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

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Contributions: We explored the utility of quantitative diffusion-tensor tractography (QT) metrics to identify associations between specific cognitive functions and the structural integrity of specific white matter pathways.

Background: QT assesses the structural integrity of entire white matter pathways. Prior studies have shown associations between diffusion tensor imaging (DTI) scalar parameters and cognitive functions in cortical white matter [1] ,but we are unaware of studies that have demonstrated such associations using QT. Epstein et al. [2] showed an association between QT metrics in the superior longitudinal fasciculus and working memory in patients with CADASIL (Cerebral Autosomal Dominant Arteriopathy with Subcortical Infarcts and Leukoencephalopathy), an inherited form of subcortical vascular dementia. Based on previous research we predicted associations between QT metrics in specific white matter pathways and cognitive functions in a sample of patients with CADASIL and healthy controls. These predictions are tabulated together with results.

Methods: Participants were 12 patients with CADASIL (age = 52.09 ± 7.37) and 9 healthy subjects (age = 53.17 ± 5.21). DTI data was collected using a double spin-echo, echo-planar diffusion-weighted sequence on a 1.5T Siemens Symphony scanner (12 directions, b=1000 s/mm^2). Data volumes were seeded at a density of one seed per .85mm^3. Streamtubes start at a seed point and continue through the major eigenvector field. Second-order Runge-Kutta integration was used to find the trajectory of a streamtube passing through a seed point[3]. 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. We calculated the total fiber length weighted by FA (TWL_{FA}) [4] averaged across all fibers in each tract. 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). Average age-corrected T-scores were calculated for domains measured with more than one test. Associations between TWL_{FA} and cognitive metrics were assessed in the entire sample using bivariate Pearson correlation. Alpha was set to $p < .025$ as a balance between guarding against Type I and Type II error in this exploratory study with a small sample.

Results: The groups did not differ significantly by age ($p = .712$). The CADASIL group had significantly lower values of TWL_{FA} in all tracts except the left ILF and performed significantly more poorly on all cognitive measures except visual naming.

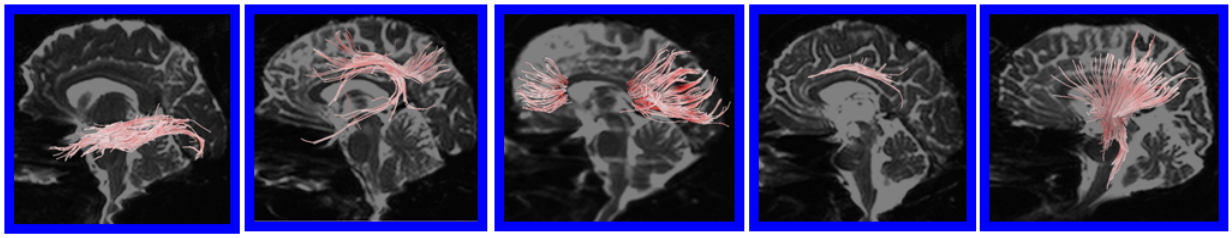

Figure 1. Selected tracts: left ILF, left SLF, Genu, Splenium, left Cingulum Bundle, left CST

	Processing Speed	Executive Function	Motor Speed	Visual Naming	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=.021	– √	+ √ r=.538, p=.012
Right ILF		– √	– √	– √	
Left ILF		– √	– √	– √	
Right C. B.	+ X			– √	
Left C. B.	+ √ r=-573, p=.007			– √	
Genu	+ X	+ X		– √	
Splenum		+ X	– √	– √	
Right CST	○ r=-.505, p<.019		– √	– √	
Left CST	○ r=-.522, p<.015		+ √ r=.648, p=.001	– √	

Table 1. Summary of hypotheses (+ expected correlation, – expected disassociation, ○ no hypothesis) and findings (√ hypothesis supported, X hypothesis not supported)

Discussion: The results generally confirmed our hypothesized pattern of significant and non-significant correlations but were more consistent for our predictions of non-significance. Significant correlations were not restricted to the white matter pathways we hypothesized; they extended to other (but not all) pathways. This is not unexpected given that performance on the cognitive measures 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 measures, 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 have resulted from failure to select the relevant pathways, lack of cognitive measures needed to show an association, or to insufficient power due to small sample size. Our results, however, demonstrate that it is possible, even in a small sample, to dissociate specific associations between cognitive functions and certain, but not all, white matter pathways, using quantitative tractography.

References: [1]Johansen-Berg & Behrens: Diffusion MRI, C.11 [2]S. Epstein et al. INS. 2008 [3]S. Zhang et al. IEEE Trans. Vis. Comput. Graph. 2003 [4]S. Correia et al. NeuroImage. 2008