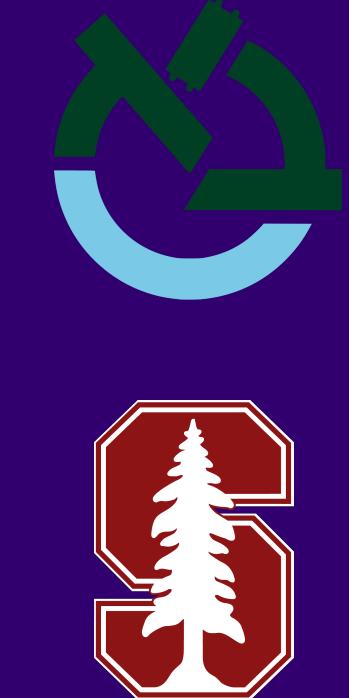


Structural cerebellar connectivity in schizophrenia: support for the cognitive dysmetria theory

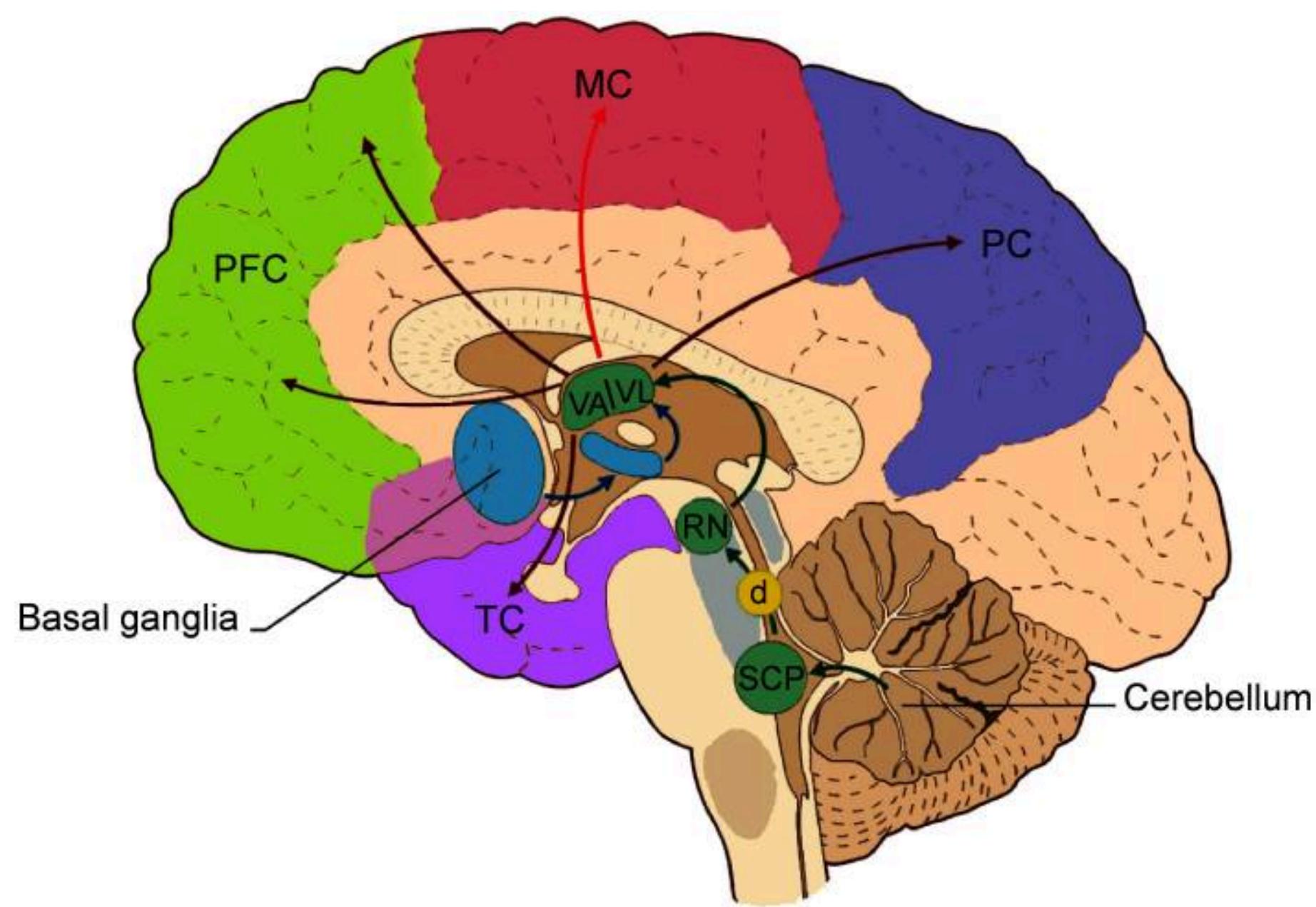


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Background

- Schizophrenia (SZ) is a neurodevelopmental psychiatric disorder that carries significant health burden.
- The *cognitive dysmetria* theory of schizophrenia posits that the core cognitive deficits arise from dysfunctions of cortical-thalamic-cerebellar (CTC) circuits. (1)
- Previous research found increased functional connectivity in the cerebello-thalamo-cortical circuits in individuals at clinical high risk for psychosis. (2)
- This hyperconnectivity was more pronounced in individuals who converted to psychosis, correlated to the severity of symptoms, and was predictive of the time to conversion.
- The cerebellum sends its output through the superior cerebellar peduncle (SCP), the contralateral red nucleus (RN), and VA/VL of the thalamus to various cerebral areas. The decussation (d) of the cerebro-thalamo-cortical pathway is indicated by the yellow circle (image taken from (3)).



