

Persistent Neurovascular Coupling Dysregulation During Subacute Recovery Phase Following Concussion

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ABSTRACT

Concussion diagnosis is characterized by a lack of objective markers, as there is a paucity of better understanding of the pathophysiology. Neurovascular coupling (NVC), an important factor in cerebral blood flow (CBF) regulation, is a tight temporal relationship between neuronal activity and CBF in order to meet cerebral metabolism. **PURPOSE:** To examine NVC on Day-3, Day-21, and Day-90 following a concussion in comparison to the non-injured healthy controls. **METHODS:** Twenty-nine male and female collegiate athletes (20±1years) sustaining a sports-related concussion were enrolled in a longitudinal study. For the concussed athletes, data were obtained on Day-3 (N=29), Day-21 (N=26), and Day-90 (N= 21) following the head injury. Thirty-two sports-matched non-injured controls were also enrolled and data were obtained at a single time point. Symptom number and severity and cognition were assessed using the Sports Concussion Assessment Tool-3rd Edition (SCAT-3). To assess NVC, continuous middle cerebral artery blood flow velocity (MCAV) was obtained bilaterally with 2 MHz transcranial Doppler ultrasonography (TCD) while subjects were seated in an upright position. As a measure of working memory and executive function, the 0-Back (control task) and 2-Back (cognitive task) tasks were performed for 3 minutes each. NVC was estimated as the percentage change in MCAV between the 2-Back (MCAV_{2Bk}) and 0-Back (MCAV_{0Bk}) tasks for each subject. The equation used was $NVC (\%) = [(MCAV_{2Bk} - MCAV_{0Bk}) / MCAV_{0Bk}] \times 100$. A non-parametric Wilcoxon rank sum test was utilized to compare NVC means between the controls and concussed athletes at the three time points. **RESULTS:** On Day-3 subsequent to the head injury, concussed athletes, compared to the controls, displayed higher symptom number (12.2±6.8 vs. 2.4±3.4; p<0.001) and symptom severity (4±6 vs. 28±23) with resolution of symptoms by Day-21. The concussed group exhibited lower percentage of correct responses on the 2-Back task in comparison to the controls on Day-3 (82±13 vs. 90±5; p=0.02), Day-21 (89±12 p=0.012), and Day-90 (90±5 p=0.018). Compared to non-injured controls (2.73±3.7), lower NVC was observed on Day-3 (0.36±3.62 p=0.03) and Day-21 (0.18±3.31 p=0.01) with persistent decline observed on Day-90 (-0.5±2.9 p=0.003) following concussion. No difference in NVC was observed within the three points post-concussion. **CONCLUSION:** NVC remained dysregulated during the acute phase and worsened during subacute phases following concussion suggesting persistent physiological impairment beyond symptom resolution. Future studies with a large sample size and longer follow-up period are needed to track the physiological recovery trajectory and examine if there is an association between dysregulation of NVC and higher risk of secondary injuries post-concussion.