The use of diffusion-weighted imaging to assess structural brain connectivity in early demyelinating clinically-isolated syndrome – a preliminary analysis

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Introduction

The use of magnetic resonance imaging (MRI) in demyelinating clinically-isolated syndrome (CIS) is well-described. Here we explore how connectivity analysis from diffusion-weighted imaging (DWI) can be applied to patients with CIS, and its relationship to clinical outcomes.

Methods

44 patients with CIS and 16 healthy controls (HC) were prospectively recruited between 2014 and 2017 and followed-up clinically and radiologically at 6, 12 and 36 months. Disability was assessed with the extended disability status scale (EDSS) and multiple sclerosis functional composite (MSFC). Conversion to multiple sclerosis (MS) was defined using the 2017 McDonald criteria.

Multi-shell DWI was acquired at each visit, as well as conventional sequences of the brain and spinal cord. After DWI post-processing with denoising and correction, a connectome from baseline imaging was generated using the FMRIB Software Library (FSL) and MRTrix, and connectivity metrics produced with the Brain Connectivity Toolbox. Global efficiency, mean local efficiency, transitivity, assortativity coefficient, mean node strength and mean betweenness centrality were investigated. Statistical analysis was performed with R.

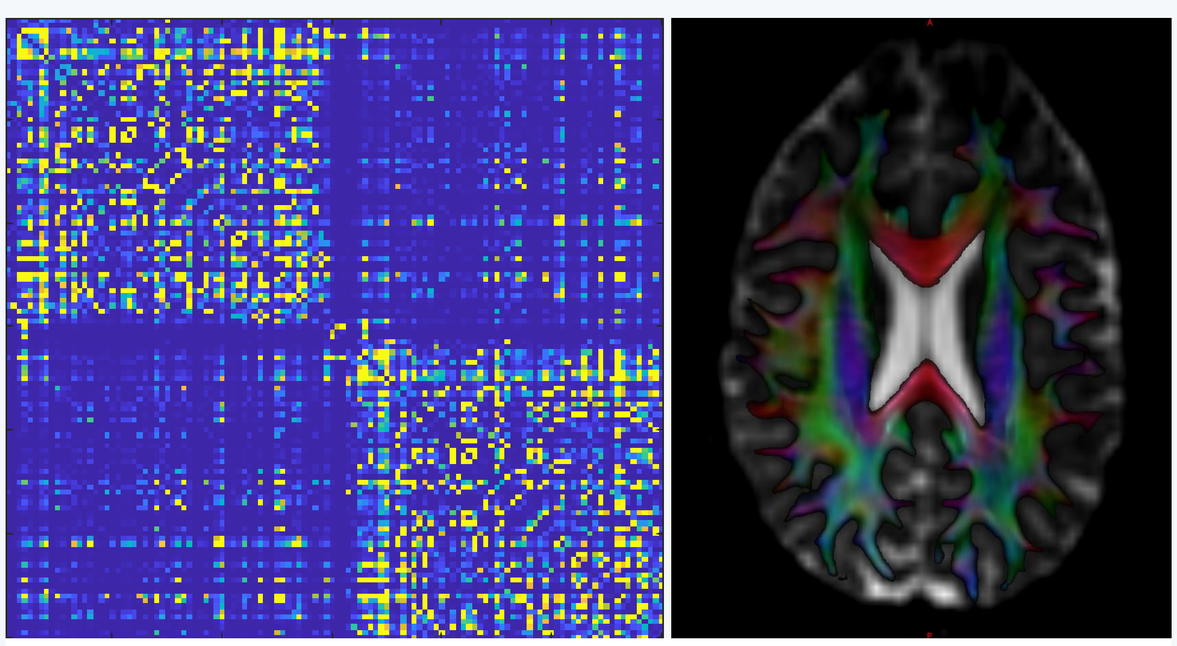

Figure 2: A structural connection network generated with FSL and MRTrix (L), and a track density image representing the generated streamlines (R)

	EDSS		Lesion Volume	
Metric	**Correlation**	**P value**	**Correlation**	**P value**
Global Efficiency	-0.248	0.105	-0.017	0.913
Mean Local Efficiency	**-0.307**	**0.043**	-0.172	0.263
Transitivity	**-0.318**	**0.035**	-0.219	0.152
Assortativity Coefficient	0.282	0.064	0.100	0.520
Mean Node Strength	-0.271	0.075	-0.061	0.694
Mean Betweenness Centrality	0.271	0.075	**0.328**	**0.030**

