Brainstem Encoding of Speech and Corticofugal Modulation in Children with Specific Language Impairment

Krithika Gururaj
Register Number: 15AUD010

This Dissertation is submitted as part fulfilment

For the Degree of Master of Science

(Audiology)

University of Mysore, Mysore

ALL INDIA INSTITUTE OF SPEECH AND HEARING

MANASAGANGOTHRI, MYSORE – 570006

May, 2017

CERTIFICATE

This is to certify that this dissertation entitled **"Brainstem Encoding of Speech and Corticofugal Modulation in Children with Specific Language Impairment"** is a bonafide work submitted in part fulfilment for degree of Master of Science (Audiology) of the student Registration Number: 15AUD010. This has been carried out under the guidance of a faculty of this institute and has not been submitted earlier to any other University for the award of any other Diploma or Degree.

Mysore
May, 2017

Prof. S.R. Savithri
Director
All India Institute of Speech and Hearing
Manasagangothri, Mysore-570006

CERTIFICATE

This is to certify that this dissertation entitled **"Brainstem Encoding of Speech and Corticofugal Modulation in Children with Specific Language Impairment"** has been prepared under my supervision and guidance. It is also being certified that this dissertation has not been submitted earlier to any other University for the award of any other Diploma or Degree.

Mysore
May, 2017

Dr. Sujeet Kumar Sinha
Guide
Reader in Audiology
Department of Audiology
All India Institute of Speech and Hearing
Manasagangothri, Mysore-570006

DECLARATION

This is to certify that this dissertation entitled **"Brainstem Encoding of Speech and Corticofugal Modulation in Children with Specific Language Impairment"** is the result of my own study under the guidance of Dr. Sujeet Kumar Sinha, Reader in Audiology, Department of Audiology, All India Institute of Speech and Hearing, Mysore, and has not been submitted earlier to any other University for the award of any other Diploma or Degree.

Mysore **Registration No: 15AUD010**

May, 2017

Acknowledgement

"Family: Anchor during rough times". Amma and Appa, you have been with me through out, and thanking you here isn't just enough. I am what I am only because of you both. Appa, you have always supported me and stood by me no matter what. And Maa, you are wonderful and I will always be grateful to you. ***Abhishek****, you are annoying as always but I could not have made it without you.*

It is said that "The influence of a good teacher can never be erased", and you are an inspiration, motivation and the impact you have had on my life is enormous Sir. I would like to thank my guide, ***Dr. Sujeet Kumar Sinha,*** *for making life easier by making the dissertation days pass by as smoothly as possible. Thank you so much Sir for helping me find the right path and working as your student was always more fun than work.*

I would like to thank the director ***Dr. S R Savithri*** *and* ***Dr. Sandeep M****, HoD of Audiology department for permitting me to carry out the dissertation work and to use the department for data collection.*

I would like to express my gratitude to the research staff, ***Mr. Srikar Sir, Mr. Vikas Sir, Mr. Anoop Sir, and Mr. Rakesh Gatla*** *for opening the department for my data collection. Thank you so much to all of you Sir, for being ready to open the department on weekends or after college hours without thinking twice.*

I would like to acknowledge and thank ***Mr. Santosh C D*** *for his help regarding the statistical analysis of the data.*

Dr. Niraj Sir*, our JC Guide, you are an inspiration and the most wonderful teacher. Pediatric audio and vestibular classes were fun and informative only because of your style of teaching. I will always be thankful to you sir.*

*After being done with the formal vote of thanks, how can I not mention my 7 wonders…..****Kulli, Chakke, Nayana, Priya, Shama, Meghu****……these 6 years in AIISH would be disastrous without you guys. Kulli and Chakke….my 3 years of bachelors, I can remember only the time spent with you both….triple ride, bunking classes, best CC with Kulli…..how I wish I could go back to those days. In 2nd year of bachelors enter Nayana (my sweetheart), priya, shama, meghu…..life just got better with chakke being the entertainer. We became the 7 wonders. I hope we stand up to our* words when we promised each other we will be meeting once in a year after masters.

Oh I forgot to mention….internship….when another wonderful person came into my life……**Manishaaaa** (Ghantiiii)….you changed my outlook towards life….towards family….U are one hell of a counsellor (remember pondi). I have wonderful memories only because of you….and with you everything was so much easier. You understand me and correct me when am wrong and hold me when I need you. I don't want to thank you, thanking is being too formal…I want you to be there in my life forever, no matter where we go. (Thank you for being there with me even during data collection…..)

Anuj…my best friend, you are the best thing that happened to me in these six years. The difference you have made in my life is enormous and beyond words. I have one thing to say….I adore you. You are my support system and understand me better than anyone else.

Mightymasters, my classmates, it was a wonderful journey with all of you. Thank you for being there throughout.

I would like to thank the parents of the **children** who participated in the study and for getting their children for data collection.

These two pages are not enough to thank all the wonderful people who have made the SIX years of AIISH memorable and wonderful……it has been a roller coaster ride…..but made me stronger and a better person to face the real world.

Table of Contents

List of Tables

List of Figures

Abstract

Specific language impairment is a developmental language disorder and characterized by auditory processing deficits. Due to the auditory processing deficits, these children tend to have language learning problem. Research has shown that children with similar language learning problems, such developmental dyslexia and central auditory processing deficits have deficits in the corticofugal modulations which results in improper auditory brainstem response coding. These studies were carried out by recording auditory brainstem responses to speech stimulus in various contexts. The present study is also on a similar line, which is to assess the context dependent brainstem encoding of speech in children with specific language impairment. The study comprised of 15 typically developing children and 15 children with specific language impairment in the age range of 4 to 11 years. Speech evoked ABR was recorded using /da/ stimulus in three paradigms- original /da/, filtered /da/ and original + filtered /da/. Results showed that there was significant difference between the wave V latency for stimulus and between groups. There was significant difference between amplitude of fundamental frequency, first harmonic and second harmonic for the three stimulus. The enhancement of fundamental frequency and the harmonics was due to the repeated exposure, inducing online plasticity via the corticofugal pathway. Also, the encoding of fundamental frequency and its harmonics was present in the filtered /da/ stimulus for both the groups. This can be explained by the fact that brainstem uses the stimulus envelope cues which continues to be present in the stimulus even after filtering. The present study justifies the enhancement of amplitude due to the online plasticity occurring through the corticofugal modulations in typically developing children and children with specific language impairment.

Chapter 1

INTRODUCTION

Specific Language Impairment (SLI) is a developmental language disorder in children, where the delay in learning language is not attributed to any kind of sensory impairment, motor dysfunction, neurological condition, intellectual disability, emotional problems or environmental deprivation (Johnston, 1988; Leonard, 1991; Speaks, 2013). The deficits can be seen either only in expressive language, or in both receptive and expressive language. The lag in language usually leads to further problems such as reading and writing difficulties during the scholastic years (Catts, 1993). There are mainly grammatical errors in the language and reduced vocabulary, leading to incorrect sentence formation (Speaks, 2013).

Over the decades, researchers have reported that children with specific language impairment have, temporal auditory processing deficit and abnormal neural coding of auditory information (Farmer & Klein, 1995; Tallal & Piercy, 1974), deficits in spectral resolution (Wright et al., 1997), deficits in phonological processing (Briscoe, Bishop, & Norbury, 2001), deficits in selective auditory attention (Stevens, Sanders, & Neville, 2006), and deficits in semantics and syntax processing (Van der Lely, Rosen, & McClelland, 1998). Due to these deficits, children with specific language impairment encounter problem in processing speech and as a result lag in learning language compared to the typically developing children. These deficits in children with specific language impairment have been measured either behaviourally or electrophysiologically, speech evoked ABR being one of them.

Recently, speech evoked auditory brainstem response has been introduced as a tool to study the brainstem encoding of speech sounds in children with learning disability (Banai, Abrams, & Kraus, 2007; Ghannoum, Shalaby, Dabbous, Abd-El-

Raouf, & Abd-El-Hady, 2014), in children with autism (Russo, Nicol, Trommer, Zecker, & Kraus, 2009; Russo et al., 2008), in children with central auditory processing disorders (Kumar & Singh, 2015; Rocha-Muniz, Befi-Lopes, & Schochat, 2012), in older adults (Anderson, Parbery-Clark, Yi, & Kraus, 2011; Vander Werff & Burns, 2011) and in musicians (Musacchia, Strait, & Kraus, 2008; Strait, O'connell, Parbery-Clark, & Kraus, 2014).

Gabr and Darwish (2016) have shown from their study that children with specific language impairment have abnormal encoding of speech. The results exhibited prolonged wave V latency of speech evoked ABR and reduced FFR amplitude in children with specific language impairment. Similar results have been obtained by K. Banai and Kraus (2007) and Wible, Nicol, and Kraus (2004) in children with language learning disabilities. Karun (2013) studied the brainstem correlates of auditory temporal processing in children with specific language impairment in comparison to typically developing children at three different repetition rates (6.9/s, 10.9/s and 15.4/s) for the speech stimulus /da/. They found that there was no significant difference between the groups for wave V latency and amplitude of FFR. Although, one of the major findings of the study was that speech evoked ABR was absent in three children with SLI. This abnormal brainstem coding of speech may be attributed to an initial cortical deficit, which might have an effect on the coding through the corticofugal modulation (Banai et al., 2007).

The auditory system consists of both the ascending and descending (corticofugal) pathways. Corticofugal system is the descending pathway of the auditory system which improves and reorganizes the auditory signal processing of the sub cortical auditory nuclei and is also important for plasticity of the auditory system (Suga, Gao, Zhang, Ma, & Olsen, 2000; Suga, Xiao, Ma, & Ji, 2002). Corticofugal modulation helps listening during adverse signal- to- noise conditions by enhancing the response properties of selectively amplifying relevant information in the signal, and inhibiting irrelevant information at the earliest stages of auditory processing (Luo, Wang, Kashani, & Yan, 2008; Nahum, Nelken, & Ahissar, 2008).

Need for the study in SLI

Research has established that children with SLI are at considerable risk for social and behavioural problems and also educational difficulties (Catts, 1993; Rice, Sell, & Hadley, 1991). They also have difficulty in understanding and formulating language and specific social tasks affecting group cooperation (Brinton, Fujiki, & McKee, 1998). Moreover, one of the main deficits reported in children with specific language impairment is auditory processing deficits. Lowe and Campbell (1965) and Tallal and Piercy (1973) established that children with SLI have temporal processing deficits. In support to that, Miller and Wagstaff (2011) reported that children with CAPD and children with SLI have similar deficits in auditory processing, reading fluency, working memory grammar and vocabulary. Along with the behavioral studies relating to auditory processing deficits in children with SLI, some of the electrophysiological studies have established that there is impaired encoding of the speech sounds at the level of brainstem and cortex (Gabr & Darwish, 2016; Holopainen, Korpilahti, Juottonen, Lang, & Sillanpää, 1998; Neville, Coffey, Holcomb, & Tallal, 1993; Wible et al., 2004). Basu, Krishnan, and Weber-Fox (2010) exhibited deficit in temporal processing by recording FFR in children with SLI using non-speech stimulus (tone bursts). Whereas, Karun (2013) used speech stimulus /da/ and recorded speech evoked ABR in children with SLI to find absent speech evoked ABR in three of these children. Recently, a study in the Finnish population on children with specific language impairment has reported that there was a statistically significant increase in the prevalence of children with SLI (Hannus, Kauppila, & Launonen, 2009). Since there is an increase in the prevalence of children with SLI and no evidence for the cause of difficulty in learning language, there is a need to study the auditory pathways in these children.

Need for Speech evoked ABR

Speech evoked ABR has three components, the onset response, the frequency following response (FFR) and the offset response. The FFR is a non-invasive method to document the regularity detection mechanism in the brainstem (Chandrasekaran, Hornickel, Skoe, Nicol, & Kraus, 2009; Parbery-Clark, Strait, & Kraus, 2011; Strait, Hornickel, & Kraus, 2011). Compared to cortical potentials, the scalp recorded FFR is highly consistent, smaller in amplitude, less susceptible to adaptation with repetition, and demonstrates earlier maturation (Chandrasekaran & Kraus, 2010). Speech evoked ABR has been recorded in children with learning disability (Ghannoum et al., 2014), auditory processing deficits (Miller & Wagstaff, 2011), autism spectrum disorder (Russo et al., 2008), and for children at risk for (C)APD without reading difficulties (Kumar & Singh, 2015).

Basu et al. (2010) using a non-speech stimulus reported that ABR latencies are prolonged and frequency following responses reduced in amplitude in children with specific language impairment. But, in the above study authors have used a click stimulus to record the ABR. The major problem with the click stimulus is that it is a non-speech stimulus and it does not reflect any auditory processing ability to speech. Recently, Gabr and Darwish (2016) using a speech stimuli reported significantly delayed latencies and reduced amplitudes of waves A, C, D, E, F and O components of speech evoked ABR in the study group compared with the controls. However, the above authors have reported only the latencies and amplitude of various peaks but not the encoding of F0, F1 and F2 in children with SLI. Hence there is a need to study the speech evoked ABR in children with specific language impairment.

Need to assess the functioning of corticofugal pathways

Hearing in adverse conditions is facilitated by the descending (corticofugal) pathways of the auditory system, by improving the signal-to-noise ratio (Chandrasekaran et al., 2009; Parbery-Clark et al., 2011; Strait et al., 2011). This is a normal phenomenon occurring in all typically developing children and in normal adults (Gnanateja, Ranjan, Firdose, Sinha, & Maruthy, 2013). Chandrasekaran and Kraus (2010) have shown that auditory brainstem responses are tuned by learning related experience over a period of days to years. Also, Skoe, Krizman, Spitzer, and Kraus (2013) provided evidence to establish that auditory brainstem is sensitive to learning occurring over minutes. Additionally, Skoe and Kraus (2010) studied the online subcortical plasticity in young adults by presenting a four note melody containing a repeated note over the course of 1.5 hours. The authors concluded that there is real time subcortical transformations occurring through which listeners can adjust to behaviourally relevant signals that occur over different time scales due to the corticofugal modulations. Previous studies have shown that corticofugal modulation is affected in children with developmental dyslexia (Chandrasekaran et al., 2009). Since children with SLI also have language impairment and the difficulty in learning language is not attributed to any sensory impairment, motor dysfunction, neurological damage, intellectual disability, emotional problems or environmental deprivation, it might be a possibility that corticofugal modulations are affected. There is a dearth of information on corticofugal modulations in children with specific language impairment. Hence, there is a need to study the corticofugal modulation in these children.

