A COMBINED DTI AND STRUCTURAL MRI STUDY IN MEDICATED-NAÏVE CHRONIC SCHIZOPHRENIA

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Target audience: This study is designed for radiologists and psychiatrists with an interest in MRI.

Purpose: Abnormal white matter (WM) connectivity among brain regions may play a critical role in the etiology of schizophrenia. And cortical morphometry alterations have been also described in schizophrenia. It is still uncertain whether the damage of WM integrity is entirely due to a primary WM abnormality or whether it is partly related to gray matter (GM) alterations in anatomically connected areas. Most of the patients included in previous studies that have used antipsychotic medication[1]. Studies have shown that antipsychotic drug can affect WM anisotropy and cortical morphology[1, 2]. We aimed to detected WM integrity damage and cortical morphometry alterations in medicated-naïve chronic schizophrenia patients and healthy controls and investigate the relationship between damage WM and their connecting cortex regions.

Methods: All the imagings were performed on a 3.0-T MRI scanner (Signa HDx; GE Medical Systems, Milwaukee, WI, USA) with 8-channel brain-phased array coil. DTI were obtained using single-shot echo-planar imaging (acquisition matrix=256×288; TE=Minium; TR=16000.0ms; field of view=240mm; slice thickness=2.5mm) with 25 isotropically distributed orientations for the diffusion-sensitising gradients at a *b* value of 1000s.mm^{-2} and one *b*=0 images. T1-weighted imaging were acquired using three-dimensional fast spoiled-gradient recalled acquisition in the steady state (acquisition matrix=256×288; TE=3.9ms; TR=9.6ms; field of view=1.0mm; slice thickness=0mm). We used the FSL 4.1.9 (FMRIB Software Library, http://www.fmrib.ox.ac.uk/fsl) to preprocess DTI image. The FreeSurfer version 5.1.0 (http://surfer.nmr.mgh.harvard.edu/fswiki) was used to estimate GM volume, cortical thickness and surface area that corresponding to abnormal WM fiber tracts with default processing settings. A *P* value of <0.05 was regarded as significant.

Result: We found one cluster of reduced FA in schizophrenia in the left temporal (fig 1). We extracted regions of the cortex regions that corresponding to abnormal white matter fiber tracts (fig 2). Patients had smaller volume in the left medialorbitofrontal, lateralorbitofrontal, superior and inferior temporal, fusiform and lateroccipital (*P*<0.05). The cortical thickness reducted in the left medialorbitofrontal, inferior temporal, fusiform and lingual (*P*<0.05). The surface area reduction was in superior temporal (*P*<0.05). Furthermore, in the gender-combined analysis, no significant correlations between FA and cortical morphometry were found in patients. In the gender-separated analysis found the male patients had a significant positive correlation between FA and lateralorbitofrontal thickness (r=0.976), superior temporal thickness (r=0.96). The female patients showed a significant positive correlation between FA and lateralorbitofrontal volume (r=0.778) and negative correlations with temporal pole surface area (r=-0.772).

Discussion: Patients with schizophrenia decreased FA in the left temporal contains inferior fronto-occipital fasciculus (IFOF) and inferior longitudinal fasciculus (ILF), which suggests that the integrity of the white matter is disrupted in schizophrenia. Several cortical regions connected by the left ILF and IFOF have morphometry changed. This result has also implicated for the psychopathology of schizophrenia both from an anatomical and connection perspective. That relationship between decreased FA and anatomical correspondence GM regions in patients was only seen when gender-separated. Recent neuroimaging studies suggest gender differences in some parts of the brain in schizophrenia and there is a gender-dependent alteration in the brain [3]. We failed to find damage in WM integrity was linked to connective gray matter morphology in gender-combined. That may attributed to various confounding factors, including patients' characteristics, sample size or impaired WM connectivity and regionally alteration in cortex may also be independent features of the disorder.

Conclusion: Schizophrenia patients have reduced FA in the left ILF/IFOF and widespread reduction in anatomical correspondence cortex in patients. White matter damage and gray matter alteration in schizophrenia are interdependent in gender-separated analysis.

References: [1] Kakeda S, Korogi Y. The efficacy of a voxel-based morphometry on the analysis of imaging in schizophrenia, temporal lobe epilepsy, and Alzheimer's disease/mild cognitive impairment: a review. Neuroradiology 2010;52(8):711-721. [2] Navari S, Dazzan P. Do antipsychotic drugs affect brain structure? A systematic and critical review of MRI findings. Psychol Med 2009;39(11):1763-1777. [3] Tepest R, Vogeley K, Viebahn B, et al. Automated gray level index measurements reveal only minor cytoarchitectonic changes of Brodmann area 9 in schizophrenia. Psychiatry Res 2008;163(2):183-192.

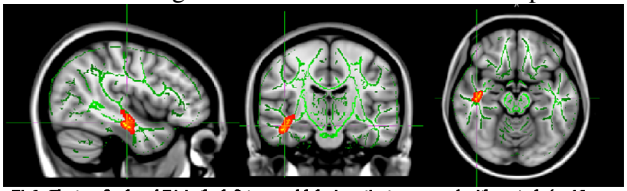

Fig1. Cluster of reduced FA in the left temporal lobe in patients compared with controls (x=46, y=-14, z=-24). Significant cluster (*P*<0.05, corrected by TFCE) highlighted in red-yellow are showed on the mean FA image.

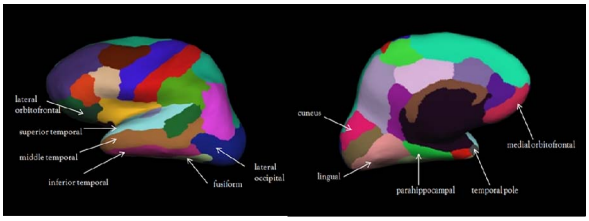

Fig2. Lateral, medial surface of the left hemisphere derived surface-based morphing procedure by using FreeSurfer. The cerebral cortex is parcellated into Desikan-Killiany cortical atlas.