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Physiological and Behavioral Evidence of Auditory Processing Deficit in Children Suspected of Auditory Processing Disorder

Sangamanatha Ankmnal Veeranna, *The University of Western Ontario*

Supervisor: Prudence Allen, *The University of Western Ontario*

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Abstract

A series of studies were carried out to examine the neural and behavioral processing of acoustic stimuli in children with suspected auditory processing disorder (sAPD).

The click-evoked auditory brainstem responses recorded from children with sAPD and adults were analyzed using traditional clinical measures and detailed analysis seeking to explore the separate contributions of axonal conduction and synaptic transmission. Clinical measures revealed significant prolongation of absolute latencies and interwave intervals in children with sAPD compared to adults. Examination of responses delineating axonal vs. synaptic transmission showed frequent delays in synaptic factors and fewer instances of delays related to axonal conduction in children with sAPD compared to adults.

Inefficient neural transmission in the auditory brainstem may lead to difficulty in coding of dynamic acoustic cues (envelope, fine structure or spectral shape) that are necessary for recognizing speech in quiet and in noise. The ability to use envelope and fine structure cues to recognize speech in noise was therefore examined in children with sAPD, typically developing children and adults. Typically developing children showed developmental trend in use of envelope cues. Whereas children with sAPD were less efficient in using envelope and fine structure cues to recognize speech in noise compared to age-matched children and adults. Perception of speech based on fine structure alone was difficult for both TD children and children with sAPD compared to adults. This could be due to developmental difficulty in integrating frequency information from different bands.

Difficulty in integrating auditory filter outputs may lead to the inadequate representation of spectral shape, which is necessary for recognizing speech sounds. Spectral shape perception was assessed using a spectral ripple discrimination task in typically developing children, children with sAPD, and adults. Young children could resolve fewer of ripples per octave when compared older children and adults. The performance of children with sAPD was poor compared to age-matched controls and young adults. Spectral-ripple discrimination showed a strong trend for improvement in thresholds as a function of age in both typically developing

children and children with sAPD. This suggests that spectral shape is a learned cue and may take a longer time to mature.

Keywords: Click-evoked auditory brainstem response, Auditory Processing Disorder, Envelope, Fine structure, Spectral shape, Spectral Ripple discrimination

List of Abbreviations

A		
	AAA	American Academy of Audiology
	ANOVA	Analysis of variance
	ABR	Auditory Brainstem Response
	AEP.	Auditory Evoked Potential
	AN	Auditory Nerve
	ASHA	American Speech-Language-Hearing Association
	APD	Auditory Processing Disorder
B		
	BSA	British Society of Audiology
C		
	CA	Conception Age
	CNC	Cochlear Nucleus Complex
D		
	dB	Decibel
E		
	E	Envelope
F		
	FS	Fine Structure
G		
	GUI	Graphical User Interface
H		
	HINT-C	Hearing in Noise for Children
I		
	IC	Inferior Colliculus
	IHC	Inner hair Cells
M		
	MLS	Maximum Length Sequence
	MSO	Medial Superior Olivary complex

O		
	OTD	Older Typically Developing
R		
	RAU	Rationalized Arcsine Units
R		
	RMANOVA	Repeated Measure of Analysis of variance
	RPO	Ripple per Octave
S		
	SD	Standard Deviation
	SOC	Superior Olivary complex
	SMD	Spectral Modulation Detection
	SNR	Signal to Noise Ratio
	SRD	Spectral Ripple Discrimination
	SSN	Speech Shaped noise
T		
	TD	Typically Developing
Y		
	YTD	Young Typically Developing

Co-Authorship Statement

This thesis is comprised of an introductory chapter (Chapter 1), four integrated manuscripts (Chapter 2 to 5) and concluding chapter (Chapter 6). I am the main author for all the chapters as I was responsible for designing the methods of the experiments, collecting the data, statistical analysis of the results and writing the manuscripts. I, Sangamanatha Ankmnal Veeranna, am the sole author for chapter 1 and Chapter 6. Dr. Chris Allan and Dr. Prudence Allen are co-authors in chapters 2-5 as they participated in study design and analyses. Additionally, Dr. Chris Allan was responsible for recruiting and assessing children's auditory processing skills. Chapter 2 has been submitted for peer review (Sangamanatha Ankmnal Veeranna, Chris Allan and Prudence Allen).

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Chapter 1

1 Overview

School children may be referred to audiology for central auditory processing assessment because their parents or school teachers expressed concerns over their hearing and difficulty understanding speech in noise. These children are suspected of having an auditory processing disorder (sAPD). The American Speech-Language-Hearing Association [ASHA] defines APD as a perceptual deficit in the processing of acoustic information. Children with APD should demonstrate abnormal neural processing of auditory stimuli that is not attributable to deficit in cognition or language (ASHA, 2005). For an APD evaluation, ASHA recommends including electrophysiological measures to assess the integrity of the auditory nervous system. Even at the Bruton Conference held at the Callier Centre in Dallas, Jerger and Musick, (2000) suggested to include ABR and middle latency responses (MLR) in an APD assessment battery. However, less than 15 % of audiologists include electrophysiology [ABR, MLR and Late Latency Response (LLR)] in their routine battery (Emanuel, Ficca, & Korczak, 2011). One reason for this disconnect may be the position of the American Academy of Audiology (American Academy of Audiology [AAA], 2010) who described the value of click-evoked auditory brainstem response (ABR) as limited, agreeing with prominent authors (Katz et al., 2002) who have criticized the inclusion of ABR in a routine diagnostic battery due to lack of evidence to support its inclusion. This is unfortunate because there is evidence that children with APD do show a measurable physiologic deficit at lower levels of the auditory system, similar to that observed in individuals with auditory neuropathy. ABR responses are often characterized by increased wave latencies and interwave intervals, reduced wave amplitudes and abnormal latency shifts at faster stimulation rates (Allen & Allan, 2014; Gopal & Kowalski, 1999; Jirsa, 2001). These findings suggest a disruption in neural timing. Neural disruption may arise from axonal conduction or synaptic transmission delays in the auditory brainstem pathway. Ponton, Moore, and Eggermont, (1996) have demonstrated that maturation of these parameters can be seen in the click-evoked ABR.

The peripheral auditory system of typically developing children's is mature early enough to provide an acoustic signal that can be well represented in the higher level auditory system; however, young children require a higher signal to noise ratio (SNR) to perceive speech signal in noise (Fallon, Trehub, & Schneider, 2000; Hall, Grose, Buss, & Dev, 2002; Nittrouer & Boothroyd, 1990). Recognizing speech in noise becomes especially important when children enter school. In school, teaching and learning may not take place in a quiet environment, as there are several sources of background noise (e.g. children chatting, noise from the corridor).

There is general agreement that typically developing children's ability to understand speech in noise improves with age (Fallon et al., 2000; Wilson, Farmer, Gandhi, Shelburne, & Weaver, 2010). The prolonged maturation of recognizing speech in noise could be due to differences in maturation of the perception of dynamic acoustic cues (fine structure and envelope cues). Envelope cues are slowly varying amplitudes over time and fine structure cues are rapid variations in amplitude over time. Both envelope and fine structure are known to provide important cues for speech recognition (Rosen, 1992). Listeners use both envelope and fine structure cues to recognize speech. Developmental studies indicate that typically developing children may weight fine structure cues more heavily than envelope cues (Allen & Bond, 1997). Perception of speech based on fine structure cues is matured by 5-7 years of age (Bertoncini, Serniclaes, & Lorenzi, 2009). Typically developing children can extract speech from envelope cues by 5-7 years of age but reaches adult level by 10 years old (Eisenberg, Shannon, Martinez, Wygonski, & Boothroyd, 2000). In quiet, typically developing children can use both envelope and fine structure cues to recognize speech. However, it is not clear how these cues are used to recognize speech in noise by typically developing children.

One of the most frequent listening complaints of children with sAPD is that they have difficulty understanding speech in the presence of background noise (Bamiou, Musiek, & Luxon, 2001; Chermak, Hall, & Musiek, 1999; Lagacé, Jutras, Giguère, & Gagné, 2011; Vanniasegaram, Cohen, & Rosen, 2004). Unfortunately, only a handful of studies have tested speech in noise directly. Such studies suggest that children with listening disorders and suspected of having APD require higher SNRs to achieve similar speech recognition

scores to age-matched controls (Lagacé et al., 2011; Vanniasegaram et al., 2004a). However, the underlying cause for the poor recognition in noise by APD children has not been specifically identified. One possibility is that children with listening disorders may be less proficient at extracting important envelope and fine structure cues. However, this has not been examined directly.

Previous studies, both developmental and in APD, have examined speech in noise ability by mixing speech in noise at different SNRs. By mixing speech and noise at various SNRs, it may not be clear to what extent envelope and fine structure cues are masked and what cues are used to recognize speech. Apoux, Yoho, Youngdahl, and Healy (2013) proposed to use auditory chimera (Smith, Delgutte, & Oxenham, 2002) signal processing strategies to study the importance of envelope and fine structure cues in recognizing speech in noise. They demonstrated that adults rely heavily on envelope cues rather than fine structure cues to recognize speech in noise. However, it is not clear how envelope and fine structure cues are used in noise by typically developing children and children with APD.

Spectrally, a listener may use spectral shape, periodicity, spectral peaks or rapid spectral changes to recognize speech from background noise (Assmann & Summerfield, 2004). The ability to discriminate spectral shape in complex sounds is important for accurate speech perception (Allen & Wightman, 1992; Henry, Turner, & Behrens, 2005). Spectral shape refers to the overall shape of the spectrum of an acoustic signal. Perception of spectral shape relies on identifying frequency-amplitude information from each auditory filter and integrate them (across-channel integration). Any difficulty in across-channel integration may lead to the inadequate representation of spectral shape. Psychoacoustic studies have been used to understand the perception of these cues in adults. However, only a handful of studies have been carried on typically developing children (Allen & Wightman, 1992; Peter et al., 2014; Rayes, Sheft, & Shafiro, 2014). The perception of spectral shape in children with sAPD has not been explored.

The main focus of this dissertation was to understand why children with sAPD find it difficult to understand speech in the presence of noise. A combination of physiological,

speech perception and psychoacoustic tasks that tap different aspects of auditory processing was used. Study 1 analyzed the click-evoked ABRs in children with sAPD and adults using traditional clinical measures and responses that delineate axonal conduction and synaptic transmission times. This study provides novel evidence for the underlying source of neural disruption in children with sAPD. Study 2 focused on understanding the ability of typically developing children, children with sAPD and adult's to use envelope and fine structure cues to recognize speech in noise. Study 3 focused on the perception of speech with only fine structure cues in typically developing children, children with sAPD and adults. Study 4 assessed the perception of spectral shape using psychoacoustic measures in typically developing children, children with sAPD and adults. The main focus of this study is to understand whether children with sAPD abilities to integrate frequency-amplitude information is similar to that of age-matched adults.

1.1 Auditory processing disorder

1.1.1 Definition

ASHA (2005) defines APD as a deficit processing auditory information in the auditory nervous system in the presence of normal audibility. Children with APD may demonstrate a deficiency in auditory discrimination, localization, temporal processing, or detecting sound in noise (ASHA, 2005). ASHA also highlights that the diagnosis of APD requires demonstration of a neural deficit in the processing of acoustic stimuli that is not due to the influence of cognition or language.

1.1.2 Criteria for making a diagnosis

The diagnosis of APD can be made based on the identification of difficulties in auditory discrimination, localization of sounds, temporal processing (resolution or patterning), dichotic listening and recognition of degraded acoustic signals. Professional bodies (e.g ASHA, 2005) have recommended certain diagnostic guidelines to be used with APD assessment. These diagnostic guidelines typically involve a battery of behavioral and objective tests consisting of multiple subtests presumed to examine the integrity of

auditory processing. The test batteries can include tests of auditory discrimination, temporal processing, binaural processing, monaural low-redundancy test, and electrophysiological measurements. The diagnosis of APD can be made if a child's performance is poor on two or more tests in the battery falling at least two standard deviations below the mean (Chermak & Musiek, 1997). If only one test is administered then, a diagnosis of APD should only be made if the result falls three standard deviations below the mean (ASHA, 2005). However, ASHA did not specify whether the auditory deficit should be present in one ear or both ears. The AAA (2010) requires that the deficit be present in at least one ear.

There is no standard clinical protocol for APD diagnosis. More recently, Wilson and Arnott (2013) reviewed the files of 150 children who had completed an APD assessment, including low-pass filtered speech, competing sentences, dichotic digits and frequency patterns tests. From performance on these tests, children were classified as having APD or not having APD based on nine different sets of recommended diagnostic criteria. The diagnosis of APD ranged from 7.3% to 96% depending on the criteria used for diagnosis. The researchers suggested not using the APD as a global label. The presence of ongoing debate on the diagnosis of APD make it difficult for the audiologist to diagnose and provide adequate rehabilitation for these children.

1.1.3 Objective assessment of APD

For APD evaluation, ASHA recommends the inclusion of electrophysiological measures to assess the integrity of the auditory nervous system. However, less than 15 % of audiologists include electrophysiology in their assessments (Emanuel et al., 2011). This could be due to the limited availability of advanced equipment in some clinics and limited research on objective indicators of APD. Another reason for this disconnect may be the position of the AAA (2010) who described the value of click-evoked auditory brainstem response (ABR) as limited, agreeing with prominent authors (Katz et al., 2002) who have criticized the inclusion of ABR in routine diagnostic battery due to lack of evidence to support auditory deficit in these children.

The advantage of using objective measures is that no overt behavioral response is required and responses can be acquired passively. Acoustic reflex measurements (acoustic reflex thresholds, acoustic reflex growth function), otoacoustic emissions, and electrophysiological measures (click or speech evoked ABR, MLR, P300) can be used to assess neural integrity in children with APD. Jerger and Musiek (2000) recommended using auditory evoked potentials and otoacoustic emissions (OAE) along with behavioral measures of APD. Studies have reported abnormal acoustic reflex thresholds and growth functions (Allen & Allan, 2014; Saxena, Allan, & Allen, 2015, 2016), abnormal click-evoked ABRs (Allen & Allan, 2014; Gopal & Kowalski, 1999; Jirsa, 2001), and abnormal speech evoked ABRs (Kumar & Singh, 2015). Results from these studies suggest the objective measures may aid in the diagnosis of APD.

1.1.4 Comorbidity

The classification of APD as a separate disorder is controversial as this disorder often co-exists/co-occur with other conditions. Children with APD often show associated difficulties in language learning, reading, writing, memory and attention (ASHA, 2005; Allen and Allan, 2014). Children with language-learning related difficulties often demonstrate auditory processing difficulties, behaviorally (Corriveau, Pasquini, & Goswami, 2007; Fraser, Goswami, & Conti-Ramsden, 2010) and neurally (Banai, Nicol, Zecker, & Kraus, 2005). These groups of children are known to have difficulties in processing acoustic stimuli both at the level of the brainstem (Banai et al., 2005; Billiet & Bellis, 2011) and at the level of auditory cortex (Sharma et al., 2006). Researchers have also reported difficulty in processing speech (Russo, Nicol, Zecker, Hayes, & Kraus, 2005) and non-speech stimuli (Mody, Studdert-Kennedy, & Brady, 1997). Some authors have questioned these findings (Bishop, Carlyon, Deeks, & Bishop, 1999) and argue that not all children demonstrate auditory deficits, only some portion of these children carry auditory deficits. Since the presence of heterogeneity of APD, it becomes difficult to differentially diagnose the child as APD. Objective measures showing poor auditory neural integrity may help clarify.

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Chapter 2

2 Auditory brainstem responses in children with auditory processing disorder

2.1 Introduction

School-aged children are often referred to audiology for assessment because of concern about their hearing in difficult listening situations. These children, when found to have normal hearing threshold levels, may be suspected of having an auditory processing disorder (APD). The diagnosis of APD is challenging because there is no one diagnostic procedure that is agreed upon by hearing healthcare professionals, potentially leading to inconsistent identification (Hind, 2006). Professional guidelines (ASHA, 2005; AAA, 2010) typically recommend behavioral test batteries consisting of speech and non-speech tests designed to examine auditory skills. An assessment battery can include tests of auditory discrimination, temporal processing, auditory pattern recognition, binaural interaction and the perception of monaural low-redundancy and dichotic speech (ASHA, 2005). A diagnosis of APD is made based upon overall performance on the test battery. Although the manner in which test results are combined may vary, typically performance deficits in at least two or more tests in the battery falling at least two standard deviations below age expectations are used to support an APD diagnosis (Chermak & Musiek, 1997). If only one test is administered the child would be identified as APD only if performance was at least three standard deviations below expectations (ASHA, 2005). The use of behavioral measures in diagnosing children with APD is controversial. Speech tests (word or sentence repetition) have linguistic information, making it difficult to distinguish between listening and language skills (Hall, 2007). Test results may also be affected by attention (Sharma, Purdy, & Kelly, 2009).

The use of neurophysiologic techniques may provide some assistance in avoiding language and attentional issues (Dawes & Bishop, 2009). Professional guidelines often recommend the inclusion of objective/physiological measures to assess the integrity of

the auditory nervous system for APD. However, very few clinicians include objective measures in their test battery. A survey of audiologists on protocols used to assess APD revealed that less than 15 percent of clinicians indicated using electrophysiology tools such as the auditory brainstem response (ABR), middle latency response or cortical evoked potentials as part of their standard central auditory battery (Emanuel et al., 2011). AAA (2010) described the value of click-evoked ABR as limited and some authors have criticized the inclusion of ABR in a routine diagnostic battery due to lack of evidence (Katz et al., 2002). This is unfortunate because the ABR has the potential to provide useful information regarding the integrity of the ascending auditory pathway.

The ABR is widely used for objective hearing threshold and neuro-diagnostic assessment (Stapells & Oates, 1997; Starr & Achor, 1975). It is a robust response characterized by low intra-subject variability in both amplitude and latency (Lauter & Loomis, 1986). The time at which peaks are generated provides information regarding travel time in the brainstem. A delay in absolute or interwave intervals may suggest impairment as may the ability of the system to maintain integrity at increasing stimulation rates. The ABR has been used as an objective tool to study auditory neural integrity in children suspected of an auditory processing disorder (Allen & Allan, 2014; Gopal & Kowalski, 1999; Jirsa, 2001) although the number of reported studies is limited and patient populations are often small. For example, Gopal and Kowalski (1999) recorded ABRs in 9 children with APD and 9 typically developing children. They used slope vector analysis which calculates the amplitude difference between a positive peak and the following negative peak divided by the travel time. The slope decreases when the amplitude of the peaks is low or the travel time is lengthened. Children with APD demonstrated lower slopes compared to age-matched controls. The effect of stimulus repetition rate was studied by Jirsa (2001) who recorded Maximum Length Sequence ABRs in 37 children diagnosed with APD and age-matched controls. They found wave V latency was significantly delayed in the children with APD when the stimuli were presented at a very high rate (909.1/sec). Allen and Allan (2014) recorded ABRs for slow (21.7 -27.7/sec) and faster rates (57.7/sec) in 62 children with suspected APD and 8 normal hearing adults. Approximately 25% of the children showed delayed wave V latencies at the slower stimulation rate with many showing large rate dependent delays.

Maturation must be considered when using the ABR as a neuro-diagnostic tool for infants and very young children but responses are mature by school age, when most APD testing is recommended. The ABR can be recorded as early as 27 weeks conceptual age (CA) but responses are characterized by prolonged absolute and interpeak latencies and poor amplitude when compared to older children and adults (Hecox & Galambos, 1974). Peak I matures rapidly and is expected to be seen at adult latencies by 2-3 months of age, while peaks III and V do not mature until 1-2 years of age (Gorga, Kaminski, Beauchaine, Jesteadt, & Neely, 1989; Hall, 2006; Salamy, 1984). Peaks II and IV, seldom evaluated in clinical settings, are found to follow behind the maturation of peaks I and V, respectively (Salamy, 1984). Longer maturation times for the later occurring waves than for the earlier ones results in maturational delays in the inter-peak intervals of very young children, reflecting increased transmission time through the brainstem. Changes in ABR wave amplitudes can also act as an index of maturation of the auditory brainstem. V/I amplitude ratios are greater than 1.0 in normal hearing adults (Starr & Achor, 1975) but are typically less than 1 until 3-4 years of age, after which there is an increase in peak V amplitude resulting in an increased V/I ratio (Jiang et al., 1993; Mochizuki et al., 1982). Maturational changes in the ABR likely arise from increased axonal myelination and synaptic maturation (Eggermont & Salamy, 1988; Ponton et al., 1996). Understanding how axonal and synaptic factors are impacted by maturation and pathologic processes could prove useful when assessing auditory neural integrity in clinically referred children.

Ponton et al. (1996) developed a model of ABR generation and maturation based on age-related changes in axonal conduction and synaptic transmission. The model was derived from extensive review of the literature, anatomical and electrophysiological data from infants and adults, intra-surgical recordings, and direct recording of the human cochlear nuclear complex (CNC) through a brainstem implant device. The model argues that peaks I and II are generated from the auditory nerve. The I-II interval is largely determined by axonal conduction and is adult-like even for premature infants, 29-34 weeks CA. Peak III is assumed to be generated by axons emerging from the CNC in the ventral acoustic stria and the II-III interval is therefore dominated by synaptic contributions. It does not become adult-like until 18 months post term. Peaks IV and V are generated from the rostral brainstem location (medial olivary nucleus). The III-IV interval is axonal and

attains adult levels by 40 weeks CA. In contrast, the IV-V interval, reflecting synaptic responses in the medial olivary nucleus, does not become adult-like until 11-12 months post term. The non-linear best-fit functions to the synaptically dominated II-III and IV-V intervals are parallel and slower than the axonally dominated I-II and III-IV intervals. This closely matches the findings of Mochizuki et al. (1982) showing little change in I-II and III-IV (axonal) intervals from infancy to adulthood but significant changes in the maturation of II-III and IV-V (synaptic) intervals.

In this study, ABRs recorded from normal hearing adults and children referred for APD assessment elicited both at slow (13.3 clicks/sec) and faster stimulation rates (57.7 clicks/sec) were analysed using traditional clinical measures (absolute and interwave intervals for waves I, III and V, and the effect of stimulus presentation rate on wave V latency) and using Ponton et al.'s model to separate axonal (I-II and III-IV) and synaptic (II-III and IV-V) factors. The goal was to determine if the more detailed analysis could provide useful clinical insights not visible with traditional, clinical inspection. Because the ABR is mature within the first few years of life, the data from our clinical population who were aged 5 to 15 years were compared directly to data from normal-hearing adults.

2.2 Methods

2.2.1 Participants

Participants included 20 normal hearing adults (20 to 35 years of age, mean age: 23.71 years, standard deviation [SD]: 3.90 years) and 108 children (5.25-15.7 years of age, mean age: 9.63 years, SD: 2.70 years) with sAPD. The children had been referred to our clinic because of concerns about their hearing as a contributor to poor academic performance. As part of their clinical assessment all children underwent pure tone audiometry to ensure that they had normal (< 20 dB HL) air-conduction thresholds at octave frequencies from 250 to 8000 Hz and tympanometry to verify normal middle ear function. Distortion product otoacoustic emissions (DPOAEs) were recorded to ensure normal functioning of outer hair cells. Adult participants received a similar evaluation of hearing threshold levels and had no reports of listening difficulties. The Health Sciences Research Ethics Board of Western University, Canada approved the study methods.