Aim of the study

Present study aimed at studying online plasticity in children with specific language impairment in comparison to typically developing children.

Objectives of the study

1. To study the brainstem encoding of speech sounds in children with specific language impairment
2. To assess whether the auditory brainstem responses can be modulated online by context in children with specific language impairment.

Chapter 2

REVIEW OF LITERATURE

Specific language impairment is a developmental language learning disorder which is characterized by normal intelligence, normal motor function, no neurological pathology, no sensory impairment, or environmental deprivation(Leonard, 1991).

Prevalence of SLI reported in literature varies depending on how language impairment is defined, the population studied, and due to the variations caused by methodology (Law, Boyle, Harris, Harkness, & Nye, 2000; Pinborough-Zimmerman et al., 2007).The prevalence of children with SLI in the upper Midwestern region of United States was 6% in girls, 8% in boys and 7.4% overall. No students of Asian origin presented with SLI (Tomblin et al., 1997); however, other research does indicate that children with SLI are present of Asian parentage (Lahey & Edwards, 1999). Tallal, Ross, and Curtiss (1989) estimated that approximately 8- 15% of all preschool going children had some form of speech and language impairment. In congruence, Hartley, Hill, and Moore (2003) also reported a prevalence of 3 to 10% of SLI in children. A retrospective study by Hannus et al. (2009), conducted on Finnish population, showed that there is a significant increase in the prevalence of children with SLI. Prevalence was reported to be higher in boys than girls. It has also been reported that around half a million children in the age range of 3 to 16 years have had speech and/or language impairments in the absence of hearing loss, mental handicap or emotional disorders (AFASIC, 1989).

2.1 Etiology of Specific Language Impairment

Specific Language Impairment is defined as a language disorder without evidence of neurological impairment such as seizure activity or brain lesions

(Jernigan, Hesselink, Sowell, & Tallal, 1991; Plante, Swisher, Vance, & Rapcsak, 1991). However, subtle irregularities in brain structure or function have been stated in children with SLI. And these mild abnormalities can contribute to some developmental disorders affecting higher cognitive functions (Bishop, 1997). Plante, Swisher, and Vance (1989) and Plante et al. (1991)studied the brain structure through MRI and reported abnormal asymmetries of the peri-sylvian region of the temporal lobes between right and left hemisphere. Genetic evidences have estimated that neuronal migration is affected causing disruption in the brain connectivity (Bishop, 1997). Other prenatal and perinatal factors, such as viral infections, lack of oxygen, or trauma, are reported as not significant that cause SLI (Bishop, 1997).

The precise nature and etiology of the deficits in SLI remain unresolved (Leonard, 1998). One of the controversial hypothesis states that, auditory processing deficits play a causal role in SLI (Dawes, Bishop, Sirimanna, & Bamiou, 2008; Moore, 2006; Rosen, 2003). Although, it has been reported that children with SLI have difficulty processing brief, rapidly presented stimuli, and these individuals perform within the normal range on auditory processing tasks (Banai, Nicol, Zecker, & Kraus, 2005; Bishop & McArthur, 2005; McArthur & Bishop, 2005). In regard to these studies it can be understood that SLI can be present without auditory processing deficits.

2.2 Auditory processing defects in SLI

Specific language impairment and central auditory processing disorder are defined as developmental communication disorders (Jerger & Musiak, 2002; Leonard, 1998). The differential diagnosis of the two communication disorders are confounded due to the co-occurrence (comorbidity) with other developmental disorders. Literature reports the similarities in symptoms presented between SLI and (C) APD, making it demanding for differential diagnosis. ASHA (2005) has reported that not only does CAPD and SLI have overlapping symptoms but also suggest that CAPD attributes to some language impairments.

Miller and Wagstaff (2011) reported no statistical significant mean difference between children diagnosed as CAPD (n=35) by an audiologist and children with SLI (n=29) by a SLP, in tasks such as auditory processing, reading fluency, working memory, grammar and vocabulary. Similar results were reported by Ferguson, Hall, Riley, and Moore (2011) presenting that the two clinical groups (APD, n=19; SLI, n=22) showed group mean differences on very few variables, but performed more poorly than the control group. Children with SLI have poor non word repetition, spatial working memory, SSW total errors, and left ear score for dichotic digits.

Dlouha, Novak, and Vokral (2007) administered dichotic CV and dichotic digit test on 90 children with SLI in the age range of 6-7 years (67 boys and 23 girls) and 20 typically developing age and gender matched children. The results of the study showed that children with SLI had degraded performance on these two tests compared to typically developing children. Therefore the authors concluded that a relationship exists between auditory processing deficit and language impairment in children with SLI.

Vandewalle, Boets, Ghesquiere, and Zink (2012) studied auditory temporal processing (frequency modulation and between channel gap detection) and speech perception (speech in noise and categorical perception) in 8 children with SLI and 14 typically developing children. The SLI group with literacy delay scored significantly lower than both the other groups on speech perception but not on temporal auditory processing. Also, the authors probed to find correlation between speech perception skills and auditory temporal processing skills with oral language and literacy skills. It was found that speech perception ability is more associated with development of literacy skills than oral language ability.

Lowe and Campbell (1965) studied the temporal ordering and sequencing ability in 8 children with SLI (age range 7-14 years) and 8 age matched normal children. The authors established significant difference in performance between the two groups on ordering task only. Children with SLI also show difficulty in perceiving formant transition.

Tallal and Piercy (1973) studied auditory temporal processing skills in 12 children with SLI (9 boys and 3 girls) aged 6.8 to 9.2 years and 12 normal age and gender matched children. The children were trained to associate two complex tones with a specific key press response. Children with SLI performed accurately when the tones were separated by an inter stimulus interval (ISI) of 300ms, and their performance deteriorated when shorter ISI was used. In contrast, control group had high level of performance at ISI as short as 8ms. The temporal sequencing test also showed similar performance in control group. Similarly the effect of shortening of the absolute duration of the tonal signal was studied in children with SLI. The results exhibited that performance of children with SLI reduced significantly when the absolute duration of the signal was decreased from 250ms to 75ms. The authors concluded that these children have temporal processing deficit of transient signals which leads to difficulty in speech perception.

Tallal and Piercy (1974) presented synthesized consonant and vowel stimuli to 12 children with SLI in the age range of 6.9 to 9.3 years (9 boys and 3 girls) and 12 age and gender matched typically developing children. The findings of the study indicated that children with SLI find it difficult to discriminate the consonant stimuli due to the brief duration of the formant transition. It was also hypothesized that this deficit may be sufficient to cause the language impairment in these children. However, there was no marked difference in discriminating when consonants were artificially stretched or vowels artificially shortened in children with developmental aphasia(P. Tallal & Piercy, 1975).

Miller, Kail, Leonard, and Tomblin (2001) tested the reaction time for various auditory tasks in 29 children with SLI and in control group of 29 children. The tasks included both linguistic and non- linguistic tasks. The results of the study showed that the children with SLI performed poorly for both linguistic and non- linguistic tasks in comparison to normal children. The results of the analyses support the hypothesis that speed of processing in children with SLI was slow than that of children with normal language. However, some children with SLI did not appear to show temporal deficits.

Some researchers claim that language impairment results from fundamental problem which affects the acoustic distinctions among successive brief sounds of speech (Elliott & Hammer, 1988; Kraus, McGee, Carrell, & Zecker, 1996; Tallal & Piercy, 1973). Wright et al. (1997) used psychophysical tests of simultaneous and non- simultaneous masking, employing simple tones and noises in 8 children with SLI and 8 age matched typically developing children. The authors reported that children with SLI have severe auditory perceptual deficits for brief tone but not for longer duration tones in certain acoustic contexts. Thresholds of simultaneous and forward masking were similar for both children with SLI and normal children. Whereas, backward masking showed a difference of 40dB in threshold with normal children showing minor masking effect.

Bishop, Carlyon, Deeks, and Bishop (1999) have pointed out that, an auditory deficit is neither necessary nor sufficient to cause SLI. The study included 11 children with SLI and 11 typically developing children age matched. Bishop et al. (1999) estimated thresholds for backward and forward masking, frequency modulation and pitch discrimination. There was no significant difference between children with SLI and typically developing children. The authors found no link between auditory deficit and language impairment. It was speculated by the authors that the discrepancy might be due to disproportionate number of cases whose difficulties had a non- auditory basis.

Another study which supports the hypothesis that not all children with SLI have auditory processing deficits was given by Montgomery (1999). In this study, 21 children with SLI, 21 children matched for chronological age and 21 vocabulary matched children participated in a forward gating task in which they were made to listen to successive temporal chunks of familiar monosyllabic nouns. Results were interpreted to suggest that children with SLI performed similarly to children matched for chronological age and vocabulary skills on tasks based on lexical mapping (i.e., acoustic- phonetic analysis) of auditory word recognition.

Literatures on electrophysiological tasks support the results of the behavioural tasks indicating auditory processing deficit in children with specific language impairment. Higher cortical potentials are said to be prolonged in latency in children with SLI. Neville et al. (1993) recorded N400 in children with language impairment while the subjects were reading a series of sentences ending with either an appropriate or anomalous final word. The authors reported that the amplitude of P150, and P350, over occipital regions, component was significantly reduced in those children whose performance on auditory temporal discrimination task was poor. However, it was noticed that N400 response was significantly larger in children with language impairment than control group, recorded from occipital regions. In the sentence processing task abnormal hemispheric specialization was observed in a subset of children who scored poorly on grammar tests.

Holopainen et al. (1998) recorded mismatch negativity (MMN) in 12 children with SLI, 13 children with language impairment secondary to mental retardation and 10 normal children. The MMN was elicited using pure tone stimuli of 500Hz as standard stimulus and 553 Hz as deviant stimulus. Amplitude of MMN was significantly reduced for both mentally retarded and SLI groups in comparison to the group with normal children. Attenuated frequency mismatch negativity was related to impairment of linguistic skills irrespective of the child's cognitive skills, and thus the authors concluded that it can be used as an indicator of linguistic deficits in children with SLI.

Basu et al. (2010) reported temporal processing deficit in children with SLI. The study included 10 children with SLI in the age range of 4- 11 years and control group of age matched typically developing children. The authors recorded frequency following response with different pure tone stimuli and also studied the effects of reducing inter- stimulus interval. The results showed reduced phase locking in children with SLI at higher repetition rate suggesting temporal deficits. The findings of the study suggests that children with SLI might greater susceptibility to neural adaptation.

Al-Saif, Abdeltawwab, and Khamis (2012) studied children with SLI to demonstrate evidence of absent or abnormal auditory middle latency response (AMLR). The study consisted of 19 children with SLI, in the age range of 4- 11 years (7 females and 12 males). The control group included 15 typically developing children in the age range of 4- 11 years (10 males and 5 females). The results showed lesser amplitude of Na-Pa complex and also prolonged latency of the peaks in children with SLI in comparison to the control group. Although, the differences in amplitude and latency were not statistically significant between the two groups. The authors concluded that children with SLI have normal auditory system at the level of AMLR generating systems.

2.3 Speech evoked auditory brainstem response

2.3.1 Speech evoked ABR in normal children

Brainstem encoding of speech have been studied in quiet as well as in background noise (Russo, Nicol, Musacchia, & Kraus, 2004), also using speech stimulus other than /ba/ (Johnson et al., 2008; Russo et al., 2008). Russo et al. (2004) established reliable procedures and normative values to quantify brainstem encoding of speech sounds. Response from brainstem was elicited using speech stimulus /ba/ in quiet and in background noise from 38 normal children. The authors obtained high test- retest reliability and low variability across subjects. All components of the brainstem response were robust in quiet. Background noise disrupted the transient responses whereas the sustained response was more resistant to the deleterious effects of noise. The authors concluded that the speech-evoked brainstem response faithfully reflects many acoustic properties of the speech signal.

Johnson et al. (2008) conducted a study to understand how the human auditory brainstem encodes temporal and spectral acoustic cues in voiced stop consonant-vowel syllables. The authors recorded auditory evoked potentials from brainstem of 22 normal children using /ba/, /da/ and /ga/ stimulus. The results showed that there was a predictable change in the response latencies to systematic alterations in a speech syllable. Spectral analyses of the responses revealed frequency distribution differences across stimuli (some of which appear to represent acoustic characteristics created by difference tones of the stimulus formants) indicating that neural phase-locking is also important for encoding these acoustic elements.

2.3.1 Speech evoked ABR in children with language impairment

King, Warrier, Hayes, and Kraus (2002) recorded speech evoked auditory brainstem responses in 33 normal children and 54 children with learning disability (8-12 years). The latency of the peaks A, C and F were significantly prolonged in children with learning disability in comparison to normal children. These findings indicate that there might be an alteration in the onset synchrony response of the auditory brainstem neurons in children with learning disability compared to normal children. Additionally, deficits in cortical processing of signals in noise were seen for those learning disabled children with delayed brainstem responses to the /da/, but not for children with learning disability with normal brainstem measures.

Ghannoum et al. (2014) assessed the coding of speech at the level brainstem using speech evoked auditory brainstem responses. The study comprised of 30 normal hearing children without learning disability and 30 children with learning disability (sub groups age range: 6-8 years, 8-10 years, 10-12 years). The parameters considered for analysis are the latency and amplitude of onset and sustained response (waves V, A, C, D, E and F). The results of the study is in coherence to the study by King et al (2001), showing statistically significant delayed latencies of waves V, A and F in both the ears in all subgroups compared to control group. The amplitude of wave F was also found to be reduced significantly in both the ears in all subgroups in comparison to control group. In the 6-8 years subgroup, there was a statistically significant reduction in the amplitude of waves D and E. Also, a significant attenuation in amplitude of waves C and D in subgroup of 8-10 years. In concise, speech evoked ABR can be used as a tool to assess children with learning disability as it reflects abnormalities in encoding of speech stimulus at the level of brainstem.

