

Session/Poster#

Presenter

B18

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Investigating the role of CB1 and GABA receptors in human EEG biomarkers associated with schizophrenia using a multiscale model of auditory thalamocortical circuits

GABA receptor deficits and increased CB1 receptor availability have both been related to changes in EEG waveforms observed in Schizophrenic patients. Abnormalities in auditory cortex oscillations have been observed in pathologies that include auditory processing deficits, such as schizophrenia. We will therefore use a previously developed model of auditory (A1) thalamocortical circuits to reproduce an experimental dataset measuring the effects of CB1 and GABA on human EEG data. The A1 model simulates a cortical column with a depth of 2000 $\hat{1}$ /₄m and 200 $\hat{1}$ /₄m diameter, containing over 12k neurons and 30M synapses. Neuron densities, laminar locations, classes, morphology and biophysics, and connectivity at the long-range, local and dendritic scale were derived from published experimental data. Auditory stimulus-related inputs to the MGB were simulated using phenomenological models of the cochlear/auditory nerve and the inferior colliculus. The model reproduced in vivo cell type and layer-specific firing rates, and accurately simulated the corresponding local field potentials (LFPs) and electroencephalogram (EEG) signals. The experimental dataset comes from experimental collaborators at Yale and consists of human EEG recordings under different conditions, including placebo, THC (CB1 agonist), lomazenil (GABA deficit) and THC plus lomazenil. This dataset includes cognitive and behavioral measures. We will also employ PET imaging data on CB1 receptor availability (n=58) and synaptic density (n=90) in healthy individuals. We will first simulate the baseline EEG in the A1 model and validate it against the human EEG data in the control condition. We will then simulate the stimulus-specific adaptation (SSA) paradigm in the model and systematically explore the effects of CB1 and GABA alterations in order to reproduce the experimental EEG data. We will use the model to gain insights into the underlying cellular and circuit biophysical mechanisms associated with schizophrenia.