Computational Modeling of Neuronal Networks: Clarifying Neural Dynamics for Neuropathological Investigations

Wang, Zhitong

Current understanding of schizophrenia concerns mainly molecular, single cell, or gross-system levels of brain function; however, the disruption of patterned dynamics in neuronal clusters yet remain unclarified. In vivo imaging studies of schizophrenia are largely constrained by inflexible animal models and complex disease pathology. Computational modeling provides a flexible and inexpensive alternative to investigate neural circuitry and the interplay between multiple synaptic channels, inspiring this study to design a novel in silico model of neuronal networks in a schizophrenic (SZ) setting. The control model observed similar biophysical accuracy to previous in vitro recordings, exhibiting neuronal connectivity governed by a “rich-club” organization. The SZ model reflected profound alterations in the network’s framework, where neurons were hyperactive along with increased cell-cell interaction strength ($p<0.01$), however observed decreased cluster-cluster interaction strength ($p<0.01$). Further evaluation demonstrated reduced gamma-Aminobutyric acid (GABA) neurotransmitters alone accounted for the increased cell-cell interaction strength ($p<0.01$), while reduction in N-methyl-D-aspartate (NMDA) receptors alone led to decreased cluster-cluster interaction strength ($p<0.01$). This study was the first to identify the causal role of reduced NMDA and GABA in altering neuronal clusters’ connectivity in schizophrenia, directing attention to restoring NMDA and GABA levels simultaneously for future antipsychotic medications. Future modeling studies should reference the current model as a template to study other psychotic systems such as bipolar disorder, as well as improving upon current model design to establish a virtual pharmacological testing system.

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