Increased Diffusion Kurtosis of Gray Matter in Schizophrenia

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Introduction

- Gray matter (GM) alterations have been long known to exist in schizophrenia (SZ), with cortical thinning consistently reported by previous studies [1]; however, there is little understanding of how gray matter is affected at the microstructural level, with most knowledge to date arising from invasive, postmortem studies.
- In this study, we employed diffusional kurtosis imaging (DKI) [3] to describe microstructural properties of gray matter in patients with chronic SZ compared to healthy controls (HC).
  - DKI is an extension of the diffusion tensor imaging (DTI) that derives mean kurtosis (MK), a metric that describes non-gaussian effects of water diffusion in tissues and reflects tissue complexity.
  - MK was previously shown to be sensitive to GM changes due to both development [4] and pathology, such as inflammation [4].
  - Cognitive impairment in schizophrenia has documented by the Wisconsin Cart Sorting Test (WCST) and linked to abnormalities in frontal lobe structures [6].

Objective: To use MK, axial kurtosis (AK), radial kurtosis (RK) and mean diffusion (MD), measures to quantify microstructural properties of gray matter in SZ.

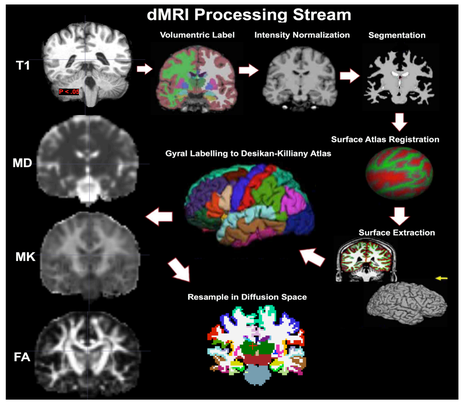
- **H_{01}:** Altered diffusion metrics will be found in gray matter in the SZ compared to HC group.
- **H_{02}:** Microstructural asymmetry patterns will differ in the SZ versus HC group.
- **H_{03}:** Executive function measured by cognitive assessments will be correlated to alterations in gray matter diffusivity.

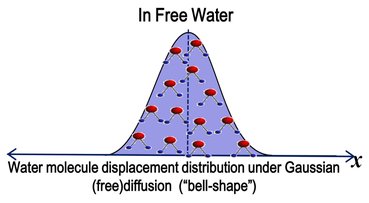
Methods

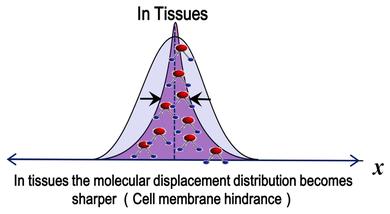
- DKI, B_0 field map, and anatomical MPRAGE T1-weighted data was acquired using a 3T Trio Siemens scanner.
- All participants were right-handed males aged 30 to 55 years old
- dMRI data preprocessing included motion and eddy current correction and distortions from B0 field inhomogeneities.
- MK, RK,AK and MD maps were calculated using in-house developed software.
- ROIs were first derived in each subject using Freesurfer processing of the T1-weighted images and then transferred into the diffusion space.
- Cognitive assessments were administered by a trained psychologist to test a range of executive cognitive functions.

Table 1. Demographic and clinical characteristics of the subjects.

	Schizophrenia (n = 18) Mean ± SD (range)	Healthy Control (n = 19) Mean ± SD (range)
Male/female	18/0	19/0
Age (years)	45 ± 6	42 ± 6
Handedness (right/left)	18/0	19/0
SES participants (score)	1.9 ± 4	4.5±1.3
SES parents (score)	3.8 ± 1.7	4.6±1.5

