MRI Morphological and Functional Connectivity Analysis of Thalamus in Mild Traumatic Brain Injury

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Introduction: The etiology of a disabling array of symptoms denoted post concussive syndrome (PCS) in mild traumatic brain injury (MTBI) is still unknown. Accumulating evidence is pointing towards the injury of thalamus and thalamocortical pathways that may account for PCS in MTBI [1]. In this study, we used recently developed shape and thickness analysis as well as resting state fMRI (RS-fMRI) to detect whether there are thalamic morphological and thalamocortical connectivity changes in patients with MTBI.

Methods: Twenty-three patients with clinically-defined MTBI participated in the experiments with a mean interval between MRI and trauma of 22 days (3~53 days), and have various cognitive symptoms. For comparison, 18 age-matched healthy controls were also recruited. 3D high resolution T1-MPRAGE (TR/TE/TI=2300/2.98/900ms, flip angle=9°, resolution=1x1x1mm^3) and standard RS-fMRI images (TR/TE=2sec/30msec, flip angle=75°, FOV=220x220 mm^2, matrix=128x128) were obtained at 3T MR. Thalamic mask images as well as caudate and putamen images for comparison were generated from MEDx software based on MPRAGE images.

All the functional MRI datasets were realigned and co-registered to the 3D T1 image and then normalized to the MNI template. Each voxel of the thalamus in the template space was correlated with all 45 cortical Brodmann Areas (BAs). The voxel will be classified to a BA that has the maximum correlation among all the BAs to the voxel. Group analysis was done to investigate whether there was voxel number or correlation strength difference between MTBI and control for the classified BAs within the thalamus.

The shape and thickness analysis were performed in 9 patients and 10 controls. For shape analysis, the binary ROI mask images of each structure generated from MEDx (for delineation) were transformed to a template space chosen from the control population; and averaged to generate the final map for each group. Shape analysis was also done using harmonic approximation shape toolbox in [2]. For the thickness analysis, the brain volume of each subject with an isotropic resolution of 1mm first went through the segmentation step using the SPM8 to generate gray and white matter segmentation. Then the gray and white matter mask images went through the standard cortical thickness mesh step from the thickness analysis tool [2] to generate the boundary and inside cortical thickness map, the gray matter Danielson map and white matter distance map metrics. For across-subject quantification, the four metric images were scaled to each subject's intracranial volume. The average thickness or distance measure of each ROI was done by the average of the scaled metric images within these ROIs for each subject.

Results: Figure 1 shows the group average results of the left thalamus of MTBI patients (right side not shown) compared to controls in axial, coronal and sagittal views (top row). Overall MTBI showed shrinkage in the medial ventral anterior and medial central lateral nuclei of the thalamus (red color). Bottom row shows the difference (hot color, $p<0.05$) between the two groups in 3D surface rendering views. We also found significant difference of structural thickness measure of thalamus between controls and MTBI patients ($p \leq 0.001$, Table 1) but not other deep gray matter structures except for right putamen ($p<0.05$).

Figure 2 shows representative images of thalamus functional voxel-wised classification from back projection of whole brain 45 BAs according to their highest correlation strength. Within thalamus, a significant difference of number of voxels associated with BA39 angular area was found between controls and patients (median 27 voxels in control vs. median 10 voxels in MTBI; $p=0.0456$, orange color). The strength value comparison shows that BA20 bilateral inferior temporal area (BA20) has higher median value in MTBI (correlation coefficient: 0.615 in control vs. 0.683 in MTBI with $p=0.03$, green color).
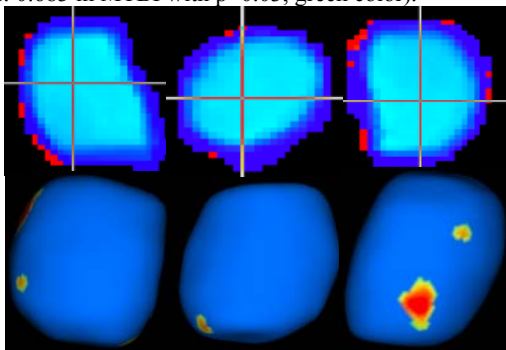

Fig.1 Shape analysis of thalamus (left side) shows the morphological difference between groups of MTBI and control. Top row: overlay axial (left), coronal (middle) and sagittal views of two groups (MTBI: blue; control: red). Such differences are shown in 3D rendering views (Bottom row).
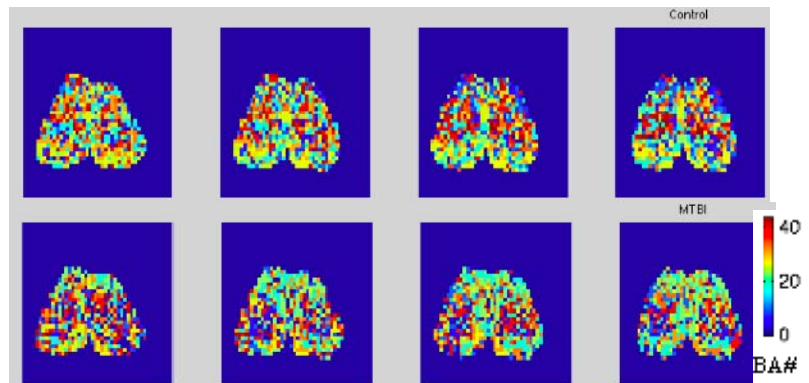

Fig2. Thalamus classification based on fMRI connectivity at resting state from all BAs with color showing BA region number. Four continuous slices were shown.

Conclusion: Shape and thickness analysis showed slightly morphological changes (shrinkage) of thalamus in MTBI compared to control group. We also found the disruption of thalamocortical networks indicated by reduced projected voxel number from BA39 (parietal angular area) and increased correlation strength with BA 20 (inferior temporal area) in patients, which might explain the aphasia and memory problem often seen in MTBI [3,4].

Thickness (mm)	MTBI	Control	P-value
Left Thalamus	1.608±0.111	2.059±0.207	0.00003
Right Thalamus	1.660±0.145	2.014±0.230	0.00101
Both Thalamus	1.617±0.086	2.041±0.159	0.00000
Left Caudate	2.360±0.211	2.421±0.451	0.709
Right Caudate	2.229±0.302	2.413±0.582	0.397
Both Caudates	2.288±0.251	2.418±0.487	0.469
Left Putamen	1.917±0.243	2.117±0.386	0.193
Right Putamen	2.772±0.320	3.518±0.744	0.027
Both Putamens	2.236±0.131	2.582±0.590	0.101

Table 1 ROI-based Thickness Measure and Comparison

References
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[4] McAllister T W et al. NeuroImage 2001; 14: 1004-1012.