

Cortical Auditory Evoked Potentials of Children with Normal Hearing Following a Short
Auditory Training with a Remote Microphone System

By

Carlos R. Benítez-Barrera

Dissertation

Submitted to the Faculty of the

Graduate School of Vanderbilt University

in partial fulfillment of the requirements

for the degree of

DOCTOR OF PHILOSOPHY

in

Hearing and Speech Sciences

May 31, 2020

Nashville, Tennessee

Approved:

Anne Marie Tharpe, Ph.D.

Alexandra Key, Ph.D.

Todd Ricketts, Ph.D.

Troy Hackett, Ph.D.

Micah Murray, Ph.D.

A D. José Barrera Serrano, quien me
enseñó que la pasión por aprender es el único secreto
de una vida con sentido.
Nunca te olvidaré, abuelo.

For Mr. José Barrera-Serrano, who taught me
that passion for learning is the only secret
of a meaningful life.
I will never forget you, grandpa.

ACKNOWLEDGEMENTS

I would like to extend my sincere gratitude to all individuals who have helped me in this research endeavor. Without their active guidance, help, cooperation, and encouragement, I certainly would not have advanced this project. Most notably, I would like to thank my advisor Dr. Anne Marie Tharpe, her guidance and mentorship throughout my doctoral studies (including my dissertation) were a vital component of my development as a researcher. Only I know the support and encouragement she provided during all these years. There are no words to express my gratitude to her. I also extend particular thanks to the members of my dissertation committee, Drs. Alexandra Key, Todd Ricketts, Troy Hackett, and Micah Murray. Their ideas, insights, and constructive feedback during the conception of the study enhanced my thought process. Moreover, their willingness to assist me during the preparation stage was key to the successful implementation of this study. A substantial part of this project belongs to them. This project would not have been possible without the financial support from the American Academy of Audiology Research in Hearing and Balance Grant and Phonak A.G Research Grant. Support of this work was also provided by Annalise Valle, Fiona Higgins, Ling Zhong, Delphanie Wu, Tiffany Fowler, and Sydnie Bailey who assisted with data collection and data analyses.

Additionally, I am grateful to all of those with whom I have had the pleasure to work during my time at Vanderbilt University. I am particularly thankful to Drs. Benjamin Hornsby and Tiffany Woynaroski who allowed me to develop research projects with them, and Dr. Daniel Ashmead who allowed me to serve as his teaching assistant for his statistics classes. Their mentorship and guidance were critical for my development as a scholar and mentor. Special thanks to all members of the Auditory Development Laboratory during my time there (Drs. Samantha Gustafson, Dana Kan, Gina Anglely, Uma Soman, Adrienne Roman, Emily Thompson,

and Hilary Davis); they were incredibly supportive throughout my Ph.D. program. I hope they learned from me as much as I learned from all of them. I also offer a deep “thank you” to all my fellow Ph.D. students with special mention to Jean Paul Noel, Travis Moore, Pumpki Sue, Anna Diedesch, Alison Hessling, and Natalie Covington; they were each an incredible source of support.

Most importantly, I express sincere gratitude to my family and close friends who supported me right from the start of my emerging idea of completing a Ph.D. in a place far away from home. To my mother, Amparo Barrera-Gómez, I am forever grateful. Her support of my choice to move from Spain across the Atlantic Ocean to pursue my education was unconditional. I also want to thank my wife, Laura Obra-Garrido. She suffered with me the uncertainties and sometimes frustrations of being a Ph.D. student. I thank her for her patience and unconditional support. Lastly, I want to express my gratitude to my grandfather, José Barrera-Serrano, who taught me to enjoy the process of learning. His lesson allowed me to value my progress in the Ph.D. program based on my learning achievements as opposed to other merit based standards. This was especially important during times in which the finish line seemed to be very far away. I will carry this life lesson with me during my entire academic career. *Muchas gracias, abuelo.*

TABLE OF CONTENTS

	Page
DEDICATION.....	ii
ACKNOWLEDGMENTS	iii
LIST OF TABLES.....	vii
LIST OF FIGURES	viii
Chapter	
I. INTRODUCTION.....	1
Development of Speech Perception Skills in Children	2
Neural Foundations for Speech Perception Development in Children.....	4
Sound and Speech Processing in the Auditory System.....	6
Cortical Auditory Evoked Potentials (CAEPs) as an Index of Speech Perception at the Neural Level.....	10
Plasticity in the Auditory System	13
Sensitive Periods for Auditory Processing.....	16
Auditory Experience Determines Neural and Behavioral Speech Processing Skills	18
Research Aims and Research Hypothesis	24
II. METHODS.....	26
Participants	26
Study Equipment and Materials	28
Pre-Experimental Materials and Procedures	29
Study Procedures.....	30
Data Processing and Analyses.....	34
III. RESULTS.....	38
Training Effects on CAEPs	38
Training Effects on Behavioral Measures of Speech Perception in Noise.....	43
Relationship Between Neural and Behavioral Indices of Speech Perception in Noise.....	44

IV. DISCUSSION.....	46
Aim 1 – Training Effects on CAEPs	47
Aim 2 – Training Effects on Behavioral Measures of Speech Perception in Noise.....	50
Aim 3 – Relationship Between Neural and Behavioral Indices of Speech Perception in Noise.....	51
Clinical Implications.....	52
Future Directions	53
Limitations.....	55
Conclusions	57
REFERENCES	58

LIST OF TABLES

Table		Page
1.	Study aims and research hypotheses	25
2.	Demographic information across studies	27
3.	CAEP mean amplitudes for quiet, pre-training and post-training conditions	42

LIST OF FIGURES

Figure		Page
1.	Study procedures diagram	32
2.	Modulations in response strength assessed through global field power waveforms	39
3.	Topographic maps corresponding to pre- and post- training conditions.....	41
4.	CAEP grand average waveforms for each study group	42
5.	Interaction effect in the pre- and post-training conditions	43
6.	Speech perception in noise scores pre- and post-training for each study group.....	44

CHAPTER I

INTRODUCTION

Encoding speech in the presence of background noise is important for assuring children's access to language in academic and non-academic settings. It is well documented that children who struggle with listening in noise (e.g., children with hearing difficulties) are also at risk for academic and social deficits (Crandell, 1993; Gifford, Olund, & DeJong, 2011; Pittman, Lewis, Hoover, & Stelmachowicz, 1999). Efforts have been made to improve speech-perception-in-noise skills for children to ensure they have adequate access to speech in learning environments. For example, the use of hearing technology and computer-based auditory training have been suggested as possible interventions to improve children's listening in noise (Hayes, Warrier, Nicol, Zecker, & Kraus, 2003; Kraus & Chandrasekaran, 2010; Rayes, Al-Malky, & Vickers, 2019).

Assistive listening devices such as remote microphone systems (RM systems) have been traditionally used in classroom settings to overcome the negative effects of background noise on children's speech perception. RM systems, as the contemporary version of frequency-modulated or FM systems, are a type of assistive listening device in which a speaker of interest (e.g., the teacher) wears a microphone transmitter and the listener (typically a child with hearing loss) wears a receiver. The signal captured by the microphone (e.g., teacher's voice) is transmitted wirelessly to the receiver. This arrangement allows individuals to have access to speech from a distance and typically improves the signal-to-noise ratio (SNR) for the listener, thus, facilitating speech perception in noise.

More recently, RM systems have been shown to improve not only speech perception

when used at school (Bertachini et al., 2015), but also access and attention to language (Benítez-Barrera, Angley, & Tharpe, 2018; Benítez-Barrera, Thompson, Angley, Woynaroski, & Tharpe, 2019; Thompson, Benítez-Barrera, Angley, Woynaroski, & Tharpe, 2020) and development of language skills when used by children with hearing loss in their homes (Curran, Walker, Roush, & Spratford, 2019). Although evidence for behavioral effects of improved SNRs for children is building, it is still unknown whether exposure to improved SNRs will have a positive impact on anatomical and functional changes in the neural auditory system of children. The present project targets this knowledge gap in the research literature by investigating whether a brief speech-in-noise training with an RM system induces short-term changes in cortical auditory evoked potentials (CAEPs) of children with normal hearing and whether said training has an impact on children's ability to perceive speech in the presence of background noise.

The development of speech perception skills and neural foundations underlying speech perception deficits during childhood are reviewed in the following sections. Then, CAEPs, an available tool to measure neural speech processing, are described in detail. The concept of sensitive periods and how they determine the acquisition of speech-perception-in-noise skills and timing of intervention in children is also introduced. Finally, possible factors that should be considered in the acquisition of speech-perception-in-noise skills (e.g., impoverished versus enhanced auditory experience) and the effects that varying SNRs have on ongoing speech processing at the neural level are discussed. This review of the literature establishes the basis for the present study including the research aims and research hypotheses.

Development of Speech Perception Skills in Children

Basic perceptual capacities of the auditory system develop slowly and continuously throughout childhood (Schneider, Trehub, & Bull, 1979). Among these basic capacities, are pure tone detection (Bargones & Werner, 1994; Elliott & Katz, 1980; Nozza & Wilson, 1984; Tharpe & Ashmead, 2001; Trehub, Schneider, & Endman, 1980), temporal processing (Davis & McCroskey, 1980; Irwin, Ball, Kay, Stillman, & Rosser, 1985), and frequency resolution (Allen, Wightman, Kistler, & Dolan, 1989; Irwin, Stillman, & Schade, 1986). These skills are necessary to encode complex sounds, such as speech and speech in noise (Holt & Lotto, 2008). As a result, the ability to encode speech in the presence of background noise also develops and improves with age (Boothroyd, 1970, 1997).

Infants as young as six months demonstrate the ability to discriminate phonemes related to their native and non-native language (Kuhl, 1992), and systematic improvements in speech perception performance occur as children have experience with sound and mature to adolescence (Boothroyd, 1968; Eisenberg, Shannon, Schaefer Martinez, Wygonski, & Boothroyd, 2000; Siegenthaler, 1969). Furthermore, in the presence of noise or reverberation, young children show more difficulty encoding speech than adults or older children (Johnson, 2000; Nittrouer & Boothroyd, 1990; Stelmachowicz, Hoover, Lewis, Kortekaas, & Pittman, 2000). It has been proposed that speech perception abilities of children with normal hearing in reverberant conditions might not fully mature until the age of 13 years (Neuman & Hochberg, 1983), 13 to 15 years of age in noisy conditions (Elliott & Katz, 1980), and mid-to-late-teen years when reverberation and noise are combined (Johnson, 2000). One consequence of these immature speech perception skills is that younger children require up to +20 dB greater SNRs when listening in adverse conditions than older children to perceive speech in the presence of

background noise accurately (Johnson, 2000; Klatte, Lachmann, & Meis, 2010; Neuman & Hochberg, 1983).

Neural Foundations for Speech Perception Development in Children

Speech-processing differences between adults and children with normal hearing appear to arise from structural and functional immaturities in the peripheral and central areas of the auditory system. Childhood is characterized by anatomical and functional modifications of the brain circuits during development, which have been observed in human and animal models. The developmental organization of brain circuits, including those related to the auditory system, is remarkably complex and is influenced by genetic predispositions and neuroplastic responses to environmental demands (Stiles & Jernigan, 2010; Tau & Peterson, 2010). The interplay of inherent genetic programs and environmental experiences determines the formation (neurogenesis) and elimination (apoptosis) of neurons as well as the formation (synaptogenesis), pruning, and reorganization (synaptic remodeling) of their axons, dendrites, and synapses. This, ultimately, determines the configuration of neural circuits during development.

These developmental modifications in neural circuits occur continuously from birth to adolescence and in some cases they extend to adulthood (Tau & Peterson, 2010). However, certain periods of development are characterized by the prevalence of particular neural mechanisms. For example, neurogenesis, which is mostly influenced by genetic predispositions, is prevalent during gestation and the first months of life (Stiles & Jernigan, 2010; Tau & Peterson, 2010). Although present during the entire life, synaptogenesis, which is highly experience-dependent, reaches its peak by approximately five years of age (Stiles & Jernigan, 2010; Tau & Peterson, 2010). Synaptic exuberance is thought to underlie the increase in cortical

gray matter and metabolic activity that characterizes this period of life (Chugani, 1994; Levitt, 2003). Pruning and synaptic remodeling, two processes highly determined by experience, start at age one year and reach their maximum activity by about 12 years (Huttenlocher & Dabholkar, 1997; Stiles & Jernigan, 2010). Synaptic pruning is thought to underlie gradual cortical thinning and reduction of grey matter that takes place later in childhood (Stiles & Jernigan, 2010; Tau & Peterson, 2010).

Another important aspect in the maturation of neural circuits is the myelination of neurons, including axons and dendrites (Stiles & Jernigan, 2010; Tau & Peterson, 2010). Myelination of neural circuits is also highly experience dependent and is present throughout life but reaches peak activity during childhood. It is worth noting that these anatomical changes in neural circuits have been observed throughout different areas of the brain, including the auditory system (Moore, 2002; Moore & Guan, 2001). Synaptogenesis, pruning, remodeling, and increased myelination during development results in more efficient neural circuits that are able to fire at a faster rate and with greater synchronization than earlier in development (Eggermont, 1992). In addition to these structural changes, a host of pre- and post-synaptic changes at the molecular level also contributes to alterations in synaptic efficacy during maturation (e.g., Larsen & Sjöström, 2015). These changes are initiated by input from multiple neuromodulatory systems, which tend to be enhanced during attentive states (e.g., Fritz, Elhilali, David, & Shamma, 2007a, 2007b).

Therefore, it is reasonable to conclude that immature auditory systems of children underlie auditory processing difficulties in speech-perception-in-noise tasks. This has been corroborated in studies that have found immature subcortical and cortical responses in children with poor auditory processing outcomes (Cardon & Sharma, 2013; Sharma, Cardon, Henion, &

Roland, 2011). Therefore, a fully developed auditory system appears necessary to exhibit adult-like abilities when processing speech under difficult listening conditions.

Sound and Speech Processing in the Auditory System

The central auditory system receives input from the organ of Corti in the cochlea. The organ of Corti is composed of two different membranes, known as the tectorial and the basilar membrane, and mechanosensory cells, known as outer and inner hair cells. Hair cells are located between the two membranes and differ in their function (Purves et al., 2001). While inner hair cells receive afferent inputs from auditory pathways, outer hair cells receive mostly efferent input. Thus, the inner hair cells are the actual sensory receptors of the auditory system that transform sound energy into electrical signals, whereas outer hair cells act as mechanical amplifiers of sound entering the cochlea (Purves et al., 2001). Inner hair cells (the sensory cells), following the length of the basilar membrane, are tuned to progressively higher frequencies when moving from the apex to the base of the cochlea (tonotopicity). Input vibrations of the cochlea produce the well-known traveling wave of the basilar membrane mapping stimulus frequency to place of stimulation in the cochlea. That is, the cochlea serves as a sound frequency analyzer such that specific regions of the basilar membrane are maximally responsive to specific frequencies of the original sound wave (Pickles, 2015). This tonotopic representation of sound established in the cochlea is maintained throughout the auditory system including the auditory nerve, subcortical nuclei, and primary auditory cortex.

Auditory information is conveyed from the inner hair cells to the brain through two types of afferent auditory pathways. These non-primary auditory pathways connect auditory information leaving the cochlea with other sensory information. The main function of these

pathways is to select which type of sensory information is most relevant and should be treated first; this is important for environment adaptation (Pickles, 2013, 2015). However, the main function of the auditory system, which is to decode auditory information, is primarily driven by a different set of auditory pathways. These are called primary auditory pathways. Because the present project is focused on auditory perception, primary auditory pathways are described in more detail below.

Central auditory pathways. Cochlear hair cells are connected to the brain via spiral ganglion neurons whose centrally directed axons form the auditory nerve. Central auditory pathways carry the auditory input from the cochlea to the auditory cortex. These inputs are processed bilaterally in an interconnected series of subcortical nuclei in the brainstem and thalamus (cochlear nuclei, superior olivary complex, inferior colliculus, and medial geniculate body). At each level of processing, the spectrotemporal properties of the input are encoded and recoded for the extraction of spatial and object-related features (Jenison, 2001). Processing and feature-extraction continues in the auditory cortex and associated areas where auditory information is available for perceptual processes (Pickles, 2013, 2015).

Auditory cortex. The human primary auditory cortex is located in Heschl's gyrus in the superior part of the temporal lobes of both brain hemispheres (Hackett, 2015). Although recent imaging studies have provided some light on the anatomical and functional characteristics of the auditory cortex in humans, much of our knowledge about how human audition might operate comes largely from studies in animals (Hackett, 2015). Across primate species, the auditory cortex shows patterns of hierarchical structure, topographic mapping, and streams of functional processing (Rauschecker & Scott, 2009). Assuming that differences between the human auditory cortex and the animal models might exist, we can presume three main regions within the auditory

cortex: the primary (core), secondary (belt), and tertiary (parabelt) regions (Kaas & Hackett, 2000; Purves et al., 2001). The core area is divided into three different auditory fields including a most caudal, a more rostral field, and an even more rostral field (Kaas & Hackett, 2000). These fields are characterized by having different systematic representations of the cochlea. In caudal fields, neurons are best activated by high-frequency tones, whereas neurons in rostral field neurons are best activated by low-frequency tones (Kaas & Hackett, 2000). One common characteristic of these primary auditory cortex fields is that they preserve the tonotopic organization of the cochlea and brainstem structures. Therefore, receptive fields of single neurons in these regions are specialized in responding to very specific spectral-temporal characteristics of auditory stimuli. Hyper-specialized lower-order neurons in the core project to belt areas, then onto parabelt areas. These areas have a less strict tonotopic organization. However, complex response properties are generated in these peripheral regions by convergence from hyper-specialized neurons in core areas and by nonlinear summation, a process that it is called “combination sensitivity” (Rauschecker, Tian, & Hauser, 1995). That is, higher order specificity is generated by combining input from lower-level neurons specific to relatively simple features of sound (Rauschecker & Scott, 2009).