Rocha-Muniz, Befi-Lopes, and Schochat (2014) elicited auditory brainstem responses to speech stimulus /da/ in children with auditory processing disorder (n=25), children with specific language impairment (n=25) and typically developing children (n=25). The sensitivity and specificity were calculated and receiver operating characteristic analysis were performed to determine optimum cut-off. Statistical analysis of the data revealed significant prolonged latency of waves V and A in the auditory processing disorder and specific language impairment groups compared with the typically developing group. Additionally, wave V was significantly prolonged in the SLI group than normal and auditory processing group. No group differences were observed in the amplitude of the spectral component of F0 and F1. In contrast, a significant difference was noted in the encoding of higher harmonic among the three groups. SLI group demonstrated significant lower spectral magnitude for higher harmonic compared with normal and auditory processing disorder group. Hence, the authors concluded that speech evoked ABR has better sensitivity for SLI group than the auditory processing disorder group. Nevertheless, it can be used as a tool to identify both auditory processing disorder as well as language impairment.

A study by Gabr and Darwish (2016) aimed to evaluate speech-evoked auditory brainstem responses in 20 normal children and 20 children with SLI. The results exhibited significantly delayed latencies and reduced amplitude of waves A, C, D, E, F and O components of speech evoked ABR in the experimental group compared with control group. Hence, the authors concluded that children with SLI have abnormal encoding of speech.

Wible et al. (2004) studied the correlation between brainstem and cortical auditory processing in 20 normal and 11 language impaired children. Auditory evoked potentials were used to investigate brainstem and cortical responses to the speech sound /da/. The results demonstrated abnormal encoding of speech sound in both cortical and subcortical structures. There was prolongation of wave V-Vn complex reflecting diminished synchrony of response generator mechanisms. Furthermore, the experimental group failed to demonstrate a relationship between brainstem and cortical measures, which were quite strong across all normal children.

2.3.2 Speech evoked ABR in children with Autism

Russo et al. (2008) examined the subcortical representations of prosodic speech in 21 children with ASD (19 boys, 2 girls) and 21 typically developing children (13 boys, 8 girls) in the age range of 7- 13 years. The stimulus was naturally spoken /ya/ syllable with descending and ascending pitch contours. Results showed that children with autism spectrum disorder showed more frequency error and slope error in encoding of F0 in comparison to normal children. Also, frequency error was significantly higher in encoding of second harmonic between the 2 groups, whereas slope error did not differ between them.

Russo et al. (2009) measured brainstem response to syllable /da/ in quiet and in background noise in children with autism spectrum disorder (n=21) and without autistic spectrum disorder (n=19) who had normal intelligence and hearing, in the age range of 7-13 years. In quiet, speech ABR was recorded at 80dB SPL and in noise, at same intensity with white background noise at 75dB. Children with autistic spectrum disorder exhibit deficits in both the transient response and sustain responses despite normal click-evoked brainstem. There was a significant delay in the latency of waves V, A, D and F in children with autism spectrum disorder in comparison to normal children in quiet condition. In the same condition onset response duration was also significantly prolonged in the autism spectrum disorder group. Wave F amplitude was significantly reduced in the children with autism spectrum disorder, however there was no between group differences in amplitude of F0. The authors suggested that the speech-evoked brainstem response may serve as a clinical tool to assess auditory processing in children with autistic spectrum disorder.

2.3.3 Speech evoked auditory brainstem response in children with CAPD

Rocha-Muniz et al. (2012) investigated the speech evoked auditory brainstem response in children with central auditory processing disorder (n=18), children with language impairment (n= 21) and typically developing children (n=18) in the age range of 6 to 12 years. A comparative analysis of the latency of peaks V, A, C, E, F and O revealed significantly delayed responses between the language impairment group and typically developing children and children with central auditory processing disorder. Despite the finding that the central auditory processing disorder group had later latencies than the TD group, statistically significant differences were only found for peak A. The results also revealed no group differences in the amplitudes of F0 and F1. In contrast, there was a significant difference in the encoding of the higher harmonics among the three groups, with the typically developing and central auditory processing disorder groups showing larger amplitudes than the language impairment group.

Kumar and Singh (2015) recorded speech ABR from a total of 336 school going children in the age range of 8-12 years were screened for presence of central auditory processing deficits. Among the 51 children who were identified as at risk, 15 were randomly selected and served as experimental group. The control group comprised of 15 age matched children. The statistical analysis revealed prolonged waves V and A latencies along with marginal reduction in V/A slope and amplitude of first formant. The affected speech evoked ABR probably indicates the presence of abnormal brainstem encoding of speech signal in children with central auditory processing disorder without reading deficits.

2.3.4 Speech evoked ABR in older adults

Vander Werff and Burns (2011) recorded speech-evoked ABRs using a synthetic 40-mesc /da/ stimulus in normal hearing younger adults and older adults. The statistical analysis of the onset and sustained responses revealed no significant difference in latency or amplitude between the two ears across the two groups or within the young adult group. However, there was significant difference between the ears in the older adult group in terms of latency (left ear longer than right ear) and amplitude (left ear larger than right ear) of wave A. The FFR analysis of amplitude of F0, F1 and higher harmonics revealed no significant difference between the ears for either of the groups. Although the overall RMS amplitude did not vary significantly between groups, the spectral magnitudes of the three harmonic components were all significantly smaller for the older adult group compared with the younger adult group.

These results suggest that the ability of neurons at the brain stem level to phase-lock to these components of the stimulus seems to be reduced for the older adults.

Anderson et al. (2011) investigated a neural basis of speech in noise perception in older adults (28 adults, age: 60-73 years), speech evoked auditory brainstem responses were recorded in quiet and in presence of background noise. The results revealed significant differences in quiet and in noise conditions of F0 amplitude. However, there was no main effect for the response of higher harmonics (H2- H10) both in quiet and noise conditions. The authors reported that poorer speech in noise perception was due to the reduction in neural synchrony in encoding of F0. Thus, the older adults with poorer speech in noise perception demonstrate impairment in the subcortical representation of speech.

2.4 Corticofugal modulations

The auditory system consists of both ascending and descending (corticofugal) pathways. The corticofugal system forms multiple feedback loops. Repetitive acoustic or auditory cortical electric stimulation activates the cortical neural net and the corticofugal system. The corticofugal system has multiple functions. One of the most important functions is the improvement and adjustment (reorganization) of subcortical auditory signal processing for cortical signal processing (Suga, 2008).

The auditory system of humans (Skoe & Kraus, 2010), non-human primates (Hauser, Newport, & Aslin, 2001) and rodents (Toro & Trobalon, 2005) have the extraordinary ability to identify regularities from a sound stream which makes it possible to detect a novel stimulus.

Research in bats has also shown that corticofugal projections are involved in one of the most common type of auditory processing, frequency tuning. A study by Zhang, Suga, and Yan (1997) exhibited that when cortical neurons tuned to a specific frequency are inactivated, the auditory responses of subcortical neurons tuned to the same frequency are reduced. Moreover, the responses of other subcortical neurons tuned to different frequencies are increased, and their preferred frequencies are shifted towards that of the inactivated cortical neurons. Thus the corticofugal system mediates a positive feedback which, in combination with widespread lateral inhibition, sharpens and adjusts the tuning of neurons at earlier stages in the auditory processing pathway.

Literature has revealed that the brainstem is sensitive to statistical properties of the stimulus in real time (Skoe & Kraus, 2010; Skoe & Kraus, 2013) leading to changes in the response throughout the recording, making it an online process. Chandrasekaran et al. (2009) recorded FFRs for the speech stimulus /da/ in repetitive context and a variable context in normal children and children with developmental dyslexia. This stimulus paradigm was used to record FFRs and study the encoding of regular and irregular sequences in the sound stream by the brainstem. Results have shown that there is enhancement of the brainstem responses in a repetitive context, relative to variable context in typically developing children. In contrast, children with developmental dyslexia exhibited impairment in the ability to modify representation in predictable contexts. This context dependent encoding of speech is evidence of online regularity detection and modulation of sub-cortical responses. The corticofugal model states that the modulation of the brainstem responses are through the corticofugal efferent pathway from the auditory cortex (Suga, 2008; Suga et al., 2002; Zhang et al., 1997). This model also states that there are moment-to-moment changes in brain function as a result of top-down feedback.

This new found context dependent brainstem encoding of speech is evidence of online regularity detection and modulation of the subcortical responses. Gnanateja et al. (2013) studied the influence of spectral structure of the contextual stimulus on context dependent encoding of speech at the brainstem. 14 normal hearing adults participated in the study. Brainstem responses for a high pass filtered /da/ in the context of syllables, that either had same or different spectral structure were compared with each other. The findings suggest that spectral structure is one of the parameters which cue the context dependent sub-cortical encoding of speech. Interestingly, the results also revealed that, brainstem can encode pitch even with negligible acoustic information below the second formant frequency.

In support to the above mentioned studies it was reported that subcortical auditory system is sensitive to local sound statistics as reflected in an enhanced response to repetitive as compared to pseudo random stimulus paradigm (Chandrasekaran et al., 2009). Skoe and Kraus (2010) probed the online subcortical plasticity using a paradigm that assessed the encoding of brainstem responses to a five note melody containing a repeated note and monitored how the response changed over 1.5 hours of recording. The results demonstrated that despite the stimulus being physically invariant and not paid attention, it will be constantly monitored in the auditory system. These real-time subcortical transformations, likely reflect a mix of local and top-down processes that are influenced by implicit and explicit knowledge about the auditory stimulus and expectation (Repp, 2007).

To summarize, specific language impairment is a developmental language disorder which cannot be attributed to any motor or neurological impairment, poor intelligence, sensory impairment or environmental deprivation. The prevalence of this is found to be increasing and the precise nature and etiology of the deficits in SLI remain unresolved. However, there exists a hypothesis that auditory processing deficits play a causal role in SLI. Speech evoked ABR in various populations with communication disorders, such as, central auditory processing disorder (CAPD), autism spectrum disorder (ASD), and with language impairment have shown that these children have abnormal coding of the speech sounds at the level of brainstem. Also, literature reports that in children with learning disability might have affected corticofugal pathways due to which the context dependent encoding is absent (Chandrasekaran et al., 2009).

Chapter 3

METHOD

The study aimed at assessing the brainstem encoding of speech and corticofugal modulations in children with specific language impairment and in typically developing children. Static group comparison design was used to estimate the difference in encoding of speech in children between specific language impairment and typically developing children.

3.1 Participants

The participants were divided into two groups:

Group I consisted of 15 participants in the age range of 4 to 11years with mean age of 6 years. The group comprised of 5 females and 10 males, who have been diagnosed as children with specific language impairment by a speech language pathologist according to Leonard (1991) criteria.

Group II consisted of 15 age and gender matched typically developing children. The mean age was 6.5 years. Children of the control group had normal speech and motor milestones as reported by the parents/ caretaker. This was verified using a developmental chart given by WHO.

3.1.1 Participant selection criteria for both the groups

1) All the participants were diagnosed as having normal hearing sensitivity (within 15 dB HL) at octave frequencies between 250 Hz and 8000 Hz for air conduction and between 250 Hz and 4000 Hz for bone conduction.
2) Immittance evaluation showed type ‘A’ tympanogram with normal ipsilateral as well as contralateral reflexes, indicative of normal middle ear functioning in all the participants.

3) No history of any relevant otological or neurological dysfunction

4) No known medical or surgically treatable ear related conditions

5) No evidence of any retrocochlear pathology based on auditory brainstem responses.

6) Participants of **Group I** were diagnosed as children with specific language impairment by a Speech language pathologist.

7) Children with SLI were not undergoing speech therapy and also were not exposed to music on a regular basis.

3.2 Instrumentation

1. A calibrated GSI audiometer (GSI VIASYS Healthcare, Wisconsin, USA) was used for the purpose of threshold estimation and speech audiometry. Calibrated TDH 39 headphones (Telephonics, 815 Broad Hollow Road, Farmingdale, New York 11735) for AC threshold and calibrated B-71 bone vibrator (Radioear, KIMMETRICS, 22050 Mohawk Drive, Smithsburg, MD 21783) for BC threshold was used for the same.
2. Calibrated GSI Tympstar Immittance meter (GSI VIASYS Healthcare, Wisconsin, USA) was used for tympanometry with a probe tone frequency of 226Hz and reflexometry was carried out at 500Hz, 1k Hz, 2k Hz and 4k Hz.
3. Calibrated Biologic Navigator Pro EP ((Bio-logic Systems Corp., a Natus Medical Inc., Mundelin, IL, USA) was used for recording of the click and speech evoked auditory brainstem responses with ER-3A insert phones (Etymotic Research, Inc., 61 Martin Lane, Elk Grove Village, IL 60007, USA).

3.3Procedure

3.3.1 Pure tone audiometry

Pure-tone thresholds were obtained at octave frequencies between 250 Hz to 8000 Hz for air conduction and for bone conduction between 250 Hz to 4000 Hz using the modified Hughson Westlake procedure (Carhart & Jerger, 1959). Pure tone average was calculated by taking an average of 500, 1000, 2000 and 4000 Hz.

3.3.2 Immittance evaluation

Tympanometry was carried out utilizing a probe tone frequency of 226 Hz at 85dB SPL. Ipsilateral and contralateral acoustic reflexes thresholds were elicited at 500, 1000, 2000, and 4000 Hz, for all the participants from both the ears.

