Asymmetry Patterns of Association Fibers in Schizophrenia: Preliminary Results Using Diffusion Spectrum Imaging Tractography

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Introduction Schizophrenia is a mental disorder with a prevalence rate of 1% of the adult population in the world. The clinical manifestations include auditory hallucinations, paranoid or bizarre delusions, or disorganized speech and thinking with significant social or occupational dysfunction. To date, data from neruoimaging studies has provided important evidence implicating that white matter abnormalities play a role in the disorder. Findings from diffusion tensor imaging (DTI) studies suggest plausible possibility of pathology of schizophrenia is the involvement of the corpus callosum and the white matter in the frontal lobes. In this study, we investigated three association fibers connecting the frontal and temporal lobes (cingulums [CG], arcuate fasciculi [AF], uncinate fasciculi [UF]) and three commissural fibers connecting the bilateral orbitofrontal lobes, bilateral inferior frontal gyri, and bilateral superior temporal gyri related to the social and language functions that might serve the neuropsychopathology of patients with schizophrenia inferred from diffusion spectrum imaging (DSI) [Figure 1].

Materials and Methods Seven right-handed Taiwanese adults with schizophrenia (3 males and 4 females), as well as seven matched neurotypical participants were examined using DSI. Images were acquired on a 3T MRI system with a 32-channel head coil (Tim Trio, Siemens, Erlangen, Germany). DSI was performed using a twice-refocused balanced echo diffusion echo planar imaging (EPI) sequence, TR/TE = 9600/130 ms, image matrix size = 80 x 80, spatial resolution = 2.5 x 2.5 mm^2, and slice thickness = 2.5 mm. A total of 102 diffusion encoding gradients with the maximum diffusion sensitivity b_{max} = 4000 s/mm^2 were sampled on the grid points in the 3D q-space with $|q| \leq 3.6$ units [1]. DSI analysis was performed based on the relationship that the echo signal S(q) and the diffusion probability density function P(r) were a Fourier pair, i.e., S(q)=FT{P(r)}. The orientation distribution function (ODF) was determined by computing the second moment of P(r) along each radial direction. The intravoxel fiber orientations were determined by decomposing the original ODF into several constituent ODFs [2]. Further, those primary fiber orientations were used for tractography reconstruction. Generalized fractional anisotropy (GFA) at each voxel was quantified based on the shape of the original ODF [3]. Tractography was reconstructed using a streamline-based algorithm adapted for DSI data and the targeted tracts were selected by specific regions-of-interest (ROIs). A method that projected the GFA onto a single mean path of a specific white matter tract, called mean path analysis, was used to analyze local changes in microstructure coherence along the individual tract bundles [4]. The asymmetry patterns were also assessed in CG, AF, and UF.

Results Our findings provided evidence of abnormal white matter microstructures in schizophrenia as inferred from DSI. In neurotypical participants, we found a consistent leftward asymmetry in the three pairs of association fibers. However, adults with schizophrenia did not demonstrate such asymmetry [Figure 2]. Moreover, the results did not show significant differences of the mean GFA values in the three pairs of the association fibers and the three commissural fibers between the adults with schizophrenia and neurotypical participants.

Discussion DSI tractography is a method which allows segmentations and visualization of white matter tracts along with measurement of various characteristics, such as average GFA. This facilitates a more direct comparison of specific neuronal networks. Using DSI technique, the GFA of CG, AF, and UF, were analyzed and represented the integrity of white matter structural connectivity. We found that there were no significant differences in GFA of the three pairs of association fibers and three commissural fibers between adults with schizophrenia and neurotypical participants. This result is consistent with a previous DTI tractography study [5]. Moreover, the structural asymmetry pattern is an important component of long range connectivity in white matter and worth to be investigated. Previous DTI studies of white matter asymmetry reported that a leftward asymmetry pattern of the diffusion anisotropy has been observed in the CG [6], AF [7], and UF [8] in right-handed healthy participants. The loss of leftward asymmetry in adults with schizophrenia in CG [9], AF, and UF [8] suggests alteration of long-range connectivity involved in social and language functions which related to core symptoms of schizophrenia. Lack of leftward asymmetry in schizophrenia may imply a disruption in the normal pattern of structural and functional connectivity in frontal-temporal brain regions. Further studies with larger sample sizes are warranted to examine the correlations between GFA and the severity of clinical symptoms.

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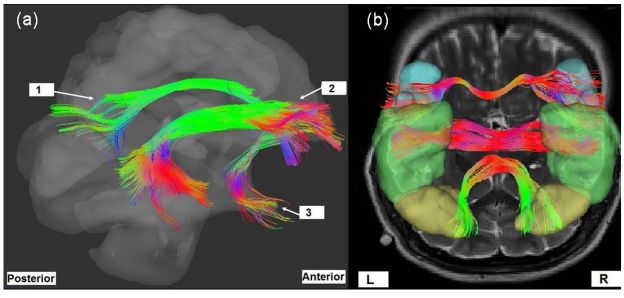

Figure 1 (a) Three association fibers in the right hemisphere. 1 is the cingulum, 2 is the arcuate fasciculus, and 3 is the uncinate fasciculus. (b) The regions of interest (ROIs) and reconstructed commissural fibers. The ROIs at the bilateral orbitofrontal lobes (yellow), bilateral Broca's areas (green), and bilateral Wernicke's areas (blue) are shown.

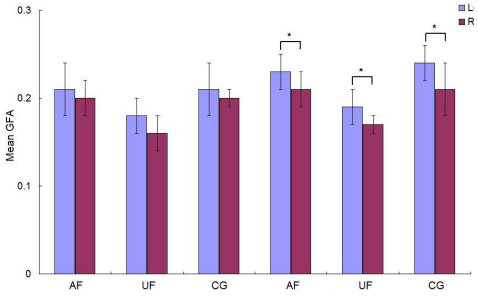

Figure 2 The loss of leftward asymmetry of the cingulums (CG), arcuate fasciculus (AF), and uncinate fasciculus (UF) in schizophrenia. There was a significant left asymmetry of the CG, AF, and UF in neurotypical participants.