Single-subject diffusion tensor imaging changes after concussion

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Introduction: Sports-related mild traumatic brain injury (mTBI) is a prominent risk at every level. Concussion is a complex phenomenon and the neurological basis is still poorly understood. The current standard of care involves a series of clinical tests to diagnose the concussion, advise on an appropriate recovery time and estimate when it is feasible to return to play. Multiple concussion events during childhood can be especially severe with long-lasting symptoms that considerably affect many aspects of life. Diffusion tensor imaging (DTI) could provide insight into the neurological basis of this injury, and possibly aid in diagnosis and determining when it is safe to return to play. Though concussion is believed to be a global injury, there may also be injury-specific changes that are lost in a average group analysis.

Purpose: The objective of this ongoing study is to determine (a) DTI changes on the single-subject and group level post-concussion and (b) assess the longevity of these changes.

Methods: Male hockey players (age 10-12) are involved in this longitudinal study. A group of 15 hockey players were evaluated prior to the beginning of the season and acted as an independent control baseline group. We then followed multiple boys hockey teams where concussed players (n = 8) were assessed within 48hrs of the injury, and 3-months later (n = 6). The 3T MRI (Tim Trio; Siemens, Erlangen, Germany) scanning protocol includes an MPRAGE anatomical (TE/TR = 2.94/2300 ms, flip angle = 9°, matrix size = 256x64, FOV = 256x240 mm, # slices = 160, slice thickness = 1.20 mm) and a diffusion tensor imaging (DTI) EPI sequence (TE/TR = 79/7200 ms, matrix size = 98x98, FOV = 200x200mm, # slices = 64, slice thickness = 2.0mm, 64 directions). DTI data was first eddy-current corrected and then a diffusion tensor model was fit to each voxel. From this fractional anisotropy (FA) and mean diffusivity (MD) maps were calculated. This data was then registered and transformed to standard space, where binary masks were created for 11 major white matter tracts based on the John Hopkins University White-Matter Tractography Atlas. DTI data was statistically analyzed using independent samples t-tests comparing baseline, post-concussion and 3-month follow-up groups. Concussed individuals were also compared to the baseline control group on a per subject basis, and each individual from the baseline group was compared to the entire baseline group as a control.

Results: The lead author is currently blind to clinical results. The FA in the left and right cingulate gyrus was significantly lower post-concussion ($p = 0.02$ and $p = 0.002$ respectively), and the right FA ($p = 0.02$) and the left MD ($p = 0.04$) remained significantly different 3-months later (Figure 1(a)) in the grouped analysis. The MD in the right superior longitudinal fasciculus was also significantly lower post-concussion ($p = 0.04$) and 3-months later ($p = 0.003$) at the group level (Figure 1(b)). The hockey baseline group was randomly split in half and compared with no significantly different FA or MD values. Comparing individual concussed data to the baseline group rendered even more significantly different tracts. For example, one concussed individual had 25 significantly different FA and MD values including other tracts like the inferior longitudinal fasciculus, inferior fronto-occipital fasciculus and the corticospinal tract. The affected tract and number of significantly different tracts varied from individual to individual, however in each case the FA maps allowed one to distinguish a concussed *individual* from the controls (Figure 1(c)). To control for this exploratory analysis, each individual baseline DTI data was compared to the baseline group and no significant differences were found.

Conclusions: Though there have been a number of reports of changing FA and MD values in mTBI[1,2], some injury-specific information may be lost. DTI data on an individual basis may be an informative biomarker for concussion diagnosis and recovery. Future work includes correlating clinical symptom severity with the appropriate affected tracts.

References: [1]Cubon et al. A diffusion tensor imaging study on the white matter skeleton in individuals with sports-related concussion. Journal of Neurotrauma. 2011;28:189-201. [2]Henry et al. Acute and chronic changes in diffusivity measures after sports concussion. Journal of Neurotrauma. 2011;28:2049-2059. ***Figure 1:***(a-b) *=significant difference from baseline (c) A concussed subject (top) and control subject (bottom) subtracted from the average FA control group map.