The Conceptualization of a Theoretical Framework for a Music Intervention to Improve Auditory Development in Very Preterm Infants

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Abstract

Very preterm infants are at a high risk for language delays that can persist throughout their lifetime. The auditory system is rapidly developing and highly sensitive to acoustic stimulation during the third trimester of pregnancy. The acoustic nature of the womb provides the essential foundation for auditory perceptual skills necessary for language acquisition. In contrast, the NICU environment presents a wider spectrum of sounds that can alter the early development of the auditory system and cause delays in language acquisition. Research supports the importance of early exposure to speech sounds for optimal development of auditory perceptual ability and the critical role of the intrauterine characteristics of language. Pitches below 300 Hz, as well as rhythmic patterns and prosodic contours are highly salient intrauterine features of language that make up the infant's initial auditory experience. The purpose of this study is to form a theoretical framework as a structure for understanding how intrauterine speech characteristics of pitch, rhythm, and prosody can be implemented as active ingredients in a music intervention to improve auditory development and long-term language outcomes in very premature infants. The framework is presented and described in detail. Implications for a future research agenda and applications for clinical practice are explored.

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Chapter 1

Introduction

The number of premature births in the United States has been on the rise since 2015. In 2017 the United States received a “C” rating from the March of Dimes as the premature birth rate rose to 9.9% of live births (March of Dimes Premature Birth Report Card, 2019). Very preterm (VP) infants are a subset of premature infants that are born between 28- and 32-weeks gestation (World Health Organization, 2018). Early life experiences in the extrauterine environment of the neonatal intensive care unit (NICU) expose the developing auditory system of VP infants to stimulation that is vastly different from the intrauterine environment (Lahav & Skoe, 2014). The third trimester of fetal development, which coincides with the period of time that VP infants spend in the NICU, is a critical period for auditory perceptual development (He & Parikh, 2016). Therefore, auditory development for VP infants may be altered as a result of this stark change in auditory stimulation (Graven & Brown, 2008).

An interconnected relationship exists between early auditory experiences, auditory perceptual development, and later language acquisition (Guzzetta, Conti & Mercuri, 2011; McMahon, Wintermark & Lahav, 2012). Language delays in VP infants are frequently cited as a developmental concern associated with this population (Charollais, Stumpf & Pasquet, 2014; Joseph et al., 2016; Ramon-Casas, Bosch, Iriondo & Krauel, 2013). The relationship between auditory perception and language acquisition may be a significant component in understanding the risk for language delays in VP infants (Guzzetta et al., 2011). Language delays can result in long-term difficulty that effects social and cognitive development during childhood and persists throughout the lifetime (Bagwell et al., 2005; Durkin & Conti-Ramsden, 2010; Silverman, 2005). Understanding how the early postnatal auditory experience of VP infants impacts auditory perceptual development, a prerequisite to language acquisition, may provide a potential path for a preventive intervention to change language outcomes for VP infants in the NICU.

Importance of Language

Language is the uniquely human ability to create meaning out of a sequence of conventionalized sounds for the purpose of communication ("Language", 2019). Developing the capacity to use language is a complex process that relies on auditory development, memory, learning, and motor function (Kuczaj, 1982; Kuhl, 2009). The ability to comprehend and produce language is a significant human behavior that is intimately connected to the development of social and cognitive capacities (Durkin & Conti-Ramsden, 2010; Vallance, Im, & Cohen, 1999). Connection between individuals, sharing ideas, expressing thoughts, and understanding others are rooted in the ability to use language. Cognition relies on receptive understanding of language and forming new ideas based on knowledge. As early acquisition of language progresses to adulthood the demands of language become more complex (Kuczaj, 1982). As a result, the impact of delayed language is cumulative over time.

Child-directed speech. The development of language proficiency in children is dependent upon both early experiences with language, as well as auditory perceptual skills that are established before birth and during infancy (Chonchaiya et al., 2012; Rowe & Goldin-Meadow, 2009; Tsao, Liu & Kuhl, 2004; Weisleder & Fernald, 2013). Many adult caregivers naturally use child-directed speech when interacting with infants and young children. Exaggerated speech patterns that emphasize the prosody, elongated vowel sounds, and decreased complexity of speech are characteristics that define child-directed speech and the innately musical sound of this type of interaction (Papousek & Papousek, 1981; Head Zauche, Thul, Darcy Mahoney, & Stapel-Wax, 2016). Child-directed speech has been researched as to its function in several developmental domains including language (Dominey & Dodane, 2004).

It is known that the characteristics of child-directed speech help establish joint attention which is engagement in a shared communication experience that is essential for language development (Corkum & Moore, 1995). Children who receive exposure to child-directed language develop larger vocabularies and more efficient language processing skills (Weisleder & Fernald, 2013). Delays in auditory perception can impact the ability of an infant to engage in joint-attention during child-directed speech and as a result provide further risk to language acquisition (Dominey & Dodane, 2004). As language skills become more complex over time, early language delay can cause significant academic struggles that escalate as demands become more advanced (Snowling, Bishop, & Stothard, 2000).

Language and cognitive ability. The important role early language environment plays in long-term academic success is evident from the cumulative effects of language development seen through longitudinal investigation (Head Zauche et al., 2016). Language processing and vocabulary skills developed during preschool years are shown to predict reading and academic success at later developmental levels (Dickinson & Porche, 2011; Rowe, Raudenbush & Goldin-Meadow, 2012). When children enter school, their language abilities can be determined by their vocabulary at age three (Botting, Simkin & Conti-Ramsden, 2006). In addition to academic difficulty that results from delayed language, without sufficient language skill, children and adolescents are also at a higher risk for experiencing social difficulty (Durken & Conti-Ramsden, 2007).

Language and social relationships. Loneliness, stress, and psychological risks as a result of lack of friendship can occur from the inability to successfully engage in language exchanges with peers (Bagwell et al., 2005; Silverman, 2005). All the way into adolescents, compared to children without language delays, children with language delays experience poorer quality friendships (Durken & Conti-Ramsden, 2007). Challenges in social engagement due to language delay cause children to enter adolescence unprepared for new communication demands associated with more developed peer relationships (Durkin & Conti-Ramsden, 2010). Language delays can result in persistent academic and social challenges throughout the lifetime.

Language and auditory perception. One of the first prerequisites to language development is auditory perceptual development which begins before birth and continues through infancy (Chonchaiya et al., 2012). The ability to perceive sounds that make up human speech must be established prior to the more complex tasks of comprehension and production of language. Optimal development of auditory perception requires frequent repetition of speech sounds in order to strengthen neural pathways and create strong representation of those sounds in the auditory cortex of the brain (Zhang, Bao & Merzenich, 2001). Early speech perceptual skill and vocabulary development serve as strong predictors of language achievement (Rowe, 2012). The influence of incoming auditory stimulation on early perceptual skill development is a cause for further investigation of the unique auditory experience of VP infants in the NICU environment and its possible relationship to delayed language outcomes and opportunity for enhancing these outcomes.

Neonatal Care

Advancements in neonatal care beginning in the 1990's have included the use of surfactant therapy and ventilator support to address immature lung development in VP infants. These medical advancements have played a major role in improved survival rates of this population (Wilson-Costello, Friedman, Minich, Fanaroff, & Hack et al., 2005). As survival rates of the most fragile premature infants has risen, so too have neurodevelopmental impairments such as auditory perception. Earlier gestational age at birth and longer NICU hospitalization has turned more attention to developmentally supportive environments and interventions that aim to lessen the negative long-term outcomes associated with prematurity has increased (Altimier & Phillips, 2016).

Developmental care. Developmental care in the NICU is a philosophy that emphasizes the need to not only attend to the medical needs, but also very specific developmental needs of VP infants (Altimier & Phillips, 2016). The past three decades have brought a rise in efforts to minimize exposure to harsh extrauterine elements that are considered detrimental to the fragile developing systems of VP infants (Als & McAnulty, 2011). Premature birth causes infants to lose exposure to intrauterine sensory characteristics that support early neuro-development of language.

A significant amount of developmental care research focuses on providing a more "womb-like" sensory experience through the use of interventions and environmental adaptations. Swaddling, range of motion, cycled lighting, skin-to-skin contact, non-nutritive sucking, maternal voice, and womb sounds are all techniques that have been used to provide neuro-developmental support during NICU hospitalization (Darcy, Hancock, & Ware, 2008; de Róiste, 2004; Lessen, 2011; Lickliter, 2011; Loewy, Stewart, Dassler, Telsey, & Homel, 2013; Moyer-Mileur, Brunstetter, McNaught, Gill, & Chan, 2000; van Sleuwen et al., 2007). Studies support intervention and environmental modifications for short-term outcomes such as physiologic stability, pain, nutrition, sleep, and weight gain and long-term outcomes such as language and cognitive ability are being positively impacted by developmental care practices in the NICU (Altimier & Phillips, 2016; Aylward, 2005; Moody, Callahan, Aldrich, Gance-Cleveland, & Sables-Baus, 2017; Pineda et al., 2014; Platt, 2008). Many NICUs aim to provide developmentally supportive care in order to protect early neurodevelopmental needs (Moody et al., 2017).

NICU environment. The impact of light and noise in the NICU environment on physiologic stability and neurodevelopmental outcomes is perhaps the most researched and modified component of developmental care. Reducing lights and noise and educating staff and parents on the impact of the environment on VP infants are associated with many positive benefits for premature infants. Increased sleep, reduced stress, improved physiological stability, improved weight gain and decreased length of stay have been positively impacted as a result of environmental changes (Altimier & Phillips, 2016; Kellam & Bhatia, 2008; Laudert et al., 2007). Single family room designs have emerged as a way to increase individualization of the environment and reduce the problem of noisy ambient sounds associated with large open units (Dunn, MacMillan-York & Robson, 2016). Single-family rooms benefit developmental care practice by creating an improved atmosphere for implementing interventions that target neuro-developmental outcomes.

Reducing the amount of stimulation, such as noise, in the environment solves one problem, but it does not solve the problem of providing sensory input that is matched to the developmental needs of the infant. Exposure to speech sounds, an important component of auditory perceptual development, is severely lacking in the NICU despite attempts to reduce noise, sound levels, and frequencies in order to optimize the acoustic environment (Caskey, Stevens, Tucker, Vohr, 2011; Pineda et al., 2017). There is growing recognition that improving the auditory development of very preterm infants cannot merely consist of reduction of sound but must also include the purposeful addition of optimized auditory experiences (Pineda et al., 2014).

Premature birth causes the infant to lose access to filtered sounds of the human voice that have been identified as essential experiences for auditory development (Abboub, Boll-Avetisyan, Bhatara, Höhle, & Nazzi, 2016). Within the past decade, research to increase exposure to human voice in the NICU has primarily investigated short-term outcomes such as infant heart rate, oxygenation, and pain through the use of the mother's voice (Filippa, Devouche, Arioni, Imberty, & Gratier, 2013) There is some evidence that exposure to the maternal voice during NICU hospitalization increases the size of the auditory cortex which may have a positive link to language development (Webb, Heller, Benson, & Lahav, 2015). The auditory environment experience for premature infants continues to be improved as increased understanding emerges regarding how the auditory environment impacts the overall wellbeing of VP infants (Als et al., 2004). Major advances to create a more healing environment include reducing sound sources through new unit designs and updating equipment to newer models. (Szymczak & Shellhaas, 2014).

Advancement in developmental care practices and unit designs have dramatically improved NICU environments; however, carefully designed interventions that target specific needs of very preterm infants are still lacking. This may be partially influenced by the historical belief that reducing contact provides the most appropriate and safest care for very preterm infants (Lahav & Skoe, 2014; Pineda et al., 2014). The dependence of the auditory system on external stimulation from the environment suggests that consideration is warranted for a preventive intervention to enhance the auditory environment. Drawing from what is known about intrauterine auditory characteristics and implementation of neurosensory developmental care practice in the NICU, it may be possible to enhance early auditory development through intervention.

At this time, there is no research that considers the use of specific intrauterine speech characteristics in an intervention to target auditory development of VP infants in the NICU. Speech in the intrauterine environment is filtered through the maternal tissues and fluids so only sounds that pass through are low frequency sounds (Dealessandri & Vivalda, 2018). Filtering creates speech sounds with emphasized rhythmic and prosodic qualities and de-emphasized word meaning (Kisilevsky et al., 2009). Consider how language sounds when filtered through a wall from one room to another. While it is difficult to understand individual words, the overall speech contour, pitch and rhythm, is intact. Mimicking some of the emphasized characteristics that are experienced as a result of filtering inside the womb may be done efficiently through music. Highly rhythmic and melodic sounds of filtered speech share overlapping qualities with simple sung melody lines (Patel, 2008). Building a theoretical framework that considers the filtered speech characteristics of pitch, rhythm, and prosody can lead to a deeper understanding of how singing may be a specific way to use the voice with VP infants in the NICU in order to match the developmental expectation of the auditory system during the critical period of the third trimester.

Experience dependent neural plasticity, the impact of experience on the development of neurosensory functions such as auditory perception is the construct underpinning the the use of an intervention to benefit auditory development in VP infants (Kraus & Banai, 2007). Auditory experiences during the critical period of development are essential in establishing a functional foundation for auditory perception on which more complex language skills can be built. Therefore, the purpose of this study is to form a theoretical framework as a structure for understanding how intrauterine speech characteristics of pitch, rhythm, and prosody can be implemented as active ingredients in a music intervention to improve auditory development and long-term language outcomes in very premature infants. An iterative process that integrates relevant literature with the researcher’s insight gained from clinical practice will form the basis for the development of the theoretical framework. Implications for a phased research agenda to test the effectiveness and acceptability of the intervention will be explored in the discussion.

Chapter 2

Review of Literature

Prematurity is a prevalent health concern. Infants born very early, prior to 32-weeks gestational age, have sensory experiences vastly different than those of the full-term infant (Als & Gilkerson, 1997; Aylward, 2005). The fetus grows and develops in a rich sensory atmosphere protected by the maternal uterine environment. The intrauterine environment provides the optimal experience necessary for competent developmental capacity during the onset of sensory organization, particularly for long-term language development. Premature birth places the infant in the significantly altered sensory environment of the NICU. Emerging evidence suggests limited and/or inappropriate auditory experiences in the NICU have detrimental implications for long-term language development, particularly for VP infants (Lahav, 2015; Lahav & Skoe, 2014). At this time there are no early interventions for VP infants that target auditory sensory experiences necessary for long-term language development. The purpose of this study is to form a theoretical framework as a structure for understanding how intrauterine speech characteristics of pitch, rhythm, and prosody can be implemented as active ingredients in a music intervention to improve auditory development and long-term language outcomes in very premature infants; this theory will inform the key ingredients of a future preventive music intervention. This chapter will illustrate the complex concepts that inform language development, specifically including: (a) auditory experience and development of very preterm infants; (b) characteristics of expected language development; (c) predictors of language development challenges due to very premature birth and the NICU environment; (d) protective factors from maternal voice; and (e) the translation of language concepts to music characteristics supportive to the development of a causal model theoretical framework for a music intervention.

Auditory Experience and Development of Very Preterm Infants

Critical periods for development are defined as time periods in which rapid organization of neural networks create optimal windows for specific sensory skills. During a critical period, sensory experiences are essential in developing the optimal sensory functioning that lays the foundation for more complex skills, such as language. If sensory experiences are not optimal and a critical period has passed, it becomes increasingly more difficult to acquire the skill associated with that critical period (Kral, 2013). A critical period of rapid auditory development has been established as occurring during the third trimester (28-40 weeks) of fetal development and continuing through the first 7-10 months after birth (Graven & Browne, 2008).

Developing the ability to understand language and communicate begins with auditory perceptual abilities acquired during the third trimester (Belin & Grosbras, 2010; Prather, 2013). During the critical period of auditory development, organization of the auditory system is influenced by characteristics of the acoustic environment (Zhang et al., 2001). Alterations to the auditory system during the onset of functioning and neural organization as a result of sensory input, can cause negative effects in the development of auditory perception and later language acquisition (Zubiaurre-Elorza et al., 2017).

Functional development of the auditory system. Development of the auditory system is a complex process that involves the structural components of the auditory pathway, responsivity to incoming stimulation and transmission of stimulation to the brain (Hall, 2000; Prather, 2013). Auditory processing capabilities are present very early in life and infants possess near adult like capabilities to perceive, distinguish and prefer human speech sounds when they are only a few days old (Nishida et al., 2008). While a significant portion of auditory development occurs before birth, some aspects, such as the perception of subtle changes in inflection, do not reach their fullest potential until late adolescence and early adulthood which demonstrates the ongoing plasticity of the auditory system. Due to their complexity, research his still examining the intricate connection between the development of auditory structures and neural pathways, and the important role of outside stimulation and early experience in language acquisition (For a full review of the auditory system see Werner, Richard, Arthur, & Dick, 2012).

Auditory structures. Structures of the outer-, middle-, and inner-ear make up the peripheral auditory system where acoustic stimulation is transmitted to the auditory nerve. Very early in fetal development, before 20-weeks gestation, these structures are completely formed but not yet functional. The peripheral auditory system begins with the external ear structure, the pinna, which leads to the middle ear via the ear canal. The middle ear contains a chain of three bones and the tympanic membrane that transmit acoustic vibration into the cochlea (Graven & Browne, 2008; Hall, 2000; Werner et al., 2012). By 20-weeks gestation, the cochlea, a primary structure in hearing, is physiologically functional and begins randomly firing auditory signals to the auditory nerve. Random auditory nerve firing, independent from external stimulation, primes the auditory pathway for responding to external sound. However, there are no physiologic responses to external auditory stimulation until approximately 25-weeks gestation (Graven & Browne, 2008).

Onset of hearing. Around 25-weeks gestation, external auditory input begins to stimulate the auditory pathway signaling the onset of hearing and the start of a critical period for the development of auditory perception that is dependent on external stimulation (Sanes & Bao, 2009). This critical period is a significant time of neurologic maturation and organization of the auditory system (Bureš, Pysanenko, Lindovsky, & Syka, 2018; Hall, 2000). Tonotopic organization is the arrangement of the auditory cortex based on pitch frequencies that stimulate the hair cells within the cochlea. The basilar membrane in the cochlea and Heschl's gyrus (HG) in the auditory cortex rely on external auditory input for the tonotopic organization of sound that allows for efficient auditory processing. (Humphries, Liebenthal, & Binder, 2010; Warrier et al., 2009). Beginning between 26- and 28-weeks gestation, tiny hair cells within the cochlea are displaced (i.e. hair cell movement) to different extents based upon the pitch and intensity of an external sound. The mechanical displacement of the hair cell stimulates corresponding auditory nerve cells converting the signal from mechanical energy to an electric signal (Krishnan, Bidelman, & Gandour, 2010). The electrical energy is transmitted to the brain via the central auditory pathway (Eldredge & Salamy, 1996; Hall, 2000; McMahon et al., 2012; Oberholtzer, 1999).

Auditory perception of speech. Perceptual ability begins when auditory neural circuitry is stimulated from an outside sound, and neurons process the information within the auditory cortex. Maturation of the ability of the auditory system to perceive specific speech sounds involves frequency tuning, tonotopic organization and myelination, which are shaped through auditory input of speech sounds (Bureš et al., 2018; Mahmoudzadeh, Wallois, Kongolo, Goudjil & Dehaene-Lambertz, 2017). For example, prior to birth the fetus is exposed to the external auditory stimulus of the mother's voice which begins to stimulate the auditory system and build neural networks for the perception of the maternal voice sounds.

