EFFECTIVENESS OF LATE IMPLANTATION IN CHILDREN WITH PRELINGUISTIC DEAFNESS: AN EVIDENCE-BASED STUDY OF AUDIOLOGICAL OUTCOME IN RELATION TO AUDITORY PLASTICITY AND LIMITING DETERMINANTS

Janie Chobot-Rodd

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Thesis Committee:

Linda J. Hood, Ph.D	Committee Chair
Anne Marie Tharpe, Ph.D.	Faculty Member
Cheryl DeConde Johnson, Ed.D.	Faculty Member
May 27, 2011	Date of Defense
Roger Coles, Ph.D.	Dean College of Graduate Studies
July 12, 2011	Approved by the College of Graduate Studies

This is dedicated to my family and
colleagues for all of their support,
as well as the children and families
who participated in this project.

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ABSTRACT

EFFECTIVENESS OF LATE IMPLANTATION IN CHILDREN WITH PRELINGUISTIC DEAFNESS: AN EVIDENCE-BASED STUDY OF AUDIOLOGICAL OUTCOME IN RELATION TO AUDITORY PLASTICITY AND LIMITING DETERMINANTS

by Janie Chobot-Rodd

The use of cochlear implants to restore hearing is an effective way to enhance auditory, language and communication skills, promoting more normal maturation and efficient transmission of neural signals within the central auditory system. Current research suggests that when children with pre-linguistic deafness (PLD) miss opportunities to receive auditory input during receptive periods in early development, delayed intervention yields negligible improvement in auditory performance. The absence of early auditory experience is found to retard the otherwise natural progress from primitive signal integration expressed in early life to more sophisticated auditory processing. This makes it harder, if not impossible, for change to occur after prescribed time periods within various sensitive and critical periods of the auditory and language system. The quality and quantity of achievable auditory function ultimately depend on this ability to integrate auditory cues into meaningful perceptual events. A consistent theme in implant outcome has been the inability to generalize about expected benefit in certain groups of children. The purpose of this chart review is to provide information about auditory outcome over the first four years of CI use in children with PLD implanted after the maximum period of plasticity (seven or more years). The retrospective case study compares individual auditory function of eight cases as it changes over time in relation to other variables potentially able to influence performance in late implantation. The main objective is to identify which aspects of auditory function can be readily changed following implant activation, which functions are plastic and can improve with sustained implant use, and which are difficult, if not impossible to

alter. Auditory results appear to be most strongly linked to the pre-implant characteristics of auditory and speech perception development, the ability to resume a more normal maturational sequence following biologically appropriate sound stimulation, the amount of plasticity that exists within the neural networks of the CAS at the time of implantation, and the motivational reasons for implantation. These factors may help to predict the auditory benefits a child will receive with a cochlear implant and provide useful information specific to older children and families considering late implantation.

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DEFINITION OF TERMS

A	auditory only
A1	primary auditory cortex
AS	auditory system
ABR	auditory brainstem response
ACE	Advanced Combination Encoder
AEP	auditory evoked potential
AI	articulation index
ASL	American Sign Language
AT	auditory training
AV	auditory visual
CAEP	obligatory cortical potentials
CAS	central auditory system
CASP	categories of Auditory/Speech Perception
CDC	congenitally deaf cats
CI	cochlear implant
CID	Central Institute for the Deaf
CN	cochlear nucleus
CNIC	central nucleus of the inferior colliculus
EABR	electric auditory brainstem response
ECAP	electrical evoked compound potential
eMLR	electrical evoked middle latency response
ES	electrical stimulation
ESL	English as a Second Language
ESP	Early Speech Perception
FDG-PET	F-fluorodeoxyglucose positron emission tomography
GPA	Graded Profile Analysis
IAC	industrial acoustic company
IC	inferior colliculus

MGB	medial geniculate body
MLR	middle latency response
MMN	mismatch negativity
NLL	lateral lemniscal nuclei
NRT	neural response telementry
OC	aural communication
PET	positron emission tymography
PLD	prelinguistic deaf
SERT	Sound Effects Recognition Test
SGC	spiral ganglion cells
SNR	single noise ratio
SOC	superior olivery complex
TC	total communication
V	visual only

CHAPTER I

INTRODUCTION

The use of a cochlear implant (CI) to promote hearing in young, pre-linguistically deaf (PLD) children has become an effective way to enhance auditory, language and communication skills, promoting more normal maturation and efficient transmission of neural signals within the central auditory system (CAS) (Osberger et al., 2002; Ponton et al., 1999; Ryugo et al., 1997; Sharma et al., 2002). Implantation in early childhood can restore significant auditory capacity to subcortical and cortical auditory systems (AS), permitting a more normal rate of development in higher levels of the pathway (Gordon et al., 2001), and can potentially enhance auditory function following auditory experience (Boothroyd, 2004). This would provide higher brain centers with more consistent and differentiable information about speech sounds (Boothroyd et al., 1997; Eisenberg et al., 2004). Not only would this help regain the ability to detect sounds but also aid in the recognition of auditory spoken language. To what extent a CI can provide improved sensation and the capacity to discriminate the basic acoustic features of time, intensity and frequency necessary for categorization and identification of auditory signals in late-implanted children with PLD continues to be debated (Naito et al., 1997). Consistent to the “information processing” model as discussed by Dowell and colleagues (1995), sensation is dependent on sound stimulation being received at the peripheral level while perception requires processing of auditory signals as they are shaped by the action of the central auditory system (Dowell et al., 1995; Ruben R., 1997).

Current research suggests that when children with PLD miss opportunities to receive auditory input during receptive periods in early development, delayed intervention yields negligible improvement in auditory performance (Kral et al., 2001, 2006; Kral & Eggermont, 2008; Merzenich & Jenkins, 1995). Merzenich and Jenkins consider cortical plastic processes to be competitive and influenced by sensitive/critical periods. They suggest that absence of early sound stimulation could potentially retard the otherwise natural progress from primitive signal integration expressed in early life to more sophisticate auditory processing, making it harder, if not impossible, for change to occur after a certain prescribed time period. Merzenich and Jenkins further argue that as cortical plasticity processes are competitive, a dominance of early visual American Sign Language (ASL) would "competitively occupy language areas normally dominated by auditory inputs, and without (probably even with) heavy training, competitively limit the establishment of hearing-based speech constructs across these same forebrain zones" (p. 255 in Julesz & Kovacs, 1995). According to Eggermont and Ponton (2003), specific limitations imposed on cortical maturation following prolonged early auditory deprivation appear to correlate with changes in structural, electrophysiological, and behavioral outcome. Their review produced evidence that certain subsystems within the cortex mature in the absence of sound stimulation while others require stimulation during a limited critical period in order for maturation to proceed. Their investigation concluded that PLD children implanted at the end of a relevant critical/sensitive period achieve only limited subsequent maturation within their central auditory pathways. When developmental windows for brain plasticity are lost, implantation might yield only minimal effects on the capacity to represent new response patterns, and thus retard the CAS's ability to integrate new acoustic cues into meaningful perceptual events. Based on Cortical Auditory Evoked Potential (CAEP) studies of congenitally deaf children, a sensitive period has been identified in the CAS that is time-locked during development. Implantation after the age of seven has been suggested to mark the end of maximal plasticity in the auditory pathways for complex/speech sounds (Sharma et al., 2009).

Understanding the basic principles of neurobiology such as maturation, myelination, synaptic growth, plasticity, stimulation and deprivation is important as it carries significant implications for auditory function in terms of the ability to self-organize during development and reorganize following changes in sensory input (Illing, 2004; Stiles, in Julesz & Kovacs ed., 1995). Although much has been written about the potential for lifelong learning and adaptation to changing environments from brain plasticity, maladaptive plasticity can also occur and affect aspects of auditory development when appropriate speech/sound stimulation does not occur during specific critical/sensitive periods in early life (Eggermont, 2008).

A consistent theme in clinical CI outcomes has been the inability to generalize about expected benefit in certain groups of children (Dowell et al., 1995). Not all children implanted early perform well nor do all children implanted late perform poorly. Although there are many demographic characteristics explaining 35-51% of the observed variance in outcome among implanted children (Dowell et al., 1995; Geers et al., 2003; Surant et al., 2001), age of implantation in children with early auditory deprivation has been reported to be the major determinant of auditory outcome (Nikolopoulos et al., 1999). Research has shown that a better chance of improvement in speech perception and language is noted when implantation occurs early (Busby et al., 1992; Fryauf-Bertschy et al., 1997). As a general rule, when implantation occurs after the speech acquisition period, speech sound perception and language develop more slowly with poorer performance outcome (Kirk et al., 2002; Zwolan et al., 2004). Consistent with this, studies using animal model also report much slower auditory learning in late-implanted congenitally deaf cats' central auditory development (CDC) (Klinke et al., 1999, 2001; Kral et al., 2002).

While humans have a genetic predisposition to acquire speech, spoken language requires exposure to auditory speech sounds (Rauschecker, 1999). The effects of inactivity can be reversed by subsequent auditory stimulation, but only when activation occurs within prescribed critical/sensitive periods (Kral et al., 1999, 2001). Unfortunately, sustained effects of inactivity causing auditory deprivation can lead to a loss of responsiveness and selectivity within the AS. Both neural (bottom-up influences) and cognitive operations (top-down influences) appear to be the most malleable only during early development (Kral & Eggermont 2007; Pisoni et al., 2000). The functional capabilities of the auditory pathways begin at the level of the auditory brainstem with its multiple nuclei facilitating extensive subcortical processing of auditory information (Ryugo et al., 1997). Ryugo et al. suggest that the endbulbs of Held, a large synaptic structure capable of promoting function in the temporal domain, provide high-fidelity synaptic transmission along with temporal analysis of speech sounds such as prosody and phoneme duration critical to effective speech recognition. In a more recent study, restoration of auditory nerve synapses of the endbulbs of Held was documented in CDCs following early chronic stimulation (Ryugo et al., 2005). The experiment, however, did not assess whether a sensitive period existed in late-implanted CDC but Huttenlocker & Dabholkar (1997) reported that after four years of life, synaptogenesis begins its pruning process in the AS.

Statement of Problem

Little attention has been focused on behavioral auditory findings when implantation occurs in PLD children who sustain prolonged auditory deprivation. Few clinical studies have looked at auditory outcome in relation to individual variables in this population and few studies have attempted to integrate auditory outcome in the late-implanted child with basic principles of neurobiology. Given the large individual differences generally reported in auditory performance of children with PLD, narrowing the age focus to when plasticity of the AS and auditory performance is known to be at a minimum may reveal unique demographic identifiers that potentially affect auditory speech perception performance (Dowell et al., 2002; Fryauf-Bertschy et al., 1997; Oh et al., 2003; Robinson, K., 1998; Sharma et al., 2002). Research in auditory pathway maturation and neural plasticity may help explain what potential benefits and/or constraints occur following late implantation as it relates to the ability to obtain new neuronal response patterns. The quality and quantity of achievable auditory function following implantation ultimately depends on this ability to integrate acoustic cues into meaningful perceptual events (Polley et al., 2008). Moreover, speech perception ability appears to be dependent on auditory pathway encoding at one or more levels of the AS, as referenced by neurophysiologic response data (Firszt et al., 2002).

The purpose of this research is to provide a descriptive analysis of change in auditory function over the first four years of CI use in late-implanted PLD children. Behavioral data are viewed in relation to the growing information from research in neuroplasticity. The main objective is to identify which aspects of auditory function can be readily changed following CI activation, which functions are plastic and can improve with chronic CI use and which are difficult, if not impossible to reverse. Using an "information processing" model as described by Dowell et al. (1995), auditory outcome from a CI will be viewed in terms of the amount of auditory information being received from the environment (sensation) and the ability to process this information successfully (perception). In this model individual patient demographics are used as identifiers of speech perception outcome (Dowell et al., 1995; Teoh et al., 2004). Auditory function in late-implanted children with PLD will be reviewed in relation to behavioral results in a single-listener design. Attention will be drawn to studies that address how auditory pathway response to prolonged pre-linguistic deafness are differentially affected when implantation occurs in a time window beyond the period for maximal plasticity (Dorman et al., 2007; Eggermont & Ponton, 2003; Eggermont, 1988; Firszt et al., 2002; Gordon et al., 2003, 2005; Groenen et al., 1997; Harrison et al., 2005; Lee et al., 2001; Moore D., 2002; Moore & Guan, 2001; Naito et al., 1997; Lee et al., 2001, 2005; Ponton et al., 2002, 2000, 1996; Ryugo et al., 1997, 2005; Sharma et al., 2002a, b, c, 2005; Truy et al., 1995).

Although this type of study is not expected to support definitive conclusions, it may suggest some common baseline from which auditory development and function can proceed in late-implanted children with PLD over long-term CI use. This information could help clinicians and families make informed rehabilitative choices.

CHAPTER II

REVIEW OF THE LITERATURE

Early Auditory and Language Deprivation Affects Maturation of Auditory and Language Systems

Early hearing appears to strongly affect the development of auditory and language competence, and overall functional capacity of the central auditory pathways. A series of studies in animal and human experiments looking at the maturational status of auditory pathways in normal and deaf subjects have observed change in central auditory pathway maturation as a function of early and ongoing development with and without biologically relevant sensory stimulation (Eggermont, 1985; Kral et al., 2001; Ponton & Eggermont 1996; Sharma et al., 2002). Normal development takes place during an age span when the auditory-language system requires external stimulation to develop competence for processing both acoustic and language inputs (Kral et al., 2001). The literature supports the existence of a positive relationship between a normal maturational sequence of central auditory pathways and normal development of auditory/speech perceptual skills (Firszt et al., 2002; Harrison et al., 2005; Sharma et al., 2004). Implanted children are observed to go through a developmental trajectory similar to normal hearing children (Ponton et al., 1999; 2001; Sharma et al., 2002, 2004). Prolonged deafness appears to limit developmental plasticity within the AS (Moore, D. 1985) Age-appropriate cortical responses can be recorded in deaf children following chronic electrical stimulation (ES) when implantation occurs within a sensitive period of 12 years (Ponton & Eggermont 2001) for simple tonal sounds and 3.5 years for complex speech sounds (Sharma et al., 2002, 2005). Using the latency of the P1 CAEP as an objective measure to infer maturity of central auditory pathways, evidence has shown different age cutoffs for maximal malleability in the CAS (Harrison et al., 2005).

Studies of deprivation in the language system have also shown significant interference with normal developmental processes in the absence of biologically relevant early sensory stimulation. Auditory evoked potentials (AEPs) are physiological measures of sound/speech processing routinely used to quantify central auditory function (Tremblay et al., 2007). AEP findings have identified several aspects of language development related to critical-sensitive periods, each affecting different elements of language and each with a different maturational time course (Neville et al., 1992, 1997; Ruben R., 1997). Language has been reported to consist of several sub-systems with different developmental periods (Neville et al., 1992). According to Ruben's (1997) review, phonology matures during the first eight to ten months of life, semantics matures in the first two to four years of life and syntax matures by fifteen years. These functions will be irreversibly affected if hearing is impaired during the given developmental periods. To further complicate this, there are many language areas that are multimodal and receive projections from visual, somatosensory, and auditory systems (Perault et al., 2003). Interestingly, multimodal areas are capable of great cross-modal compensatory plasticity (Rauschecker, 1995). It is therefore difficult to differentiate between deficits in the main input system (the AS), deficits in the language system, and all their interrelated synapses. Late-implantation in children with PLD may thus cause an insufficient activation of the language and related areas for speech sound analysis, making language acquisition difficult if not impossible to achieve (Kral et al., 2001).

The timing of sensory deprivation has a huge impact on the type of functional organization/reorganization that occurs within the deprived and related brain systems. When auditory stimulation is not restored within a specific time frame, animal and human studies show significant functional limitations in physiological, language and auditory performance (Busby et al., 1999; Kral et al., 2001; Ponton et al., 1999, 2001; Sharma et al., 2002, 2005; Skinner et al., 1992). The immature auditory system has a higher capacity for plasticity than a more mature system, suggesting that there is a sensitive/critical period during development (Kral et al., 2002; Sharma et al., 2005). Malleability across brain systems varies in time as a function of the onset of biologically meaningful sound stimulation (Bavelier & Neville, 2002) and appears to be level-specific within the central auditory system (Rauschecker, 1999). The expected ratio of change in existing neural networks compared to the promotion of new pathways is dependent on the point during the developmental time-span at which implantation occurs (Harrison et al., 2005). At one end of the spectrum during early development, Harrison's team speculates that electrical stimulation (ES) will drive organization in neural networks for the first time. At the other end of the spectrum, the mature AS will be affected by ES through modification of previously existing neural networks to constitute a true reorganization. When implantation occurs somewhere between these two ends of the continuum, the affect on the AS will come in part from organization and in part from reorganization. The ratio of organization to reorganization is dependent on the developmental age at implantation and the amount of salient sound stimulation received prior to and following appropriate sound stimulation.

Benefits of Cochlear Implantation

A CI device overcomes the lack of or reduced cochlear function by encoding acoustic information into ES and directing it to the auditory nerve. Spectral information is transmitted to the auditory nerve by allocating a frequency range to each electrode channel according to the cochlea's tonotopic organization (Thai-Van et al., 2007). The CI provides important cues necessary for auditory awareness of sounds and speech perception. A range of sounds from high to low frequencies is conveyed by the electrodes located at the basal to apical ends of the CI electrode array. The stimulation delivered to the auditory nerve is then conveyed through the brainstem auditory pathways to the auditory cortex in a similar way to the acoustic processing of sound. Unlike the cochlea, which is fully developed at birth, central auditory pathway maturation is an activity-dependent process and can be promoted either by acoustic or electrical input, provided that chronic ES occurs early in PLD children. The literature supports maturation following a centripetal theory from the auditory nerve towards central auditory neurons with completion of maturation occurring into the teen years in more central areas of the pathway (Ponton et al., 2001). The benefit of a CI in late-implanted children appears to be dependent on the condition of the auditory pathways at the onset of deafness and the available developmental plasticity within the AS (Harrison et al., 2005; Ponton & Eggermont, 2001; Sharma et al., 2002, 2005).

