Brain Bases of Auditory Processing in Infants: Localization and Statistical Regularities Radhika Santhanagopalan University of Michigan

Mentor: Ioulia Kovelman

A Thesis Submitted in Partial Fulfillment of the Requirements for the Degree of Bachelor of Science with Honors in Biopsychology, Cognition, and Neuroscience from the University of Michigan 2016

Author Note

Thank you to Dr. Silvia Bisconti, Dr. Frank Hu, Dr. Anne-Michelle Tessier, & Dr. Renee Lajiness-O'Neill for providing me with the facilities and resources needed to conduct this study. A huge thank you to Neelima Wagley, my graduate student advisor, whose mentorship, support, and remarkable aptitude have undoubtedly shaped my learning and strengthened my desire to pursue research. Finally, thank you Dr. Ioulia Kovelman for the opportunity to work in your lab and the dedication and passion with which you inspire your lab members to pursue research.

Contact: radhisan@umich.edu

Abstract

We have all at some stage questioned our sensibilities when we 'baby talk' – can babies really understand language, or are we overreaching in vain? Despite an inability to articulate to us their prowess, infants have a remarkable capacity to understand familiar sounds and apply language rules to novel stimuli. Neuroimaging techniques reveal the complex process of language acquisition in infants, specifically as it relates to statistical regularities and localization of language at infancy. Using functional Near-Infrared Spectroscopy (fNIRS), this present study examines brain activity associated with an infant's ability to differentiate between high and low probability phonemes in the frontotemporal, temporal, and temporoparietal brain regions. Consistent with previous findings, our results show that infants between 7-9 months are already able to identify familiar phoneme categories (sounds occurring more often in their native language). Interestingly, evidence from temporal regions suggests that infants already have a penchant for speech sounds compared to non-speech, nature sounds. Lastly, our results indicate hemispheric differences in temporoparietal regions, which, albeit marginal, may reveal the inchoate stages of left-hemisphere language localization. On top of biological predispositions, exposure to language from the environment can permanently alter the neural architecture of the developing brain. This could have significant implications for atypical populations with specific language impairments where making early interventions is pivotal. Thus, we can capitalize on an infant's ability to identify statistical cues and localize language in the brain to predict the course of their language and cognitive development.

Keywords: fNIRS, phonology, statistical regularities, localization, language acquisition, phoneme

Brain Bases of Auditory Processing in Infants: Localization and Statistical Regularities using fNIRS

Spoken language is a continuous stream of linguistic input, and it is this very fluidity that constitutes one of the first challenges of language acquisition in infants: the ability to parse sounds into meaningful units. Natural speech offers cues that help infants detect and extract syllable and word boundaries; these cues can manifest in multiple ways: suprasegmental cues (e.g. pitch), phonotactic cues (e.g. legal consonant clusters), social cues, or even statistical cues (regularities like transitional probability; Gervain & Mehler, 2010). Language-based statistical learning is a domain-general, implicit and passive means of extracting patterns, or statistical regularities, in a given language (Aslin & Newport, 2012). Infants as young as 4 months have the propensity to learn which syllables are paired together, gauge how frequently these patterns and combinations occur in their environment (Friederici, 2007), and, according to Aslin & Newport (2012), distinguish between what constitutes part-words and full words (including the case of pseudo words) in a given language. In fact, even with limited exposure to language, infants have the capacity to learn statistical relationships and distinguish between syllables that are always paired together and those that are rarely paired together. The relationship between external statistical cues and internal mental representations describes an inductive cognitive leap that constitute the building blocks to infants' understanding of phonotactics (Gervain & Mehler, 2010).

Phonotactics are the rules and boundaries that govern a particular language: word order, legality of these formations, and the various combinations of phonemes within syllables or words (Gervain & Mehler, 2010). For example, in English, certain syllables and sounds often occur together (e.g. '*ba*') while other syllables and sounds are not as frequently observed (e.g. '*td*').

3

Over time, infants learn implicitly the probability of syllable occurrences, and are increasingly able to form and distinguish syllable clusters (Romberg & Saffran, 2011). Whether statistical and phonotactic learning operate in parallel with a child's innate and unique predispositions to language, or whether this learning renders any innate differences obsolete, remains contentious. However, our experiment relies on the theory that typically developing brains can capitalize on statistical and phonotactic cues, which lead to the formation and development of language. We thus acknowledge the prodigious role environmental stimuli plays on language acquisition in developing infants.

Given the role of environmental stimuli on language development in infants, the present study uses a paradigm in which statistical regularities are measured by the relative frequency (and infrequency) of certain paired phonemes in the English language. Thus, we are testing an infant's ability to recognize familiar speech sounds compared to both unfamiliar speech sounds of their native language (English) and non-speech nature sounds. More brain activation for high frequency phonemes would indicate familiarity with the phoneme pair (because children are more sensitive to native phonemes), whereas we would expect lower brain activation for those phoneme pairs that are uncommon in English. Additionally, we expect that non-speech nature sounds elicit more activation in the left hemisphere and less activation in the right hemisphere, which is predominantly responsible for music and other non-speech sounds (Werker, 2015).