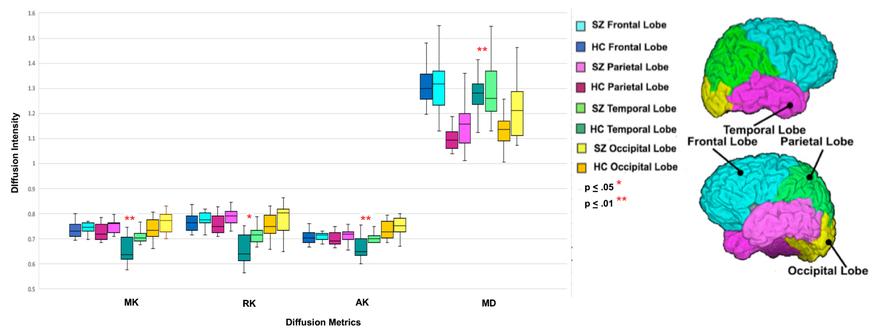


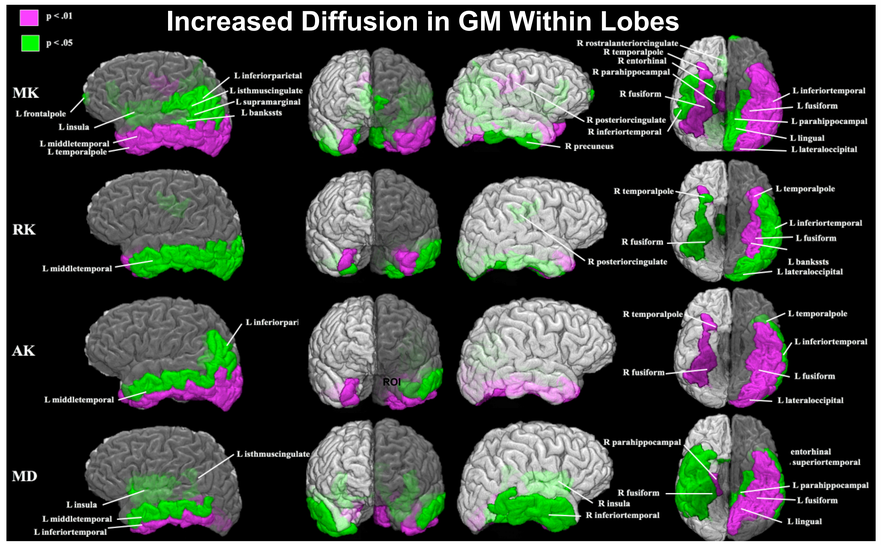




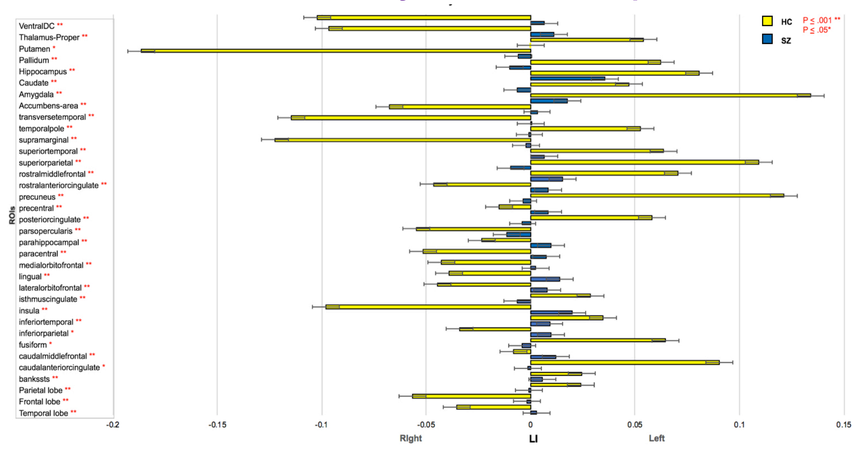
Results

Diffusion in GM of Lobes





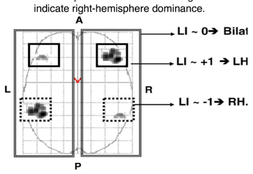
Abnormal Laterality of MK in Schizophrenia

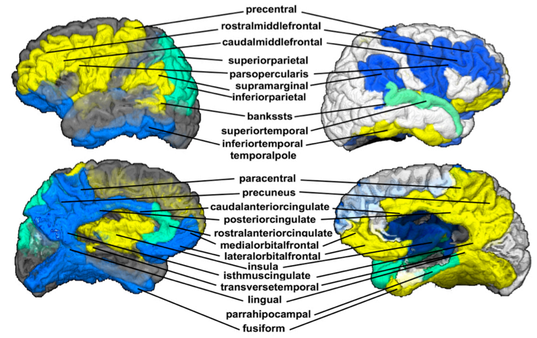


Laterality Index

$$LI=(L-R)/(L+R)$$

L represents the number of active voxels in the left-hemisphere ROI or Lobe in the brain, and R is the number active voxels in the right-hemisphere ROI or Lobe in the bra This yeilds a value of LI that -1 < LI < +1, and positive valu indicate left-hemisphere dominance and negative values indicate right-hemisphere dominance.



