A Quantitative Tractography Approach for Exploring Associations Between White Matter Pathways and Cognitive Functions

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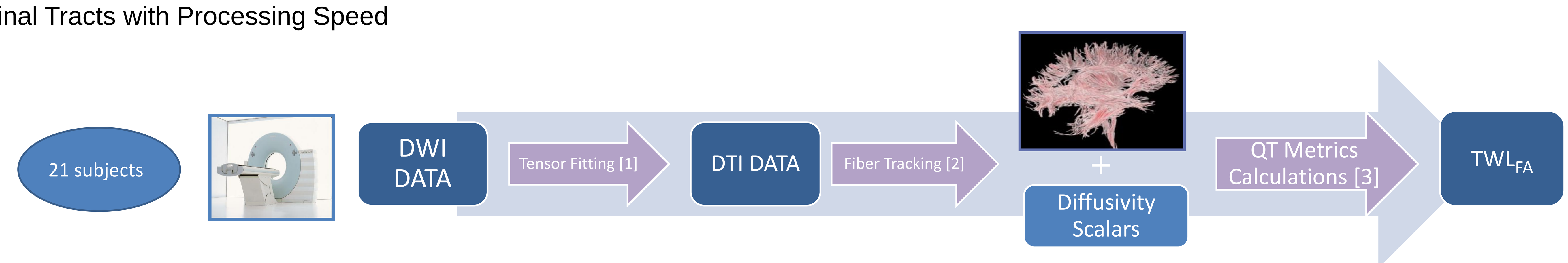
Contributions

Identified the following associations between white matter pathways and cognitive functions:

- Superior Longitudinal Fasciculus with Working Memory, Processing Speed, and Motor Speed
- Left Corticospinal Tract with Motor Speed
- Left Cingulum Bundle and Corticospinal Tracts with Processing Speed

Demonstrated that quantitative tractography (QT) metrics are more effective than diffusivity scalars alone in exploring these relationships

Methods



- 12 patients with CADASIL (age = 52.09 ± 7.37) and 9 healthy subjects (age = 53.17 ± 5.21)
- Double spin-echo, echo-planar diffusion-weighted sequences were obtained on a 1.5T Siemens Symphony scanner (12 directions, b=1000 s/mm²).
- After tensor fitting, a fiber tracking algorithm was used to generate whole brain tractography models. Streamtubes started at a seed point and continued through the major eigenvector field. Second-order Runge-Kutta integration was used to find the trajectory of a streamtube passing through a seed point. The algorithm minimizes redundancy through a careful seeding and culling process.
- Expert raters selected the following tracts (bilaterally): the corticospinal tracts (CST), cingulum bundles (CB), superior longitudinal fasciculi (SLF), inferior longitudinal fasciculi (ILF), and the genu and splenium of the corpus callosum (Fig.1). We calculated the total fiber length weighted by fractional anisotropy, linear anisotropy, as well as mean, radial, and axial diffusivity (TWL_{FA}, TWL_{CL}, TWL_{MD}, TWL_{RD}, TWL_{AD} respectively).
- Cognitive domains and the measures used to assess them were as follows: Processing Speed (Trail Making Test part A & Symbol-Digit Modalities Test; Stroop Color-Word Test); Working Memory (verbal 2-back); Executive Functions (Trail Making Test part B); Motor (Grooved Pegboard Test, dominant hand only) and Visual Naming (Boston Naming Test).
- Based on previous research we formulated the following hypotheses: verbal working memory would be associated with QT metrics in the superior longitudinal fasciculus (SLF) but not the inferior longitudinal fasciculus (ILF); motor speed and dexterity would be associated with the corticospinal tract (CST) but not the ILF or splenium of the corpus callosum; processing speed would be associated with the cingulum bundles (CB) and genu of the corpus callosum; executive functions (i.e., cognitive switching) would be associated with widespread white matter regions but not in inferior regions (i.e., ILF); visual naming would not show significant associations with any white matter pathways.
- Associations were assessed in the entire sample using bivariate Pearson correlation.

