ABSTRACT

Title of Thesis: AN EXPLORATION OF AUDITORY BRAINSTEM ENCODING OF STOP CONSONANTS IN INFANTS AND IMPLICATIONS FOR LANGUAGE OUTCOMES.

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Current trends in speech-language pathology focus on early intervention as the preferred tool for promoting the best possible outcomes in children with language disorders. Neuroimaging techniques are being studied as promising tools for flagging at-risk infants. In this study, the auditory brainstem response (ABR) to the syllables /ba/ and /ga/ was examined in 41 infants between 3 and 12 months of age as a possible tool to predict language development in toddlerhood. The MacArthur-Bates Communicative Development Inventory (MCDI) was used to assess language development at 18 months of age. The current study compared the periodicity of the responses to the stop consonants and phase differences between /ba/ and /ga/ in both at-risk and low-risk groups. The study also examined whether there are correlations among ABR measures (periodicity and phase differentiation) and language development. The study found that these measures predict language development at 18 months.

AN EXPLORATION OF AUDITORY BRAINSTEM ENCODING OF STOP CONSONANTS IN INFANTS AND IMPLICATIONS FOR LANGUAGE OUTCOMES

by

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Introduction

According to the American Speech-Language and Hearing Association's (ASHA) Treatment Efficacy Summary on Child Language Disorders, seven percent of children in preschool and grade school have significant language impairments (ASHA, 2015). In this position statement, ASHA also refers to the well-documented advantage of early intervention for a variety of language disorders. Currently, childhood language disorders are not diagnosed until children have demonstrated significant delays compared to their peers. The farther behind children fall before receiving appropriate intervention, the more difficult it will be for them to catch up to their peers, thus making early diagnosis and early intervention crucial.

There are a limited number of tools available to screen for possible language disorders in infancy and toddlerhood, and the reliability of many of these tools at young ages is relatively low (Fisch, 2012). Tools such as the MacArthur-Bates Communicative Development Inventory (MCDI) are very reliable in toddlers but less so in infancy (Fenson et al., 1994). Because of this, language disorders are currently not diagnosed in the first year of life and many are not diagnosed until elementary school. Many current infant language measures require participation from the child, which can be very difficult to obtain given infants' difficulty with following directions and short attention spans. This inherently lowers the validity of the results of such measures. An objective, reliable measure that is easy to obtain would enable mass screenings by a variety of professionals in order to provide infants with the early diagnosis and intervention that they need to achieve improved language outcomes.

The Link between Auditory Processing and Language

The foundation of language in children is the input that they receive, and language output will typically only be as good as the input (Benasich, Thomas, Choudhury & Leppanen, 2001). The quality of input that infants receive may be significantly impacted by their ability to process this input. If infants have difficulty accessing language, they will likely have difficulty learning language and will therefore have poor language outcomes. Because of the relationship between language input and output, auditory processing abilities have long been linked to language outcomes (Tallal, 1980). Auditory processing is very complex and multifaceted and the impact of its elements on language outcomes has been widely studied. These facets include rapid auditory processing (Tallal, 1980) and segmenting (the knowledge of where one word ends and the next begins) (Newman, Ratner, Jusczyk, Jusczyk & Dow, 2006) among many others. Rapid auditory processing (RAP) is the processing of the fast-rate changes in speech, such as consonant transitions (Tallal, 1980). Differences in RAP may predict the development of language and literacy skills (Johnson, Pennington, Lee & Boada, 2009), as RAP is crucial to the representation of speech phonemes which are crucial to language learning. Most current research on auditory processing in infants is being conducted using behavioral paradigms (e.g. Newman et al., 2006), but there is a growing trend towards using brain imaging to quantify different factors relating to language and cognitive development in infants.

Predicting Language Delay from Brain Imaging

Researchers are currently exploring different brain imaging techniques as potential objective measures that can be used to assess multiple areas of intelligence and learning in infants (Choudhury & Benasich, 2011; Leppanen et al., 2012). The hope is that if we can learn to use brain imaging to differentiate between infants who vary on certain measures (i.e., language skills, intelligence), we can identify those who are not developing typically. Within the area of brain imaging, there is growing interest in the study of auditory responses in infancy as an early language predictor. One example of such research was done on cortical-evoked auditory potentials, responses in the cortex that are elicited by auditory stimuli. These potentials mature more quickly in infants without family histories of language impairments than in infants with family histories of language impairments, and cortical responses to fast-rate stimuli predict later language abilities (Choudhury & Benasich, 2011). The mismatch negativity response (MMN) is a cortical-evoked potential that uses an oddball paradigm to compare responses to frequently-occurring stimuli to rarely-occurring stimuli. The MMN is delayed in 2-month-olds with family histories of specific language impairments (Friedrich, Weber & Friederici, 2004). Though this research has implications for our knowledge of infant auditory development and language learning, cortical responses are meaningful on a group level but may be too variable to be used clinically to identify individual deficits.

