

# Neuropsychological

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# Changes in brain activation measured by functional Near-Infrared Spectroscopy associated with continuing to play following sport-related concussion among adolescent athletes

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ABSTRACT

*Athletes who continue to play following sport-related concussion (SRC) have worse clinical outcomes compared to those removed from play immediately. This prospective study examined brain activation (i.e., oxygenated hemoglobin concentration [HbO<sub>2</sub>]), using functional near-infrared spectroscopy (fNIRS), in 20 adolescent athletes who either continued to play (PLAYED) or were immediately removed (REMOVED) following SRC. A linear mixed effects model found the PLAYED group demonstrated an increase of [HbO<sub>2</sub>] in the left hemisphere at the initial visit ( $p_{FDR} < .001$ ) and the REMOVED group had a reduction in [HbO<sub>2</sub>] in the right hemisphere at clinical recovery ( $p_{FDR} = 0.024$ ). There was a significant group\*timepoint interaction ( $p_{FDR} < 0.011$ ), in which the PLAYED group had greater increase in [HbO<sub>2</sub>] in the left hemisphere at the initial visit compared with the REMOVED group, but no differences at clinical recovery. Athletes who remain in play following SRC exhibited more pronounced brain hyperactivation, which may be associated with worse clinical recovery outcomes.*

*Keywords: functional near-infrared spectroscopy; sport-related concussion; brain activity; neurocognitive testing; adolescent*

## 1. INTRODUCTION

Sport-related concussion (SRC) is a significant public health concern, with nearly 2 million SRCs occurring among youth in the U.S. annually (Bryan et al., 2016). SRC is associated with diverse symptoms (e.g., headache, dizziness) and impairments (cognitive, vestibular/ocular). Despite large-scale awareness initiatives, it is estimated that 50% to 70% of concussions go unreported due to limited knowledge of signs and symptoms (McCrea et al., 2004), delayed symptom onset (Duhaime et al., 2012; Giza et al., 2013), pressures to continue to play (Kroshus et al., 2015) and limited understanding of the injury risks (Youth, 2013). Adolescence is a crucial phase of brain development and maturation, in which changes in regional blood flow coincide with acquisition of cognitive skills, potentially representing a vulnerable period for head injury (Chiron et al., 1992; Giedd, 2008). Both high school and collegiate athletes who remain in play after sustaining a concussion have worse outcomes compared to those removed from play immediately following injury, including worse symptoms and cognitive impairments, and longer recoveries (Asken et al., 2016; Charek et al., 2020; Elbin et al., 2016). However, the underlying mechanisms for these clinical differences have yet to be examined empirically.

One hypothesis is that physiological injury to the brain is exacerbated through continued play. A concussion is caused by direct (e.g., helmet to helmet contact) or indirect (e.g., whiplash) forces on the brain. These forces result in a neurometabolic cascade wherein the brain experiences an energy crisis, involving an influx of  $\text{Ca}^{2+}$  and efflux of  $\text{K}^{+}$  in the brain, together with a concomitant increase in demand for glucose and decrease in cerebral blood flow (CBF) (Giza & Hovda, 2001). Both animal models and retrospective human studies provide evidence for impaired recovery with immediate physical and cognitive activity (Griesbach et al., 2004) with evidence for decreased neuroplasticity (Griesbach et al., 2004) and increased neuroinflammation (Piao et al., 2013). Sustaining a secondary injury within 24 hours is also associated with exacerbated axonal injury and astrocytic reactivity (Giza & Hovda, 2014). As such, it is feasible that decreased CBF from the initial injury is exacerbated by exposure to additional biomechanical force to the brain and physical activity. This hypothesis is supported by recent research for a “dose response” effect of estimated time “in play” following SRC (Charek et al., 2020). However, researchers have yet to examine differences in CBF among athletes who continued to play compared to those who were removed immediately following SRC. The most pronounced changes in CBF have been documented in the acute period post injury, with lack of agreement upon expected resolution (Banks & Domínguez, 2019) and concern that dysfunction of CBF can persist beyond clinical clearance (Purkayastha et al., 2019).

