

# Brain State and Trait Dynamics in Mental Illnesses

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Symposium

This symposium aims to address a critical need to reveal the complex relationship between brain dynamics and mental illnesses across psychiatric spectra. In an era marked by notable advancements in precision imaging, understanding the temporal evolution of neural patterns is imperative for developing reliable neural markers of psychopathology. This symposium navigates the methodological challenges inherent in such innovations, providing a platform for experts to present cutting-edge insights. The learning outcomes are tailored to empower the audience with a nuanced understanding of neuroimaging-based brain-behavior association studies, optimizing sample size and scan duration for resting-state fMRI, and integrating state and trait dynamics in both brain and behavior. The symposium will delve into stable variations in human brain network architecture, shedding light on network variants as potential clinically relevant neural targets. Furthermore, the exploration of precision mapping in individuals with depression promises to unveil trait-like expansions in the salience network and state-dependent connectivity fluctuations linked to specific symptoms. As the field strives for actionable neural markers, this symposium aligns with the pressing need for methodological clarity and substantive insights into psychiatric neuroimaging.

## Objective

1. Understanding the Considerations for Neuroimaging-based Brain-Behavior Association Studies: (1) Gain insights into the optimal balance between sample size and scan duration in resting-state fMRI, (2) Understand the empirical considerations for enhancing prediction accuracy and reliability of brain-behavior relationships.
2. Integration of State and Trait Dynamics in Brain and Behavior: (1) Explore reproducible state and trait-related features of brain co-activation patterns. (2) Understand how these dynamics relate to individual life functional outcomes.

3. Exploration of Stable Network Variations and Precision Imaging in Clinical Context: (1) Examine the concept of stable variations in human brain network architecture, focusing on network "variants.". (2) Understand the potential of these stable variations as systematic elements with high reliability and stability over time. (3) Investigate the trait-like features of psychopathology, with a specific focus on variants in individuals with depression. (4) Gain insights into the application of precision imaging techniques in psychiatry.

## Target Audience

Our primary audience comprises the broad OHBM membership attending the annual OHBM meeting. Individuals with research backgrounds and interests in neuroimaging, psychiatry, psychology, cognitive neuroscience, clinical neuroscience, and machine learning will benefit from the topics covered by this symposium.

## Presentations

### MRI meets economics: Balancing sample size and scan duration

Resting-state functional connectivity is widely used to predict behavioral traits in individuals. A pervasive dilemma in neuroimaging is whether to prioritize sample size or scan duration given fixed resources. Here, we systematically investigate the trade-off between sample size and scan time in the context of the accuracy and reliability of brain-behavior relationships using resting-state fMRI. For prediction accuracy of individual-level behavioral measures, we find that the contributions of increasing sample size and scan duration are similar up to approximately 20-30 minutes of scan-time per participant. In particular, total scan duration (sample size  $\times$  scan time per participant) robustly explains prediction accuracy via a logarithmic function. On the other hand, when considering the reliability of brain-behavior associations, sample size dominates individual participant scan durations beyond 6 to 10 minutes. These results replicate across a wide range of behavioral measures from two large-scale datasets. Overall, our findings establish an empirically informed reference for calibrating scan duration and sample size to maximize prediction of behavioral performance and reliability of brain-behavior association.

## Presenter

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### State-trait dynamics of the human brain reflect individual behavior and life functions

Spontaneous fluctuations of brain activity are embedded in time and space, exhibiting rich spatial-temporal information that varies within (state) and between (trait) individuals. The joint properties of state-trait resting-state fMRI signal variation and the mapping of these neural variation to behavior remain poorly understood. To fill this gap, we quantify moment-to-moment changes in brain-wide co-activation patterns (CAPs) derived from resting-state fMRI in healthy young adults ( $n=337$ ). We demonstrate spatiotemporal features of CAP dynamics that are reproducible at the individual level. We found that distinct parameters of CAP temporal characteristics, such as occupancy and persistence, can be studied together and represented as either state or trait features. A joint analysis of state-trait neural variations and feature reduction reveal general motifs of individual differences, encompassing state-specific and general neural features that exhibit day-to-day variability. The principal neural variations co-vary with the principal variations of 262 behavioral phenotypes. Specifically, people who showed longer time spent in a given CAP, longer persistent periods within a CAP, as well as higher variation in transitioning

between all CAPs, also showed higher cognitive function, improved emotion regulation, and lower alcohol and substance use. Critically, person-specific probability of occupying a particular CAP was highly reproducible and associated with both neural and behavioral features. This highlights the importance of studying CAP-derived measures as a neural marker that may be altered as a function of mental health symptoms and may change developmentally. Collectively, these results show a reproducible pattern of neural co-activation dynamics in humans, which capture both within- and between-subject variance that in turn maps onto functional life outcomes across people.

## Presenter

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## **Stable variations in human brain network architecture: applications to psychopathology**

While human brain networks follow a canonical organization, every individual measured so far differs from this archetypal pattern. A central question in clinical neuroscience is the extent to which these individual differences are informative regarding neuropathological traits versus less temporally stable features of psychiatric disorders. In past work, we have used a combination of precision and big-N datasets to investigate the properties of locations that differ most strongly between individuals and the canonical group-average brain network organization. In our work, we refer to these locations with idiosyncratic brain connectivity profiles as network “variants”. In neurotypical samples, variants appear most frequently in frontal regions and near the temporo-parietal junction, with a higher prevalence in the right hemisphere ( $d = 0.57$ ;  $p < 0.001$ ; a pattern that reproduces across datasets). With sufficient individual-level data, variants are highly reliable (test-retest  $r > 0.8$ ) and stable over years (average  $r = 0.79$  longitudinally). When examined across task conditions, variants show some state-dependent features, but are largely trait-like. In a preliminary investigation, we also show that variants have potential for revealing trait-like features of psychopathology, as variants differ in individuals with schizophrenia, with a higher frequency of variants in the dorsolateral prefrontal cortex, relative to matched controls ( $p < 0.01$ ,  $d = 0.64$ ). Jointly, this work suggests that network variants are stable, systematic elements of brain networks in individuals, with potential for revealing clinically-relevant neural targets. We close by considering experimental designs that may be useful for untangling trait and state like features of brain networks in clinical neuroscience.

## Presenter

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## **Precision mapping of functional brain networks in individuals with depression**

Precision functional mapping is the emerging practice of delineating functional brain areas or networks and studying brain-behavior relationships within individuals, as opposed to at the group-level, typically using a large amount of fMRI data per-subject acquired longitudinally. Here, we applied precision functional mapping in individuals with major depression who were studied for up to 1.5 years, and found that the salience network is expanded nearly 2-fold due to borders of the network shifting outwards and encroaching upon neighboring functional systems. Cortical expansion of the salience network was trait-like – stable over time, unaffected by mood

state, and detectable in a separate sample of children scanned before the onset of depression symptoms later in adolescence. In contrast, functional connectivity between different pairs of frontostriatal salience network nodes was state-dependent and closely tracked fluctuations in distinct symptoms (anhedonia, anxiety) over time within and across individuals. Together, these findings reveal new patterns of functional network topography and connectivity that are neural traits and states, respectively, characteristic of depression, and highlight the utility of deeper characterizations of functional neuroanatomy and behavior within individuals as an alternative to studying population-level central tendencies.

## Presenter

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