Binaural Sensitivity in Children with Normal Hearing and Children with Bilateral Cochlear Implants

By

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BINAURAL SENSITIVITY IN CHILDREN WITH NORMAL HEARING AND CHILDREN WITH BILATERAL COCHLEAR IMPLANTS

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Binaural hearing provides a listener with access to interaural time and interaural level differences (ITDs and ILDs). Binaural hearing aids in spatial hearing skills, such as sound localization or the ability to segregate speech in noisy environments. These spatial hearing abilities are vital for young children, as they spend a remarkable amount of time in noisy environments, such as a classrooms or playgrounds. Children with normal hearing (NH) perform well on spatial hearing tasks by the age of 4-5. Although children with bilateral cochlear implants (BiCIs) perform better than children with unilateral implants, they still perform worse than their NH peers when tested on the same tasks. Some factors that may be responsible for this gap in performance include (1) the lack of temporal fine structure present in current clinical processing, (2) neural degradation due to lack of early acoustic hearing, (3) surgical issues leading to differing depths of electrode array insertion between the two ears, and (4) the lack of temporal synchronization between the two implants.

The specific aims of this dissertation are to (1) investigate the extent to which the high-rate amplitude modulated stimuli are the limiting factor in performance by studying the ability of NH children to utilize envelope ITDs as transmitted by stimuli that renders fine structure information for ITDs imperceptible, (2) examine binaural sensitivity to binaural cues in children with BiCIs using low-rate pulsatile stimuli on pitch matched pairs to understand whether children with BiCIs have the ability to utilize these cues, (3) examine the effects of perceived interaural pitch mismatch on a pitch comparison task and a task measuring ITD sensitivity to evaluate the efficacy of pitch matching in children, (4) examine the effects of stimulus rate on ITD sensitivity in order to determine if high-rate amplitude modulated stimuli can elicit ITD sensitivity, and (5) investigate cognitive factors that may predict performance on tasks of binaural sensitivity, to better understand if specific cognitive factors may be predictors of binaural performance. Together, the five aims of this dissertation are designed to provide a better insight into why children with BiCIs demonstrate poor spatial hearing abilities.

DEDICATION

In loving memory of Mark Constancio.

To all my family and friends that have been my biggest support system. I could not have done it without you.

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Chapter I: Background and Introduction

Spatial hearing allows children to identify content and location of sound sources and is vital for navigation of their everyday environment. Spatial hearing abilities are largely related to the extent of which the binaural auditory system is able to integrate acoustic inputs arriving at the ears from various sources [1], [2]. This integration of acoustic inputs, or binaural hearing, provides a listener with cues that aid in spatial hearing tasks such as sound localization or listening to speech in noisy environments. Two cues specific to binaural hearing are interaural time and interaural level differences (ITDs and ILDs, respectively). Children spend much of their time attending to sound sources in complex acoustic environments, like classrooms, where there is one target talker with various distracting auditory signals, a situation known as the “cocktail party” environment [3]. As a result, it is necessary to understand the binaural hearing abilities of normal hearing (NH) children and children with profound hearing loss who use bilateral cochlear implants (BiCIs). However, little is currently known about children’s sensitivity to specific binaural cues that aid in sound localization and listening in noisy environments.

Binaural Hearing

ITDs and ILDs are important cues for sound localization in the horizontal plane. ITDs are typically the most robust for low-frequency sounds (<1,500 Hz) and ILDs are the more prominent cue for high-frequency sounds (>2,000 Hz) [2]. In addition, ITDs in the envelopes of modulated high-frequency carriers are also important for sound localization [4], [5]. Both ITDs and ILDs are determined by the location of the sound source relative to the listener’s head. An ITD is the difference in time between the arrival of the sound at the ear closest to the source and the ear furthest from the sound source. Similarly, an ILD is the difference in sound pressure level between the ear closest to the source and the ear furthest from the source. This difference in sound pressure level is caused by a phenomenon called the “head shadow effect” in which the head physically blocks sound waves, thus causing a decrease in level in the opposite ear [6]. In an adult human, the maximum ITD is approximately 700-800 μs based on the size of the average human head [7]. ILDs can be as large as 20 dB, also based on head size and location of the sound source [8].

In addition to providing important cues for sound source localization and improved hearing in noise, binaural hearing can also provide increased loudness through binaural summation, which is when sound presented binaurally is perceived as louder than sound presented monaurally [9]. It has also been reported that having two functional ears makes listening and communication less tiresome than for individuals with only one functioning ear [10].

Binaural hearing in normal hearing adults

The literature on binaural hearing in NH adult listeners is extensive. NH adult listeners show good sensitivity to binaural cues and are able to make use of these cues to complete spatial hearing tasks efficiently. For example, on a free field localization task, NH adults demonstrated an average root-mean-square (RMS) error of as low as 6.7º [11]. NH adult listeners can also benefit from spatially separating interferers and target sources, an occurrence known as spatial release from masking (SRM). NH adults can show as much as a 15 dB in improvement of thresholds when the target and masker are spatially separated [12]. The amount of SRM that occurs is dependent on the location of both target and masker. In an asymmetrical placement of target and masker (target at 0° and one masker at 90°), more SRM occurs as listeners are able to use the monaural head shadow cue. However, with a symmetrical placement of maskers (target at 0° and two maskers at ± 90°) there is a reduction of the monaural head shadow cue and listeners are forced to rely more on binaural cues [13], [14]. Finally, when given binaural cues via headphones, NH adults demonstrate sensitivity to ITDs as low as 11.5 µs [15], [16] and less than 1dB for ILDs [17].

Although the binaural abilities of NH adults are well documented, the abilities of young children are not fully understood. Since binaural cues, such as ITDs and ILDs are vital for all spatial hearing tasks, such as listening in complex environments and locating sound sources, it is necessary to understand the developmental trajectory of binaural hearing in both children with NH and children with BiCIs.

Binaural hearing in normal hearing children

To date, spatial hearing abilities in NH children have been primarily studied in the free field [18]–[20]. Two main approaches have been used to investigate spatial hearing skills in children: discrimination and localization. In the discrimination task, a minimum audible angle (MAA) threshold is found, which is the smallest change in location an individual can detect [21]–[23]. MAA thresholds undergo significant maturation throughout the first few years of life, with thresholds estimated to be 12º by 6 months of age and 4-6º by 18 months of age in NH children [21]. By ages 4-5, spatial hearing abilities are fairly developed, with children having adult-like MAA thresholds of 1-2º [21]. The second task commonly used to test spatial hearing perception in children is localization. Localization studies typically involve a target signal that varies in location and is presented from an array of loudspeakers. Results for sound localization experiments show that RMS errors for sound localization can be as low as 8º in NH children, which, like MAA thresholds, is similar to adult performance [18], [19], [24], [25].

Along with adult-like sound localization abilities at a young age, children with NH have also shown SRM as early as 3-4 years of age [26]. Even more recently, SRM has been shown in toddlers 2-3 years of age [27]. Although SRM has been shown at such a young age, it appears to be an auditory skill that continues to develop throughout adolescence, with NH children showing less benefit from the separation of target and masker than adults [14], [25].

Previous work on binaural hearing in NH children has investigated spatial hearing abilities, such as sound localization and SRM in the free field, in which both binaural cues and monaural spectral information are available to a listener. Therefore, research investigating children's sensitivity to specific binaural cues has been sparse. However, some research shows that NH children listening to acoustic stimuli are able to detect the presence of both ITDs and ILDs [28]–[30]. In fact, children as young as 6 months of age make directional responses to ITDs when presented with the cue over earphones [31].

The above findings, both in the free-field and earphone studies, confirm that young NH children are able to take advantage of binaural hearing to perform well on spatial hearing tasks, both to localize sounds and to segregate auditory sources when listening in noise. However, to date, research has not been conducted on the ability of NH children to utilize binaural cues when given stimuli that mimics aspects of CI processing.

Binaural hearing in children with bilateral cochlear implants

The goal of providing a child with bilateral cochlear implants is to restore binaural hearing. In fact, individuals with BiCIs do demonstrate improved sound localization abilities when compared to testing with a single CI [18], [24], [32], [33]. However, true binaural hearing is not fully restored when an individual is provided with two implants [18], [28], [34]. Therefore, a different developmental trajectory for spatial hearing tasks occurs for children with BiCIs than children with NH. For example, on a sound localization task, children with BiCIs had RMS errors that ranged from 19-56°, which is considerably poorer than their NH peers who had RMS errors of 9-29° [18]. This gap in performance between NH children and children with BiCIs remains, even after several years of experience with both implants [33]. In addition, children with BiCIs show little to no SRM in symmetric conditions where the monaural head shadow is reduced and do not appear to develop these abilities even after several years of experience [14], [35].

As with NH children, research investigating the spatial hearing of children with BiCIs in the free-field is abundant, whereas information regarding sensitivity to the specific binaural cues that aid in spatial hearing, ITDs and ILDs, is less prominent. Unlike preliminary research on NH children, who demonstrate sensitivity to ITDs and ILDs, there is some evidence to suggest that children with BiCIs show reliable sensitivity to ILDs, but are less reliable in detecting the presence of ITDs [29], [28]. However, in the Gordon et al. [29] study, the task involved the detection of a binaural cue, rather than the discrimination of a binaural cue. Therefore, it is unknown how sensitive children with BiCIs are to small changes in ITDs or ILDs. Additionally, in the Gordon et al. [29] study, when comparing NH children to children with BiCIs, the acoustic stimuli presented to NH children did not simulate CI processing, thus it remains unclear whether NH children were simply relying on fine structure cues, something that is not available to children with BiCIs in current clinical processing.

Finally, other factors regarding why there was a lack of ITD sensitivity in this pediatric population, including neural degradation, device limitations, and non-sensory factors such as cognitive abilities, have not been investigated further. It remains uncertain what effect these factors have on the ability of the binaural hearing pathways to develop early in life, particularly because current clinical processing provides inconsistent binaural input.

Factors Affecting Binaural Sensitivity

Numerous factors can be attributed to the gap in performance between BiCI users and NH children on tasks requiring spatial hearing. Factors affecting binaural hearing in BiCI users can include (but are not limited to) cochlear implant software limitations, surgical procedure variations, peripheral development (neural development of the auditory pathways), and central development, or higher order processing of auditory stimuli [36].

Children with BiCIs provide a unique population to investigate and cannot be thought of in the same manner as adults with BiCIs. Many adults with BiCIs either have long periods of deafness prior to receiving implants (pre-lingually deafened) or had long periods of natural acoustic hearing (post-lingually deafened). However, children with BiCIs may demonstrate a variety of patterns in regards to their hearing history. Although some children may have a few years of early acoustic hearing prior to implantation, many children with BiCIs receive their CIs within the first few years of life. This means that they will only receive sound through electrical stimulation (a lack of acoustic stimulation), and will not have long periods of deafness prior to receiving the implants. An additional factor to consider is whether children have received simultaneous or sequential implants. If the child is implanted sequentially, the inter-implantation delay can impact auditory development as research shows an inter-implantation delay of less than 1.5 years is beneficial to the development of binaural hearing [24], [37]. Therefore, for the current set of studies, factors that may affect binaural sensitivity must be considered differently from that of adults, thus taking into account pediatric auditory development.

Software-based limitations

Clinical CIs typically provide stimulation through biphasic current pulses. Stimulation in current speech processing strategies is multi-channel and non-simultaneous. Band pass filters are used to filter the incoming signal into a number of frequency bands (ranging from 12 to 22 depending on device manufacturer). There is a limitation in the ability of the speech processors to encode the acoustic signal with fine resolution. The detailed temporal fine structure of the original sound gets discarded and replaced with constant-rate pulsatile stimulation [38], [39], leaving the listener with the envelope of the signal. However, because the processors are not temporally synchronized (essentially functioning as two monaural systems), the ITD cue present in the envelope of the signal may also be unreliable [36], [38]. ILDs are also affected by the lack of synchronization between processors as the gain control is adjusted independently between implants, eliminating the consistency of the ILD cue [40].

Lastly, current clinical programming is typically high-rate, amplitude modulated stimulation with a rate of stimulation at 900+ pulses per second [41]. This high rate of stimulation provides excellent speech understanding in many users, but is not ideal for ITD sensitivity, which is known to be better at lower rates [42]. On the contrary, speech understanding is poorer at low-rates, suggesting there is a trade-off between binaural sensitivity and speech understanding.

Surgical issues

Variations in surgical placement of the electrode array can lead to differing insertion depths of the electrode arrays in the two ears, thus yielding differences in the anatomical location that is being stimulated between the ears. The average human cochlea is approximately 35 mm long. The majority of current internal devices for cochlear implants are only inserted roughly 20-30mm into the cochlea [43], [44]. Since the electrode array is not being inserted into the full length of the cochlea, differing depths of insertion is highly likely between the ears. As current clinical processing stimulates the same frequency band in each ear rather than the same anatomical region, this could cause differing inputs in frequency between the ears. A mismatch in anatomical place of stimulation between ears causes differing frequencies to be compared by the brain, thus leading to a decrease in binaural sensitivity.

Research has shown that ILDs are less susceptible to interaural mismatch than ITDs [45]. In this study by Kan et al. [45], two tasks including binaural fusion and lateralization were conducted with increasing amounts of mismatch. A pitch-matched electrode pair was found. The pitch-matched electrode pair was tested as well as intentionally mismatched pairs of electrodes (± 2, 4, and 6 electrodes from the pitch matched pair). Both the pitch-matched and "mismatched" electrode pairs were tested on the two tasks. Results showed that even a small mismatch of two electrodes (1.5mm) could cause a shift in perception of the auditory signal. ITDs were more likely to be affected by a small mismatch than ILDs [45].

Pathology of the peripheral auditory system

Many pre-lingually deaf children lack early access to acoustic binaural input, thus their auditory system may be insensitive to binaural cues, as the auditory pathways may not have developed properly. Therefore, even if current cochlear implant processing provided reliable ITD and ILD cues, a lack of development of the auditory pathway may not allow for use of these cues on spatial hearing tasks. It has been shown that a lack of early acoustic stimulation can cause peripheral and central processing degradation to occur [46], [47]. Specifically, spiral ganglion cells within the auditory system can shrink in size and number after a long period of auditory deprivation [47].

In addition, many children receive one implant at a young age and do not receive their second implant until years later. Electrophysiological studies have shown that binaural auditory pathways may degrade if *bilateral* stimulation is not received within a sensitive period [37], [48], [49]. More recent research has shown that children who have a duration of longer than 1.5 years between implants have abnormal strengthening of both contralateral and ipsilateral auditory pathways from the first implanted ear. This unilateral strengthening and reorganization can cause abnormalities in the development of binaural hearing, which can be detrimental to integration of cues provided for spatial hearing tasks [37].

As mentioned previously, some research shows that children with CIs demonstrate sensitivity to ILDs but not ITDs [28], [29]. ITDs and ILDs are processed separately in the brain. ITDs are thought to be processed in the medial superior olive located in the brainstem and are detected by the brain based on coincidence of excitatory inputs [50]. ILDs are thought to be processed in the lateral superior olive of the brainstem and are processed through the inhibition/excitation patterns of both ipsilateral and contralateral inputs. ITDs present in the envelope of high-rate amplitude modulated sounds are also thought to be processed in the lateral superior olive [51], [52]. Therefore, it may be that these pathways develop differently throughout infancy and childhood. It may be that the ITD pathway requires a greater amount of early acoustic hearing in order to develop to its full potential.

Central processing abilities

The above factors discuss how “bottom-up” peripheral processing in bilaterally implanted patients affect the ability to utilize binaural cues in complex listening environments. However, it has also important to investigate how “top-down” central processing, such as executive function, can interact with “bottom-up” peripheral processes to impact hearing abilities [53]. In order to understand how these top down processes might impact the peripheral hearing system it is important to first define these processes. Executive function is an overarching term that can include working memory, attention, problem solving, planning, inhibition, processing speed, etc. There are many models of executive function; however, for the purposes of this dissertation, the model used will be Miyake et al. [54]. In this model, a confirmatory factor analysis analyzed latent variables and found three aspects of executive functioning, which include working memory (updating), shifting, and inhibition. Working memory, or updating, involves keeping relevant information in the mind while discarding old or no longer important information. Shifting involves the shifting of attention between mental tasks or sets. Finally, inhibition is required to block out prepotent or predominant stimuli, ongoing responses, and maintain interference control. Working memory is thought to be the workspace for other aspects of executive function and its function is to keep relevant items in mind that allows one to shift attention or inhibit distractors appropriately [54].

The ability to localize a sound or attend to an auditory target requires the ability to focus on the stimuli of interest while inhibiting or ignoring the distracting stimuli. Research has shown that in complex listening environments, peripheral auditory and central cognitive factors can influence the ability to locate sounds and segregate speech [55], [56]. In addition, it has been shown that working memory is a predictor of NH adult's ability to segregate speech in noise, even more so than general IQ [57]. Therefore, it may be that children who demonstrate better cognitive abilities may also perform better on difficult tasks of binaural sensitivity.

The investigation of executive function abilities as a whole is also important in this population. It has been shown that executive function abilities may suffer when an individual is stressed or fatigued [58]. As children with cochlear implants have a high amount of listening effort required in any given situation, particularly in the classroom, fatigue may cause a depletion of cognitive resources, thus affecting their ability to hold items in working memory, shift attention, and inhibit outside distractors. Investigating the effect of executive function on results may be important for an understanding of variability in data analysis and for future clinical implications in identifying children at risk for executive function disorders.

In summary, it is unclear which of the above factors contribute most significantly in the gap in performance between NH children and children with BiCIs on spatial hearing tasks. This dissertation will explore the ability of children with NH and children with BICIs to use binaural cues such as ITDs and ILDs. Therefore, the aims of this dissertation are (1) Investigate the extent to which high rate stimuli are the limiting factor in performance by studying the ability of NH children to utilize envelope ITDs as transmitted by stimuli that renders fine structure information for ITDs imperceptible. (2) Examine binaural sensitivity in children with BiCIs to investigate performance with ITDs and ILDs using low-rate pulsatile stimuli on pitch matched pairs of electrodes. (3) Examine the effects of perceived interaural pitch mismatch on a pitch comparison task and a task measuring ITD sensitivity. (4) Examine the effects of stimulus rate on ITD sensitivity. (5) Investigate cognitive factors that may predict performance on tasks of binaural sensitivity. The second and third chapters aim to evaluate and compare binaural sensitivity abilities of children with NH and children with BICIs. The fourth chapter isolates the group with BiCIs and attempts to uncover why children with BiCIs may be demonstrating poor sensitivity to ITDs. Finally, the fifth chapter investigates non-auditory abilities and their relationship to spatial hearing.

As many children with BiCIs demonstrate difficulty on spatial hearing tasks such as sound localization or speech in noise, it is important to understand their abilities to utilize binaural cues important for spatial hearing tasks, and to compare their abilities to NH peers. In addition, understanding why children with BiCIs are having difficulty utilizing the important cues for sound localization, specifically ITDs, will help drive future clinical decisions such as bilateral mapping programs.

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Chapter 2: Binaural hearing in children using Gaussian enveloped and transposed tones (*in press in J. Acoust. Soc. Am., 2016)

Abstract

Children who use bilateral cochlear implants (CIs) show significantly poorer sound localization skills than their normal hearing (NH) peers. This difference has been attributed, in part, to the fact that CIs do not faithfully transmit interaural time differences (ITDs) and interaural level differences (ILDs), which are known to be important cues for sound localization. Interestingly, little is known about binaural sensitivity in NH children, in particular with stimuli that constrain acoustic cues in a manner representative of CI processing. In order to better understand and evaluate binaural hearing in children with bilateral cochlear implants (BiCIs), we first undertook a study on binaural sensitivity in NH children ages 8-10, and in adults. Experiments evaluated sound discrimination and lateralization using ITD and ILD cues, for stimuli with robust envelope cues, but poor representation of temporal fine structure. Stimuli were: spondaic words, Gaussian-enveloped tone pulse trains (100 pulse-per-second), and transposed tones. Results showed that discrimination thresholds in children were adult-like (15-389 µs for ITDs and 0.5-6.0 dB for ILDs). However, lateralization based on the same binaural cues showed higher variability than seen in adults. Results are discussed in the context of factors that that may be responsible for poor representation of binaural cues in bilaterally implanted children.

Introduction

Spatial hearing is essential for the ability of children to navigate their everyday environments, including location of important sound sources (e.g. parents and teachers), and perceptually separating speech from competing sources. Although children spend much of their time having to attend to important sound sources based on their location in the environment, little is known about their sensitivity to spatial hearing cues that are likely to be involved in performing these tasks.

Spatial hearing abilities rest largely on the extent to which the binaural auditory system is able to integrate acoustic inputs that arrive at the two ears from sounds in the auditory environment [1], [2]. Normal hearing (NH) listeners localize sounds in the horizontal plane by relying on variations in interaural differences in time and level (ITDs and ILDs, respectively) as a function of sound source location. ITDs are present in the low frequency region, as well is in the low-frequency envelope of high-frequency carriers. The auditory system has mechanisms that enable binaural processing for both types of ITD stimuli. Sensitivity to ITDs in the envelope of stimuli has been demonstrated in psychophysical studies [3] and in physiological responses of neurons in the auditory brainstem [4]–[7]. Finally, there are spatial cues that do not depend on interaural differences, such as monaural spectral and loudness cues; although for sound localization in the horizontal plane the utility of these cues is relatively weak.

To date, spatial hearing abilities in children have been studied primarily in free-field environments, where all spatial cues are naturally combined, and therefore not independently controlled. Studies on the ability of children to locate sound sources in the free field [8], [9] and on the ability of children to discriminate changes in a sound source location (estimating the minimum audible angle, MAA) [10], [11] have been informative regarding emergence of spatial hearing accuracy and acuity, respectively. By 4-5 years of age, root-mean-square (RMS) errors for sound localization can be as low as 8°**,** similar to that of adults [8], [9], [12]. MAA thresholds for single source (non-reverberant) stimuli undergo substantial maturation in infancy and early childhood, with thresholds estimated to be ~12° at 6-months of age, 4-6° at 18-months of age, and 1-2° (adult-like) by 5 years of age [10]. Thus, assuming that the auditory signal reaches the developing auditory system with fidelity, spatial hearing abilities undergo substantial maturation, and come to approximate those of adults, during early childhood.

A different developmental trajectory appears to be emerging from studies with children who receive cochlear implants (CIs) in both ears, i.e., bilateral CIs (BiCIs). MAA thresholds are better (smaller) when children listen with both CIs (bilateral condition) compared to when they listen with a single CI (unilateral condition) [8], [11]. RMS localization errors are also generally better in the bilateral condition compared with the unilateral condition [8]. However, even when using BiCIs, these children show significantly poorer performance compared to their NH age-matched peers; this gap in performance is observed even after several years of experience with BiCIs [13].

The gap in spatial hearing abilities between NH children and children with BiCIs may be attributed to numerous factors. First, in the BiCI population there may be poor neural survival due to a lack of early acoustic hearing, leading to degraded processing of auditory cues that are important for binaural hearing [14]. Second, surgical issues can lead to different depths in the insertion of electrode arrays in the cochleae in the two ears, thus yielding mismatched place of stimulation across the ears for same-frequency information which has been shown to affect sensitivity to ITDs [15]–[17]. Third, CI processors act as independent systems that do not recognize frequency-specific interaural differences. Fourth, in CI processing the detailed temporal structure of the original sound is replaced with constant-rate pulsatile stimulation [18], [19], but the rate is generally too high to provide reliable ITD cues from the temporal fine structure. For a further review of these issues see Kan and Litovsky [20]. It is not clear which of these factors contribute most significantly to the gap in performance described above. As a first step, the present study was concerned with the extent to which a lack of temporal fine structure ITDs are the limiting factor in performance.

This study focused on the fact that, while short-term ITDs in the fine structure are not available in CI processors, BiCI users might have access to ITDs in the ongoing envelopes of signals [19]. Psychophysical data suggest that adult BiCI users are sensitive to such envelope ITD cues [21], [22]. Therefore, the important question is whether NH children demonstrate the ability to extract ITDs in the envelope. If not, then there may be additional constraints imposed on the ability of pediatric users of BiCIs to perform spatial hearing tasks using the limited cues available to them. To date, research on binaural sensitivity in the BiCI pediatric population has been sparse. There is evidence to suggest that, when stimuli are synchronized via research hardware, children with BiCIs show reliable sensitivity to ILDs, but are much less sensitive in to large ITDs [23]. In contrast, NH children listening to acoustic sounds are able to detect the presence of either ILD or ITD cues [23]. However, in the aforementioned study, when testing NH children CI processing was not simulated, thus it remains unclear whether NH children were relying on fine structure cues, which are not available to CI users.

Here we asked whether NH children are capable of using envelope ITDs as transmitted by CI-like processing. CI simulations have been used to ascertain aspects of speech perception and psychophysics that are affected by some basic elements of CI processing [24], [25]. The present study used simulations that were designed to provide insight into the manner by which a specific aspect of CI processing (i.e. envelope ITDs) might provide access to binaural cues in particular. Two stimuli were selected: transposed tones and Gaussian envelope tone (GET) pulse trains. Both stimuli provide only envelope ITD cues, as temporal fine structure cues are restricted to high-frequency regions, rendering them imperceptible (as they are in CI processing across the entire frequency spectrum). Transposed tones have been used extensively in binaural studies with NH adult listeners [3], [26], [27], but never with children. Typically, transposed tones have been the focus of studies aimed at exploring auditory mechanisms involved in ITD sensitivity that occurs with high-frequency modulated signals [26]. Here, for the transposed tone, a 125 Hz modulation rate was chosen in order to compare to previous literature, which demonstrated that this modulation rate provided the best ITD sensitivity [26]. A GET pulse train [15], [28] is similar to a transposed tone, but can be used to approximate the spread of current that occurs with monopolar stimulation in CIs [29] by varying the bandwidth of the GET. Finally, the spondaic words were also used because they have been used in the past for studies on sound localization in the free field with children due to their ecological validity and ease of obtaining responses from the subjects [8].

