Rapid development of cortical auditory evoked potentials after early cochlear implantation

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The aim of our research was to estimate the time course of development and plasticity of the human central auditory pathways following cochlear implantation. We recorded cortical auditory-evoked potentials in 3-year-old congenitally deaf children after they were fitted with cochlear implants. Immediately after implantation cortical response latencies resembled those of normal-hearing newborns. Over the next few months, the cortical evoked responses showed rapid changes in morphology and latency that resulted in age-appropriate latencies by 8 months after implantation. Overall, the development of cortical response latencies for the implanted children was more rapid than for their normal-hearing age-matched peers. Our results demonstrate a high degree of central auditory system plasticity during early human development. *NeuroReport* 13:1365–1368 © 2002 Lippincott Williams & Wilkins.

Key words: Cochlear implant; Cortical auditory-evoked potentials; Plasticity

INTRODUCTION

The effects of congenital deafness on the human auditory pathways are not well understood. The effects are of sufficient magnitude that adults who have been deaf since birth receive essentially no speech understanding from electrical stimulation of the cochlea provided by a cochlear implant [1,2]. However, many congenitally deaf children, after receiving a cochlear implant, are able to acquire oral language [3,4]. The different outcomes occur, presumably, because degenerative changes take time to develop [5] and because young nervous systems exhibit a high degree of neural plasticity [6,7]. These findings suggest that the best time to implant a congenitally deaf child would be before the degenerative effects of sensory deprivation substantially alter the plasticity of the central auditory system. In humans, however, the time course of central auditory system plasticity is largely unknown.

We are investigating the time course of development and plasticity of the central auditory system in congenitally deaf children following cochlear implantation. Our response measure is the latency of the P1 cortical auditory- evoked potential. The P1 response is generated by auditory thalamic and cortical sources [8–10]. P1 latency reflects the accumulated sum of delays in synaptic propagation through the peripheral and central auditory pathways [11]. Because P1 latency varies as a function of chronological age [12], P1 latency can be used to infer the development of auditory pathways in children fitted with an implant.

In a previous study [13], we compared P1 latencies from 18 congenitally deaf children who were fitted with a cochlear implant by age 3.5 and from 18 age-matched normal-hearing peers. We found that the P1 latencies of implanted children after 6 months of implant use were not significantly different from their age-matched normal-hearing peers, suggesting that the functional development of central pathways was age-appropriate by 6 months after early implantation.

We have since replicated this finding in a larger group of cochlear-implanted children [14]. In that study we examined the P1 latencies of 97 pre-lingually deaf children fitted with implants at ages ranging from 1.5 years to 17 years against the 95% confidence intervals of P1 latencies derived from 124 normal-hearing children ranging in age from 0.1 to 17 years. The results showed that children implanted under 3.5 years of age had age-appropriate P1 latencies after 6 months of implantation, while children implanted after age 7 had delayed P1 responses, sometimes even after years of implant use. Taken together, the results of these two studies suggest that there is a sensitive period of about 3.5 years during early development when cochlear implantation occurs into a relatively non-degenerate and/or highly plastic central auditory system. This view is supported by animal studies of deaf rats and congenitally deaf white cats fitted with cochlear implants who demonstrate the existence of a sensitive period for the development of auditory pathways [15–17]. Our finding of normal P1 latencies in children who had experienced about 3 years of auditory deprivation could be accommodated by either of the following views of early development. One view is that central auditory pathways begin developing normally and remain minimally degenerate following periods of auditory deprivation for about 3 years. This period corresponds closely to the period of intrinsically driven synaptogenesis, or synaptic proliferation, in the auditory cortex [18]. Perhaps synaptogenesis protects central pathways from measurable effects of deprivation. In this case we would expect to see age-appropriate latencies immediately following implantation and subsequently an age-appropriate rate of development.

An alternate hypothesis is that early implantation occurs into a highly plastic system where the effects of deprivation can be overcome in a relatively short period of time. There is evidence for such rapid functional development from the visual system [7]. From this point of view, we would expect to see delayed cortical response latencies immediately post-implantation, followed by a rate of development that is faster than that shown by age-matched controls resulting in age-appropriate latencies after a period of implant use.

The aim of this study was to test the two hypotheses described above. Towards this aim, we examined the changes in morphology and latency of the P1 response during the initial 8 months after the initiation of electrical stimulation in 22 pre-lingually deaf children fitted with a cochlear implant.

