Comparison of in vivo MRI Methods for Examining White Matter Abnormalities in Schizophrenia

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BACKGROUND: Previous MR imaging studies have found white matter abnormalities in subjects with schizophrenia. Methods used in past work include diffusion tensor imaging (DTI), which is a method for examining tissue microstructure, magnetization transfer imaging (MTI), which provides a measure of protons bound to large molecules, and T_2 relaxography (T2R), which measures water protons with a short transverse relaxation time. The water component with a short (0-50ms) T_2 relaxation time, known as the myelin water signal, is thought to reflect water trapped between the myelin bilayers. Differences between patients with schizophrenia and control subjects have been observed with all three imaging methods[1-4]. We are conducting a neuroimaging study of patients with schizophrenia and age matched controls in which the three modalities (DTI, MTI, T2R) are collected on every subject. T2R data is collected using a novel multi echo, multi slice, linear combination method that allows multiple slices to be collected instead of the standard single slice method[5].

METHODS: Subjects for this analysis consisted of 12 individuals with schizophrenia (6 male, mean age 39) and 11 age matched healthy controls (5 male, mean age 35). MRI data were collected on a Siemens 3T Trio scanner. T_1 and proton density images were acquired for subject registration and tissue classification. DTI data consisted of 64 consecutive 2mm thick slices, 256 FOV, 30 directions, b=1000. A field map sequence was acquired to correct for the spatial distortions in the DTI data. The MTI acquisition consisted of a pair of consecutive 3D GRE scans, with and without MT selected, and a voxel size of 2x1x2mm. T_2 relaxography data were collected aligned to the AC-PC plane, using three consecutive multi-slice, spin echo acquisitions with TR/TE (1290/8, 1310/33, 1390ms/110ms), with twelve slices and a voxel size of 2x2x8mm. Data from the three T2R acquisitions were linearly combined to obtain estimates of the myelin water fraction (MWF), defined as the myelin water divided by the total water signal.[5] The magnetization transfer ratio (MTR) was computed on a voxel-wise basis as the difference between the data without and with MT, divided by the value without MT. The diffusion tensor was computed, and the scalar maps were then distortion corrected using custom software incorporating multiple FSL routines.[6] A white matter mask derived from tissue segmentation was used to select voxels to include in the white matter evaluation. White matter in frontal and superior regions where evaluated for group differences, with the frontal region, defined as anterior to the coronal plane located at the anterior extent of the genu and perpendicular to the AC-PC line and the superior region, defined as superior to the AC-PC aligned plane located at the superior extent of the corpus callosum at the midline (figure 1). The masks were translated to the original acquisition, and voxels estimated to be at least 90% white matter were included in the computation of the regional averages.

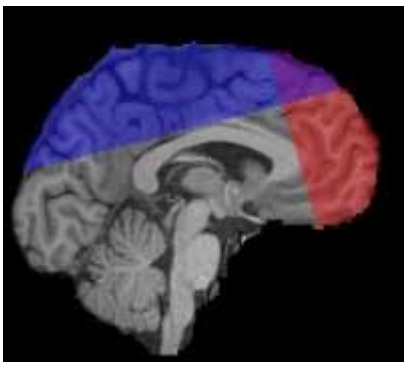

Figure 1 Frontal (red, purple) and superior (blue, purple) regions.

RESULTS: There was no significant difference in the mean age of the two groups. Mean MWF, MTR, fractional anisotropy (FA), and mean diffusivity (MD) in the two white matter regions were computed for each subject. No group differences were observed in either region for the MTR and MWF. Subjects with schizophrenia were found to have significantly lower mean FA in the superior region and trend lower FA in the frontal region (frontal: $F(1,20)=3.42$, $p=0.079$ Cohen's d effect size ($d=0.78$); superior: $F(1,20)=6.83$, $p=0.016$ ($d=1.11$)). Subjects with schizophrenia were found to have significantly higher MD in both regions (frontal: $F(1,20)=5.19$, $p=0.033$ ($d=0.96$); superior: $F(1,20)=9.35$, $p=0.006$ ($d=1.29$)).

DISCUSSION: These preliminary results show reduced FA and increased MD in frontal and superior white matter in subjects with schizophrenia relative to controls, in line with published results from other studies. No significant difference was observed in the MTR and T2R data. Inclusion of additional subjects may reveal group differences in the MTR and T2R data. Future plans include comparisons utilizing voxel based analyses.

REFERENCES:

(1) Flynn et al. Molecular Psychiatry, 8, 811-820, 2003.
(2) Lim et al. Archives of General Psychiatry, 56, 367-74, 1999.
(3) Kubicki et al. NeuroImaging, 26, 1109-1118, 2005.
(4) Kalus et al. Neuroscience Letters, 375, 151-156, 2005.
(5) Vidarsson et al. Magnetic Resonance in Medicine, 53, 398-407, 2005.
(6) http://www.fmrib.ox.ac.uk/fsl/

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