Concussion Incidence and Recovery Among Youth Athletes With ADHD Taking Stimulant-Based Therapy

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Background: Attention deficit hyperactivity disorder (ADHD) may affect concussion risk and recovery in youth athletes.

Purpose: To evaluate the association between incidence of concussion and postinjury recovery of symptoms and neurocognitive dysfunction among youth athletes with ADHD and differential stimulant use.

Study Design: Cohort study; Level of evidence, 3.

Methods: From 2009 to 2019, the authors administered the Immediate Post-concussion Assessment and Cognitive Testing (ImPACT) to youth athletes at the beginning of each season. Throughout the season, athletes with concussions were examined and readministered the ImPACT both postinjury and again 7 days after the postinjury administration. These athletes (N = 7453) were divided into those with ADHD on stimulant-based therapy (ADHD+meds; n = 167), those with ADHD not on stimulant-based therapy (ADHD-only; n = 354), and those with no ADHD (non-ADHD; n = 6932). Recovery of neurocognitive dysfunction at postinjury and follow-up was calculated using the ImPACT symptom score, verbal memory, visual memory, visual motor skills, and reaction time (calculated as standardized deviations from baseline). Univariate results were confirmed with multivariate analysis.

Results: The ADHD+meds cohort had a lower incidence of concussion (37.3 concussions per 100 patient-years) compared with the ADHD-only group (57.0 concussions per 100 patient-years) (odds ratio [OR], 0.51 [95% CI, 0.37-0.71]; P < .0001) and non-ADHD group (52.8 concussions per 100 patient-years) (OR, 0.50 [95% CI, 0.37-0.67]; P < .0001). At postinjury, ImPACT scores were elevated from baseline to a similar extent in the ADHD+meds cohort compared with the other 2 groups. By follow-up, however, deviations from baseline were lower among the ADHD+meds group compared with the non-ADHD group in verbal memory (OR, 0.46 [95% CI, 0.28-0.76]; P = .002), visual memory (OR, 0.27 [95% CI, 0.10-0.66]; P = .005), and visual motor skills (OR, 0.58 [95% CI, 0.33-0.99]; P = .048). The deviation at follow-up was also lower among the ADHD+meds group compared with the ADHD+meds group in visual memory (OR, 0.42 [95% CI, 0.22-0.81]; P = .01).

Conclusion: Stimulant use among youth athletes with ADHD was independently associated with reduced incidence for concussion and lower deviation from baseline in verbal memory, visual memory, and visual motor skills at 7 days postconcussion, suggesting lower neurocognitive impairment at follow-up in this group versus their peers.

Keywords: ADHD; concussion; ImPACT; stimulants

INTRODUCTION

Concussions are the most prevalent injury among youth athletes in the United States. In 2014, the Centers for Disease Control and Prevention (CDC) reported that 812,000 children under the age of 17 were treated for concussion in US emergency departments.⁴ According to the Concussion in Sport Group, some factors that affect concussion risk and recovery include sex, age, education level, and psychiatric illness such as depression and attention deficit hyperactivity disorder (ADHD). 4,19

Youth with ADHD are twice as likely to have a selfreported history of concussion.^{12,25} Youth with ADHD also experience prolonged concussion recovery.^{1,8,18} Even though 30% of the 3 million adolescents with ADHD use stimulants to treat their disorder, the effects of stimulants on concussion risk and recovery remain unclear.²⁰ Some studies have found that stimulants reduce the risk of concussion among youth with ADHD.^{10,12} Others have found that stimulants have an increased risk or no effect on

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concussion risk.^{14,16} The stimulant methylphenidate has been shown to improve attention in youth without ADHD after concussion, but no such analysis exists in patients with ADHD.⁹ Combined, these studies suggest that stimulants might have a protective effect on concussion risk and recovery.

The aim of this study was to examine concussion incidence and longitudinal neurocognitive testing among a large cohort of young athletes with ADHD and differential stimulant use. We analyzed results from the Immediate Post-concussion Assessment and Cognitive Testing (ImPACT; ImPACT Applications) administered at baseline and twice postinjury to explore whether stimulant therapy is independently associated with reduced concussion incidence and improved ImPACT scores among youth athletes with ADHD as compared with their peers.

