Neural Efficiency Among Concussed and Uninjured Adolescents during an N-Back Task: a Preliminary fNIRS Study

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Introduction:

Over 1.9 million children sustain a concussion in the US annually, with adolescents accounting for over 50% of these injuries (Bryan et al., 2016). Current methods for diagnosing concussions and monitoring recovery rely on self-reported symptoms, which are neither objective nor specific (McCrory et al., 2017). Common sequelae of concussion include neurocognitive deficits that, in adolescents, can persist after symptom resolution (Sroufe et al., 2010; Shrey et al., 2011). Functional near-infrared spectroscopy (fNIRS) is a non-invasive, portable neuroimaging technology that has proven to be valuable in monitoring the recovery of cognitive function and the effects of rehabilitation strategies on adult patients with traumatic brain injury (TBI), (Hashimoto et al., 2007; Hibino et al., 2013; Rodriguez Merzagora et al., 2014). fNIRS has also been used to study brain activation differences in concussed adults aged 18-45 (Kontos et al., 2014) and adults with persistent post-concussive syndrome (Helmich et al., 2015). The prefrontal cortex, the brain region intricately linked to cognition (Spear, 2013), rapidly and variably develops during adolescence, making it inappropriate to directly translate findings in adults to youth. The uneven pace of development may affect cognitive ability, making it potentially difficult to detect differences between groups based solely on prefrontal cortical activation as measured by fNIRS. Neural efficiency analyses, however, provide an approach that is useful for group comparison by capturing not only the performance on tasks of varying demands but also measuring how hard the brain is working to achieve that performance, as measured by fNIRS. Combining both the neurophysiological measure of cortical activity and an individual's given behavioral performance allows for powerful insight into the neurofunction of the brain (Sayala et al., 2006; Neubauer and Fink, 2009; Curtin and Ayaz, 2019). Thus, the goal of this study was to use this approach to understand the dysfunction created by concussion by investigating differences in neural efficiency during a standard assessment of working memory, an N-back task, among concussed adolescents and uninjured controls.

Methods:

This was a case-control comparison of concussed and uninjured adolescents, ages 16.5 to 18 years. Concussed participants were recruited from The Children's Hospital of Philadelphia care network, and uninjured controls were recruited from the greater Philadelphia region. Participants completed an N-back task, which requires participants to react when the current stimulus is the same as the n-th letter before the stimulus letter. This task consisted of 4 trials each of 0-, 1-, and 2-back tasks, presented in a pseudorandomized order. Each trial contained 4±1 stimuli which were the same as the 0-, 1-, or 2- stimuli previously. Twenty-two stimuli were present in each trial, with each stimulus displayed for 0.5 seconds, followed by a blank screen for 1.5 seconds. A rest period of 15 seconds was present between each trial, and after every third trial, a 30 second rest period was provided (Stoet, 2010, 2017). Reaction times were captured with increased reaction time indicating worse performance. During the N-back task, fNIRS data from the anterior pre-frontal cortex was collected at 10 Hz using a 6 optode fNIR2000M imager (fNIR Devices, LLC, Potomac, MD). The fNIRS sensor was symmetrically centered on each participant's forehead. The light intensity and detector gain were adjusted for each participant to optimize signal. Raw light intensity data were low pass filtered to attenuate cardiac and respiratory cycle effects. Motion artifacts were removed using the SMAR algorithm (Ayaz et al., 2010). Trial data was extracted using time synchronized markers. Relative changes in oxygenated hemoglobin concentrations (HbO) during each trial were calculated via the Modified Beer Lambert Law using pre-task baselines, defined as 5 seconds prior to the start of each trial (Kocsis et al., 2006). Neural efficiency was calculated as the projection of normalized reaction time and mean HbO onto the line where the normalized reaction time equals the normalized mean HbO value, as this is where neural efficiency is zero (Causse et al., 2017; Curtin and Ayaz, 2019). Neural efficiency values were then averaged across all four trials of each condition. A linear mixed effect model was used to evaluate the fixed effects of N-back task condition (0-, 1-, or 2-), injury status and their interaction, and the random effect of subject, on average neural efficiency. The model was evaluated with restricted maximum likelihood. Denominator degrees of freedom and p-values were estimated via Kenward-Rogers corrections in R (Bates et al., 2014; Kuznetsova et al., 2017; R Core Team, 2019).