Changes in CBF, which are a proxy for brain activation, are measured using various imaging modalities. Results of imaging studies integrating neurocognitive testing studies post-concussion are largely conflicting with some studies showing brain hypoactivation, hyperactivation or no abnormalities, attributed to differences in time from injury, task type, and sample characteristics (Chen et al., 2008; Chen et al., 2004; Jantzen et al., 2004; Slobounov et al., 2010). At resting state, functional neuroimaging has provided evidence for differential patterns of cerebral activation following concussion, including reduced inter-hemispheric connectivity (Johnson et al., 2012) and reduced connectivity strength (Nakamura et al., 2009). Although preliminary evidence is promising regarding the use of neuroimaging to quantify CBF differences following concussion, many of these modalities (e.g., functional magnetic resonance imaging [fMRI], positron emission tomography [PET]) are limited due to their cost and lack of portability. Functional near-infrared spectroscopy (fNIRS) represents a novel, portable imaging tool that measures cerebral blood oxygenation during task performance (Huppert et al., 2006) and has been utilized with concussion patients. Kontos and colleagues (2014) reported reduced brain activation with fNIRS during computerized neurocognitive testing, which was associated with poorer test performance, among athletes evaluated 15–45 days following SRC. The majority of fNIRS studies are limited in that they involve nonathletes or retired athletes at chronic (i.e., months to years from injury) timepoints, and have examined a wide variety of parameters, including interhemispheric connectivity and communication (Hocke et al., 2018; Urban et al., 2015) in addition to change in CBF during non-cognitive tasks (Helmich et al., 2020; Neary et al., 2020; Sharma et al., 2020). To date, fNIRS has not been employed in an acute population at multiple time intervals post injury or at clinical recovery.

The present study sought to examine one potential underlying mechanism for detrimental effects of continuing to play following an SRC by utilizing fNIRS to quantify changes in brain activation associated with reported clinical effects. The primary aim of this study was to compare brain activation, as measured by fNIRS, during an attentional visual search task, between adolescent athletes who remained in play or were removed immediately following SRC. A secondary aim was to examine changes in brain activation in the two groups from the first week following injury to date of medical clearance for full return to sport. We expected the groups to differ on brain activation patterns while completing a visual search task the first week post injury, with the group who remained in play to have a more pronounced decrease in CBF but expected differences to resolve at clearance. We hypothesized that participants who continued to play would have worse visual search performance in the first week post injury.

## 2. METHODS

### *2.1 Participants and study design*

A prospective, repeated measures design was used to assess athletes within 7 days of diagnosed SRC and at clearance/clinical recovery from SRC. Twenty athletes (12-18 years old) seeking care for SRC at a concussion specialty clinic between September 2017 and May 2018 were recruited. Inclusion criteria: 1) SRC within 7 days, 2) ability to recall the moment he/she sustained a head impact resulting in on-field SRC symptoms (e.g., dizziness) and/or changes in mental status (e.g., amnesia), 3) persistent symptoms at initial visit, and 4) no other brain injury within 3 months. SRCs were diagnosed per consensus criteria by clinicians (e.g., physician, neuropsychologist) trained in concussion management. In order to determine group designation, athletes were asked if they experienced concussion signs and/or symptoms AND were subsequently removed from that game or practice. Athletes who responded, “yes” to this question comprised the “REMOVED” group and athletes who responded “no” (i.e., continued to participate with concussion symptoms) comprised the “PLAYED” group. Participants were matched for age (+/-1 year) and gender. Participants were consecutively recruited regardless of group membership until it was necessary to only recruit participants that would be a match to reach target of 10 pairs.