By 30-weeks gestation, neurons are processing auditory input in the same capacity that is seen in infants who are three-months post-term but tonotopic organization is still immature (Mahmoudzadeh et al., 2017). Tonotopic organization across a broad pitch range continues throughout the first several months after birth when the infant is no longer protected from high frequencies by the womb. Sounds that are later used in language and communication are initially learned through exposure to the sounds of language that organize and refine auditory processing and perception prior to understanding of word meanings (Zhang et al., 2001). Rich auditory experiences of voices and repeated sounds of speech, as well as repetitive, rhythmic, low frequency sounds of the mother's heartbeat, digestion, and footsteps during the third trimester of pregnancy help build strong neural connections and organization of the auditory cortex that are foundational for perceiving human speech sounds (Mahmoudzadeh et al., 2017). The abundant repetition of language sounds present in-utero may be key for developing perceptual abilities through optimal organization and refinement of the auditory system.

Refinement of auditory perception in support of language acquisition spans from 32-weeks gestation through the first year of life (Werker & Tees, 2002). Increased speed and synchronization of auditory signal processing relies on myelination of the auditory nerve (Belin & Grosbras, 2010; Stipdonk et al., 2016). Incoming stimulation activates the peripheral and central auditory pathways and repetition of stimulation strengthens neural connections through continued activation of the pathways. Increased pathway stimulation leads to faster processing of the auditory signal as a result of myelination (Dahmen & King, 2007). Myelination of the central auditory pathway begins during the third trimester of gestation which allows the speed of auditory processing to be near adult-like at full term gestation (Amin, Vogler-Elias, Orlando & Wang, 2014). After birth, myelination continues past the initial critical period throughout the first year of life (Dahmen & King, 2007). See Table 1 for a summary of the primary tasks of auditory development that have significant implications in the development of language.

Table 1

Third trimester auditory milestones

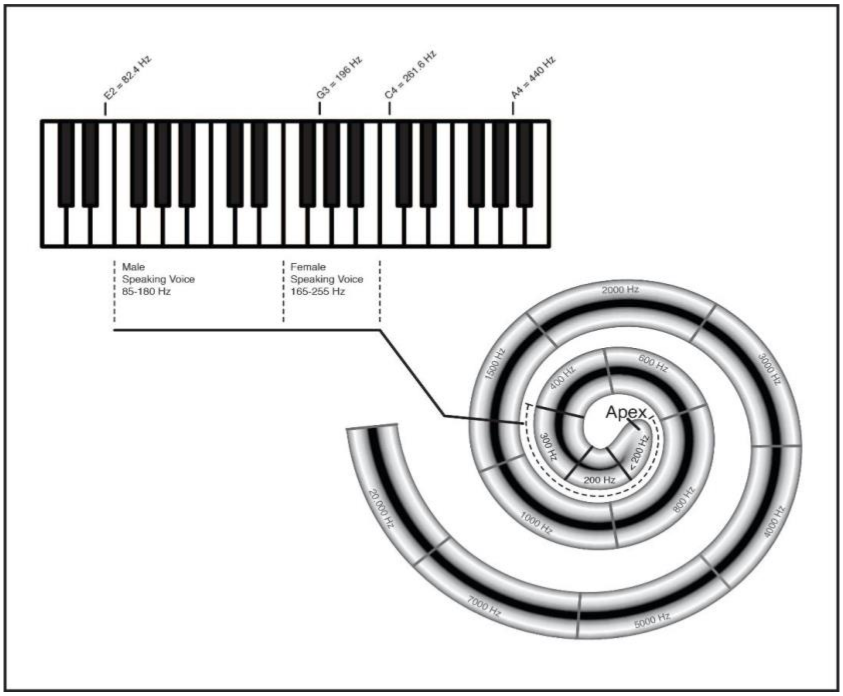
Gestational age (GA)	Primary tasks of auditory development
Prior to 25th week	Development of peripheral and central auditory structures
25th week	Activation of central auditory pathway from external stimulation Onset behavioral and physiologic responses to auditory stimulation indicating hearing
26th -28th week	Beginning of tonotopic organization of the auditory cortex stimulated by external stimulation
30th week	Beginning of myelination of the central auditory pathway stimulated by repetition of auditory input
32nd week - term	Strengthening of auditory processing to near adult-like efficiency Auditory learning of most salient language components and voice features in utero

Early auditory experience. The characteristics of incoming stimulation are important in the development of processing capacity at this early stage of the auditory system (May, Byers-Heinlein, Gervain & Werker, 2011). Input that consists of language is essential to myelination that will lead to the rapid processing of language. The quality and repetition of incoming stimulation during the critical period plays a key role in development of perceptual ability and language acquisition (Suresh, Krishnan & Gandour, 2017). Quality auditory experience includes frequent exposure to the pitches, rhythms, and prosody present in language (May et al., 2011). Developing strong neural networks that can efficiently process language requires repetitive sensory exposure to language sounds during the third trimester. Strong auditory neural functioning is the foundation for language perception skills that allow infants to become proficient in a native language during the first year after birth (Intartaglia et al., 2016; Werker & Tees, 2002). The third trimester and early postnatal auditory environments are crucial in the basic functional organization of language sounds and processing capability that persist throughout development (Zhang et al., 2001). Auditory processing that is impaired can negatively impact quality of life as language and cognitive abilities are threatened (Kraus & Banai, 2007).

Perception of the frequencies that are specific to the human speaking voice is a primary perceptual skill that develops during the critical period of the third trimester and requires robust rapid processing and tonotopic organization achieved through experience with those sounds (Bureš et al., 2018; Prather, 2013). The typical fundamental frequency, or mean pitch range, of an adult voice is between 85 and 255 Hz (Stoicheff, 1981). This voice range coincides with the earliest frequencies that are responsive to auditory stimulation in the cochlea during the third trimester (see Figure 1). The inflection present when speaking, as well as the production of consonants that are essential for word meaning, produce frequencies well above this range, but the fundamental frequency carried primarily in the vowel sounds produces the average frequency where the majority of sounds fall. Even though the high frequency sounds of some consonants are filtered out through the uterus, the fundamental pitches, rhythm and prosody of language remains intact. Repeated exposure to these specific speech characteristics during the third trimester is considered an important component that is essential for the acquisition of language (Abboub et al., 2016; Patel, 2008).

Before birth, infants hear language being spoken by the mother as well as others in the immediate environment of the mother. This language experience provides the auditory input needed to stimulate the sensory system. The quality of language sounds transmitted through the tissues and fluids of the womb provides stimulation that specifically emphasizes pitch, rhythm and prosody while diminishing other aspects such as word meaning and high frequencies (Abboub, Nazzi, & Gervain, 2016; Lahav, 2015). Vowel sounds, which contain lower frequencies than consonants carry the prosodic contours of language and make up the majority of the speech sounds that are experienced inside the womb. Hearing, with great repetition, vocalizations during the critical period allows for acute sensitivity for detecting human voice sounds in the extrauterine environment after birth, which further refines the auditory system for the development and use of language (Sanes & Wooley, 2011).

Figure 1: Tonotopic organization and location of speech frequencies in the cochlea



Bottom-up, top-down processing. The process of how rapid auditory signals in language develop into a sophisticated and efficient system used for communication is complex. Increasing evidence supports an interplay between both subcortical and cortical networks that enhance auditory functioning (Intartaglia et al., 2016; Kral & Eggermont, 2007). Bottom-up processing refers to the process of the peripheral auditory structures, such as the cochlea, transmitting auditory input to neural signals which travel from the auditory nerve to the primary auditory cortex (Kral & Eggermont, 2007). Experience and repetition of external stimulation is essential to bottom-up auditory processing by initiating the firing process, increasing processing speed and organizing the auditory cortex (Intartaglia, et al., 2016).

Through the robust organization of the auditory cortex as a result of repeated exposure to linguistic elements, top-down processing allows the cortical regions of the auditory system to send predictions of auditory input to the peripheral system. Based on prior experiences with sound patterns in language, these predictions allow for faster processing as a result of anticipating the next sound based on frequent patterns found in language (Kral & Eggermont, 2007). For example, in the English language consonant sounds are most often followed by vowel sounds. High levels of representations of this language specific pattern due to exposure in the environment allows the auditory cortex to predict, through top-down processing, what sounds to listen for next. More rapid and efficient processing due to the interaction between bottom-up and top-down processes aids in the task of language learning as a result of experience with auditory sounds (Intartaglia et al., 2016).

Language Development

The speed with which language develops over the first few years of life as well as the impact of language on other long-term outcomes, causes it to be at the center of many fields of study. Understanding how language emerges from perception to comprehension and finally communication is complex. Without a robust ability to perceive the sounds of human speech, discriminating speech sounds among the vast acoustics present in the environment is more challenging, thus acquisition of language is at-risk (Moore, 2002; Stipdonk et al., 2016). For typically developing individuals the early acquisition of language occurs without formal instruction but instead as a developmental progression involving both perceptual and production tasks (Chonchaiya et al., 2013; Gervain & Mehler, 2010; Kuhl, 2004).

Exposure to voices and low frequency human sounds during the third trimester creates a bias for attending to human voice sounds over other environmental sounds (Vouloumanos & Werker, 2007). After birth this bias facilitates joint attention with a caregiver. Hearing the caregiver's voice attracts the infant's attention to the caregiver; infants attention to caregiver reinforces the caregivers response and supports episodes of joint attention (Mundy et al., 2007; Tomasello, 1995; Vuksanovic & Bjekic, 2013). Although there may be a genetic predisposition for language to develop, in order to reach the fullest capacity, language is dependent upon the early experience of hearing language (Chonchaiya et al., 2013).

Characteristics of language. Language is built from the combination of sounds, pulse, and pitch contour that create communication (Kuczaj, 1982). The pulse of stressed and unstressed sounds in language make up its rhythm, while the rise and fall of speech pitches create the contour, or prosody as it is referred to in language. Rhythm and prosody of language are the first auditory elements that infants are exposed to in utero (Mampe, Friederici, Christophe, & Wermke, 2009). Within the first hours of birth, term infants demonstrate the ability to recognize their native language based on prosodic and rhythmic elements (Abboub et al., 2016). Sensitivity to rhythmic structure allows infants to distinguish between, (a) different languages, and (b) language versus non-language sounds (Nazzi, Bertoncini, & Mehler, 1998). A primary function of prosody for early language processing is the grouping of acoustic information. Prenatal exposure to language prosody allows infants to recognize prosodic changes such as pitch inflection that indicates the end of a sentence (Partanen et al., 2013).

Due to familiarity with language sounds experienced prior to birth, infants demonstrate a preference for their native language and other rhythmically similar languages compared to rhythmically contrasting languages (Moon, Panneton Cooper & Fifer, 1993; Nazzi et al., 1998). Beginning around five to six months post birth, infants develop the capacity to use rhythm and prosody to distinguish their native language from all other languages. Exposure to unfiltered language after birth refines the neural pathways for fine-tuned processing of more nuanced language sounds (Nazzi & Ramus, 2003). Exposure to specific language characteristics during the prenatal period plays a role in developing the preliminary perceptual skills necessary to acquire language at later developmental stages. Continued postnatal language exposure refines processing for specific language fluency (Kuhl, 2004).

Experience-dependent plasticity. Experience-dependent plasticity refers to "changes in neural circuits and synapses occurring throughout life that result from the environment and specific ways in which the individual interacts with the environment" (Skoe & Chandrasekaran, 2014, p. 37). For example, a professional pianist has had a significant amount of experience playing music on the piano. As a result of that experience, neural networks develop that make the task of playing the piano more efficient. Differences in environment and life situations change the strength of cortical development. Long-term experience with auditory events such as language, sharpens specific processing mechanisms which allows for the development of sensitivities to sounds that are linguistically relevant (Krishnan, Gandour, & Bidelman, 2012). This increases the efficiency of language processing for the use of language for communication.

Long-term experience with language sounds that begins in utero increases the ability to perceive, process and use language in degraded listening conditions (Ross et al., 2018; Suresh et al., 2017). Discriminating language sounds in a complex environment with competing speech and non-speech sounds is a complicated higher-order auditory task. During the earliest stage of auditory development, when subcortical processing paves the way for cortical organization, repeated experience with language plays a particularly important role in the foundation for higher order auditory tasks such as the connection between auditory and motor neurons that leads to the use of language for communication. (Krishnan et al., 2012; Werner et al., 2012).

Malleability of the auditory system is present in varying capacities across the lifespan; however, experience during the early period of auditory development can impact later perceptual abilities. Studies of song birds reveal similarities to humans in the need for early auditory experience to develop the capacity to learn their species-specific native calls (Doupe & Kuhl, 1999; Prather, Okanoya, & Bolhuis, 2017). Throughout development, auditory perceptual abilities become increasingly refined based on experience with the native language while perceptual skills that are not needed in the native language are pruned in favor of more efficient native language processing (Jacobs, 1988). Neural circuits and synapses change as a result of the environment and the specific ways in which individuals interact with the environment (Skoe & Chandrasekaran, 2014).

Studies involving musicians, auditory enrichment and language deprivation provide excellent examples of how individual experiences and behaviors shape auditory plasticity. Individuals who have studied music show greater representation in the brain for sounds that are specific to music such as pitch; whereas individuals with no music background do not have the same robustness of this specific brain area indicating that it is a result of experience (Bidelman, Gandour, & Krishnan, 2011; Pantev et al., 1998). Research involving animals raised in engaging and complex auditory environments are shown to have more robust neural connections overall compared to those raised in isolation (Sampedro-Piquero & Begega, 2017). Investigation of language capacity of children found living in an environment void of language indicates that isolation from language exposure diminishes the ability to acquire language at all (Lederber, Schick, & Spencer, 2013; Rand & Lahav, 2013). Similarly, research from children receiving cochlear implants shows that implantation before age one increases language acquisition ability as a result of increased exposure to language that establishes auditory perceptual ability (Feng et al, 2018; Mouvet, Matthijs, Loots, Traverniers, & Herreweghe, 2013).

Intrauterine Environment

Throughout the gestational period, human infants experience acoustic stimulation that is both rich with sounds and developmentally timed to support the neurologic progression of the auditory system (Gervain, 2018). Studies using recordings from the inside of a sheep uterus show that language contours are highly perceivable in-utero and comprise a significant amount of the entire auditory environment before birth (Gerhardt & Abrams, 2000). At the onset of functional hearing around 25-weeks gestation, the first frequencies ready for stimulation are low frequencies below 300Hz. The intrauterine environment not only provides rich exposure to low frequency and low intensity sounds, but simultaneously provides protection from high frequencies and high intensities to support the developmental progression of tonotopic organization from low to high (Abrams & Gerhardt, 2000; Lahav & Skoe, 2014; Werner et al., 2012). Closer to term the uterine walls become thinner and amniotic fluid reduces gradually allowing higher frequencies to be heard while still providing protection from harsh intensities. The mother's voice along with internal sounds of the beating heart and digestion are the primary sources of low frequency stimulation required prior to birth (Abrams & Gerhardt, 2000).

One of the most significant sounds within the womb environment is the mother's speaking voice. This voice component of the intrauterine sound scape is a building block for the foundation of speech perception (Dehaene-Lambertz et al., 2010). During the process of auditory development, rich exposure to the mother's voice frequencies and prosodic characteristics of language in utero allows for the organization of the auditory cortex (Abrams & Gerhardt, 2000; Chang & Merzenich, 2003; Krishnan, Xu, Gandour, & Cariani, 2005). Low-pass filtering of the voice through the uterine tissues and fluid causes only low frequency language sounds such as vowels to pass into the womb environment (Moon Lagercrantz, & Kuhl, 1992). The modified signal of the voice that is transmitted in utero further refines the auditory system for specialization of language processing by saturating the intrauterine environment with the rhythm and pitch frequencies of spoken language (Graven & Browne, 2008; Pysanenko, Bureš, Lindovsky, & Syka, 2018). Emphasized melodic contour and rhythmic characteristics prime the infant for rapid and robust perception of speech sounds that aid in the understanding and use of verbal communication (Chang & Merzenich, 2003; Griffiths, Brown & Gerhardt, 1994; Pysanenko et al., 2018). The intrauterine environment provides essential protection as well as a rich soundscape of auditory input, and may be more essential than previously believed, for the onset of neural organization of the auditory system (Gervain, 2018).

NICU Environment

In contrast to intrauterine conditions, environmental acoustics of the NICU are difficult to control. Large rooms with multiple beds are filled with noises and voices that blend together creating a high ambient background volume level (Pineda et al., 2017; Shoemark, Harcourt, Arnup, & Hunt, 2016). The sources of noise in the NICU produce sounds at high frequencies (Lahav, 2015), ambient sound levels cover up meaningful speech (Kellam & Bhatia, 2008), and premature infants have shown negative physiologic responses such as increased heart rate in the presence of noise (Cardoso, Kozlowskic, Moreira, Marquesa, & Ribasd, 2015; Grecco, Tsunemi, Balieiro, Kakehashi, & Pinheiro, 2013). Altered cerebral development as a result of the NICU environment has been linked to slower processing of auditory input as well as a predictor of language outcomes in preterm infants (Baldoli et al., 2015; Stipdonk, et al., 2016; Therien, Worwa, Mattia, & de Regnier, 2004). The stark contrast between the acoustics of the womb and NICU environments may have a serious impact on auditory development by causing changes in connectivity between brain regions (Wilke, Hauser, Krägeloh-Mann, & Lidzba 2014).

Changes in NICU care philosophies and unit designs have brought increased awareness to the impact that noise can have on the auditory development of a preterm infant, as well as attempts at noise reduction (Graven, 2000; Jobe, 2014). However, redesigning units with new sound absorbing materials, has not shown to significantly decrease noise or increase desirable acoustics as overall ambient sound continues to be well above recommended levels (Shoemark et al., 2016). The existence of higher frequencies and louder sound intensity in the NICU overwhelms biological expectations of the auditory system (Graven & Browne, 2008; McMahon et al., 2012). Reconfiguring NICUs as private rooms, rather than open bays, has resulted in the additional acoustic challenge of too much silence that inhibits necessary input during the critical period of the third trimester (Pineda et al., 2014).

Private NICU rooms can become a vacuum of silence, void of any auditory stimulation. The shift in NICU design from open bay to private rooms has reduced exposure to high ambient noise levels, but also increased periods of silence (Pineda et al., 2017; White, Smith, & Shepley, 2013). Increased silence causes isolated sound events, such as alarm bells, to be even more invasive due to the large decibel contrast between a near silent ambient sound environment and an alarm (Shoemark et al., 2016). In a private room NICU, frequent exposure to long periods of silence are more prevalent than human voice input (Pineda et al., 2017; Vohr et al., 2017). Premature infants in private rooms have been shown to have reduced activation in areas of the auditory cortex assigned to human speech perception and lower language scores at age two (Pineda et al., 2014).

With movement toward creating more neurodevelopmentally supportive acoustic environments in the NICU, attempts at reducing noise have resulted in silence as the gold standard (Jobe, 2014). As such, reduction in all acoustic stimulation has led to inconsistent exposure to speech. While it is not known the appropriate amount or type of auditory exposure that is needed for VP infants in the NICU, auditory exposure is important for the developing auditory system (Pineda et al., 2017). Attempts to increase speech exposure have primarily involved conversational speech versus a tailored speech experience that provides exposure to the intrauterine qualities of language (Caskey et al., 2011).

