Universität Basel

Research Project

EEG resting-state connectivity and psychosis: Dopaminergic influences

Third-party funded project

Project title EEG resting-state connectivity and psychosis: Dopaminergic influences
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The dopamine hypothesis has proven to be the most enduring neurobiological model of psychosis, and all currently licensed antipsychotic drugs are dopamine antagonists. Although the pharmacological actions of antipsychotics have been extensively investigated, research into how these translate into their effects on symptoms is relatively new. The present project focuses on the relationships between medication-induced changes in dopaminergic activity and brain connectivity, disturbances of which are considered to be a core neurophysiological characteristic of psychotic disorders. It uses electroencephalography (EEG) to assess how dopaminergic agents affect the fast dynamics of brain networks, drawing upon two complementary lines of research: a drug challenge study, and a longitudinal patient study. Method: The project consists of two parts: a drug-challenge study in healthy individuals (Project A), and a longitudinal study with medication-naïve patients with psychotic disorders before and after antipsychotic treatment (Project B). -Participants: Project A includes single-dose administration of a dopaminergic agonist (L-dopa 100 mg), a dopaminergic antagonist (haloperidol 2 mg) and placebo to 60 healthy subjects within a randomized, double-blind, cross-over design. Project B will investigate 40 medication-naïve patients with psychotic disorders before and after 8-10 weeks of antipsychotic medication treatment. -Measures of interest: Analyses will be performed based on 10-min, eyes-closed, resting-state 64-channel EEG data. Three different measures of interest will be assessed: (1) lagged phase coherence (multivariate interaction method) and (2) orthogonalized power envelope correlation at the level of brain electrical sources in the theta and gamma frequency band; and (3) resting-state EEG microstates as a measure of global brain connectivity. -Statistical analyses: In Project A, regressors will be defined for linear and quadratic substance contrasts; in Project B, differences between pre-and post-treatment will be assessed. For measures (1) and (2), a cluster-based permutation method (network-based statistic) will be used for analyses. Microstate parameters (3) will be subjected to repeated-measures ANOVAs with microstate class as a within-subject factor. Expected value of the project: The project aims to fill a significant knowledge gap regarding the mechanisms of action of antipsychotic drugs. Beyond their theoretical value in understanding the pathophysiology of psychosis, results are expected to be valuable in informing use-inspired research, especially given the growing interest in non-invasive neuromodulation techniques for the treatment of neuropsychiatric disorders.

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