### *2.2 Measures*

Functional Near-infrared spectroscopy (fNIRS) is an optical imaging technology that provides a non-invasive, safe, portable, and low-cost method to assess brain activation by monitoring oxygenated cerebrovascular blood flow in cortical regions of the brain during the performance of a task (Huppert et al., 2006). FNIRS employs a series of LED sources and detectors that measure refractory light to calculate continuous blood oxygenation levels, similar to blood oxygen level dependent (BOLD) imaging in fMRI. A continuous wave fNIRS instrument (Cw6 real-time system; TechEN Inc, Milford, MA) was used in this study. Prior to the start of the recording, the fNIRS cap consisting of 2 sources and 5 detectors over each hemisphere was placed over the dorsolateral prefrontal region of the brain, resulting in 7 channels on each side. Using the nearest neighbour principle, optode distances ranged from 28-46 mm. Two wavelengths of light, 690 and 830 nm, were generated for each channel to measure the De-oxy-hemoglobin [Hb] and Oxy-hemoglobin

[HbO<sub>2</sub>] concentration, respectively. The amplification of the detectors was adjusted via down sampling from 20 Hz to 4 Hz to maximize the signal-to-noise level for all measurement pairs. fNIRS brain signals were recorded at rest (baseline) for approximately one minute and then during completion of the Ruff 2&7.

The Ruff 2&7 (Ruff & Allen, 1996) is a sustained visual search test lasting 5 minutes. The visual search and cancellation test consists of a series of 20 trials (15s each) where the respondent detects and marks all occurrences of the two target digits: 2 and 7. There are two different conditions randomly sequenced across 20 trials – automatic (AUTO) detection and controlled (CONT) search. In the 10 AUTO trials, the target digits are embedded among alphabetical letters that serve as distractors. In the 10 CONT trials, the target digits are embedded among other numbers that serve as distractors. Three scores are calculated for each condition (CONT and AUTO) and total trials during the test - speed, errors, and accuracy.

### *2.3 Procedure*

The study was approved by the institution's review board for human subject research. Participants and their parents provided informed written consent and assent prior to the study. All participants completed the Ruff 2&7 while wearing the fNIRS cap at the conclusion of their two clinic visits. Total testing time was 7 minutes. Recovery time was defined as the total number of days from the date of injury to the date of receiving medical clearance for return to sports by a neuropsychologist and physician, which was defined based on international consensus (McCrory et al., 2017). All participants were symptom free, remained symptom free throughout an exertion test administered by a physical therapist or certified athletic trainer, and performed normally on computerized neurocognitive testing at the time of clearance.

### *2.4 Statistical analyses*

Descriptive statistics were calculated to describe participant demographics (e.g., age, gender, concussion history, time until first clinic visit). The approach to analyzing the fNIRS data using a 2-level analysis was based on previous work (Huppert et al., 2009). The changes in optical density are related to changes in concentration of oxy-hemoglobin and deoxy-hemoglobin via the modified Beer-Lambert law with a differential pathlength factor of 6 and partial volume correction of 1/60 (Cope et al., 1988). In the first level, a canonical general linear model is computed for each subject and each channel, using the time-



