

Title: Investigating cognitive control in Multiple Sclerosis using diffusion MRI tractography

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Structured Abstract:

Introduction: Multiple Sclerosis (MS) is a progressive, inflammatory, and demyelinating condition characterized by extensive lesions in the central nervous system. Consequently, about half of MS patients will experience a form of cognitive impairment, of which the causal links remain poorly understood (Rao et al., Neurology, 1991). Diffusion MRI tractography can be used to probe white matter connections that link grey matter regions to one another. Such methods can be used to interrogate the corticostriatal circuit which plays a fundamental role in aspects of cognition. To that end, we (1) used a data-driven tractography approach to classify the corticostriatal circuit, and (2) investigated correlates of structural MR measures with a measure of information processing speed. We hypothesize that MS pathology implicated in corticostriatal circuitry leads to reduce cognitive function.

Methods: T1-weighted (T1w) and multi-shell diffusion MRI (dMRI) scans were acquired at 7 Tesla from MS patients (n=14) recruited from London's MS clinic. Each participant performed a cognitive battery which included the PASAT, a measure of information processing speed. The T1w scans were preprocessed using FreeSurfer (v6.0.0), and the dMRI scans were preprocessed using software from github.com/khanlab/prepdwi. Probabilistic tractography was performed by seeding in standard space from grey matter to generate a connectivity matrix of streamline visitation counts for each of 68,539 seeds to 80,090 possible targets (voxels in standard space). This matrix was reduced using a principal component analysis, followed by independent component analysis imposed on the seed-space to identify 50 grey matter networks. A network that included the dorsal lateral prefrontal cortex (DLPFC) involved in the corticostriatal circuit was identified and used as region of interest to extract quantitative-T1 (qT1) values. A general linear model was used to examine the relationship between qT1 and PASAT performance.

Results: Analyses identified prefrontal grey matter networks composed of cortical and striatal components. Organization of corticostriatal circuitry matched topographical gradients described in track tracing experiments, specifically a ventral to dorsal, and a medial to lateral gradient (Haber et al., Dialogues in clinical neuroscience, 2016). PASAT score was significantly correlated to average qT1 from the DLPFC ($B=-0.0138$, $p=0.046$), but not with its subcortical counterpart ($B=-0.0110$, $p=0.141$).

Discussion: Myelin is a dominant source of contrast in T1w images. The results of the current study suggest that demyelination (increase in qT1) of the DLPFC is associated with reduced information processing speed. Further investigation into the role of corticostriatal circuitry in cognitive impairment within the MS population is needed.