Acute DKI Alterations in Mild Traumatic Brain Injury Patients with and without Eventual Symptomatic Improvement

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Purpose: To investigate diffusional kurtosis imaging (DKI) as a means to infer mechanisms of microstructural alterations following mild traumatic brain injury (mTBI), and its ability to distinguish patients who experience symptomatic improvement from those who do not. TBI affects approximately 1.7 million in the United States each year,[1] with 75% of cases classified as mild.[2] Mechanisms of injury and recovery in mTBI are complex and poorly understood, particularly in cases without evidence of acute damage through traditional imaging techniques. DKI has shown to provide complementary information about subtle tissue microstructure changes to diffusion tensor imaging following mTBI.[3] We investigated whether mTBI patients demonstrate alterations in diffusion and kurtosis-related parameters derived from DKI. More importantly, we sought to investigate whether these changes at the acute stage will reveal information about symptom recovery in mTBI patients at chronic stages.

Methods: As part of the MagNeT (**Mag**netic Resonance Imaging of **Ne**uro**T**rauma) Study, 30 mTBI patients (Glasgow Coma Scale score=13-15) received an MRI evaluation in the acute (≤10 days) and sub-acute (1 month), and chronic (6 months) stages of injury. DKI data was compared to that from 30 healthy controls. Patients also completed the Rivermead Post-Concussion Symptoms Questionnaire, which asks participants to rate a series of common post-concussive symptoms they may be experiencing on a scale of 0-4.[4] Because several patients were still hospitalized at the acute scan, incomplete Rivermead data were available at this stage; however, complete Rivermead data were available for all patients at the sub-acute and chronic stages, and complete DKI data were available at all stages. The change in total Rivermead score from the sub-acute to chronic stages was used to subdivide patients into those whose symptoms reduced (n=14) and those whose symptoms remained static or increased (n=11). Five patients who reported no symptoms at either stage were excluded from this subdivision. There were no significant differences among control and patient groups in age, gender, or years of education. Patient groups did not differ significantly in Rivermead score at the sub-acute stage, incidence of positive CT or clinical MRI, or in time between injury and MRI at any stage.

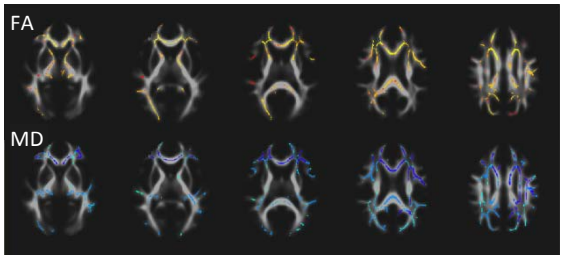

Fig. 1. Acute FA and MD: Symptoms Reduced vs. Not Reduced. FA in significantly higher and MD significantly lower in patients whose symptoms reduced. Significant regions of skeleton overlaid on mean FA map. Darker red and lighter blue indicate more significance.

Imaging was performed using a 3T Siemens Tim Trio Scanner. Diffusion weighted images were obtained with b = 1000, 2000s/mm^2 at 30 directions, together with 4 b0 images, in-plane resolution = 2.7mm^2, TE/TR = 101ms/6000ms at a slice thickness of 2.7mm with two averages. A high resolution T1-weighted-MPRAGE (TE = 3.44 ms, TR = 2250ms, TI = 900ms, flip angle = 9º, resolution = 256 × 256 × 96, FOV = 22 cm, sl. Thick. = 1.5 mm) image was acquired for anatomic reference. Diffusion weighted images were motion corrected using SPM8. 3D Gaussian smoothing with FWHM = 3.0mm was applied to improve the signal SNR. DKI reconstruction was then carried out on each voxel using in-house MATLAB program. Voxelwise statistical analysis of DKI data was carried out using TBSS (Tract-Based Spatial Statistics,[5] part of FSL[6]). All subjects' fractional anisotropy (FA), mean diffusivity (MD), and mean kurtosis (MK) data were projected onto a mean FA tract skeleton, before applying voxelwise cross-subject statistics.[5] Region of interest (ROI) analysis was performed for major white matter tracts, with each ROI representing the portion of the white matter skeleton falling within a given region of the JHU white matter atlas.[7]

Results: Voxelwise analysis showed no difference between controls and mTBI patients as a whole at the acute or sub-acute stages. Based on ROI analysis at the acute stage, patients showed increased MD in the genu of the corpus callosum (CCG), and decreased MK in bilateral posterior internal capsules (PIC) and superior corona radiata (SCR). Patients experiencing symptomatic improvement demonstrated widespread voxelwise differences compared to those whose symptoms did not improve. Patients with improving symptoms showed higher FA and lower MD in several white matter tracts acutely (Fig. 1). Upon ROI analysis, patients without symptomatic improvement showed significant differences compared to both controls and those with symptomatic improvement (Fig. 2), showing decreased FA and MK and increased MD in several regions at the acute stage. While no voxel-wise changes in MK were noticed acutely, ROI analysis revealed changes in the bilateral PIC that were not depicted by FA or MD.

Discussion and Conclusion: There was a stark distinction in acute DKI measures between patients who experience symptomatic improvement and those who do not at the chronic state. Increased FA and MD and decreased MK in patients with persistent symptoms indicate microstructural damage to white matter tracts likely missed by convention imaging. These patterns emerged at an early stage and despite similar incidence of positive CT and MRI in both patient groups, indicating potential prognostic value of DKI. MK also appears more sensitive to PIC damage than the Gaussian diffusion parameters investigated. Further research is needed to elucidate the predictive value of DKI.

References: [1]Faul M et al., 2010. [2]Centers for Disease Control and Prevention, 2003. [3]Grossman, 2012. [4]King et al., 1995. 5Smith et al., 2006. 6Smith et al., 2004. [7]Oishiet al., 2008

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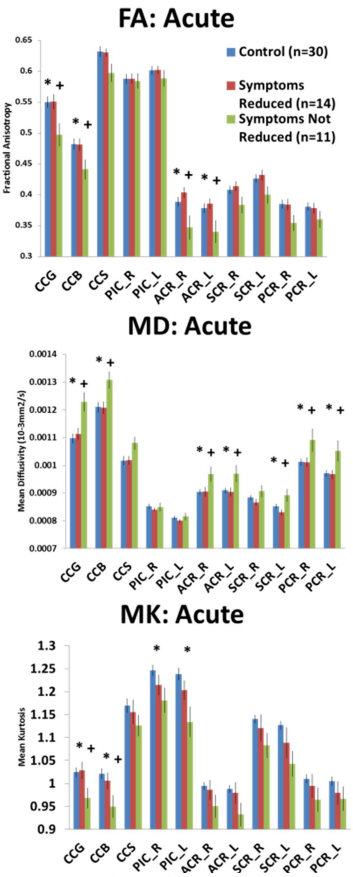

Fig. 2. Acute FA, MD, & MK: ROI. R: right; L: left. * Symptom not improved vs. control; + Symptom not improved vs. symptom improved; p<0.05. CCB: corpus callosum body; CCS: corpus callosum splenium; ACR: anterior corona radiata; PCR: posterior corona radiata.