Critical Review: Using cortical auditory evoked potentials (CAEP) as the outcome measure of cortical maturation, is there an optimal age to implant deaf children to provide better auditory development?

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This critical review examined the effects of auditory deprivation on the central auditory system in children with cochlear implants as compared to children and adults with normal hearing, using CAEPs as the outcome measurement. Study designs included five between group non-randomized intervention studies. Overall, research suggests that cochlear implantation at an earlier age will produce smaller maturational delays compared to implantation at a later age, and implantation at an earlier age will produce P1 latencies that are normal or within-normal limits compared to age-matched norms. However, a definitive statement regarding a sensitive period for cochlear implantation in children cannot be made due to conflicting findings, and research limitations, such as small sample sizes, differences in methodologies and subject criteria across studies. Additional studies involving more subjects, control of subject criteria, standardized research methods, and longitudinal effects are recommended.

Introduction

Children born with congenital deafness or who are pre-lingually deaf in childhood are faced with an auditory system that does not experience any auditory input. The central auditory system depends on this sensory input to mature and develop normally, and if disrupted, normal developmental processes are altered. The maturation of the central auditory system is not fully complete until age 12 and in some cases even into the teenage years (Kral & Tillein, 2006). With cochlear implants, some aspects of the auditory cortex can be restored with electrical stimulation of the auditory nerve. This prosthetic device can provide deaf children with new auditory inputs, instead of a system that would otherwise be deprived of auditory stimulation (Kral & Tillein, 2006).

To determine the effectiveness of the cochlear implant on the maturing central auditory system, objective measures such as CAEPs can be used. CAEPs are a useful objective tool because they can measure the maturational processes for auditory cortical function, since the P1 latency varies as a function of chronological age (Sharma et al., 2002a). ‘P1 latency reflects the accumulated sum of delays in synaptic propagation through the peripheral and central auditory pathways’ (Sharma et al., p.1365, 2002b). With these objective measurements, CAEPs can determine how the central auditory system is developing with electrical stimulation from the cochlear implant. It is valuable to understand the critical timeframe in which to implant a congenitally deaf child with a cochlear implant while the auditory system is still highly plastic. Neural plasticity is known as the ability of the nervous system to alter its structure and function based on new or varying external and internal inputs (Kral & Tillein, 2006). The brain’s plasticity is greater in children than in adults.

There have been numerous animal studies measuring the effects of cochlear implantation and the optimal period for implantation as it relates to the development of the auditory cortex. These past studies have shown that ‘most of the signs of plastic reorganization that occurred after cochlear implant stimulation became less pronounced the later in life the stimulation was begun’ (Kral & Tillein, p.99, 2006). Animal studies have supported the idea that there is a developmentally sensitive period for cochlear implantation, showing that earlier ages will produce better results.

There are few human based published reports on sensitive periods for cochlear implantation on children using CAEP outcomes. A critical review of the effects of sensitive periods for children with cochlear implantation is considered to be an important topic to the pediatric field of audiology. It is a critical issue to determine the optimal age range for implanting deaf children. If the critical review suggests a sensitive period, this information can guide future treatment recommendations to provide the best possible rehabilitation for this population.

Objectives

The primary objective of this paper was to outline and critically evaluate the current body of research on CAEP outcome measures in implanted deaf children as compared to normal hearing children at different ages to determine the effects of auditory deprivation on the central auditory system; and to determine if there is a developmental sensitive period to implant deaf children.

Methods

Search Strategy

Computerized databases, including PubMed, Medline, CINAHL, and the Universities libraries search engine were searched using the following search strategy: (cochlear implant) AND (auditory evoked potentials) AND (auditory system plasticity) OR (auditory maturation). The search was limited to peer-reviewed articles written in English and involving human participants. Reference lists in obtained journal articles were also examined to seek out additional relevant sources.

Selection Criteria

Studies selected for inclusion in this critical review were required to investigate CAEP measurements of implanted children (< 18 yearsyears) as compared to normal hearing children and adults. The studies were limited to those including children with unilateral cochlear implants only and sample sizes greater than five. The studies were limited to CAEPs as the outcome measure, and not speech perception abilities or other electrophysiological measures. No limits were set on the age of implantation or the research methods used.

Data Collection

Results of the literature search yielded five articles that were congruent with the selection criteria above: five between group non-randomized intervention studies which only come from two different research groups. According to the level of evidence hierarchy for high quality studies, all studies provided a level 3 of evidence (Cox, 2005).

