Comparison of Neural Response to Language in Infants at Elevated Risk for ASD and in Infants with Nonsyndromic Craniosynostosis

Sun AH1,2, Rolison M2, Halligan T3, Chuang C1,2, Yang JF1,2, Hashim PW2, Stavropoulos KKM2, Chawarska K1, Steinbacher DM2, Landi N2,4, Mayes LC1, Persing JA2 & McPartland J1

1McPartland Lab, Child Study Center, Yale School of Medicine, 2Section of Plastic and Reconstructive Surgery, Yale School of Medicine, 3Haskins Laboratories, New Haven, CT, 4Department of Psychology, University of Connecticut, 5Graduate School of Education, University of California, Riverside

Introduction

Background: Autism spectrum disorder (ASD) is characterized by impaired social interaction and communication.1 While language skills vary widely among individuals with ASD, language delay in infants is an important prognostic feature of ASD severity. The study of auditory event-related potentials (ERPs) in infants at higher risk for ASD (HR-ASD) has demonstrated atypical responses in several ERP components compared to typically-developing (TD) controls.2]\n
Methods

Participants
- HR-ASD and TD subjects were recruited from the Yale Child Study Center, and MSO subjects were recruited from the Yale Craniofacial Center.
- Subjects were tested at two time points (T1 and T2). For MSO subjects, T1 was prior to surgical correction of deformity and T2 was after surgical correction.
- In total, there were 12 HR-ASD, 15 MSO (6 of which were severe, S-MSO), and 33 TD subjects.

Experimental Design:
- Auditory presentations of retroflex phoneme /D/ and dental phoneme /d/ (non-native phoneme discrimination task) with 5 blocks and 20 trials per block.
- Each phoneme was presented 10 times per block in random order.
- Stimulus duration: 250ms; inter-stimulus interval: 610ms.

Data Acquisition and Processing:
- EEG recorded at 250 Hz using 128 channel HydroCel Geodesic Sensor Net.
- EEG was segmented from 100ms before to 700ms after the stimulus, filtered from 0.1-30 Hz, and artifact corrected using NetStation 4.5.4.
- The difference wave was computed between cortical and retroflex waveform responses, and the MMN was defined as the largest negative amplitude between 80-300ms.
- Clusters of central and frontal electrodes were selected based on previous literature (Figure 2).
- Severity of metopic synostosis was determined from 3D reconstruction of CT imaging in Materialise Mimics (Leuven, Belgium) based on the previously-defined endocranial bifrontal angle5.

Results

One-way analysis of variance (ANOVA) was performed for three groups: HR-ASD, MSO, and TD subjects, as well as a sub-analysis for severe metopic patients (S-MSO). Homogeneity of variance was tested using Levene's test with Tukey's HSD and Games-Howell tests were performed post hoc.

Table 1. Mean MMN voltages (µV) by group. P-value is for one-way ANOVA between HR-ASD, MSO, and TD.

<table>
<thead>
<tr>
<th>Group</th>
<th>T1 HR-ASD (n=12) Mean ± SD (µV)</th>
<th>T2 HR-ASD (n=7) Mean ± SD (µV)</th>
<th>Controls (n=27) Mean ± SD (µV)</th>
<th>MSO (n=15) Mean ± SD (µV)</th>
<th>ANOVA p-val</th>
</tr>
</thead>
<tbody>
<tr>
<td>Left Frontal</td>
<td>-3.30±2.77</td>
<td>-0.36±4.40</td>
<td>-6.31±4.55</td>
<td>0.090</td>
<td></td>
</tr>
<tr>
<td>Right Frontal</td>
<td>-5.80±3.99</td>
<td>-4.03±3.74</td>
<td>-4.05±1.96</td>
<td>0.623</td>
<td></td>
</tr>
<tr>
<td>Left Central</td>
<td>-2.95±3.12</td>
<td>-2.56±4.05</td>
<td>-4.05±1.96</td>
<td>0.498</td>
<td></td>
</tr>
<tr>
<td>Right Central</td>
<td>-5.16±3.27</td>
<td>-2.66±1.68</td>
<td>-3.61±4.87</td>
<td>0.344</td>
<td></td>
</tr>
</tbody>
</table>

Table 2. Electrode layout. Frontal (blue) and central (red) clusters were used for analysis.

Conclusions

- HR-ASD and MSO subjects had reduced MMN amplitude in the left frontal electrodes compared to controls, but this was not significant.
- Individuals with severe forms of MSO had greater MMN attenuation compared to controls (p=0.004).
- There were no significant differences in MMN found between postoperative metopic synostosis, HR-ASD, or control subjects.
- Our previous work demonstrated shared abnormalities in the P150 in HR-ASD and SSO infants, suggesting abnormal processing as a shared basis for atypical language development in HR-ASD and SSO subjects.
- However, abnormal auditory MMN does not appear to be a shared feature of atypical language processing in HR-ASD and severe MSO subjects.
- Atypical language development in HR-ASD and NSC subjects reflects shared and distinct neural processes, highlighting the importance of considering functional profiles when characterizing language deficits in clinical populations.

Acknowledgements

This research was supported by NIH MH82507 (JM), Simons Foundation 94924 (JM), C TSA Grant Number U1L RR021439 (LM, JM), the American Society of Maxillofacial Surgeons (IP), the plastic Surgery Foundation (IP), and the office of Student Research at the Yale School of Medicine (AS).

References