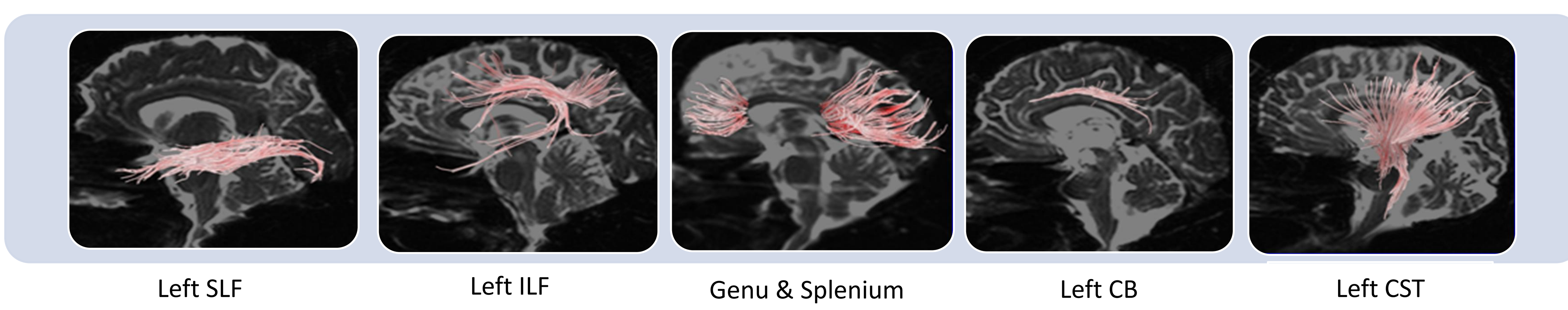


Figure 1: Selected Tracts

Results

- Groups did not differ significantly by age (p = .712).
- The CADASIL group had significantly lower values of QT metrics in all tracts except the left ILF and performed significantly more poorly on all cognitive measures except visual naming.
- All QT metrics were highly correlated among each other. They also correlated well with the diffusivity scalars
- Significant correlations are summarized in Table 1. These values come from one of the QT metrics (TWL_{FA}) since they all followed the same pattern.
- Overall, correlations of cognitive functions with fiber tract integrity remained when QT metrics were substituted with diffusivity scalars, except in the CST-Processing Speed case. Correlation factors were exclusively lower, however.

	Processing Speed	Motor Speed	Working Memory
Right SLF	r=-.719,p=.000	r=-.545,p=.011	r=.544,p=.011
Left SLF	r=-.632, p=.002	r=-.498,p=0.021	r=.538,p=.012
Left C B	r-=-.573,p=.007		
Right CST	r=-.505,p=.019		
Left CST	r=-.522, p=.015	r=-.648,p=.001	

Table 1: Summary of significant correlations

Discussion

Results generally confirmed our hypothesized pattern of significant and non-significant correlations. Significant correlations were extended to white matter pathways and cognitive function pairs for which we had no hypothesis. This is not unexpected given that performance on the cognitive tests used in this study is not orthogonally dependent on specific brain regions or networks.

As expected, visual naming, which is less dependent on the integrity of white matter pathways than the other functions, did not correlate with TWL_{FA} in any pathway.

The lack of associations between executive function and white matter pathways and between the genu and splenium and any cognitive function may be due to insufficient power resulting from the small sample size.

Our findings however support speculations that relate the SLF to motor control, processing speed, and working memory, based on the cortical regions these fibers interconnect [4].

Since right hand motor functions are controlled by the left hemisphere, performance in motor tasks should correlate with structural variations in left hemisphere tracts -- and it does.

Our subjects were all right handed. CSTs, known to carry signals that control motor function, exhibit lateral bias during motor tasks. Structural integrity of the left CST strongly correlates with motor performance, but that of the right CST does not. Correlations between right and left CST with processing speed could result from the motor component in tasks that assess this function, as well as the wide span of cortical area that CST fibers project on.

Correlation of the left, but not the right, CB with processing speed could also result from the effect of a motor component in processing speed assessment.

Conclusion

Our results demonstrate that it is possible to dissociate specific relations between cognitive functions and white matter pathways using quantitative tractography.

Future studies, with larger samples, targeting more discrete cognitive functions and more specific functional subdivisions of white matter pathways may help refine our current results.

References

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[4] Johansen-Berg & Brehens: Diffusion MRI, C.11

Acknowledgement

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