**Metabolic alterations in corpus callosum may compromise brain functional connectivity in mTBI patients: An 1H-MRS study**

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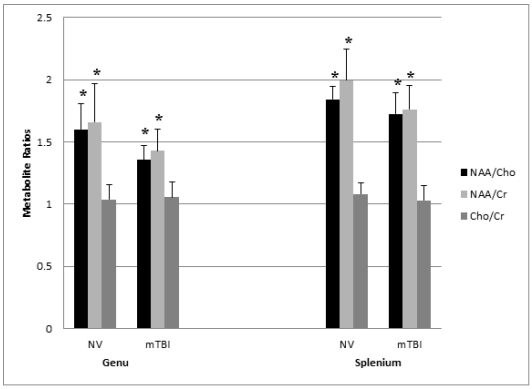
**Introduction:** Mild traumatic brain injury (mTBI) accounts for 70-90% of the 1.4 million annual incidence of traumatic brain injury in the United States [1]. A single episode of mTBI sets off a complex chain of neurochemical and neurometabolic reactions due to mechanical trauma that produces acceleration and deceleration forces on the brain. As a result of the complex pathophysiological response to mTBI individuals present with many clinical symptoms including: headache, nausea, visual disturbances, light sensitivity, dizziness, fatigue, and irritability. Even more disturbing is the timeframe for mTBI symptoms resolution with 15% of cases where individuals report physical, cognitive, and emotional symptoms that persist for more than one year post-injury [2]. Few studies to date have investigated both structural and functional connectivity of large-scale cognitive networks, although the use of multimodal studies combining functional and structural information are valuable in understanding how brain injury disconnects or disrupts brain networks [3]. Based upon our previous research and prior hypothesis that reduced interhemispheric functional connectivity may result from compromised integrity of the corpus callosum; the aim of this study was to evaluate the metabolic profile of the corpus callosum with magnetic resonance spectroscopy ($^1$H-MRS) in the subacute phase of mTBI.

**Methods:** 15 student-athletes (mean age 20.6 +/- 1.2) who had recently suffered from a sports-related mTBI and 15 neurologically normal volunteer (NV) student-athletes with no history of mTBI (mean age 20.4 +/- 0.8) were recruited. $^1$H-MRS and anatomical images were acquired on a 3.0 Tesla Siemens Trio whole-body scanner using a 12 channel head coil. 3-D multivoxel $^1$H-MRS Chemical Shift Imaging (CSI) (120mm x 120mm x 80mm FOV, 10.0mm x 10.0mm x 12.5mm voxel size, TE=135ms, TR=1510ms, NSA= 1) was implemented to evaluate *in-vivo* NAA, Cho, and Cr metabolite peaks. The $^1$H-MRS CSI data were processed off-line using standard scanner software (spectroscopy Card, Siemens) and included zero filling, eddy current correction, water suppression, Fourier transform, baseline and phase correction post processing steps. The genu and splenium of the corpus callosum were demarcated into 2 separate regions of interest (ROIs). Each ROI consisted of 6 voxels that were individually selected to be within the genu and splenium of the corpus callosum based upon overlaid anatomical T1 images. NAA/Cho, NAA/Cr, and Cho/Cr ratios of these selected voxels were then averaged to come up with a mean value for each ROI [4]. Metabolite ratios between the mTBI group and NV group were compared by one way ANOVA and considered significant if $p < 0.05$.




**Results:** Similar findings were found in both the genu and splenium of the corpus callosum. In the genu both NAA/Cho ($p=0.001$) and NAA/Cr ($p=0.022$) ratios were significantly lower in the mTBI group compared to the NVs. However, there was no difference between groups in the Cho/Cr ratio for the genu. As seen in the Genu, the splenium showed significantly lower NAA/Cho ($p=0.04$) and NAA/Cr ($p=0.01$) ratios. Again Cho/Cr ratio was not significantly different between groups.

**Conclusion:** While functional connectivity does not necessarily mean structural connectivity due to indirect pathways and compensatory measures, there is growing evidence that the two are related to a certain degree. Although there is limited research on structural and functional connectivity, the evidence out there suggests that disruptions in one affect the other [3]. Future research combining both structural and functional information is important to see the effects that structural connectivity has on functional connectivity and vice versa. mTBI produces an imbalance in brain metabolites that is not yet restored to pre-injury levels even when there has been clinical symptoms resolution and a return to baseline on neuropsycholgical testing [4]. There is growing evidence through advanced neuroimaging techniques that despite a return to premorbid status based upon current clinical measures there are still deficits in structural and functional connectivity in the subacute phase of mTBI. This is of major concern when returning athletes to play due to the fact that previous history of mTBI puts an individual at a higher risk for recurrent mTBI.

**References:**

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