Laminar Neural Mass Model for Representing Alzheimer's Disease Electrophysiological Biomarkers

Roser Sanchez Todo | Neuroelectrics Barcelona SL

Roser Sanchez-Todo1, 2 , Borja Mercadal1, Edmundo Lopez-Sola1, 2 ,Giulio Ruffini1
1 Neuroelectrics Barcelona SLU, Barcelona, Spain
2 Universitat Pompeu Fabra, Barcelona, Spain

Alzheimer's disease (AD) is characterized by progressive cognitive decline associated with amyloid beta (Aβ) plaques and hyperphosphorylated tau (hp-τ) proteins. Despite advances in identifying its biomarkers, more research is needed to understand disease progression and early, non-invasive, or cost-effective biomarkers like MEG or EEG. Modeling the disease in a physical-physiologically realistic fashion is also crucial to building whole-brain models of patients for treatments such as noninvasive brain stimulation, including transcranial alternating current stimulation. Here, we employ the mesoscale Laminar Neural Mass Model (LaNMM) framework to model the impact of disease on the electrophysiological biomarkers of AD, including alpha and gamma oscillations, which are critical for understanding disease mechanisms and progression.

Our computational model integrates our laminar framework and uses biologically informed parameters to represent the impact of Aβ and hp-τ on neural circuitry. The model incorporates physiologically realistic mechanisms, focusing on reducing parvalbumin-positive (PV+) interneuron connectivity to represent Aβ effects and the associated excitation-inhibition imbalance. The LaNMM offers a novel platform to replicate electrophysiological biomarkers observed in M/EEG across the disease continuum by simulating alpha and gamma oscillatory activity.

The model successfully replicates alpha band slowing and gamma power reductions, which is consistent with clinical observations in AD. It demonstrates the interplay between neural hyperexcitability, spectral slowing, and oscillatory disruptions driven by Aβ and hp-τ dynamics. Importantly, this is the first biologically realistic model to replicate these biomarkers within a mesoscale framework.

This work advances our understanding of AD pathophysiology by linking molecular pathology to electrophysiological biomarkers using the LaNMM. It provides a foundation for developing computational tools to optimize diagnostic and therapeutic approaches in AD.
