Mapping White Matter Degradation Following Mild Traumatic Brain Injury: A Diffusion Tensor Imaging Study

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Introduction: Conventional neuroimaging techniques (e.g. CT and structural MRI) are inadequate for direct assessment of diffuse axonal injury (DAI), a major contributor to neurocognitive dysfunctions that may persist long after an incident of mild traumatic brain injury (TBI) [1]. Diffusion tensor imaging (DTI), as a promising, noninvasive tool for measuring axonal integrity, revealed fractional anisotropy (FA) reduction in various white matter (WM) regions of interest associated with post-concussive syndrome [2-3]. However, regional distribution and temporal evolution of brain damage following a TBI incident are poorly understood. The damage may involve a series of events, including cellular disruption, edema, axonal swelling / disconnection, de-myelination, and WM atrophy [4-5]. In the present DTI study, we aim to detect pattern and progression of WM degradation at a voxelwise level in both acute and chronic mild TBI patients, using postinjury time (PIT) as the quantification to the post-traumatic process.

Methods: Volunteers of N=12 acute TBI patients (f=1, age=29±7 yrs) with PIT of 1~7 weeks (20±12 days), and N=10 chronic TBI patients (f=0, age=33±7 yrs) with PIT of more than two years (>781 days) participated the present MRI study at 4T. All patients were clinically classified under criteria of initial Glasgow Coma Score (GCS) of 13-15, loss of consciousness (LOC) less then 30 minutes, and posttraumatic amnesia (PTA) of less than 24 hours. Two healthy groups (N=12 and N=10) with matched age and gender served as the controls to the acute and chronic TBI groups, respectively. Subjects were excluded if they had diagnosis of any other neurological disorder, central nervous system infection, seizures, or history of alcohol and/or drug abuse. Each subject had MRI scans at 4T (Siemens) to acquire DTI, fluid-attenuated inversion recovery (FLAIR), and T1-weighted imaging (MPRAGE) data. The EPI-based DTI sequence were scanned at b=800 s/mm^2 using parallel imaging (GRAPPA) with two fold acceleration. DTI acquisitions were repeated 4 times to boost the signal-to-noise ratio (SNR). MRI data showing strong motion artifact or with substantial presence of WM lesion, identified as abnormal hyperintensities in the FLAIR image, were also excluded from the analysis. The tract-based spatial statistics (TBSS) technique [6] was implemented for DTI post-processing and spatial normalization. A 3-D multivariate linear regression analysis program (3dRegAna) from the Analysis of Functional NeuroImage (AFNI) [7] was applied to identify the voxelwise WM alternations associated with TBI and accounting for age.

Results: Compared with controls, reduced FA ($p<0.01$) is shown as blue clusters overlaid on the mean FA map in Fig.1 (a) and (b), for the acute and chronic TBI, respectively. Both groups exhibit FA reductions near posterior cingulate, although distinct clusters are found in dorsal posterior cingulate cortex in the acute TBI group and internal capsule in the chronic TBI group. The relative FA changes from acute to chronic TBI are shown in Fig.2, where smaller FA in corticospinal / thalamic tracts and larger FA in corpus callosum / fornix regions are found for the chronic group. In Fig.3, negative correlations ($p<0.01$) between FA and PIT are detected in the acute TBI group at regions approximating anterior /posterior cingulate and corpus callosum. No significant correlations between DTI and PIT are found in the chronic group.

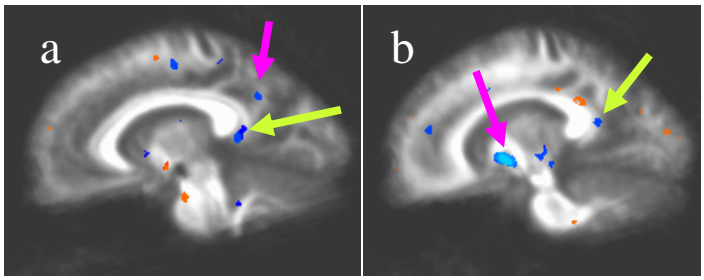

Fig 1: FA alterations associated with (a) acute TBI, and (b) chronic TBI.

Discussion: Distinct regional patterns of TBI related FA reductions are revealed in acute and chronic patient groups, suggesting first that specific brain areas are particularly vulnerable to TBI and second that the neuronal alterations spread to different areas in different postinjury phases. In general, WM degradation tends to appear in the cingulate and corpus callosum in the acute stage, whereas the WM alterations in chronic stage extend to other areas associated with cognitive and motor functions, such as frontal lobe and corticospinal tract. Significant FA decrease in corpus callosum - fornix conjunction observed in acute TBI disappear in the chronic TBI group (FA increase in Fig.2), may indicate a neuronal re-generation during the late TBI recovery, as previously suggested [3]. Further investigations are directed toward longitudinal studies and integration of other modalities, such as MR spectroscopy and susceptibility weighted imaging, in order to better characterize the dynamic pathology following TBI.

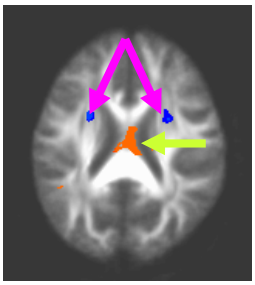
Fig 2: Acute-Chronic FA changes.

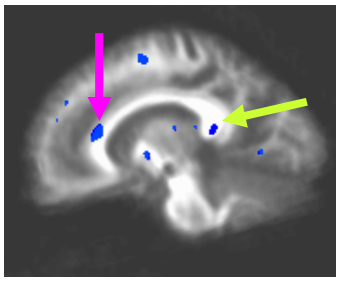
Fig 3: FA~PIT correlation in acute TBI.

Reference: [1] Silver et al., Textbook of traumatic brain injury, 2005. [2] Lee et al., J Neurotrauma, 25:1049-1056, 2008. [3] Sidaros et al., Brain, 131:559-572, 2008. [4] Povlishock et al., J Head Trauma Rehabil, 20:76-94, 2005. [5] Newcombe, et al., Bri. J. Neurosurgery, 21:340-348, 2008. [6] Smith S.M, et al., NeuroImage, 31:1487-1505, 2006. [7] http://afni.nimh.nih.gov/afni