series of oxy-hemoglobin or de-oxyhemoglobin concentration as the dependent variable, and Block (Rest, Ruff 2&7) as the independent variable. Thus, regression coefficients indicating the change in concentration were estimated for each combination of Condition (AUTO, CONT) and Timepoint (INITIAL, RECOVERY), using the robust statistical model described previously (Barker et al., 2013) and implemented in the NIRS AnalyzIR toolbox (Santosa et al., 2018). The change in brain activity (oxy-and deoxy-hemoglobin) from the first level general linear model (GLM) was used for a second, group-level analysis. Group-level analysis was performed via a linear mixed effects model that included random intercept terms for each subject to model within-subject correlations (Abdelnour & Huppert, 2010). The group-level model was estimated using an iteratively-estimated robust linear mixed-effects model and initial covariance prewhitening based on first-level statistical noise estimates as part of the NIRS AnalyzIR toolbox (Santosa et al., 2018). For each channel, estimates of the regression coefficients for [HbO<sub>2</sub>] and [Hb], as well as the standard error, were computed for each Ruff 2&7 task (AUTO and CONT), each timepoint (INITIAL and RECOVERY), and each group (REMOVED and PLAYED). A region-of-interest (ROI) analysis using all channels for each hemisphere was performed to test if there was a difference in [HbO<sub>2</sub>] and [Hb] between Ruff 2&7 tasks, time points, and groups. Multiple t-tests were used to compare the estimates (and standard error) of the regression coefficients using a false discovery rate (FDR) method (Benjamini & Hochberg, 1995) to adjust the p-value (pFDR<0.05). Due to the number of overall comparisons, which includes factors of oxyhemoglobin and deoxyhemoglobin concentrations, multiple channels, and the group, time and condition factors, the Benjamini-Hochberg FDR method was used because the FWER Bonferroni method is stricter and results in more false negatives.

To examine performance on the Ruff 2&7, repeated measures GLMs were conducted with between-subjects factor of group (PLAYED or REMOVED), using SPSS (version 25). Statistical significance was set at  $p \leq 0.05$  and Bonferroni correction was used for multiple comparison.

## 3. RESULTS

## 3.1 Sample demographics and descriptives

A summary of demographic and medical/injury history data for the total sample and groups (PLAYED, REMOVED) is provided in Table 1. Participants included 20 athletes (18 males, 2 females) aged 12-18 ( $14.4 \pm 1.7$ ) years who sustained an SRC within the past 7 days ( $4.2 \pm 2.0$ ). Participants represented sports including soccer ( $n=5$ ), football ( $n=3$ ), hockey ( $n=6$ ), lacrosse ( $n=4$ ), and volleyball ( $n=2$ ). Approximately 30% ( $n=6$ ) of participants reported a history of concussion. The groups did not differ on any other clinical variables.

Table 1. Participant demographics,  $N=20$ 

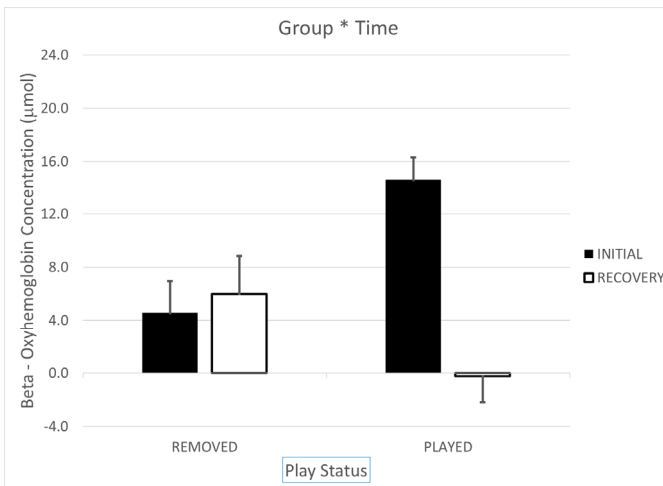
	Total ( $N=20$ )	PLAYED ( $n=10$ )	REMOVE D ( $n=10$ )	$p$ value (t- test or chi- square)
Age, $M$ (SD), years	14.4 (1.7)	14.6 (1.9)	14.2 (1.5)	0.61
Sex				1.00
Female	2 (10%)	1	1	
Male	18 (90%)	9	9	
Sport, $n$ (%)				-
American football	3 (15%)	2	1	
Soccer	5 (25%)	3	2	
Ice hockey	6 (30%)	2	4	
Volleyball	2 (10%)	1	1	
Lacrosse	4 (20%)	2	2	
Prior concussion (% yes)	6 (30%)	3	3	1.00
History of migraine	2 (10%)	2	0	0.47
Anxiety	1 (5%)	1	0	1.00
Depression	1 (5%)	1	0	1.00
ADHD	1 (5%)	0	1	1.00
Days from injury to initial visit, $M$ (SD)	4.2 (2.02)	4.8 (1.6)	3.6 (2.3)	0.19
Days from injury to recovery, $M$ (SD)	32.8 (44.4)	31.5 (26.0)	34.0 (58.9)	0.90