Ample evidence from non-human and human studies indicates that the auditory cortex projects to higher-order areas of the brain via two main parallel streams or processing pathways, each of which maintains the hierarchical structure observed in the auditory cortex. While anterior areas of belt areas project to ventrolateral prefrontal cortex, the caudal belt areas project to dorsolateral PFC (Ahveninen et al., 2006; Hackett, 2011; Kaas & Hackett, 1999; Romanski et al., 1999). These two parallel pathways differ in function. The neurons in antero-ventral or “what”

pathways are responsive to auditory objects¹, including recognition of speech sounds (Ahveninen et al., 2006; Binder et al., 2000; Hackett, 2011; Kaas & Hackett, 1999). The neurons in the anterior-postero-dorsal or “where” pathways are responsive to spatial location cues (e.g., Ahveninen et al., 2006; Hackett, 2011; Kaas & Hackett, 1999) supporting the perception of auditory space and motion (Rauschecker, 1998; Rauschecker, 2007).

All these areas involved in auditory processing are highly interconnected with each other and with other areas of the brain. It is important to note that these connections are both afferent and efferent. That is, top-down projections also emanate from higher-order areas to primary areas of the auditory system, including the brainstem. These systems of afferent and efferent connections regulate information processing in the auditory system (Pickles, 2015). Therefore, sound processing in the auditory cortex is modulated not only by the specific features of sound in a bottom-up fashion, but also by top-down projections coming from other sensory cues as well as experience, memory, and attention (King, Teki, & Willmore, 2018). The complexity of afferent and efferent connections makes it scientifically challenging to tease out how the brain processes auditory objects, in general, and speech sounds in particular. For example, although the dual parallel stream hypothesis of auditory processing is well founded, regions belonging to the “where” pathway (e.g., posterior superior temporal region or the inferior parietal lobule) also serve a role in speech perception (Belin & Zatorre, 2003; Griffiths & Warren, 2002; Obleser, Wise, Dresner, & Scott, 2007). Moreover, neurophysiological evidence suggests that belt areas of the auditory cortex not only respond to auditory input but also show multimodal responses (e.g., vision and motor stimuli, Fu et al., 2003; Kayser, Petkov, Augath, & Logothetis, 2007).

¹ Auditory objects are formed by different acoustic attributes, such as timbre, pitch and loudness, which give each its distinctive perceptual identity. More specifically, auditory objects are defined as neuronal representations of a delimited acoustic pattern (Griffiths & Warren, 2004).

This phenomenon, typically referred to as multisensory integration, has been observed at lower levels of the auditory system, including the brainstem and the primary auditory cortex.

Therefore, this evidence demonstrates that auditory processing is accomplished by converging sensory information from multiple senses and not just the auditory object.

Cortical Auditory Evoked Potentials (CAEPs) as an Index of Speech Perception at the Neurophysiological Level

Neural processes at the cortical level underlying behavioral speech perception can be evaluated using objective measures that quantify changes in electrical activity in the brain following the presentation of a speech stimulus. The magnitude of the response (e.g., amplitude) and the time course relative to the stimulus onset (e.g., latency) provide valuable information about speech processing. These neural speech processing measures or cortical auditory evoked potentials (CAEPs) are categorized as exogenous and endogenous CAEPs, which reflect different stages of cortical processing. Exogenous, or sensory, CAEPs primarily reflect the acoustic properties of the stimuli and the integrity of the primary auditory pathway including the auditory cortex. Conversely, the endogenous CAEPs are modulated by the interaction between the listener and the auditory stimulus; that is, they reflect the listener's reaction to an auditory event. This differentiation of exogenous and endogenous CAEPs suggests a hierarchical or serial model of auditory processing, which has been challenged by contemporary studies. For example, lexical and semantic discrimination of sounds of environmental objects might be achieved at very early stages of cortical processing (e.g., De Santis, Clarke, & Murray, 2007; MacGregor, Pulvermüller, Van Casteren, & Shtyrov, 2012; Murray, Camen, Andino, Bovet, & Clarke, 2006). This suggests that the auditory system processes sound in general and speech in particular in a

holistic manner, instead of in a serial fashion. That being said, hierarchical models are still believed to be appropriate for understanding the different processes involved during auditory object processing (Friederici, 2012; Specht, 2014). In this study, a hierarchical model of auditory processing formed the basis of the hypotheses, acknowledging that parallel auditory processing occurs in the auditory system (De Santis et al., 2007; Murray et al., 2006). In the present study, we focus on early stages of cortical processing reflected in exogenous or sensory CAEPs, which are described in more detail in the following section.

Sensory CAEPs. Adult sensory CAEPs have been characterized by a multiphasic waveform with a small positive peak at around 50ms (P1) and a large negative peak at around 100ms (N1), followed by a large positive peak at around 175-200ms (P2) and a small negative peak at around 250ms (N2; Wunderlich & Cone-Wesson, 2006). Assuming a hierarchical model, P1 and N1 reflect detection and encoding of basic acoustic properties of the stimuli such as frequency and timing (Martin, Kurtzberg, & Stapells, 1999), P2 and N2 reflect synthesis of these features into a higher order representation such as stimulus familiarization and auditory object representation (Čeponienė, Alku, Westerfield, Torki, & Townsend, 2005; Crowley & Colrain, 2004; Tremblay, Ross, Inoue, McClannahan, & Collet, 2014). Auditory sensory components are observed around the centro-frontal areas of the scalp and they are generally found to be maximal around the vertex (Key, Dove, & Maguire, 2005). Finally, neural generators of the auditory CAEPs are primarily located at the level of AI and auditory association areas of the temporal lobe (AII and belt area; Picton et al., 1999; Wunderlich & Cone-Wesson, 2006). Importantly, because the auditory cortex receives top-down projections from higher-order areas of the brain, these sensory components (except P1) are strongly modulated by attention and show greater

amplitudes and shorter latencies when the stimuli are attended than when unattended (e.g., De Boer, & Krumbholz, 2018).

Development of Sensory CAEPs. Not all of the auditory CAEPs that characterize the adult multiphasic waveform are present during childhood. In fact, sensory components experience changes during development, reaching adult-like morphology during adolescence (Sharma, Kraus, McGee, & Nicol, 1997; Wunderlich & Cone-Wesson, 2006; Wunderlich, Cone-Wesson, & Shepherd, 2006).

Cortical responses to any detected auditory stimuli (including speech sounds) in infants and young children (0 to 6 years of age) are characterized by a biphasic waveform with a broad positive peak at 200–250ms post-stimulus onset (referred to as P1) followed by a broad negative peak at 200-250ms (referred to as N2; Molfese, 2000; Wunderlich & Cone-Wesson, 2006). This biphasic response tends to be maximal at central locations, but is also observed in frontal, parietal, and temporal areas of the scalp (Barnet, 1971). As children mature to adolescence, P1 amplitudes and latencies decrease (Albrecht, Suchodoletz, & Uwer, 2000; Ponton, Eggermont, Kwong, & Don, 2000; Sharma, Dorman, & Spahr, 2002), while N2 latencies decrease and N2 amplitudes increase (Albrecht et al., 2000; Gilley, Sharma, Dorman, & Martin, 2005; Ponton et al., 2000; Sharma et al., 1997; Wunderlich & Cone-Wesson, 2006). At approximately six years of age, a negative peak at about 100 to 150ms (referred to as N1; Bruneau, Roux, Guérin, Barthélémy, & Lelord, 1997; Cunningham, Nicol, Zecker, & Kraus, 2000; Johnstone, Barry, Anderson, & Coyle, 1996) and a positive peak at 140 to 210ms (referred as P2; Lavoie, Robaey, Stauder, Glorieux, & Lefebvre, 1997; Ponton et al., 2000) start to appear. Generally, by age 18 years the classic adult multiphasic waveform is fully formed, displaying the P1 (at 50ms), N1 (at 100ms), P2 (at 175 to 200ms), and N2 (at 250ms) components that characterize the adult cortical

response (Wunderlich & Cone-Wesson, 2006).

These gradual changes in CAEP amplitudes and latencies observed in children are related to the anatomical and functional changes in neural circuits noted previously. For example, maturation of cortical layers triggers the formation of the adult N1 response (Eggermont & Ponton, 2003). Increased myelination and synaptic efficiency during development is associated with changes in sensory CAEPs as well as with an increased ability to detect and discriminate sounds, including speech, as children mature to adulthood (Eggermont & Ponton, 2003).

Plasticity in the Auditory System

The auditory system is highly plastic in response to environmental demands. Plasticity changes in the auditory cortex have been observed in animals and humans using a variety of techniques, ranging from single-unit measurements in animals to electroencephalography (EEG) in humans (Fritz et al., 2007a, 2007b). More specifically, neuronal receptive fields in primary auditory cortex of animals are rapidly reshaped while performing auditory discrimination tasks, including tone detection in the presence of background noise (Atiani, Elhilali, David, Fritz, & Shamma, 2009; Fritz, et al., 2007a, 2007b; Fritz, Elhilali, & Shamma, 2005; Kaya & Elhilali, 2017). Reshaping of neuronal receptive fields enhances responsiveness to spectral frequencies of the signals of interest, which at the same time are highly correlated with improvements in behavior (Fritz, et al., 2007a, 2007b; Fritz, et al., 2005; Kaya & Elhilali, 2017). This enhanced responsiveness to auditory stimuli is also observable in humans. Short auditory training (about 10 minutes) can lead to greater amplitudes of CAEP sensory components (Seppänen, Hämäläinen, Pesonen, & Tervaniemi, 2012; Tremblay, Kraus, McGee, Ponton, & Otis, 2001; Tremblay & Kraus, 2002), suggesting enhanced auditory processing at the cortical level after

training. It is thought that rapid plasticity changes, if reinforced over time, foster permanent changes in the auditory system (Kral, 2013).

Plastic changes in the primary auditory cortex are also modulated by attention (Fritz, et al., 2007b; Kaya & Elhilali, 2017). Two different types of attention foster plasticity changes in the primary auditory cortex -- bottom-up stimulus-driven attention and top-down task-driven attention. While bottom-up attention relies on the salience of the signal of interest in respect to other auditory distractors or maskers (Kaya & Elhilali, 2017), top-down attention refers to task-driven attention such as active versus passive listening (Kaya & Elhilali, 2017). These two attentional mechanisms driving plasticity are explored in the following sections.

Top-down attention. In the auditory domain, top-down attention refers to voluntary direction of attention to the target sound, or more specifically to distinct auditory features of the target sound. There is ample evidence suggesting that it produces rapid changes in spectrotemporal receptive fields (SRTFs) of individual neurons (David, Fritz, & Shamma, 2012; Fritz, Elhilali, & Shamma, 2007; Yin, Fritz, & Shamma, 2014), improves neural sensitivity (Caras & Sanes, 2017), and induces topographic map changes in the auditory cortex (Polley, Steinberg, & Merzenich, 2006). This process is rapid and dependent on task and reward structure (Kaya & Elhilali, 2017). Attention is also highly correlated with perceptual learning (Caras & Sanes, 2017; Polley et al., 2006; Zurita, Villa, De Ribaupierre, De Ribaupierre, & Rouiller, 1994) and spans both primary and higher auditory areas of the brain (Fritz et al., 2007).

Findings at the single-neuron level in animal models have been corroborated by human studies using magnetoencephalography (MEG) and EEG. Collectively, these studies have shown that there is not only greater cortical activity to attended sounds compared to unattended sounds (Ding & Simon, 2012; Hillyard, Hink, Schwent, & Picton, 1973; Mesgarani & Chang, 2012;

Okamoto, Stracke, Wolters, Schmael, & Pantev, 2007) but also suppression of task-irrelevant neural activity in the human auditory cortex (Okamoto, Stracke, Lagemann, & Pantev, 2010; Okamoto, et al., 2007). Brief attention-driven auditory training also leads to greater cortical activity post-training. Specifically, increased amplitudes of sensory components within the first 200 ms after stimulus onset are observed after training (Alain, Snyder, He, & Reinke, 2007; Seppänen et al., 2012; Tremblay et al., 2001; Tremblay & Kraus, 2002). Larger ERP amplitudes after training can reflect a number of potential mechanisms including an increase in the number of responsive neurons, increased neural synchrony in the discharge of the responding population of neurons, increased specificity of which neural populations are responding to the stimuli and their firing rate, or topographic changes in the response. Nevertheless, it suggests that top-down attention drives changes in the human auditory cortex that are maintained after training (e.g., Alain et al., 2007).

Bottom-up attention. Auditory stimuli are often encoded in the presence of other auditory distractors or maskers in the environment (e.g., background noise). When the stimulus of interest is perceptually distinct from the masker (high SNR), spectrotemporal features of the auditory object of interest (e.g., frequency, intensity, or timbre) can be extracted by the auditory cortex. On the other hand, when the auditory object of interest is completely masked by the distractor (low SNR), extraction of spectrotemporal features of the sound is not possible (Kaya & Elhilali, 2017). In animal models, extraction of spectrotemporal features at high SNR reshapes STRFs in neural networks in charge of encoding the signal (Atiani et al., 2009). These SRTF shape changes are excitatory and specific to neurons with best or characteristic frequencies in the frequency range used in training (i.e., in the “area of representation” of those frequencies) near the target signal (i.e., tone; Atiani et al., 2009). In other words, neural representation of the sound

of interest relative to the background noise is enhanced when the sound of interest is salient in respect to the masker (high SNR). These changes are not observable at poor SNR when the sound of interest is perceptually indistinguishable from the masker. Adaptive changes in STRF are highly correlated with behavior, suggesting that plasticity changes at the neural level are related to changes in the ability of the animal to distinguish the sound of interest from the masker (Atiani et al., 2009).

Rapid plasticity changes related to bottom-up attention have not been observed in humans performing speech-in-noise perception tasks. However, it has been widely reported that manipulating the SNRs or the saliency of the signal does have an immediate effect on brain responses (Almeqbel & McMahon, 2015; Benítez-Barrera, Key, Ricketts, & Tharpe, 2019). Specifically, increasing the SNR reduces CAEP latencies and increases CAEP amplitudes when adults listen to speech in the presence of background noise (e.g., Whiting, Martin, & Stapells, 1998). The same effect has been also observed in children with normal hearing (Anderson, Chandrasekaran, Yi, & Kraus, 2010), and in children with learning disabilities (Hayes et al., 2003). More favorable SNRs produce greater amplitudes and shorter latencies in all sensory components (P1, N1, and P2) of the CAEP relative to less favorable SNRs. As SNR increases, there is greater engagement of auditory neural networks in response to sound, which in turn, facilitates speech processing.

Sensitive Periods for Auditory Processing

It is well accepted that the development of sensory areas of the brain is regulated by intrinsic homeostatic mechanisms shaped by extrinsic environmental experiences (Altevogt & Hougan, 2008; Greenough, Black, & Wallace, 1987; Ismail, Fatemi, & Johnston, 2017). The

interplay between genetic and environmental factors has led to the concept of *experience-dependent* mechanisms that characterize neuroplasticity (Greenough et al., 1987). This concept establishes that human brains have evolved to take advantage of experiences to shape the development of sensory and motor brain systems (Greenough et al., 1987). The time windows in early development in which the brain is especially susceptible or malleable to change as a result of environmental stimulation are known as sensitive periods (Greenough et al., 1987).

As noted previously, children exhibit adult-like speech-in-noise skills during adolescence. Therefore, it is reasonable to assume that auditory systems in childhood are still malleable and incorporate changes in neural networks that are responsible for speech and speech-in-noise processing. In fact, auditory brainstem responses (ABR) evoked by simple auditory stimuli (e.g., clicks) and speech stimuli in pre-school and school-age children, differ across ages. While these two groups of children show equivalent ABRs to clicks, pre-school children display less synchronous and less sustained neural responses to speech as compared to those from school-age children (Johnson, Nicol, Zecker, & Kraus, 2008). The authors concluded that neural pathways involved in processing speech sounds are more malleable and more susceptible to experience-dependent plasticity than simple sounds (e.g., clicks). Electrophysiological and behavioral data suggest that auditory pathways responsible for processing complex stimuli might have a longer sensitive period than those involved in processing simple auditory stimuli such as tones or clicks. As discussed below, these data support the idea that interventions aiming to improve speech processing can be effective with pre-school and school-age children.

Sensitive periods and intervention. Length of sensitive periods vary according to the behavioral skill in question, such as perception of stereoscopic depth, language processing, or developing social relationship skills (Knudsen, 2004). Moreover, each skill requires an

experience of a certain kind that must occur within that sensitive period for the behavior to develop normally (Knudsen, 2004). For example, Sharma, Campbell, and Cardon (2015) showed that auditory stimulation before seven years of age is necessary to achieve age appropriate P1 amplitudes and latencies. Although the relationship between auditory experience and the development of auditory areas of the brain has been established, the specific type of experience required to develop adequate speech processing and, more specifically, speech-perception-in-noise skills is unknown. We are still far from understanding how and for how long exposure to specific speech features should occur to develop effective auditory feature maps.