Sound frequency exposure. Research interest in how the frequency of sounds in the NICU impact auditory development is increasing in an effort to more fully understand and optimize characteristics of the acoustic environment. Acoustic analysis of NICU sound reveals higher frequencies than what an infant is exposed to in utero (Lahav, 2015; Shoemark et al., 2016). Electronic sounds from monitors, pumps, phones and other necessary medical equipment create repeated exposure to frequencies that the still developing auditory pathway of a premature infant is not prepared to handle. Infants requiring supplemental oxygen are exposed to greater amounts of high frequency noise from medical equipment and the need for oxygen is greater for very preterm infants during the critical auditory stage (Lahav, 2015). While it is unknown exactly how the frequency of sounds in the NICU impacts early auditory development, due to the tuning process of the cochlear hair cells it is important to consider how exposure to a wide range of unfiltered sound frequencies will change hair cell sensitivity. High intensity sounds can cause hair cells to lose their sensitivity to a specific frequency by damaging or completely breaking off the hair. Damaged hair cells are unable to send frequency information to the auditory nerve which reduces perceptual abilities. (Jiang, Brosi, & Wilkinson, 2006; Moore, 2002).

Language exposure. Exposure to rhythm and prosody through repeated human voice input is required to build the neural networks necessary for auditory perception and language acquisition (Krishnan et al., 2005). However, considerations must be made for how to increase exposure to certain language characteristics without increasing unit noise levels and causing overstimulation. Environmental characteristics, parent visitation, and NICU culture, are factors that impact premature infants from being exposed to the intrauterine rhythm and prosody sounds of language (Vohr, 2014).

Speech present in the NICU environment is likely to be masked by background noise and competing high frequency sounds that are overstimulating to preterm infants (Kellam & Bhatia, 2008; Pineda et al., 2017). Excessive noise and high frequency sound have been shown to impact speech perception by diminishing exposure to rhythm and pitch contours of language (i.e. prosody). Conversational speech present in the NICU environment adds to the ambient background noise that is overstimulating to very preterm infants (Shoemark et al., 2016). Exposure to electronic sound and silence dominate the sound environment of the NICU causing deprivation from important language input (Caskey et al., 2011; Caskey & Vohr, 2013). The NICU presents many challenges that prevent control over the acoustic environment. It is essential to begin measuring the qualities of sounds currently present in order to determine how interventions may work to optimize exposure to essential speech components (Abboub et al., 2016).

Parents are the primary deliverers of language exposure in the NICU; yet barriers such as caring for other children, distance to the hospital, stress, and expenses related to long-term hospitalization, prevent parents from being consistently present at the bedside (Caskey et al., 2011; Harris, Gibbs, Mangin-Heimos, & Pineda, 2018). Despite dramatic shifts toward family-centered care in the NICU, total exposure to speech sounds is sometimes as low as 1% of total time over the course of a day. Using the Language Environment Analysis device (LENA) to record and measure environmental language, the percentage of duration of language present increases only slightly as infants get older (Caskey et al., 2011). LENA research demonstrates that parent presence may not be enough to increase exposure to language as the amount of individually delivered language only significantly increases when parents are engaged in holding their infant (Pineda et al., 2017).

While the auditory structures are physically mature early in gestation, NICU hospitalization during the period of critical auditory development between 28 and 32-weeks gestation may impact the progression of auditory perception leading to language difficulties that persist throughout life (Nishida et al, 2008; Zubiaurre-Elorza et al., 2017). Research has shown fundamental changes in auditory processing within key brain areas as a result of early life in the acoustic environment of the NICU (Pineda et al., 2014). Animal studies help to increase understanding of how the early acoustic environment can change brain structure. Exposing rats to a degraded acoustic environment involving continuous clicking noise during the onset of hearing shows changes to overall processing within the auditory cortex. Rats exposed to the altered environment had slower processing of frequencies above the frequency of the click stimulus (Oliver, Izquierdo, & Malmierca, 2011). Disorganization of the auditory cortex as a result of continuous, low-level noise exposure, delays the emergence of audult like autiory processing by limiting neural organization of speech processing centers in the auditory cortex (Chang & Merzenich, 2003).

Language Outcomes in Very Preterm Infants

Research continues to indicate that language development is a significant concern for the VP infant population (Vohr, 2016). VP infants are at an increased risk for language acquisition difficulty that persists throughout their lifetime. Born before 32-weeks gestation, this subset of preterm infants is consistently recognized as experiencing deficits in cognitive function that include language (Sansavini, et al., 2011). In recent years, the study of language outcomes in VP infants has provided more specific insight into the types of language difficulty, predictors of language skill, and long-term implications of language outcomes for VP infants. In a systematic review and meta-analysis evaluating language outcomes of preterm infants from age three to 12 years, preterm infants not only experience lower language scores than term born peers, but also experience increasing difficulty over time as language competence becomes more complex (van Noort-van der Spek, Franken, & Weisglas-Kuperus, 2012).

Preverbal communication skills that develop prior to word production include babbling, gesture and word comprehension. There is only limited research that looks specifically at how these early language behaviors are affected by preterm birth as well as how they might be related to later language development. Preterm infants with and without additional diagnoses both experience delayed babbling behaviors between nine and 22 months compared to full-term controls (Byers-Brown, Bendersky, & Chapman, 1986). When comparing gesture and word comprehension of VP infants with full-term infants at 12, 18, and 24 months, evidence is emerging which suggests that VP infants have slower acquisition of gesture and language comprehension. Additionally, the divergence between preterm and term born infants appears to increase at each age benchmark indicating that the effects of early language skills on later language skills are cumulative (Sansavini et al., 2011). Beginning around age two, when toddlers typically begin communicating with multi-word phrases, VP infants are using significantly fewer words and shorter utterances compared to term-born infants (Charollais et al., 2014). The magnitude of this difference is correlated with GA: infants born before 32-weeks gestation have the smallest vocabularies and greatest difficulty with word production (Foster-Cohen, Edgin, Champion, & Woodward, 2007).

Language acquisition tasks become more difficult as the demands of communication move beyond simple vocabulary and require more complex conversational and comprehension skills. VP infants may appear to be on target with language until the demands require more advanced skills (Aylward, 2005). VP infants are found to be deficient in complex verbal processes upon entering childhood. More mature language skills such as word meaning, grammar, understanding sounds, and pragmatic skills, build on earlier language ability (Aylward, 2005; Vohr, 2016). As a result, longitudinal studies of school age and adolescents, VP infants continue to score lower on language tasks and the gap becomes larger as language demands increase (Aarnoudse-Moens, Weisglas-Kuperus, Duivenvoorden, Oosterlaan, & Van Goudoever, 2013; Wolke & Meyer, 1999). By age five, one-in-five premature infants meets the criteria for a language impairment (Woods, Rieger, Wocaldo & Gordon, 2014). While the language difficulty in VP infants may not be immediately obvious, the compounding nature of slower response time, vocabulary acquisition, understanding, and use of language are critically important to social and academic achievement.

Predicting language outcomes in VP infants. One of the distinct challenges in mitigating language difficulty in VP infants is that multiple factors play a role in affecting language outcomes. Understanding multiple factors that can help predict language outcomes of VP infants is of interest as developmental care in the NICU and early intervention programs strive to provide individualized interventions to meet early developmental needs. NICU design and gestational age have the most research supporting their ability to predict language outcomes in the VP infant population (Joseph et al, 2016). Additional risk factors include medical complications, ethnicity, and socioeconomic status (Freeman Duncan et al., 2012; Perez-Pareira, Fernandez, Gomez-Taibo, & Resches, 2014; Pineda et al, 2014).

Single family rooms. In recent years, the study of single-family room NICU design on language outcomes has emerged as hospitals move from open units to private rooms in an attempt to provide more developmentally supportive care. However, language deprivation has become concern for infants in single-family rooms. Language outcomes at age two for infants in single-family rooms are lower than those in an open unit as a result of longer durations of silence associated with single-family rooms (Pineda et al, 2014). Language stimulation, especially maternal voice use, is an important factor of early auditory development and has been shown to positively increase language outcomes for VP infants especially in single-family rooms. However, many barriers, especially those associated with SES and maternal education, prevent maternal presence which impacts the amount of language exposure for VP infants (Vohr et al., 2017). High variability in duration of language across studies does not allow for recommendations about the amount of language exposure needed for VP infants in the NICU (Pineda et al., 2014; Pineda et al., 2017). Regardless, the benefits of language exposure are emerging which supports the need for more cohesive research in order to adequately use language as an intervention.

Gestational age. Low-risk preterm infants, those born between 32- and 36-weeks gestation without medical complications, do not consistently show a language delay when followed-up between the age of two and three. However, infants born at lower gestational ages are consistently reported as having lower language outcomes (Perez-Pareira et al., 2014). Thus, it is commonly agreed upon that lower gestational age is a risk factor for language outcomes. The extent of language delay in VP infants may not be fully identified until language skills become more advanced when children enter school. VP infants and late preterm infants test similarly on early language tasks, whereas the older developmental age shows a larger gap in language ability that is predicted by gestational age at birth. (Woods et al., 2014). Lower gestational age and lower birthweight are factors that are directly related. Compared to normal birthweight infants, very low birthweight infants, those with lower gestational ages, scored lower on language and cognitive tasks (Ortiz-Mantilla, Choudhury, Leevers, & Benasich, 2008). This further supports VP infants being at a higher risk for poor language outcomes.

Medical complications. VP infants are born earlier which means they have longer NICU hospitalization and are at a higher risk for developing medical complications (McCormick & Litt, 2017). Medical complications and physiologic instability may impact blood flow to key brain areas delaying fundamental processes of auditory development from becoming established. In order to protect the physiologic stability of very ill infants, they may experience less language exposure compared to other preterm infants, which can also impact auditory processing. Chronic lung disease is a complication of prematurity that has been linked to language outcomes. While the incidence of chronic lung disease is more prevalent in VP infants making it difficult to separate the effects on language outcomes, it has been suggested that longer periods of oxygen support are associated with an increased number of hypoxic events which impacts auditory cell development. As a result, chronic lung disease may be an additional factor that provides increase accuracy in predicting language outcomes compared to gestational age alone (Guarinia et al., 2009; Singer et al., 2001).

Ethnicity and socioeconomic factors. Language outcomes associated with ethnicity and socioeconomic factors have been considered but not as widely represented in the research. VP infants, regardless of ethnicity, have all been shown to have lower than expected language outcomes when compared to full-term infants. However, after accounting for socioeconomic and medical factors, African American and Hispanic infants scored the same as Caucasian infants on cognitive measure but maintained lower language scores compared to white infants (Freeman Duncan et al., 2012). It is not currently known the source of this disparity in language outcomes. SES and maternal education may put minority groups at a higher risk for language delays even in the absence of additional risk factors and/or genetic differences between ethnicities may describe some of the outcome variability (Freeman Duncan et al., 2012). Understanding the difference in language outcomes for different ethnic groups allows for interventions to specifically target the highest need in order to help prevent long-term language delay.

Measuring Auditory and Language Development

The compound relationship between auditory and language development coupled with the multifaceted complexities of premature birth are critical factors within the NICU context for understanding the relationship between the environment, early auditory development and language acquisition. Different methods of measuring early auditory and behavioral responses to stimulation have yielded contradictory results. In many studies, a lack of description of NICU design, which has been shown to significantly impact the early auditory experience of premature infants, makes cross-study comparison difficult (Cardoso et al, 2015; Pineda et al, 2017). Additionally, measuring early language outcomes is difficult as different fields tend to use a variety of outcomes to measure pre-language capacity.

Auditory evoked brainstem response. Auditory evoked brainstem (ABR) response testing is a standard test used in the NICU to measure the response time of auditory signals. Jiang and colleagues (2006) report VP infants with chronic lung disease having significantly delayed auditory response times, whereas the response times of VP infants without chronic lung disease were similar to term born infants. Infants with medical complications, such as chronic lung disease, experience more frequent hypoxic events that may cause cell changes in the cochlea thus impacting auditory development independent from the auditory environment. These changes in auditory response can be measured with ABR. However, another study found no difference in ABR between very preterm, moderately preterm and late preterm infants (Seethapathy, Boominathan, Uppunda, & Ninan, 2018). ABR may not be sensitive enough to determine differences in auditory processing among groups of premature infants. As such, this suggests that additional health complexities that impact physiologic stability such as intraventricular hemorrhage, gastrointestinal disease or heart diagnoses, which are more common in VP infants, may have a greater effect on ABR response times than gestational age alone. Slower response time observed early on indicates the potential for difficulty in the acquisition of more complex language skills at later ages (Loi, Marchman, Fernald, & Feldman, 2017).

Functional magnetic resonance imaging. Increasing use of another non-invasive measurement, functional magnetic resonance imaging (fMRI) is expanding what is known about early brain processing of auditory signals. Strength of auditory processing regions has been shown on fMRI to increase in very premature infants between 32- and 52-weeks indicating growth during the period of NICU hospitalization (He & Parikh, 2016). However, optimal development of auditory processing skill is still considered to be directly related to environmental input during the critical period and the best predictor of later language acquisition (Guzzetta et al., 2011). Studies using fMRI suggest auditory and language functions are networked differently in VP infant brains compared to term-born infants (Aylward, 2005). It has been shown that VP infants have increased right hemisphere connectivity for language regions compared to the typical left dominance in term born infants (Myers et al., 2010). Reliance on alternative pathways have shown a strong correlation with cognitive and language deficits. Preterm birth during a critical period of neural development, specifically within the auditory system, increases the risk for alternative neural pathways for auditory processing. Alternative pathways viewed using fMRI may be useful indicators of language outcomes (Aylward, 2005).

Near infrared spectroscopy. More recently, near infrared spectroscopy (NIRS) has been used to measure concentrations of cerebral oxygenation associated with brain activation which is thought to be a valid measurement of auditory processing. The portability and non-invasive nature of NIRS make it ideal for vulnerable populations (Arimitsu et al, 2018). May and colleagues (2011) used NIRS to examine associations between infant brain responses to familiar (forward sentence) and unfamiliar (backward sentence) and language processing in full term infants within the first two days after birth. They discovered that cerebral oxygenation is greater when exposed to familiar language sounds compared to unfamiliar sounds. This finding indicates that intrauterine language experience plays an important role in robust processing of familiar sounds. The significant change in language input between the intrauterine environment and the NICU during the rapid development of the third trimester has been shown to have great effect on the formation of auditory networks and delay cortical responses to verbal stimulation in preterm infants (Nishida et al., 2008).

Behavioral outcomes. Sucking, and visual habituation and dishabituation are behavioral indicators of auditory discrimination that are used to determine recognition of language sounds in infants (Friederici & Thierry, 2008). Sucking rates for infants are a behavioral response within the paradigm of discrimination ability in very young infants. Greater arousal in the presence of a familiar or preferred auditory stimulus is marked by an increased sucking rate. Sucking rate also increases when a novel change is perceived after a period of familiarization through repetition (Moon & Fifer, 1990). Sucking behavior demonstrates the ability of very young infants to discriminate differences in language based on prior experience shaping their auditory perceptual skills (Mehler et al., 1988).

Look durations in response to paired auditory and visual stimulation can also indicate perception of language sounds. Compared to term infants, premature infants at nine months demonstrated longer looking times in response to auditory stimulation as well as increased number of trials needed for habituation of the auditory stimulus. This indicates slower auditory processing ability in the group of preterm infants (Oriz-Mantilla et al., 2008). In the same study, perceptual skills at nine months were compared to standardized cognitive and language tests at age seven. The Looking While Listening (LWL) test measures eye movement duration when directed toward a picture with the presentation of a familiar auditory stimulus (eg. "look at the dog") indicating processing time of auditory stimulation (Loi et al., 2017). At 16, 18, and 22 months corrected age, VP infants show longer look durations and slower orientation to target picture indicating longer processing time (Loi et al., 2017; Ramon-Casas et al., 2013). When matched with term-born control subjects on socioeconomic status and quality of linguistic environment, VP infants continued to differ significantly on the behavior measures of language processing. Studies that compare language processing ability with language ability at later developmental stages consistently find a positive correlation between slower language processing and language delays (Loi et al., 2017; Mehler et al., 1988; Ortiz-Mantilla et al., 2008; Ramon-Casas et al., 2013).

Challenges in comparing outcome measures. Challenges exist for synthesizing available research on language outcomes for VP infants. Heterogeneity of tests used to demonstrate language outcomes cause difficulty when comparing results. Additionally, age at follow-up and duration of follow-up for longitudinal research are inconsistent across studies. It is well documented however that there is a higher risk for language difficulty associated with VP infants compared to other preterm populations and full-term infants (Eldredge & Salamy, 1996; Singer et al., 2001; Vohr, 2014). This increased risk appears to be consistent when additional risk-factors such as medical complexity, socioeconomic status and ethnicity, associated with language development are removed. While parental involvement, medical stability and developmental care practice may positively benefit language outcomes in VP infants, low gestational age at birth continues to be a risk factor on its own.

Very premature infants are born at a time when the auditory system is forming initial neural connections. Typical networking of the auditory pathway for optimal functioning relies on quality and developmentally timed input from the environment. The acoustic experience of the NICU is vastly different from the womb and may cause very premature infants to be at risk for the development of atypical neural pathways in the auditory system. Changes to the early auditory development, that are essential building blocks for language acquisition, may result in persistent language delays for VP infants (Jobe, 2014; Lahav & Skoe, 2014). However, identification of potential protective factors may assist in the development of interventions to minimize the risks of language delays noted in VP infants.

Protective Factors

One way that has been explored to increase exposure to nurturing stimulation and familiar womb-like characteristics is through use of the mother's voice. Significant exposure to the maternal voice in utero provides a natural interest in the clinical use of the maternal voice in interventions for the benefit of premature infants in the NICU (Krueger, Parker, Chiu, & Theriaque, 2010). In utero, maternal voice is heard in a muffled sense, as high frequencies are not present due to filtering through the maternal fluids and tissues. It has been determined that word meaning is not present in utero, but that rhythm and prosody of language remain salient (Teie, 2016). Recreating the womb environment is not possible in the NICU; however, presenting stimulation that may closely represent the womb environment is frequently considered in NICU developmental interventions. Exposure to maternal voice may have possible protective effects when included as a component of developmental interventions.

Among the literature reviewed, maternal voice interventions have been used to positively impact a variety of outcome measures including: short-term physiologic measures (Krueger et al, 2010), behavior state (Choi, Kang, & Kim, 2014), feeding (Lessen, 2011), and pain (Azarmnejad, Sarhangi, Javadi, & Rejeh, 2015; Filippa, Devouches, Arioni, Imberty, & Gratier, 2013). However, there is very limited research that explicitly explores the use of maternal voice interventions on language and brain development. Even though direct research that explores a link between maternal voice in the NICU and language development is limited, indirect benefits of physiological, behavioral, feeing and pain outcomes may have protective qualities for VP infant's language development by mitigating some of the experiences of early life in the NICU.

Short-term physiologic measures. Heart rate, respiratory rate and oxygen saturation are a primary interest in maternal voice research. The physiologic measures are also associated with language outcomes as prolonged physiologic instability can impact neurodevelopmental outcomes (Mattia & deRegnier, 1998). Recorded maternal voice has been effective in lowering heart rate and respiration rate, as well as increasing oxygen saturation (Choi et al., 2014; Sajjadian, Mohammadzadeh, Taheri, & Shariat, 2017). Maternal voice recordings have included maternal singing, speaking, and reading, making it difficult to discern if there are specific qualities of the maternal voice that are essential in impacting short-term physiologic status. These studies also include variability in the duration of the voice exposure ranging from five minutes a day to more than three hours of continuous exposure. In a systematic review of maternal voice interventions, short-term physiologic status was inconsistent across studies making it difficult to determine if there is a positive benefit on physiological status using recordings of the maternal voice in the NICU (Provenzi, Broso, & Montirosso, 2018). Nevertheless, physiologic stability is an important factor for VP infants in the NICU and maintaining optimal physiologic stability may help protect auditory development.

