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Simultaneous versus sequential bilateral implantation in young children: Effects on central auditory system development and plasticity

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Abstract

The aim of this study was to determine whether children who received early, simultaneous, bilateral cochlear implants showed more rapid development of the central auditory pathways compared to children who received early, sequential, bilateral implants. In 20 children, over the first 15 months following bilateral implantation, we assessed longitudinal changes in the morphology and latency of the P1 cortical response, which is generated within the auditory cortex. Our results showed that by 3.5 months post-implantation, mean P1 latencies for both groups of children were within normal limits. Overall, the developmental trajectory of the P1 response did not differ significantly for the two groups over the 15-month period. Our results suggest that bilateral implantation, whether sequential or simultaneous, occurring within a sensitive period of 3.5 years, takes advantage of the high degree of plasticity in the developing central auditory nervous system.

Key words: *cochlear implants, cortical auditory evoked potentials (CAEP), P1, development, plasticity*

Introduction

Over the last few years, bilateral implantation of young children has become increasingly common in clinical practice. Among the benefits of bilateral cochlear implantation is the restoration of some of the advantages of binaural hearing such as localization, improved listening in noise, directional hearing, binaural summation, and squelch. Typically, young hearing-impaired children are being provided with two implants either at the same time (simultaneous implantation) or at different times in early childhood (sequential implantation). However, there are no developmental studies that have examined the advantages and disadvantages of sequential versus simultaneous implantation in a systematic way. In the absence of such data, parents and surgeons are often concerned that sequential bilateral implantation (even at a young age) may be less beneficial compared to early simultaneous bilateral implantation. Therefore, a clinically relevant issue is whether there is a significant benefit to providing young children with implants simultaneously versus sequentially. Factors that weigh on this decision include difficulty and cost of simultaneous implantation surgery, difficulty in obtaining cooperation from medical insurance providers for simultaneous bilateral implantation, fatigue associated with mapping two implants at the same time in young children, lack of reimbursement to audiologists for simultaneous implant mapping sessions and whether bimodal (hearing aid + CI) amplification would provide more benefit than bilateral implantation.

In addition to providing the benefits of binaural hearing in young children, bilateral implantation may serve to ameliorate the morphological and physiological effects of auditory deprivation, given that normal maturation of the auditory system depends on receiving auditory input very early in childhood. In young children, development and plasticity of the central auditory pathways has been studied using latency and morphology of the P1 cortical auditory evoked potential (CAEP) (1,2). The P1 is generated by activity within the auditory cortex including recurrent, cortico-cortical input to the auditory cortex. The latency of the P1 CAEP decreases systematically as age increases, reflecting the maturation of the central auditory pathways. In a

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series of studies, Sharma et al. (3–5) examined maturation of the central auditory system in prelingually deafened children with unilateral cochlear implants. Results of those studies revealed that children who were implanted before age 3.5 years exhibited normal development of the P1 CAEP, while children implanted after age seven years exhibited delayed P1 latencies. Those results indicate that there is a sensitive period of about 3.5 years during which implantation occurs into a highly plastic central auditory system. Furthermore, failure to provide auditory input during early development leads to cortical reorganization with negative implications for speech perception abilities in children implanted later in childhood (6).

Because P1 latency reliably reflects maturation of auditory cortical pathways it may be used as a biomarker to assess central auditory development in children with hearing impairment, such as in deaf children who have had hearing restored with a cochlear implant (2,7). The large, rapid decreases in P1 latency that are typically seen in early implanted children within the first year after implantation are an indication of the high degree of plasticity in the developing auditory nervous system (5,8).

The relative benefit of simultaneous versus sequential bilateral implantation is an important clinical issue. However, it is often difficult to measure benefit objectively in young children. Typically, infants and young children are not able to perform complex behavioral tasks that could demonstrate the effects of binaural listening such as speech perception in noise, selective listening and directional hearing. Measurement of P1 latencies provides an objective means, in young children, of evaluating benefit from bilateral implantation by assessing development and plasticity of the central auditory pathways immediately following implantation.