Based on previous findings from animal models, it could be argued that children might need to be exposed consistently to salient speech signals relative to maskers early in life to incorporate, through bottom-up plasticity, spectrotemporal auditory features into their auditory feature maps. Theoretically, these optimized auditory feature maps would allow individuals to encode speech embedded in background noise more effectively later in life. The following section provide evidence for the bottom-up plasticity hypothesis in children's long-term auditory processing outcomes.

Auditory Experience Determines Neural and Behavioral Speech Processing Skills

The type of auditory experience one has (impoverished versus enriched) determines the degree of auditory brain development, which ultimately impacts the development of auditory skills, including speech perception in noise. The following is a review of how auditory impoverishment and auditory enrichment can impact development.

Auditory impoverishment. For purposes of this manuscript, *auditory impoverishment* is defined as any type of experience that diminishes access to auditory stimuli (including speech).

Deafness and listening in the presence of environmental noise are examples of impoverished auditory experiences.

Deafness. One of the most powerful demonstrations of the impact of auditory impoverishment on the developing brain comes from studies of congenitally deaf animals and humans. Several studies have shown that auditory areas of congenitally deaf cats are drastically altered relative to normal hearing cats (Kral, 2007; Kral, Yusuf, & Land, 2017). For example, deafness resulting from noise trauma induces reorganization of the tonotopic map of the primary auditory cortex in cats, as reflected in broadened spectral tuning and reduced neural synchrony in the cortical maps (Eggermont, 2008).

Additionally, congenitally deaf cats display a phenomenon called *cross-modal plasticity*, in which non-stimulated auditory areas of the brain start to strengthen neural connections with visual and somatosensory areas (Kral, 2007; Meredith & Lomber, 2011). In these studies, auditory deprivation secondary to deafness was shown to reorganize the pattern of auditory neural connections to such an extent that auditory areas started processing information from other sensory modalities. Similarly, in humans, brain regions of individuals deprived of auditory stimulation early in life have been found to demonstrate cross-modal reorganization (Kral, 2007; Kral & Sharma, 2012; Neville & Bavelier, 2002). For example, studies looking at activation patterns of auditory cortices of individuals who are congenitally deaf have shown that auditory cortices are activated while the individuals perform visual tasks (Buckley & Tobey, 2011; Finney, Fine, & Dobkins, 2001; Sharma et al., 2015). Cross-modal reorganization is not restricted to congenital and profound deafness. Recruitment of auditory cortex for visual processing has also been observed in adult individuals with lesser degrees of hearing loss acquired in adulthood (Campbell & Sharma, 2014). This suggests that not only early and total

deprivation but also impoverished auditory experience later in life results in neuroplastic changes at the cortical level.

Significant degrees of cross-modal reorganization in children and adults result in reduced CAEP amplitudes and prolonged latencies (Kral, 2007; Sharma et al., 2015; Sharma, Dorman, & Kral, 2005). In addition, cross-modal reorganization and altered CAEPs are related to behavioral performance in children and adults with hearing loss. In individuals with either profound or mild-moderate losses whose hearing is restored via cochlear implants and hearing aids, the degree to which auditory cortices are activated by visual stimuli have been shown to predict speech-perception-in-noise skills (Buckley & Tobey, 2011; Campbell & Sharma, 2014; Strelnikov et al., 2013). In individuals with profound hearing losses, the degree to which auditory cortices are activated by visual stimuli is also associated with age of cochlear implantation (Buckley & Tobey, 2011) as well as with the amount of residual hearing (Lambertz, Gizewski, de Greiff, & Forsting, 2005). Therefore, individuals deprived of auditory stimulation for a longer time (later age of implantation and less residual hearing) demonstrate greater degrees of cross-modal reorganization and poorer speech-perception-in-noise skills than those exposed to lesser degrees of auditory deprivation (through residual hearing) for a shorter periods of time (early implantation).

Environmental noise. Prolonged exposure to noisy auditory environments has also been shown to impact the development of auditory areas of the brain in animals. Tonotopic reorganization and malformation of cortical maps has been observed in animals that were reared in environments with high levels of background noise (Bao, Chang, Davis, Gobeske, & Merzenich, 2003; Chang & Merzenich, 2003; Zhang, Bao, & Merzenich, 2001, 2002). That is, animals exposed to high levels of background noise show topographic maps in the primary

auditory cortex that reflect broadened spectral tuning and reduced spontaneous discharged correlation (Bao et al., 2003; Chang & Merzenich, 2003). Persistent exposure to background noise is also associated with poorer development of auditory function in humans. For example, children raised in socioeconomically disadvantaged environments experience higher levels of noise pollution than children from high socioeconomic backgrounds (e.g., Evans & Kantrowitz, 2002) and demonstrate poorer speech-evoked auditory brainstem responses (Skoe, Krizman, & Kraus, 2013) and more difficulty suppressing irrelevant auditory input during behavioral listening tasks (D'Angiulli, Herdman, Stapells, & Hertzman, 2008; Neville et al., 2013; Stevens, Lauinger, & Neville, 2009). Similarly, high levels of high-frequency noise experienced by pre-term infants in neonatal intensive care units, as opposed to the quiet auditory experience provided by the womb to the fetus, have been proposed to underlie, at least in part, auditory and language deficits often observed in pre-term children (Lahav & Skoe, 2014). Collectively, these studies suggest that auditory deprivation and auditory impoverishment can have a negative impact on the development of auditory cortices as well as the development of speech-perception-in-noise skills.

Auditory enrichment. For purposes of this manuscript, *auditory enrichment* is defined as any type of technology or intervention that seeks to improve access to auditory stimuli. Hearing technology (e.g., cochlear implants or RM systems) and auditory training for individuals who are deaf are examples of interventions that provide auditory enrichment.

Hearing technology. It is well known that children who are congenitally deaf and receive cochlear implants within the first three years of life have significantly better speech processing and language skills than those who are implanted after three years of age (Buckley & Tobey, 2011; Peterson, Pisoni, & Miyamoto, 2010). Early implanted children have more mature CAEPs

(greater amplitudes and shorter latencies) and a lesser degree of cross-modal reorganization than late-implanted children (Buckley & Tobey, 2011; Sharma et al., 2015). Although causality cannot be determined, auditory experience early in life, maturation of the brain auditory system, and speech perception skills seem to be related.

Early amplification does not only benefit congenitally profound deaf individuals. Recent studies have shown that in children with lesser degrees of hearing loss, age of amplification explains most of the variance on speech perception outcomes and language skills later in life (e.g., Sininger, Grimes, & Christensen, 2010). Similarly, accessing early intervention services focused on auditory outcomes also predicts speech and language outcomes of children with residual hearing (Yoshinaga-Itano, Sedey, Coulter, & Mehl, 1998). That is, having access to an enriched auditory environment through hearing aids and early auditory intervention appears to enhance development of top-down, bottom-up, or both processes in the auditory system resulting in enhanced auditory outcomes.

Finally, a few studies have investigated whether having consistent access to enriched auditory experiences through assistive listening devices, such as RM systems, impact cortical and subcortical responses to speech in noise and language outcomes in children with disabilities. Hornickel, Zecker, Bradlow, and Kraus (2012) found that after one year of classroom RM system use, a group of school-age children with dyslexia had enhanced subcortical neural consistency to speech than a matched control group of children who were non-users. Moreover, improvements in neural representation of sound (e.g., greater neural consistency) at the subcortical level were related to improvements in phonological awareness and reading skills. Consistent use of RM systems has also been related to improvements in cortical processing of speech in school-age children with auditory processing disorders (Friederichs & Friederichs,

2005; Sharma, Purdy, & Kelly, 2014). More specifically, children who used RM systems for over a year at school, showed better auditory object representation reflected in larger P2 (Friederichs & Friederichs, 2005) and N2 amplitudes (Sharma, et al., 2014) than an age-matched control group who used hearing aids but did not use an RM system during the same period. These cortical changes were related to improvements in frequency discrimination skills (Friederichs & Friederichs, 2005). Finally, RM system use at home has also been associated with better discourse skills in children with hearing loss (Curran et al., 2019). Therefore, it appears that by providing clarity of the acoustic signal, consistent use of RM systems can result in neural and behavioral changes in children. This might suggest an accelerated neuro-maturational process associated with having access to enriched auditory environments.

Auditory training. Another intervention that has been used to enhance auditory experience aimed at improving individuals' speech processing skills is auditory training. In its present-day form, auditory training provides computer-based sound training designed to teach the brain to perceive sound contrasts through repetition and variation of stimuli together with effective feedback (Rayes et al., 2019). An ultimate goal of auditory training is to train a listener to distinguish, or discriminate, between sound contrasts (Schow & Nerbonne, 2007). Two examples of auditory training approaches include the analytic approach (bottom-up), which trains the listener to decode speech sounds with no context (e.g., vowels or consonants) and, the synthetic approach (top-down), which uses one's linguistic knowledge (e.g., semantic, syntactic, lexical, and phonological) to fill in the gaps in the sensory information. Both auditory training approaches have been shown to be effective in teaching adults and children to encode sounds (including speech) at least in the short term (Fu & Galvin, 2008; Fu, Galvin, Wang, & Nogaki, 2004; Henshaw & Ferguson, 2013; Rayes et al., 2019; Rubinstein & Boothroyd, 1987; Sweetow

& Palmer, 2005; Zhang, Dorman, Fu, & Spahr, 2012). It has been suggested that combining analytic and synthetic training results in maximum intervention benefits (Amitay, Irwin, & Moore, 2006; Rayes et al., 2019).

As noted previously, auditory training effects at the neural level have also been cited as an example of brain plasticity. In fact, auditory training has been shown to produce short-term changes in neural pathways and synapses reflected by changes in CAEPs in adults (Tremblay et al., 2001; Tremblay, Shahin, Picton, & Ross, 2009). More specifically, amplitudes are increased in early sensory components (N1 and P2) after training (Alain, et al., 2007; Seppänen et al., 2012; Tremblay et al., 2001; Tremblay & Kraus, 2002) suggesting neuroplastic changes as a result of training.

In summary to this point, early and consistent access to enriched auditory environments through the use of hearing technologies and auditory training is a clear example of how quality of auditory experience can shape the development of auditory areas of the brain as well as the development of speech perception and language skills. Therefore, enriching the auditory experience seems to facilitate auditory neuroplastic changes that are linked to improvements of a variety of behavioral outcomes, including speech perception in noise.

Research Aims and Research Hypotheses

The purpose of this project was to investigate whether a short period of active syllable discrimination training with an RM system (at a favorable SNR) enhances CAEPs and improves speech-in-noise perception skills of children with normal hearing as compared to children who receive the same training without the RM system (at a poorer SNR). We hypothesized that similar to what has been observed in animal models, salience of the signal via an enhanced SNR

would increase neural engagement by reshaping STRFs within feature maps. This process would facilitate incorporation of spectrotemporal features of the stimuli via bottom-up attention mechanisms in the auditory feature maps, resulting in enhanced CAEPs and improved speech-in-noise perception skills after training even when the RM was not in use. No changes were expected to be observed as a result of training in the group that did not use the RM system. Table 1 outlines the three specific aims that were addressed in the current study.

Table 1. Study aims and hypotheses

Aim 1	To evaluate whether a brief auditory training with an RM system (greater SNR) will result in changes in children’s CAEP activity post-training that is different than CAEP activity in children receiving the same training without the RM system.
Hypothesis 1	Following the RM system training, children will show significantly greater improvement in cortical activity (reflected by greater modulations in response to strength, assessed via global field power [GFP], and greater amplitudes and shorter latencies of sensory CAEPs) relative to the pre-training condition than children in the control (no-RM) group. Children in the no-RM group will not show a significant difference between their pre- and post-training conditions.
Aim 2	To evaluate whether the same auditory training will result in improved speech-in-noise ability post-training by children using an RM system but not in the group of children receiving training without the RM system.
Hypothesis 2	No differences will be observed between the groups in pre-training speech-in-noise scores. However, the children trained with an RM system will have significantly better speech-in-noise scores compared to their baseline condition. This change pre- and post-training for the RM system (RM) group will not be observed in the no-RM group.
Aim 3	To describe the relationship, if any, between CAEPs and speech-in-noise ability pre- and post-auditory training with both groups of children.
Hypothesis 3	Cortical responses to speech in noise will be related to speech-in-noise scores pre- and post-training for both groups. Moreover, children with greater CAEP improvement after the RM system training will show more improvement in their speech-in-noise scores after training than those with less improvement in CAEPs.

CHAPTER II

METHODS

Participants

A total of 49 typically developing children with normal hearing (27 females) were consented. Children were between the ages of 8:5 months and 12:7 (M = 10:8; SD = 1:1, years:months). School-age children were selected based on the assumption that sensitive periods for the acquisition of speech processing skills are available for school-age children and also because plasticity changes have been observed as a result of auditory training in this age population (Rayes et al., 2019). All children passed an air-conduction pure tone screening at 20 dB HL at octave intervals from 250 to 4000 Hz at 20dB in both ears. All children used English as the primary language at home and had typical cognitive skills as evidenced by standard scores of no lower than 85 (M= 113.3; SD = 14.0) on the Kaufman Brief Intelligent Test (KBIT-2; Kaufman & Kaufman, 2004). The children were randomly assigned to two different groups. One group (RM group) received training with an RM system. The other group (no-RM group) received the same training but without an RM system. Informed assent was obtained from all children and consent from all their legal guardians. All procedures conformed to the protocol approved by the Vanderbilt University Institutional Review Board (#162044).

Five of the initial 49 children were excluded from data analyses. One child was unable to complete the electrophysiology and behavioral testing because of behavioral issues. The remaining four children were excluded from the study due to an excessive number of contaminated trials in the electrophysiology tasks. Therefore, 44 children were included in the final analyses. As a result, 22 children were included in each study group (RM group and no-RM

group) for data analyses. Children from these groups did not differ in age [$t(41.6) = -1.9, p > .05$], sex [$\chi^2(1) = 0.38, p > .05$], maternal education [$\chi^2(4) = 0.8, p > .05$], musical experience [$\chi^2(2) = 0.78, p > .05$], or cognitive abilities [$t(40.5) = -0.22, p > .05$]. Demographic information for both groups is provided in Table 2.

Table 2. Demographic information across study groups (no-RM and RM). Means (SDs) are shown for age, KBIT-2 scores and NST pre-training scores.

Participant Characteristics		Group		
		no-RM	RM	Total
Number of children		22	22	44
Age (years:months)		10:5 (1:1)	11:0 (1:0)	10:8 (1:1)
Sex	Female	15	12	27
	Male	7	10	17
KBIT-2		112.9 (15.4)	113.8 (12.7)	113.3 (14.0)
Maternal Education	High School	4	4	8
	Community College	3	3	6
	College	6	4	10
	Masters	5	5	10
	Ph.D.	4	6	10
Duration Instrument Experience	≤2 years	4	2	6
	>2 years	6	7	13
	0 years	12	13	25
NST score (pre-training)	+5 dB SNR	71.4% (6.3)	75.1% (7.3)	73.2% (7.2)
	0 dB SNR	70.1% (7.8)	70.2% (5.4)	70.1% (6.5)
	-5 dB SNR	64.2% (9.1)	63.9% (6.6)	64% (7.7)
	-10 dB SNR	54.6% (10.5)	60% (10.0)	57.5% (10.4)

Note. RM = remote microphone; KBIT = Kauffman Brief Intelligence Test; NST = Nonsense Syllable Test; dB = decibel; SNR = signal-to-noise ratio

Study Equipment and Materials

Remote Microphone (RM) System. The Phonak Roger Inspiro™ transmitter was programmed using the Phonak iPOP protocol (iPOP™ - Phonak Dynamic Offset Protocol, 2009). The mix ratio between the output from the ear-level receiver microphones and the RM system transmitter was set at +10dB. RM system transparency was verified with the Audioscan Verifit testbox. Children who received training with the RM system were bilaterally fitted with pediatric Phonak ear level receivers (Roger™ Focus) during the training portion of the study. To control for stimulus presentation level at the participants' ears, non-custom eartips (COMPLY™ Canal Tips, Slim 0) were used to deliver the speech signal through the ear level receiver.

Nonsense Syllable Test (NST). Phoneme recognition is the most basic and analytic process involved in speech perception. We predicted that if any improvement in speech perception was observed after the short training, it was likely to occur at the phonemic level. Moreover, the fact the previous studies looking at the relationship between CAEPs and speech-perception-in-noise skills measured at the sentence level in adults and school-age children reported inconclusive findings (Anderson et al., 2010; Benítez-Barrera, Key et al., 2019; Gustafson, 2017; Parbery-Clark, Marmel, Bair, & Kraus, 2011), led us to explore more basic features of speech perception. The idea was that behavioral metrics of speech perception that more closely resembled the speech stimuli used to elicit the CAEPs, might reveal a relationship between neural and behavioral measures of speech-perception-in-noise in school-age children. For that reason, the Edgerton-Danhauer Nonsense Syllable Test (NST; Danhauer & Edgerton, 1988) was selected to assess speech perception in noise in the current study. The NST is a widely used recorded speech perception test that contains 50 different English-based nonsense

bisyllables (consonant-vowel-consonant-vowel structure; CVCV) produced by a male speaker. These nonsense syllables are distributed across two different forms (Form A and Form B). Within each form, the test provides six different lists of 25 nonsense syllables each that contain the same nonsense syllables but in different orders.

Electroencephalography (EEG) equipment. Cortical responses were digitally recorded using a high-density system Geodesic Sensor Net with 128 electrodes (Electrical Geodesics Inc., Eugene, OR, USA) and NetAmp 400 amplifiers. EEG signals were acquired at a sampling rate of 250 Hz using the NetStation program running on a Macintosh computer. The Cz served as the reference during data acquisition, and average reference was used for analysis.