Infant-directed speech (IDS) is an effective method of making statistical and phonological cues more accessible to infants (thereby leading to effective phoneme parsing), because it helps convey linguistic importance and socioemotional value (Perryman et al., 2013). The most prominent characteristics of IDS include slower rate of speech, higher frequency, greater pitch variation, longer pauses, hyperarticulated vowels, simplified sentence structure and repetitive intonational structures (Kitamura & Burnham, 2003). Through the parsing of phonemes into appropriate word and syllable boundaries, IDS assists infants in learning patterns of high frequency and low frequency sounds; cues given from IDS help facilitate the recognition and formation of boundaries of syllables and words (Saffran, Newport & Aslin, 1996). Moreover, IDS is shown to elicit increased neural activity for familiar words (Zangl & Mills, 2007). Thus, an in-depth understanding of the perceptual and neural correlates associated with IDS and phoneme clustering may help to better understand the mechanisms behind the earliest milestones of language acquisition. Given the overwhelming support of IDS in language development, our auditory paradigm for high and low probability phonemes both use IDS with the expectation that infants will be more receptive to our auditory stimuli and thus produce more salient brain responses to the linguistic manipulations.

Brain Bases of Language Acquisition

The neural mechanism behind an infant's ability to parse these aforementioned phonemes still remains unclear, though new technologies are now able to examine nascent stages of development. Previous findings using fNIRS show more activation in language areas for speech over non-speech, as well as native languages compared to non-native languages (Werker, 2015). Even though infants up until 6 months are sensitive to nonnative phonemes, they eventually lose this affinity through linguistic experience (Kuhl, 1992). Interestingly, some studies even reveal left-hemisphere language specialization at birth. Given this evidence, in our study we would expect lateralized processing in the left hemisphere for high and low probability phonemes, and more right hemisphere processing for nature sounds. fMRI studies of sleeping 3-month-old infants show active left-lateralized brain regions (similar to adults), suggesting precursors of adult cortical language areas are already active (Dehaene-Lambertz, Dehaene, & Hertz-Pannier, 2006). This is further evidence that infants' brains can reveal much about their state of language processing preceding actual speech production. Given this evidence, studies that then observe language within a chronological framework (starting at speech production), may fail to acknowledge the significant neural organizational changes that occur before speech develops. More research is necessary to see whether individual differences at infancy can render some babies at an early (and possibly permanent) disadvantage from the onset of life, a disadvantage that likely compounds over time. Tangentially, these early imaging studies may allow us to identify those at high-risk for language impairments even before infant verbalization. For example, infants exhibiting early signs of hyper-connectivity (a common occurrence in ASD) related to brain volume and prevalence and position of commissural fibers, projection fibers, and association (Conti et al., 2015).

One theory bridging language experience with neural changes is the native language neural commitment (NLNC), which suggests that language learning results in neural patterns and networks that code native speech (Kuhl, 2004). With the development of these networks come a heightened ability to process new speech that is consistent with existing patterns. Speech from environmental stimuli thus provide a foundation that makes native languages more conducive to learning. This epigenetic-esque interaction between environmental speech stimuli and neural organization evokes interesting questions about the nature-nurture paradigm as previously discussed; from these findings we might extrapolate that the brain is prewired to sounds, but it is the interaction of language in the environment with the brain that bring about an infant's impressive language acquisition abilities. In this experiment we can thus observe the intricate relationship between the brain and language from the environment. Additionally, it is thought that the structural asymmetries observed in macroscopic and cytoarchitectonic levels (for example a longer left sylvian fissure and left planum temporale), can explain the why the left hemisphere is able to code complex speech patterns better than the right hemisphere (Dehaene-Lambertz, Dehaene, Hertz-Pannier, 2006). It is as yet unclear however whether these differences are a result of prewiring or normative and hegemonic environmental influences that maintain the status quo, thus producing the same brain patterns.

Given the emerging use of fNIRS in understanding language acquisition in infants, we can inspect neural correlates of language processing during the early milestones of typical and atypical development, which can help map trajectories as infants come to master their native languages. Using our knowledge of phonotactics and statistical learning (in particular high and low phoneme clustering as phonotactic cues), we can investigate the organization of phonological structures in the brain by measuring hemodynamic responses and examining activation patterns in language-processing areas.

Present Study

This present study examines the neural underpinnings of phonotactic cues (high and low frequency clusters) in infants, as well as the lateralization and localization of phonological processing. We aim to address the following questions: 1) Are infants able to capitalize on statistical cues by differentiating between phoneme clusters? 2) Is phonological development localized in infants' brains by 7-9 months? Does each language-related brain region (frontotemporal, temporal, & temporoparietal) invoke similar patterns to each other? 3) Based on these research questions, what could we expect in infants at risk for language impairments (from a neurodevelopmental and environmental perspective)? Specifically, we are looking at three important language-related brain areas: bilateral frontotemporal, temporal, and temporoparietal

regions. Despite their relation to language, it would be interesting to identify differences in the way each brain region processes auditory paradigms based on their own unique cytoarchitectonic structure.

A useful method of studying the neural mechanisms involved in language acquisition in infants, is the functional near-infrared spectroscopy (fNIRS), a neuroimaging tool with high temporal resolution (Masataka, Perlovsky, & Hiraki, 2015). It uses the infrared wavelength of light to measure oxygenated and deoxygenated hemoglobin concentration changes (Lloyd-Fox, Blasi, & Elwell, 2010). It can therefore be used to track nonverbal brain responses to verbal stimuli in a naturalistic environment and does not rely on the ability of infants to articulate their ability to discriminate legal and illegal phonemes (Gervain & Mehler, 2010). fNIRS is one of the leading brain imaging options for infants, and despite a relatively shallow depth of 2-3cm into the cortex, it is ideal for this study because it is non-invasive, quiet, child-friendly, portable and ecologically valid. Not to mention, due to the relatively amorphous and shallow nature of an infant's brain, this depth should not prove to be a substantial limitation.