3.3.3 Click Evoked Auditory Brainstem Responses (ABRs)

Auditory brainstem response testing was carried out in a sound treated room. The participants were instructed to sit in a reclining chair. The skin surface at the two mastoids (M1, M2), and forehead (Fz) was cleaned with skin abrasive, to obtain skin impedance of less than 5 KΩ for intra electrode and less than 2 KΩ inter electrode. The electrodes were placed with the help of skin conduction paste and tape was used to secure them tightly in the respective places. Participants were instructed to relax and refrain from extraneous body movements to minimize artifacts. The testing was done monaurally (right ear).

3.3.3.1 Protocol for click evoked ABR

ABR was recorded using click stimuli initially, to rule out retrocochlear pathology. Duration of the click stimulus was 100µs and was presented at 80dBnHL. The repetition rate was 30.1/s and presented at a rarefaction polarity ipsilaterally (right ear only). The responses were filtered with band pass filtering from 100Hz to 3000 Hz. Analysis time was set to 10ms. The responses were averaged for 1500 sweeps. Recording was done twice to check for replicability of the peaks.

3.3.4 Speech evoked ABR

The test stimulus used (/da/) in the present study was the default stimulus available with the BIOLOGIC NAVIGATOR PRO instrument in the BIOMARK protocol. This /da/ stimulus was a 40 ms synthesized speech syllable, which had been produced using KLATT synthesizer (Klatt, 1980). The stimulus comprised of initial transient burst and formant transition between the consonant and vowel. The fundamental frequency (F0) linearly rises from 103 to 125 Hz with voicing beginning at 5ms and an onset noise burst during the first 10ms. The first formant (F1) rises from 220 to 720 Hz, while the second formant (F2) decreases from 1700 to 1240 Hz over the duration of the stimulus. The third formant (F3) falls slightly from 2580 to 2500 Hz, while the fourth (F4) and fifth formants (F5) remain constant at 3600 and 4500 Hz, respectively (Krizman, Skoe, & Kraus, 2010). The figure of /da/ stimulus is given in figure 2.

3.3.4.1 Stimulus paradigm

To investigate the context dependent encoding it was necessary to record speech evoked ABR in three stimulus paradigms. Out of the three, two paradigm had same spectral structure and the third paradigm had different spectral structure. The same spectral structure paradigm had presentation of the same stimulus, that is, original /da/ (first paradigm) and filtered /da/ (second paradigm). The filtered /da/ differed from the original /da/ in the spectral content, the /da/ syllable was high-pass filtered using a sixth order Butterworth filter with a cut off frequency of 1000 Hz. High-pass filtering removed the fundamental frequency and the first two formants of the syllable without altering the higher harmonics.

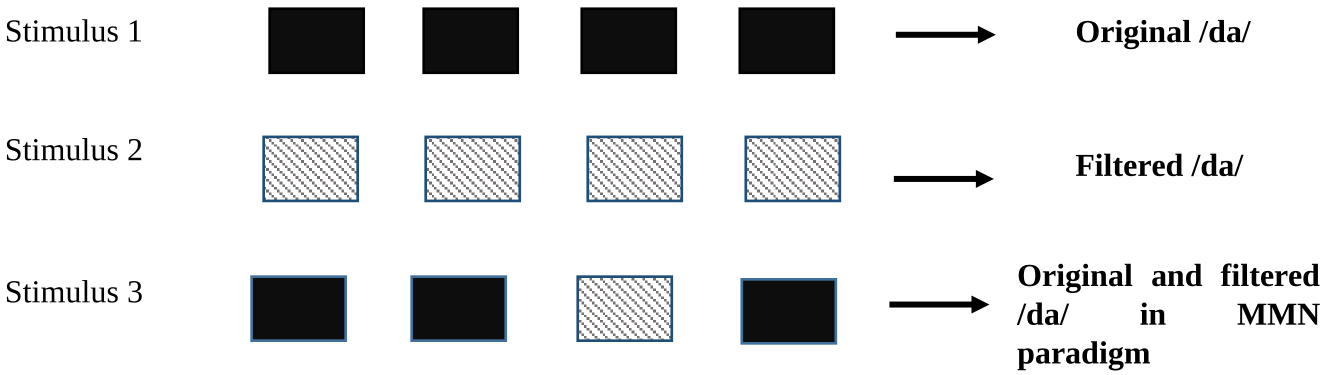
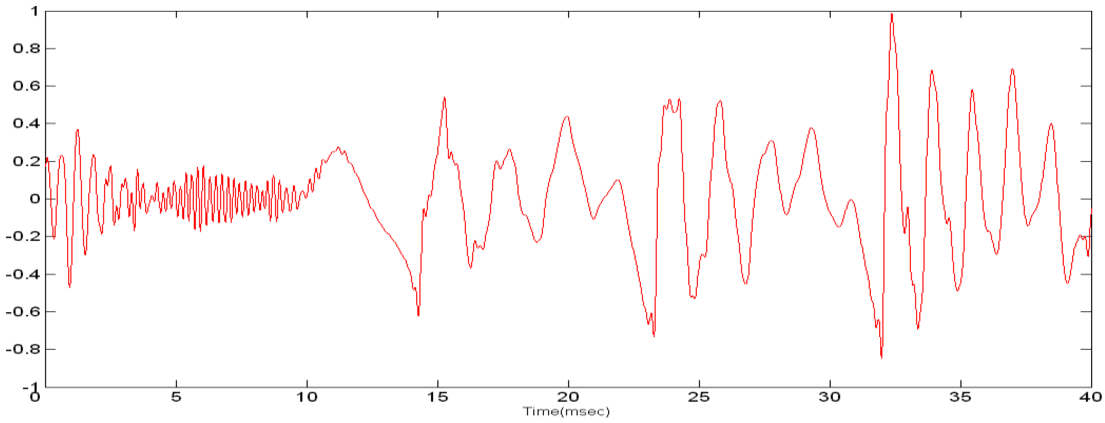


Figure 3.1. Representation of the stimulus paradigm used for assessing the context dependent encoding.

The different spectral structure stimulus consisted of a primary stimulus in context of spectrally different stimulus. The recording was carried out in the P300 paradigm. The original /da/ and filtered /da/ was presented in the ratio of 3:1. The original /da/ was considered as the frequent stimulus and the filtered /da/ was considered as the infrequent stimulus (Gnanateja et al., 2013).



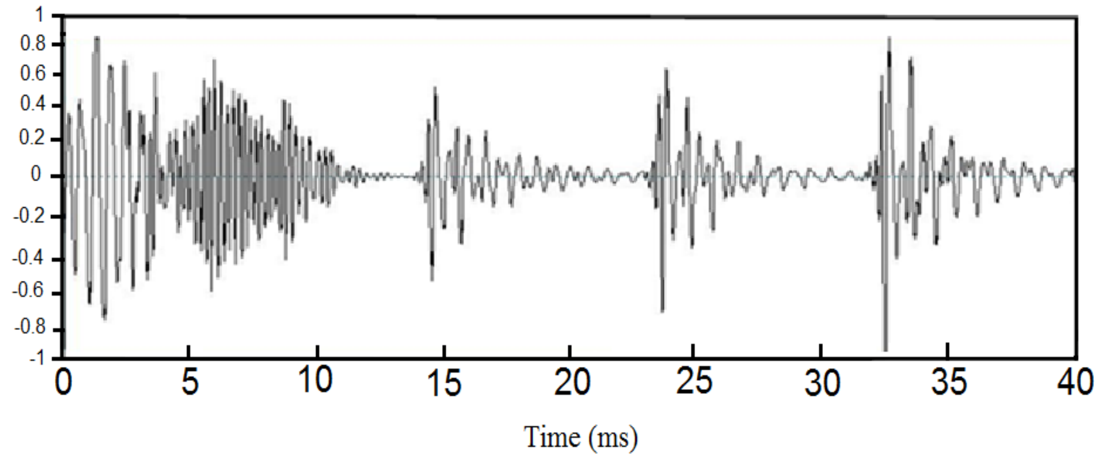
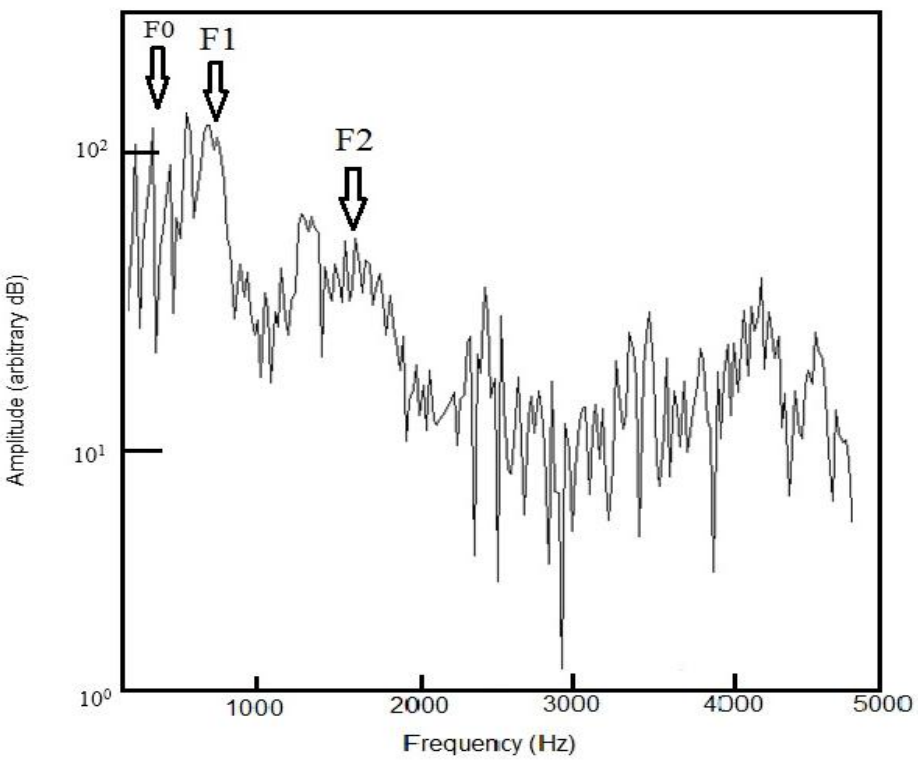
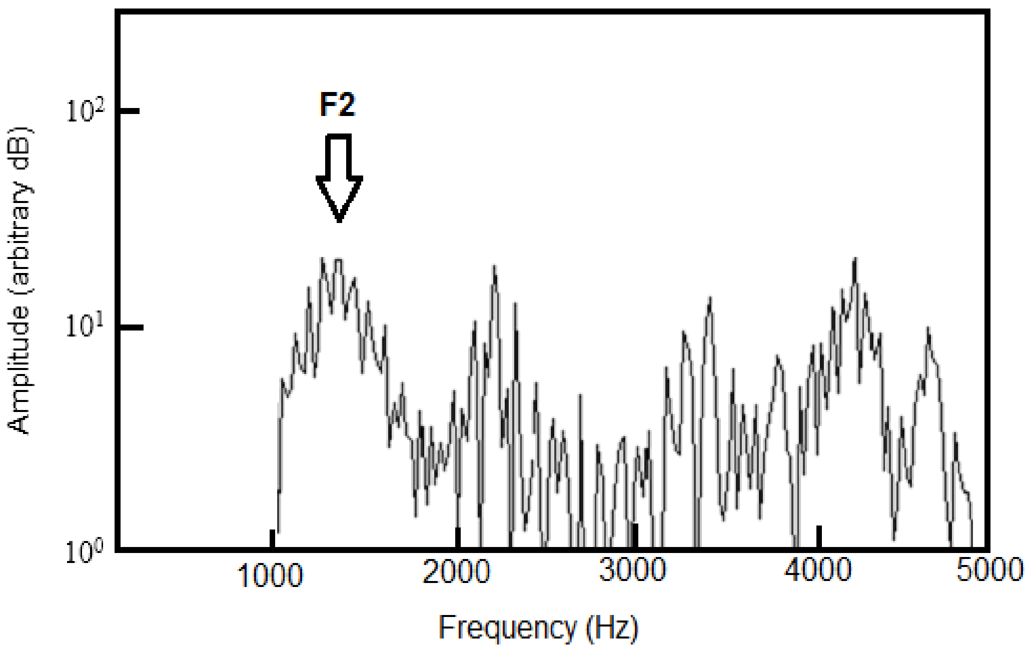


Figure 3.2. Stimulus waveform of original /da/ (above) and filtered /da/ (below) stimulus.



(a)



(b)

Figure 3.3. (a) Spectrum of original /da/ stimulus, (b) spectrum of filtered /da/ stimulus. Please note that there is no energy below 1000 Hz in the filtered stimulus.

3.3.4.2 Recording protocol for speech evoked ABR

The Biologic Navigator Pro EP was used to record the ABR. Vertical montage was used for the recording of responses. The inverting electrode was placed on the mastoid (M1) of the test ear, non- inverting on upper forehead (Fz) and ground on the contralateral ear mastoid (M2). The /da/ stimulus was presented at 80dB SPL at the rate of 10.9 stimuli per second. Alternating polarity was used for presentation. The total time window was kept for 70ms including a 10ms pre stimulus recording. The responses were averaged for 1500 sweeps in each paradigm. Speech evoked ABR was recorded twice each for all the three paradigms to check for replicability.

The stimulus and acquisition parameters used for recording brainstem responses are given in the Table below.

Table 3.1 Protocol for recording speech evoked auditory brainstem responses

Parameters	**Target setting for Speech evoked ABR**
Stimulus	Filtered /da/ Original /da/
Duration	40 ms
Polarity	Alternating
Stimulus Intensity	80dBSPL
Repetition Rate	10.9/s
Mode	Ipsilateral
Analysis Time	70msec including pre-stimulus period of 10msec
Band Pass Filter	100 to 3000Hz
Electrode Montage	Inverting- M1 Non Inverting- FZ Ground- M2
Sweeps	1500
Transducer	Biologic Insert
InterElectrode Impedance	<2 Kilo Ohms
No. of Channels	One
No. of Replications	Two

3.4 Data Analysis

The transient response which consists of the response within 10ms includes the wave V. The latency of the wave V was analysed for both the groups. Within the groups, wave V was also analysed for the responses obtained from original /da/ stimulus, filtered /da/ stimulus and original and filtered /da/ in P300 paradigm.

