Combining voxel-based morphometry and diffusion tensor imaging to probe neural substrate of schizophrenia on first episode treatment naive patients

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Introduction

Meta-analysis of voxel-based morphometry(VBM) studies revealed that grey and white matter deficits in schizophrenia amounted to a total of 50 brain regions [1]. Diffusion tensor imaging (DTI) studies also reported impaired white matter integrity in schizophrenia, quantified as lower fractional anisotropy (FA) [2, 3]. The combination of volumetric and DTI data had been proposed to detect and characterize subtle brain tissue alterations in schizophrenia [4]. However, no study has combined these two modalities to explore the whole brain structural and functional deficit in schizophrenia yet. In the present study, we aim to investigate the neural substrate of schizophrenia on first episode treatment naive patients by using optimized voxel based analysis of high resolution T1 weighted images and diffusion tensor images acquired using a 3.0T MR scanner.

Method

The study was approved by the local ethical committee and written informed consent was obtained from all subjects. Eighteen patients (mean age = 25.23 ± 7.01, range 18 to 39, eight males) experiencing a first episode of schizophrenia according to the diagnostic criterion of DSM-IV and nineteen healthy age and gender matched volunteers were recruited. All subjects were right handed. MRI scanning was performed prior to any antipsychotic treatment using a 3T MR imaging system (EXCITE, General Electric, Milwaukee, USA) with an 8 channel phase array head coil. High-resolution T1-weighted images were acquired by 3D SPGR pulse sequence (TR/TE = 8.5/3.4 msec; slice thickness = 1 mm; matrix = 256 x 256; flip angle = 12°). DTI was acquired using a single shot spin echo EPI sequence (TR/TE = 10000/70.8 ms; slice thickness = 3 mm, matrix = 128x128, b value = 1000s/mm^2) with 15 directions. SPGR images were preprocessed in SPM2 (http://www.fil.ion.ucl.ac.uk/spm/software/) using the optimized protocol. Fractional anisotropy（FA) maps were generated from each participant's DTI scan by DTIstudio (http:// cmrm.med.jhmi.edu/). The b = 0 images of all control subjects and patients were first normalized and averaged to form a study-specific template, to which all raw b=0 images were normalized again. Then the derived mapping parameters for each subject were applied to the FA maps. Voxel-based analysis of smoothed grey matter and FA maps was carried out using two sample t test and statistical threshold was set at t>3.24 (P<.001, uncorrected) voxel level.

Result

Schizophrenia patients exhibited significantly reduced grey matter density in brain regions including bilateral occipital lobe (P<.05 after correction), bilateral insular, right temporal lobe, right orbitofrontal cortex and bilateral thalamus (P<.05 after correction). The FA value was decreased in patients with first-episode schizophrenia in the bilateral optic radiations, right splenium, and right superior longitudinal fasciculus. No area of increased grey matter density or FA value was found in schizophrenia group.

Conclusion

Schizophrenia is now widely recognized as a disorder which is not only manifested by brain abnormalities involving multiple regions but also by the disconnectivity amongst these regions [5]. Our results of the reduction of grey matter density in occipital lobe and decrease of FA value in related white matter of optic radiation are consistent with known early-stage visual processing dysfunction in schizophrenia [6], whereas grey matter reduction in bilateral thalamus, bilateral insular, right orbitofrontal cortex area combines with FA decrease in splenium and superior longitudinal fasciculus suggest the disruption of limbic system. Present study provide convergent evidence of the involvement of the two cerebral circuits in schizophrenia at early stage of the disease, and combination of different MR modalities may help to provide in depth information about the cerebral alteration in future studies.

Reference

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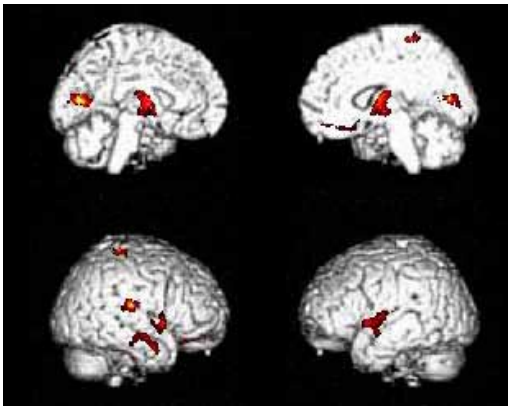

Figure 1.Rendering images from VBM analysis showing areas of grey matter density reduction in schizophrenia in bilateral occipital lobe, bilateral thalamus (P<.05 after correction at cluster level), bilateral insular, right orbitofrontal cortex and right temporal lobe.

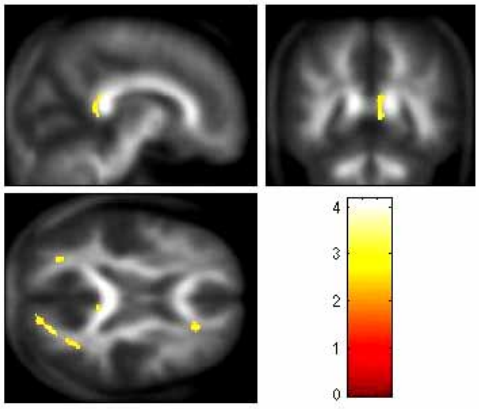

Figure 2. Orthogonal sections of averaged FA maps showing FA decrease in schizophrenia patients in the bilateral optical radiations, right splenium and right superior longitudinal fasciculus (t>3.24, P<.001, uncorrected).