The study will involve behavioral assessments informed by Mullen Scales of Early Learning (Mullen, 1995), as well as parent reports of child behaviors using the Infant Behavior Questionnaire-Revised (IBQ-R, Gartstein & Rothbart, 2003). The subsequent fNIRS experiment involves using a 6-minute auditory paradigm (with 2 experimental conditions and 1 control condition) to examine an infant's familiarity with phonotactic rules (conditions differ on phoneme frequency), and measuring their brain's hemodynamic levels during auditory stimulation. Moreover, fNIRS probes and channels provide physiological data from both the left and right hemisphere, thus allowing us to examine the lateralization of phonemic cues. Through this we can then examine an infant's ability to differentiate between high and low probability phonemes, as well as establish localization and hemispheric differences in language processing.

We expect higher brain activation for high-probability phoneme clusters, indicating that these are more salient units of information for infants who are babbling and are about to start producing words reflecting the high frequency patterns of their native language. In the same vein, we anticipate less brain activation for low-probability phoneme clusters as these are less relevant to children's language acquisition at 9 months of age. We might also expect that nature sounds show more activation in the right hemisphere, which is mostly responsible for processing non-speech sounds like music (Molfese, 1984). We hypothesize that the three different brain regions will produce similar results because they are all associated with language processing. However, any potential differences in their output might be related to the specificity of our phonotactic paradigm – that is, if we were to take the aggregate effects of prosody, transitional probabilities, phonotactics and so on, those differences between different brain regions might prove inconsequential. In essence, we surmise main effects for condition (phoneme clusters) and hemispheric differences.

Method

Participants

Twenty-four typically developing infants between the ages of 7 and 9 months (M = 278 days or 7.6 months, SD = 9.50 days) were recruited from the OB registry in the Department of Psychiatry at the University of Michigan, of which a subset of 15 were analyzed. Infants, who came from native English speaking homes, also had no hearing or known neurodevelopmental impairments. Regarding the inclusion criteria, infants were within a 37-42-week gestation

bracket, and had a birth weight of at least 2500g. In addition, they had no history of prenatal or intrapartum complication, brain injury, neurological illnesses, diseases (e.g. seizures), or known genetic disorders. All participants were offered monetary compensation for taking part in this study, and informed consent was obtained prior to participation from caregivers. This study was approved by the Institutional Review Board (IRB MED).

Behavioral Measures of Development

Infant Behavior Questionnaire – Revised (IBQ-R, Gartstein & Rothbart, 2003). The IBQ-R involves parent reports of temperament in infants between the ages of 3 and 12 months. It encompasses various different interrelated criterion: activity level, distress to limitations, approach, fear, duration of orienting, smiling and laughter, vocal reactivity, sadness, perceptual sensitivity, high intensity pleasure, low intensity pleasure, cuddliness, soothability, and falling reactivity.

Mullens Scales for Early Learning (Mullen, 1995). Mullens is often used to evaluate intellectual development vis-à-vis five scales of measurement: fine and gross motor skills, receptive and expressive language production, and visual reception. For the purpose of this study, we were interested in an infant's receptive and expressive language because these facets of language are often compromised in high-risk ASD infants. Within our 7-9 month age bracket, measures of receptivity included comprehending words and phrases such as their name, as well as attentional gaze, while expressive language involved measuring vowel production and producing meaningful gestures (Weismer, Lord, & Esler, 2011).

Verbal and Nonverbal Communication Paradigm

While undergoing fNIRS imaging, infants listened to an auditory paradigm that lasted approximately 6 minutes, with a recurring structure: 2 experimental conditions and a control condition (see Figure 1). Each condition segment lasted 18 seconds, and there was an 8 second rest between each segment. To ensure the infant's attention and physical stillness during data acquisition, moving non-social stimuli (distractor video with abstract images played on mute) were presented during the study, and there were toys available to distract the infant if necessary.

The two experimental conditions were recorded in lively IDS by a native, Englishspeaking woman: nonsense high-frequency phonemes, and nonsense low-frequency phonemes. The 18-second nature control condition involved a combination of nature sounds like waves, rain, and wind. Apart from its importance as a control (for comparison), this control condition provided insight into the development of right hemisphere specialization of non-speech, musical sounds.

fNIRS Optical Brain Imaging

fNIRS Imaging Apparatus. Using a TechEN-CW6 system, this non-invasive optical mechanism measured hemodynamic changes related to neural activity (using a sampling rate of 50 Hz). Using near-infrared light (690 and 830 nm) to penetrate the skull, we measured oxygenated and deoxygenated hemoglobin. Even though data from frontal, parietal and occipital cortices were also collected, for the purpose of this study, we focused specifically on the temporal regions (frontotemporal, temporal, and temporoparietal). fNIRS provided 28 channels (source-detector pairs, see Figure 2), and the distance between light emitter and detector was 2.0cm.

5-10 head measurements were taken and probes were then placed on the infant's head (who sat on their caregiver's lap for the entirety of the experiment). The stimuli were presented using MATLAB (MathWorks), Psychtoolbox Version 3, presented with an iMac "Core 2 Duo" 3.06 (2009 model) with a 27-inch screen, and auditory stimuli was played through the Mac stereo speakers.

fNIRS Cap Design. This fNIRS cap, designed by Atlas Viewer Gui software, was used to measure frontal, temporal, parietal, and occipital cortices using the 10-20 system (Jurcak, Tsuzuki, & Dan, 2007). Each participant wore the fNIRS cap for the entire auditory paradigm, and pictures were taken of the infants with a cap to ensure standardized probe positions (Figure 3). I chose to analyze data from the temporal subregions of the brain: frontotemporal, temporal, and temporoparietal brain regions. The frontotemporal brain region for both the left and right hemispheres was examined using 4 probe-detector pairs and 8 channels. Similarly, the temporal region was assessed using 4 probe-detector pairs and 8 channels. The temporoparietal region was measured by 2 probe-detector pairs and 4 channels.

