Comparison of the Auditory Mismatch Negativity ERP in Infants at Risk for ASD and Infants with Craniosynostosis

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Introduction

Background: Language delay impairing communication is a primary feature of autism spectrum disorder (ASD). Children with ASD display social and communicative impairments and present with varying levels of language functioning.[1] One approach to studying language processing in infants at high risk for ASD (HRASD) is the use of auditory event-related potentials (ERPs). Previous work, including our own, has demonstrated irregularities in the P150 component in HRASD infants as an indicator of abnormal speech processing.[2,3] The P150 reflects neural correlates of acoustic processing (recognizing physical features of auditory stimuli, such as fundamental frequency).[4]

The auditory mismatch negativity (MMN) ERP component is also thought to be associated with language processing, however via phonetic processing (processing lexical semantics in which words are based). This includes language perception, memory, and auditory discrimination.[5] When abnormal, the MMN has been associated with language impairment.[6] Previous studies have reported conflicting MMN findings in HRASD populations.[7]

Study of language development is also of interest in craniosynostosis (CSO), a congenital condition of premature skull fusion in infants causing abnormal skull shape and distribution of brain volume. Sagittal CSO is the most common form, characterized by premature fusion of the sagittal suture. Photographs illustrating headshape morphology in sagittal CSO are shown in Figure 1. CSO has been associated with delayed speech and decreased abilities in both reading and spelling.[8]

Objective: Compare language processing using the MMN component in infants across two groups at risk for language impairment—HRASD and sagittal CSO.

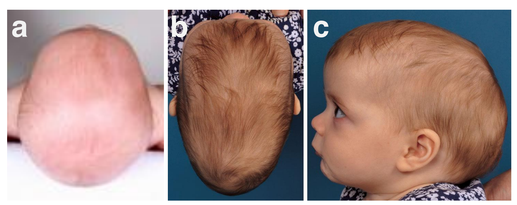

Figure 1. Graphic comparison of headshape between (a) normal infant[9] and (b, c) sagittal CSO infant[10].

Methods

Participants: The number of participants in each group is shown in Table 1.

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

Methods

Table 1. Sample size and age per group

	Typically Developing (TD)	HR ASD	Sagittal CSO
# of Participants	34	12	14
Mean age, days (SD)	206 (94)	226 (126)	234 (277)

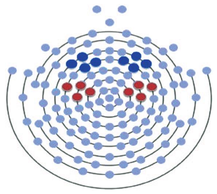

Figure 2. Electrode layout of the frontal (blue) and central (red) electrodes used for analysis

Data Acquisition and Analysis:
- EEG recorded at 250 Hz using 128 channel HydroCel Geodesic Sensor Net
- EEG was segmented, filtered, and artifact corrected using Net Station 4.5.4
- MMN was computed as the largest negative amplitude in the difference wave (obtained by subtracting the dental from the retroflex waveform response) between 80-300ms
- Clusters of central and frontal electrodes were selected for analysis (Figure 2)
- Repeated measures analysis of variance (ANOVA) was performed with group as a between-subjects factor and brain region and hemisphere as within-subjects factors

Results

- Grand-averaged waveforms to the retroflex and dental phonemes and the difference waves are shown in Figures 3-5 for the TD, HRASD, and CSO groups, respectively
- Significant effects of Group ($F(2,57)=4.658$, $p=0.013$) and Region*Group ($F(2,57)=3.252$, $p=0.046$) were observed
- Group
  - Pairwise comparisons revealed CSO infants displayed attenuated MMN compared to controls ($p=0.004$) and HRASD infants ($p=0.036$) (See Figure 6)
- Region*Group
  - A statistically significant impact of group was observed in the frontal region ($F(2,57)=6.254$, $p=0.004$) but not in the central region ($F(2,57)=1.264$, $p=0.290$)
  - In the frontal region, pairwise comparisons revealed sagittal CSO infants displayed attenuated MMN compared to controls ($p=0.001$) and HRASD infants ($p=0.026$) (See Figure 7)

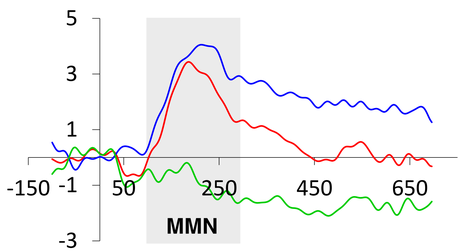

Figure 3. TD grand averaged waveforms

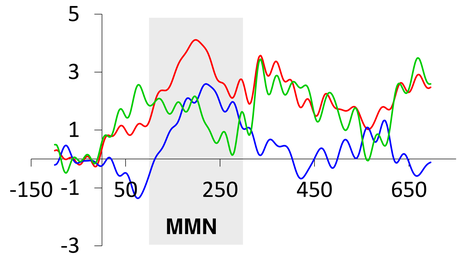

Figure 4. HRASD grand averaged waveforms

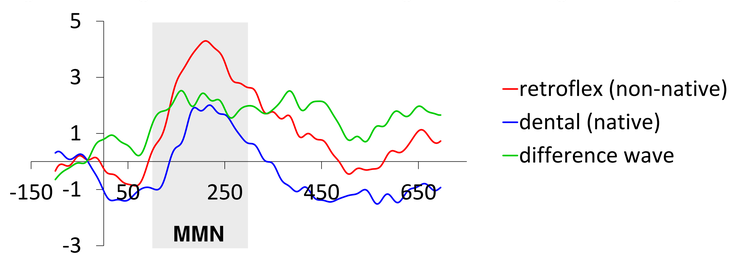

Figure 5. Sagittal CSO grand averaged waveforms

Results

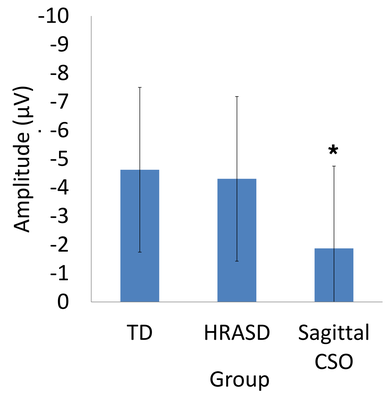

Figure 6. Overall average MMN amplitude differences by group

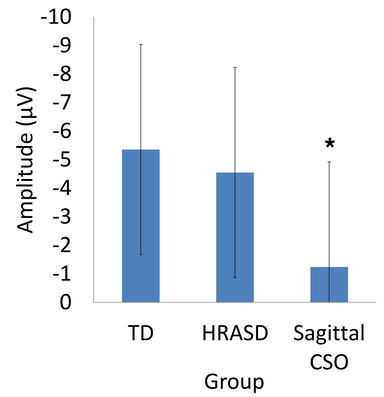

Figure 7. Frontal region average MMN amplitude differences by group

* indicates statistically significant difference from the other two groups.
Error bars indicate standard deviation above and below the mean.

Conclusions

- No significant difference in auditory MMN was observed between TD infants and HRASD infants
- CSO infants demonstrated attenuated auditory MMN compared to TD infants and HRASD infants, suggesting abnormal phonetic processing in CSO infants
- Abnormal auditory MMN is not a shared feature of atypical language development in HRASD and sagittal CSO infants
- Our previous work[11] demonstrated shared abnormalities in the P150 in HRASD and CSO infants, suggesting abnormal acoustic processing as a shared basis for atypical language development in HRASD and CSO
- Atypical language development in HRASD and CSO are contributed to by shared and differing neural processes, highlighting importance of considering profiles of function when characterizing language deficits in clinical populations

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