Results

Group Study#1. Sharma, Dorman, and Spahr (2002a) recorded CAEPs from 136 normal hearing persons ranging in age from 0.1 yr to 20 yr, and 121 hearing impaired persons with cochlear implants ranging in age from 2.3 yr to 35 yr. Fourteen hearing impaired subjects were excluded from the study due to stimulus artifact in the recording, and 107 cochlear implant subjects were included. The hearing impaired subjects were either congenitally deafened or had severe to profound hearing loss by age 1. Post hoc, the cochlear implant users were divided into three groups. The early implanted group consisted of 57 subjects who had been implanted by age 3.5 years. The middle implanted group consisted of 29 subjects who had been implanted between 3.6 and 6.5 yr. The late implanted group consisted of 21 subjects who had been implanted after 7 years of age. CAEPs were recorded with a 90 msec synthesized speech syllable /ba/. Each subject had at least two averaged waveforms of 300 sweeps, and if replicable, the waveforms were averaged together. The P1 was identified, and the latency values were recorded regardless of chronological age or age of implantation in subjects.

The results from the normal hearing subjects were best fit by a growth function based on the natural log of age ($R2= 0.78$; $p<0.0001$). It revealed that P1 latencies decreased rapidly from 0 to 10 yr, and decreased more slowly from 10 to 20 yr. For the cochlear implant subjects, 55 out of 57 subjects in the early implanted group had P1 latencies within the normal range. 19 out of 29 subjects in the middle implanted group were outside the normal range, and 20 out of 21 of the late implanted subjects were outside of the normal range. Both the middle and late implanted group differed significantly from the early implanted group with the proportion of P1 latencies falling within normal range (Fishers Exact Test for two proportions, $p=0.0000001$). The results showed that the early implanted group showed normal P1 latencies by 6 months post-implantation. The late implanted group showed delayed P1 latencies if implanted after 7 years, which reflects abnormal central auditory maturation. Interpretation of the results suggested that children have a sensitive period of up to 3.5 yr where the brain has maximum plasticity. In discussing the results, the authors state that other variables can affect the P1 latency responses, such as age and duration of use of amplification prior to cochlear implants, and amount/type of aural habilitation.

Group Study #2. Sharma, Dorman and Spahr (2002b) recorded CAEPs from 22 pre-lingually deaf children with cochlear implants, ranging in age from 1.25 to 5.65 yr (mean age 3 years). Subjects were divided into four groups, depending on duration of stimulation with implant, with 1 week, 2 months, 5 months and 8 months. CAEPs were recorded using a synthesized speech syllable /ba/ presented at an interstimulus interval of 500ms with a loudspeaker placed 45 degrees to subject's implanted side. The P1 latencies were recorded and averaged within the groups to create grand-average waveforms.

Statistical analysis revealed that the subjects did not significantly differ in respect to age at time of fitting ($F (3,18)= 0.04$; $p=0.98$), and at time of testing ($F (3,18)= 0.39$; $p= 0.76$). The 1 week group had a mean fitting age of 2.63 years, and mean age at test 2.64 years. The 2 months group had a mean fitting age of 2.48 years and mean age at test 2.61 years. The 5 months group had a mean fitting age of 2.64 years, and mean age at test 3.1 years. The 8 months group had a mean fitting range of 2.8 years, and mean age at test 3.49 years. The grand-averaged waveforms showed distinct changes in the morphology in the different groups with negativity at about 150ms in week1, and by

8 months the waveform was similar to age-matched normal hearing peers. For the mean P1 latencies, a one-way ANOVA showed a significant effect of duration of stimulation of implant with P1 latency ($F(3,18) = 20.39; p=0.000005$). Interpretation of the results suggested that congenitally deaf children implanted at an early age can have age appropriate P1 latencies 8 months post implantation. Results showed that there is a high degree of plasticity in the central auditory system in children implanted at an early age due to the drastic waveform morphology changes and the decrease in mean P1 latencies within 8 months post implantation. The study only included early implanted children, and omitted late implanted children, which could have limited the validity of these results. Other variables that could affect the outcomes of the P1 responses were not included, and could have biased the results in a positive direction.

Group Study #3. Ponton, Don, Eggermont, Waring, & Masuda (1996a) recorded CAEPS from 14 children and 10 adults with normal hearing, and 6 children and 6 adults with profound hearing loss that received a unilateral cochlear implant. The average age of implantation in the children was 4.5 years, ranging from 1.5 to 6 years. The subjects were tested in a comfortable reclining chair in a sound-attenuated booth with stimuli consisting of 100us clicks for normal hearing subjects and 200us/phase biphasic electric pulses for the implanted subjects. The pulses were presented at a rate of 1.3 per second at 65 dB nHL for the normal hearing subjects, and at most comfortable levels for the implanted subjects. There were 30 electrodes used on the scalp, and the responses reported are from the vertex (Cz) location.