In Experiment I, a left-right discrimination task was used to estimate just-noticeable-differences (JNDs) for ITDs and ILDs in children, and results are compared with published data in NH adults [26], [28]. In Experiment II, a lateralization task was used to investigate the ability of NH children to perceive an intra-cranial position of stimuli that had either an ITD or ILD imposed on them. The lateralization task is designed to measure the ability of listeners to map binaural cues to perceptual space, providing more information than acuity-based measurements of cue discrimination. The lateralization task is important for ascertaining spatial mapping, rather than sensitivity to changing cues; this task also provides different information than the free-field localization task, because ITDs and ILDs can be manipulated independently. Together the lateralization and discrimination experiments provide information that benchmarks sensitivity to envelope ITDs in NH children using stimuli that simulate an important aspect of the cues received by BiCI users under ideal listening conditions.

Experiment I: Discrimination of Binaural Cues

A. Methods

1. Subjects and Equipment

Results are presented from 11 NH children (8 years, 7 months to 10 years, 8 months; mean 9.5 years). Data were collected over three two-hour sessions (spread over an average of 10.6 weeks). All subjects had hearing thresholds at or below 20 dB HL in both ears, measured at octave interval frequencies between 250-8,000 Hz. None of the subjects had a known illness or ear infections on the day of testing. In addition to the 11 NH children, for Experiment I, six NH adults were tested on ILD discrimination using the transposed stimuli, as there are no previously published data with these stimuli in adults.

The experiments were performed in a single-walled sound booth (Acoustic Systems; Texas). Stimuli were generated in MATLAB (Mathworks; Massachusetts, USA). A Tucker-

Davis Technologies System 3 (RP2.1, PA5, and HB7; Florida, USA) was used to deliver the stimuli to the ear-insert headphones (ER-2, Etymotic; Illinois). All sounds presented were calibrated to 60 dB-A. ER-2 headphones were used because they could be deeply inserted into the ear canal; therefore bypassing the resonances of the ear canal and outer ear. This is much like what occurs for behind-the-ear microphones of CIs, thus providing a better simulation of CI processing. Additionally, ER-2 headphones have good isolation of external sounds and have a relatively flat frequency response up to 10 kHz.

Subjects were paid $7.50/hour for their participation. All experimental procedures followed the regulations set by the National Institutes of Health and were approved by the University of Wisconsin's Human Subjects Institutional Review Board. Each parent of a child participant signed a consent form. In addition, each child signed an assent form prior to commencing the experiment.

2. Stimuli

Stimuli consisted of two types of acoustic pulse trains, which had two different envelope shapes, shown in Fig. 1. The first was a GET pulse train with a 4 kHz center frequency that was presented at a rate of 100 pps (pulses per second; see Fig. 1a) with a 1.5 mm (~861 Hz) bandwidth [28]. The second was a transposed tone with a 4 kHz carrier tone modulated at a rate of 125 Hz; this essentially shifts the positive temporal envelope of a 125 Hz tone up to the 4 kHz region (Fig. 1b), where the ITDs present in the fine structure should be unusable, leaving only envelope cues [26]. Both stimuli had a 300 ms duration, and were presented at a typical conversation level of 60 dBA. For the ILD condition stimulus levels were randomly varied between 50 and 70 dBA (roved by ± 10 dB) from trial to trial.

ILDs or ITDs were imposed on the stimuli and each cue was tested in separate blocks of trials. In this paper, positive ILDs indicate a higher level (louder) in the right ear and negative ILDs indicate a higher level in the left ear. ILDs were applied by shifting the louder channel up by half of the ILD, and shifting the quieter channel down by the other half of the ILD. Similarly, positive ITDs indicate the right ear was leading and negative ITDs indicate the left ear was leading. Like, ILDs, ITDs were applied by shifting the lead channel earlier by half of the ITD and shifting the lag channel later by the other half of the ITD.

3. Procedure

In this experiment, listeners' ability to determine whether the sound shifted intracranially, from left to right, or from right to left, was measured. Feedback regarding correct/incorrect responses was provided on each trial. Testing was conducted using an adaptive tracking algorithm, and within each run, either ITDs or ILDs were adjusted adaptively using a two-down, one-up procedure. During testing, initial values were 800 μs for ITDs and 15 dB for ILDs. ITDs changed by a factor of 3 for the first two turnarounds, 2 for the next two, and then √2 for the rest of the run. For the ILD condition, ILDs were changed by 2 dB for the first 2 turnarounds, 1 for the next two, and 0.5 for the remainder of the test. The last six turnarounds were averaged and that value was used to estimate the 70.7% JND thresholds [30]. This procedure is consistent with previous literature on experiments conducted on NH listeners [28]. Subjects were first tested with the GET stimuli followed by the transposed stimuli. Testing was done in blocks of trials in which only one cue was varied at a time (i.e., when varying ILD, ITD was set to zero, and vice versa). Order of blocks was randomized within subject.

B. Results

Results from Experiment I are shown in Figs. 2 and 3, for the ILD and ITD data, respectively. In Figs. 2a and 3a, individual JND thresholds are shown, for ILDs and ITDs, respectively. In Figs. 2b and 3b the group average and standard error are shown, for ILDs and ITDs, respectively. Note that JND values shown here have been doubled to reflect methodological differences and simplify comparison with existing literature, where JND thresholds are typically measured with a center reference [26]. All subjects demonstrated measureable JNDs for both ILDs and ITDs, but performance varied amongst the children. Regarding the ILD data, the four best-performing children (left-most in Fig. 2a) showed little or no difference between the transposed and GET stimuli, whereas the remaining children showed low JNDs for the transposed tone and higher JNDs for the GET stimulus. A repeated measures analysis of variance (ANOVA) confirmed that, on average, ILD JNDs were significantly lower for the transposed tone than the GET stimuli [$F(1, 10) = 14.813$, $p=0.003$]. Regarding ITD data, all children but one showed very low JNDs with the GET stimulus, and there was some variation in the transposed tone JNDs. Contrary to the ILD data, a repeated measures ANOVA on ITDs revealed no significant differences between JNDs for the transposed tone and GET stimuli.

In Fig. 4, individual ITD JNDs are plotted with their corresponding ILD JNDs, for the GET and transposed stimuli. A Pearson correlation test confirmed a significant correlation between JNDs in the ILD and ITD tasks for the GET stimuli ($R^2=0.921$, $p < 0.01$); however, no significant correlation was found for the transposed tone ($R^2= 0.174$, $p=0.608$).

Fig. 5 compares results from the present study with previously published results from adult listeners using the same stimuli [26], [28]. Fig. 5a shows data for ITD JNDs and 5b shows the ILD JNDs. One-way ANOVAs were conducted to compare the effect of group (child and adult) for each of the stimuli (transposed or GET). Results revealed no significant differences between adults and children for the ILD or ITD JNDs with either stimulus ($p>0.05$), suggesting that, as a group, children with an average age of 9.5 years have a mature ability to extract ILD and ITD cues from the stimuli used here. However, individual data from Figs. 2-3 do suggest that some of the children's JND thresholds are on the high end of the distribution. Although there were no statistically significant differences between children and adults, it should be noted that there were some methodological differences between the studies, which may affect interpretation of these results. In prior studies in adults, low levels of noise have been typically used to mask low-frequency distortion products that occur in the cochlea with the use of transposed stimuli. Low-frequency distortion products may potentially provide an unintended low-frequency ITD cue [26], [28], [31]. Low-frequency masking noise was not included in these experiments because pilot testing indicated that the introduction of low-frequency masking noise rendered the task difficult and confusing for young children. Thus, we may be over-estimating performance in children, especially for ITD estimates where low-frequency ITD cues are dominant. Another methodological difference between our study and previous work is that Bernstein & Trahiotis [26] used a four-interval, two-cue, two-alternative forced choice task, where the first and fourth interval were diotic and the listener was required to detect an ITD in the 2nd or 3rd interval. In contrast, our task was a two-interval, two alternative forced choice task, where the listener indicated the direction of the second sound relative to the first. This methodological difference may have an effect on measured thresholds because a four-interval task may require a greater memory load compared to a two-interval task. As such, our results may again be over-estimating performance in children.

Experiment II: Lateralization

A. Methods

1. Subjects and Equipment

The same 11 subjects that participated in Experiment I also participated in Experiment II. The same equipment as Experiment I was used.

2. Stimuli

In addition to the two stimuli tested in Experiment I, spondaic words were also used here, in order to draw comparisons to previous free-field data. ILDs (0, ±1.5, ±3, ±6, ±9, and ±15 dB) or ITDs (0, ±50, ±100, ±200, ±400, and ±800μs) were imposed on the stimuli and each cue was tested in separate blocks of trials.

3. Procedure

For this experiment, subjects sat facing a computer monitor that displayed a cartoon image of a head with a red shaded area spanning between the right and left ears, to provide subjects with a visual scale that would enable them to indicate the perceived intracranial location of sound sources. Each trial was initiated by the subject selecting a "start" icon on the monitor. After stimulus presentation, subjects indicated the perceived intracranial position of the sound source by using the computer mouse to move a visual pointer to a selected position inside the red shaded area of the head. This method was selected for data collection after extensive pilot testing showed that both adult and child listeners were able to follow the instructions and to reliably use the pointer method to indicate perceived intracranial positions. Similar approaches were taken in recent studies [15], [32]. Responses were coded using an arbitrary scale from -10 (at the left ear) to +10 (at the right ear), with 0 being at the center of the head. This scale was linearly transformed for analysis (described below). Subjects were allowed to repeat sound presentation on each trial as many times as they wished, although the majority of subjects selected their response after a single presentation.

Before testing began, each subject underwent a familiarization procedure for approximately 30 minutes, so that they were comfortable using the testing interface and reporting the perceived intracranial position of stimuli on the computer. Once familiarization was completed, subjects were tested with 10 repetitions for each level of each binaural cue, for the three stimulus types. Cue levels were randomized within blocks of cue type and stimulus type. In addition, although every participant began with spondees, both cue and the remaining two stimulus types were randomized among listeners.

B. Analysis

Psychometric functions relating perceived intra-cranial position to ILD or ITD values were modeled using the R software [33] with a non-linear least squares (NLS) curve fitting procedure using the Levenberg-Marquardt algorithm available in the ‘minpack.lm’ package. A standard four-parameter logistic function was used, scaled to the input and output levels for each cue type. The form of the function was as follows:

$$Position = \frac{Range}{1+e^{(-Slope \times ILD\, +\, Shift)}} + Floor - 10$$

“*Position*” refers to the intracranial location response of the participant. “Range” refers to the space between the upper and lower ends of the range of lateralization responses, which was roughly 20 (-10 to +10). "*Floor*" refers to the lower end of this range, (which was typically -10). "*Shift*" refers to the overall bias in responses, which might occur if listeners shifted all responses uniformly to the left or right; in general, no listener demonstrated such behavior. "*ILD*" refers to the ILD applied to the stimuli (or ITD, as appropriate). ILDs were varied within the range of -15 to +15 dB and ITDs were between -800 to +800 µs. The formula used the standard logistic function, including the natural *e* exponential as a growth curve from min to max. The value of the slope is an index of the listeners' perceptual mapping of the cues to the response range, and refers to the natural log change in output value (lateralization response between -10 and 10) resulting from a change in input level by one unit (either one microsecond ITD or one decibel ILD). The -10 on the right-hand side of the equation translates the predicted values between 0 and 20 back to the results scale between -10 to +10. All four terms of the model were free to vary across individuals; this flexible modeling approach proved to provide much better fits than an approach with fixed terms for the minimum or maximum asymptotes.

F. Results

Data from Experiment II are plotted in Fig. 6, showing individual subjects' average intracranial locations as a function of ILD (6a) and ITD (6b). Within each column (subject), results are compared for the three stimulus conditions (GET pulse train, transposed tones and spondees). Children's performance in the lateralization task was highly variable, akin to performance in the discrimination task described above. Some children had patterns of responses that were more categorical in nature and lateralized sounds mainly to the right or left (i.e. subject CNB), while others used the entire range, showing smaller changes for each ITD/ILD (i.e. subject CQV).

A repeated measures one-way ANOVA was conducted to compare the effects of stimuli (spondees, transposed tones, and GET) on subject’s slope, revealing no significant differences between stimulus type for ILD cues. In addition, when running a linear model instead of an ANOVA for ILD cues, no comparisons reached significance, even when a random effect of listener was used (i.e. to produce a mixed-effects model). A repeated measures one-way ANOVA for ITD cues revealed no significant main effects. However, a linear model suggested marginally smaller slope values obtained from the GET and transposed tone stimuli compared to the spondees. GET stimuli were subsequently chosen as the default stimuli for the linear mixed model because they yielded psychometric functions that were intermediate to the other two conditions and could therefore be used to test significant differences in either direction. A linear mixed-effects model was created, using a random effect of listener in addition to the stimulus-type predictor. P-values were estimated using the z-distribution as a substitute for the t-distribution; using that approach, the spondee slope values were found to be significantly smaller in magnitude compared to the default (GET) stimulus type ($p < 0.05$), but slopes for transposed tones were not found to be significantly different from those for GET stimuli. These general trends can be seen in Fig. 7 for both ILDs (7a) and ITDs (7b), where average slopes are compared. Comparison of the three stimuli for ILD revealed no significant differences and although the ITD spondees were significantly different from the GET and transposed stimuli, this only occurred with a linear effects model. This suggests a weak effect of stimulus type on slope.

Data collected from 10 adults using GET stimuli (replotted, with permission, from the condition without low-frequency masking noise in Goupell et al. [28] are also included in Fig. 7 for comparison (far right panels). Data for ILD (7a) and ITD (7b) stimuli were analyzed using the same NLS curve-fitting model that was used for the children's data. Between-subjects one-way ANOVAs revealed no significant differences between the slopes of the data from children and adults for ILDs [*F*(1, 18)=0.622, p=0.440] or ITDs [*F*(1, 18)=0.496, p=0.490]. One note regarding the range of ILD cues: the adults were only tested on ILDs as large as 9 dB, however, when testing children the ILD range was extended to 15 dB, as some of the children required a larger value in order to perceptually lateralize the stimuli to the most extreme locations (near the ears). The data were thus also analyzed to compare children and adult lateralization functions with the restricted ILD range (up to 9dB only for both groups). A between-subjects one way ANOVA revealed no statistically significant differences [F(1, 18)=0.826, p=0.375] between children and adults. In summary, children were tested using three stimuli, and results from the GET stimuli were compared with those from adults published earlier. Overall, findings suggest that by age 8-10 years, the ability of NH children to lateralize sounds using ILDs or ITDs is not different than observations reported in adults.

General Discussion

These experiments were motivated by the fact that children with BiCIs show significantly worse sound localization skills than their NH peers, but there is no clear understanding of what contributes to this deficit. In two experiments, we investigated binaural sensitivity in NH children in order to begin understanding the factors that contribute to limitations observed in the pediatric BiCI population. We used acoustic stimuli that were (1) same as those used in free field studies with BiCI users (spondees); or (2) required listeners to rely on the ITD information present in the envelope (transposed and GET) which is similar to the manner in which CI processing disregards fine structure information. This study is also the first to systematically test discrimination and lateralization abilities of ITDs and ILDs in NH children; it thus contributes to our knowledge about the sensitivity of the binaural system in children in this age range.

In experiment I, common methods for assessing binaural sensitivity were used to measure JNDs. For both the GET and transposed stimuli, children demonstrated JNDs that may be comparable to those obtained in NH adult subjects, suggesting that in a discrimination paradigm, NH children demonstrate sensitivity to ITD and ILD cues by age 8-10. Notably, this occurs even when using stimuli that require use of envelope ITDs, when the fine structure ITD cues are presented in a frequency range known to be too high to be reliable. This approach simulates aspects of CI processing and current findings will thus be a useful benchmark for research with children who have CIs. Interestingly, there was an effect of stimulus type on performance with the ILD cues for 7 of 11 children. Note that the four children with lowest thresholds did not show a difference in performance based on stimulus type; however, the differences seen in the other seven children suggest that it may have been easier to extract ILD cues from the transposed stimuli than from the GET stimuli. The reason for this difference is not obvious. Prior work in adults shows better performance with transposed vs. sinusoid amplitude modulated (SAM) tones [26]; however, that difference was only reported for ITD cues, as opposed to the difference seen here which is with ILD cues. We speculate that the wider bandwidth of the transposed tone compared to the GET may be providing a wider-band signal for an interaural level comparison. However, because so little is known about ILD sensitivity with any of these stimuli, further research is required. In particular, because CIs transmit ILDs better than ITDs [18], [34], [35] children with CIs may show better ILD than ITD sensitivity, in which case future research should explore the importance of envelope shape for ILD sensitivity. Another possibility is that the difference between GET and transposed for ILD stimuli was due to an order effect because GET was always tested before the transposed tone stimuli. However, this is unlikely because the effect was found only in the ILD but not the ITD condition. If this was an order effect, performance should have been poorer for both ITDs and ILDs with the GET stimuli.

Experiment II further investigated usability of binaural cues for perceptual mapping of auditory space to a range of intracranial positions. Data showed that children ages 8-10 can map ITD and ILD cues to perceived intracranial position in a manner consistent with adult performance, regardless of the stimulus type. To our knowledge, there is prior literature on the ability of children to locate sounds from a select known set of stimulus locations, but there is no previous literature on the ability of children to perceptually map lateralized images on a continuous scale. The lateralization task is unique because it does not restrict responses to a predetermined set of options; rather subjects use a continuous scale to report perceived locations in the head. Experiment II also differs from prior work because the task was specifically designed to test the ability of children to utilize a single binaural cue at a time (ITD or ILD). This differs from free-field stimulus presentation, whereby spatial cues can potentially include not only ITDs and ILDs, but also monaural head shadow and spectral cues.

Although the statistical tests revealed no differences between groups, there was notable variability in performance for the children on both tasks used here. As has been noted in prior literature, psychophysical tasks may require the use of non-sensory abilities and selective attention, which are undergoing continued maturation throughout childhood beyond 8-10 years [10], [36]–[38]. These non-auditory factors may be underlying the variability in performance seen in both experiments. In particular, the variability is greater for lateralization (Experiment

II), which requires a listener to perceptually map auditory cues to intracranial position. This may be more challenging for listeners because unlike discrimination, there is no perceptual reference to make a judgement as it is a one-interval task. In addition, this task required that children be able to translate continuously varying cues into a response system to which they are not accustomed. Several hours of testing may not have been sufficient to maximize their performance on the task. Future work involving auditory training for many more hours may reveal that lateralization abilities can improve with training. To date, work on training of auditory cues has focused on improved performance measured with discrimination tasks, similar to that used in Experiment I [39]. The notion of training may also be applicable to children with BiCIs, who might benefit from feedback-driven experiences with spatial cues. Finally, other unknown factors that may contribute to the variability include top-down processes that depend on more mature executive function and working memory [37].

In sum, the motivation behind this study was to help us better understand why children with BiCIs might perform more poorly on spatial hearing tasks than their NH peers. It is reasonable to presume that in BiCI users, a great limitation in use of ITDs is lack of temporal fine structure cues in the signal, as discussed above, which renders use of ITDs difficult or impossible to perceive. In the present study, NH children performed similarly to adults with NH when tested using stimuli that have the fine structure ITD cue deliberately neutralized. Therefore, the conclusion is that the deficits in BiCI localization for stimuli comparable to those used in this study are likely due to other factors besides the lack of fine structure ITDs. For example, the children may suffer from lack of exposure to fine structure ITDs during development, or degradation of neural substrates that mediate binaural sensitivity. Another factor is binaural frequency mismatch, which has been shown to limit binaural sensitivity in both NH adults and adults who use BiCIs [15], [16], [28]. These factors and others are discussed in greater detail elsewhere [20]. The impact of these factors on spatial hearing acuity is not well understood even in adults, and further research is needed in order to better understand the cause of the performance gap between NH and BiCI children.

V. Summary and Conclusions

Two experiments were conducted in children with normal hearing, measuring binaural discrimination and lateralization. The following conclusions were made:

1. On discrimination tasks, children might show ITD and ILD sensitivity comparable to adults, even with stimuli that rendered fine structure ITDs unusable.

2. Performance on tasks of binaural sensitivity is variable at this age. However, performance on tasks with ILDs was correlated with performance on tasks requiring use of ITDs, suggesting that ILD and ITD sensitivity may be linked in terms of binaural sensitivity for NH children.

3. Future research on children with BiCIs could reveal factors other than binaural sensitivity, such as neural degradation or interaural frequency mismatch that may be responsible for poor binaural performance with BiCIs.

4. This work serves as a starting point towards improving our understanding of the auditory cues that children might need to utilize to localize sounds, which should promote better listening in complex environments such as classrooms and playgrounds.

Figures

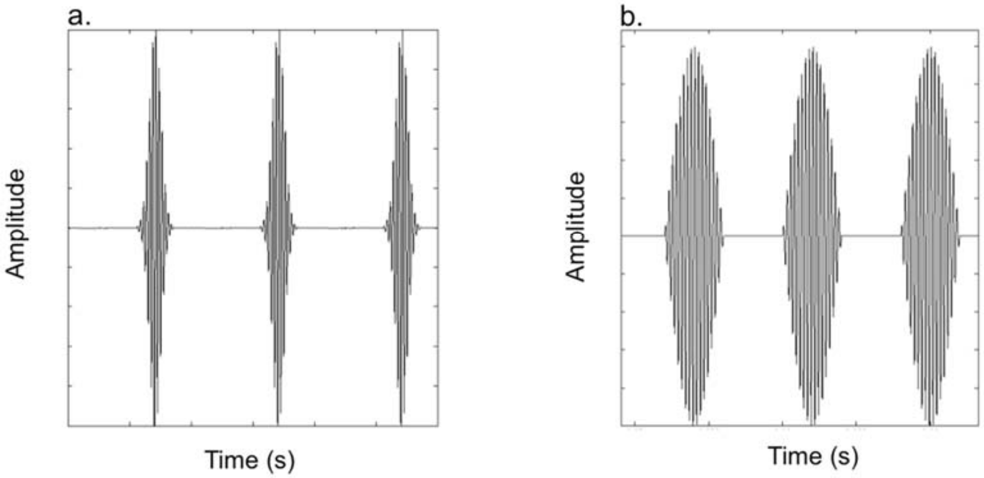

FIG 1. Waveforms for the two stimuli selected to simulate CI processing: (a) a Gaussian-enveloped tone pulse train, demonstrating the bell-shaped curve, which causes greater spread of excitation in the cochlea and (b) a transposed tone, which shows the low-frequency envelope (125 Hz) imposed on a high frequency carrier (4kHz).

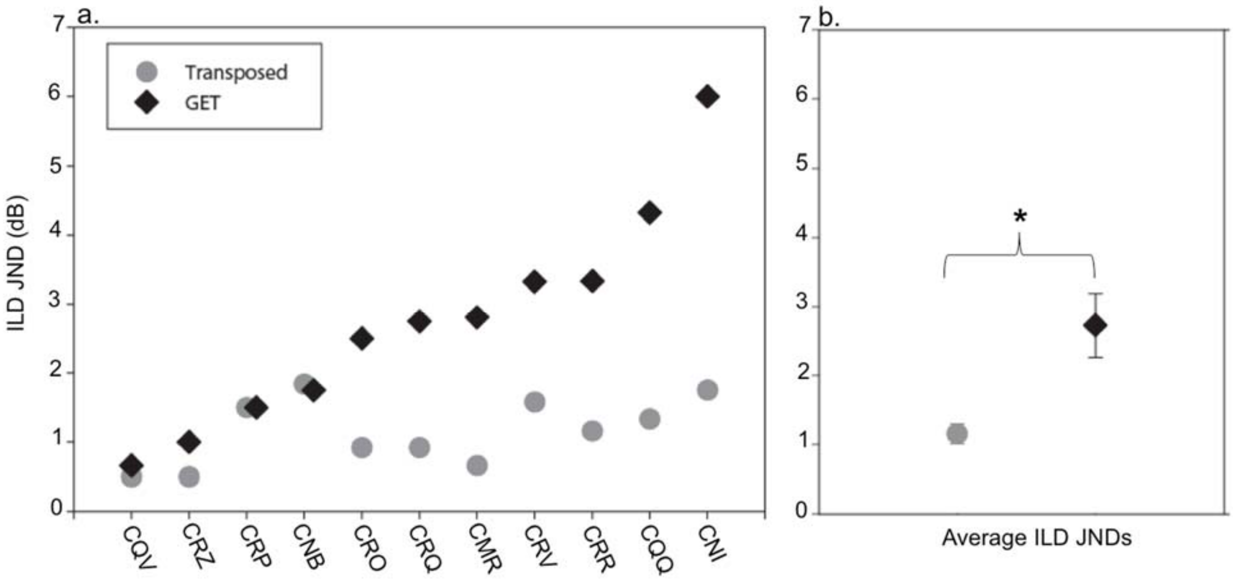

FIG 2. ILD JND data are shown for the GET (diamond) and transposed stimuli (circle). Panel (a): individual ILD JND values. Panel (b): average (+/- standard error). Significant differences are indicated with an asterisk (*).