The amplitude of fundamental frequency and its harmonics (second and third) was obtained using FFT analysis for both the control and experimental group. The amplitude of F0, second harmonic and third harmonic was recorded for responses obtained from original /da/ stimulus, filtered /da/ stimulus and original and filtered /da/ stimulus in MMN paradigm for both the groups.

3.5 FFT Analysis

The latency of wave V were analysed. Additionally, to know the encoding of the first formant frequency and higher harmonics, a Fast Fourier transform (FFT) of the waveform was done. FFT was analysed from 16 ms to 44 ms of the waveform. To do the FFT analysis, activity occurring in the frequency range of the response corresponding to the fundamental frequency of the speech stimulus (103-121 Hz), and second harmonics of the stimulus (200-300 Hz) and third harmonic (310 Hz to 400 Hz) were measured for all the subjects. All FFT analysis was done using a custom-made programme using MATLAB software. Brainstem Toolbox developed at North-western University was also utilized along with MATLAB, to get the FFT information.

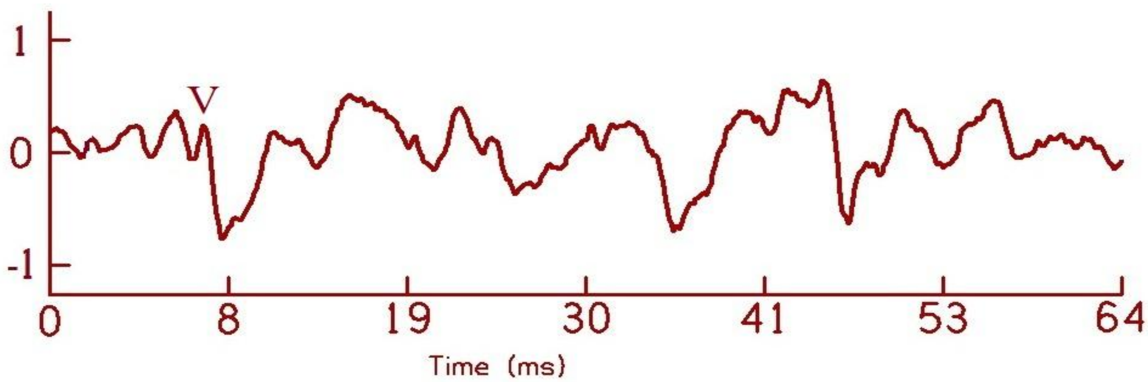
Chapter 4

RESULTS

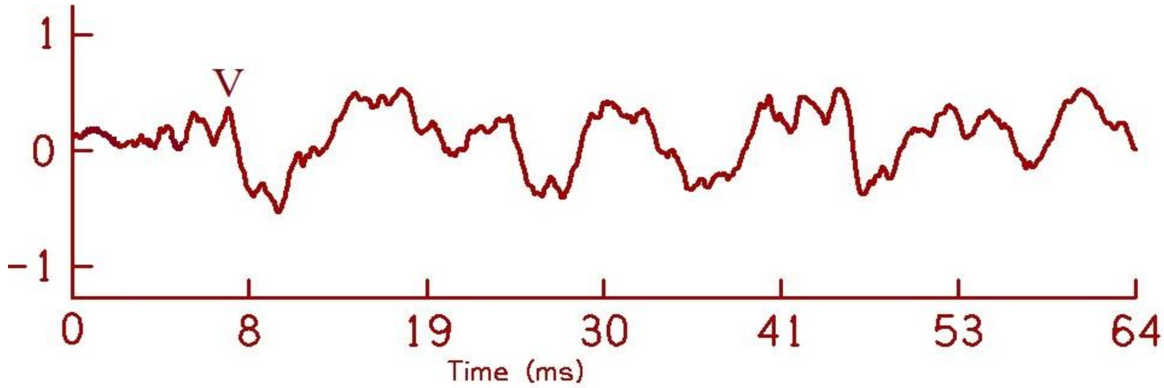
The objective of the present study was to assess the brainstem encoding of speech sounds in children with specific language impairment and to assess whether the auditory brainstem responses can be modulated online by context in children with specific language impairment. Speech evoked ABR was elicited using /da/ stimulus, and wave V latency and amplitude of F0, H1 and H2 was considered for comparison between children with SLI and typically developing children.

4.1 Wave V latency

A total of 15 children with SLI and 15 typically developing children participated in the study and speech evoked ABR was recorded from the right ear using original /da/, filtered /da/ and original + filtered /da/ in P300 paradigm. Wave V was present in all the subjects in all the stimulus paradigm in both the groups. The V peak was analysed for the three different stimulus paradigm (original /da/, filtered/da/, and original + filtered /da/ in P300 paradigm). The figure below shows the grand average of the calculated waveforms elicited using original /da/ stimulus paradigm for children with specific language impairment and typically developing children.



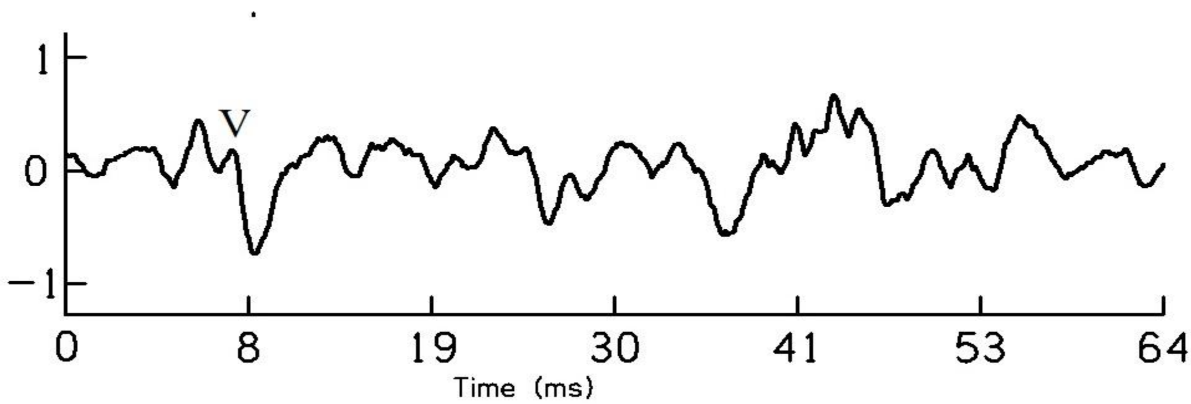
(a)



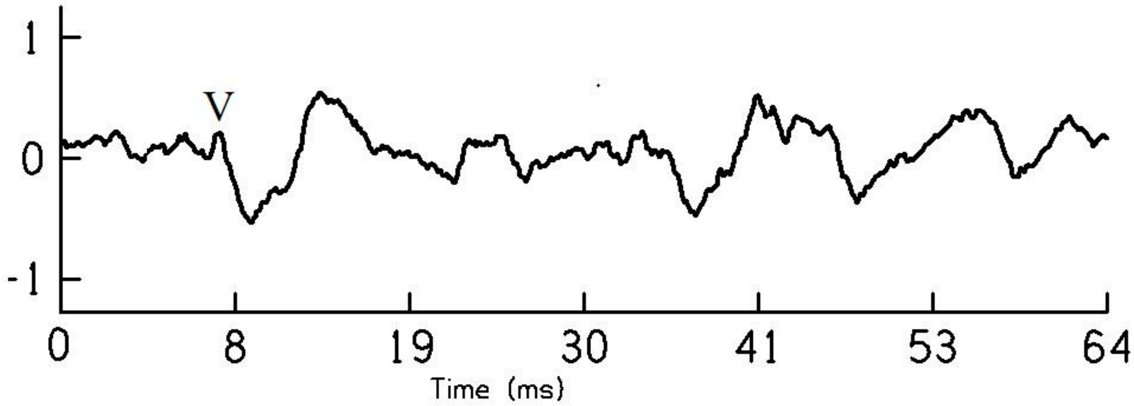
(b)

Figure 4.1 Grand average of the calculated waveforms of speech evoked ABR using original /da/ stimulus in (a) typically developing children and (b) children with specific language impairment

The filtered /da/ differed from the original /da/ in the spectral content. The /da/ syllable was high-pass filtered with a cut off frequency of 1000Hz removing the fundamental frequency and the first two formants without altering the higher harmonics. Figure below shows the grand average of the calculated waveforms elicited using filtered /da/ in normal children and children with specific language impairment.



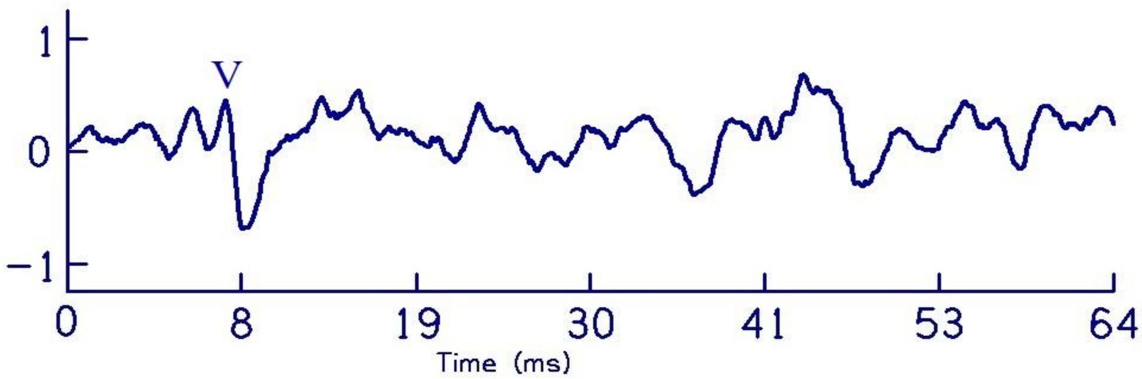
(a)



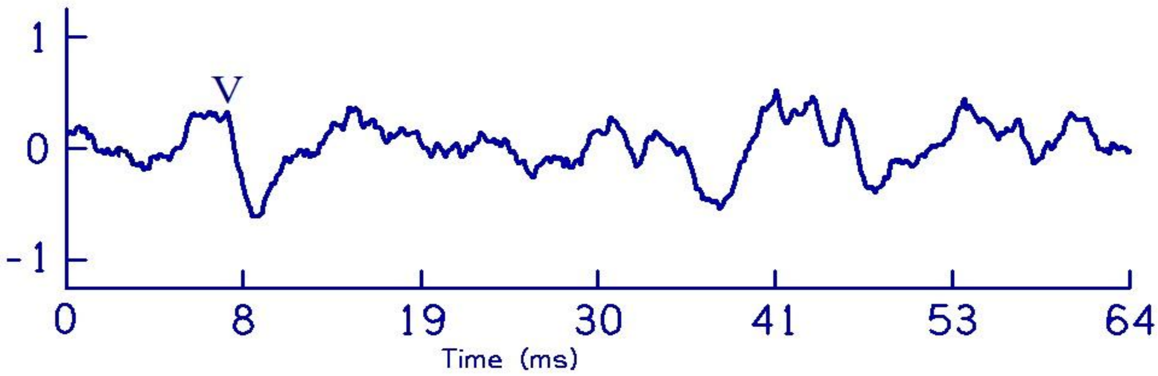
(b)

Figure 4.2 Grand average of the calculated waveforms of speech evoked ABR using filtered /da/ stimulus in (a) typically developing children and (b) children with specific language impairment.

The third recording was elicited in a P300 paradigm wherein the frequent stimulus was the original /da/ and infrequent stimulus was the filtered /da/ in 3:1 ratio in both the groups. The figure below shows the grand average of the calculated waveforms elicited by original + filtered /da/ paradigm for both the groups.



(a)



(b)

Figure 4.3 Grand average of calculated waveforms of speech evoked ABR of original + filtered /da/ in P300 paradigm of (a) typically developing children and (b) children with specific language impairment.

Descriptive statistics was carried out to find out the mean and standard deviation for latency of wave V for both the groups. Table 4.1 shows the mean and standard deviation of wave V latency for all three stimulus paradigm.

Table 4.1 Mean and standard deviation of wave V latency for three stimulus paradigm- original /da/, filtered /da/, and original + filtered /da/ in P300 paradigm for both the groups.

Stimulus paradigm	**Original /da/**		**Filtered /da/**		**Original + filtered /da/**	
Groups	Mean (ms)	SD	Mean (ms)	SD	Mean (ms)	SD
Normals	6.30	0.17	6.73	0.27	6.78	0.26
SLI	6.46	0.34	7.11	0.61	7.05	0.42

It can be observed from the above table that the wave V latency is prolonged in children with specific language impairment in comparison to typically developing children across all three conditions. Also, in the normal group it can be seen that wave V latency is the longest in original + filtered /da/ paradigm, and the shortest in the response elicited using original /da/ stimulus. However, in children with SLI wave V latency is longest in the filtered /da/ stimulus paradigm and shortest for original /da/ stimulus. The same can be seen in figure 4.4 also.

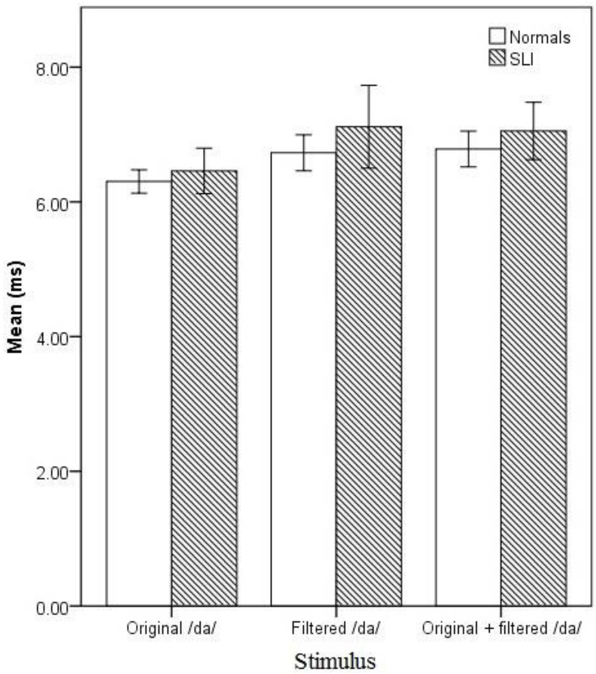


Figure 4.4 Mean and standard deviation of wave V latency for original /da/, filtered /da/ and original + filtered /da/ for normal children and children with SLI.

