Diffusion tensor imaging and magnitization transfer parameters correlate with the white matter pathology in mild traumatic brain injury

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Introduction

Parameters of diffusion tensor imaging (DTI) and magnetization transfer ratio (MTR) have been reported sensitivitve to reflect diffuse axonal injury in mild traumatic brain injury (TBI).[1,2] However, the relation between the changes of these imaging parameters and the underlying white matter injury pathologies is still greatly unknown. The goal of this study is to establish a direct correlation of the imaging parameters to the specific underlying neuropathologies itdentified by immuno-histochemistry (IHC) using the animal model of mild TBI.

Materials and Methods

Animal Diffuse axonal injury was generated on 35 female 8-week-old Wistar rats by 2-m height weight drop TBI without focal contusions. *MRI* Animals were imaged for baseline (n=26), 1 (n=35), 10 (n=28), 20 (n=21), and 30 (n=17) days post-injury (DPI). MRI data were acquired in vivo using a Doty quadrature coil on a Bruker 7T. DTI was acquired using 3D SE EPI: TR 700ms, TE 37ms; segment 4, Δ 15 ms; δ 5 ms; *b*-value 0 and 800 s/mm^2 with 17 encoding directions. FOV 3.5 × 2.56 × 1.4 (cm), voxel size 200 (μm, isotropic). MT images was acquired by SE with (M_S) and without (M_0) MT pulses. Parameters for MT pulse were: offset 6kHz (20ppm), amplitude 4μT, duration 1ms, pulse number 20. FOV 2.56 × 2.56 × 0.5 (cm), in-plane resolution 100 (μm^2). DTI parameters, fractional anisotropy (FA), axial diffusivity (AD) and radial diffusivity (RD), were derived by Tortoise. MTR maps were calculated by ($1-M_S/M_0$). *Immunohistochemical staining (IHC)* After MRI, 3 animals per group were randomly chosen for histology. Tissues obtained from 3 sections (2.5mm in distance) covering the whole corpuse callosum from genu to splenium were immuno-stained for axon (SMI31), myelin (MBP), microglia (IBA1), and astrocyte (GFAP). *Data Analysis* MRI data were quantified by ROIs encompassing the exact locations of the IHC images. One-way ANOVA with repeated measures, Pearson correlation coefficient and corresponding significance test were calculated by Prism.

Results

The time course DTI and MTR maps are shown in Figure 1. FA, AD, and MTR were significantly decreased at 1DPI, while RD was increased significantly at 20DPI (Fig. 2). Time course IHC stainings reveal axonal injury at 1 and 10 DPI. Less compact myelin was seen at from 1 to 30 DPI. Microgliosis was increased after injury peaking in numbers at 10DPI, while astrogliosis increased progressively over time (Fig. 3). Figure 4 shows the Pearson correlation analysis of the MRI and IHC data.

Discussions and Conclusions

Comparable to the previous reports[3], results of our correlation analysis suggest that AD and FA are sensitive in reflecting axonal integrity, while RD is capable of showing myelin compactness. In addition, our results also show that the MTR at 20 ppm correlates with the extent of astrogliosis over time following TBI. Reactive astrocytes were also increased indicative of injured white matter. MTR at 20 ppm may reflect the increased of water exchanging rate in the process of the reactive astrocytes rich in the aquaporin 4 water channel.[4] In conclusion, our data indicate that DTI and MTR are sensitive in reflecting multiple injury pathologies, and maybe useful in detecting the injury status of mild close head TBI.

Reference (1) Niogi et al., J Head Trauma Rehabil, 2010; 25:241-55. (2) Bagley et al., JMRI, 2000; 11:1-8. (3) Song et al., Neuroimage, 2003; 20:1714-22; (4) Myer et al., Brain, 2006; 129:2761-72