EEG stimuli. Speech stimuli consisted of recorded natural speech syllables (/da/, /ga/) produced by an adult female native English speaker. Length of the syllables was 350ms. During noise conditions, a 4-talker babble noise (three female talkers and a male talker) was also presented to the children.

Pre-Experimental Materials and Procedures

Demographic History. Demographic information about the children's medical and educational backgrounds was collected from their caregivers. In addition, families were asked about maternal education, which has been used before as a proxy for family socioeconomic status (Mueller & Parcel, 1981), and the amount of experience their child had playing a musical instrument, if any. Socioeconomic status and musical experience were included as part of the demographic history because these two variables have been found to predict speech-perception-in-noise skills of children (D'Angiulli et al., 2008; Slater et al., 2015)

Audiometric Screening. Hearing was screened at 20 dB HL in an IAC soundbooth via pure tone air conduction stimuli at octave intervals from 250 to 4000 Hz in both ears using a Grason Stadler 16 diagnostic audiometer.

Cognitive Screening. Kaufman Brief Intelligence Test (K-BIT; 2nd; Kaufman & Kaufman, 2004). This measure evaluated verbal and nonverbal abilities and is standardized for people between 4 and 90 years of age. The test was administered according to published instructions to each child prior to study initiation by either the principal investigator or a qualified research assistant.

Study Procedures

EEG. Testing was conducted in a sound-treated laboratory while children actively discriminated between the two syllables by pressing one of two computer keys. EEG data collection occurred in two different blocks. During the first EEG block completed prior to training, children listened to the speech-in-quiet condition followed by the speech-in-noise condition (+5 dB SNR). This noise condition was considered a pre-training baseline condition. The second EEG block occurred immediately after the training session and consisted of the noise condition (+5 dB SNR) only.

In each block, syllables were presented in the free field at 70dB SPL at the participant's location from a front loudspeaker (0° azimuth and 0° elevation; RCA, 02A04) at one-meter distance relative to the participant and measured by a sound level meter (Brüel & Kjaer™, model 2250). During noise conditions, the 4-talker-babble background noise was delivered at 65dB SPL at the participant's location from four different loudspeakers located at 90°, 270°, 225°, and 135° azimuth and 0° elevation at one-meter distance relative to the participant. This speaker

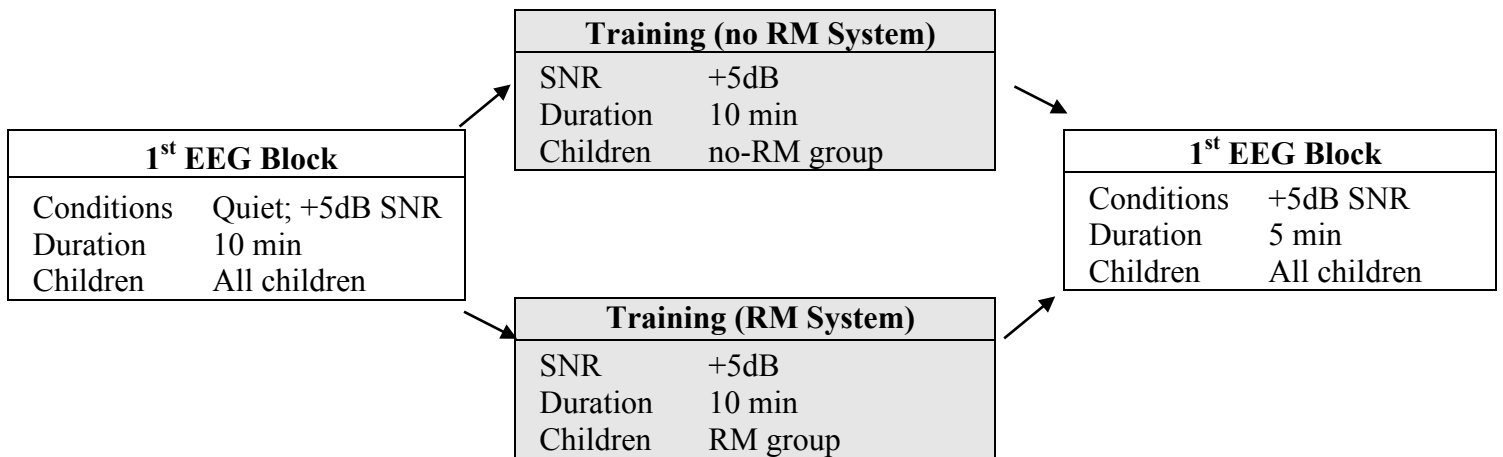
configuration (speech coming from the front and noise coming from the sides and back of the participant) was selected to simulate a classroom situation with preferential seating, which is a typical classroom seating arrangement for children who are most likely to use RM systems (e.g., children with hearing difficulties). To ensure an accurate and stable +5dB SNR, each signal from the 4-talker babble noise was spectrally matched within +/-5 dB to the long-term average speech spectra (LTASS). One hundred trials for each syllable were presented per condition, for a total of 200 trials. E-prime v.2.0 controlled sound presentation and behavioral response collection. Syllables were presented in random order with a variable inter-stimulus interval (ISI) ranging between one and two seconds. Each condition lasted about seven minutes. No feedback was provided during these listening tasks.

Training. The training portion of the study took place between the first and second EEG blocks. Children were randomly assigned to one of two groups (no-RM and RM). Children in the RM group were fitted with the receivers (one on each ear). The transmitter microphone was placed eight inches in front of the loudspeaker used to deliver the speech signal (0° azimuth) The SNR through the RM system was measured using a pair of real ear simulators (G.R.A.S. RA0401) mounted bilaterally in an acoustic mannequin (Knowles Electronics Manikin for Acoustic Research; KEMAR). The output of the real ear simulators was routed to a computer for signal recording via a G.R.A.S. 12AA power module. The RM system consisted of the same pair of pediatric Phonak ear level receivers (Roger™ Focus) with occluding ear molds fitted to KEMAR, and wirelessly coupled to the Phonak Roger Inspiro™ microphone. The +5 dB SNR speech and babble noise were presented to KEMAR and the resultant SNR after processing through the RM system was +15dB. Therefore, while children in the no-RM group were trained at

a +5dB SNR, children from the RM group were trained at +15dB SNR due to the additional increase in SNR provided by this system.

During training, children from both groups performed the same speech-in-noise sound discrimination task described above, except feedback was provided through a computer program designed for that purpose. Length of the training was about 10 minutes. The training session was slightly longer than the baseline and post-training conditions because of the time necessary for the computer program to provide feedback to the child after each response. Figure 1 displays a diagram of the EEG part of the study for clarification.

Figure 1. Study procedures diagram. White boxes indicate EEG blocks. Light grey boxes indicate training portions of the study.



Note. SNR = signal-to-noise ratio; EEG = electroencephalography; dB = decibel; RM = remote microphone.

Nonsense Syllable Test (NST) in Noise. The NST was administered in the same sound-treated room as the EEG testing. The test was administered twice in two different blocks. That is, the first NST block test took place before the EEG testing and training, and the second NST

block test took place right after the EEG testing and training. That way, pre- and post-training NST scores could be compared. All NST testing was conducted in noise.

Nonsense syllables were presented at 70 dB SPL from the same point-source loudspeaker used in the EEG tasks. The same four-talker-babble masking noise used in the electrophysiology testing was presented from four source loudspeakers placed one meter from the child at 90°, 270°, 225°, and 135° azimuth (same set up as in the EEG testing). For each NST block, four different SNRs were evaluated (-10dB SNR, -5dB SNR, 0dB SNR, +5dB SNR) with four different lists for each NST block for a total of eight lists used for each participant (four lists from Form A and four lists from Form B). To obtain the desired SNRs, the babble noise was adjusted from the four loudspeakers to a total level of 80 dB SPL, 75 dB SPL, 70 dB SPL, and 65 dB SPL. To ensure accurate and stable SNRs, the 4-talker babble noise was spectrally matched to each NST list within +/-5 dB to the long-term average speech spectra (LTASS).

To administer the test, one list of 25 nonsense syllables was selected. The participant listened to each nonsense syllable and repeated the word out loud. The examiner determined the accuracy of each phoneme (CVCV) produced by the participant. To obtain full credit for a given nonsense syllable, all phonemes must be repeated accurately by the participant. The NST total score was computed as a percentage correct of nonsense syllable productions out of the total number of syllables in the list. Administering each NST block took between 12 and 15 minutes (three minutes per list). On average, participants spent a total of 30 minutes on NST testing. The order of NST list presentation as well as the order of noise conditions was randomized across children using a Latin square design. Finally, NST responses from each participant and condition were recorded. A native English speaking graduate student research assistant with training in linguistics and phonetics listened to the recordings and scored the responses. Moreover, to

ensure accurate and non-biased NST scoring, the research assistant was blind to the child's study group, listening conditions, and NST condition (pre- or post-training).

Data Processing and Analyses

EEG Data Processing. EEG data were bandpass filtered with high-pass filter cutoff at 0.1 Hz and low-pass filter cutoff at 30 Hz, and segmented on syllable onset to include a 100 ms pre-stimulus baseline and 500 post-stimulus interval. The resulting epochs were screened for artifact using Cartool software (Brunet, Murray, & Michel, 2011; brainmapping.unige.ch/cartool), and trials contaminated by eye blinks, eye movements, other motor noise, or bad channels in excess of 15 were excluded. Next, individual EEGs were averaged, re-referenced to an average reference, and baseline corrected. For a data set to be included in the statistical analyses, individual listening condition averages had to include more than 100 trials (>50 trials for each of the syllables).

EEG data. To investigate whether pre-training CAEPs differed from post-training CAEPs across groups, we conducted CAEP analyses at the global strength of the electric field at the scalp (global field power [GFP]) and at the single waveform level. GFP is a reference-independent index that quantifies the strength of the electric field at each time point throughout the scalp considering the data from all recording electrodes (Skrandies, 1990). That is, GFP provides a reference independent index of the brain activity as a function of time. GFP is calculated as the square root of the mean of the squared value recorded at each electrode (versus the average reference) and is equal to the spatial standard deviation across electrodes at a given instant in time (Michel & Murray, 2012). Larger GFP values are associated with greater synchronized neural activity. Therefore, we assessed training effects across groups by analyzing

GFP modulations over the post-stimulus period averaged across syllables (/da/ and /ga/) between pre- and post-training conditions within each group using paired sample t-tests.

We used time windows (e.g., time windows of interest) in which GFP differences were observed across groups to identify regions of maximum activity across the scalp. Then, single waveform analyses were computed at that location of maximum activity within each time window. Early sensory components' (P1-N1 and P2-N2) amplitudes and latencies averaged across syllables (/da/ and /ga/) were then explored within the time windows in which GFP significant differences were observed between pre- and post-training conditions. Amplitude values were reported as mean amplitudes, and peak latency values were measured relative to stimulus onset (if any peak was identified within the time window).

At the single waveform analysis level, a two-way mixed model analysis of variance (ANOVA) was conducted with testing condition (quiet, pre-training, and post-training) serving as within-group variables and group (No-RM, RM) serving as between-group variables. Mean amplitudes and peak latencies averaged across syllables (/da/ and /ga/) served as the dependent variables. The main effects of condition and group were analyzed to explore whether background noise had an impact on the cortical responses and to analyze whether there were overall differences in cortical responses between the groups across listening conditions. The interaction of *group x condition* was explored to analyze whether there was a difference in cortical responses as a function of listening conditions between the groups. All ANOVA results reported herein reflect two-tailed values. When applicable, ANOVA p values were reported with Huynh-Feldt correction for sphericity.

Behavioral speech perception in noise data. The percentage of correct phonemes identified by participants in each listening condition was used to quantify speech-perception-in-

noise skills (NST score). A three way, mixed model ANOVA with noise condition (+5dB SNR, 0dB SNR, -5dB SNR, and -10dB SNR) and testing condition (pre-training and post-training) serving as within-group variables and group (No-RM, RM) serving as between-group variables was computed. The NST score served as the dependent variable. Main effects of group, noise condition, and testing condition were analyzed to explore whether the two groups differed in their NST scores across conditions, whether background noise had an effect on NST scores, and whether there were pre- and post-training differences across both groups and listening conditions. The interaction *group x testing condition* was explored to analyze whether NST scores differed between the groups as a function of testing condition. Again, all ANOVA results reported herein reflect two-tailed values. When applicable, ANOVA p values were reported with Huynh-Feldt correction for sphericity.

Relationship of CAEPs and speech-perception-in-noise skills. The relationship between CAEPs to speech in noise and behavioral responses to speech in noise were explored implementing correlational analyses. First, to explore whether CAEPs to speech in noise were related to behavioral skills, Pearson's correlations were calculated for pre-training NST scores and pre-training GFP values independently for each NST noise condition. Pearson's correlations were also computed between pre-training NST scores and mean amplitudes and peak latencies (averaged across syllables) in the pre-training condition independently for each NST noise condition. These correlations were also computed in the post-training listening conditions.

To explore whether the CAEP changes from the pre- to post-training sessions had a behavioral correlate in both groups, we computed Pearson's correlations between the difference NST score (pre- versus post-training) and the difference in GFP values (pre- versus post-training), independently for each NST listening condition and study group. Pearson's

correlations were also computed between the difference NST score and the difference between mean amplitude values (averaged across syllables), independently for each NST listening condition and study group. Finally, Pearson's correlations were computed for all participants to explore whether age had an effect on CAEPs and speech-in-noise scores. Age and GFP values, and amplitudes and latencies in the pre- and post-training conditions over the time windows of interest were averaged across syllables. Then, Pearson's correlations were computed between age and NST scores at each listening condition.

CHAPTER III

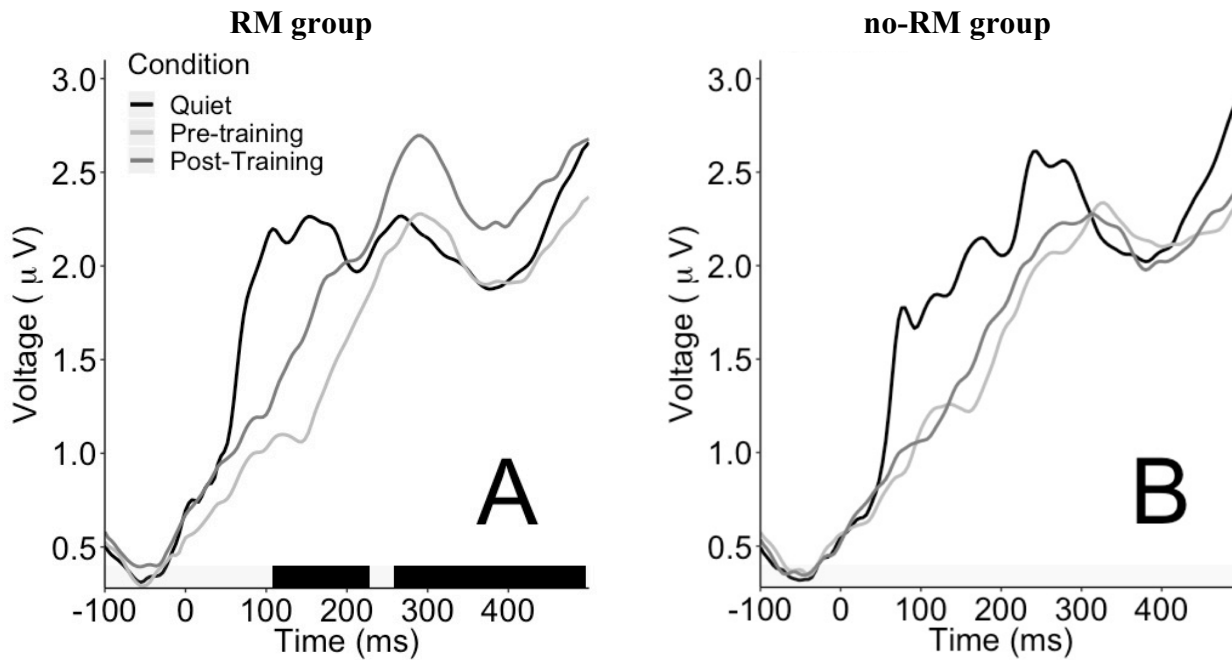
RESULTS

Training Effects on CAEPs

Global measures of the electric field. Significant modulations in response to strength, assessed via GFP, were found between the pre- and post-training conditions in the RM group over the 108-228 ms interval and >248ms interval post-stimulus onset (Figure 2A), with post-training eliciting stronger responses than pre-training in such intervals. No differences were found in modulations in response to strength between pre- and post-training in the no-RM group (Figure 2B). Additionally, modulations in response to strength did not differ in quiet or in pre-training conditions across groups, suggesting that the strength of the cortical response was equivalent across the groups before receiving training.

Sensory CAEP modulations at individual electrodes. Visual inspection of topographic maps revealed greater cortical activity at frontal areas of the brain in the time-windows of interests (108-228 ms and >248ms) in both groups during the pre- and post-training conditions (Figure 3). Therefore, waveform analyses were computed at frontal electrodes (Fz). A bi-phasic waveform characterized the cortical response at Fz across conditions in both groups, with a positive peak (P1) at around 100 ms post-stimulus onset and a negative peak (N2) between 250-300 ms post-stimulus onset (Figure 4). A main effect of listening condition was found for mean amplitudes in the 108-228ms ($F_{2,84} = 28.0$, $p < .001$, $\eta^2_G = .2$; Table 3) suggesting an effect of background noise over the time window. However, no main effect of group ($F_{1,42} = 1.15$, $p > .05$, $\eta^2_G = .02$) nor interaction effect ($F_{2,84} = 1.97$, $p > .05$, $\eta^2_G = .02$) were observed, suggesting no difference between groups across listening conditions.

