# Assessment of prefrontal hemodynamic activity in concussion during a rapid number naming task

Christina Master,[1,2,3] Eileen Storey,[3] Lei Wang,[4] Matthew Grady,[1,2] Catherine McDonald,[5] Susan Margulies,[6] Kristy Arbogast,[1,3] Hasan Ayaz[7, 8 ,9, 3, 5]

[1]University of Pennsylvania Perelman School of Medicine, Philadelphia, PA
[2]Children's Hospital of Philadelphia, Sports Medicine and Performance Center, Philadelphia, PA
[3]Children's Hospital of Philadelphia, Center for Injury Research and Prevention, Philadelphia, PA
[4]Department of Information Science, College of Computing and Informatics, Drexel University, Philadelphia, PA
[5] University of Pennsylvania, School of Nursing, Philadelphia, PA
[6] Department of Biomedical Engineering, Georgia Institute of Technology and Emory University, Atlanta, GA
[7] School of Biomedical Engineering Science and Health Systems, Drexel University, Philadelphia, PA
[8] Department of Psychology, College of Arts and Sciences, Drexel University, Philadelphia, PA
[9] Drexel Solutions Institute, Drexel University, Philadelphia, PA

## Background

Concussion is a common injury in adolescents with an estimated 1.9 million occurring annually in the US. Despite the prevalence and burden of concussion, it remains a primarily a clinical diagnosis, based on a history of injury followed by the onset of a constellation of subjective symptoms. In addition, the King-Devick (KD) test[1], a standardized, timed, rapid number-naming card test, has also demonstrated utility, aiding in the diagnosis of sports related concussion on the sidelines. However, while these clinical behavioral approaches provide additional support for the diagnosis of concussion, they remain nonspecific, and are not always able to accurately distinguish concussed from healthy adolescents. Thus, there remains an urgent need for a useful objective diagnostic tool for concussion.

The wide distribution of visio-motor control centers within the central nervous system, including the dorsolateral prefrontal cortex and frontal eye fields[2], along with the diffuse distribution of neuronal injury after concussion, likely contribute to the prevalence of visio-motor deficits associated with concussion. The quantitative objective assessment of visio-motor function may serve as a potential diagnostic physiologic biomarker for concussion. Functional near infrared spectroscopy (fNIRS) is an emerging portable neuroimaging modality[3] that is able to capture localized brain activity data in relevant, real-life settings[4] using mobile and wearable sensors[5], even during movement and physical activity[6]. By capitalizing on the optical window differences between oxygenated and deoxygenated hemoglobin, fNIRS is able to measure regional task-related cortical activation via neurovascular coupling. This hemodynamic measure is similar to blood-oxygenation-level-dependent (BOLD) of fMRI, but has the additional advantage of capturing such responses without the restrictions, noise or cost of fMRI. To date, fNIRS has demonstrated utility in measuring cognitive workload during various tasks, including complex ones such as driving. It has also been shown to capture learning effects, adaptation, and compensation, demonstrating robust utility in aiding our understanding of the underlying neurophysiology of various clinical neurologic conditions[7-12].

The goal of this study was to use fNIRS to identify any differences in visual task-related cortical activation between concussed adolescents and healthy controls while performing the KD test[1] and to further characterize the relationship of cognitive load to concussion-related symptom provocation.

## Methods

We enrolled 112 adolescents, ages 12-18 years, with recent concussion and 165 healthy controls as part of a large observational prospective cohort. The KD test was used as the visio-motor task of interest. As a rapid number-naming test, participants are instructed to read the single digit numbers from left to right, top to bottom, as rapidly and accurately as possible, beginning with a simplest practice card, followed by three test cards of increasing difficulty due to the spacing and offset of numbers on the card. Time to read each individual card and overall total time were recorded, as well as any errors made during reading, or symptoms provoked with testing. Participants were provided standardized instructions to read the KD cards while wearing the fNIRS sensor pad.

## fNIRS Acquisition and Analysis

Participant brain activation while performing the task was obtained using a continuous wave four-optode fNIRS device with 4 Hz sampling rate positioned over the forehead to record prefrontal cortical activity (1200W, fNIR Devices, Potomac, MD). Data from the sleft and right hemisphere, and lateral and medial areas were collected via COBI Studio[13].

