Changes of White Matter Integrity and Brain Activation in Diffuse Brain Injuries: Assessed by fMRI and DTI

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Introduction Diffuse axonal injury is a common consequence of **tr**aumatic brain injury (TBI) that often causes significant impairments in cognitive functions such as memory, language and attention. The clinical dilemma of diffuse axonal injury is the lack of accurate diagnosis of its neuroanatomical underpinnings, therefore, it is often left undetected by routine radiological workups. The ability to evaluate the relationship between the functional deficit and structural perturbation in diffuse axonal injuries can be important in development of non-invasive imaging tools to improve the diagnosis of diffuse axonal injuries and to assist the clinical management of such patients. Here we report the results of our study of using combination of functional MRI (fMRI) and diffusion tensor imaging (DTI) to investigate diffuse axonal injuries.

Experimental Methods

Subjects Twelve patients (age 21-40, Glasgow Coma Score: 9-13) and ten neurologically intact healthy controls participated in the study. All injuries occurred less than 12 months prior to the study. All patients had routine MRI and/or CT scans after the injury. Additional anatomic MRI scans were also performed for the most of the participants at the time of fMRI and DTI study.

Functional MRI A 3T whole body scanner (Philips Intera) was used for all MRI scans. Blood oxygenation level dependent (BOLD) functional images were acquired as 25 contiguous, 5mm axial slices without gap using susceptibility weighted gradient echo EPI method. The imaging parameters include: TR/TE of 3000/32ms, flip angle of 90, FOV of 224 mm and image matrix of 64 x 64. A blocked design N-back task for working memory was used for investigating the change of the brain activation pattern that may be associated to the brain injury. Visual stimuli were consisted of 10 black and white photographs of faces of adult men and women. Each condition was presented for 24 seconds at a rate of 3 seconds per stimulus. In the 0-back control condition, the subject was asked to press a button on the response box each time a man's face is appeared and to press the button each time when a face matches the immediately preceding face (1-Back) and when the face appeared identical to the face presented immediately before the previous face (2-Back). The image volume for each fMRI scan was 110 (4 min 10 sec). A 3D anatomic image set was also collected to co-register activation maps and DTI for anatomic assignment. Functional data were analyzed using SPM2 (Wellcome Department of Cognitive Neurology, London) software package. Image realignment and co-registration for motion corrections and temporal and spatial smoothing were done using routines of SPM before activation maps were calculated.

Diffusion Tensor Imaging DTI were performed after fMRI exam for each subject. Diffusion images with the isotropic pixel (2 mm) were recorded using 16 directional sensitized gradients. In the axial planes, 60 slices with 2 mm thickness without gap were used. Fractional anisotropy (FA) were measured and averaged in the regions of interest (ROIs) from four axial sections of the frontal lobe (8 mm thick/section, 2mm slice thickness) for each subject using a software (PRIDE) provided by Philips Medical System.

Results and Discussions **Ten of 12 TBI patients showed significant reduction of FA in the selected frontal regions compared to those of neurological intact controls. Four of the patients with abnormal DTI further exhibited asymmetrical reduction of FA in the frontal lobe, suggesting possible focal injuries. For example, 15% difference in FA between the left frontal area and right frontal lobe was observed in one of patients as shown in Figure 1. Averaged FA values for patients were measured at 0.27±0.12 (from 0.24 to 0.29) while averaged FA in the similar areas was averaged at 0.36±0.11 (from 0.34 to 0.39) in control subjects. Prefrontal brain activation is related to the memory load. It appears that activation is greater in TBI patients as compared to the healthy controls. In particular, controls exhibited a greater focal pattern of activity within the right frontal lobe, whereas the brain-injured patients had more extensive bilateral activation. When examining the individuals from the group, it appeared that the bilateral activation increased (or decreased laterality) in those with more severe deficits compared to those of less impaired patients. Among those with reduction of FA (lower than 0.26), 8 patients showed positive correlation with their fMRI results, i.e., increased activation areas and more bilateral presentation in N-back working memory tests**

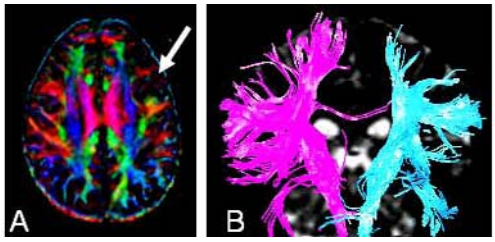

Figure 1. PA maps (**A**) showed reduction of FA values in the area of left inferior frontal lobe (arrows) while DTI derived tractography showed fewer fiber bundles in the left hemisphere (Blue color), particularly in the frontal region, when compared to the opposite hemisphere.

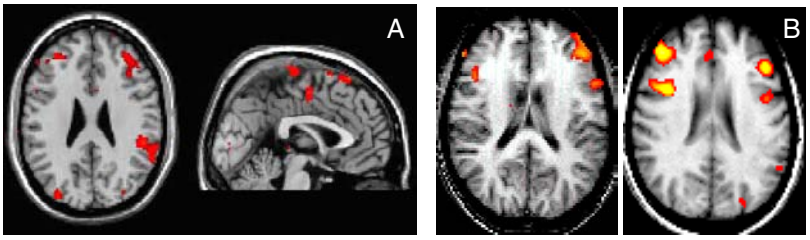

Figure 2. Group wised difference in activation during the N-back task when comparing TBI patients (N=6) with lower FA vs. the control group (**A**). (**B**) A patient with lower FA (0.24) exhibited more extended and bilateral activation in performing N-back task than the patient with less decrease in FA (0.29)