CENTRE DE RECERCA MATEMÀTICA CENTRE DE RECERCA MATEMÀTICA 2022 - 2025

A Laminar Whole-brain Model of Serotonergic Psychedelics: Restoring Oscillatory Dynamics in Alzheimer's Disease

Edmundo Lopez | Neuroelectrics Barcelona

Classical serotonergic psychedelics show promise in addressing neurodegenerative disorders such as Alzheimer's disease by modulating pathological brain dynamics. However, the precise neurobiological mechanisms underlying their effects remain elusive. This work introduces a personalized whole-brain model built upon a laminar neural mass framework to elucidate these effects. Using multimodal neuroimaging data from thirty subjects diagnosed with Alzheimer's disease, we simulate the impact of serotonin 2A receptor activation, characteristic of psychedelics, on cortical dynamics. By modulating the excitability of layer 5 pyramidal neurons, our models reproduce hallmark changes in EEG power spectra observed under psychedelics, including alpha power suppression and gamma power enhancement. These spectral shifts are shown to correlate strongly with the regional distribution of serotonin 2A receptors. Furthermore, simulated EEG reveals increased complexity and entropy, suggesting restored network function. These findings underscore the potential of serotonergic psychedelics to reestablish healthy oscillatory dynamics in the prodromal and early phases of Alzheimer's disease and offer mechanistic insights into their potential therapeutic effects in neurodegenerative disorders.

MATHEMATICAL NEUROSCIENC

😁 June 17 - 20, 2025

PRBB, Barcelona