Experimental Procedure

Prior to starting the experiment, fNIRS signals were assessed and verified to ensure correct optode placement. Upon arrival, caregivers completed a consent form and were then asked to report their child's behaviors through the Infant Behavior Questionnaire-Revised. This provided caregiver assessments of motor, sleep, feeding, communication/cognition, and socialemotional measures of their child. Next, head measurements of the infant were taken to ensure proper fitting of the imaging cap. Then, depending on a pre-set randomized order, participants either took part in Mullens Scales of Early Learning or completed the fNIRS neuroimaging task. Once participants completed these behavioral measures, the infant and their caregiver were taken to the fNIRS testing room, where they were given time to get acquainted. Using the infant's head measurements, the fNIRS cap was then placed on their head according to pre-existing configurations of the 10-20 system (Jurcak, Tsuzuki, & Dan, 2007). At this time, (both during set-up and the auditory paradigm) infants' attention was directed towards the computer and their neural responses to the auditory stimuli were recorded. Breaks were offered when needed for feeding or resting. A trained experimenter also sat next to the baby to both ensure that their attention was directed to the computer screen, and to restrict as much as possible the baby's head movements. After the experiment, subjects were compensated for participating in the study.

Data Analysis

Behavioral Measures Analysis. Once they completed the IBQ-R, parents were asked to read each description of the infant's temperament based on how often they pursued those behaviors in the last seven days. The format of this response was a seven-point, Likert scale (Gartstein & Rothbart, 2003): never, very rarely, less than half the time, half the time, more than half the time, almost always, always. The Mullens Scales for Early Learning was assessed in a laboratory setting with a trained researcher. Sessions would be coded for on-task and off-task behaviors in 10-second intervals. Continued behaviors over more than one interval were scored in each subsequent interval.

fNIRS Analysis. Homer2, a software developed for MATLAB (Huppert, Diamong, Franceschini, & Boas, 2009), was used to analyze our fNIRS data. Within the pre-processing stage, raw fNIRS data was converted into optical density change, motion artifacts were assessed (removed or modified) for physiological and system noise, and data was converted into hemoglobin concentration changes. The post-analysis phase involved converting our data (post pre-processing) from optical density, into oxygenated and deoxygenated hemoglobin concentrations. Applying the modified Beer-Lambert law, we measured relative differences in absorption of light by brain tissue, and used this to calculate hemoglobin concentrations. Using R statistical computing software, we ran a 2x3 ANOVA to find main effects of hemisphere (left and right) and main effects of condition (high frequency phoneme clusters, low frequency phoneme clusters, and nature sounds) for each brain region (frontotemporal, temporal, and temporoparietal).

Results

Behavioral Measures

Averages and standard deviations on the battery of standardized measures: infants' scores on the expressive and receptive subtests of the Mullens Scale of Early Learning, and parent reports from the Infant Behavior Questionnaire - Revised, are reported in Table 1. Based on the IBQ-R results, all infants in our sample fall within the average or normal range of temperamental measurements. Similarly, they exhibited average expressive and receptive language scores (M= 50.16, SD= 9.01).

fNIRS Imaging

For each ROI, a two-way repeated measures ANOVA [Hemisphere (Left, Right) x Phoneme Cluster Conditions (High Frequency, Low Frequency, Nature)] was used to assess mean hemoglobin concentration changes, using a threshold p value of .05 (see figure 4). A 2x3 ANOVA on brain activation patterns for the frontotemporal region of interest revealed a significant main effect of condition on hemoglobin concentration for the three phoneme conditions (F(2, 4)=4.13, p=.03)). Similarly, a 2x3 ANOVA on brain activation patterns for the temporal region of interest revealed a significant main effect of condition on hemoglobin concentration for the three phoneme conditions (F(2,1)=7.58, p = .02)). We can infer from this that there is generalized pattern of neural activity associated with phonemic cues at varying frequency levels in both the frontotemporal and temporal brain regions.

Additionally, a 2x3 ANOVA on brain activation patterns for the temporoparietal region of interest revealed a marginally significant main effect of hemisphere on hemoglobin concentration for both hemispheres (F(1,3)=4.33, p = .06)). The variation of hemoglobin concentration means between both hemispheres is larger than the variation of hemoglobin within a single hemisphere. We found no significant interaction effects in all three regions of interest.

In order to further corroborate our results, a post hoc paired samples t-test was run to assess condition effects in the frontotemporal and temporal regions, and hemisphere effects in the temporoparietal region. In the frontotemporal brain region, there was a marginal significance in mean HbO concentration between the low frequency and nature condition (t(8)=-2.24, p = .55)). The temporal region however showed no significant difference between conditions; of the various pair combinations, the most significant result (relative to other condition pairs in this brain region) was between high and low frequency clusters in the left hemisphere (t(8)=1.60, p = .15)). Lastly, the temporoparietal region also provided no significant results in any of the hemisphere pairs, of which the most significant (in relative terms) was the hemispheric difference in nature sounds (t(6)=0.97, p = .37)). The somewhat conflicting results between these post hoc tests and the results from the ANOVA suggest that more data should be collected in order to produce more consistent results.

Discussion

The present study investigated the brain bases of phoneme discrimination in infants between 7 and 9 months, as well as the localization of such phonetic understanding within the developing brain. Apart from undergoing multiple behavioral measures that served to reify their typicality in reaching their linguistic milestones, infants' hemoglobin levels in frontotemporal, temporal, and temporoparietal brain regions were measured in response to auditory verbal and nonverbal stimuli using functional near infrared spectroscopy (fNIRS).