Figure 2. Modulations in response strength assessed through global field power waveforms for the RM group (Panel A) and for the no-RM group (Panel B). Differences between pre- and post-training conditions emerged in the 108-228 ms and >248 ms post-stimulus onset only for the RM group (black bars).

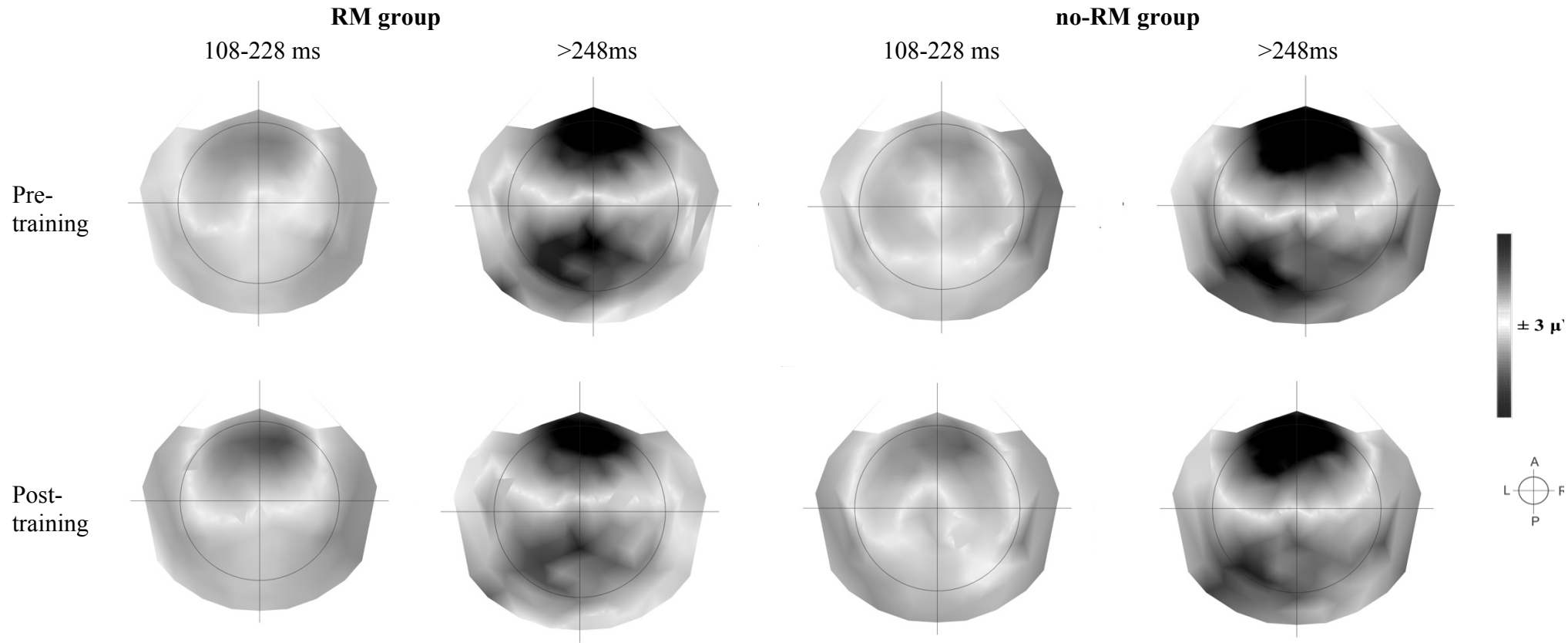


Note. Note: μV = microvolts; ms = milliseconds; RM = remote microphone.

ANOVA main effects were not significant over the >28ms interval (Group: $F_{1,42} = .02$, $p > .05$, $\eta^2_G = .00$; Condition: $F_{2,84} = 1.36$, $p > .05$, $\eta^2_G = .00$), suggesting no effect of background nor overall mean amplitude differences between groups over the time window. However, a significant *group x listening condition* interaction was found over the > 248ms time window ($F_{4,84} = 7.73$, $p < .001$, $\eta^2_G = .04$; Table 3). A follow-up mini-ANOVA was computed with the pre- and post-training conditions serving as a within-group variable and group (No-RM, RM) serving as a between group variable. Similar to the overall ANOVA, the mini-ANOVA revealed a significant group x listening condition interaction effect ($F_{1,42} = 6.97$, $p < .01$, $\eta^2_G = .02$). Main effects were non-significant (Group: $F_{1,42} = .46$, $p > .05$, $\eta^2_G = .01$; Condition: $F_{1,42} = 0.19$, $p > .05$, $\eta^2_G = .00$). The significant interaction suggested a greater amplitude change post-training in

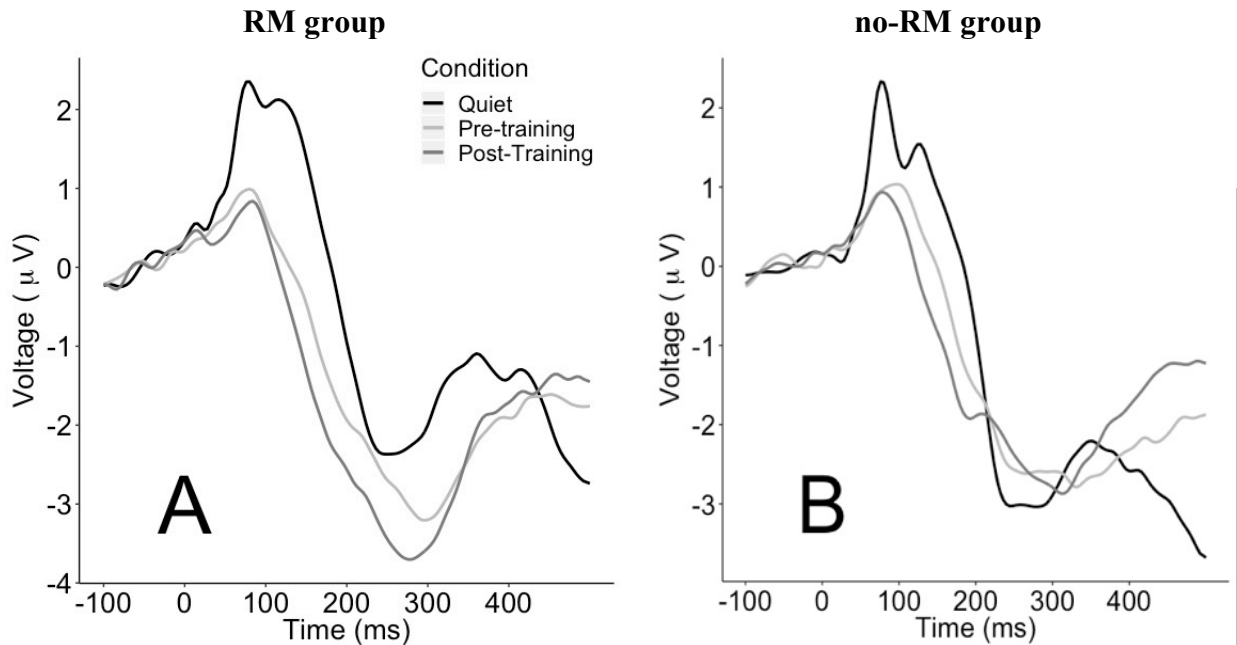
the RM group than in the no-RM (Figure 5). Additionally, mean amplitudes and latencies in the time-windows of interest did not differ in quiet or in pre-training conditions across the groups, suggesting that CAEPs were equivalent across groups before receiving the training.

Figure 3. Topographic maps corresponding to pre- and post-training conditions in the time windows of interests for both groups (RM and no-RM). Maximum cortical activity (darker areas) was located in frontal areas (Fz) across groups, time windows and listening conditions.



Note. RM = remote microphone; ms = milliseconds

Figure 4. CAEP grand average waveforms averaged across /da/ and /ga/ for each study group (panel A: RM; panel B: no-RM group). Black, light grey and dark grey correspond to quiet, pre-training and post-training conditions, respectively.



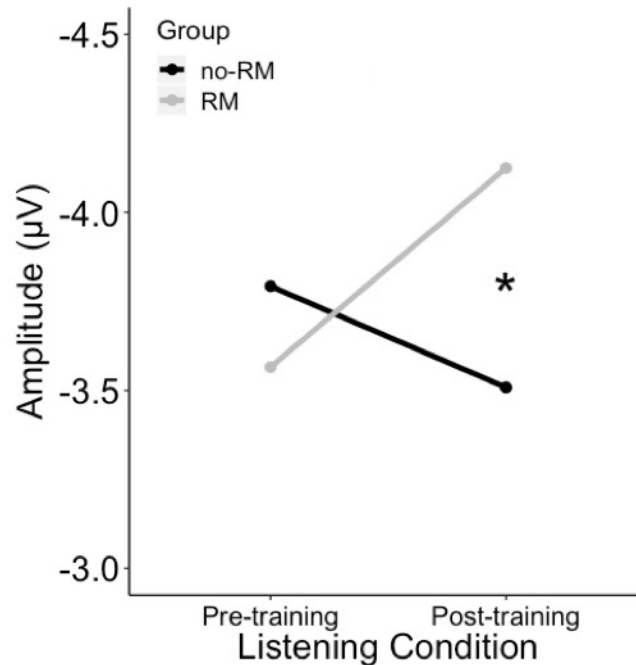
Note. μV = Microvolts; ms = milliseconds; RM = remote microphone

Table 3. CAEP mean (SE) amplitudes in microvolts for the 108-228 ms and > 248 ms in quiet, pre-training and post-training conditions at Fz.

Group	Time window: 108-228 ms			Time window: >248 ms		
	Quiet	Pre-training	Post-training	Quiet	Pre-training	Post-training
no-RM	0.21 (0.75)	-0.67 (0.49)	-1.16 (0.61)	-2.47 (0.73)	-2.15 (0.72)	-2.06 (0.57)
RM	0.19 (0.77)	-0.98 (0.35)	-1.79 (0.62)	-1.81 (0.62)	-2.43 (0.49)	-2.67 (0.77)

Note. ms = milliseconds; RM = remote microphone; CAEP = cortical auditory evoked potential

Figure 5. Mean amplitude differences between no-RM (black line) and RM (grey line) groups in the pre- and post-training conditions in the >258ms time window. A significant interaction between the pre- and post-training conditions for the two groups ($p < .05$) with $RM > no-RM$ only in post-training.



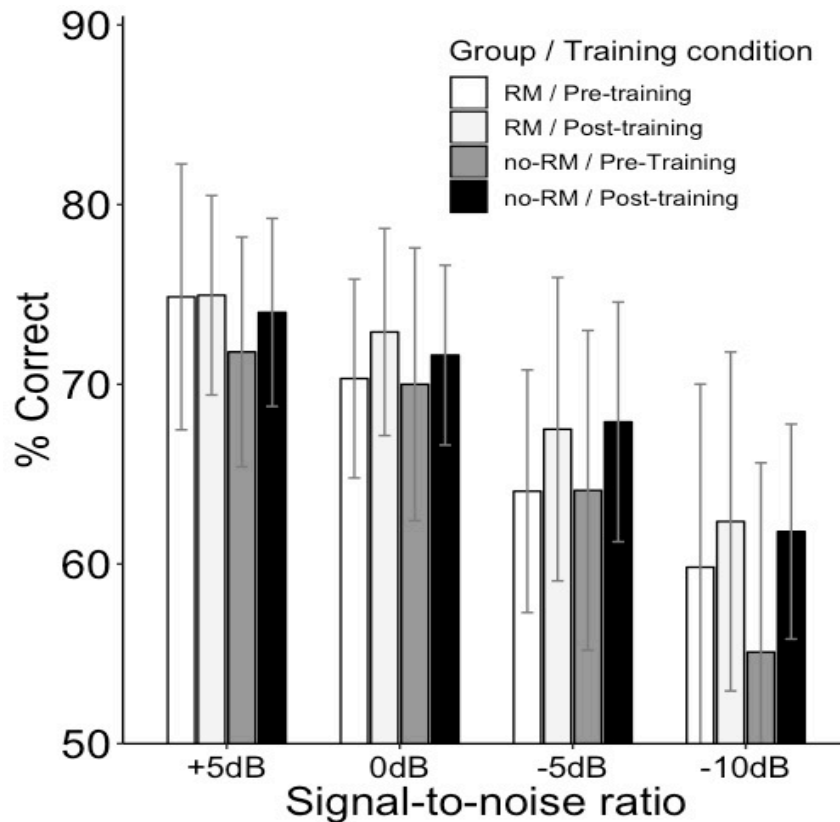
Note: μV = Microvolts; RM = remote microphone.

Training Effects on Behavioral Measures of Speech Perception in Noise

One additional child from the no-RM group in the study was unable to complete the behavioral post-training condition. As a result, behavioral analyses were computed on 43 children (21 children from the no-RM group and 22 children from the RM group). Main effects of listening condition ($F_{3, 123} = 80.7, p < .001, \eta^2_G = .36$) were found, indicating a negative effect of background noise on speech-in-noise performance across groups. A main effect of testing condition (pre-training vs post-training) was also found ($F_{1,41} = 13.6, p < .001, \eta^2_G = .04$), with post-training condition showing better NST scores across groups; however, no significant interaction of *group x testing condition* was found ($F_{1,41} = .5, p > .05, \eta^2_G = .00$), indicating that speech-perception-in-noise scores improved for both groups equivalently post training. See

Figure 6 for a visual representation of speech-in-noise performance across groups, testing, and listening conditions. Additionally, there was no main effect of group, which suggests that speech-perception-in-noise skills were equivalent across groups at pre- and post-training assessments.

Figure 6. Speech-perception-in-noise scores at +5 dB, 0dB, -5dB and -10dB SNR pre- and post-training for each study group (white bars: RM pre-training; light grey bars: RM post-training; dark grey bars: no-RM pre-training; black bars: no-RM post-training). Higher scores reflect better speech-perception-in-noise skills.



Note. RM = remote microphone; dB = decibels.

Relationship Between Neural and Behavioral Indices of Speech Perception in Noise

Weak ($r < .35$) and non-significant correlations were found between pre- and post-training NST scores at all SNRs and CAEPs (including GFP values and amplitudes and latencies

over the time windows of interest). Similarly, weak ($r < .35$) and non-significant correlations were found between pre- and post-training NST difference scores and pre- and post-training CAEPs (including GFP values as well as amplitudes and latencies pre- and post-training over the time windows of interests). Finally, the relationship between age and NST scores (pre- and post-training) was very weak ($r < .2$) and non-significant at every NST SNR. The same was found for the relationship between age and GFP values and amplitudes and latencies in the pre- and post-training with correlation values being very weak ($r < .2$) and non-significant between the variables.

CHAPTER IV

DISCUSSION

The present study was designed to evaluate whether the use of an RM system with a brief speech-in-noise training improved speech-in-noise processing (as indexed by CAEPs and behavioral responses) compared to children receiving the same training without use of an RM system. In addition, the relationship between speech-in-noise processing at the cortical level and behavioral speech perception in noise skills of children was explored. It was hypothesized that children using an RM system during training would show greater improvement in cortical activity and better speech-perception-in-noise skills post-training relative to a pre-training condition than children who received training without the RM system. Moreover, it was hypothesized that CAEPs to speech in noise would be related to behavioral indices of speech perception in noise, with children showing greater CAEP improvement when using an RM system during training also showing greater improvement on their speech-perception-in-noise performance post-training.

Both groups of children participating in the study shared equivalent demographic variables such as age, gender, socioeconomic status, and amount of musical experience. Moreover, participants had equivalent cognitive skills, speech-perception-in-noise skills pre-training, and CAEPs to speech in quiet and in noise prior to training. By controlling these variables, we were able to attribute post-training changes in CAEPs and behavioral indices of speech-in-noise processing to training effects and not to pre-existing differences between the groups.

Our main findings can be summarized as follows: (1) children receiving training with an RM system showed increased cortical activity (reflected in greater modulations in the strength of the response and greater amplitudes in the N2 response time-window) in response to speech in noise post-training compared to pre-training, than children receiving training without the RM system; (2) children in both groups (RM and no-RM) showed better speech-perception-in-noise skills post-training than pre-training; (3) CAEPs evoked by speech in noise were not related to behavioral measures of speech perception in noise.

Aim1 - Training Effects on CAEPs

We found that a brief training with an RM system improved speech processing at the cortical level. That is, we confirmed our hypothesis that children in the RM group would demonstrate greater improvement in cortical activity post training than children in the no-RM group. Specifically, this improvement was reflected by enhanced modulations on the strength of the response (i.e., GFP) across the scalp and greater CAEP amplitudes over the N2 time-window (>248ms) while processing speech in noise post-training compared to the pre-training condition. Also confirming our hypothesis, children from the no-RM group did not show any change on these indices of cortical speech-in-noise processing post-training compared to the pre-training condition. Greater GFP and larger CAEP amplitudes are thought to reflect increased neural synchrony in response to a stimulus. The N2 time-window has been shown to reflect stimulus categorization during cortical auditory processing (Čeponienė et al., 2005; Crowley & Colrain, 2004; Tremblay et al., 2014); therefore, our results also suggest that the RM system training allowed children to categorize the syllables in noise more effectively after training.