In this study, we compared longitudinal changes in P1 latency in young children who received either simultaneous or sequential bilateral implants within the sensitive period for development of the central auditory pathways (i.e. under 3.5 years of age). At issue was whether central pathways develop more rapidly following early, simultaneous, bilateral implantation compared to early, sequential, bilateral implantation.

Methods

Twenty children with cochlear implants were tested. All children received bilateral implants under age 3.5 years. The children were divided into two groups based on whether they received their implants simultaneously or sequentially. The simultaneous implant group consisted of 10 children. Mean age of implant fitting was 1.57 years. The sequential implant group comprised 10 children whose mean age at first implant activation was 1.3 years, and 2.26 years at activation of the second implant. The time period between activation of the two implants ranged from 0.25 years to 1.68 years with a mean time period of 0.84 years.

P1 latencies were measured on average at implant activation, and at post- implantation intervals of one week, one month, three months, five months, eight months, 11 months and 15 months. Not every subject had P1 latency measurements at each of the post-implantation intervals specified above.

Evoked responses were recorded in response to a synthesized speech syllable – ba – presented at an interstimulus interval of 610 ms via a loudspeaker placed at an angle of 45 degrees to the side of the patient's implant. A full description of the stimulus can be found in a previous article (9). Implant speech processors were set to each child's usual settings. CAEPs were recorded in response to individual ears, i.e. a child's left side implant was turned off when the right ear was being tested and vice versa.

Subjects were seated comfortably in a sound booth while they watched a videotape movie. Videotape audio levels were kept below 45dB SPL. Evoked potentials were collected using a Synamps EEG amplifer (Compumedics/Neuroscan, El Paso, TX). Ag/AgCl electrodes were used for the recordings. The active electrode was placed at CZ, referenced to an optimized differential reference (10). The ODR is a point along the isopotential field of the CI stimulus artifact (typically along the forehead), which defines a point of null polarity for the artifact. Eye blinks were monitored from a separate bipolar recording channel placed at the lateral canthus of the eye, and referenced to the superior orbit. Averaging was suspended when eye blinks were detected. The recording window included 100 ms pre-stimulus and 600 ms post-stimulus time. Responses were analog filtered from 0.1 to 100 Hz. Two runs of 300 sweeps were collected per subject.

Sweeps larger than 100 uV were rejected offline. After that the remaining sweeps were averaged to compute a mean waveform for individual subjects. CAEPs were generated by averaging the epochs in each test block, separately. Replicable responses were then averaged together to create a grand average waveform for each subject. The P1 CAEP was defined as the first robust positivity in the waveform, or if the peak was broad, at the midpoint. P1 latencies were computed for each subject at each of the time- points described above.

Results

The longitudinal changes in P1 latencies for simultaneously and sequentially implanted children in the first year after implantation are shown in Figure 1.

P1 latencies from the two groups of subjects were treated as the response variable in a partially repeated measures analysis of variance (ANOVA) design under a general linear model for unbalanced data. Implant group (sequential or simultaneous) and duration of implant use were treated as between-group factors, and test ear (1st or 2nd CI for sequential, and left or right CI for simultaneous) as within-group factors. Results of the ANOVA revealed a main effect for duration of implant use, ($F(7.21) = 46.25$, $p < 0.0001$), but no effects for implant group (sequential vs. simultaneous), ($F(3.16) = 0.64$, $p = 0.602$). The main effect of duration corroborates previous results of a decrease in P1 latency as experience with the implant increases (5). An analysis of all possible pairwise comparisons (Scheffe's correction for multiple comparisons) revealed no significant differences for P1 latency between either group or either test ear compared within each time at test (i.e. duration of implant use) (alpha = 0.05).

As shown in Figure 1, P1 latencies were not significantly different for the two groups at any of the post-implantation time intervals shown in Figure 1. Compared to 95% confidence intervals for normal development of the P1 response (4), mean P1 response latencies for both groups were outside normal limits at implant activation, one week and one month post-implantation. For both groups of children, P1 latencies reached normal limits at three months post-activation and continued to decrease normally at the five, eight, 11 and 15-month post-implantation time-points.