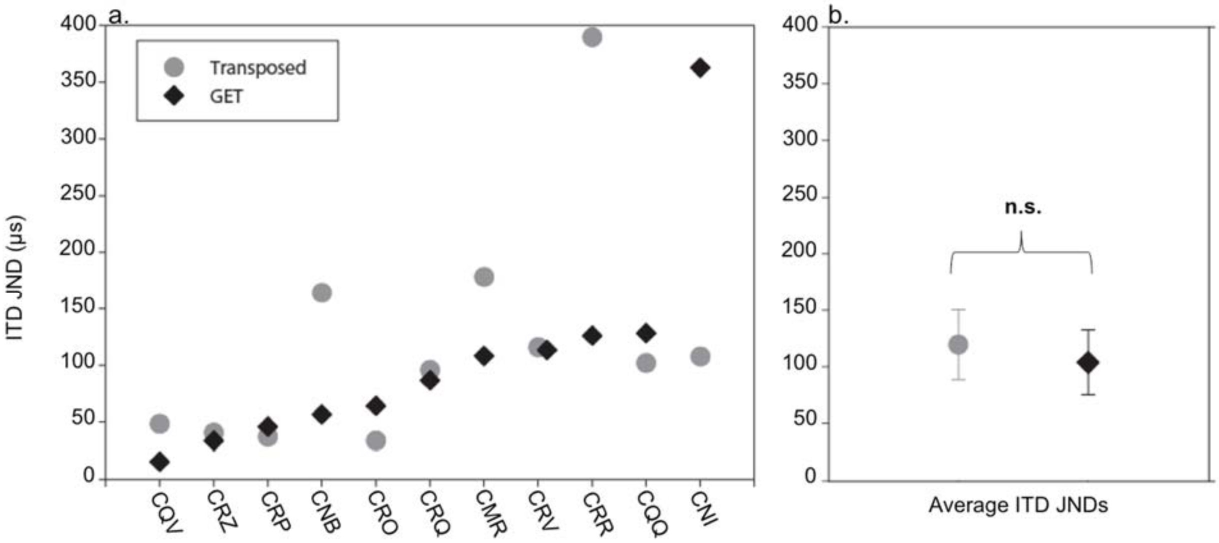

FIG 3. ITD JND values are shown for the GET and transposed stimuli, in the same arrangement as shown in Fig. 2.

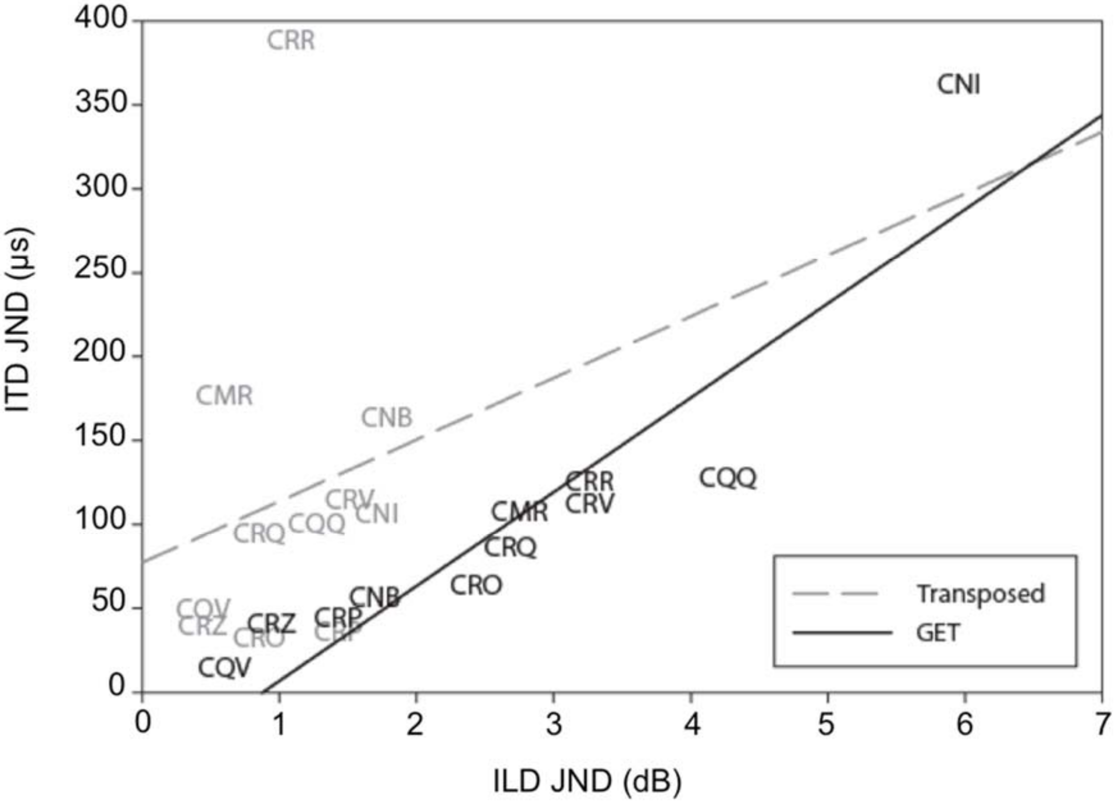

FIG 4. ITD JND values are plotted as a function of ILD JNDs for individual subjects.

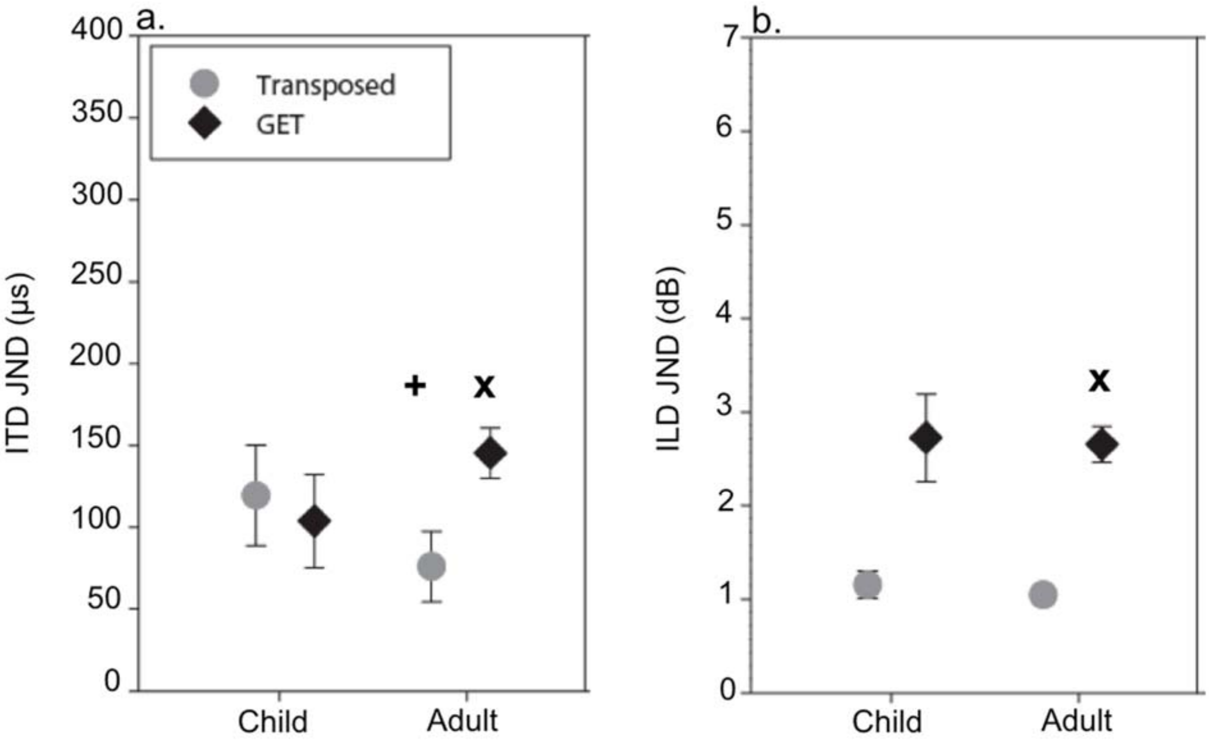

FIG 5. Average (+/- standard error) ILD JNDs (a), and ITD JNDs (b) are shown for the transposed tones and GET stimuli, for children and adults. In addition, comparisons are made with data that were previously published in adult listeners (x depicts data replotted with permission from Goupell et al, 2013; + depicts data replotted with permission from Bernstein & Trahiotis, 2002).

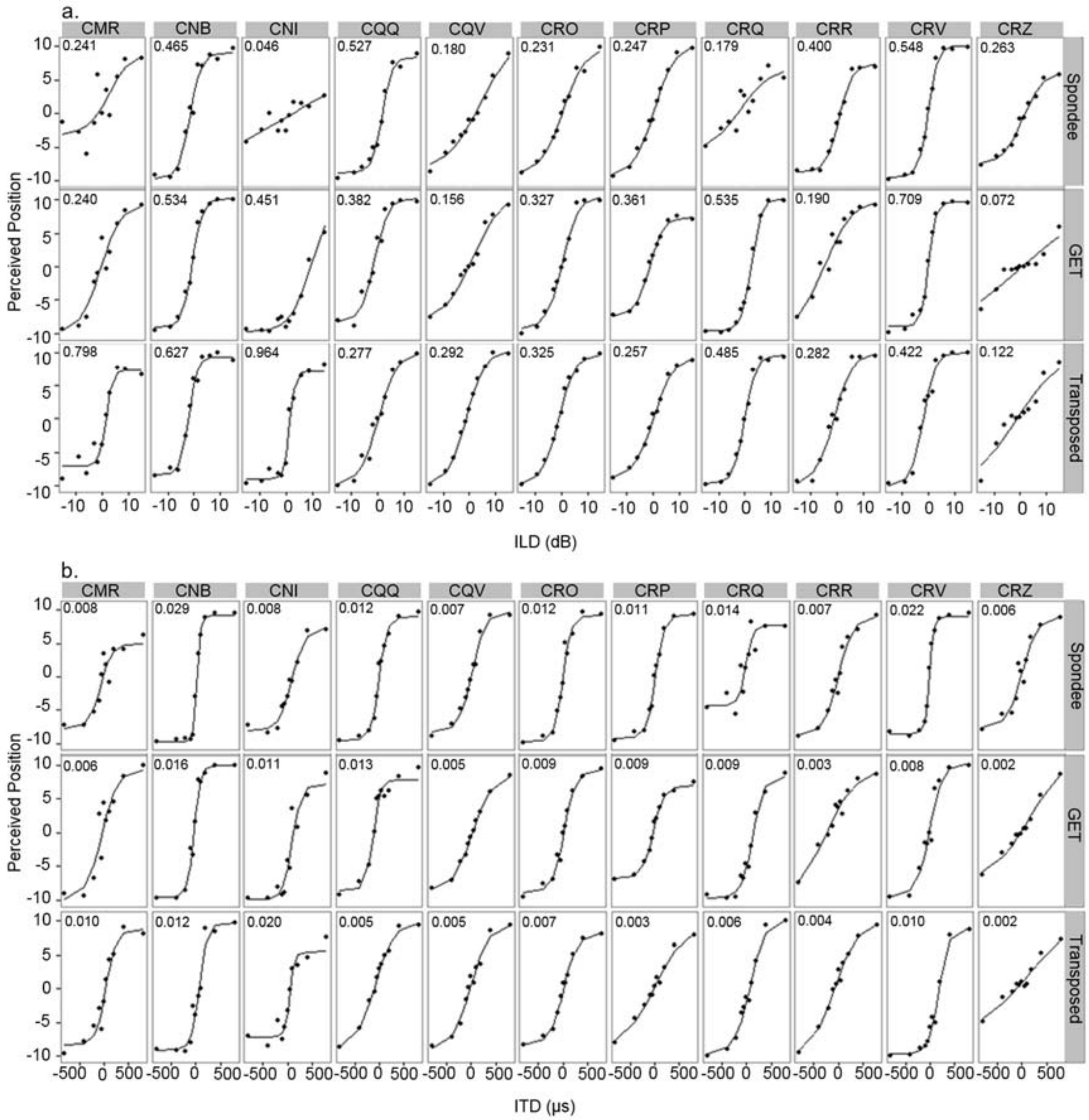

FIG 6. Individual data from the lateralization task are shown. In each panel, data from a single listener showing the average perceived intracranial position as a function of ILD (a) or ITD (b). In (a) and (b), panels are arranged in rows according to the three stimuli that were tested (GET, spondee, transposed), with subjects in each column. Slope values are inserted in the top left corner of each panel.

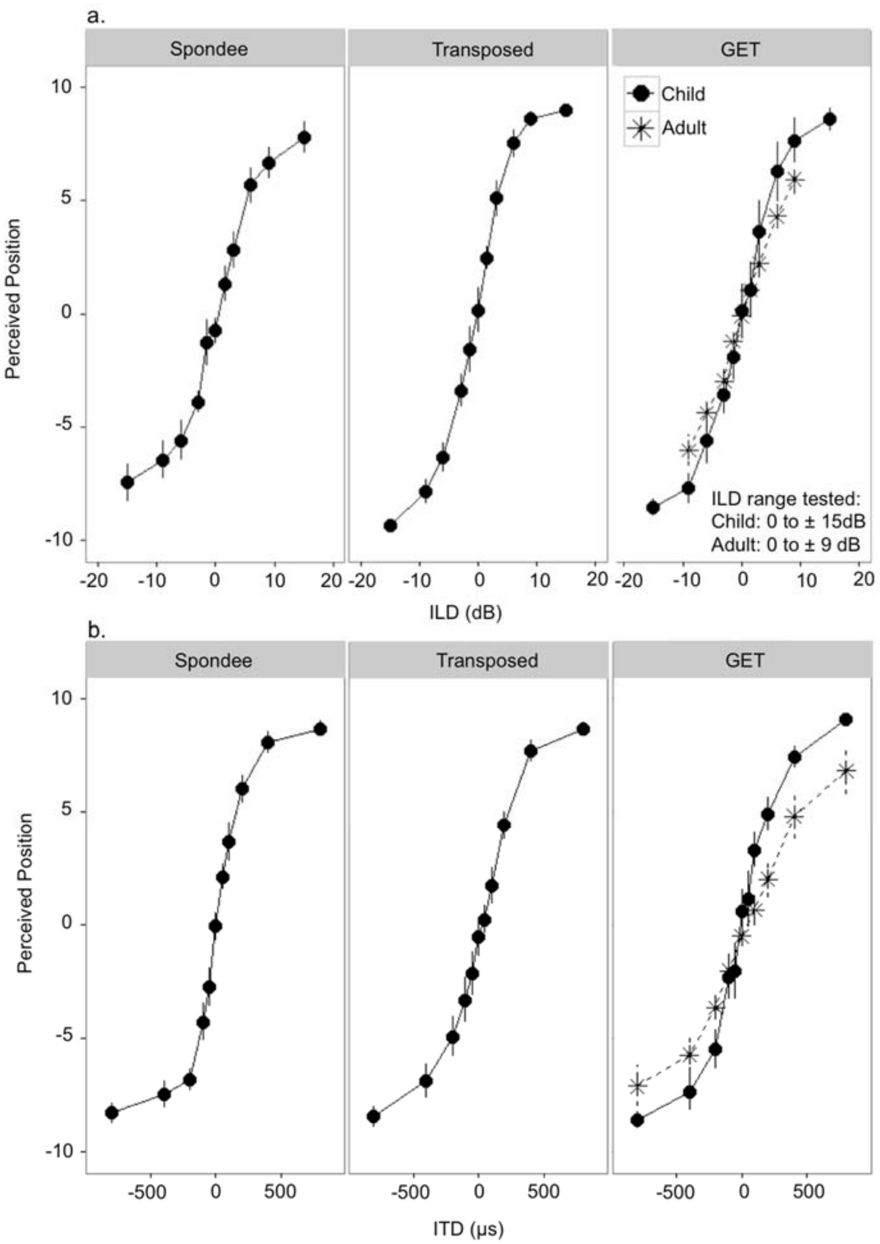

FIG 7. Average lateralization data are summarized for the ILD (a) and ITD (b) tasks. Included in the right-most panel are data from NH adults and replotted with permission from Goupell et al, 2013.

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Chapter 3: Binaural sensitivity in children who use bilateral cochlear implants

Abstract

Children who are deaf and receive bilateral cochlear implants (BiCIs) perform better on spatial hearing tasks with bilateral implants than unilateral devices. Nevertheless, they underperform relative to normal hearing (NH) peers. There are many factors as to why this gap in performance occurs, including the inability of speech processors to deliver binaural cues reliably. However, although much is known regarding binaural sensitivity of adults with BiCIs, currently little is known regarding the development of binaural hearing in children with BiCIs. Here, 16 children ages 9-17 were tested using synchronized research processors. Interaural time and level differences (ITDs and ILDs) were presented to pairs of pitch-matched electrodes. Stimuli were 300-ms, 100 pulses per second, constant amplitude pulse trains. On a discrimination task, sensitivity to sounds presented right-left vs. left-right was measured. On a lateralization task, subjects reported the perceived intra-cranial position of the stimuli. Results from both tasks showed that although all children demonstrated sensitivity to ILDs, the majority of children with BiCIs have weak or absent sensitivity to ITDs. The lack of ITD sensitivity in pre-lingually deafened children who use BiCIs may be due to the lack of access to reliable ITD information through the speech processors of the CIs. Sensitivity to ILDs may occur because ILDs are presented through the processors in everyday listening. Of the small number of children who did show ITD sensitivity, most had exposure to acoustic hearing early in life. Therefore, it may be that factors such auditory deprivation and binaural maturation are responsible for the lack of ITD sensitivity in children with BiCIs.

Introduction

Humans rely on binaural cues to localize sounds, and to segregate speech from interfering sounds in the environment. Normal hearing (NH) individuals enjoy the benefits of binaural processing, which utilizes interaural timing differences (ITDs) and interaural level differences (ILDs) to accomplish spatial hearing tasks in everyday listening environments [1]–[3]. ITD information is also useable when a slow modulation is imposed on a high frequency carrier [4]. Recent work in NH children suggests that by 8 years of age, discrimination thresholds for ITDs in the envelope are similar to those of adults [5]. In fact, children with NH show fairly well developed sound localization ability by age 4-5 years, and some children show adult-like localization performance, with root-mean-square (RMS) errors as low as 8° [6]–[8].

In contrast, children of the same age who are deaf and are fitted with bilateral cochlear implants (BiCIs) perform significantly worse on spatial hearing tasks than their NH peers [6]–[8], even after several years of experience with BiCIs [7]. That is not to say that children with BiCIs do not receive benefits from the access to sound in both ears; there is ample evidence to suggest that they perform better while using two CIs than while listening through a single CI [6], [9]. However, the gap in performance between children with BiCIs and with NH has implications for the ability of these children to function in complex noisy environments, such as classrooms, and many other everyday listening situations.

The reason for poorer performance in individuals with BiCIs compared with NH peers has been a topic of considerable interest in recent years [10]–[14]. One known limitation is the inability of today's CIs to deliver binaural cues with fidelity [14]–[16]. There are many reasons for this. First, due in part to the lack of coordinated inputs to the electrode arrays in the two ears. Second, cochlear implant speech processors discard temporal fine structure, which is an important cue for ITD processing. Third, spread of excitation along the cochlear arrays due to monopolar stimulation is likely to result in stimulation of more than one channel, which presents a non-ideal stimulation mode for maximizing presentation of ITDs at specific locations along the cochlear arrays [13], [14]. Other limitations include the fact that today's clinical programming approaches present information at the same frequency range to electrodes that have the same numbers in the right and left ears, regardless of specific anatomical locations. This approach has the potential to cause inputs between the two ears that are not matched by frequency [12], [14]. Finally, beyond the cochlea, auditory deprivation resulting in loss of neural function, both peripherally and centrally, may lead to degraded abilities to use binaural inputs [17], [18].

In the event that CI speech processors were able to deliver binaural cues to BiCI users, little is known about the usability of these cues, because binaural sensitivity in children with BiCIs is poorly understood. In contrast, studies on adults with BiCIs have been conducted for decades using research processors that carefully control which electrodes are stimulated, and to deliver synchronized binaural stimulation to selected pairs of electrodes in the right and left cochlear arrays. Studies have shown that there is great variability in the sensitivity of adult BiCI users to binaural cues, but in particular to ITDs [12], [19]–[22]. The factors that account for the variability are not well understood, but one likely candidate is the age at onset of deafness. Adults with early onset of deafness generally have weak or absent ITD sensitivity whereas adults with auditory experience prior to onset of deafness can have excellent ITD sensitivity, even if they experience may years of auditory deprivation between the time of onset of deafness and time of implantation [13], [19], [23]. Unlike the dependence of ITDs on experience, adult BiCI users generally have excellent sensitivity to ILD cues [14], [19].

While there is much to learn from studies conducted in adults, it is unclear whether knowledge about adults is sufficient for understanding binaural mechanisms in children. This issue is particularly important, because children are likely to have different auditory histories and periods of auditory deprivation than adults. Because many children who are fitted with BiCIs are congenitally deaf, and have never been exposed to non-distorted binaural acoustic cues, there is an open question regarding their capacity to process binaural cues. Conversely, it is unclear whether children who are born hearing and lose their hearing during childhood will demonstrate binaural sensitivity if provided with the appropriate cues.

A small number of studies to date using synchronized research processors with children who use BiCIs have focused on presenting stimuli to a single pair of electrodes. Gordon and colleagues reported that sensitivity to ILDs is good while ITD sensitivity is poor [11], [24]. Other studies using research processors have focused on the ability of children to use interaural decorrelation cues to hear tones in noise [25], [26]. This binaural unmasking paradigm most likely explores abilities related to hearing speech in noise and is measuring the ability to detect changes in interaural correlation or fluctuating ILDs, but is not revealing about the use of ITDs. In fact, it was recently shown that children could have binaural unmasking even if their ITD sensitivity is poor [26].

The present study evaluated binaural sensitivity in children with BiCIs in two experiments, using low-rate pulsatile stimulation delivered to the electrode arrays through synchronized research processors. In Experiments I and II, children performed a left-right discrimination task so that just-noticeable-difference (JND) thresholds could be estimated for ITDs and ILDs. In Experiment III, the perceived intracranial location of sound sources was measured using a lateralization task, which offers a more direct estimate regarding the contribution of binaural cues to spatial mapping abilities. Overall, the purpose of this work was to understand whether children who are deaf and use unsynchronized bilateral processors in everyday situations could use ITD and/or ILD cues on acute psychophysical tasks when binaural cues are controlled. The study was also aimed at extending the work done in adults to continue understanding whether neural mechanisms mediating ITDs are less resistant to neural degeneration caused by auditory deprivation than mechanisms that mediate ILD processing.

II. General Methods

A. Subjects

Sixteen children who were profoundly deaf and use BiCIs participated in two experiments. Table I shows the profiles for each subject. All children wore Cochlear Ltd. devices that were either from the CI24 or CI512 family of implants. These internal devices have an electrode array of 22 intra-cochlear stimulation electrodes and two extra cochlear ground electrodes. The electrodes are numbered from the basal end to the apical end, or 1-22 respectively.

Participants traveled to Madison, WI with a legal guardian and testing was conducted at the Waisman Center on the University of Wisconsin-Madison campus. Travel costs were covered and a stipend was provided. To complete the battery of tests, participants were typically in Madison, WI for 2-3 days. All experiments conducted followed regulations created by the National Institute of Health and were also overseen by the University of Wisconsin's Human Subjects Institutional Review Board.

B. Experimental Set up:

The experiments were controlled by a laptop computer using MATLAB (MATHWORKS, Natick, MA). A Nucleus Implant Communicator (NIC; Cochlear Ltd., Sydney, Australia) was used to deliver all stimuli to each subject's own internal devices. Subjects provided all responses by interfacing with a touch screen computer monitor that was connected to the laptop.

C. Stimuli:

Bilaterally synchronized, electric pulse trains were used. The pulses were biphasic, with a 25 µs phase duration, and had an 8 µs phase gap, which is consistent with current clinical CI programming. The pulse trains were constant amplitude, 300 ms, and were presented at a rate of 100 pulses per second (pps). The rate of stimulation was lower than typical clinical CI stimulation in this study in order to maximize sensitivity to ITDs, which are better at low stimulation rates [20]. This stimulation rate is also consistent with previous research completed with adults [12], [19].

D. Implant Mapping

Subjects' clinical MAPs were provided by their audiologist through direct request from the children's parents. These MAPs were used as a starting point for setting stimulation levels during the experiments. Three stimulation levels were carefully determined for all even-numbered electrodes in both ears: Threshold (T, the lowest level of audibility), Comfortable (C, a level that was comfortable enough for a patient to tolerate listening to for an extended period of time), and Maximum Comfortable (M, the highest amount of current that a subject could accept briefly without the stimulation being uncomfortably loud).

Once these loudness levels were determined, C levels were loudness-balanced within each ear, and then across ears (the procedure for loudness balancing across ears is described below). For within-ear balancing, subjects were presented with series of five-electrode sets at a time and asked to judge the relative loudness, in particular focusing on any electrodes that were judged to be “soft” or “loud” relative to the others in the series. Adjustments were manually made, until all C levels within each group of 5 were perceived as having “equal loudness.” The procedure was iterated within each ear, until all 11 electrodes were tested, and a final sweep across all 11 electrodes was made in order to ensure balanced loudness. This approach is consistent with methods used in previous studies with adults [12], [19].