The age at which deaf recipients receive an implant is critical to successful auditory and speech/language performance (Harrison et al., 2005; Kirk et al. 2002; Lee et al., 2004; Nikolopoulos et al., 1999; Osberger et al., 1991; Snik et al., 1997; Waltzman et al., 2002; Zwolan et al., 2004). This is consistent with data from animal models showing enhanced development in functional networks of auditory pathways following early ES as compared to late stimulation (Harrison et al., 1993; Hartmann et al., 2004; Hsu et al., 2001; Kral et al., 2001, 2005, 2006; Shepherd et al., 1997). In the human AS, change following chronic ES has been inferred by improved auditory skill development (Kirk et al., 2002; Tyler et al., 1997). PLD Children implanted at older ages demonstrate poorer speech perception than younger children with similar CI experience. Depending on the type of speech perception test used, different critical age cut-offs have been obtained due to bias introduced by the specific behavioral test performed (El-Hakim et al., 2002; Harrison et al., 2005). Despite this, evidence of critical age-of-implant cutoffs on behavioral outcome has been reported when implantation occurred prior to age three (Kirk et al., 2002), prior to age four (Tyler et al., 1997), prior to age five (Geers et al., 2002), and prior to age six to seven (Lee et al., 2005; Oh et al., 2003; Papsin et al., 2000). Teoh et al. (Part 1, 2004) observed that auditory performance in late-implanted adults with PLD is inversely related to their duration of deafness, with those sustaining ten or more years of sound deprivation reaching performance asymptote after only a year of CI use. Reviewing long-term outcome of cochlear implantation over a four-year period, Oh's group (2003) found that post-linguistically deaf adults did not improve further after the first two years of CI use. They also reported that children with PLD continued to improve and those implanted prior to age five had a faster rate of recovery of speech perception than those who had been implanted after five years of deafness. Furthermore, they observed that children with PLD implanted between five to seven years had the widest variability in individual outcome. Overall, the literature concludes that children implanted under the age of four years show significantly better auditory and speech/language outcome than children implanted after age six and a half (Geers, 2006; Kirk et al., 2002).

The variability in auditory performance appears to relate to neurophysiologic responses at one or more levels of the auditory pathway. The structural maturation of the human auditory cortex is necessary to improve conduction time in individual neurons, which allows auditory information from the thalamus and other cortical areas to arrive synchronously. This results in shorter latency and sharply defined waveform morphology, and may relate to temporal aspects of speech-sound perception necessary for adequate processing (Eggermont & Ponton, 2003; Firszt et al., 2002). Auditory evoked potentials and F-fluorodeoxyglucose positron emission tomography (FDG-PET) imaging of glucose metabolism in brain cortices provide objective evidence of the integrity within the auditory system; poorly formed or absent evoked potentials or lack of hypometabolism in auditory-related cortices are reported to correlate with poorer speech perception outcome and duration of deafness (Firszt et al., 2002; Kelly et al., 2005; Lee et al., 2001; Naito et al., 1997; Nishimura et al., 1999; Oh et al., 2003, 2005; Truy et al., 1995). Evidence recorded from generator sites at one or more levels of the auditory pathway and association areas reflects the ability of ES to promote a more natural maturational sequence within the AS, which ultimately affects overall auditory/speech perception outcome. Measures in brain cortices have provided objective evidence of integrity of the auditory system across different implant age groups. AEPs are dependent on neural synchrony and thus may evaluate critical synchronous components of neural encoding (Firszt et al., 2002). Firszt's group reported that late-implanted PLD adults had limited neural synchrony in their electrophysiologic responses recorded in the thalamocortical pathway and also had poorer behavioral outcome, presumably because it was harder to follow temporal change. Using the P1 of the CAEP as a biomarker for central auditory system development and re-organization, Sharma's data for complex stimuli consistently demonstrated persistent immaturity and/or reorganization as related to P1 latency shifts and waveform morphology in late-implanted PLD children, when implantation occurred after the age of seven (Sharma et al., 2002). The data correspond to previous findings of significantly poorer speech perception and language skills of PLD children implanted after the age of six or seven (Geers, 2006; Kirk et al., 2002; Sharma et al., 2005, 2007, 2009).

Basic Structures and Functions of the Central Auditory System

How early deafness interferes with basic structure and function of the CAS and how it affects information processing operations once auditory stimulation is resumed, can provide important insights into the basis of individual outcome (Pisoni et al., 2000). We know that sound travels along many nerve fibers and nuclei to reach the auditory cortex. Not only is the CAS a collection of nuclei and tracts that relay auditory signals from the ear to the thalamus and auditory cortex, but it also contains parallel and serial processing centers used to analyze and code complex sound stimulation (Webster, 1999). The acoustic content of a signal (i.e., frequency, intensity and timing information) is coded by highly organized neural systems. Humans code acoustic information at birth, but essential maturation is required in the CAS that can only occur as a function of auditory stimulation. During maturation, these changes appear as neural reorganizations and occur throughout the lifespan according to the specific acoustic input delivered to the brain. The auditory signal is delivered from the cochlea in the peripheral AS to the spiral ganglion cells (SGCs) and conducted to the cochlear nucleus through the eighth nerve. From here, two major ascending auditory systems arise: the lemniscal or classical system (part of the ventral pathway) with its tonotopic organization from the cochlea to the cortex, and the non-lemniscal system commonly activated by a multi-modal sensory system starting from the dorsal cochlear nucleus, mixing with the lemniscal pathway in the inferior colliculus (IC) and separating in the nuclei of the medial geniculate body (MGB) to project to the secondary and association auditory areas (Eggermont, 2008). Although both systems conduct auditory signals to the cerebral cortex, it is the lemniscal pathway, with major nuclei in the superior olivery complex of the brainstem (rhombencephalon), the IC of the midbrain, and the MGB of the thalamus, that are the major contributors involved in the fine-tuning of auditory information in the auditory cortex (Illing, 2004). It is the lemniscal pathway that responds to acoustic stimulation and represents stimulus features.

Figure 1 is a block diagram of the various levels of the CAS, which draws attention to the divergence of information to the cochlear nucleus (CN) complex, the establishment of parallel pathways, the convergence to the IC nucleus and a second divergence to the MGB and cerebral cortex (Webster, 1999).

Webster suggests that what distinguishes the AS from other sensory systems is the projections from first order neurons (spiral ganglion cells) which deviate from the classic pattern; they do not all decussate and extend to the thalamus but rather project to several brainstem nuclei in the superior olivery complex (SOC), lateral lemniscal nuclei (NLL) and the central nucleus of the inferior colliculus (CNIC) before sending third-order

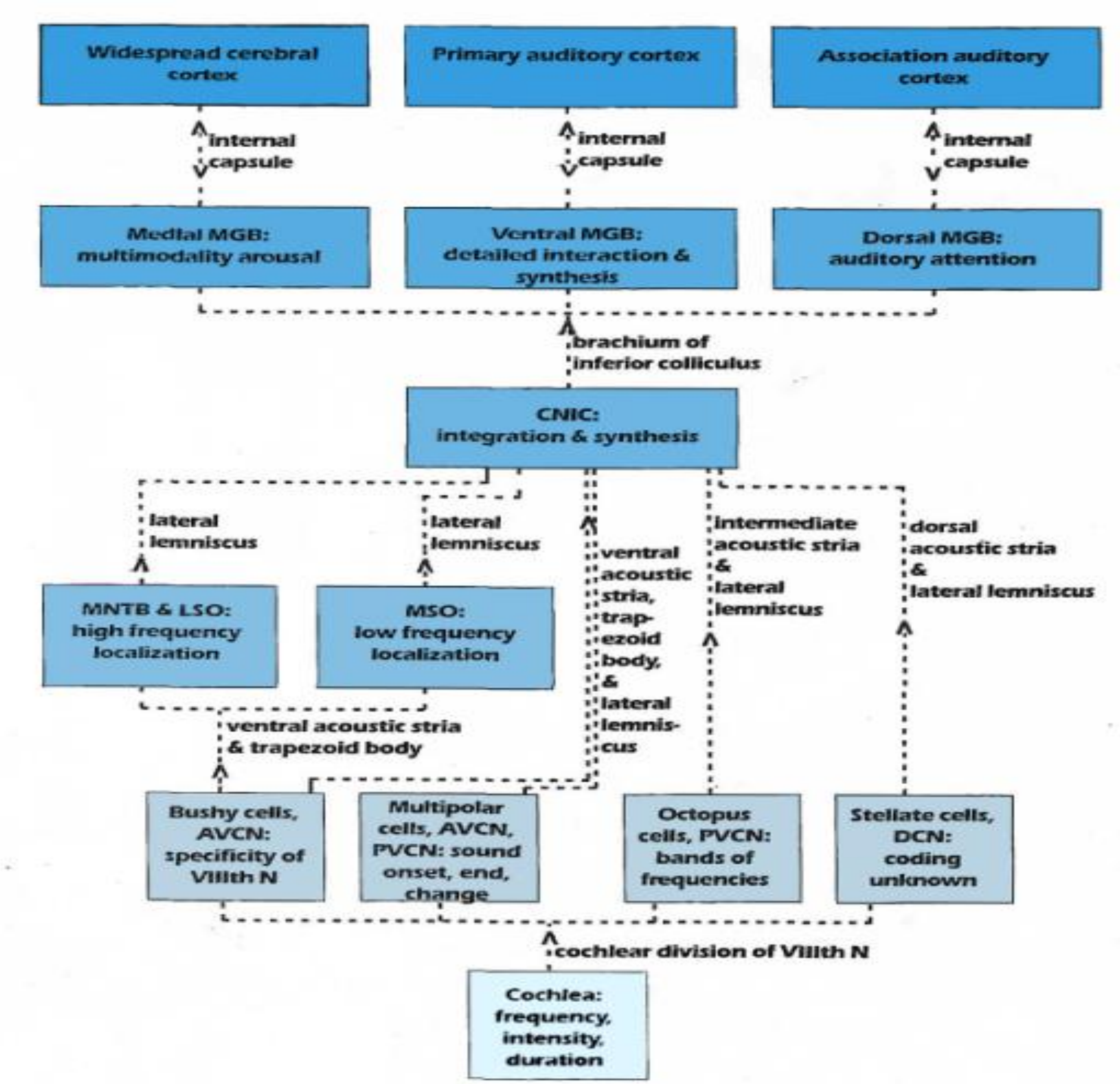

Figure 1. Information processing model of parallel central auditory pathways moving from the cochlea to the cerebral cortex with a pattern of divergence, convergence and another divergence of auditory information (Webster, 1999).

neurons to the thalamus. At the fourth-order neurons, from the thalamus to the A1, the extensive subcortically-processed auditory information is sent to the transverse gyri of Heschl at the auditory cortex. Thus, there exists extensive processing of the auditory signal, starting at the brainstem and mid-brain prior to reaching the auditory cortex and association areas. Results from animal and human studies suggest that the central auditory pathways may play a more important role in the speech and language outcome of CI children and therefore warrants further study (Pisoni et al., 2000).

Maturational Differences in the Auditory Nervous Systems of Normal Hearing and Deaf Children

Auditory experience, with its ensuing neural activity, has a powerful impact during early development. This is demonstrated by the effects of sensorineural hearing loss, which causes changes to the auditory signal and reduced, broadened and/or abolished nerve activity at the cochlea. This impoverished signal is then passed to and through various centers of the AS for processing and into the auditory cortex for understanding, integration and action. The type of signal that is presented will shape the future of the auditory brain. It will either enhance developmental shaping of speech processing circuits when some meaningful input is present or produce neurodegeneration and reorganizations within processing brain centers when there is a lack of meaningful auditory stimulation (Moore D., 2002).

It is helpful to understand the basic stages of normal maturation when studying deaf children with prolonged auditory deprivation; the status of CAS development at the time of implantation appears to play a large role in determining to what extent acoustic information will be made relevant to behavior. The normal maturational sequence progresses differently across CAS development during the first decade of life. Without sound stimulation, the CAS remains at various stages of immaturity (Ponton & Eggermont, 2001). This would affect neural transmission of sound by slower axonal conduction velocities and synaptic transmission time, poorer synchronization, poorer processing capability, and ultimately cause inadequate ability to process temporal aspects of speech sounds (Eggermont & Ponton, 2003; Moore, J., 2002).

Age-related changes in evoked potentials reflect a centripetal developmental time course in auditory pathways to the cortex. The auditory brainstem response (ABR), which is generated in the brainstem, decreases in latency with increasing age until about two years; the middle latency response (MLR), reflects activity in the auditory thalamus and cortex, and is not noted to mature until approximately five years. The cortical P1 response, generated by auditory thalamic and cortical sources, decreases with increasing age, up to about age twelve (Ponton & Eggermont, 2001). These measures have been used in deaf research as an index of maturation of the auditory pathway (Ponton et al., 1996). Using tonal stimulation to elicit a response, observed developmental changes in CAEP extended to around 12 years of age. In the absence of early sound, however, this development would be delayed by the length of sound deprivation (Ponton et al., 1996, 1999). Looking at age-dependent recovery of function in congenitally deaf children, Sharma et al. (2002, 2005, 2008) observed a more normal maturation of CAEP waveform morphology and response latency change when implantation occurred during early development, specifically prior to age four. Using speech stimuli to elicit a response, their data identified that late-implanted children are less likely to exhibit responses similar to those of normal hearing children even after many years of implant use.

A series of studies in animal and human experiments looking at the maturational status of auditory pathways in normal and deaf subjects have shown change in central auditory pathway maturation as a function of early and ongoing development with and without biologically relevant sensory stimulation (Eggermont, 1985; Kral et al., 2001; Ponton et al., 1996; Sharma et al., 2002). Normal development takes place during an age span when the auditory-language system requires external stimulation to develop competence for processing both acoustic and language inputs (Kral et al., 2001). The literature supports the existence of a positive relationship between normal maturational sequence of central auditory pathways and normal development of auditory/speech perceptual skills (Firszt et a., 2002; Gordon et al., 2006; Harrison et al., 2005; Sharma et al., 2004). Implanted children are observed to go through a similar developmental trajectory to normal hearing children, reflecting a general response to sound stimulation but limited by the extent of the auditory deprivation and stimuli used (Ponton et al., 1999; 2000; Sharma et al., 2002; 2004). Prolonged deafness appears to limit developmental plasticity within the AS and potentially leads to permanent deleterious effects throughout the auditory and language systems (Moore D., 1985; Ponton et al., 1999).

Animal Models of Deafness-Induced Limitations in the Auditory Pathway

Using altrical animals, Sheperd and Hardie (2001) found that gross connectivity within the AS was in place prior to the onset of hearing. Studies of long-term deafened animals suggest the maintenance of at least a rudimentary cochleotopic organization within the IC in the absence of afferent input over many years (Sheperd et al., 1999).

They reviewed deafness-induced changes in the auditory pathway of deaf animals and found potential functional neural responses able to:

> 1) Generate and propagate action potentials via CI from partially degenerated SGCs;
>
> 2) Activate partially degenerated SGCs by ES and remain unaffected following long-term deafness;
>
> 3) Establish functional neural connections along the central auditory pathway with minimal auditory experience;
>
> 4) Find a rudimentary cochleotopic organization in the central auditory pathway in the absence of extensive auditory experience;
>
> 5) Find temporal resolution, albeit reduced, in the auditory nerve fibers and central auditory neurons;
>
> 6) Find a significant increase in the response latency of central auditory neurons. The authors conclude that the central auditory pathway of long-term deafened animals remains capable of undergoing functional reorganization following reactivation of the auditory nerve using CI.

Maturation and Plasticity of the CAS and Potential Limitations in Deafness

The ability of neuronal networks to change their structure and responsiveness using changing patterns of incoming stimulation is defined by Illing (2004) as plasticity. Many studies demonstrate that plastic changes occur throughout life (Eggermont, 2008; Illing, 2004). When cortical plasticity and the resultant reorganization of the CAS takes place during maturation, the results manifest as long-lasting and profound effects that can be either beneficial or maladaptive to speech/sound development. To obtain maximum adaptation and learning from either acoustic or electric stimulation, early neural activity is necessary to maintain the brain’s plasticity (Eggermont, 2008). Timing of auditory neuronal activity is a crucial factor; the age at which a child becomes deaf and the time when meaningful sound stimulation is introduced have significant impact on the establishment of a wide range of auditory functions starting with cochleotopic representation and ending with development of language-specific phonetic prototypes (filters). A relevant review of CAS maturation and plasticity by Illing (2004) identified seven levels of neuronal organization linking subcortical and cortical mammalian auditory development and function. They are:

a) Neurogenesis: CAS neurons are activated at different times of ontogeny in an evolutionary rather than functional pattern; activation does not begin from lower to higher centers along the pathway (Illing 2004).

b) Axonal growth: Growth begins without instructive help from sensory input but requires patterned sensory activity to maintain the proper course of development. Before birth, axons begin to sprout at the level of the auditory brainstem due to genetic instruction. A critical period is found in ferrets demonstrating a complete loss of plasticity at three months of age, evidenced by the inability of certain neuronal networks to alter their structure and responsiveness to sound.

c) Axonal maturation: Maturational changes of axonal neurofilaments are used as markers of onset of function as it affects the onset of rapid conduction velocity within intracortical axons. Four separate indices of auditory axonal maturation and function are identified with one stage occurring in the brainstem and three within the auditory cortex, each with its own distinct time course influencing a distinct level within the AS (Moore et al., 1996, 1997; Moore & Guan, 2001). The developmental course becomes much slower at higher levels of the AS with the last stage not fully mature until approximately age 15 (Moore & Guan, 2001).

d) Synaptic maturation: synaptic maturation is closely linked to axonal maturation. The endbulbs of Held, one of the largest presynaptic endings of the central nervous system, are located in the lower brainstem and are linked to temporal transmission in cat model (Ryugo et al., 1997, 2005). The authors identified a restoration of auditory nerve synapses in cats by CI and consider that high-fidelity temporal features of sound can be used to mediate more complex functions occurring in the auditory cortex.

e) Cochleotopy: Orderly frequency representation of cochlear loci is noted at all levels of the lemniscal auditory pathway. In the absence of sound stimulation only a rudimentary order is seen without the emergence of any orderly and complete progression of frequencies (Zhang et al., 2002). Of note, deviant sound stimulation is capable of changing the rudimentary order of frequencies by expanding frequency representation and causing either a maladaptive or adaptive reorganization (Reconzone et al., 1993; Schwaber et al., 1993).

f) Descending auditory system: Little is known about the development of the descending countercurrent system except that it is a final link with the brainstem and cochlea. It connects potential inputs to motor projections, feedback and inhibitory interactions on all levels of the CAS. The reduced effectiveness of feedback loops is suspected following early deafness (Kral et al., 2002; Busby et al., 1999).

g) Adult plasticity: Following new auditory experience, animal studies have shown changes in gene expression (c-fos) as noted by neurons responding in the ventral cochlear nucleus in a cochleotopic manner.

Critical, Sensitive, and Age-Related Plasticity

Both human and animal studies show that physiological and perceptual plasticity occurs, to varying extents, within CAS structures following implantation. The language system is also known to have critical/sensitive periods that underlie a finite period of cortical plasticity for development to proceed normally (Ruben, 1997). The effects of auditory deprivation, maturation and plasticity on the CAS are also influenced by specific critical-sensitive periods causing wide variability in auditory outcome, dependent on the duration of deafness (Eggermont & Ponton, 2003; Harrison et al., 2005; Sharma et al., 2005). Age-related plasticity, sensitive periods and critical periods cause a gradation of ensuing developmental effects on neural change, ranging from the less abrupt transitions following age-related plasticity to the specific and very abrupt transition occurring from a specific critical period (Harrison et al., 2005). In between these two extremes and occurring during development is the sensitive period when the maximum effects of experience on brain development occur during a limited time period. During each window of opportunity, experience plays a strong role in the instruction of neural circuits to represent information in a way that is adaptive to future function (Knudsen, 2004).

