Disruption of Default Mode Network following Mild Traumatic Brain Injury

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Introduction

The default mode network (DMN) is a network of regions consistently found to be deactivated during task related activities while remaining active during rest (2). The network includes lateral parietal cortex, posterior cingulate cortex (PCC), anterior cingulate cortex (ACC), medial temporal lobe (MTL), and medial frontal cortex. This network has been found to be disrupted in multiple patient populations with cognitive deficits including Alzheimer's (3) and schizophrenia (1). Furthermore, functional connectivity within the network has been correlated to performance on working memory tasks in healthy controls (4). Due to the diffuse axonal injuries and cognitive deficits associated with mild traumatic brain injury (TBI), we hypothesize that the functional connectivity within the DMN will be decreased during the acute stage in individuals suffering from mild TBI.

Methods

Resting state MRI data was obtained on patients suffering from mild TBI within ten days of initial injury (N=16; avg 3 days) and again one month following initial injury (N=6; avg 39 days). All imaging was performed on a Siemens 3T MRI scanner using an 12-channel receive onlyhead coil. T2*-weighted images were acquired using a single-shot EPI sequence (TE = 30 ms, TR =2000 ms, FOV = 220 mm, resolution = 64 × 64) with 24 axial slices (sl. thick. = 6 mm) over 6 min 42 s that yielded 171 time points. A high resolution T1-weighted-MPRAGE (TE = 3.44 ms, TR = 2250ms, TI = 900ms, flip angle = 9º, resolution = 256 × 256 × 96, FOV = 22 cm, sl. Thick. = 1.5 mm) was also acquired for anatomic reference. Data were analyzed using AFNI (Robert Cox, NIH) and MATLAB (MathWorks Inc., Natick, MA). Each subject's functional images were corrected for slice timing, optionally filtered to remove physiological artifacts, and registered to the first volume of the functional scan. A 6mm FWHM Gaussian blur was applied to the registered functional scans. Five mm ROI spheres were made in the posterior cingulate cortex (PCC) in original space and the average time series was correlated with every voxel in the brain to create an individual whole brain correlation map. These whole brain correlation maps along with the T1-MPRAGE images for each individual were transformed to Talairach space. Whole brain correlation maps were converted to Z-scores using the Fisher transformation and t-tests were run on the data to create a group correlation map which was then transformed to correlation coefficients and thresholded at r = +/- 0.500. In addition average correlation coefficients between a 5mm temporal ROI from the PCC and 5mm ROI spheres in the bilateral MTL, frontal, thalamus, parietal and medial ACC were computed. These values were used as a measure of the strength of functional connectivity. The same analysis was run on a control group (N=7) which was compared to the results of the TBI groups.

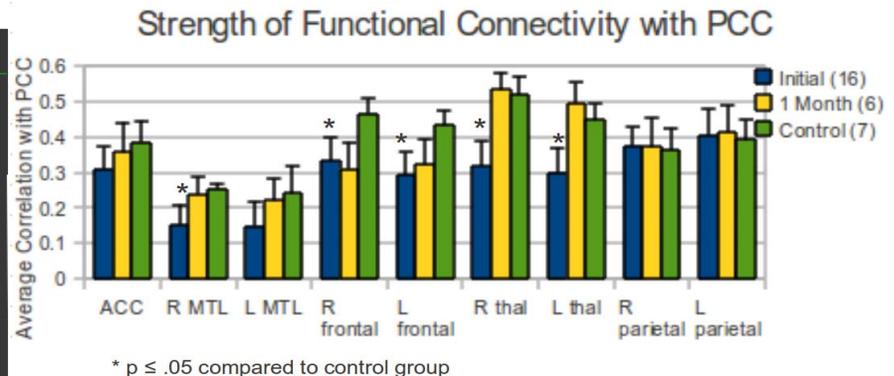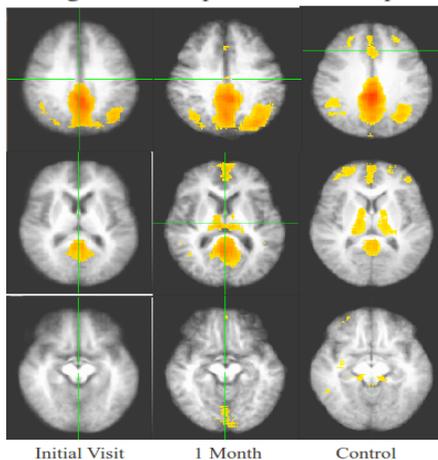## Results and Discussion

Figure 1: Group Correlation Maps

Figure 1 shows the group maps between the control subjects and the mild TBI patients during their initial visit and four week visit following mild TBI. Based on our ROI analysis (as shown in the histograms above), we observe a significant decrease in functional connectivity among the mild TBI patients during their initial visit in the right MTL (p=.036), right frontal (p=.027), left frontal (p=.020), right thalamus (p=.006), and left thalamus (p=.026) compared to controls. Very little effect was seen in the bilateral posterior parietal areas (right: p=.428; left: p=.431) and ACC (p=.153) among the mild TBI patients. The DMN begins to show signs of normalization after one month with increased functional connectivity in the bilateral thalamus, and right MTL and left frontal compared to the initial visit. However, there remains a decrease in functional connectivity in the right frontal cortex compared to controls at one month (p=.041). This normalization to the normal control values at the four week time point can be visualized in the group correlation maps shown in Figure 1.

Conclusion

Functional connectivity within the DMN is disrupted initially following mild TBI with decreased functional connectivity in the bilateral frontal cortex, right MTL, and bilateral thalamus. This disruption began to normalize at one month with the functional connectivity approaching that of the controls in the thalamus, right MTL, left frontal but still showing decreased functional connectivity within the right frontal cortex. The frontal cortex is involved in executive function and working memory which are common deficits of mild TBI. We believe that this longitudinal analysis of functional connectivity within the resting state helps to explain some of the cognitive deficits associated with mild TBI that persist for over one month after the initial injury.

References

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