E. Selection of electrode pairs

Numerous studies to date have assumed that in order to maximize binaural sensitivity, stimulation should be provided to pairs of electrodes in the two ears that are perceived to be matched by pitch, i.e., to stimulate populations of neurons that are tuned to the same frequency [12], [13], [15], [19], [27]. In fact, there is evidence to suggest that mismatched pairs of electrodes result in reduced ITD sensitivity [12], [28]. Thus, here too, effort was made to use pitch-matched electrodes, and two tasks were employed. The first task was aimed at having subjects assign a value to the perceived pitch, also known as pitch magnitude estimation [12], [19]. While stimulation was presented at the subject’s self-reported comfortable level, the task was to provide a value that represents the perceived pitch of the stimulus, on an arbitrary scale ranging from 1 (low pitch) to 100 (high pitch). The stimuli were presented in random order to the 22 electrodes (11 in each ear) and repeated 10 times at each electrode. Prior to initiation of the task, subjects were familiarized with task of assigning a value to the perceived pitch of a stimulus, via verbal discussion and practice, as well as encouragement to use the full scale from 1-100 when subjectively judging the pitch.

The second task involved a direct comparison of perceived pitch between select pairs of electrodes in the two ears. Based on the rankings in the pitch magnitude estimation task, electrodes in the right and left ear that had similar rankings were selected. Of those two electrodes, the one in the left ear was held constant, and compared to five electrodes in the right ear, including the matched electrode, as well as two electrodes more basal and two electrodes more apical. The direct pitch comparison task was conducted using a two interval, five-alternative forced choice task. The subject was asked to directly compare the pitch of the electrode in the left ear, with each of the electrodes in the right ear and to determine if the pitch in the right relative to the left was: “much higher”, “higher”, “same”, “lower”, or “much lower”. Twenty repetitions were completed per electrode pair. Pitch-matched electrode pairs chosen for testing with binaural stimuli are shown for each subject in table II.

F. Loudness Balance

In order to elicit an auditory image that is perceived to be centered in the head, a task aimed at loudness balancing across ears was performed. In this task the amplitude in the left electrode was held constant, while the amplitude in the right was varied. Subjects were able to control the stimulation level of the right electrode themselves, increasing or decreasing the level until the stimulation in the right and left electrodes was judged to be of equal loudness.

Experiment I and II: Discrimination

A. Methods

In Experiments I and II, ITD and ILD sensitivity were measured for each subject. In Experiment I, discrimination was measured at an electrode pair that was in the middle of the electrode arrays, for both ITD (N=10) and ILD (N=8). Subsequently, Experiment II served as a follow-up study in which performance was measured on three electrode pairs, located at the basal, medial and apical regions of the electrode arrays. An exception to this is subject CIAY, who was not tested with an electrode pair located at the base due to visit time constraints. Four subjects completed both Experiments I and II. Some subjects in Experiment II were not tested on both ITDs and ILDs due to time constraints, hence the slightly different N sizes.

Testing was conducted in blocks of trials where either an ITD or ILD was imposed on the pulsatile stimulation. ITDs were applied by delaying the stimulation in the ear contralateral to the intended direction of the sound. ILDs were applied by reducing the stimulation level at the contralateral ear relative to the direction of the sound. Subjects participated in a left-right discrimination task using a two-interval, two-alternative forced choice. In the first interval, the cue favored one ear, and in the second interval the cue favored the opposite ear (left-right followed by right-left, or vice versa). Subjects responded by indicating the direction of the sound in the second interval when compared to the first. When testing ITDs, ILD values were set to 0, and vice versa when testing ILDs. Typical ITD values were ±100, ±200, ±400, and ±800 μs. Typical ILD values were ±2, ±5, ±10, ±20 current units (CUs). However, these values varied for some subjects depending on their sensitivity to these cues. Subjects were tested on 40 trials (20 repetitions right-left and 20 repetitions left-right) per cue per condition. All subjects were tested with ITD cues; due to time constraints, subjects CIDX, CIAG, and CIDQ were only tested with the ITD cues, but not with the ILD cues. Percent correct data were fit to a psychometric function and just-noticeable-difference (JND) thresholds were calculated at the point on the psychometric function intersecting with 70.7% correct [29].

B. Analysis

One of the questions that arises regarding binaural sensitivity in children with BiCIs is whether they perform similarly to, or significantly worse than their peers with NH. Data from the current study were compared to NH children tested on the same task [5]. It is worth nothing that there is currently no feasible way to directly compare electric CUs to acoustic dB. However, for the purposes of comparison, expressing ILD JNDs as a percentage of dynamic range (DR) between NH children and children with BiCIs can be informative. This approach shares some characteristics with a previous study that compared ILD lateralization ranges between NH and BiCI adults [30]. For the current study, the DR for NH listeners was estimated to be 65 dB SPL based on the loudness growth function in NH adults for a 4kHz tone [31], which was the carrier frequency for the pulse train presented to NH children in Ehlers et al [5]. Research has shown that children and adults show similar loudness growth functions [32]. For subjects with BiCIs, the DR was estimated as:

$$DR = \min\{ [C_R - T_R + M_L - C_L] , [C_L - T_L + M_R - C_R] \}$$

where C, T and M are the comfortable, threshold and maximum comfortable levels, respectively, and the subscripts R and L denote the right and left ears, respectively. As there are two dynamic ranges that may differ between the ears, the smaller of the two was chosen in order to be conservative. ILD JNDs were then calculated as a percentage of DR for both NH subjects [5] and subjects with BiCIs. For example, if a NH subject had an ILD JND of 5 dB, this would utilize 8.3% of their DR. If a subject with BiCIs had an across ear DR of 50 and an ILD JND of 5 CUs, this would utilize 10% of their DR.

C. Results

Figures 1 and 2 show individual data from Experiment I and II, for ILDs and ITDs, respectively. Individual and average ILD and ITD JNDs from Experiments I and II are shown in Figures 1a and 2a, and Figures 1b and 2b, respectively. Subjects whose code is highlighted in bold completed both experiments. Results show that all subjects had measureable JNDs for ILDs at all tested electrode pairs, but performance varied in a number of ways. First, one subject

(CIEH) had extremely high ILD JNDs. Second, four subjects had ILD JNDs that did not vary much across electrode pair location (CIAP, CIEH, CIAQ, CIDJ). Finally, the remaining subjects showed larger variability in JND with electrode pair location. Similar variability in binaural JNDs across electrode pair locations has been found in adults [21], [33] and the implications are discussed in more detail below.

A different pattern emerged for ITD discrimination. Of the ten subjects tested in Experiment I where only the middle of the electrode array was tested, three had measureable JNDs (Fig. 2a). In Experiment II when subjects were tested at three locations along the electrode arrays, six of the 10 subjects showed measureable JNDs on at least one electrode pair. For the purpose of this study, only JNDs <1600 μs were considered measureable, and even 1600 μs is over twice as large than the ITD produced by an adult human head (approximately 700 μs). This value is consistent with previous studies conducted with adult subjects using similar paradigms [11], [12], [19]. In addition, 4/10 subjects (CIAQ, CIAY, CIAP, CIBO) demonstrated ITD sensitivity at more than one electrode location, and 2/10 subjects demonstrated sensitivity to ITDs at only the apical electrode pair (i.e. CIAG and CIDJ).

Recent data from Ehlers et al. [5] are included in Fig. 3, where performance of children with BiCIs and NH children are compared (ILDs in 3a and ITDs in 3b). When calculating the average ITD JNDs, only data from subjects with measurable ITD sensitivity were included. In addition, for middle electrode pair, data from experiment I and II were both included in the average for ITDs and for ILDs. Data were analyzed using a one-way repeated-measures analysis of variance (ANOVA), conducted on location (base, middle, and apex) for ITDs or ILDs. There were no significant main effects of location for either ITD [$F(2, 4)=0.272$, p=0.775] or ILD [$F(2, 12)=0.747$, p=0.494]. Next, ITD JNDs were compared between children with BiCIs who had measureable JNDs (n=7) and NH children (n=11). A between-group one-way ANOVA confirmed significantly higher ITD JNDs for the children with BiCIs (using JNDs found at all locations) when compared to the ITD JNDs for the NH children [*F*(1, 23)=27.267, p=0.0002].

Figure 4 shows ILD JNDs as a percentage of DR, for children with BiCIs tested here, and also DR data calculated from the NH data in Ehlers et al. [5]. A between group one-way ANOVA was conducted on ILD JND DR for the two groups of children; for the BiCI group all JNDs were used, including those found at the base, middle, and apex. The ANOVA confirmed significantly higher percentages of ILD JND DR for the children with BiCIs when compared to the NH children [*F*(1,42)=12.327,p=0.001].

Experiment III: Lateralization

A. Methods

Nine of the subjects that participated in Experiment I also participated in Experiment III. Due to visit time constraints one subject, CIAG, was not tested with ILDs for Experiment III. Subjects sat facing a computer monitor that displayed a cartoon of a head; a red shaded area spanned between the left and right ears provided subjects with a visual scale designed to enable them to accurately indicate the perceived intracranial position of sound sources. The values for ITDs (0, ±100, ±200, ±400, ±800, and ±1600μs) and ILDs (0, ±2, ±4, ±10, and, ±20 CUs) were tested separately for each cue type, although these varied based on subject performance. Similar to the discrimination task in Experiments I and II, positive cues values indicate that the cue favors the right ear and negative values indicate that the cue favors the left ear. After each stimulus presentation, subjects were asked to indicate the perceived intracranial position of the sound using a computer mouse to move a pointer positioned in the horizontal red shaded area of the head. Responses of perceived intracranial position were coded using an arbitrary scale from -

10 to 10 (with 0 being center and the right ear being 10). Prior to the initiation of the experiment, each subject was familiarized with the task. Once familiarization was completed, subjects were tested with 20 repetitions of each condition, and the cue levels were randomized within blocks of ILD or ITD.

B. Analysis

A linear effects model predicted slope values for the lateralization results in Experiment III. The psychometric functions relating perceived intra-cranial position to ILD or ITD level were modeled using the R software [34] with a non-linear least squares (NLS) curve fitting procedure using the Levenberg-Marquardt algorithm available in the 'minipack.lm; package. For further review of analysis, please consult Ehlers et al [5].

C. Results

Individual ILD data from Experiment III are plotted in Fig. 5, showing each subject's average responses as a function of ILD, with the model's predicted slope located in the upper left-hand corner. Each panel in Fig. 5 represents data from an individual subject.

ILD data could be modeled using the NLS curve fitting for all subjects. In the bottom right panel of the figure, average data from NH children are shown [5]. They have been re-plotted with permission, and analyzed using the same NLS curve-fitting model. A between groups one-way ANOVA revealed no significant differences in slope between the NH and BiCI groups [$F(1, 17)=0.135$, $p=0.717$] for ILD data. Two subjects' data (CIEB and CIFF) had very shallow slopes, implying that even the largest ILD given (±20 CUs) was not enough to pull the auditory image to either one ear or the other. However, other subjects (CIEU and CIAW) showed small changes in perceived intracranial location for each given ILD. Subject CIDJ was only tested on ILDs as large as 10 CUs, as this delivered enough of a difference to pull the auditory image all the way to one ear or the other. Subject CIDJ had a small overall across ear dynamic range of 12 CUs (as calculated in Experiment II); therefore, an ILD of 10 CUs would represent a large portion (83%) of the DR.

Individual ITD data from Experiment II are plotted in Fig. 6 showing each subject's average responses as a function of ITD. Due to the fact that subjects' performance was highly variable, the model was not able to predict performance in a meaningful way; therefore, there are no slope values for the ITD data. Once again, the bottom panel represents the NH average intracranial location as a function of ITD [5]. The general trends of the functions can be compared across subject groups. Results suggest that NH children could provide a more cue-dependent, finely-grained response distribution; that is, NH children distinguished a more gradual shift in perceived position as the ITDs varied. In contrast, children with BiCIs were unable to use the ITD cues reliably to indicate intracranial position. For example, subject CIAG had a very strong right-sided bias, never reporting sound on the left. An alternate example is subject CIFF, who reported that nearly all given ITDs were perceived from the center.

V. General Discussion

The experiments reported here were motived by the fact that children with BiCIs perform notably poorer than NH peers on spatial hearing tasks. The reasons for this finding are not clear. In the present set of experiments, the binaural abilities of children with BiCIs were investigated and compared to those of NH children studied in Ehlers et al. [5] using the same tasks, in order to better understand how children with BiCIs can use important cues for spatial hearing tasks such as sound localization or listening to speech in noise.

Experiment I and II utilized methods that have been previously utilized to study similar effects in adults. The discrimination task has been applied frequently in the literature for all populations [5], [12], [35], [36]. However, this is the first study to make comparisons to NH peers that were tested on the same task with stimuli designed to limit accessibility of fine structure ITD cues. On the discrimination task, all children with BiCIs had measureable sensitivity and were able to make use of ILD cues. When evaluating ILD JNDs for NH children and children with BiCIs there is no direct way to compare ILD sensitivity, because the CU does not equate to a specific change in dB. The definition of clinical current units is independent of sound pressure level. Past research has attempted to express current level as a percentage of DR [30]. Other research has attempted to quantify current level in terms of dB. For example, Litovsky et al [19] reported that ILD JNDs in adults were as small as 0.5 difference in CU, and suggested that, in the research processors, assuming a dynamic range of 175-255 CUs, a change of 1 CU corresponds to 0.176 dB in stimulation current (20 log 10 (175) /255). For the purposes of this study, the across ear DR was calculated for each individual subject with BiCIs in order to determine the maximum ILD the subject could receive through research processors. For the purposes of comparison, NH DR was assumed to be 65 dB based on the loudness growth functions for a 4kHz tone [31], which high frequency carrier presented to NH children in Ehlers et al [5]. ILD JNDs for children with BiCIs took up a significantly larger portion of DR than NH children, suggesting that they may not be as sensitive to small changes in ILD as their NH peers. However, some caution is warranted when interpreting this finding, given the lack of direct comparison for ILDs across acoustic and electric hearing.

For ITD values, NH children and children with BICIs can be directly compared, as both were tested in microseconds. The small amount of children with BiCIs who had sensitivity to

ITDs show poorer sensitivity reflected with higher JNDs than their NH peers using stimuli that mimics CI processing. This suggests that by age 8, although the NH binaural system is well developed for the discrimination task [5], children with BiCIs are falling behind their NH peers, specifically for use of ITDs. This previous research suggests that NH children are able to utilize ITDs present in the envelope, similar to what is provided via the processing of CIs [5]; therefore, suggesting that these deficits are not simply due to development of the binaural system, rather they may be related to other factors such as neural degradation.

Experiment III continued the investigation of sensitivity to binaural cues through perceptual mapping of auditory stimuli to a range of intracranial positions on a continuous scale. All children were able to perceive an intracranial position associated with ILD cues. When comparing the slopes of the ILD data for the children with BiCIs to the children with NH, there were no significant differences. Contrary to the ILD data, children with BiCIs were not able to map perceptual position of ITDs in any meaningful or predictable manner. Previous research with NH children demonstrated large amounts of variability on the lateralization task when compared with NH adults [5]. Therefore, lateralization, particularly with ILDs, may be a skill that could improve in children with BiCIs as their auditory system develops.

Previous reports on children with BiCIs have examined responses to binaural stimuli in children with BiCIs [11], [24]. Salloum and colleagues asked children to describe stimuli as coming from the left side, right side, middle of the head, or from both right and left simultaneously; performance was poor for stimuli with non-zero ITDs but good for ILDs. Gordon and colleagues suggested that sensitivity to ITDs occurs in children with BiCIs after over 4 years of bilateral implant use. However, a difference in task between Gordon et al. [11] and the present study may explain the findings. Gordon et al. [11] study reported the percentage of times that subjects reported the sound as coming from either the left or the right, thus the task involved a detection of a binaural cue. Here, both the discrimination and lateralization tasks required that subjects be able to hear the sounds as lateralized. In the discrimination task they had to note the direction of the sound movement (right-left or left-right). In the lateralization task they had to perceptually map binaural cues to a continuous range of intracranial positions. These two tasks may be more challenging than the same/different task used by Gordon et al. [11].

Finally, the population tested in this set of experiments was dissimilar to the groups of children tested by Gordon et al. [11], as most of the children in this study were sequentially implanted, with few having received simultaneous implants; the mean inter-implantation time was 35.13 ± 29.97 months, which is contradictory to previous results that found better ITD sensitivity in subjects who had an inter-implantation delay of less than 1.5 years [11], [37]. It may be that a large inter-implantation delay causes unilateral reorganization of the auditory system, thus affecting the ability to integrate binaural cues [37], [38].

The lack of ITD sensitivity in 11/16 children studied here is consistent with what is known about binaural sensitivity in pre-lingually deafened adult BiCI users, tested on the same task as the one used here [19]. Six of the seven subjects with ITD sensitivity had a progressive or fluctuating loss, with one subject (CIAY) having 42 months of normal acoustic hearing. The subject that did not have any early acoustic hearing (CIDX) had an inter-implantation delay of 1 year, 2 months, which is within the window suggested by Gordon et al. [37] for development of binaural pathways. It may be that early access to acoustic cues is required for the development of ITD pathways in the auditory system, although studies in non-human mammalian species suggest that neural circuits involved with binaural hearing remain somewhat plastic throughout life [39]. In addition, research in the animal literature has shown that through training and experience can help with plasticity of neural circuits in regards to spatial hearing [39], [40]. ILD circuitry appears to recover function following deprivation more easily than ITD circuitry [14], [19]. One theory suggests that ITDs are only processed by a small number of nuclei [41]; thus potentially causing the effect that the ITD pathway is preset. On the contrary, ILDs show several brainstem nuclei that respond to level differences, thus potentially making it less susceptible to early deafness [14], [42].

With regard to the effect of auditory deprivation on the use of binaural cues, it is not clear that deprivation obliterates binaural processing altogether. Two studies in children with BiCIs have measured binaural masking level differences (BMLDs), which require the detection of tone in noise in conditions with vs. without interaural difference cues, that is, the binaural cue that is used is known as interaural decorrelation present in the envelope of the signal. BMLDs are found regardless of whether the children have ITD sensitivity or not [25], [26]. It thus appears that the ability to detect interaural decorrelation, similar to the ability to detect a sound with an ITD [11], reveal aspects of binaural sensitivity not evident from ITD discrimination and lateralization measures.

Another issue for consideration is the underlying neural substrates involved in the complex tasks used here. As has been demonstrated in many studies over the years, the auditory system undergoes continued maturation into the teenage years [8]. With regard to binaural hearing, the recent study on binaural discrimination and lateralization in NH children showed that at 8-10 years of age some children perform similarly to adults on tasks of lateralization, utilizing the entire range of responses, while others had responses more categorical in nature (favoring responses at the extremes) [5]. In addition, other aspects of audition, such as gap detection [43] and backward masking [44] undergo maturation and refinement into adolescence.

Due to many factors, including auditory deprivation early in life and the need to learn to use auditory input through electrical stimulation provided by the CI, it is possible that binaural hearing abilities are undergoing developmental changes that are more protracted in children with BiCIs than in NH children. Future research investigating these issues in greater detail may be more revealing regarding the developmental trajectory of binaural sensitivity in this specific population.

A final consideration in regards to the tasks used in this study, particularly lateralization, is the potential influence of cognitive abilities such as working memory and attention. Lateralization may require greater concentration and attention, or the use of top-down processes that depend on more mature executive function and working memory. The lateralization task differs from the discrimination task as there is no perceptual reference to make a judgement. It is a one-interval task. Therefore, hours of testing may not have been sufficient to maximize their performance on the task. Future work involving auditory training for many more hours may reveal that lateralization abilities can improve with training. To date, work on training of auditory cues has focused on improved performance measured with discrimination tasks, similar to that used in Experiment I [45].

In summary, the motivation behind this study was to understand possible reasons why children with BiCIs might perform more poorly than their NH peers on tasks of spatial hearing. A known limitation contributing to poor ITD sensitivity is the lack of temporal fine structure present in everyday clinical CI processing. However, previous research with NH children demonstrates that when rendering the temporal fine structure ITD cues inaccessible, the performance of NH children on a discrimination task remained excellent, even adult-like [5]. This suggests that deficits in children with BiCIs may not be solely related to the lack of fine structure present in CI processing; rather, other factors are more likely to be the cause of this gap in performance, such as neural degradation and lack of coordinated inputs to the implants in the two ears. The impact of these factors on spatial hearing is not well understand even in adults with BiCIs and therefore further research is necessary to more fully understand the performance gap and to determine possible ways in which performance can be improved using better engineering of bilateral devices and better ways of protecting the auditory system from the effects of auditory deprivation.

Conclusions

Two tasks were conducted in children with BiCIs: discrimination and lateralization. The following results were found:

1. On the discrimination task, all children with BiCIs had measurable sensitivity to ILDs. However, only 50% of children had measureable sensitivity to ITDs, and those that did had significantly higher JNDs than NH children tested on stimuli that render fine structure ITDs inaccessible.

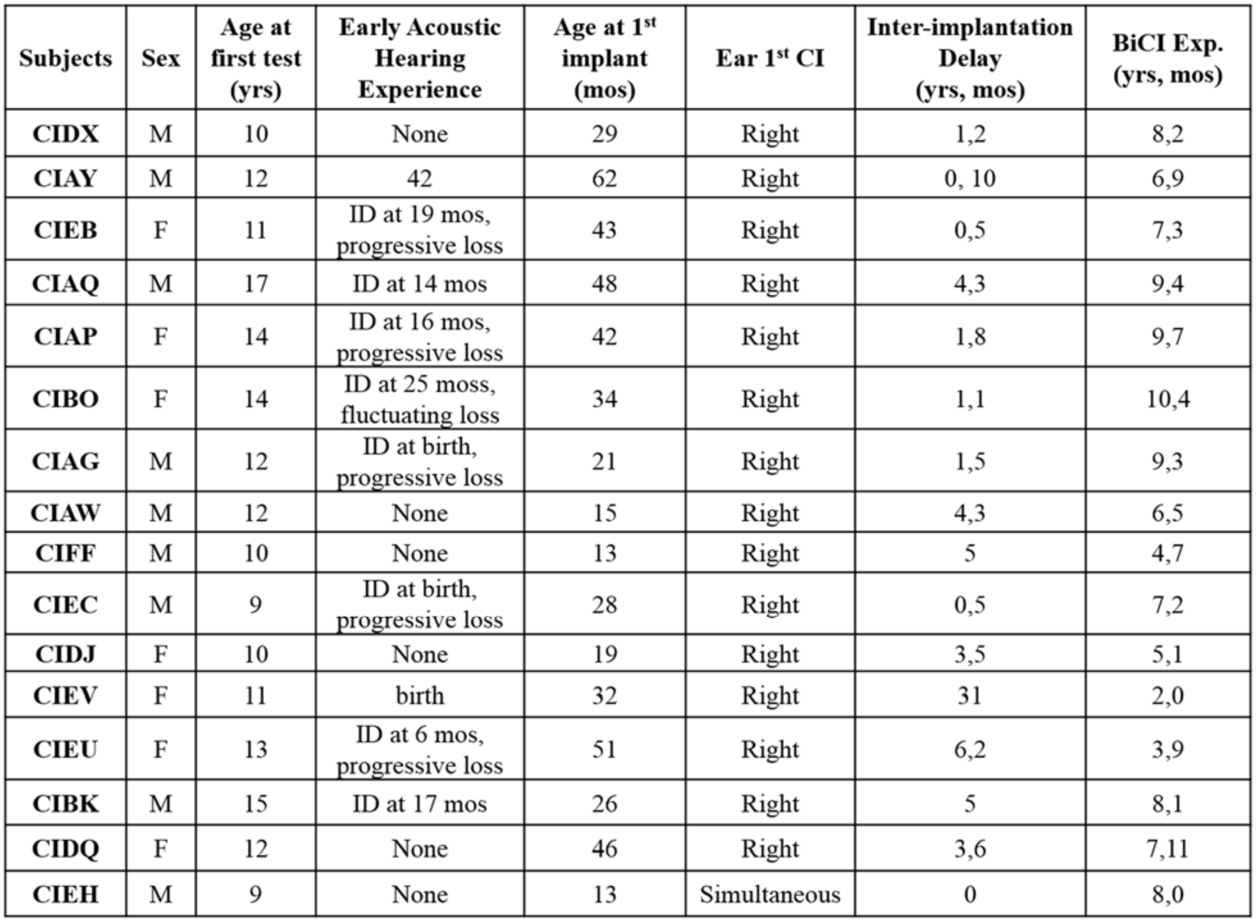
2. On the lateralization task, children with BiCIs had measureable slopes and showed sensitivity to ILDs. For ITDs, children with BiCIs did not have data that could be modeled in any predictable manner. This is contrary to previous research in NH children in which they showed sensitivity to both ITDs and ILDs when tested on the same task.

3. This work serves as an important benchmark for future studies regarding binaural sensitivity in this population. Further research is necessary to investigate other factors that may be barriers to binaural sensitivity, specifically with ITDs, such as neural

degradation, interaural frequency mismatch, or non-auditory factors like working memory and attention.

