Diffusion Tensor Imaging of the Corpus Callosum in Patients with First-Episode and Chronic Schizophrenia


(1) Psychiatry Neuroimaging Laboratory, Department of Psychiatry, Brigham and Women’s Hospital, Harvard Medical School, Boston, MA
(2) Massachusetts Mental Health Center, Public Psychiatry Division, Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, MA
(3) Division of Women’s Health, Connors Center for Women’s Health & Gender Biology, Departments of Psychiatry and Medicine, Brigham and Women’s Hospital, Harvard Medical School, Boston, MA
(4) Clinical Neuroscience Division, Laboratory of Neuroscience, Department of Psychiatry, VA Boston Healthcare System, Brockton, MA.

BACKGROUND
Abnormalities in inter-hemispheric communication have been consistently reported in patients with schizophrenia. The Corpus Callosum is the primary commissural fasciculus in the brain, responsible for inter-hemispheric communication, and structural abnormalities of the Corpus Callosum have been repeatedly observed in schizophrenia patients. Studies comparing patients with schizophrenia to healthy controls on diffusion indices in the Corpus Callosum such as Fractional Anisotropy, Trace, and Mode, have found diffusion abnormalities in schizophrenia patients to be related to the severity of their symptoms (Kubicki, 2007). However, the time-course and development of these structural abnormalities remains unclear, and requires further examination of schizophrenia patients at different stages of the illness. By comparing diffusion measures in the Corpus Callosum of first-episode schizophrenia patients to those of patients with chronic schizophrenia, we can get a better sense of changes in the Corpus Callosum over the course of the disease.

METHODS

• 18 first-episode schizophrenia patients, 20 chronic schizophrenia patients, 20 healthy controls matched to the first-episode patients, and 20 controls matched to the chronic patients participated in the study.
• Diffusion-weighted images were acquired from all participants on a GE 3T MRI scanner at a resolution of 1.7 mm x 1.7 mm x 1.7 mm (51 diffusion directions, b=900, TR 17000 ms, TE 78 ms, FOV 24 cm, 144x144 matrix)
• Whole-Brain Tractography was carried out on each participant, which generated approximately twenty thousand diffusion fibers per subject (Fig. 1 A). Fibers were then automatically grouped into 200 fiber clusters on the basis of shape and spatial position (Fig. 1 B)
• Fiber clusters constituting the Corpus Callosum were manually defined on two representative participant images and then automatically extracted from the remaining 76 participant images (Fig. 1 C). The Corpus Callosum was segmented into 6 regions (CC1 through CC6, anterior to posterior), on the basis of spatial position and fiber trajectories to the cortex (Fig. 1 D and Fig. 1 E)
• Average Fractional Anisotropy (FA), Trace, and Mode were calculated for each Corpus region. FA is an index of diffusion sphericity, Trace is a measure of diffusion extent, and Mode is a measure of diffusion morphology from oblate to prolate.

RESULTS

First-Episode Schizophrenia Patients Compared to Healthy Controls:
• Relative to healthy controls, First-Episode Schizophrenia patients exhibited reduced FA in CC2 (p=.022) (Fig. 2 A)
• Relative to healthy controls, First-Episode Schizophrenia patients exhibited increased Trace in CC2 (p=.007), CC3 (p=.006), CC5 (p=.017), and CC6 (p=.001) (Fig. 2 B)

First-Episode Schizophrenia Patients Compared to Chronic Schizophrenia Patients:
• Relative to First-Episode patients Chronic Schizophrenia Patients exhibited reduced FA in CC1 (p=.046) and CC2 (p=.020) (Fig. 2 A)
• Relative to First-Episode patients Chronic Schizophrenia Patients exhibited reduced Trace in CC6 (p=.005) (Fig. 2 B)

CONCLUSIONS
These Fractional Anisotropy findings suggest that the structural abnormalities reflected by FA are present at First Episode, change over the duration of the disease and are most pronounced in the anterior half of the Corpus Callosum.

The Trace findings in the first episode subjects suggest an increase in overall diffusivity throughout the Corpus Callosum in comparison to normal controls. The finding of decreased Trace in Chronic patients compared to First Episode suggests a progressive decrease in overall diffusion that is most prominent in the posterior portion of the Corpus Callosum. The abnormally high Trace in First Episode patients potentially reflects an inflammatory process in the early stages of the disease.

This study illustrates the advantages of using a battery of orthogonal diffusion metrics when investigating white-matter pathology, as opposed to using FA alone, as is common in the DTI literature.