Probabilistic tractography in patients with schizophrenia

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Introduction

Diffusion tensor imaging has been widely utilized to examine the status of white matter integrity in both healthy and clinical populations, including schizophrenia. To date, several reports indicate widespread white matter deficits in several brain regions in patients with schizophrenia compared to healthy controls[1]. Recent reports suggest that the illness may be progressive and that age should be considered when studying white matter integrity in patients with schizophrenia[2,3]. The goal of the current study was to explore the fronto-temporal circuitry highlighted in previous reports and to expand upon this analysis strategy by a.) using an automated probabilistic tractography method and b.) examining additional white matter pathways.

Method

Thirty-four individuals with schizophrenia (21 male, ages 19-59) and thirty-four age and gender matched controls were studied. Participants underwent a structured clinical interview to confirm diagnosis in patients and to probe for exclusion criteria in both patients and controls. Imaging was performed on a Siemens Trio 3T system using an 8 channel head coil, and included a T1-weighted MPRAGE sequence, a 30 direction DTI sequence and a GRE field map sequence. The DTI volumes were corrected for eddy current distortion and then the field map was used to correct for magnetic field inhomogeneity distortion. FreeSurfer (http://surfer.nmr.mgh.harvard.edu) parcellation was performed on the T1-weighted images to determine white matter regions of interest that were then used to seed the tractography analyses. BEDPOSTX and ProbtrackX from the FMRIB software library[4] were used to perform probabilistic tractography on six bilateral tracts; cingulum bundle (CB), cortico-spinal (CST), inferior fronto-occipital fasciculus (IFOF), inferior longitudinal fasciculus(ILF), superior longitudinal fasciculus (SLF), and uncinate fasciculus(UNCI) (see Figure 1., for 3D rendering of the tracts). Mean fractional anisotropy (FA) was computed along each tract. A univariate ANCOVA with age entered as a covariate was used to examine the effect of group, age and the interaction between age and group on tract integrity. To reduce the Type I error probability, and because the literature is still inconsistent regarding unilateral findings, an average tract scalar was computed from left and right tracts.

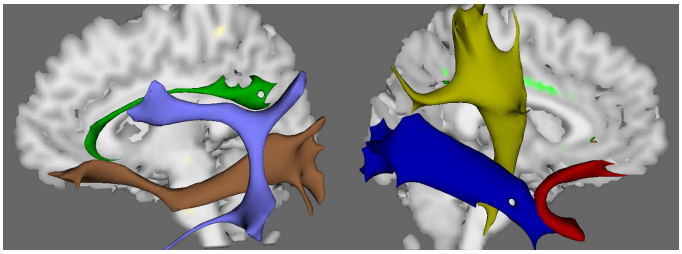

Figure 1. Left panel, green is CING, brown is IFOF, and blue is SLF. Right panel, yellow is CST, dark blue is ILF, and red is UNCI.

Results

There was no significant effect of group in mean FA for any of the tracts examined. There was a significant effect of age and also an age by group interaction effect in the UNCI. Mean FA within the UNCI showed a steeper age by FA slope in patients when compared to controls. Mean FA in the CB, the IFOF, and the SLF showed a significant effect of age, but not a main effect of group or an interaction between age and group. To further investigate the impact of age on tract integrity in patients and controls, the sample was divided into older and younger groups based on a median age split. Older patients showed significantly lower FA in the IFOF, SLF, and the UNCI (see figure 2) compared to older controls. Mean FA in younger patients was not different from mean FA in younger controls in any of the tracts. Both young patients and controls showed significantly higher FA in the IFOF, SLF and UNCI when compared to the older patients.

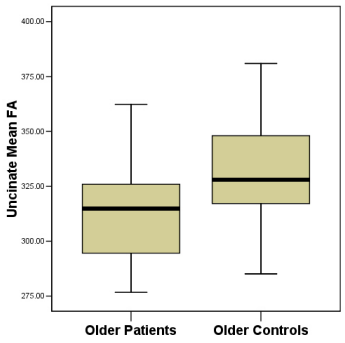

Figure 2. Mean FA in the UNCI

Conclusions

These data corroborate other tractography reports indicating age-related fronto-temporal deficits in FA in patients with schizophrenia[3]. This study expands upon the current literature by utilizing a fully-automated fiber tractography method, examining additional white matter pathways and by replicating the finding of an interaction between age and group. Incorporating additional information on medication dose years, genetic susceptibility, and neurocognitive performance into the analysis may be helpful in identifying further modifiers of white matter microstructure in schizophrenia.

Acknowledgments

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References

1. White, T, et al, (2008). Topics in Magnetic Resonance Imaging, 19:97-109.
2. Mori , T, et al., (2007). Psychiatry Research, 154:133-145.
3. Rosenberger, G, (2008). Schizophrenia Research, 102:181-188.
4. Smith, S. et al. (2004). NeuroImage, 23(S1):208-219 (www.fmrib.ox.ac.uk/fsl)