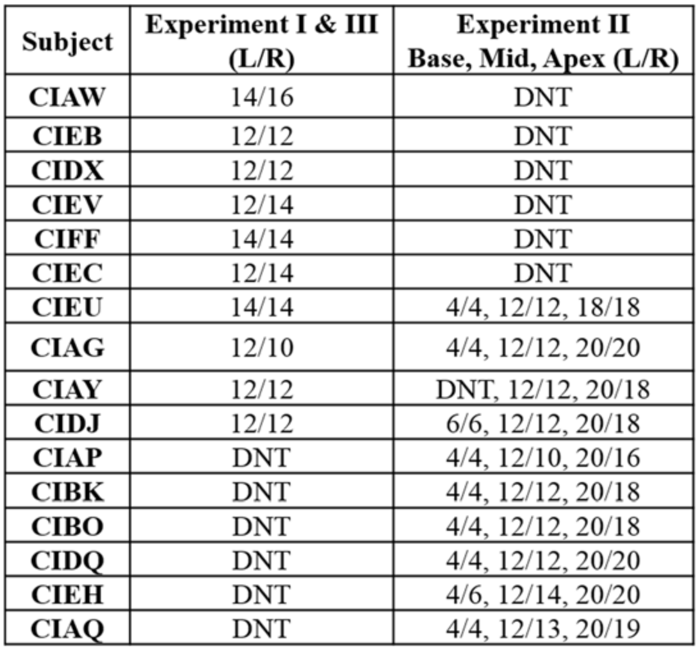
Tables

Table I. Subject Characteristics



Subjects	**Sex**	**Age at first test (yrs)**	**Early Acoustic Hearing Experience**	**Age at 1st implant (mos)**	**Ear 1st CI**	**Inter-implantation Delay (yrs, mos)**	**BiCI Exp. (yrs, mos)**
CIDX	M	10	None	29	Right	1,2	8,2
CIAY	M	12	42	62	Right	0, 10	6,9
CIEB	F	11	ID at 19 mos, progressive loss	43	Right	0,5	7,3
CIAQ	M	17	ID at 14 mos	48	Right	4,3	9,4
CIAP	F	14	ID at 16 mos, progressive loss	42	Right	1,8	9,7
CIBO	F	14	ID at 25 moss, fluctuating loss	34	Right	1,1	10,4
CIAG	M	12	ID at birth, progressive loss	21	Right	1,5	9,3
CIAW	M	12	None	15	Right	4,3	6,5
CIFF	M	10	None	13	Right	5	4,7
CIEC	M	9	ID at birth, progressive loss	28	Right	0,5	7,2
CIDJ	F	10	None	19	Right	3,5	5,1
CIEV	F	11	birth	32	Right	31	2,0
CIEU	F	13	ID at 6 mos, progressive loss	51	Right	6,2	3,9
CIBK	M	15	ID at 17 mos	26	Right	5	8,1
CIDQ	F	12	None	46	Right	3,6	7,11
CIEH	M	9	None	13	Simultaneous	0	8,0

Table II. Chosen electrode pairs



Subject	**Experiment I & III (L/R)**	**Experiment II Base, Mid, Apex (L/R)**
CIAW	14/16	DNT
CIEB	12/12	DNT
CIDX	12/12	DNT
CIEV	12/14	DNT
CIFF	14/14	DNT
CIEC	12/14	DNT
CIEU	14/14	4/4, 12/12, 18/18
CIAG	12/10	4/4, 12/12, 20/20
CIAY	12/12	DNT, 12/12, 20/18
CIDJ	12/12	6/6, 12/12, 20/18
CIAP	DNT	4/4, 12/10, 20/16
CIBK	DNT	4/4, 12/12, 20/18
CIBO	DNT	4/4, 12/12, 20/18
CIDQ	DNT	4/4, 12/12, 20/20
CIEH	DNT	4/6, 12/14, 20/20
CIAQ	DNT	4/4, 12/13, 20/19

Figures

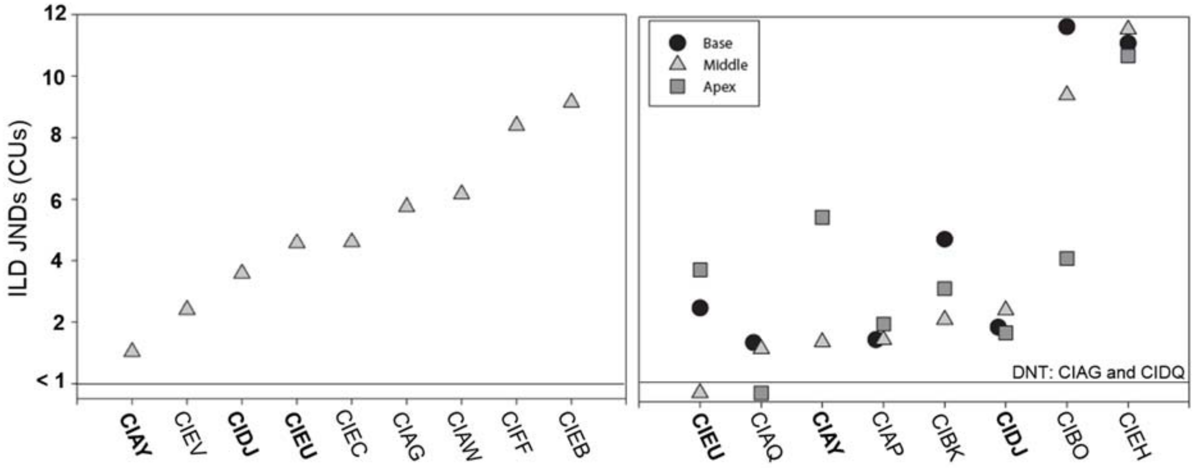


FIG 1. Individual ILD JNDs for subjects tested on a single medial electrode pair (n=9) in Experiment I (a) and for subjects tested on three electrode pairs located at the base, middle, and apex of the electrode array (n=8) in Experiment II (b). Subjects in bold were tested in both experiments (n=4).

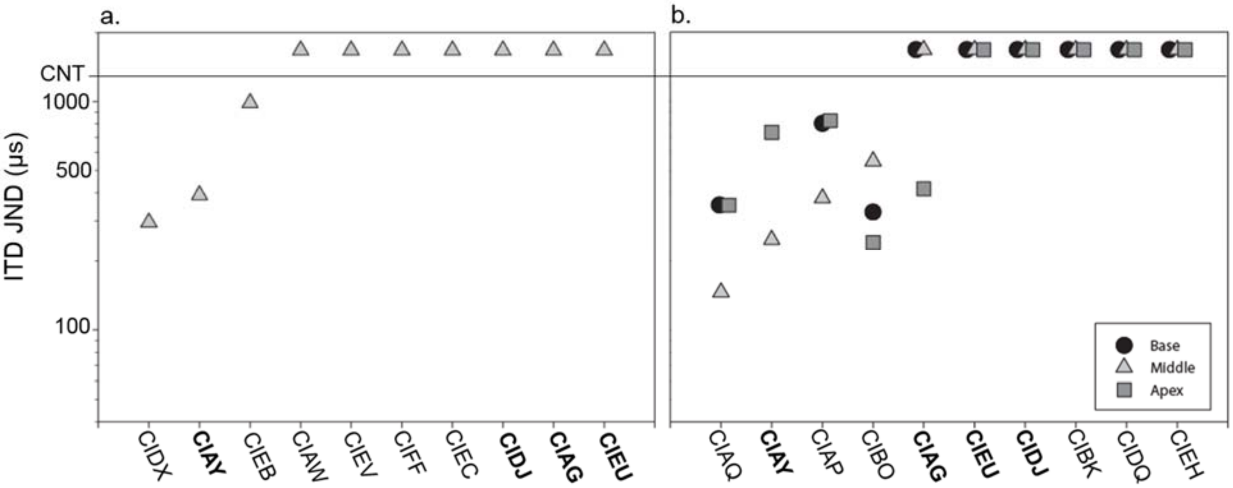


FIG 2. Individual ITD JNDs for subjects tested on a single medial electrode pair (n=10) in Experiment I (a) and for subjects tested on three electrode pairs located at the base, middle, and apex of the electrode array (n=10) in Experiment II (b). Subjects in bold were tested in both experiments (n=4).

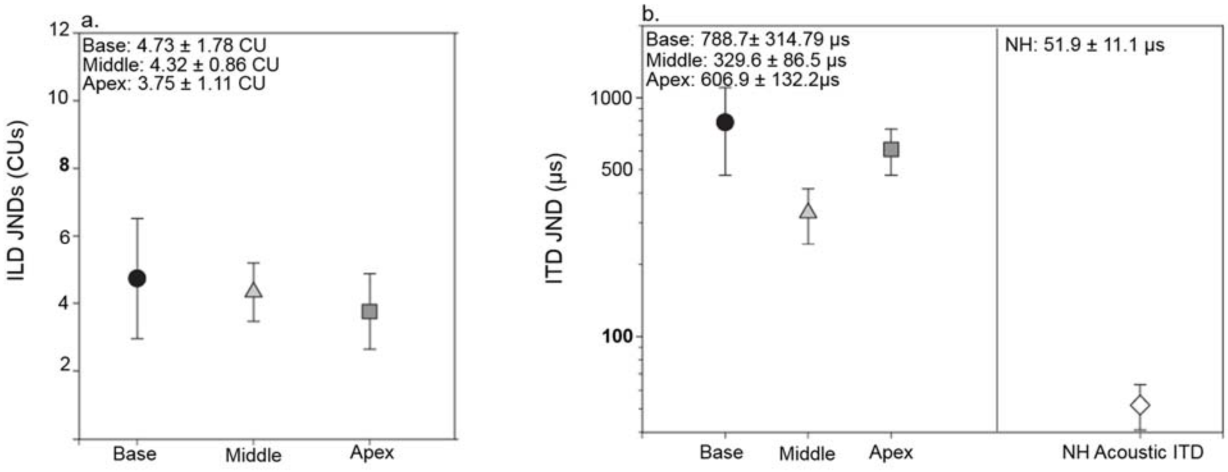


FIG 3. Average (+/- standard error) ILD JNDs (a), and ITD JNDs (b) are shown for the three locations across the array. In addition, comparisons are made with data that were previously published in NH children for ITDs (Ehlers et al, 2016).

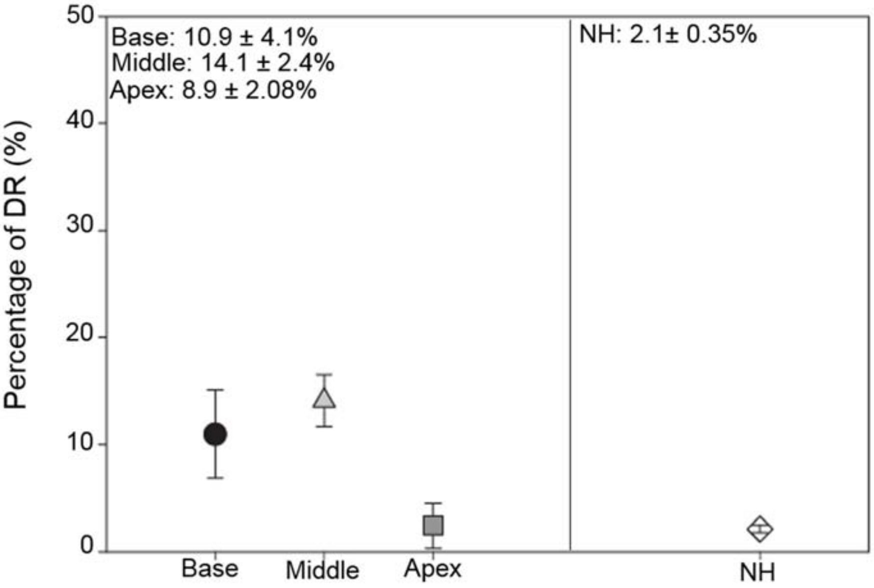


FIG 4. ILD JNDs expressed as a percentage of DR (average +/- standard error) are shown for the three locations across the array In addition, comparisons are made with data that were previously published in NH children (Ehlers et al, 2016).

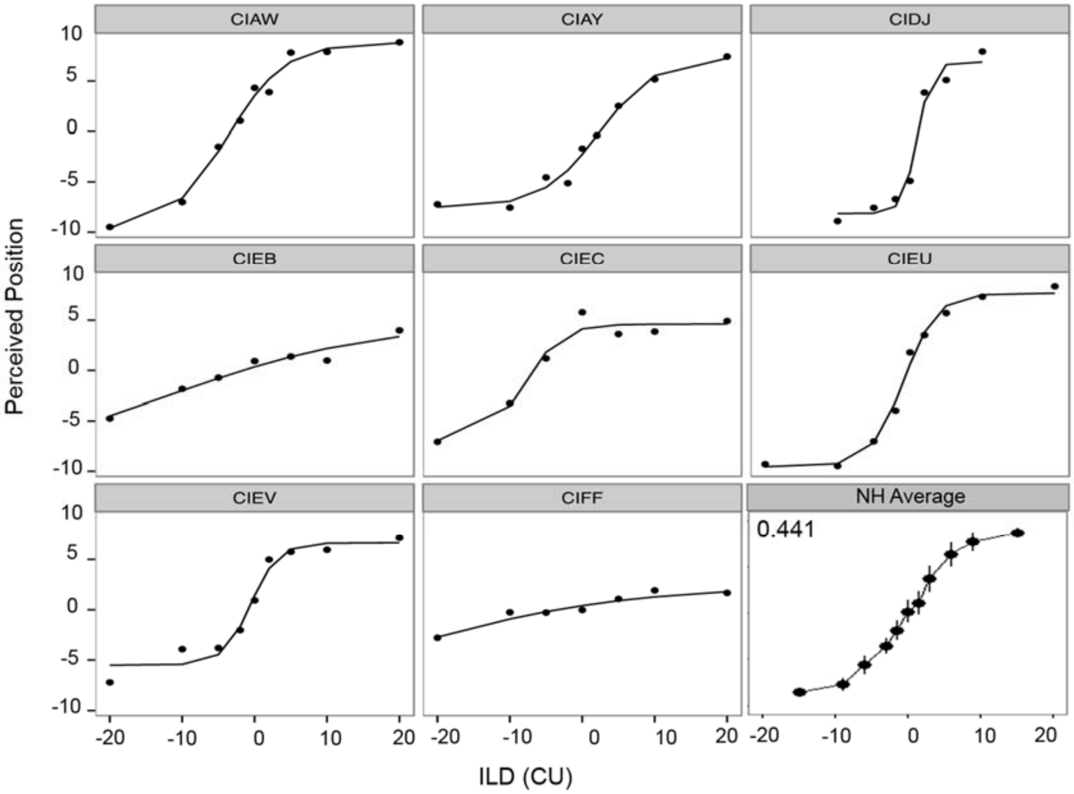


FIG 5. Individual data from the lateralization task are shown for ILD data. In each panel, data from a single listener indicate the average perceived intracranial position as a function of ILD. Slope values are inserted in the top left corner of each panel. In the bottom right panel the overall average intracranial positions for NH children as a function of ILD are replotted with permission from Ehlers et al., 2016. The average ILD slope value for the NH children is inserted in the top left corner of the panel.

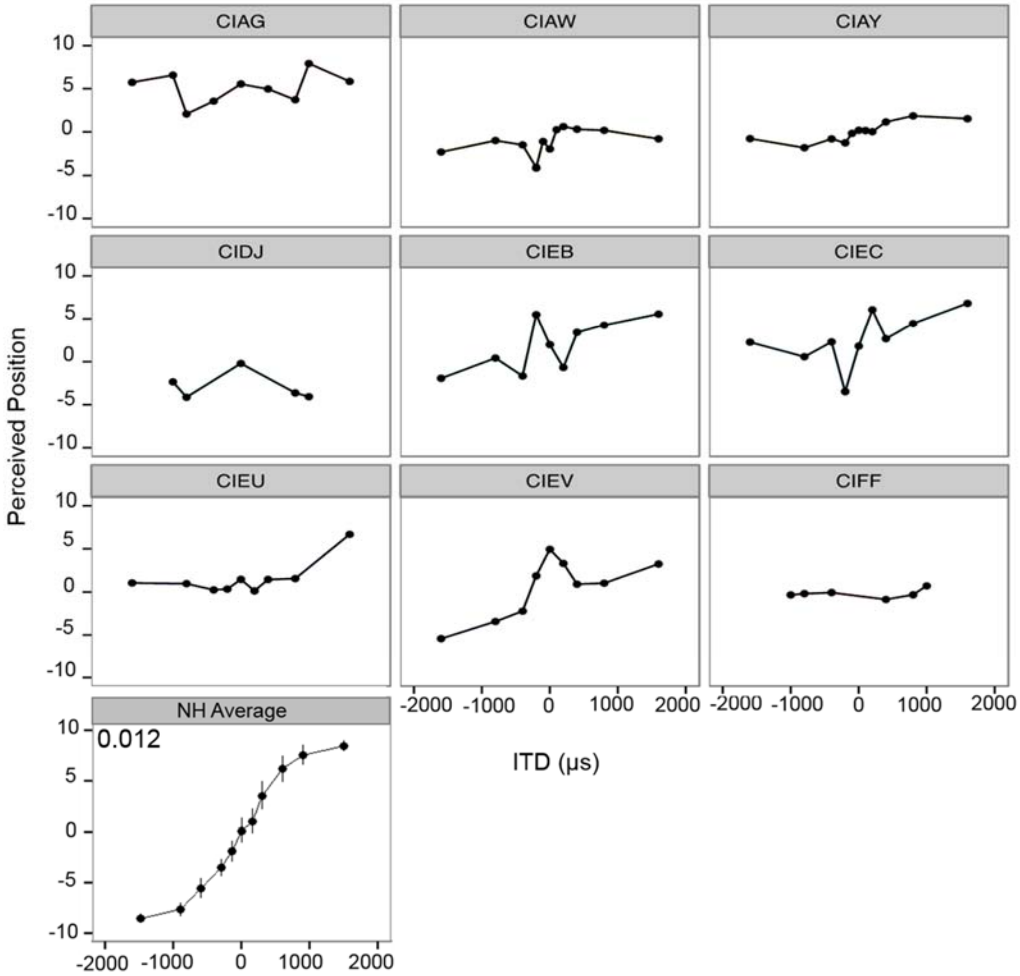


FIG 6. Individual data from the lateralization task are shown for ITD data. In each panel, data from a single listener indicate the average perceived intracranial position as a function of ITD. Slope values are not listed as the model could not be run for the ITD condition. In the bottom left panel the overall average intracranial positions for NH children as a function of ITD are replotted with permission from Ehlers et al., 2016. The average ITD slope value for the NH children is inserted in the top left corner of the panel.

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Chapter 4: Factors affecting interaural timing difference sensitivity in children with bilateral cochlear implants

Abstract

A main motivation behind bilateral cochlear implantation is the provision of access to binaural cues, namely interaural time and level differences (ITDs and ILDs, respectively), in order to improve spatial hearing abilities. Previous research with low-rate stimulation of 100 pulses per second (pps) suggest that bilaterally implanted children generally have sensitivity to ILDs, whereas sensitivity to ITDs is weak or absent. Lack of ITD sensitivity may arise from numerous factors including interaural mismatch between electrode arrays and rate of stimulation. In order to examine these factors in greater detail, children (ages 10-17) with bilateral Cochlear Nucleus implants participated in three experiments. In Experiment I (direct pitch comparison) subjects compared the perceived pitch for different interaural pairs of electrodes. ITD just-noticeable-difference (JND) thresholds were then also measured using the same electrode pairs. In Experiment II, ITD JNDs were measured using a pitch-matched electrode pair with low rate, unmodulated stimuli (100 pps) and high rate amplitude modulated stimuli (1000 pps modulated at 100 Hz). Some children had ITD sensitivity, and pitch-matched electrode pairs typically yielded the lowest (best) ITD JND, in line with results from adults with bilateral CIs. Children who demonstrated ITD sensitivity at 100 pps had comparable performance with high-rate, amplitude-modulated stimulation. The fact that most children had absent or weak sensitivity to ITDs suggests that neither the rate of stimulation nor the choice of interaural electrode pair can account for poor ITD sensitivity and that other factors must be explored.

Introduction

Bilateral cochlear implantation is aimed at providing patients with the auditory cues needed to function on spatial hearing tasks. For listeners with normal hearing (NH) interaural timing differences (ITDs) and interaural level differences (ILDs) are known to aid in the ability to effectively perform spatial hearing tasks [1], [2]. On tasks that require discrimination of changes in sound source location, or minimum audible angle, NH children display spatial hearing abilities that are adult-like (as low as 1-2º) by 4-5 years of age [3]. In addition, on sound location identification tasks with multiple loudspeakers, some NH children perform like adults, with root-mean-square errors as low as 8º [4]–[7]. In a recent study in which ITDs and ILDs were individually manipulated, NH children were found to have relatively mature binaural sensitivity by 8 years of age, with just-noticeable-difference (JND) thresholds similar to those of NH adults [8].

Children with bilateral cochlear implants (BiCIs) display a different developmental trajectory for spatial hearing than their NH peers. Although they typically perform better on spatial hearing tasks, such as the minimum audible angle when using two vs. one implants [5], [9], they generally perform poorer than their age-matched peers with NH. Similar group differences have been reported for sound location identification tasks, even after 3-4 years of experience with BiCIs [10]. In addition, as shown in Chapter 3 of this dissertation, when given binaural cues through synchronized research processors, children with BiCIs do not demonstrate the ability to use these cues in the same manner as their NH peers, particularly for ITDs. Recent studies, also conducted with synchronized research processors, report that children with BiCIs can use interaural decorrelation to hear tones in noise [11], [12], even if they do not have sensitivity to ITDs [12]. However, this binaural unmasking paradigm is more closely related to the segregation of speech from noise than sound localization abilities, hence the present study seeks to improve understanding of the mechanisms involved in mediating sensitivity to binaural cues. There are a variety of reasons as to why children who use BiCIs are poor at using ITDs; two of these factors were investigated in the present study (1) the relationship between pitch-matching and ITD sensitivity and (2) the relationship between stimulation rate and ITD sensitivity.

In Chapter 3 of this dissertation, children with BiCIs were tested using synchronized research processors and pitch-matched pairs of electrodes in the right and left ears were selected, at basal, medial and apical places along the cochlear arrays. Surgical procedures for bilateral cochlear implantation may not be precise enough to guarantee that the electrode arrays in the two ears are physically matched for insertion depth. In addition, clinical best practices typically distribute the frequency spectrum across the active electrodes and thus the same electrode numbers in the right and left ears are given the same frequency range, regardless of location of the electrodes along the basilar membrane. It is possible that such an approach would cause differing frequency inputs (mismatch) between the ears. In numerous studies to date, pitch-matching has been considered to be an important prerequisite for maximizing binaural sensitivity, because this approach approximates stimulation of the same cochlear places and is aimed at optimizing binaural sensitivity. In fact, it has been shown that interaural mismatch limits binaural sensitivity in both NH adults and adults with BiCIs [13], [14]. Furthermore, there is evidence to suggest that mismatched pairs of electrodes result in reduced ITD sensitivity specifically [13], [15].

With regard to children with BiCIs, little is known about the potential importance of pitch-matched stimulation, or the consequences of mismatching stimulation across the ears on binaural sensitivity. Most children who use BiCIs have had limited access to acoustic hearing early in life, which means that perception of pitch is acquired by listening to electrical stimulation. Clinical speech coding strategies are designed such that frequency allocation tables are used to determine the acoustic frequency range associated with each electrode. The importance of this frequency allocation and the extent to which it bears significance for binaural hearing is not known. In adults it has been shown that the perception of pitch is malleable and may be influenced by the frequency allocation tables of the implant programming [16]. If children perceive pitch based on their frequency allocation tables, then using a pitch-matched pair of electrodes could actually be detrimental to binaural sensitivity because it might lead to a mismatch in the frequency that children have become accustomed to. An important question is whether the pitch-matching tasks that have been previously used provide the best approach for probing the matched anatomical places in the right and left implants, or if the children who perform pitch-matching tasks have used information that they learned through use of their clinical MAPs on a daily basis. If the latter is true then there may still be an underlying difference in anatomical stimulation present, which may help to explain why many of these children have weak or absent sensitivity to ITDs.

A second factor that may be affecting sensitivity to ITDs in children with BiCIs is the stimulation rate used in studies to date. Studies in adults with BiCIs show that ITD sensitivity is best at fairly low rates, below a few hundred pulses per second (pps) [17]–[19]. While low rates are ideal for binaural hearing, it is well established that higher stimulation rates are needed for speech understanding [20]. Clinical processors generally provide carrier rates that are fixed at 900+ pps, with slower rates of modulation imposed on the stimulus envelope as per the incoming speech signal. As a result, there appears to be a trade-off between the best stimulation rates for speech understanding and ITD sensitivity. In Chapter 3, low rates of 100 pps were used to test binaural sensitivity for ITDs and ILDs; these rates were selected based on prior research in adults that focused on low-rate stimuli [13], [21]. Adults with BiCIs also show ITD sensitivity with high rate (1000 pps) stimulation modulated at low rates (100 Hz) that is comparable to the performance with the 100 pps stimuli [17], [22]. The present study was aimed at determining whether ITD sensitivity could be improved if they were tested with amplitude-modulated high-rate stimulation, which is more similar to the high-rate stimuli that they hear in everyday listening.

