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MSc Computational Neuroscience
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Master Thesis

TMS Evoked Potentials in Alzheimer's Disease: A Whole-Brain Computational Model Approach

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Abstract

Aim: Non-pharmacological approaches in Alzheimer's Disease (AD) have gained significant interest due to the limited effectiveness of current pharmacological treatments. Non-invasive brain stimulation techniques such as Transcranial Magnetic Stimulation (TMS) have shown promise. TMS-evoked potentials (TEP) up to 300ms have been shown to differ significantly in excitability and are used for diagnosing and evaluating AD's progression.

This study looks at AD as a "circuitopathy" and utilizes connectivity-informed whole-brain computational modeling to simulate AD, Mild Cognitive Impairment (MCI), and Healthy Control (HC) brains. The aim was to replicate the varying amplitudes of TEPs observed in individuals with AD and gain a better understanding of their underlying causes.

Method: Data from 5 AD, 5 MCI, and 5 HC participants from the Alzheimer's Disease Neuroimaging Initiative is used.

Personalized TMS electric fields are simulated using SimNIBS. The T1 and T2 MRI brain scans of each participant are used to create a head model, onto which a TMS figure-8 coil is placed posteriorly over the primary motor cortex. The electric field is simulated using finite element method.

TVB platform is used to construct a personalized whole-brain network model for each participant. The brain is divided into 360 regions, each populated by the Jansen Rit neural mass model to replicate local brain activity. Regions are connected using connectome matrices derived from diffusion-weighted and structural MRI scans, to simulate global brain dynamics.

TEPs are generated for each participant by simulating the brain network model with their respective TMS electric field as the stimulus. Global model parameter exploration and dynamical system analysis is used to investigate the factors contributing to the inter-group differences in the amplitude of the P30 component.

Result: The study successfully replicated higher P30 amplitudes in AD than HC and MCI, consistent with findings in existing literature. Simulated P30 amplitudes were significantly higher in AD, than in HC, than in MCI. The analysis indicated that these variations in P30 amplitudes were primarily influenced by differences in cortical geometry resulting from atrophy. Moreover, the simulated P30 amplitudes in AD were mildly correlated with the decline in cognitive function as measured by MMSE scores.

This study is the first to establish a robust and empirical data-driven whole-brain modeling pipeline for recreating and investigating the effects of TMS in AD. This paves way for future multiscale explorations of TMS in AD by utilizing modeling parameters.