In Figure 2, mean P1 latencies for each test ear for subjects in the two groups are plotted by duration of implant use. In the sequential group, at implant activation and up to three months later, the P1 latency for the second implanted ear tended to be shorter than in the first implanted ear, although this trend was not statistically significant.

CAEP waveforms from two representative subjects are shown in Figure 3. The left panel shows recordings made at the time of implant activation and then four months later from a child who received simultaneous implants at age 1.35 years. On the right panel are recordings made at the time of implant activation and five months later from a child who received his first implant at age 1.14 years and his second implant at age 2.13 years. As shown in Figure 3, there are distinct changes in the morphology of the CAEP and in P1 latency within the first few months after implantation, consistent with our previous reports (2,5).

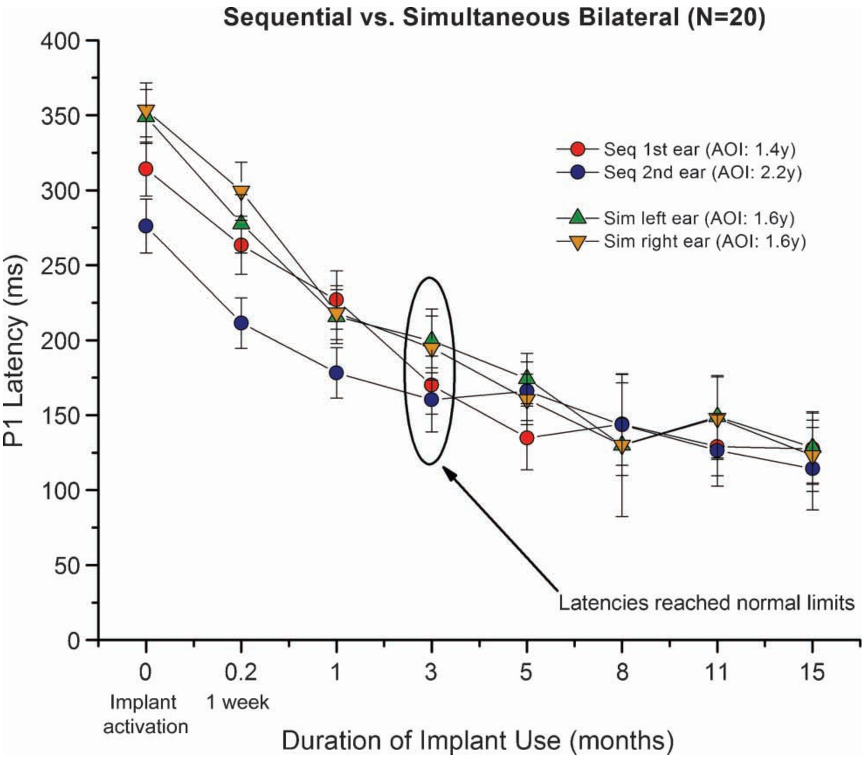

Figure 1. Mean P1 latencies for sequentially and simultaneously implanted subjects at various post-implantation time intervals. Error bars represent SEM.