Experiment I: Place of stimulation and ITD sensitivity

A. Methods

1. Participants

Ten bilaterally implanted children between the ages of 9-17 years participated in this study. All children had Cochlear Ltd. devices that were either from the CI24 or CI512 family of implants in order to be compatible with the direct stimulation research processors. These internal devices have an electrode array of 22 intra-cochlear stimulation electrodes and two extra cochlear ground electrodes. The electrodes are numbered from the basal end to the apical end, or 1-22 respectively. An additional inclusion criterion was that the main mode of communication for participants was oral with English as their first language. More detailed participant information is displayed in Table I.

Participants and legal guardians traveled to the Waisman Center at University of Wisconsin-Madison for testing. Travel costs were covered for these experiments and were given a stipend for their time. Testing lasted two to three days for each subject.

2. Experimental set up

All testing with auditory stimuli was conducted in a quiet room. The experiments were conducted on a personal computer using MATLAB (MATHWORKS, Natick, MA) software to generate stimuli. A research interface (Nucleus Implant Communicator; Cochlear ltd., Sydney, Australia) was used to deliver all stimuli to each subject's own internal devices. Subjects used a touch screen computer monitor to record their responses throughout all auditory experiments.

3. Implant mapping

Clinical MAPs for subjects were provided by their audiologist through direct request from the children's parents. Each subject's clinical map was used as a starting point for setting stimulation levels during the experiments. Three stimulation levels were determined for all even-numbered electrodes in each ear: Threshold (T), comfortable (C), and maximum comfortable (M). T is defined as the lowest level of audibility. C is defined as a level that is comfortable enough for a patient to tolerate listening to for an extended period of time. M is the highest amount of current that a subject can tolerate briefly without being uncomfortable.

Once T, C, and M levels were obtained, C levels were loudness-balanced within an ear. A series of five electrodes at a time were swept and the subjects were asked to report soft or loud electrodes. Adjustments continued to be made until all C levels within each group of 5 were perceived as equally loud. Finally, a sweep across all 11 electrodes was made in order to ensure balanced loudness. This approach is consistent with methods used in previous studies with adults [13], [17], [21] and in children as conducted in Chapter 3.

In order to elicit a perception of a centered image between the ears, subjects were asked to balance the loudness across ears. In this task, the amplitude in the left electrode was held constant, while the amplitude in the right electrode varied. Subjects were also asked to indicate on a cartoon version of a head where they perceived the sound, in order to confirm the sound was centered, thus reducing unwanted ILD cues. This was completed for each interaural electrode pair being tested.

4. Stimuli

Bilaterally synchronized, electric pulse trains were used in this series of experiments. A biphasic, 300 ms, constant amplitude, 100 pulses per second (pps) pulse train was presented at the subject's C level. The pulses had a 25 μs phase duration and an 8 μs phase gap, consistent with current clinical CI programming. This stimulation rate is lower than typical clinical CI stimulation in order to maximize sensitivity to ITDs, which are known to be better at low stimulation rates [17]. This stimulation rate is also consistent with previous research completed with adults [13], [17], [21] and in children in Chapter 3.

5. Tasks

Each subject participated in three tasks given in the following order: (1) Pitch Magnitude Estimate (PME), (2) Direct pitch comparison (DPC), and (3) ITD discrimination. The PME task required subjects to rank the perceived pitch of even numbered electrodes in each ear [13], [21]. Stimulation was presented at the subject's self-reported C level. The task required subjects to provide a value that represented the perceived pitch of the stimulus on an arbitrary scale ranging from 1 (low pitch) to 100 (high pitch). The stimuli were presented in random order to the even numbered electrodes in each ear and repeated 10 times at each electrode. Prior to the initiation of the task, subjects were familiarized with assigning a value to the perceived pitch of a stimulus via verbal discussion and practice. Subjects were also encouraged the use the full range of the scale (1-100) when subjectively judging the pitch. Ten repetitions per electrode in each ear were completed.

On the DPC task subjects were asked to directly compare the perceived pitch between specified electrodes in the right and left ears. For the present study, only electrodes in the middle of the electrode arrays were used. The left ear electrode was held constant and compared to the electrode in the right ear that had been judged as 'pitch matched' in the PME task, plus six other electrodes: three higher in number and three lower in number ($\pm \Delta 2$, $\Delta 4$, and $\Delta 6$ electrodes). This task was completed in a two interval, five-alternative forced choice task. Twenty repetitions per electrode pair were completed for each subject. The subject was asked to report whether the right ear electrode was "much higher", "higher", "same", "lower", or "much lower" than the electrode in the left ear. A metric, μ, was calculated by giving the above responses values of 2, 1, 0, -1, and -2 respectively and summing together [13].

$\mu = (2)N_{\text{much higher}} + (1)N_{\text{higher}} + (0)N_{\text{same}} + (-1)N_{\text{lower}} + (-2)N_{\text{muchlower}}$, where N is the number of times a particular response is chosen.

Finally, ITD sensitivity was measured on each electrode pair tested in the above direct pitch comparison task. Testing was conducted in blocks of trials where were a series of ITDs were imposed on the pulsatile stimulation. ITDs were applied by delaying the stimulation in the ear contralateral to the intended direction of the sound. Each ITD was presented 40 times (20 reps left and 20 reps right). The task on each trial consisted of a two-interval, two-alternative forced choice procedure, in which an ITD is presented in the left or right direct for the first interval, and in the opposite direction for the second interval. Subjects responded by indicating the direction of the sound in the second interval when compared to the first. ILDs were always 0. Typical ITD values were ±100, ±200, ±400, and ±800 μs; however, these varied for some subjects depending on individual ITD sensitivity.

Percent correct scores were measured and fit with a psychometric function [23], [24]. The ITD JND thresholds are calculated at the 71% point on the psychometric function. Finally, feedback was given after each trial. Frequent breaks were given to the subjects throughout testing in order to keep them attentive and motivated. Children were reinforced during the tasks with both prizes and monetary earnings.

B. Results

Results from the PME task are displayed in Figure 1. Subjects' data are divided according to performance on the binaural sensitivity measures. The left and right sets of panels (Fig. 1a and 1b) include subjects who either did or did not demonstrate ITD sensitivity, respectively. All subjects were able to complete the PME task. However, there was large variability both within and between subjects on this task. For example, subject CIAW was able to use the full scale provided (0 to 100), whereas subject CIBI had a more condensed range (30 to 70) on the scale. In addition, some subjects (e.g., CIAY, CIBO, and CIAW) had more steeply sloping functions, suggesting larger perceived changes in pitch between electrodes. Other subjects, (e.g., CIDJ or CIBI) had more flat functions, suggesting smaller changes in perceived pitch between electrodes.

Results from both the DPC and ITD discrimination task are shown in Figure 2. For each pair of electrodes tested, panel 2a shows results from the four subjects with ITD sensitivity (DPC on the top ITD JNDs on the bottom). Panel 2b shows results from the DPC task for the 6 subjects who did not demonstrate sensitivity to ITDs at 1600 μs or greater, and were thus not considered sensitive to ITDs.

With regard to the DPC findings, it is important to recall that the pitch-matched pairs were first determined based on the PME task (see Figure 1), and that interaural differences in electrodes (Δ values) were imposed on those electrode pairs for the DPC task. Most of the children tested here showed increasing μ values (differences in perceived pitch across ears) as the difference in electrode pair numbers increased away from the pitch-matched pair. For example, subjects CIAY, CIBO, and CIAW showed the highest μ values for electrode pairs L12/R18 and L12/R6. Two subjects, CIAY and CIBO had very low μ values for the pitch matched pair (12/12) and increasing μ values for all other pairs. However, not all subjects demonstrated this pattern (e.g., CIAP, CIBI and CIDJ). Interestingly, the DPC data for CIAP were fairly flat, and anecdotally this subject frequently reported that many of the electrode pairs sounded the same within each ear, hence the μ values less than 0.05 except for L12/R/16 and L12/R18.

Three of the four subjects with ITD sensitivity (CIAY, CIBO, and CIAP) demonstrated sensitivity to ITDs at all electrode pairs tested, and one subject (CIAW) only demonstrated sensitivity to ITDs at the pitch-matched electrode pair. The effect of interaural mismatch on ITD sensitivity was not consistent across all subjects; CIAY showed increased JNDs with increased Δ values; CIBO and CIAP did not appear to be affected by the Δ values, such that ITD JNDs were fairly similar for most of the electrode pairs tested.

Experiment II: Stimulation rate and ITD sensitivity

A. Methods

The same participants, experimental set-up and implant mapping strategy used in experiment I was used in experiment II.

1. Stimuli

ITD sensitivity was measured for two stimuli: 100 pps unmodulated and 1000 pps AM modulated at 100 Hz.

2. Tasks

ITD sensitivity was measured using the same left/right discrimination task as experiment I. ITD sensitivity for all three stimuli was tested on a pitch matched pair chosen from the DPC data collected in experiment I. A new MAP was created for each of the stimuli. Then, the MAP for each individual stimulus was loudness balanced to provide perception of a centered auditory image. The MAPs were also loudness balanced across stimuli to ensure they were comparable for ITD discrimination.

B. Results

Figure 3a shows the individual ITD JNDs for each stimulus condition and Figure 3b shows the average measurable JNDs from each condition. As in experiment I, subjects who did not demonstrate sensitivity to ITDs at 1600 μs or greater not considered sensitive to ITDs. The same four subjects who demonstrated ITD sensitivity to the 100 pps stimulus in Exp. I continued to do so here. Of these four subjects, three also showed sensitivity the high-rate modulated stimuli (1000pps with 100 Hz AM); subject CIBO did not show sensitivity to the high-rate AM stimuli. The remaining 6 subjects did not show ITD sensitivity for either stimulation rate.

Due to the small n-size of subjects with ITD sensitivity (n=4) statistical analyses were not conducted to compare between stimuli. However for subjects with sensitivity to both the low-rate stimuli (100 pps) and the high-rate amplitude modulated stimuli (1000 pps with 100 Hz AM) there did not appear to be notable differences in JND for the unmodulated and modulated stimuli.

Table II shows a summary of the results from two of the experiments in the current paper as well as previous results from Chapter 3. Of particular note, subject CIAW did not show ITD sensitivity at a pitch-matched pair of L14/R16 in Chapter 2, but did show ITD sensitivity to low-rate stimuli at a pitch-matched pair of L12/R10 in the current experiment. The remaining subjects (n=5) that did not show ITD sensitivity in the previous experiment were still not sensitive to ITDs regardless of rate or chosen interaural electrode pair, suggesting that other factors such as neural survival, binaural maturation, or a lack of early acoustic hearing experience may be responsible for the lack of ITD sensitivity.

General Discussion

The current set of experiments was motivated by the fact that, when children with BICIs are given ITD cues using research processors they perform much worse than NH peers [25], [26]. Chapter 3 showed that approximately 50% of children tested to date have not demonstrated sensitivity to ITDs, even when tested at different locations (base, middle, and apex) along the electrode array. Because little is known about the reason for poor sensitivity to ITD cues in these children, the present set of experiments attempted to examine two factors that may be important to consider: (a) the relationship between pitch-matching and ITD sensitivity, and (b) the relationship between stimulation rate and ITD sensitivity.

Experiment I utilized pitch-matching methods that are often used with adult BiCI users [13], [17], [21]. This is the first study in children to test ITD sensitivity at pairs of electrodes that are deliberately and systematically mismatched relative to measured pitch-matched electrodes. The mis-match was used here to test the hypothesis that for children who did not previously show ITD sensitivity at a pitch-matched pair, they may show ITD sensitivity at a different interaural electrode pair; one is better matched for anatomical sensitivity. Electrodes tested include a pair of L12/R/12 plus 6 other pairs, 3 that were mismatched towards the base and 3 that were mismatched towards the apex. While 4/10 subjects demonstrated sensitivity to ITDs at all, 3 of the 4 had best ITD sensitivity at the pitch-matched pair. The subject that did not show the best JND at the pitch-matched pair showed an inconsistent ability to rank pitch on the PME task and to compare pitch on the DPC task, which may have affected the selection of a pitch-matched pair. This finding suggests that when ITD sensitivity is found in children with BiCIs, the pitch-matching approach used with adults yields similarly best performance. A mis-match in anatomical stimulation did not appear to be the reason for the lack of ITD sensitivity in the 10 subjects tested here. Therefore, it seems that although pitch has been shown to be malleable and influenced by frequency allocation tables in adults [16] it does not appear to be affecting children in regards to selection of a pitch-matched pair to optimize binaural sensitivity. Current CI processing is monopolar, which causes spread across the cochlea and stimulation of populations of neurons in multiple channels [14]. Thus, it may be that current clinical stimulation is not precise enough to cause re-organization of pitch that is large enough to affect binaural sensitivity in bilaterally implanted children [27]. In fact, some research has shown that typical tonotopic reorganization is maintained in children who are born deaf and receive cochlear implants [27], [28].

Experiment II used the pitch-matched pair found in experiment I to examine the effect of using high-rate pulsatile stimulation that is amplitude modulated, which is more similar to the stimulation rates used in the children daily use of clinical processors. High rates are used because they appear to produce better speech understanding [20], high rates are a poor choice of stimulus for ITD sensitivity [17]. Chapter 3 of this dissertation as well as previous research in children with BiCIs has used low-rate pulsatile stimulation [25], which does not bear resemblance to daily electrical stimulation used by these children. By using modulated high-rate stimulation ITDs in the envelopes were presented and were akin to the envelope ITDs used in children with NH in a recent study [8]. Results showed that ITD sensitivity was comparable for the high rate modulated and low-rate pulsatile stimulation. This is consistent with previous research on adults [17], [19],

[29]. This is also consistent with results from NH children who demonstrated sensitivity to high-rate stimuli that rendered fine-structure ITD cues imperceptible, forcing subjects to rely on the envelope for ITD detection [8].

One subject (CIAW) who showed ITD sensitivity in the current study (pitch-matched electrode pair of L12/R10) had failed to show ITD sensitivity on the experiments conducted in Chapter 3 with a different pair of electrodes (L14/R16). The difference is not easy to account for; the two binaural electrode pairs may be stimulating spiral ganglion cells that differ in health (survival), which could create regions that respond more poorly to stimulation with one pair than with another pair [30]–[32]. The two pairs could also differ in in spread of excitation. Either of these problems would limit the extent to which the poorer electrode feeds information to the brainstem with fidelity. An alternate explanation is that the subject had improved binaural sensitivity due to additional experience with BiCIs, as participation in the current set of experiments occurred two years after initial study conducted in Chapter 3. Research has shown that sensitivity to ITDs may emerge in some subjects after greater than 4 years of bilateral experience [25]. This issue is complex and cannot be resolved with the small number of subjects studied here; in fact, more than half of the subjects did not show ITD sensitivity in previous experiments and still lacked ITD sensitivity here regardless of the rate of stimulation or the interaural electrode pair.

Experiments I and II investigated the relationship of pitch-matching and rate of stimulation to ITD sensitivity. However, neither changes in interaural electrode pair or rate of stimulation elicited ITD sensitivity in subjects who did not show it previously. Therefore, other factors such as lack of exposure to acoustic hearing early in life may be responsible for the lack of ITD sensitivity. Three of the four subjects with ITD sensitivity in this study had at least a small amount of early acoustic hearing. Research on adults with BiCIs shows that many post-lingually deafened adults with BiCIs demonstrate ITD sensitivity similar to that of NH adults; however, pre-lingually deafned adults do not typically demonstrate ITD sensitivity [21]. This supports the idea that early acoustic hearing may be important for development of the auditory pathways that process ITDs, an experience that does not pertain to the many children with BiCIs who are congenitally or pre-lingually deaf. Finally, although all children with BiCIs showed good sensitivity to ILDs even if they do not show sensitivity to ITDs, research has shown that ILDs are less susceptible to auditory deprivation [21].

Because the children tested here showed ILD sensitivity in Chapter 3, and overall poor ITD sensitivity, in order to undersatnd what cues they have access to, it is important to consider findings from other studies regarding tasks that they perform well on when listening through research processors. Recent studies have shown that children with BiCIs without ITD sensitivity demonstrate binaural masking level differences (BMLDs) of comparable magnitude to values seen in children with ITD sensitivity [33], [12]. Note however that the BMLD task does not require subjects to lateralize sounds, rather the task involves detecting a perceptually different stimulus. It appears that children with BiCIs have the ability to use interaural decorrelation in absence of being able to discriminate differences in interaural timing as is the case with ITDs, and this ability seems to exist even if they have not had access to early acoustic hearing. Further research regarding interaural decorrelation and binaural unmasking is warranted to understand the effects of auditory deprivation on spatial hearing.

Binaural maturation may also play a role in determining ITD sensitivity. Research on NH children demonstrated high variability between subjects on tasks of discrimination and lateralization with binaural cues, suggesting that binaural sensitivity is a skill that develops throughout childhood [8]. In addition, other aspects of audition that do not involve binaural hearing, such as backward masking and gap detection develop throughout childhood into adolescence [34]–[37]. Therefore, it reasonable to consider that binaural sensitivity is a skill that is still developing in this population. Future work is required on a large age range of children with BiCIs in order to understand the developmental trajectory of binaural hearing in this population.

In sum two possible factors affecting ITD sensitivity were investigated in this series of experiments: (1) the relationship of pitch-matching and ITD sensitivity and (2) the relationship of stimulation rate and ITD sensitivity. Results suggest that pitch-matching appears to be an effective method to provide optimal binaural sensitivity in a small group of children who demonstrate ITD sensitivity. Furthermore, high-rate amplitude modulated stimuli that are more similar to the stimuli children hear in their everyday clinically programmed processors did not elicit better ITD sensitivity in subjects who had not previously demonstrate ITD sensitivity. Therefore, further research is necessary to investigate other factors that may affect ITD sensitivity such as early acoustic experience, binaural maturation, and/or neural survival.

Conclusions

1) Experiment I demonstrated that pitch-matching appears to be an effective method for identifying an electrode pair that can yield ITD sensitivity for children who use bilateral cochlear implants.
2) Experiment II confirmed that, for most subjects, ITD sensitivity is comparable for low-rate (100pps) stimuli and high-rate (1000 pps) stimuli amplitude modulated at a low rate of 100pps.
3) Subjects who had ITD sensitivity in previous experiments conducted in Chapter 3 maintained ITD sensitivity in the current experiments. However, neither a change in rate

of stimulation nor interaural place of stimulation provided ITD cues to subjects who did not previously demonstrate ITD sensitivity.

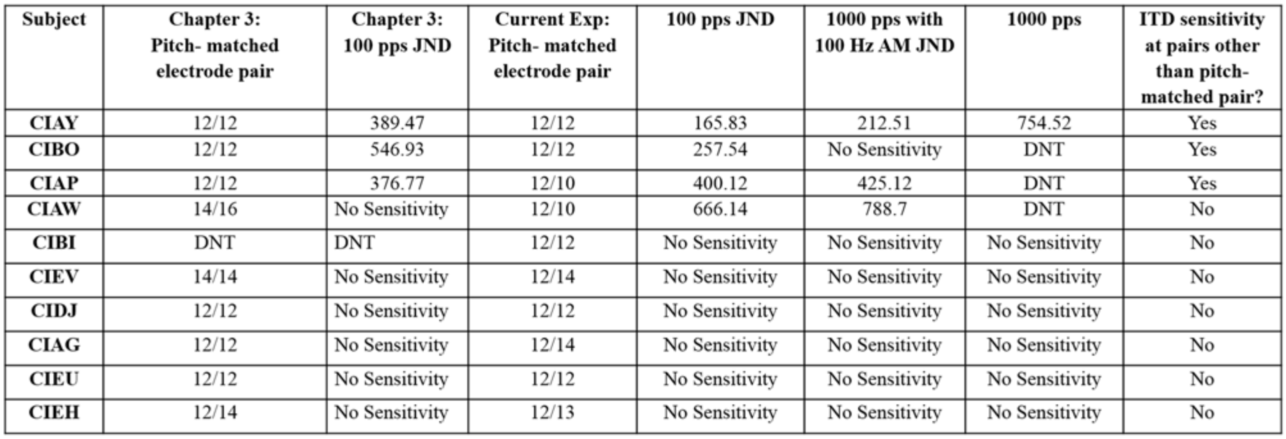
4) The current set of experiments suggest that factors other than anatomical mismatch between the two ears, and stimulus rate may be responsible for a lack of ITD sensitivity in this population. Another possible hypothesis is that early acoustic experience and/or binaural maturation may be required for ITD sensitivity.

Tables

Table I. Subject characteristics

Subject	Sex	Age	Early Acoustic Hearing Experience (mos)	Age at 1st implant (mos)	Inter-implantation Delay (yrs, mos)	BiCI Exp. (yrs, mos)
CIAY	M	15	42	62	0, 10	9, 12
CIBO	F	16	ID at 25, fluctuating	34	1, 1	10,4
CIAP	F	16	ID at 16, progressive	42	1, 8	9,7
CIAW	M	15	None	15	4, 3	9,9
CIBI	F	13	None	13	1, 9	10,10
CIEV	F	14	ID at birth, progressive	32	8, 3	2,0
CIDJ	F	14	None	19	3, 5	9,0
CIAG	M	14	ID at birth, progressive	21	1, 5	11,10
CIEU	F	17	ID at 6, progressive	51	6, 2	3,9
CIEH	M	10	None	13	0	9,0

Table II. Summary of chosen pitch-matched pairs and ITD JNDs for previous research (Chapter 3) and for the current set of experiments.



Subject	Chapter 3: Pitch- matched electrode pair	Chapter 3: 100 pps JND	Current Exp: Pitch- matched electrode pair	100 pps JND	1000 pps with 100 Hz AM JND	1000 pps	ITD sensitivity at pairs other than pitch-matched pair?
CIAY	12/12	389.47	12/12	165.83	212.51	754.52	Yes
CIBO	12/12	546.93	12/12	257.54	No Sensitivity	DNT	Yes
CIAP	12/12	376.77	12/10	400.12	425.12	DNT	Yes
CIAW	14/16	No Sensitivity	12/10	666.14	788.7	DNT	No
CIBI	DNT	DNT	12/12	No Sensitivity	No Sensitivity	No Sensitivity	No
CIEV	14/14	No Sensitivity	12/14	No Sensitivity	No Sensitivity	No Sensitivity	No
CIDJ	12/12	No Sensitivity	12/12	No Sensitivity	No Sensitivity	No Sensitivity	No
CIAG	12/12	No Sensitivity	12/14	No Sensitivity	No Sensitivity	No Sensitivity	No
CIEU	12/12	No Sensitivity	12/12	No Sensitivity	No Sensitivity	No Sensitivity	No
CIEH	12/14	No Sensitivity	12/13	No Sensitivity	No Sensitivity	No Sensitivity	No

Figures

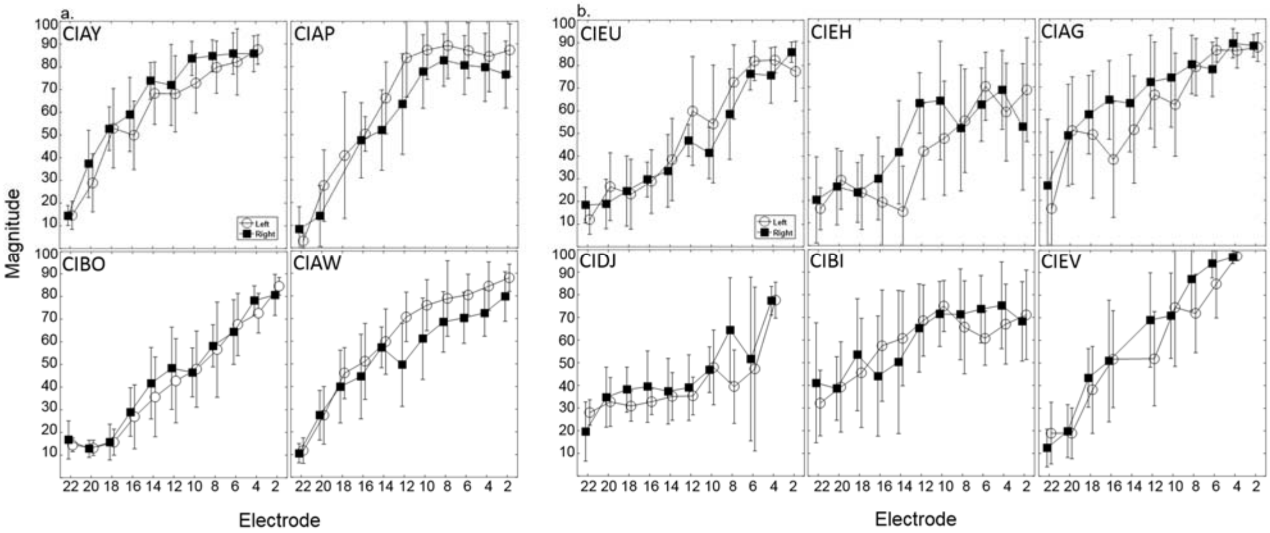


FIG 1. Individual pitch magnitude estimation results for subjects with ITD sensitivity (a) and subjects without ITD sensitivity (b). Average (± SD) change in magnitude response as a function of electrode pair is shown for the right ear (square) and the left ear (circle).