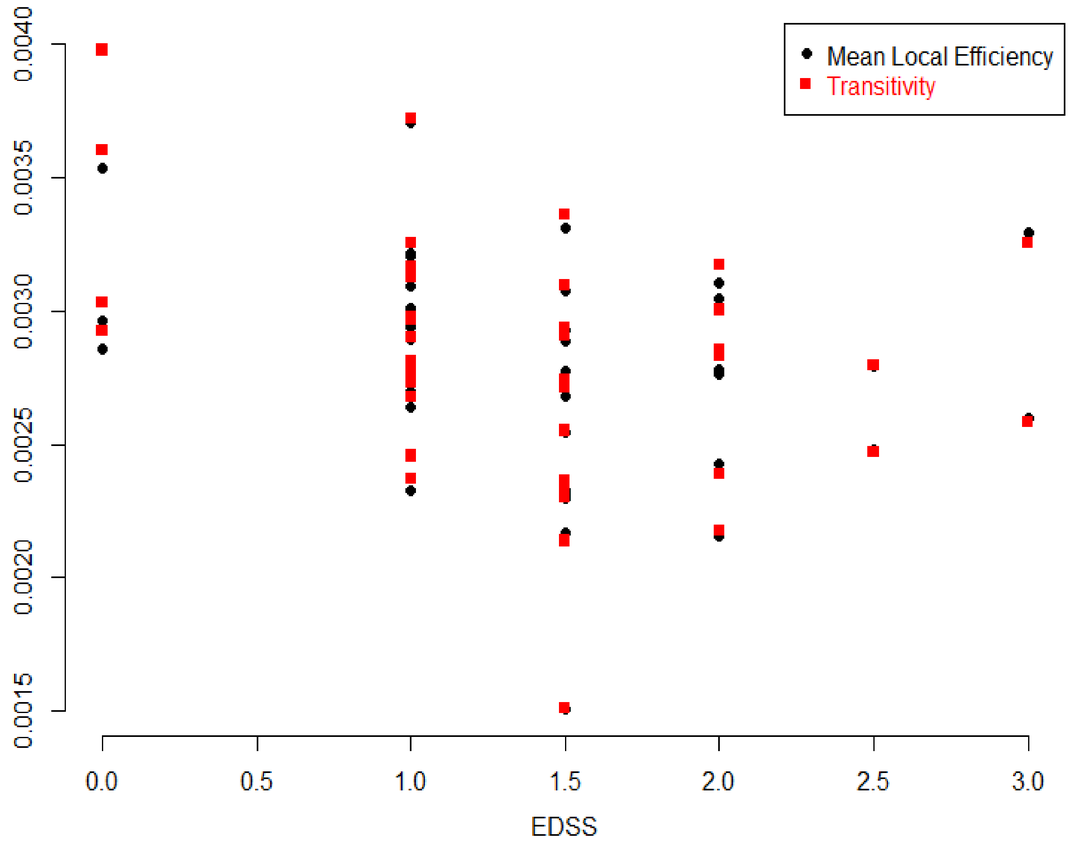

Figure 1: Mean local efficiency (black) and transitivity (red) plotted against EDSS, all at baseline

Results

Disease state of 33 patients was known at 36 months. 6 remained as CIS, with an average of 10 T2-hyperintense lesions at baseline (range 0-21). 27 had developed MS, with average 37 lesions at baseline (0-121); 11 patients had baseline gadolinium enhancement. Mean EDSS change from baseline to 36 months was -0.3 (-1.5 to 1.5).

At baseline, two metrics had significant correlation with EDSS: greater EDSS was associated with lower mean local efficiency (rho= -0.31, p=0.04) and lower transitivity (rho= -0.32, p=0.04). Also, greater baseline total lesion volume was correlated with greater mean betweenness centrality (rho=0.33, p=0.03). For MSFC components, faster 25-foot timed walk was associated with a higher assortativity coefficient (rho=0.39, p=0.01).

No significant differences were detected in connectivity between patient and HC groups at baseline, or between patients with MS or CIS at 36 months.

Interpretation

The negative correlation between connectivity metrics and EDSS suggests they reflect mechanisms underlying disability in CIS. The lack of overall difference between patients and HCs may reflect the low sample size, or might suggest a window of opportunity for treatment in early MS to maintain structural connectivity. Further longitudinal analyses are planned.

Disclosures

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