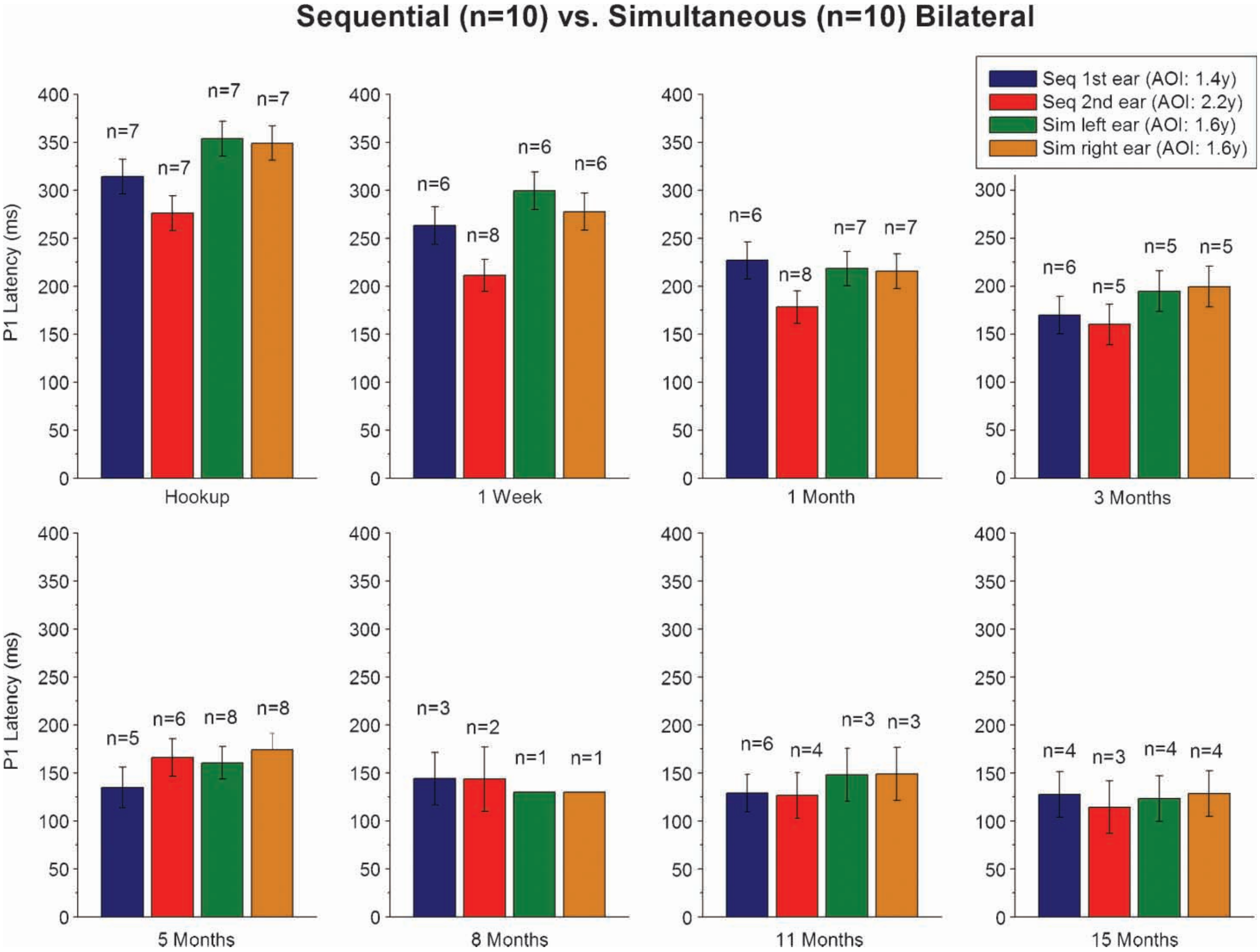

Figure 2. Mean P1 latencies for each test ear for subjects in the simultaneous and sequential implant groups are plotted by duration of implant use. The number of subjects within each group that were tested at each time interval is reported above the representative bar. Error bars represent the SEM.

Discussion

Our goal was to determine if there was a difference in development and plasticity of the central auditory pathways for young children receiving either simultaneous or sequential bilateral implants in early childhood. We measured changes in P1 latency and CAEP morphology in two groups of subjects who received either simultaneous or sequential implants under age 3.5 years, i.e. within the sensitive period for central auditory development described by Sharma, Dorman and Spahr (2002).

