Prospective study of changes in regional brain myelin content after concussion

Elham Shahinfard1, Michael Jarrett1, Irene Vavasour1, Shannon Kolling1, Enedino Hernández-Torres1, Jack Taunton1, David K Li1, and Alexander Rauscher1

1University of British Columbia, Vancouver, BC, Canada

Target Audience: Radiologists, neurologists, medical physicists, sports physicians

Purpose: Mild traumatic brain injury (mTBI) is characterized by diffuse axonal injury and is not detectable on traditional computed tomography or MRI. While diffusion tensor imaging (DTI) measures are often used as indirect markers for myelination, it is preferable to use a direct, validated marker. Apart from axonal rupture as a direct consequence of an impact, axons also undergo secondary axotomy, as a consequence of the biochemical cascade following impact. Both scenarios result in Wallerian degeneration accompanied by degradation of the myelin sheath. A non-invasive method for myelin assessment would therefore be a valuable addition to the neuroimaging portfolio available for the evaluation of TBI. Here, we use myelin water fraction (MWF, a marker for myelin3) to measure demyelination and remyelination in the human brain after concussion.

Subjects: 25 male and 20 female college-aged (17 to 22 yrs old) amateur hockey players participated over one hockey season. All players underwent MRI scanning and neuropsychological testing (SCAT2) before and after the hockey season. Players who were identified as concussed by an independent neurologist underwent additional scans and testing at 72-hours, 2-days, 2-weeks, and 2-months after injury.

MRI: MRI data were acquired on a Philips Achieva 3T scanner equipped with Quasar Dual Gradients and an eight-channel SENSE head coil. A 32 echo T2 scan was acquired for myelin assessment (TR-1000 ms, TE-10 ms, flip angle=90°, acquisition matrix=232x192, acquired voxel size 0.99x0.99x5mm, reconstructed voxel size=0.96x0.95x2.5mm). A high-angular resolution DTI scan was acquired with TR=7015ms, TE=60ms, flip angle=90°, acquisition matrix=100x99, FOV=224x224x154mm, acquired voxel size=2.2x2.2x2.2mm, reconstructed voxel size=2x2x2.2mm (SENSE factor of 2.1, b0=6, b=700, 60 directions).

Analysis Methods: The T2 decay was decomposed into myelin water, and intra- and extra-cellular water using a non-negative least squares fit with an extended phase graph algorithm and flip angle optimization4. MWF was calculated as T2 signal from 0-40ms divided by the total T2 signal. MWF measures were compared at the various time-points via voxelwise and region of interest (ROI) based analysis. For both methods, we compared the end-of-season scans for the full cohort with their baseline scans. Baseline scans of the concussed subjects were compared to the scans at all other time-points. ROI analysis was performed based on the John Hopkins University (JHU) white matter atlas. For each ROI, a MWF threshold was defined at two standard deviations below the mean of the baseline measurement for that ROI. A score was calculated for each ROI by subtracting the number of subjects with MWF below the threshold at baseline from the number of subjects with MWF below the threshold at end of season. This method allows us to measure diffuse changes in MWF without requiring the MWF changes to be localized in the same ROI in all subjects. In addition, voxelwise statistical analysis of the data was performed using FSL’s tract-based spatial statistics (TBSS)5, which uses DTI data to create a white matter skeleton; MWF values were then projected onto this skeleton. Voxelwise cross-subject statistics were then carried out while controlling for age, gender and SCAT2 results. These methods were chosen explicitly to examine diffuse changes in brain structure while compensating for multiple comparisons.

Results: Eleven players sustained a concussion during the ice hockey season. ROI analysis showed the ROI score distribution across all ROIs to be significantly non-zero. Fig. 1 shows one of 42 sample ROIs (left cerebellar peduncle), with grey dots representing baseline MWF, green dots as end of season MWF, and the low edge of the blue box as the threshold. Serial scans of concussed players did not have sufficient power to show significant differences with this approach. However, voxelwise tract-based statistics showed significant decreases in myelin content at 2 weeks post injury, with no significant change at the end of the season compared to baseline. Most significant changes were in the splenium of corpus callosum, posterior thalamic radiation, superior corona radiata and posterior limb of the internal capsule (as shown in Fig. 2).

Discussion: The short-term reduction in myelin observed after concussion, and subsequent normalization is consistent with the typical neurological progression of concussion. The full season changes in myelin content observed in the ROI analysis was not replicated in the TBSS results, but this is not unexpected, as TBSS relies on the assumption that changes in brain structure will be found in identical brain regions across all (or most) subjects. While this may be true occasionally in concussion, we must consider the possibility of diverse brain regions being affected throughout the cohort. Our ROI analysis accounts for this and clearly shows a full season effect.