A critical/sensitive period has been reported to exist in humans under the age of six in which sound stimulation in the CAS is necessary for a more natural sequence of maturation to occur. When appropriate sound activation in the CAS occurs after the age of six, a profound immaturity or absence of the N1 in the CAEP is observed (Eggermont, 2008) and a true reorganization or immaturity is maintained, as noted by the polyphasic waveform morphology (Sharma et al., 2005). The behavioral consequences of these immaturities may be subtle in relation to the absence of wave N1, or significant when the morphology of CAEP is extensively immature for all waveforms. In a review of various aspects of auditory cortical plasticity, Eggermont (2008) suggests that a maladaptive plasticity accompanied by undesirable side effects occurs following prolonged early deafness. Early, biologically meaningful neural activity is necessary to trigger and/or maintain normal maturational and adaptive mechanisms (Knudson, 2004). Using CAEP studies, parts of the auditory cortex responsible for generating the long-latency AEP components were arrested during early development in deafness but resumed and/or continued to develop following ES (Eggermont, 2008; Ponton et al., 1996, 1999). After six months of CI use, Sharma's (2005) data show a more normal maturational sequence as evidenced by CAEP recordings. In late implantation, however, there is no clear indication of maturational changes or a catching up to age-appropriate responses despite long-term CI use (Ponton & Eggermont, 2001; Sharma et al., 2005). Interestingly, when deafness occurred at the completion of the normal maturational sequence, the effects on

AEP findings appeared negligible on waveform morphology (Gordon et al., 2003; Ponton & Eggermont 2001; Sharma et al., 2002, 2006).

Development of human central auditory pathways also demonstrates a sensitive period for maximal CI outcome (Harrison et al., 2005; Ponton et al., 2001; Sharma et al., 2002). While a period of prolonged early deafness is sufficient to arrest functional maturation in the CAS, restoration by chronic stimulation from a CI appears possible to at least partly restore a more natural sequence of development (Ponton & Eggermont, 2001). However PLD children implanted after six years of age have been reported to maintain significantly poorer speech perception and language skills than early-implanted PLD children (Kirk et al., 2002; Manrique, 2002). Poor development of speech perception and language skills after the age of seven has been correlated with loss of central auditory plasticity (Oh et al., 2003; Sharma et al., 2002). Studies of speech perception in PLD children implanted at various ages also demonstrate that a sensitive period/age-related plasticity exists, dependent on the specific outcome measure used (El-Hakim et al., 2002; Harrison et al., 2005). A relationship in PLD children exists between age at implantation and long-term speech perception and spoken language abilities (Lee et al., 2004; Oh et al., 2003; Ponton & Eggermont, 2001; Snik et al., 1997). AEP's obtained from implanted children reveal significant maturational delays and deviations in neural activation using non-speech stimuli (Ponton & Eggermont, 2001).

Behavioral, Electrophysiological and Structural Correlates of Human Brainstem and Cortical Maturation

The sequence of prolonged cortical maturation is not specific to the A1 but occurs simultaneously in all auditory cortical, somatosensory and visual cortical areas (Moore &

Guan 2001). The maturation of human auditory cortex has implications for speech perception. In their seminal study, three developmental time periods of cortical maturation were identified beginning from infancy to young adulthood as defined by three distinct axonal systems determined by onset of rapid conduction. Furthermore, axonal maturation is found to parallel human behavioral and electrophysiological maturation (Eggermont & Ponton, 2003).

The perinatal period of auditory maturation and function (from the third trimester of gestation to fourth postnatal month) indicates that the onset of information conduction occurs only through the brain stem. It increases rapidly in axonal conduction velocity and synaptic transmission time to produce relatively mature function (Moore et al., 1996, 1997). This initial period correlates with data from click-evoked brain stem auditory potentials, which demonstrate function at birth, with close to adult values by the first year of life along with rapid synchronous conduction-time responses (Eggermont & Ponton, 2003). The authors report that synchronization is necessary for adequate temporal processing required in speech perception. Using neurofilament immunostaining as a marker of maturation, onset of function in neuronal systems has been found to precede myelination and rapid conduction of transmission of information (Moore & Guan, 2001). The investigators found below age 4.5 months, a fairly mature auditory brainstem with mature and functional axons only in marginal layer I of the auditory cortex. Corresponding to this structural index, only the ABR waves P2 and N2 of CAEP response are observed (Eggermont & Ponton, 2003) as is the auditory-facial reflex which is intact and functional during infancy (Illing, 2004). In the absence of sound stimulation, the electric auditory brainstem response (EABR) is reported to remain arrested until appropriate sound stimulation restores the normal chronology of maturational processes similar to that of a normal development child (Gordon et al., 2005; Thai-Van et al., 2007). Of note, neither the characteristic waveform nor the P1 response latency of the CAEP will even begin the maturational process without sensory input.

The behavioral ability to discriminate speech sounds also develops during the perinatal period in infants. Infants are noted to accurately distinguish individual speech sounds and changes in speech (Eimas et al., 1971; Nozza et al., 1987). Despite the very mature cochlea, brainstem, and mature axons of layer one of the auditory cortex, there is no route for transmission of auditory information to the cortex during early infancy. Layer one has not been found to play any significant role in carrying auditory information to the cortex (Moore & Guan, 2001). Yet during this early period, the infant is able to develop and categorize sounds to form phonetic prototypes prior to word meaning (Kuhl et al., 1992). The ability to form these perceptual-cognitive building blocks without the participation of the auditory cortex suggests to some the plastic potential and analytical abilities of the brainstem (Eggermont & Ponton 2003; Gordon et al., 2003; Moore, J. 2002). Prior to age six months, individual speech sounds in both native and non-native language can be discriminated equally well (Kuhl, 1992). Infants can process many stimulus parameters, such as speech sounds, that differ in many acoustic characteristics across varying speakers. The ability to retain previously heard stimuli for as long as a day demonstrates the beginning of auditory memory (Jusczyk, 1992).

At around five months to one year of age, a second axonal system of cortical development is identified by neurofilament-expressing axons beginning in the deeper layers of the auditory cortex (lower III, IV, V, and VI) which continues to mature and increase in maturity until age five. As part of the thalamocortical system, they are an obligatory link to the ascending AS. The developmental course of this axonal system begins the process for auditory information to be transmitted from the ear and brainstem to the cortex, with full maturation and function occurring until three to five years of age (Moore, J., 2002). Thus, in early childhood, maturing thalamocortical afferents in the deeper cortical layers are the first source of input to the A1 from lower levels of the AS. Parallel to the structural maturity, most scalp-positive evoked potential components come from excitatory synaptic activity in layers IV and lower III (middle latency response, mismatch negativity (MMN), along with the emergence of the P1 late-evoked response) and appear fully mature with respect to latency, amplitude and waveform morphology by age three to five years (Eggermont & Ponton 2003). At this level, the P1 component of the CAEP emerges and begins to mature with sound activation. The function of the thalamorcortical afferents is to carry input from the lower levels of the auditory system to the cortex (Moore J., 2002). Behaviorally, a noticeable transition in speech perception occurs starting at age five to six months when infants are able to differentially discriminate sounds that are specific to their mother tongue (Kuhl, 1992). Using neurophysiological correlates of auditory discrimination, reports have cited differential cortical responses emerging during this time frame in the MMN between native and nonnative language contrasts (Eggermont & Ponton, 2003). At around this time, infants have begun to establish speech filters (prototypes) to categorize sounds into a set of phonetic prototypes and acquire word meaning (Illing, 2004). By six to nine months of age, infants start to take more notice of words that have stress patterns similar to their language and monosyllables that occur within their own language (Trehub, 1976). This shift to a stronger focus on sounds of the environmental language is suggested to be a reflection of maturation in thalamocortical afferents and deeper cortical layers in the process of auditory perception (Moore J., 2002). Eggermont and Ponton (2003) draw the distinction that the development of this deep axonal system coincides in time with the onset and development of perceptual language and specific electrophysiological findings such as the maturing of MLR, T-complex and MMN.

The third axonal system (age period five to twelve years) includes association fibers, which interconnect different areas of auditory cortex within the same hemisphere, and reflects the maturation of axons in cortical superficial layers II and upper III with axonal density reaching that of a young adult. It is largely between this period of age five to twelve that axons in layer II and upper layer III begin to develop increasing action potential conduction velocity and neural synchronization to generate a recordable N1 component of the CAEP (Eggermont, 2008). During this stage, the P1 response matures and N1 response emerges with asymptotic maturation extending into adolescence (Eggermont & Ponton, 2003). The maturation of the N1 appears to be associated with activity coming from upper layer II synaptic activity. Because of the prolonged maturation of superficial cortical layers, the N1 response cannot be recorded using a stimulus rate of 1Hz or faster below the age of approximately seven years (Eggermont & Ponton, 2003). This last axonal system has both intra and interhemispheric axons and forms the basis for greater complexity in cortical processing of auditory input (Moore, J., 2002). Fibers at this level have been reported to belong to the corticocortical systems linking auditory cortex to a variety of areas in temporal, parietal and prefrontal cortical lobes through interconnections in the cerebral hemispheres, allowing the two halves of the brain to work together (Illing, 2004).

Thus, this final stage of maturation of the human auditory cortex parallels maturation of the N1 response and represents the final time course in auditory perception of masked and degraded auditory stimuli (Moore J., 2002). Behaviorally, perception of degraded and masked speech begins to mature and improve steadily between five to twelve years of age (Eisenberg et al., 2000). Moore (2002) draws a parallel between maturation of perception with its improvements in processing skills and the maturation of this last axonal system. During late childhood, maturation of commissural and association axons in the superficial cortical layers provides communication within different areas of the auditory cortex to promote more complex cortical processing. In total, Moore and Guan's three cortical stages of axonal maturation appear to parallel maturation of frequency resolution at around age six, temporal resolution maturing past age 12 and the ability to hear in noise matures at around age 15 years.

Limitations in Cortical Development Stages Following Prolonged Early Deafness in Animal Models

Animal models have demonstrated development of the ascending thalamocortical afferents accompanied by basic connections from the auditory periphery to the A1 following prolonged congenital deafness (Sheperd et al., 1997). Like the brainstem and midbrain, the auditory cortex retains some rudimentary level of cochleotopic organization (Shepherd et al., 2001). Of note, the primary cortex obtains its main input from the lemniscal auditory pathways (Kral et al., 2003). CDC's were also able to retain some rudimentary level of cochleotopic organization in the cortex, even in deafness. Evidence from animal model overwhelmingly reveals that prolonged congenital deafness does not completely arrest the basic connections of the peripheral AS to the articulation index (AI) since some aspects of normal developmental sequence of ascending thalamocortical afferents are retained (Teoh et al., 2004, Part II). Activity-independent processes are proposed to continue to develop, as in the rudimentary tonotopic projections and growth of nerves that occur to certain degrees throughout the AS (Kral et al., 2005; Shepherd et al., 2001). Using PET imaging technique, prelinguistically deaf human adults remain responsive to ES in the A1 but show absence or minimal speech activation of the secondary auditory cortex (Naito et al., 1997; Truy et al., 1995). They speculate this reduction in speech activation might be due to either reorganized or incomplete development within neuronal networks of auditory language processing or their degeneration due to lack of biologically appropriate neuronal stimulation.

The maturing A1 is very sensitive to auditory experience based on functional deficits noted during early development in CDC model (Kral A., 2007). While early chronic ES is able to counter these deficits in a CDC model, malleability decreases with increasing age of deafness. Furthermore, a sensitive period from the second to the sixth month of cat life is observed, coinciding approximately with the onset of puberty. Layer-specific deficits within the A1 are observed during the developmental sequence, as noted by alterations in gross synaptic currents, spread of activation, and morphology of local field potentials (Kral et al., 2002, 2006). The pyramidal cells of layers II/III are affected, projecting to higher-order secondary auditory cortex and infragranular layers which receive feedback (top-down) projections from higher-order auditory cortex.

When ES is initiated at the end of the sensitive period in CDC animal model (after 4-5 months), Kral and colleagues have observed delays in activation of supragranular layers in the cortex and reduction or absence of activity at longer latencies in infragranular layers V and VI (Kral et al., 2007). Their evidence suggests that early, prolonged deafness causes a very different reorganization during postnatal development within the A1. The minimal outward currents in layers IV and III are proposed to indicate incomplete development of inhibitory synapses accompanied by alterations of neural activity from layer IV to supragranular layers. Feedback projections from association areas to A1, primarily to the infragranular layers V and VI, are poorly developed and corticofugal projections to subcortical auditory structures, which send long-ranged feedback projections to subcortical auditory areas, become inefficient. Thus, lack of sound stimulation in the A1 produces an inability to process thalamic input accurately and generate output within the infragranular layers, ultimately leading to the inability to process top-down modulations from higher order auditory cortex to the A1 (Kral et al., 2006, 2007).

Thus, in the absence of prolonged auditory experience, effects are not reversible and infragranular activity becomes severely compromised. Projections from higher order auditory cortex to A1 do not develop normally, and thus feedback loops become weakened. The absence of activity in infragranular layers is seen as a functional decoupling of A1 from higher-order auditory cortex when auditory experience is not restored within the sensitive period for recovery (Kral et al., 2002; Kral, 2007). The ensuing disconnect in cortical areas necessary for auditory and language processing would make efficient analysis of incoming auditory stimuli more challenging once misguided postnatal development, poorer malleability within primary auditory areas, and cross-modal reorganization by other systems has occurred. A model depicting deficiencies in the auditory cortex is depicted in Figure 2, showing insufficient connections in the lemniscal input targets of CDC model. Six potential sites of insufficient connections are illustrated by dashed crosses at differential corticocortical areas of A1 and in higher-order auditory cortices. This model implicates extensive deficits in top-down modulations of higher-order cortices and the inability for feed-forward transmission to activate higher-order areas via lemniscal thalamic input in primary auditory areas (Kral, 2007).

Based on work in animal model, Kral et al. (2006) cite three phases of plastic adaptation which occur during maturational changes in CAEP following implantation. An initial fast reorganization phase with no specific sensitive period, as reflected in a fast decrease of P1 latency, is observed within the first few weeks of initial stimulation, apparently due to a quick development of immature synaptic currents and the appearance of more synchronized evoked activity. This is followed by a second slower reorganization phase that takes place within the first months after implantation with a sensitive period of under four years of age in PLD children and five months in CDCs. According to Kral's group, the primary areas during this second stage reorganize and sharpen their feature-detection abilities as suggested by changes observed in the latencies of field potentials, increase in cortical representation of the stimulated cortical region, restoration of the functionality in cortical intrinsic networks, and the appearance of long-latency responses. And lastly, a third, and much slower phase, with its own sensitive period, is speculated to occur, which appears to restore functionality to the primary cortical areas, involving increased activation of higher order cortical areas.

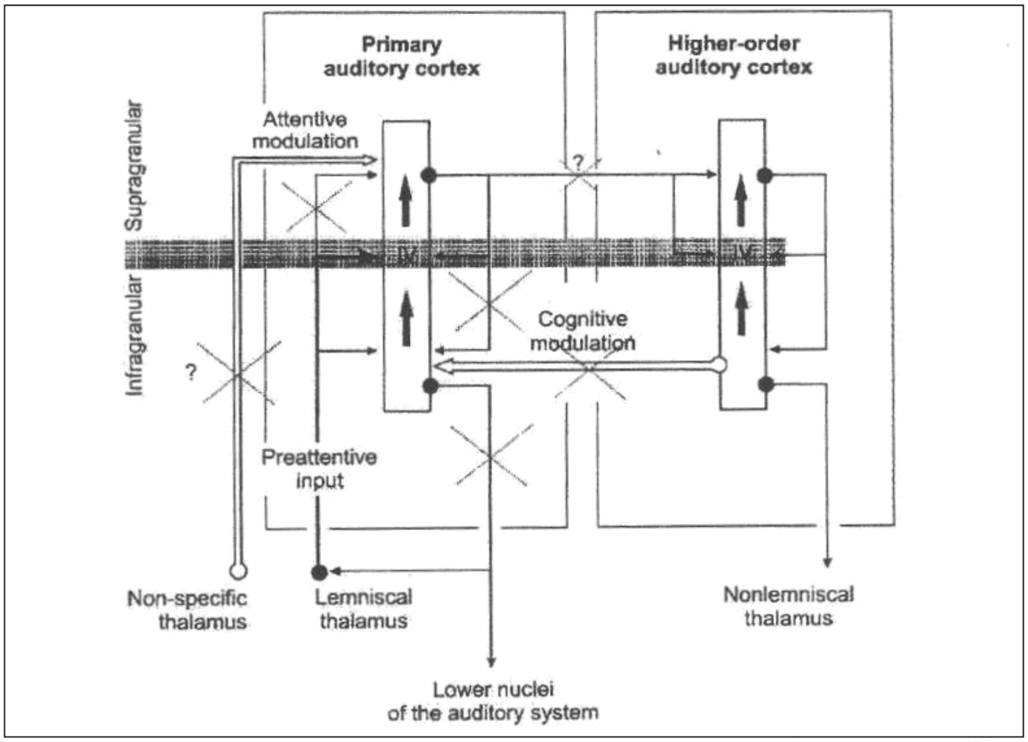

Figure 2. Animal model of deafness deficits as noted in the auditory cortex. Lemniscal inputs are noted to target mostly layer IV and also supragranular and infragranular layers. Neurons in the infragranular layers project to layer IV, layer IV projects to supragranular layers, and supragranular layers project back to layer IV and infragranular layers (‘folded feedback’). Infragranular layers send descending fibers to subcortical nuclei, and feed-forward coupling to the higher-order auditory areas is accomplished via supragranular layers. Descending projections from higher-order cortex target the infragranular layers in A1 (cognitive modulation). This is based on data from Kral et al., (2007) by permission from author.

During this stage, the formation of descending projections from higher order areas to the A1 begin to occur along with the emergence of the N1 component and later CAEPs. These findings are corroborated by Sharma et al. (2007, 2009) CAEP data in congenitally deaf children.

Limitations in Auditory Association Area Development in Human Deafness

During prolonged auditory deprivation, the targets of the secondary auditory and association areas do not atrophy but become colonized or rewired by other sensory modalities due to their inherent cortical plasticity, while the dormant A1 remains reserved for auditory sound (Nishimura et al., 1999; Teoh et al., 2004, Part II). As age of sound deprivation increases, these higher-order cortices undergo cross modal reorganization, making it less likely for them to process auditory input (Naito et al., 1997). While elementary function appears to be preserved despite early deprivation, more complex functions have been reported to be significantly compromised. This implicates processing in primary areas to a lesser degree, and instead targets the more extensive deficits in higher-order cortical areas and its effect of top-down modulation on primary areas (Kral & Eggermont, 2007).

