Reduced diffusion anisotropy in schizophrenia: a voxel-based diffusion tensor MR study

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INTRODUCTION

Disruptions in connectivity may explain some of the symptoms in schizophrenia. Several magnetic resonance (MR) diffusion tensor imaging (DTI) studies have shown reduced diffusion anisotropy in patients with schizophrenia (1-3). However, these studies have yielded inconsistent results. The purpose of this study is to investigate diffusion anisotropy in schizophrenic brain by voxel-based analysis of DTI in our institute, using statistical parametric mapping (SPM).

MATERIALS and METHODS

We studied 32 patients (21 men and 11 women, ages 22-58) with schizophrenia diagnosed by DSM-IV criteria, and 42 age-matched controls (38 men and 6 women, ages 19-55). The data were obtained with a 1.5-T Signa Horizon LX MRI system (GE Medical Systems, Milwaukee, WI, U.S.A.). A circularly polarized head coil was used for both RF transmission and reception of the NMR signal. We used single-shot spin-echo echo-planar sequences (TR / TE = 5000 / 102 msec, 5 mm slice thickness and l.5 mm gap, FOV = 21 x 21 cm^2, NEX = 4, l28 x 128 pixel matrix) for diffusion tensor acquisition. Diffusion gradients (b-value of 500 or 1000 s/mm^2) were always applied on two axes simultaneously. Diffusion properties was measured along 6 non-collinear directions: (G_x, G_y, G_z)=[(0, 0, 0), (1/√2, 0, 1/√2), (-1/√2, 0, 1/√2), (0, 1/√2, 1/√2), (0, 1/√2, -1/√2), (1/√2, 1/√2, 0), (-1/√2, 1/√2, 0)]. The diffusion-weighted images were transferred to a workstation supplied by the manufacturer (Advantage Workstation, GE Medical Systems), and the structural distortion induced by the large diffusion gradients was corrected, based on each T2-weighted echo-planar images (b = 0 s/mm^2). The fractional anisotropy (FA) maps were generated on a voxel-by-voxel basis and converted into Analyze format (Mayo Foundation, Rochester, MN, USA). T2-weighted echo-planar images of the normal controls were then segmented into gray, white matter, and cerebrospinal fluid, using SPM2 (Wellcome Department of Cognitive Neurology, London) running on MATLAB6.5.1 (Mathworks, Sherborn, MA). The segmented white matter images in native space were transformed to the white matter templates supplied by SPM, using the residual sum of squared differences as the matching criterion, and the parameter of the transformation was applied to each FA map. The normalized FA maps were smoothed with 8-mm-full-width at half-maximum (FWHM) isotropic Gaussian kernel and a mean image (FA template) was created. Then, all FA maps in native space were transformed to the stereotactic space by registering each of the images to the same FA template image. The normalized data were smoothed with 12-mm FWHM isotropic Gaussian kernel, and were analyzed using SPM employing the framework of the General Linear Model. Age and gender were treated as confounding covariates, and significance levels were set at corrected $P < 0.05$.

RESULTS

Figure 1 shows a result of SPM analysis of FA data. Statistical parametric map in the three orthogonal maximum intensity projections shows voxels with less FA values in patients compared with the normal controls. The significant FA decrease in the patient group was found in the parahippocampal white matter (WM) of the left limbic lobe {peak coordinate [x, y, z (mm)] = (-26 –24 –12), T score = 6.68}, the parahippocampal WM of the right limbic lobe {peak coordinate [x, y, z (mm)] = (-26 –22 –14), T score = 6.57}, middle frontal WM of the right frontal lobe {peak coordinate [x, y, z (mm)] = (-24 26 -2), T score = 5.47}, and so on. No significant increased region was noted.

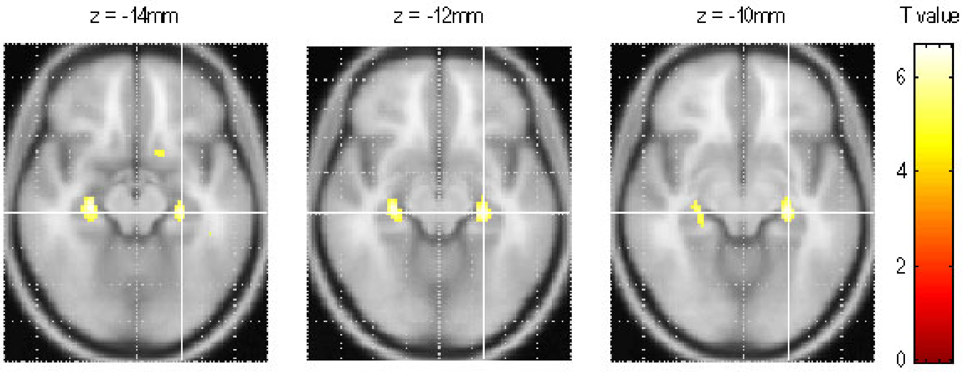

Figure 1.
Significantly decreased FA regions in patients than in normal controls. Bilateral parahippocampal WM and medial frontal region of the left frontal lobe are highlighted.

DISCUSSION AND CONCLUSION

Limbic system such as the hippocampus is considered to have relation with schizophrenia. The parahippocampal gyrus, which is known to be disturbed in schizophrenia with other mesial temporal lobe regions, plays a role in the higher cognitive processes such as learning and memory. Our result may reflect reduced diffusion anisotropy of the white matter pathway of the limbic system as decreased FA indices. Manual region-of-interest (ROI) analysis is usually more sensitive than voxel-based analysis, but it is subjective and difficult to set with anatomical reproducibility. Voxel-based analysis of the diffusion tensor data set allows a voxel-wise comparison encompassing the whole brain without operational bias or hypothesis. This study suggests that the voxel-based diffusion tensor analysis may be robust enough to perceive changes in diffusional anisotropy in patients with schizophrenia.

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