Statistical analysis revealed mean and standard deviations of the P1 latencies, and plotted the P1 latency change data on a non-linear curve fit analysis. The best fit functions showed that the latencies decrease with age at the same rate for implanted and normal hearing children. The best fit function is displaced to the right for the implanted children, and this showed that the maturation of the P1 latency is delayed. The latencies for the adult implanted group showed shorter P1 latencies for the implanted group, but provide information to compare against the maturation of the P1 responses in the implanted children. The P1 latencies become adult-like for normal hearing children at age 15, and by extrapolation from the data, the P1 latencies will mature for implanted subjects at age 20. One of the main findings was that the implanted children will have mature P1 latencies about 5 years later than the normal hearing children, which can possibly be related to the close similarity between the period of deafness and the maturational delay. Another main finding was that the waveform morphology in the implanted children showed no 'classical N1/P2 components, which emphasized delayed maturation in the auditory cortex. Overall, the results of this study showed that implanted children can restore normal auditory cortical function following implantation, but with a maturational delay. The authors suggest that the near normal responses with the adult implanted subjects cannot predict normal responses in the implanted children since the adults had normal hearing or residual hearing into adulthood. Also, the small number of implanted children (n=6) most likely resulted in an unrepresentative sampling of this group compared to the larger sample size (n=107) from Sharma, et al., 2002a.

Group Study #4. Ponton, Don, Eggermont, Waring, Kwong and Masuda (1996b) recorded CAEPs from 39 normal hearing children and adults, and 18 hearing impaired children and adults with cochlear implants. The average age between detection of profound hearing loss and cochlear implantation was 4 years 5 months. Cochlear implanted subjects were tested with brief trains of 10 clicks or pulses at a rate of 1.3/s and at an individually loud, but comfortable level. Normal hearing subjects were presented with clicks monaurally to left ear at 65dB above threshold.

Statistical analysis revealed mean P1 latencies for the adults and children. The cochlear implanted children were grouped into three categories based on duration of auditory deprivation. Short auditory deprivation had an average of 1.1 years, medium deprivation had an average of 4.9 years, and long deprivation group with only two children had 8 years 4 months and 8 years 10 months of deprivation. The P1 latencies were described with a decaying exponential fit function, which assumes P1 latencies decrease with age. The data were plotted with a best-fit function from the first analysis as well. It showed that P1 latencies mature at the same rate in the different groups of auditory deprivation and normal hearing controls, however, maturation is delayed for the cochlear implanted subjects. By extrapolation of the best fit function data, the P1 latencies did not mature until age 17, 20, and 25.5 for the short, medium and long deprivation implant groups. This study showed that the auditory system is plastic in deaf children, and when auditory stimulation from a cochlear implant is provided, the cortex can still resume normal maturation but is delayed by the period of auditory deprivation.

Group Study #5. Eggermont, Ponton, Don, Waring & Kwong (1997) measured CAEPs on 8 adults and 31 children with normal hearing, and 6 adults and 12 children fitted with cochlear implants. In the implanted children, the deafness occurred between birth and 5 years 1 month, and the duration of deafness ranged between 5 months and 8 years 10 months. For normal hearing subjects, clicks were presented monaurally at 65 dB HL above threshold to left ear, and for implanted subjects, clicks were presented at loud but comfortable levels. Potentials were recorded from 30 electrode locations and the vertex (Cz) location was used to report the data. Statistical data used the exponential fit function on a semi-logarithmic scale. Post hoc, the implanted subjects were divided into three groups based on the duration of deafness prior to implant, with short duration, medium and long duration. The results showed that the maturation rate is the same for both implanted and normal hearing children. For the short duration deafness group, the P1 latencies are near the upper boundary of normal range. For the long duration deafness group, the P1 latencies are well above the normal range and considerably longer than medium duration deafness group's exponential fitting curve. Overall, the results found that children implanted at an earlier age will only show minor maturational delays, but if implanted at a later age, the maturational process will equal the duration of deafness. The authors stated that it is not known at what age limit cochlear implantation will be not effective in restoring cochlear maturation, and therefore, a longitudinal study needs to be conducted.