<sup>a</sup> $p < .05$

### 3.2 *fNIRS* outcomes

The linear mixed effects model indicated that only three of eight conditions (2 groups x 2 timepoints x 2 tasks) had a significant change in [HbO<sub>2</sub>] concentration relative to baseline. The PLAYED group had a significant increase in [HbO<sub>2</sub>] in the left hemisphere region of interest for both the AUTO ( $\beta=14.6$ , SE=2.0, T=7.2,  $p_{FDR}<0.001$ ) and CONT ( $\beta=14.5$ , SE=2.0, T=7.2,  $p_{FDR}<0.001$ ) tasks during the INITIAL timepoint. The REMOVED group had a significant reduction in [HbO<sub>2</sub>] in the right hemisphere during the CONT ( $\beta=-5.3$ , SE=1.8, T=-2.9,  $p_{FDR}=0.024$ ) trial at the RECOVERY timepoint.

Results of the linear mixed effects model supported a significant group\*timepoint interaction ( $\beta=8.1$ , SE=2.3, T=3.5,  $p_{FDR}<0.011$ ), such that the PLAYED group had greater increase in [HbO<sub>2</sub>] in the left hemisphere at the INITIAL timepoint compared with the REMOVED group, whereas their activity did not differ during the RECOVERY timepoint (Figure 1). There was a significant main effect for time, with a greater increase in [HbO<sub>2</sub>] at the INITIAL timepoint compared to the RECOVERY timepoint for both the left ( $\beta=6.7$ , SE=2.3, T=2.9,  $p_{FDR}=0.040$ ) and right ( $\beta=4.2$ , SE=1.5, T=2.8,  $p_{FDR}<0.040$ ) hemispheres (Figure 2). The results of a sensitivity analysis using the age of the participants and days from injury to INITIAL timepoint as covariates did not show appreciable differences from the main findings.



*Figure 1. A significant group\*timepoint interaction in linear mixed effects model*