2.2.2 Auditory Brainstem Responses

For all participants, ABRs had been acquired as part of their standard APD evaluation using a Bio-logic Navigator Pro AEP system (Natus Medica, Inc). A 100 µs rarefaction click was presented at 13.3 (slow) and 57.7 (fast) clicks/sec. Stimuli were presented monaurally via insert earphones (ER-3A, Etymotic Research, Inc) to the right and left ears at 80 dBnHL. Recordings were made with four surface electrodes placed at Cz and Fz (ground) positions and referenced to the right and left earlobes. Electrode impedance was below 5kΩ. The responses were averaged over a 10 msec window, amplified (100k) and filtered (100-1500Hz). Artifact rejection was set at 23.8 µV. Click responses to 2000 repetitions were averaged for each response with a minimum of two replications. Lights in the testing room were turned off during recording to minimize electric interferences.

2.2.3 ABR analysis

Waves I to V were identified by an experienced audiologist and verified by a second experienced audiologist. Wave V was always marked on the prominent 'shoulder' following the peak (expected time between 5 to 6 msec). Interwave intervals and the effect of stimulation rate on wave V were calculated. The ABR data were compared to published data (Schwartz, Pratt, & Schwartz, 1989) and evaluated according to the model proposed by Ponton et al. (1996). For the Ponton model, the ABR data were analyzed using interwave intervals that represents axonal conduction times (I-II and III-IV) and synaptic transmission times (II-III and IV-V). A repeated measure of ANOVA was used to evaluate group differences and effect sizes are reported as partial Eta-Squared (η^2_p). Whenever the assumption of sphericity was violated the Greenhouse-Geisser correction was used. The analysis was conducted in SPSS (SPSS INC., Chicago, IL, USA).

2.3 Results

2.3.1 Clinical measures

Absolute latencies. Figure 2.1 shows the individual absolute wave I, III and V latencies for children and adults plotted as a function of age to facilitate visualization of individual data. Responses from the children are shown by the unfilled circles and triangles for right and left ears, respectively. Adult responses are shown by the filled circles and triangles for right and left ears, respectively. Lower, middle and upper panels display latencies for waves I, III and V, respectively. Solid horizontal black lines represent expected means from published data (Schwartz et al., 1989). Dashed and filled grey lines represent ±1 and ±2 standard deviations, respectively.

As can be seen in the Figure 2.1, there was no apparent age effect in the children's data but there was a trend for the children's latencies to be longer than those of the adults, [$F(1, 126) = 15.75$, $p < 0.001$, $\eta^2_p = 0.111$]. This was especially obvious for the later waves, seen in a significant latency by group interaction [$F(1.75, 220.77) = 5.03$, $p = 0.010$, $\eta^2_p = 0.038$]. Post hoc t-tests revealed a significant group difference for wave I [$t(254) = 2.44$, $p = 0.015$], III [$t(254) = 4.16$, $p < 0.001$], and V [$t(254) = 5.26$, $p < 0.001$] with longer latencies measured in the children compared to adults. There were no significant differences between ears [$F(1, 126) = .819$, $p = 0.367$, $\eta^2_p = 0.006$]. Individual latencies for adults fell within 2 SD of published data (Schwartz et al., 1989) but the mean latencies for the children were higher and several children showed wave latencies more than 2 SD beyond expectations for wave I, III and V. At slower stimulation rates, 51 of the 108 (47.22%) children had clinically abnormal absolute latencies (either in one or more of waves I, III and V). Of these children, 33 (30.55%) children were unilateral and 18 (16.66%) were bilateral. Only 1 adult showed absolute latency (wave III) more than 2 SD later than expected mean.

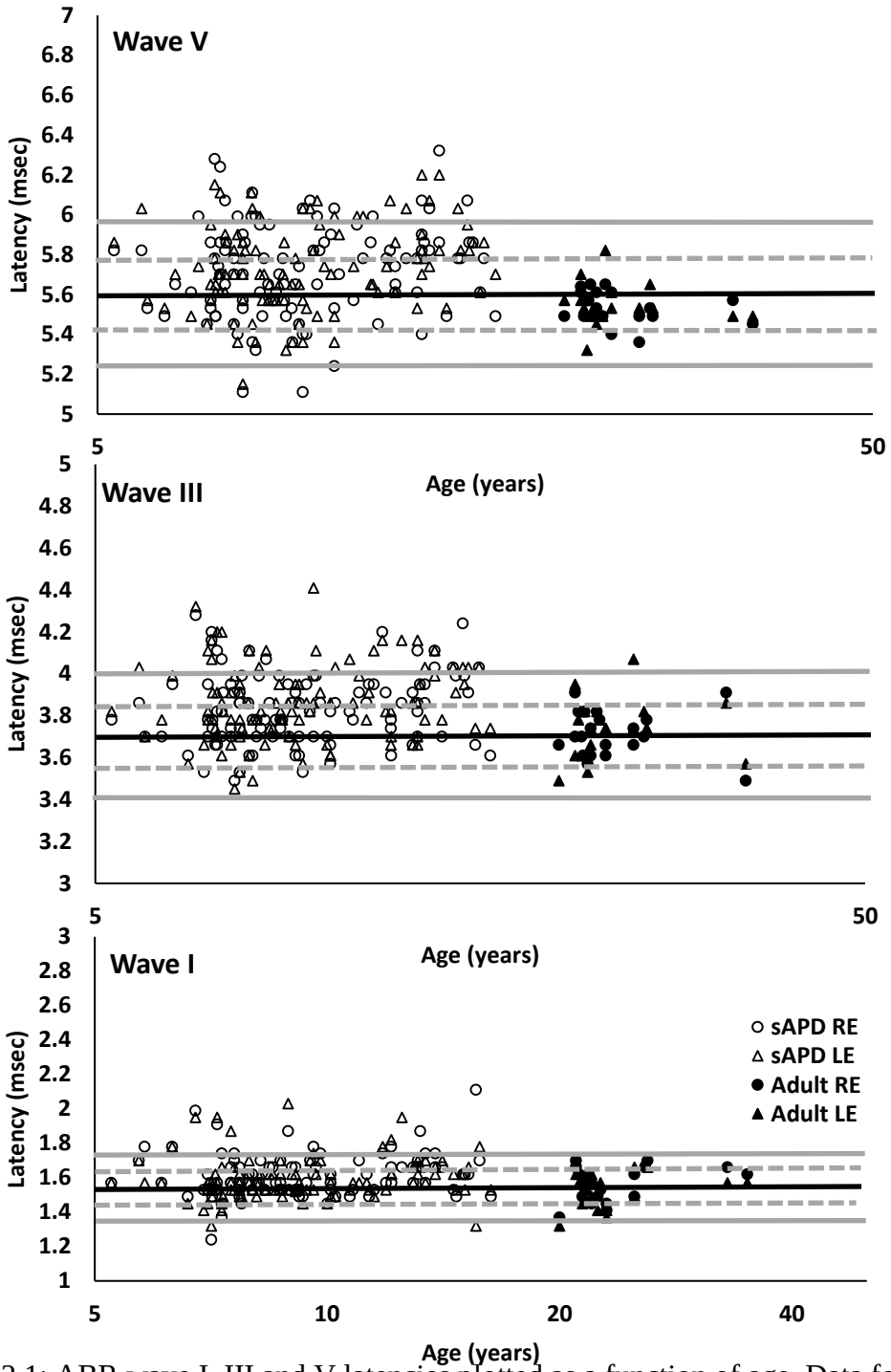

Figure 2.1: ABR wave I, III and V latencies plotted as a function of age. Data for sAPD children are shown as unfilled circles and unfilled triangles for right and left ears, respectively. Adult responses are shown as filled circles and filled triangles for right and left ears, respectively. Filled horizontal black line, unfilled and filled grey lines represents mean, ±1 and ±2 SD, respectively.

Interwave intervals. Figure 2.2 shows I-III and III-V interwave intervals in lower and upper panels, respectively, plotted as a function of age. Symbols are the same as in Figure 2.1 for individual children and adults. Horizontal lines represent expected means ±1 and ±2 standard deviations from published data (Schwartz et al., 1989).

Interwave intervals (both I-III and III-V) were significantly prolonged in children when compared to adults [$F(1, 126) = 7.16$, $p = 0.008$, $\eta^2_p = 0.054$]. Interwave intervals showed no significant difference between ears [$F(1, 126) = 2.63$, $p = 0.107$, $\eta^2_p = 0.020$] and the interwave interval by group interaction was not significant [$F(1, 126) = .006$, $p = 0.938$, $\eta^2_p = 0.000$]. Latencies from individual adults and children largely fell within 2 SD of published data but several children showed interwave latencies more than 2 SD beyond expectations. Twenty children (18.51%) demonstrated unilateral abnormal interwave intervals (either I-III or III-V). None were prolonged bilaterally. The incidence of abnormalities was similar in the lower [I-III, n = 11 (10.18%)] and upper brainstem [III-V, n = 9 (8.33 %)].

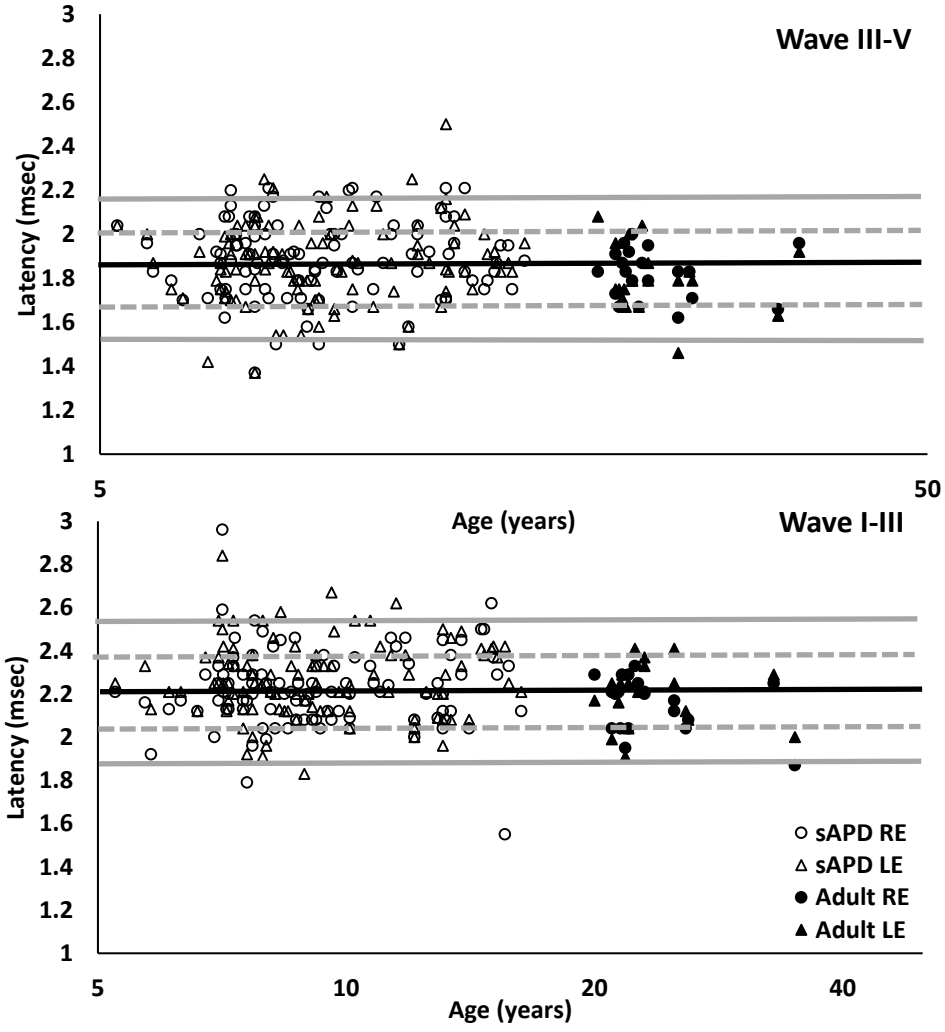

Figure 2.2: ABR interwave intervals I-III and III-V plotted as a function of age. Data for sAPD children are shown as unfilled circles and unfilled triangles for right and left ears, respectively. Adult response are shown as filled circles and filled triangles for right and left ears, respectively. Filled horizontal black line, unfilled and filled grey lines represent mean, ±1 and ±2 SD, respectively.

Stimulus rate effects. In Figure 2.3, wave V latencies for faster rates of stimulation are plotted as a function of slow rate latencies for children (left panel) and adults (right panel). Data for the right and left ear are shown by circles and triangles, respectively.

The solid diagonal line shows no change and the dotted line shows an expected latency shift of 0.36 msec (Jiang et al., 2009). The wave V shift was not significantly different between groups [F (1, 126) = 1.60, p = 0.207, $\eta^2_p = 0.013$]. There were no significant difference between ears [F (1, 126) = 0.097, p = 0.756, $\eta^2_p = 0.001$]. Although there were no significant group effects several individual children showed large shifts in wave V latency. Thirty-two of the 108 (29.62%) children showed abnormal shifts in wave V latency ($\geq$ 0.4ms) when stimulation rate changed from slow to fast. Of these, 24 were unilateral and 8 were bilateral. Of the 32 children, 18 (16.66%) had shown clinically abnormal absolute latencies at the slow rate.

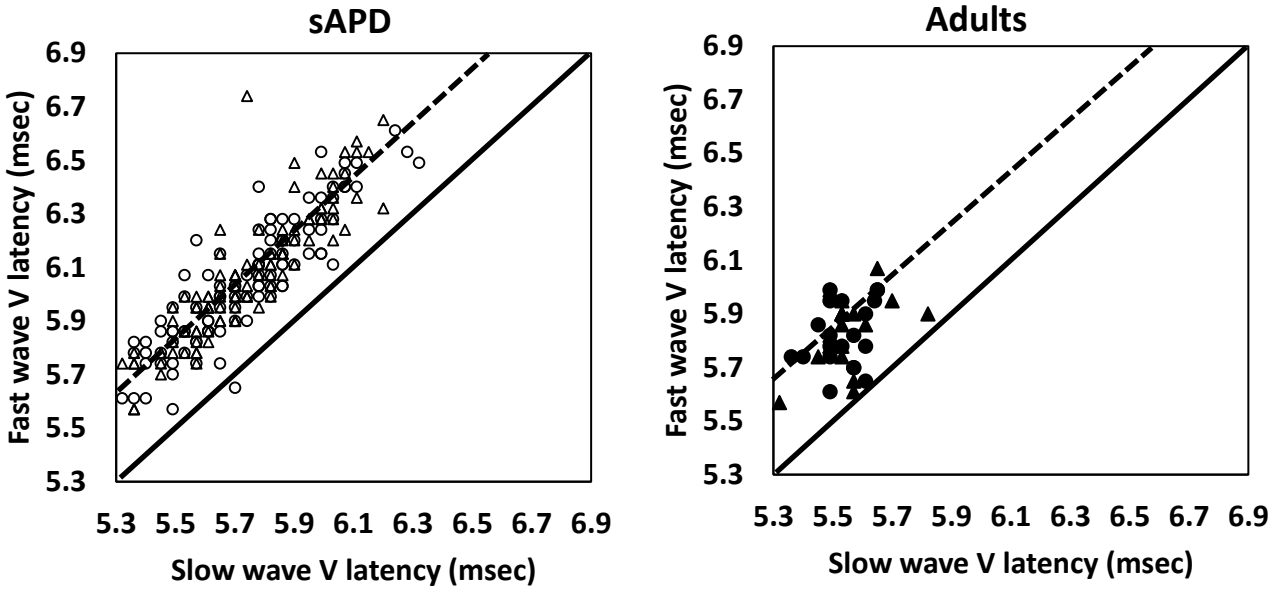

Figure 2.3: Individual wave V latency shift in the faster stimulation rate (57.7 clicks/sec) plotted as a function of slower stimulation rate (13.3 clicks/sec). Data for the right and left ears are shown by unfilled circles and triangles for children sAPD, respectively. Adult data for the right and left ear are shown by filled circles and triangles, respectively.

Summary. Both group and individual data suggest that many of the children in this clinically referred group showed objective indicators of reduced neural integrity that could contribute to their reported listening difficulties. However, these clinical measures do not provide any information about whether the observed delay in absolute or

interwave latency was due to the atypical functioning of axonal or synaptic factors. Evaluation of responses according to the model proposed by Ponton et al. (1996) was used to understand the axonal conduction and synaptic contribution to abnormalities in the children's data.

2.3.2 Evaluation of axonal conduction and synaptic transmission

Figure 2.4 shows I-II, II-III, III-IV and IV-V interwave intervals at slow (leftmost panel) and faster (rightmost panel) stimulation rates, plotted as a function of age. Symbols are the same as in Figure 2.1 for individual children and adults. Solid horizontal black, dashed and filled lines represent expected means, ±1 and ±2 standard deviations from adult data, respectively.

As the figure shows, there was no trend for age effects within the group of children but the children did show a tendency for longer interwave intervals in the intervals dominated by synaptic factors (II-III and IV-V) than those dominated by axonal transmission (I-II and III-IV) when compared to the adult data. A repeated measure of ANOVA was applied to the responses with the ear (right and left), interwave interval (I-II, II-III, III-IV, and IV-V) and stimulation rate (slow and fast) as within-subject factors and group (children and adults) as a between-subject factor. There were statistically significant differences between groups [$F(1, 52) = 25.39$, $p < 0.001$, $\eta^2_p = 0.328$] and a significant interaction between interwave interval and group [$F(3, 156) = 6.08$, $p = 0.001$, $\eta^2_p = 0.105$]. Post hoc t-tests revealed no significant group difference in intervals measuring axonal conduction time (I-II [$p = 0.986$] and III-IV [$p = 0.664$]), but intervals representing synaptic transmission were significantly longer in the children (interwave II-III [$p < 0.001$] and IV-V [$p < 0.001$]). There were no differences between ears [$F(1, 52) = 2.89$, $p = 0.095$, $\eta^2_p = 0.053$].

There were significant differences in interwave intervals at slow and faster stimulation rates [$F(1, 52) = 189.87$, $p < 0.001$, $\eta^2_p = 0.785$] but the rate by group interaction was not significant [$F(1, 52) = 1.45$, $p = 0.233$, $\eta^2_p = 0.027$]. The interaction between rate and interwave interval showed a significant rate dependent prolongation [$F(1.95, 156) = 19.54$, $p < 0.001$, $\eta^2_p = 0.273$]. Post-hoc analysis showed that stimulation rate significantly

prolonged interwave intervals that measures synaptic transmission time (interwave interval II-III [$p < 0.001$] and IV-V [$p < 0.001$]) but stimulation rate had no effect on intervals measuring axonal conduction time (I-II [$p = 0.621$] and III-IV [$p = 0.429$]). The three-way interaction (interpeak interval by rate by groups) was not significant [$F(3,156) = 1.05$, $p = 0.372$, $\eta^2_p = 0.020$].

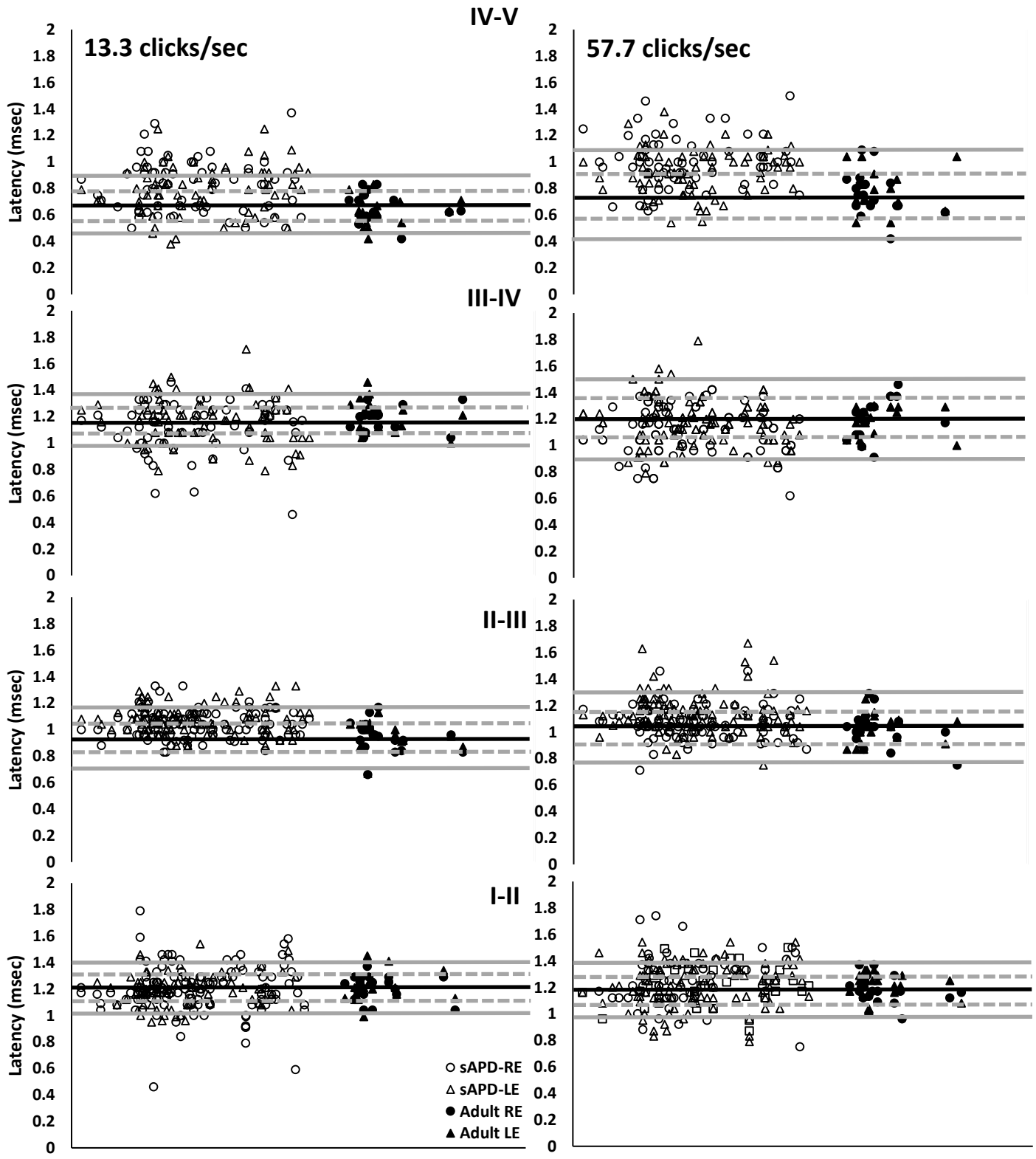

Figure 2.4: ABR interwave latencies I-II, II-III, III-IV and IV-V plotted as a function of age for slow and fast rates in left and right panel, respectively. Data for sAPD children are shown as unfilled circles and unfilled triangles for right and left ears, respectively. Adult responses are shown as filled circles and filled triangles for right and left ears, respectively. Filled horizontal black line, unfilled and filled grey lines represent mean, ±1 and ±2 SD, respectively.

Although the group trends suggested a preponderance of delays in the synaptically dominated intervals of the children, it can be seen that many individual children showed delays in axonal intervals. To better examine individual trends for the occurrence and co-occurrence of synaptic and/or axonal delays and whether effects were unilateral or bilateral, Venn diagrams were constructed. Figure 2.5 shows the number of children showing axonal and synaptic transmission delays that exceeded 2 standard deviations relative to the adult data. The upper and lower figures show the incidences of delays that were observed at the slow and fast stimulation rates, respectively. Delays that were unilateral are shown in the leftmost figures, and bilateral delays are on the right.

