The specificity of atypical neural responses to language in infants at risk for ASD

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Introduction

Background: Language delay and difficulties in communication are characteristic features of autism spectrum disorder (ASD). Atypical patterns of neurophysiological responses to language emerge between 6 and 12 months in infants at elevated risk for ASD (Seery et al., 2012).

Delays in language are also associated with non-syndromic craniosynostosis (NSC; Magge et al., 2000). NSC is the result of premature fusion at one or more skull growth sites, and it affects roughly roughly 1 in 2000 live births (Cohen and MacLean, 2000). The delays observed in infants with NSC are due to impaired cranial expansion, which, in turn, restricts anatomical brain development. Preliminary evidence suggests that infants with NSC display atypical neurophysiological responses to linguistic stimuli (Hashim et al., 2013).

It remains unclear which atypical neurophysiological responses to linguistic stimuli are non-specific markers of general language delay and which are specific to each of these two conditions.

Study Aims: To contrast local and global oscillatory characteristics of electrophysiological responses to language stimuli in infants at high-risk for ASD, infants with NSC, and infants at low-risk for ASD:

- Inter-trial coherence (ITC) is a measure of localized synchronization in the EEG signal across trials that can be interpreted as an index of consistent stimulus-driven neurophysiological responses.
- Phase coherence is a measure of synchronization in the EEG signal across sites that can be interpreted as an index of functional connectivity.

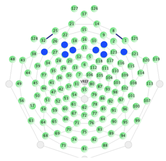

Figure 1: ITC was computed within left and right electrode groupings (electrodes chosen to match Hashim et al., 2013)

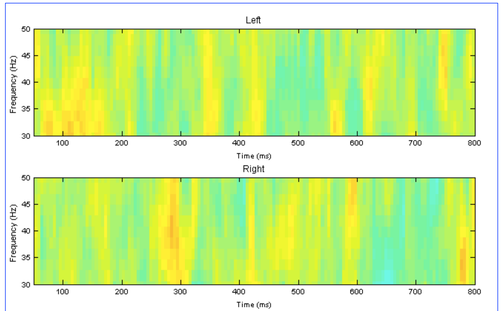

Figure 2: ITC in the gamma band in infants at **low-risk for ASD (LR)** computed between left frontal electrodes (top panel) and right frontal electrodes (bottom panel)

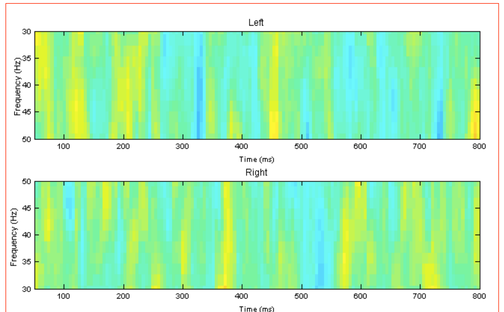

Figure 3: ITC in the gamma band in infants at **high-risk for ASD (HR)** computed between left frontal electrodes (top panel) and right frontal electrodes (bottom panel)

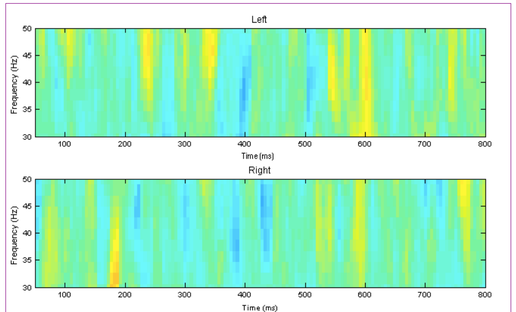

Figure 4: ITC in the gamma band in infants with **craniosynostosis (NSC)** computed between left frontal electrodes (top panel) and right frontal electrodes (bottom panel)

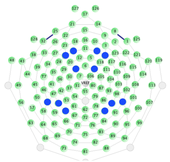

Figure 5: Coherence was calculated between anterior and posterior electrode groupings within each hemisphere (electrodes chosen to match Righi et al., under review).

