Clinical and Neuropsychological Correlates of Diffusion Tensor Imaging Indices in First-Episode Schizophrenia

JX Zuo1,2, E Fredman3, J Duskin1, Z Kikinis1, K Green2, LJ Seidman3,4, JM Goldstein2,5, TL Petryshen6,7, RI Mesholam-Gately2, J Wojciak3,4, RW McCarley1,2, M Kubicki4*, ME Shenton2,8

(1) Harvard College, Cambridge, MA; (2) Department of Psychiatry, Brigham and Women’s Hospital, Harvard Medical School, Boston, MA; (3) Massachusetts Mental Health Center, Public Psychiatry Division, Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, MA; (4) Department of Psychiatry, Massachusetts General Hospital, Harvard Medical School, Boston, MA; (5) Department of Medicine, Brigham and Women’s Hospital, Harvard Medical School, Boston, MA; (6) Stanley Center for Psychiatric Research, Broad Institute of MIT and Harvard, Boston, MA; (7) Psychiatric and Neurodevelopmental Genetics Unit, Center for Human Genetic Research, Massachusetts General Hospital, Boston, MA; (8) Department of Psychiatry, Veterans Affairs Boston Healthcare System, Brockton Division, Brockton, MA; * denotes equal last authorship

**BACKGROUND**

- Diffusion tensor imaging (DTI) studies have shown that reduced white matter integrity is related to schizophrenia, which supports the disconnectivity theory of the disease.1,2
- Here, in first-episode schizophrenia patients (FESZ), we studied 5 tracts that have been implicated in schizophrenia: uncinate fasciculus (UF), cingulum bundle (CB), inferior longitudinal fasciculus (ILF), superior longitudinal fasciculus (SLF), and arcuate fasciculus (AF).
- We hypothesized that these tracts would exhibit reduced white matter integrity (indicated by lower fractional anisotropy (FA) and/or increased trace), and that these DTI indices would correlate with hypothesized clinical symptoms and performance on neuropsychological tests.

**METHODS**

- Subjects: 30 FESZ and 30 healthy control subjects (HC), group-matched for age, sex, and parental socioeconomic status.
- Clinical and neuropsychological measures:
  - Scale for the Assessment of Positive Symptoms3
  - Scale for the Assessment of Negative Symptoms3
  - Wisconsin Card Sorting Test5
  - Trails A6
  - Wechsler Memory Scale-III spatial span7
- Image acquisition: Diffusion weighted images were acquired on a 3-Tesla General Electric scanner.
- Tractography: Manual ROIs were first drawn for each case. For CB, ILF, and SLF/AF, ROIs were based on earlier methodologies.8 SLF and AF were further distinguished based on connectivity.9 ROIs for UF were placed a single axial slice. Tractography was performed using 3D Slicer version 3. All tracts were visually inspected and exclusion ROIs were used as needed.

**RESULTS**

- FESZ exhibited significantly lower FA in the right CB, AF, and ILF, but not in either hemisphere of the UF or SLF.
- There was no overall group difference in trace.
- In FESZ, right ILF FA negatively correlated with the severity of hallucinations.
- In patients, FA did not significantly correlate with any hypothesized clinical or neuropsychological measures.

**CONCLUSIONS**

- These results suggest that the right CB, AF, and ILF white matter are disrupted early in the course of schizophrenia.
- Since FA but not trace was affected in these tracts, the tract abnormalities are likely to stem more from disturbances in fiber organization than reduced fiber density or demyelination.
- Additionally, the significant correlation between ILF integrity and the severity of hallucinations suggests that the ILF plays a role in this disturbance.

**REFERENCES**

3. Andreasen, N. Scale for the assessment of positive symptoms (SAPS). (University of Iowa College of Medicine, 1984).
4. Andreasen, N. Scale for the assessment of negative symptoms (SANS). (University of Iowa College of Medicine, 1981).

**ACKNOWLEDGEMENTS**

This work was supported, in part, by a MH11 PSID CIDAR Grant (RWM, MES, LJS, JMP, TLF, RHM, JWW), Department of Veterans Affairs Merit Awards (MES), and the Harvard College Research Program (JXZ).