Auditory Brainstem Response

The Auditory Brainstem Response (ABR) is an electrophysiological measure that objectively measures the neural response to sound, requiring no active response from the individual. ABR has traditionally been used to measure hearing thresholds using clicks or pure tones and is currently being explored as a possible tool for measuring auditory processing with speech stimuli. ABRs have become the gold standard for assessing hearing in infancy (Joint Committee on Infant Hearing [JCIH], 2007) and are widely used to diagnose a variety of auditory disorders including Auditory Neuropathy Spectrum

Disorder (Starr, Picton, Sininger, Hood, & Berlin, 1996). ABR could be considered ideal for use in infancy as it is fast and easy to administer, employs equipment that is readily accessible to most audiologists and is highly reliable. Transient stimuli, clicks and tonebursts, are used to perform ABR threshold testing; additionally, speech stimuli may be used to assess suprathreshold auditory processing. One disadvantage of the ABR is that it can be difficult to use on infants who are awake, as movement and noise can interfere with the ABR responses and many older infants are resistant to wearing electrodes and earphones. Despite this disadvantage, ABR can be an ideal tool for studying language, because infants as young as three months may show robust subcortical representation of the fundamental frequency and harmonics of sounds (Anderson, Parbery-Clark, White-Schwoch & Kraus, 2015). These results demonstrate that speech-ABRs might be used to assess encoding accuracy of specific speech components.

ABRs to Stop Consonants

Speech syllables may be used to assess neural encoding accuracy of both the consonant and vowel components. Consonants are frequently used to study auditory processing because their spectral patterns change rapidly, while the spectral patterns of vowels are longer and more stable (Wallace & Blumstein, 2008). Response timing of consonant encoding provides one means of measuring neural encoding accuracy. The principles behind the use of response timing in studying neural encoding accuracy stem from the anatomy and physiology of the cochlea. Sounds enter the cochlea through the base and travel up towards the apex through the traveling wave. The cochlea is organized tonotopically, meaning that it is organized by frequency, with high frequencies encoded near the base of the cochlea and lower frequencies towards the apex. Because of this tonotopic arrangement, sounds that are higher in frequency should be processed earlier than lower frequency sounds. Earlier processing may be reflected in earlier peak latencies for a higher frequency consonant compared to a lower frequency consonant. Because the second formant in the stop consonant /g/ is higher in frequency than that of /b/, the response timing to /g/ should be earlier than /b/.

Timing may also be assessed by calculating phase differences between two stimuli (Skoe, Nicol & Kraus, 2011). Phase differences between different syllables containing stop consonants (e.g., /ba/ vs. /ga/) have been documented in the ABR response when there is a sufficient difference in the formant frequencies of the consonants (White-Schwoch & Kraus, 2013). For example, the /ga/ transition starts at a higher second formant frequency (2480 Hz) than the /ba/ transition (900 Hz), and this difference in formant frequency results in phase differences. These phase differences have been referred to as brainstem “stop-consonant differentiation” (Skoe & Kraus, 2011).

Accurate brainstem stop-consonant differentiation may be a factor in phonological awareness and language development. Language development involves learning the complex patterns of speech and therefore requires a strong representation of phonemes. Children with delayed language have poorer performance on phonological awareness tasks compared to children with typically developing language (Claesen, Leitao, & Williams, 2013). Stop-consonant differentiation is related to phonological awareness in preschool (White-Schwoch & Kraus, 2013) and school-age children (Hornickel, Skoe, Nicol, Zecker, & Kraus, 2009), such that greater stop-consonant differentiation is found in children who have better phonological awareness. However, the relationship between stop-consonant differentiation and language development has not yet been demonstrated.

