Examining Neural Synchrony in Autism Spectrum Disorders with Magnetoencephalography (MEG) During Resting State

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Introduction

- Autism spectrum disorders (ASD) are characterized by impairments in social functioning and communication as well as restricted repetitive behaviors (RRBs). One in 68 children are affected (CDC, 2014) necessitating our need to understand the neurophysiological mechanisms underlying these disorders.
- Recent reports suggest that impaired neural synchrony (phase coherence) may be a primary pathophysiological mechanism in ASD. Disruptions in neural synchrony are believed to contribute to hyperexcitability, unstable cortical network development, and aberrant connectivity.
- Studies have identified abnormal functional connectivity in the brain's of individual's with ASD in resting state networks (RSNs). The Default Mode Network (a key RSN) is believed critical for internal cognitive tasks such as taking others' perspectives and self reflection, known areas of impairment in ASD, making the DMN a vital area of investigation.
- To date, a very limited number of studies have explored neural synchronization with MEG during resting state in ASD and none have examined the DMN.
- Functional connectivity is mediated by various rhythms of cortical oscillatory activity. It also remains unclear how specific frequency bands contribute to this complex pattern of over- and underconnectivity.

Objectives:

- This study investigated whole-brain patterns of coherence during rest in ASD compared to neurotypicals (NT) to: 1) explore regional brain differences in the DMN, and 2) identify how connectivity is mediated by the various rhythms.

Hypotheses:

- We hypothesized there would be decreased coherence between cortical regions of the DMN (e.g. medial prefrontal, posterior cingulate, ventral precuneus, medial/lateral/inferior parietal cortex) coupled with increased posterior synchronous activity in ASD consistent with their often-noted perceptual-cognitive style.
- Based on prior work in our lab, we further hypothesized:
  - Decreased coherence in the gamma frequency band (30-80 Hz) in ASD in frontal regions and their connections
  - Increased alpha (8-12 Hz) and beta (13-30 Hz) coherence in posterior regions
  - Interhemispheric and right intrahemispheric coherence in NT>ASD
  - Stronger relationships between measures of social functioning and DMN mean coherence in NT

Methods

Participants:

- 12 ASD, 13 NT (ASD matched on Perceptual-Reasoning or FSIQ with NT)
- ASD Age (M = 8.9; SD= 1.0) and FSIQ (M = 102.6; SD = 14.9)
- NT Age (M = 9.3; SD = 1.3) and FSIQ (M = 112.0; SD = 9.0)

Inclusion/Exclusion Criteria:

- ASD: Diagnoses made with DSM-5 criteria and confirmed with ADOS-2, no history of comorbid genetic disorder or seizure disorder
- NT: No history of ASD in a first-degree relative, no history of learning disorder, neurological disorder or other psychopathology
- ASD and NT: FSIQ ≥ 70. No history of head injury with LOC, no metal implants

Psychometric Measures: Social Communication Questionnaire, Social Responsiveness Scale, Vineland Adaptive Behavior Scales, Test of Problem Solving

Psychometric Group Differences: Independent t-tests or chi-squares were computed to examine group differences on psychometric measures. Pearson correlations were computed to examine relationships between coherence values in ASD and NT and psychometric measures of social, communication, and RRBs.

Magnetoencephalography (MEG):

- 5 minutes of eyes-open passive recording during MEG scanning.

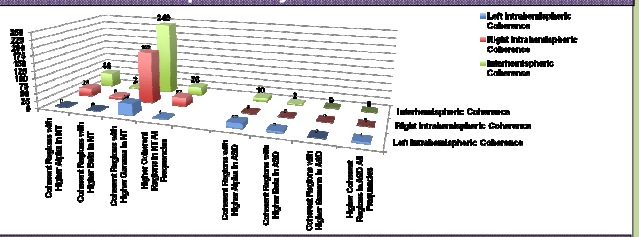
***MEG Preprocessing & Data Analysis*:** 148 channel whole head MEG (4D Neuroimaging, Magnes WH2500) collected cortical activity. Data were band-pass filtered 3-85 Hz, digitally sampled at 508.63 Hz, and artifacts eliminated with ICA.

Synchronization of neuronal activity during resting state was quantified by calculating coherence between cortical sites from MEG imaged brain activations (Elisevich K, Shukla N, Moran J, et al. 2011). Cortical coherence levels (0 to 1) were used to quantify differences in connectivity. Coherence was calculated for each pair of 54 brain regions in alpha (8-12 Hz), beta (13-30 Hz), and gamma (30-80 Hz) frequency bands and combined frequency bands (1-80 Hz).

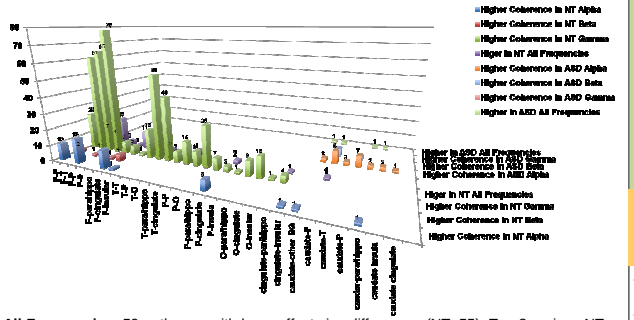
***MEG Group Difference Testing*:** For each frequency and with frequencies combined, a t-test was used to assess for a difference in average coherence values between groups for each pair of brain regions (N=1431). The False Discovery Rate was controlled at 0.10. From each t-test, a z-score was computed according to the method of Efron to summarize the difference in coherence values between ASD and NT.

