Functional Asymmetry in Alzheimer's Disease: A computational approach using TheVirtualBrain (TVB)

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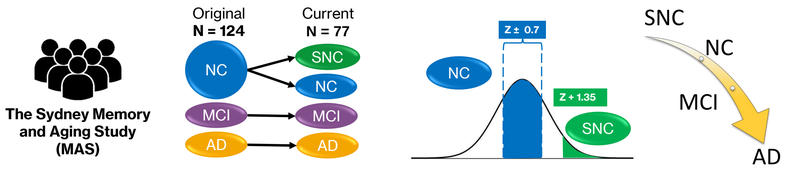
INTRODUCTION

Alzheimer's Disease (AD), the most prevalent form of dementia is associated with widespread brain degeneration. Interestingly, asymmetry of its neuropathological manifestations between left and right hemispheres have been reported from the aggregation of Amyloid-Beta and Tau to regional atrophy and anatomical functional connectivity.

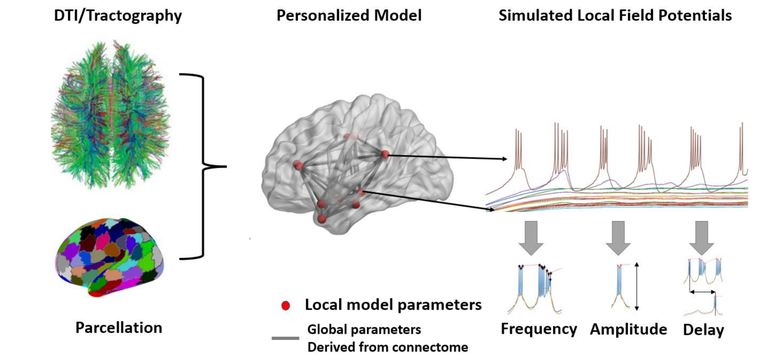
Even with the great amount of data on the neuropathology of AD, we still lack curative treatments. It maybe due to lack of knowledge in disease mechanism. In this context, TheVirturalBrain have uncovered evidence of mechanisms associated to changes in brain dynamics (Zimmermann et al., 2018; Stefanovski et al., 2019; Triebkorn et al., 2022). In this study, we used several computational biophysical methods to explore changes of brain asymmetry in AD.

METHODS // MATERIALS

Participants



Model-Base Analysis: TheVirtualBrain

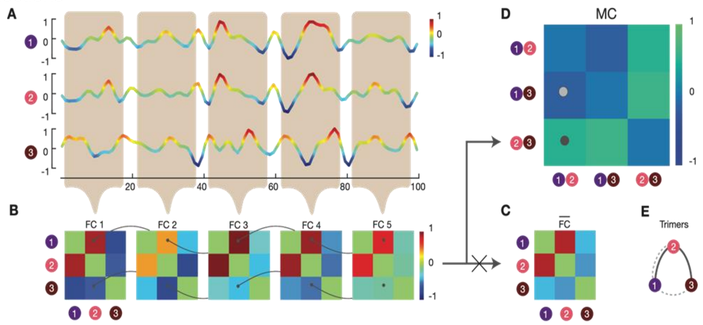


Simulation of LFPs: Empirical input: Tract weights and lengths (DTI); Local biophysical model: Stefanescu-Jirsa 3D model

Model-Free Analyses

1. DTI Structural Connectivity: Weights and Lengths: intra-hemispheric and interhemispheric connectivity

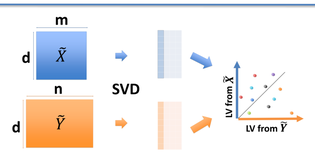
2. Metaconnectivity: Edge-centered analysis derived from dynamical functional connections