METHODS

Participants

The study cohort included 7453 student-athletes who had reported to concussion centers in Westminster, Colorado; Durango, Colorado; Orlando, Florida; and Tallahassee, Florida; from 2009 to 2019. All students had undergone baseline ImPACT testing at the beginning of the season. They received standardized care, head-injury assessment on the field by physicians and athletic trainers, and postinjury ImPACT testing. Data were primarily collected for medical care and repurposed for research. The concussion centers had agreements with ImPACT Applications that allowed the data to be repurposed as such. Specifically, the participants' legal guardians were aware that the data may be used in future research studies and provided consent. The data were deidentified before acquisition, and retrospective analysis of the data set was approved by an institutional review board.

Baseline Data Collection

Data collected at the beginning of each season included (1) a survey of patient information and clinical history, (2) the ImPACT Post-Concussion Symptom Scale (PCSS) survey, and (3) 40 separate neurocognitive tests on ImPACT. Students indicated their sport at the baseline test. Sports were dichotomized into 2 types: contact and limited contact. Contact sports included football, lacrosse, wrestling, and ice hockey. Limited contact sports included soccer, basketball, volleyball, baseball or softball, and cheerleading. The survey included yes/no questions about disease diagnoses, including ADHD and other psychiatric illnesses. The ImPACT PCSS survey was used to calculate the symptom score composite, and the ImPACT neurocognitive tests were used to calculate verbal memory, visual memory, visual motor skills, and reaction time composites.^{6,11}

Study Cohorts

The 7453 athletes who were diagnosed with concussion were divided into 3 categories: those diagnosed with ADHD and taking one of either amphetamine/dextroamphetamine, methylphenidate, or lisdexamfetamine (ADHD+meds; n = 167); those diagnosed with ADHD but not taking stimulants (ADHD-only; n = 354); and those not diagnosed with ADHD (non-ADHD; n = 6932). The study was approved by the institutional review board for human research and deemed exempt from informed consent as the data were deidentified before analysis.

Concussion Definition and Incidence

Throughout the season, physicians and athletic trainers examined head injuries. Physicians were employed by high schools and had backgrounds in family and/or physical medicine and rehabilitation. Concussions were defined as blunt trauma to the head followed by either the sudden alteration of mental status or the appearance of multiple pathological symptoms, including headaches, nausea, vomiting, dizziness, and vision problems. The incidence of concussion was defined as the total number of concussions per total patient-years for each of the 3 cohorts. Patientyears were calculated according to US CDC guidelines.²⁴ Briefly, patients required a baseline test to be considered at risk for concussion for that year. Patients with more than 2 years between baseline tests were considered lost to follow-up; these patients were given 1 patient-year.

Longitudinal Neurocognitive Testing

To track recovery from symptoms and neurocognitive measures postinjury, ImPACT was administered at 2 sequential follow-up visits. ImPACT was readministered postinjury and again at follow-up a median of 7 days after the postinjury administration. The recovery of symptoms and neurocognitive dysfunction postinjury is reported as standardized deviations from baseline to postinjury and baseline to follow-up in the 5 composite ImPACT scores. Deviations were standardized by the standard error of the

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Ethical approval for this study was obtained from the Icahn School of Medicine at Mount Sinai (project 18-01083)

					Р	
	(A) ADHD+Meds	(B) ADHD-Only	(C) Non-ADHD	A vs B	A vs C	B vs C
Patients/baseline tests, n	167/205	354/426	6932/10,932			
Age, y, mean \pm SD	15.5 ± 1.5	15.2 ± 1.6	15.6 ± 1.6	$.10^b$.50	$.13^{b}$
Male sex	71.7	76.8	65.4	$.17^b$	$.059^b$	<.0001 ^b
Contact sport ^{c}	55.8	52.1	49.9	.32	$.11^b$.37
Limited contact sport	36.9	37.5	36.1	.90	.77	.54
DLD	19.5	18.5	1.8	.78	<.0001	<.0001
Dyslexia	2.0	3.1	2.0	.40	.97	$.11^b$
Autism	1.0	1.5	0.3	.56	$.04^{b}$	$.008^{b}$
Special education	7.8	6.6	1.5	.57	<.0001 ^b	<.0001 ^b
History of epilepsy	1.1	0.2	1.1	$.21^b$.82	$.08^b$
Depression/anxiety	13.7	11.5	3.2	.44	<.0001 ^b	<.0001 ^b
Depression/anxiety SSRIs	2.0	0.7	0.5	$.16^b$	$.004^{b}$.55
History of >2 concussions	11.0	12.2	8.3	.73	$.04^{b}$	$.03^b$
Chronic headaches	10.9	8.2	15.1	$.08^b$	$.06^{b}$	$.008^{b}$
Chronic migraines	7.8	4.9	7.7	$.15^b$.97	$.03^b$