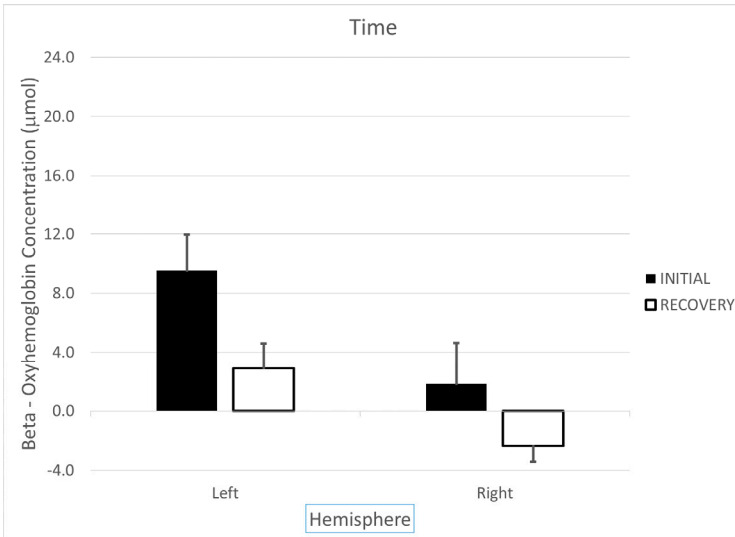


Figure 2. A significant main effect for time in linear mixed effects model

### 3.3 Ruff 2&7 Performance

Results of repeated measures GLMs supported main effects for total accuracy, ( $F[1,18]=6.2$ ,  $p=0.023$ , Wilks' $\Lambda=0.7$ , partial  $\eta^2=0.3$ ), AUTO errors, ( $F[1,18]=4.5$ ,  $p=0.049$ , Wilks' $\Lambda=0.8$ , partial  $\eta^2=0.2$ ), CONT accuracy, ( $F[1,18]=5.1$ ,  $p=0.036$ , Wilks' $\Lambda=0.8$ , partial  $\eta^2=0.2$ ), and CONT errors, ( $F[1,18]=4.7$ ,  $p=0.045$ , Wilks' $\Lambda=0.8$ , partial  $\eta^2=0.2$ ) on timepoint (INITIAL and RECOVERY), with both groups performing with greater total accuracy at RECOVERY. There were no significant main effects for total speed, ( $F[1,18]=.7$ ,  $p=0.400$ , Wilks' $\Lambda=1.0$ , partial  $\eta^2=0.0$ ), AUTO accuracy, ( $F[1,18]=4.2$ ,  $p=0.054$ , Wilks' $\Lambda=0.8$ , partial  $\eta^2=0.2$ ), AUTO speed, ( $F[1,18]=0.4$ ,  $p=0.538$ , Wilks' $\Lambda=1.0$ , partial  $\eta^2=0.0$ ), or CONT speed, ( $F[1,18]=2.6$ ,  $p=0.124$ , Wilks' $\Lambda=0.9$ , partial  $\eta^2=0.1$ ) on timepoint (INITIAL and RECOVERY, Table 2). The results also did not support any statistically significant interactions for group (PLAYED and REMOVED)\*timepoint (INITIAL and RECOVERY) for total accuracy, ( $F[1,18]=0.8$ ,  $p=0.380$ , Wilks' $\Lambda=1.0$ , partial  $\eta^2=0.0$ ), total speed, ( $F[1,18]=0.5$ ,  $p=0.496$ , Wilks' $\Lambda=1.0$ , partial  $\eta^2=0.0$ ), AUTO accuracy, ( $F[1,18]=1.6$ ,  $p=0.223$ , Wilks' $\Lambda=0.9$ , partial  $\eta^2=0.1$ ), AUTO speed, ( $F[1,18]=.5$ ,  $p=0.499$ , Wilks' $\Lambda=1.0$ , partial  $\eta^2=0.0$ ), AUTO errors, ( $F[1,18]=1.8$ ,  $p=0.197$ , Wilks' $\Lambda=0.9$ , partial  $\eta^2=0.1$ ), CONT

accuracy, ( $F[1, 18]=0.4, p=0.551, \text{Wilks}'\Lambda=1.0, \text{partial } \eta^2=0.0$ ), CONT speed, ( $F[1, 18]=0.6, p=0.451, \text{Wilks}'\Lambda=1.0, \text{partial } \eta^2=0.0$ ), or CONT errors, ( $F[1, 18]=.3, p=0.578, \text{Wilks}'\Lambda=1.0, \text{partial } \eta^2=0.0$ ).

*Table 2. Ruff 2&7 scores at initial clinic visit (INITIAL) and clearance (RECOVERY) timepoints among athletes who played through injury (PLAYED) and athletes removed from play (REMOVED)*