Additionally, the degree of cross-modal reorganization, as noted by glucose metabolism of the secondary auditory and association cortices, is directly proportional to the duration of early deafness (Lee et al., 2001). Unlike the A1, the auditory association area has been shown to be responsive to sign language in PLD adults (Neville et al., 1997). Lee and colleagues suggest that if cross-modal plasticity restores metabolism prior to implantation, children with PLD will show little to no improvement in their hearing function even after long-term auditory rehabilitation. Many have interpreted this to mean that the auditory language areas are rewired to process visual rather than auditory signals, while the dormant A1 remains reserved but underused for auditory processing (Lee et al., 2005; Nishimura et al., 1999). Lee et al. (2001) showed that the amount of cross-modal reorganization (colonization) of the auditory association areas was directly affected by the length of auditory deprivation, which dictated the amount of inherent cortical plasticity found at this level. The amount of early auditory deprivation was found to inversely correlate with speech perception outcome following implantation (Oh et al., 2004). These authors, along with others, suggest that an alternative communication modality could colonize the underused secondary auditory cortical areas after prolonged auditory deprivation, and once rewired, potential improvements in speech perception outcome would be drastically impeded, even after implantation (Merzenich & Jenkins, 1995, p. 247-264). Current findings show that the colonization phenomenon observed in the higher-order auditory cortex is not able to be reversed once the sensitive period for cortical development has ended (Teoh et al., Part II 2004). Collectively, these findings support the theory that functional maturation of auditory, visual and multisensory brain systems are regulated during discrete sensitive periods and a developmental window for brain plasticity exists (Polley et al., 2008).

Deafness-Induced Limitations in Midbrain Auditory Development

Apparently related to normal maturational sequence, the electrically evoked middle latency response (eMLR) was rarely detected at the time of implantation (Gordon et al., 2005). Acute ES did not evoke synchronous activity in the thalamocortical pathways to produce responses particularly in a low arousal or sleeping state. Following six months of chronic CI use, the investigators found better responses in children older than five years versus younger children, suggestive of age-related activity-dependent plasticity in the auditory thalamocortical pathways, but dependent upon length of early sound deprivation. It has been proposed by McGee and Kraus (1991) that MLR generating systems involves not only auditory pathways from midbrain to cortex but also involve contributions from multimodal stimuli coming from reticular formation and non-primary divisions of the auditory thalamocortical pathway. Thus, both the lemniscal, with its sharply tuned neurons responding only to auditory input, and the multisensory, non-lemniscal pathway responding to broadly tuned auditory stimuli and multisensory input, can be activated.

Since the MLR is affected by attention and arousal and the non-primary pathways are influenced by sleep state, due to the connections in the limbic system and reticular formation (Kraus & McGee, 1993), it has been suggested that an added role of attention is required in young children to process sounds at the thalamocortical level (Gordon et al., 2005). Moller & Rollins (2002) suggest that there is a difference in contributions of primary and non-primary pathways related to age and development; early development of primary pathways appears to involve predominately the non-lemniscal system until the phylogenetically younger lemniscal system can take over function during late childhood, and the non-primary system function recedes. Using this theory, a conceptual model was proposed. The non-primary auditory pathways (reticular activating system and lemniscal-adjunct pathways), with its multimodal inputs mature, appears to be somewhat unaffected by a period of auditory deprivation (Gordon et al., 2005).

Activity-Dependent Development of the Auditory Nerve and Brainstem after CI Use

Responses following the electrically evoked auditory brainstem response (EABR) and electrically evoked compound potential (ECAP) demonstrated that the auditory pathway up to the level of the midbrain was not influenced by any period of auditory deprivation or limited by a critical period during childhood (Gordon et al., 2003). Furthermore, chronic stimulation with a CI promoted a seemingly normal developmental time course in children of a wide range of ages and was not dependent on the duration of deafness at the time of surgery (Gordon et al., 2005). The ECAP developed the quickest with the most extensive changes occurring within the first two months of activation, while the later waves of the EABR changed over longer periods of implant use. In line with the ABR Wave V latency in normal hearing children, findings in early-onset PLD children support the theory that auditory pathways remain arrested during deafness, but following implantation a restoration of normal chronology of maturational processes is observed typical to that of normal hearing children over the course of two years (Thai-Van et al., 2007). Thus no critical or sensitive period has been identified at the level of the brainstem even after long periods of prolonged deafness. And, while the auditory cortex demonstrates a lack of functional cortical projections during the first six months of development, it has been suggested that early auditory processing occurs mainly in the brainstem (Gordon et al., 2003). Gordon's group posits that the brainstem takes a more active role in developing some basic auditory discrimination abilities in children when auditory cortices are unable to function sufficiently following long-term deprivation.

CHAPTER III

METHODOLOGY

Chart Selection

The clinical setting used in the chart review is an urban pediatric CI center located in The Bronx, New York. Of the sixty children implanted, only eight charts met all of the following inclusion criteria:

1) Severe to profound pre-linguistic deafness in the frequency region necessary for communication development.

2) Implantation at or after seven years of age and less than sixteen years of age.

3) Absence of early OC training.

4) Minimum of four years of CI use from the date of implantation.

For the purposes of this study, prelinguistic is defined as early-onset hearing loss diagnosed prior to age three, or when diagnosis occurred after this age precluded development of speech until after intervention. All children selected for review used either the Nucleus 24 implant by Cochlear Limited or the next generation Freedom CI system. Unlike many studies in the past, there will be no bias exclusion in the study due to low performers, socioeconomic status, ethnicity, communication mode, functional equivalent hearing level, gender or any disabilities in addition to the child's deafness.

All children received their hearing and cochlear implant management at a single implant facility. Their ages ranged from 9 to 15 years at the time of implantation. A study of this kind ideally requires a homogeneous population where subject characteristics are similar enough not to adversely affect the comparability of performance outcomes. The group of children followed by our center and reviewed in this study is homogeneous with regard to fitting expertise. Each was fitted by the same programming audiologist using consistent parameters and method. All but Case 7 attended the same school for the deaf using total communication (TC) with dominance in sign English vs. oral communication (OC). Each was subject to the same selection criterion for implantation, and each received the same speech processor model, except for Case 8. Identical test protocols and judgment criteria for correct responses were used and applied by a single tester. The children come from a similar subject pool with families from low socioeconomic backgrounds, and no outside rehabilitation was received for any, except Case 1. All children were also well controlled for early onset of deafness, had minimal meaningful early auditory experience and poor early auditory-oral development. Seven cases came from Hispanic backgrounds and one lived in Africa until age eleven. While all cases reviewed were trained in TC and used a combination of OC (spoken and lipreading), their auditory skills varied greatly. Case 7 depended primarily on OC (spoken and lipreading) with sign assist, Case 5 primarily used a combination of sign English and OC, and all others were dominant in Signed English and used lip-reading to communicate.

Table 1a summarizes the general demographic details of each case. Prior to implantation, all children underwent the Graded Profile Analysis (GPA) to document the level of audiological, developmental, academic, and social concern (Daya et al., 1999). The GPA provides an objective measure of concern that reflects a prediction of potential speech perception outcome following CI device (MacDonald et al., 2004). According to Daya et al., 1999, a significant association is observed between speech perception and GPA score. A high level of concern in CI outcome (level 1) was noted for five of the eight children, some level of concern (level 2) for two of the eight, and minimal to no concern (level 3) for one child. None of the children spoke prior to hearing aid usage. The dominant mode of communication in the school environment for seven cases was TC (signed English dominant). Case 7 did not attend a school for the deaf and used primarily OC with sign support. Most families did not present with strong Signed English skills. Spanish or English as a second language (ESL) was spoken in six of the eight families.

Table 1b contains a summary of pre-implant characteristics regarding each child's auditory function and characteristics potentially affecting implant outcome. Each child demonstrated a minimum of two and a half years to a maximum of ten years of auditory deprivation prior to obtaining analog hearing aids. While concern in speech language development was noted in all children, concerns in daily living skills was observed only in one child. All demonstrated reliable responses during threshold determination. Only Case 1's family committed to auditory rehabilitation outside of school therapy. All but one case were full-time users of amplification once aided. Using the count-the-dot-matrix for the calculation of the articulation index (AI), FM-tone sound field threshold levels (Mueller & Killion, 1990) were obtained and all demonstrated 0% AI unaided and less than 20% aided. Although all used some combination of TC, only two cases showed an interest to use OC. The other six cases reported hearing rather than speech was their motivation to obtain a CI and preferred a TC-combination strongly dependent on Signed English. Three of the eight subjects demonstrated adequate lip reading skills of 45% or better on the Craig Test of lipreading.

Mapping Parameters

Seven children in the study were implanted with the Nucleus 24 contour CI using the Esprit 3G speech processor and one received the newer generation Freedom CI device. By the end of their third year all were upgraded to the Freedom speech processor. In every case all 22 active electrodes were placed in the cochlea and medical follow-up was uneventful. All children were mapped by the same audiologist and received the Advanced Combination Encoder (ACE) speech coding strategy set to 25 us/phase, monopolar stimulation, and 8 maxima. All started on 900 pulses per second/channel (pps/ch) stimulation. The parameters were maintained for all with the exception of the child with the longest auditory deprivation who was changed to a slower pulse rate of 500 after two years of use.

General Procedures

The study was designed as a retrospective chart review of auditory plasticity in children with PLD prior to and following chronic electrical stimulation. Implementation of the study was performed under the approval of the Institutional Review Board at both Albert Einstein College of Medicine and Central Michigan University. Behavioral data were obtained from a chart review of children with PLD followed by our center. A single-subject design was used to collect longitudinal data to avoid obscuring facts from group results and to allow examination of both intra and inter-subject variations in auditory outcome. Clinic protocol at our center requires each child considered for implantation to be tested preoperatively and at six-month intervals after initial stimulation to evaluate benefit. Auditory data were therefore available for review at the following time points: preoperatively; approximately six months and then twelve months after activation; and yearly thereafter. Preoperatively, audiometric data were often used over personal hearing aid outcome when maximum gain and output characteristics could not be reached using dated linear analog instruments (as opposed to newer digital instruments). The objective was to assess auditory function and not appropriateness of hearing aid fitting capability.

Tests of speech perception and warble tones were routinely performed in a double-walled industrial acoustic company (IAC) soundproof test suite through a loudspeaker placed at ear-level height at 0 degrees azimuth and approximately 1.5 meters from the center of the subjects' heads. All speech perception testing was administered by the same female talker at hearing levels of 70 dB HL, 55 dB HL, or 40 dB HL via monitored live voice, presented using a face screen that preserves acoustic features while obscuring visual facial features. Test results were first obtained at the higher 70 dB HL as infants and young children with little auditory experience and immature auditory systems required an increased intensity of about 25-28 dB HL above adults to be able to detect speech sound stimulation (Nozza et al., 1990). Nozza's team found infants had much poorer discrimination of speech sounds at softer hearing levels of 40 dB HL and that discrimination improved over time. Testing therefore always began at louder sensation levels due to the immaturity of the AS. Detection thresholds in sound field at pulsed warble tones of 250, 500, 1000, 2000, and 4000 Hz were evaluated along with the detection and discrimination results using the Ling 6-sound test. Speech perception testing was always performed in the auditory-only (A) condition but in those cases with poor auditory skills during pre implant testing, auditory-visual (AV) condition and visual-only (V) condition was also monitored periodically. Testing in these visual modes was conducted in the same room at a distance of one meter from the child with full facial view at a typical conversational level using the same examiner.

Test Measures

The auditory function and language capability of children followed by our center influenced the selection of tests used to evaluate their speech perception skills. The tests selected were chosen to represent a variety of auditory skills and perceptual capabilities and included measures deemed appropriate for our population. Our test protocol consisted of the following closed- and open-set tests: standard three subtests from the Early Speech Perception (ESP) test battery for profoundly hearing-impaired children (Moog & Geers, 1990), the Word Intelligibility by Picture Identification test (WIPI) (Ross & Lerman, 1971); and the Northwestern University Children's Perception of Speech (NU-CHIPS) (Elliot & Katz, 1980). Protocol for open-set tests of word recognition included: the Phonetically Balanced Kindergarten Word lists (PB-K: Haskins, 1949); Lexical Neighborhood Test easy list (LNT; Kirk & Pison, 2000), Central Institute for the Deaf (CID) W-22 word list (Hirsh et al., 1952) and the HINT words presented at 15 dB HL single noise ratio SNR.

Warble-tone thresholds as well as Ling-speech discrimination abilities in sound field were retrieved using a paradigm determined by acceptance of three or more correct responses from five presentations. In the Ling test, three or more sounds needed to be discriminated accurately. We recorded data defining each child's CI behavioral dynamic range for electrical stimulation (determined by finding the difference between the threshold response and the upper limits of comfort) on two electrodes that represent basal, mid or apical locations within the cochlea.

Additionally, the Craig Lipreading test and Sound Effects Recognition Test (SERT) were administered during pre-assessment and an informal numerosity measure was obtained at least twice during the first two years of post-implant use. To assess numerosity, a non-standard, simplified version of the numerosity test described by Busby et al., (1992). The numerosity task requires accuracy of counting to repeated short tones in a temporal series as a function of the number of presentations in the series. A more complex temporal processing measure than detection, this task has been linked to memory processes of recall and/or higher level cognitive functions (Busby et al., 1992, 1999; Kral et al., 2002; Tong et al., 1988).The ability to detect temporal gaps requires a certain level of auditory development involving auditory memory and/or auditory attention (Busby et al., 1992; Kral et al., 2002; Tong et al., 1988). It requires children to count a series of stimuli in each run to obtain an index of short-term memory and/or attention represented by the largest number of beeps recalled at conversational levels (Busby et al., 1992, 1993; Klinke et al., 1999; Kral et al., 2002). It was anticipated that any significant auditory benefits for the perception of speech provided by the CI would be apparent from the above battery of tests.

Categories of Auditory Speech Perception

Due to the large variance of auditory performance noted in late-implanted children with PLD, direct comparison of speech perception among a group of such children is difficult. Several researchers have suggested categorizing the level of performance based on better-than-chance performance levels in the skill being tested (Moog & Geers, 1990; Dowell et al., 1995). No single test provided a suitable measure of speech perception to cover the wide range of performance encountered. Using a categorization approach has been reported to be a successful way to measure outcome when performance is very variable. Dowell's group, and Moog & Geers have used similar categorization scales to measure children with very varied outcomes to determine whether a child is consistently demonstrating a particular perceptual skill from the available battery of tests used by a clinic. Categorization scaling provides a way to look at performance that can reflect change-over-time in performance across age group by using multiple hierarchical tests. All tests used in their battery of tests were standardized tests. The Categories of Auditory Speech Perception (CASP) utilized in this study incorporates nine of these categories using the same scaling parameters, the first seven subtests of the CID Early Speech Perception (ESP) test battery (Geers & Moog, 1990; Geers, 1994) and the next three categories from Dowell et al., 1995). In addition, an easier perceptual skill (category 2) was included in the CASP scale using the Ling-sound discrimination test, a hierarchically easier skill to accomplish than the pattern perception test on the ESP (now category 3) which requires more sophisticated auditory temporal and memory skills. Two other categories were also introduced into the CASP as some of our better performers required more difficult perceptual skills. Category 11 used open-set words at a softer intensity level (40 dB HL) and category 12 used a noise test utilizing an SNR of +15 dB. In addition, Geers and Moog's word identification through word recognition category (Category 6) used an increased in presentation level of 70 dB HL with a score of 28% or more to place into the category rather than 55 dB HL. This differentiation is based on Nozza et al., (1987), where it is reported that infants require an increased intensity to detect speech sounds. Although not infants, our cases initially needed a louder presentation level to access speech cues. The final six categories on the CASP come from Dowell's group, in which more advanced open-set standardized tests are employed to reflect speech perception outcome in children with better performance (Dowell et al., 1995). The CASP used in this study incorporates both scales using the same sub-tests and similar if not identical scoring to define benefit in the category tested.

Thus, using this battery of tests permits a useful measure of auditory performance where no single test could provide a suitable measure of speech perception to cover the wide range of performance displayed by late-implanted CI children. The CASP becomes a vehicle for hierarchically categorizing auditory change in performance. It provides a way to look at performance across age group to determine if a child is consistently demonstrating a particular skill. Each child is placed into one of these categories during each designated time period and a CASP profile is generated over time. As explained above, the CASP scale includes a combination of thirteen closed- and open-set tests (detailed below) that cover the wide range of performance outcomes represented in the chart review. The CASP profile represents a wide range of auditory abilities beginning with no detection of speech sound input to the recognition of speech presented in noise. The tests were chosen because they monitor the essential features of auditory function, ranked in order of increasing difficulty based on above-chance performance from Moogs & Geers (1990) and Dowell et al., (1995). The thirteen-level scale consists of the following criteria:

0 - No detection of auditory/speech sounds at conversational levels (65 dB HL or lower)

1 - Detection of auditory and/or speech sounds at conversational levels only

2 - Discrimination of Ling sounds above chance using a two-pair combination of same or different Ling sounds presented randomly using different combinations of “same and different” Ling sounds. Over 50% correct identification of same and different discriminations is required in at least three or more different Ling sounds

3 - Discrimination of supra-segmental aspects (temporal and stress) of speech patterns in addition to 1-2 but unable to use spectral information among vowels or consonant sounds (>66% score) (patterns subtest of ESP)

4 - Some discrimination of and recognition of vowels in word identification in addition to 1-3. This category demonstrates minimal ability in use of spectral information to identify words in addition to 1-3 (score of >33%) using spondee subtest of the ESP

5 - Consistent word identification (ability to use spectral information for discrimination) and 1-4 (score >50%) (monosyllable subtest of ESP)

6 - Minimal discrimination and recognition of consonants in addition to 1-5 using the closed-set WIPI or NU-CHIPS test (WIPI 28% or higher or NU-Chips 40% or higher) at 70 dB HL. The WIPI utilizes a 6-choice picture format with scores by chance is16% while Nu-CHIPS scores by chance are 25% on a 4-choice format

7 - Discrimination and recognition of consonants on the more difficult WIPI test (50% or higher) or the easier NU-CHIPS test (60% or greater) at 55 dB HL

8 - Minimal open-set speech perception on the LNT, PBK, or W-22 (scores of 20-40%) at 55 dB HL. Each correct word recognition score is 4% using a half list format on the PBK and W-22 word list and a score by chance is 0. The LNT used a full list representation and was scored according to test parameters (Kirk & Pisoni 2000)

9 - Good open-set speech perception (greater than 40%) on LNT test, PBK, or W-22 at 55 dB HL

10 - Greater than 60% on LNT or W-22 word list at 55 dB HL

11 - Greater than 50% on LNT or W-22 word list at 40 dB HL

12 - Greater than 50% on HINT words at SNR of +15 dB with speech at 55 dB

For each measure in the hierarchy, a criterion level of performance is required before proceeding to the next level of difficulty, so every level test has a different criterion level. Results were reviewed by the same clinician who assigned each child to a specific benefit category based on at least two speech perception test scores that indicated significantly above-chance performance, as specified in each category of the particular skill being assessed.