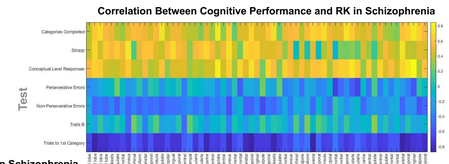


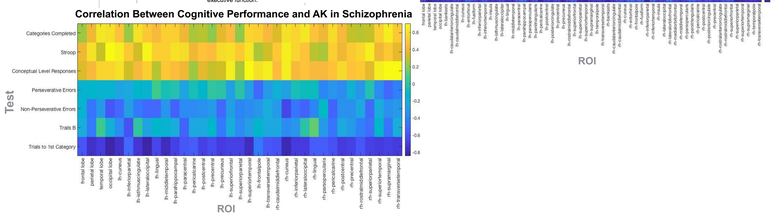
Results

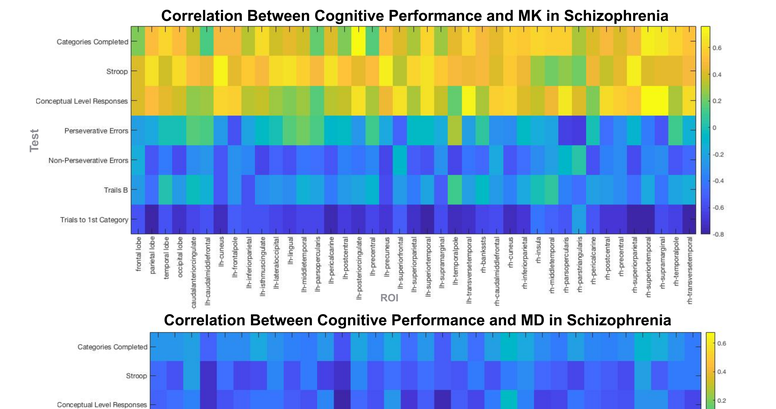
Cognitive Impairment Correlated to GM dMRI abnormalities in Schizophrenia

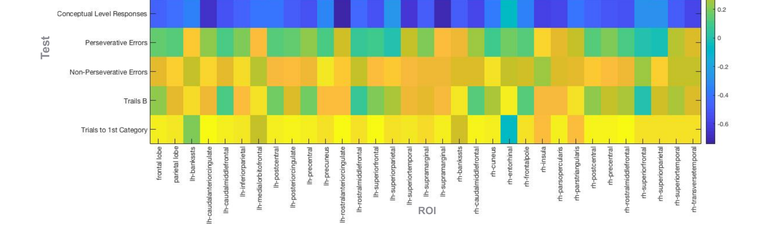
Cognitive Assessment Index

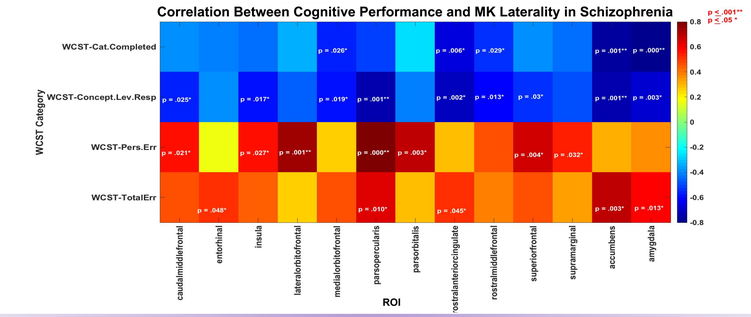
TEST	CATEGORY	FUNCTION
WCST	Categories Completed	The greater the score, the better executive function.
STROOP	Stroop	The greater the score, the better processing speed and selective attention.
WCST	Conceptual Level Responses	The greater the score, the better abstract reasoning and insight.
WCST	Perseverative Errors	The lower the score, the better perseveration function.
WCST	Non-Perseverative Errors	The lower the score, the better executive function.
TMT	Trails B	The lower the score, the better speed of processing and mental flexibility.
WCST	Trials to 1st Category	The lower the score, the better the executive function.











Conclusions

These results support our hypotheses that gray matter microstructure is altered in schizophrenia. These alterations may be a direct result of microstructural reorganization due cortical thinning or may reflect other microstructural alterations such as inflammation or dysmyelination [5]. We note that the dMRI increase pattern observed here was previously reported to reflect astrogliosis in a rat model of traumatic brain injury [4]. Future studies will further examine these hypotheses using a multimodal approach that includes Magnetic Resonance Spectroscopy and quantitative Magnetization Transfer in addition to the DKI approach.

References

1. Watsky, R. E., Pollard, K. L., Greenstein, et al. Psychiatry. 2016 *;55*(2), 130-136. 2. Seitz J, Rathi Y, Lyall A, et al. Brain Imaging Behav. 2017, in press. 3. Jensen JH, Helpern JA, Ramani A, et al. Magn Reson Med. 2005 Jun;53(6):1432-40. 4. Zhuo J, Xu S, Proctor JL, et al. Neuroimage. 2012;59:467-77. 5. Uranova NA, Vikhreva OV,Rachmanova VI, et al. Schizophr Res Treatment;2011:325789. 6. Rüsch, N. *et al.* Prefrontal-thalamic-cerebellar gray matter networks and executive functioning in schizophrenia. *Schizophr. Res.* **93,** 79–89 (2007).

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