A diffusion tensor imaging study of white matter integrity in adult major depressive disorder

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Introduction

Diffusion tensor imaging (DTI) provides information about cerebral white matter integrity in vivo, and fractional anisotropy (FA) is a commonly used index to describe the anisotropy of diffusion. Past studies have reported microstructural white matter abnormalities in widespread prefrontal regions in late-life depression [1, 2] and found prefrontal white matter alterations to be associated with neuropsychological function [3]. In latest study, the authors used DTI to test the hypothesis that MDD had microstructural white matter abnormalities in cortico-striato-limbic networks implicated in geriatric depression [4]. However, most DTI studies recruited elderly patients, and no studies yet have detected the white matter change in adult major depressive disorder (MDD). The aim of the present study is to examine for the white matter microstructural abnormalities in MDD using a rigorous voxel-based analysis of DTI data.

Material and Method

Fifty one patients experiencing MDD (mean age = 34.6±12.7, twenty five males and twenty eight females) according to the diagnostic criterion of DSM-IV, who had a score of 18 or greater on the 17-item Hamilton Depression Rating Scale (HAMD), and fifty two age and sex matched normal controls (mean age = 37.2±16.1, twenty three males and twenty eight females) were recruited. DTI was acquired using a 3.0T MR scanner (GE EXCITE, Milwaukee, USA) by employing a single shot spin echo EPI sequence (TR/TE = 10000/70.8 ms, slice thickness = 3.0 mm, FOV = 24 cm, matrix = 128x128, b value = 1000s/mm^2). FA maps were generated from each participant's DTI scan. Voxel-based analysis was carried out using SPM2 (http://www.fil.ion.ucl.ac.uk/spm/software/). Prior to the analysis, FA maps were normalized using the parameters determined from the normalization of the b = 0 image followed by smoothing with a 6-mm FWHM isotropic Gaussian kernel. Statistical comparisons were performed using two sample t test between patients and normal controls. The correlation between the microstructure abnormalities of white matter and the HAMD which represented the severity of depressive symptoms was examined. A corrected *p* value of less than 0.05 was deemed to be significant.

Results

Patients with MDD exhibited lower FA values than healthy controls in multiple brain regions including right paracentral lobule, paracentral lobule, parietal lobe, left parietal lobe and right cerebellum (cluster level $p<0.05$, corrected) (Table 1). No brain areas in patients showed significantly higher FA values than controls. Significant negative correlation between the FA value and HAMD scores were found in left caudate head (r=-0.36, $p<0.01$, MNI coordinates [-14, 18, 8]) and right insulae (MNI coordinates [34, 24, 12]) (r=-0.37, $p<0.01$) after controlling for age, years of education and duration of illness (Table 1 and Figure 1).

Table 1. Regions with reduced FA values in major depression patients compared with those in normal controls, and correlation of the FA value with the HAMD scores ($p < 0.01$).

Description of extent of cluster	L/R	Cluster size[a]	T score	Z score	※Peak coordinates voxel (x, y, z)	Correlation coefficient	*p* value
Caudate Body	L	71	3.89	3.74	-14, 18, 8	-0.363	0.008
Insulae	R	111	4.00	3.85	34, 24, 12	-0.369	0.007
Paracentral lobule	R	173	6.07	5.59	14, -33, 48	-0.079	0.576
Parietal Lobe	L	317	5.29	4.96	-30, -43, 30	0.117	0.407
Cerebellum	R	326	4.99	4.70	18,-59, -21	0.188	0.182
Parietal Lobe	R	167	4.78	4.53	38, -36, 24	-0.037	0.795
Parietal Lobe	L	156	3.78	3.65	-30, -38, 48	0.002	0.987

※Listed are coordinates corresponding to the voxels with maximum (peak) effects sizes defined in Montreal Neurological Institute (MNI) space.

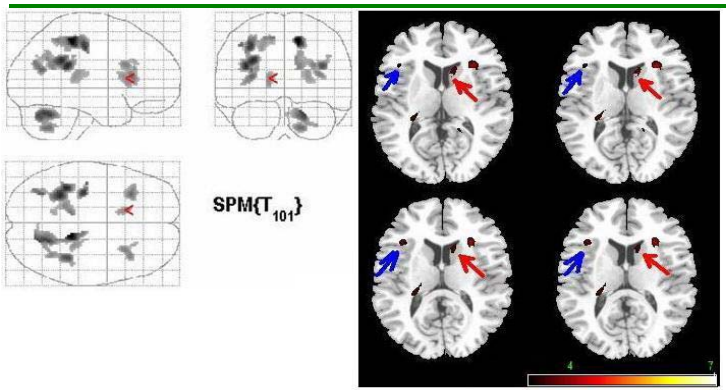

Figure 1. Glass brain maps (left) and statistic parameter maps overlaid on the corresponding T1 images (right) showing significant negative correlation between the FA value and HAMD scores in left caudate head and right insulae ($p<0.01$).

Discussion and Conclusion

Present study demonstrated that adult MDD have compromised white matter integrity in multiple brain areas. The reduction of white matter anisotropy observed in our DTI study is suggestive of possible loss of integrity in MDD and these alterations generally support the theory that microstructural alterations in white matter may reflect disconnection of cortical and subcortical regions in MDD [5]. To our knowledge, this is the first study to investigate the whole brain abnormalities between the adult MDD and normal controls with relatively large sample size. Although there had been many reports showing reduced FA in caudate and insula in late-life depression, no report reveal significant correlation between the FA value of and depression severity [6,7]. Significant negative correlation between the FA value and HAMD scores in left caudate head and right insulae found in present study revealed that FA change is sensitive to disease severity, and also further evidenced the microstructural white matter abnormalities in cortico-striato-limbic networks in patients with major depression [4].

Reference

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