Analysis

Data from a multidisciplinary analysis using the GPA are presented to quantify the degree of concern at the audiologic, developmental, academic and social level. The GPA is calculated from 14 items prior to implantation to determine the degree of concern. Scores qualify each case into one of the following three categories of benefit: 1) scores between -14 and +4 indicate great concern and poor speech perception potential for CI benefit following implantation and were placed into Level one; 2) scores between +5 and +8 indicate some concern and questionable speech perception outcome and were placed into Level two; 3) scores from +9 to +14 indicate little to no concern and suggest good speech perception potential for CI benefit and constitute the highest category at Level three (Daya et al., 1999).

The CASP profile allows a composite of performance in terms of growth function over a wide range of individual abilities and over an extended period of time. The highest level of performance achieved within a prescribed range of scores, as referenced within each specific category, is recorded and graphed at the various time periods to obtain a CASP profile. Children who are unable to use auditory input for the most basic syllabic contrasts were placed into the lowest end of the scale while those who have strong communication skills using only auditory input fell into the higher end of the scale. With a small sample size of eight, both single-subject and group data were comparatively analyzed over a four-year span. Findings from each child's file were used as their own control to avoid obscuring facts following group analysis and allowed examination of intra- and inter-subject variation in auditory outcome. Profiles of auditory performance on the CASP were graphed to allow for visual comparison of both individual and group change over time. Change in auditory ability over the four years yields an auditory plastic potential from which the magnitude of change was used to quantify the capacity within the AS to adapt to altered environmental cues.

Additionally, an information processing model as described by Dowell et al., (1995) was used to assess potential benefit obtained from a CI in relation to general pre-implant demographic identifiers and other auditory characteristics potentially influencing implant success, provided from Table 1a and 1b, and Table 3. From this model, one can capture fine distinctions using a comparison of speech perception progress obtained over time in the CASP data with independent factors that may have a limiting effect on CI success. The model assumes the extent of CI benefit will be directly related to the amount of auditory information received from the environment and the ability of this information to be processed successfully by the individual. The model divides potential limiting variables into those affecting information delivered to the peripheral AS (implant technology, auditory neural reserve/spiral ganglion survival) with those affecting processing of information at higher levels of the AS (central auditory pathway development, sensory deprivation, critical/sensory periods for speech development, meaningful and consistent auditory input, cognitive and other handicaps). Results are graphed and show changes in both audibility and perception in each subject over time with a CI device.

Table 1a. General Pre-Implant Demographics: Background data for eight PLD children obtained at the beginning of the present study.
English as a second language (ESL) and Total communication (TC) are abbreviated.

Subject	1	2	3	4	5	6	7	8
GPA Level and (raw score)*	2 (6)	1 (1)	1 (1)	1 (3)	2 (5)	1 (-1)	3 (10)	1 (3)
Gender	male	female	Female	female	female	female	Female	Female
Age Amplification Begun	Age 4	Age 1.6	Age 10	Age 3.5	Age 2.5	Age 4.5	Age 4.5	Age 3.5
Etiology	genetic	genetic	waardenburg	unknown	congenital	unknown	Genetic	Unknown
Ethnicity	Hispanic	Hispanic	African	Hispanic	Hispanic	Hispanic	Hispanic	Hispanic
Additional Handicaps: 1, 2, 2+	none	None	None	none	2	2+	1	2
Dominant Language used by Family	Spanish	Spanish/ ESL	English	Spanish	Spanish/ ESL	Spanish/ English	Spanish/ ESL	Spanish
Fluent Sign by Family: yes/no	yes	no	no	no	no	no	no	no
Dominant Mode of Communication	TC-sign	TC-sign	TC-sign	TC-sign	TC-sign	gesture	TC-OC	TC-sign
Use of Voice to Communicate	no	no	no	no	yes	no	Yes	
Use of Lipreading to Communicate	yes	yes	no	no	yes	no	yes	no
Mouths or Signs Words While Reading	neither	both	sign	neither	both	can't read	neither	sign
Spoke Prior to Hearing Aids: yes/no	no	no	no	no	no	no	no	n o

* The GPA score is broken into three levels; scores of less than 5 are considered Level 1 and reflect a poor prognostic value; those with scores between 5 and 8 are considered Level 2 and are questionable in prognosis; and those with scores between 9 and 14 are considered Level 3 and reflect a good prognostic value (Daya et al, 1999).

Table 1b. Characteristics potentially able to affect auditory outcome obtained from eight implanted children.

Individual aspects on the GPA provide an index of level of concern. Early support for OC is assumed when family is using only oral language with no sign support.

Subject Identifiers: gender/age implanted/ear implanted	1. M12L	2. F9R	3. F12R	4. F9R	5.F15R	6.F12R	7. F14R	8.F11R
Age in years at Implantation	11.8	9.2	12	9	15	12	13.7	10.7
Unaided Best 2-Frequency PTA (125-4000) in HL	42 dB	90 dB	100 dB	75 dB	70 dB	80 dB	70 dB	78 dB
Unaided Audibility Index (AI %)	0%	0%	0%	0%	0%	0%	0%	0%
Age Hearing Aid use/Habilitation Begun	4	1.6	10	3..5	2.5	4.5	4.5	3.6
Aided AI %	11%	5%	0%	0%	15%	6%	19%	3%
Educational Setting: School for Deaf	yes	yes	Yes	yes	Yes	yes	no	Yes
Full Time Use of Hearing Aids	yes	no	yes	yes	Yes	yes	yes	Yes
Spontaneous use of Voice	no	no	no	no	Yes	no	yes	No
SERT Score:chance/ above chance	50%	chance	chance	chance	chance	chance	78%	chance
Craig Lipreading Score: above chance	74%	45%	chance	35%	chance	chance	66%	chance
Reason for CI - hear vs. oral comm. (OC)	hear	hear	hear/OC	hear/OC	OC	hear	OC	hear
Daily Living Skill Concerns: yes/no	no	no	no	no	Yes	yes	no	no
Motor Developmental Concern: yes/no	no	no	no	no	yes	yes	no	yes
Social Developmental Concern: yes/no	no	no	no	no	yes	yes	no	no
Early Support for Oral Communication (OC)	yes	no	no	no	Yes	no	yes	no

CHAPTER IV

PRESENTATION OF DATA

Pre-implantation Auditory and Non-Auditory Function

Auditory performance varied among the eight cases prior to implantation. Tables 1a and 1b illustrate general pre-implant demographic information and various auditory characteristics potentially able to affect outcome. Based on a multi-disciplinary assessment (GPA), the children qualified into one of three groups of concern. Case 7 scored high enough to be placed into group 3, indicative of no concern in speech perception outcome and a faster rate of improvement following implantation. Cases 1 and 5 obtained scores that placed them in group 2, suggestive of some concern in CI speech perception benefit and a questionable rate of improvement. The others attained scores of less than 5 placing them into group 1, consistent with poor prognostic outcome and the slowest rate of improvement. All cases obtained an unaided AI of 0%. Unaided best 2-frequency pure tone averages calculated using frequencies at octave intervals from 125 Hz to 4000 Hz, however, revealed individual differences between 42 dB HL to 100 dB HL. To distinguish auditory benefit and individual plastic potential over a four-year time period, audibility and perception of sound stimulation were measured first with hearing aids and then over time with a CI. Using an information-processing model as described by Dowell et al. (1995), one assumes benefit from a CI in terms of audibility and speech perception if the child receives a maximal amount of auditory information from the peripheral AS, and is successful in processing this information. This model divides potential limiting factors into those that affect the information presented to the AS and those that affect the processing of this information using CASP profile and AI as the dependent variables. Many of the children were unable to recognize even the most basic syllable contrasts with hearing aids.

For the most part, children with better tonal thresholds (Cases 1 and 7) achieved higher pre-implant rankings on the AI and CASP. Not surprisingly, they also held higher ratings (group 2 or 3) on the GPA along with better performance in speech perception. Case 1 attained a CASP level of 6 and was able to use auditory input to minimally discriminate consonants while Case 7 functioned at a CASP level of 8 by performing minimal open-set perception. Despite being the best performers preoperatively, Cases 1 and 7 sustained the longest period of auditory deprivation prior to identification and amplification (age four and five respectively) and were some of the oldest to be implanted (age 12 and 14 years respectively). On other tests of auditory performance, Cases 1 and 7 also scored the highest on the Craig test of lip-reading and the SERT test of environmental sounds. They obtained scores of 50% or greater on the Craig test and achieved scores of 50% or higher on the SERT. Both cases revealed the lowest hearing thresholds in this group, reflecting the important role hearing played in auditory performance prior to implantation.

Based on characteristics potentially affecting outcome, all but Case 2 were motivated to hear, as noted by their full-time use of hearing aids, but only Cases 1 and 5 received weekly auditory therapy to promote auditory listening. Of note, Case 3 came to the United States at age eleven without any formal education or amplification experience. She was enrolled in the local school for the deaf, obtained amplification and was highly motivated to develop her auditory skills. While all children in the sample cited better hearing as their reason to obtain a CI, Cases 3, 4, 5, and 7 additionally expressed a desire to develop oral speech. Case 1 demonstrated the ability to communicate using OC, but showed little interest in developing these skills in real-world situations. Case 5, on the other hand, enjoyed communicating using both sign and OC and used her skills in real-world situations. Most of the families failed to learn sign language sufficiently, which may have encouraged OC by default. Although a good user of hearing aids and with residual hearing comparable to the better achievers in the group, Case 6 demonstrated the poorest overall score on the GPA, with major concerns in daily living skills significant enough to impact overall functional development. Cases 2, 5, and 8 revealed good lip-reading ability on the Craig test but poor development in their auditory skills.

Auditory Responses at Initial Stimulation with CI

Age at time of implantation ranged from 9 to 15 years. No formal speech perception testing was measured during this initial time period. At the time of surgery or during initial stimulation, two or more ECAP's were recorded at different points on the electrode array using Neural Response Telemetry (NRT). Table 2 illustrates specific auditory characteristics at initial stimulation. The typical dynamic range between threshold and most comfortable level during mapping was 30 to 40 CL (current levels) but Cases 2, 3, and 4 revealed a restricted range of less than 25 CL. The most abnormal loudness growth function occurred in Case 3, who also represented the most extreme case of auditory deprivation in the group. While ECAP responses were observable at initial stimulation (IS), the waveform morphology was often poorly defined, it demonstrated the ability of ES to produce a response from the caudal region of the brainstem upon acute stimulation. All eight cases also readily detected sound stimulation at different frequencies and at substantially lower levels of audibility necessary for conversational speech perception.

Table 2. Auditory identifiers for eight PLD children observed during initial stimulation

Auditory Characteristics at Initial Stimulation								
Subject: (gender/age CI/ear implanted	1. M12L	2. F9R	3. F12R	4. F9R	5. F15R	6. F12R	7. F14R	8. F11R
Device Implanted: Nucleus 24 Contour	yes	yes	yes	yes	yes	Yes	yes	Freedom
Speech Processor: ESPrit 3-G	yes	yes	yes	yes	yes	Yes	yes	Freedom
ACE Strategy:: yes/no	yes	yes	yes	yes	yes	Yes	yes	yes
Rate of Stimulation 900 rate: yes/no	yes	yes	yes	yes	yes	Yes	yes	yes
Mode MP 1+2: yes/no	yes	yes	yes	yes	yes	Yes	yes	yes
Full Electrode Insertion: yes/no	yes	yes	yes	yes	yes	Yes	yes	yes
Restricted Map Dynamic Range: < 25 CL	no	yes	yes	yes	no	No	no	no
CI Audibility Index (CI-AI%):	85%	50%	17%	21%	40%	44%	89%	32%
Best 2-Frequency CI PTA (250-4K Hz.)	23 dB	35 dB	40 dB	47 dB	35 dB	30 dB	20 dB	35 dB
Numerosity:Test (Detect 3 or more beeps in a series):	yes	no	no	no	yes	No	yes	yes
ECAP Response detected at 2 different positions on array	yes	yes	yes	yes	yes	Yes	yes	yes

Post-operative FM warble-tone thresholds obtained with a CI revealed immediate improvements in detection with the CI when compared with pre-operative thresholds obtained with hearing aids, resulting in greater audibility of the speech spectrum. When CI-AI thresholds were calculated and compared with aided-AI results, improvements ranged from 17% in Case 3 to 74% in Case 1. Interestingly, response reliability at 4000 Hz was often poor, especially for the inexperienced listener, as demonstrated by thresholds generally being poorer and/or inconsistent at this frequency. Using a simple version of the numerosity test that required children to correctly identify the number of warble beeps presented in a series of varying beeps up to a series of sixteen presentations, only half of the cohort (Cases 1, 5, 7, and 8) was able to distinguish a series of up to three or more beeps accurately.

Individual Characteristics During the First Four Years of CI Use

Auditory Detection/Auditory Sensation

Figure 3 shows the group average AI calculations over three different time periods using warble-tone sound field threshold levels plotted on the "count-the-dots" matrix (Mueller & Killion, 1990). Values increased substantially following implantation, going from .07 to .47 at initial stimulation and continued to improve over the next four years to .70 as the children became better able to detect and tolerate sound delivered by a CI device. A potential for plasticity is therefore noted in the group average with the largest change at initial stimulation but continuing over the course of four years of CI use.

Individual AI changes are presented in Figure 4 and reveal improved detection thresholds over time for all cases, but to different degrees. Differences in CI-AI change are greatest at the time of initial stimulation for Cases 1 and 7, who attained the highest AI scores of .85 and .89, respectively, while Cases 3 and 4 achieved the lowest scores of .17 and .21, respectively. Over the next three to four years, the large variability in AI outcome narrows but continues to show a sizable difference of .52 between the poorest and best AI scores. Better pre-implant residual hearing and the ability to use OC appear to be positive factors in late-implanted PLD children, allowing better access to auditory cues and increased appreciation for the audibility of sound that carries over for the next four years of CI use.

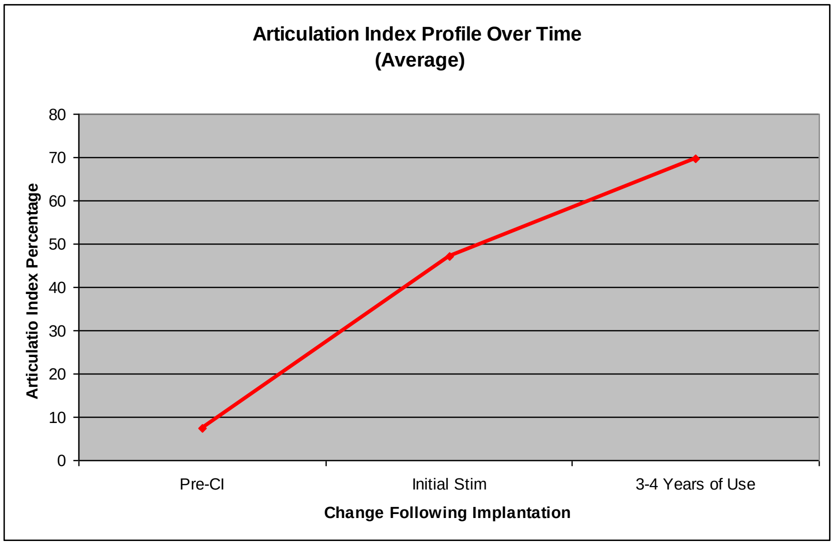

Figure 3. Articulation Index Profile Over Time (Average).
AI percentage plotted on Mueller and Killion's (1990) count-the-dots matrix. Calculation of the articulation index occurs at three different time periods from aided condition, initial stimulation and within the first 3 to 4 year post-implant period.

Auditory Speech Perception

The CASP profile was tabulated for all cases at multiple points starting from pre-implantation and followed over the next four-years of post-CI use. During each period, cases were evaluated and placed into one of thirteen hierarchical categories to index their auditory speech perception achievement level. By connecting a child's overall performance obtained on the CASP at different time intervals, an auditory trajectory of speech perception outcome can be measured over time. Figure 5 depicts average change in CASP levels obtained prior to and following four years of CI use. All cases were able to pass through category 0 as they were able to detect some speech sounds at conversational levels. Generally, there is a slow but steady change in auditory performance over time continuing into the fourth year. This differs from the children's AI scores, where the ability to detect softer sounds initially improved quickly and then slowed over time.

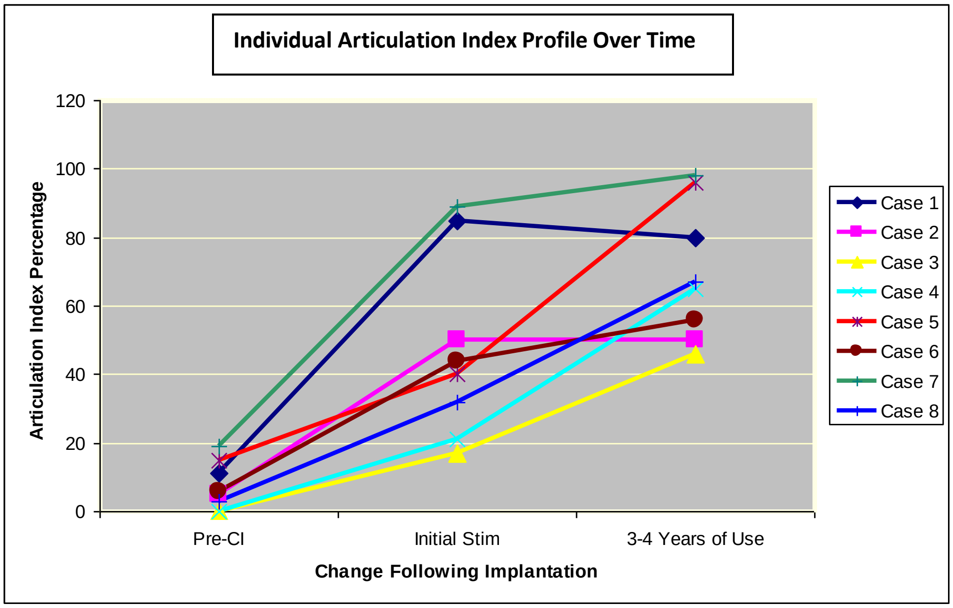

Figure 4. Individual AI profile over time.
Scores start in the hearing aid condition prior to CI, followed by scores obtained at initial stimulation and then after three to four years of CI use.