Raw light intensity data from each subject (4 optodes x 2 wavelengths) were low-pass filtered with a finite impulse response, linear phase filter with order 50 and cut-off frequency of 0.1 Hz to attenuate noise and physiological artifacts, such as respiration and cardiac cycle. A sliding-window motion artifact rejection algorithm was adopted to detect and remove any movement contamination and saturation. For each task block, fNIRS data was extracted using time synchronization markers. The changes in hemoglobin concentration over each card for each brain area were calculated via the Modified Beer-Lambert Law using local baselines. The averaged difference in oxy- and deoxy-hemoglobin concentration changes for each task period were used for statistical analysis of group (e.g., concussed vs. healthy). A separate linear-mixed-effects model with restricted-maximum-likelihood was used to estimate the effects on both cerebral hemodynamics and behavioral performance on the KD test.

**Results**

The concussed adolescents (n=112) and healthy controls (n=165) were demographically comparable with respect to age, sex, and race/ethnicity. The concussed group was more likely to have a history of prior concussion ($p = <.0001$) and migraine ($p = .0001$) compared to the healthy control group. The concussed adolescents were assessed a median of 10 days after injury (IQR 4-16) with fNIRS while performing a visual task (KD test).

Analysis of fNIRS measures indicated that the concussed group exhibited altered cortical activation, particularly with a deficit at the left lateral prefrontal area ($p<.005$, FDR $q<.005$), as an indicated by a reduced task-evoked response. This location in Brodmann area 46 roughly corresponds to the dorsolateral prefrontal cortex (DLPFC) that plays a central role in sustaining attention and working memory[7, 14]. In particular, the attention network coordinated in the DLPFC supports basic cognitive selection of sensory information and response. The reduced activation here can be explained by the disruption of the distributed attention network that results in 'functionally inactivating' the dorsal network[14]. The activity deficit also correlates with lower performance, with significantly higher task completion time, measured with each card for the concussed group ($p<.0001$). Moreover, there was also a main effect for task condition at the right lateral prefrontal cortex ($p<.001$, FDR $q<.005$) corresponding to increasing task difficulty across cards. Again, this correlated with increasing task execution time for each card ($p<.0001$). Finally, task card times had an interaction for both group and block ($p<.0001$).

**Conclusions**

fNIRS distinguished concussed adolescents from healthy controls while performing a visual-cognitive task, the K-D test, which involved rapid number-naming. Injured adolescents with concussion demonstrated altered cortical activation suggesting localized dysfunction, distinguishing it from the pattern of cortical activation in healthy controls, specifically at left lateral prefrontal area. fNIRS, as a modality, is not only able to differentiate concussion from healthy controls, but also captures the compensatory mechanisms of cortical activation that underlie visual cognitive dysfunction after injury.