Behavior state. Maintaining an optimal behavior state, such as quiet alert or sleeping, as well as transitioning between behavior states, can be a significant challenge for premature infants. Protecting infant sleep in the NICU is important as brain development is consistently linked to sleep quality (White, 2015). Periods of deep sleep are required for neural network development and in this way, sleep is a protective factor for the language development of VP infants (Huber & Born, 2014). Exposure to maternal voice is thought to have a calming effect on infants that has led to research on maternal voice and sleep in the premature infant population. Infants who are 35-weeks and older experienced significantly enhanced sleep quality with exposure to recorded maternal voice reading a book. Infants younger than 35-weeks did not experience a significant difference in sleep quality (Shellhaas, Barks, Burns, Hassan, & Chervin, 2018). Compared to other studies that report early exposure to maternal voice stimulation, Shellhaas and colleagues (2018) suggest that sensitivity to maternal voice may increase closer the infant is to term as the infant has increased experience with the maternal voice.

Feeding. As premature infants progress toward discharge from the NICU, regardless of age, feeding and weight gain can be a barrier to leaving the hospital. Learning to feed is a significant skill that develops for premature infants during NICU hospitalization. For a variety of reasons, this skill can be impacted by premature birth and become a hurdle for weight gain and discharge from the unit. Feeding difficulty has also been associated with poor language outcomes in VP infants (Adams-Chapman, Bann, Vaucher, & Stoll, 2013). Rates of non-nutritive sucking (NNS), a precursor skill to feeding by mouth, have been shown to increase with presentation of maternal-speech (Butler, O'Sullivan, Shah, & Berthier, 2014). Better NNS skills in premature infants can lead to more successful feeding and reduced length of stay (Butler et al., 2014). Feeding intolerance can be a significant setback for premature infants leading to longer hospitalization. The use of maternal voice recordings early during hospitalization have been shown to reduce feeding intolerance in very preterm infants compared with receiving the maternal voice exposure later during hospitalization or not at all (Krueger et al., 2010). This study supports the protective capacity of early exposure to maternal voice during NICU hospitalization for very preterm infants.

Pain. Medical care provided during NICU hospitalization involves frequent painful procedures such as heel sticks and intravenous line placement. It is now known that premature infants are susceptible to the stress that pain can cause. Non-pharmacological pain relief is desirable due to the side effects and long-term impact of pain medication (Grunau et al., 2009). Term infants benefit from the closeness and soothing sounds of mother's voice to calm and reduce discomfort. In the NICU, premature infants may receive blood draws without the presence of the maternal or other caregiver present for closeness and comfort. Frequent and repeated pain experiences impact neural networks and long-term neurodevelopmental outcomes including language (Grunau, 2002).

Recordings of the mother's voice before and after a painful procedure such as a blood draw significantly reduces pain scores on the Neonatal Infant Pain Score (NIPS) for preterm infants who are at least 36-weeks gestation (Azarmnejad et al., 2015). Johnston and colleagues (2007) investigated the effects of recorded maternal voice on premature infants between 32- and 36-weeks during a heel stick and found that no significant difference on pain between maternal voice and other voices. Currently, there is not enough research to recommend the use of recorded mother's voice to reduce pain in premature infants, although the emerging potential of maternal voice on premature infant outcomes suggests it is necessary to understand how certain elements of the voice, maternal or other, can benefit the developing premature brain.

Auditory and brain development. Two studies have been found that investigate the effects of maternal voice on auditory or brain development (Saito, Fukuhara, Aoyama, & Toshima, 2009; Webb et al., 2015). In the NICU infants are exposed to both maternal voices and the voices of family members and medical caregivers in the environment. When comparing maternal speech with nurse provided infant-directed speech, frontal cerebral blood flow on both sides of the infant's brain was significantly impacted. Cerebral blood flow was reduced with the use of monotonous presentation of adult-directed speech which indicates habituation to auditory stimulation that does not have infant-directed qualities. This suggests that variations in the prosodic patterns of language inherently present in mother's speech, or a nurse using infant-directed speech play a similar role in activating the brain of premature infants (Saito et al., 2009).

Webb and colleagues, (2015) inquired more specifically about the impact of maternal sounds on the auditory development of preterm infants by looking at neonatal cranial ultrasounds at 30 days of life. When the mother's voice was combined with heartbeat sounds and played inside the incubator four times a day for 45 minutes each, infants had significantly larger auditory cortex regions on the ultrasound. This study demonstrates that preterm infant brains are sensitive to the sensory experience of maternal sounds during NICU hospitalization but does not determine any differential benefit between heartbeat or maternal voice. The study also does not indicate how many days the infants receive the maternal sounds.

Singing and speaking to infants while in the NICU is frequently encouraged as part of standard care. Nurses and other medical caregivers encourage parents to sing, speak or read to their infant. This type of interaction is valued as normal within the NICU environment and has not been associated with higher ambient sound levels like conversational speaking making it a safe addition to infant care (Chow & Shellhass, 2016; Jobe, 2014). Infant-directed vocalization has emerged as the standard for interacting with infants of all ages due to its characteristically exaggerated prosody, ability to engage infant attention, and facilitate language development (Saito et al., 2009). Interventions in the NICU that specifically involve increasing exposure to vocalizations are primarily focused on the mother's voice and are found in nursing, psychobiology, neurologic, medical, and music therapy literature. Research that investigates the use of the voice for premature infants includes a variety of targeted outcomes, mode of voice delivery, duration and patient population (Filippa et al, 2017; Provenzi et al., 2018). Additionally, the majority of research involving maternal voice includes singing, speaking and reading within a single intervention and it has been noted that additional understanding of specific mechanisms of the maternal voice is needed in order to develop targeted interventions that can be used to target specific needs of VP infants in the NICU (Provenzi et al., 2018).

Translating Language into Music Elements

Music and language share a natural connection with many overlapping acoustic components. Both music and language appear in all cultures throughout human history and have evolved out of the necessity for communication (Bright, 1963). Early evidence of mothers singing to their infants supports the function of singing to create a sense of closeness and communication during activities where the baby could not be held, such as while gathering food (Falk, 2004). The way that many adults naturally speak with infants, known as infant-directed speech, has many musical qualities embedded in the characteristic style. Slower tempo, increased pitch variability to emphasize language contour, elongated vowel sounds, frequent pauses, and repetition are some of the music characteristics that are known to define infant-directed speech (Falk, 2012; Trehub, 2003). Traditional lullabies and play-songs used in multiple languages with infants also incorporate these same infant-directed speech characteristics. The style of singing to an infant is known as infant-directed singing and it mimics the rhythmic and prosodic qualities of the spoken language (Trehub & Trainor, 1998).

Differences between language and music exist primarily in how pitches and rhythms are organized, and specific rules of grammar essential to language that are not present in musical compositions. However, these differences seem less apparent when considering how many musical characteristics are already present in infant-directed communication. Additionally, the differences may be even more reduced as the scope is narrowed further to consider only the qualities of language that remain salient in the intrauterine environment during the third trimester of development. The pitch, rhythm, and prosody of language is highly represented inside the womb making up a significant portion of the acoustic environment. Specific word meaning and carriers of grammar that are distinct differences between language and music are filtered out in the womb environment. While there is evidence that supports music and language share only minimal cerebral overlap, another perspective promotes shared basic processing of the common characteristics between music and language (Patel, 2008).

Defining the characteristics of pitch, rhythm, and prosody from a music-based perspective will help guide understanding of how music can be used in a targeted intervention to enhance the early auditory development of VP infants. Overall, music is widely considered beneficial for infants and many studies that have used music as a therapeutic modality within the NICU report positive outcomes (Haslbeck, 2013; Loewy et al., 2013; Standley & Swedberg, 2011; Walworth et al., 2012; Whipple, 2005). Therefore, it is essential to clearly articulate how the elements of music function to produce the anticipated mechanism of change. This research-based approach to examining the function of individual music elements before composing them into a whole for a music intervention increases understanding and predictability in outcomes (Hanson-Abromeit, 2015).

Pitch. Pitch is the most fundamental element of both language and music because it allows sound to be organized in a recognizable system from high to low (Coutinho & Dibben, 2013, Patel, 2008). In the voice, pitch is a result of the vibration of the vocal folds as air passes through the vocal mechanism. In traditional western music, the scale system is comprised of 12 equal sized intervals. Use of the symmetrical scale system creates a natural bias for the familiar sound of music with a clear tonal center. Individual pitches are arranged in a sequence of varying intervals which creates a melodic musical phrase that can be sung or played on an instrument. This predisposition for the equally tuned scale is also reflected in the interval relationships in western speech prosody (Patel, 2008). Other organizations of pitches and musical scales are used throughout the world and the same influence between music and language can be observed (Bright, 1963). This indicates the need for cultural sensitivity and knowledge of the primary language when considering the use of music to enhance auditory development and language acquisition.

Language sounds are made up of phonemes. Phonemes are the smallest speech unit or sound that when combined create different words. The standardized system for representing phonemes is the International Phonetic Alphabet (IPA). Combinations of phonemes create syllables. Syllables play an important role in speech rhythm and are combined to create words. European languages do not rely on pitch to indicate word meaning as is the case in the tonal languages of the world. However, pitch variation carried in the inflection that a speaker uses implies different aspects of linguistic, attitudinal and emotional information. Some universal examples of pitch variation in European language include a higher pitch at the end of a phrase indicating inquiry, happiness being characterized by a wider pitch range and sadness characterized by a narrower pitch range. Pitch variation is also present in the sounds of individual phonemes. Consonants and vowels each have different pitch characteristics based on how they are produced. For example, the initial non-voiced consonant sound in the word "chew" creates a high pitch sound as air is forced out between the tongue and the roof of the mouth (Patel, 2008). Combinations of pitch produced by both the vocal folds and certain non-voiced consonants share many similarities to pitch in a sung melodic line thus making the use of acapella singing a viable consideration for introducing the pitches present in language during the early critical period of auditory development.

Rhythm. Both language and music have an underlying organization that combines the timing, accent, and grouping of sounds. This organization is referred to as rhythm. Speaking language with native fluency requires mastering not only the sounds but also the timing and accentuation patterns inherent in the language (Patel, 2008). Mastering the rhythmic qualities of language begins before birth with frequent exposure to the native language as a result of exposure to the maternal voice, as well as other voices in the environment of the mother. Early and repeated experience with the native language creates strong neural representation of rhythmic patterns during the early stage of development (Abboub et al., 2016).

Rhythm in music is organized in a hierarchical pattern of stronger and weaker beats. Simply put, in Western music, the patterns of beat strength are governed by general principles of rhythmic patterns including regular beat, grouping of events into phrases, and strong beats followed by weaker beats. Emphasizing the ability of musical rhythm to mimic language rhythm is a primary interest of this study (Latham, 2002; Patel, 2008); thus, simple musical rhythm will be the focus rather than addressing the complexity of rhythmic analysis in music.

Every language of the world is spoken with some kind of rhythmic pulse that emerges from pronunciation of sounds, stressed and un-stressed syllables or sounds, and other individual characteristics of the language. It is traditionally believed that the languages of the world fall into two distinct categories, either “stress-timed” or “syllable-timed.” Stress-timed languages such as English or Arabic are characterized by having roughly equal time intervals between stresses. For example, consider the English sentence:

x x x x
The boy is looking to buy a ball.

The x’s above the sentence indicate where the natural stressed sounds falls. The time relationship between the stressed sounds is more or less equal creating a predictable perception of rhythm. In stress-timed languages there are a variable number of syllables between the intervals. In contrast, syllable-timed languages, such as French, the equal timing intervals are tied to individual syllables. However, this strict notion of the rhythmic construct of language is challenged by the more contemporary idea that rhythm in language is naturally determined as a result of the temporal, accentual and phrase patterns within a given language (Langus, Mehler, & Nespor, 2016; Patel, 2008).

Music has a long history of exploiting the rhythms in language in the composition of songs with words. It is very common for composers to align language stresses with stronger beats in a melodic line. Children's songs are frequently composed using rhythmic patterns that closely match the native language (Patel, 2008; Patel, Iversen, & Rosenberg, 2006). The difference in language and music rhythms is most notably the construction of rhythm in the music composition versus the consequence of rhythm that occurs naturally in language. However, construction of rhythm to closely represent language may be useful in bridging the gap in rhythm exposure from filtered language for VP infants.

Prosody. The combined rhythm, pitch, accentuation, tempo and dynamic elements of language that convey a rich variety of information independent from word meaning is known as language prosody (Coutinho & Dibben, 2013). Vocal inflection and speech sounds create intervallic relationships similar to note intervals in music, while the rhythmic stressed and un-stressed sounds are compared to the musical beat (Mazuka, 1996; Patel, 2008). An important purpose of prosody is grouping continuous speech into larger prosodic phrases. Certain prosodic characteristics form boundaries that turn many small speech elements such as syllables and words into larger phrases with specific contour properties. Common prosodic characteristics that cue phrase boundaries include phrase-final lengthening, phrase-final pitch lowering, and pauses (Carvalho, Dautriche, & Christophe, 2016; Patel, 2008). Phrase groupings as a result of prosody create a "big picture" effect of language. Because of the universal function of the prosodic elements in a particular language, infants learn to recognize their native language and begin to learn word order, communication intent and emotional meaning as a result of the prosodic contours (Benavides-Varela & Gervain, 2017; Nazzi et al., 1998).

In music, melody is created through the arrangement of notes into a specific sequence of interval relationships. Rules associated with various musical cultures govern the scales and intervals that are commonly associated with that culture's music. Familiarity with the music from a particular culture creates neurologic expectations for the melodies of that culture similar to the learned expectation of prosodic information in the native language. Unlike speech prosody, which occurs naturally as a phenomenon of language and has limited pitch range characteristics, music is composed around a stable set of pitches with much richer contours and intervallic relationships. Despite this difference in music and speech contours, music can be composed using similar characteristics of speech prosody, such as a narrow pitch range, increased duration of notes at the end of the phrase, and pitch variation to indicate the end of a phrase (Patel, 2008).

Prosodic information carries an important role that is independent from word meaning. Within the intrauterine environment, prosodic qualities of speech are preserved while characteristics necessary for word meaning are filtered out (Abboub et al., 2016). Exposure to prosody is likely an important factor in enhancing the auditory environment for VP infants due to its role in establishing early perception of language. Musical melodies that closely represent the universal prosodic qualities present in language can be composed and sung on a sustained vowel or hummed in order to isolate the prosody in a way that is more representative of the intrauterine environment.

Form. Broadly speaking, musical form refers to the structure of a musical composition (Burnham, 2001). Repetition of a verse-chorus structure is an example of musical form. The repetition of language sounds is necessary for robust neurologic pathway development. Strophic form is characterized by the repetition of the same musical material through several verses (Tilmouth, 1980). Due to the universal characteristics of pitch, rhythm and prosody that are repeated throughout language, music compositions in strophic form may emphasize these salient aspects and benefit VP infants' language development in the NICU.

Synthesizing how musical elements that are present in language and emphasized due to the filtering of language present in the intrauterine environment helps to define the potential for a music intervention for VP infants in the NICU. Table 2 provides a summary comparison of each musical elements within the context of both the intrauterine environment and the NICU in order to highlight significant differences. Following descriptions of each environment are implications for how differences between the environments potentially impact auditory development and language acquisition. The final column presents the hypothesized role for each musical element in the development of an intervention targeting auditory development in VP infants in the NICU.

Table 2

Language components represented in the intrauterine environment and the NICU

Necessary experiences for pre-language development	Intrauterine environment	NICU	Implications for auditory development	Implications for language acquisition	Hypothesized role in a music intervention
Pitch *Individual frequencies of language sounds*	**Frequencies above 600Hz are attenuated in the womb environment** causing the fine details of language, especially consonants to be non-existent (Gervain, 2018; Griffiths et al, 1994).	Infants experience a **broad spectrum of pitches** that are produced by humans and machines (Kellam & Bhatia, 2008).	The auditory system develops systematically from low frequencies to high frequencies. Repetition of the **low frequencies sounds of language develop the auditory pathways for robust processing** of the pitches needed to perceive language (Lahav & Skoe, 2014; Prather, 2013).	Language acquisition requires **prior perceptual development of pitches** represented in speech sounds (Kuhl, 2004).	Composed melodies can **emphasize lower frequencies** that are appropriate for the developing auditory system guided by gestational age of very preterm infants.
Rhythm *Combination of stress and un-stressed sounds in*	The rhythmic characteristics of language are **highly present in the womb**.	In the midst of the full spectrum of speech sounds,	Regular repetition of language rhythm strengthens auditory pathways	Rhythmic patterns of language are associated with the ability to	Song compositions can mimic language rhythms and

language (Langus et al., 2016) "The systematic patterning of sound in terms of timing, accent, and grouping" (Patel, 2008, pg 96)	(Dealessandri & Vivalda, 2018; Mampe et al., 2009)	**infants are not exposed to the isolated presentation of rhythm** (Langus et al., 2016)	and **develops sensitivity for recognizing rhythms of the primary language** (Langus et al., 2016; Teie, 2016)	**discriminate native language sounds in the midst of other sounds,** as well as learning word order (Benavides-Varela & Gervain, 2017; Langus et al., 2016)	when presented through singing can **emphasize rhythmic contour of language.**
Prosody *Acoustic variation in speech that conveys meaning independent from verbal understanding (Coutinho & Dibben, 2013) Combined rhythm and pitch that creates a distinct contour (Gervain, 2018; Patel, 2008)*	Attenuation of the speech signal preserves the prosodic characteristics of language making it a **salient feature of the prenatal auditory environment** (Gervain, 2018; Griffiths et al., 1994; Moon et al., 2012).	In the midst of the full spectrum of speech sounds, **infants are not exposed to isolated presentation to prosody** (Gervain, 2018).	The sequence of experiencing prosody alone before the full spectrum of speech sounds may play a **significant role in developing auditory pathways** and allow infants to build strong neural pathways for fundamental language characteristics (Benavides-Varela & Gervain, 2017; Gervain, 2018)	Infants rely on prosody to **break up continuous speech signals into smaller units which lays the foundation for language acquisition.** (Benavides-Varela & Gervain, 2017; Moon et al., 2012).	Sung melodies **elongate vowel duration and emphasize prosody**. Humming, or singing a single vowel removes consonants that are naturally attenuated in the womb which further emphasizes prosodic contour.
Form *Organization of a musical composition (Tilmouth, 1980)*	In the womb, infants are exposed to language elements with **great repetition** through both the voice of the mother and voices in the environment (Gervain, 2018)	In the NICU infants do not receive repetitive exposure to the essential isolated language sounds. **Background noise and/or long periods of silence prevent repeated exposure** (Graven, 2000; Jobe, 2014.	The development of **strong neural pathways depends upon repeated exposure**. (Aslin & Schlaggar, 2004; Oliver et al., 2011)	Strong **auditory pathways created during the critical period are the foundation for the processing ability** needed for language acquisition (Aslin & Schlaggar, 2004	Song can be implemented using a **strophic form to increase exposure to the repetition** of language characteristics.

Problem Statement

Language delays are a frequently cited long-term problem associated with very preterm birth. Very preterm infants are born during a critical period of auditory development. They spend their first months of life in the NICU where the acoustic environment is vastly different from the intrauterine experience. A lack of exposure to the acoustic characteristics of language in the NICU alters the auditory pathways for perception and sensitivity that build the foundation for language acquisition. There are currently no interventions that target early auditory development in this population; yet substantial research in language-outcomes of VP infants, understanding of the mechanisms of auditory and language development, and rationales for the need to improve early auditory experiences all contribute to a strong basis for the development of a theory-driven intervention that targets the language outcomes of very preterm infants. Characteristics of how language in represented in the intrauterine environment are similar to the musical constructs of pitch, rhythm and melody. Simple melodies can be composed and presented through singing to provide access to the specific parameters of language exposure in utero. Enhancing the auditory environment with stimulation that mimics the intrauterine environment can provide developmentally supportive input into the auditory system during the critical period of development.