Figure 6 allows for a finer inspection of individual difference in CASP profile. Individual data appears to be somewhat different in the degree of change in categories and the time required for change to occur. Over time all but one case demonstrates some benefit on the CASP regardless of starting point prior to implantation. Although case 6 shows no growth in perceptual performance over time in sound, audibility continued to improve from .38 at IS to .50 following three to four years of CI use. Cases 1 and 7 continued to make slow and steady change on the CASP over the four years, while Cases 2, 5, and 8 required more time using CI before benefit was detected on the CASP. The pattern of change in categories for Cases 3 and 4 was also different with no clear benefit on the CASP detected after the first year or two of CI use.

From the seven cases demonstrating change, three distinctive groups based on change emerge over time. Pre-implantation, Case 1 was able to perform minimal discrimination and recognition of consonants using a closed-set test and Case 7 was able to perform minimal open-set speech perception test. Over four years of CI use, both cases were able to improve their open-set perceptual skills in a slow but steady manner and followed a similar developmental trajectory ending with a plastic potential of three categories.

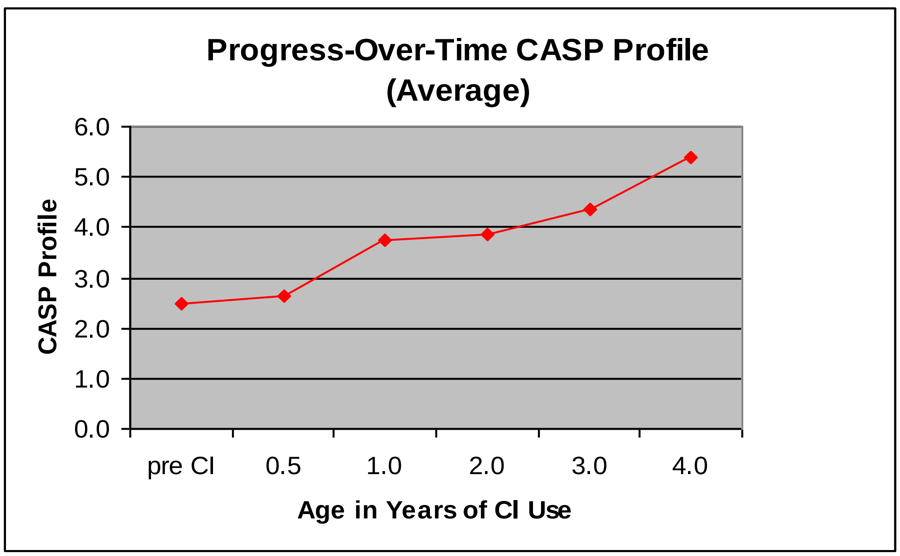

Figure 5. Progress-Over-Time CASP Profile (Average).
Eight cases obtained as six different time periods in the A-only (A) condition beginning with hearing aids and followed over four years of CI use

Group two (Cases 2, 5, and 8) follows a different course of improvement in speech perception ability. Initially they were able to detect only tones and Ling sounds at conversational levels, but over a protracted period of time auditory function improved minimally until the fourth year when all cases in this group performed at category 6, obtaining scores significantly above chance on formal closed-set tests of consonant discrimination and recognition. Interestingly, these three cases each demonstrate a plastic potential of 5 categories after four years of CI use.

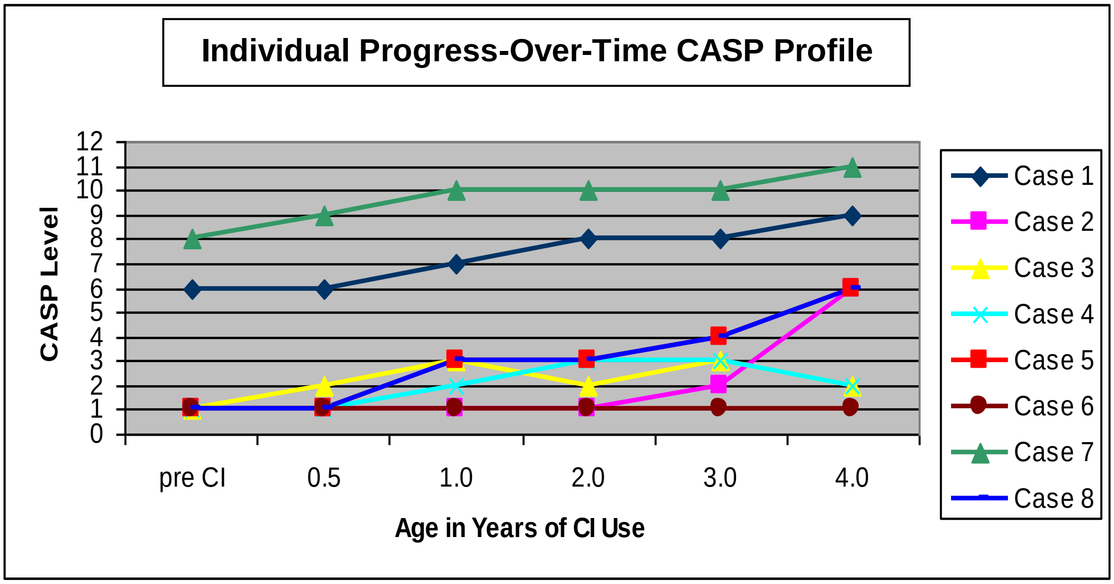

Figure 6. Individual Progress-Over-Time CASP Profile.
Results are obtained over a four-year time span in the A condition with hearing aids and at multiple time points after implantation.

Cases 3 and 4 comprise the third group. Each demonstrated an increase of 2 CASP categories in the second to third year of CI use, followed by a one category decline in CASP performance. Neither case maintained category 3 through the end of the study period. Both ended the fourth year at category 2.

The maximum individual change in categories recorded in this group in auditory speech perceptual benefit over four years is illustrated in Figure 7. The incremental increase in CASP performance varied from no change in Case 6 to five levels of improvement noted in Cases 2, 5, and 8. All cases that improved by five categories initially performed at a CASP category 1. At the other extreme, the best pre-CI performers (Cases 1 and 7) improved over the next four years by three categories. Not surprisingly, advancement in this hierarchical categorization of auditory function becomes more demanding, requiring more complex auditory and speech perceptual development at the higher levels. In Dowell's study using a similar categorization scale, perceptual ability was observed to improve by approximately one category for every two years of CI use (Dowell et al., 1995).

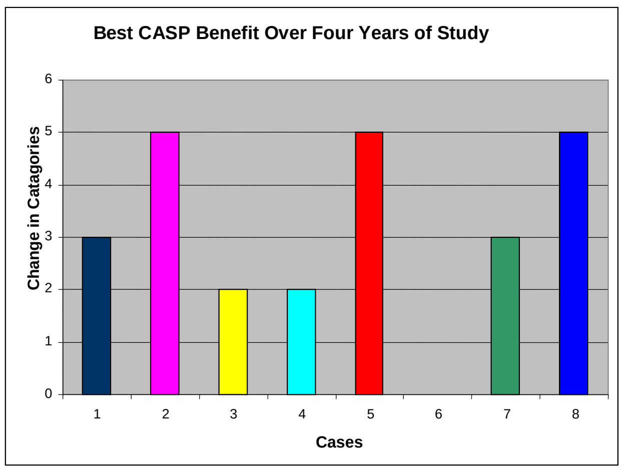

Figure 7. Best CASP Benefit Over Four Years of Study.
Individual A-only CASP increase in categories over four years, from pre-implantation to maximum change recorded within the four years of CI use. The Y axis shows the number of categories each case improved by over a four-year period. Case 6 reveals no change and is thus shown as being absent.

Children who performed poorly on speech perception tests in the A condition and relied on visual speech perception (lip-reading) to access speech cues were also tested in the AV and/or V condition. Both Case 6, due to cognitive function, and Case 7, who could access speech cues in the A condition, were precluded from this mode of testing. Case 1, also a strong auditory performer, was tested in the AV condition prior to implantation and then in the AV and V condition after four years of CI use. Figure 8 illustrates CASP results in the A condition compared with CASP results using AV and V

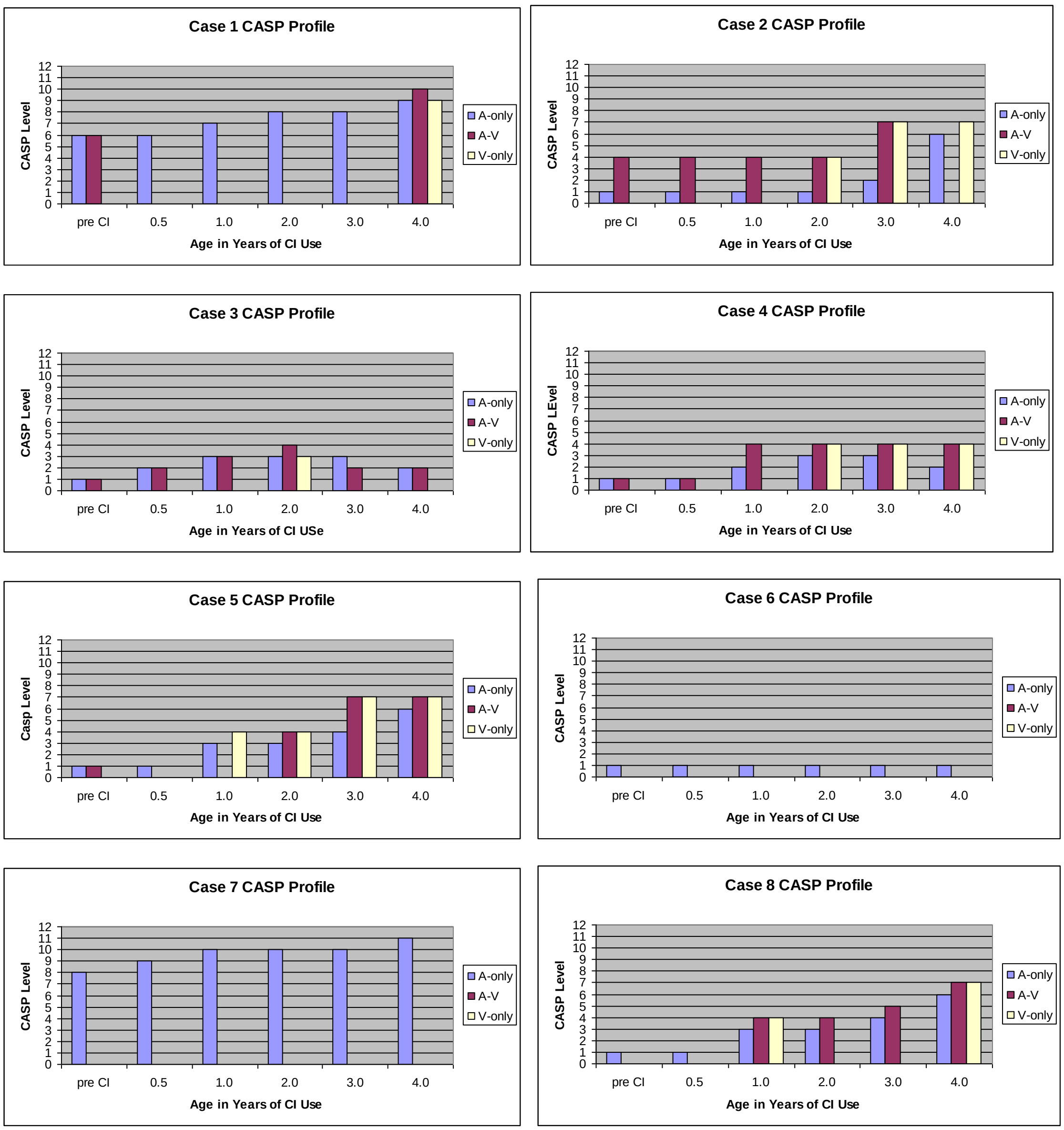

Figure 8. Individual CASP profiles over four years in auditory-only mode, A-V mode, and visual mode.
Results are obtained in pre-CI, at six months, one year and yearly thereafter until four years following implantation.

conditions. While most cases (except Case 2) performed pre- CI at the same category, varying degrees of change in performance in the auditory and visual modes began to occur and individual patterns began to emerge. A lip-reading enhancement is observed in both the AV and V conditions over the A condition in many cases. The AV enhancement varied individually with improvements ranging from a minimum of one level to a maximum of five levels over the A condition. Only Case 2 revealed a strong visual component prior to implantation. When AV and V CASP results are observed in relation to A CASP results, there was an inability to integrate auditory and visual information to improve performance in the AV condition observed in all cases except for Case 1 and Case 3 were multisensory integration appears to have occurred as noted by a small AV advantage.

Table 3 reviews individual characteristics noted for the eight cases, following four years of hearing experience. All cases made some improvements in their numerosity judgments, suggesting increase in memory span, auditory attention, or other cognitive functions that allowed them to perform the task. The best performers, Cases 1 and 7, both demonstrated the ability to count more than 10 beeps in a series. Interestingly, the best performer, Case 7 was able to count the most beeps in a series of 15. Many of the responses have no objective metrics and are either self-reports or reports by the family.

Both Cases 2 and 5 suffered from severe headaches prior to implantation and according to reports from parents and children these increased following CI use. Cases 1, 2, 3, and 5 have reported a lower tolerance to sound, particularly at the end of the day.

Table 3. Individual characteristics identified over four years related to CI use. Motivation to use or improve OC (oral communication) indexed by child's response regarding OC in daily life.

Individual Characteristics Over Four Years of CI Use

Subject: gender/age of CI/ear CI	1. M12.L	2. F9.R	3. F12.R	4. F9.R	5. F15.R	6. D12.R	7.F14.R	8. F11R
Tolerance Problem	no	Yes	yes	No	yes	no	no	no
Headaches with CI use	no	Yes	yes	No	yes	no	yes	no
Audibility Index (AI): increase/same/less	less	increase	increase	Increase	increase	increase	increase	increase
Numerosity task of recall	10 beep	4 beep	6 beep	5 beep	4 beep	4 beep	15 beep	5 beep
Full, Partial, or Non Use of Device	partial	Partial	partial	full	full	partial	full	full
Motivated to use OC	no	No	no	no	yes	no	yes	no
Realistic Expectations	yes	Yes	no	Yes	yes	yes	yes	yes

While no metrics were available to measure the child's expectations and motivation to use OC, both parents' and the children's reports were collected and recorded.

Analysis of CI Outcome Using an Information Processing Model

To better understand whether auditory performance in any particular case follows well-defined rules of skill development once biologically relevant neural stimulation is introduced by a CI, the Dowell et al., (1995) information processing model is adapted for analysis. As auditory development requires an intact peripheral and central auditory system, the model divides potential limiting factors between those that affect information presented to the AS and those that affect the successful processing of auditory information. Table 4a contains individual demographic variables obtained from the chart review applied in relation to each child's CASP performance following four years of CI use. While there are a large number of predictor variables reported in the literature to affect outcome, only those pre- and post-operative parameters observed to be relevant in this cohort (by visual inspection of tables 1-3) were included. CI benefit is assumed in terms of improved outcome if the child obtains a maximal amount of auditory information (tonal sensation of sound), and if the child demonstrates an ability to successfully process this information (perception). CASP and AI results are individually assessed in relation to the limiting independent variables obtained for each case. This model assesses whether factors affecting auditory outcome can be attributed to either peripheral or central AS disruption. Since all cases are prelinguistically deaf, age at onset of hearing loss and the duration of severe to profound deafness will be considered close to if not equal to the age of implantation. The independent variables reviewed are:

1) Age at time of implantation in years (AGE);
2) Pre-implant residual hearing loss based on best 2-frequency PTA (2-freq)
3) Aided AI (Aid-AI)
4) CI-AI index after four years of CI use: (CI-AI);
5) Dynamic range for electrical stimulation (DYN);
6) Measured t-NRT obtained in at least two different areas in the array (t-NRT);
7) Dominant mode of TC communication: sign dominant vs. OC dominant
8) Full-time versus part-time use of device (Full/Part);
9) Child's motivation for CI: to speak versus to hear versus to do both;
10) GPA level of concern at time of implantation (Level 1, 2, or 3).

As the dependent variable, CASP results over four years are illustrated in Table 4b. Children who where ranked at higher levels on the CASP also had higher AI scores, suggesting a main variable associated with better performance at the peripheral level was the ability to accept increased minimum stimulation levels to obtain lower-level thresholds during mapping. Looking at factors affecting information presented to the peripheral AS recorded in Table 4a, residual hearing prior to CI appears to improve auditory benefit which could increase a child's acceptance of sound stimulation during mapping. Little difference in speech perception outcome emerged between cases in

Table 4a. Independent variables used in the information processing model to separate those important to sensation versus perception. Each case was asked whether their motivation for CI was to improve hearing or oral communication. Auditory attention was determined by the ability to obtain reliable and consistent tonal thresholds over time.

Variables important to Sensation-Sensory (Audibility)

Subject Identifiers: case/gender/age CI/ear CI	1.M.L	2 F.R	3 F.R	4 F.R	5 F.R	6 F.R	7 F.R	8 F.R
Age at Implantation (in years)	12 yr	9 yr	12 yr	9 yr	15 yr	12 yr	14 yr	11 yr
Unaided best 2 frequency PTA	42 dB HL	90 dB HL	100 dB HL	75 dB HL	70 dB HL	80 dB HL	70 dB HL	78 dB HL
Aided AI	11%	5%	0%	0%	15%	6%	19%	3%
CI-AI after 3-4 years of use	80%	50%	46%	65%	96%	56%	98%	67%
CI-AI Improves over 4 years: yes/no	no	no	yes	no	no	no	no	yes
ECAP response in at least 2 diff areas	yes	yes	yes	yes	yes	yes	yes	yes
Reduced dynamic range (<25 CL) in Map parameters	no	yes	yes	yes	no	no	no	No

Variables Important to Perception -Cognitive

Maintain Consistent Auditory Attention:for thresholds: yes/no	yes	yes	no	no	yes	yes	yes	Yes
Auditory Memory: (numerosity count) Increases Over Time	yes	yes	yes	yes	yes	yes	Yes	Yes
Pre-CI mode: (TC-sign or TC-OCl)	sign	sign	sign	sign	sign	gestures	OC/sign	sign
post mode of comm.TC-Dominance	sign	sign	sign	sign	OC	gestures	OC	sign
Graded Profile Analysis (GPA) level (1-3)	2	1	1	1	2	1	3	1
Motivation for CI: OC vs. Hear	Hear	Hear	Hear	Hear	OC	Hear	OC	Hear
Craig lipreading scores pre CI	74%	45%	poor	35%	poor	noone	66%	poor
Age Auditory Therapy Begun	4 yr	1.6 yr	9 yr	3.5 yr	2.5 yr	4.5 yr	4.5 yr	3.6 yr
Numerosity judgment count	10	4	6	5	4	4	15	5

relation to implant technology, surgical results, surviving auditory neurons as noted by NRT data, speech processing schemes and technology following device use and time in sound. NRT results suggest there are adequate spiral ganglion cells to promote compound action potentials at various areas in the electrode array. Cases 2, 3, and 4 displayed a rapid sensitivity to sound stimulation that restricted map dynamic range. These cases continued to display a restricted dynamic range for ES over four years. Interestingly, Cases 2, 3 and 5 also suffered from headaches when map parameters were increased to widen the dynamic range.

