Aberrant brain network dynamics underlying cognitive inflexibility in childhood autism revealed by variational Bayes hidden Markov modeling.

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Background: Cognitive flexibility depends on the ability to efficiently integrate information across specialized brain networks over time, yet little is known about these dynamic processes in autism spectrum disorder (ASD)—a disorder in which cognitive inflexibility is a core deficit. Here we characterize intrinsic time-varying functional interactions among the salience (SN), default mode (DMN), and central executive (CEN) networks—three core brain networks critical for higher-order cognition—in 50 children with ASD and 50 typically-developing (TD) children using a novel variational Bayes hidden Markov model (VB-HMM) method.

Methods: rsfMRI timeseries were extracted from six key network nodes of the SN, DMN and CEN. We developed a novel VB-HMM method that overcomes the limitations of existing approaches, including the sliding-window procedure for estimating time-varying functional interactions between brain regions. VB-HMM uses a state-space approach to model multivariate non-stationary time series data and cluster them into distinct states, each with a different covariance matrix reflecting the interactions between brain regions. Importantly, VB-HMM automatically prunes redundant states, retaining only those that significantly contribute to the underlying dynamics of the fMRI data. We applied VB-HMM to the extracted timeseries to identify brain states and estimate the probability of each identified brain state at each time point in the two groups. To determine whether the learned HMM models can be used to discriminate ASD from TD children, we computed the likelihood of observing the TD data given the ASD model and vice versa. Lastly, we measured the relationship between state dwelling times and ASD symptom severity.

Results: In both groups of children, we found that brain connectivity fluctuated between two states: a ‘segregated state’ during which the three networks were disconnected from each other and an ‘integrated state’ characterized by strong cross-network coupling. Critically, patterns of intrinsic brain dynamics distinguished children with ASD from TD with an accuracy of 86%. Furthermore, compared to TD, children with ASD demonstrated shorter dwelling times in the ‘integrated state’. Notably, ASD children who showed the lowest levels of network integration had the most severe repetitive behaviors.

Conclusions: Taken together, our findings provide novel evidence that the intrinsic dynamics of functional segregation and integration among the SN, CEN, and DMN networks are aberrant in children with ASD, and that the dynamical temporal properties of cross-network interactions not only provide a distinguishing neurobiological signature of childhood autism but also link temporal inflexibility of brain networks with core ASD symptomatology. We demonstrate for the first time that at earlier ages closer to disorder onset, the temporal dynamics of core brain networks in children with ASD are inflexible in ways that contribute to cognitive inflexibility, which is a hallmark of the disorder.