At the slow stimulation rate, shown in the 2 upper diagrams, 69 of the 108 children (63.88%) showed delays, the majority, 53 (49.07%), were unilateral and 16 (14.81%) were bilateral. As was indicated in the group level analysis, significant delays in synaptically dominated intervals (II-III and IV-V shown by solid circles) were nearly 4 times more likely than delays in axonally dominated intervals (I-II and III-IV shown by the patterned circles). Unilateral delays in axonal transmission, when they did occur, were more likely to occur in the I-II interval. The presence of delays in both synaptic and axonal intervals, as shown by the numbers in the intersection of solid and patterned circles was consistently low.

At faster stimulation rates, the incidence and pattern of delays were very similar to that observed at the slower rate. Sixty-one of the 108 children (56.48%) showed delays that were much more often unilateral (n = 50, 46.29%) than bilateral (n = 11, 10.18%). The incidence of axonal delays increased, especially in the lower level I-II response from the auditory nerve. Although both groups had shown increased delays in the synaptic intervals, the children were more likely to show large rate dependent axonal delays. The incidence of abnormalities in both axonal and synaptic transmission was rare.

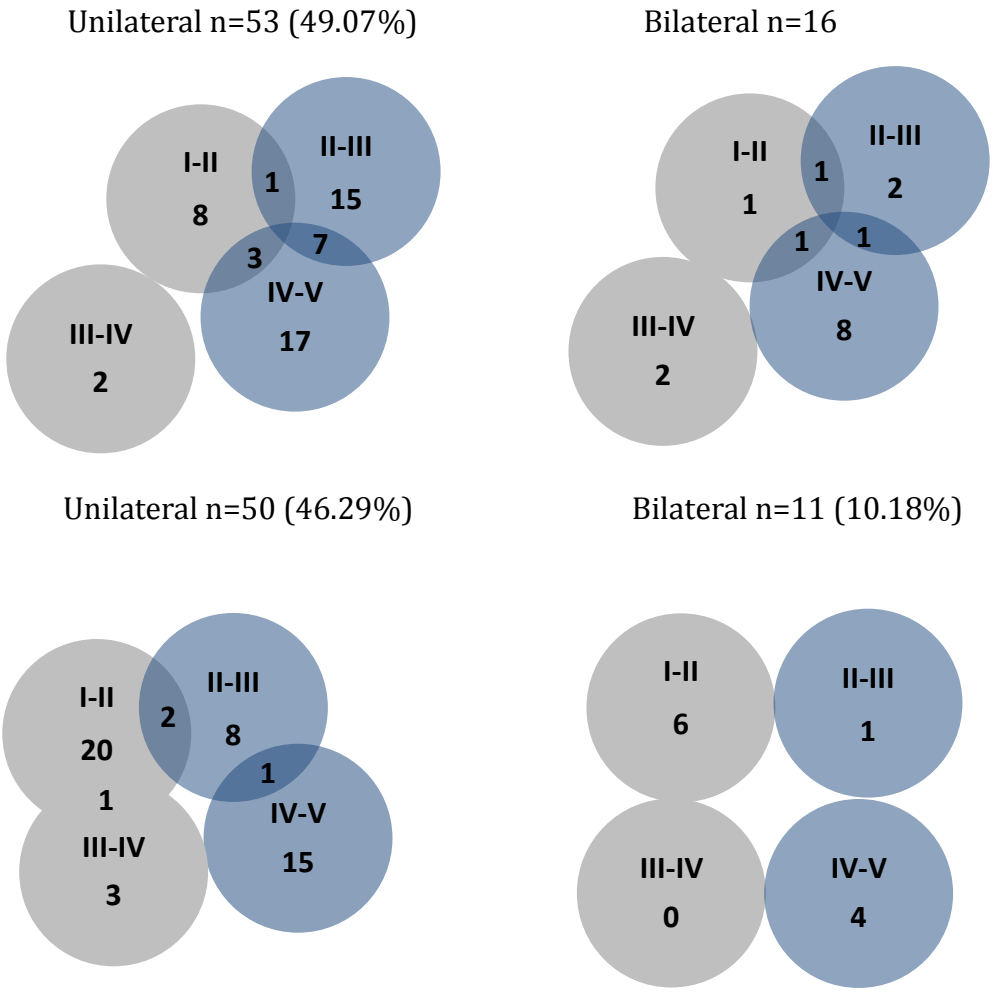

Figure 2.5: Venn diagrams illustrating number of children with clinically abnormal interwave latencies at slower (top panel) and faster stimulation rates (bottom panel) in unilateral and bilateral. I-II and III-IV interwave interval represents the axonal conduction times and II-III and IV-V represents the synaptic transmission times.

2.4 Discussion

Professional guidelines (ASHA, 2005) argue that a disorder in auditory processing should be attributable to a deficit in the neural processing of auditory stimuli and not to deficits in cognitive or language-related functions. Although the ABR provides a potentially useful tool for exploring the integrity of the auditory brainstem pathways, it is not widely used for APD assessment (Emanuel et al., 2011) largely because of a lack of supporting evidence (AAA, 2010; Katz et al., 2002). This study was aimed at exploring ABRs recorded in children reporting listening difficulties using standard clinical measures (absolute latencies, interwave intervals and effect of stimulus rate on wave V latency) and a more detailed analysis that attempts to separate, as much as possible, axonal and synaptic factors contributing to brainstem transmission (Ponton et al., 1996).

Many of the children whose data were included in this retrospective analysis of ABRs showed clinically abnormal neural functioning in the auditory brainstem when compared to normal hearing adults. Analysis of waves I, III and V showed that these abnormalities occurred as prolonged absolute latencies and interwave intervals, most often occurring with similar frequency in the lower and upper brainstem pathways. Most abnormalities were unilateral and equally likely in right or left ears. Similar findings have been reported in the literature (Allen and Allan, 2014; Gopal and Kowalski, 1999; Jirsa, 2001). Contributions from axonal versus synaptic factors are difficult to tease apart using these clinical measures, such as the I-III and III-V intervals, which are each vulnerable to both factors.

The ABR relies on faithful transmission of rapidly occurring acoustic stimuli across and between axons and synapses. The auditory synapses are especially specialized for reliable synaptic transmission at faster stimulation rates (Fuchs, 2005), and axonal myelination ensures rapid travel between synapses. ABRs recorded from infants and children have shown prolonged latencies at slower stimulation rates and greater shifts in latency at faster stimulation rates when compared to adults that can be attributable to incomplete myelination and reduced synaptic efficiency (Jiang, Brosi, & Wilkinson, 1998; Lasky,

1997), both of which show strong maturational changes during the first few years of life (Kral & Sharma, 2012; Moore & Linthicum, 2007).

Comparison of successive interwave intervals from all 5 major ABR peaks with similar measures from adults identified more children with abnormal interwave intervals in a slow rate ABR (n = 69, 63.88%). The model proposed by Ponton et al. (1996) helped in differentiating children with the atypical synaptic transmission (n = 50, 46.29%) from those with atypical axonal conduction (n = 13, 12.03%). Very few (n = 6, 5.55%) showed both. Axonal conduction, dominating the I-II and III-IV intervals were adult-like. The II-III and IV-V intervals, which were prolonged for many of the clinically referred children in this study, represent synaptic transmission within the CNC and the contralateral MSO, respectively. Synaptic function in the auditory nerve itself is not assessed unless the absolute latency of wave I is examined. As can be seen in the lower most panel of Figure 2.1, wave I latency was prolonged in the data from many individual children. Given that all children had normal middle ear function this delay in wave I can only be attributable to deficiencies in the very first auditory synapse in some children.

At a faster stimulation rate, clinical analysis of rate-dependent changes in wave V showed delays of a predictable magnitude in nearly all listeners (Jirsa, 2001). It has been suggested that a faster stimulation rate may have a greater effect on synaptic transmission than on axonal conduction (Pratt, Ben-David, Peled, Podoshin, & Scharf, 1981). Detailed analysis showed that the II-III and IV-V intervals for both adults and children were increased when the stimulus rate increased, consistent with synaptic influences. However, in the group of clinically referred children, there was a high incidence of unexpected delays in the auditory nerve transduction as shown in the I-II interval.

This ABR study showed that a significant portion of children referred for clinical evaluation of listening difficulties show atypical synaptic transmission times, and a smaller number show atypical axonal conduction. The causes of these delays are unclear but animal models may provide some insight into potential factors. Mouse models of mutant genes that affect axonal conduction (e.g. Kv3.3, Kv1.1 proteins) or synaptic transmission (e.g. α2δ3, Cav1.3, complexin proteins) have provided evidence of impaired

auditory processing. The voltage-gated potassium channels (Kv channels) are important for the generation and propagation of electrical impulses within the axons. Any variation in the functioning of these channels can lead to abnormal transmission of neural impulses. The Kv3.3 ion channel protein is important for auditory coding. This protein modulates the high-voltage potassium channels which is the vital component for the repolarization of action potentials in the auditory nervous system (Johnston, Forsythe, & Kopp-Scheinpflug, 2010). This protein is encoded by a gene KCNC3 (Middlebrooks et al., 2013). A mutation of KCNC3 could lead to a complete lack of potassium channel activity. This protein is expressed more in the auditory brainstem especially in the medial nucleus of the trapezoid body (MNTB), which is crucial for sound localization (Middlebrooks et al. 2013). Middlebrooks et al. (2013) reported elevated thresholds for the detection of interaural differences in level and time in normal hearing humans with $KCNC3^{R420H}$ mutation. This indicates deficits in binaural comparison. These symptoms are frequently observed/reported in APD children.

Another protein that is essential for axonal conduction is the Kv1.1 subunit. This protein is encoded by the KCNA1 gene and strongly expressed in the VCN and MNTB of the auditory pathway. Researchers (Kopp-Scheinpflug, Fuchs, Lippe, Tempel, & Rübsamen, 2003) believe that the Kv1.1 subunit is vital for temporally precise action potentials along axons. Kopp-Scheinpflug et al. (2003) studied the contribution of Kv1.1 in neural coding of auditory stimuli. Single cell recordings in KCNA1 mutant mouse model showed abnormal evoked response in VCN and MNTB neurons. The variability of first spike latency was high in both VCN and MNTB neurons, suggesting poor temporal precision. The auxiliary subunits α2δ3 protein modulates biophysical properties of voltage-gated calcium channels and is encoded by the CACNA2D3 gene. This α2δ3 protein is required for normal auditory processing. The α2δ3 is not expressed in the cochlea, but it is expressed in the spiral ganglia and brainstem neurons (Pirone et al., 2014). Genetic deletion of α2δ3 protein in mice leads to reduced levels of Ca2+ channels and smaller auditory nerve fibers terminals contacting CNC. Changes in the cellular structure were reflected in the ABRs, characterized by reduced amplitude (waves II to IV) and delayed latencies (Pirone et al., 2014). The Cav1.3 protein is encoded by the CACNA1D gene, and it plays an important role in the release of neurotransmitter in presynaptic terminals.

This gene is known to cause hearing loss (Platzer et al., 2000). Mutation of CACNA1D gene in a mouse lead to the absence of calcium channels from the SOC but the expression of this was preserved within the cochlea. The ABR recorded in these mice showed no differences in latencies but wave II and III were merged and the amplitude of wave I was reduced compared to control mouse models (Satheesh et al., 2012). This suggests that any alteration in Cav1.3 protein can lead to changes in the acoustic signal processing in the auditory brainstem. The complexin (CPX I-IV) proteins are known to play an important role in synaptic transmission in different levels of the auditory pathway. In the auditory system, cochlear hair cells do not express CPX-I, but it is expressed in spiral ganglions (Strenzke et al., 2009). Mutation of CPX-I in mouse showed a small increase in threshold (~15 dB) in the mid frequency region at 3 - 4 weeks of age. The hearing impairment was large (~30 dB) at 6 - 10 weeks of age. The ABRs were characterized by reduced amplitude and delayed latencies in both young and older mice. The reduced resting release probability in the endbulb of Held synapses of the auditory nerve fibers, which provides the primary input from the auditory nerve to VCN bushy cells was reduced. This resulted in decreased spike rates, longer and variable first spike latencies explaining abnormal ABRs. The reduced temporal precision may lead to loss of synchrony along the auditory pathway. This indicates that absence/variation of CPX-I may result in changes in sound encoding within the CNC. These findings in mouse models provide preliminary evidence of cellular mechanisms underlying abnormal auditory processing that could theoretically contribute to abnormal ABRs such as those observed in the children examined in this study.

2.5 Summary and Conclusion

The current study demonstrated that a significant portion of children suspected of APD showed significant abnormalities in ABRs that differentially impact axonal or synaptic transmission in the auditory brainstem. The auditory neurons in the brainstem are known to phase lock to stimuli (Joris, Schreiner, & Rees, 2004). A delay in synaptic transmission in the lower level of the auditory system (e.g. CNC) may have irreversible effects on the encoding of sound at higher levels in the auditory system producing temporal coding deficits, frequently reported in children with an APD. These findings suggest that the ABR is a valuable tool in the assessment and diagnosis of APD and highlights the importance of including objective/physiological measures in APD test battery.

2.6 Reference

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Chapter 3

3 Sensitivity to Envelope and Fine Structure Cues In Speech: Data from Adults, Typically Developing Children and Children with Suspected Auditory Processing Difficulties

3.1 Introduction

Recognizing speech in noise can be challenging for listeners of all ages, but it may be especially hard for children whose auditory skills and language proficiency are maturing rapidly. It is well-known that young typically developing children require a higher SNRs to recognize speech in noise compared to adults (Fallon et al., 2000; Hall et al., 2002; Nittrouer & Boothroyd, 1990). Noise can reduce the availability of relevant acoustic cues (temporal or spectral) for speech recognition, but specifically, what cues are used in different signal-to-noise conditions and whether young children use and shift emphasis on cues as SNR varies is not well understood. Cognitive factors including attention, memory, fatigue and language proficiency may also affect speech recognition in noise (Allen & Wightman, 1992; Oh, Wightman, & Lutfi, 2001). These abilities are still developing in children which may force greater reliance on acoustic cues (bottom-up processing) while listening to speech in noise. Yet acoustic feature processing may also be developing during this time placing a still greater burden on the child listening to unfamiliar and/or degraded sounds.

Listeners recognize speech by extracting both envelope (slowly varying amplitudes over time) and fine structure (rapid variations in amplitude over time) cues. The envelope cues are known to provide segmental information about the manner of articulation and voicing (Rosen, 1992). The fine structure provides information regarding voicing, manner, stress and intonation (Rosen, 1992) and it also plays a major role in stream segregation (Smith et al., 2002). Physiological data indicate that

envelope and fine structure cues are encoded through phase locking pattern in the auditory nervous system. The phase locking pattern to envelope cues is accurate for carrier frequencies up to 6 kHz (Joris, Schreiner, & Rees, 2004) whereas the fine structure remain constant up to 1-2 kHz (Johnson, 1980). These temporally dynamic cues are believed to play an important role in understanding speech in quiet and in presence of background noise (Apoux, et al., 2013; Smith et al., 2002).

Speech perception studies have been carried out to understand the contribution of the envelope and fine structure cues for speech recognition (Bertoncini, Nazzi, Cabrera, & Lorenzi, 2011; Cabrera, Lorenzi, & Bertoncini, 2015; Eisenberg et al., 2000). In these studies, signal processing algorithms have been used to extract one cue (e.g. envelope) by altering the other cue (e.g. fine structure). One of the widely used signal processing method to extract envelope and fine structure cues is by the Hilbert transform (Hilbert, 1912). The Hilbert transform derives the analytic (real and imaginary part) representation of the signal. The real part of the analytic signal contains the original data and the imaginary part contains the original data with a phase shift of $\pi/2$ radians. The Hilbert envelope of a signal is the magnitude of the amplitude contour of the signal and the fine structure is the cosine phase of the signal. Mathematically, the Hilbert envelope and the fine structure components are assumed to be independent of each other.

The Hilbert transform method is efficient if the signal is split into narrow analysis bands (e.g. 4, 8, 16 or 32 adjacent bands). Envelope cues are extracted from the (slow) time varying energy in each band. The extracted envelope is used to modulate a sinusoidal tone or a narrow band noise centered at the frequency of the band from which the envelope was extracted (Shannon, Zeng, Kamath, Wygonski, & Ekelid, 1995). By doing this, fine structure information is degraded/removed while envelope information is retained. The fine structure cues are extracted by similarly splitting the speech into adjacent analysis bands. The fast time-varying energy in each band is extracted by discarding the slow varying time energy. The resulting stimulus will contain an equal amplitude in each band. Listeners are forced to rely on fine structure information to recognize the speech.

Developmental studies indicate that typically developing children are able recognize speech based on envelope (Bertoncini et al., 2009; Eisenberg et al., 2000; Newman & Chatterjee, 2013; Nittrouer & Lowenstein, 2010) and fine structure cues alone in quiet (Bertoncini et al., 2009). These studies suggest that in quiet, typically developing children are able to use both envelope and fine structure cues to recognize speech. However, it is not clear how these cues are used to recognize speech in noise by typically developing children.

Normal hearing adults are able to obtain high levels of speech intelligibility in quiet using envelope cues alone (Drullman, 1995; Shannon et al., 1995; Smith et al., 2002; Zeng et al., 2004) but require training to achieve similar levels of performance on the basis of fine structure cues alone (Gilbert & Lorenzi, 2006; Lorenzi, Husson, Ardoint, & Debruille, 2006). However, in the presence of background noise, the perception of speech with envelope cues alone is greatly reduced (Apoux & Healy, 2011; Füllgrabe, Berthommier, & Lorenzi, 2006). This indicates that in presence of noise adults require fine structure cues to recognize speech (Hopkins, Moore, & Stone, 2008). But, some authors have raised concern regarding the signal processing strategy used to study the contribution of the envelope and fine structure cues in recognizing speech from the noise (Apoux et al., 2013).

Adding noise to speech will corrupt both envelope and fine structure cues but it is not clear to what extent these cues are distorted. Simply using speech and noise mixed at different SNR to study speech perception may not provide sufficient information regarding which cues (envelope or fine structure) are more important for speech recognition. Apoux et al. (2013) used the auditory chimera technique (Smith et al., 2002) to address this. In the chimeric approach, stimuli are synthesized by interchanging the envelope of a signal such as speech with the fine structure of another sound such as noise. Using this analogy Apoux et al, mixed speech and noise at various SNRs. Envelope and fine structure cues were extracted from each SNR combination. The extracted envelope and fine structure information were then re-mixed using different SNRs to create stimuli with the envelope of one sound mixture (e.g. +10 dB SNR) and the fine structure of the another (e.g. -10 dB SNR). The

resulting speech sample would have envelope cues at +10 dB SNR and fine structure of at -10dB SNR. Using this method, synthesized stimuli will have two original carriers, the relationship between the envelope and the fine structure is maintained. Results demonstrated that recognition accuracy was tightly tied to the SNR at which the envelope was extracted with minimal contribution of fine structure cues, suggesting that adults rely more on envelope than fine structure to understand speech in noise. No comparable data are available for children.

Auditory processing disorder (APD) is a perceptual deficit in the processing of auditory information in the presence of normal audibility (AAA, 2010) . Children with APD may demonstrate a deficiency in auditory discrimination, localization, temporal processing, or detecting sound in noise (ASHA, 2005). One of the most frequent listening complaints of these children is that they have difficulty understanding speech in the presence of background noise (Bamiou et al., 2001; Chermak et al., 1999; Lagacé et al., 2011; Vanniasegaram et al., 2004). Unfortunately, only a handful of studies have tested speech in noise directly. Such studies suggest that children with listening disorders and suspected of having APD require higher SNRs to achieve similar speech recognition scores than for age-matched controls (Lagacé et al., 2011; Vanniasegaram et al., 2004). However, the underlying cause for the poor recognition in noise by APD children has not been specifically identified. One possibility is that children with listening disorders may be less proficient at extracting important envelope cues.

The current study used the speech cue extraction techniques reported by Apoux et al. (2013) to explore the fine structure and envelope cue utilization in perceiving speech in noise by typically developing children and those reporting listening difficulties and therefore suspected of having an APD. The hypothesis was that the poorer speech recognition in noise seen in young children and those with suspected APD might involve atypical processing of envelope and fine structure cues.

3.2 Method

3.2.1 Participants

Participants in this study included 10 normal hearing adults (21-28 years, mean age: 24.6 years, SD: 2.45 years), 21 typically developing children (TD) (5-14 years, mean age: 8.70 years, SD: 2.93 years) children and 22 (5.7 – 14.1 years, mean age: 9.41 years, SD: 2.68 years) children with sAPD. Children with sAPD were referred to Western HA Leeper Speech and Hearing clinic because their parents or teachers expressed concerns over their hearing. TD children, children with sAPD and adults underwent basic pure tone audiometry to ensure that they had normal (≤ 20 dB HL) air-conduction thresholds at octave frequencies from 250 to 8000 Hz and tympanometry to verify normal middle ear function.

3.2.2 Signal processing

Hearing in Noise Test (HINT) sentences were used as stimuli (Nilsson, Soli, & Sullivan, 1994). 260 (10 practice sentences and 250 target stimuli) stimuli were used. The stimuli were created as shown in Figure 3.1. Clear HINT sentences were equated for root-mean-squared (RMS) amplitude. Speech shaped noise (SSN) was leveled to the RMS amplitude that is required to produce SNRs of -12, -6, 0, +6 and +12 dB. The masked sentences were passed through 30 variable finite impulse response (FIR) band pass filters (order n = 6635). The cutoff frequencies of these filters were chosen using those suggested by Greenwood (Greenwood, 1990), spanning a frequency range from 80 to 7563 Hz. The cut-off frequencies for the 30 bands were 80, 106, 136, 170, 208, 251, 300, 354, 416, 486, 564, 653, 753, 866, 993, 1136, 1298, 1480, 1686, 1918, 2180, 2475, 2808, 3184, 3607, 4085, 4624, 5232, 5917, 6690, and 7563 Hz. Stimuli were filtered in both the forward and reverse directions to avoid phase distortion resulting from the filtering. The Hilbert transform was used to extract the envelope (i.e., the magnitude of the Hilbert analytic signal) and the fine structure (i.e., the cosine phase of the Hilbert analytic signal) in each band, resulting in isolated envelope and fine structure properties in each bands. Chimeric stimuli were prepared by extracting the envelope of one version of the sound mixture

(e.g. 12 dB SNR) and the fine structure of the version of the same sound mixture at a different SNR (e.g. -12 dB SNR), thus the resulting stimuli would contain independently degraded envelope and the fine structure components of the original speech signal (envelope of 12 dB SNR and the fine structure of the -12 dB SNR). This mixing was carried out using a Chimerizing algorithm using MATLAB code developed by Smith and colleagues (Smith et al., 2002). The SNR of the sound mixture from which the envelope was extracted is referred to as SNR E and the SNR from which the fine structure was extracted is referred to as SNR FS. All signal processing was performed in MATLAB-14 (Mathworks, Natick, MA). The processed stimuli were stored as .WAV files on laptop (Lenovo ThinkPad CSL-14122). The reference condition (REF) corresponds to the baseline performance in which the SNR of the envelope and the SNR of the fine structures were the same. If at a given SNR the chimera containing the predominant envelope (e.g. +10 dB SNR E -10 dB SNR FS) produces the highest intelligible speech we would conclude that the envelope is the dominant cue. If in contrast the chimera containing predominant fine structure cue is more intelligible, we would conclude that fine structure (e.g. -10 dB SNR E +10 dB SNR FS) is the dominant cue. Figure 3.2 displays the waveform and spectrogram for a sample sentence processed to retain predominant envelope (center column) and fine structure (right column).

