The Integrity of Corpus Callosum and Cingulum in Schizophrenia Assessed by Diffusion Tensor Tractography

C-J. R. CHEN[1], H-L. WANG[1], S-K. LIU[2], V. J. WEDEEN[3], T. G. REESE[3], and W-Y. I. TSENG[1,4]

[1]Center for Optoelectronic Biomedicine, National Taiwan University College of Medicine, Taipei, Taiwan, [2]Psychiatry Department, Far Eastern Memorial Hospital, Taipei, Taiwan, [3]MGH Martinos Center for Biomedical Imaging, Harvard Medical School, MA, United States, [4]Department of Medical Imaging, National Taiwan University Hospital, Taipei, Taiwan

Abstract

The present study aims to detect subtle structural changes in the organization and integrity of corpus callosum and cingulum of schizophrenic patients. The finding suggests that there is no disruption to the integrity of corpus callosum and cingulum for schizophrenic patients. It also raises the possibility that the neuro-pathological abnormalities may be progressive slowly.

Introduction

Diffusion tensor imaging (DTI) technique has shed light on the research of schizophrenia, particularly with respect to speculative changes in the sub-cortical connectivity. Since corpus callosum (CC) and cingulum (CG) play crucial roles in the inter-hemispheric and intra-hemispheric communication, it has been hypothesized that under-connectivity shown in corpus callosum and cingulum may explain some of the clinical symptoms and cognitive dysfunction in people with schizophrenia [1; 2]. However, evidence suggesting the disrupted neural network has been inconsistent [3]. There is a lack of compelling study to systematically investigate both connective fiber tracts at the same time.

In this study, we applied DTI to test the hypothesis that alterations of corpus callosum and cingulum may be significant in schizophrenic patients. We divided each tract into four segments and examined tract integrity by assessing mean fractional anisotropy of each section.

Materials and Methods

Subjects

Eight patients were recruited with a DSM-IV diagnosis of schizophrenia (4 males and 4 females; age range from 23 to 47; mean age ± S.D.=33.25 ± 9.62). Ten normal controls were selected to match the patient group for age, gender, race and handedness (4 males and 6 females; age range from 23 to 45; mean age ± S.D.=35.30 ± 9.17). None of the participants had a history of head injury, neurological illness, mental retardation or substance abuse. All subjects were right handed. Informed consent was signed by them.

Diffusion Tensor Imaging

All images were acquired on 3T MRI system (Trio, Siemens, Germany). A pulsed-gradient spin-echo diffusion EPI sequence was used to acquire diffusion-weight images. The DTI experiment was performed by applying 37 diffusion gradient vectors, TR/TE=5300/120 ms and maximum diffusion sensitivity b=1000s/mm^2. After interpolating thickness from 3.9mm to 1.95mm, isotropic spatial resolution was obtained with both in-plane and through-plane resolution=1.95 mm. Thirty-three trans-axial slices were acquired encompassing the whole brain. The DTI scanning completed in 4 min. DTI analysis was based on the diffusion-dependent attenuation of the NMR signal. The measured signal is related to the diffusion tensor **D** by $\ln(Si/S0) = -\int \mathbf{K}^T_i(t)\mathbf{D}\mathbf{K}_i(t)dt$, where Si and S0 represent attenuated and non-attenuated images, $\mathbf{K}_i(t) = \int \gamma G_i(\tau)d\tau$ is the spatial modulation of magnetization, Gi is diffusion-sensitizing gradient in nth direction, i=1, 2,…., 37, γ is the proton gyromagnetic ratio. By measuring the attenuation Si and S0, we can reconstruct **D** and solve for the first eigenvector, representing the local fiber orientation, and three eigenvalues, allowing us to estimate the fractional anisotropy (FA) of individual fibers.

Tractography

Tractography was based on a simple algorithm that was adapted for DTI data. All fiber orientations of nearest voxels were used to decide the proceeding orientation for the next step; the most coincident orientation less than 45 degree was chosen. A new starting point was then obtained to repeat the same tracking procedure. Tracking stopped if there was no coincident orientation in the nearest voxels. The algorithm started with placing the seed points in CC from genu, body, and splenium in mid-sagittal plane. For left and right CG, seed points were selected from the anterior-posterior orientated fibers above CC based on color-coded maps of the first eigenvector orientation in mid-coronal plane. CC was bounded by minor forceps anteriorly and major forceps posteriorly, whose coordinates in mid-sagittal plane were defined as anterior and posterior boundaries. The coordinates of mass centers of left CG and right CG were defined as left and right boundaries. Four equally-distanced sections were then divided in the regions between anterior and posterior boundary. FA along tracts of CC and CG within the defined boundaries was analyzed.

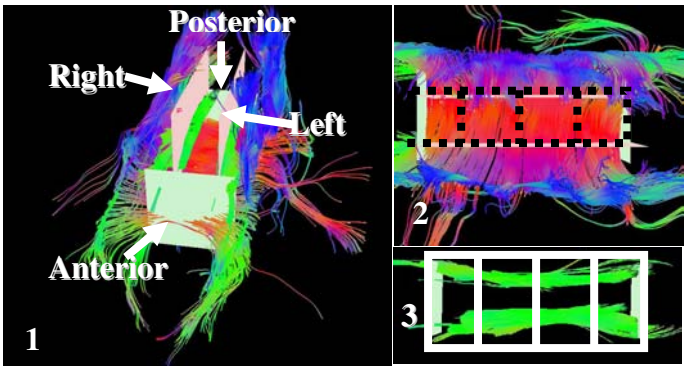

Figure 1. Tractography of Corpus Callosum and Cingulum. Pink planes indicate left and right boundaries. Light green planes indicate anterior and posterior boundaries. Four equally-distanced sub-regions of CC and CG were defined according to the boundaries as illustrated in Figure 2. and Figure 3.

Statistic Analysis

Multivariable analysis of variance (ANOVA) with age and gender as covariates was performed to compare the FA values of corpus callosum and cingulum between schizophrenic patients and normal controls. The FA differences in each section of corpus callosum and cingulum were tested with group (patients, controls) as a between-subject factor. The 2-tailed statistical significance level was set at $p < 0.05$.

Results

Multivariate ANOVA revealed no significant group effects in all sub-regions of corpus callosum and cingulum. Regarding the corpus callosum, there was no significant difference in FA values between schizophrenic and control groups (CC1, F=2.293, p=0.152; CC2, F=0.052, p=0.823; CC3, F=1.038, p=0.326; CC4, F=0.069, p=0.797). Also, FA in the left cingulum and right cingulum did not significantly differ between two groups (Left: CG1, F=0.180, p=0.678; CG2, F=0.032, p=0.860; CG3, F=0.018, p=0.896; CG4, F=0.014, p=0.908; Right: CG1, F=0.783, p=0.391; CG2, F=2.310, p=0.151; CG3, F=0.004, p=0.952; CG4, F=0.289, p=0.599).

Conclusions

Against some previous reports, our study failed to demonstrate abnormalities in the corpus callosum and cingulum in patients with schizophrenia. Negative findings of our study suggest that neuro-pathological changes in schizophrenia might be subtle or heterogeneous. Further studies on different phenotypes of schizophrenia might reveal distinct neural substrates for different phenotypes.

Reference

[1] Brambilla, P et al. Schizophrenia Research 2005; 79: 201
[2] Wang, F et al. Am J Psychiatry 2004; 161:573
[3] Kanaan, RAA et al. Biological Psychiatry 2005; 58(12): 921