Shapiro-Wilks test of normality was done to check for normal distribution of the data. The test revealed normal distribution of data (p>0.05) for both the groups. Since the data shows normal distribution parametric tests were administered. Repeated measure ANOVA was administered, with group as within subject factor, to see the significant main effect of the variant stimulus of /da/ on latency of wave V, and also significant interaction between wave V latency and groups.

Repeated measure ANOVA showed significant main effect wave wave V latency [F (2, 56) = 51.66, p=0.00] and also showed significant main effect between groups [F (1, 28) = 5.26, p<0.05]. However, repeated measure ANOVA failed to show any interaction between latency of wave V and groups [F (2, 56) = 1.74, p>0.05].

As there was significant main effect of all the three stimuli on wave V latency, Bonferroni pairwise comparison was carried out to check which two stimuli were significantly different, in both the groups separately. In both the groups, Bonferroni pairwise comparison revealed significant difference between original /da/ and filtered /da/ stimulus (p<0.05), original /da/ and original + filtered /da/ (p<0.05). Yet, no significant difference was found between the filtered /da/ and original + filtered /da/ (p>0.05).

Since Repeated measure ANOVA showed main effect of groups, independent sample t-test was administered for latency of wave V for each stimuli separately. The independent sample t-test revealed no significant difference between normal children and children with SLI for wave V of original /da/ stimulus [t (28) = 1.60, p>0.05]. However, it revealed significant difference between the normal children and children with SLI for wave V latency of filtered /da/ [t (28) = 2.22, p<0.05] and original + filtered /da/ [t (28) = 2.06, p<0.05]. Thus, latency of wave V was earlier in normal children compared to children with SLI.

4.2 Amplitude of fundamental frequency (F0)

Descriptive statistics was carried out to obtain the mean and standard deviation for amplitude of F0 for both the groups, for all three stimuli. The mean amplitude of F0 and standard deviation is given in the table below.

Table 4.2 Mean and standard deviation of amplitude of F0 for three stimulus paradigm- original /da/, filtered /da/, and original and filtered /da/ in P300 paradigm for both the groups.

Stimulus paradigm	Original /da/		Filtered /da/		Original + filtered /da/	
Groups	Mean (µV)	SD	Mean (µV)	SD	Mean (µV)	SD
Normals	8.04	2.31	6.50	1.68	4.28	2.10
SLI	8.50	2.43	5..96	1.89	3.60	1.41

It can be seen from the Table 4.2 that amplitude of F0 is higher for normals when elicited using filtered /da/ stimulus and original +filtered /da/ stimulus. On the contrary it was observed that SLI group had higher amplitude of F0 obtained using original /da/ stimulus. The same can be observed in figure 4.5.

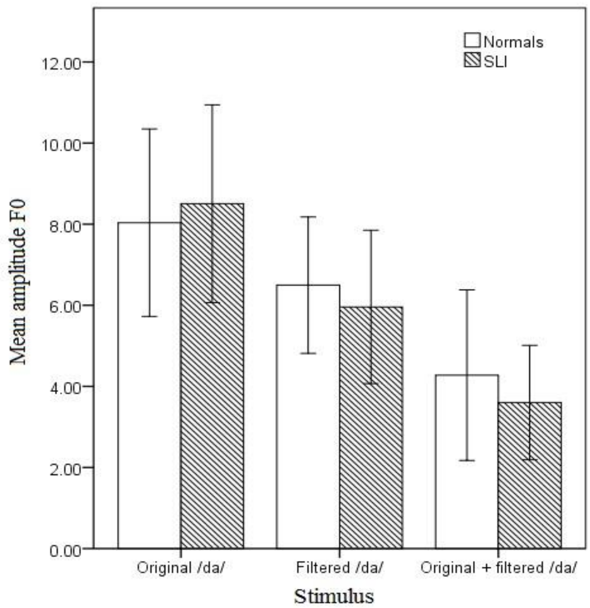


Figure 4.5 Mean and standard deviation of amplitude of F0 for original /da/, filtered /da/ and original + filtered /da/ for normal children and children with SLI.

Repeated measure ANOVA with group as between subject factor was administered to check the main effect of stimulus on the amplitude. It revealed significant main effect for the stimulus for the two groups [$F (2, 56) = 65.77$, $p= 0.00$]. But, there was no interaction between the amplitude and groups [$F (2, 56) = 1.37$, $p > 0.05$] and also no significant difference was found between the two groups for all three stimuli [$F (1, 28) = 0.18$, $p > 0.05$].

As there was significant main effect of all the three stimuli on amplitude of F0 within the groups, Bonferroni pairwise comparison was carried out to check which two stimuli were significantly different, in both the groups separately. In normals, Bonferroni pairwise comparison revealed significant difference between original /da/ and original + filtered /da/ stimulus ($p<0.05$), filtered /da/ and original + filtered /da/ ($p<0.05$). However, no significant difference was found between the original /da/ and filtered /da/ ($p>0.05$).

In the SLI group, Bonferroni pairwise comparison revealed significant difference between all the three stimuli, that is, between original /da/ and filtered /da/, between filtered /da/ and original + filtered /da/, and between original /da/ and original + filtered /da/ ($p<0.05$) for amplitude of F0.

4.3 Amplitude of first harmonic (H1)

Descriptive statistics was carried out to obtain the mean and standard deviation for amplitude of first harmonic (H1) for both the groups, for all three stimuli. The mean amplitude of H1 and standard deviation are given in the table below.

Table 4.3 Mean and standard deviation of amplitude of H1 for three stimulus paradigm- original /da/, filtered /da/, and original and filtered /da/ in P300 paradigm for both the groups.

Stimulus paradigm	**Original /da/**		**Filtered /da/**		**Original + filtered /da/**	
Groups	Mean (µV)	SD	Mean (µV)	SD	Mean (µV)	SD
Normals	4.01	1.58	3.26	1.43	2.74	1.41
SLI	3.65	1.22	2.71	0.94	2.48	0.73

From the above Table it can be seen that normal children had greater amplitude of first harmonic for all the three stimulus paradigm in comparison to children with specific language impairment. The amplitude of H1 is highest for response elicited from original /da/ and lowest for original + filtered /da/ for both the groups. The same can be seen in figure 4.6.

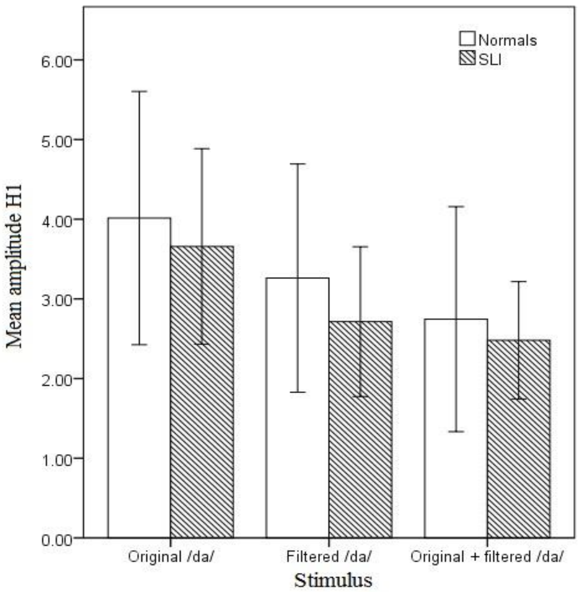


Figure 4.6 Mean and standard deviation of amplitude of first harmonic (H1) for original /da/, filtered /da/ and original + filtered /da/ for normal children and children with SLI.

To check for significant main effect and interaction between the three stimulus recording within the group, Repeated measure ANOVA was administered with group as between subject factors. It showed that there was a significant difference between the amplitude of H1 obtained from three stimulus within the groups [$F (2, 56) = 12.78$, $p=0.00$]. However, the analysis showed that there was no interaction between the amplitude of H1 and groups [$F (2, 56) = 0.168$, $p>0.05$] and also no significant difference between the groups for amplitude of H1 [$F (1, 28) = 1.17$, $p>0.05$].

As there was significant main effect of all the three stimuli on amplitude of first harmonic (H1) within the groups, Bonferroni pairwise comparison was carried out to check which two stimuli were significantly different, in both the groups separately. In both the groups, Bonferroni pairwise comparison revealed significant difference between original /da/ and original + filtered /da/ ($p<0.05$). Yet, no significant difference was found between the original and filtered /da/, and also between filtered /da/ and original + filtered /da/ ($p>0.05$) for H1 amplitude.

4.4 Amplitude of second harmonic (H2)

Descriptive statistics was carried out to obtain the mean and standard deviation for amplitude of second harmonic (H2) for both the groups, for all three stimuli. The mean amplitude of H2 and standard deviation are given in the table below.

Table 4.4 Mean and standard deviation of amplitude of H2 for three stimulus paradigm- original /da/, filtered /da/, and original and filtered /da/ in P300 paradigm for both the groups.

Stimulus paradigm	**Original /da/**		**Filtered /da/**		**Original + filtered /da/**	
Groups	Mean (μV)	SD	Mean (μV)	SD	Mean (μV)	SD
Normals	3.00	1.36	2.46	0.77	2.16	1.13
SLI	2.48	0.70	2.09	0.65	1.82	0.56

The above Table displays the amplitude of H2, and it can be observed that typically developing children have larger amplitude for all three stimuli in comparison to the children with SLI. Within the group, largest amplitude was obtained for original /da/ and shortest amplitude was obtained for original + filtered /da/ stimulus for both the groups. The same be seen in figure 4.7.

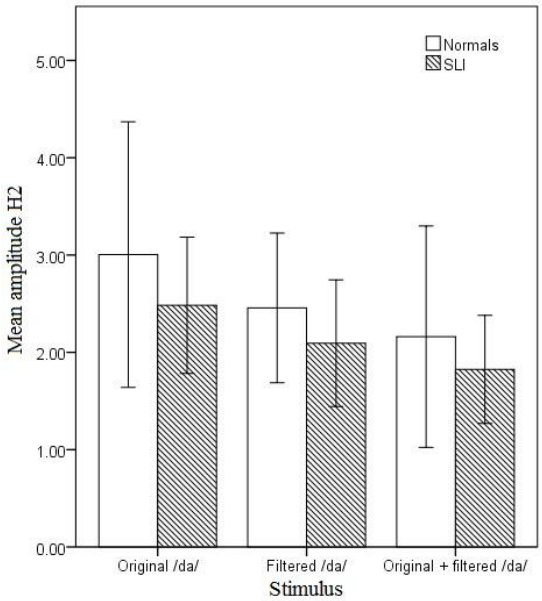


Figure 4.7 Mean and standard deviation of amplitude of second harmonic (H2) for original /da/, filtered /da/ and original + filtered /da/ for normal children and children with SLI.

As the data showed normal distribution parametric test, Repeated measure ANOVA was administered. It revealed significant difference between the amplitude of H2 for the three stimuli, within the groups [F (2, 56) = 10.04, p<0.05]. But, it did not show any significant difference for amplitude of H2 between the groups [F (1, 28) = 2.29, p>0.05]. Also the tests revealed no significant interaction between amplitude of H2 and the groups [F (2, 56) = 0.18, p>0.05].

As there was significant main effect of all the three stimuli on amplitude of second harmonic (H2), Bonferroni pairwise comparison was carried out to check which two stimuli were significantly different, in both the groups separately. In normal children, it revealed no significant difference between the stimuli for amplitude of H2. Whereas, in children with SLI, it exhibited significant difference between original /da/ and original + filtered /da/ (p<0.05). Yet, no significant difference was found between original and filtered /da/ and also between filtered /da/ and original + filtered /da/ (p>0.05).

In summary, there was a significant difference between the wave V latency of the three stimuli and between the groups. There was no interaction between latency of wave V and groups. The analysis showed a significant main effect for stimulus for the two groups for amplitude of fundamental frequency, first harmonic and second harmonic. But there was no interaction between amplitude and groups. Also no significant difference between the groups for amplitude of fundamental frequency, first and second harmonic.

Chapter 5

DISCUSSION

The aim of the present study was to assess the brainstem encoding of speech sounds in children with specific language impairment and to assess whether the auditory brainstem responses can be modulated online by context in these children. Speech evoked ABR was elicited using /da/ stimulus. Wave V latency and amplitude of F0, H1 and H2 was considered for analysis for both the groups.

5.1 Wave V latency

Statistical analysis of the results showed that there was a significant main effect between wave V latency of original /da/, filtered /da/ and original +filtered /da/ and also showed significant main effect between groups. Independent sample t-test revealed no significant difference between normal children and children with SLI for wave V latency of original /da/. However, it revealed significant difference between normal children and children with SLI for wave V latency of filtered /da/ and original + filtered /da/.

The results revealed no significant delay in latency of wave V for original /da/ between normal children and children with SLI. Similar results have been obtained by Filippini, Befi-Lopes, and Schochat (2012) and Karun (2013) in normal children and children with SLI. The present study is in congruence with Filippini et al. (2012) and Karun (2013), indicating that these children with SLI might not have any neural synchrony problems. Also the small number of subjects was probably insufficient to reveal differences between the groups. Karun (2013) reported that out of 24 children with SLI, in 3 children with SLI the speech evoked ABR was absent and in rest of the children it was not different from normal children. This indicates a heterogeneity of the specific language impairment children. This heterogeneity of the disorder also has been mentioned by Banai et al. (2007). Banai et al. (2007) reported that that not all children with same disorder exhibit deficits in speech ABR.