	PLAYED (n =10)	REMOVED (n = 10)	TOTAL (N = 20)
<b>Ruff 2&amp;7</b>			
Total accuracy <sup>b</sup>			
INITIAL	76.4 (19.9)	80.0 (14.3)	78.4 (16.6)
RECOVERY	93.1 (15.9)	87.8 (22.9)	90.2 (19.8)
Total speed			
INITIAL	78.1 (20.5)	79.8 (20.0)	79.1 (19.7)
RECOVERY	78.7 (13.6)	85.0 (23.1)	82.2 (19.2)
AUTO accuracy			
INITIAL	94.0 (4.0)	94.2 (2.2)	94.1 (3.1)
RECOVERY	97.0 (3.1)	95.0 (4.3)	95.9 (3.9)
AUTO speed			
INITIAL	137.9 (36.2)	134.0 (29.6)	135.8 (31.9)
RECOVERY	137.6 (20.8)	141.1 (34.2)	139.5 (28.3)
AUTO errors <sup>b</sup>			
INITIAL	9.3 (7.5)	8.2 (3.6)	8.7 (5.5)
RECOVERY	4.4 (4.8)	7.1 (5.8)	5.9 (5.4)
CONT accuracy <sup>b</sup>			
INITIAL	85.5 (6.4)	87.3 (5.8)	86.5 (6.0)
RECOVERY	90.5 (5.2)	90.1 (7.5)	90.3 (6.4)
CONT speed			
INITIAL	101.9 (23.5)	105.6 (17.4)	103.9 (19.9)
RECOVERY	104.6 (15.1)	113.1 (26.2)	109.3 (21.8)
CONT errors <sup>b</sup>			
INITIAL	19.0 (12.7)	16.2 (9.5)	17.5 (10.8)
RECOVERY	12.0 (7.9)	12.1 (8.5)	12.1 (8.0)

<sup>a</sup>Values are expressed as M (SD); <sup>b</sup>Main effect for timepoint,  $p < .05$

#### 4. DISCUSSION

Our study was the first to examine changes in brain activation using fNIRS in athletes who continued to play compared to those who were immediately removed from play after SRC. The primary finding indicated that athletes who remained in play experienced greater increases in [HbO<sub>2</sub>] during a visual search task compared to those immediately removed from play. Further, there was a greater increase in [HbO<sub>2</sub>] at the initial timepoint <7 days post-injury compared to the recovery timepoint in both the left and right hemispheres of the brain. However, these differences resolved by athletes' date of clearance for return to sport. All athletes exhibited improved accuracy and decreased errors from the initial to recovery timepoints, but no group differences were supported for task performance.

The increases in brain activation reported in the current study contrasted from our hypothesis based on prior fNIRS research that documented decreases in brain activation in athletes with SRC (Kontos et al., 2014; Master et al., 2022). Further, decreased cerebral activation following SRC has been reported in neuroimaging studies employing functional magnetic resonance imaging (fMRI) and working memory tasks (Chen et al., 2008; Chen et al., 2004). However, compared to the current study, these studies compared concussed to control participants, used a broader post-injury time interval, and employed different test paradigms. Despite these discrepant findings, another recent fNIRS study examining youth athletes injured within the past 2 weeks found hyperactivation and recruitment of additional brain regions during administration of a dual task paradigm, compared to control participants (Urban et al., 2021), generally consistent with our results. Researchers have reported patterns of increased fMRI measured brain activation during cognitive task performance post-concussion (Jantzen et al., 2004; Slobounov et al., 2010), with hyperactivation associated with protracted recovery (Lovell et al., 2007). These findings suggest that athletes with hyperactivation may be more significantly injured, similar to athletes in the current study that continued to play. It has been speculated that discrepant patterns of activation in concussed and control groups represent decreased neural efficiency (Jain et al., 2022) or a compensatory pattern of activation (Master et al., 2022).

The current study was the first to examine athletes using fNIRS imaging within 7 days of injury and at clinical recovery. Previous neuroimaging studies evaluating differences in brain activation following SRC typically compare athletes with acute concussion to matched controls (Churchill et al., 2017; Kontos et al., 2014; Master et al., 2022) or those who are medically cleared versus asymptomatic at just one timepoint, return to play (Johnson et al., 2012). The current findings support a greater increase in [HbO<sub>2</sub>] at the initial