ABR Periodicity

ABR trial-to-trial consistency is another measure that may be used as a possible predictor of language ability. This measure is thought to be important because robust neural representation of a phoneme requires synchronous neural firing. A decrease in neural synchrony, as reflected in reduced response consistency or periodicity, may lead to imprecise representation of speech components and thus affect language learning since language learning requires stable representations of the sounds that compose the language. Inconsistent brainstem responses to speech correlate with poor reading ability (Hornickel & Kraus, 2013), indicating that response consistency or periodicity may be a useful measure for predicting language ability.

The purpose of the current investigation is to determine the feasibility of using auditory brainstem responses to speech in normal-hearing infants to predict later language outcomes.

Research Questions

1. Can brainstem differentiation of stop consonants assessed between 3 and 12 months of age be used to predict later language outcomes?
2. Does ABR periodicity in responses to speech stimuli predict later language outcomes in infants?

Method

Participants

Forty-one infants between the ages of 3 and 12 months were recruited through the University of Maryland Infants and Child Studies Consortium database. All of the infants were born full-term, had no history of hearing loss or recent ear infections, and were from the Washington D.C. metro area. An infant hearing questionnaire was administered to the parents prior to testing. Criteria for participation in the study included passing the newborn hearing screening, no familial history of hearing loss, normal developmental history, and normal otologic history.

Before participating in the study, each infant's middle ear function was tested through immittance using an Interacoustics Titan Middle Ear Analyzer. Criteria for normal middle ear function was an ear canal volume between 0.2 and 0.8 cc, compliance of at least 0.2 mmho and a tympanometric peak pressure between +150 and -150 daPa. Outer hair cell function was tested using distortion-product otoacoustic emissions (DPOAEs) using the Titan system and the criterion for passing was +6 SNR at 3 of 4 frequencies tested from 2000 to 8000 Hz. Finally, responses to an 80 decibels peak equivalent sound pressure level (dB peSPL) 100-µs click were used to verify neural integrity. Two blocks of 2000 sweeps were collected in the right ear at a rate of 32 Hz with rarefaction polarity using the Intelligent Hearing System SmartEP system (IHS; Miami, FL). Criterion for inclusion was replicable wave V latencies that were normal for the infant's gestational age by visual inspection (Hyde, Riko & Malizia, 1990).

Approval from the University of Maryland Internal Review Board was obtained prior to the beginning of the study. Each family was compensated $20 and a baby book of their choice for participating in the study.

Stimuli

The syllables /ba/ and /ga/ were created in Praat using a Klatt-based synthesizer (Klatt, 1980) at a sampling rate of 20 kHz. The stimuli were calibrated using a sound level meter prior to the infant's arrival at the lab. The output level was set to 80 dB peSPL. Both stimuli were 120 ms long with voicing onset at 10 ms and a transition period of 50 ms between the consonant and the vowel. The vowel was then sustained for 60 ms in both conditions. The two syllables had identical fundamental frequency (100 Hz) and formants, except for the second formant. The second formant onset in /ba/ was lower in frequency (900 Hz) than the second formant onset of /ga/ (2480 Hz). Since both syllables have the same vowel, the second formant in the vowel region was identical in both syllables (1240 Hz).

Recording

The study was conducted in an electrically-shielded sound-attenuated booth. The syllables /ba/ and /ga/ were presented in randomized order to the right ear using the IHS system with alternating polarities at 80 dB SPL at a rate of 6.67 sweeps/second through insert earphones. The ABR was collected using a vertical montage of three electrodes (Cz active, forehead ground, right earlobe reference). Impedance values were ≤ 3 kΩ.

During the recording, infants were either seated on their parents' laps or held by their parents while standing. Parents were instructed to entertain their children while making minimal noise, to feed their infants, or to allow them to nap depending on the infants' needs.

Responses were digitally bandpass filtered offline from 70 to 2000 Hz. This frequency range was selected to filter out cortical activity while maximizing signal to noise ratio (Smith et al., 1975; Galbraith et al., 2000). The artifact rejection criterion was set to ±30 mv.

Language Assessment

The MacArthur-Bates Communicative Development Inventory (MCDI) (Fenson et al., 1994) is an infant and toddler assessment tool that assesses language development at a very early age. It contains a checklist of 680 words that are typically the earliest to develop and asks parents to check off all of the words that their child attempts to say independently. The MCDI is the current gold standard for research on language development in infants and young toddlers and is frequently used diagnostically in conjunction with other measures. It was chosen to measure the infants' language development because it is well-normed and well-validated, and the scores for toddlers are highly reliable (Fenson et al., 1994). It was sent to the parents of all of the infants when they turned 18 months old.

