Diffusion Tensor Imaging Of Children With Early Onset Of Schizophrenia

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Purpose: To examine white matter integrity of brain regions in patients with early onset of schizophrenia as compared with healthy comparison subjects usin a voxel based analysis of DTI maps.

Materials and Methods: Subjects: Twenty patients (13 male) with a DSM-IV diagnosis of schizophrenia or schizoaffective disorder and a mean age of 16.65 were recruited from inpatient and outpatient facilities at the Zucker-Hillside Hospital. The normal control group consisted of seventeen subjects (7 Male) and mean age of 14.18. Normal subjects were obtained from advertisements and community centers. Normal controls were screened for any neurological an psychological impairment. After describing the study to the subjects and their parents, written assent and informed consent were obtained. The institutional review board at the North Shore-Long Island Jewish Health System approved this study.

Image Acquisition. In addition to routine clinical scans (T1, T2 and FLAIR) for clinical purposes, diffusion tensor images (DTI) with matching fast spin echo (FSE) double echo sequence for segmentation and 3D spoiled gradient recalled (SPGR) with inversion prep (IR-Prep) for registration were obtained. DTI (TR=10,000 msec, TE=Minimum Full, Ramp Sample=On, FOV=22 (cm)^2, Slice Thickness=5.0mm, Gap=0.0, Matrix=128x128, NEX=2, Time=9.00 min) slices were graphically prescribed parallel to the AC-PC. The current DTI protocol runs with twenty-five gradient directions and provides twenty-three 5mm contiguous slices covering the whole brain. Double echo FSE sequence (TR=4000 msec, TEs=17, 102 msec, ETL=16, BW= 20.83, FOV=22 (cm)^2, Matrix = 256x192, NEX = 2 Time=3.24 min) was obtained with matching slices to the DTI locations.

Image Analysis: Image analysis sections were comprised of intra and inter subject registrations. All 3D brain images were extracted into brain and non-brain. For the inter subject registration a brain extracted template image was selected from all the subjects and transferred into Talairach space using AFNI (Cox, 1996). In order to transform all other subjects' images into this common space a 3D warping technique was applied to all individual extracted brains using the template image as the target. This transformation results into a warp field and Talairach transformed images. The warp field (W3D) of each individual subject was stored for the transformation of the FA map into the common Talairach space.

The intra subject registration is accomplished using a linear rigid-body transformation to register subject's T2 and PD into their original 3D SPGR. The resultants matrix (M) is stored for registering the FA maps of all subjects. Another important stage is the susceptibility induced spatial distortions correction of diffusion images. This correction was carried out using the extracted T2 volume of each subject and a non-linear 2D warping algorithm (Ardekani, 2003). The resultant warp field (W2D) of each subject is stored for correction of FA maps for susceptibility distortion.

Individual FA map was computed from the 26 DTI volumes for each subject using the methods described in (Basser& Pierpaoli, 1998). The FA map of each subject was then transformed to the Talairach coordinates by combining the transformations M, W2D, and W3D into a single transformation and applying it to the original FA map by a single interpolation operation.

Statistical Analysis: Mann-Whitney and t tests were used for statistical analysis of FA maps. We applied a threshold criterion to the resulting *t*-map at 2.4 ($p<0.01$, one-tailed) followed by an extent threshold criterion of at least 200 contiguous voxels. Those voxels, which met both criteria, were considered to hav a significantly reduced or increased mean FA value in the patient group relative to the healthy comparison group.

Results: Several brain areas were found to have lower FA values in patients with schizophrenia compared to normal controls. These included bilateral Heshel's gyri (Fig. 1), the inferior parietal lobule bilaterally; the left frontal gyrus dorsal and lateral to the genu of the corpus callosum; the genu of the corpus callosum (Fig. 2); left superior temporal gyrus; middle temporal gyri (Fig 3); and bilateral parahippocampal gyri (Fig. 4).

Conclusions: Using a robust voxel-based analysis technique, we have demonstrated lower FA values in patients with early onset of schizophrenia as compared to healthy comparison subjects. These areas of lower FA are consistent with a recent diffusion tensor imaging study in adult patients with chronic schizophrenia with an unspecified age of onset (Ardekani, 2003). In conclusion, voxel-based analysis of DTI maps provides a comprehensive brain assessment revealing areas of compromised white matter integrity throughout the whole brain in adolescents with early-onset schizophrenia. These data are consistent with the results of a recent postmortem study in patients with chronic schizophrenia that have implicated a cluster of genes involved in the formatior and maintenance of myelin sheaths (Hakak et al., 2001).

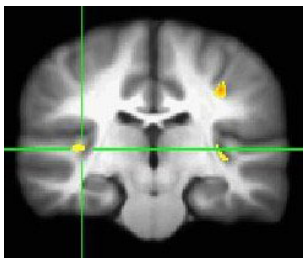

Figure 1: Reduced FA at Bilateral Heshel's gyri

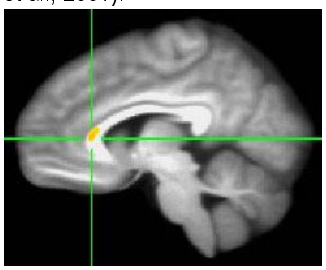

Figure 2: Reduced FA at Genu of CC

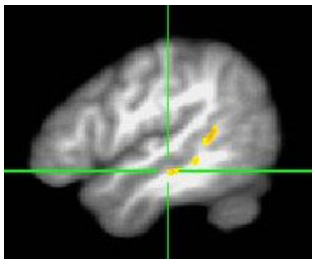

Figure 3: Middle Temporal reduced FA areas

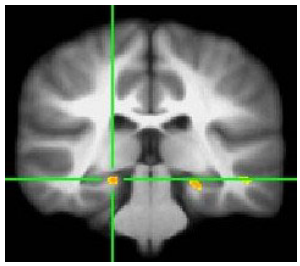

Figure 4: Bilateral Hippocampal FA Reduction

Ardekani BA. An improved method for intersubject registration in 3D volumetric brain MRI. *World Cong. on Med. Phys. and Bio Eng.*; Sydney, AU, 2003; 452.

Basser PJ, Pierpaoli C. A simplified method to measure the diffusion tensor from seven MR images. Magn Reson Med 1998; 39:928-934.

Hakak Y, Walker JR, Li C, Wong WH, Davis KL, Buxbaum JD, Haroutunian V, Feinberg AA. Genome-wide expression analysis reveals dysregulation of myelination-related genes in chronic schizophrenia. Proc Natl Acad Sci U S A 2001; 98(8):4746-51.

Cox RW. AFNI: software for analysis and visualization of functional magnetic resonance neuroimages. Comput Biomed Res 1996; 29:162-173.