Rationale for Intervention Theory Construction

Deeper understanding is the foundational tenet of theory construction and complex intervention conceptualization. Answering the “why” questions and being able to predict how active ingredients of an intervention may impact the outcome motivate researchers to spend time constructing theoretical frameworks that guide multiple future research endeavors (Robb, 2012). A theory becomes the solid foundation that forms a systematic empirical research agenda contributing to a cohesive understanding of an intervention. Without construction of a theoretical framework for intervention research, studies fail to move toward a more sophisticated and detailed understanding of treating the problem. (Fleury & Sidani, 2012; Ravitch & Riggan, 2012).

VP infants experience an altered auditory environment and are at a higher risk for difficulty processing speech sounds essential for language acquisition (Moore, 2002). Designing a complex intervention to impact the language outcomes of very preterm infants involves understanding the key constructs of auditory development, influences of the auditory environment, and language acquisition which notably share causal relationships with one another. The first relationship of interest exists between the auditory system and sensory input. Auditory perceptual development is affected by the quality of auditory exposure. In the case of very preterm infants, the auditory experience in the NICU is different from the intrauterine auditory environment (Lahv & Skoe, 2014). Another complex relationship exists between auditory development and language acquisition. One factor in developing the capacity to use language is the ability to process specific sounds and patterns present within language (Gonzalez-Gomez & Nazzi, 2012). While these broad relationships have been well established in the research literature, there are many more concepts such as the specific language elements of pitch, rhythm, and prosody, that have not been explored with regards to how they relate to early auditory development and language acquisition.

Using theory to provide insight into the active ingredients for an intervention aimed at improving language development for very preterm infants will help explain the role that individual acoustic elements may play in a targeted intervention. Because the phenomenon is complex and longitudinal, it is essential to establish a strong theory to answer preliminary "why" questions about each element and build a path toward predicting how the nature of relationships between variables is represented and its potential impact on the language development outcomes of very preterm infants (Fleury & Sidani, 2012). Proceeding straight to an intervention study without a clear foundation creates a greater risk for ambiguous results and research that lacks impact and influence in the field (Robb, 2012).

Reducing research waste. Research waste is identified as the result of studies that fail to yield social and scientific value by meeting the obligation to advance scientific understanding or redeem human and material costs due to lack of contributing results (Hey, 2018). There are multiple reasons why a study might fail to fulfill this obligation. Poor study design or inappropriate analysis can create misleading results while lack of planning, theoretical foundation, or poorly articulated research questions can cause unnecessary studies that do not contribute to furthering understanding (Bleijenberg et al., 2018; Chalmers & Glasziou, 2009; Hey, 2018). Researching complex interventions with multiple influencing factors are at a higher risk of having limited impact. Careful theory building and intervention construction is an essential first step (Craig et al., 2013). Commitment to filling a research gap through well designed and conceptualized research studies has caused this researcher to spend additional time in the development phase prior to advancing to empirical studies.

Research Questions

1) What evidence-based constructs are present in a theoretical model that supports auditory perceptual development in very preterm infants in the NICU?
2) How do the music elements: pitch, rhythm, and melody, provide enhanced delivery of intrauterine-like speech for very premature infants in the NICU?

Chapter 3

Methods

Research Philosophy

Merging the researchers 10-year experience as a music therapist in the NICU with new insight gained from reviewing relevant literature creates a deeper understanding of how specific acoustic elements of language may function as mechanisms of change in a complex music intervention, thus supporting the construction of a theoretical framework. The research philosophy guiding this inquiry is interpretivism, a stance which suggests human behavior should be studied in a naturalistic manner reflecting as many aspects of the phenomenon as possible in order to appreciate a wider understanding of the problem within its naturally occurring context (Schwandt, 2000). The goal of interpretivism is to obtain a deeper understanding and description of the unique, specific or deviant characteristics of a phenomenon (Crotty, 1998; Miller, 2004). Derived from phenomenology, interpretivism involves the researcher’s direct experience, interaction and interpretation of the phenomenon to uncover meaningful new knowledge rooted in context, culture and values (Miller, 2004). Nuance and variability are innate characteristics of intervention research because humans in different contexts, with varied experiences and varied biological makeup will respond differently to the same intervention. Therefore, the researcher’s direct experience working with very preterm infants is a significant lens through which the evaluation of research and construction of the theoretical framework are viewed. Causal modeling has been selected as the method for developing a theoretical framework because it allows the researcher to consider multiple, complex factors associated with understanding the problem and articulate a solution with insight into what causes the change and why. Constructing a theoretical framework through causal modeling will illustrate how specific acoustic qualities of language form the active ingredients for a preventive music intervention to improve language outcomes for very preterm infants situated in the environmental, medical and social context of the population, i.e. the Neonatal Intensive Care Unit (NICU). Seeking this understanding through a lens that considers the context of the phenomenon allows for the development of a deeper theoretical foundation for the use of specific voice characteristics with very preterm infants in the NICU to support long-term language development.

Researcher's experiences that shape this inquiry. Generating the ideas for this theoretical model emerged from my clinical career as a music therapist in the NICU as well as recent coursework completed during time as a PhD student. As a clinician I worked closely with the developmental care teams at each hospital where I was employed. I have been immersed in the trends of developmental care and felt frustrated by the lack of forward movement in the creation of developmental interventions for the very premature population. I have observed the "hands off" approach to providing developmental enrichment to very premature infants and have long questioned the appropriateness of reducing stimulation without replacing it with something of value to benefit the trajectory of development.

As a music therapist, the auditory environment has been a primary interest of mine as I brought music into an environment where so many sounds already existed. Multiple times I have experienced the phenomenon of an entire NICU pod quieting from loud conversation, and the hustle of footsteps and movement slowing as staff and parents listen to the live music, I was creating for a patient. I have also experienced many moments with infants and families being soothed, comforted, uplifted and inspired through a music interaction. Yet, there was an almost daily barrier to providing music therapy wrought with questions of safety, effectiveness, value, and necessity for patients and families. The chasm between, "music is nice" and "music is a beneficial therapy" keeps music therapy on the periphery. Research supports the many benefits of music in the NICU environment, and staff and families generally value the role of music with infants, but there is limited understanding of the music beyond being "just music."

When I came back to school in pursuit of a PhD I came with curiosities about music and premature infants as a result of my clinical experiences in the NICU. I came wanting to understand not only *why* music was effective but *how*. I was interested in the connection between the critical period of early auditory development that coincides with very preterm birth, and the consistent reporting of language delays in this population. Not knowing exactly how to shape a research agenda in order to study the questions I had, I was fortunate to take several classes that contributed to my understanding of research methodology, theory construction, intervention research, and cohesive research trajectories. Throughout completion of my coursework, components of this project emerged in many different forms which has allowed me to approach my original questions with new insight, depth and understanding each time.

Drawing on what I knew of rhythm being a substantive sensory experience in the womb and having experienced the lack of rhythm in the acoustic nature of the NICU; I dove into the messy and complicated realm of dissecting the notion of music as an intervention strategy. My desire was to discover greater understanding of how to compose music that causes an intentional change in the auditory development of very preterm infants. Spending time in this messy place opened up understanding of additional elements of music that play a significant role in language development and lead me to the use of causal modeling as a way to describe the possible mediating effects these elements have in language outcomes for very preterm infants.

Causal Modeling

Causal modeling is a powerful methodological tool bridging the gap between theory and research. Philosophers, such as Aristotle, were fascinated with cause/effect relationships that were based on everyday observation of events (Biddle & Martin, 1987). Humankind's early interest in predicting outcomes based on observation led to documentation of forecasting future events based on prior observations. While not scientifically rooted, these early predictions followed the form, if X happens then Y will happen. This formula has since become the foundation for causal modeling in research development and is particularly helpful in instances of complex problems with multiple variables. The rise of research inquiry based on causal modeling demonstrates an ever-emerging depth of understanding that brings the rigors of scientific investigation to the perception of causation. (Anderson & Evans, 1974; Frosini, 2006).

The term "cause" when applied to causal modeling does not imply that one variable directly and immediately results in a change in another variable. This view does not acknowledge the vastly complicated nature of understanding multifaceted, human issues within their cultural, environmental or social context (Frosini, 2006). Research problems that involve multiple complex variables require researchers to go beyond the simple bi-variate relationship of X causes Y and attempt to construct bridges that explain in greater detail additional contextual variables that interact with the relationship between X and Y and cause variation in the outcome of interest (Wu & Zumbo, 2008). Conditions that must be present to make inferences of cause and effect include: (a) there must be a relationship between the variables, (b) the presumed cause must occur prior to the effect, (c) the relationship between the variables must be supported, and (d) there are no other relevant hidden factors that carry the causal relationship. In theory building, these conditions are met using prior research to build connections between the variables, thus developing a theory through causal modeling which allows for inferences of cause and effect to be drawn (Keith, 2015).

Development of a causal model involves a systematic process. Building a causal model is an iterative systematic process of identifying individual variables and assigning relationships based on understanding informed by prior research, and the evaluation and re-evaluation of variables and their relationships as the model emerges and additional variables are added (Jaccard & Jacoby, 2010). Systematic construction of a causal model begins with the identification of the outcome or dependent variable of interest along with a limited number of independent variables thought to cause the dependent variable. This will be followed by examination of mediator and moderator variables. Varying types of relationships between the independent and dependent variables will be evaluated. There are three primary types of relationships that can occur between variables within a causal model; direct, mediated, and moderated. Additional relationships include reciprocal or bidirectional relationships, spuriousness, unanalyzed relationships, and disturbance terms (Jaccard & Jacoby, 2010). Strong causal models include robust detail of intervening variables that clarify boundaries of an intervention and allow for more precise prediction of outcomes based on the presence or absence of those variables. Causal modeling is the very important first step in answering the question of *how* an intervention is expected to work in order to obtain a desired outcome (Jaccard & Jacoby, 2010; Wu & Zumbo, 2008).

The method used to build this causal model closely followed the systematic approach suggested by Jaccard and Jacoby (2010) in *Theory Construction and Model-Building Skills: A Practical Guide for Social Scientists.* Constructing the causal model began by identifying the outcome variable of interest. In the case of this causal model, the outcome variable that has been identified is auditory perceptual development of VP infants in the NICU. Once the outcome variable is identified, additional variables are added through examination of the core relationships found in causal models and include: (a) direct causes, (b) mediated relationships, (c) moderated relationships, (d) reciprocal causality, (e) spurious effects, and (f) unanalyzed relationships. Constructing a causal model is an iterative process that is not linear and may include additional variables that are not part of the initial process. Guidance from statistics, including multiple regression and structural equation modeling (SEM) provide terminology and relationship analysis that are beneficial to building a theoretical model that can be tested (Keith, 2015). The use of disturbance terms, while not necessarily indicated in the core relationships is taken from SEM in order to indicate additional variation or influence that is not part of the current model but will impact future results. The following sections provide detailed descriptions of the variables and relationships that will be considered in the construction of the theoretical causal model.

Dependent variables. At the essence of a causal model are dependent, or outcome, variables that the theory is attempting to explain. Initially a single outcome variable is identified as the phenomenon of interest (Jaccard & Jacoby, 2010). In the case of this theory, the initial outcome variable of interest is auditory perceptual development of VP infants in the NICU. VP infants experience delays in language and that those delays can be linked to deficits in auditory perceptual development. Because of this relationship between early perceptual abilities, language acquisition is also included as a secondary dependent variable of long-term interest. Although it is not the primary aim of this theory its supported connection to auditory development makes it important to include it in the model as a music intervention is considered to improve auditory perception. As the theory emerges, there may be additional outcome variables that are added to strengthen understanding of the problem.

Independent variables. Independent variables are the components of the intervention that are manipulated in order to discover their effect on the dependent variable (Jaccard & Jacoby, 2010). After conducting an extensive review of literature in order to understand the phenomenon of early auditory perceptual development in very preterm infants, the independent variable identified in the model is language exposure during NICU hospitalization as a music-based intervention will seek to alter factors of language exposure in this environment.

Throughout the process of building the model, additional independent variables may be included to improve the ability of the model to predict the outcome.

Mediators. Further elaboration of how an effect comes about between independent and dependent variables in the model are explained by mediator variables. Mediators turn direct cause/effect relationships into indirect or mediated relationships by explaining how the relationship occurs. If a cause/effect relationship is identified, the logical next question is how the independent variable functions as an influencer on the dependent variable. When added to the model, mediators begin to provide insight into how the effect happens and why there is variability in the outcome (Jaccard & Jacoby, 2010). Intrauterine boundaries of speech pitch, rhythm and prosody are the hypothesized mediators for this model. These characteristics of speech are very different between the intrauterine and NICU environments and may help describe specific characteristics of language that essential to mitigating the effects of the NICU environment on auditory outcomes.

Mediator variables might describe the entire relationship between two variables as in full mediation or may only partially represent an influence on the outcome in which case it is described as partial mediation. When the direct relationship between the independent and dependent variable is statistically zero with the addition of a mediator, complete mediation exists. This means that the cause/effect relationship is only present when the mediator is present. Due to lack of statistical testing at this stage of model development all mediators are hypothesized as being partial mediators. In this model, possible mediators will be considered for all direct relationships, based on prior research and the researcher's clinical experience (Jaccard & Jacoby, 2010; Keith, 2015; Wu & Zumbo, 2008).

Moderators. Sometimes the cause/effect relationship between two variables is stronger or weaker when certain conditions are present. Those identified conditions are another type of variable called moderators. Moderators are additional variables that influence the strength of a relationship between two variables. Moderators assist in characterizing which population and individual characteristics can be most effectively treated by the intervention. The magnitude of an effect may be explained by a moderator which further refines the ability to predict how an intervention will function to elicit the outcome. In the statistical analysis of multiple regression, moderators are represented by differences in the slope between groups with varying characteristics. Both direct and mediated relationships can be influenced by moderators (Jaccard & Jacoby, 2010; Keith, 2015; Wu & Zumbo, 2008).

By asking *why* questions about moderated relationships, additional mediators might be identified that further describe the function of the moderator. When a mediator can be identified for why a moderator exists, the relationship is referred to as mediated moderation. Additionally, moderated mediation relationships may occur when the magnitude of a mediated path varies as a result of a moderator. A final moderated relationship to consider is moderated moderation which occurs when a second moderator changes the moderating effect of the first moderator. The first-order moderator has a direct impact on the cause/effect relationship while the second-order moderator has an indirect relationship (Jaccard & Jacoby, 2010).

For each relationship in the model at this point, moderators will be considered by asking if the relationship is the same under all circumstances, or if there are conditions which change the strength of the relationships. Throughout the process of building the model, each type of moderated relationship will be analyzed for inclusion, but it is possible that not all types of relationships will be present in the final model (Jaccard & Jacoby, 2010). In this model there are multiple moderators that have been initially identified as changing the strength of the effect of language exposure on auditory outcomes. These hypothesized moderators are: maternal voice, parent presence, environmental characteristics and medical stability. Each of these factors is represented in the literature as impacting access to language or quality of language available which potentially strengthens or weakens the relationship between language exposure and auditory development.

Direct Relationships. Direct relationships imply an uninterrupted link between two variables. It is most simple to think about direct relationships in terms of X causes Y; regardless of any other additional factors, X will always cause Y. Mediated relationships are a type of indirect relationship where an additional variable must be present in order for X to cause Y. A mediated relationship might appear as X causes Q, and Q causes Y. In this case Q is mediating the relationship between X and Y. Moderated relationships occur when an additional variable changes the strength or direction of the relationship between x and y. In moderated relationships X causes Y, but X is more or less effective if Z is present. In this case Z is moderating the relationship between X and Y (Biddle & Martin, 1987; Jaccard & Jacoby, 2010; Keith, 2015; Wu & Zumbo, 2008).

In this theoretical framework, direct relationships will be considered first between the independent and dependent variables. Direct relationships imply that one variable causes the other. Initially, only a limited number of direct causes will be added to the model in order to begin with a simple representation of the model that can develop more elaborately without becoming overwhelming. Additional direct relationships may be added to the model later if needed to further explain the outcome (Jaccard & Jacoby, 2010).

Reciprocal or bidirectional relationships. After a period of time, if the dependent variable influences the independent variable in a feedback loop, it is considered a reciprocal or bidirectional relationship. Auditory development is by nature a longitudinal phenomenon that occurs in tandem with maturation. At the same time a premature infant is experiencing the auditory environment of the NICU, they are growing. In this model, maturation toward more term-like behaviors may produce a feedback loop where variables share different relationships at different points in time (Jaccard & Jacoby, 2010).

Spuriousness. As causal modeling becomes more complex with the addition of variables and examining relationships between variables, the potential for identifying spurious relationships becomes more relevant. Spurious relationships may appear to be causal but are erroneously inferred as a result of coincidence or an unanalyzed variable. An example of a spurious relationships is that of increased ice cream sales causing drowning. In this case, there is a hidden variable, summer, that impacts both ice cream sales and swimming. The hidden variable is overlooked when inferring causation of ice cream sales and drowning. Spurious relationships may be part of a theoretical model and further refined as a result of empirical testing and statistical analysis. Any suspicion of spurious relationships that arise as a result of building this model based on research understanding will be explored within the discussion section (Jacoby & Jaccard, 2010; Keith, 2015).

Unanalyzed relationships. Development of a causal model that explains an identified phenomenon of interest may result in identification of causal relationships between the independent variables that are not of interest given the phenomenon. Unanalyzed relationships are included in this model using curved arrows to represent acknowledgement of the correlation between the variables, but they are not analyzed as part of the causal model (Jaccard & Jacoby, 2010; Keith, 2015).

Disturbance terms. There may be some variables that are related to the identified variables within the model but are not a central focus of the theory. For those variables, a disturbance term is used to explicitly acknowledge that additional factors are present but are not part of present theory. In the statistical analysis of a causal model, disturbance terms represent any variance that is unaccounted for in the relationship between independent and dependent variables. In order to provide the most thorough representation of the theoretical model that can lead to empirical testing of the components, disturbance terms will be included at this point. Disturbance terms will be added to the variables within the model to represent unspecified influences that are not the central focus of the theory (Jaccard & Jacoby, 2010).

Visual Representation

Visual representation of a causal model is traditionally expressed through the use of a path diagram. A path diagram employs boxes and ovals to depict individual variables and arrows to represent the quality and direction of individual relationships between variables (Jaccard & Jacoby, 2010). A path diagram typically includes independent variables on the left, intervening or additional variables such as mediators and moderators in the middle and the dependent variable on the right. Straight arrows show the hypothesized causal relationships between variables and curved double headed arrows depict unanalyzed correlations. In the theoretical stage of the model, all relationships are presumed based on relevant research and observation. Empirical research examines and validates the relationships to the variables and correlation coefficients are added into the path diagram to represent the statistical strength of the relationships between variables (Biddle & Martin, 1987; Jaccard & Jacoby, 2010; Keith, 2015)

Theoretical Synthesis

This project is the development of a theoretical framework derived from causal modeling with the intent to inform the development of a music intervention to addresses long-term language outcomes in very premature infants. Causal modeling in intervention research allows for the focus to center around interactions between the independent, mediator, moderator and dependent variables. A prepared model that presents a research-based causal hypothesis of the intervention can then be tested using rigorous experimental design and statistical methods in order to isolate separate effects within the model and describe the statistical strength of causal inferences from the theoretical model. Furthermore, a theoretical causal model, paired with future systematic empirical research, will provide the foundation to develop a music-based intervention, to explain how and why the intervention works, and strengthen the validity of music interventions for premature infants in the NICU (Anderson & Evans, 1974; Biddle & Martin, 1987; Keith, 2015).