 $\begin{array}{c} {\rm TABLE \ 1} \\ {\rm Cohort \ Characteristics \ and \ Univariate \ Analysis}^a \end{array}$

^{*a*}Data are reported as percentage of group unless otherwise indicated. Bolded *P* values indicate statistically significant differences between groups (P < .05). ADHD, attention deficit hyperactivity disorder; DLD, diagnosed learning disability; SSRIs, selective serotonin reuptake inhibitors.

^bCovariate in multivariate analysis.

^cIncludes football, lacrosse, wrestling, and ice hockey.

difference. Of note, only valid ImPACT tests were included in the analysis.

Statistical Analysis

GraphPad Prism 7.0 (GraphPad Software) and RStudio (RStudio Software) were used for statistical analysis. The chi-square test with Bonferroni post hoc comparison and 1-way ANOVA with Tukey post hoc comparison were used for univariate analysis. Patient and clinical history covariates, including age, sex, contact sports, diagnosed learning disability (DLD), epilepsy, dyslexia, autism, depression/anxiety, selective serotonin reuptake inhibitor (SSRI) use (fluoxetine, escitalopram, and sertraline), special education, chronic premorbid headaches, chronic premorbid migraines, and a history of 2 or more concussions, with univariate P values $\leq .20$ were used as covariates in multivariate logistic regression models. Premorbid headaches and migraines lasting longer than 1 year were considered chronic. P < .05 was considered significant for all tests.

RESULTS

Cohort Characteristics

The mean age of the non-ADHD group was 15.6 years (range, 12-22 years) for the non-ADHD group, 15.5 years (range, 12-22 years) for the ADHD+meds group, and 15.2 years (range, 12-20 years) for the ADHD-only group. Additionally, 99% of the athletes were adolescents aged 12 to 18 years. Baseline characteristics between the 3 study groups are shown in Table 1. There were no significant differences between the ADHD+meds and ADHD-only groups on any variables tested. Both ADHD cohorts had a significantly greater percentage of DLDs and individuals enrolled in special education than the non-ADHD group (P < .0001 for all). Additionally, the ADHD+meds group had a greater incidence of depression or anxiety (P < .0001) and past concussions (P = .04) than the non-ADHD group. The ADHD-only group also had a greater incidence of depression or anxiety (P < .0001) and past concussions (P = .04) than the non-ADHD group. The ADHD-only group also had a greater incidence of depression or anxiety (P < .0001) and past concussions (P = .03) than the non-ADHD group had a lower incidence of premorbid headaches (P = .008) and migraines (P = .03) than the non-ADHD group.

Concussion Incidence

The ADHD+meds group had an incidence of 37.3 concussions per 100 patient-years. This was lower than the concussion incidence of both the non-ADHD (52.8 concussions per 100 patient-years; P < .0001) and ADHD-only (57.0 concussions per 100 patient-years; P < .0001) groups (Table 2). Differences in concussion incidence remained significant after multivariate analysis after accounting for age, percentage male, contact sport, epilepsy, autism, depression/anxiety, SSRI use, special education, chronic headaches, chronic migraines, and a significant history of concussions. The ADHD+meds cohort had a 2 times lower incidence of concussion than both the ADHD-only group (odds ratio [OR], 0.51 [95% CI, 0.37-0.71]; P < .0001) and the non-ADHD group (OR, 0.50 [95% CI, 0.37-0.67]; P < .0001) (Table 3).

