

Central Auditory Development in Children With Bilateral Cochlear Implants

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Objective: To examine the time course of maturation of P1 latencies in infant sequential and simultaneous bilateral cochlear implant recipients.

Design: Retrospective case series.

Setting: Pediatric collaborative cochlear implant program.

Patients: Four children who received bilateral cochlear implants prior to age 2 years.

Intervention: Cortical auditory evoked potential was completed to determine the latency of the P1 response in 4 children with bilateral cochlear implants.

Main Outcome Measures: Longitudinal development of the latency of the P1 cortical auditory evoked

potential in children who received bilateral cochlear implants prior to age 2 years.

Results: In 2 patients who received sequential bilateral implants, P1 latencies recorded from the first implanted ear were within normal limits after 3 to 6 months of implant use. By comparison, P1 latencies from the second implanted ear reached normal limits as early as 1 month after implant use. In 2 patients who received simultaneous bilateral implants, P1 latencies from both ears were also within normal limits in a very short time frame (ie, by 1 month poststimulation).

Conclusions: Our data suggest a high degree of plasticity of the central auditory pathways after early bilateral implantation. We find that P1 latencies provide a clinically useful biomarker of central auditory system development in children after cochlear implantation.

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BILATERAL PEDIATRIC COCHLEAR implantation is becoming increasingly common in clinical practice. One factor for this is an attempt to achieve the binaural benefit enjoyed by listeners with normal hearing. The binaural benefit includes improved performance in noise, binaural summation, binaural squelch, and localization of sound. These benefits have been previously established in adults using bilateral implants.¹⁻⁶

A motivation for and benefit of bilateral implantation in young children is to ameliorate the effects of auditory deprivation. It is known that speech recognition ability can become worse in the unaided ear for individuals who have bilateral hearing loss but unilateral hearing aid amplification.⁷ This deterioration is often attributed to a lack of auditory stimulation or auditory deprivation in the unaided ear. Studies in animal models have shown that spiral ganglion survival is decreased in the nonstimulated ear, that intracochlear electrical stimulation promotes survival of spiral ganglion neurons, and that the normal cochleotopic organization of the inferior

colliculus is severely reduced if electrical stimulation is not initiated at an early age.⁸⁻¹⁰ In humans, the effects of auditory deprivation on the central auditory system have been indirectly examined by computing P1 cortical auditory-evoked response latencies as an indicator of cortical maturation in response to sound.^{11,12} The P1 response is generated by auditory thalamic and cortical sources and varies with chronological age. Therefore, P1 latency can be used to infer the maturational status of auditory pathways after cochlear implantation.^{11,13} The rapid decreases in P1 latency after cochlear implantation are an indirect reflection of central auditory plasticity. Central auditory plasticity is affected by age, with earlier age implantation associated with a shorter time interval to normal latency values for the P1 response latency.¹⁴⁻¹⁶

Demonstrating benefit from bilateral cochlear implantation in very young children is difficult. Computing P1 latencies from cortical evoked responses provides an objective measure of benefit that has been clinically correlated with the development of early communicative behav-

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iors.¹⁶ We report results from 4 children who underwent bilateral implantation before the age of 2 years. Two of these children were fitted with implants sequentially, and the other 2 received their bilateral implants simultaneously. The P1 response latencies were recorded at various time intervals following implantation to assess the effects of bilateral implantation on the maturation of the central auditory pathways.

METHODS

Four children undergoing bilateral cochlear implantation between the ages of 12 to 24 months were identified, and their cortical evoked responses were reviewed in retrospect. Medical charts were reviewed to identify the etiology of hearing loss, time course and experience with hearing aids, and timing of cochlear implantation as these factors relate to the intervals of cortical evoked response testing. This research was approved by the institutional review boards of the University of Texas Southwestern Medical Center, Dallas, and the University of Texas at Dallas.