Criteria for Inclusion in Analysis

In order for their results to be used in the analysis, all infants had to have at least one set of 2500 sweeps with a positive signal-to-noise ratio (SNR) (/ba/: N = 25, 12 females, mean age = 240 days; /ga/: N = 29, 10 females, mean age = 238 days). The SNRs were calculated by subtracting the root-mean-square amplitude (RMS) of the pre-stimulus region (-20-0 ms) from the RMS amplitude of the response region (5-120 ms).

The infants whose parents returned the MCDIs were divided into two groups based on their MCDI scores. The at-risk MCDI group consisted of eleven infants with MCDI scores between the first and twentieth percentiles. The low-risk MCDI group consisted of seven infants whose scores fell between the 40th and 85th percentiles. No infants had MCDI scores higher than the 85th percentile.

Data Analysis

Phase differences in radians between /ba/ and /ga/ were calculated in the consonant transition and steady-state regions using MATLAB's (MathWorks, Natick, MA) cross-power spectral density function. Phaseogram calculation required good SNRs for both /ba/ and /ga/. Because there are differences in second formant frequencies between only the consonant portions of the two stimuli, the two stimuli were predicted to be out of phase during the consonant transition portion and then in phase during the steady-state vowel portion.

Periodicity was assessed using an auto-correlation for the consonant transition and steady-state regions. The periodicity of the stimulus is represented in the speech-evoked brainstem response (Figure 1). Higher auto-correlation values indicate lower periodicity, because a highly periodic signal will have correlation values approaching zero when comparing the signal to a shifted version of itself. The infants were divided into two groups based on their periodicity. The low periodicity group consisted of seven infants with auto-correlation values higher than 0.0015. The high periodicity group consisted of 11 infants with auto-correlation values lower than 0.0015.

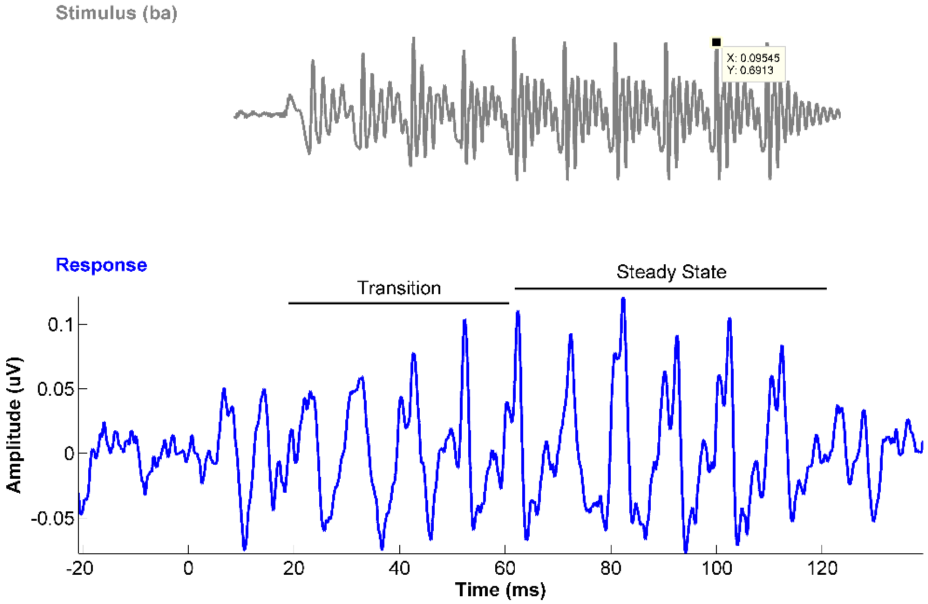

Figure 1. *Periodicity in the grand average of the neural response to /ba/ closely mirrors the periodicity of the stimulus waveform, which has been temporally aligned with the response waveform. The transition (20-60 ms) and steady-state (60-120 ms) regions are indicated.*

The MCDIs of each infant were scored according to the test's manual and a percentile score for total words spoken for each child was calculated.