Results:

Eight concussed participants (8 female, average age:17.6±0.7 years, average days since injury:22.2±9.4) and sixteen uninjured controls (9 female, average age:17.9±0.6 years) completed the N-back task. N-back task condition ($F_{2,257.1}$=26.23, p<0.0001), as well as the interaction of injury status and N-back task condition, ($F_{2,257.1}$=3.55, p=0.03) were statistically significant. Post-hoc testing revealed injury status was only statistically significant during the 2-back, with concussed adolescents displaying significantly worse neural efficiency as compared to uninjured controls (p = 0.04). Mean neural efficiency values during the N-back task are in Figure 1.

Discussion:

In this preliminary study, there were significant differences in neural efficiency between concussed adolescents and uninjured controls during an N-back task. These results suggest that fNIRS may be a useful tool in monitoring recovery from concussion and the metric of neural efficiency may potentially account for differences in cognitive ability due to variable maturation of the frontal lobe in adolescents by accounting for both task performance and cortical activity. The association of injury status with decreased neural efficiency was limited to the most difficult condition (2-back), indicating that while concussed adolescents were able to meet the task demands of the simpler 0- and 1-back conditions efficiently, they were unable to do so during the complex 2-back condition. Although statistically insignificant, there is a trend towards concussed adolescents completing the 0- and 1-back conditions with greater efficiency than controls. This may be due to few participants or other factors such as the presence of ADD/ADHD diagnoses in the control group. These findings warrant study of neural efficiency metrics in a larger sample of adolescents at different time points throughout recovery and exploration of sex-specific differences.

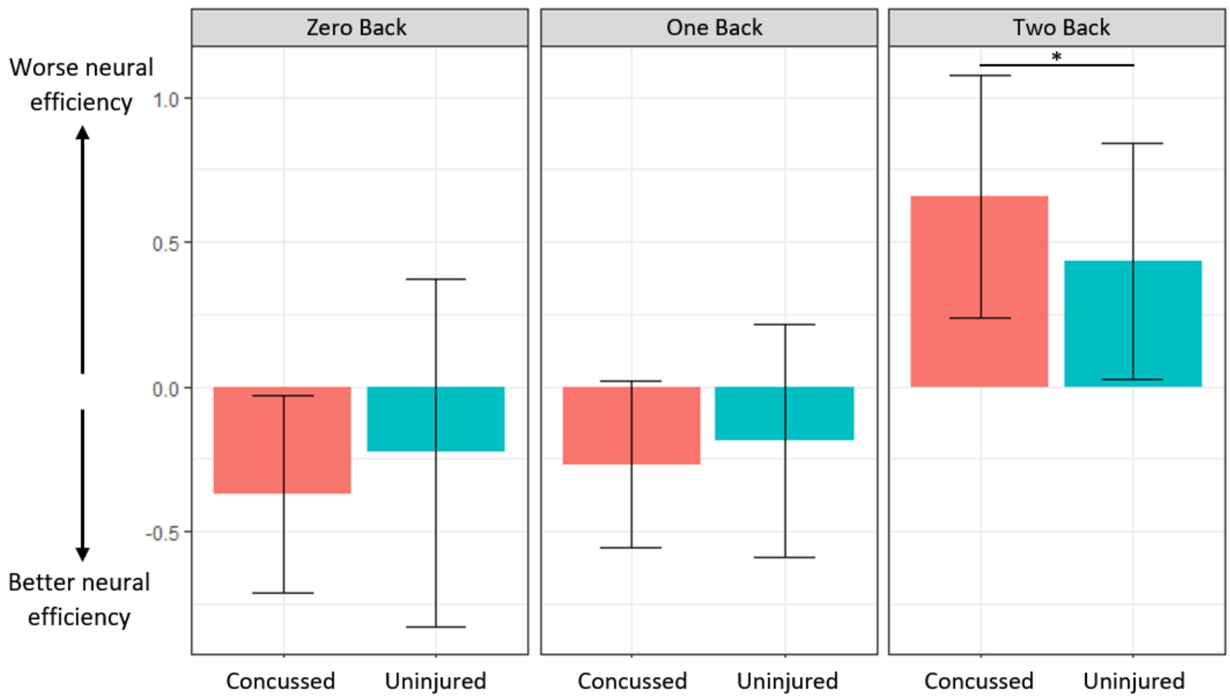

*Figure 1. Mean neural efficiency values and standard deviation for each condition of the N-back task for cases and controls. A higher positive value indicates worse neural efficiency. Neural efficiency was only significantly affected by injury status during the most difficult condition, 2-back, with concussed adolescents presenting with significantly worse neural efficiency than uninjured controls. * indicates p < 0.05.*

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