Cortical auditory-evoked responses were recorded in response to a synthesized speech syllable /ba/. Full information on the stimulus has been previously published.¹⁷ The stimulus was presented via a loudspeaker placed at an angle of 45° to the implanted side. Processors were set to the children's usual processor settings. Subjects were seated comfortably in a reclining chair placed in a sound booth. Subjects watched a videotaped movie or cartoon of their choice on a television monitor placed in front of them in the sound booth. Videotape audio levels were kept below a 45-dB sound pressure level. Evoked potentials were collected using Cz as the active electrode (Cz refers to the vertex midline placement). The reference electrode was placed on the mastoid and a ground electrode on the forehead. On some of the children with bilateral implants, the P1 response was obscured by the presence of a stimulus artifact in the first 100 ms of the recording. In these cases, the reference electrode was moved along the isopotential field of the artifact (typically around the forehead) to a point of null polarity, where the amplitude of the artifact was minimal and the response could be easily visualized.¹⁸ Eye movements were monitored using a bipolar electrode montage (lateral outer canthus to superior outer canthus). The reference electrodes were placed on the mastoids. Averaging was automatically suspended by the recording computer when eye blinks were detected. The recording window included a 100-ms prestimulus time and 600-ms poststimulus time. Incoming evoked responses were analog filtered from 0.1 to 100 Hz. Approximately 300 response sweeps were collected for each subject. The test session, including electrode application and evoked response recording, lasted for about 30 minutes. Sweeps greater than 100 μ V were rejected off-line, and the remaining sweeps were averaged to compute a grand average waveform for the individual subjects. We defined P1 as the first robust positivity in the auditory evoked potential waveform in the 50- to 175-ms range.¹⁷ The P1 latency was labeled at the peak of the response or, if the peak was broad, at the midpoint. The P1 response latencies were plotted against the 95% confidence interval for normal development of the P1 response.¹⁷

RESULTS

Patient 1 has asymptomatic congenital cytomegalovirus infection as the etiology to her profound sensorineural hearing loss. When the patient was tested at age 8 months, the results of auditory brainstem response testing showed

a profound hearing loss bilaterally. Aided thresholds tested in a sound field revealed a pure-tone average (PTA) of 90-dB hearing level (HL). Patient 1 met the criteria for cochlear implantation and underwent implantation in the left ear at age 12 months and in the right ear at age 24 months. The postimplantation developmental trajectory for P1 latencies is shown in the **Figure, A**. At the time of hook-up in the left ear, the P1 latency was significantly delayed, which is indicative of an unstimulated auditory system.¹³ Consistent with our previous findings, as experience with the implant increased, rapid decreases in P1 latency were observed, and the P1 response latency was within normal limits after 3 months of implant use.¹³ At the time of initiation of stimulation of the second (right) ear, the P1 latency was less delayed compared with the hook-up latency of the first ear. The P1 latency in the second ear reached normal limits within a month of initial stimulation. When tested at age 3½ years, P1 latencies from both ears continued to show normal development.

Patient 2 has *GJB2* (connexin 26 and 30) mutations (312del14 and del342kb) as the etiology to his profound sensorineural hearing loss. Behavioral testing revealed unaided and aided thresholds in the severe to profound hearing loss range. Patient 2 underwent cochlear implantation in the left ear at age 10 months and in the right ear at age 15 months. The developmental trajectory for the P1 response is shown in the **Figure, B**. At the time of hook-up in the left ear, consistent with the profound hearing loss, the P1 latency was significantly delayed. Unfortunately, no data points could be obtained in this ear until 6 months poststimulation, at which time the P1 latency was well within normal limits. The hook-up data point of the right ear was contaminated by an artifact; however, we were able to infer a latency value that was less delayed compared to the hook-up latency for the first ear. The P1 latency in the right ear continued to decrease as expected, and when tested at age 1½ and at age 2 years, the P1 latency from both ears was developing normally.

Patient 3 has asymptomatic congenital cytomegalovirus infection as the etiology of her profound sensorineural hearing loss. Behavioral testing showed that she had an unaided PTA of 98-dB HL in the right ear and 105-dB HL in the left ear. The aided PTA was 75-dB HL when tested in the sound field. Patient 3 met the standard candidacy criteria for cochlear implantation and underwent simultaneous bilateral implantation at age 12 months. The developmental trajectory for the P1 response latency is shown in the **Figure, C**. In this case, although the P1 latencies from both ears were significantly delayed at the time of activation, the latencies from both ears were within normal limits as early as 1 month after initial stimulation.