Statistical Analysis

The data failed Levene's test of homogeneity of variance. Therefore, the Kruskal-Wallace test was used to compare phase differences and periodicity between the low-risk and at-risk MCDI groups. Spearman's correlations were used to assess relationships among MCDI percentiles and periodicity and phase differences for the /ba/ and /ga/ syllables in both the steady-state and transition regions. Spearman's correlations were also used to assess relationships among age and periodicity and phase differences to ensure that there was no age effect driving the group differences.

Results

Periodicity

The MCDI percentile score correlated with periodicity in the /ba/ consonant transition region (ρ = -0.509, p = 0.009; Figure 2) but not in the steady-state region (ρ = -0.272, p = 0.189). The MCDI percentile score did not correlate with periodicity in the /ga/ consonant transition region (ρ = 0.280, p = 0.141) or steady-state region (ρ = 0.020, p = 0.918).

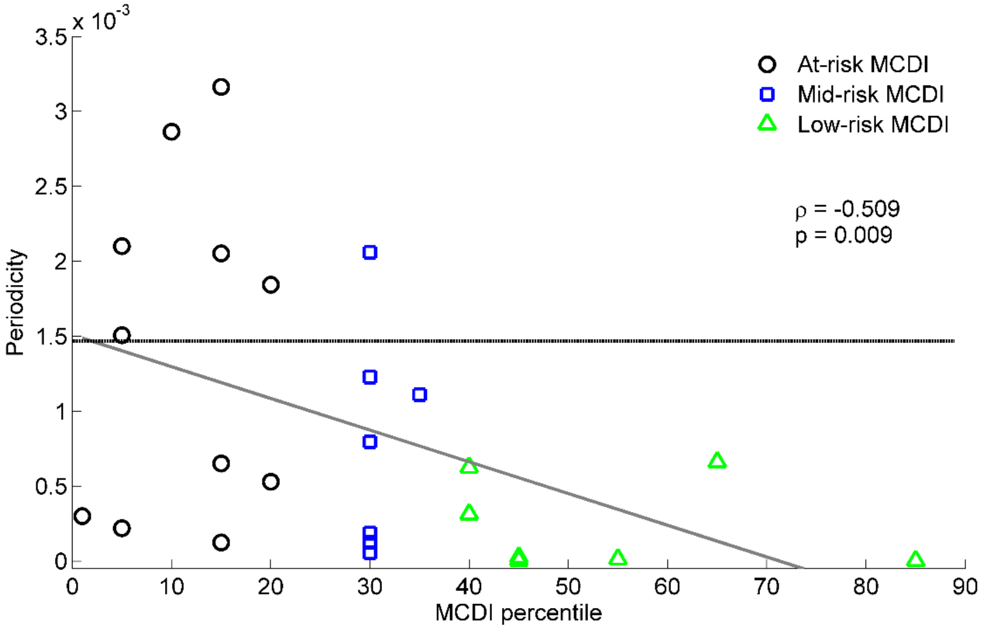

Figure 2. MCDI percentile scores correlate with autocorrelation values (a measure of periodicity) in the consonant transition region, with infants in the low-risk MCDI group (green) consistently having high periodicity and infants in the at-risk MCDI group (black) having values that range from low to high periodicity. Note that 6/7 infants with low periodicity (values higher than 0.0015) have MCDI scores that are ≤ 20.

Responses to the consonant transition in the /ba/ syllable were more periodic in the low-risk MCDI group than the at-risk MCDI group (χ^2 = 5.760, p = 0.01; Figure 3). There were no group differences for the steady-state region in the /ba/ syllable (χ^2 = 1.725, p = 0.189) or the consonant transition (χ^2 = 1.993, p = 0.158) or steady-state regions (z = 0.130, p = 0.718) in the /ga/ syllable.

