Functional MRI of Working Memory in Patients of Mild Traumatic Brain Injury

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Introduction

Previous functional MRI (fMRI) studies of MTBI patients have indeed shown altered patterns of activation during working memory task. However, the results were inconsistent. Study of McAllister et al. showed "increased" activation in the dorsolateral prefrontal and posterior parietal areas during an n-back task (1), while Chen et al. showed "decreased" activation in the dorsolateral prefrontal cortex during an externally ordered task (2). This study was aimed to analyze the brain activation patterns in response to n-back working memory (WM) loads after mild traumatic brain injury (MTBI). To settle the controversy of the aforementioned fMRI results, in this study we used same n-back WM task as McAllister et al. to explore the brain activation in response to different WM loads in MTBI patients. A 6-week follow-up study was also performed.

Methods and Materials

This prospective study was local research ethics committee approved. All subjects participating gave written informed consent. During April 2010 and September 2010, patients ≥ 17 years old and diagnosed as MTBI in our hospitals were convinced to enter this study. As a control group, healthy volunteers were recruited from hospital coworkers and were screened for handedness, neurological, medical or any psychiatric illness. The n-back (n = 1, 2, 3) conditions were presented using E-prime v2.0 installed on a desktop computer. Each condition was conducted in a single run, which consisted of three epochs. Each epoch contained 30 seconds of presentation with numbers and 30 seconds of fixation on a crosshair. Conditions were counterbalanced among participants, i.e. each condition was equally often preceded and followed by each of the other conditions. All participants were trained prior to scanning to ensure that they could perform 1-back condition at an accuracy criterion of 70%. Imaging was performed on a 3.0T MR system (Discovery MR750, GE Healthcare, Milwaukee, WI). An eight-channel head coil was used. Functional data were collected by using an Echo Planar Imaging (EPI) sequence (repetition time (TR) = 3000 millisecond (ms), echo time (TE) = 35 ms, flip angle (FA)= 90°, field of view (FOV) = 230 mm^2, matrix = 64 x 64, 40 slices, slice thickness = 3 mm, and 1-mm inter-slice gap). fMRI data were analyzed by Statistical Parametric Mapping version 5 (SPM5, Wellcome Department, University College London, London, UK) implemented in Matlab version 7.9 (MathWorks, Sherborn, MA).

Results

Both groups did not differ significantly in years of education, digit span, continuous performance test, and accuracy of n-back WM performance. Brain activation patterns differed between MTBI patients and controls in response to increasing WM loads (Figure 1). Controls maintained their ability to increase activation in the WM circuitry with each increase in WM load Figure 2). On the contrary, MTBI patients impaired their ability to increase activation in WM circuitry in both moderate and high WM load conditions. However, MTBI patients did show cerebral plasticity with more activation than controls in some areas outside and inside the WM circuitry (Figure 3). In the 6-week follow-up study, MTBI patients showed an improvement of activation in response to increasing WM loads (Figure 4).

Conclusion

MTBI-induced differences in WM functional activity were observed in the absence of differences in neuropsychological performance, suggesting that this approach may increase sensitivity to MTBI compared with neuropsychological evaluation alone. The results also lend further evidence to the potential for cerebral plasticity to maintain performance levels on WM tasks after MTBI.

References (1) McAllister et al. Neuroimage 2001; 14:1004-1012. (2) Chen et al. Neuroimage 2004; 22:68-82

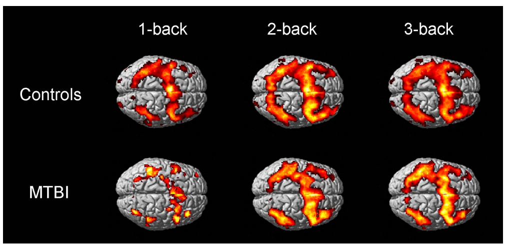

Figure 1 Activation maps of 1-, 2-, and 3-back conditions of MTBI patients and controls (uncorrected p<0.01)

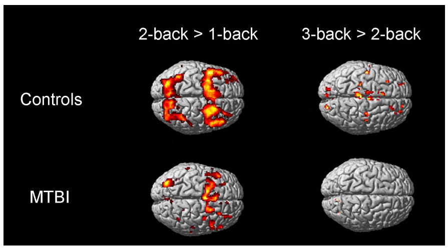

Figure 2 Activation maps of 2-back >1-back and 3-back > 2-back conditions of MTBI patients and controls (uncorrected p<0.01)

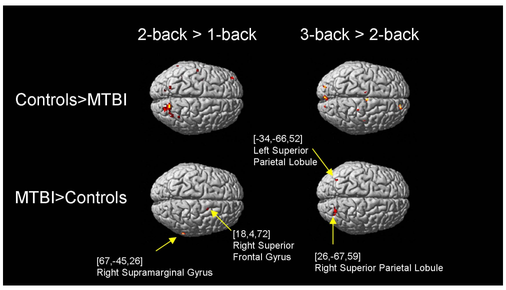

Figure 3 Activation differences between the MTBI and the controls as a function of WM processing load (uncorrected p<0.01)

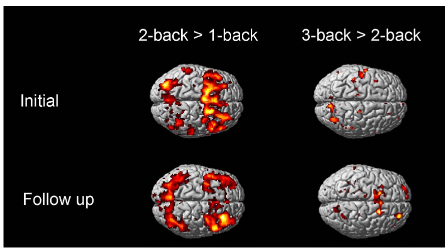

Figure 4 Activation maps of the initial and 6-week follow-up in 9 MTBI patients (uncorrected p<0.01)