Results from the ANOVA show a significant effect of phoneme condition on hemoglobin concentration in the frontotemporal and temporal regions of the brain. That is, there is a phonemic pattern exhibited in both hemispheres as they relate to the relative frequency and infrequency of a speech sound. This corroborates previous findings that infants are already sensitive to native speech sounds by 8 and 10 months of life (Jusczyk, Friederici, Wessels, Svenkerud, & Jusczyk, 1993). However, it is possible that this effect operates on a gradient depending on brain region: results from the temporal region show more marginal effects of phoneme condition on hemoglobin levels, while data from the temporoparietal region show no significant differences. To extrapolate further, this gradient might interact in parallel with a similar gradient in language-dependent memory traces, as seen through MEG studies marking phonemic memory traces of native language (Näätäneiv et al, 1997). Perhaps stronger auditory memory paths correlate with those brain areas (like the frontotemporal region) that are more highly active in phonemic discrimination. Multiple studies have supported the role of frontotemporal regions in mediating receptive language (Binder et al, 1997). This offers an alternate explanation to the idea of a gradient - different elements of language (receptive, expressive, prosodic cues, statistical cues) may activate different language-related subregions of

the brain. Future research could delve into the intricacies of these neural underpinnings of various facets of language.

Based on previous findings, we would not only expect these phoneme discriminating abilities, but we would also expect that the right hemisphere shows a higher affinity for the nature sounds than for speech sounds. However the results from this study were inconclusive, which may imply that while phoneme sensitivity has increased, localization of speech sounds may not necessarily have developed in parallel simultaneously.

Apart from phoneme cluster condition effects, the temporoparietal region shows marginally significant hemispheric differences in hemoglobin concentrations. While this might prove inconsequential upon further investigation, it elicits interesting questions regarding the localization of different facets of language acquisition in the brain. It seems there are multiple localized structural connections between language cortices (Friederici, 2011), some stronger than others depending on which element of language is being examined - for example, semantic processing is higher in frontotemporal regions (which is incidentally, less lateralized than temporal regions). How are different elements of language broken down in the brain? Is there a somatosensory homunculus equivalent for different subsets of language? Are brains prewired this way or do these hemispheric differences result from hegemonic environmental stimuli? What about cultural differences in localization?

Auditory processing of phonemes, albeit crucial, is by no means the only valid measure of language acquisition. Metrical and statistical cues for example may or may not operate similarly across different language-related brain areas. At the same time, while these language cues might exhibit differences at a mechanistic level, it is likely that prosodic, rhythmical, and statistical cues alike, do in fact align at a more abstract, cognitive level (Werker, 2015). It is

17

because of this that we purposefully chose high and low frequency phoneme clusters – as it is likely that high frequency clusters align with native speech sounds and prosodic cues, while low frequency clusters align with nonnative speech and even non-speech sounds. So while phoneme clusters may not necessarily be the best paradigm to examine language, it allows us to extrapolate our findings to language processing more generally, abstractly, and suprasegmentally.

It is well documented that infants are sensitive to nonnative phonemes, but lose this ability over time (Cheour et al, 1998). In this case we would expect equal activation for both low and high probability phoneme clusters. Since there were significant differences in their detection of different phoneme groups, we can extrapolate that by 7-9 months, infants have already lost this inclination towards low probability phonemes, or nonnative sounds; universal phoneme discrimination becomes more culture-bound. At the same time, these results were not as significant in temporal and temporoparietal regions, which might evoke interesting questions about the unique localization of native and nonnative speech sounds across the ipsilateral left hemisphere. Tangentially, it would be interesting to consider whether the increased sensitivity of native phonemes is independent of the decreased sensitivity to nonnative phonemes, or whether they have an incontrovertible inverse relationship.

Limitations

As with most studies using brain imaging technology, our sample size of fifteen limited the generalizability of our data. However, given the preliminary nature of this study, its results still are credible enough to pursue further research on neural underpinnings of phonemic discrimination in atypical populations. Similarly, the nature of our subject pool means much of our data was removed due to observed discomfort by infants and/or their inability to sit still to allow for clear hemodynamic readings. On top of recruiting infants with high-risk autism, we also intend to further expand our typically developing infant population in order to get a more generalizable data set and potentially incur more pellucid results.

Additionally, if we accept the assumption that typically developing children are already prewired to recognize certain speech sounds, then our study could be conflating important individual differences in language acquisition. In other words, to elicit meaningful comparative data between ASD populations and typical infants, it is important that these typically developing infants do not significantly vary in their genetic predisposition to language. Despite controlling for language exposure (participants were recruited from monolingual households) there may still be confounding influences like growing up in a multilingual neighborhood or the fact that some new studies have shown that even neonates are receptive to their mother's language (Werker, 2015), which may have affected the trajectory of their language development by 6 months of age.

It might be useful to combine EEG methods with fNIRS to allow for a more comprehensive understanding of electrical and hemodynamic responses of the cortex to further consolidate and advance knowledge using multiple levels of analysis.

A potential limitation with behavioral assessments like the IBQ-R is that of subjective reporting. Parents may overestimate their child's cognitive and behavioral abilities (Miller, 1988), or possibly even underestimate their child's ability as seen from gender bias studies in mothers (Mondschein, 2000). This could lead to data output that suggests that a child is typically developing even if they are not. Given that we intend to use this study as a stepping stone to investigate atypical populations, it could potentially conflate our results by obscuring differences between groups.