Chapter 4

Defining the Theoretical Framework

Very premature infants are admitted to the NICU during a time of critical neurosensory development. The auditory system, which is highly impacted by the quality of external stimulation, is particularly vulnerable to the stark differences between the womb and the NICU (Graven & Browne, 2008). Specific pitch ranges and emphasized rhythmic and prosodic contours of speech are unique auditory experiences presented in the womb with great saturation due to transmission of the mother's voice and other voices around the mother through the maternal tissues and fluids (Abboub et al., 2016). However, these speech qualities are not present in the NICU due to a wide range of environmental, social, and medical factors (Lahav, 2015). Experience with speech pitch, rhythm and prosody is key in the organization and function of auditory perceptual skills which are an important foundation for the acquisition of language (Chonchaiya et al., 2013; Kisilevsky et al., 2009; Stipdonk, Franken, & Dudink, 2018). Currently, there are no interventions that employ the specific elements of speech pitch, rhythm and prosody in a highly tailored way that reflect the intrauterine experience. Prior to developing a targeted intervention, the constructs which inform later language development must be defined. Therefore, the research questions being investigated by this theory development through causal modeling included: (a) What evidence-based constructs emerge in a theoretical model to support auditory perceptual development in very preterm infants in the NICU? and (b) How do the music elements: pitch, rhythm, and melody, provide enhanced delivery of an intrauterine-like auditory experience for very preterm infants in the NICU?

Reducing exposure to harsh sounds and lights, providing tucked positioning, and encouraging parental closeness through skin-to-skin holding are three examples of developmental care practice that bring characteristics of the intrauterine environment into the

NICU environment in order to protect neurodevelopment (Altimier & Phillips, 2016). Advancing toward a deeper understanding of the rich filtered sensory experience within the womb, that exists as a mechanism to protect the premature infant's developing auditory system, should be a significant consideration for future developmental care interventions. Identifying appropriate characteristics of auditory exposure that are present in the womb and can be supplemented in the NICU may provide support for the development of auditory perceptual skills that are pre-requisites to language acquisition.

Causal modeling is a process that can uncover new insights through examining relationships between many concepts within a phenomenon (Jaccard & Jacoby, 2010). The use of iterative examination of relevant published research throughout the process, brought a new perception of auditory development in the altered auditory environment of the NICU, characteristics of the intrauterine environment, and the interconnection between auditory development and language. As a result of using causal modeling to construct the theoretical framework, intrauterine characteristics of pitch, rhythm, and prosody that are present in speech, have been identified as significant components of the auditory environment that play a major role in the development of the auditory system.

A theoretical framework that provides in depth understanding in the development of an intervention includes multiple variables and relationships beyond just direct relationships. Additional variables that have the potential to impact the relationship between language exposure and auditory development for VP infants are determined from the literature review. While inclusion of multiple variables and relationships increases the complexity of the framework, they provide the most robust explanation of the phenomenon. Identifying moderator variables requires further comparison of the literature in order to determine what type of variation the moderators may induce on the relationship. Some variables, such as maternal voice, are richly represented in the literature while other variables are more obscure. Due to limited research that explicitly examines early auditory development of VP infants, at this point in the theoretical framework, the variables and their relationships are hypothesized. Additional research of the framework is required in order to determine the accuracy of included components and their relationships to one another.

This theoretical framework is nested in the grand theory of experience-dependent neural plasticity. This grand theory provides context for understanding how alterations of auditory experience during early phases of development impact the quality and outcome of auditory development (Skoe & Chandrasekaran, 2014). Experience-dependent neural plasticity also provides the rationale for how an intervention that alters the early auditory experience has the capacity to change the outcome of auditory development. During the initial establishment of the auditory pathway and neuronal connection within the auditory cortex, incoming stimulation sets the process in motion. The quality of stimulation during this early period of development determines early auditory capabilities (Stipdonk et al., 2016). Changes to auditory input as a result of NICU hospitalization alter the extent of the initial auditory capabilities (Kisilevsky et al., 2009).

This chapter defines the variables in the model and provides a research-based rationale for their relationships to one another. Path diagrams are the traditional way to express a causal model graphically. This causal model is presented in phases through a series of path diagrams that provide pictorial representation of the variables and relationships. Research citations that validate the model are indicated by sub script numbers in the path diagram and Appendix A includes a full list of diagram references.

Dependent Variable

A dependent variable is the outcome of interest that the theory is aiming to explain (Jaccard & Jacoby, 2010). The primary dependent variable of interest is auditory perceptual development. The reliance of the auditory system on the quality of early sensory input is evident in the research (Skoe & Chandrasekaran, 2014). Initiating activation of the auditory pathway and strengthening neural connections for efficient processing of auditory stimulation are directly related to early auditory experiences (Dahmen & King, 2007). An infant that is born during the critical period of auditory development when the auditory system is the most vulnerable to the quality of incoming stimulation is at a high risk for long term difficulty as a result of altered development (Baldoli et al., 2015).

Specific aspects of auditory development that are particularly vulnerable to early experiences are myelination of neurons, structural organization of the auditory cortex, and functioning of the auditory pathway. Auditory development can be measured by several different non-invasive methods: Auditory Brainstem Response (ABR), Functional Magnetic Resonance Imaging (fMRI) and Near Infrared Spectroscopy (NIRS) (Baldoli et al., 2015; May et al., 2011; Seethapathy et al., 2018). Additionally, behavioral responses such as eye gaze and looking duration have also been identified as having the potential to provide valuable information regarding auditory discrimination capacity (Mehler et al., 1988). The non-invasive and early use of these measurement tools with premature infants provides a promising path to understanding the impact of early auditory experiences on auditory perceptual development. Because each method of measurement reveals a slightly different, yet essential aspect of auditory development, they are presented together in the framework as possible measurements of the dependent variable, auditory perceptual development.

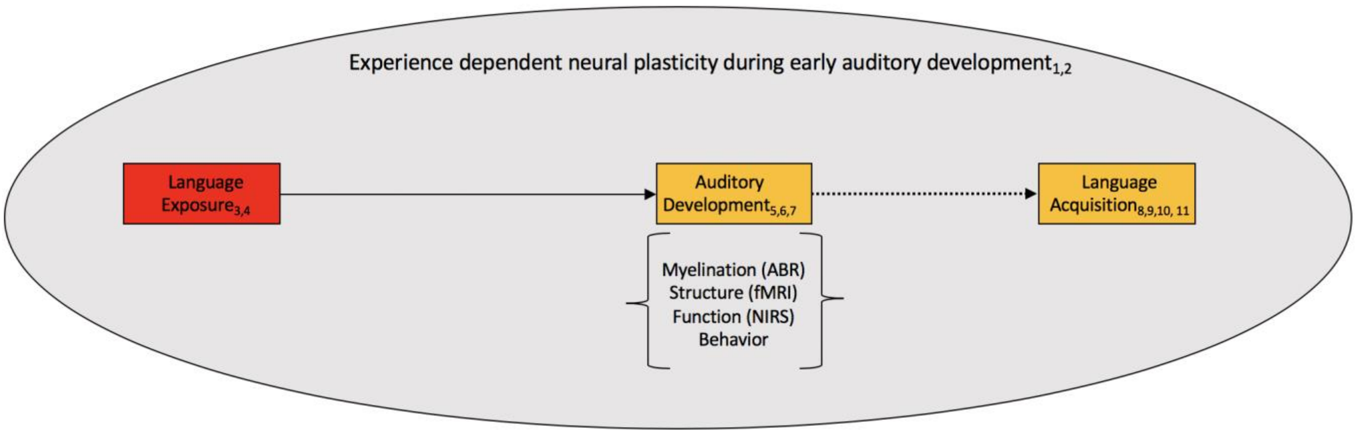
Due to the significant amount of research that links auditory development to long-term language outcomes in VP infants, language acquisition is identified as a secondary dependent variable (Chonchaiya et al., 2012; Kisilevsky et al., 2009; Stipdonk et al., 2018). Increased understanding of the relationship between auditory development and language acquisition in VP infants is essential in the long-term goal of improving language outcomes in the VP infant population. While language acquisition is not the primary focus of this model, it is included for the purpose of conceptualization of the problem and a goal of future longitudinal research.

Independent Variable

In causal modeling, independent variables are the factors that can be manipulated through an intervention to change the dependent variable (Jaccard & Jacoby, 2010). The essence of this theoretical framework is developed through considering how changes to early auditory experiences of VP infants impact auditory perceptual development. The critical period of auditory development that occurs during the third trimester of development is reliant on the experience of language sounds in order to establish sensitivity to language (Joseph et al., 2016). As such, the independent variable in the model has been identified as language exposure.

Exposure to language from the onset of hearing is an essential component of the early auditory experience that impacts auditory development (Caskey et al., 2011; Caskey, Stephens, Tucker, & Vohr, 2014). Additionally, the quality of language exposure is significantly changed as a result of premature birth (Lahav & Skoe, 2014). Language present in utero is filtered through maternal tissues and fluids. The process of filtering allows only low frequencies to pass through causing language quality to include increased emphasis on rhythm and prosody carried by vowel sounds. Figure 2 is a path diagram that represents the direct relationship between language exposure and auditory perceptual development, as well as the secondary direct relationship of interest between auditory perceptual development and language acquisition. The independent and dependent variables are inside the grey oval that represents how the model is situated in the grand theory of experience dependent neural plasticity.

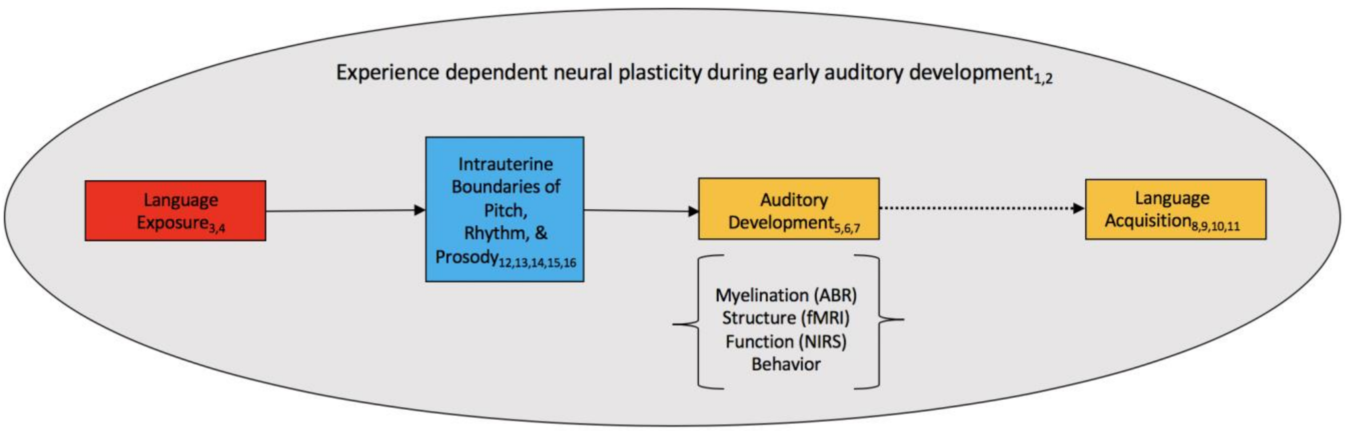
Figure 2: Independent and dependent variables



Mediators

Variables that must be present in order for the relationship to exist between an independent and dependent variable are known as mediators (Jaccard & Jacoby, 2010). Mediators are also referred to as the active ingredients, or mechanisms of change in an intervention (Keith, 2015). Mediator variables are essential components that are required to achieve the predicted outcome of an intervention. In this model, three characteristics of language sounds in utero are included as a single mediator variable. These characteristics are: pitch in a range that is less than 300 Hz, rhythm that follows the iambic pattern of the English language, and prosody that mimics the universal acoustic boundaries of the English language. The characteristics are presented as a single acoustic signal in speech which led to combining them in the model as a single mediator variable. The intrauterine boundaries of pitch, rhythm and prosody are known to impact early auditory perceptual development by creating strong auditory neural pathways for the perception of speech sounds (Gerhardt & Abrams, 2000; Belin & Grosbras, 2010; Nazzi & Ramus, 2003). Language sounds are significantly altered and/or reduced as a result of very preterm birth and NICU hospitalization does not afford the VP infant exposure to the intrauterine characteristics of language. Figure 3 illustrates how the three language characteristics are represented in the model as a single unit of "intrauterine boundaries" due to the simultaneous presentation of pitch, rhythm and prosody that is present in speech.

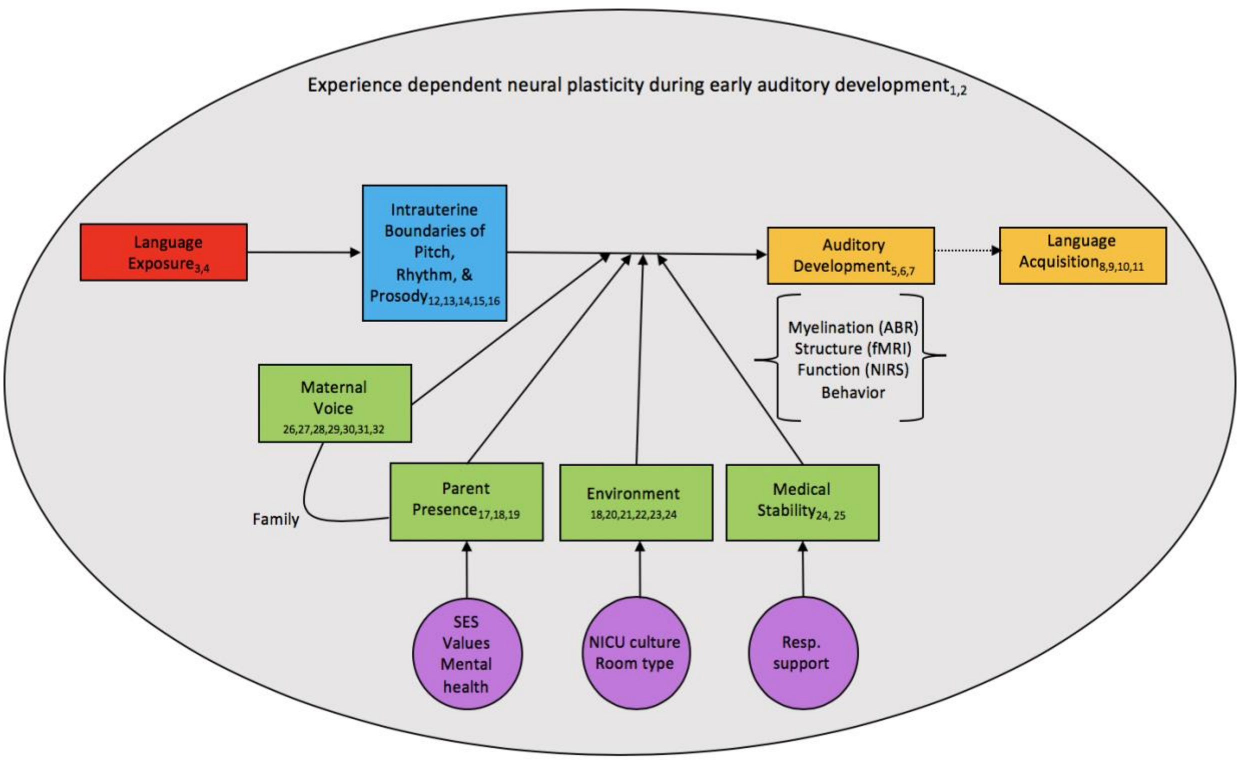
Figure 3: Mediators



Moderators and Disturbance Terms

Moderator variables are factors that change the strength of the influence that one variable has on another (Jaccoby & Jacard, 2010). In intervention research, moderators are factors that must be considered to define variability in outcomes of an intervention on the population for which it is intended (Fleury & Sidani, 2012). The outcomes of any intervention for VP infants will vary due to the complex and individualized nature of developmental processes. There are many environmental, family and medical components that can change the strength of the relationship between language exposure and auditory development as a result of preterm birth. To design a model that describes critical sources of individual variation, multiple moderators have been identified. Figure 4 demonstrates the inclusion of four primary moderators that directly impact the relationship between language exposure and auditory development. Each of the identified moderators also has a set of disturbance terms associated with it. Disturbance terms are variables that are related to another variable but are not the central focus of the model (Jaccoby & Jacard, 2010). Based on the available research evidence, the disturbance terms in this model are additional factors that provide further explanation of potential variation in the moderators. Identifying the disturbance terms at this point in the model allows for them to be considered during intervention development and to be tested at later stages of research to determine their variation and influence on the model.

Figure 4: Moderators and disturbance terms



Moderator: Parent presence. Having a parent present at the bedside provides more accurately opportunities for an infant to be exposed to individualized speech sounds thus strengthening the relationship between language exposure and auditory development. Especially in private rooms where overall language is greatly decreased, parent presence is essential (Pineda et al., 2014). Parents who hold their infants while at the bedside are shown to provide even more language through talking and singing to their infant than parents who are present but not holding (Pineda et al., 2017). Although there are many barriers that prevent parent presence in United States' NICUs, based on the benefits to auditory development, it is necessary to include parent delivery of speech sounds of as a component of an intervention that targets auditory development.

Disturbance term: Socioeconomic status. Parents of low socioeconomic status (SES) are overrepresented in the NICU environment due to disparities in preterm birth among this population (MacDorman & Mathews, 2011). Costs associated with hospitalization such as travel to and from the medical center, loss of wages due to time away from work, child care, and medical bills are significant stressors that may prevent parents from being present at the bedside and complicates the financial situation (Enlow et al., 2017). Thus, SES may cause variation in parent presence and should be considered as a disturbance term of this moderator.

Disturbance term: Family value systems. There was no explicit research that described the impact of family values on parental presence in the NICU. However, in the study of values and behaviors from other areas of social research, it is well documented that values are a basic motivator of behavior (Maio, 2010). Value systems act as guiding principles that influence attitude, goals, and behavior (Maio, 2010). Translating this into the behavior of parents experiencing the NICU hospitalization of an infant, it must be considered that value systems could impact parent presence in the NICU. As a result, this model accounts for family value systems impacting parent presence by including it as a disturbance term.

Disturbance term: Mental health. Maternal mental health is an additional factor that influences parent presence at the beside as well as the quality of interactions. Mothers experiencing psychological distress have more challenges being present with their infants and engaging in care of their infant during NICU hospitalization (Harris, Gibbs, Mangin-Heimos &

Pineda, 2018). Evidence exists for a positive influence on maternal mental health when the mother is included in healthcare routines with the infant in the NICU (Horsch et al., 2016). While it is outside the initial scope of this model to fully describe the complex relationship between maternal mental health and auditory development, including maternal mental health as a disturbance term acknowledges it as a factor that could vary the moderator of parent presence.

Moderator: Environment. The environment is identified as a moderator because many auditory characteristics present in the NICU influence the quality of exposure to beneficial speech sounds. In the context of experience-dependent language development, environmental characteristics play a large part in the strength of an intervention for very premature infants. Environmental features present in the NICU such as loudness, random sound peaks and silence are very different from intrauterine characteristics and are known to negatively impact auditory development (Graven & Brown, 2008; Rand & Lahav, 2013). Background noises mask important speech sounds while too much silence creates possible deprivation from speech sounds all together (Pineda et al., 2017). Auditory factors of the NICU environment can impact outcomes of infant weight gain, infant irritability, state regulation, and parent sensitivity (Cusson, 2006). These outcomes have all have been associated with long-term language outcomes in VP infants.