3.2.3 Procedure

In each condition, the SNR of the fine structure (e.g. +12 dB SNR FS) was held constant and SNR of the envelope was varied from -12 to 12 dB in 6 dB steps in descending and ascending method (Figure 3.3). This was repeated ten times, resulting in an average 50 sentences per condition. There were five conditions (-12, -6, 0 6 and 12 dB) resulting total of 250 sentences and these conditions were randomized (Table 3.1). Participants were given breaks as needed during data collection. For all conditions stimuli were presented via a laptop (Lenovo ThinkPad CSL-14122) connected to a Creative Sound Blaster Extigy external sound card through ER- 3A insert ear phones. Stimuli were presented at a level of 65 dBA, calibrated using HINT SSN. Calibration was completed in an artificial ear (Type 4152) using a Bruel and Kjaer amplifier (Type 2610). The same attenuator setting was used for all the conditions. Stimuli were presented binaurally. A

custom graphical user interface (GUI) was created using MATLAB to present the stimuli. The listener's task was to press a space bar or any key on the keyboard to begin a sentence. Listeners were asked to repeat all the words in each sentences. No sentences were repeated in any condition. In the HINT test, the listener's task is to repeat correctly all words in the sentence and the sentence is scored as either correct or incorrect. In this study, each correctly repeated key word was given a score of one. Number of words per sentence ranged from four to seven. Participants were tested individually in a sound attenuated booth. The total duration of the testing was approximately 45 minutes.

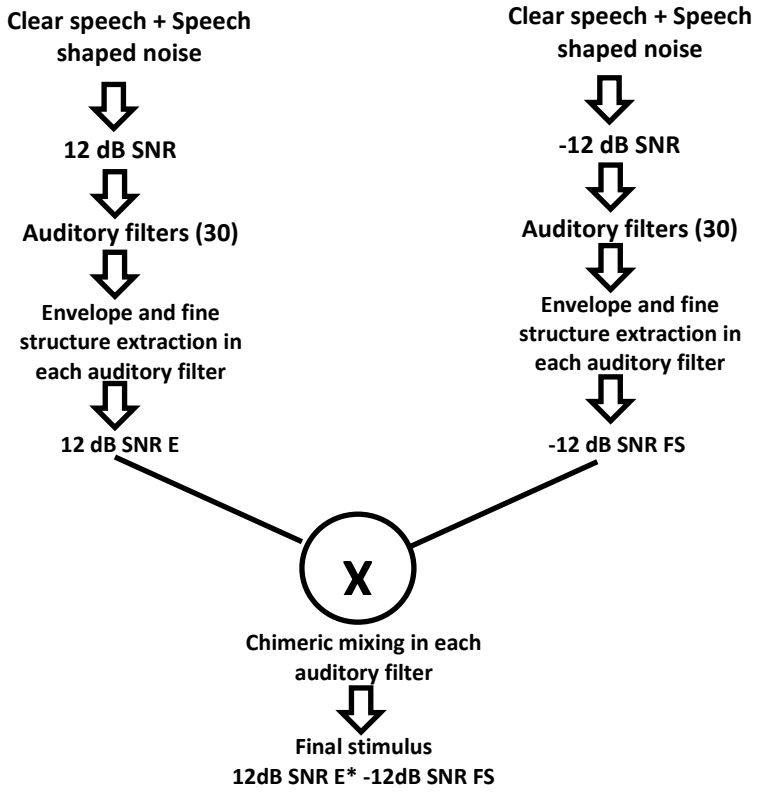

Figure 3.1: Simplified flow chart showing steps involved in creating stimuli. Abbreviations: dB, decibel; SNR, signal-to-noise ratio; E, envelope; FS, fine structure.

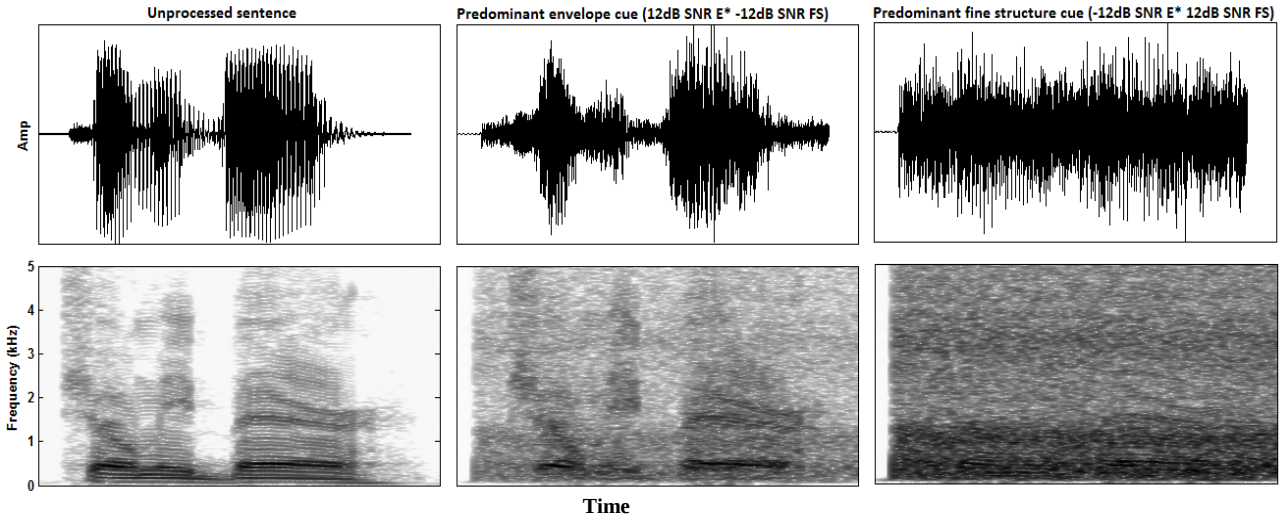

Figure 3.2: Stimulus processing examples. Each cell displays the amplitude waveform and spectrogram (0-5000Hz) for that condition. The original unprocessed sentence "Show me bear" is shown in the left column. Processed stimulus examples are shown in the center and right columns. Center column shows processed stimuli with dominant envelope (E) cues and reduced fine structure (FS). Right column shows processed stimuli with predominant fine structure cues and reduced envelope cues.

Table 3.1: Number of key words in different experimental conditions.

		SNR dB FS					
		-12	**-6**	**0**	**6**	**12**	
SNR dB E	**-12**	55	49	53	53	53	**263**
	-6	51	55	50	53	52	**261**
	0	53	55	54	51	57	**270**
	6	52	56	55	55	51	**269**
	12	51	50	52	51	55	**259**
	Total	**262**	**265**	**264**	**263**	**268**	**1322**

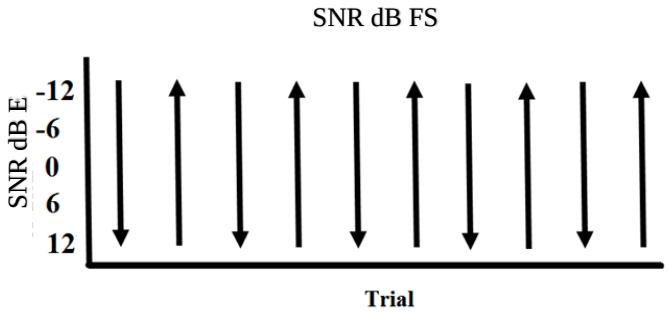

Figure 3.3: Schematic of stimulus presentation.

3.3 Results

3.3.1 Reference condition

Data for individual listeners at different SNRs in the reference condition are plotted in Figure 3.4 as a function of age. Open symbols indicate scores for TD children and adults, filled symbols indicate speech recognition scores for children with sAPD. All three groups showed improvement in speech recognition scores as the SNR was increased from -12 dB to + 12 dB.

A mixed ANOVA was performed on rationalized arcsine units (RAU; Studebaker, 1985). Whenever the assumption of sphericity was violated the Greenhouse-Geisser correction was used. Performance across SNRs in the reference condition varied between [$F(2, 50) = 8.91$, $p < 0.001$, $\eta^2_p = 0.263$] and within group [$F(3.38, 169.46) = 1145.03$, $p < 0.001$, $\eta^2_p = 0.958$]. There was a significant two-way interaction between SNRs in the reference condition and group [$F(6.77, 169.46) = 3.18$, $p = 0.004$, $\eta^2_p = 0.113$]. Post-hoc analysis, corrected for multiple comparison by using Bonferroni corrections, demonstrated that at -12 dB SNR condition, adults had better speech recognition scores compared to children with sAPD ($p = 0.008$). There were no significant differences in speech recognition scores between adults vs TD children ($p = 0.168$) and TD children vs children with sAPD ($p = 0.436$). At -6 dB SNR, children with sAPD had poorer speech recognition scores compared to adults ($p < 0.001$) and TD children ($p = 0.025$). There were no significant differences in speech recognition scores between the groups in other SNR conditions (0 dB, 6 dB and 12 dB SNR).

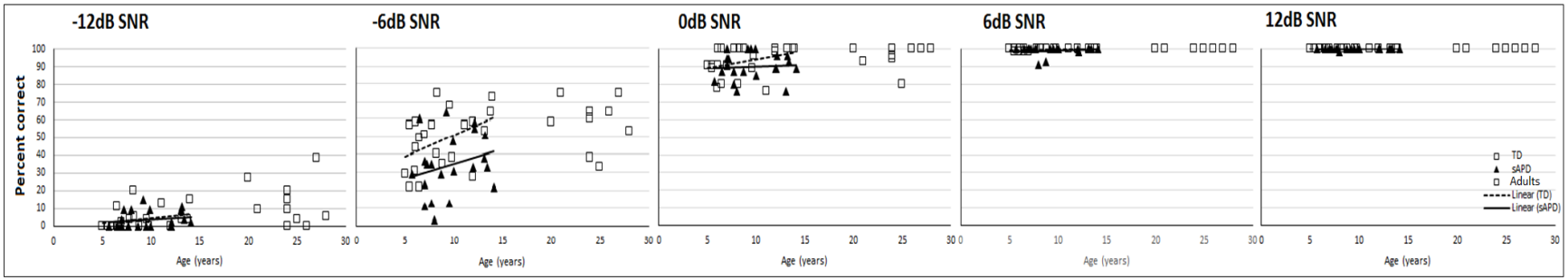

Figure 3.4: Individual speech recognition scores at different SNR. Open symbols indicate scores for TD children and adults. Filled symbols indicate scores for children with sAPD. Best-fit lines are shown separately for the two groups of children.

3.3.2 Varied envelope and fine structure condition

Speech recognition scores for individual listeners across different SNR envelope and SNR fine structure conditions are plotted as a function of age in Figure 3.5. Open symbols indicate scores for TD children and adults, filled symbols indicate scores for children with sAPD. The best-fit linear functions were plotted as a function of age for TD children (dashed) and children with sAPD (solid). The SNR of envelope varies by column; the first column represents the poorest SNR for envelope. Similarly, SNR of fine structure varies by row; the bottommost row represents the poorest SNR for fine structure. The diagonal graphs (indicated in grey) represent the reference condition in which the envelope and the fine structure SNRs were equal.

A mixed ANOVA was performed on RAUs with two within-subject factors (SNR E and SNR FS) and one between subject factors (group). Speech recognition scores varied by group [$F(2, 50) = 9.83$, $p < 0.001$, $\eta^2_p = 0.282$]. Speech recognition also varied by SNR E [$F(2.28, 114.46) = 1728.31$, $p < 0.001$, $\eta^2_p = 0.972$] and SNR FS [$F(4, 200) = 90.70$, $p < 0.001$, $\eta^2_p = 0.645$]. The two-way interaction between SNR E and SNR FS [$F(9.72, 486.09) = 18.59$, $p < 0.001$, $\eta^2_p = 0.271$] as well as the three-way interaction between SNR E, SNR FS and group was significant [$F(19.44, 486.09) = 1.64$, $p = 0.042$, $\eta^2_p = 0.062$] was significant. The significant three-way interaction suggests group differences in extracting speech from noise as the availability of temporal cues were varied.

Post-hoc analysis, corrected for multiple comparison by using Bonferroni corrections, is shown in Table 3.2. Significant group differences were evident between children with sAPD and adults in -12 dB FS condition (last row) and in -6 dB E condition (second column).

Within group post-hoc analysis was carried out to examine how one temporal cue (e.g. fine structure) was utilized for speech recognition when the availability of the other temporal cue (e.g. envelope cue) was minimal. This was examined in -12 dB SNR FS (bottommost row), -12 dB SNR E (first column) and -6 dB SNR E (second column).

A. Use of envelope cue for speech recognition:

When fine structure cues were minimal [at -12 dB SNR FS (last row)], speech recognition scores of all three groups at -6dB SNR E were significantly higher [TD children, $p < 0.001$; children with sAPD, $p < 0.001$; Adults, $p < 0.001$] compared to -12 dB SNR E. TD children showed no further improvement ($p = 1.00$) as the SNR of envelope was increased further. Adult performance was at ceiling 0 to 12 dB SNR E. Children with sAPD showed significant improvement in speech recognition scores between 6 dB SNR E to 12 dB SNR E ($p < 0.001$). These results indicate that when fine structure cues are minimal, children with sAPD, require stronger envelope cues compared to TD children and adults for better speech recognition. In other words, while the addition of envelope cues is helpful to adults and typically developing children when fine structure is poor, children with sAPD seem less able to use these cues to improve their performance.

B. Use of fine structure cues for speech recognition:

When envelope cues were minimal [at -12dB SNR E (first column)], speech recognition scores of all three groups at 6dB SNR FS were significantly higher [TD children, $p < 0.001$; children sAPD, $p > 0.001$; Adults, $p < 0.001$] compared to -12 dB SNR FS. This suggests that in poor envelope conditions, listeners can take advantage of fine structure cues to better recognize speech. At -6dB SNR E of condition (second column), speech recognition scores of all three groups at 0dB SNR FS were significantly higher compared to -12 dB SNR FS ($p < 0.001$), suggesting that all three groups were similarly able to benefit from the fine structure cues.

Table 3.2: Bonferroni post hoc analysis for different SNR E and SNR FS conditions ($p<0.01$).

SNR Fine structure(dB)	SNR Envelope (dB)					
		-12	**-6**	**0**	**6**	**12**
	12		**Adults vs sAPD (p=.010)**			
	6					
	0		**Adults vs sAPD (p=.010)**			
	-6		**Adults vs sAPD (p=.001)**	**Adults vs sAPD (p=.004)**		
	-12	**Adults vs sAPD (p=.008)**		**Adults vs sAPD (p=.000)**	**Adults vs sAPD (p=.002)**	

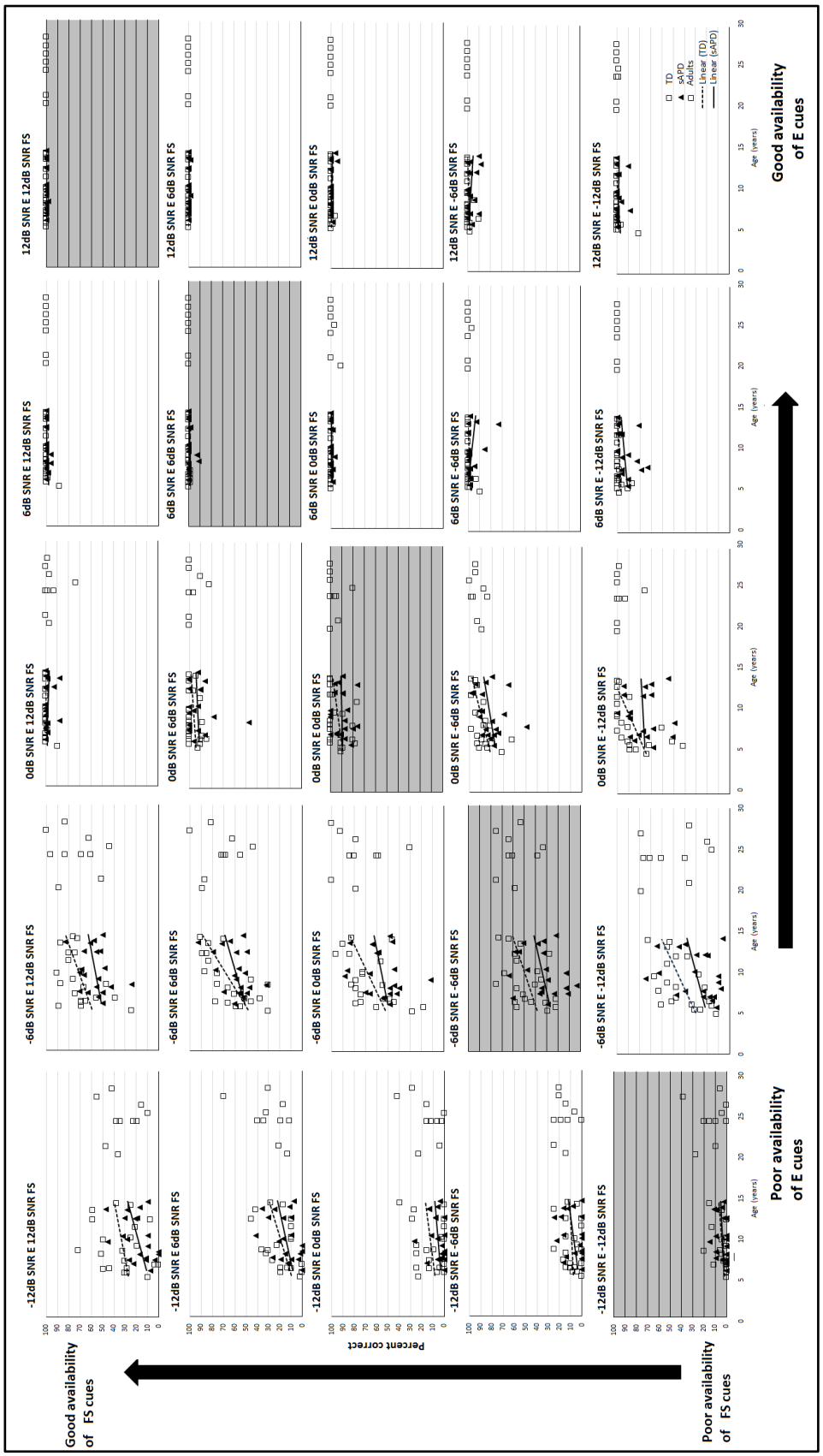

Figure 3.5: Individual speech recognition scores at different SNR dB E and SNR dB FS conditions. Open symbols indicate scores for TD children and adults. Filled symbols indicate scores for children with sAPD. Best-fit lines are shown separately for two groups of children. Abbreviations: SNR, signal to noise ratio; E, envelope; FS, fine structure.

3.4 Discussion

If unprocessed speech signals are used to understand speech perception difficulties in children with sAPD, it becomes difficult to determine whether observed differences between children with sAPD and TD children involve reduced sensitivity to the particular temporal structure. In this study, sentences were mixed with speech-shaped noise. This noise overlaps with a target sentence in time and frequency at the cochlear level (energetic masking). Using the auditory chimera technique, mixed sentences were processed to retain the availability of envelope and fine structure at equal SNRs (reference condition) while varied the availability of one temporal cue while masking the other. Perception of speech with varied envelope and fine structure cues depend on how well the listener extracts these cues (envelope or fine structure) (bottom-up processing). If a listener is able to extract speech-related cues accurately, then decoding of these cues is easier at higher levels compared to a listener who has poor access to these cues.

In this study speech recognition ability of TD children, children with sAPD and adults was studied. In reference condition, envelope and fine structure information are mixed at equal SNR. Regardless of the SNRs, as a group, TD children (mean age = 9.48 years) performance was similar to that of adults. These results closely match with that of Hall et al. (2002) study. On the other hand at poor SNR (-6 dB) the performance of children with sAPD was poor compared to age-matched TD children and adults. Providing direct evidence of speech recognition difficulties in these children. A handful of studies have been carried out to assess this directly (Legace, et al., 2011; Vannisegaram et al., 2004). These studies have consistently reported the speech perception difficulty at low SNRs. The difficulty in recognizing speech in noise at low SNRs may indicate that children with sAPD have significant difficulty in extracting relevant acoustic cues to recognize speech in noise. But as the SNR increased the performance was similar to that of age-matched controls and adults. This indicates that to achieve similar speech recognition scores, children with sAPD require higher SNR.

When the availability of the envelope and fine structure cue was varied, the listener was forced to rely on available cues to recognize speech in noise. Though there were apparent

differences between groups, listeners in all three groups demonstrated that they rely on both envelope and fine structure cue. The contribution of envelope cues was strong compared to fine structure cues. Findings of our study are similar to that of Apoux et al. (2013). Their study with adults reported that the envelope cue is the major contributor for speech perception and fine structure contributes when temporal cues are minimal. Recently, Swaminathan and Heinz (2012) examined the contribution of envelope and fine structure cue to speech recognition in noise using simple regression (auditory nerve) model and demonstrated that envelope cue was the main contributor to speech recognition in noise.

In varied envelope and fine structure conditions, as a group, the performance of TD children was similar to that of adults. When the availability of fine structure cue was poor (bottommost row in Figure 3.5, left to right), as the SNR of the envelope was increased in 6 dB steps, TD children and adults showed improved scores. By 0 and 6 dB SNR E adult's and TD children speech recognition scores reached ceiling levels, respectively. This may indicate that TD children may require slightly stronger envelope cues to reach ceiling levels. The speech recognition scores of children with sAPD were significantly poor when compared to adults. Children with sAPD also demonstrated that they require strong SNR of envelope cue to (6-12 dB) reach ceiling levels. These results suggest that children with sAPD are poor at using envelope cues to recognize speech.

When the availability of envelope cue was poor (first column in Figure 3.5, bottom to top), as the SNR of the fine structure was increased in 6 dB step, the mean performance of TD children was again similar to that of adults. This may indicate that TD children's ability to use fine structure cues to recognize speech from the noise are similar to that of adults. The mean performance of children with sAPD was poor compared to age-matched children and adults. This may indicate that children with sAPD are poor at utilizing available fine structure cues to recognize speech. When compared to adults, some individual TD children were using fine structure cues to recognize speech when SNR of the envelope was increased by 6 dB (Figure 3.5, second column -6dB SNR E). This suggests that when envelope cues are not strong, TD children may use fine structure cues to recognize speech. This may be due to differences in maturation of fine structure and

envelope cues in children (Allen & Wightman, 1997). Developmental studies have shown that young TD children prefer fine structure cues over envelope cues (Allen and Bond, 1997). It could be possible that in unfavorable conditions TD children may use additional fine structure information along with envelope cues to improve their speech recognition. Whereas adult may not rely on fine structure cues to recognize speech but they may rely heavily on envelope cues. Like TD children, children with sAPD demonstrated a similar trend of use of fine structure cues but they were lagging behind TD children and speech recognition scores were significantly poor compared to adults. This suggests that children with sAPD failed to utilize the SNR of the fine structure cues to improve their speech recognition scores when envelope cues were poor.

