INNOVATIVE COMPUTATIONAL STUDY OF BRAINS AFFECTED BY MS

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Introduction

Multiple sclerosis (MS)

- Neurodegenerative autoimmune disease
- Immune system targets central nervous system (CNS)
- White blood cells enter the CNS, produce destructive inflammation
- Triggered chemical responses lead to lesion formation, disruption of structural and functional connections between brain regions
- Axonal disruption believed to lead to grey matter cell death (atrophy) via Wallerian degeneration (WD)

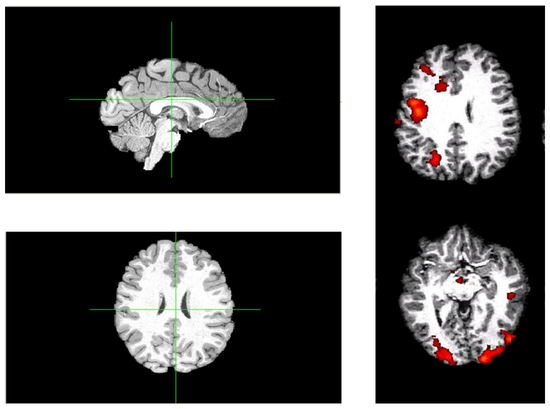

Figure 1: Structural (left) and functional (right) MRI Data

Magnetic Resonance Imaging (MRI)

- Method of in vivo assessment of anatomy and physiology
- Strong magnetic field aligns nuclear spin of protons, in particular, hydrogen atoms
- Radiofrequency pulses excite proton spin, realignment releases electromagnetic energy
- Magnetic field gradient allows localization
- Speed of energy released differentiates molecular composition of tissue
- Various imaging modalities and enhancements, e.g., T1w, T2w, diffusion
- Functional MRI detects neural activity as a result of oxygenated blood levels increasing within activated brain regions
- Increased oxygen level causes signal fluctuation which translates to fMRI data

Aim

The goal of our research is -

- To derive connectomics data from MRI of MS
- To analyze the brain as a network, measuring connection and lesion based disconnection of regions
- Leverage neuropsychological data to investigate the impact of lesions and atrophy on cognition and personality

Results will lead to advancement of therapeutic approaches in treatment and an improved understanding of MS

Methods and Results

Dis-connectomics

- Term coined to describe structural connectome disruption
- Employ Network Modification (NeMo) Tool to overlay lesions derived from MRI on database of healthy structural connectome data
- Measures of probable disconnection may be determined
- Machine learning used to model and predict the effects of disconnection on cognition and personality

Dis-connectomics Results

- Regional disconnection correlates with regional atrophy indicative of WD

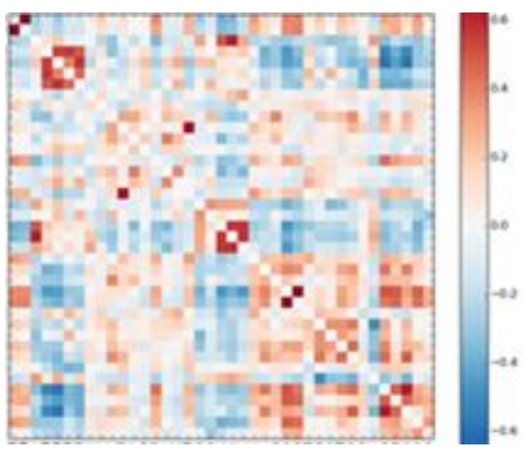

Figure 2: Connectivity matrix illustrating relative connection strengths between brain regions

Methods and Results (cont'd)

Probabilistic Tractography

- Map water diffusion through probabilistic path illustrating white matter tracts connecting regions
- Generate structural connectivity matrices in DSI Studio

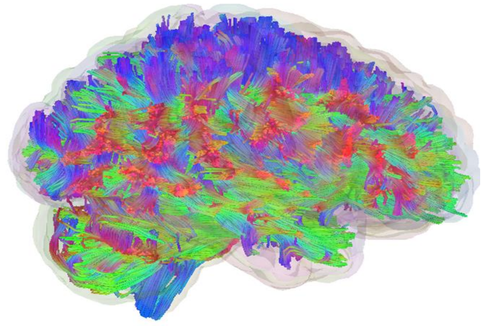

Figure 3: Mapped connectome via probabilistic tractography

Functional Connectome

- Established resting state functional networks are template for expected resting state activation patterns
- De-noise based on these expected activation patterns
- Generate functional connectivity matrices from de-noised data, representing correlation of activity between brain regions across time
- Matrices describe functional connectivity of networks disrupted by disease pathology

Network Based Statistical Analysis

- Employ dis-connectome matrices from the NeMo tool
- Generate weighted connectome matrices where disconnection from lesions of different types contribute according to the amount white matter damage inflicted
- Perform network based statistical analyses with neuropsychological measures accounting for statistical controls
- Identifies brain regions which are significantly associated with the neuropsychological outcomes of interest

Methods and Results (cont'd)

Neuropsychological Measures

- Extensive screening including cognitive and personality measures
- For example, the symbol digit modalities test (SDMT) quantifies working visual memory and cognitve processing speed

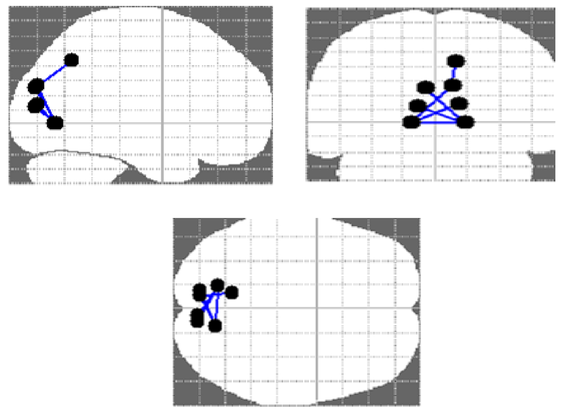

Figure 4: Damage to occipital network found significantly associated with lower SDMT scores in people with MS

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