Unaided residual hearing varied among the eight children appears to be a contributing factor to CASP performance. Those cases with better 2-frequency PTA obtained better speech perception outcome than those with poorer hearing. Furthermore, children with poorer auditory development required more time in sound to perceive higher frequencies at softer thresholds and also to tolerate those sounds. After four years of CI use, the CI-AI improved for all cases except Cases 1 and 2. In the eight cases, it appears that the primary limiting factor to providing information to the peripheral AS is potentially the neural survival within the cochlea as it relates to poorer detection thresholds and a persistent restriction in the dynamic range obtained during mapping. This reduction could cause poorer audibility in the sound spectrum.

Table 4b. Best CASP profile over four years of CI use for eight PLD cases looking at the CASP findings in both V-only and V or A-V modes.

Subject Identifiers: case/gender/age CI/ear CI	1.M.L	2..F.R	3F.R	4. F.R	5.F.R	6..F.R	7.F.R	8..F.R
Highest CASP Level Achieved	9	6	2	3	6	1	11	6
CASP A-only plastic potential	3	5	2	2	5	0	3	5
CASP V or AV plastic potential	4	2	3	3	6	DNT	DNT	6

When factors affecting successful processing of auditory information are reviewed in relation to CASP results over four years, several variables may be associated with better performance. The effects of long-term early deprivation on the development of auditory pathways and the ensuing critical/sensitive periods in the CAS may be a main limiting factor to successful perceptual outcome. The lack of early experience to sound stimulation on cortical maturation and reorganization in A1 and cross-modal reorganization in secondary and association areas has been noted to affect the AS interaction with the language system (Eggermont, 2008; Kral, 2009). Both systems are suggested to have several sensitive/critical periods which limit the ability to use auditory information effectively in late-implanted PLD children. Cases with better auditory experience (cases 1 and7) demonstrated better CASP outcome.

Prior to implantation, cases with better CASP outcome were also found to have better lipreading skills as measured on the Craig test (cases 1 and 7). Good lipreading skills could be a contributing factor to better perceptual outcome which might interact with increased integration of multisensory information. Motivation to use voice during communication also appeared to be a influencing variable as noted by better CASP outcome. The score on the GPA also appeared to have a relationship with CASP outcome, those cases obtaining a level of 2 or 3 obtained better CASP outcomes.

Figure 9 illustrates individual timelines for auditory development based on effectiveness of sound stimulation prior to and following amplification and then after four years of implantation. The time line is based on the development of the CAS which continues to develop for at least the first decade of life. During this period the type of activity-driven neural input to the brain, especially during the very early stages of development will strongly influences central function (Moore, J., 2002). Limited or no auditory input during early periods of development will cause a disruption in activity. The early environmental influence can cause either harmful or beneficial outcome depending on the type and amount of auditory experience. While a relationship exists between the developing aspects of hearing and other aspects of cognition and behavior, the overall outcome will depend on the underlying neural basis of auditory system plasticity (Moore, D., 2002). Figure 9 suggests a ratio of organization and reorganization occurring following critical, sensitive and activity-dependent plasticity at the level of the brainstem, midbrain, auditory cortex and higher-level auditory cortices. The ratio of organization and reorganization is related to the level of the CAS and research suggesting either the presence or absence of critical, sensitive period on sound-dependent plasticity. The levels and age period are summarized as:

1) The auditory nerve and brainstem reflects a true organizational change following CI which is activity-driven and not under the influence of critical/sensitive periods following implantation (Gordon et al., 2003).

2) A possible sensitive period in the activation of the midbrain reflecting a possible reorganization in the thalamocortical areas following implantation after age eight years (Gordon et al., 2005).

3) A sensitive period in A1 is reflected by a reorganization in the P1 wave response with maximum plasticity noted up to the fourth year followed by a minimum plasticity at the end of the sixth year (Sharma et al., 2002, 2009).

4) A critical period in the activation of higher-order auditory areas reflects reorganization by the absence of N1 wave in late-implanted children with over three years of early deafness (Ponton & Eggermont, 2001).

5) A critical/sensitive period in the cross-modal reorganization in secondary and association areas occurring after the age of four (Lee et al., 2001; Oh et al., 2003).

6) A critical/sensitive period prior to termination of normal synaptogenesis is identified by three to four years of human life (Huttenlocher and Dabholkar, 1997).

Although Cases 1, 5 and 7 were implanted at the older ages of 12, 15 and 14, respectively, these three demonstrated the lowest best 2-frequency PTA during early development despite demonstrating severe to profound loss above 1000 Hz. All were able to use OC when requested. All three categorized into GPA levels of 2 or 3, consistent with little to no concern for CI outcome. Cases 1 and 7 were both identified and amplified after the age of four and yet achieved the two highest CASP outcomes for the group. Case 5's poorer performance of the CASP and Craig lipreading test could be explained by her GPA profile that identified cognitive limitations as a major concern.

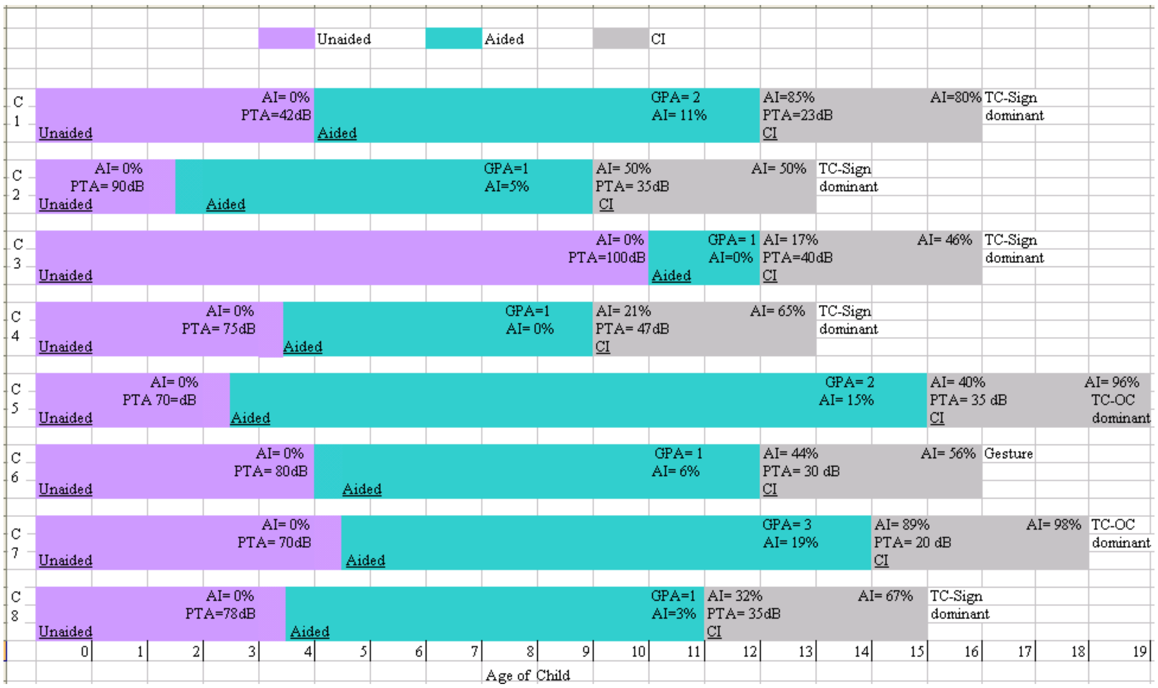

Figure 9. Individual timeline of auditory development in the eight cases, based on audibility in the unaided, aided and CI condition.
The Graded Profile Analysis (GPA) results are shown for each case prior to implantation. Following four years of CI use, the mode of communication preference is listed for each case using the descriptors: Total Communication (TC), Oral Communication (OC) and Sign English (Sign).

CHAPTER V

CONCLUSIONS AND RECOMMENDATIONS

Summary and Interpretation of Findings

A retrospective chart review of eight children with PLD is presented over a four-year period of CI use provides information about the ability of late-implanted children to regain sensation to sounds as well as aid in the recognition of auditory speech perception. The literature review provides evidence that when children miss opportunities to receive biologically relevant sound stimulation during receptive periods in early development, the natural progression from primitive sound integration noted in infancy to more complicated auditory speech perception will be impaired (Merzenich and Jenkins, 1995). When the developmental windows of auditory plasticity is lost following prolonged auditory deprivation, the resultant limitations imposed on CAS maturation leads to structural, electrophysiological and behavioral deficits (Eggermont & Ponton, 2003).

Looking at the literature review, there appears to be specific well-defined, rules of auditory response development in the CAS of late-implanted PLD children. While this needs to be interpreted cautiously, the evidence suggests that auditory results demonstrate a dependence on: a) the pre-implant characteristics of auditory and speech perception function; b) the ratio of organization/re-organization within the neural networks of the CAS at the time of implantation; c) level-specific critical/sensitive periods or age-related plasticity within the AS; d) a decoupling between primary auditory cortex and language association cortices; e) a colonization factor following cross modal reorganization by other sensory systems. Although this type of study is not expected to support definitive conclusions, it may suggest a baseline for auditory development and function in late-implanted PLD children over long-term CI use and suggest important implications between active vs. passive listening. This information will help clinicians and families make informed rehabilitative choices.

First Objective

The first objective of this study is to identify which aspects of auditory function can be readily changed following CI activation, which functions are plastic and can improve with long term CI use and which are difficult if not impossible to improve. At initial stimulation, all cases demonstrated at least two ECAP responses at different areas on the electrode array. All cases showed significant improvements in their detection of warble tones across the speech spectrum. The ability to achieve audibility at IS is not surprising as the auditory nerve and brainstem are activity-driven by ES with no apparent critical or sensitive periods reported (Gordon et al., 2003, 2005). Over the next four years, additional improvements in AI occurred for all cases. Cases 1 and 7 achieved the highest percentage AI scores after implantation and through the four years of the study. Case 5 also had higher pre-implantation AI, but initially showed less AI improvement than Cases 1 and 7 after implantation. However, by the third and fourth years, Case 5 had improved to AI levels comparable to Cases 1 and 7. This catch-up by Case 5 may have been due to exceptionally high motivation to use and improve OC. This higher degree of AI improvement is expected to help Cases 1, 5, and 7 perceive soft speech, and improve speech perception access, further increasing the likelihood of spontaneous learning when the sound source or speaker is beyond a distance of one meter (Skinner et al., 2002). This advantage was also noted in their vocal quality (as reported by the families of Cases 1, 5 and 7) when they wore their CI.

Specifically, when looking at the AI profile, improvements in audibility are observed from the thresholds obtained at initial stimulation and throughout the four years of CI use. Cases 1, 5 and 7, achieved AI scores of .80 or higher by the fourth years while Cases 2, 4, 6, and 8 all achieved poorer scores ranging from .50 to 67. Only Case 3 demonstrated an AI below .50. According to the AI Theory, poorer audibility could be a limiting factor in their ability to improve speech perception development (Skinner et al., 2006). Prior to implantation, Cases 1, 5, and 7 demonstrated better residual hearing. Cases 4 and 8 attained smaller but sizeable increases in their AI over four years of CI use, while Cases 2, 3, and 6 relied the least on auditory skills and show the least benefit to AI in the group. Three of the cases (Cases 2, 3, and 4) continued over time in sound to maintain a reduced dynamic range between threshold and maximum comfort levels for intra-cochlear ES. It has been reported in adults that speech perception scores can be associated with a wider dynamic range in map parameters, particularly for vowel recognition (Blamey et al., 2001, 1992). The restricted growth of loudness as evidenced by a restricted dynamic range may be an additional factor that diminishes the potential for speech development.

Improvements in auditory and speech perception on the CASP, however, followed a more diverse and slower course than is observed in early implanted children. Only two of the eight cases showed any improvement in speech perception by six months following initial stimulation. By one year following stimulation, six of the eight showed improvement and by two years all but one case had improved speech perception and all but two continued to improve through the fourth year (See Figure 6, above). Only Case 6 was unable to achieve any perceptual skills had cognitive problems that precluded even the use of sign language.

This is not a surprise when looking at the auditory characteristics of these cases prior to implantation. Prior to implantation, Cases 1 and 7 were higher performers who relied on auditory cues and were able to perform on closed-set tests of speech perception above chance (Case 1) and open-set tests above chance (Case 7). Looking at their pre-implant unaided 2-frequency PTA, both cases had significantly better low frequencies. Case 1 had a 42 dB HL coming from thresholds at 125-250 Hz, not sufficient to develop speech prior to amplification at age four but perhaps adequate to stimulate a more normal early maturational sequence in the auditory pathways of the CAS. Case 7 demonstrated better thresholds throughout the entire frequency range of 125-4000 Hz and her best 2-freq PTA was 70 dB. She also did not speak until she received hearing aids at age four and a half. She remained in a self-contained classroom using OC and sign support and her family never learned any form of sign language.

It is known that in young children earlier implantation increases the effectiveness of the CI in the acquisition of communication skills. This study suggests that the benefits that older children may obtain from CI depend not on relative age, but on other factors, including the child's pre-implantation levels of residual hearing and speech perception and motivation to improve OC. Cases 1 and 7, implanted at ages 12 and 14, respectively, show the most overall improvement and except for Case 5 (implanted at age 15) were the oldest to be implanted, and they both had the advantage of better residual hearing. They were both identified after age four, which means they did not use sign language before age four and had early exposure to and opportunity to develop some degree of visual and auditory speech perception skills using OC. Although Case 7 did not speak until after amplification was obtained at age five, little was known about her hearing status prior to diagnosis.

Over four years of CI use, Cases 1 and 7 increased the amount of detail extracted in their speech perception as shown by their three category improvements on the CASP. Case 1 was able to advance to category 9, reflecting good open-set speech perception of greater than 40% at 55 dB HL and Case 7 was able to advance to category 11 by obtaining greater than 50% on W-22 word list presented at 40 dB HL. When A and AV conditions were observed with A condition at initial stimulation, Case 1 placed in the same category for both conditions. At the four-year mark, the A outcome was compared with both the V and AV condition and showed a small AV advantage. It is possible that he was able to integrate information from both the auditory and visual modes, producing a true AV advantage. Yet despite the strong outcome on auditory and visual speech perception and his ability to communicate in OC when urged, Case 1 showed no motivation to transition into OC and continues to maintain TC-sign dominance as his main communication mode.

Cases 2, 5, and 8 were implanted at ages 9, 15 and 11, respectively. They performed poorly at initial stimulation, placing into category 1 of the CASP. This suggested they were only able to detect tonal and speech sounds at conversational levels. Their auditory skills developed very slowly and it was only by the third to fourth year of CI use that all three were able to reach a category 6 by performing minimal discrimination and recognition of consonants above chance on closed-set tests of greater than 28% on the WIPI at 70 dB HL. Interestingly, Case 2 revealed no change in the A condition on the CASP until her third year when she advanced one level and then jumped an additional four levels by the fourth year to match performance with Cases 5 and 8. Unlike adults whose speech perception was found to plateau by the first to second year (Teoh et al., 2004 Part I), the three cases continue to improve over time with no evidence of a plateau in performance. Bt the fourth year, all three cases demonstrated minimal discrimination and recognition of consonants using a closed-set test (category 6 on the CASP).

Results on multimodal conditions revealed that Cases 2, 5, and 8 all relied on visual rather than auditory cues. Performance in the visual conditions consistently bested auditory performance on the CASP. What is intriguing in this group is that all three cases were unable to integrate visual and auditory cues together to obtain a true AV advantage. There was no difference in performance between the V and AV conditions over time. This suggests that the visual mode was the dominant mode and primarily working alone without any integration from the auditory mode. A second trend noted is that while visual and auditory modes seem to function separately, each condition continued to improve with CI use with the visual mode outperforming the auditory mode.

An interesting outcome was seen in Case 5, our oldest case to be implanted at age15, who continued to demonstrate a strong determination to use OC despite her CASP performance. Her specific demographic and auditory characteristics revealed residual hearing of 70 dB HL (best 2-frequency PTA). She received early auditory therapy, but received poor sign language implementation by her family. Despite her poorer CASP standing she, along with Case 7, continued to be the strongest OC communicators in the eight cases.

Cases 2, 5, and 8 were also strong lip-readers as evidenced by their CASP findings in visual speech perception. Cases 2, 5, and 8 probably demonstrate the strongest effects of auditory deprivation following late implantation due to their poor auditory development and the ensuing effects of critical sensitive periods as they involve speech and language learning. The inability of this group to integrate auditory and visual speech perception is in line with data from positron emission tomography (PET) studies illustrating that visual speech perception is not critically dependent on the A1 (Bernstein et al., 2002). While vision can influence "heard" speech as noted by the McGurk effect, visual speech perception apparently can also function alone. Bernstein's group suggests the possibility of a modality-specific pathway for the processing of phonetic speech stimuli using the visual mode as a separate pathway from the auditory pathway. This would suggest that the auditory and visual pathways are not wired together, probably do not fire together and thus are not enhanced under the domain of Hebbian principles.

Another explanation for the absence of auditory-visual integration is that long-term auditory deprivation causes a persistent slower temporal processing of auditory input (Sharma et al., 2002; 2005). This ensuing mismatch in real time would negatively interact with the coordinated temporal treatment of visual speech perception, lipreading-facial expression and tactile representation (Bavelier & Neville, 2002). The result is a maladaptive AS lacking appropriate temporal processing in the hearing and visual domains, and thus separate processing would be maintained with visual trumping auditory. This is consistent with Merzenich and Jenkins (1995), who suggest that the brain and its multisensory systems become used to the deafness-induced slowed auditory-temporal processing with adverse affects noted on long-term speech perception remediation. They seem to come to this conclusion based solely on their knowledge of basic principles of neurobiology without any empirical study.

The last three, Cases 3, 4, and 6 (implanted at ages 12, 9 and 12, respectively) were weaker performers, measured by their ultimately poorer improvement on the CASP over time. It is possible to identify factors applicable to these cases that suggest reasons for this poor performance.