The results showed significant difference in the latency of wave V recorded by using filtered /da/ in children with SLI compared to normal children. The results thus indicate that when the stimulus complexity is increased the latency becomes prolonged in children with SLI as compared to that of typically developing children. Several studies have indicated that the speech perception in noise is poorer in children with language difficulties compared to that of typically developing children. For example, Vance and Martindale (2012) studied speech perception using Stimuli which varied in phonetic contrast. The stimulus was presented in quiet and in presence of noise. The results revealed that the presence of noise affected the speech perception in noise in both normal and children with language related deficits. However, the performance of children with language deficits was more compared to the normal children.

In another study Ziegler, Pech-Georgel, George, and Lorenzi (2009) investigated speech perception in quiet and in noise in children with dyslexia. The authors reported that the speech perception deficits in the presence of noise was more in children with dyslexia compared to the normal children. Not only behavioural measures but utilising the electrophysiological methods also authors have reported an abnormality in children with language deficits. Basu et al. (2010) recorded FFR using tone burst stimuli in children with specific language impairment. At a normal repetition rate the FFR amplitude in children with specific language impairment was similar to that of normal children. However, when the repetition rate was increased children with specific language impairment showed deficits in FFR amplitude compared to the normal children. In a study by Russo et al. (2009), the authors showed that there was significant delay in latency of wave V for speech presented in presence of background noise in children with autism spectrum disorder. In the present study also when the fundamental frequency cues, first harmonic cues and second harmonic cues were removed from the stimulus the latency of wave V was prolonged in children with specific language impairment compared to the normal children.

The delay in latency of wave V recorded using filtered stimulus could be to deficit in onset synchrony and reduced fidelity of response in absence of the important cues present in speech stimulus (Cunningham, Nicol, Zecker, Bradlow, & Kraus, 2001; Johnson, Nicol, Zecker, & Kraus, 2007; King et al., 2002). The complex spectro-temporal structure of speech signal requires a synchronized neural response for accurate encoding. Further if the acoustic cues are removed from speech stimuli it will depend more upon the synchronisation of the nerve fibers. Deficit in neural synchrony and reduced neural fidelity can be accounted for delayed wave V latency in children with SLI for the present study as the filtered stimulus is similar to the speech in noise condition wherein, some of the spectral cues are unavailable due to masking (Herbert & Kenet, 2007).

5.2 Amplitude of fundamental frequency (F0), First Harmonics and second harmonics

The filtering of the fundamental frequency and its harmonics from the stimuli, did not alter the encoding of fundamental frequency and harmonics in the frequency following response in both the groups. However, a statistical significant difference could not be observed between the two groups.

The results of the present study are in agreement to a similar study conducted by Gnanateja et al. (2013) on young adults. The encoding of F0 and its harmonics using a filtered stimulus, even though it was devoid of the fundamental frequency, can be attributed to the capability of brainstem to code the fundamental frequency using the stimulus envelope cues which continues to be present in the stimulus even after filtering (Gnanateja, Ranjan, & Sandeep, 2012). Although the concept of 'missing fundamental' (Schouten, Ritsma, & Cardozo, 1962) is a well-known fact in the tone complexes, it was first established using speech stimulus by Gnanateja et al. (2012).

The higher amplitude of F0, H1 and H2 was recorded from original /da/ in the present study suggesting that the human auditory system is influenced by exposure to short term stimulus. Chandrasekaran et al. (2009), recorded speech evoked ABR in normal children and children with developmental dyslexia using /da/ in a repetitive and variable context. The results revealed larger amplitude of F0 and its harmonics for repetitive /da/ context than variable context in normals. The enhancement of F0 and the harmonics was due to the repeated exposure, inducing online plasticity. This phenomenon of modulating the neural plasticity is crucial for speech in noise perception also (Luo et al., 2008).

Two hypotheses that explain the experience dependent brainstem plasticity are the corticofugal model and local reorganization model. The former model states that the top-down (efferent) pathway modulates the functioning of the brainstem in response to the cortical function and expects moment to moment changes (Suga, 2008; Suga et al., 2002). Whereas, the latter model states that brainstem function is modulated over a longer timescale during frequently encountered sounds (Krishnan & Gandour, 2009; Krishnan, Swaminathan, & Gandour, 2009). Therefore, both the model predicts plasticity but in different timescales.

The present study justifies the enhancement of amplitude due to the online plasticity occurring from the intact corticofugal modulations in typically developing children and children with SLI.

Chapter 6

SUMMARY AND CONCLUSION

Specific Language Impairment (SLI) is a developmental language disorder in children, where the delay in learning language is not attributed to any kind of sensory impairment, motor dysfunction, neurological condition, intellectual disability, emotional problems or environmental deprivation. Tallal et al. (1989) estimated that approximately 8- 15% of all preschool going children had some form speech and language impairment. Since there is an increase in the prevalence of children with SLI (Hannus et al., 2009) and no evidence for the cause of difficulty in learning language, there is a need to study the auditory pathways in these children.

Hearing in adverse conditions is facilitated by the descending (corticofugal) pathways of the auditory system, by improving the signal-to-noise ratio (Chandrasekaran et al., 2009; Parbery-Clark et al., 2011; Strait et al., 2011). Since children with SLI also have language impairment and the difficulty in learning language is not attributed to any sensory impairment, motor dysfunction, neurological damage, intellectual disability, emotional problems or environmental deprivation, it might be a possibility that corticofugal modulations are affected. There is a dearth of information on corticofugal modulations in children with specific language impairment. Hence, there is a need to study the corticofugal modulation in these children.

The objective of the present study was to study the brainstem encoding of speech sounds in children with specific language impairment and to assess whether the auditory brainstem responses can be modulated online by context in children with specific language impairment.

To achieve the aim the study, 15 children with specific language impairment and 15 typically developing children (age range: 4 – 11 years) participated for the study. These children did not have any history of ontological, neurological and psychological problems as reported.

Routine audiological evaluations such as pure tone audiometry, immittance evaluations and click evoked ABR revealed normal hearing sensitivity for both the groups. Subsequently, speech evoked ABR was recorded from all the participants at 80dB SPL using three different stimulus conditions, original biomark stimulus /da/, filtered /da/ stimulus (low pass cut off of 1000Hz) and original + filtered /da/ together. The recording parameter was similar for all the three conditions. Non- inverting electrode was placed on upper forehead (Fz), inverting electrode was placed on the mastoid (M1) of the test ear, and ground on the contralateral ear mastoid (M2). The /da/ stimulus was presented at the rate of 10.9 stimuli per second in alternating polarity. The post stimulus time window was kept for 64ms and 10ms pre stimulus recording. The responses were averaged for 1500 sweeps in each paradigm and responses were band pass filtered from 100 Hz to 3000 Hz.

Latency of wave V and amplitude of fundamental frequency (F0), first harmonic (H1) and second harmonic (H2) were analysed for all the three stimuli for both the groups. FFT analysis was done using MATLAB software.

Descriptive statistics was done to find the mean and standard deviation for wave V latency and amplitude of F0, H1 and H2. Normality check revealed normal distribution, hence parametric tests were administered. Accordingly, Repeated measure ANOVA and independent sample t-test were administered.

Results revealed that there was a significant main effect between wave V latency of original /da/, filtered /da/ and original +filtered /da/ and also showed significant main effect between groups. Independent sample t-test revealed no significant difference between normal children and children with SLI for wave V latency of original /da/. However, it revealed significant difference between normal children and children with SLI for wave V latency of filtered /da/ and original + filtered /da/.

The delay in latency of wave V recorded using filtered stimulus could be due to deficit in onset synchrony and reduced fidelity of response in absence of the important cues present in speech stimulus (Cunningham et al., 2001; Johnson et al., 2007; King et al., 2002). However, no significant delay in latency of wave V for original /da/ between normal children and children with SLI was probably insufficient to reveal differences between the groups and also indicates a heterogeneity of the specific language impairment children.

The filtering of the fundamental frequency and its harmonics from the stimuli, did not alter the encoding of fundamental frequency and harmonics in the frequency following response in both the groups. However, a statistical significant difference could not be observed between the two groups.

The higher amplitude of F0, H1 and H2 recorded from original /da/ in the present study was due to the repeated exposure, inducing online plasticity. This phenomenon of modulating the neural plasticity is crucial for speech in noise perception also. The experience dependent brainstem plasticity are due to the corticofugal modulations or the modulations of the brainstem responses via the top down feedback, by the cortical structures. The present study justifies the enhancement of amplitude due to the online plasticity occurring from the intact corticofugal modulations in typically developing children and children with SLI.

To conclude, in the present study, effect of context dependent encoding on the amplitude of fundamental frequency or its harmonics was observed in both typically developing and children with specific language impairment. However, there was a significant prolongation in latency of wave V in children with SLI in comparison to normal children when filtered stimulus was used. Whereas, the latency of wave V recorded from original /da/ was not prolonged in SLI children. This implies that when there is a complex stimulus used such as filtered speech stimulus in the present study it shows a prolongation of wave V. The results indicate a timing related problem in children with specific language impairment. It is suggested that for assessment of encoding of speech sounds at the brainstem through speech evoked ABR shall be done with a more complex stimulus.

Implications of the study

1. Study helped in understanding the pattern of speech encoding at the brainstem level in children with specific language impairment.

2. This study helped us to understand the corticofugal modulations in typically developing children and children with specific language impairment.

3. It adds to the literature.

REFERENCES

AFASIC (1989). Breaking Down the Communication Barrier, London: AFASIC.

Al-Saif, S. S., Abdeltawwab, M. M., & Khamis, M. (2012). Auditory middle latency responses in children with specific language impairment. *European Archives of Oto-Rhino-Laryngology, 269*(6), 1697-1702.

Anderson, S., Parbery-Clark, A., Yi, H.-G., & Kraus, N. (2011). A neural basis of speech-in-noise perception in older adults. *Ear and Hearing, 32*(6), 750.

Banai, Abrams, D., & Kraus, N. (2007). Sensory-based learning disability: Insights from brainstem processing of speech sounds. *International Journal of Audiology, 46*(9), 524-532.

Banai, Nicol, T., Zecker, S. G., & Kraus, N. (2005). Brainstem timing: implications for cortical processing and literacy. *Journal of Neuroscience, 25*(43), 9850-9857.

Banai, K., & Kraus, N. (2007). Neurobiology of (central) auditory processing disorder and language-based learning disability. *Handbook of (central) auditory processing disorder, 1*, 89-116.

Basu, M., Krishnan, A., & Weber-Fox, C. (2010). Brainstem correlates of temporal auditory processing in children with specific language impairment. *Developmental Science, 13*(1), 77-91.

Bishop. (1997). Uncommon understanding. Development and language disorders in children: Hove, UK: Psychology Press.

Bishop, Carlyon, R., Deeks, J., & Bishop, S. (1999). Auditory Temporal Processing ImpairmentNeither Necessary nor Sufficient for Causing Language

Impairment in Children. *Journal of Speech, Language, and Hearing Research, 42*(6), 1295-1310.

Bishop, & McArthur, G. M. (2005). Individual differences in auditory processing in specific language impairment: a follow-up study using event-related potentials and behavioural thresholds. *Cortex, 41*(3), 327-341.

Brinton, B., Fujiki, M., & McKee, L. (1998). Negotiation skills of children with specific language impairment. *Journal of Speech, Language, and Hearing Research, 41*(4), 927-940.

Briscoe, J., Bishop, D. V., & Norbury, C. F. (2001). Phonological processing, language, and literacy: A comparison of children with mild-to-moderate sensorineural hearing loss and those with specific language impairment. *Journal of Child Psychology and Psychiatry, 42*(03), 329-340.

Carhart, R., & Jerger, J. (1959). Preferred method for clinical determination of pure-tone thresholds. *Journal of Speech & Hearing Disorders*.

Catts, H. W. (1993). The relationship between speech-language impairments and reading disabilities. *Journal of Speech, Language, and Hearing Research, 36*(5), 948-958.

Chandrasekaran, B., Hornickel, J., Skoe, E., Nicol, T., & Kraus, N. (2009). Context-dependent encoding in the human auditory brainstem relates to hearing speech in noise: implications for developmental dyslexia. *Neuron, 64*(3), 311-319.

Chandrasekaran, B., & Kraus, N. (2010). The scalp-recorded brainstem response to speech: Neural origins and plasticity. *Psychophysiology, 47*(2), 236-246.

Cunningham, J., Nicol, T., Zecker, S. G., Bradlow, A., & Kraus, N. (2001). Neurobiologic responses to speech in noise in children with learning problems: deficits and strategies for improvement. *Clinical Neurophysiology, 112*(5), 758-767.

Dawes, P., Bishop, D. V., Sirimanna, T., & Bamiou, D.-E. (2008). Profile and aetiology of children diagnosed with auditory processing disorder (APD). *International Journal of Pediatric Otorhinolaryngology, 72*(4), 483-489.

Dlouha, O., Novak, A., & Vokral, J. (2007). Central auditory processing disorder (CAPD) in children with specific language impairment (SLI). Central auditory tests. *International Journal of Pediatric Otorhinolaryngology, 71*(6), 903-907.

Elliott, L. L., & Hammer, M. A. (1988). Longitudinal changes in auditory discrimination in normal children and children with language-learning problems. *Journal of Speech and Hearing Disorders, 53*(4), 467-474.

Farmer, M. E., & Klein, R. M. (1995). The evidence for a temporal processing deficit linked to dyslexia: A review. *Psychonomic bulletin & review, 2*(4), 460-493.

Ferguson, M. A., Hall, R. L., Riley, A., & Moore, D. R. (2011). Communication, listening, cognitive and speech perception skills in children with auditory processing disorder (APD) or Specific Language Impairment (SLI). *Journal of Speech, Language and Hearing Research, 54*(1), 211-227.

