A neurocomputational biomarker assay for schizophrenia based on E/I-balance (IMBALANCE)

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Schizophrenia is a severe mental disorder that remains poorly understood. The accuracy of the clinical diagnosis is poor and the search for biomarkers that could aid diagnosis and individualized treatment has remained elusive. The present project aims to develop and validate a novel biomarker assay that is firmly grounded in a recent mechanistic theory regarding higher brain function and the pathophysiology of schizophrenia: The balance between excitatory and inhibitory neurons in the cerebral cortex ('E/I balance'), which is key for brain function, is fundamentally disturbed in schizophrenia. We will assess several candidate biomarkers of E/I balance, in an interdisciplinary translational neuroscience approach that will bridge across levels of brain organization via an integrated computational framework. Pharmacological interventions in healthy humans will target the key neurotransmitter systems involved in E/I balance to establish a set of non-invasive electrophysiological and behavioural biomarkers. Neural recordings in a mouse models of the disease with selective circuit perturbations and multi-scale computational modeling will bridge the gap between large-scale neural signals and microcircuits. Candidate neurocomputational biomarkers will be translated to patient data, probing the utility of neural and behavioural readouts of E/I balance in clinical diagnosis. This integrated approach holds promise to establish a novel mechanism-based biomarker assay for schizophrenia.