Patient 4 has congenital severe-profound sensorineural hearing loss. Behavioral testing showed that his unaided PTAs were 78-dB HL in the right ear and 83-dB HL in the left ear. His aided PTA was 53-dB HL when tested in the sound field. He underwent simultaneous bilateral cochlear implantation at age 15 months. The developmental trajectory of the P1 response is shown in the **Figure, D**. At hook-up, P1 latencies from both ears were

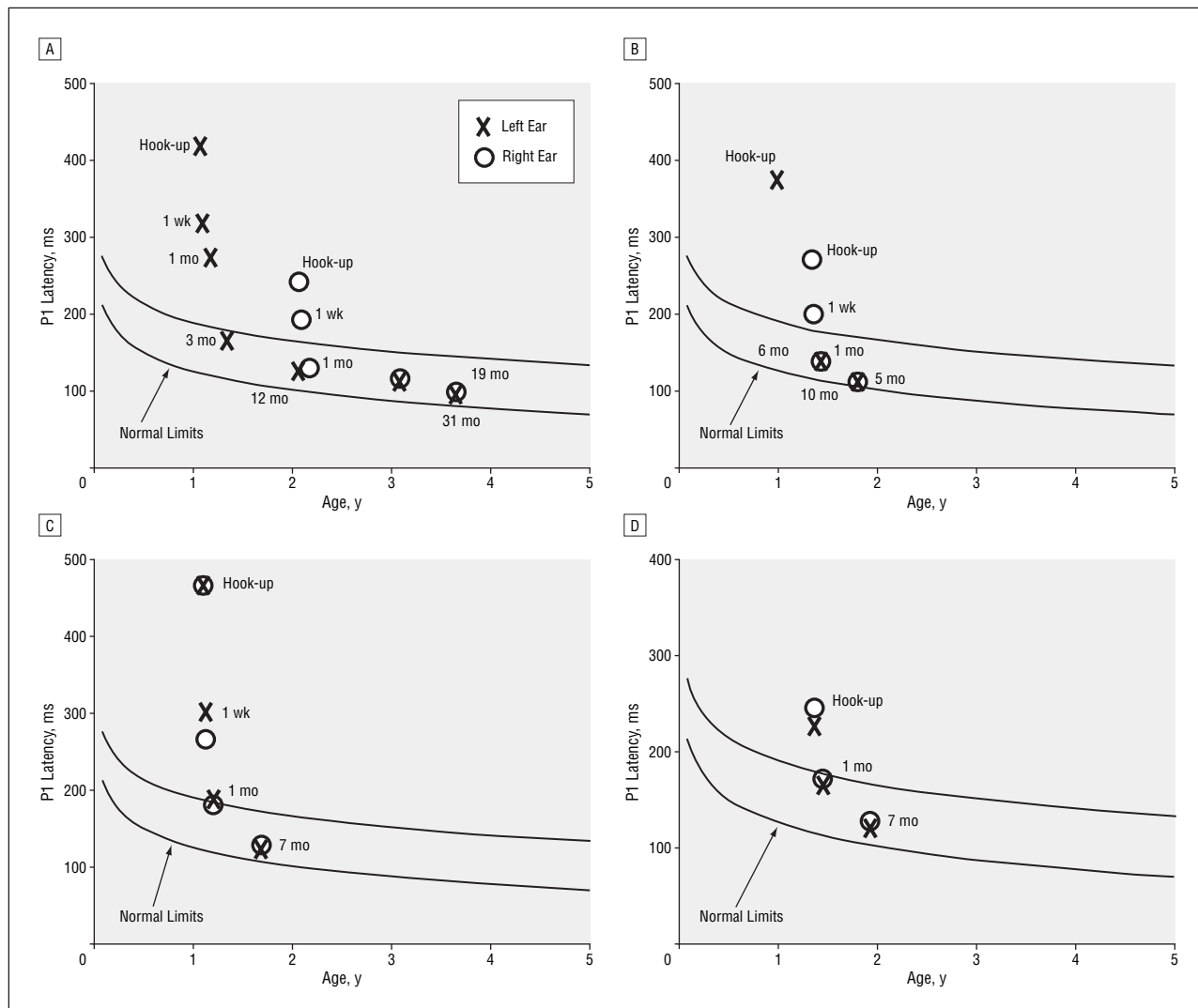


Figure. Trajectories for P1 latency changes following sequential bilateral implantation for (A) patient 1, (B) patient 2, (C) patient 3, and (D) patient 4. The solid lines represent the 95% confidence intervals for normal development of P1 latencies.

delayed. The delay in P1 latencies is less than that seen for patients 1, 2, and 3, consistent with the fact that this child had better aided thresholds than those children. That is, P1 latencies in this patient reflected auditory pathways that had received some (albeit not enough) degree of stimulation with hearing aids. After implantation, P1 latencies reached normal limits bilaterally after 1 month of implant use. As shown in the Figure, D, P1 latencies continued to show normal development after 7 months of implant use.

COMMENT

We have described the time course of maturation of the central auditory pathways (as reflected by P1 latencies) in 4 patients who received bilateral cochlear implants early in life (ie, younger than 2 years). In the 2 patients who received sequential implants, P1 latencies recorded from the first implanted ear were within normal limits after 3 to 6 months of implant use. This result is consistent with the trajectory for P1 latency development in children who

are fitted with a unilateral cochlear implant at an early age.¹⁴ For the sequentially implanted children, the P1 latency from their second implanted ear was less delayed at hook-up than the P1 latency from their first implanted ear. This finding is consistent with brain imaging and current source density data in both animal and human models that show a robust contralateral and weak ipsilateral stimulation (crossed and uncrossed fibers of the central auditory pathways) after unilateral implantation.¹⁹ Therefore, it is perhaps not surprising that the P1 latencies in the second implanted ear are within normal limits by about 1 month after stimulation because they have a shorter distance to travel.