All three groups mean speech recognition scores in envelope distortion conditions (first column in Figure 3.5) were poor when compared to fine structure distortion conditions (last row in Figure 3.5). This indicates that these listeners rely more on envelope cues to recognize speech in presence of noise. But due to reduced sensitivity to envelope and fine structure cues, the performance of children with sAPD was poor compared to age-matched children and adults. This may explain their difficulty in recognizing speech in degraded conditions. However, when SNR of the envelope and fine structure were high, children with sAPD performance was equal to age-matched TD children and adults. This indicates that children with sAPD require a stronger envelope and fine structure cues to recognize speech in noise.

It was evident that children with sAPD demonstrated difficulty in extracting speech from the envelope and fine structure cues. We argue that children with sAPD performed poorly compared to age-matched controls because peripherally they failed to extract relevant speech envelope and fine structure cues from the noise. The poor ability to extract envelope and fine structure cue related to speech can be attributed to the poor neural integrity of the ascending auditory nervous system. The ascending auditory system is specialized to code temporal aspect of stimuli. The auditory neurons in the brainstem are specialized to phase lock precisely to each cycle of a temporally structured stimulus (Joris et al., 2004). The envelope cues in the auditory nervous system are represented by fluctuations in firing rate over time and the fine structure is coded by patterns of phase

locking to individual stimulus cycle (Sachs & Young, 1979). If there is any neural delay in transmission of temporal aspects of stimuli at the brainstem level, it may have an irreversible effect on the encoding of these structure at higher levels in the auditory system (Wible, Nicol, & Kraus, 2005). Results from Chapter 2 indicated that children with sAPD have abnormal neural processing at the lower brainstem level. The ABRs were characterized by significantly prolonged absolute and interwave latencies. Some portion of children with sAPD demonstrated an abnormal shift in wave V latency at faster stimulation rates, suggesting a compromise of rapid temporal processing of stimuli. The observed delay in neural timing was significantly due to atypical synaptic transmission and axonal conduction time in some portion of children with sAPD. It has also been suggested that children with sAPD have abnormal brainstem physiology, characterized by abnormal auditory brainstem responses to clicks (Allen & Allan, 2014; Gopal & Pierel, 1999) and speech stimuli (Kumar & Singh, 2015); abnormal acoustic reflexes (Allen & Allan, 2014; Saxena, Allan, & Allen, 2015, 2016). Results from these studies suggest that children with sAPD may have poor neural synchrony at the level of the auditory brainstem. Thus the abnormal neural processing in children with sAPD may have a large impact on the processing of temporally dynamic cues that are important for recognizing speech, such as envelope and the fine structure cues. Hence, children with sAPD may find it difficult to process envelope and fine structure cues related to speech in presence of background noise.

It is also important to remember that in the fine structure predominant condition (-12dB SNR E 12dBSNR FS), the envelope cues were masked, yet they were not eliminated completely, thus retaining the relation between the envelope and the fine structure. Swaminathan and Heinz (2012), using an auditory nerve physiological model demonstrated that the contribution of fine structure cues was mainly in the presence of envelope cues and rarely as a primary cue for speech perception. The auditory chimera signal processing used in this study maintained the natural relationship between the envelope and fine structure cues. The contribution of fine structure in speech perception is always in presence of detectable envelope cues. If envelope cues are removed completely, the perception of speech with fine structure cue alone may be challenging and it may be difficult for both TD children and children with sAPD.

3.5 Summary and Conclusion

The relative contribution of the envelope and fine structure cues in recognizing speech was examined in typically developing children, children with sAPD and adults. Though there were group differences, listeners from all three groups demonstrated that they rely more heavily on envelope than fine structure cues to recognize speech in noise. These results are highly consistent with current theories of the envelope and fine structure processing. Typically developing children and adults utilized available temporal cues similarly. Children with sAPD failed to utilize available envelope cues to recognize the speech from the noise. Hence, they performed poorer than age-matched typically developing children and adults.

3.6 Reference

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Chapter 4

4 Perception of Speech with Fine Structure Cues: Data from Adults, Typically Developing Children and Children with Suspected Auditory Processing Difficulties

4.1 Introduction

In Chapter 3 typically developing (TD) children, children suspected of having auditory processing disorder (sAPD) and adults were found to rely more heavily on envelope, rather than fine structure cues to recognize speech in noise. The performance of children with sAPD was poor in comparison to age-matched TD children and adults, and suggests that they may not be as efficient at extracting the relevant cues for recognizing speech in noise. The auditory-chimera signal processing strategy used in Chapter 3 was such that it retained both envelope and fine structure cues in the speech and noise. Results suggested that the contribution of fine structure cues to speech recognition in noise was nominal and only occurred in the presence of the envelope cue. Because the perception of speech with fine structure cues alone (no envelope cue) may be difficult for both TD children and children with sAPD. This study investigated the possibility that fine structure cues may contribute to speech recognition only in the presence of envelope cues. The signal processing strategy used to create a speech signal with fine-structure cues alone discarded as much of the envelope cue information as possible while still retaining fine structure.

The Hilbert Transform (Hilbert, 1912) defines envelope as the magnitude of the amplitude contour of the signal and the fine structure as the cosine phase of the signal. These two components are assumed to exist independently of each other. Speech with fine structure cues alone is created by initially dividing the speech signal into different analysis bands. Envelope and fine structure cues in each analysis band are extracted and then the envelope is discarded so that only the fine structure cues remain. The resulting signal will have fine-structure with equal amplitude in each band. The band signals are

then combined to form a speech with fine structure cue alone. The fine structure cues related to speech are in this way retained while the information related to the envelope is discarded, requiring the listener to rely on fine structure cues alone. It is important to remember that when fine structure is extracted using broad auditory filters, processed stimulus may contain envelope cues. However, this can be avoided if narrow auditory filters are used (Ghitza, 2001; Gilbert & Lorenzi, 2006).

There is evidence that children as young as six months old can understand speech with envelope cues alone (Bertoncini et al., 2011; Cabrera et al., 2015) but very few studies have been conducted to explore the perception of fine structure cues in school-aged children. Bertoncini et al. (2009) studied the ability of 5, 6, and 7-year-old children and adults to process speech with only envelope or fine structure cues. French vowel-consonant-vowel (VCV) syllables were processed in 16 frequency analysis bands to isolate and retain envelope and fine structure cues. Discrimination scores and response latency for each type of cue were examined in all participants. Regardless of the age, listeners demonstrated better discrimination and shorter response latency for speech with envelope cues than for speech with fine structure cues. Age differences were not evident in recognition scores for speech with only fine structure cues. Results of this study imply that the ability to process envelope cues is essential for speech recognition and that children and adults process fine structure cues in a similar fashion.

Studies have reported high levels of intelligibility (~90 %) for fine structure speech in quiet (Gilbert & Lorenzi, 2006; Gilbert, Bergeras, Voillery, & Lorenzi, 2007) for adults suggesting that fine structure speech does provide sufficient information for speech recognition under ideal conditions. To attain high levels of intelligibility when the number of analysis bands are high, adults required intense training (Gilbert & Lorenzi, 2006). This implies that perception of fine structure speech alone is difficult. The lack of envelope cues and the possibility that the fine structure cues are distorted through the signal extraction process have been postulated as potential reasons for the poor speech recognition scores when only fine structure cues are made available to listeners.

Auditory processing disorder (APD) is a perceptual deficit of processing auditory information in the central auditory nervous system (ASHA, 2005; AAA, 2010). One of the most frequent listening complaints of these children is that they cannot recognize speech in noise (Bamiou et al., 2001; Chermak et al., 1999; Lagacé et al., 2011; Vanniasegaram et al., 2004). Chapter 3 suggested that these children may have failed to recognize speech in noise because of their poor ability to extract envelope and fine structure cues in noise. Experimental conditions in Chapter 3 included signals for which the fine structure cues were large and envelope cues were minimal (e.g. -12 dB SNR envelope +12 dB SNR fine-structure). In these conditions the mean performance of children with sAPD was poor in comparison to TD children. This finding may suggest poor ability to extract fine structure information in individuals with auditory processing disorder when compared to their typically developing comparison group. However, the method did not remove the envelope cues completely and the listeners might have used envelope information to aid recognition.

When envelope cues are degraded by noise, listeners may place significant perceptual weight on fine structure cues to assist in recognizing speech (Fogerty, 2011). There is some evidence to suggest that in the presence of noise fine structure information is beneficial for source segregation (Apoux et al., 2013) which in turn can lead to better recognition. Fine structure is also known to play a major role in the integration of speech fragments (Gilbert & Lorenzi, 2010). Studies investigating the perception of speech with fine structure cues alone in the APD population are lacking. Such studies are important given the importance of the cue to speech understanding and source location segregation. It is also possible that the use of fine structure may be compromised in children with sAPD because these children found to have abnormal brainstem functioning, as demonstrated in Chapter 2.

4.2 Method

4.2.1 Participants

Participants included 12 adults (21 to 28 years, mean age: 23.65 years, SD: 2.28 years), 32 typically developing (TD) children (4.1 to14 years, mean age: 8.11 years, SD: 2.56 years) and 23 children with sAPD (6.5 to 13.4 years, mean age; 8.84 years, SD: 1.65 years). Children with sAPD were referred to Western HA Leeper Speech and Hearing clinic because their parents or teachers expressed concerns over their hearing. TD children, children with sAPD and adults underwent basic pure tone audiometry to ensure that they had normal (≤ 20 dB HL) air-conduction thresholds at octave frequencies from 250 to 8000 Hz (ANSI, 2004, 2010) and tympanometry to verify normal middle ear function.

4.2.2 Signal processing

The acoustic stimuli for this study were compiled from 50 (10 practice and 40 target stimuli) of the HINT (Nilsson et al., 1994) sentences. The stimuli were processed as depicted in Figure 4.1. Pre-recorded sentences were passed through a variable number of finite impulse response (FIR) bandpass filters [4 (order n = 579), 8 (order n = 1487), 16 (order n = 3351), and 30 (order n = 6635)]. Using the Greenwood, (1990) equation, auditory filter (or frequency analysis band) center frequencies were selected that represent equal lengths along the basilar membrane and span a frequency range from 80 to 7563 Hz. Stimuli were filtered in both the forward and reverse directions to avoid phase distortion that could result from the filtering. The Hilbert transform (Hilbert, 1912) was used to extract the magnitude (envelope) and the cosine phase of the analytic signal (fine structure) in each auditory filter. The envelope information was discarded from each auditory filter and the fine structure information in each auditory filter was retained. The bands were then recombined to form a speech signal with only fine structure information. Figure 4.2 displays the waveform and spectrogram for a HINT sentence (left column) and spectrograms for various band conditions following acoustic manipulation of the signal (right column).

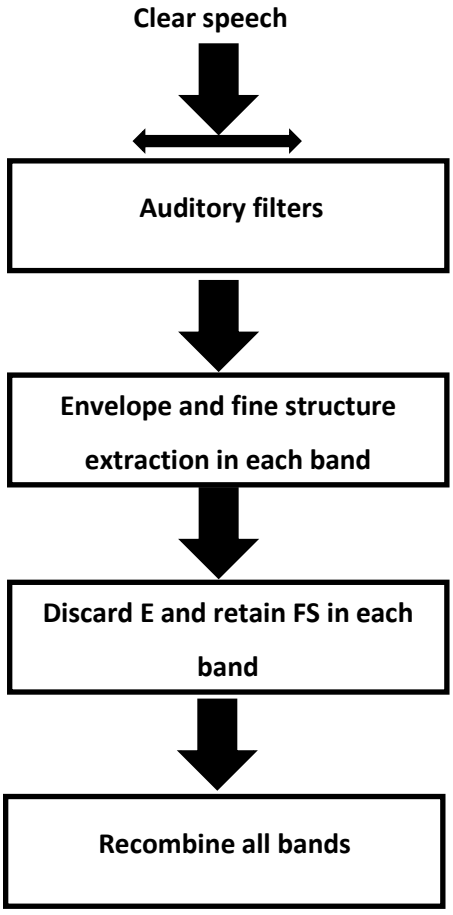

Figure 4.1: Simplified flow chart showing the steps involved in creating speech signals that include only fine structure acoustic cues. Abbreviations: E, Envelope; FS, fine structure.

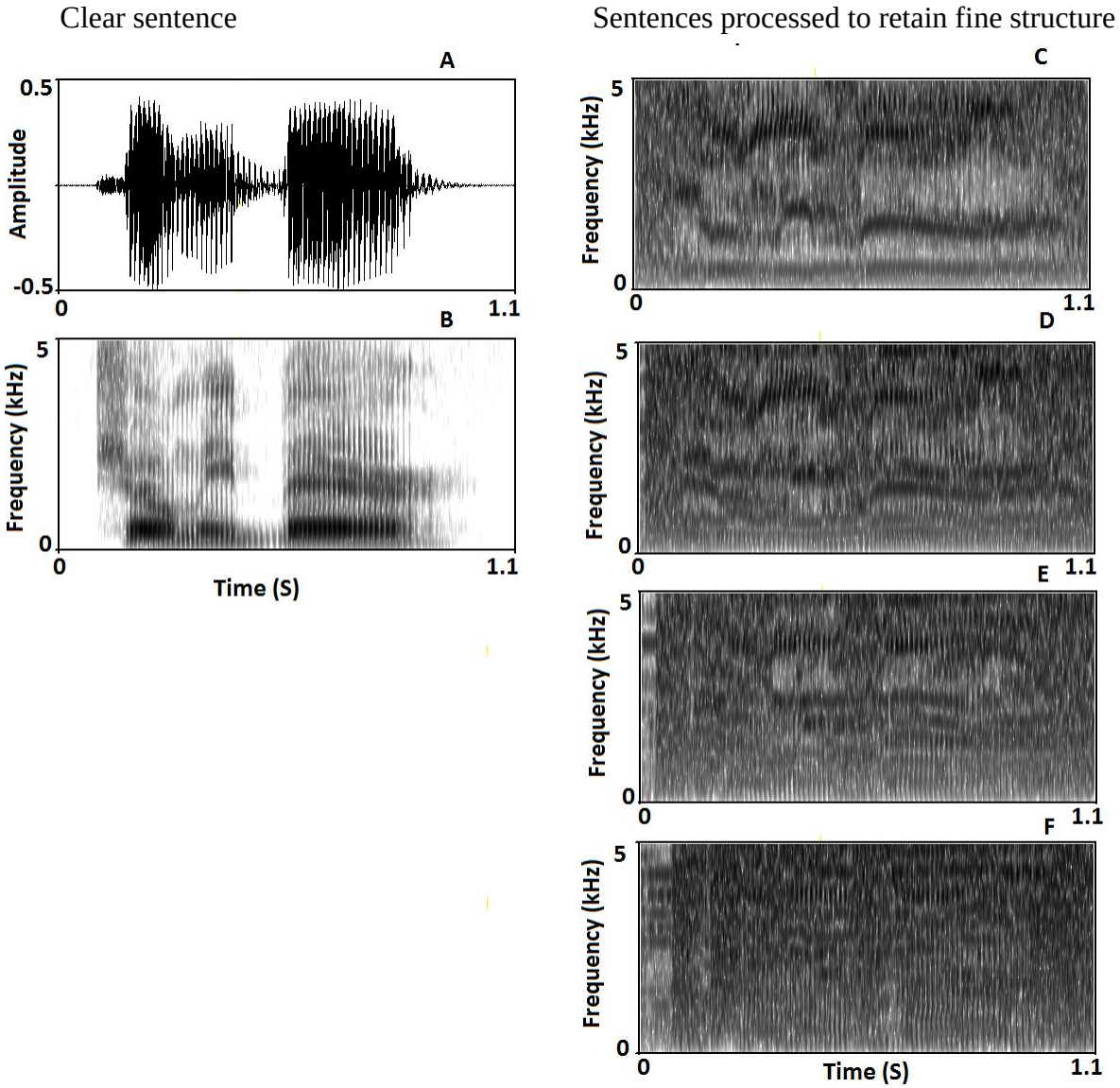

Figure 4.2: Stimulus processing examples. The original unprocessed sentence “Show me bear” is shown in the left column; waveform (A) and spectrogram (B). Spectrograms of the processed sentence to retain fine structure in the 4 bands (C), 8 bands (D), 16 bands (E), and 30 bands (F) conditions are shown in the right column.

4.2.3 Procedure

Sentences were presented in a descending and ascending order based on the number of filter bands included in the signal (Figure 4.3). In each band condition there were ten sentences, resulting in a total of 40 sentences (4 bands conditions X 10 sentences). For all conditions stimuli were presented via a laptop (Lenovo ThinkPad CSL-14122) connected to a Creative Sound Blaster Extigy external sound card through ER- 3A insert ear phones. The output of the earphones was calibrated to produce 65 dBA, using HINT SSN. Calibration was completed in an artificial ear (Type 4152) using a Bruel and Kjaer amplifier (Type 2610). The same attenuator setting was used for all the conditions. Stimuli were presented binaurally. A custom graphical user interface (GUI) was created, using MATLAB, to present the stimuli. The participant's task was to press the space bar on the keyboard and listen to the sentence that was played by the laptop. The listener was asked to repeat all the words in a sentence. No sentence was repeated in any condition. Each correctly repeated word was given a score of 1. Maximum number of words for each sentence varied from four to seven. Participants were tested individually in a sound attenuated booth. The test duration was approximately 10 minutes.

Figure 4.3: Schematic representation of stimulus presentation

4.3 Results

Individual listener data for different bands are plotted in Figure 4.4 as a function of age. The number of keywords identified correctly for each condition was converted to a percent correct score. Open symbols represent speech recognition scores for TD children and adults. Filled symbols represent speech recognition scores for children with sAPD. Large individual differences in speech recognition scores were evident in all three groups. This scatter of performance within groups suggests the presence of a significant amount of variability in listeners' ability to extract speech from fine structure cues.

All groups had better speech recognition scores in the four band condition and as the number of bands used to extract fine structure was increased there was a reduction in speech recognition scores. A mixed ANOVA was performed on RAUs. Whenever the assumption of sphericity was violated the Greenhouse-Geisser correction was used. The performance across different band condition varied within group ($F [1.74, 111.42] = 196.75$, $p < 0.001$, $\eta^2_p = 0.755$).

In all band conditions, the adults had the best speech recognition followed by TD children and children with sAPD displayed the poorest performance. The performance between group was significant ($F [2, 64] = 25.92$, $p < 0.001$, $\eta^2_p = 0.448$) and the interaction between group and number of bands was significant ($F [3.48, 111.42] = 8.58$, $p < 0.001$, $\eta^2_p = 0.21$).

In the four bands condition, there was a general trend for improvement in speech recognition score as a function of age in both groups of children. This finding suggests that older children had better speech recognition scores in comparison to young children. The mean performance of children with sAPD was always poorer than age-matched TD children and adults although there were some TD developing children who achieved performance that was similar to the adults. Few children with sAPD demonstrated performance that was akin to the age-matched TD children. Some individual TD children and children with sAPD could not recognize speech. At the eight bands condition, the

mean speech recognition scores of all three groups were reduced. Some individual TD children and several children with sAPD could not recognize speech. The performance of some children with sAPD was similar to that of their age-matched peers. At the 16 bands condition, the majority of children and some adults could not recognize speech. At 30 bands there was a substantial increase in the number of TD children, children with sAPD and adults who could not recognize speech with TFS cues alone. Post-hoc analysis, corrected for multiple comparison by using Bonferroni corrections, demonstrated that in the 4 band condition, the adults performed better than TD children ($p = 0.002$) and children with sAPD ($p < 0.001$); TD children performed better than children with sAPD ($p= 0.038$). In the 8 bands condition, the adults performed better than TD children ($p < 0.001$) and children with sAPD ($p < 0.001$); TD children performed better than children with sAPD ($p = 0.024$). In the 16 band condition, the adults performed better than TD children ($p < 0.001$) and children with sAPD ($p < 0.001$); there was no significant difference between TD children and children with sAPD ($p = 0.158$). In the 30 bands condition, adult performance was better than children with sAPD ($p = 0.033$), but there were no significant differences between the adult and TD children performance ($p = 0.072$), and there was no significant difference between the performance of the children's groups ($p = 1.00$).

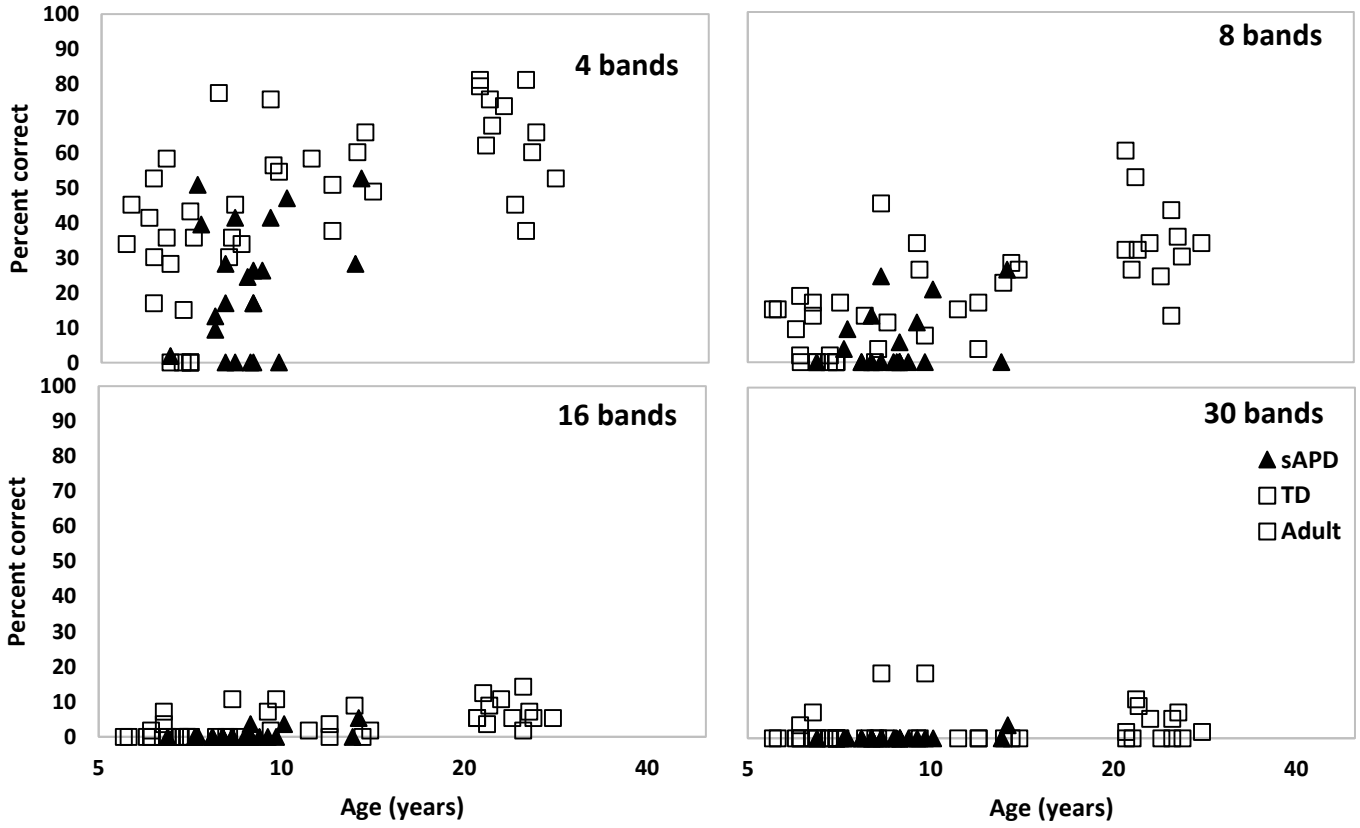

Figure 4.4: Individual speech recognition scores, in percent correct, obtained for TFS speech extracted from different filter band conditions. Open symbols indicate scores for TD children and young adults. Filled symbols indicate scores for children sAPD.