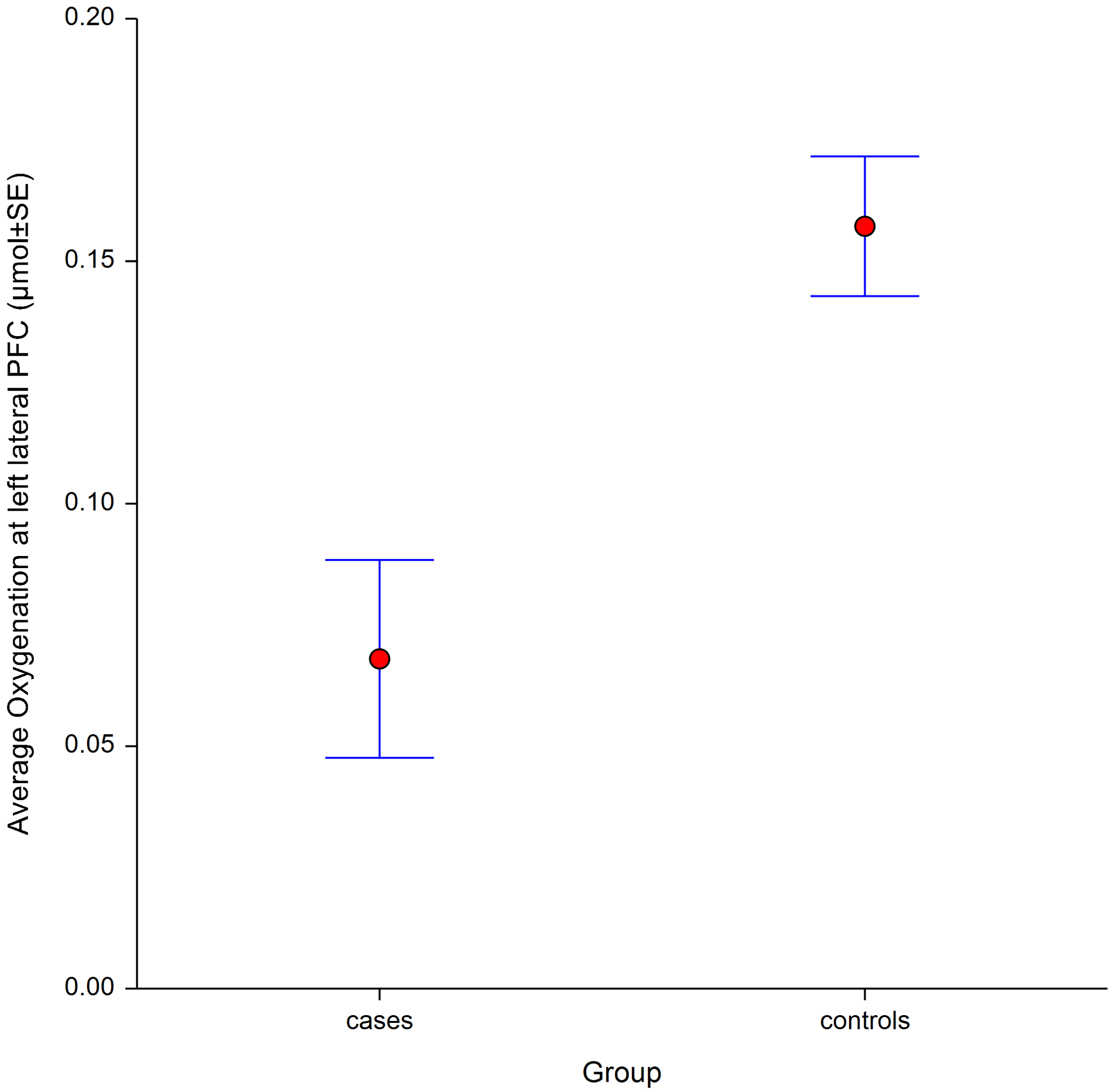


Figure 1. Significant difference in average oxygenation at left lateral prefrontal cortex between concussed participants and healthy controls (p<.005, FDR q<.005)

## References


1. Galetta, K., et al., *The King-Devick test as a determinant of head trauma and concussion in boxers and MMA fighters.* Neurology, 2011. **76**(17): p. 1456-1462.
2. Cameron, I.G., J.M. Riddle, and M. D'Esposito, *Dissociable roles of dorsolateral prefrontal cortex and frontal eye fields during saccadic eye movements.* Frontiers in human neuroscience, 2015. **9**: p. 613.
3. Villringer, A. and B. Chance, *Non-invasive optical spectroscopy and imaging of human brain function.* Trends Neurosci, 1997. **20**(10): p. 435-42.
4. Quaresima, V. and M. Ferrari, *Functional Near-Infrared Spectroscopy (fNIRS) for Assessing Cerebral Cortex Function During Human Behavior in Natural/Social Situations: A Concise Review.* Organizational Research Methods, 2016.
5. Ayaz, H., et al., *Continuous monitoring of brain dynamics with functional near infrared spectroscopy as a tool for neuroergonomic research: Empirical examples and a technological development.* Frontiers in Human Neuroscience, 2013. **7**: p. 1-13.
6. McKendrick, R., et al., *Prefrontal Hemodynamics of Physical Activity and Environmental Complexity During Cognitive Work.* Human Factors, 2017. **59**(1): p. 147-162.
7. Ayaz, H., et al., *Optical brain monitoring for operator training and mental workload assessment.* Neuroimage, 2012. **59**(1): p. 36-47.
8. Lai, C.Y.Y., et al., *Functional near-infrared spectroscopy in psychiatry.* BJPsych Advances, 2017. **23**(5): p. 324-330.
9. Pinti, P., et al., *The present and future use of functional near-infrared spectroscopy (fNIRS) for cognitive neuroscience.* Ann N Y Acad Sci, 2018.
10. Kim, Y.H., B.-J. Kim, and J.S. Bae, *Application of near-infrared spectroscopy in clinical neurology.* Annals of Clinical Neurophysiology, 2018. **20**(2).
11. Master, C.L., et al., *Cognitive workload as the physiologic basis for symptom provocation with task performance in concussion: an fNIRS study of prefrontal brain activity*, in *2nd International Neuroergonomics Conference*. 2018, Frontiers in Human Neuroscience: Philadelphia, PA.
12. Ayaz, H., et al., *fNIRS differentiates cognitive workload between concussed adolescents and healthy controls*, in *2nd International Neuroergonomics Conference*. 2018, Frontiers in Human Neuroscience: Philadelphia, PA.
13. Ayaz, H., et al., *Using MazeSuite and Functional Near Infrared Spectroscopy to Study Learning in Spatial Navigation.* J Vis Exp, 2011(56): p. e3443.
14. Corbetta, M. and G.L. Shulman, *Control of goal-directed and stimulus-driven attention in the brain.* Nat Rev Neurosci, 2002. **3**(3): p. 201-15.