Filippini, R., Befi-Lopes, D. M., & Schochat, E. (2012). Efficacy of auditory training using the auditory brainstem response to complex sounds: auditory processing disorder and specific language impairment. *Folia Phoniatrica et Logopaedica, 64*(5), 217-226.

Gabr, T. A., & Darwish, M. E. (2016). Speech auditory brainstem response audiometry in children with specific language impairment. *Hearing, Balance and Communication, 14*(1), 50-58.

Ghannoum, M. T., Shalaby, A. A., Dabbous, A. O., Abd-El-Raouf, E. R., & Abd-El-Hady, H. S. (2014). Speech evoked auditory brainstem response in learning disabled children. *Hearing, Balance and Communication, 12*(3), 126-142.

Gnanateja, G. N., Ranjan, R., Firdose, H., Sinha, S. K., & Maruthy, S. (2013). Acoustic basis of context dependent brainstem encoding of speech. *Hearing Research, 304*, 28-32.

Gnanateja, G. N., Ranjan, R., & Sandeep, M. (2012). Physiological bases of the encoding of speech evoked frequency following responses. *Journal of All India Institute of Speech and Hearing, 31*, 215-219.

Hannus, S., Kauppila, T., & Launonen, K. (2009). Increasing prevalence of specific language impairment (SLI) in primary healthcare of a Finnish town, 1989-99. *International Journal of Language and Communication Disorders, 44*(1), 79-97.

Hartley, D. E., Hill, P. R., & Moore, D. R. (2003). The auditory basis of language impairments: temporal processing versus processing efficiency hypotheses. *International Journal of Pediatric Otorhinolaryngology, 67*, S137-S142.

Hauser, M. D., Newport, E. L., & Aslin, R. N. (2001). Segmentation of the speech stream in a non-human primate: statistical learning in cotton-top tamarins. *Cognition, 78*(3), B53-B64.

Herbert, M. R., & Kenet, T. (2007). Brain abnormalities in language disorders and in autism. *Pediatric Clinics of North America, 54*(3), 563-583.

Holopainen, I. E., Korpilahti, P., Juottonen, K., Lang, H., & Sillanpää, M. (1998). Abnormal frequency mismatch negativity in mentally retarded children and in children with developmental dysphasia. *Journal of Child Neurology, 13*(4), 178-183.

Jernigan, T. L., Hesselink, J. R., Sowell, E., & Tallal, P. A. (1991). Cerebral structure on magnetic resonance imaging in language-and learning-impaired children. *Archives of neurology, 48*(5), 539-545.

Johnson, K. L., Nicol, T., Zecker, S. G., Bradlow, A. R., Skoe, E., & Kraus, N. (2008). Brainstem encoding of voiced consonant–vowel stop syllables. *Clinical Neurophysiology, 119*(11), 2623-2635.

Johnson, K. L., Nicol, T. G., Zecker, S. G., & Kraus, N. (2007). Auditory brainstem correlates of perceptual timing deficits. *Journal of Cognitive Neuroscience, 19*(3), 376-385.

Johnston, J. (1988). Specific language disorders in the child. *Handbook of speech-language pathology and audiology*, 685-715.

King, C., Warrier, C. M., Hayes, E., & Kraus, N. (2002). Deficits in auditory brainstem pathway encoding of speech sounds in children with learning problems. *Neuroscience Letters, 319*(2), 111-115.

Klatt, D. H. (1980). Software for a cascade/parallel formant synthesizer. *Journal of Acoustical Society of America, 67*(3), 971-995.

Kraus, N., McGee, T. J., Carrell, T. D., & Zecker, S. G. (1996). Auditory neurophysiologic responses and discrimination deficits in children with learning problems. *Science, 273*(5277), 971.

Krishnan, A., & Gandour, J. T. (2009). The role of the auditory brainstem in processing linguistically-relevant pitch patterns. *Brain Language*, *110*(3), 135-148.

Krishnan, A., Swaminathan, J., & Gandour, J. T. (2009). Experience-dependent enhancement of linguistic pitch representation in the brainstem is not specific to a speech context. *Journal of Cognitive Neuroscience, 21*(6), 1092-1105.

Krizman, J. L., Skoe, E., & Kraus, N. (2010). Stimulus rate and subcortical auditory processing of speech. *Audiology and Neurootology, 15*(5), 332-342.

Kumar, P., & Singh, N. K. (2015). BioMARK as electrophysiological tool for assessing children at risk for (central) auditory processing disorders without reading deficits. *Hearing Research, 324,* 54-58.

Lahey, M., & Edwards, J. (1999). Naming errors of children with specific language impairment. *Journal of Speech, Language, and Hearing Research, 42*(1), 195-205.

Law, J., Boyle, J., Harris, F., Harkness, A., & Nye, C. (2000). Prevalence and natural history of primary speech and language delay: findings from a systematic review of the literature. *International Journal of Language and Communication Disorders, 35*, 165-188.

Leonard, L. B. (1991). Specific language impairment as a clinical category. *Language, Speech, and Hearing Services in Schools, 22*(2), 66-68.

Lowe, A. D., & Campbell, R. A. (1965). Temporal discrimination in aphasoid and normal children. *Journal of Speech and Hearing Research, 8*(3), 313-314.

Luo, F., Wang, Q., Kashani, A., & Yan, J. (2008). Corticofugal modulation of initial sound processing in the brain. *The Journal of Neuroscience, 28*(45), 11615-11621.

McArthur, G., & Bishop, D. V. (2005). Speech and non-speech processing in people with specific language impairment: A behavioural and electrophysiological study. *Brain Language, 94*(3), 260-273.

Miller, C. A., Kail, R., Leonard, L. B., & Tomblin, J. B. (2001). Speed of processing in children with specific language impairment. *Journal of Speech, Language, and Hearing Research, 44*(2), 416-433.

Miller, C. A., & Wagstaff, D. A. (2011). Behavioral profiles associated with auditory processing disorder and specific language impairment. *Journal of Communication Disorders, 44*(6), 745-763.

Montgomery, J. W. (1999). Recognition of Gated Words by Children With Specific Language ImpairmentAn Examination of Lexical Mapping. *Journal of Speech, Language, and Hearing Research, 42*(3), 735-743.

Moore, D. R. (2006). Auditory processing disorder (APD): Definition, diagnosis, neural basis, and intervention. *Audiological Medicine, 4*(1), 4-11.

Musacchia, G., Strait, D., & Kraus, N. (2008). Relationships between behavior, brainstem and cortical encoding of seen and heard speech in musicians and non-musicians. *Hearing Research, 241*(1), 34-42.

Nahum, M., Nelken, I., & Ahissar, M. (2008). Low-level information and high-level perception: the case of speech in noise. *Public Library of Science Biology, 6*(5), e126.

Neville, H. J., Coffey, S. A., Holcomb, P. J., & Tallal, P. (1993). The neurobiology of sensory and language processing in language-impaired children. *Journal of Cognitive Neuroscience, 5*(2), 235-253.

Parbery-Clark, A., Strait, D., & Kraus, N. (2011). Context-dependent encoding in the auditory brainstem subserves enhanced speech-in-noise perception in musicians. *Neuropsychologia, 49*(12), 3338-3345.

Pinborough-Zimmerman, J., Satterfield, R., Miller, J., Bilder, D., Hossain, S., & McMahon, W. (2007). Communication disorders: Prevalence and comorbid intellectual disability, autism, and emotional/behavioral disorders. *American Journal of Speech-Language Pathology, 16*(4), 359-367.

Plante, E., Swisher, L., & Vance, R. (1989). Anatomical correlates of normal and impaired language in a set of dizygotic twins. *Brain Lang, 37*(4), 643-655.

Plante, E., Swisher, L., Vance, R., & Rapcsak, S. (1991). MRI findings in boys with specific language impairment. *Brain Language*, *41*(1), 52-66.

Repp, B. H. (2007). Hearing a melody in different ways: Multistability of metrical interpretation, reflected in rate limits of sensorimotor synchronization. *Cognition, 102*(3), 434-454.

Rice, M. L., Sell, M. A., & Hadley, P. A. (1991). Social interactions of speech, and language-impaired children. *Journal of Speech, Language, and Hearing Research, 34*(6), 1299-1307.

Rocha-Muniz, C. N., Befi-Lopes, D. M., & Schochat, E. (2012). Investigation of auditory processing disorder and language impairment using the speech-evoked auditory brainstem response. *Hearing Research*, *294*(1-2), 143-152.

Rocha-Muniz, C. N., Befi-Lopes, D. M., & Schochat, E. (2014). Sensitivity, specificity and efficiency of speech-evoked ABR. *Hearing Research*, *317*, 15-22.

Rosen, S. (2003). Auditory processing in dyslexia and specific language impairment: is there a deficit? What is its nature? Does it explain anything? *Journal of phonetics, 31*(3), 509-527.

Russo, Nicol, T., Musacchia, G., & Kraus, N. (2004). Brainstem responses to speech syllables. *Clinical Neurophysiology, 115*(9), 2021-2030.

Russo, Nicol, T., Trommer, B., Zecker, S., & Kraus, N. (2009). Brainstem transcription of speech is disrupted in children with autism spectrum disorders. *Developmental Science, 12*(4), 557-567.

Russo, Skoe, E., Trommer, B., Nicol, T., Zecker, S., Bradlow, A., & Kraus, N. (2008). Deficient brainstem encoding of pitch in children with autism spectrum disorders. *Clinical Neurophysiology, 119*(8), 1720-1731.

Schouten, J. F., Ritsma, R., & Cardozo, B. L. (1962). Pitch of the residue. *Journal of Acoustical Society of America, 34*(9B), 1418-1424.

Skoe, & Kraus, N. (2010). Hearing it again and again: on-line subcortical plasticity in humans. *Public Library of Sciences One, 5*(10), e13645.

Skoe, & Kraus, N. (2013). Musical training heightens auditory brainstem function during sensitive periods in development. *Frontiers in Psychology, 4,* 622.

Skoe, Krizman, J., Spitzer, E., & Kraus, N. (2013). The auditory brainstem is a barometer of rapid auditory learning. *Neuroscience, 243*, 104-114.

Speaks, A. (2013). DSM-5 diagnostic criteria. *Retrieved August, 12*, 2013.

Stevens, C., Sanders, L., & Neville, H. (2006). Neurophysiological evidence for selective auditory attention deficits in children with specific language impairment. *Brain Research, 1111*(1), 143-152.

Strait, D. L., Hornickel, J., & Kraus, N. (2011). Subcortical processing of speech regularities underlies reading and music aptitude in children. *Behavioral and Brain Functions, 7*(1), 1.

Strait, D. L., O'connell, S., Parbery-Clark, A., & Kraus, N. (2014). Musicians' enhanced neural differentiation of speech sounds arises early in life: developmental evidence from ages 3 to 30. *Cerebral Cortex, 24*(9), 2512-2521.

Suga, N. (2008). Role of corticofugal feedback in hearing. *Journal of Comparative Physiology A, 194*(2), 169-183.

Suga, N., Gao, E., Zhang, Y., Ma, X., & Olsen, J. F. (2000). The corticofugal system for hearing: recent progress. *Proceedings of the National Academy of Sciences, 97*(22), 11807-11814.

Suga, N., Xiao, Z., Ma, X., & Ji, W. (2002). Plasticity and corticofugal modulation for hearing in adult animals. *Neuron*, *36*(1), 9-18.

Tallal, & Piercy, M. (1973). Defects of non-verbal auditory perception in children with developmental aphasia. *Nature*, *241*(5390), 468-469.

Tallal, & Piercy, M. (1974). Developmental aphasia: rate of auditory processing and selective impairment of consonant perception. *Neuropsychologia*, *12*(1), 83-93.

Tallal, Ross, R., & Curtiss, S. (1989). Familial aggregation in specific language impairment. *Journal of Speech and Hearing Disorders, 54*(2), 167-173.

Tallal, P., & Piercy, M. (1975). Developmental aphasia: the perception of brief vowels and extended stop consonants. *Neuropsychologia*, *13*(1), 69-74.

Tomblin, J. B., Records, N. L., Buckwalter, P., Zhang, X., Smith, E., & OÔÇÖBrien, M. (1997). Prevalence of specific language impairment in kindergarten children. *Journal of Speech, Language, and Hearing Research*, *40*(6), 1245-1260.

Toro, J. M., & Trobalon, J. B. (2005). Statistical computations over a speech stream in a rodent. *Attention, Perception, & Psychophysics, 67*(5), 867-875.

Van der Lely, H. K., Rosen, S., & McClelland, A. (1998). Evidence for a grammar-specific deficit in children. *Current Biology, 8*(23), 1253-1258.

Vance, M., & Martindale, N. (2012). Assessing speech perception in children with language difficulties: Effects of background noise and phonetic contrast. *International Journal of Speech-Language Pathology, 14*(1), 48-58.

Vander Werff, K. R., & Burns, K. S. (2011). Brain stem responses to speech in younger and older adults. *Ear and Hearing*, *32*(2), 168-180.

Vandewalle, E., Boets, B., Ghesquiere, P., & Zink, I. (2012). Auditory processing and speech perception in children with specific language impairment: Relations with oral language and literacy skills. *Research in Developmental Disabilities, 33*(2), 635-644.

Wible, B., Nicol, T., & Kraus, N. (2004). Atypical brainstem representation of onset and formant structure of speech sounds in children with language-based learning problems. *Biological Psychology, 67*(3), 299-317.

Wright, B. A., Lombardino, L. J., King, W. M., Puranik, C. S., Leonard, C. M., & Merzenich, M. M. (1997). Deficits in auditory temporal and spectral resolution in language-impaired children. *Nature*, *387*(6629), 176-178.

Zhang, Y., Suga, N., & Yan, J. (1997). Corticofugal modulation of frequency processing in bat auditory system. *Nature, 387*(6636), 900.

Ziegler, J. C., Pech-Georgel, C., George, F., & Lorenzi, C. (2009). Speech-perception-in-noise deficits in dyslexia. *Developmental Science, 12*(5), 732-745.