Resting-State EEG Asymmetry and Irritability in Children with ASD: The Autism Biomarkers Consortium for Clinical Trials


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Background

• Autism Spectrum Disorder (ASD) is a neurodevelopmental disorder characterized by social communication and behavioral impairments.
• Irritability, or a proromene experience negative affective states like anger or frustration, is associated with several mental health disorders and is an important target of clinical trials for ASD (Barata et al., 2016; Brotman et al., 2017; Elbe & Lanahl, 2012).
• Electroencephalography (EEG) measures neural activity and has been discussed as a potential biomarker in several mental health disorders. EEG is particularly important in ASD research due to its non-invasive protocol and flexibility (Webb et al., 2015).
• Acquired during resting state EEG, Alpha power, represents frequency in the 6 to 12Hz and has been shown to be increased in ASD (representing decreased activity), although findings are mixed (Wang et al., 2013). Right Frontal Alpha-Aymmetry (FAA) may index behaviors associated with withdrawal and other negative temperament characteristics. Additionally, infants at higher risk for ASD begin with a left relative fronto asymmetry that shifts toward the right as they develop (Gabor-Sunthorn et al., 2015; Sutton et al., 2005).

This study investigates the relationship between fronto alpha asymmetry and irritability in ASD children.

• Hypothesis 1: Compared to TD, ASD children will show both higher parent-reported irritability and greater alpha power in the right than left frontal lobe (Right FAA).
• Hypothesis 2: Children with ASD who score clinically high in irritability will show Right FAA compared to ASD children with low irritability.

Methods

The Autism Biomarkers Consortium for Clinical Trials (ABC-CT) is a NIH-funded five-site longitudinal study investigating potential biomarkers in children ages 6-11.5 with ASD compared to typically developing peers. Data collected includes clinical/social functioning, eye-tracking, and EEG. Measures include Autism Diagnostic Observation Schedule (ADOS) for ASD severity, Differential Ability Scale (DAS) for IQ, Aberrant Behavior Checklist – Irritability Subscale, Resting-state EEG data – High and Low Alpha Power.

Resting-State EEG Collection & Processing

• EEG System: EEG 128 Channel HydroCel Geodesic Sensor Net, with either 300 or 400 amps, at a 1000 Hz sampling rate, with a 0.1-2000 Hz filter, and a 0.1Hz high pass filter post-acquisition.
• Resting-state EEG stimuli consisted of 180 seconds of non-social abstract images presented as 6 videos divided into 3 blocks. Participants were reminded to sit still and watch the videos without talking.
• Log EEG, videos, and EEG loss was reviewed for protocol fidelity, child compliance, and file integrity. Resting-state data was processed through the Batch EEG Automated Processing Platform (BEAPP, Levin et al., 2018) to derive power within the chosen frequency bands–study this uses alpha (8.99-12.99Hz) and low alpha (9.12-9.99Hz).

Participants

• 399 (280 ASD) were enrolled in the study (365+25 ASD provided ≥200 seconds of attended, artifact-free EEG data).
• Using a raw irritability score clinical cutoff of ≥21, participants with ASD were divided into high (H=9) and low (L=183) irritability groups (Brinkley et al., 2007).
• There were no participants in the TD group that met the threshold for high irritability and therefore were not analyzed by High and Low Irritability.

Analysis

• FAA was calculated using mean Alpha Power as described in Sun, Plerakylia, & Hartikainen (2017) for: - Left Frontal (E20, E23, E24, E27, E28) and - Right Frontal (E3, E117, E118, E123, E124)
• FAA = Right Frontal Power – Left Frontal Power
• A score >0 reflects Right FAA
• Analyses utilized ANOVA(s) and correlations.

Results

H2a. Correlations within ASD

• No relationships between High FAA or Low FAA and IQ, ASD severity, or parent-reported irritability.

H2b. ANOVAs within ASD

• There was no significant difference between (H) and (L) irritability ASD groups in either High FAA, (F1,250=0.011 or Low FAA, F1,250=0.677) as shown in the graph below.

Discussion

• Irritability is a transdiagnostic characteristic and is found across childhood neurodevelopmental disorders and childhood mental health disorders. Irritability is a target of treatment for ASD. Our goal was to examine if frontal asymmetry in the alpha band was related to irritability in children with ASD.

Conclusion

• Children with ASD compared to children with TD were reported as having more behaviors that were characterized as reflecting "irritability" by their parents.
• However, we neither found differences in FAA in children with ASD and TD, nor within children with ASD who had High or Low Irritability scores on the ABC.
• Additionally, there were no relationships between ASD severity, IQ, irritability, and High or Low FAA.

Future Steps

• It may be that FAA in a child is a related to parent report of irritability or irritability that could matter (state) during the EEG may influence FAA. As a follow up, we will be able to look at mood ratings taken by the experimenter during acquisition.

Table 1. Mean and (SD) for TD and ASD participants at T1.

<table>
<thead>
<tr>
<th></th>
<th>TD</th>
<th>ASD</th>
<th>ASD Only</th>
</tr>
</thead>
<tbody>
<tr>
<td>All</td>
<td>All</td>
<td>Irritability</td>
<td>Irritability</td>
</tr>
<tr>
<td>Total N</td>
<td>116</td>
<td>252</td>
<td>69</td>
</tr>
<tr>
<td>Female N</td>
<td>36 / 31.03%</td>
<td>61 / 24.21%</td>
<td>11 / 15.94%</td>
</tr>
<tr>
<td>Age in years</td>
<td>8.49 (1.61)</td>
<td>8.58 (1.64)</td>
<td>8.67 (1.75)</td>
</tr>
<tr>
<td>DAS Full Scale IQ</td>
<td>115.22 (12.32)</td>
<td>96.65 (20.97)</td>
<td>98.51 (21.01)</td>
</tr>
<tr>
<td>ADOS CSS</td>
<td>1.59 (0.875)</td>
<td>7.58 (1.787)</td>
<td>7.39 (1.89)</td>
</tr>
<tr>
<td>ABC Irritability</td>
<td>1.23 (0.24)</td>
<td>12.49 (2.92)</td>
<td>24.93 (6.02)</td>
</tr>
<tr>
<td>High FAA</td>
<td>-0.011 (0.274)</td>
<td>0.016 (0.259)</td>
<td>0.036 (0.264)</td>
</tr>
<tr>
<td>Low FAA</td>
<td>-0.053 (0.276)</td>
<td>-0.013 (0.262)</td>
<td>0.005 (0.273)</td>
</tr>
</tbody>
</table>

Table 2: irritability and FAA Correlations in ASD T1.

Frontal Alpha Asymmetry by Low and High Irritability in ASD (N=252)

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