ImPACT at Postinjury Assessment

Deviations from baseline to postinjury in the 5 composite ImPACT scores were consistent between the ADHD+meds

	TABLE 2				
Univariate Analysis of Concussion	Incidence and	d ImPACT	Scores a	at Postinju	ry

					P^{a}	
		$\begin{array}{l} \text{(B) ADHD-only} \\ \text{(n}=354) \end{array}$	$\begin{array}{l} \text{(C) Non-ADHD} \\ \text{(n = 6932)} \end{array}$	A vs B	A vs C	B vs C
Concussion incidence per 100 patient-years	37.3	57.0	52.8	<.0001 ^b	<.0001 ^b	$.10^b$
ImPACT score, deviation from baseline (95% CI)	1.00 (0.70 1.49)	1.00 (1.10.1.00)	1 10 (1 00 1 10)	01	0.70	0.00
Symptom score	1.08(0.72 - 1.43)	1.36 (1.10-1.62)	1.13(1.08-1.18)	.21	0.78	0.06
Verbal memory	0.80(0.46 - 1.15)	0.87(0.67-1.06)	0.68(0.64 - 0.71)	.66	.35	.03 ^b
Visual memory	$0.45\ (0.25 - 0.64)$	$0.42\ (0.31 \text{-} 0.53)$	$0.40\ (0.38 \text{-} 0.42)$.80	.58	.69
Visual motor skills	0.44 (0.18-0.70)	$0.40\ (0.28 - 0.53)$	0.37 (0.34-0.39)	.74	.43	.54
Reaction time	$0.98\ (0.47 \text{-} 1.49)$	$1.25\ (0.83-1.66)$	$0.96\;(0.90\text{-}1.01)$.91	.30	$.04^{b}$

^{*a*}Bolded *P* values indicate statistically significant differences between groups (P < .05). ADHD, attention deficit hyperactivity disorder; ImPACT, Immediate Post-concussion Assessment and Cognitive Testing.

^bChecked in multivariate analysis.

TABLE 3 Multivariate Analysis of Concussion Incidence and ImPACT at Postinjury

	OR (95% CI)	P^{a}
$ADHD+meds vs ADHD-only^b$		
Concussion incidence	0.51 (0.37-0.71)	<.0001
$ADHD+meds vs non-ADHD^{c}$		
Concussion incidence	0.50 (0.37-0.67)	<.0001
ADHD-only vs non-ADHD d		
Concussion incidence	$1.09 (0.89 - 1.34)^e$.42
ImPACT symptom score	$1.05~(0.98-1.12)^{e}$.14
ImPACT verbal memory	$1.11 (1.01 - 1.22)^e$.03
ImPACT reaction time	$1.05 (1.00-1.10)^{e}$.049

^{*a*}Bolded *P* values indicate statistical significance (P < .05). ADHD, attention deficit hyperactivity disorder; ImPACT, Immediate Post-concussion Assessment and Cognitive Testing.

^bCovariates: age, percentage male, history of epilepsy, depression/anxiety medication, chronic headaches, chronic migraines.

^cCovariates: percentage male, contact sport, autism, special education, depression/anxiety, depression/anxiety medication, history of concussions, chronic headaches.

^dCovariates: age, percentage male, dyslexia, autism, special education, history of epilepsy, depression/anxiety, history of concussions, chronic headaches, chronic migraines.

^eOdds ratio per point.

cohort and the other 2 groups. However, the ADHD-only group had a greater deviation from baseline compared with the non-ADHD group in postinjury verbal memory (0.87 vs 0.8; P = .03) and reaction time (1.25 vs 0.98; P = .04) (Table 2). After multivariate analysis, the ADHD-only group still had greater deviations from baseline than the non-ADHD cohort in postinjury verbal memory (OR per point, 1.11 [95% CI, 1.01-1.22]; P = .0343) and reaction time (OR per point, 1.05 [95% CI, 1.00-1.10]; P = .0489) (Table 3).

ImPACT at Follow-up Assessment

Approximately 70% of the patients across all 3 cohorts returned for the follow-up test (P > .99), which was

TABLE 4				
Multivariate Analysis of ImPACT at Follow-up ^a				

	$OR (95\% CI)^b$	P Value
ADHD+meds vs ADHD-only		
ImPACT visual memory	$0.56\ (0.33-0.96)$.04
ImPACT visual motor skills	$0.42\ (0.22 \text{-} 0.81)$.01
ADHD+meds vs non-ADHD		
ImPACT verbal memory	$0.46\ (0.28-0.76)$.002
ImPACT visual memory	0.27 (0.10-0.66)	.005
ImPACT visual motor skills	$0.58\ (0.33-0.99)$.048

^{*a*}Covariates: postinjury ImpACT scores, loss to follow-up, and latency to follow-up (by day), as well as significant patient and clinical variables mentioned in Table 3. Bolded *P* values indicate statistical significance (P < .05).

