

# Structural cerebellar connectivity in schizophrenia

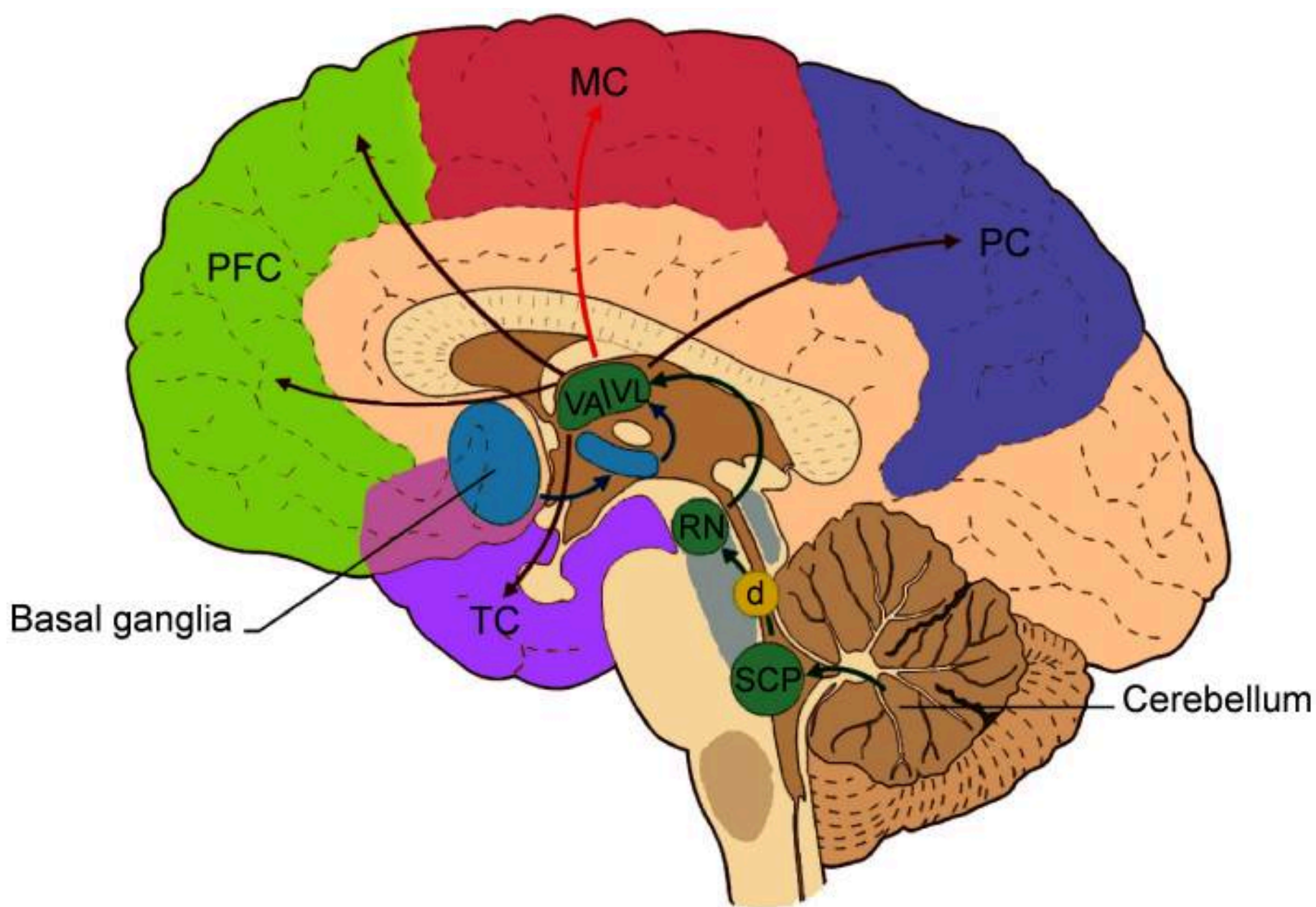
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## Background

- 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.