4.4 Discussion

The goal of this study was to examine whether speech can be recognized when only fine structure cues are available to the listener. All three groups included in this study showed a decrease in speech recognition scores with an increasing number of processed filter bands. The speech recognition trend seen in young adults is similar to that of previously published studies (Gilbert & Lorenzi, 2006; Léger, Desloge, Braida, & Swaminathan, 2015). However, the mean speech recognition scores of adults in our study were lower when compared to the previously published data. This could be due to differences in the material used and/or training/exposure to fine structure speech (Gilbert & Lorenzi, 2006; Léger et al., 2015). Previous studies with adults have used syllables (closed set), and the participants have had more exposure (training) to fine structure stimuli. In this study, each sentence was presented only once, and they were not repeated. Perhaps with a longer training period with sentences, the adults may be able to achieve the higher levels of speech recognition scores as reported in previous studies.

Similar to adults, TD children showed the best performance in the four band condition. Regardless of the number of bands used to extract the speech signal fine structure, TD children's mean performance was significantly poorer than adult performance until the number of bands were at its largest they outperformed the children with sAPD. The data from the study conflict with Bertoncini et al. (2009) who reported that fine structure speech recognition in 5, 6 and 7-year-old TD children was similar to that of adults. The differences in results between the current study and Bertoncini et al. study could be attributed to differences in methodology. In their study, participants were asked discriminate closed set of nonsense syllables. Whereas in the present study, listeners task was to repeat sentences that they hear (open task).

Regardless of the number of bands used to extract fine structure speech, the performance of children with sAPD was consistently poorer than the performance of TD children and adults. This result suggests that children with sAPD experience greater challenges

processing speech with only fine structure cues and that perception of speech without envelope cues is difficult for this group.

Stimuli used in this experiment had only fine structure cues. Envelope cues play a major role in understanding speech both in quiet and in the presence of background noise (Apoux et al., 2013; Shannon et al., 1995; Chapter 3). Adults were able to accept the degradation in envelope cues, and they were able to recognize speech with fine structure cue alone (in the fewer number of bands condition). The auditory system of TD children may be less able to handle speech without envelope cues (or fine structure speech only). The study highlights the importance of envelope cues for speech recognition and indicates that fine structure cues alone cannot act as the primary cue for speech recognition. It is also important to remember that the speech recognition scores for a large number of bands (16 and 30) were poor for all the listeners and likely do not contain perceptually relevant cues.

Researchers conducting modeling work in the use of envelope and fine structure in speech coding have reported that a physically removed envelope cue can be reconstructed at the output of peripheral auditory filters, and listeners may use these reconstructed-envelope cues for identification tasks (Ghitza, 2001; Gilbert & Lorenzi, 2006; Heinz & Swaminathan, 2009; Zeng et al., 2004). When fewer bands are used to extract fine structure speech, the reconstructed envelope from an output of the auditory filter is stronger than to when a large number of bands are present in the signal (Gilbert & Lorenzi, 2006; Sheft, Ardoint, & Lorenzi, 2008). In our study, when a small number of bands was used to extract speech fine structure, the listener might have used reconstructed envelope cues to recognize speech, leading to better speech recognition scores. As the number of bands was increased, the likelihood of envelope reconstruction was reduced at the cochlear output and speech recognition deteriorated. The mean speech recognition scores in the four bands condition for TD children were significantly poorer when compared to adult performance. This may imply that the ability of TD children to process speech with fine structure is poor due to an immature ability to encode reconstructed envelope cues.

Typically developing children's performance was better than children with sAPD. One possible explanation for poor performance of children with sAPD is that they have a deficit in recognizing reconstructed envelope cues. At a large number of bands (16 and 30), listeners from all groups had difficulty recognizing fine structure speech. This could be due to reduced availability of reconstructed envelope cues, implying that the fine-structure alone may not act as a primary cue for speech recognition. Previous studies have reported that children can recognize a closed-set of syllables based on the basis of the fine structure speech extracted using a large number of bands (16 bands) (Bertoncini et al., 2009). With training, adults can recognize fine structure speech extracted from a large number of bands (16 bands) (Gilbert and Lorenzi, 2006). However, in our study speech recognition scores were poor at large numbers of bands and the poor performance could be due to lack of training.

The auditory brainstem is specialized for rapid transmission of acoustic signals (Fuchs, 2005). Delay in rapid transmission may lead to difficulties in the encoding of acoustic signals at higher levels of the auditory system. It can be speculated that the observed difficulty in processing speech with fine structure cues in children with sAPD may be due to abnormal brainstem functioning. Chapter 2 demonstrated that significant portion of children with sAPD have abnormal click-evoked ABRs. Examination of responses delineating axonal vs. synaptic transmission showed frequent delays in synaptic transmission and fewer instances of delays related to axonal conduction. Thus, the atypical functioning of auditory brainstem may have a large impact on the coding of fine structure speech.

One of the potential problems with the speech processed to retain fine structure is the presence of unwanted noise (Apoux et al., 2013; Hopkins, Moore, & Stone, 2010). Fine structure signal processing involves discarding the envelope structure and retaining the fine structure. The original amplitude of the envelope in a given frequency analysis band is discarded as much as possible, and the output envelope amplitude in the remaining fine structure is made constant across all analysis bands. If there is any low-level recording noise in any analysis band, it will be amplified to the same level as the speech information. Analysis bands with no speech information are also filled with distracting

background sound (e.g. low-level recording noise). The unwanted noise can be present within the band along with the target signal or several bands away from the target signal band. As the number of frequency analysis bands are increased, there is an increase in the unwanted noise. Even in our study, the amount of noise increased as the number of analysis bands increased and the presence of the noise was clearly evident in spectrograms (Figure 4.2, right column). The effect of signal processing noise was reflected in the speech recognition scores, particularly in the higher number of bands condition.

Previous studies have used syllables to examine speech recognition with fine structure cues, but in this study, sentences were used. Since sentences are longer in duration than syllables, fine structure signal processing might have induced more noise to corrupt the reconstructed envelope cues. Hence, speech recognition based on reconstructed envelope cues may be challenging for TD children and children with sAPD compared to adults.

Recognition of speech with fine structure cues was difficult, especially in a large number of bands condition (n=30). This could be due to the signal processing strategy that is used to process fine structure speech. Figure 4.5 shows mean speech recognition scores for chimeric mixing (Chapter 3) and the Hilbert-fine structure speech (current study, 30 bands fine structure condition). Filled triangles and squares represent the mean speech recognition scores for chimeric mixing and the Hilbert fine structure speech, respectively. Both chimeric mixing and the Hilbert transform speech were processed using 30 analysis bands. In chimeric mixing, typically developing children and adults showed nearly 30% mean speech recognition scores but the mean speech recognition was less than 5% in Hilbert fine structure speech. Children with sAPD showed 20% mean speech recognition scores in chimeric mixing and less than 1% in the Hilbert fine structure speech. These differences in scores might be due to differences in signal processing used to study the importance of fine structure cues.

In chimeric mixing (Chapter 3), the fine structure is dominant, and the envelope is minimal or masked (-12 dB SNR envelope 12 dB SNR fine-structure) but not removed completely. This type of mixing retains the relation between the envelope and the fine

structure at the cochlear output. Hence, listeners performed better. On the other hand, in speech with fine structure cues alone (Hilbert transform), the envelope related to the original stimuli is discarded and the fine structure information is retained. This processing distorts the relationship between the envelope and the fine structure cues at the cochlear output and leads to poor speech recognition. This signal processing also induces unwanted noise into the target signal, making it difficult to recognize speech. These results suggest that the fine structure alone may not act as a primary cue but that it may contribute to speech recognition only in the presence of envelope cues. This was evident in all three groups. Similar findings have been reported using an auditory nerve model (Swaminathan & Heinz, 2012).

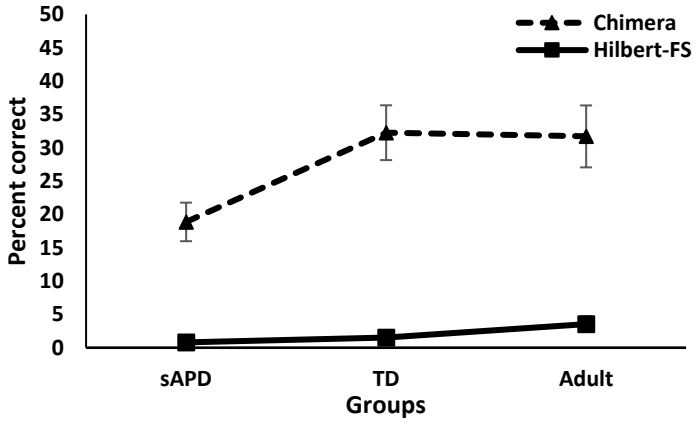

Figure 4.5: Mean speech recognition scores obtained for children suspected of auditory processing disorder (sAPD), typically developing children (TD) and adults in Chimeric mixing and Hilbert fine structure (Hilbert-FS) speech. The error bar shows the standard error of the mean.

4.5 Summary and Conclusion

In this study, TD children, children with sAPD, and adults ability to recognize speech with fine structure cue was assessed. Typically developing children and children with sAPD are poor, in comparison to adults, in recognizing speech based on the fine structure cues. Children with sAPD performance was poor compared to age-matched typically developing children and adults. These results suggest that it is difficult for typically developing children auditory system to handle speech without envelope cues. Removal of envelope cue had a larger negative impact on children with sAPD as their performance was poor than age-matched typically developing children. The mean speech recognition scores of Hilbert fine structure speech (30 bands) were poor when compared to chimeric fine structure predominant condition. This likely reflects the idea that the contribution of fine structure cues is always in the presence of the envelope cue and may not act as a primary cue for speech recognition.

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Chapter 5

5 Perception of Spectral Shape: Data from Adults, Typically Developing Children and Children with Suspected Auditory Processing Difficulties

5.1 Introduction

Good speech recognition in noise depends on the accurate extraction of temporal and spectral acoustic cues. Listeners can use temporal cues including signal envelope and fine structure to isolate speech from background noise (Apoux et al., 2013; Chapter 3). Listeners may derive benefit from the spectral aspects of sound, such as overall spectral shape to perceive speech (Assmann, & Summerfield, 2004). The spectral shape has been shown to be particularly important for accurate speech recognition (Allen & Wightman, 1992; Henry et al., 2005). The perception of spectral shape relies upon the extraction of frequency-amplitude information from each auditory filter and the successful cross-channel integration of this acoustic information. Any difficulty in integrating auditory filter outputs may lead to an inadequate representation of spectral shape. This could result in difficulty discriminating speech sounds that have subtle differences in spectral shape.

The perception of spectral shape is often studied by measuring the ability to detect or discriminate differences in complex acoustic stimuli such as speech. But non-speech stimuli with complex spectra can also be used. A ripple spectrum stimulus is a complex acoustic signal that can be used to investigate spectral shape. This type of stimulus can be created by adding sinusoids with frequencies spaced logarithmically. The spectrum of the complex stimulus is modulated (or rippled) by applying a sinusoidal spectral envelope with sine (or cosine) as the starting phase. The resulting rippled spectrum stimulus can be used to quantify the perception of spectral shape by manipulating modulation parameters such as depth, density, or phase.

Psychoacoustic studies with children have shown that typically developing (TD) children can discriminate between sounds of varied spectral shape. Allen and Wightman (1992) evaluated children and adults spectral shape discrimination using both speech and non-speech sounds that differed only in the shape of their spectral amplitude in children and adults. The study showed that 4-7 year-old children demonstrated poor spectral shape discrimination and poor speech sound discrimination abilities. Children aged 9 years and adults performed better. Differences were evident for signals presented in quiet and in the presence of a noise masker. Similar results were obtained for the discrimination of spectral patterns associated with vowel and consonant sounds. A significant correlation was observed between speech sound discrimination in quiet, and ripple discrimination thresholds. Taken together, these results suggest that ripple discrimination ability improves with age in children. Peter et al. (2014) examined the capacity of young children (8 - 11 years), older children (12 - 18 years), and adults to discriminate between spectral ripples of differing density. Their results showed that young children performed poorer on this task than adult group, while the performance of older children did not differ from adults. Finally, Rayes, Sheft, and Shafiro (2014) studied the discrimination of static and dynamic spectral patterns in 20 children (5.4 to 12.8 years), and 20 adults (19-27 years). For static patterns, they used a cued two intervals forced choice method (2IFC) to evaluate just noticeable differences in the phase of modulation. The dynamic spectral pattern discrimination was quantified as the signal-to-noise ratio required to discriminate between 5 Hz low-pass noise-modulated pure tones in the presence of a masker. Along with these non-speech tasks, speech recognition in the presence of multi-talker babble was examined. In comparison to adults the children demonstrated poor performance on both static and dynamic spectral pattern discrimination tasks, but only the children showed a significant correlation between dynamic spectral pattern discrimination and speech-in-noise perception.

In summary, studies manipulating the depth, density, and phase of modulation suggest that young children are poor at processing spectral shape when performance compared to older children and adults. While one study has shown spectral ripple discrimination abilities in TD children (Peter et al., 2014), that study was limited to children aged eight years and older; it is not clear whether younger children can discriminate between

spectral ripple stimuli. Discrimination of spectral shape may depend on an individual's ability to resolve acoustic signal frequencies. Young, typically developing children are known to have poor frequency resolving ability (Allan, 2011; Allen, Wightman, Kistler, & Dolan, 1989). Hence, we hypothesized that young typically developing children may have difficulty with spectral shape discrimination.

In addition to an absence of data from young children, we are unaware of any study that has investigated spectral shape perception in children who complain about difficulty understanding speech in the presence of background noise and children with sAPD. An APD presents as a deficit in the perceptual processing of auditory information in the central auditory nervous system (AAA, 2010), and children with APD demonstrate a deficiency in one or more following behaviors: auditory discrimination, localization, temporal processing, or hearing in the presence of background noise (ASHA, 2005). There is strong evidence to suggest that these behavioral deficits arise from difficulty in coding the basic structure of acoustic signals in comparison to age-matched typically developing children (Allan, 2011). Since the perception of spectral shape is a complex task involving the extraction and integration of frequency-amplitude information across auditory channels, we hypothesized that children with APD would display poor performance this task. Indeed, we previously demonstrated that children with APD were poor at processing speech that contained only fine structure or envelope cues in comparison to TD children and young adults. It was speculated that this poor performance could be due to an impaired ability to extract and integrate frequency information across different frequency channels. Examining the perception of spectral ripple discrimination in children with APD may provide direct evidence of a spectral shape perception deficit, which could help explain the difficulty these children experience recognizing speech in noisy conditions.

The current experiment had two goals. The first was to measure/describe any developmental trend that may be evident in spectral shape discrimination in typically developing children. It was hypothesized that young children would perform poorer than older children and adults. The second aim was to compare spectral shape discrimination ability in children with suspected APD and age-matched typically developing children. It

was hypothesized that children with APD would perform poorly in comparison to age-matched TD children and adults on a spectral ripple discrimination task.

5.2 Method

5.2.1 Participants

This experiment includes data from 14 adults (19 - 35 years, mean age: 24.28 years, SD: 4.59 years), 12 children with sAPD (6.9-10 years, mean age: 8.7 years, SD: 0.95 years) and 18 typically developing (TD) children who were divided into a group of ten young (5.1 - 7.9 years, mean age=6.49 years, SD: 0.51 years) and eight older children (8.1 - 13.9 years, mean age: 10.78 years, SD: 1.83 years). Children with sAPD were referred to our clinic because their parents or teachers expressed concerns about their listening abilities. TD children, sAPD children, and adults underwent basic pure tone audiometry to ensure that they had normal (< 20 dB HL) air-conduction thresholds at octave frequencies from 250 to 8000 Hz (ANSI, 2004, 2010), and tympanometry to verify normal middle ear function in both ears.

5.2.2 Signal processing

Spectral shape discrimination was assessed using a spectral ripple discrimination task. The spectral ripple stimuli were generated using MATLAB software (MathWorks, Natick, MA). The broadband stimulus was constructed by adding 200 sinusoidal tones with frequencies spaced logarithmically between 100 to 6400 Hz (six octaves). The spectrum of the broadband stimulus was modulated using logarithmically spaced sinusoidal modulation (peak-to-peak modulation depth of 30 dB) with either zero or $\pi/2$ radians as the starting phase (as in Won et al., 2011). The number of ripples per octave (ripple density) was varied between 0.125 and 10. The duration of the stimulus was 500 msec, including 150 msec raised cosine onset and offset ramps. Figure 5.1 shows examples of stimuli spectrum. The frequency spectra of these types of signals are often described as having a series of peaks and troughs resembling ripples, giving rise to the name spectral ripple stimuli.

5.2.3 Procedure

The listener's task was to discriminate between standard (spectral envelope with zero radians) and inverted (spectral envelope with π/2 radians) spectral rippled stimuli. As the ripple density increases (modulation depth is held constant), the distance between spectral peaks becomes smaller, and it becomes increasingly difficult for listeners to discriminate between stimuli. The threshold for spectral ripple discrimination is defined as the highest ripple density at which an individual can differentiate between the standard and inverted ripple stimuli.

Stimuli were presented via a personnel computer (Intel Core i3 processor) connected to a Creative Sound Blaster Extigy external sound card through an ER-3A insert earphone (right ear). Stimuli were presented at a level of 60 dB SPL, calibrated using unmodulated noise (100 - 6400Hz). Calibration was completed in an artificial ear (Type 4152) using a Bruel and Kjaer amplifier (Type 2610). Discrimination was measured using a three-alternative forced choice (3AFC) procedure. To facilitate testing in young children, an animated sequence was displayed marking the three listening intervals. In two of the intervals, the phase of the sinusoidal spectral envelope was set to zero radians (reference) and the target interval was set to π/2 phase (Figure 5.1). The starting ripple density was set to 0.125 ripples per octave (RPO), and the ripple rate was varied adaptively using a 2-down-1-up procedure (Levitt, 1971). The inter-stimulus interval was 500 msec. The RPO depth increased or decreased by a ratio of 1.41 with each reversal in the tracking direction. The 3AFC trials were grouped into blocks. For a given block, each participant completed a minimum of six reversals and the last four reversal points were used to compute a mean arithmetic threshold. Higher spectral ripple discrimination thresholds indicate better performance. Spectra of ripple stimuli at 1 RPO are provided in Figure 5.1.

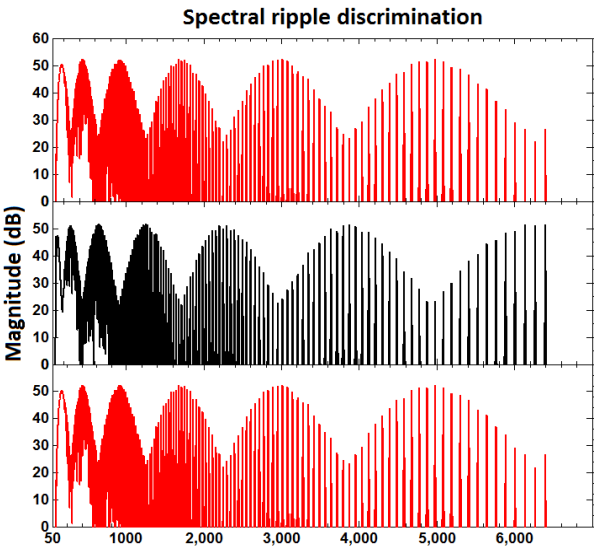

Figure 5.1: Spectra of spectral ripple stimuli for reference (top and bottom) and target conditions (middle).

5.3 Results

5.3.1 Maturation of spectral ripple discrimination

Figure 5.2 shows individual subject thresholds as a function of age. It is evident that young TD children demonstrated smaller spectral ripple discrimination thresholds compared to older TD children and adults. There was a significant positive correlation between age and spectral ripple discrimination thresholds ($r = 0.78$, $p < 0.001$). This suggests that as children mature, their ability to resolve an increasing spectral density improves. A one-way ANOVA revealed significant differences between groups [$F(2, 29) = 21.94$, $p < 0.001$]. Post-hoc comparisons using a Bonferroni test demonstrated that young TD children had smaller spectral ripple discrimination thresholds in comparison to older TD children ($p = 0.001$) and adults ($p < 0.001$). There were no significant differences ($p = 0.402$) between the spectral ripple discrimination thresholds achieved by older TD children and adults.

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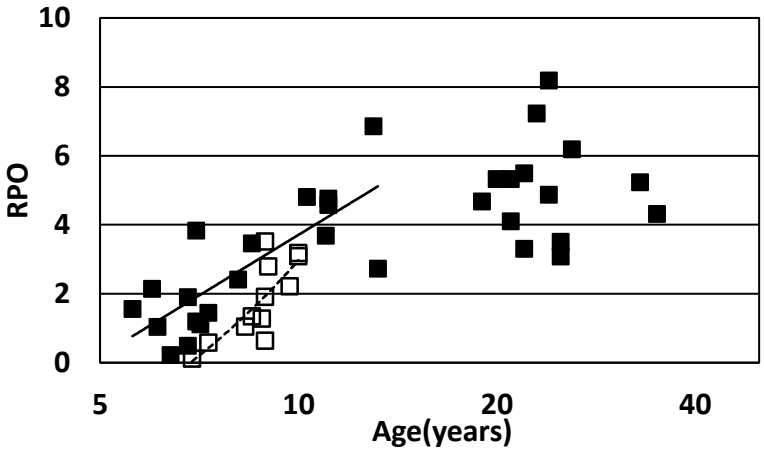

Figure 5.2: Spectral ripple discrimination thresholds as a function of age for all listeners. Typically developing children and adults are represented by the filled squares. Unfilled squares represent the children with sAPD. The dark line characterizes the relationship between age and spectral ripple discrimination threshold. Best-fit lines are shown separately for typically developing children (filled line) and children with sAPD (unfilled lines).

5.3.2 Spectral ripple discrimination by children suspected with APD

The performance of children referred to our clinic with suspected APD on the spectral ripple discrimination task was compared with age matched TD children (6.9- 13.2 years, mean age = 10.4 years, n=10), and normal hearing adults. Independent sample t-test revealed no significant differences in age between children sAPD and age-matched TD children [t (20) =-1.76, p=.094]. In figure 5.2 it is evident that the performance of adults on the spectral ripple discrimination task was best followed by TD children and children with sAPD. There was a significant positive correlation between children with sAPD age and spectral ripple discrimination thresholds ($r = 0.78$, $p = 0.003$). This suggests that as children mature, their ability to resolve an increasing spectral density may improve. To determine whether there were differences in mean performance between groups, a one-way ANOVA was conducted with Bonferroni posthoc tests. Significant differences between groups were observed [$F (2, 33) = 17.15$, $p < 0.001$], with posthoc comparisons revealing that sAPD children had lower spectral ripple discrimination thresholds when compared to TD children ($p = 0.013$) and adults ($p < 0.001$). There were no statistically significant differences ($p = 0.067$) between TD children and adults.