Preliminary Results

Difference in Number of Interhemispheric and L & R Intrahemispheric Synchronous Connections

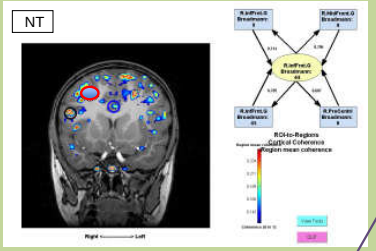


Regional Differences in Number of Synchronous Connections for Alpha, Beta, and Gamma Frequency Bands



- **Across All Frequencies:** 59 pathways with large effect size differences (NT=55). Top 3 regions NT > ASD - Right Cingulate to Right Inferior, Middle, and Orbitofrontal Gyri. 4 regions ASD > NT - Left Caudate to Left Putamen, Hippocampus, Insula, and Inferior Frontal regions.
- **Alpha band**: 72 pathways with large effect size differences (NT=47). Top 3 regions NT > ASD – Left Superior Parietal to Right Inferior Frontal, Left Precuneus to Right Lateral Orbitofrontal, Right Cingulate to Right Middle Frontal. All regions ASD > NT – Left Caudate to Left Frontal, Temporal, Parietal or subcortical regions.
- **Beta band**: 16 pathways with large effect size differences (NT=8). Top 3 regions NT > ASD – Right Cingulate to Right Lateral Orbitofrontal, Inferior Frontal, and Middle Frontal. All regions ASD > NT – Left Caudate to Left Parietal (e.g. Postcental) and Frontal (e.g. Precentral).
- **Gamma band**: 447 pathways with large effect size differences (NT=446). Top 3 regions NT > ASD – Right Middle Temporal to Right Precentral, Left Middle Occipital to Right Inferior Frontal, Right Fusiform to Right Postcentral. ASD > NT – Left Caudate to Left Hippocampus.

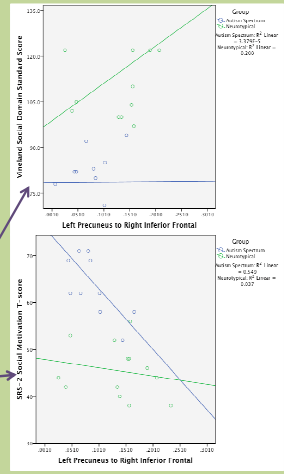
ASD and NT Subjects Depicting Cortical Areas with Greatest Effect Size Differences in Region-to-Region Coherence and Relationship to Social and Language Functioning

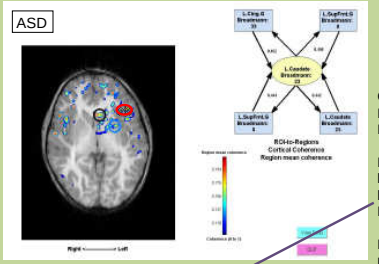


Coherence between Right Inferior and Middle Frontal, Cingulate, and Left Precuneus in NT>ASD.

•Higher social skills on Vineland related to higher coherence between these regions in NT.

•Lower social motivation (higher scores are poorer) on SRS related to lower coherence between these regions in ASD.

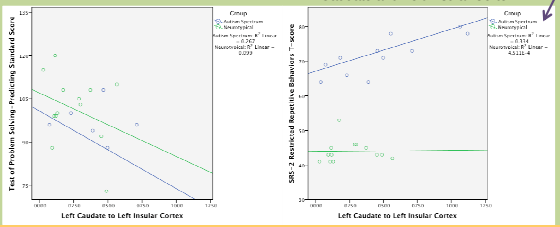




Coherence between Left Caudate, Left Putamen, and Left Frontal, Temporal, and Parietal regions higher in ASD.

Lower performance on test that integrates linguistic skills and problems solving related to higher coherence between Left Caudate and Left Insular Cortex.

More restricted, repetitive behaviors in ASD related to higher coherence between Left Caudate and Left Insular Cortex.



Conclusion

- Preliminary results reveal increased coherence between DMN regions (medial prefrontal, cingulate, precuneus, and medial/lateral/inferior parietal cortex) in NT compared to ASD.
- A significantly higher number of interhemispheric and right intrahemispheric (association) synchronous connections, particularly in the gamma frequency band was noted in NT. Gamma band synchrony was essentially non-existent in ASD during rest.
- Higher coherence was consistently noted between left caudate and left hemispheric regions in ASD.
- Higher social and language functioning was related to increased coherence in DMN regions while lower social and language functioning and higher RRBs were related to increased coherence between left caudate and left hemispheric regions.

Implications:

Findings support a model of aberrant neural synchrony in ASD revealing underconnectivity in the DMN and enhanced connectivity between left subcortical regions known to be critical for voluntary movement, the integration of spatial/motor behavior, goal-directed behavior, learning/memory, and social behaviors. Increased caudate volumes have been linked to OCD, and enhanced coherence between these regions may underlie the rigid social, communicative, and motor behaviors in ASD.