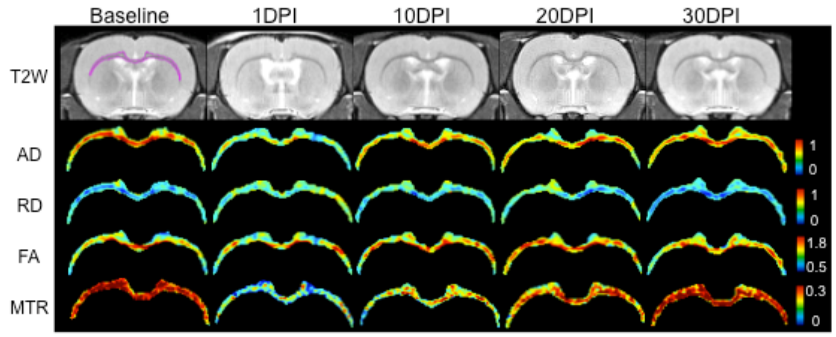

Fig. 1 Representative *in vivo* T2W, DTI, and MTR maps in mild TBI time course. T2W images show that the ventricle volume is significantly increased at 1 DPI, where the contrast of FA, AD and MTR is significantly loss. RD increases at 1DPI and 20DPI. The DTI and MTR maps are extracted from the ROI in T2W images for visualization of the changes in corpus callosum.

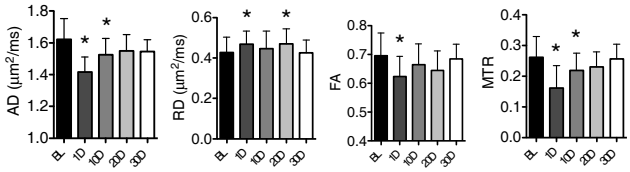

Fig 2. Group averaged data of AD, RD, FA and MTR values in the TBI time course. Data were acquired from corpus callosum indicated in figure 1. *p < 0.05.

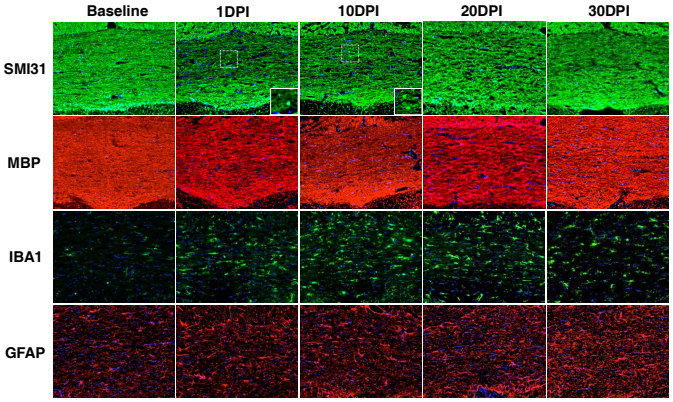

Fig. 3. IHC images of axon (SMI31), myelin (MBP), microglia (IBA1), and astrocyte (GFAP) in TBI time course. Clear axonal injury is seen at 1DPI and 10DPI (axonal beadings in zoom-in), then gradually return to baseline condition at 30DPI. Loss of MBP staining is seen after the introduction of injury. Microglia increases after injury and decreases gradually after 10DPI. Astrogliosis increases progressively after injury.

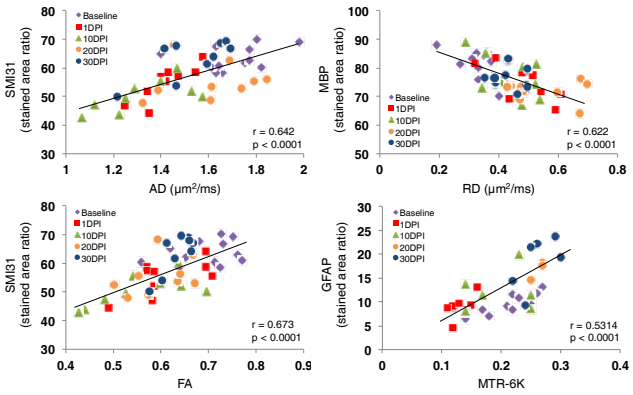

Fig. 4 Correlation analysis. Strong correlations exist between AD and SMI31 (r=0.642), RD and MBP (r=-0.622), FA and SMI31 (r=0.673), and MTR and GFAP (r=0.531). All correlations were significant (p<0.0001).