5.4 Discussion

5.4.1 Maturation of spectral ripple discrimination

In our spectral discrimination task, listener performance relied on the perception of the relative amplitude of the frequency components within a stimulus. The auditory system must analyze the cochlear output which consists of the summed output from each auditory filter, and then integrate that information to perceive the signal. In our study, young TD children had lower spectral ripple discrimination thresholds in comparison to older TD children and adults. This suggests that the perception of spectral shape is still immature in children younger than 8 years of age. Importantly, this was not due to the listening task demands, as children as young as 5.6 years old were able to understand and complete the task. Results of this study showed a significant correlation between spectral ripple discrimination thresholds and age which shows a strong developmental trend in spectral shape discrimination. It is also an important factor to be considered if spectral ripple discrimination tasks are to be used clinically. There were no significant differences between older TD children and young adults, suggesting maturation of spectral ripple discrimination occurs by approximately nine years of age. Peter et al. (2014) reported similar trend that spectral ripple discrimination in 8 to 11-year-old children was poor when compared to 12- to 18-year-old children and young adults. Differences in age groupings between the present study and Peter et al. make direct comparisons challenging.

Allen and Wightman (1992) reported that spectral modulation detection matures by a nine years of age. This closely matches the current finding. It can be speculated that the performance of young TD children was poor due to their inability to evaluate information across auditory filters. Young TD children have been shown to integrate information over a larger number of auditory filters than mature listeners (Oh et al., 2001).

Young TD children have been shown to exhibit a significant deficit in understanding speech in the presence of noise (Elliot et al., 1979). The auditory system is tasked with determining which parts of the cochlear output correspond to speech and which

correspond to noise in poor listening conditions. Background noise can alter the shape of the speech spectrum, reducing the distinction between signal peaks and valleys, and changing its spectral slope (Assmann, & Summerfield, 2004). The prolonged maturation of spectral shape perception could be a possible reason or contributing factor for the poor performance of young children in noise.

5.4.2 Spectral-ripple discrimination by children with sAPD

The novel finding of this study is the poor performance on a spectral ripple discrimination task by children with sAPD in comparison to age-matched TD children and adults. The spectral ripple discrimination task directly assessed the across-channel integration of frequency and amplitude information. The poor performance by children with sAPD on this task suggests that they are having difficulty combining frequency-amplitude information contained in the cochlear output of greater than one filter. As in young children, this finding may reflect difficulty combining and evaluating the outputs of large numbers of auditory filters, or difficulty resolving individual frequency components.

5.5 Summary and Conclusion

The current study examined the perception of spectral ripple discrimination in typically developing children, children with sAPD, and adults. Younger typically developing children's spectral discrimination thresholds were significantly lower (performance was poorer) compared to older children. This suggests that spectral shape discrimination is immature in children aged 5 - 8 years. The performance of children with sAPD was poorer than age-matched typically developing children, providing direct evidence of a deficit for spectral shape perception in children with sAPD. This deficit may arise from an inability to integrate information across cochlear channels, an impaired ability to resolve individual frequency components or some combination of the two.

5.6 References

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Chapter 6

6 Summary, Future direction and Clinical implications

6.1 Summary

The central aim of this thesis was to examine the auditory processing in children with sAPD. These children were referred to Leeper Speech and Hearing Clinic because their parents or teachers expressed concerns about hearing and/or listening abilities. Physiological and behavioral experiments were carried out to understand the auditory processing in children with sAPD and compared to age-matched typically developing children and young adults. A focus was on auditory skills related to speech in noise understanding and the underlying neural integrity that supports those skills.

ASHA recommends including electrophysiological measures in their auditory processing disorder (APD) assessment battery. However, few audiologists do so due to lack of evidence (AAA, 2010; Katz et al., 2002). Some previous studies have reported increased ABR wave latencies, reduced wave amplitudes and abnormal latency shifts at faster stimulation rates in APD children (Allen & Allan, 2014; Gopal & Kowalski, 1999; Jirsa, 2001). The analysis of ABRs in Chapter 2 also revealed significantly prolonged absolute latencies and interwave intervals in children with sAPD compared to adults. These findings provide physiological evidence that many children with listening difficulties have abnormal auditory brainstem functioning. ABRs in infants and very young children have reported prolonged latency at slower stimulation rates and a greater shift in latency at faster stimulation rates (Jiang et al., 1998; Lasky, 1997). This can be attributed to incomplete myelination and reduced synaptic efficiency in the auditory brainstem (Lasky, 1997; Jiang et al., 1998). Based on this it can be assumed that ABR abnormalities observed in sAPD children of our study (Chapter 2) could be due to either atypical axonal or synaptic transmission in the auditory brainstem. ABR analysis using the Ponton et al. (1996) model demonstrated significant prolongation of interwave intervals (II-III and IV-V) that represents synaptic transmission. Some individual children also showed

prolonged interwave intervals (> 2SD from the adult mean) that represent the axonal conduction times (I-II and III-IV). There is evidence that atypical axonal or synaptic transmission can impair auditory processing in animals (Johnston et al., 2010; Middlebrooks et al., 2013; Pirone et al., 2014; Satheesh et al., 2012). Hence, it can be speculated that the observed abnormal synaptic transmission and axonal conduction times in the brainstem may be partly responsible for listening difficulties that are frequently reported in these group of children.

Allen and Allan (2014) reported ABR abnormalities in both children diagnosed as APD and non-APD based on behavioral tests. Hence, in study 2, children with sAPD were not divided into APD vs non-APD for the statistical analysis. The ABR was recorded in 108 children with sAPD. Out of 108 children, 68 were diagnosed as APD and 40 were diagnosed as non-APD based on behavioral test performance. It was interesting to note that children in both groups demonstrated abnormal ABRs. Children who received the diagnosis of non-APD may have adequate cognitive and linguistic skills, potentially elevating performance in behavioral tests, many of which are speech based. However, these children still evidence listening difficulties that may arise from reduced auditory brainstem transmission. This may suggest that the behavioral tests alone may not be justified children with APD. The use of click-evoked ABRs may assist in identifying children with APD. Future studies should focus more on understanding functioning of the peripheral auditory system.

Findings of ABR abnormalities in children with sAPD suggest that these children may have a measurable physiological deficit at a lower level of the auditory system. Studies also suggest the presence of lower level abnormalities, such as abnormal acoustic reflex threshold and growth function, (Allen & Allan, 2014; Saxena et al., 2015, 2016) and abnormal cochlear and efferent system (Boothalingam, Allan, Allen, & Purcell, 2015). Accurate coding of an acoustic signal (either in quiet or noise) at lower levels of the auditory system is essential for adequate representation at higher levels of the auditory system. If the functioning of the brainstem is atypical, then it may send faulty neuronal signals to the auditory cortex, leading to the faulty representation of acoustic signals. Based on this it can be speculated that a significant portion of children with listening

difficulties may have difficulty in processing the acoustic signal at the lower level of the auditory system.

Inefficient neural (axonal and synaptic) transmission may cause an unexpected delay in transmitting an acoustic signal within the auditory brainstem. This delay in neural transmission may lead to difficulty in the coding of dynamic acoustic cues (temporal envelope, fine structure or spectral shape) that are necessary for recognizing speech. The auditory neurons in the brainstem are known to phase lock precisely to each cycle of a temporally structured stimulus (Joris et al., 2004). If the delay in the synaptic transmission of the temporal aspect of stimuli starts in the lower level of the auditory system (e.g. CNC), it may have an irreversible effect on the encoding of these structure at higher levels in the auditory system. Hence, the abnormal synaptic transmission may cause temporal coding deficits, which is frequently reported in APD children.

In Chapter-3, using auditory-chimera signal processing, the availability of the envelope and the fine structure was varied. This signal processing retains the relation between the envelope and the fine structure cues but allows the evaluation of the use of both envelope and the fine structure cues in noise. Listener's task was to recognize the speech based on the available envelope or the fine structure cues. When SNR of the envelope and fine structure cues were equal, at low SNRs the performance of children with sAPD was poor compared to age-matched children. This provided direct evidence of speech recognition difficulties faced by these children. When the availability of envelope and fine structure cues were varied, all listeners showed better speech recognition based on envelope cue than fine structure cue. Typically developing children and children with sAPD demonstrated developmental trends when they were forced to identify speech based on envelope cues but the performanc eof the children with with sAPD lagged behind that of typically developing children. Children with sAPD showed performance that was significantly poorer when compared to age-matched children and adults. There were no significant differences between groups in recognizing speech based on fine structure cues. However, the mean performance of children with sAPD was always poorer than age-matched children. These results indicate that the processing of fine structure likely

matured earlier while the maturation of envelope processing, which is much more important to speech processing may be more protracted.

It is important to note however, remember that in fine structure predominant condition (e.g. -12dB SNR E 12dBSNR TFS), the envelope cues were masked but not entirely eliminated. The relation between the envelope and the fine structure was retained. If envelope cues are removed completely, the perception of speech with fine structure cue alone may be more challenging, and it may be difficult for both TD children and children with sAPD (chapter 4). Children with sAPD showed performance that was poor compared to age-matched typically developing children and adults. These results suggest that it may be difficult for typically developing children's auditory systems to handle speech without envelope cues. Removal of envelope cue entirely had a larger negative impact on children with sAPD. The mean speech recognition scores of Hilbert fine structure speech (30 bands) were poor when compared to chimeric fine structure predominant condition. This likely reflects the idea that the contribution of fine structure cues is always in the presence of the envelope cue and may not act as a primary cue for speech recognition.

The signal processing used to extract the fine structure cues induced unwanted noise into the signal. Similar findings have been reported by previous researchers (Apoux et al., 2013; Hopkins et al., 2010). The presence of unwanted noise might have impaired the recognition of speech with fine structure cues in typically developing children and children with sAPD compared to adults. With a large number of bands (16 and 30) condition, all three groups showed poor speech recognition scores. Regardless of the noise, children could have recognized the speech based on fine structure information, but they failed to do so. It could be due to their poor ability to integrate frequency information from different bands (across-channel integration).

Extracting spectral shape is crucial for understanding the speech either in quiet or in the presence of noise. The perception of spectral shape relies on the extraction of frequency-amplitude information from each auditory filter and combining that information across channel. Difficulty in combining and comparing auditory filter outputs may lead an

inadequate representation of the spectral shape. This, in turn, may result in difficulty in discriminating speech sounds that have subtle differences in spectral shape. Spectral shape perception was studied in Chapter 5 using a spectral ripple discrimination task with typically developing children, children with sAPD, and young adults. Young typically developing children (5-8 years) could resolve fewer number of ripples per octave compared to older typically developing children (8.1-14 years) and adults. This suggests that spectral shape perception is still immature in younger children. The performance of children with sAPD was reduced compared to age-matched controls and young adults. Spectral-ripple discrimination showed a strong trend for improvement in thresholds as a function of age in both typically developing children and children with sAPD. This may indicate that spectral shape is a learned cue that may take a longer time to mature. Similar findings have been reported in previous studies (Allen & Wightman, 1992). Results from this psychoacoustic study provided direct evidence of spectral shape perception deficit in children with sAPD. If a listener has poor ability to extract spectral shape they may find it difficult to recognize speech in noise. This may explain children with sAPD difficult to understand speech in presence noise.

It is important to remember that results of chapter 3 to 5 might have been influenced by non-auditory factors (attention, cognition and language), especially in (young) typically developing children and children with sAPD. Researchers believe that attention and memory plays a major role in speech and non-speech behavioral tasks (Dawes & Bishop, 2009; Moore, Ferguson, Edmondson-Jones, Ratib, and Riley, 2010). Poor performance on these task may indicate that individual may be poor at encoding the basic acoustic signals in the central auditory nervous system or could be a problem in decoding the basic structure of language (phonology, semantics and syntax) or problems in attention and memory. The task in study 3 was to repeat sentences in noise. This process may involve, extracting words (by neglecting the background noise) and storing them in working memory, and repeating them in the sequence they heard. Any difficulty in this process may lead to difficulty in recognizing the speech. Even with good auditory skills, children with poor language skills may fail to perform in tests that are linguistically loaded (Allen and Allan, 2014). It can be speculated that results of study 3 might have been influenced to some extent by linguistic factors.

Furthermore, the spectral ripple discrimination task (chapter 5) is cognitively demanding, as both standard and the target stimuli keep varying during the task. As such, difficulties maintaining attention can lead to elevated thresholds. Young typically developing children show elevated thresholds on psychoacoustic tasks due to poor attention (Moore, Ferguson, Halliday, & Riley, 2008). In our study, young children performance might have been influenced by their attention. Some individual children sAPD spectral ripple discrimination thresholds were similar to that of age-matched TD children. This may suggest that some individual children sAPD are roughly attentive to the task, but those who fail to do more poorly than TD children. As a group, the performance of children sAPD was poor compared to age-matched typically developing children, and this could be either due to poor attention to the signal or due to poor (complex) signal encoding.

6.2 Future directions

1. Wave I of the ABR is believed to be generated by IHC and spiral ganglion neurons. Studies on animal models have reported that disruption in IHCs activity can significantly reduce the ABR waveform without altering OHCs activity (Harrison, 1998). This indicates that impaired processing within the cochlea can influence signal coding at the auditory nerve (AN) or higher levels in the auditory system. A significant portion of children with sAPD (in Chapter 2) demonstrated prolonged wave I latency at high-intensity levels (80 dB nHL). This indicates that these children may have atypical cochlear processing (IHC) leading to abnormal wave I response. Current research on electrophysiology in APD has focused on AN and beyond (e.g., ABR) but there is a lack of research on cochlear potentials. Recording cochlear potentials may provide novel information regarding pre-neural activity in children with sAPD.
2. In children with sAPD the ABR was recorded in quiet but not in the presence of noise. Recording ABR in noise may prolong absolute latencies. The amount of shift in latency may be abnormal in children with sAPD compared to age-matched typically developing children and adults. Hence, future should focus on recording ABR in noise.

3. In our lab, follow-up assessment of some individual children with sAPD (n=4) several years later did not show changes in their ABRs compared to their initial assessment, even though some behavioral measures improved. This may indicate that the ABR may not show changes due to maturation and that some children may retain these brainstem abnormalities. This should be examined in a larger number of children with sAPD.
4. The perception of envelope (amplitude modulation) and fine structure (frequency modulation) were assessed using speech stimuli. Currently, there are few studies examining the perception of these cues using non-speech stimuli in children with sAPD. Hence, future studies should be carried out to assess the perception of the non-speech envelope and fine structure cues in children with sAPD.
5. Currently, the spectral ripple discrimination task is not widely used in APD assessment. This could be due to lack of normative data. Future studies should be carried out to develop age-specific norms so that this test can be used in APD assessment.

6.3 Clinical implications

The finding of these studies suggests that the click-evoked auditory brainstem response in children with sAPD can provide significant information regarding the auditory brainstem integrity. The clinical measures failed to identify the specific neural mechanism responsible for the neural disruption. The Ponton et al. model helped in characterizing the nature of the disruption in the neural transmission observed in children with sAPD. Several individual children with sAPD demonstrated atypical axonal and synaptic processing. However, the more significant portion of children with sAPD had prolonged synaptic transmission, evident both at slow and faster stimulation rates. These results indicate that Ponton model may provide useful information regarding the nature of disruption in a clinical population.

Clinically, it is important to analyze ABRs on an individual basis and identify the nature of neural disruption. About 5-15 % of adult patients complain of understanding speech in the presence of noise, despite the presence of normal hearing thresholds (Hind et al.,

2011; Kumar, Amen, & Roy, 2007). These symptoms are similar to that of APD children. Currently, it is not clear whether these adults with listening difficulties have atypical axonal or synaptic processing. The Ponton model may help to identify the nature of disruption in these population.

There is evidence that mutation of a gene can affect auditory processing in humans (e.g. ROBO1 gene, Lamminmäki, Massinen, Nopola-Hemmi, Kere, & Hari, (2012); $KCNC3^{R420H}$ gene, Middlebrooks et al., (2013). Some studies have demonstrated abnormal auditory processing in family members of affected individuals with language-learning disorders (Addis et al., 2010; Neuhoff et al., 2012). Thus, the Ponton et al. model of axonal and synaptic transmission can be used in genetic linkage studies of auditory and language-learning related disorders. The model may help in identifying individuals with axonal and synaptic difficulties. These kinds of studies may assist in identifying those who are at risk, allowing for appropriate interventions at a younger age. It also helps in understanding the primary pathway leading to the disorder/deficits and improving the understanding of the neurobiological bases of these disorders/deficits.

The perception of spectral shape is crucial for recognizing speech in quiet and in noise. The spectral ripple discrimination task in Chapter 5 demonstrated that children with sAPD can resolve fewer ripples per octave, indicating a deficit in spectral shape perception. All the listeners in this study were able to complete the test. Hence, this test may be an ideal tool to examine spectral shape perception in a clinical population. Since the perception of spectral ripple depends on resolving individual frequencies, this test may also provide information regarding the frequency resolution in cochlear implant users.

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Appendices

Appendix A: Approval for Research Involving Human Participants

Western Research

Research Ethics

Use of Human Participants - Ethics Approval Notice

Principal Investigator: Dr. Prudence Allen
File Number:102932
Review Level: Delegated
Approved Local Adult Participants:0
Approved Local Minor Participants:480
Protocol Title: Auditory function and acoustic signal encoding in school-aged children
Department & Institution: Health Sciences\Communication Sciences & Disorders,Western University
Sponsor:
Ethics Approval Date: March 28, 2013 **Expiry Date:**December 30, 2014
Documents Reviewed & Approved & Documents Received for Information:

Document Name	Comments	Version Date
Letter of Information	102932 Letter of Information	
Assent	102932 Assent letter	

This is to notify you that The University of Western Ontario Research Ethics Board for Health Sciences Research Involving Human Subjects (HSREB) which is organized and operates according to the Tri-Council Policy Statement: Ethical Conduct of Research Involving Humans and the Health Canada/ICH Good Clinical Practice Practices: Consolidated Guidelines; and the applicable laws and regulations of Ontario has reviewed and granted approval to the above referenced revision(s) or amendment(s) on the approval date noted above. The membership of this REB also complies with the membership requirements for REB's as defined in Division 5 of the Food and Drug Regulations.

The ethics approval for this study shall remain valid until the expiry date noted above assuming timely and acceptable responses to the HSREB's periodic requests for surveillance and monitoring information. If you require an updated approval notice prior to that time you must request it using the University of Western Ontario Updated Approval Request Form.

Members of the HSREB who are named as investigators in research studies, or declare a conflict of interest, do not participate in discussion related to, nor vote on, such studies when they are presented to the HSREB.

The Chair of the HSREB is Dr. Joseph Gilbert. The HSREB is registered with the U.S. Department of Health & Human Services under the IRB registration number IRB 00000940.

Ethics Officer to Contact for Further Information

This is an official document. Please retain the original in your files.

Office of Research Ethics

The University of Western Ontario

Western

Use of Human Subjects - Ethics Approval Notice

Principal Investigator: Dr. P. Allen

Review Number: 16505E **Review Level:** Expedited

Review Date: September 30, 2009

Protocol Title: Testing the efficacy and efficiency of an improved comprehensive test battery for the assessment of auditory processing disorders.

Department and Institution: Health & Rehabilitation Sciences, University of Western Ontario

Sponsor: Ontario Research Fund

Ethics Approval Date: October 27, 2009 **Expiry Date:** December 31, 2014

Documents Reviewed and Approved: UWO Protocol, Letter of Information and Consent (LHSC Victoria Hospital), Letter of Information and Consent (UWO National Centre for Audiology)

Documents Received for Information:

This is to notify you that The University of Western Ontario Research Ethics Board for Health Sciences Research Involving Human Subjects (HSREB) which is organized and operates according to the Tri-Council Policy Statement: Ethical Conduct of Research Involving Humans and the Health Canada/ICH Good Clinical Practice Practices: Consolidated Guidelines; and the applicable laws and regulations of Ontario has reviewed and granted approval to the above referenced study on the approval date noted above. The membership of this REB also complies with the membership requirements for REB's as defined in Division 5 of the Food and Drug Regulations.

The ethics approval for this study shall remain valid until the expiry date noted above assuming timely and acceptable responses to the HSREB's periodic requests for surveillance and monitoring information. If you require an updated approval notice prior to that time you must request it using the UWO Updated Approval Request Form.

During the course of the research, no deviations from, or changes to, the protocol or consent form may be initiated without prior written approval from the HSREB except when necessary to eliminate immediate hazards to the subject or when the change(s) involve only logistical or administrative aspects of the study (e.g. change of monitor, telephone number). Expedited review of minor change(s) in ongoing studies will be considered. Subjects must receive a copy of the signed information/consent documentation.

Investigators must promptly also report to the HSREB:

a) changes increasing the risk to the participant(s) and/or affecting significantly the conduct of the study;
b) all adverse and unexpected experiences or events that are both serious and unexpected;
c) new information that may adversely affect the safety of the subjects or the conduct of the study.

If these changes/adverse events require a change to the information/consent documentation, and/or recruitment advertisement, the newly revised information/consent documentation, and/or advertisement, must be submitted to this office for approval.

Members of the HSREB who are named as investigators in research studies, or declare a conflict of interest, do not participate in discussion related to, nor vote on, such studies when they are presented to the HSREB.

Chair of HSREB: Dr. Joseph Gilbert

Ethics Officer to Contact for Further Information

This is an official document. Please retain the original in your files.

cc: ORE File
LHRI

LAWSON HEALTH RESEARCH INSTITUTE

FINAL APPROVAL NOTICE

RESEARCH OFFICE REVIEW NO.: R-09-503

PROJECT TITLE: Testing the efficacy and efficiency of an improved comprehensive test battery for the assessment of auditory processing disorders.

PRINCIPAL INVESTIGATOR: Dr. P Allen

DATE OF REVIEW BY CRIC: November 18, 2010

Health Sciences REB#: 16505E

Please be advised that the above project was reviewed by the Clinical Research Impact Committee and the project:

Was Approved

PLEASE INFORM THE APPROPRIATE NURSING UNITS, LABORATORIES, ETC. BEFORE STARTING THIS PROTOCOL. THE RESEARCH OFFICE NUMBER MUST BE USED WHEN COMMUNICATING WITH THESE AREAS.

V.P. Research
Lawson Health Research Institute

All future correspondence concerning this study should include the Research Office Review

cc: Administration

Western Research

Research Ethics

Western University Health Science Research Ethics Board
HSREB Annual Continuing Ethics Approval Notice

Date: October 10, 2016
Principal Investigator: Dr. Prudence Allen
Department & Institution: Health Sciences\Communication Sciences & Disorders,Western University

Review Type: Delegated
HSREB File Number: 6551
Study Title: Testing the efficacy and efficiency of an improved comprehensive test battery for the assessment of auditory processing disorders.
Sponsor: Ontario Research fund

HSREB Renewal Due Date & HSREB Expiry Date:
Renewal Due -2017/09/30
Expiry Date -2017/10/27

The Western University Health Science Research Ethics Board (HSREB) has reviewed the Continuing Ethics Review (CER) Form and is re-issuing approval for the above noted study.

The Western University HSREB operates in compliance with the Tri-Council Policy Statement Ethical Conduct for Research Involving Humans (TCPS2), the International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use Guideline for Good Clinical Practice (ICH E6 R1), the Ontario Freedom of Information and Protection of Privacy Act (FIPPA, 1990), the Ontario Personal Health Information Protection Act (PHIPA, 2004), Part 4 of the Natural Health Product Regulations, Health Canada Medical Device Regulations and Part C, Division 5, of the Food and Drug Regulations of Health Canada.

Members of the HSREB who are named as Investigators in research studies do not participate in discussions related to, nor vote on such studies when they are presented to the REB.

The HSREB is registered with the U.S. Department of Health & Human Services under the IRB registration number IRB 00000940.