It seems probable that Case 6 performed poorly on the CASP due to cognitive difficulties, suggested by the fact that by age 12 she had no communication skills, including sign language and by concerns identified in her GPA with regard to daily living skills. However, Case 6 improved over the four-year period on tasks that were not heavily loaded in the cognitive area, showing strong performance in audibility and even some improvement on an auditory memory task using numerosity judgments.

Cases 3 and 4 both demonstrated a very restricted dynamic range in map parameters causing distortion in vowel discrimination and optimal loudness growth characteristics (Geers et al., 2003). While both cases were able to detect sounds at conversational levels, they continued to reveal limited speech perception abilities.

Case 3 demonstrated the largest amount of auditory deprivation, which severely compromised development within auditory pathways. Her continued severe tolerance problem with sound stimulation never improved. She demonstrated at pre-implantation poor auditory and visual speech perception development and over time continued to maintain inconsistent outcome in A, V and AV CASP. The persistent inconsistencies and regression in performance may, in part, reflect lack of auditory focus and motivation to task, rather than low auditory capacity. It is possible that her initial improvements were entirely based on cognitive "top-down" influences interacting with audibility for perception rather than true auditory-perceptual capacity.

Case 4 also demonstrated poor skill development, reaching a plateau by the second and third years at category 3 only to drop back one category in the fourth year. Despite her lack of progress, she continued to be highly motivated as a "hearing" listener. Her results in the AV and V condition remained stable over time and her visual speech perception continued to outperform her A mode by 2 categories. Here again it seems that, rather than a true plastic change in auditory capacity, her performance may be due to cognitive "top-down" influences interacting with perceptual audibility.

When looking at evidence from deafness research, the findings overwhelmingly report that prolonged congenital deafness does not completely arrest the basic connections of the peripheral AS to the A1. Some aspects of the normal developmental sequence of ascending thalamocortical afferents are retained (Teoh et al., 2004, part II). Activity-independent processes continue to develop as in the rudimentary tonotopic projections and growth of nerves that occur to certain degrees throughout the AS (Kral et al., 2005; Shepherd et al., 2001). One can speculate that the malleability noted in the audibility of sound over time may be due to maturational factors similarly noted in infants who initially required louder intensities to hear due to their immature CAS (Nozza et al., 1987, 1990). Another possible explanation for the change in audibility, however, could come from more central-cognitive factors (top-down influences) influenced by variables affecting CAS development and individual preferences to hear more based on the meaningfulness of the auditory information.

Second Objective

The second objective compared results from audibility and CASP outcomes to the results implied by the information processing model with regard to potential contributing factors that affect the amount of auditory information being received from a CI at the periphery and the ability to successfully process this auditory information by the CAS. While the chart review identified many demographic variables and auditory characteristics in individual cases prior to and following four years of CI use, only those variables that seemed relevant to AI and CASP outcome were included in Tables 4a and 4b. Looking at the variables that could affect performance at the level of the periphery, two main limiting factors were observed in this group. One limiting variable was the amount of residual hearing prior to surgery. Looking at graph 9, Cases with poorer residual hearing showed poorer AI scores compared to others in the group after four years of CI use. This is observed in Cases 2 and 3, who attained the poorest AI scores and also weaker improvement in speech perception measured on the CASP. Each of these cases had minimal early auditory experience and both demonstrated the poorest pre-implant best 2-frequency PTA of 90 and 100 dB HL, respectively. Case 3 was identified and received hearing aids after the age of eight and Case 2, despite early detection and hearing aid intervention, was an inconsistent user of hearing aids and irregularly attended preschool classes at the local school for the deaf during her early years. While the audibility of sounds noticeably improved at initial stimulation for all cases, the next four years of CI use continued to show improvements. This suggests that the ability to develop better detection skills and/or improved tolerance to accept more sounds does change over time. It is important to note that children who used or were able to use an OC mode of communication maintained the highest AI. This trend suggests that the amount of audibility may be dependent on the communication mode of the CI recipient.

A second limiting variable observed to affect outcome in this group is the reduced dynamic range between threshold and maximum comfort level in the fitted CI map. Representing some of the poorest auditory thresholds in the group, Cases 2 and 3 demonstrated the narrowest dynamic ranges for electrical stimulation. A very narrow dynamic range is expected to produce a reduction in optimal growth of loudness characteristics, ultimately affecting how a child perceives speech. Graph 9 shows that Cases 2 and 3 had the poorest residual hearing prior to implantation of the group. Whether a link exists between reduced dynamic range and the status of surviving neural populations (SGC) is the subject of debate.

When perceptual cognitive factors affecting successful processing of auditory stimuli within the CAS were visually analyzed using the information processing model, the amount of auditory experience obtained during early development appeared to be a main limiting factor in this group. Cases with better auditory experience did better on the CASP prior to implantation. Auditory experience is also related to the amount of unaided residual hearing prior to implantation and thus part of the peripheral system. This is consistent with findings in deafness research reviewed in this study which suggest that the organization and reorganization that occurs in auditory pathways of deaf children with PLD is directly related to early experience of behaviorally relevant sound stimulation (Eggermont, 2008; Kral & Eggermont 2007; Sharma et al., 2009). Thus, early auditory experience affects the neural development within the CAS which ultimately affects auditory performance. Studies have suggested a relationship between slower processing or delayed neurotransmission and speech recognition scores (Gordon et al., 2003; Ponton & Eggermont, 2001; Sharma et al., 2002). Research collectively suggests slower or compromised neurotransmission in the neural auditory pathways following prolonged auditory deprivation. This slower processing can be expected to play a critical role in the abnormal auditory and speech perception and processing observed in PLD children who are implanted late (Gordon et al., 2005; Moore, J. 2002).

While all cases in the present study were implanted after the critical ages for speech, language and auditory development, and all demonstrated significant auditory deprivation, there were differences in these variables that might have differentially impacted individual CI outcome. The pre-implant auditory function evidenced by unaided audibility and aided CASP benefit appeared to play an important role on future outcomes with a CI. Those cases with better pre-implant auditory function showed better initial outcome after implantation and continued to outperform the other cases regardless of age of implantation. In the three oldest children implanted in the group, responses prior to and following implantation reveal some of our best outcomes from a CI. Cases 1, 5, and 7 were implanted at age 12, 15 and 14, respectively. These three cases were the only ones that did not show significant concerns on the GPA. While all cases revealed improvement over time, only Cases 1 and 7 demonstrated stronger ability to remember the number of beeps in a series of beeps. Auditory memory is suspected to play a key role in speech perception outcome. Cases 2, 3, 4, 5, and 8 all demonstrated difficulty with temporal cues noted on the CASP by their inability to perform at a basic level of discrimination of speech patterns using temporal and stress cues for the first year of CI use. The inability to perceive temporal cues in these cases suggests that temporal perception is a function that may not be benefited to a significant degree in late-implanted children.

One other variable that appears to affect this group's CASP outcome is the motivation the child brings to CI use. Those interested in hearing as opposed to speech (Cases 2, 4 and 8) were motivated only to use their CI to hear more sounds. Those expressing a desire to improve OC (Cases 3, 5 and 7) were inclined to use their CI to improve speech perception. Of these, Case 3 expressed a desire to use OC but due to her profound hearing loss, the absence of hearing aid use prior to age nine and lack of formal education, she was not able to achieve the auditory skills to do so. Cases 5 and 7 were able to improve OC after implantation, but both had some ability to communicate in the OC mode before implantation. Case 1, who did have the skills, did not have the motivation to use OC in real world situations.

Using a multidisciplinary approach to assess a child's potential, the GPA provided a means to access and quantify individual variables that could impact outcome with a CI. The GPA incorporates assessments in the degree of hearing loss, duration of hearing loss, age of child, medical constrains, speech and language development, educational setting, home environment, developmental millstones, and assessment of other handicaps from which a level of concern is assigned to each variable and for all variables as a whole. Cases 1, 5 and 7 all showed less concern on their GPA scores consistent with their CASP outcome and/or ability to use OC. All other cases showed great concern with varying results in final outcome over four years. Cases 2, 4, and 8 continued to improve and reached a category of 6 on the CASP by the fourth year while Cases 3, 4 and 6 showed very little ability to access speech perceptual cues.

Cases with better ability to count successfully the number of beeps in a temporal sequence of beeps also revealed better outcome on CASP testing. Case 1, 5 and 7 were more “active” listeners and able to access speech cues while the other cases in the group approached listening in a more “passive” fashion. The “passive” listeners were not able to access speech cues in the environment with any reliability which is consistent with their reason for obtaining a CI.

One factor not found to be a contributing variable was the age of implantation for children implanted after age seven. Cases 1, 5, and 7 were all implanted after the age of eleven (Case 5 and 7 were implanted at ages 15 and 14, respectively) and were the most successful of the group in their use of CI. In the present group, it was early experience with sound rather than earlier implantation that was critical to their outcome.

Recommendations for Future Research

One of the recommendations for future research comes out of the limitations of this study to obtain a measure of speech perception in a group of children over a four year period using one test. While the CASP offers a possible solution, further investigation is needed to determine if all selected categories are appropriate to measure outcome in the late-implanted PLD population. The range of scores within a specific category and the actual tests used within the test protocol will require more scrutiny before it can be used as a standard tool to record speech perception.

With the exception of Cases 1 and 7, all cases demonstrated poor auditory skills accompanied by poor development of skills prior to and following implantation. Results of the numerosity show that the cases that were better able to count the number of beeps were also better able to perform on the CASP. Although the test used here is a simplified version of the numerosity test described by Busby et al., (1999), the findings in the present review suggest a possible relationship between poor auditory memory and poorer performance on the CASP. A recommendation is therefore made to address this issue with a more in-depth analysis of auditory memory in late-implanted children. A standardized clinical tool to measure auditory memory is needed.

The literature also suggests that the brainstem and non-lemniscal pathways are not under the influence of critical sensitive periods in the absence of sound even after long periods of deafness (Gordon et al., 2003, 2006). Infant research in speech perception shows the ability to develop some behavioral discrimination in the absence of A1 function (Moore, J., 2002). Studies of normal hearing infants using electrophysiological ABR and CAEP responses observe deficits in the conduction time of neural signals, poor synchronous transmission and long latencies throughout the CAS. This all makes auditory development following implantation difficult as noted by the CASP results after four years of CI use. We know from the literature review that accurate speech sound encoding and perception depends on precise timing of neural events and cognitive influences. Auditory training has long been used to improve precision. Furthermore, the preconscious encoding of sound has been reported to be plastic even in adulthood. Looking at my eight cases, Cases 2, 3, 4, 5, and 8 all had significant difficulty with temporal issues. The above cases all seem to require more “active” listening to retain the auditory information they hear and the motivation to use this information in everyday situations. There is opportunity for more research with this population using aggressive auditory training (AT) focused on “active” and meaningful listener participation. While the present case review suggests that auditory memory was impaired in many of the cases, further information needs to be obtained to clarify the extent of deficit. While numerosity testing may be a viable tool, a standardized test should be used to confirm findings and made available for clinical use.

A trend in this chart review was the lack of auditory integration observed in A, AV, and V condition testing with the CASP. The question arises of whether there are two separate pathways used by children with PLD, and whether multisensory integration is possible with time in sound. The quality and quantity of achievable auditory function following implantation needs to be addressed related to the ability to integrate acoustic cues into meaningful perceptual events using all modalities. Bernstein’s group suggests the possibility of a modality-specific pathway for the processing of phonetic speech stimuli using the visual mode as a separate pathway from the auditory pathway. This would suggest that the auditory and visual pathways are not wired together, probably do not fire together and thus are not enhanced under the domain of Hebbian principles. Another theory comes from Merzenich and Jenkins (1995), who suggest that the brain and its multisensory systems become used to the deafness-induced slowed auditory-temporal processing, with adverse effects noted on long-term auditory visual speech perception remediation. Further investigation is necessary to understand the relationship of auditory and visual speech perception on ultimate benefit from auditory oral or auditory verbal therapy.

Limitations of Study

A retrospective chart review using only eight cases poses some difficulties in interpretation which will affect how the findings can be used. While this study may suggest some common baseline similarities and/or differences in the cases presented, the findings cannot be treated as conclusive and may require further study. With a small sample size, this study can only describe trends and not support any definitive conclusions. While it lacks the rigor of a formally planned prospective study, it can be useful in its collection and analysis of longitudinal datum which permits the identification of potentially significant facts that may be lost in a large group study.

The preliminary data suggests the CASP is a useful means to describe and track speech perception over a period of time, specific categories within the CASP should be confirmed using a larger patient group. The numerosity test also needs to be assessed on a larger patient group to assess whether it is actually measuring auditory memory. The specific beeps presented, the length of each beep and presentation series using number of beeps all needs to be tightened in the implementation of the test.

A language assessment of age-equivalent scores and vocabulary level both prior to and after four years of CI use would have helped to explain speech perception outcome.

Conclusions

While early implantation restores hearing and is an effective way to enhance auditory, language and communication skills, promoting more normal maturation and efficient transmission of neural signals within the central auditory system, this is not the case in late-implanted PLD children. The missed opportunity to receive auditory input during receptive periods in early development places late-implanted PLD children at a severe disadvantage to their younger-implanted peers. The literature review suggests that auditory experience is vital for proper activation of secondary and association areas in the auditory cortex. The available auditory capacity following implantation is reflected by the ability of cortical and sub-cortical auditory systems to relay consistent and differentiable information about neural patterned afferent stimulation to higher centers of the brain. Auditory capacity depends on early experience for both relevant hearing sensitivity and auditory resolution. While the CI is not able to restore normal auditory capacity, it appears that auditory capacity is somewhat malleable and subject to enhancement by experience and training. Depending on the developmental age when implantation occurs, evidence in both human and animal models suggest some form of plasticity exilsts in cortical and sub-cortical systems to adapt in response to stimulation and to promote auditory capacity (Boothroyd et al., 2002; Harrison et al., 2005; Reconzone et al., 1993; Sharma et al., 2002).

Auditory results in this late-implanted group appear to be most strongly linked to the pre-implant characteristics of auditory and speech perception development, the ability to resume a more normal maturational sequence following biologically appropriate sound stimulation, the amount of plasticity that exists within the neural networks of the CAS at the time of implantation, and the motivational reasons for implantation. Based on an information processing model, important identifiers prior to implantation were the amount of residual hearing, speech perception performance and level of concern on the GPA and communication mode establish early in life all appeared to be related to CI outcome after four years of CI use. Post implantation, motivational factor to promote better hearing or better access to OC was an important factor. Another possible determinant of auditory outcome appears to be the degree of available auditory memory.

While the data clearly reveal that auditory information is getting to the peripheral AS, late-implanted children were less successful in processing this auditory information. Of the five cases that, prior to implantation, were unable to use auditory input for even the most basic syllabic contrasts or pattern perception, three cases ultimately demonstrated improved perceptual development, consistent with their ability to use lip-reading skills. It is observed in these five cases that visual speech perception was always dominant over auditory speech perception. Further, no difference was noted between the visual and auditory-visual conditions, suggesting the visual mode alone was providing information and the auditory mode provided no additional help. Children that were "active" and not "passive" listeners showed greater improvement in their overall outcome.

The absence of early auditory experience appears to retard the otherwise natural progress from primitive signal integration expressed in early life to more complex auditory processing, making it harder or impossible for change to occur. A theory is suggested by Kral & Eggermont that when auditory experience does not occur within the critical sensitive period for proper activation of secondary and association areas, top-down descending modulation to A1 is impaired. This has been suggested to cause a deficit in the thalamocortical feedback loops that are suspected to be important to auditory memory (Kral et al., 2002). This could explain why most of our cases had difficulty remembering the number of beeps presented in a sequence.

The absence of top-down modulation according to Kral and Eggermont (2007) is the result of poorly developed bottom-up connections to the A1 due to lack of neural stimulation. Kral and Eggermont's conceptual model suggests that a reduction in synaptic plasticity within the lemniscal auditory pathways will occur after the critical sensitive period which will ultimately affect synaptic plasticity and the ability to differentiate distinctive features of sound. This also plays into another conceptual model that has been proposed by Gordon et al., (2003, 3005). They suggest because the prolonged auditory deprivation within the CAS produces an immature or reorganized CAS which is incapable of higher-order processing, auditory processing continues to play the more dominant role within the brainstem (Moore J., 2002) and the phylogenetically older non-lemniscal pathways, similar to that of an infant (Gordon et al., 2005). These primitive pathways, with a subcortical route beginning at the dorsal cochlear nucleus and a higher-level route leading to secondary and association areas are suspected to be primarily used during early infant and child development. In late implanted children with PLD, the more primitive brainstem and non-lemniscal pathways are suggested to remain the dominant pathways in processing of auditory information. If this is true, a much more "active" role is necessary in listening (Kraus & McGee, 1995; Galambos et al., 1961; Moller & Rollins, 2002).

While all of the children in this study were implanted after the critical ages for speech-language development and each had significant auditory and language deprivation, there were differences in these variables that impacted individual CI outcome. It seems that any single failure in one limiting variable affecting successful processing of auditory information may have less consequence in these children when other factors are favorable. The quality and quantity of achievable auditory function ultimately depends on the particular child's ability to integrate auditory speech cues into meaningful perceptual events. After four years of CI use, two cases were able to use auditory input only to recognize minor syllabic contrasts of speech, three cases were able to recognize minimal discrimination of consonants using closed-set tests, two cases were able to show good open-set speech perception, and one case was unable to make sense of sound. All cases that had the cognitive ability to develop visual speech perception were able to improve to some extent their auditory speech perception over the four years post-implantation. Children identified pre-implantation as having very poor auditory development had significant problems in developing those perceptual skills that depend on the precise timing of neural events, as evidenced by their slow development perceiving pattern perception (temporal and stress patterns of speech).

However, this study demonstrates that late-implanted PLD children can receive benefits from a CI within realistic expectations. As to these eight children, the CI, by permitting higher levels of audibility and perception, has enriched their hearing experience to increase connectivity to family, friends and the world they live in. All eight patients described in this study continue to wear their CI device on a part- or full-time basis. Many report that full-time use of the device is fatiguing and half opt not to use their CI at home. In late-implanted children, learning to listen requires a more active role to understand auditory speech sounds. The children in this study were each motivated to improve their hearing and/or speech perception and, notwithstanding the limitations to which they are subject due to late implantation, each has benefited from their CI. However, to maximize these benefits, it is recommended that all children implanted late should receive intensive auditory training focused on active listening and enhancement of auditory memory. Further, this study confirms the importance of the clinician's obtaining a detailed description of demographic identifiers and auditory characteristics in assessing the future benefit that may be obtained with a CI. This will be helpful in counseling families, establishing realistic expectations and planning appropriate intervention following implantation. Finally, it is important to understand that while many variables must be reviewed to try to predict to what degree a given child may be able to benefit from cochlear implantation, for children over age six or seven, age alone does not appear to be a significant factor. These preliminary data should be confirmed in a lager patient group.

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