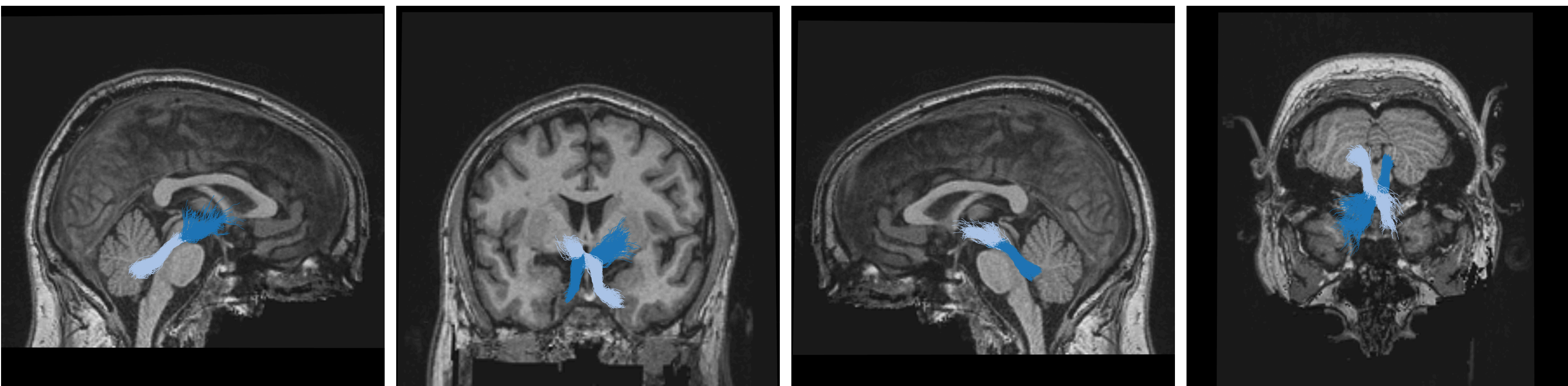


The cerebellum sends its output through the superior cerebellar peduncle (SCP), the contralateral red nucleus (RN), and VA/VL of the thalamus to various cerebral areas... The decussation (d) of the cerebro-thalamo-cortical pathway is indicated by the yellow circle. (3)