Our findings align with other human studies that have shown that auditory training triggers amplitude increases in the P2-N2 time window in adults, which has been suggested as an indicator of increased auditory perceptual learning (Seppänen et al., 2012; Tremblay & Kraus, 2002). Taking into account that RM systems increase the SNR to the user and that greater SNRs enhance CAEP amplitudes, it is reasonable to suspect that providing access to a more salient input via an RM system contributed to greater neural firing during training (Almeqbel & McMahon, 2015; Benítez-Barrera, Key, et al., 2019; Whiting, et al., 1998). Considering findings from animal models, it is possible that increased neural activity during training in our participants reshaped the SRTFs in the neural network (Atiani et al., 2009). A possible mechanism for this increased neural activity could be that neuromodulatory inputs were engaged during training through bottom-up attention, which in turn improved the cortical response post training. And, because children receiving training without an RM system did not listen to an enhanced SNR, no bottom-up attention mechanism was activated. As a result, CAEPs were equivalent between pre- and post-training conditions in that group.

It could also be argued that children in the RM group could have been more attentive during training than children in the no-RM group because of the enhanced SNR they received during CAEP testing. Plasticity changes in the auditory cortex have previously been shown to be modulated by top-down attention (David et al., 2012; Fritz et al., 2007; Yin et al., 2014). Therefore, if attention was actually enhanced in the RM group, increased neural activity in this group post-training could be explained by top-down attention-driven plasticity. However, three different factors argue against this explanation. First, children in the no-RM group could actually have to attend more to the stimuli during training than children from the RM group because of the extra effort needed to discriminate the syllables with a poorer SNR. This hypothesis is

supported by previous fMRI findings that showed increased activation in the superior temporal gyrus (which contains the auditory cortex and other language related areas) as a function of reduction in SNR when participants actively discriminated between syllables in quiet and noise conditions (Wong, Uppunda, Parrish, & Dhar, 2008). Authors interpreted this increased cortical activation in superior temporal gyrus as an effect of increased attention and listening effort during the noisier tasks. Second, in post-hoc analyses, we found that behavioral accuracy and response time when discriminating the syllables were not significantly different between groups during training or in the post-training condition; thus, both groups were equally attentive during this task. Therefore, it is believed that plasticity changes observed in the RM group were primarily driven by stimulus-driven or bottom-up plasticity and not by top-down modulatory effects.

Third, the fact that cortical responses to speech-in-noise did not change between pre- and post-training in the no-RM group, indicates that plasticity changes driven by top-down attention might not occur in speech-in-noise discrimination tasks in children. Although top-down attention plasticity changes have been observed in animals and humans in other types of listening tasks (e.g., voice-onset-time discrimination or frequency discrimination), it is possible that attending to masked speech for 10 minutes is not sufficient to drive the associated plasticity changes in the human auditory cortex (Fritz et al., 2007a, 2007b; Tremblay & Kraus, 2002). This is an important finding from a clinical standpoint because it suggests that listening to an enhanced SNR might result in greater improvement in speech-in-noise processing than simply “practicing” listening in noise.

Therefore, this study is believed to be the first to provide evidence of rapid bottom-up but not top-down plasticity driven changes in the human auditory cortex during a speech-in-noise

discrimination task. Previous human EEG studies have shown enhancement of P2 amplitudes after a short period (approximately 15 minutes) of both passive and active exposure to speech syllables in quiet (Ross & Tremblay, 2009; Seppänen et al., 2012; Tremblay & Kraus, 2002). This aligns with previous studies showing that long-term access to enriched auditory stimuli (via an RM system) improves cortical responses of children to speech-in-noise even when the RM system is not in use (Friederichs & Friederichs, 2005; Sharma et al., 2014). Our study supports the notion that plasticity changes occur quickly in the auditory system when listening to an enhanced SNR. It is then feasible to assume that if these plastic changes are reinforced over time, permanent changes in children's auditory systems can occur.

Overall, our study suggests that auditory systems of school-age children are susceptible to neuroplastic changes through auditory experience. Our study also supports previous findings with animals and humans that have shown that enhanced auditory experience (e.g., listening at a greater SNR) leads to better neural outcomes than impoverished auditory experience (Bao et al., 2003; Chang & Merzenich, 2003; Skoe et al., 2013). That is, our results support the idea proposed by Skoe and colleagues (2013) that the quality of auditory experience (enhanced versus impoverished) during childhood underlies the brain's ability to follow a speech signal of interest masked by noise. Moreover, we provide evidence of rapid *experience-dependent* plasticity in the auditory system outside of the early sensitive period (Kral, 2013).

Aim 2 - Training Effects on Behavioral Measures of Speech Perception in Noise Skills

Although we confirmed our hypothesis relating RM system training to changes in cortical responses to speech in noise post-training, we did not see between-group improvements in behavioral speech-in-noise testing post training. Children in the RM group improved their

behavioral performance on the NST task across all measured SNRs post-training; however, we found the same improvement for the children in the no-RM group. This improvement in speech perception skills post-training could be attributed to the fact that all children were familiarized with the NST stimuli during the pre-training condition, and this improvement was not specific to the use of the RM system.

Nevertheless, we did not find differential improvement in behavioral speech-perception-in-noise scores when an RM system was used. It is possible that longer training might be required to see plastic changes transferred to behavioral performance. It is well known that trained auditory processing skills can be generalized to untrained skills (Henshaw & Ferguson, 2013; Rayes et al., 2019). However, generalization is more likely to occur when auditory training is sustained over time. The fact that our speech stimuli were different between the training component of the study (/da/ and /ga/) and the NST (nonsense syllables composed by multiple phonemes) and that the training was of very short duration, might have reduced our ability to detect generalization effects from trained skills to untrained skills.

Aim 3 – Relationship Between Neural and Behavioral Indices of Speech Perception in Noise

We hypothesized that there would be a relationship between CAEPs and speech-perception-in-noise scores; specifically, that as CAEPs improved, speech perception scores would improve. Previous studies using sentence material in behavioral tasks found weak to moderate correlations with CAEPs measured at favorable SNRs (e.g., +10/+15dB SNR; Anderson et al., 2010; Benítez-Barrera, Key et al., 2019; Gustafson, 2017; Parbery-Clark et al., 2011). We used nonsense syllables to evaluate speech-in-noise performance in an attempt to use stimuli that were similar to those used in the CAEP task. However, no such relationship was

found. It is possible that phonetic differences between the EEG (/da/ and /ga/) and the speech-perception-in-noise tasks (nonsense words) were still large enough to impede observing a relationship between both measures. It is also likely that greater levels of top-down control were necessary for children to discriminate the unfamiliar nonsense words than for the more familiar EEG syllables (/da/ and /ga/). That could have limited our ability to see a relationship between both measures.

Clinical Implications

Sensitive periods for the acquisition of auditory and language skills are presumed to last until about seven and three years, respectively (Buckley & Tobey, 2011; Peterson et al., 2010; Sharma et al., 2015). That is, to develop adequate auditory and language skills, children need to have access to auditory stimuli early in life. Our findings suggest that plastic changes can occur, at least in the short term, at the cortical level in school-age children with normal hearing during complex listening tasks (e.g., speech-perception-in-noise). These findings support the idea that sensitive periods for the acquisition of more complex listening skills are extended to later in childhood (Johnson et al., 2008). Therefore, auditory intervention strategies targeting more complex listening skills could be effective from early childhood to at least the elementary school years. This is particularly relevant for clinical populations (e.g., children with hearing loss) who are known to struggle listening in the presence of background noise (Crandell, 1993; Gifford et al., 2011; Pittman et al., 1999). Furthermore, our findings suggest that successful auditory interventions with children could be those that incorporate enriched auditory experience through the use of technologies such as RM systems.

Future Directions

This study provides important insights regarding rapid plasticity changes occurring in the human auditory cortex. Furthermore, our findings support clinical practices that enhance auditory experience for children (e.g., RM systems) and facilitate cortical development via bottom-up attention plasticity changes. Future studies should investigate both rapid plasticity mechanisms occurring in the human auditory cortex (top-down versus bottom-up) and the impact of long-term enhancement of auditory experience on neural and behavioral indices of speech-in-noise processing in children.

Plasticity mechanisms studies. In the present study, we used an active training task for both groups of children. The only difference between groups was the SNR at which they were trained. Therefore, we found bottom-up plasticity changes related to the enhanced auditory signal in the group that received training with the RM system during an active listening task. However, in day-to-day life, children often listen to speech in a passive manner (i.e., overhearing). Therefore, it would be of interest to explore stimulus-driven plasticity with a passive speech-in-noise training-by-exposure task. It would be also of interest to see whether there are differences between bottom-up plasticity changes in an active versus a passive task. This could inform our understanding of the extent to which task engagement is necessary to generate bottom-up attention plasticity changes in the human auditory cortex.

Also, in our current study we did not find a training effect on speech-in-noise behavioral performance or a relationship between cortical responses and behavioral speech-in-noise performance. This is an important translational link to demonstrate that training has a meaningful impact on behavioral outcomes of children. To increase the likelihood of finding a relationship between neural and behavioral indices of speech processing, future studies could incorporate

different options. One possibility would be to use behavioral responses (e.g., response time and accuracy) at different SNRs for the same syllables (/da/ and /ga/) as an index of speech-in-noise perception skills. Theoretically, using the same speech stimuli in both tasks should control for top-down attention effects, potentially increasing the chances of finding a relationship between both measures as well as observing a training effect on behavioral performance. Also, future studies might consider using a dual-task paradigm as a measure of behavioral performance pre- and post- training. For example, a dual-task paradigm could pair an auditory discrimination task with another sensory discrimination task (e.g., visual tasks). Presence of plasticity changes related to auditory training would allow better performance on the visual discrimination task post- training than pre-training. This is based on the assumption that training would facilitate auditory discrimination resulting in an advantage when completing the dual task. Finally, another possible line of research could examine the impact of longer trainings with the RM system on generalization effects from trained stimuli (e.g., /da/ and /ga/) to untrained stimuli (e.g., nonsense words).

Auditory experience. Apart from investigations of rapid plasticity mechanisms in the auditory system, the present study provides additional support to the idea that the quality of the auditory experience is related to neural and behavioral outcomes of children. Future studies could investigate the neural and behavioral effects of long-term exposure to enhanced versus impoverished auditory environments in children. Based on our findings of rapid plasticity, we hypothesize that the quality of the auditory environments in which children are reared plays an important role in their ability to process speech in noise at the neural and behavioral level. Future studies could focus on measuring the quality of children's auditory daily environments such as background noise levels, SNRs, and examining the relationship with neural and behavioral

indices of speech perception in noise. It should be expected that children reared in environments with higher levels of background noise and poorer SNRs would show poorer cortical responses to speech-in-noise and poorer speech-in-noise perception skills than children reared in quiet environments.

Similarly, future studies could investigate whether providing clinical populations with access to enriched auditory stimuli via hearing technology has a positive impact on the development of auditory areas of the brain as well as on speech perception in noise skills of children. Longitudinal studies examining speech-in-noise cortical responses as well as growth curves in speech-in-noise behavioral skills are warranted. Because speech-in-noise perception is strongly associated with cognitive skills, language skills, and academic performance, it is possible that benefits related to enhanced auditory experience might extend beyond speech-in-noise perception (Anderson, White-Schwoch, Parbery-Clark, & Kraus, 2013; Boets, Ghesquière, Van Wieringen, & Wouters, 2007; Boets, Wouters, Van Wieringen, De Smedt, & Ghesquiere, 2008). This is supported by the connectome hypothesis of brain function, which proffers that changes in sensory areas of the brain (e.g., speech perception) produce cascade plasticity effects benefiting higher order processing areas such as memory, attention, and language (Kral, Kronenberger, Pisoni, & O'Donoghue, 2016). Longitudinal studies could investigate whether long-term access to enriched auditory experience, via RM systems or other hearing technologies, improve children's general behavioral functioning.

Limitations

There are several methodological caveats that must be considered when interpreting the study findings. First, we did not measure the input level at the ear when the stimuli were

delivered through the RM system. It is possible that because we used custom ear tips, the stimuli were delivered to the children receiving training with the RM system at a higher intensity level than to those receiving training in the free-field without the RM system (70 dB SPL). Therefore, plasticity changes related to RM use could be attributed to differences in sound level instead of differences in SNR during training between the groups. Although this is a limitation of the study, the fact that differences in SNR has been shown to trigger bottom-up plasticity changes in animal models supports our conclusions. Moreover, pilot participants in the RM group were trained without the device. That is, they were trained in the free field at +15 dB SNR (same SNR as those who were trained with the RM system). These pilot participants demonstrated the same effect as participants receiving training with the RM system. Therefore, attributing plasticity changes in the RM group to differences in SNR rather than level seems to be a reasonable argument.

Also as previously stated, the use of a relatively favorable SNR in the EEG tasks likely influenced the magnitude of the effect of noise on CAEPs and potentially affected its relationship with behavior. However, we decided to use a +5dB SNR in the EEG pre-training and post-training conditions because when poorer SNRs were used with pilot participants we were often unable to detect clear CAEP components. Therefore, using a +5dB SNR improved the likelihood that training effects would be measurable in our group of participants. Also, the fact that NST post-training testing occurred approximately 15 to 20 minutes post training could have impeded our ability to detect shorter-term training effects.

This study is also limited by the convenience sample of the children of university faculty and staff. Our sample represented a portion of the population with higher than usual cognitive and language skills, which are known to predict speech-perception-in-noise skills (e.g., Hnath-

Chisolm, Laipply, & Boothroyd, 1998). A more diverse sample might have allowed for greater variability in the impact of noise on CAEPs and behavioral measures of speech in noise.

Nonetheless, these results contribute to the knowledge base in this area by detecting training effects at the neural level for this group of children. It remains to be seen if RM system use could be an effective auditory training tool for children known to have difficulty with speech in noise (e.g., children with hearing loss).

Conclusions

This study utilized neural and behavioral indices of speech-in-noise processing to evaluate the impact of RM system use on children's CAEPs and speech-perception-in-noise scores. Results suggest that a brief period of RM system training triggers bottom-up plasticity changes in the auditory cortex, improving speech processing at the cortical level post-training. Therefore, it is possible that prolonged use of RM systems in clinical populations of children could enhance the development of their speech processing skills. This could potentially not only increase children's ability to encode speech in noise when the RM system is not used but also, as suggested by one recent study (Curran et al., 2019), enhance the development of other language and cognitive skills that are known to be associated with speech processing.

REFERENCES

- Ahveninen, J., Jääskeläinen, I. P., Raij, T., Bonmassar, G., Devore, S., Hämäläinen, M., ... & Witzel, T. (2006). Task-modulated “What” and “Where” Pathways in Human Auditory Cortex. *Proceedings of the National Academy of Sciences*, *103*(39), 14608-14613.
- Alain, C., Snyder, J. S., He, Y., & Reinke, K. S. (2007). Changes in auditory cortex parallel rapid perceptual learning. *Cerebral Cortex*, *17*(5), 1074-1084.
- Albrecht, R., Suchodoletz, W. V., & Uwer, R. (2000). The Development of Auditory Evoked Dipole Source Activity from Childhood to Adulthood. *Clinical Neurophysiology*, *111*(12), 2268-2276.
- Allen, P., Wightman, F., Kistler, D., & Dolan, T. (1989). Frequency Resolution in Children. *Journal of Speech, Language, and Hearing Research*, *32*(2), 317-322.
- Almeqbel, A., & McMahon, C. (2015). Objective Measurement of High-level Auditory Cortical Function in Children. *International Journal of Pediatric Otorhinolaryngology*, *79*(7), 1055-1062.
- Altevogt, B., & Hougan, M. (Eds.). (2008). *From Molecules to Minds: Challenges for the 21st Century: Workshop Summary*. National Academies Press.
- Amitay, S., Irwin, A., & Moore, D. R. (2006). Discrimination Learning Induced by Training with Identical Stimuli. *Nature Neuroscience*, *9*(11), 1446–1448.
- Anderson, S., Chandrasekaran, B., Yi, H. G., & Kraus, N. (2010). Cortical-evoked Potentials Reflect Speech-in-noise Perception in Children. *European Journal of Neuroscience*, *32*(8), 1407-1413.

- Anderson, S., White-Schwoch, T., Parbery-Clark, A., & Kraus, N. (2013). A Dynamic Auditory-Cognitive System Supports Speech-in-noise Perception in Older Adults. *Hearing Research, 300*, 18-32.
- Atiani, S., Elhilali, M., David, S. V., Fritz, J. B., & Shamma, S. A. (2009). Task Difficulty and Performance Induce Diverse Adaptive Patterns in Gain and Shape of Primary Auditory Cortical Receptive Fields. *Neuron, 61*(3), 467-480.
- Bao, S., Chang, E. F., Davis, J. D., Gobeske, K. T., & Merzenich, M. M. (2003). Progressive Degradation and Subsequent Refinement of Acoustic Representations in the Adult Auditory Cortex. *The Journal of Neuroscience, 23*(34), 10765-10775.
- Bargones, J. Y., & Werner, L. A. (1994). Adults Listen Selectively; Infants Do Not. *Psychological Science, 5*(3), 170-174.
- Barnet, A. B. (1971). EEG Audiometry in Children under 3 years of Age. *Acta Otolaryngologica, 72*, 1-13.
- Belin, P., & Zatorre, R. J. (2003). Adaptation to Speaker's Voice in Right Anterior Temporal Lobe. *Neuroreport, 14*(16), 2105-2109.
- Benítez-Barrera, C. R., Angley, G. P., & Tharpe, A. M. (2018). Remote Microphone System Use at Home: Impact on Caregiver Talk. *Journal of Speech Language & Hearing Research, 61*(2), 399-409.
- Benítez-Barrera, C. R., Key, A., Ricketts, T., & Tharpe, A. M. (2019). *Central Auditory Responses from Children While Listening to Speech in Noise*. Manuscript submitted for publication.