19

Future Directions

We can use this study as a platform to examine whether atypical populations (specifically those at high risk for developing language-specific learning impairments) can provide information on early biological markers of language impairment, potentially leading to more effective interventions. Because language organization and processing begins well before infancy, it might be beneficial to look into ways to capitalize on early stages of processing in order to attenuate the negative compounding effects of atypical language development. Particularly, the main focus of the current project is to recruit families with infants born preterm. Not to mention, fNIRS imaging is slowly making its mark as a leading tool for studying development; given its portability, studies can be conducted in schools and in other more naturalistic learning settings. Phonemic discrimination reveals much about the state of language acquisition in infants as young as 6 months, and further research on neural correlates of language in infants can help change the trajectory of language development in atypical populations, as well as harness and capitalize on untapped potential in typically developing infants.

References

- Akshoomoff, N. (2006). Use of the Mullen Scales of Early Learning for the assessment of young children with autism spectrum disorders. *Child Neuropsychology*, *12*(4-5), 269-277. doi: 10.1080/09297040500473714
- Aslin, R. N., & Newport, E. L. (2012). Statistical learning from acquiring specific items to forming general rules. *Current Directions in Psychological Science*,21(3), 170-176. doi: 10.1177/0963721412436806
- Best, C. T., McRoberts, G. W., & Sithole, N. M. (1988). Examination of perceptual reorganization for nonnative speech contrasts: Zulu click discrimination by Englishspeaking adults and infants. *Journal of experimental psychology: human perception and performance*, 14(3), 345. <u>http://dx.doi.org/10.1037/0096-1523.14.3.345</u>
- Binder, J. R., Frost, J. A., Hammeke, T. A., Cox, R. W., Rao, S. M., & Prieto, T. (1997). Human brain language areas identified by functional magnetic resonance imaging. *The Journal of Neuroscience*, 17(1), 353-362.
- Centers for Disease Control and Prevention. (2014). CDC estimates 1 in 68 children has been identified with autism spectrum disorder. Retrieved from http://www.cdc.gov/media/releases/2014/p0327-autism-spectrum-disorder.html
- Chambers, K. E., Onishi, K. H., & Fisher, C. (2003). Infants learn phonotactic regularities from brief auditory experience. *Cognition*, *87*(2), B69-B77. doi:10.1016/s0010-0277(02)00233-0
- Cheour, M., Ceponiene, R., Lehtokoski, A., Luuk, A., Allik, J., Alho, K., & Näätänen, R. (1998). Development of language-specific phoneme representations in the infant brain. *Nature neuroscience*, 1(5), 351-353. doi:10.1038/1561

- Conti, E., Calderoni, S., Marchi, V., Muratori, F., Cioni, G., & Guzzetta, A. (2015). The first 1000 days of the autistic brain: a systematic review of diffusion imaging studies. *Frontiers in human neuroscience*, *9*. doi: 10.3389/fnhum.2015.00159
- Dehaene-Lambertz, G., Dehaene, S., & Hertz-Pannier, L. (2002). Functional neuroimaging of speech perception in infants. *Science*, *298*(5600), 2013-2015. doi: 10.1126/science.1077066
- gocognitive. (2011, May 5). angela friederici the N400 and word meaning. the N400 and word meaning. [Video File]. Retrieved from https://www.youtube.com/watch?v=5d9DPhGSKVo
- Irwin, O. C., & Chen, H. P. (1946). Development of speech during infancy: curve of phonemic types. *Journal of experimental psychology*, 36(5), 431. <u>http://dx.doi.org/10.1037/h0056861</u>
- Iverson, P., Kuhl, P. K., Akahane-Yamada, R., Diesch, E., Tohkura, Y. I., Kettermann, A., & Siebert, C. (2003). A perceptual interference account of acquisition difficulties for nonnative phonemes. *Cognition*, 87(1), B47-B57. doi:10.1016/S0010-0277(02)00198-1
- E-Prime 2 (Version 2.0) [Computer Software]. Sharpsburg, PA: Psychology Software Tools, Inc. Ferguson, C. A. (1964). Baby talk in six languages. *American* anthropologist,66(6_PART2). doi: 10.1525/aa.1964.66.suppl_3.02a00060
- Eilers, R. E., Gavin, W., & Wilson, W. R. (1979). Linguistic experience and phonemic perception in infancy: A crosslinguistic study. *Child Development*, 14-18. doi: 10.2307/1129035
- Fowler, A. E. (1991). How early phonological development might set the stage for phoneme awareness. *Phonological processes in literacy: A tribute to Isabelle Y. Liberman*, 97, 117.

- Friederici, A. D., Friedrich, M., & Christophe, A. (2007). Brain responses in 4-month-old infants are already language specific. *Current Biology*, 17(14), 1208-1211. doi: 10.1016/j.cub.2007.06.011
- Friederici, A. D. (2011). The brain basis of language processing: from structure to function. *Physiological reviews*, 91(4), 1357-1392. doi: 10.1152/physrev.00006.2011
- Fujioka, T., Mourad, N., & Trainor, L. J. (2011). Development of auditory-specific brain rhythm in infants. *European Journal of Neuroscience*, 33(3), 521-529. doi: 10.1111/j.1460-9568.2010.07544.x
- Gartstein, M. A., & Rothbart, M. K. (2003). Studying infant temperament via the revised infant behavior questionnaire. *Infant Behavior and Development*, 26(1), 64-86.
 doi:10.1016/S0163-6383(02)00169-8
- Gervain, J., & Mehler, J. (2010). Speech perception and language acquisition in the first year of life. *Annual review of psychology*, 61, 191-218. doi:

10.1146/annurev.psych.093008.100408

- Huppert, T. J., Diamond, S. G., Franceschini, M. A., & Boas, D. A. (2009). HomER: a review of time-series analysis methods for near-infrared spectroscopy of the brain. *Applied optics*, *48*(10), D280-D298. doi: 10.1364/AO.48.00D280
- Jochaut, D., Lehongre, K., Saitovitch, A., Devauchelle, A. D., Olasagasti, I., Chabane, N., ... & Giraud, A. L. (2015). Atypical coordination of cortical oscillations in response to speech in autism. *Frontiers in human neuroscience*, *9*. doi: 10.3389/fnhum.2015.00171
- Jurcak, V., Tsuzuki, D., & Dan, I. (2007). 10/20, 10/10, and 10/5 systems revisited: their validity as relative head-surface-based positioning systems. *Neuroimage*, *34*(4), 1600-1611. doi: 10.1016/j.neuroimage.2006.09.024

- Jusczyk, P. W., Friederici, A. D., Wessels, J. M., Svenkerud, V. Y., & Jusczyk, A. M. (1993). Infants' sensitivity to the sound patterns of native language words. *Journal of memory and language*, 32(3), 402-420. doi:10.1006/jmla.1993.1022
- Karzon, R. G. (1985). Discrimination of polysyllabic sequences by one-to four-month-old infants. *Journal of Experimental Child Psychology*, 39(2), 326-342. doi:10.1016/0022-0965(85)90044-X

Kitamura, C., & Burnham, D. (2003). Pitch and communicative intent in mother's speech:
Adjustments for age and sex in the first year. *Infancy*, 4(1), 85-110. doi:
10.1207/S15327078IN0401 5

- Kovelman, I., Mascho, K., Millott, L., Mastic, A., Moiseff, B., & Shalinsky, M. H. (2012). At the rhythm of language: Brain bases of language-related frequency perception in children. *NeuroImage*, 60(1), 673-682. doi:10.1016/j.neuroimage.2011.12.066
- Kuhl, P. K., Williams, K. A., Lacerda, F., Stevens, K. N., & Lindblom, B. (1992). Linguistic experience alters phonetic perception in infants by 6 months of age. *Science*, 255(5044), 606-608. doi: 10.1126/science.1736364
- Kuhl, P. K. (2004). Early language acquisition: cracking the speech code. *Nature reviews neuroscience*, *5*(11), 831-843. doi:10.1038/nrn1533
- Lew-Williams, C., & Saffran, J. R. (2012). All words are not created equal: Expectations about word length guide infant statistical learning. *Cognition*, *122*(2), 241-246.

doi:10.1016/j.cognition.2011.10.007

Lloyd-Fox, S., Blasi, A., & Elwell, C. E. (2010). Illuminating the developing brain: the past, present and future of functional near infrared spectroscopy. *Neuroscience & Biobehavioral Reviews*, 34(3), 269-284. doi:10.1016/j.neubiorev.2009.07.008

- Lombardo, M. V., Pierce, K., Eyler, L. T., Barnes, C. C., Ahrens-Barbeau, C., Solso, S., ... & Courchesne, E. (2015). Different functional neural substrates for good and poor language outcome in autism. *Neuron*, 86(2), 567-577. doi:10.1016/j.neuron.2015.03.023
- MacKain, K. S. (1982). Assessing the role of experience on infants' speech discrimination. *Journal of Child Language*, 9(03), 527-542. doi: 10.1017/S030500090000489X
- Masataka, N., Perlovsky, L., & Hiraki, K. (2015). Near-infrared spectroscopy (NIRS) in functional research of prefrontal cortex. *Frontiers in Human Neuroscience*, 9. doi: 10.3389/fnhum.2015.00274
- Maye, J., & Gerken, L. (2000, March). Learning phonemes without minimal pairs. In Proceedings of the 24th Annual Boston University Conference on Language Development (Vol. 2, pp. 522-533).
- Maye, J., & Gerken, L. (2001). Learning phonemes: How far can the input take us. In *Proceedings of the 25th annual Boston University conference on language development* (Vol. 1, p. 480). Somerville, MA: Cascadilla Press.
- Miller, S. A. (1988). Parents' beliefs about children's cognitive development. *Child development*, 259-285. doi: 10.2307/1130311
- Minagawa-Kawai, Y., Mori, K., Naoi, N., & Kojima, S. (2007). Neural attunement processes in infants during the acquisition of a language-specific phonemic contrast. *The Journal of Neuroscience*, 27(2), 315-321. doi: 10.1523/JNEUROSCI.1984-06.2007
- Molfese, D. L. (1984). Left hemisphere sensitivity to consonant sounds not displayed by the right hemisphere: Electrophysiological correlates. *Brain and language*, 22(1), 109-127. doi: 10.1016/0093-934X(84)90082-8

- Mondschein, E. R., Adolph, K. E., & Tamis-LeMonda, C. S. (2000). Gender bias in mothers' expectations about infant crawling. *Journal of experimental child psychology*, 77(4), 304-316. doi:10.1006/jecp.2000.2597
- Mullen, E. M. (1995). Mullen scales of early learning (pp. 58-64). Circle Pines, MN: AGS.
- Näätäneiv, R., Lehtokoski, A., Lennest, M., Luuki, A., Alliki, J., Sinkkonen, J., & Alho, K. (1997). Language-specific phoneme representations revealed by electric and magnetic brain responses. *Nature*, *385*, 432-434. doi:10.1038/385432a0
- NuroSy. (2011, October 11). Functional Near-Infrared Spectroscopy (fNIRS) Experimental Protocol. [Video Blog]. Retrieved from <u>https://www.youtube.com/watch?v=e79-LYNgBc4</u>
- Perryman, T. Y., Carter, A. S., Messinger, D. S., Stone, W. L., Ivanescu, A. E., & Yoder, P. J. (2013). Brief report: parental child-directed speech as a predictor of receptive language in children with autism symptomatology. *Journal of autism and developmental disorders*, *43*(8), 1983-1987. doi: 10.1007/s10803-012-1725-3
- Quaresima, V., Bisconti, S., & Ferrari, M. (2012). A brief review on the use of functional nearinfrared spectroscopy (fNIRS) for language imaging studies in human newborns and adults. *Brain and Language*, 121(2), 79-89. doi:10.1016/j.bandl.2011.03.009
- R Core Team (2013). R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria. URL <u>http://www.R-project.org/</u>.
- Rossi, S., Jürgenson, I. B., Hanulíková, A., Telkemeyer, S., Wartenburger, I., & Obrig, H.
 (2011). Implicit processing of phonotactic cues: evidence from electrophysiological and vascular responses. *Journal of Cognitive Neuroscience*, *23*(7), 1752-1764.
 doi:10.1162/jocn.2010.21547