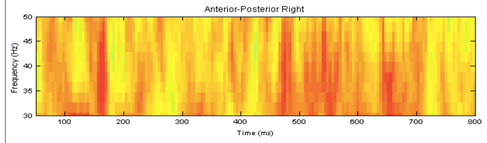

Figure 6: Coherence in the gamma band in infants at **low-risk for ASD (LR)** computed between left anterior-posterior electrodes (top panel) and right anterior-posterior electrodes (bottom panel)

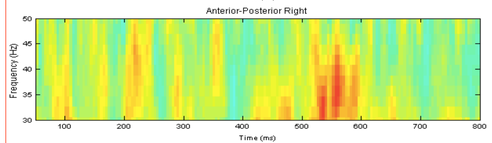

Figure 7: Coherence in the gamma band in infants at **high- risk for ASD (HR)** computed between left anterior-posterior electrodes (top panel) and right anterior-posterior electrodes (bottom panel)

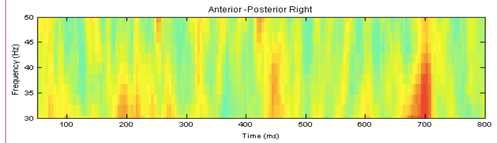

Figure 8: Coherence in the gamma band in infants with **craniosynostosis (NSC)** computed between left anterior-posterior electrodes (top panel) and right anterior-posterior electrodes (bottom panel)

Methods

Participants:

	Low Risk for ASD (LR)	High Risk for ASD (HR)	Craniosynostosis (NSC)
Participants	21	14	7
Mean age (months)	11.7	9.9	11.2

Experimental Design:

- Auditory presentations of English retroflex phoneme /Da/ and Hindi dental phoneme /da/
- 5 blocks, 20 trials per block
- Stimulus duration= 250 ms; ISI = 610 ms

Data Acquisition and Analysis:

- EEG recorded at 250 Hz using 128 channel HydroCel Geodesic Sensor Net
- EEG was segmented, filtered, artifact corrected, and hand-edited
- Inter-trial coherence (ITC) and phase coherence in the gamma band (30-50 Hz) were computed using EEGLAB (Delorme and Makeig, 2004).

Preliminary Results

- ITC and coherence were averaged in 100ms time windows from 100ms to 700ms post stimulus onset
  - Data was analyzed using repeated-measure factorial mixed-model ANOVA separately for each time window
  - Models included group (3 levels; between-subjects) and hemisphere (2 levels; within-subjects) as factors

	ITC	Coherence
100-200ms	• **LR > HR, $p < 0.05$** • **LR > NSC, $p < 0.01$** • No hemispheric differences, No interactions	• **LR > HR, $p < 0.01$** • **LR > NSC, $p < 0.05$** • **Right > Left, $p < 0.05$**
200-300ms	• **LR > HR, $p < 0.05$** • **LR > NSC, , $p < 0.01$** • No hemispheric differences, No interactions	• **LR > HR, $p < 0.05$** • **LR > NSC, $p < 0.1$** • No hemispheric differences, No interactions
300-400ms	• **LR > HR, $p < 0.05$** • **LR > NSC, , $p < 0.01$** • **Left > Right in HR, $p < 0.01$**	• **LR > HR, $p < 0.01$** • **LR > NSC, $p < 0.05$** • **Right > Left, $p < 0.05$**
400-500ms	• No group differences • No hemispheric differences • No interactions	• **LR > HR, $p < 0.01$** • **LR > NSC, $p < 0.05$** • **Right > Left, $p < 0.05$**
500-600ms	• No group differences • No hemispheric differences • No interactions	• **LR > HR, $p < 0.05$** • **LR > NSC, $p < 0.05$** • **Right > Left for LR, $p < 0.01$, and HR, $p < 0.01$**
600-700ms	• No group differences • No hemispheric differences • Left > Right in LR, $p < 0.01$	• **LR > HR, $p < 0.01$** • **LR > NSC, $p < 0.05$** • No hemispheric differences, No interactions
700-800ms	• No group differences • No hemispheric differences • No interactions	• **LR > HR, $p < 0.01$** • **LR > NSC, $p < 0.1$** • No hemispheric differences, No interactions

Table 1: Results of post-hoc simple effect tests following significant main effects and interactions

Conclusions

- Infants at low-risk for ASD show higher local and global synchronization in response to speech sounds, compared to both infants at high-risk for ASD and infants with NSC.
- Atypical oscillatory responses in the gamma band in response to speech sounds might be indicative of non-syndrome specific disruptions in brain development.
- Lower synchronization in neural activity might give rise to the language delays observed in infants at high-risk for ASD and infants with NSC.
- Results emphasize the importance of including clinical control groups in studies of at-risk infants to provide information about the specificity of developmental differences

Acknowledgments

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