Statistical Analysis: Permutation tests FDR corrected

Correlation with Cognition

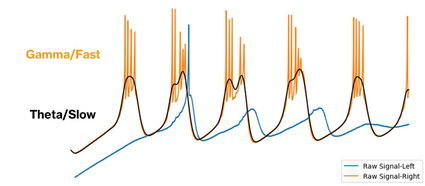
Partial Least Square Correlation



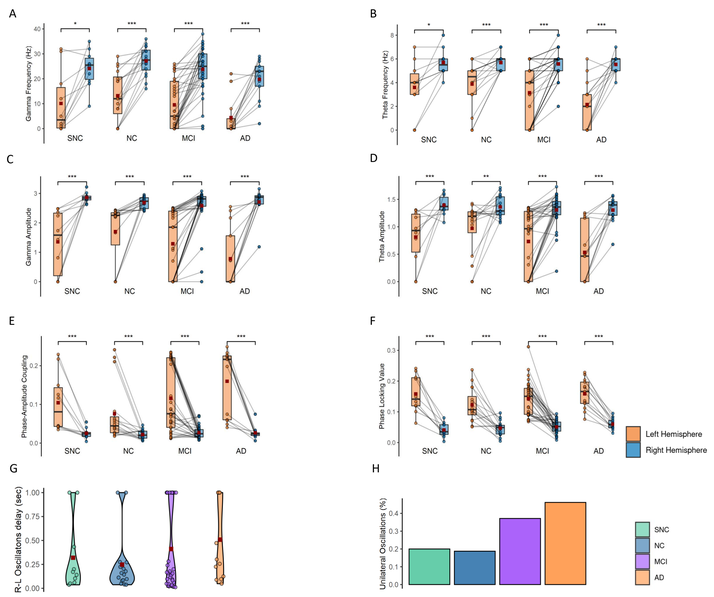
RESULTS

Model-Based Analysis: TVB

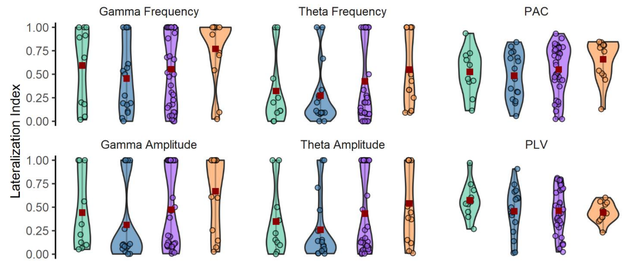
LFPs had different morphology in right and left hemispheres



Asymmetry of LFP amplitude, frequency and phase



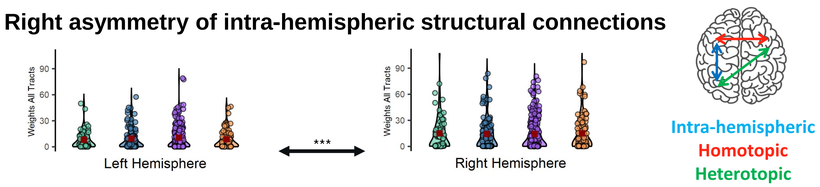
Lateralization indexes are increased in Alzheimer's Disease



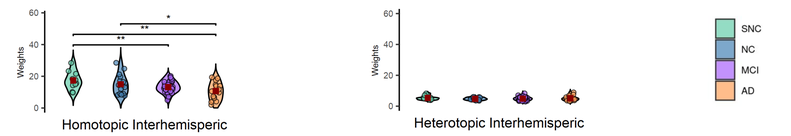
Lateralization Index: $|(\gamma^R - \gamma^L)| / (\gamma^R + \gamma^L)$. Note the quadratic trend from SNC to AD.

Model-Free Analyses

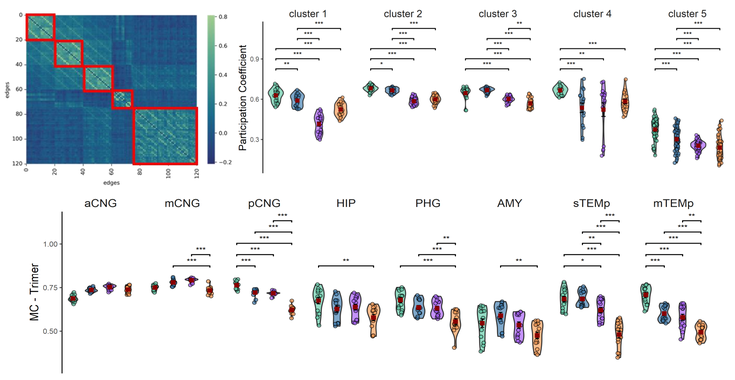
Right asymmetry of intra-hemispheric structural connections



Weights of inter-hemispheric connections were decreased in AD

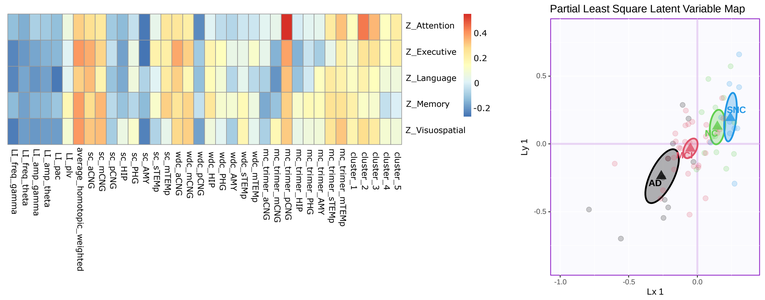


Generalized decrease in Metaconnectivity in AD



Correlation with Behavior

Inverse relationship between Lateralization and Cognition



Latent variables are segregated by group membership

DISCUSSION

Brain asymmetry of brain dynamics in AD described in this study by convergent analytical approaches complement previous neuropathological data. Of interest, larger asymmetry was seen in Alzheimer's disease compared to MCI and healthy groups. In contrast to previous studies relating brain asymmetry to specialization, our results highlight the relevance on brain integration as an essential element for maintaining cognitive health and its devastating effects when disrupted.

REFERENCES

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