- Saffran, J. R., Newport, E. L., & Aslin, R. N. (1996). Word segmentation: The role of distributional cues. *Journal of memory and language*, *35*(4), 606-621. doi:10.1006/jmla.1996.0032
- Singh, L. (2008). Influences of high and low variability on infant word recognition. *Cognition*, *106*(2), 833-870. doi:10.1016/j.cognition.2007.05.002
- Telkemeyer, S., Rossi, S., Koch, S. P., Nierhaus, T., Steinbrink, J., Poeppel, D., ... & Wartenburger, I. (2009). Sensitivity of newborn auditory cortex to the temporal structure of sounds. *The Journal of Neuroscience*, *29*(47), 14726-14733. doi: 10.1523/JNEUROSCI.1246-09.2009
- Trehub, S. E., & Rabinovitch, M. S. (1972). Auditory-linguistic sensitivity in early infancy. Developmental Psychology, 6(1), 74. <u>http://dx.doi.org/10.1037/h0032197</u>
- Vulchanova, M., Saldaña, D., Chahboun, S., & Vulchanov, V. (2015). Figurative language processing in atypical populations: the ASD perspective. *Frontiers in human neuroscience*, *9*. doi: 10.3389/fnhum.2015.00024
- Watson, L. R., Roberts, J. E., Baranek, G. T., Mandulak, K. C., & Dalton, J. C. (2012).
 Behavioral and physiological responses to child-directed speech of children with autism spectrum disorders or typical development. *Journal of autism and developmental disorders*, 42(8), 1616-1629. doi: 10.1007/s10803-011-1401-z
- Weber, C., Hahne, A., Friedrich, M., & Friederici, A. D. (2004). Discrimination of word stress in early infant perception: Electrophysiological evidence. *Cognitive Brain Research*, 18(2), 149-161. doi:10.1016/j.cogbrainres.2003.10.001

- Werker, J. F., & Hensch, T. K. (2015). Critical periods in speech perception: new directions. *Psychology*, 66(1), 173. doi: 10.1146/annurev-psych-010814-015104
- Velten, H. D. V. (1943). The growth of phonemic and lexical patterns in infant language. *Language*, *19*(4), 281-292. doi: 10.2307/409932
- Woolley, G. (2011). Reading Comprehension: Assisting Children with Learning Difficulties. Retrieved from <u>http://link.springer.com.proxy.lib.umich.edu/book/10.1007/978-94-007-1174-7</u>
- Zangl, R., & Mills, D. L. (2007). Increased brain activity to infant-directed speech in 6-and 13month-old infants. *Infancy*, *11*(1), 31-62. doi: 10.1080/15250000709336869

Tables

Table 1

Mean and standard deviation scores of infant temperamental characteristics using the IBQ-R assessment (N = 16) and expressive and receptive language subsets of the Mullens Scales for Early Learning (N = 24).

	Mean	Std. Deviation		
IBQ-R				
Activity Level	4.90	0.76		
Distress to Limitations	3.60	0.89		
Fear	2.74	0.85		
Duration of Orienting	4.20	1.03		
Smiling	5.52	0.86		
High Intensity	(17	0.62		
Pleasure	6.4/			
Low Intensity Pleasure	5.36	0.93		
Soothability	5.21	0.60		
Falling Reactivity	5.56	0.61		
Cuddliness	5.84	0.51		
Perceptual Sensitivity	4.34	1.48		
Sadness	2.98	1.09		
Approach	6.08	0.71		
Vocal Reactivity	5.30	0.91		
Mullens Scale of Early Learning				
Receptive Language	48.67	6.94		
Expressive	51 56	11.10		
Language	31.30			

Table 2

		Condition		
		HFQ	LFQ	NAT
Frontotemporal	L	-0.06(2.97)	-1.29(4.78)	2.59(11.23)
	R	0.10(6.90)	-2.85(5.63)	3.79(8.80)
Temporal	L	0.72(6.09)	-3.35(4.50)	0.87(10.41)
	R	1.20(3.80)	-0.88(8.46)	-1.49(6.24)
Temporoparietal	L	2.21(14.91)	-5.27(11.66)	1.11(7.05)
	R	1.15(8.94)	-7.92(19.50)	-2.83(8.51)

Mean (standard deviation) hemodynamic response for all ROIs for each experimental condition





Figure 1. Illustration of the auditory stimuli presentation in block design; all stimuli followed a pre-set randomized sequence



Figure 2. Probe configuration as depicted in Homer-2 (MATLAB) including 28 channels of source (letters)-detector (numbers) pairs



Figure 3. Cap design and probe placement fitted to the head of an infant using 10-20 configuration



Figure 4. Mean oxygenated hemoglobin (HbO) levels for high frequency (HFQ), low frequency (LFQ), and nature (NAT) phoneme clusters in bilateral frontotemporal, temporal and temporoparietal brain regions (also separated by hemisphere)