Disruption of Regional White Matter Integrity in Schizophrenia: A High Resolution Diffusion Tensor Imaging Study
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Abstract
Alterations in whole brain white matter (WM) in schizophrenia have thus far been inconclusive. DTI, however, allows for a more thorough analysis of WM alteration than more conventional MR measures. Here we used high resolution 3T DTI to evaluate whole brain white matter in schizophrenia.

We found decreased FA and increased Trace in whole brain WM of chronic schizophrenics, compared with normal controls (n = 15, 15). Within cerebral WM, temporal and occipital WM showed decreased FA more than other regions, while Trace was increased in all areas except the temporal lobe. Additionally, there was no change in WM volume in any area other than the temporal lobe.

Background
Impairments in neural connectivity, particularly in the frontal and temporal lobes, have been implicated in the pathophysiology of schizophrenia (e.g., Bullmore, 1997; Andreasen, 1997). White matter appears homogeneous under conventional structural MRI and thus does not allow for thorough analysis of white matter abnormalities in schizophrenia (see review in Kubicki, et al., 2007). DTI provides much more comprehensive measures from which one can infer differences in white matter integrity.

Methods
Subjects
15 male chronic schizophrenics and 15 male normal controls, matched by age, parental socioeconomic status, and handedness (all right-handed).

Image Acquisition and Processing
Images were acquired on a 3T GE shortbore magnet. Axially acquired 176 slice spgr (1mmx1mmx1mm) series were coregistered to axially acquired DTI (1mmx1mmx1mm) series. An automated, intensity based segmentation was applied to coregistered structural images to acquire white matter labelmaps.

DTI baseline images (1.7mmx1.7mmx1.7mm) and tensors were analysed with Slicer 2.8. Diffusion weighted tensors were converted to 2 corresponding scalars: trace and fractional anisotropy (FA).

ROI Analysis
Exclusion ROIs were drawn on SPGR images and applied to white matter, generating white matter ROIs

• All structural images and labelmaps were co-registered to diffusion weighted scans and the white matter was manually segmented into lobes.

Results
• We observed significant differences in whole brain white matter fractional anisotropy (p = 0.003) and trace (p = 0.003) between chronic schizophrenics and normal controls.

• More specifically, there was a significant decrease in FA in the temporal and occipital lobes (p = 0.007, p = 0.033), while Trace was significantly increased in prefrontal, fronto-parietal, and occipital lobes (p = 0.007, p = 0.010, p = 0.024). Additionally, the only significant difference in volume was an increase in white matter in the temporal lobe (p = 0.011).

Whole Brain White Matter Abnormalities

Discussion
These findings suggest that whole brain WM abnormalities are present in schizophrenia. Furthermore, cerebral WM abnormalities were observed more in the temporal and occipital lobar regions. In the temporal lobe, where there was a difference in FA with no difference in Trace, that differences are likely primarily organizational and architectural, whereas, in areas where both FA and Trace differed, the changes would be more based in the structural components of WM (i.e. the axons themselves and their myelin sheaths). The fact that these abnormalities were primarily found in diffusion measures, with minimal obvious differences in volume, further emphasizes the importance of DTI as a modality for studying differences in WM, in contrast to conventional structural MRI.