Neural Coherence During Natural Story Listening as a Biomarker for Autism

Jonathan Brennan1, Neelima Wagley1, Margaret Ugolini1, Annette Richard2, Ioulia Kovelman1, Susan Bowyer3 & Renee Lajiness-O'Neill2

jobrenn@umich.edu

1University of Michigan, 2Eastern Michigan University, 3Henry Ford Hospital

Introduction

A major thread in current neuroimaging research on Autism Spectrum Disorders (ASD) focuses on biomarkers sensitive to diagnostic status and/or treatment efficacy that can be passively measured in pediatric populations.

Recent work on resting state brain activity has suggested that ASD may be associated with impaired functional connectivity between brain networks (e.g., Dinstein et al., 2011; Cohen et al., 2008; Lajiness-O'Neill et al., 2014), raising the possibility that a short segment of electrophysiological activity, easily collected with minimal task demands, may provide clinically useful information.

In parallel, neural responses to simple auditory stimuli and speech sounds also show atypical patterns that correlate with clinical language scores (Roberts et al., 2010; Edgar et al., 2013). This correlation raises the possibility that connectivity patterns during language processing may be more divergent between children with ASD and those with neurotypical (NT) development compared to resting state connectivity, where variance in brain states between individuals is expected to be high.

Listening to a short story is a simple, familiar and, for many children, enjoyable activity that requires minimal extraneous task demands. Accordingly, we tested whether neural coherence, measured using magnetoencephalography (MEG), during passive story listening could distinguish children with and without ASD.

Methods

Participants

19 children (9 NT and 10 ASD), aged between 8 and 12. Diagnosis confirmed with the Autism Diagnostic Observation Schedule (ADOS-2).

Design

We analyzed passive listening data from three experimental datasets: (1) Ten minutes of data collected during eyes-open REST. (2) Ten minutes of data collection while participants listened to a segment of a children’s STORY also with eyes open. (3) Ten minutes of data collected while participants listened to speech in a FOREIGN language (Italian) which was unfamiliar to all participants.

Data Collection

Data were recorded from 148 magnetometers (4D Neuroimaging) with a band-pass of 0.1 to 100Hz and sampling rate of 508.25Hz.

Data Analysis

After preprocessing to remove cardiac artifacts, data were band-pass filtered 30 and 80Hz (γ-band) and MR-FOCUSS (Moran et al., 2005) was used to localize brain activity within a 4000 dipole source grid spanning the grey matter of a pediatric template which was morphed into each subject’s digitized head shape.

Sources were grouped in to 54 anatomical regions spanning both hemispheres and pairwise coherence was computed. A logistic classifier was constructed modeling group membership (NT or ASD) as features a coherence subspace defined by the first two principle components derived from the pairwise coherences. Leave-one-out cross-validation was used to test the predictive power of each model.

Results: Biomarker Performance

Model Details

Classifiers for each block were trained using two different coherence feature sets:

To facilitate comparison across blocks, a COMMON set was derived from coherences showing a the main effect of group (ASD or NT) across all blocks with a repeated-measures ANOVA (p < .05, uncorrected).

To optimize model performance per block, a SEPARATE feature set was derived from coherences showing a differences within each block with paired t-tests (p < .1 REST; p < .05 STORY, FOREIGN).

Model Evaluation

Accuracy (proportion of correct model predictions; leave-one-out cross-validation) and Confidence (match between model prediction and actual diagnosis; 1 - (||y - ŷ||)^2)

More regions showed coherence differences between groups in the STORY and FOREIGN conditions, compared to REST (see below) with differences found in left middle temporal, middle frontal, pre- and post-central gyr and other regions.

STORY shows the highest diagnostic accuracy and confidence across feature sets.

Results: Network Analysis

Preliminary efforts to characterize the connectivity patterns exploited for diagnosis explored the network structure of the six models (3 blocks x 2 feature sets)

Edges show pairwise coherences, line thicknesses are weighted by the model coefficients multiplied by the two sets of principle component loadings. Node sizes scale with the average of edge weights. Nodes from the left and right hemisphere are distinguished; edges in light blue indicate negative weights.

*“Interchange*” regions commonly implicated in learning, control (caudate, putamen) and memory (hippocampus), are prominent network hubs and a left-hemispheric bias is evident with different balances of connectivity across datasets.

Interestingly, differences between diagnostic groups do not lean heavily on familiar language regions.

Conclusions

Neural coherence in the gamma-band successfully predicts ASD diagnostic status with better performance from story-listening than from listening to an unfamiliar language or resting with eyes-open.

Group differences in cortico-subcortical pathways implicated, perhaps with downstream consequences for language performance.

Neuromagnetic activity collected during a simple passive story-listening task may be valuable in constructing neurophysiological biomarkers for ASD.