White Matter Degradation in Fornix after Mild Traumatic Brain Injury: Cross-Sectional and Longitudinal MRI Investigations

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Introduction: The fornix is the primary white matter (WM) pathway interconnecting the hippocampus and the rest of limbic system [1]. A postmortem study [2] suggested that the fornix may be susceptible to traumatic brain injury (TBI), resulting in impaired learning and memory functions in post-concussion syndrome [3]. Several MRI studies [4-5] reported damage to the fornix in TBI, but the effect of mild TBI (mTBI), which is clinically much more common [6], has not been thoroughly investigated. Furthermore, longitudinal post-injury changes in the fornix have not been reported. In the present study, we used both structural and diffusion tensor imaging (DTI) techniques to assess WM degradation of the fornix in mTBI, and to test if these WM alterations can be detected during 6 month recovery.

Methods: Mild TBI patients (N=24, age=31±8 years, female=7) (Initial Glasgow Coma Score of 13-15, loss of consciousness less than 30 minutes, and posttraumatic amnesia of less than 24 hours) volunteered in the MRI study at acute stage (post injury time of 24 ± 11 days) for baseline study (TP1), and half of them (N=12, age=31±8 years, female=3) participated a follow up study after 6 months (TP2). Subjects were excluded for substantial presence of MRI-visible concussion lesions, history of multiple head injuries or other neuropsychological disorders. A group of N=24 healthy controls with no history of head trauma were selected with matched age, gender, and year of educations. All subjects were scanned on a Siemens 4-Tesla MRI system using DTI (2x2x3 mm, b=800 s/mm²) and T1-MPRAGE (1x1x1 mm) images for the whole brain. For DTI data, the superior section of fornix (s. Fx) was identified on the fraction anisotropy (FA) map for each individual. For anatomical image, a fornix-to-brain ratio (FBR) was estimated based on the cross-sectional area of the superior section of fornix bundles and the total area of the brain at the same axial level of the fornix.

Results: Fig.1a shows that the FA of the superior section of fornix WM is significantly lower (p<0.001) in mTBI at baseline (TP1) than in controls. For most patients (10 out 12), the fornix degradation progressed slightly with further decreased FA at the 6 month follow-up study (TP2) (p<0.07) based on a paired-sample T-test, whereas the group-wise FA differences between TP1 and TP2 are not significant (p=0.6). Fig 1b depicts structural image measurement of fornix-to-brain ratio (FBR), indicating that the mild TBI patients had a significant FBR reduction (p<0.00001) in the acute stage at TP1 compared to the controls, and continued atrophy after 6 months of recovery with lower FBR at TP2 (p<0.001). Again, the group-wise FBR differences between TP1 and TP2 are marginal (p=0.06), although all 12 follow-up participants show slightly smaller FBR at TP2.

Conclusion and Discussion: Both micro- and macro-structural degradations of fornix white matter pathways onset in the acute stage of mild TBI, and these degradations continued in the following 6 month period of recovery. Our data suggest that using DTI and structural MRI together can effectively detect the fornix alterations for both cross-sectional and longitudinal investigations. Further studies are warranted to examine the association between the fornix alterations and neurocognitive performance of TBI patients.

References