QUESTION: Are the physical properties of the white matter tracts of the CTC different in individuals with SZ?

Methods

Data:

- Diffusion MRI data (64 directions, $b=1,000 \text{ s/mm}^2$) from the UCLA Consortium for Neuropsychiatric Phenomics LA5c study (Open Neuro DS00030).
- Participants: SZ (N=12F/37M, age: $36.2 \pm 8.8 \text{ SD}$), ADHD (N=20F/20M F/M age: 31.95 ± 10.3), bipolar disorder (BD; N=21F/28M, age: 35.3 ± 9.0), Healthy control (HC 58F/65M, age: 31.6 ± 8.8).

Processing:

- QSIPREP (4) and pyAFQ (5) for preprocessing, QC, and tractometry (FA/MD tract profiles).
- Bilateral SCP were identified in each individual using anatomical criteria that capture the decussation (6).
- Group-blinded QC of SCP bundle was conducted by two expert observers (TG and AR).

Analysis:

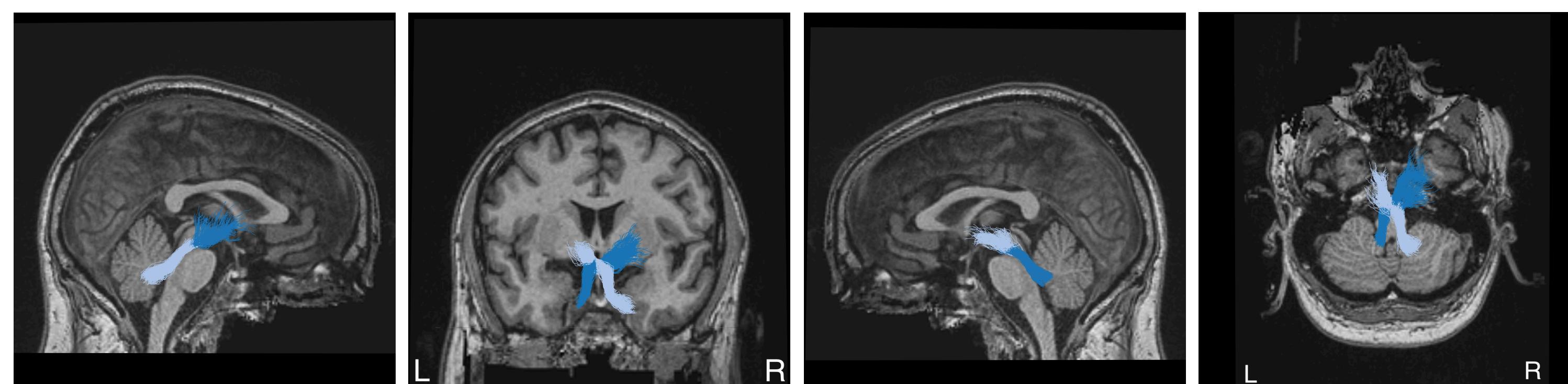
- Data quality confounds were mitigated by matching each SZ/ADHD/BD to a HC with similar age, sex and data quality (neighbor correlations, NDC).
- Generalized additive models (GAMs) for FA and MD in each SCP as (7):
$$\text{FA/MD} \sim \text{group} + s(\text{nodeID}, k, \text{by}=\text{group}) + \text{age} + \text{sex} + \text{QC} + s(\text{subjectID}, \text{bs}=\text{"re"})$$