Discussion

The evidence from these five studies needs to be interpreted with caution because all of these studies, (except Sharma et al., 2002a) included fairly small sample sizes for the subjects with cochlear implants and no study used random selection to obtain subjects. The sample sizes for studies #2-5 ranged from 12 to 22 cochlear implanted subjects. However, study #1, Sharma et al., 2002 had 107 cochlear implanted subjects, which was statistically significant. In addition, the experimental methodologies were diverse which made it difficult to make comparisons across studies and could have a large effect on the overall findings extrapolated from the studies. For the CAEP procedure and data analysis, some of the differences included; stimuli, duration and rate of stimuli, presentation levels, transducers used to test, averaging, artifact rejection and sweeps criteria for data analysis. Despite the sample size limitations and the diversity of experimental CAEP procedures used, some important and contradicting trends emerged. First, all the studies demonstrated differences in P1 latencies measured in cochlear implant subjects at different ages, however, only one study, Sharma et al., 2002a showed an optimal age limit for implantation for development of the central auditory system. Sharma et al., (2002a), demonstrated a sensitive period of about 3.5 years where the central auditory system remains maximally plastic. This study had sufficient statistical significance to support the conclusion that cochlear implantation should be done prior to age 3.5 in congenitally deaf children, and that after age 7, the plasticity in the brain is greatly reduced. Also, the research from Sharma and colleagues found that P1 latencies will be in normal range within months after initiation of a cochlear implant for early implanted children (Sharma et al, 2002a, 2002b). In comparison, the results from Ponton and colleagues did not suggest a critical period for implantation for deaf children. Ponton and colleagues, however, demonstrated that children with cochlear implants will have P1 latencies develop at the same rate as normal hearing subjects, but with a maturational delay that is related to the amount of years of auditory deprivation (Ponton et al., 1996, 1996 & Eggermont et al., 1997). Also, these three studies showed that the morphology is different in children with cochlear implants, as the typical N1/P2 complex will either be delayed or absent compared to age matched normal hearing children, which demonstrates the maturational delay. Therefore, the shorter duration deafness subjects or earlier implantation will provide P1 latencies that are closer to normal range than the longer duration deafness subjects. These three studies failed to provide sufficient statistical evidence to allow for an accurate evaluation of the experimental evidence, and the findings should be viewed cautiously.

Another limitation in interpreting the findings of this research involves differences in the subjects across the studies. The studies varied in their tendency to control for differences between cochlear implant subjects on variables that can affect the CAEP results, such as age of implantation, duration of implant use, type of implant, amount of habilitation or hearing aid use prior to implantation, and timing of deafness. Three of the review studies selected the cochlear implant subjects based on considerable improvement in speech recognition with the device (Ponton et al., 1996, 1996 & Eggermont et al., 1997). The first two studies (Sharma et al., 2002a,b) selected the cochlear implant subjects based on the timing of deafness, either congenitally deafened or severe to profound hearing loss by age 1 year. Therefore, the differences in selection criteria and the aforementioned confounding variables can limit the validity of comparisons across studies.

The overall conclusion of this review is that a shorter duration of deafness or earlier implantation in children with congenital deafness or profound hearing loss will produce P1 latencies that are within or near normal range for CAEP responses. However, the present review suggests conflicting results regarding a critical period for implanting deaf children. The research from Ponton and colleagues indicated that there is a maturational delay in CAEPs in cochlear implant users compared to normal hearing subjects, and even greater maturational delays for late implanted children. Yet, this maturational delay in implanted children suggested that the auditory system can resume normal development after a period of auditory deprivation, which showed that there is no sensitive period for implanting deaf children. In comparison, the overall findings from Sharma and colleagues suggested that cochlear implantation in congenitally deaf children should be done prior to age 3.5 years when the central auditory cortex remains maximally plastic. Given the contradiction between the two research groups, a definitive critical period for cochlear implantation in deaf children remains difficult to suggest. Further research is needed to more clearly understand if there is a critical period to implant deaf children to provide the best possible treatment after auditory deprivation.

Clinical Implications

Clinically, the present review can provide some valuable information to the pediatric cochlear implant field. To determine an optimal age range for implantation would be clinically useful in the future. Since only Sharma and colleagues have suggested a developmental sensitive period for cochlear implantation; a strong recommendation for this age range to be used as the time frame for cochlear implants in children needs to be viewed cautiously.

Future research with longitudinal studies is needed to understand the long-term effects of deafness and auditory stimulation from a cochlear implant on the development of the central auditory system. Future research should include larger sample sizes, and focus on determining the relationship between auditory cortex development and the many different confounding variables (i.e., age of implant, timing of deafness, etc). This potentially could provide clinicians and parents more information regarding the appropriate time frame for cochlear implantation. CAEP responses could also be used as a counseling tool to describe the development and maturation of the auditory cortex pre and post cochlear implantation.

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