- Benítez-Barrera, C. R., Thompson, E., Angley, G. P., Woynaroski, T., & Tharpe, A. M. (2019). Remote Microphone System Use at Home: Impact on Child-directed Speech. *Journal of Speech Language & Hearing Research*, 62(6), 2002-2008
- Bertachini, A. L. L., Pupo, A. C., Morettin, M., Martinez, M. A. N., Bevilacqua, M. C., Moret, A. L. M., ... & Jacob, R. T. D. S. (2015). Frequency Modulation System and Speech Perception in the Classroom: A Systematic Literature Review. In *CoDAS* (Vol. 27, No. 3, pp. 292-300). Sociedade Brasileira de Fonoaudiologia.
- Binder, J. R., Frost, J. A., Hammeke, T. A., Bellgowan, P. S., Springer, J. A., Kaufman, J. N., & Possing, E. T. (2000). Human Temporal Lobe Activation by Speech and Nonspeech Sounds. *Cerebral Cortex*, 10(5), 512-528.
- Boets, B., Ghesquière, P., Van Wieringen, A., & Wouters, J. (2007). Speech Perception in Preschoolers at Family Risk for Dyslexia: Relations with Low-level Auditory Processing and Phonological Ability. *Brain and Language*, 101(1), 19-30.
- Boets, B., Wouters, J., Van Wieringen, A., De Smedt, B., & Ghesquiere, P. (2008). Modelling Relations Between Sensory Processing, Speech Perception, Orthographic and Phonological Ability, and Literacy Achievement. *Brain and Language*, 106(1), 29-40.
- Boothroyd, A. (1968). Developments in Speech Audiometry. *British Journal of Audiology*, 2(1), 3-10.
- Boothroyd, A. (1970). Developmental Factors in Speech Recognition. *International Journal of Audiology*, 9(1), 30-38.
- Boothroyd, A. (1997). Auditory Development of the Hearing Child. *Scandinavian Audiology-Supplement Only*, 46, 9-16.

- Bruneau, N., Roux, S., Guérin, P., Barthélémy, C., & Lelord, G. (1997). Temporal Prominence of Auditory Evoked Potentials (N1wave) in 4–8-year-old Children. *Psychophysiology* 34, 32–38
- Brunet, D., Murray, M. M., & Michel, C. M. (2011). Spatiotemporal Analysis of Multichannel EEG: CARTOOL. *Computational Intelligence and Neuroscience*, 2011, 2.
- Buckley, K. A., & Tobey, E. A. (2011). Cross-modal Plasticity and Speech Perception in Pre-and Postlingually Deaf Cochlear Implant Users. *Ear and hearing*, 32(1), 2-15.
- Campbell, J., & Sharma, A. (2014). Cross-modal Re-organization in Adults with Early Stage Hearing Loss. *PloS One*, 9(2).
- Caras, M. L., & Sanes, D. H. (2017). Top-down Modulation of Sensory Cortex Gates Perceptual Learning. *Proceedings of the National Academy of Sciences*, 114(37), 9972-9977.
- Cardon, G., & Sharma, A. (2013). Central Auditory Maturation and Behavioral Outcome in Children with Auditory Neuropathy Spectrum Disorder who use Cochlear Implants. *International Journal of Audiology*, 52(9), 577-586.
- Čeponienė, R., Alku, P., Westerfield, M., Toriki, M., & Townsend, J. (2005). ERPs Differentiate Syllable and Non-phonetic Sound Processing in Children and Adults. *Psychophysiology*, 42(4), 391-406.
- Chang, E. F., & Merzenich, M. M. (2003). Environmental Noise Retards Auditory Cortical Development. *Science*, 300(5618), 498-502.
- Chugani, H. T. (1994). Development of Regional Brain Glucose Metabolism in Relation to Behavior and Plasticity. In G. Dawson & K. W. Fischer (Eds.), *Human Behavior and the Developing Brain* (pp. 153–175). New York: Guilford Press.
- Crandell, C. C. (1993). Speech Recognition in Noise by Children with Minimal Degrees of

- Sensorineural Hearing Loss. *Ear and Hearing*, 14(3), 210–216.
- Crowley, K. E., & Colrain, I. M. (2004). A Review of the Evidence for P2 Being an Independent Component Process: Age, Sleep and Modality. *Clinical Neurophysiology*, 115(4), 732-744.
- Cunningham, J., Nicol, T., Zecker, S., & Kraus, N. (2000). Speech-evoked Neurophysiologic Responses in Children with Learning Problems: Development and Behavioral Correlates of Perception. *Ear & Hearing*, 21, 554–568
- Curran, M., Walker, E. A., Roush, P., & Spratford, M. (2019). Using Propensity Score Matching to Address Clinical Questions: The Impact of Remote Microphone Systems on Language Outcomes in Children Who Are Hard of Hearing. *Journal of Speech, Language, and Hearing Research*, 62(3), 564-576.
- D'Angiulli, A., Herdman, A., Stapells, D., & Hertzman, C. (2008). Children's Event-related Potentials of Auditory Selective Attention Vary with their Socioeconomic Status. *Neuropsychology*, 22(3), 293.
- Danhauer, J. L., & Edgerton, B. J. (1988). Edgerton-Danhaeur Nonsense Syllable Test. Auditec, Inc. CD and CD-Rom
- David, S. V., Fritz, J. B., & Shamma, S. A. (2012). Task Reward Structure Shapes Rapid Receptive Field Plasticity in Auditory Cortex. *Proceedings of the National Academy of Sciences*, 109(6), 2144-2149.
- Davis, S. M., & McCroskey, R. L. (1980). Auditory Fusion in Children. *Child Development*, 75-80.

- De Boer, J., & Krumbholz, K. (2018). Auditory Attention Causes Gain Enhancement and Frequency Sharpening at Successive Stages of Cortical Processing—Evidence from Human Electroencephalography. *Journal of Cognitive Neuroscience*, *30*(6), 785-798.
- De Santis, L., Clarke, S., & Murray, M. M. (2007). Automatic and Intrinsic Auditory “What” and “Where” Processing in Humans Revealed by Electrical Neuroimaging. *Cerebral Cortex*, *17*(1), 9-17.
- Ding, N., & Simon, J. Z. (2012). Emergence of Neural Encoding of Auditory Objects while Listening to Competing Speakers. *Proceedings of the National Academy of Sciences*, *109*(29), 11854-11859.
- Eggermont, J. J. (1992). Development of Auditory Evoked Potentials. *Acta OtoLaryngologica*, *112*(2), 197-200.
- Eggermont, J. J. (2008). The Role of Sound in Adult and Developmental Auditory Cortical Plasticity. *Ear and Hearing*, *29*(6), 819-829.
- Eggermont, J. J., & Ponton, C. W. (2003). Auditory-evoked Potential Studies of Cortical Maturation in Normal Hearing and Implanted Children: Correlations with Changes in Structure and Speech perception. *Acta Oto-laryngologica*, *123*(2), 249-252.
- Eisenberg, L. S., Shannon, R. V., Schaefer Martinez, A., Wygonski, J., & Boothroyd, A. (2000). Speech Recognition with Reduced Spectral Cues as a Function of Age. *The Journal of the Acoustical Society of America*, *107*(5), 2704-2710.
- Elliott, L. L., & Katz, D. R. (1980). Children’s Pure-tone Detection. *The Journal of the Acoustical Society of America*, *67*(1), 343-344.
- Evans, G. W., & Kantrowitz, E. (2002). Socioeconomic Status and Health: The Potential Role of Environmental Risk Exposure. *Annual Review of Public Health*, *23*(1), 303-331.

- Finney, E. M., Fine, I., & Dobkins, K. R. (2001). Visual Stimuli Activate Auditory Cortex in the Deaf. *Nature Neuroscience*, 4(12), 1171.
- Friederichs, E., & Friederichs, P. (2005). Electrophysiologic and Psycho-acoustic Findings Following One-year Application of a Personal Ear-level FM Device in Children with Attention Deficit and Suspected Central Auditory Processing Disorder. *Journal of Educational Audiology*, 12, 31-36.
- Friederici, A. D. (2012). The Cortical Language Circuit: From Auditory Perception to Sentence Comprehension. *Trends in Cognitive Sciences*, 16(5), 262-268.
- Fritz, J. B., Elhilali, M., David, S. V., & Shamma, S. A. (2007a). Auditory Attention— Focusing the Searchlight on Sound. *Current Opinion in Neurobiology*, 17(4), 437-455.
- Fritz, J. B., Elhilali, M., David, S. V., & Shamma, S. A. (2007b). Does Attention Play a Role in Dynamic Receptive Field Adaptation to Changing Acoustic Salience in A1? *Hearing Research*, 229(1-2), 186-203.
- Fritz, J. B., Elhilali, M., & Shamma, S. A. (2005). Differential Dynamic Plasticity of A1 Receptive Fields During Multiple Spectral Tasks. *Journal of Neuroscience*, 25(33), 7623-7635.
- Fritz, J. B., Elhilali, M., & Shamma, S. A. (2007). Adaptive Changes in Cortical Receptive Fields Induced by Attention to Complex Sounds. *Journal of Neurophysiology*, 98(4), 2337-2346.
- Fu, K. M. G., Johnston, T. A., Shah, A. S., Arnold, L., Smiley, J., Hackett, T. A., ... & Schroeder, C. E. (2003). Auditory Cortical Neurons Respond to Somatosensory Stimulation. *Journal of Neuroscience*, 23(20), 7510-7515.
- Fu, Q. J., & Galvin, J. J., III. (2008). Maximizing Cochlear Implant Patients' Performance with

- Advanced Speech Training Procedures. *Hearing Research*, 242(1–2), 198–208
- Fu, Q. J., Galvin, J. J., III., Wang, X., & Nogaki, G. (2004). Effects of Auditory Training on Adult Cochlear Implant Patients: A Preliminary Report. *Cochlear Implants International*, 5(Suppl. 1), 84–90
- Gifford, R. H., Olund, A. P., & DeJong, M. (2011). Improving Speech Perception in Noise for Children with Cochlear Implants. *Journal of the American Academy of Audiology*, 22(9), 623–632.
- Gilley, P. M., Sharma, A., Dorman, M., & Martin, K. (2005). Developmental Changes in Refractoriness of the Cortical Auditory Evoked Potential. *Clinical Neurophysiology*, 116(3), 648-657.
- Greenough, W. T., Black, J. E., & Wallace, C. S. (1987). Experience and Brain Development. *Child Development*, 539-559.
- Griffiths, T. D., & Warren, J. D. (2002). The Planum Temporale as a Computational Hub. *Trends in Neurosciences*, 25(7), 348-353.
- Gustafson, S. J. (2017). *Cortical Associates of Speech-in-noise Perception from Childhood to Adulthood* (Doctoral dissertation, Vanderbilt University).
- Hackett, T. A. (2011). Information Flow in the Auditory Cortical Network. *Hearing Research*, 271(1-2), 133-146.
- Hackett, T. A. (2015). Anatomic Organization of the Auditory Cortex. In *Handbook of Clinical Neurology* (Vol. 129, pp. 27-53). Elsevier.
- Hayes, E. A., Warrier, C. M., Nicol, T. G., Zecker, S. G., & Kraus, N. (2003). Neural Plasticity Following Auditory Training in Children with Learning Problems. *Clinical Neurophysiology*, 114(4), 673-684.

- Henshaw, H., & Ferguson, M. A. (2013). Efficacy of Individual Computer-based Auditory Training for People with Hearing Loss: A Systematic Review of the Evidence. *PLoS One*, 8(5), e62836.
- Hillyard, S. A., Hink, R. F., Schwent, V. L., & Picton, T. W. (1973). Electrical Signs of Selective Attention in the Human Brain. *Science*, 182(4108), 177-180.
- Hnath-Chisolm, T. E., Laipply, E., & Boothroyd, A. (1998). Age-related Changes on a Children's Test of Sensory-level Speech Perception Capacity. *Journal of Speech, Language, and Hearing Research*, 41(1), 94-106.
- Holt, L. L., & Lotto, A. J. (2008). Speech Perception Within an Auditory Cognitive Science Framework. *Current Directions in Psychological Science*, 17(1), 42-46.
- Hornickel, J., Zecker, S. G., Bradlow, A. R., & Kraus, N. (2012). Assistive Listening Devices Drive Neuroplasticity in Children with Dyslexia. *Proceedings of the National Academy of Sciences*, 109(41), 16731-16736.
- Huttenlocher, P. R., & Dabholkar, A. S. (1997). Regional Differences in Synaptogenesis in Human Cerebral Cortex. *Journal of Comparative Neurology*, 387(2), 167-178.
- Irwin, R. J., Ball, A. K. R., Kay, N., Stillman, J. A., & Rosser, J. (1985). The Development of Auditory Temporal Acuity in Children. *Child Development*, 614-620.
- Irwin, R. J., Stillman, J. A., & Schade, A. (1986). The Width of the Auditory Filter in Children. *Journal of Experimental Child Psychology*, 41(3), 429-442.
- Ismail, F. Y., Fatemi, A., & Johnston, M. V. (2017). Cerebral Plasticity: Windows of Opportunity in the Developing Brain. *European Journal of Paediatric Neurology*, 21(1), 23-48.

- Jenison, R. L. (2001). Auditory System. In *International Encyclopedia of the Social & Behavioral Sciences*. Pages 936-952. Pergamon.
- Johnson, C. E. (2000). Children's Phoneme Identification in Reverberation and Noise. *Journal of Speech, Language, and Hearing Research*, 43(1), 144-157.
- Johnson, K. L., Nicol, T., Zecker, S. G., & Kraus, N. (2008). Developmental Plasticity in The Human Auditory Brainstem. *Journal of Neuroscience*, 28(15), 4000-4007.
- Johnstone, S. J., Barry, R. J., Anderson, J. W., & Coyle, S. F. (1996). Age-related Changes in Child and Adolescent Event-related Potential Component Morphology, Amplitude and Latency to Standard and Target Stimuli in an Auditory Oddball Task. *International Journal of Psychophysiology*. 24, 223–238.
- Kaas, J. H., & Hackett, T. A. (1999). 'What' and 'Where' Processing in Auditory Cortex. *Nature Neuroscience*, 2(12), 1045-1047.
- Kaas, J. H., & Hackett, T. A. (2000). Subdivisions of Auditory Cortex and Processing Streams in Primates. *Proceedings of the National Academy of Sciences*, 97(22), 11793-11799.
- Kaufman, A. S., & Kaufman, N. L. (2004). Kaufman Brief Intelligence Test 2. London: Pearson.
- Kaya, E. M., & Elhilali, M. (2017). Modelling Auditory Attention. *Philosophical Transactions of the Royal Society B: Biological Sciences*, 372(1714), 20160101.
- Kayser, C., Petkov, C. I., Augath, M., & Logothetis, N. K. (2007). Functional Imaging Reveals Visual Modulation of Specific Fields in Auditory Cortex. *Journal of Neuroscience*, 27(8), 1824-1835.
- Key, A. P., Dove, G. O., & Maguire, M. J. (2005). Linking Brainwaves to the Brain: An ERP Primer. *Developmental Neuropsychology*, 27(2), 183–215.

- King, A. J., Teki, S., & Willmore, B. (2018). Recent Advances in Understanding the Auditory Cortex. *F1000Research*, 7, F1000 Faculty Rev-1555.
- Klatte, M., Lachmann, T., & Meis, M. (2010). Effects of Noise and Reverberation on Speech Perception and Listening Comprehension of Children and Adults in a Classroom-like Setting. *Noise and Health*, 12(49), 270.
- Knudsen, E. I. (2004). Sensitive Periods in the Development of the Brain and Behavior. *Journal of Cognitive Neuroscience*, 16(8), 1412-1425.
- Kral, A. (2007). Unimodal and Cross-modal Plasticity in the 'Deaf' Auditory Cortex. *International Journal of Audiology*, 46(9), 479-493.
- Kral, A. (2013). Auditory Critical Periods: A Review from System's Perspective. *Neuroscience*, 247, 117-133.
- Kral, A., Kronenberger, W. G., Pisoni, D. B., & O'Donoghue, G. M. (2016). Neurocognitive Factors in Sensory Restoration of Early Deafness: A Connectome Model. *The Lancet Neurology*, 15(6), 610-621.
- Kral, A., & Sharma, A. (2012). Developmental Neuroplasticity After Cochlear Implantation. *Trends in Neurosciences*, 35(2), 111-122.
- Kral, A., Yusuf, P. A., & Land, R. (2017). Higher-order Auditory Areas in Congenital Deafness: Top-down Interactions and Corticocortical Decoupling. *Hearing Research*, 343, 50-63.
- Kraus, N., & Chandrasekaran, B. (2010). Music Training for the Development of Auditory Skills. *Nature Reviews Neuroscience*, 11(8), 599.
- Kuhl, P. K. (1992). Psychoacoustics and Speech Perception: Internal Standards, Perceptual Anchors, and Prototypes. In L. A. Werner & E. W. Rubel (Eds.), *Developmental Psychoacoustics* (pp. 293–332). Washington, DC: American Psychological Association.