^bOdds ratio per point.

administered at a median of 7 days (IQR, 5-13; range, 3-39 days) after the postinjury tests. There was no difference in medians among the 3 cohorts (P = .39). Multivariate analysis controlling for postinjury ImPACT scores, loss to follow-up, and latency to follow-up in addition to patient data and clinical history demonstrated that the ADHD+meds cohort had a lower deviation from baseline to follow-up in verbal memory (OR per point, 0.46 [95% CI, 0.28-0.76]; P = .002), visual memory (OR per point, 0.27) [95% CI, 0.10-0.66]; P = .005), and visual motor skills (OR per point, 0.58 [95% CI, 0.33-0.99]; P = .048) than the non-ADHD group. A second set of multivariate analysis demonstrated that the ADHD+meds cohort also had a lower deviation from baseline to follow-up in visual memory (OR per point, 0.56 [95% CI, 0.33-0.96]; P = .04) and visual motor skills (OR per point, 0.42 [95% CI, 0.22-0.81]; *P* = .01) as compared with the ADHD-only group (Table 4).

DISCUSSION

This study evaluated concussion trends among 521 youth athletes with ADHD and differential stimulant use as compared with 6932 of their peers. The ADHD+meds cohort had 2-fold lower odds of experiencing a concussion than both the non-ADHD (OR, 0.50; P < .0001) and ADHD-only groups (OR, 0.51; P < .0001). At postinjury, the 5 composite ImPACT scores were elevated from baseline to a similar extent in the ADHD+meds cohort as compared with the other 2 groups. By follow-up, however, deviations from baseline in verbal memory, visual memory, and visual motor skills were 2 times lower among the ADHD+meds group as compared with both the non-ADHD (verbal memory: OR, 0.46 [P = .002]; visual memory: OR, 0.27 [P = .005]; visual motor skills: OR, 0.58 [P = .048]) and ADHD-only (visual memory: OR, 0.56 [P = .04]; visual motor skills: OR, 0.42 [P = .01]) groups, suggesting lower neurocognitive impairment at follow-up.

Concussion Incidence

The effects of stimulants on concussion incidence have been debated. Liao et al¹⁴ found that methylphenidate prescriptions were indirectly associated with concussion incidence (OR, 0.49). Liou et al¹⁶ also found that stimulant treatment was indirectly associated with concussion incidence (OR, 0.93). Other studies found either an increased incidence of past concussions in children with ADHD who were treated with stimulants (OR, 1.42) or no effect of stimulants on concussion risk.^{10,12} However, the latter set of studies did not address confounding variables, whereas the former set of studies used multivariate analysis accounting for age, sex, and comorbid illnesses. Similar to the first set of studies, we found that the ADHD+meds group had a lower incidence of concussion as compared with both the ADHD-only (OR, 0.51) and non-ADHD (OR, 0.50) groups after accounting for patient and clinical data.^{14,16}

Stimulant use has been associated with reduced risk for nonconcussive trauma. Man et al¹⁷ found that traumarelated emergency department admission was lower when patients were exposed to stimulants (OR, 0.91). Further, in a prospective study, Dalsgaard et al² found that 6 months of stimulant use reduced the risk of various kinds of injuries among youth with ADHD by 40%.

Multiple hypotheses may explain the protective effects of stimulants on the incidence of traumatic brain injury (TBI).¹⁶ Stimulants temper impulsivity in ADHD and improve executive functioning.^{5,17,21} Untreated impulsivity increases near misses, leading to more car accidents and associated TBI.²² Deficits in executive function inhibit higher-order planning, also leading to more car accidents and TBI.²³ Stimulants also reduce the likelihood of ADHD-associated violence and risky behavior.^{15,26} Violence and risky behavior lead to more traumatic injury, increasing the likelihood of concussion. Finally, stimulant use is associated with depression and anxiety.²⁷ Individuals with mood disorders are more likely to be sidelined by coaches,¹³ thus avoiding serious head trauma.