with k chosen to minimize AIC and neighbor correlations (8) for QC.

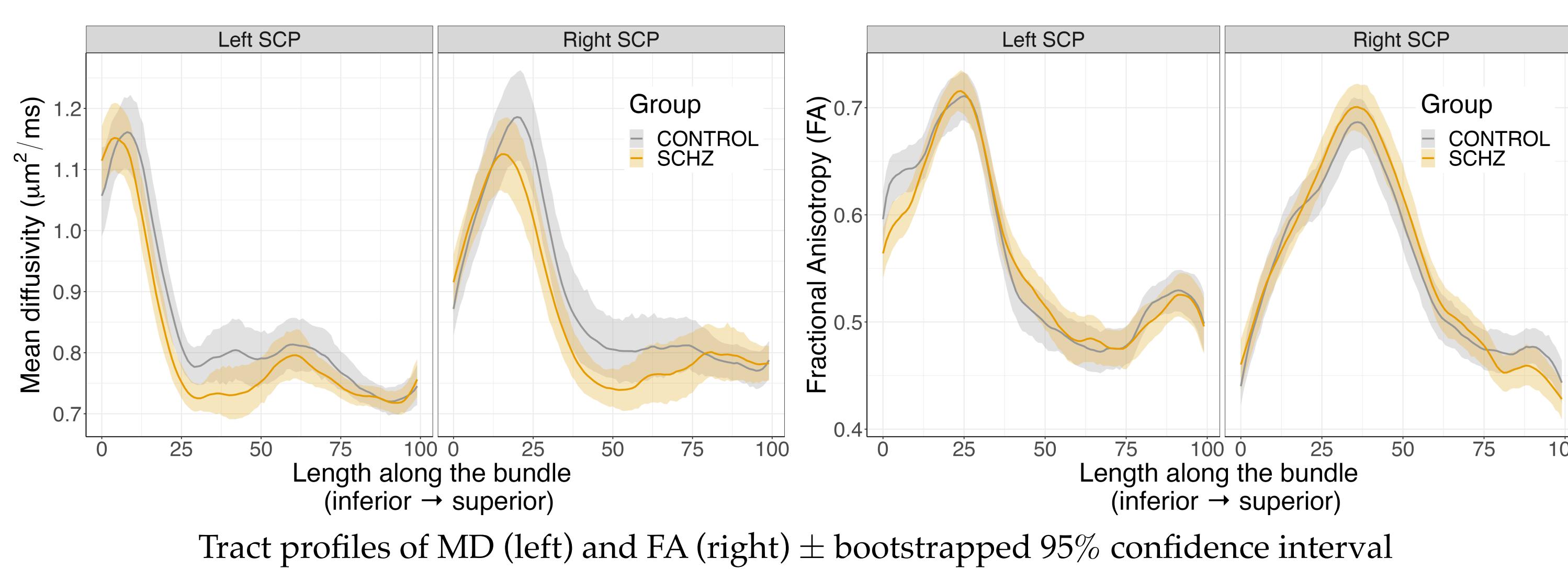
Acknowledgements

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Results



The left (dark blue) and right (light blue) SCP bundles visualized in an individual with SZ, with sagittal, coronal and axial anatomical views of the T1-weighted scan of this individual.