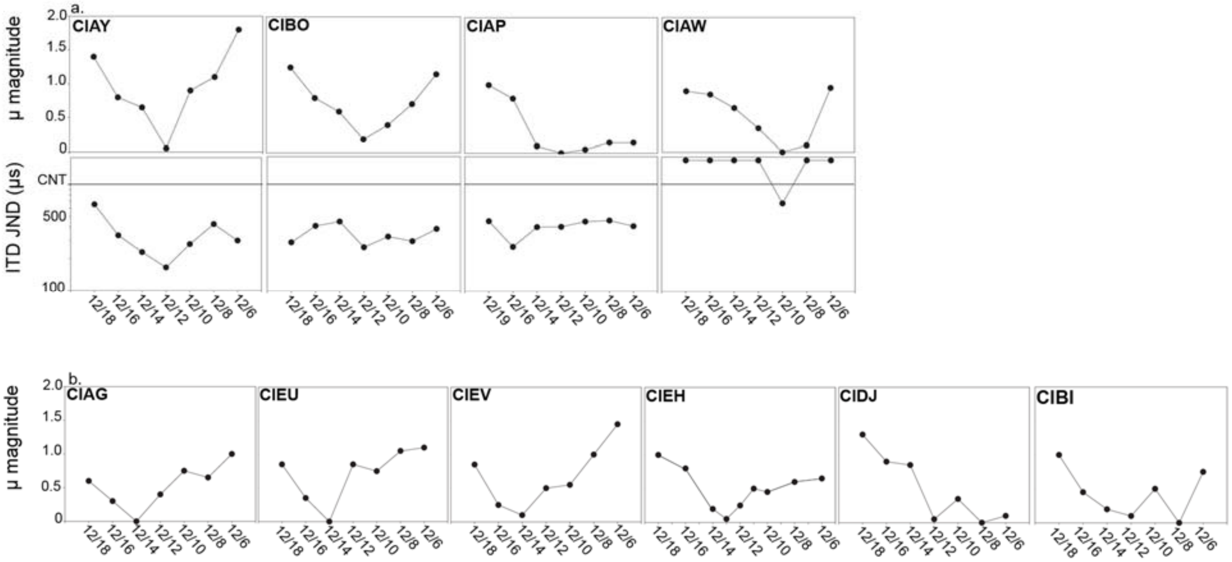


FIG 2. Individual direct pitch comparison (top) and ITD discrimination (bottom) results for the four subjects with ITD sensitivity (a). Individual direct pitch comparison results are also shown for the 6 subjects without ITD sensitivity (b).

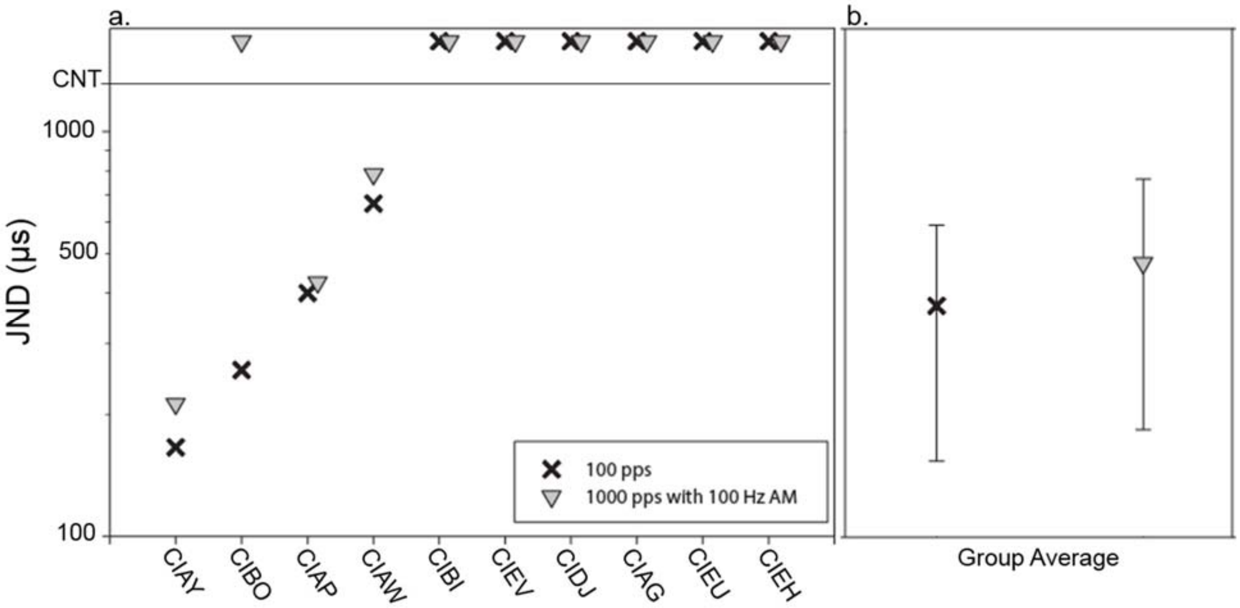


FIG 3. Individual ITD JNDs each stimulus condition (a) and average (±SD) measurable JNDs for each stimulus condition (b).

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Chapter 5: Cognitive abilities in children with bilateral cochlear implants

Abstract

Children with cochlear implants (CIs) perform more poorly than their NH peers on many tasks, including spatial hearing tasks, even when listening with bilateral CIs (BiCIs), and high variability in performance exists among BiCI users. It may be that the ability to inhibit interfering stimuli, shift attention, and hold more items in working memory is related to performance on tasks of spatial hearing. In the current experiment, children with BiCIs were tested using the Tasks of Executive Control (TEC) in order to investigate visual working memory, inhibition, and selective attention. In addition to the TEC, auditory working memory, non-verbal IQ, and expressive vocabulary were also tested. Results demonstrated that the majority of children performed within the range observed in NH peers on all cognitive tasks, suggesting that for this cohort of children the limitations observed on spatial hearing tasks cannot be easily attributed to cognitive function limitations. However, these results should be interpreted with caution as the population tested in this study may not be representative of the population of children with BiCIs as a whole.

Introduction

Chapters 3 and 4 discussed how “bottom-up” peripheral processing in bilaterally implanted patients affects the ability to utilize binaural cues in complex listening environments. However, it is also important to investigate how “top-down” central processing, such as executive function, can interact with “bottom-up” peripheral processes to impact hearing abilities [1]. Children with bilateral cochlear implants (BiCIs) have shown notable variability on measures of speech perception and production, language acquisition, and spatial hearing abilities [2]–[4]. Research suggests that some of the variance in performance, specifically on tasks involving the identification of speech in noise, derives from differences in central processing mechanisms, i.e. executive function [5].

In order to understand how these cognitive mechanisms might impact spatial hearing abilities it is important to first define them. Executive function is an overarching term that can include cognitive abilities such as working memory, attention, problem solving, planning, inhibition, processing speed, etc. There are many models of executive function abilities [6]–[8]; however, for the purposes of this work, the model used will be Miyake et al. [9]. This model was chosen as it includes working memory, attention shifting (or selective attention), and inhibition: three of the major components of executive function that were hypothesized to impact performance on tasks of binaural sensitivity. Working memory is thought to be the “workspace” of executive function and involves holding relevant information in the stream of consciousness while continually discarding old or irrelevant information from the workspace. More specifically, it is thought to consist of the processes that are used to store, manipulate, and integrate incoming information [8], [10]. Attention shifting involves the changing of attention between mental tasks or sets. Finally, inhibition is required to block out prepotent or predominant stimuli, ongoing responses, and maintain interference control. In this model, working memory is thought to be the control station for the other aspects of executive function [9].

Executive function abilities, such as working memory, short-term memory, attention, and inhibition may play a role in the processing of auditory stimuli, specifically spatial hearing abilities. Processing and understanding complex auditory stimuli requires that a listener monitor the incoming signals and combine input with prior knowledge, thus requiring working memory [11]. The ability to localize a sound and attend to an auditory target requires the individual to focus on the stimuli of interest while inhibiting or ignoring the distracting stimuli. To do this, one must hold an item in working memory, shift attention, and inhibit conflicting information.

When listening in complex listening environments, peripheral auditory and central cognitive factors can both influence the ability to locate sounds and segregate speech [12]. A number of studies have investigated peripheral factors that influence performance outcomes of children on speech in noise tasks and have found that, in general, children, unlike adults, include unnecessary auditory information when extracting a target signal from background noise [13]–[15]. More specific to peripheral hearing of children with CIs, the electrical signal received by individuals with CIs is degraded with multiple features compared to the acoustic signal [16], [17], which may affect the ability of the peripheral auditory system to filter sound in complex environments.

The degraded signal provided by CIs may affect central processes as well. For example, research has shown that the added demand on listening from a degraded signal may also require a greater cognitive load in order to decode the signal [18]. In addition, it has been shown that executive function may be reduced when an individual is stressed or fatigued [7]. The theory of limited cognitive resources [19] suggests that an individual has a limited number of cognitive resources that can be allocated to ongoing mental tasks. That is, if one tasks requires a large proportion of cognitive resources (e.g., listening in noise), there will be fewer resources available to allocate to other tasks that are performed simultaneously. Of specific interest to this work, children with hearing impairment exert additional listening effort to decode the degraded signal [20], [21], specifically in noise; therefore, they may have fewer resources available to learn from the auditory signal, maintain social interactions, etc. [20]. Therefore, children with CIs may be at a disadvantage in the classroom compared to their NH peers if the high amount of listening effort is reducing the cognitive resources that are available to hold items in working memory, shift attention, and inhibit outside distractors. It has been shown that children with bilateral stimulation expend less listening effort than children with unilateral stimulation [20]; therefore, for the purpose of this study only children with BiCIs will be tested in order to provide a "best case scenario".

Previous research has investigated cognitive processes that affect performance of children with CIs. There is evidence to suggest that cognitive skills, specifically working memory and attention, are highly associated with speech and language development in children with CIs [22]–[24]. The investigation of executive function abilities as a whole is also important in this population. For example, Figueras et al. [25] compared 8-12 year-olds with NH and with CIs on multiple measures of cognition. They found that, on average, children with CIs performed more poorly than their NH peers on measures of working memory and attention [25]. In addition, compared to NH peers, children with CIs show differences in working memory capacity, including slower processing speeds for rehearsing and retrieving verbal information [26].

Specific to this work, investigating executive function may provide a deeper understanding of the variability in performance on auditory tasks for children with BiCIs. These results may also give insight into clinical implications for identifying children who are at risk for executive function disorders. In the current study, cognitive factors such as attention shifting, working memory, and inhibition were be examined. In addition, standardized tests of expressive vocabulary and non-verbal IQ were administered. Research demonstrates that some of the variance in performance on tasks of hearing, such as speech in noise, derives from central rather than peripheral processing [5]. Therefore, we hypothesize that those who are better able to inhibit interfering stimuli, shift attention, and hold more items in working memory will be better performers on tasks of binaural sensitivity, as this task requires the ability to attend for long periods of time, inhibit outside distractions, and hold the direction of the sound in memory.

Methods

A. Participants

Ten children who were profoundly deaf and used BiCIs participated in the experiment. Table I shows the profiles for each subject. Additionally, all subjects used oral language as their mode of communication and were native English speakers.

Participants traveled to Madison, WI with a legal guardian and testing was conducted at the Waisman Center on the University of Wisconsin-Madison campus. All travel-related expenses were paid and a stipend was provided. All experiments conducted followed regulations created by the National Institute of Health and were also overseen by the University of Wisconsin's Human Subjects Institutional Review Board.

B. Experimental set-up

Testing on measures of cognition was conducted in a quiet office space and a personal computer was used for the computer-based tasks.

C. Tasks

This experiment included four different tests. The tasks of executive control (TEC) was used investigate non-verbal working memory, selective attention, and inhibition. The forward and backward digit span sub-tests from the *Weschler Intelligence Scale for Children-III* (WISC-III) [27] was used to investigate auditory working memory. The Kaufman Brief Intelligence test, Second Edition (KBIT-2) was used to measure non-verbal intelligence. Finally, the Expressive Vocabulary Test, Second Edition (EVT-2) was used to measure expressive vocabulary.

1. Tasks of Executive Control (TEC)

The TEC was used in order to measure working memory, selective attention, and inhibitory skills using n-back and “go/no-go” tasks. The n-back has been used in a variety of literature and performance involving accuracy and speed have been shown to increase with age in NH children [28]. The “go/no-go” task is a measure of an inhibitory control that presents “go” and “no-go” stimuli throughout an experiment. This task has been used frequently to investigate the neural circuitry associated with inhibitory control [29], [30]. The TEC consists of six short subtests (2-3 minutes each). The subtests included three n-back tasks: 0-back, 1-back, and 2-back (explained below). The three n-back tasks were then repeated to include “go/no-go” trials. For all tasks, stimuli were presented on the computer screen, and subjects responded by pressing specific buttons on the computer keyboard.

In the n-back paradigm the subject was presented with a series of stimuli (such as animals, food, etc.) and was asked to press the right and left shift keys depending on the stimulus that appeared. The subject was asked to press the right shift key each time that a standard stimulus appeared, which occurred frequently. Then, they were asked to press the left shift key each time a target stimulus appears, which occurred infrequently, or less often than the standard stimulus. In the 0-back, a target stimulus was specified in the opening instructions (zebra). The task required participants to press a target button each time the zebra appeared, and press the standard button in response to any other image. In the 1-back condition, there was no single target stimulus. The subject only pressed the target button when the stimulus matched the picture immediately preceding, or 1-back (e.g. monkey followed by another monkey). The subject pressed the standard button for all other stimuli. Finally, the 2-back condition required the subject press the target button only when a stimulus matched the one presented two stimuli before it, or 2-back (e.g. an egg, followed by a monkey, followed by an egg). Once again, the standard button was pressed for all other stimuli.

The “go/no-go” task was used to measure inhibitory control. The “go” stimuli consisted of a rapid response (in this case the push of a standard or target button in the n-back task), which established an automatic response (i.e. repetitive pressing of the shift button). When the “no-go” stimulus appears, it required the subject to inhibit the created automatic response. For this task, the “go” trials were all of the standard and target stimuli trials. Then, for the “no-go” trials, a new stimulus of a brown box surrounding the objects was included. The brown box indicated a “no-go” trials and subjects were instructed not to press either shift key when the box was present. The n-back (0, 1, and 2) was presented both without inhibition (not including “no-go” trials”) and with inhibition (including “no-go” trials) for a total of 6 sections that the subject participated in.

2. Digit Span

The forward and backward digit span sub-tests from the *Weschler Intelligence Scale for Children-III* (WISC-III) [27] were used to assess short-term and working memory (forward digit span and backward digit span, respectively). These tests were presented using live-voice with the experimenter speaking at a rate of approximately one digit per second [23]. Prior to initiation of the task the audibility of digits was confirmed for each subject. The forward digit span task required subjects to repeat a list of digits in the order they were presented. The backward digit span task instructed subjects to repeat lists of digits in reverse order. The lists started at two digits and increased in length if subjects provided correct repetitions. Testing ceased when two lists, within a trial, were repeated incorrectly.

3. The Kaufman Brief Intelligence test, Second Edition

The Kaufman Brief Intelligence test, Second Edition (KBIT-2) was used to measure non-verbal intelligence. The task included a test of matrices, which measured the ability to complete complex visual puzzles. If the subject solved four consecutive puzzles incorrectly the task was terminated.

4. The Expressive Vocabulary Test, Second Edition

The Expressive Vocabulary Test, Second Edition (EVT-2) was used to measure expressive vocabulary. This task measured expressive vocabulary knowledge using labeling and synonyms. The participant was shown a picture and responded with one word that was an acceptable label of the picture, a word that answered a question about the picture, or a word that was synonym for the picture context. The participant had to respond within 10 seconds. If the subject provided an incorrect answer for five consecutive pictures then the test was terminated.

Analysis

The TEC calculated performance accuracy in a variety of ways. First, target correct scores were calculated for all subjects. The target correct score is the number of correct responses to target stimuli. Then, the target correct *T* score (standardized score) was calculated by taking the target correct score relative to the scores obtained by participants of the same age in the normative sample. Scores lower than 50 reflect better than average performance and scores higher than 50 reflect poorer than average performance. Scores deemed to be in the normal range fall within one standard deviation of the average.

Next, specific aspects of executive function were examined including, sustained accuracy, processing speed, and selective attention. For each of the aforementioned executive function abilities, a factor score was calculated. Sustained accuracy measured accuracy in responding to the high frequency stimuli (standard) with a faster speed than the low-frequency stimuli (target). This factor score includes the number of correct responses and reaction time for standard stimuli. Processing speed measured the general speed of correct responding (includes the reaction time to both the target and standard stimuli). Finally, selective attention measured how well the subject coordinated and controlled responses (includes the target correct score as well as the overall number of errors). Then, standardized scores (*T* scores) were calculated for all three factors based normative data.

The digit span was scored based on the number of digits a subject could correctly repeat back. Participants received one point for each correct trial when all digits within the given list were repeated back correctly. Scores for the digit span were calculated separately for the forward and backward digit span. Then, the raw scores were converted to the standardized scores, which take into account the normative data.

Standardized scores were also used for the KBIT-2 and the EVT, as the standardized score compares performance against the normative sample. In addition, the standardized scores for these tests take into account the subject age, therefore making it feasible to compare across a wide age range of subjects.

Results

Fig. 1 shows the results of the TEC for the n-back tasks. Panel a shows target correct *T* scores for the n-back without inhibition (only “go” trials) and panel b shows target correct *T* scores with inhibition (including “no-go” trials). A score of 50 is the average and is indicated on the graph with a solid black line. Scores deemed to be in the normal range fall within one standard deviation of the average (indicated on the graph with the gray bars). Scores are ordered based on the subject’s performance on the 2-back in the condition without inhibition. The majority of subjects fell within the normal range on all tasks. In addition, two of the subjects who are the best performers also demonstrated sensitivity to ITDs in Chapter 4.

Fig. 2 shows the average (± standard deviation) target correct *T* score for all subjects for the n-back without inhibition and the n-back with inhibition. Repeated-measures analysis of variance (ANOVAs) were conducted in order to compare across tasks (0-back, 1-back, and 2-back) for the conditions with and without inhibition. Results revealed no significant differences between the tasks for either condition: with inhibition ($p=0.132$) and without inhibition ($p=0.106$), suggesting that overall children with BICIs did not demonstrate worse performance as working memory demands increased.

Although there were not statistical differences found between tasks, as seen in Fig. 1, it is interesting to note that subjects did seem to vary in performance on the tasks. Subjects CIEH and CIAY appeared to improve on conditions without inhibition and subjects CIEV and CIAW showed improvement on conditions with inhibition. That is, performance was better on the 2-back than the 0-back, even though the former is a more challenging task. This suggests that for these subjects it may take longer to understand and engage in the task. On the contrary, one subject (e.g. CIAP), performed very well on the easiest task, the 0-back, but demonstrated poorer performance as working memory demands increased for the 2-back.

Fig. 3 shows the overall factor score analysis for the 6 tasks of the TEC including sustained accuracy, processing speed, and selective attention. Subject data are in order of their factor score for selective attention. A score of 50 is the average and is indicated on the graph with a solid black line. Scores deemed to be in the normal range fall within one standard deviation of the average (indicated on the graph with the gray bars). The majority of subjects have factor scores that fall within the range of normal performance (Fig. 3). However, between-subject variability was apparent. For example, subject CIBI, demonstrated factor scores outside the normal limits for processing speed and sustained accuracy, with sustained accuracy being over two standard deviations above the mean. In addition, subjects CIDJ and CIAG demonstrated selective attention scores that fall outside the normal range. As with the target correct *T* scores, two subjects that had ITD sensitivity in Chapter 3 (CIBO and CIAY) once again demonstrate the best factor scores, specifically for selective attention.

Fig. 4a shows the individual standardized digit span scores for both the forward and backward digit span. Data for individual subjects are ordered based on their performance with the backward digit span (assessment of working memory; higher scores indicate better performance). One subject, CIEU performed the same on both the forward and the backward digit span. Four subjects performed better on the forward digit span, which is the easier task (CIEV, CIBI, CIAG, and CIBO). The remaining 5 subjects performed better on the backward digit span than the forward digit span. Fig. 4b shows the average forward and backward digit span scores for children with BiCIs compared to their chronologically age-matched NH peers (n=10) [31]. A one-way ANOVA revealed no significant differences between the children with

BiCIs and children with NH for either the forward (p=0.147) or the backward digit span (p=0.632).

Fig. 5a shows results from the EVT. Individual standardized scores along with the average and standard deviation are shown for children with BiCIs. In addition, the average standardized scores are shown for age-matched NH children (n=10)[31]. A one-way ANOVA revealed no significant differences (p=0.974) between the children with BiCIs and with NH on the EVT. In Fig. 5b subject's non-verbal IQ based on the KBIT-2 are shown. Individual and average non-verbal IQ standardized scores for the children with BICIs are given along with the average non-verbal IQ for the same age-matched NH children as above [31]. A one-way ANOVA revealed no significant differences (p=0.061) between the children with BiCIs and the children with NH on the KBIT-2. These results suggest that all children in this sample demonstrated non-verbal IQ and expressive language scores within the normal range.

General Discussion

The current study aimed to investigate how a group of children with BiCIs, for whom data on binaural sensitivity measures is available from prior studies in Chapter 4, perform on tasks of executive function. The purpose of the work was to better understand how cognitive skills measured here might relate to performance on tasks of binaural sensitivity. When required to listen to speech in complex environments, research has shown that both working memory and short term memory are necessary [11]. Current tasks of binaural sensitivity used in Chapters 3 and 4 require the ability to attend for long periods of time, inhibit outside distractions, and hold the direction of the sound in memory. In addition, Chapter 3 and 4 revealed high variability of performance with ITD cues for children with BiCIs. It was hypothesized that due to task difficulty on the binaural measures, children with better cognitive abilities may also be better performers on tasks of binaural sensitivity.

Results of the TEC showed that the majority of subjects performed within normal limits for all tasks. In addition, all subjects but two (CIBI and CIDJ) had factor scores (sustained accuracy, processing speed, and selective attention) that fell within the normal limits. On average, no statistically significant differences were found between the 0-back, 1-back, and 2-back for either condition (with and without inhibition) suggesting that increased working memory demands did not negatively affect children with BiCIs. In addition, no statistical differences were found between children with BiCIs and their NH peers on the digit span, suggesting normal working memory abilities in the sample tested.

The results of the TEC and digit span contradict previous research on children with CIs which shows deficits in working memory and attention when compared to their NH peers [5], [24], [32], [33]. Children have also been shown to have more difficulty in speech perception and spoken language tasks that require more executive resource [26]. Furthermore, deficits in working memory are also associated with poor performance on tasks such as speech in noise [34]. However, there were differences in population between the current study and previous literature that may have affected the results. The current study only investigated children with BiCIs, whereas the aforementioned literature investigated children with unilateral and bilateral CIs. In addition, the current study had a small sample size. Finally, the children tested here were typically from families of high maternal education levels.

When investigating the relationship of ITD sensitivity and performance on the cognitive measures it is important to note that only 4 of the 10 subjects tested had sensitivity to ITDs. Therefore, due to the small sample size of children who demonstrated ITD sensitivity, results are described without statistical analyses. Two subjects, CIBO and CIAY, who demonstrated ITD sensitivity in Chapter 4 also had the best target correct *T* score on the n-back as well as the best factor score for selective attention. It is also interesting to note that both of these subjects had the longest duration of early acoustic experience (shown in Table I). It may be that early acoustic experience affects not only ITD sensitivity but also important aspects of cognition. In fact, one specific study shows that early acoustic hearing provides individuals with "auditory scaffolding", or a supportive framework, which allows an individual to interpret and process sequential information (such as the digit span) [35]. When early auditory deprivation occurs, as in some individuals with BiCIs, the effect can be neural reorganization. This may cause a disturbance to cognitive sequencing abilities which are important for ordering sounds in a speech stream [35]. Further research on a larger sample size is necessary to investigate the relationship of cognition to binaural sensitivity as well as the effect of auditory deprivation on cognition in this population.

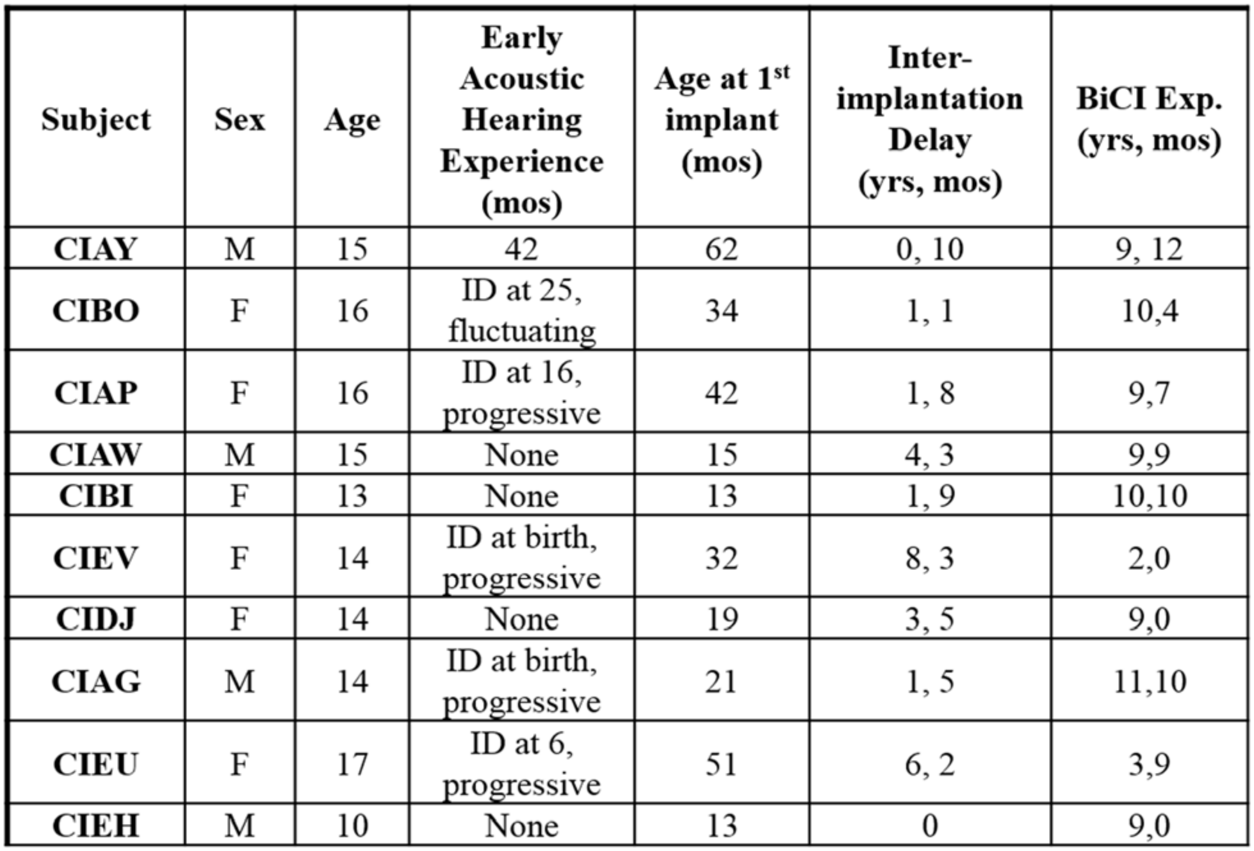
Finally, it is important to note that all subjects tested had non-verbal IQ and expressive language scores that were within the normal range (± 1 standard deviation from the mean) and were not statistically different from their NH age-matched peers. This suggests that IQ and language abilities were not confounding variables in subject performance on the auditory tasks in conducted in Chapter 4. It is important to once again note that the group of children who participated in this study were typically from families with high maternal education levels.

