Psychosis-Risk Outcomes Network (ProNET)

Project Coordinator:

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It has now been two decades since the clinical high risk for psychosis (CHR) criteria were first formulated in service of the goal of preventing psychotic disorders, one of the most urgent unmet clinical needs in behavioral health, if not in all of medicine. As with most psychiatric patients, CHR patients benefit from psychotherapies but are also often left with important treatment needs not fully addressed. Despite the critical public health need, drug development for CHR is viewed in many quarters as risky. The most daunting obstacle may be the heterogeneity of CHR course. ProNET will deeply phenotype 1040 CHR patients across the ProNET network of 26 international sites with multi-modal biomarkers that span brain structure-function (MRI and EEG), psychopathology and cognition, genetics, body fluid analytes, natural speech/language, and passive/ecological momentary digital phenotyping These biomarkers will be mapped onto a core set of clinical outcome measures and trajectories over a treatment-relevant time window at eight timepoints over 24 months. Biomarkers will be collected at two timepoints to map brain-behavior trajectories. Healthy volunteers (N=260) will complete a baseline assessment to quantify typical variation. We will also conduct exploratory studies to assess real-time behavioral data from smartphone sensors and symptom reports from surveys; novel repetition positivity and alpha-desynchronization measures derived from standard EEG paradigms; and pilot an evaluation of excitatory/inhibitory imbalance with MR spectroscopy for glutamate, glutamine, and GABA at 7 Tesla.

The ProNET network will then partner with the NIMH-selected Data Processing, Analysis, and Coordinating Center for rapid data integration. We will test the hypothesis that data-driven variation assessed by multivariate neural, genetic, and behavioral measures within the CHR syndrome predicts individualized clinical trajectories, expanding CHR stratification for broad clinical endpoints encompassing affect, anxiety, cognition, and APS with the goal of identifying behavioral and biomarker-driven patterns that can refine the CHR syndrome and promote personalized treatment decisions..