evaluation timepoint compared to the recovery timepoint for both the left and right hemispheres of the brain. Researchers have reported changes in brain activation over time in patients following SRC compared to controls (Henry, 2014). However, the differing methodology and analyses in these studies limit the conclusions that can be drawn. For example, an fMRI study of athletes scanned one week following SRC and again after clinical recovery (approximately one month) identified three networks of brain hyperactivation at the first scan, including the medial, frontal, and right temporoparietal gyri, right frontal and anterior temporal regions, and posterior parietal cortex (Lovell et al., 2007). However, the analyses in this study did not directly examine if hyperactivation resolved at recovery. Another study that examined athletes scanned 72 hours, 2 weeks, and 2 months following SRC via fMRI demonstrated increased activation in the left and right dorsolateral pre-frontal cortex persisting up to two months after injury (Dettwiler et al., 2014). In contrast, a study of pediatric athletes evaluated utilizing computerized neurocognitive testing and MRI imaging reported a predominant pattern of decreased CBF relative to matched controls up to 30 days post injury (Maugans et al., 2012). Although the current findings are consistent with previous research supporting cerebral hyperactivation in the acute stage following SRC, not all studies have demonstrated this pattern.

Athletes from both groups in the current study improved from initial clinical visit to recovery on accuracy for the controlled trials and exhibited a decreased number of errors on the Ruff 2&7. Previous imaging studies involving small samples, similar to this study, have also not supported differences in objective cognitive performance between concussed participants and controls, despite differences on imaging (Jantzen et al., 2004; Slobounov et al., 2010). This trend suggests that although performance on cognitive tests may appear intact, the underlying activation in the brain may be altered or less efficient in reaching the same performance level. A similar effect may occur within groups of concussed athletes with more (e.g., continuing to play group) or less (e.g., immediate removal group) severe injuries.

#### *4.1 Limitations*

In the study, athletes were matched by age and sex, and the sample included only collision and contact sports to allow for similar athletic exposures by group (e.g., same risk of additional contact). However, this study is limited by a small sample size and lack of a healthy control group. Ideally, an injured athlete control group would be used for comparison to normal performance. Improvements on the Ruff 2&7 may have been partially attributable to practice effects, and small sample size may explain lack of group differences in task

performance acutely. Further, the majority (90%) of participants in this study were males, limiting the application of our findings to females. Moreover, removal from play status was determined by self-report, which is subject to recall bias and inaccuracies. There is variability in the amount of exertion and/or additional head impacts, that were not measured, that may have occurred in our sample following their SRC.

## 5. CONCLUSION

The current study extends prior research on the detrimental effects to adolescent athletes who continue to play following SRC by providing evidence for underlying changes in brain activation. Although previous research demonstrates that continuing to play is associated with worse clinical outcomes and longer recovery, the current study is the first to identify underlying differences in brain activation in athletes who continued to play compared to those removed from play immediately following SRC. Specifically, athletes who remained in play demonstrated more pronounced hyperactivation during completion of a visual attention task than those who were removed immediately. The findings also suggest that the changes in brain activation resolved when athletes were clinically recovered. In conclusion, this preliminary study suggests fNIRS may provide an objective, inexpensive neuroimaging marker for injury severity and recovery of brain function following SRC.

### *Ethic Statement*

All participants and their parents gave written informed consent. The American Psychological Association's ethical standards were met in the conduct of this study and IRB approval from the University of Pittsburgh was obtained. Original data is available upon request. All authors approved the final version of this manuscript.

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### *Competing Interests*

The authors of the present manuscript certify that they have no affiliations with or involvement in any organization or entity with any financial interest or nonfinancial interest (such as personal or professional relationships, affiliations, knowledge or beliefs) in the subject matter or materials discussed in this manuscript.

### *Authors contribution*

Alicia Trbovich, PhD, conceptualized the design of the study, drafted and revised the manuscript. Patrick Sparto, PhD, and Theodore Huppert, PhD, completed data processing, analysis, and drafted components of the manuscript. Daniel Charek, PhD, and Alicia Kissinger-Knox, PsyD were responsible for data acquisition, processing of data, and drafted components of the manuscript.

RJ Elbin, PhD, Michael Collins, PhD, and Anthony Konotos, PhD contributed to drafting of the original manuscript and subsequent revisions.

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