C14

Scott McElroy Advisor(s): Salvador Dura-Bernal Ph.D.

Co-author(s): -

Title: Identifying cell-type-specific alterations underlying schizophrenia-related deficits in auditory steady-state response and aperiodic spectral activity: insights from a multiscale model of audit

Individuals with schizophrenia exhibit a variety of symptoms categorized as positive, negative, and cognitive. A cognitive symptom extensively studied using electroencephalography (EEG), is sensory processing deficits, particularly in the auditory system. These deficits manifest as abnormalities in event-related potentials and cortical oscillations. In particular, this work focuses on the reduced 40 Hz Auditory Steady State Response (ASSR) and alterations in spontaneous 1/f slope, which are thought to reflect impaired inhibitory interneuron activity and gamma oscillations. We have extended our previously developed model of auditory thalamocortical circuits to investigate the source of these schizophrenia-related EEG biomarkers. This model simulates a cortical column containing over 12k neurons and 30M synapses. Neuron densities, laminar locations, biophysics, and connectivity at the long-range, local, and dendritic scale were derived from published experimental data. Auditory stimulus-related inputs to the thalamus were simulated using a phenomenological model of the cochlea. The model reproduced in vivo cell type and layer-specific firing rates, local field potentials, and EEG signals consistent with controls. Changes made to the model to reproduce schizophrenia patient EEG biomarkers were informed using data from positron emission tomography imaging, genetics, and transcriptomics specific to schizophrenia patients. Specifically, we have employed experimental findings such as layer-specific reductions in somatostatin and parvalbumin expression in interneurons, reduced NMDA efficacy, and feedforward circuit-specific connectivity changes to explore mechanistic explanations for EEG biomarkers of schizophrenia. This work aims to bridge the gap between experimentally determined molecular and genetic changes associated with schizophrenia and the resulting circuit and network behavior that give rise to robust EEG biomarkers.