Conclusions

These results demonstrated that the majority of children with BiCIs had working memory, selective attention, and inhibition abilities similar to that of their NH peers. In addition, all children with BiCIs had expressive vocabulary skills and non-verbal IQs within the normal range. Further research is warranted on a large sample of children with BiCIs to more thoroughly investigate executive function and how it relates to spatial hearing abilities in this population.

<u>Tables</u>

Table I. Subject characteristics



Subject	Sex	Age	Early Acoustic Hearing Experience (mos)	Age at 1st implant (mos)	Inter-implantation Delay (yrs, mos)	BiCI Exp. (yrs, mos)
CIAY	M	15	42	62	0, 10	9, 12
CIBO	F	16	ID at 25, fluctuating	34	1, 1	10,4
CIAP	F	16	ID at 16, progressive	42	1, 8	9,7
CIAW	M	15	None	15	4, 3	9,9
CIBI	F	13	None	13	1, 9	10,10
CIEV	F	14	ID at birth, progressive	32	8, 3	2,0
CIDJ	F	14	None	19	3, 5	9,0
CIAG	M	14	ID at birth, progressive	21	1, 5	11,10
CIEU	F	17	ID at 6, progressive	51	6, 2	3,9
CIEH	M	10	None	13	0	9,0

Figures

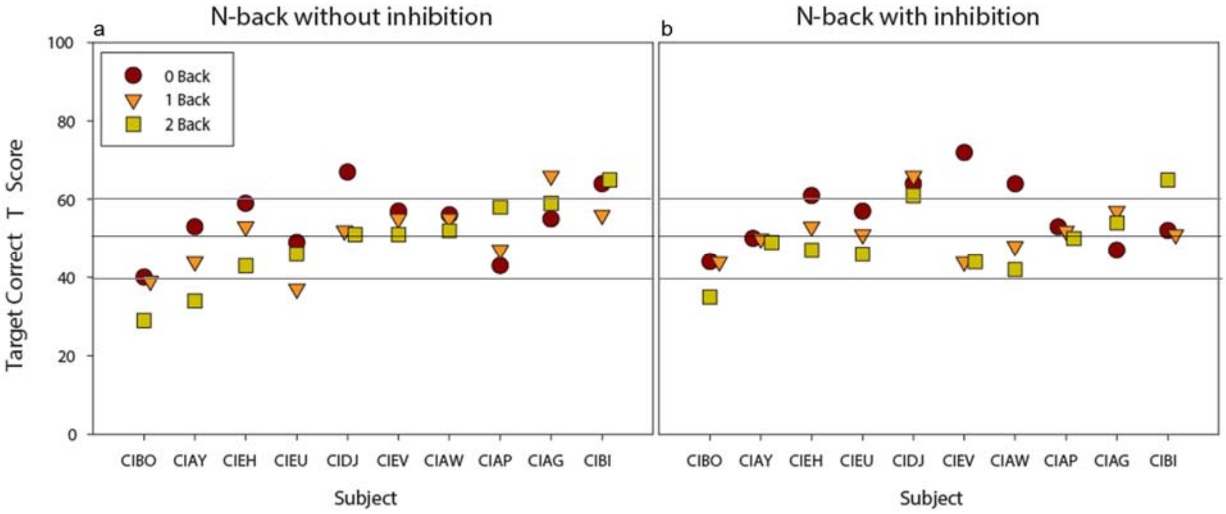


FIG 1. Individual target correct *T* scores for the 0-back (circle), 1-back (triangle), and 2-back (square). Figure 1a shows individual *T* scores for the n-back without inhibition (without "no-go" trials). Figure 1b shows individual *T* scores for the n-back with inhibition (including "no-go" trials).

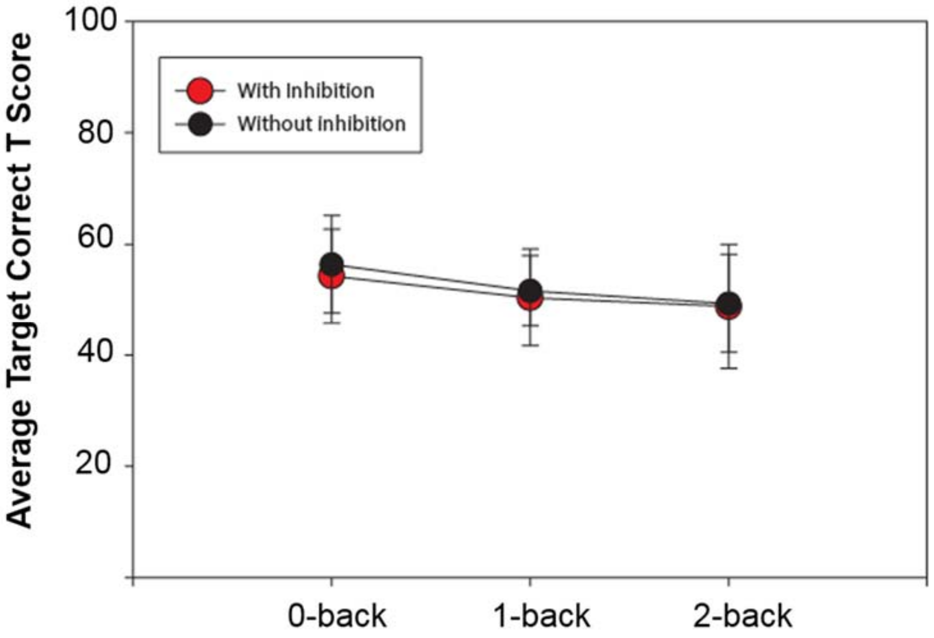


FIG 2. Average *T* score (+/- SD) across each test for inhibition (red) and without inhibition (black).

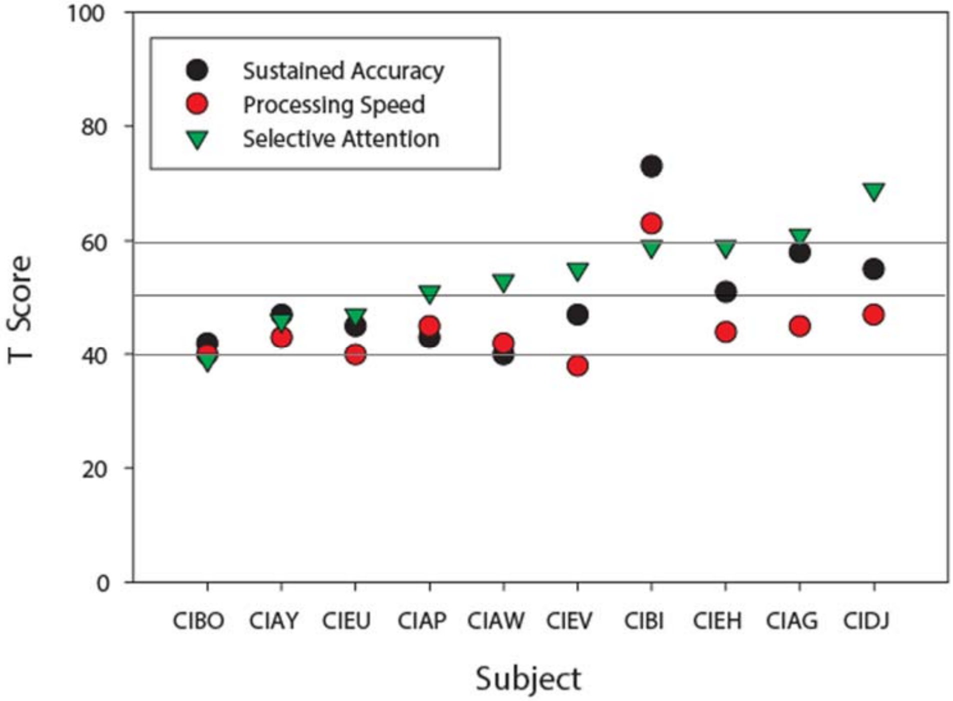


FIG 3. Individual factor scores for sustained accuracy, processing speed, and selective attention.

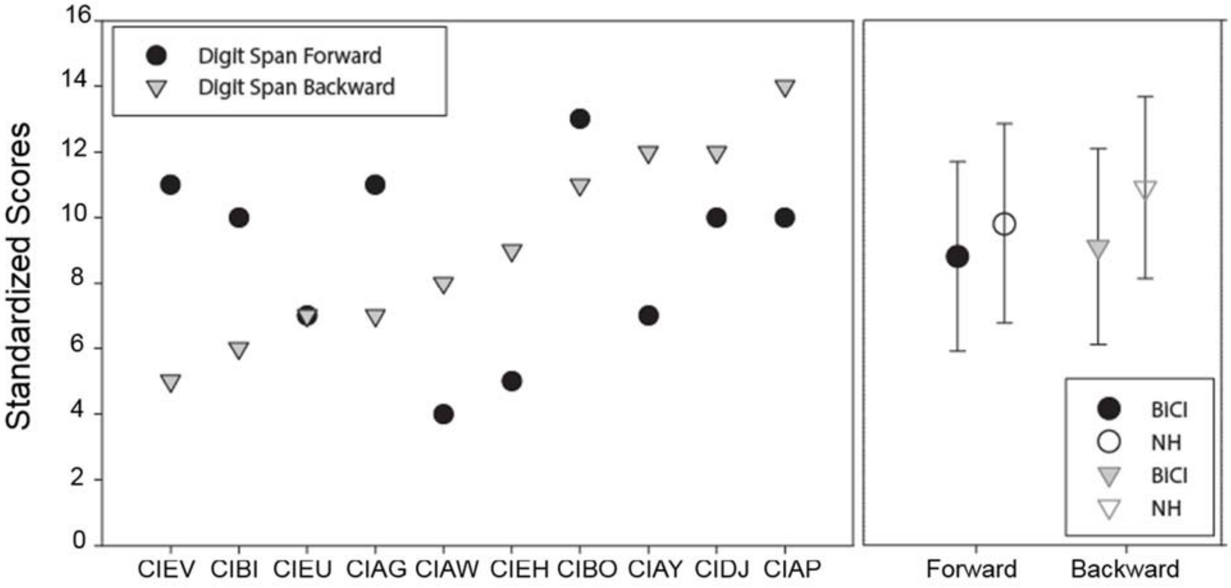


FIG 4. Standardized scores are shown for the forward (circle) and backward (triangle) digit span. Panel (a): Individual forward and backward digit span standardized scores. Panel (b): average (+/- SD) for children with BiCIs and children with NH. NH data is replotted with permission from Misurelli, 2014.

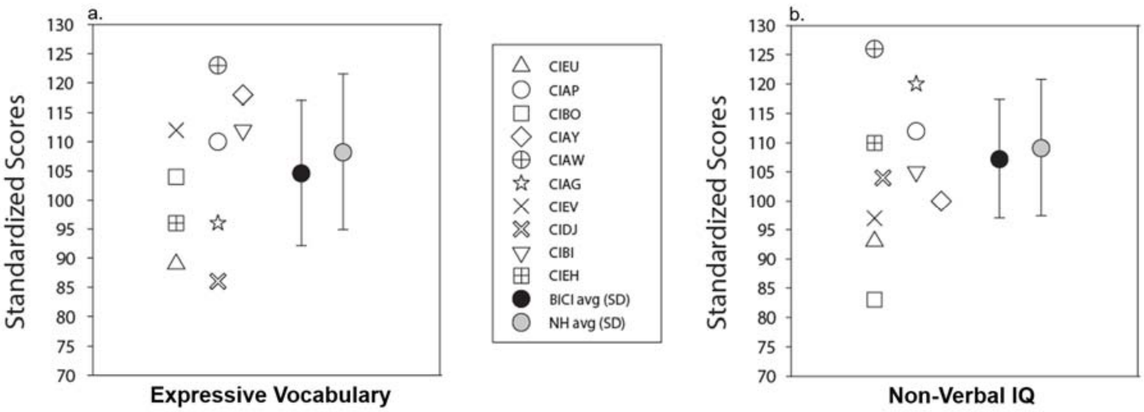


FIG 5. Standardized scores are shown for expressive vocabulary (panel a) and non-verbal IQ (panel b) digit span. On the right side of both figures is the average standardized scores (+/- SD) for children with BiCIs (black) and NH children (gray). NH data is replotted with permission from Misurelli, 2014.

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Chapter 6: Summary and Conclusions

Discussion

The focus of this dissertation was on binaural sensitivity, specifically to interaural time and level differences (ITDs and ILDs, respectively) in children with normal hearing (NH) and children with bilateral cochlear implants (BiCIs). The ability to use binaural cues is vital for spatial hearing tasks such as sound localization in the horizontal plane and segregating speech from noise in complex acoustic environments [1], [2]. Binaural sensitivity is of particular importance in children as they spend the majority of their time in complicated acoustic environments such as classrooms and playgrounds. Previous research has shown that NH children perform very well on tasks that require spatial hearing [3], [4]. However, children with BiCIs perform worse than their NH peers on similar tasks, suggesting that their binaural system is not developing in the same manner [4].

There are many factors that may be responsible for this gap in performance including the lack of fine structure temporal information in current clinical processing, the lack of temporal synchronization between the two CI devices, potential neural degradation due to lack of early acoustic hearing, surgical procedural issues that cause differing depths of electrode array insertion between the two ears, etc. [5]. However, the overall goal of this dissertation was to investigate a subset of the above-mentioned factors to understand how they contribute to the poor spatial hearing abilities in children with BiCIs. The specific aims of this dissertation were to (1) investigate how the lack of temporal fine structure information limits binaural sensitivity by studying the ability of NH children to utilize envelope ITDs, (2) examine binaural sensitivity to binaural cues in children with BiCIs using low-rate pulsatile stimulation on pitch-matched pairs using synchronized research processors, (3) examine effects of place of stimulation, i.e. perceived interaural mismatch in order to evaluate the efficacy of pitch-matching in this population, (4) study the effects of rate of stimulation on ITD sensitivity to determine if clinically relevant stimuli can be used to elicit ITD sensitivity, and (5) investigate cognitive abilities and their relationship to binaural performance.

Chapter 2 investigated the binaural sensitivity of children with NH. Very little is known about binaural sensitivity in NH children (ages 8-10 years). Previous research suggests that children with NH show the ability to detect binaural cues such as ITDs and ILDs [6], [7]. However, to date, little is known about children's sensitivity to stimuli that renders temporal fine structure imperceptible, but provides a strong envelope cue, similar to what exists in current cochlear implant processing. Children with NH were tested on two tasks (discrimination and lateralization) for three stimuli (spondaic words, Gaussian-enveloped tone (GET) pulse trains, and transposed tones). Discrimination was used to measure the left/right sensitivity of children with NH to ITDs and ILDs. Lateralization investigated the usability of binaural cues for perceptual mapping of auditory stimuli. Results showed that overall children's performance was adult-like for both the discrimination and lateralization task for ITDs and ILDs, even when tested using stimuli that rendered temporal fine structure unusable. However, compared to adults, high variability in performance was observed, specifically in regards to lateralization, suggesting that binaural abilities may still be developing in some children as old as 10 years of age.

Chapter 3 investigated the binaural sensitivity of children with BiCIs. The goal of this chapter was to understand the abilities of children with BiCIs to use binaural cues and to compare their abilities to NH children tested in chapter 2. In chapter 3, sensitivity to ITDs and ILDs were measured in 16 children with bilateral Nucleus CIs (ages 10-17 years) for two tasks: discrimination and lateralization. Tasks were conducted using temporally synchronized research processors. Pitch-matched electrode pairs were chosen at three locations along the electrode array (base, middle, and apex). Results showed that all children with BiCIs demonstrated excellent sensitivity to ILDs on both tasks for all electrode pairs tested. On the contrary, ITD sensitivity to low-rate stimulation (100 pps) was measurable in only 50% of subjects for the discrimination task. This is consistent with previous literature investigating children with BiCIs [6]. No subjects were able to utilize ITDs on the lateralization task suggesting that children have a poor spatial representation of ITDs as they lack the ability to perceptually use the ITD cue on a more finely-grained task.

In chapter 4, reasons as to why the majority of children with BiCIs lack ITD sensitivity were investigated, specifically interaural electrode pairs tested (interaural mismatch) and rate of stimulation. In Chapter 3, children with BiCIs were tested on pitch-matched electrode pairs. Pitch-matched electrode pairs are thought to optimize binaural sensitivity through stimulation of the same cochlear regions between ears, thus accounting for any interaural mismatch. Previous research in pre-lingually deafened adults with BiCIs has shown that pitch-matching is an effective manner to optimize binaural sensitivity [8]–[10]. However, children with BiCIs differ from pre-lingually deafened adults with BiCIs as many lack a long period of early acoustic experience. Furthermore, the only “pitch” they have perceived is from their cochlear implant processing (frequency allocation tables). Therefore, it cannot be assumed that pitch-matching will be as effective in children with BiCIs since pitch may be malleable [11], [12]. Due to auditory plasticity it is possible that the children’s perception of pitch is influenced by their frequency allocation tables of the implant programming [12]. However, further investigation of pitch-matching in children with BiCIs, through evaluation of a direct pitch comparison task and an ITD discrimination task, showed that for the majority of subjects with ITD sensitivity the pitch-matched pair yielded the best ITD sensitivity. Therefore, this suggests that pitch-matching is an effective method to enhance binaural sensitivity in children with BiCIs.

The second factor investigated in chapter 4 was stimulation rate. Children with BiCIs were tested on low-rate stimulation (100 pps) and high-rate amplitude modulated (AM) stimulation (1000 pps with 100 Hz AM). It was thought that the provision of more clinically relevant high-rate stimuli may elicit ITD sensitivity in subjects who did not previously demonstrate sensitivity to ITDs. Four children out of ten were sensitive to low-rate stimulation. Three of the four children were also sensitive to the high-rate AM stimulation and had comparable just-noticeable-differences (JNDs). Results from this study were similar to what has been previously found for adults with BiCIs. Like the children with BiCIs, adult BiCI users showed similar JNDs for low-rate stimuli and high-rate AM stimuli with comparable low-rate modulation [9]. This suggests that if children with BiCIs have ITD sensitivity they are able to use clinically relevant stimuli as well.

Finally, in chapter 5, non-auditory abilities were investigated through the Tasks of Executive Control (TEC) computer based program, the digit span from the Weschler Intelligence Scale for Children-III, the Expressive Vocabulary Test, Second Edition (EVT-2), and the Kaufman Brief Intelligence test, Second Edition (KBIT-2). Results of the TEC showed that the majority of children performed within normal limits on all tasks. In addition, the majority of children demonstrated normal processing speed, sustained accuracy, and selective attention. Results from the forward and backward digit span showed no significant differences between age-matched groups of children with BiCIs and children with NH [13]. Furthermore, no significant differences in expressive vocabulary or non-verbal IQ were found between groups of children with BiCIs and age-matched NH comparisons. However, these findings should be interpreted with caution as the population tested was of high maternal education; therefore, the results may be an over-representation of the non-auditory abilities of children with BiCIs. In fact, previous research on a large group of children with BiCIs shows that children with BiCIs have poorer working memory abilities than children with NH [14], [15].

Together, chapters 2-5 suggest that although children with NH are able to utilize binaural cues when given stimuli that mimics cochlear implant processing, children with BiCIs do not show the same abilities. Even when tested with temporally synchronized research processors on pitch-matched pairs of electrodes many children with BiCIs show weak or absent sensitivity to ITDs. Children with BiCIs demonstrate good sensitivity to ILDs but weak or absent sensitivity to ITDs. Chapter 4 demonstrated that changes in place and rate of stimulation did not elicit ITD sensitivity for children that did not show ITD sensitivity previously. In addition, cognitive abilities were similar to that of their NH peers. Therefore, it may suggest that other factors such as early acoustic experience or binaural maturation may be responsible for the lack of ITD sensitivity.

The lack of ITD sensitivity in many children with BiCIs is consistent with previous research on pre-lingually deafened adult BiCI users [16]. Research has shown that profound deafness early in life can cause a lack of typical tonotopic organization of the primary auditory cortex [17]; thus it is possible that other parts of the auditory pathway are affected, including pathways that are responsible for processing ITD cues. In contrast with ITD sensitivity, ILD sensitivity appears to be maintained in both children with BiCIs (as shown in Chapter 3) and prelingually deafened adults [16]. As ITDs and ILDs are at least initially processed by separate circuitry in the brain, it may be that the ITD pathway is more susceptible to auditory deprivation than the ILD pathway [5]. However, it may be that auditory deprivation does not completely eliminate binaural processing, as recent research showed that children with BiCIs without ITD sensitivity demonstrated binaural masking level differences (BMLDs) of comparable size to those of children with ITD sensitivity [18]. It may be that children with BiCIs have the ability to use interaural decorrelation in the envelope rather than specific differences in timing when given an ITD [19], [18].

An additional issue to consider is the aspect of binaural maturation as the auditory system continues to mature throughout adolescence [20]. Research on children with BiCIs has also shown that after greater than 4 years of bilateral hearing experience, some children may show the ability to detect ITDs. In addition, chapter 2 of this dissertation demonstrated variability among NH subjects, particularly on tasks of lateralization, suggesting that some aspects of binaural hearing are still developing as late as 10 years of age. Further research of children with BiCIs on a large age range is necessary in order to understand the developmental trajectory of this population.

Finally, studies in the animal literature have shown that neural circuits related to binaural hearing remain plastic throughout life [21], [22]. In addition, animal models have shown that training and experience can aid in the plasticity of spatial hearing circuitry in the brain [22], [23]. The several hours of testing for the experiments listed in this dissertation may not have been enough to maximize performance on the tasks provided. In fact, research has shown improved performance on discrimination tasks after subjects participated in over 360 trials per day for 6 days [24]. Therefore, future work involving auditory training in children with BiCIs may reveal that spatial hearing abilities can be improved.

Clinical Implications and Future Directions

Chapters 3 and 4 suggested that early acoustic hearing experience may be important for ITD sensitivity in children with BiCIs. Consequently, it is necessary to think clinically about early acoustic hearing in this population and how much is required for development of ITD pathways, especially related to early hearing aid use. Furthermore, previous research shows that children with BiCIs who have an inter-implantation delay of less than 1.5 years demonstrate better binaural sensitivity than children with longer delays [7]. Therefore, future research and should investigate how the age of implantation as well as the inter-implantation delay affects binaural sensitivity so future clinical recommendations can be made.

Chapter 4 showed pitch-matching appears to be effective in this population; therefore, it is feasible for future research to investigate children's performance with pitch-matched maps compared to their everyday clinical map. Furthermore, Chapter 4 demonstrated that children with ITD sensitivity to low-rate stimulation also had ITD sensitivity to clinically relevant stimuli when using temporally synched research processors. If future clinical devices could be temporally synchronized between the ears it is reasonable to assume that children with BiCIs may have access to ITDs in their everyday listening environments, thus providing them with more useful cues to aid in spatial hearing tasks such as sound localization or the segregation of speech from noise.

Finally, chapter 5 demonstrated that in our test population of children with BiCIs cognitive factors, such as working memory, appeared to be similar to that of their NH peers. However, our population of children with BiCIs are not necessarily representative of the population as a whole and future research should aim to target individuals of all socioeconomic status. Understanding cognitive abilities and their relation to cochlear implant patients may help drive future (re)habilitation in this population.

In summary, children with NH are able to utilize ILDs and ITDs, even with stimuli that mimics aspects of cochlear implant processing. However, children with BiCIs show good sensitivity ILDs but weak or absent sensitivity to ITDs. Neither a change in rate or interaural place of stimulation provided ITD cues to subjects that previously had absent ITD sensitivity. In addition, all children had cognitive abilities similar to that of their NH peers. Therefore, factors such as early acoustic experience and/or binaural maturation may be required for ITD sensitivity.

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