Serial Atlas-based DTI Study of Mild Traumatic Brain Injury in Adults

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Introduction: Mild traumatic brain injury (mTBI) is a major public health concern in both civilian and military populations **(1,2)**. Identifying early neuroimaging markers that relate to cognitive and behavioral changes associated with mTBI is an important application of quantitative MRI modalities **(2, 3)** such as diffusion tensor imaging (DTI). DTI offers sensitive markers of tissue microstructural integrity that could be used to model the biophysical sequela of mTBI and in the diagnosis and prognosis of injured subjects **(4)**. However, mTBI causes and effects are heterogeneous and depend on several factors such as age at injury, post-injury interval, injury severity, and location **(1,2)**. In this report, we applied DTI methods serially on cohorts of healthy orthopedic controls and mTBI to characterize regional and global macrostructural and microstructural attributes of white matter (WM), gray matter (GM) and cerebrospinal fluid (CSF) to identify and differentiate patterns of acute and short-term recovery trends. Given that a previous DTI report on mTBI in adults using regions-of-interest **(3)** implicated the left anterior corona radiata (CR), we analyzed this entire zone using atlas-based methods **(5)**. Our analysis of the cross-sectional and serial data demonstrates dissociation between volumetric (macrostructural) and tissue integrity (microstructural) attributes and show the potential utility of DTI to capture a pattern of *transient* vasogenic edema using the DTI measurements of the corona radiata.

Subjects and Methods: We included 36 mTBI patients (13 females; ages 19-50 years) imaged within 24 hours of injury (Glasgow Coma Scale score 13-15). Nineteen of these patients were imaged at baseline and 3 months. In addition, 37 orthopedic controls (10 females; 29 ± 9 years; age range = 20-49 years) recruited from emergency clinics without head injuries were imaged at baseline and 3 months (93 ± 14 days). The two cohorts were comparable on gender and age characteristics (p=0.85). All MRI studies were performed on a 3T Philips Intera scanner. The diffusion-weighted imaging (DWI) data were acquired using a single-shot spin-echo diffusion sensitized EPI sequence with 32 non-collinear encoding directions, b=1000 sec mm^{-2}, T_R/T_E = 8000/55 msec. The slice thickness was 3.0 mm with 44 contiguous axial slices covering the entire brain; FOV=256x256 mm^2: ***DTI pre-processing:*** DWI data were corrected for geometric distortions due to eddy currents using the b0 map which was used for masking or brain extraction BET-FSL (http://fsl.fmrib.ox.ac.uk/fsl/fslwiki/), the data were subsequently decoded and diagonalized **(4)**. ***Brain Tissue and CSF segmentation and Quantification***: Whole brain CSF (wbCSF) was segmented into ventricular (vCSF) and non-ventricular or sulcal CSF (sCSF), whole brain GM and WM were segmented using a DTI-ICBM atlas-based approach **(5, 6)**. The tissue segmentation utilized contrast between CSF and brain parenchyma on the mean diffusivity (MD) and fractional anisotropy (FA) maps **(7).** The approach provided volume, and corresponding DTI metrics such as FA, mean, radial and axial diffusivities. Structures were parcellated further into deep/corpus callosum and cortical/lobar which was parcellated into frontal, temporal, parietal, limbic and insular tissue according to the DTI-WM atlas **(5).** As a representative of deep non-callosal tissue, we focused on the anterior CR (ACR), posterior (PCR) and superior (SCR) segments of the corona radiata bilaterally **(3).** Regional and global volumes were normalized to the intracranial volume (ICV) obtained from each subject **(7, 8).** **Statistical Analyses**: Comparisons of regional and global mean values between groups were conducted using analysis-of-variance and generalized linear regression models were used to analyze the scatter of data as age advances.

Results: Volume-to-ICV percentage were not different in regional and global CSF, GM and WM. Sulcal and ventricular CSF volumes increased with age in both healthy controls and mTBI (**Fig. 1A**), As expected, neocortical gray matter decreased with age at comparable rates in both groups. The radial diffusivity of the anterior corona radiata was found to be significantly elevated in mTBI which was not different at 3 months hinting to the possible resolution of edema.

Discussion: In this work we analyzed data collected from two age-matched cohorts imaged at two different time points to identify patterns of acute (1 Day) and short term (90 Day) DTI characteristics. Global and regional changes in WM, GM and CSF volumetry were not different between controls and mTBI. Consistent with a previous report **(3)**, subtle changes in WM microstructure due to diffuse axonal injury was detected using the corona radiata diffusivity, hinting that this region is extremely vulnerable due possibly to its low cerebral perfusion. The non-significant serial changes in orthopedic controls indicate stable and reproducible acquisition that assures reliability. The measured regional and global age trends of CSF, WM and GM in both controls and mTBI are consistent with published and predicted trends **(8)** and assure that the methods used are sensitive to capture changes due to both age and mTBI. The serial or short term trends seen in the mTBI cohort (N=19; baseline vs. 3 months) indicate a pattern of recovery or decrease in both axial and radial diffusivity without a change in FA which could be indicative of possible resolution of transient vasogenic edema as a result of mTBI**.** The study of long term effects of mTBI on brain structure-function is warranted.

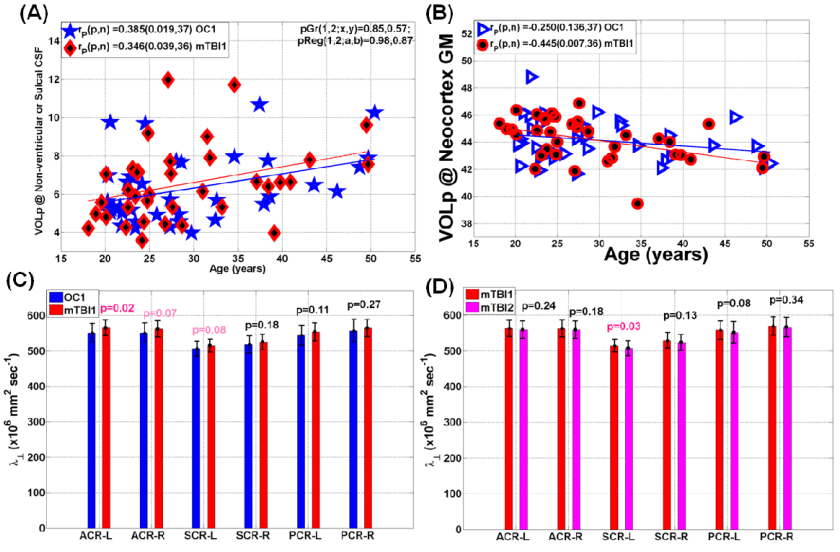

Figure 1. Representative scatter plots of global volumetry of **(A)** sulcal CSF, **(B)** neocortical GM and bar graphs of regional coronal radiata DTI metrics **(C, D)** in orthopedic controls (N=36) and mTBI (N=37) both at baseline (Day 1; **A, B, C**) and serially (**D**; N=19).

References

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