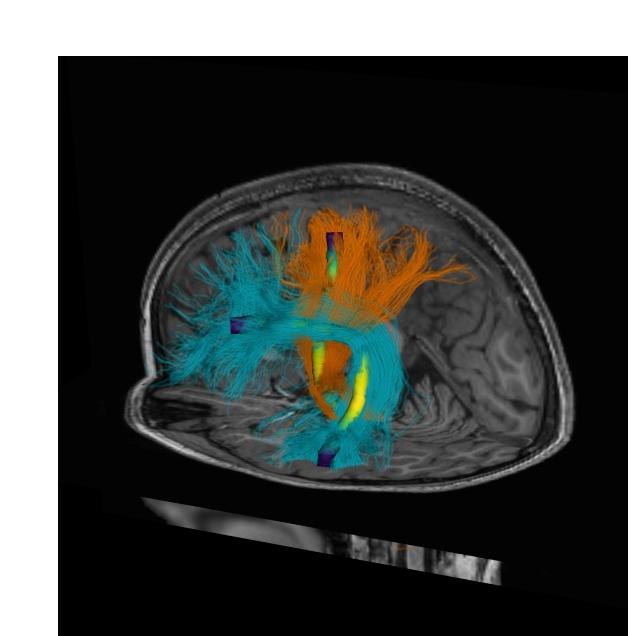
- MD differed significantly in the left superior cerebellar peduncle (SCP) between the SZ and HC groups ($p<0.05$), but not between the ADHD and HC groups or BD and HC groups.
- Individuals with SZ had lower MD in this tract than the matched controls (as indicated).
- This finding held after adding medication as a covariate (haloperidol equivalent dosage).

Conclusions

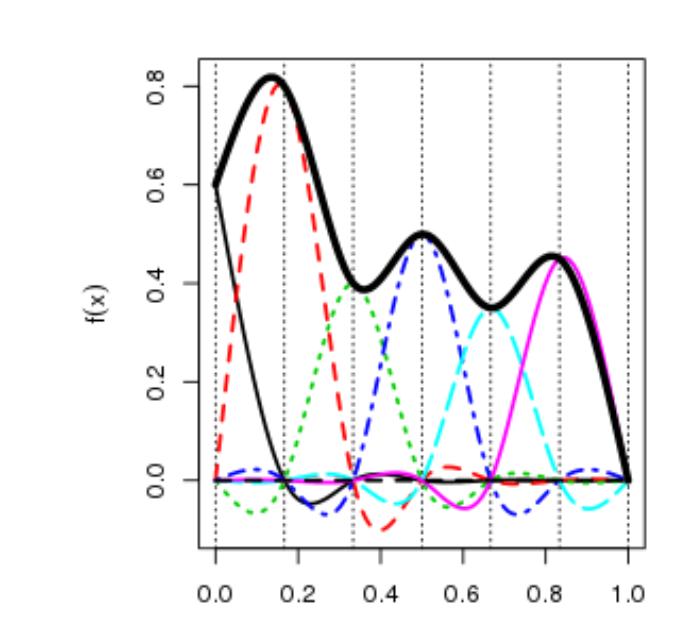
- We found decreased MD in SZ in the left SCP, a component of the CTC.
- In line with fMRI results that found increased functional connectivity in CTC in SZ. (2)
- Provides additional support for the cognitive dysmetria theory of SZ.

Software

pyAFQ: Automated Fiber Quantification / tractometry



Tractable: Statistical analysis tract profiles in R



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