White matter integrity in first-episode schizophrenia: Gender difference revealed by diffusion tensor imaging

X-Q. Huang[1], W. Deng[2], S. Lui[1], L. Ouyang[3], C-X. Li[3], T. Li[2], and Q-Y. Gong[1]

[1]Department of Radiology, West China Hospital, Chengdu, Sichuan, China, People's Republic of, [2]Department of Psychiatry, West China Hospital, Chengdu, Sichuan, China, People's Republic of, [3]School of Life Science and Technology, University of Electronic Science and Technology of China, Chengdu, Sichuan, China, People's Republic of

Introduction:

Recently, there have been regained interests in gender differences in schizophrenia, and it is thought to contribute to the heterogeneity of schizophrenia phenomenology [1]. Evidence suggests that male and female schizophrenia patients have, at least in part, different patterns of structural abnormalities [2], and EEG study reported the sex difference of functional connectivity [3]. However, the gender effect on the integrity of white matter has rarely been investigated. Present study aims to examine the gender effect on white matter abnormalities in patients with first episode drug-naive schizophrenia using a rigorous voxel-based analysis of the diffusion tensor imaging (DTI) data.

Methods:

This study was approved by the local ethical committee and written informed consent was obtained from all subjects. Twenty-six patients experiencing a first episode of schizophrenia (thirteen males, mean age = 27.62±8.69; thirteen females, mean age = 25.31±6.68) according to the diagnostic criteria of DSM-IV, and twenty-six age, sex and handedness matched normal controls (thirteen males, mean age =27.31±5.36; thirteen females, mean age=27.08±5.09) were recruited. DTI data 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 = 3mm, matrix = 128x128, b value = 1000s/mm^2) with 15 directions. Fractional anisotropy (FA) maps were generated from each participant's DTI scan using the DTIstudio (http://cmrm.med.jhmi.edu/). Voxel-based analysis was performed 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 6mm FWHM isotropic Gaussian kernel. Statistical comparisons were performed using two sample *t*-test between patients and normal controls in male and female subgroups respectively.

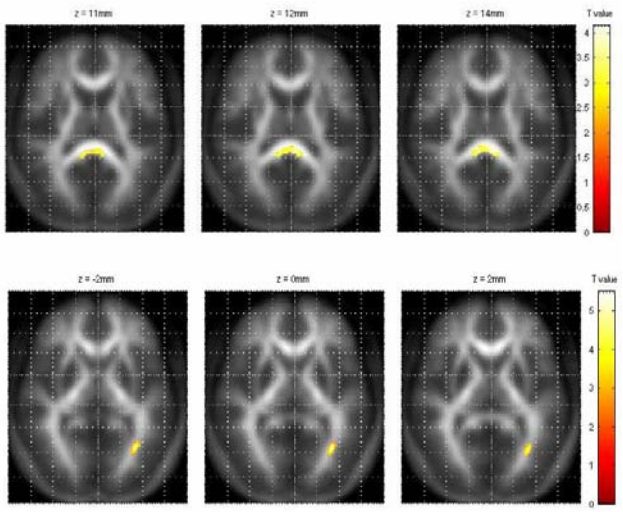

Fig 1. Significant probability maps present on backgrounds of averaged FA maps of male group showing decrease of anisotropy in male schizophrenia patients vs controls in splenium (upper pannel) and left optic radiata (lower pannel).

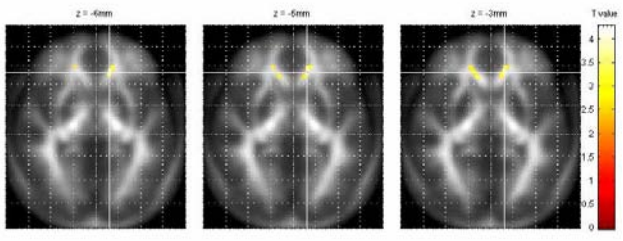

Fig 2. Significant probability maps present on backgrounds of averaged FA maps of female group showing decrease of anisotropy in female schizophrenia patients vs controls in white matter of bilateral frontal lobe.

Results:

At defined threshold value of t>3.3(p<0.001) and cluster voxel>100, significant reductions of FA value in male patients were found in splenium (-6,-38,14, cluster size 365, p<0.01 at cluster level) and left optic radiata (-33,-63,0, cluster size 150) comparing to the matched controls [fig 1]. In female patients, FA reduction was most prominent in white matter of bilateral frontal lobe adjacent to the genu of corpus callosum (-12,33,-5, cluster size 106; 14,32,-2, cluster size 119)[fig 2]. No area with significant FA increase was observed in neither male nor female patients group.

Conclusion:

Although it is generally accepted that schizophrenia is associated with neuronal deficits, it has not been possible to explain the complex features of the disorder on the basis of specific and localized structural abnormalities. It was therefore indicated that the basis of the illness could lie on abnormal interactions or disconnectivity across the brain network [4]. And the gender difference in relation to the disease course and symptom profiles may be attributed to the difference of this disconnectivity. Our findings from the voxel-based analysis of whole brain DTI data suggest that pattern of the white matter abnormalities does differ in male and female schizophrenia patients as revealed by FA maps, and future study by combining with the investigation of the functional connectivity will provide further insight into the underlying psychopathology of the schizophrenia.

Reference:

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