Overall, our results show that there were no significant differences in P1 latency for the two groups at the time of implant activation or at different post-implantation intervals (up to 15 months of implant use). At implant activation, the mean latencies of children who received simultaneous bilateral implants were not significantly different for the left and right ears, consistent with the symmetrical severe-to-profound hearing impairment for this group. For the sequentially implanted group, at implant activation and up to three months post-implantation, the P1 latencies for the ear that was implanted second tended to be less delayed than for the ear that was implanted first, although this trend was not statistically significant. This suggests either an age-related intrinsic development or a beneficial (if weaker) effect of stimulation ipsilateral to the first implanted ear or both. This finding is consistent with brain imaging and current source density data in both animal and human models that show robust stimulation of the auditory cortex contralateral to the implanted ear and a weaker stimulation of the cortex ipsilateral to the implanted ear in patients with unilateral cochlear implants (11,12). Consistent with the present findings, in previous case study reports we have also described shorter P1 latencies at implant activation for the second ear in sequentially implanted young children (8,13).

CAEP morphology at the time of implant activation was similar for both groups, in that a prominent negativity preceded the P1 response (Figure 3). We refer to this as the ‘deprivation negativity’ that is a

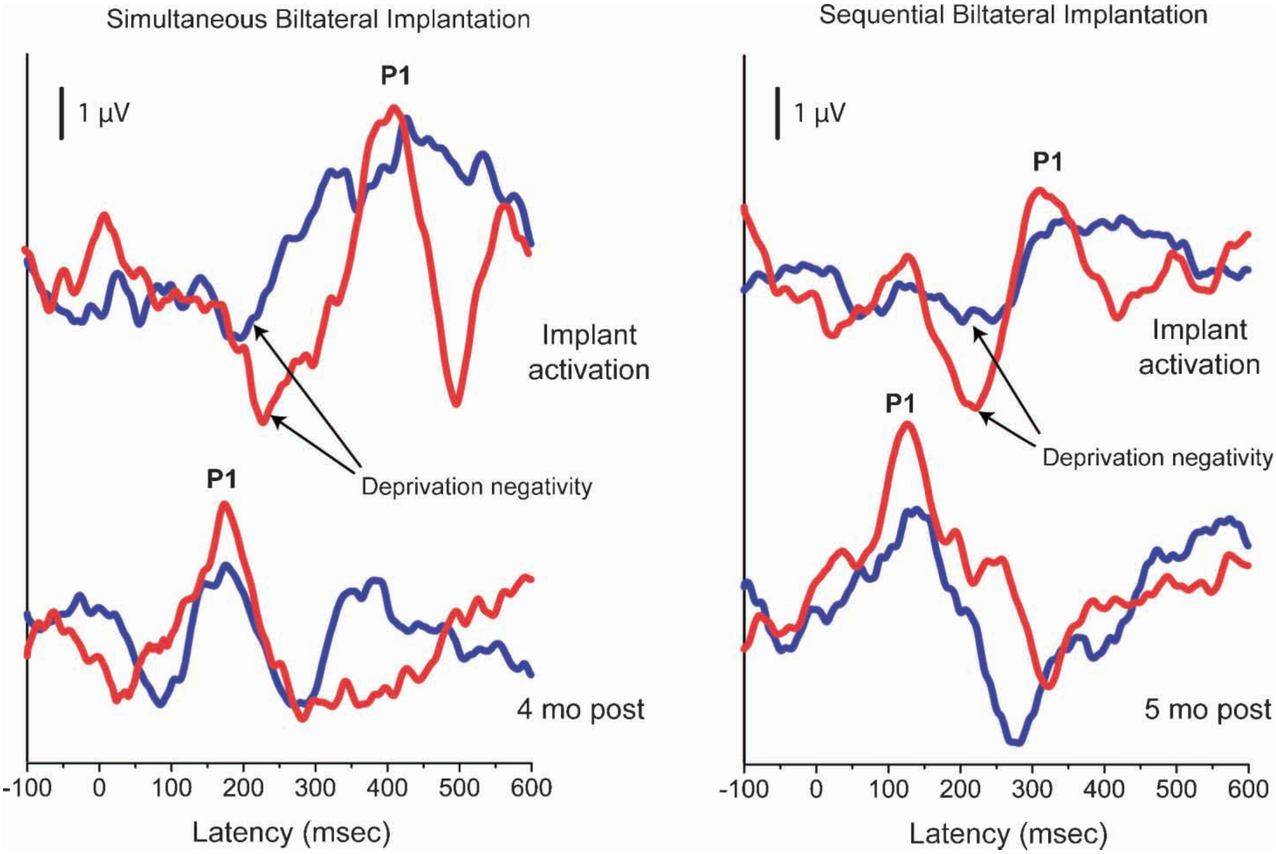

Figure 3. Grand mean CAEP waveforms for two subjects. The P1 response and the deprivation negativity response are indicated. Left panel: Left (blue) and right (red) ear waveforms are shown for a child who received simultaneous bilateral implants at age 1.35 years. Right panel: 1st CI (blue) and 2nd CI (red) waveforms are shown for a child who received sequential bilateral implants. Age at first implant was 1.14 years and at second implant was 2.13 years.

hallmark of the CAEP recorded from an unstimulated central auditory system. The presence of the deprivation negativity is consistent with severe-to profound degree of hearing impairment for children in the two groups.

By 3.5 months after implantation, both the latency of the P1 (Figure 1) and the morphology of the CAEP (Figure 3) were within normal limits for both groups. This fits the general profile of children implanted in early childhood (2). In contrast, studies have shown limited plasticity and poor behavioral performance when children receive a second implant at a sequentially later age in childhood (i.e. after age seven to nine years). Sharma, Dorman and Kral (8), Sharma and Dorman (2), and Martin (14) have described P1 responses in children who received their first implant early (under age 3.5 years) and their second implant late (after age seven years). Many (but not all) children who received their second implant after age seven years showed delayed P1 responses at time-points ranging from one to three years after the activation of the second implant. The morphology of the CAEP response from the second late implanted ear also tended to be abnormal (i.e. polyphasic or decreased in amplitude) and the children typically