

## Public Abstract

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Title:Network Coherence in Autism Spectrum Disorder:

A Multimodal Neuroimaging Study of Functional Connectivity and Spectroscopy MRI

Autism spectrum disorder (ASD) is a behaviorally defined disorder characterized by impairments in social communication and stereotyped interests and repetitive behaviors early in life. The underlying neuropathology and effects on neuronal activity are still being investigated as well as their impact on intervention and treatment outcomes. Distinct regions in the brain exhibit disrupted structural and functional connectivity between neuronal clusters in individuals with ASD and we sought to investigate the potential clinical utility of these alterations.

If differences in functional connectivity are clinically relevant to the study of ASD then treatment paradigms that improve symptom outcomes of the disorder should also affect connectivity patterns within neural networks. We found that administration of a beta-blocker, propranolol, improved information processing in a subset of individuals with ASD and that improved performance was related to drug-related changes in functional connections between neuronal clusters. These findings support the potential utility of beta-adrenergic antagonists for some patients with ASD and the clinical significance of alterations in network coherence.

There are also additional considerations for functional connectivity investigations in ASD. The cerebellum is interconnected to the cerebrum and thus has some modulatory influences on neural networks throughout the brain. The cerebellum is consistently implicated in the neuropathology of ASD but has been largely ignored in investigations of functional connectivity. We found altered patterns of functional connectivity between the cerebellum and cerebrum in a subset of individuals with ASD that were related to neurotransmitter levels, specifically glutamate, in the cerebellum. Altered connectivity with the cerebellum was also associated with language and inference abilities, suggesting a potential mechanism underlying altered connectivity in individuals with ASD as well a cognitive outcome of these alterations.