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

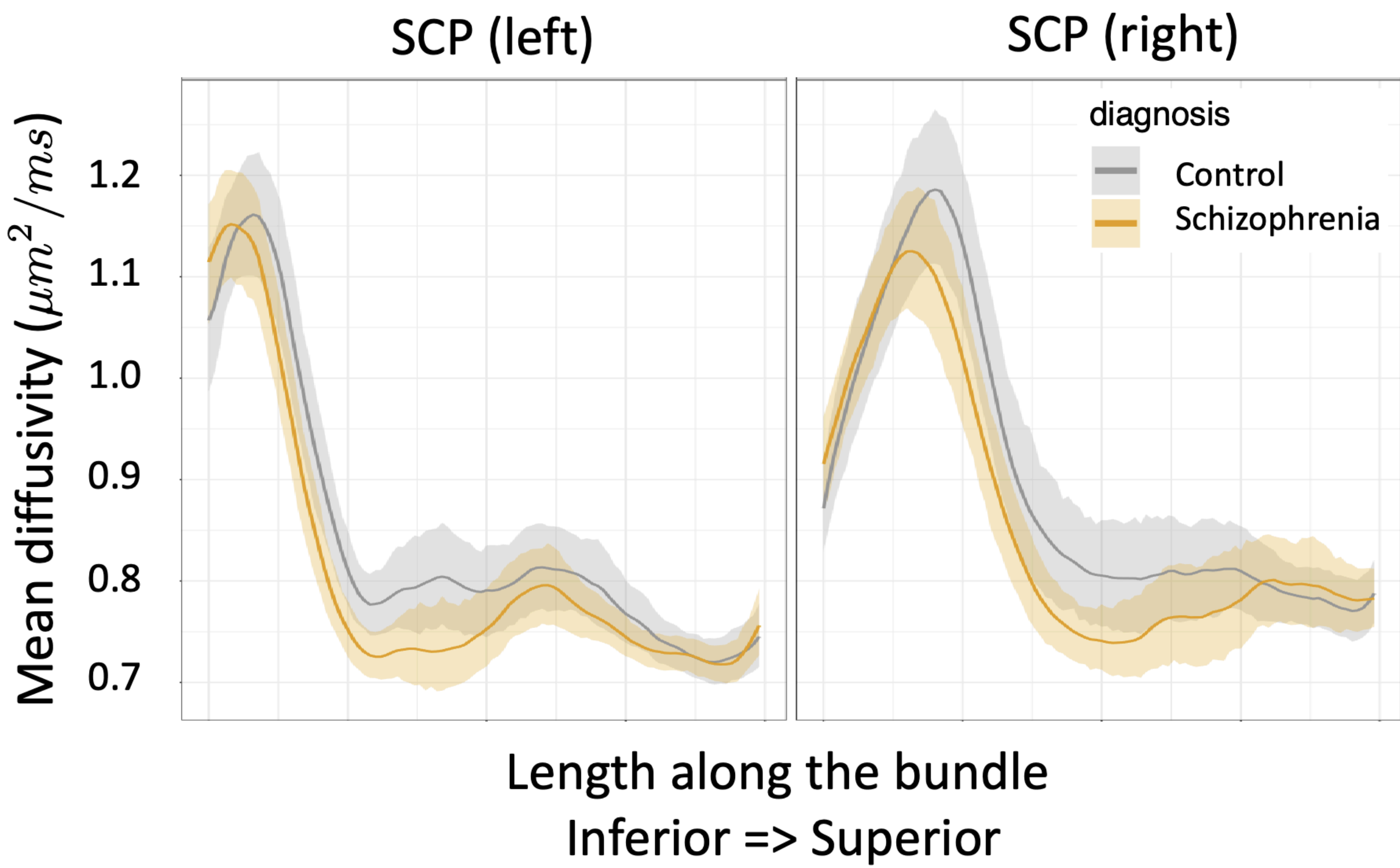
## Methods

- **Data:** the UCLA Consortium for Neuropsychiatric Phenomics LA5c Study (4), which includes diffusion MRI (dMRI) data from 49 participants with SZ (mean age: 36.2 +/- 8.8 SD; 12 female), 40 participants with ADHD (mean age: 31.95 +/- 10.3 SD; 20 female), 49 participants with bipolar disorder (BD) (mean age: 35.3 +/- 9.0 SD, 21 female), and 123 controls (CTRL) (mean age: 31.6 +/- 8.8 SD; 58 female).
- The data were processed using QSIPREP (5) and pyAFQ (6) (7)
- The SCPs were identified in each individual using pyAFQ and anatomical criteria that capture the decussation of these bundles. (8)
- This resulted in tract profiles of fractional anisotropy (FA) and mean diffusivity (MD) in each white matter pathway (100 nodes each).
- We then fit generalized additive models (GAMs) for FA and MD in each bundle as a function of diagnosis (entered as a factor: SZ or CTRL), nodeID (modeled with an adaptive smooth, where degree of the smooth is determined as the k that minimizes the AIC), age, sex (entered as a factor) and data quality (quantified as the neighbor correlation from QSIPREP). (9)



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.

## Results



- MD differed significantly in the left superior cerebellar peduncle (SCP) between the SZ and CTRL groups ( $p < 0.05$ ), but not between the ADHD and CTRL groups or BD and CTRL groups.
- Individuals with SZ had lower MD in this tract than the matched controls.
- This finding held after adding medication as a covariate (haloperidol equivalent dosage).
- No other significant differences were found.

## Conclusions

- We found decreased MD in the left SCP, a component of the CTC.
- Lower MD may indicated increased myelination and therefore increased connectivity.
- Increased density and directional coherence (but not axonal diameter) may also have similar effects on MD.
- These results appear in line with previous fMRI results that found increased functional connectivity in the CTC in individuals with SZ. (2)
- This provides additional support for the cognitive dysmetria theory of SZ.

## Acknowledgements

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## References

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