had poor speech perception in that ear (2,14). The findings of Sharma et al. are consistent with those described by Peters et al. (15) who measured speech perception in a large group of sequentially bilaterally implanted children. In the Peters et al. (15) study, all of the children tested had received their first CI before age five years and were divided into three groups based on their age at second implant: 3–5 years, 5–8 years, and 8–13 years. In general, all three groups appeared to achieve at least some benefit with binaural input. However, when testing only the second implant, children in the 8–13 years group revealed significantly poorer speech perception scores. These results and the results from our studies with evoked potentials suggest that auditory pathways and cortical regions linked to the ear of second implant commonly do not function normally when stimulation is delayed for seven to eight years. However, when bilateral implantation occurs within a sensitive period of 3.5 years, the central auditory pathways will develop rapidly and normally regardless of whether implantation occurs in a simultaneous or sequential fashion. There are however, some children who receive a second implant after age 7 years, who have normal P1 latencies and good speech perception. We are conducting studies to determine whether and how plasticity may be preserved in these children.

The results of the present study must be viewed with some caution as not all subjects had data points at all post-implantation intervals. A larger data set would be needed to determine if the trends that we have described in this paper would reach statistical significance. Furthermore, although the two groups in this study did not show differences in their central auditory developmental trajectory, there may well be functional advantages of early simultaneous bilateral implantation over sequential implantation. Gordon et al. (16) have reported that children who received simultaneous bilateral implants had shorter latencies for the auditory brainstem binaural interaction component compared with young children who were sequentially implanted. In future studies, we will compare binaural listening abilities, including speech perception in noise and directional and selective listening of the two groups, to study possible functional/behavioral advantages of early simultaneous implantation over sequential implantation.

Summary

We compared the developmental trajectory of the central auditory pathways in children who received simultaneous and sequential bilateral implants early in childhood. We measured changes in latency and morphology of the P1 CAEP response at different time-points within the first year after implantation for the two groups of children. Our results show that by 3.5 months after implantation, P1 latencies for both groups were within normal limits. The developmental trajectories for the two groups did not differ significantly at implant activation or at different post-implantation time-points (up to 15 months of implant use). Our results suggest that bilateral implantation, whether simultaneous or sequential, occurring within the sensitive period of 3.5 years, takes place within a central auditory nervous system that shows a high degree of developmental plasticity.

Acknowledgements

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