Longitudinal Neurocognitive Testing Among Youth With ADHD on Stimulants

At postinjury, the ADHD+meds cohort had comparable deviations from baseline in the 5 composite ImPACT scores

to both the non-ADHD and ADHD-only groups. Gardner et al³ found that visual memory and verbal memory scores were lower at both baseline and postinjury for youth with ADHD on stimulants as compared with the control cohort. However, Gardner et al did not track athletes longitudinally, comparing raw scores between parallel cohorts rather than deviations from baseline among the same athletes. Because the ImPACT scores were consistently lower than those of the controls at both baseline and postinjury in that study, it may explain why we did not find a difference in deviations from baseline to postinjury between the ADHD+meds cohort and the other 2 groups.

At follow-up a median of 7 days after the postinjury test, the ADHD+meds cohort had lower deviations from baseline in verbal memory, visual memory, and visual motor skills as compared with both the non-ADHD and ADHDonly groups, suggesting lower neurocognitive impairment at follow-up. Specifically, an improvement seems to occur between postinjury and follow-up, when deviations from baseline among ADHD+meds youth change from comparable to their peers to significantly lower than them. The effects of stimulants on the recovery of neurocognitive factors among youth with ADHD have not been studied previously. A meta-analysis by Huang et al⁹ found that methylphenidate use enhanced vigilance-associated attention in patients with TBI. However, the randomized trials did not examine youth with ADHD specifically, nor did they examine a wide variety of ADHD stimulants.

ADHD medications have several higher-order effects, including improved cognitive function, sometimes beyond baseline levels.^{5,17,21} Such effects have become popular among youth without ADHD who abuse stimulants for improved performance on standardized tests.⁷ Similar cognitive benefits may allow individuals to be evaluated with lower neurocognitive impairment on follow-up ImPACT as compared with their peers. In fact, lower functional impairment on follow-up ImPACT among youth with ADHD taking medications was driven by reductions in the impairment of visual memory, verbal memory, and visual motor skills but not of symptom scores.

Longitudinal Neurocognitive Testing Among Youth With ADHD Not on Stimulants

At postinjury, the ADHD-only cohort had greater deviations from baseline in verbal memory (OR per point, 1.10) and reaction time (OR per point, 1.05) than the non-ADHD group. Although these odds may seem small at first, deviation in reaction time among the ADHD-only group averages 1.25, with some scores exceeding 5.00. For a student with a deviation of 5.00, the likelihood of having ADHD is 25% greater. These findings are consistent with the assessment by the Concussion in Sport Group that ADHD is a risk factor for more severe concussions.¹⁹ Gardner et al³ found that youth with ADHD not taking stimulants had lower verbal memory, visual memory, visual motor skills, and reaction time scores as compared with the control cohort at baseline. However, they found no such difference at postinjury. Once again, had Gardner et al tracked athletes longitudinally, comparing deviations from baseline among the same athletes rather than raw scores between parallel cohorts, they may have found an increase in neurocognitive impairment postinjury for patients with ADHD not on stimulants, largely due to lower baseline and comparable postinjury ImPACT scores.

Limitations

There are several limitations to this study. Because of the retrospective nature of the study, it is subject to recall bias. Although some results are similar to those in the literature, others cannot be confirmed. For example, approximately 32% of the participants diagnosed with ADHD took stimulants to treat their condition. This is similar to the 31%reported in the literature.²⁰ However, we cannot know how long before baseline tests the participants started taking stimulants to manage their ADHD or what dosage of stimulants was taken by the participants. We can identify retention of medication use throughout the study period, though. Of those who reported medication use at postinjury, approximately 95% indicated continued use of stimulants from baseline, suggesting near-complete retention of medication use after concussion. Analysis of patient recovery is also limited by the nature of the follow-up. As this is the primary endpoint in the analysis, we cannot track recovery beyond follow-up. Finally, concussion adverse effects vary widely. The ImPACT accounts for a vast majority of symptoms and neurocognitive effects; however, it fails to account for rarer adverse effects, including vision changes and fever.

CONCLUSION

In this retrospective study of 7453 youth athletes, stimulant use among those with ADHD was associated with reduced incidence for concussions and lower deviations from baseline in verbal memory, visual memory, and visual motor skills a median of 7 days after concussion, suggesting lower neurocognitive impairment at follow-up as compared with their peers.

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