Appendix B: Letter of Information and Consent

Western
Health Sciences

Letter of Information and Consent
H.A. Leeper Speech and Hearing Clinic, UWO

Study: Comprehensive assessment of auditory processing (listening) abilities

Principal Investigator: Prudence Allen, Ph.D.
Co-Investigator: Vijay Parsa, Ph.D.
Co-Investigator: David Purcell, Ph.D.
Research Associate: Chris Allan, M.Sc.
Place of testing:

General Information:

The pronouns "you" and "your" should be read as referring to the participant rather than the parent/guardian/next-of-kin who is signing the consent form for the participant.

This letter contains information to help you decide whether or not to participate in this research. It is important for you to know why the data is being collected and the research is being conducted and what we are asking you to agree to. Please take time to read this carefully and feel free to ask questions if anything is unclear. If you have any questions let the receptionist know and someone will speak with you directly.

During the course of your treatment in the Audiology Clinic at the UWO H.A. Leeper Speech and Hearing Clinic, you will have a number of tests and treatments done as part of your regular care and a great deal of information about your past and current medical history will also be collected. This is all done as part of your standard care to help us determine how well you can hear and listen and how best to treat you if necessary.

Description and Purpose of the Research Project:

The staff in the Audiology Clinic at the UWO H.A. Leeper Speech and Hearing Clinic are engaged in ongoing research to better understand hearing and auditory processing difficulties and how best to treat these problems. We are asking for your permission to collect and use the information from your health record, for research purposes. All patients who attend our clinic will be asked to participate. One objective of this project is to investigate, in children and adults, the usefulness of a computer system in the assessment of various auditory skills such as the presence of a very brief sound or the ability to distinguish a change in the pitch, loudness, or quality of a sound. This hearing measurement device is available in a laptop as well as a handheld version and has been developed with new digital and wireless technology that has only recently become available. The auditory skills that can be assessed by these devices are ones that up until now have only been tested in research laboratories, like the University of Western Ontario Child Hearing Research Lab, because the older equipment was too large and expensive to operate in hospitals or audiology clinics. If this new device is proven to accurately measure auditory skills then, it is the intention of the researchers to commercialize the device by establishing a company for the manufacturing and sale of the device or license the software to other companies, so that the opportunity to better assess and treat hearing disorders can be moved into audiology clinics.

Protection of Your Privacy:

If you agree to participate, data relating to your health history and current care will be copied from your clinic records to a separate research database. All identifying information such as your name and address will be removed. The information in the research database will be identified by a unique code number that will link the test results in the research record. The master list that contains the link to the code number and your name and other identifying information will be kept in a very secure location at

the University of Western Ontario under the control of the Director of the research. The research database will be owned by the University of Western Ontario National Centre for Audiology and it will be stored in a secure location on the University of Western Ontario National Centre for Audiology computer system. The data in the research database will be kept as it is being collected and analyzed. Once the project is completed, all information containing participants' names and unique codes, including backup DVD's and paper documents, will be deleted and overwritten or destroyed by shredding.

If the results of the research are published or presented at scientific meetings, your name will not be used and no information that discloses your identity will be released or published without your explicit consent. Only group data will be reported and if individual data is reported, references will be made to the age group only.

Participation in the Study:

Participation in this study is voluntary. You may refuse to participate, or refuse to allow data to go to the research the database at any time with no effect on your future care.

Information that has already been transferred to the research database can be withdrawn from the study up until the data collection process is complete. At that point, all personal information will have been destroyed, leaving the unique code number and linked data anonymous so it will no longer be possible to identify and remove your data from the study. If you wish to stop your participation just let the staff at the clinic know.

Regardless of your decision to participate you can still receive continuing care through this clinic. You do not waive any legal rights by signing the consent form.

The database will also help us to identify those clients who may be eligible to participate in future research projects that involve more that just an analysis of existing data. In the

future you may be approached to participate in other research projects in the clinic. In those instances you will be given detailed information describing the project and you will have the opportunity to decide at that time, whether or not you want to participate in the new project.

Benefits and Risks:

You will not be compensated for your participation in this database.

The only known risk to your participation in this study is the possibility that, because the research database is linked to our clinical database, someone may be able to identify you. However the research database is secured in the same manner as our clinical records and access is limited to authorized personnel only.

You will not benefit directly from participation in this research however the results of our research may help other clients in the future who suffer from problems similar to yours.

Contacts for Questions about the Research Project:

Representatives of The University of Western Ontario Health Sciences Research Ethics Board may contact you or require access to your study-related records to monitor the conduct of the research.

If you have any questions about your ongoing follow-up in the Audiology Clinic at the UWO H.A. Leeper Speech and Hearing Clinic you can contact Francis Richert in the Audiology Clinic at !

If you have any questions about your rights as a research participant or the conduct of the study you may contact Dr. David Hill, Scientific Director, Lawson Health Research Institute at

This letter is for you to keep.
You will also be given a copy of the consent form if you agree to sign it.

Prudence Allen
Associate Professor

CONSENT FORM

Study: Comprehensive assessment of auditory processing (listening) abilities

Principal Investigator: Dr. Prudence Allen, Associate Professor
National Centre for Audiology
University of Western Ontario,

I have read the Letter of Information, have had the nature of the study explained to me. All questions have been answered to my satisfaction.

☐ I agree to participate OR ☐ I do not agree to participate

Name of participant (Print)

Signature of participant

Date

Name of legally authorized representative (Print)

Signature of legally authorized representative

Date

Name of person obtaining consent (Print)

Signature of person obtaining consent

Date

Letter of Information and Consent

Study: Auditory function and acoustic signal encoding in school-aged children.

Principal Investigator: Prudence Allen, Ph.D.
Research Associates: Chris Allan, Ph.D.
Udit Saxena, M.Sc.

Place of testing: Child Hearing Research Laboratory
National Centre for audiology, Elborn College

Dear Potential Participant,

The pronouns "you" and "your" should be read as referring to the participant rather than the parent/guardian/next-of-kin who is signing the consent form for the participant.

Normal hearing and good auditory processing (listening) abilities are necessary for children to experience success in school. Recent studies have shown that some children experiencing school failure have Auditory Processing Disorders. Auditory processing disorders have also been found in children that experience difficulty learning to read and/or have delays in their speech development. You are being invited to participate in a study of hearing and listening being conducted by Western's Child Hearing Research Laboratory. This study is investigating the usefulness of various listening tests, such as the ability to distinguish a change in pitch, loudness or quality of a sound. The performance of normal or typically developing children will be compared to adults and children with auditory processing disorders.

Participants Initials _____

The objective of this project is to investigate hearing and listening abilities in children so that assessment tools can be developed for early and accurate identification of children with listening problems. In this study we plan to compare the performance of typically developing children with that of adults, and children with known Auditory Processing Disorders. For both groups of children, participants between the ages of 4 to 17 years old will be included in this study.

Ear and hearing measurements

If you agree to participate, you will sit comfortably with the researchers in a quiet room, listening to different sounds while wearing earphones. The listening tasks are completed by listening to sounds while watching a regular size computer screen or handheld computer screen. You will be presented with child-friendly computer graphics and with each graphic appearance on the screen you will hear a sound. You will be asked to identify which graphic on the computer screen best corresponds to what was just heard. The responses will be recorded by the computer.

We will also be making some measurements of your ears. During these tests you will wear earplugs and you will hear a variety of different sounds. Some of the sounds will be loud but they are not harmful. You can relax during these tests because you are not required to do anything other than remain still. Each test, individually, only takes a few minutes to complete but in total there is about 1.5 hours of testing to be completed.

The test session will be arranged at your convenience.

To help promote attention and focus on the task, breaks will be taken at regular intervals and whenever necessary or requested. Most children complete the testing in one session but testing can occur over more than one session if that is more convenient for you.

Participants Initials _____

Study risks

This study will involve no known risk to you. The sounds you will be hearing are usually as loud as conversational speech and will never be so loud as to be uncomfortable or damaging. You will experience little or no discomfort during this study. At times long term use of earphones can become uncomfortable however all attempts will be made to avoid this kind of discomfort. Rest breaks will be provided at regular intervals as well as upon request to prevent fatigue or distraction due to hunger or thirst.

Privacy and confidentiality

The information gathered during this study will remain confidential at all times. Information collected at the program on the computers will be password protected to ensure it remains confidential at all times. No individual listener will be identified in any analysis or publication, however, if it is determined that you may have hearing problems that require further attention you will be notified. During the study, a 4 character unique ID code will be used to reference each participant, rather than their full names. ID codes and corresponding full names of participants will be kept in a journal and locked in a cabinet at Western. Only the local research team may have access to the cabinet. The Representatives of the University of Western Ontario Health Sciences Research Ethics Board may contact you or require access to your study-related records to monitor the conduct of the research. The data and personal information will be kept as it is being collected and analyzed. Once the project is completed, all information containing participants' names and ID codes, including backup DVD's and paper documents, will be deleted and overwritten or destroyed by shredding. Upon publication, groupdata will be reported. If individual data is reported, references will be made to the age group only.

Participants Initials _____

Voluntary participation

Participation in the study is voluntary. You may refuse to participate, refuse to answer any questions or withdraw from the study at any time. You can withdraw your data from inclusion in the study up until the data collection process for the study is complete. At that point, all personal information will have been destroyed, leaving the IDs and linked data anonymous so it will no longer be possible to identify and remove your data from the study.

Contact information

This letter is yours to keep. If you agree to participate please sign the attached form. You will receive a copy of the signed consent form. If you have questions at any time you may contact me at the above address or at the following phone number: extension
You can also speak to the research audiologist, Chris Allan at extension if you have any questions or concerns about the study. If you have any questions about the conduct of this study or your rights as a research subject you may contact the Office of Research Ethics, The University of Western Ontario, or email at:
Thank you for your time and consideration.

Sincerely,

Dr. Prudence Allen, Ph.D.

Assistant Professor

Auditory function and acoustic signal encoding in school-aged children

CONSENT FORM

I have read the accompanying Letter of Information. The nature of the study has been explained to me and I agree to allow my child, _____, to participate in this study.

All questions have been answered to my satisfaction.

Date: _____

Parent or Guardian's name: _____

Parent or Guardian's Signature: _____

Child's Age: _____years _____months

Do you have concerns about your child's development and/or academic performance? ❑ YES ❑ NO

Name of person obtaining informed consent:_____

Signature of person obtaining informed consent:_____

2013-01_v1

Western
Health Sciences

Study: **Auditory function and acoustic signal encoding in school-aged children**

Principal Investigator: Prudence Allen, Ph.D.
Research Associates: Chris Allan, M.Sc.
Udit Saxena, M.Sc.
Moumita Choudhury, M.Sc.

Place of testing: Child Hearing Research Laboratory
National Centre for Audiology, Elborn College

Assent for children ages 7 to 13 years

Why are you here?

This study is to help learn more about children's hearing and listening abilities and the kinds of tests that can be used to discover listening problems. Children with and without listening problems are being asked to be in the study. Dr. Allen and her research team are asking you to be part of this study so that they can learn more about how children listen and if the tests can help show who has listening problems.

Why are they doing this study?

They want to see how well you listen and if you are able to understand someone when they talk to you like when your teacher explains something or asks a question.

What will happen to you?

If you agree to be in the study you will be asked to do some hearing tests after school while you are waiting for your parents. This is what will happen when you see someone from the research team:

1. You will have your hearing tested. You wear earphones and raise your hand when you hear soft sounds. This will only take a few minutes.
2. Some measurements will be made of your ears. To make these measurements an earplug will be used in your ear. You will not have to do anything but you will be asked to sit very still and not move your head or talk.
3. You will play some listening games on the computer. When you play these easy games you will be wearing earphones so you can hear the sounds. The games do not take long, only a few minutes, but you may not want to finish all of them on one day.

Will the study hurt?

You will not be wearing the earphones or earplugs long enough for them to hurt your ears. Some of the sounds used for the ear measurements are loud but they will not hurt.

Will you be a better listener if you get in the study?

This study won't make you a better or worse listener. The research team hopes that this study will help them understand how children listen so that in the future they can easily find which children will have listening problems and then be able to help teach them to be better listeners.

What if you have any questions?

You can ask questions any time, now or later. You can talk to anyone on the research team, your family or someone else.

Do you have to be in the study?

You don't have to be in the study. No one will be mad at you if you don't want to participate. If you don't want to be in the study just say so. Even if you say yes now, you can change your mind later. It's up to you.

☐ Yes, I want to participate in this study

_____
Print name of child

_____ _____ _____
Signature of child Age Date

_____ _____
Signature of person obtaining consent Date

Study: **Testing the efficacy and efficiency of an improved comprehensive test battery for the assessment of auditory processing disorders.**

Principal Investigator: Prudence Allen, Ph.D.
Co-Investigators: David Purcell, Ph.D.
Vijay Parsa, Ph.D.
Research Associates: Chris Allan, M.Sc.
Udit Saxena, M.Sc.

Place of testing: National Centre for Audiology, UWO
London Health Sciences Centre Victoria Hospital Campus

Assent for children

Why you are here?

This study is to help learn more about children with listening problems and the kinds of tests that can be used to discover those problems. Children with and without listening problems are being asked to be in the study. Dr. Allen and her research team are asking you to be part of this study so that they can learn more about how children listen and if the tests can help show who has listening problems.

Why are they doing this study?

They want to see how well you listen and if you are able to understand someone when they talk to you like when your teacher explains something or asks a question.

What will happen to you?

If you agree to be in the study you will be asked to visit the Child Hearing Research Laboratory once for some hearing tests. This is what will happen when you come for your visit:

1. You will have your hearing tested. You wear earphones and raise your hand when you hear soft sounds and repeat some words that are said to you. This will only take a few minutes.
2. Some measurements will be made of your ears. To make these measurements an earplug will be used in your ear. You will not have to do anything but you will be asked to sit very still and not move your head or talk.

Will the study hurt?

You will not be wearing the earphones or earplugs long enough for them to hurt your ears. Some of the sounds used for the ear measurements are loud but they will not hurt.

Will you be a better listener if you get in the study?

This study won't make you a better or worse listener. The research team hopes that this study will help them understand how children listen so that in the future they can easily find which children will have listening problems and then be able to help teach them to be better listeners.

What if you have any questions?

You can ask questions any time, now or later. You can talk to anyone on the research team, your family or someone else.

Do you have to be in the study?

You don't have to be in the study. No one will be mad at you if you don't want to participate. If you don't want to be in the study just say so. Even if you say yes now, you can change your mind later. It's up to you.

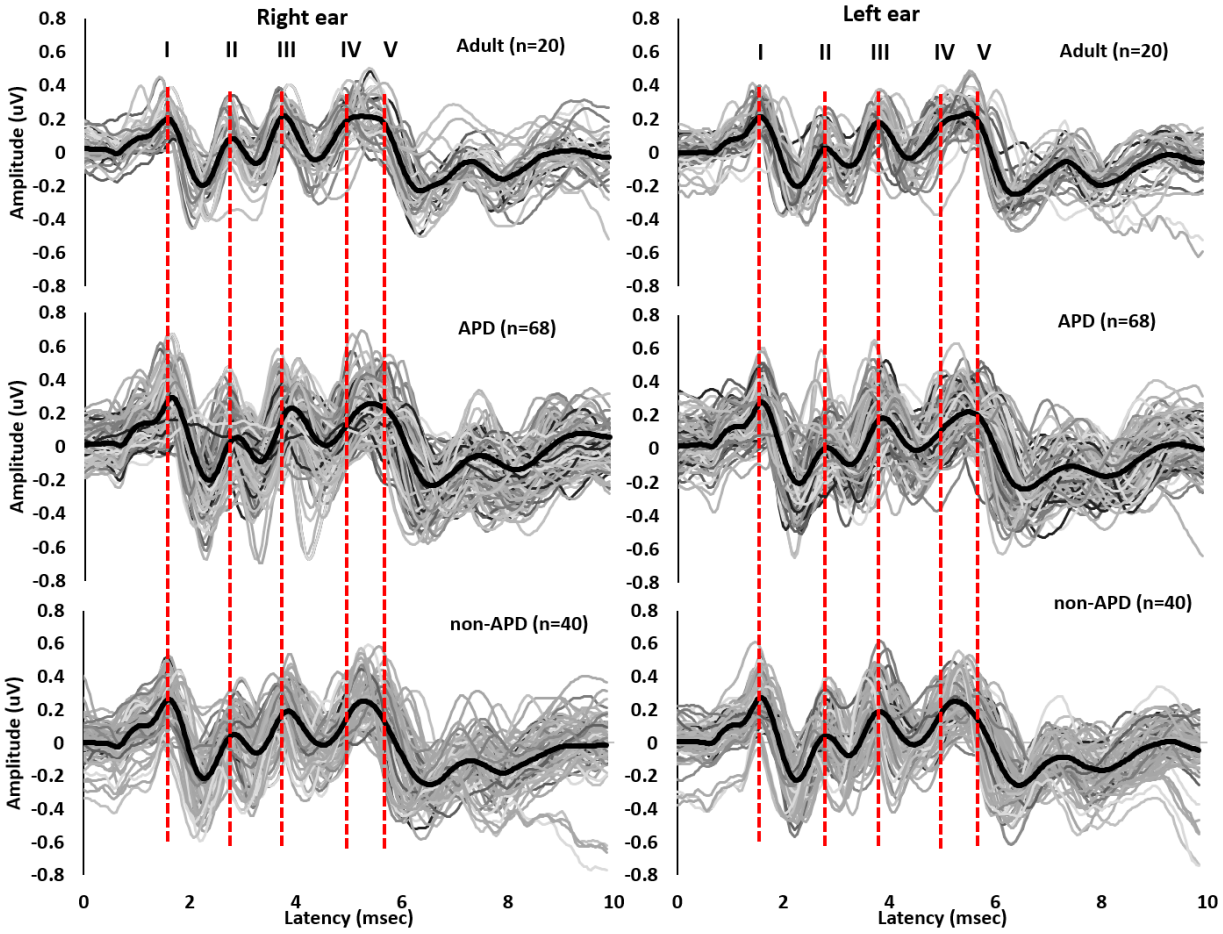
Yes, I want to participate in this study

_____
Print name of child

_____ _____ _____
Signature of child Age Date

_____ _____
Signature of person obtaining consent Date

Appendix C: Click-ABR waveforms of adults, children diagnosed as APD and non-APD.



Auditory brainstem response to a click stimulus. Individual waveforms (thin grey lines) and grand average waveforms (thick black line) for adults, children diagnosed as APD and non-APD for right and left ear.

Appendix D: Click-ABR mean (and SDs) absolute and interwave latencies.

Click-ABR Mean latencies (and SDs) for absolute waves for the adults, children diagnosed as APD and non-APD.

Adults (n=20)	I	II	III	IV	V
Right ear	1.56 (0.10)	2.77 (0.11)	3.71 (0.11)	4.89 (0.11)	5.53 (0.08)
Left ear	1.55 (0.11)	2.76 (0.15)	3.74 (0.14)	4.92 (0.11)	5.55 (0.10)
APD (n=68)					
Right ear	1.61 (0.13)	2.80 (0.14)	3.84 (0.16)	5.02 (0.20)	5.74 (0.22)
Left ear	1.60 (0.14)	2.78 (0.16)	3.86 (0.18)	5.01 (0.26)	5.74 (0.20)
non-APD (n=40)					
Right ear	1.60 (0.10)	2.77 (0.18)	3.81 (0.17)	4.95 (0.29)	5.69 (0.25)
Left ear	1.58 (0.09)	2.79 (0.15)	3.85 (0.16)	4.97 (0.20)	5.72 (0.22)

Click-ABR Mean latencies (and SDs) for interwave intervals for the adults, children diagnosed as APD and non-APD.

Adults (n=20)	**I-III**	**III-V**	**I-II**	**II-III**	**III-IV**	**IV-V**
Right ear	2.15 (0.12)	1.82 (0.11)	1.20 (0.09)	0.94 (0.11)	1.17 (0.09)	0.66 (0.11)
Left ear	2.19 (0.14)	1.80 (0.14)	1.21 (0.10)	0.98 (0.10)	1.19 (0.12)	0.62 (0.10)
APD (n=68)						
Right ear	2.23 (0.17)	1.89 (0.17)	1.19 (0.15)	1.03 (0.09)	1.15 (0.18)	0.82 (0.18)
Left ear	2.26 (0.18)	1.87 (0.17)	1.17 (0.13)	1.08 (0.10)	1.16 (0.18)	0.78 (0.18)
Non-APD (n=40)						
Right ear	2.21	1.87	1.17	1.03	1.10	0.80

	(0.20)	(0.18)	(0.21)	(0.11)	(0.19)	(0.18)
Left ear	2.26	1.87	1.21	1.06	1.14	0.80
	(0.18)	(0.19)	(0.15)	(0.09)	(0.16)	(0.18)

Appendix E: Mean (and SDs) spectral ripple discrimination thresholds for different age groups.

Mean spectral ripple discrimination (SRD) thresholds for different groups.

	Age range (mean age)	Mean SRD threshold (SD)
Young Typically developing children	5.1 – 7.9 years (6.49 years)	1.49 (1.06)
Older Typically developing children	8.1 – 13.9 years (10.78 years)	3.85 (1.60)
Children with sAPD	6.9 – 10 years (8.7 years)	1.80 (1.09)
Adults	19 -35 years (24.28 years)	5.05 (1.44)

Appendix F: Additional analysis for chapter 3.

For all participants, slopes were calculated for SNR E and SNR FS conditions from -12 dB to +12 dB SNR. A mixed ANOVA was performed on slopes with two within-subject factors (SNR E and SNR FS) and one between subject factors (group). Slopes varied by group [$F(2, 50) = 9.51$, $p < 0.001$, $\eta^2_p = 0.276$] and by temporal structure [$F(1, 50) = 1563.03$, $p < 0.001$, $\eta^2_p = 0.96$]. The three-way interaction between slopes of SNR E and SNR FS and group was significant [$F(8, 200) = 3.26$, $p = 0.002$ $\eta^2_p = 0.11$]. The Bonferroni post-hoc analysis ($p < 0.01$) revealed that at 0 dB SNR E condition, slopes were significantly different between adults and children with sAPD ($p < 0.001$). This may indicate that children with sAPD showed significant improvement in speech recognition scores as the SNR of the fine structure was increased in 6 dB steps. Whereas adults did not show significant change in speech recognition scores as the SNR of the fine structure was improved.

Curriculum Vitae

Name: Sangamanatha Ankmnal Veeranna

Post-secondary Education and Degrees:

Bangalore University
Bangalore, Karnataka, India
2003-2007 B.A.S.L.P

Mangalore University
Mangalore, Karnataka, India
2007-2009 M.A.S.L.P

The University of Western Ontario
London, Ontario, Canada
2011-2016 Ph.D.

Related Work Experience

Teaching Assistant
The University of Western Ontario
2011-2015

Assistant Professor
Department of Speech and Hearing
Kasturba Medical College (A Unit of MANIPAL University)
Mangalore, Karnataka, India
2009-2011

Publications:

1. Kumar A.U & **Sangamanatha A.V**. (2011). Temporal processing across different age groups. *Journal of American Academy of Audiology*, 22 (1), 5-12.
2. Pitchai Muthu Arivudai Nambi, Subramaniam Manoharan, Jayashree Sunil Bhat & **Sangamanatha A.V** (2012). Perception of Spectrally Shifted Speech: Implications for Cochlear Implants. *International Advanced Otology*, 7 (3), 379-384.
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