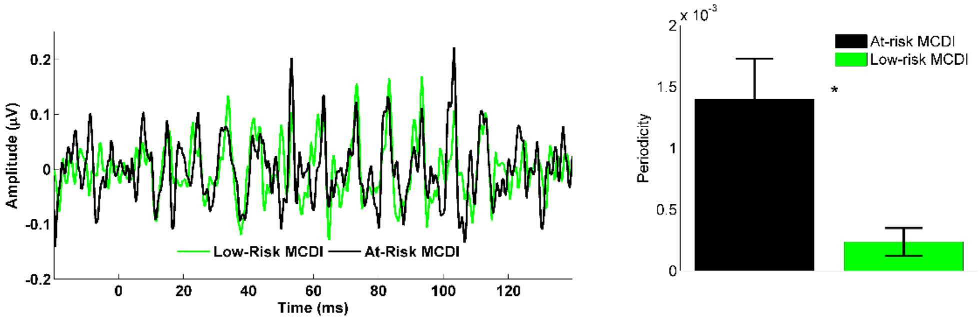

*Figure 3. Left panel: Average response waveforms to /ba/ in low (black) and high (green) MCDI groups. Right panel: The low-risk MCDI group has lower autocorrelation values (indicating higher periodicity) than the at-risk MCDI group. *p < 0.05. Error bars = 1 S.E.*

Phase Differences

The MCDI percentile did not correlate with phase differentiation between the two syllables (r = 0.230, p = 0.329). There were no MCDI group differences in phase differentiation (χ^2 = 0.857, p = 0.355; Figure 4).

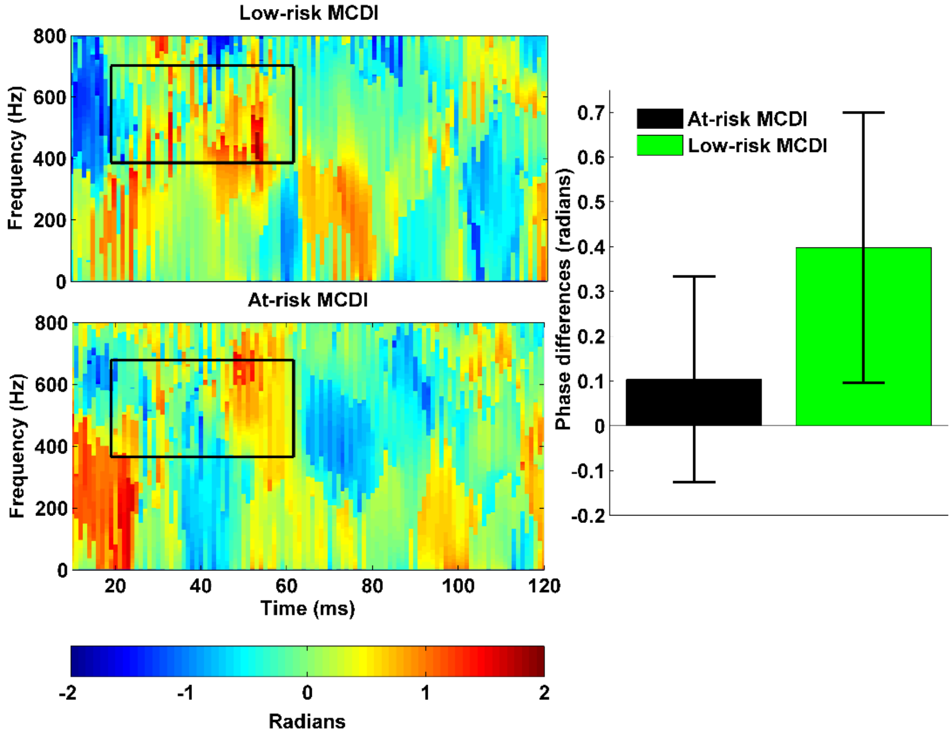

Figure 4. Left panels: Phase differentiation is seen in both at-risk and low-risk MCDI groups (indicated by red) in the frequency range corresponding to the first formant in the consonant-transition region (outlined by the black rectangles). Right panels: Although the low-risk MCDI mean phase difference is higher than in the at-risk MCDI group, high variability is present and the differences are not significant. Error bars = 1 S.E.

Age Differences

Age did not correlate with any of the ABR measures of the MCDI percentile (all ρ values > 0.05) and there were no age differences between at-risk and low-risk MCDI groups ($\chi 2 = 0.166$, $p = 0.684$). Therefore, age does not appear to be a factor in the results.

Discussion

These preliminary data support the feasibility of using objective measures of neural speech representation to identify infants who may later exhibit language delays. The low-risk MCDI group showed more periodicity than the at-risk MCDI group, and the MCDI percentile score correlated with ABR periodicity in the /ba/ consonant transition region. However, there was no correlation between MCDI percentile score and periodicity in either the transition or the steady-state regions of the /ga/ syllable or in the steady-state region of the /ba/ syllable. There was no correlation between the MCDI percentile and phase differentiation between the two syllables or group differences in phase differentiation.

