

Combined quantitative diffusion tensor and 1H magnetic resonance spectroscopic imaging findings in patients with persistent neurocognitive deficits following a mild traumatic brain injury.

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Introduction: Approximately 80% of traumatic brain injuries (TBI) are classified as mild, as defined by a loss of consciousness less than 30 minutes, post-traumatic amnesia of less than 2 hours, and a Glasgow Coma Scale (GSC) of 13-15 ⁽¹⁾. Neurocognitive deficits are estimated to occur in approximately 50-80% of mild TBI (mTBI) patients, which may persist for several years after injury ⁽²⁾ even though conventional imaging is normal. In this study, we used diffusion tensor imaging (DTI) and ¹H magnetic resonance spectroscopic imaging (MRSI), which can detect axonal injury and neuronal loss or dysfunction in normal appearing brain following TBI, to evaluate whether microstructural and/or metabolic abnormalities are present in mTBI subjects with persistent neurocognitive deficits.

Methods: Thirteen mTBI (3 – 26 months post-injury) and 5 normal control subjects of similar age were retrospectively identified and included in this study. DTI (SE-EPI TR/TE = 4800/91 msec, 2 mm slice thickness, matrix = 128 x 128, pixel size = 2³ mm, b = 1000 s/mm², 12 directions, 1 average) and 3D MRSI (PRESS TR/TE = 1700/144 ms) were acquired on a Siemens Tim Trio 3T scanner through the level of the corpus callosum and basal ganglia/internal capsule. Structural 3D T2-weighted MR images (SPACE; TR/TE = 4000/120 msec, echo train length of 15, 4 mm slice thickness) were used to assign the anatomical location of each voxel. Structural 3D T1-weighted MP-RAGE (TR/TE = 11.4/4.4 ms, 128 slices, 2mm slice thickness) were acquired to determine the tissue composition of each voxel. Fractional anisotropy (FA) and tensor maps were generated off-line using DTI Studio. LCmodel was used to obtain semi-quantitative NAA/Cr, NAA/Cho, and Cho/Cr ratios in each voxel. To obtain tissue composition, metabolic, and diffusivity information from the same anatomical position we used in-house custom designed software incorporating routines from Matlab (Version 7.0.4, MathWorks, Natick, USA) and SPM5 (Wellcome Trust Center of Neuroimaging, University College London, England) to overlay the MRSI voxel grid on the segmented white matter, grey matter and CSF images and the FA and tensor maps. Those voxels with 70% or more white matter and less than 30% CSF were included in the analysis and grouped by hemisphere and region into left or right frontal white (FW), parietal white (PW), occipital white (OW) matter and internal capsule. Within subject differences were measured using an independent samples t-test. Between-subject group differences, accounting for age and the duration between injury and the imaging study, were measured using univariate analysis of variance where $p < 0.05$ was considered significant.

Results: In the mTBI group, voxels in the left OW matter showed a 12% decrease in NAA/Cr ($p=0.037$) and a 20% decrease in NAA/Cho ($p<0.01$) compared to the same region in the right OW matter. Moreover, voxels sampling the left anterior internal capsule showed a trend towards a decrease in NAA/Cr ($p = 0.068$) and a trend towards increased FA ($p = 0.078$) compared to the right anterior internal capsule of the mTBI subjects. When the data was corrected for subject age and the time between injury and the MRI/MRS study, the mTBI group showed a decrease in NAA/Cr ($p = 0.016$) and an increase in FA ($p = 0.04$) in the left anterior internal capsule compared to controls.

Discussion: These preliminary findings show that regions suggestive of neuronal loss or dysfunction are present in the left anterior internal capsule and left occipital white matter of a group of mild TBI patients with persistent neurocognitive deficits following a remote brain injury. In addition, the increase in FA in the left anterior internal capsule may be related to an increase in extracellular space adjacent to remaining axons after the loss of a subset of corticospinal tract fibers, as suggested by Lo et. al ⁽⁴⁾. Our findings suggest that both metabolic and ultrastructural changes persist following a mild TBI which may relate to continued neurocognitive deficits seen in these subjects.

References:

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