- Lahav, A., & Skoe, E. (2014). An Acoustic Gap Between the NICU and Womb: A Potential Risk for Compromised Neuroplasticity of the Auditory System in Preterm Infants. *Frontiers in Neuroscience*, 8, 381.
- Lambertz, N., Gizewski, E. R., de Greiff, A., & Forsting, M. (2005). Cross-modal Plasticity in Deaf Subjects Dependent on the Extent of Hearing Loss. *Cognitive Brain Research*, 25(3), 884-890.
- Larsen, R. S., & Sjöström, P. J. (2015). Synapse-type-specific Plasticity in Local Circuits. *Current Opinion in Neurobiology*, 35, 127-135.
- Lavoie, M. E., Robaey, P., Stauder, J. E. A., Glorieux, J., & Lefebvre, F. (1997). A Topographical ERP Study of Healthy Premature 5-year-old Children in the Auditory and Visual Modalities. *Electroencephalography and Clinical Neurophysiology/Evoked Potentials Section*, 104(3), 228-243.
- Levitt, P. (2003). Structural and Functional Maturation of the Developing Primate Brain. *The Journal of Pediatrics*, 143(4), 35-45.
- MacGregor, L. J., Pulvermüller, F., Van Casteren, M., & Shtyrov, Y. (2012). Ultra-rapid Access to Words in the Brain. *Nature Communications*, 3(1), 1-7.
- Martin, B. A., Kurtzberg, D., & Stapells, D. R. (1999). The Effects of Decreased Audibility Produced by High-pass Noise Masking on N1 and the Mismatch Negativity to Speech Sounds /ba/ and /da/. *Journal of Speech, Language, and Hearing Research*, 42(2), 271–286.
- Meredith, M. A., & Lomber, S. G. (2011). Somatosensory and Visual Crossmodal Plasticity in the Anterior Auditory Field of Early-deaf Cats. *Hearing Research*, 280(1-2), 38-47.

- Mesgarani, N., & Chang, E. F. (2012). Selective Cortical Representation of Attended Speaker in Multi-talker Speech Perception. *Nature*, 485(7397), 233-236.
- Michel, C. M., & Murray, M. M. (2012). Towards the Utilization of EEG as a Brain Imaging tool. *Neuroimage*, 61(2), 371-385.
- Molfese, D. L. (2000). Predicting Dyslexia at 8 years of Age Using Neonatal Brain Responses. *Brain & Language*, 72, 238–245
- Moore, J. K. (2002). Maturation of Human Auditory Cortex: Implications for Speech Perception. *The Annals of Otology, Rhinology & Laryngology. Supplement*, 189, 7-10.
- Moore, J. K., & Guan, Y. L. (2001). Cytoarchitectural and Axonal Maturation in Human Auditory Cortex. *Journal of the Association for Research in Otolaryngology*, 2(4), 297-311.
- Mueller, C. W., & Parcel, T. L. (1981). Measures of Socioeconomic Status: Alternatives and Recommendations. *Child Development*, 13-30.
- Murray, M. M., Camen, C., Andino, S. L. G., Bovet, P., & Clarke, S. (2006). Rapid Brain Discrimination of Sounds of Objects. *Journal of Neuroscience*, 26(4), 1293-1302.
- Neuman, A. C., & Hochberg, I. (1983). Children's Perception of Speech in Reverberation. *The Journal of the Acoustical Society of America*, 73(6), 2145-2149.
- Neville, H., & Bavelier, D. (2002). Human Brain Plasticity: Evidence from Sensory Deprivation and Altered Language Experience. *Brain Research*, 138, 177-188.
- Neville, H. J., Stevens, C., Pakulak, E., Bell, T. A., Fanning, J., Klein, S., & Isbell, E. (2013). Family-based Training Program Improves Brain Function, Cognition, and Behavior in Lower Socioeconomic Status Preschoolers. *Proceedings of the National Academy of Sciences*, 110(29), 12138-12143.

- Nittrouer, S., & Boothroyd, A. (1990). Context Effects in Phoneme and Word Recognition by Young Children and Older Adults. *The Journal of the Acoustical Society of America*, 87(6), 2705-2715.
- Nozza, R. J., & Wilson, W. R. (1984). Masked and Unmasked Pure-Tone Thresholds of Infants and Adults Development of Auditory Frequency Selectivity and Sensitivity. *Journal of Speech, Language, and Hearing Research*, 27(4), 613-622.
- Obleser, J., Wise, R. J., Dresner, M. A., & Scott, S. K. (2007). Functional Integration across Brain Regions Improves Speech Perception under Adverse Listening Conditions. *Journal of Neuroscience*, 27(9), 2283-2289.
- Okamoto, H., Stracke, H., Lagemann, L., & Pantev, C. (2010). Bottom-up and Top-down Driven Attentional Effects on Auditory Evoked Fields. In *17th International Conference on Biomagnetism Advances in Biomagnetism–Biomag2010* (pp. 318-321). Springer, Berlin, Heidelberg.
- Okamoto, H., Stracke, H., Wolters, C. H., Schmael, F., & Pantev, C. (2007). Attention Improves Population-level Frequency Tuning in Human Auditory Cortex. *Journal of Neuroscience*, 27(39), 10383-10390.
- Parbery-Clark, A., Marmel, F., Bair, J., & Kraus, N. (2011). What Subcortical–cortical Relationships Tell Us About Processing Speech in Noise. *European Journal of Neuroscience*, 33(3), 549-557.
- Peterson, N. R., Pisoni, D. B., & Miyamoto, R. T. (2010). Cochlear Implants and Spoken Language Processing Abilities: Review and Assessment of the Literature. *Restorative Neurology and Neuroscience*, 28(2), 237-250.
- Phonak Dynamic Offset Protocol, iPOP. (2009). Retrieved from

http://www.phonak.com/content/dam/phonak/b2b/Pediatrics/campaign_2010/dynamic_fm/ipop_phonak_dynamic_fm_offset_protocol_en.pdf

- Pickles, J. O. (2013). *An Introduction to the Physiology of Hearing*. Brill.
- Pickles, J. O. (2015). Auditory Pathways: Anatomy and Physiology. In *Handbook of Clinical Neurology* (Vol. 129, pp. 3-25). Elsevier.
- Picton, T. W., Alain, C., Woods, D. L., John, M. S., Scherg, M., Valdes-Sosa, P., ... & Trujillo, N. J. (1999). Intracerebral Sources of Human Auditory-evoked Potentials. *Audiology and Neurotology*, 4(2), 64-79.
- Pittman, A. L., Lewis, D. E., Hoover, B. M., & Stelmachowicz, P. G. (1999). Recognition Performance for Four Combinations of FM System and Hearing Aid Microphone Signals in Adverse Listening Conditions. *Ear and Hearing*, 20(4), 279.
- Polley, D. B., Steinberg, E. E., & Merzenich, M. M. (2006). Perceptual Learning Directs Auditory Cortical Map Reorganization through Top-down Influences. *Journal of Neuroscience*, 26(18), 4970-4982.
- Ponton, C. W., Eggermont, J. J., Kwong, B., & Don, M. (2000). Maturation of Human Central Auditory System Activity: Evidence from Multi-channel Evoked Potentials. *Clinical Neurophysiology*, 111(2), 220-236.
- Purves, D., Augustine, G. J., Fitzpatrick, D., Katz, L. C., LaMantia, A. S., McNamara, J. O., & Williams, S. M. (2001). *Neuroscience. 2nd edition*. Sinauer Associates.
- Rauschecker, J. P. (1998). Cortical Processing of Complex Sounds. *Current Opinion in Neurobiology*, 8(4), 516-521.

- Rauschecker, J. P. (2007). Cortical Processing of Auditory Space: Pathways and Plasticity. In *Spatial Processing in Navigation, Imagery and Perception* (pp. 389-410). Springer, Boston, MA.
- Rauschecker, J. P., & Scott, S. K. (2009). Maps and Streams in the Auditory Cortex: Nonhuman Primates Illuminate Human Speech Processing. *Nature Neuroscience*, *12*(6), 718-724.
- Rauschecker, J. P., Tian, B., & Hauser, M. (1995). Processing of Complex Sounds in the Macaque Nonprimary Auditory Cortex. *Science*, *268*(5207), 111-114.
- Rayes, H., Al-Malky, G., & Vickers, D. (2019). Systematic Review of Auditory Training in Pediatric Cochlear Implant Recipients. *Journal of Speech, Language, and Hearing Research*, *62*(5), 1574-1593.
- Romanski, L. M., Tian, B., Fritz, J., Mishkin, M., Goldman-Rakic, P. S., & Rauschecker, J. P. (1999). Dual Streams of Auditory Afferents Target Multiple Domains in the Primate Prefrontal Cortex. *Nature Neuroscience*, *2*(12), 1131-1136.
- Ross, B., & Tremblay, K. (2009). Stimulus Experience Modifies Auditory Neuromagnetic Responses in Young and Older Listeners. *Hearing Research*, *248*(1-2), 48-59.
- Rubinstein, A., & Boothroyd, A. (1987). Effect of Two Approaches to Auditory Training on Speech Recognition by Hearing Impaired Adults. *Journal of Speech and Hearing Disorders*, *30*(2), 153-160.
- Schneider, B. A., Trehub, S. E., & Bull, D. (1979). The Development of Basic Auditory Processes in Infants. *Canadian Journal of Psychology/Revue Canadienne de Psychologie*, *33*(4), 306.
- Schow, R. L., & Nerbonne, M. A. (2007). *Introduction to Audiologic Rehabilitation*. Boston, MA: Allyn & Bacon.

- Seppänen, M., Hämäläinen, J., Pesonen, A. K., & Tervaniemi, M. (2012). Music Training Enhances Rapid Neural Plasticity of N1 and P2 Source Activation for Unattended Sounds. *Frontiers in Human Neuroscience*, 6, 43.
- Sharma, A., Campbell, J., & Cardon, G. (2015). Developmental and Cross-modal Plasticity in Deafness: Evidence from the P1 and N1 Event Related Potentials in Cochlear Implanted Children. *International Journal of Psychophysiology*, 95(2), 135-144.
- Sharma, A., Cardon, G., Henion, K., & Roland, P. (2011). Cortical Maturation and Behavioral Outcomes in children with Auditory Neuropathy Spectrum Disorder. *International Journal of Audiology*, 50(2), 98-106.
- Sharma, A., Dorman, M. F., & Kral, A. (2005). The Influence of a Sensitive Period on Central Auditory Development in Children with Unilateral and Bilateral Cochlear Implants. *Hearing Research*, 203(1-2), 134-143.
- Sharma, A., Dorman, M. F., & Spahr, A. J. (2002). A Sensitive Period for the Development of the Central Auditory System in Children with Cochlear Implants: Implications for Age of Implantation. *Ear and Hearing*, 23(6), 532-539.
- Sharma, A., Kraus, N., McGee, T. J., & Nicol, T. G. (1997). Developmental Changes in P1 and N1 Central Auditory Responses Elicited by Consonant-vowel Syllables. *Electroencephalography and Clinical Neurophysiology/Evoked Potentials Section*, 104(6), 540-545.
- Sharma, M., Purdy, S. C., & Kelly, A. S. (2014). The Contribution of Speech-evoked Cortical Auditory Evoked Potentials to the Diagnosis and Measurement of Intervention Outcomes in Children with Auditory Processing Disorder. In *Seminars in Hearing* (Vol. 35, No. 01, pp. 051-064). Thieme Medical Publishers.

- Siegenthaler, B. M. (1969). Maturation of Auditory Abilities in Children. *International Journal of Audiology*, 8(1), 59-71.
- Sininger, Y. S., Grimes, A., & Christensen, E. (2010). Auditory Development in Early Amplified Children: Factors Influencing Auditory-based Communication Outcomes in Children with Hearing Loss. *Ear and Hearing*, 31(2), 166.
- Skoe, E., Krizman, J., & Kraus, N. (2013). The Impoverished Brain: Disparities in Maternal Education Affect the Neural Response to Sound. *Journal of Neuroscience*, 33(44), 17221-17231.
- Skrandies, W. (1990). Global Field Power and Topographic Similarity. *Brain Topography*, 3(1), 137-141.
- Slater, J., Skoe, E., Strait, D. L., O'Connell, S., Thompson, E., & Kraus, N. (2015). Music Training Improves Speech-in-noise Perception: Longitudinal Evidence from a Community-based Music Program. *Behavioral Brain Research*, 291, 244-252.
- Specht, K. (2014). Neuronal Basis of Speech Comprehension. *Hearing Research*, 307, 121-135.
- Stelmachowicz, P. G., Hoover, B. M., Lewis, D. E., Kortekaas, R. W. L., & Pittman, A. L. (2000). The Relation Between Stimulus Context, Speech Audibility, and Perception for Normal-Hearing and Hearing-Impaired Children. *Journal of Speech, Language, and Hearing Research*, 43(4), 902-914.
- Stevens, C., Lauinger, B., & Neville, H. (2009). Differences in the Neural Mechanisms of Selective Attention in Children from Different Socioeconomic Backgrounds: An Event-Related Brain Potential Study. *Developmental Science*, 12(4), 634-646.
- Stiles, J., & Jernigan, T. L. (2010). The Basics of Brain Development. *Neuropsychology Review*, 20(4), 327-348.
- Strelnikov, K., Rouger, J., Demonet, J. F., Lagleyre, S., Fraysse, B., Deguine, O., & Barone, P.

- (2013). Visual Activity Predicts Auditory Recovery from Deafness After Adult Cochlear Implantation. *Brain*, 136(12), 3682-3695.
- Sweetow, R. W., & Palmer, C. V. (2005). Efficacy of Individual Auditory Training in Adults: A Systematic Review of the Evidence. *Journal of the American Academy of Audiology*, 16(7), 494-504.
- Tau, G. Z., & Peterson, B. S. (2010). Normal Development of Brain Circuits. *Neuropsychopharmacology*, 35(1), 147-168.
- Tharpe, A. M., & Ashmead, D. H. (2001). A Longitudinal Investigation of Infant Auditory Sensitivity. *American Journal of Audiology*, 10(2):104-12.
- Thompson, E. C., Benítez-Barrera, C. R., Angley, G. P., Woynaroski, T., & Tharpe, A. M. (2020). Remote Microphone System Use in the Homes of Children with Hearing Loss: Impact on Caregiver Communication and Child Vocalizations. *Journal of Speech, Language, and Hearing Research*. Advance online publication.
- Trehub, S. E., Schneider, B. A., & Endman, M. (1980). Developmental Changes in Infants' Sensitivity to Octave-band Noises. *Journal of Experimental Child Psychology*, 29(2), 282-293.
- Tremblay, K., Kraus, N., McGee, T., Ponton, C., & Otis, B. (2001). Central Auditory Plasticity: Changes in the N1-P2 Complex After Speech-sound Training. *Ear and Hearing*, 22(2), 79-90.
- Tremblay, K., Ross, B., Inoue, K., McClannahan, K., & Collet, G. (2014). Is the Auditory Evoked P2 Response a Biomarker of Learning? *Frontiers in Systems Neuroscience*, 8, 28.
- Tremblay, K. L., & Kraus, N. (2002). Auditory Training Induces Asymmetrical Changes in Cortical Neural Activity. *Journal of Speech, Language, and Hearing Research*, 45, 564-

- Tremblay, K. L., Shahin, A. J., Picton, T., & Ross, B. (2009). Auditory Training Alters the Physiological Detection of Stimulus-specific Cues in Humans. *Clinical Neurophysiology*, *120*(1), 128-135.
- Whiting, K. A., Martin, B. A., & Stapells, D. R. (1998). The Effects of Broadband Noise Masking on Cortical Event-related Potentials to Speech Sounds/ba/and/da/. *Ear and Hearing*, *19*(3), 218-231.
- Wong, P. C., Uppunda, A. K., Parrish, T. B., & Dhar, S. (2008). Cortical Mechanisms of Speech Perception in Noise. *Journal of Speech, Language, and Hearing Research*, *51*(4):1026–1041
- Wunderlich, J. L., & Cone-Wesson, B. K. (2006). Maturation of CAEP in Infants and Children: A Review. *Hearing Research*, *212*(1-2), 212-223.
- Wunderlich, J. L., Cone-Wesson, B. K., & Shepherd, R. (2006). Maturation of the Cortical Auditory Evoked Potential in Infants and Young Children. *Hearing Research*, *212*(1-2), 185-202.
- Yin, P., Fritz, J. B., & Shamma, S. A. (2014). Rapid Spectrotemporal Plasticity in Primary Auditory Cortex during Behavior. *Journal of Neuroscience*, *34*(12), 4396-4408.
- Yoshinaga-Itano, C., Sedey, A. L., Coulter, D. K., & Mehl, A. L. (1998). Language of Early-and Later-identified Children with Hearing Loss. *Pediatrics*, *102*(5), 1161-1171.
- Zhang, L. I., Bao, S., & Merzenich, M. M. (2001). Persistent and Specific Influences of Early Acoustic Environments on Primary Auditory Cortex. *Nature Neuroscience*, *4*(11), 1123.
- Zhang, L. I., Bao, S., & Merzenich, M. M. (2002). Disruption of Primary Auditory Cortex by Synchronous Auditory Inputs During a Critical Period. *Proceedings of the National*

Academy of Sciences, 99(4), 2309-2314.

Zhang, T., Dorman, M. F., Fu, Q. J., & Spahr, A. J. (2012). Auditory Training in Patients with Unilateral Cochlear Implant and Contralateral Acoustic Stimulation. *Ear and Hearing, 33(6)*

Zurita, P., Villa, A. E. P., De Ribaupierre, Y., De Ribaupierre, F., & Rouiller, E. M. (1994). Changes of Single Unit Activity in the Cat's Auditory Thalamus and Cortex Associated to Different Anesthetic Conditions. *Neuroscience research, 19(3), 303-316.*