Disturbance term: Room type. The type of NICU room, individual or open bay, is included as a disturbance term due to the impact the room type has on the quality of the overall auditory environment. Open bay unit designs are often too noisy which prevents essential characteristics of speech from being perceived by infants (McMahon et al., 2012; Rand & Lahav, 2013). Unit design has been a major change as NICU's shift toward individual rooms in an effort to reduce noise in the environment. Although single-family rooms provide a much quieter atmosphere, the lack of language stimulation has been shown to be detrimental to auditory development (Pineda et al., 2017). Single-family room design may provide a major benefit for the introduction of an auditory intervention due to the reduction in background noise and increased privacy.

Disturbance term: NICU culture. The culture of the NICU is also included as an environmental disturbance term due to its role in determining how professional caregivers may interact with infants in the NICU. Cultural influences include philosophy of care, professional caregiver training, and nurse's personal values and beliefs. For example, NICU's that are NIDCAP certified place emphasis on developmental care practices that influence auditory outcomes (Als & Gilkerson, 1997). Some units may have a culture that emphasizes silence and low stimulation but have not provided adequate training or resources for understanding the value of enriching stimulation that is developmentally appropriate. Along with NICU culture comes the personal values of nurses caring for infants and their families. Influences from nurse training as well as personal beliefs and values shape how nurses use their own voices during the care of premature infants as well as what information they pass along to parents. Geographic location and size of the hospital and NICU are also speculated as influential cultural factors.

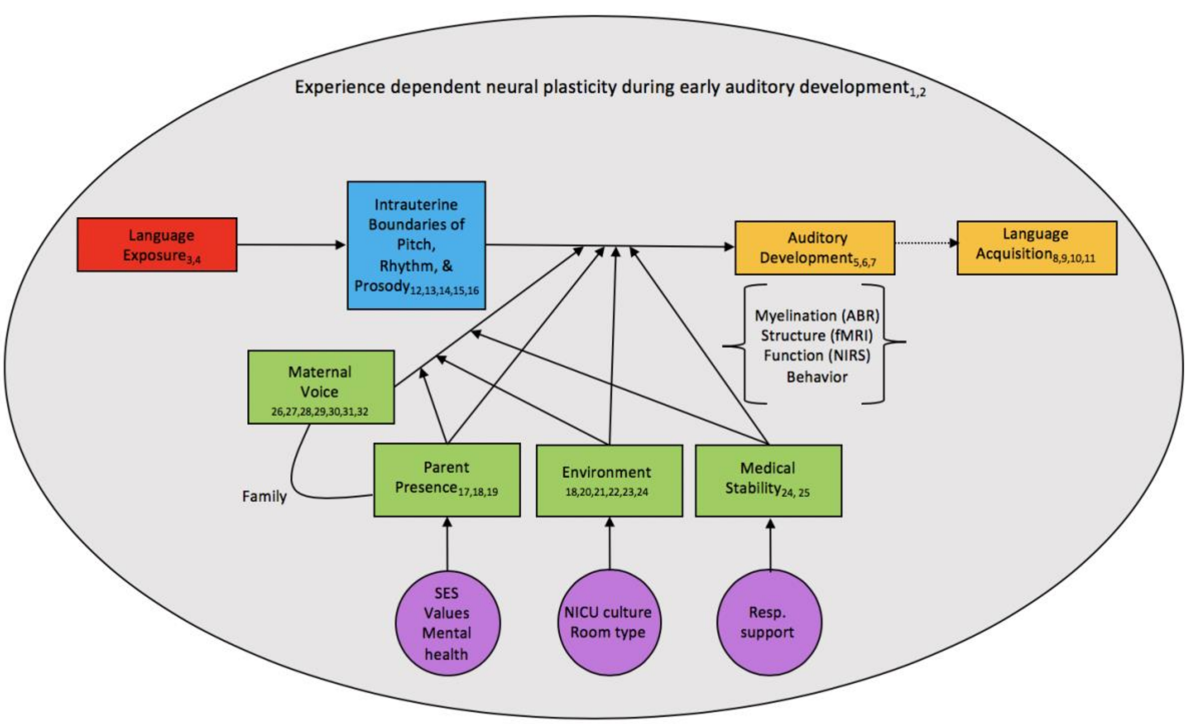
Moderator: Medical stability. Certain medical complications impact a VP infant's exposure to auditory stimulation which is why medical status is included as a moderator variable. Lack of stability and the need for respiratory support can reduce the amount of language stimulation an infant is exposed to while increasing electronic sounds from ventilators and other medical equipment required at the bedside. Increased medical complications can also increase length of stay (LOS) in the hospital which places VP infants at an increased risk for language delay as a result of sustained exposure to less than optimal auditory stimulation during a critical period of auditory development.

Disturbance term: Respiratory status. VP infants with severe lung disease that require long-term respiratory support face many developmental challenges and are at the highest risk for developmental delays during childhood and beyond. Frequent episodes of hypoxia or lack of oxygen as a result of lung disease can cause cell death that impacts the initial development of neuron pathways in the auditory system (Sansavini et al., 2011). As such, respiratory status has been identified as an individual disturbance term related to medical stability.

Moderator: Maternal voice. The amount of literature present that involves use of the maternal voice to benefit many problems associated with preterm birth has led to the inclusion of maternal voice as a moderator in auditory development. Maternal voice is one of the most salient features of the intrauterine environment which means it plays a significant role in establishing early auditory connections for robust perception of speech sounds (Dehaene-Lambertz, et al., 2010). In the NICU, maternal voice may still be present but its benefits are studied in relation to outcomes of interest in premature infants such as: short-term physiologic stability (Choi et al., 2014; Filippa et al., 2017); behavior state (Shellhaas et al., 2018); feeding (Krueger et al., 2010); pain (Johnston et al., 2007); and brain development (Webb et al., 2015). However, these outcomes of maternal voice research in the NICU may be protective factors of auditory development for the VP infant population. The significant and multi-varied impact of the maternal voice on factors related to auditory development makes maternal voice a primary factor as a moderator variable in auditory intervention.

Moderated moderation. In causal modeling, there are instances when a moderator variable influences the impact of another moderator on the primary relationship of interest. These complex relationships are called moderated moderators (Jaccard & Jacoby, 2010). In this model, the three moderators, parent presence, environment, and medical stability, are also moderated moderators in the relationship between maternal voice and auditory development. In order for maternal voice to occur, the mother has to be present in the NICU. Thus, lack of maternal presence decreases the strength of maternal voice moderation while increased maternal presence may increase the strength. Certain environments provide a more inviting and supportive situation for mothers to use their voice. In addition, the culture of the NICU environment can strengthen the maternal voice relationship if mothers are encouraged to use their voice with their infant through education or demonstration. As such, different environmental situations can strengthen or weaken the impact of maternal voice on auditory development. Lastly, medical stability may change the relationship between maternal voice and auditory development due to the impact that severe medical conditions of the infant can have on maternal mental health (Harris et al., 2018). Improved stability my cause an increase in maternal voice use and thus, strengthen the relationship to auditory development. Figure 5 provides a path diagram to highlight the relationships of moderated moderation variables.

Figure 5: Moderated moderation



Additional Disturbance Terms

Additional factors of ethnicity, gender, gestational age at birth, and genetics are identified as disturbance terms that may result in variation of auditory development outcomes for VP infants, but that cannot be modified by an intervention. Future research based on this framework will include these disturbance terms as either exclusion or randomization criteria in order to account for the effect they may have on auditory development outcomes.

There are different rates of prematurity among ethnic groups as well as differences in some outcomes associated with premature birth (Premature birth report card, 2018). As such, language outcomes may vary based on ethnicity (Freeman Duncan et al., 2012). A comparison of ethnic minority groups of very premature infants found that while all scored lower than the expected average in both receptive and expressive language, African American and Hispanic infants scored significantly lower than the Caucasian infants at 18-months. After adjusting for medical and psychosocial factors the significance remained which indicates the importance of considering the influence of ethnicity in language outcomes. (Freeman Duncan et al., 2012).

Gender is known to impact auditory development. Males and females have slightly different auditory development trajectories and sensitivities to sounds from birth. Females infants have more rapid auditory processing times than males after being matched for gestational age, birthweight, APGAR score, and ventilator days (Eldredge & Salamy, 1996). Female infants also have greater spontaneous otoacoustic emissions (SOAE), an indicator of cochlear function, than males (Morlet et al., 1995).

The earlier an infant is born before term, the higher the risk is for language delays. Earlier gestational age means infants experience a longer duration in the altered auditory environment during the critical period of auditory development (Joseph et al., 2016). Earlier gestational age at birth also increases the risk for medical complications such as chronic lung disease which can impact auditory development due to higher incidence of reduced oxygenation to the brain.

There is increasing evidence that genetics may also play a role in delayed language capacity. Family history of language delay is a possible indicator of a genetic component of language development in some cases (Rice, 2012). Although the least evidence exists for the influence of genetics in early auditory development, it is considered as a possible disturbance term.

Model Summary and Boundaries

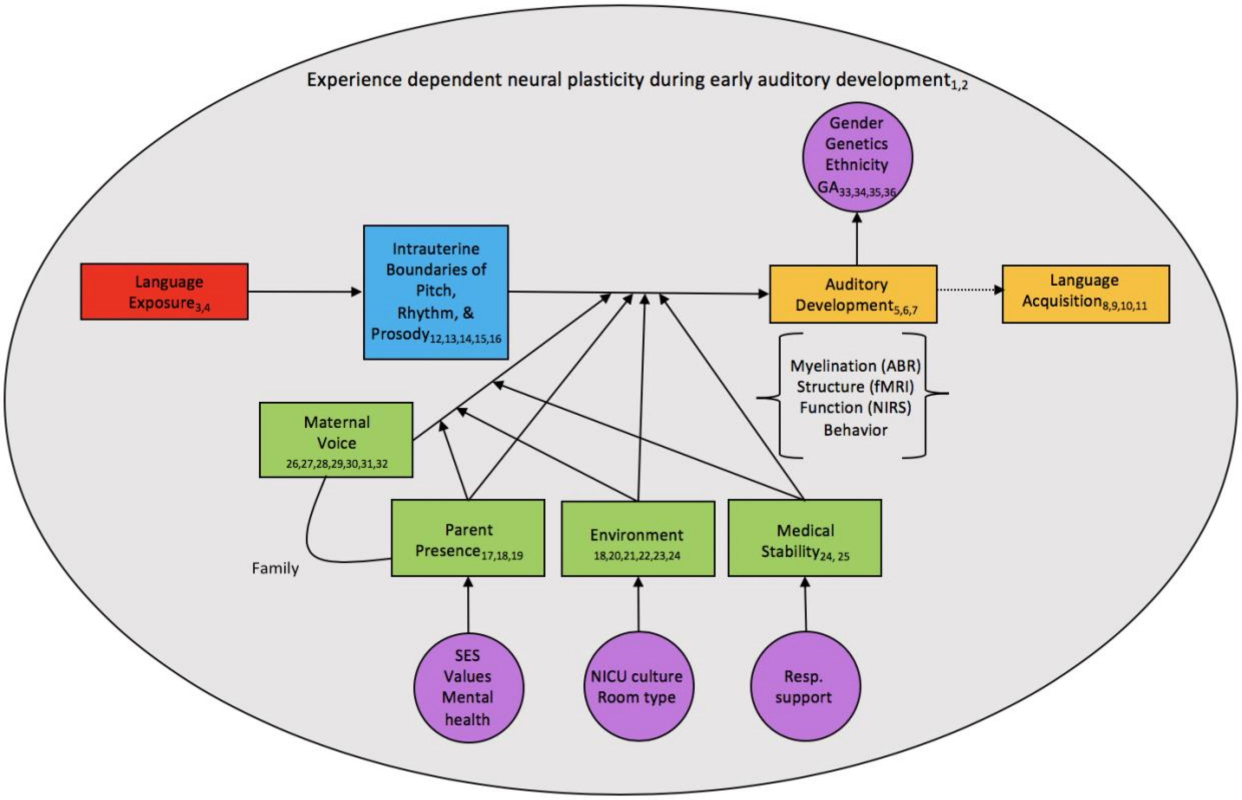
At the outset of building the theoretical framework using causal modeling, the initial relationship between early auditory experience and auditory perceptual development seemed straight forward. Based on the grand theory of experience dependent auditory plasticity it makes sense that changes to auditory input as a result of preterm birth would impact neural connections and organization of the auditory cortex. What was less understood were the constructs from the intrauterine auditory environment, speech pitch, rhythm, and prosody, that could be mimicked in the NICU to enhance auditory development. The intrauterine speech qualities were identified as essential to the early language exposure because this is a salient feature of what a fetus hears prior to birth. This essential nature allowed speech pitch, rhythm and prosody to emerge as a mediator that further describes the relationship between language exposure and auditory perceptual development.

Placing the model in the context of the NICU experience required the exploration of moderators as additional variable that describe variability of outcomes based on certain circumstances. Moderators of maternal voice, parent presence, environment, and medical stability each change the strength of the outcome due to many different factors. Disturbance terms that help define each moderator are included for clarity of this initial theoretical model.

Additionally, maternal voice is a key factor in auditory development and parent presence, environment and medical stability also moderate maternal voice by potentially changing its influence on auditory development. Inclusion of these moderated moderators helps further describe variation in outcomes based on interactions between moderators. Figure 6 provides the final path diagram that represents the emerging theoretical model with the additional disturbance terms added.

Boundaries of a theoretical model help provide further social and cultural context for the model (Swanson & Chermack, 2013). This theoretical model was developed through the lens of the researcher's own experience working in multiple NICUs in the United States. As such, it is currently situated within the cultural boundary of the United States NICUs. There are cultural aspects related to the healthcare system which present situations such as barriers to maternal presence in the NICU, that may not be present in other parts of the world. While the problem of delayed language outcomes in VP infants has been found across multiple cultures, certain considerations for the inclusion of specific variables may need to be altered for cultures outside the United States.

Figure 6: Emerging theoretical model



Music Intervention Development Based on the Theoretical Model

Based on the construction of this theoretical framework, a hypothesis has formed for the use of intrauterine boundaries of pitch, rhythm and prosody as active ingredients in a music intervention to target the early auditory development of VP infants in the NICU prior to their readiness for full spectrum speech sounds. The sounds of language inside the womb have reduced consonants which leaves vowels as the primary language characteristic. Vowels carry the pitch contours of speech so the result is intrauterine language that sounds more like a continuous musical melody than individual words. The rhythmic pulse of language remains intact in utero through stressed and unstressed sounds. Delivering speech sounds through singing vowel sounds that mimic the contour of phrases may be a feasible way to closely match the intrauterine characteristics of language in the NICU environment.

Pitch. The tissues and fluids of the womb act as a low-pass filter that prevents frequencies above 300 Hz from entering the womb environment (Lahav, 2015). Within the womb, language sounds that are the most salient are the low frequencies carried by the vowels. The fundamental frequencies, or most common pitch ranges for typical human voices of both males and females falls below 300 Hz making the voice especially well equipped to deliver frequencies that are important during early development.

Tonotopic organization of the auditory cortex based on incoming stimulation is a key early task that is essential to the perception of specific sounds in the environment. Long-term exposure to unique human voice sounds and language strengthens the auditory pathway and builds strong processing ability in the auditory brainstem (Krishnan et al., 2012). Exposure during the critical period when the connections are first being initiated increases sensitivity and processing speed for the pitches present in language spoken by the human voice (Sanes & Bao, 2009). This model suggests that robust low frequency exposure of human voice sounds has a direct relationship on myelination of auditory nerves associated with specific frequencies, as well as the tonotopic organization of the auditory cortex. Musical melodies can be composed that include only the frequencies that are the most present in the womb. Musical melodies can be presented by the human voice through humming or singing only vowels in order to remain within the low frequency pitch range.

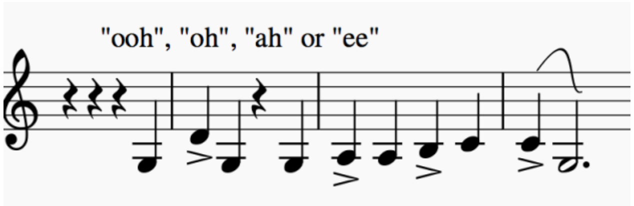
Rhythm. To develop familiarity with the rhythmic boundaries of language, the fetus is exposed to language before birth in an environment where the effects of acoustic filtering allow rhythm to be transmitted as a prominent feature of the language signal (Abrams& Gerhardt, 2000; Gervain, 2018). The pulse that makes up the rhythmic pattern of language is carried in the duration and intensity of sounds. Sensitivity to language specific rhythms is known to be an important factor in recognizing and processing speech (Gervain, 2018). Rhythmic boundaries group sounds together and allow word information to be extracted from continuous speech signals. In the English language, a “strong-weak” stress pattern, known and iambic, is the most prominent, as well as equal spacing between stresses in a sentence which is known as “stress-timed” (Nazzi & Ramus, 2003; Patel, 2008).

In the womb, high frequencies are filtered out diminishing word meaning, but rhythmic patterns remain intact. This means infants are exposed to the rhythm of language with great repetition prior to birth. Language present in the NICU does not provide the same exposure to the emphasized rhythmic structure of language. Too much background noise and overlapping conversational language present in the NICU masks the isolated rhythmic quality of language (Caskey & Vohr, 2013). Without individually provided language exposure that emphasized the rhythmic pulse, it is more difficult for very premature infants to develop the sensitivity to rhythm that is needed for language acquisition later in life. Emphasized exposure to rhythm builds stronger neural pathways for recognizing and discriminating rhythmic boundaries of a language (Nazzi & Ramus, 2003). Strong neural representation of language rhythms is a foundational auditory perception skill that allows continuous language to be grouped into segments that are more easily processed (Gervain, 2018). Without robust sensitivity for the rhythm category of the native language, more specialized rhythmic sensitivity to the native language is altered. This model supports the increased exposure to rhythm patterns of language during NICU hospitalization. To provide rhythm without the higher frequencies found in consonants, song melodies can include stressed and unstressed beats that mimic language patterns and can be sung using only vowels.

Prosody. Inside the womb, individual word meanings are not transmitted due to the filtering of high frequency sounds. What remains in addition to rhythm is the contour, or rise and fall, of the pitches as language is spoken. In English, universal prosodic patterns such as a higher pitch at the end of a question, provide boundaries that help segment large amounts of information into more manageable portions (Patel, 2008). Long-term exposure to prosodic contours of a native language create more robust recognition ability and faster processing of large amounts of language information (Krishnan et al., 2005). Early exposure to prosody in the womb through language exposure allows for encoding of the contour information at the level of the brainstem. This early encoding plays an important role in shaping the strength of perceptual abilities necessary for later stages of language acquisition (Krishnan et al., 2010). Exclusive exposure to the prosodic contour of language without the additional auditory information from individual words and higher frequency sounds, allows for early development and learning of prosodic contours that are essential for language acquisition later in development.

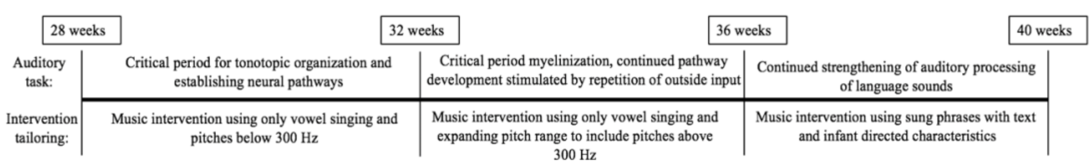
In the NICU environment, exposure to language prosody is diminished by background noise, lack of language exposure, and lack of prosody prominent stimulation. Melody, which is the organization of musical pitches, is the music element equivalent to speech prosody (Patel, 2008). This model supports the use of song melodies composed with the specific prosodic contours found in language in order to provide language stimulation that includes more intrauterine features that are necessary for auditory development. Figure 7 shows a simple example of what a melodic line composed for auditory development in the NICU might include. The prosodic and rhythmic characteristics of the spoken phrase, “good morning, let’s have a happy day” is used as an outline for the composition of the melodic contour. Accent marks are used to indicate the rhythmic inflection that mimics the syllabic contour, and the pitch range remains below 300 Hz and is within the typical adult speaking range frequency.