To our knowledge, this study presents for the first time trajectories for P1 latency development in young children who were fitted with bilateral implants simultaneously. We would predict that the P1 latency in our simultaneous early implant recipients should normalize along a trajectory similar to other unilateral early implant recipients (or, in the case of our patients, the first ear of the sequential implant recipients). However, in our patients who received simul-

taneous early bilateral cochlear implants, the P1 latency was near normal limits by 1 month after implantation. This was most pronounced in patient 3, in whom the P1 latency was significantly delayed at the time of initial hook-up. Why was the time interval to a normal P1 latency so brief in patient 3? Although to our knowledge there are no animal models or other human studies to provide insight to this question, it is likely that simultaneous early implantation creates an environment in which both the crossed and uncrossed fibers of the central auditory system on a given side are being simultaneously stimulated. We theorize that synergistic (ipsilateral and contralateral) stimulation facilitates rapid development of central auditory pathways.

In conclusion, our data suggest a high degree of plasticity of the central auditory pathways after early bilateral implantation. These results support early bilateral implantation to preserve the integrity of the central auditory system. Finally, we found that P1 latencies provide a clinically useful biomarker of central auditory development in young children who undergo cochlear implantation.

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Author Contributions: The authors had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. *Study concept and design:* Bauer, Sharma, and Dorman. *Acquisition of data:* Bauer, Sharma, and Martin. *Analysis and interpretation of data:* Bauer, Sharma, and Dorman. *Drafting of the manuscript:* Bauer, Sharma, and Dorman. *Critical revision of the manuscript for important intellectual content:* Bauer, Sharma, Martin, and Dorman. *Statistical analysis:* Sharma. *Obtained funding:* Sharma. *Administrative, technical, and material support:* Bauer, Sharma, Martin, and Dorman. *Study supervision:* Bauer and Sharma. **Financial Disclosure:** None reported.

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