

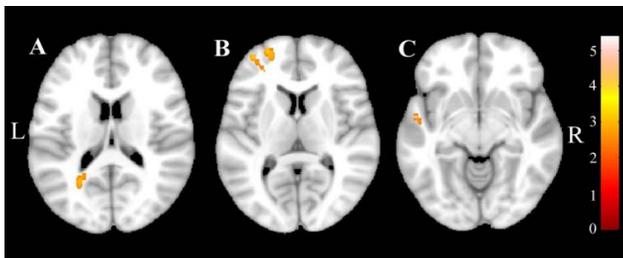
# MICROSTRUCTURAL BRAIN ABNORMALITIES IN PATIENTS WITH MAJOR EARTHQUAKE-INDUCED POSTTRAUMATIC STRESS DISORDER: A DIFFUSION TENSOR IMAGING STUDY

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**Background:** To date, previous whole-brain diffusion tensor imaging (DTI) studies have investigated white matter alterations in posttraumatic stress disorder (PTSD), however, little attention has been paid to the interregional correlations of microstructural abnormalities within these white matter regions. According to the accumulating evidences of the frontal and temporal dysfunction in PTSD, we hypothesized that the white matter abnormalities of frontal-temporal system could be found in patients with PTSD. and there would be correlations between these affected white matter regions.

**Methods:** We recruited subjects who suffering from a severe earthquake with a magnitude of 8.0 in Sichuan Province of China, 2008. 4200 survivors were screened, and 88 patients with PTSD and 91 matched survivors without PTSD (non-PTSD) were included in our study for DTI assessment. By using voxel-based analysis, fractional anisotropy (FA) value were compared between patients and controls with a two-sample t test and corrected using the false discovery rate (FDR) correlation at voxel level. The results were tested for correlation with symptom severity as measured by clinician-administered PTSD scale (CAPS). To detect the altered pattern of interregional correlations of microstructural abnormalities in PTSD compared with controls, we also conducted an exploratory research by searching for the correlations between all possible pairs of affected white matter regions.



**Fig. 1:** Parametric maps show that relative to controls, PTSD patients had significantly increased FA in the (A) forceps major of corpus callosum, (B) superior and middle frontal gyrus, and (C) superior temporal white matter. Results were considered to be significant with threshold of  $P < .05$  at voxel level after false discovery rate correction.

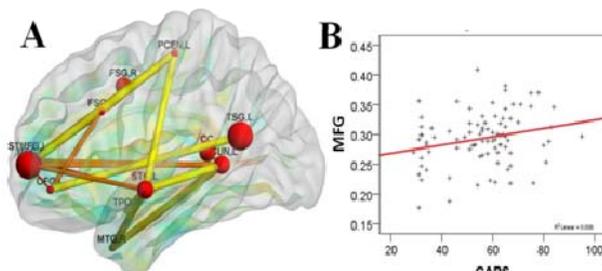
**Results:** The voxel-based analysis showed significant FA increase in the PTSD in the prefrontal lobe, including the superior and middle frontal gyrus, forceps major of the corpus callosum predominantly located in the temporal lobe, and superior temporal white matter in PTSD patients (Fig. 1). The partial correlation analysis showed that, except for some similar positive correlations of FA values between the affected white matter regions, however, significant correlations between prefrontal regions and precuneus were only observed in controls. In addition, some positive correlations were found in PTSD patients, predominantly including the significant correlations of the left orbital frontal gyrus with the left forceps major, the left precentral white matter with the left superior temporal white matter, combining with greater internal regional correlations within the frontal lobe, and correlations between left and right temporal lobes (see Fig. 2A). Moreover, in PTSD patients, the FA values in the middle frontal gyrus were positively correlated with CAPS scores (Fig. 2B).

**Discussion:** Our results demonstrated the white matter abnormality in frontal-temporal system and putative correlations between these two areas. Previous functional neuroimaging studies also have reported greater activities in the brain regions of the frontal-temporal system in PTSD patients [1]. The increased FA values in frontal-temporal system could be associated with the possible mechanism of enhanced emotional memory manifested as flashback symptoms in PTSD patients. Interestingly, we found significant positive correlations of FA values within frontal-temporal system, as the supra-regional system are believed to share a common impaired, developmental or plastic processing [2]. Moreover, the absence of positive correlation between prefrontal regions and precuneus in our results may suggest a potential disruption of the central executive network (CEN), underpinning the neuropathological mechanism of PTSD [3].

**Conclusions:** Our findings demonstrate not only regional microstructural abnormalities within the white matter of frontal-temporal system but an altered pattern of interregional correlations of microstructural abnormalities in PTSD patients from a major earthquake. Our study may help to provide new evidence for regional microstructures abnormalities in PTSD and provide further insight into the supra-regional anatomical inter-connectivities responsible of the disorder.

## References:

- [1] Patel, R. et al., *Neurosci Biobehav Rev*, 2012, 36(9): 2130-2142
- [2] Wright, I. C. et al., *Cereb Cortex*, 1999, 9(4): 366-378.
- [3] Menon, V. et al., *Trends Cogn Sci*, 2011, 15(10): 483



**Fig. 2:** (A) The region pairs showing positive correlation of FA values in PTSD patients and non-PTSD controls. These connections consist of 12 nodes and 19 connected lines. The yellow lines represent the significant positive correlations in PTSD patients, while copper-colored lines in non-PTSD controls. The slender red lines represent the similar positive correlations in both PTSD patients and non-PTSD controls.

**Fig. 2:** (B) Scatter plots of picked FA values in middle frontal gyrus against CAPS scores in PTSD patients.