Periodicity

The infants with low-risk MCDI scores consistently showed high periodicity, while the periodicity of the children with at-risk MCDI scores varied tremendously, with some showing periodicity equivalent to their low-risk MCDI peers and others showing significantly lower periodicity than any of their low-risk MCDI peers. Six of the seven infants with low periodicity had at-risk MCDI scores. This finding is important because it shows that infants who have low periodicity are likely to have poor language development when compared to their peers. If such results can be replicated at a later age, when language disorders are typically diagnosed, then periodicity in infancy can be used diagnostically to predict language delays.

The MCDI percentile score was found to correlate with the consonant transition region in /ba/ but not in /ga/. It is likely that the difference in periodicity between the two syllables is linked to /ba/ being lower in frequency than /ga/. This is consistent with previous findings that spectral representation of low frequency sounds is robustly represented in young infants, whereas representation of the high frequencies gradually increases over the first year of life (Anderson, Parbery-Clark, White-Schwoch & Kraus, 2015). If the study focused only on older infants, whose neural representations of high frequency sounds are more developed, similar relationships between periodicity and language may be found using the /ga/ syllable.

Phase Differences

Though there was no statistically significant correlation between phase difference and group, there is a general trend towards the low-risk MCDI infants showing more phase differentiation than at-risk MCDI groups during the transition period in the frequencies between 400-700 Hz. The lack of statistical significance is likely due to the large variability noted in the data. Future studies using the same design with a larger sample size should be conducted to determine whether infants with better language demonstrate more phase differentiation, as this would inform our knowledge of auditory processing and its link to language development.

Rapid Auditory Processing

The results of the current study are consistent with previous research relating to rapid auditory processing. Differences in RAP may predict developmental reading and language disabilities (Mody, Studdert-Kennedy & Brady, 1997; Johnson, Pennington, Lee & Boada, 2009), and deficits in RAP may contribute to the underlying difficulty with the representations of speech phonemes which leads to language and reading disorders. Fast ForWord (Scientific Learning Corporation, Oakland, CA) is an intervention based on these principles that trains RAP using acoustically-modified speech (Merzenich, et al, 1996). The current study shows group differences in the neural processing of the fast-changing elements of a speech syllable, which is evident through greater periodicity in the /ba/ transition region in low-risk infants than at-risk infants.

Limitations

The main limitation of the findings of this study is that it revealed only group differences and cannot yet be used to predict an individual child's language development. In order to be clinically relevant, a tool must yield results that can be applied on an individual level. The study found no age effects for the results, and robust results were obtained even when infants were sleeping. Most of the infants who had low SNRs or who were not able to complete the study did so because of a combination of them being older (typically 6 months or older) and being awake and uncooperative during the study. It is therefore likely that using younger infants (from birth to three months), who are more likely to sleep and are less active, would yield a lower dropout rate and higher SNRs.

Furthermore, the study only followed the infants until 18 months and due to resource limitations, was unable to evaluate the children in person during follow-up. Therefore, the information gained about their language development is rather limited. A number of toddlers flagged as language delayed at this age will attain normal language development on their own. Though the MCDI at the age studied is a strong enough tool to flag for risk, a more thorough in-person evaluation during the preschool years would be needed to reliably determine which of these children will actually develop later language impairment (Moyle, Stoke & Klee, 2011). This is crucial because most language disorders can typically be reliably diagnosed during preschool years. Such a study would require a larger number of infants and a more diagnostically useful tool to assess later language outcomes such as the Clinical Evaluation of Language Fundamentals – Preschool-2 (Semel, Wiig & Secord, 2004). By determining an appropriate cutoff of periodicity in the /ba/ consonant transition that reliably predicts language in preschool, researchers can use the findings of this study to predict language outcomes on an individual basis, thus making it clinically relevant.

Conclusions

This study shows that there are significant differences between the neural responses of different infants to the stop consonant /ba/ that can be used to predict later language outcomes. This pattern can be seen as early as three months of age and possibly from birth. This measure is relatively inexpensive and easy to administer, thus making it a test that could be made accessible to most infants. The current study shows promising evidence supporting the use of similar techniques to flag infants at risk for language delays, thus giving them early access to crucial early intervention.

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