Figure 7: Sample intervention melodic line



Combining the intrauterine boundaries of pitch, rhythm and prosody found in speech into a musical melody that can be sung through sustained vowel singing may be an innovative way to provide access for VP infants between 28 and 32 weeks, to the essential elements of speech that are so highly represented in utero but are significantly altered in the NICU. The movement toward private room NICU design provides an atmosphere that can be enhanced by an auditory intervention that is grounded in a theoretical model. Understanding the mechanisms that have the greatest influence on auditory development during the critical period of the third trimester allows for the development of an intervention that is specifically tailored to meet the needs of this high-risk population. As VP infants develop and become closer to term gestation, the intervention characteristics can be tailored to support the auditory task at each gestational stage. Figure 8 provides a sample timeline trajectory of how the intrauterine speech qualities of a music intervention may change based on the development of the auditory system.

Figure 8: Tailored music intervention



Chapter 5

Discussion

Music is frequently considered beneficial for preterm infants in the NICU. Recorded music, live music, lullabies, classical music, mother's voice, and womb sounds have all been used to address multiple needs of preterm infants (van der Heijden et al., 2016). The non-invasive, soothing, and historical contexts of music have been used to rationalize *why* music is effective for preterm infants. What is lacking from the research on music with preterm infants is a theoretical foundation and more knowledge that describes specific uses of explicit musical elements to impact an identified need. Theory provides insight into the nature of a problem through examining pertinent literature and constructing hypothesized relationships that define possible mechanisms of change within an intervention. In this theoretical framework it was determined that diminished early auditory perceptual ability as a result of preterm birth plays a significant role in delayed language outcomes associated with VP infants. Experience dependent neuroplasticity is the theoretical foundation that provided a context for why changes in early auditory experience could alter developmental processes, and why early intervention could be effective in mitigating negative effects of the environment (Intartaglia et al., 2016; Kral & Eggermont, 2007; Skoe & Chandrasekaran, 2014).

Causal modeling provided the systematic approach used to determine the hypothesized relationships between multiple variables that impact the auditory perceptual development of VP infants in the NICU (Jaccard & Jacoby, 2010). The theoretical framework presented in the previous chapter is the first attempt at demonstrating the hypothesized relationship that the intrauterine boundaries of pitch, rhythm and prosody found in speech (mediators), have on the auditory perceptual development of VP infants in the NICU (dependent variable). The framework includes moderating variables of, family, environment, medical stability, and maternal voice in order to provide a comprehensive representation of the how these variables further explain the complexity of the problem and may strengthen or weaken the outcomes of a potential intervention. Lastly, the theoretical framework acknowledges the direct relationship between auditory perceptual development and language acquisition as a hypothesized long-term dependent variable (Amin et al., 2014; Kisilevsky et al., 2009; Stipdonk et al., 2018).

Significance and Strengths

A substantial amount of research suggests that the sensory development of VP infants is directly impacted by the NICU environment (Cardoso et al., 2015; Lahav, 2015; Pineda et al., 2017; Stipdonk, et al., 2016; Wilke et al., 2014). Auditory perceptual development begins during the third trimester (Bureš et al., 2018; Hall, 2000), is highly dependent upon incoming stimulation (Skoe & Chandrasekaran, 2014) and is changed due to the acoustic differences between the intrauterine environment and the NICU (Kellam & Bhatia, 2008; Lahav, 2015; Pineda et al., 2017; Therien et al., 2004); thus, VP infants are at risk for altered auditory perceptual development (McMahon et al., 2012; Stipdonk, et al., 2016). A clear relationship also exists between auditory perceptual development and language acquisition which may be why long-term language delays continue to be documented for VP infants (Bosch, 2011; Guzzetta et al., 2011; Vohr et al., 2017). However, there is a gap in the current literature for strategies of early intervention during NICU hospitalization that enhance the auditory environment with characteristics of speech that are found in utero.

This theoretical framework significantly adds to the literature in two specific ways. First, it offers a synthesis of multiple constructs related to auditory perceptual development that must be considered prior to the construction of an intervention. Second, it is a research-based foundation that defines the theoretical variables that should be present in an intervention. This theoretical framework will inform intervention development and a phased research agenda to further refine and understand the individual variables and their relationships to the problem of auditory perceptual development in VP infants during NICU hospitalization. The most salient constructs that emerged as significant components to the theoretical model are: (a) auditory perceptual development, (b) differences between the intrauterine auditory environment and the NICU, (c) language exposure and auditory perception, and (d) the link between auditory perception and language acquisition.

An initial task in the process of auditory perception is activation of the auditory pathway through outside stimulation. The intrauterine environment provides attenuation of environmental and speech sounds that protect the infant from loudness and frequencies that can be damaging during the early stages of development (Gerhardt & Abrams, 2000). Additionally, specific characteristics of speech sounds within the intrauterine environment (pitch, rhythm, and prosody) appear to play an important role in preparing the auditory system to perceive language with greater potency than other types of environmental sounds (Gerhardt & Abrams, 2000; Belin & Grosbras, 2010; Nazzi & Ramus,2003; Querleu, Renard, Versyp, Paris-Delrue, & Crèpin, 1988). The relationship between quality of sound in the environment and auditory development is a significant relationship in the theoretical framework because the salience and quality of speech sounds is compromised in the NICU environment. The main delivery of speech sounds in utero comes from the maternal use of language (Dehaene-Lambertz et al., 2010). After term birth, caregivers continue to use language during interactions with the infant which creates a feedback loop between language exposure and continued auditory perceptual development that is known to be a robust predictor of later language acquisition (Adams et al., 2018; Loi et al., 2017; Stolt et al., 2014). Very preterm birth not only shortens access to the intrauterine sensory environment but under certain circumstances may also delay exposure the feedback loop created through reciprocal language interactions with a caregiver. Aspects such as the medical stability of the infant, presence of the caregiver, and NICU environment create potential barriers to caregiver/infant interactions that benefit auditory perceptual development (Chow & Shelhaas, 2016; Cusson, 2006; Lantz, 2013). Without the prerequisite auditory perceptual skills, VP infants are not able to discriminate speech sounds as efficiently which causes as high risk for delays in language acquisition (Jiang et al., 2006; Nishida et al., 2008).

This framework hypothesizes that intrauterine boundaries of pitch, rhythm, and prosody, found in speech, are significant components of auditory perceptual development that are compromised by early exposure to the extrauterine environment. It is not known exactly what the auditory experience is for an infant in utero. However, studies do support attenuation of high pitches and loudness, frequent exposure to speech sounds from the mother's voice and other voices in the environment, and ongoing background sounds generated by the mother's internal organs as key features of the intrauterine environment (Abrams & Gerhardt, 2000; Chang & Merzenich, 2003; Lahav & Skoe, 2014; Pysanenko et al., 2018; Werner et al., 2012). Immediately following term birth, infants are able to recognize their mother's voice as well as certain aspects of language (Nazzi et al., 1998; Vouloumanos & Werker, 2007). As such, these significant features of the intrauterine environment prepare the auditory system for language before birth. Considering specific intrauterine boundaries of speech and the perceptual abilities of infants related to language immediately following birth, provides support for auditory enhancement that uses characteristics of speech found in utero as essential ingredients for early intervention.

Further investigation of the quality of speech characteristics present in utero exposed several similarities to certain musical elements. The attenuation of speech through the uterine walls and fluids causes the acoustic properties to be altered in a way that the contour of pitches and rhythmic patterns become more salient than characteristics that carry word meaning. This change in acoustic properties results in a notably musical sound that is akin to a legato melodic line. Patel (2008) describes how speech and music share many characteristics and how language learning can be enhanced through exposure to music. Additionally, music is valued in the NICU environment as a possible normalizing experience for parents, enhancement of infant/parent bonding, as well as its documented benefits to physiologic stability. Using elements of music to deliver an intervention that impacts auditory perceptual development is a reasonable approach based on what is currently known.

Limitations

A possible limitation of this theoretical framework is that all variables and relationships are hypothesized based on the synthesis of the literature through the lens of the researcher's knowledge and background. The problem of language delays in the VP infant population is highly complex and involves understanding of research from many different fields. Some of the research synthesized in development of this framework was new to the researcher. Synthesizing large amounts of research from multiple fields of study leaves room for possible misinterpretation of essential concepts as well as omission of important concepts. Errors in the interpretation can cause the inclusion of variables and relationships in the model that do not accurately reflect their role in the identified problem. The absence of concepts similarly impacts the overall comprehensiveness of the model and its ability to explain the problem.

Theoretical frameworks provide a background and structure for developing complex interventions but do not themselves imply causal relationships between variables. Inferring causation between early exposure to specific speech elements in the NICU and auditory perceptual development is not intended to be implied by this theoretical framework. The researcher has taken much caution to reinforce the hypothesized relationships that will require further research testing in order to determine actual relationships and effect strengths of moderator variables. However, there is a chance that readers of this paper might interpret the theoretical model beyond its evidence-based hypothesized scope. The researcher's intention for developing this theoretical framework is to build a foundation for a future research agenda that targets understanding intervention components that can change long-term language development of VP infants.

Implications for Practice

Investigating multiple fields of study related to auditory and language development, and specifically focusing on premature infants, implications have emerged for music therapy practice with this population. The first construct is the presentation of pitch in working with VP infants. Knowing that pitches over 300 Hz are filtered out in utero, and higher frequencies are added slowly as the uterine wall becomes thinner and the infant becomes larger closer to term, brings to light that pitches presented during music therapy interventions should be highly considered when working with VP infants (Abrams & Gerhardt, 2000; Kellam & Bhatia, 2008). Some suggestions for considering the sensory readiness of VP infants for pitch based on the theoretical framework include: careful attention to avoid high frequency pitches during the use of guitar or other instruments that have the capability to produce sounds above this frequency range; singing in the modal register in order to produce pitches that are similar to the speaking voice; and avoiding high frequency consonants such as [ch] and [s]. The additional understanding of pitch can help further refine the safety of music for this fragile population.

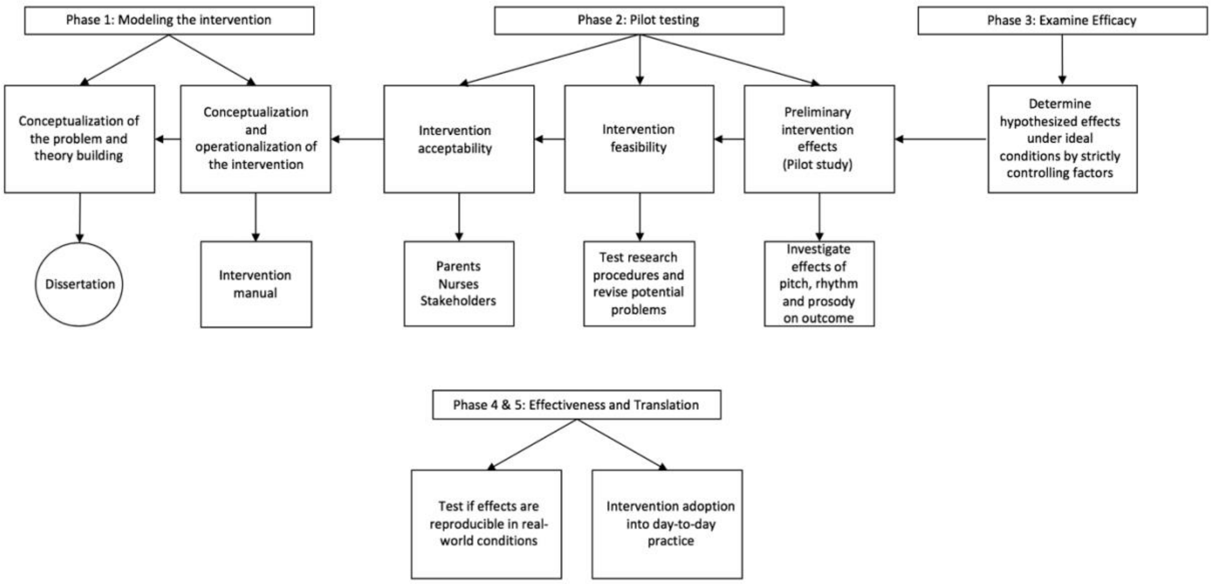
Another implication for practice that can be derived from the theoretical framework is the understanding of composition of music that provides the most auditory benefit for VP infants. At this stage in development, access to certain speech sounds appears to play the biggest role in preparing the auditory system for strong discrimination of language. As such, it may be more developmentally appropriate to deliver the sounds of the voice and contours of speech through simple humming or singing on a single vowel. Reducing the number of speech sounds present and isolating the ones that most closely reflect intrauterine sounds is yet another potential change to practice resulting from this theoretical framework.

Future Research Aims

Complex interventions are defined as those that involve several interacting components. In the case of auditory perceptual development in very preterm infants, an intervention must consider, early development of the auditory system, environmental characteristics of the NICU, and the medical and social contexts of very premature infants. Each of these constructs has its own variables that can impact the outcome of language development. As such, considerable time must be spent to gain an in depth understanding of the relationships between the components and how they will be considered in a targeted intervention.

Bleijenberg and colleagues (2018) propose a systematic framework for conceptualizing a complex intervention that involves six individual components that are considered in an iterative manner. The six components are: (a) problem identification and definition, (b) identify evidence, (c) develop theory, (d) determine needs, (e) examine current practice, and (f) model processes. The first five of these components have been addressed throughout the development of this theoretical model. The next aim is to use this theoretical model to build a research agenda that leads to development and testing of a targeted music intervention to alter auditory perceptual development in VP infants in the NICU. Figure eight models a research trajectory for this theoretical model and uses the phases of intervention research outlined by Sidani (2015). Setting up a cohesive research agenda that can build a database for inquiry of a specific need identified in a specific population brings depth of understanding and the possibility of achieving interventions that have clearly articulated active ingredients. Investing time and effort in the development phase of intervention research is essential for adding value to the field and enhancing potential effectiveness of interventions (Bleijenberg et al, 2018).

Figure 9: Phased intervention research trajectory



Modeling the intervention based on the theoretical framework includes the process of conceptualizing the essential components of the intervention and operationally defining them in an intervention manual. The intervention manual includes highly detailed descriptions of the stimulus and implementation. Developing the intervention manual marks the end of phase one and prepares the researcher to move into phase two and begin pilot testing. Testing the intervention throughout phase two also requires the intervention manual to be revised as additional knowledge is gained through research. Pilot testing involves determining if the intervention is acceptable by key stakeholders to the population of interest (e.g. Parents and nurses in the NICU), if implementation of the intervention based on the manual is feasible within the environment and with the population, and lastly if the intervention targets the outcome it is intended to target. Phase three begins the process of determining the efficacy of the intervention by testing it under strictly controlled parameters. This allows for larger scale testing of the effects under specified conditions that allow the focus to remain on determining if the intervention impacts the hypothesized outcome. The final phases of research involve removing the strictly controlled conditions in order to test the intervention in the real-world context and translating the intervention into day-to-day practice. Throughout the process of phased research, earlier models of the intervention are adapted and changed as driven by outcomes from each study (Sidani, 2015).

Intervention development and testing is not something that is undertaken by a single researcher but requires an interdisciplinary team. Building such a team in order to move this project into future phases will require identifying where researchers are already having conversations about auditory development. As a clinician, this researcher had the opportunity to work with an interdisciplinary team to develop a research project through the funding support of the Arthur Flagler Fultz Research Grant Award and the American Music Therapy Association. That research collaboration lead to presenting a poster, *The effect of live contingent singing on preterm neonates with bronchopulmonary dysplasia,* at the Graven's Conference on the Environment of Care for High Risk Newborns. A year later, this researcher presented another collaborative project at the Graven's conference, *Promoting the value of phase I research in NICU music interventions.* Both of these conference experiences have brought interest to other professional regarding the targeted use of music interventions and have set the foundation for continuing the conversation and establishing an interdisciplinary research team to begin looking at the function of this theoretical framework.

Conclusion

In order to impact the trajectory of auditory perceptual development for VP infants in the NICU, a music intervention must specifically target the early developmental needs of the auditory system. It is not enough to provide language stimulation to VP infants via singing or talking in the environment. Through synthesizing multiple fields of research that help define the problem of language delays in VP infants, a theoretical framework has been created that provides a possible mediated pathway for enhancing early auditory perception in VP infants and thus impacting long term language acquisition ability. There are specific ways that the voice can be used to maximize the speech sounds that salient in the intrauterine environment yet absent from the extrauterine environment of the NICU. Using this theoretical framework to develop an intervention and test it through a phased research agenda will provide depth of insight into possible mechanisms of change for enhancing long-term language outcomes in VP infants.

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Appendix

References for the theoretical model

1	Dahmen & King, 2007	Theoretical foundation	Early auditory experience
2	Skoe & Chandrasekaran, 2014	Theoretical foundation Disturbance term	Experience dependent neural plasticity Genetics
3	Caskey et al., 2011	Independent Variable	Language exposure
4	Caskey et al., 2014	Independent Variable	Language exposure
5	Baldoli et al., 2015	Dependent Variable	Auditory development
6	Guzetta et al., 2011	Dependent Variable	Auditory development
7	Stipdonk et al., 2016	Dependent Variable	Auditory development
8	Chonchaiya et al., 2013	Direct causal relationship	Auditory development to language acquisition
9	Amin et al., 2014	Direct causal relationship	Auditory development to language acquisition
10	Kisilevsky et al., 2014	Direct causal relationship	Auditory development to language acquisition
11	Stipdonk et al., 2018	Direct causal relationship	Auditory development to language acquisition
12	Abrams & Gerhardt, 2000	Mediator	Pitch
13	Nazzi & Ramus, 2003	Mediator	Rhythm
14	Belin & Grosbras, 2010	Mediator	Prosody
15	Querleu et al., 1988	Mediator	Pitch Rhythm
16	Teie, 2016	Mediator	Pitch Rhythm Prosody
17	Pineda et al., 2014	Moderator w/disturbance term	Parent presence
18	Chow & Shelhaas, 2016	Moderator w/disturbance term	Parent presence Environment
19	Lantz, 2013	Moderator w/disturbance term	Parent presence
20	Pineda et al., 2017	Moderator w/disturbance term	Environment
21	Rand & Lahav, 2013	Moderator w/disturbance term	Environment
22	McMahon et al., 2012	Moderator w/disturbance term	Environment
23	Graven & Browne, 2008	Moderator w/disturbance term	Environment
24	Cusson, 2003	Moderator w/disturbance term	Environment Medical stability

25	Sansavini et al., 2011	Moderator w/disturbance term	Medical stability
26	Arnon et al., 2014	Moderator	Maternal voice
27	Filippa et al., 2017	Moderator	Maternal voice
28	Kruger et al., 2010	Moderator	Maternal voice
29	Dehaene-Lambertz et al., 2010	Moderator	Maternal voice
30	Choi et al., 2014	Moderator	Maternal voice
31	Shellhass et al., 2018	Moderator	Maternal voice
32	Johnston et al., 2007	Moderator	Maternal voice
33	Duncan et al., 2012	Disturbance Term	Ethnicity
34	Morlet et al., 1995	Disturbance Term	Gender
35	Joseph et al., 2016	Disturbance Term	GA
36	Rice, 2012	Disturbance Term	Genetics