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**Dynamic Causal Modeling of Depression, Mania and Psychosis Symptoms to Inform Nosology**

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The current diagnostic system (i.e., DSM-5) includes several diagnoses related to depression, mania, and psychosis symptoms, such as schizophrenia and schizoaffective disorder etc. However, these diagnoses are based on bundles of symptoms, instead of etiology — diagnosis as the consequence, rather than the cause of a certain combination of symptoms. Prior efforts to reveal the natural clustering of these symptoms and thereby, nosology, have mainly used linear models and factor analyses on cross-sectional data. These studies, while having advanced our understanding of how these symptoms naturally co-occur across people, have left the within-individual symptom dynamics over time relatively unexamined. Recent interest in computational psychiatry has called for explicit modeling of the hidden pathophysiological and psychopathological processes. In a simulation study, Friston, Redish and Gordon (2017) have demonstrated that dynamic causal modeling (DCM) can be applied on longitudinal psychiatric data. They modeled the change of the trajectory of latent pathophysiological factors leading to psychopathology, and finally manifesting observable clinical symptoms and diagnoses. The current project pioneers applying this DCM onto real symptom data to examine the temporal trajectories of depression, mania, and psychosis symptoms.

This study uses data from first-admission patients ( $N = 553$ ) with psychosis. Depression, mania and psychosis symptoms were measured weekly over four years. Using DCM, we model three hidden pathophysiology factors giving rise to three hidden psychopathology factors (depressed mood, manic mood, and thought deficits), which in turn output observed clinical level depression, mania and psychosis symptoms. Our specific aims include: 1) to demonstrate the utility of DCM on empirical symptom data modeling; 2) to examine the nosology structure, which is to explore whether patients fall on a dimension or cluster into sub-groups based on the hidden parameters of DCM. In the presentation, I will report some early results.

This project is a first attempt to combine dynamic modeling tools, developed in theoretical neuroscience, to model psychiatric symptoms traditionally investigated using cross-sectional data and linear models. It is, therefore, likely to provide valuable novel information regarding hidden etiological process and nosology from a dynamic perspective. Such work is in line with Research Domain Criteria (RDoC), facilitating to uncover the natural symptom trajectories between depression, mania and psychosis, and provide empirical evidence on how patients vary in the dynamics between these symptom space. In turn, this will hope to inform the diagnostic structure of psychological conditions involving depression, mania, and psychosis.