

## Default-mode Resting Network in Mild Traumatic Brain Injury (MTBI)

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**Introduction:** The brain frontal regions of MTBI have been studied with auditory task while less dorso-lateral prefrontal regions were engaged with auditory task in MTBI [1]. They are also regions frequently involved in TBI. We use resting-state fMRI (RS-fMRI) to investigate the fronto-posterior resting-state functional networks (RSNs) in MTBI, particularly default mode network (DMN), which contains posterior cingulate (PCC), bilateral inferior parietal, and medial frontal nodes and is well established. Three different image-processing methods (seed-based; Informax independent component analysis (ICA)-based [2] and Probabilistic ICA (PICA) FSL-Melodic-based [3]) were used to characterize the DMN changes in MTBI.

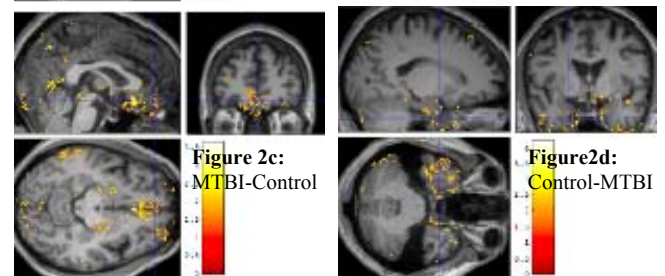
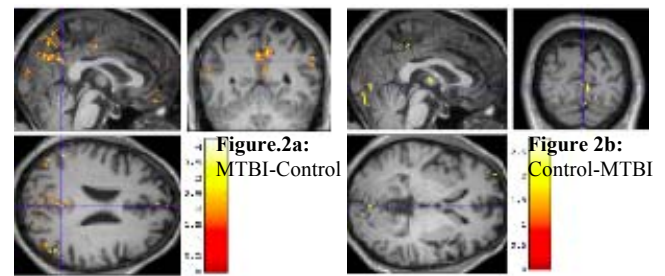
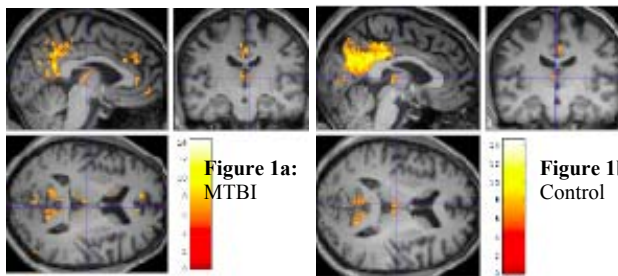
**Methods:** Standard RS-fMRI images (TR/TE=2sec/30msec, flip angle=75°, FOV=220x220 mm<sup>2</sup>, matrix=128x128) were obtained at 3T MR. Twenty-three patients with clinically-defined MTBI participated in the experiments with a mean interval between MRI and trauma of 22 days (3~53 days), and have various neurocognitive symptoms; and 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<sup>3</sup>) is also obtained for coregistration and normalization.

**Method1:** Seed-based DMN connectivity from PCC to the whole brain with a correlation coefficient  $r \geq 0.1349$  (equivalent  $p \leq 0.05$ ,  $N=150$ ). Group analysis was performed with SPM8 (2<sup>nd</sup> level Anova analysis) for DMN with their voxel numbers calculated for each subject after threshold of  $p \leq 0.05$ .

**Method2:** Informax algorithm-based ICA analysis of DMN was performed. DMN was identified from multiple ICA components via the known visual pattern of PCC connectivities, distinct low frequency spectrum, and periodic time courses fluctuation in each subject. Group results were then averaged from individuals. In addition, the subfields of thalamus (after segmentation based on FSL Juelich template) were used to correlate with Informax ICA components. Each correlation between the associated time course and average time course of the thalamus segment is computed and a component is identified with each segment based on highest correlation among all the components.

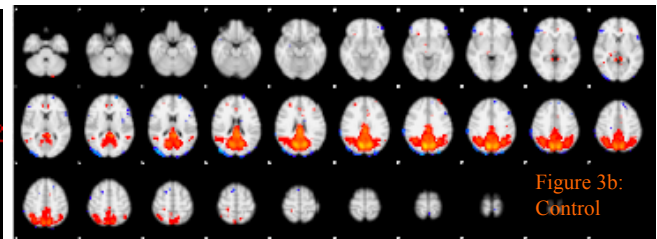
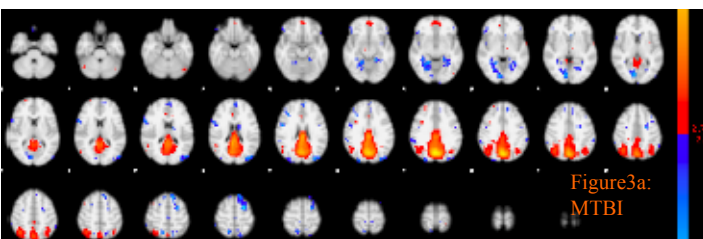
**Method3:** DMN via multiple-subject group ICA using multi-session temporal concatenation with identification of group-wise default-mode connectivity; also based on component's spectrum, low frequency fluctuation and overall spatial pattern.

### Results:



**Figure 1:** Voxel number using seed-based analysis after super-threshold did not differ between groups with  $p=0.4230$ . However DMN is more distributed in frontal regions of MTBI compared to control group ( $p < 0.05$  corrected).

**Figure 2:** Comparison results (subtraction) of DMN show more connectivity in the region of PCC in MTBI compared to control; while controls shows slightly more in thalamus and visual cortex ( $p < 0.05$ , Figure 2a-b). With reference region of thalamus segment 6, MTBI shows significantly more connectivities in the orbito-frontal region compared to control; while controls shows more connectivities of temporal area with reference region of thalamus segment7 ( $p < 0.05$ , Figure 2c-d).



**Figure 3:** With group PICA, the identified DMN also shows slightly more connectivities in frontal regions in MTBI ( $z \geq 2.36$ ,  $p \leq 0.01$ ).

**Conclusion:** The three methods of DMN demonstrate that there are increased RSNs in medial orbito-frontal regions and decreased RSNs in the dorsolateral frontal regions in patients with MTBI compared to controls. This tells us that the MTBI patients might recruit more of medial frontal regions to mediate the resting functional networks when dorsolateral prefrontal connectivity (i.e. executive function) is decreased due to injury.

References [1] Witt ST et al. Brain Imaging and Behavior 2010; 4: 232-247.

[2] [http://cnl.salk.edu/~tewon/ica\\_cnl.html](http://cnl.salk.edu/~tewon/ica_cnl.html).

[3] <http://www.fmrib.ox.ac.uk/analysis/research/melodic>.