A Tractography Approach to Studying Fronto-Temporal Fasciculi in Schizophrenia and Late Onset Schizophrenia-like Psychosis

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SYNOPSIS: DT-MRI tractography was used to study fronto-temporal fasciculi (the superior longitudinal fasciculus, the uncinate fasciculus, the inferior fronto-occipital fasciculus, and the cingulum) in (i) subjects with schizophrenia, (ii) subjects with late onset schizophrenia-like psychosis (onset after age 60), and (iii) age-matched controls. Tissue anisotropy was determined at regular intervals along the tractographically-reconstructed fiber-trajectories – thereby allowing anisotropy measurements to be localized to within particular fasciculi. Our results imply that in schizophrenia, tissue anisotropy is reduced in left-hemispheric fronto-temporal fasciculi, while it is not affected in late-onset schizophrenia-like psychosis.

METHOD: Data Acquisition: Whole brain optimized DT-MRI data with 2.5 mm isotropic resolution[1] were acquired on a GE Signa 1.5T LX system from (i) 14 right-handed males with DSM-IV criteria schizophrenia, (ii) 14 age, handedness and gender-matched control subjects; (iii) 13 subjects with very late-onset schizophrenia-like psychosis; and (iv) 15 matched elderly controls.

Deriving tract-specific measures using tractography: Following correction for eddy-current distortion, the tensor was determined in each voxel. Next for each subject, a continuous tensor field was estimated using the approach described elsewhere[2]. One of the authors, who was blinded to each individual subjects' group status, defined 3D regions of interest (ROI) believed to contain a section of desired fasciculus on fractional anisotropy (FA) maps. Tracking was initiated from within each voxel in the ROI using a streamline-propagation approach[3]. In order to exclusively select trajectories from one fasciculi where the trajectories of two or more fasciculi pass closely to one another (e.g. uncinate and inferior fronto-occipital fasciculi), a two-region of interest approach was used such that only those trajectories that passed through both ROIs were considered to be part of the fasciculus of interest, in a manner similar to that reported elsewhere[4-6]. We studied the superior longitudinal fasciculus (SLF) uncinate fasciculus, inferior fronto-occipital fasciculus (IFO) and cingulum of both hemispheres in this way for each subject. The trajectories were checked for consistency with neuroanatomical texts[7]. The FA was determined at each 0.5 mm step along the reconstructed trajectory, providing a distribution of FA values for each tract. The mean FA values were computed for each fasciculus and entered into the statistical analysis.

Statistical Analysis: As an initial step in the analysis, a limited number of statistical comparisons were performed using composite measures. A composite measure of FA in each hemisphere was generated using principal components analysis, entering FA values from each of the four fasciculi. The first principal component was used as the composite measure of FA for that hemisphere. Group comparisons were performed using a one-way ANOVA with four groups: young controls, old controls, young patients and old patients. Comparisons of anatomical patterns of any underlying group differences were then explored by *post-hoc* pair-wise comparisons of measurements from individual tracts.

RESULTS: Table 1 shows the median and range of the FA values from the different subject group comparisons. Table 2 shows the results of the statistical analysis. The p-values in the first column show the group effect, while those in the remaining columns pertain to the pairwise comparisons.

Table 1	YOUNG CONTROLS	YOUNG PATIENTS	ELDERLY CONTROLS	ELDERLY PATIENTS
Left SLF	0.432 (0.394-0.479)	0.422 (0.380-0.444)	0.429 (0.387-0.462)	0.428 (0.393-0.450)
Right SLF	0.423 (0.407-0.459)	0.411 (0.373 -0.440)	0.415 (0.394-0.452)	0.413 (0.382-0.453)
Left Uncinate	0.392 (0.362-0.427)	0.380 (0.333-0.406)	0.403 (0.346-0.435)	0.426 (0.368-0.454)
Right Uncinate	0.393 (0.346-0.418)	0.385 (0.353-0.416)	0.393 (0.364-0.410)	0.410 (0.350-0.442)
Left IFO	0.443 (0.388-0.472)	0.417 (0.360-0.474)	0.463 (0.410-0.494)	0.458 (0.426-0.497)
Right IFO	0.440 (0.388-0.490)	0.405 (0.331-0.478)	0.455 (0.400-0.501)	0.451 (0.403-0.496)
Left Cingulum	0.430 (0.382-0.464)	0.404 (0.346-0.462)	0.425 (0.389-0.503)	0.437 (0.348-0.476)
Right Cingulum	0.417 (0.375-0.455)	0.415 (0.356-0.457)	0.429 (0.375-0.481)	0.431 (0.358-0.472)

Table 2	YOUNG CONTROLS *vs* YOUNG PATIENTS	ELDERLY CONTROLS *vs* ELDERLY PATIENTS	YOUNG CONTROLS *vs* ELDERLY CONTROLS	YOUNG PATIENTS *vs* ELDERLY PATIENTS
Left Composite ($p = 0.001$)	0.040	0.990	0.973	0.005
Right Composite ($p = 0.074$)	0.300	0.990	0.990	0.170
Left SLF ($p = 0.062$)	0.072	0.964	0.964	0.648
Right SLF ($p = 0.352$)	0.358	0.990	0.892	0.988
Left Uncinate ($p = 0.003$)	0.723	0.413	0.563	0.039
Right Uncinate ($p = 0.049$)	0.972	0.610	0.994	0.170
Left IFO ($p < 0.001$)	0.321	0.990	0.270	0.002
Right IFO ($p = 0.003$)	0.126	0.963	0.995	0.006
Left Cingulum ($p = 0.165$)	0.201	0.990	0.990	0.535
Right Cingulum ($p = 0.572$)	0.989	0.998	0.949	0.966

DISCUSSION / CONCLUSION: Our results are suggestive of reduced anisotropy in left hemispheric fronto-temporal fasciculi in schizophrenia, which is not mirrored in late onset schizophrenia-like psychosis. This raises the possibility that white matter may be affected in a different manner in the two conditions – which is supported by the last column of Table 2. The novel method proposed here allows one to obtain a *distribution* of FA values for a particular tract. However, we only compared the means of these distributions in the current study. Further studies of these distributions are currently underway to see if they reveal more information about white matter in schizophrenia.

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