MATERIALS AND METHODS

Informed written consent was obtained from the parents of all children prior to testing. Informed consent procedures and the test protocol were approved by the Institutional Review Boards of the University of Texas at Dallas and Arizona State University (where the studies were conducted). Twenty-two pre-lingually deaf children with cochlear implants were tested. Subjects ranged in age from 1.25 to 5.65 years (mean age 3 years). The mean age of fitting with the cochlear implant was 2.6 years. The children were divided into four groups based on duration of stimulation with the implant: Group one consisted of five children (mean fitting age 2.63 years, mean age at test 2.64 years) whose mean duration of stimulation with the implant was 1 week (range 1 day to 8 days); Group two consisted of five children (mean fitting age 2.48 years, mean age at test 2.61 years) whose mean duration of stimulation with the implant was 2 months (range 1–2 months); Group three consisted of six children (mean fitting age 2.64 years, mean age at test 3.1 years) whose mean duration of stimulation with the implant was 5 months (range 5–7 months); Group four consisted of six children (mean fitting age 2.8 years; mean age at test 3.49 years) whose mean duration of stimulation with the implant was 8 months (range 7–9 months).

Evoked responses were recorded in response to a synthesized speech syllable/ba/presented at an interstimulus interval of 500 ms via a loudspeaker placed at an angle of 45° to the side of the patient's implant. A full description of the stimulus can be found in a previous study [12]. Implant speech processors were set to each child's usual settings.

Subjects were seated comfortably in a sound booth while they watched a videotape movie. Videotape audio levels were kept below 45 dB SPL. Evoked potentials were collected using Cz as the active electrode referenced to the mastoid of the non-implanted side, with the ground electrode at Fpz. Eye movements were monitored using electrodes near the eye of the non-implanted side at the lateral and superior outer canthi. Averaging was suspended when eyeblinks 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 $> 100\,\mu V$ were rejected offline. After that the remaining sweeps were averaged to compute a mean waveform for individual subjects. P1 latencies were computed for each subject. Evoked response waveforms were averaged across subjects within a group to compute group grand-average waveforms.

RESULTS

A one-way ANOVA showed that the children in the four groups were not significantly different with respect to their age at the time of fitting with the cochlear implant ($F = 0.04$; $p = 0.98$) or at the time of testing ($F = 0.39$; $p = 0.76$). Grand-average waveforms for the four groups are shown in Fig. 1. Distinct changes in the morphology of the cortical evoked response waveform were seen as the duration of stimulation with the implant increased. For the group which had the shortest duration of stimulation (1 week), a distinct negativity was seen at about 150 ms. As the duration of stimulation with the implant increased to 2 months the initial negativity decreased in latency and amplitude, while

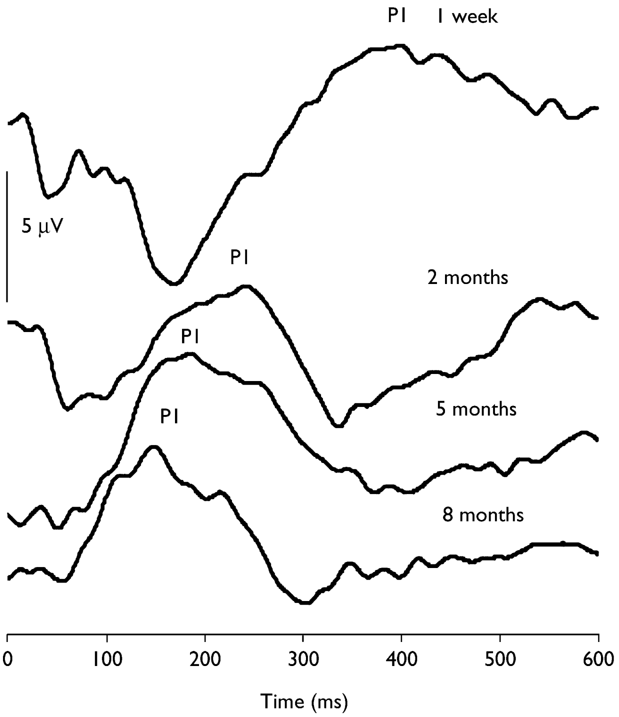

Fig. 1. Grand-average cortical auditory-evoked response waveforms for the four age-matched groups of implanted children based on their average duration of stimulation with the cochlear implant (1 week, 2 months, 5 months and 8 months).

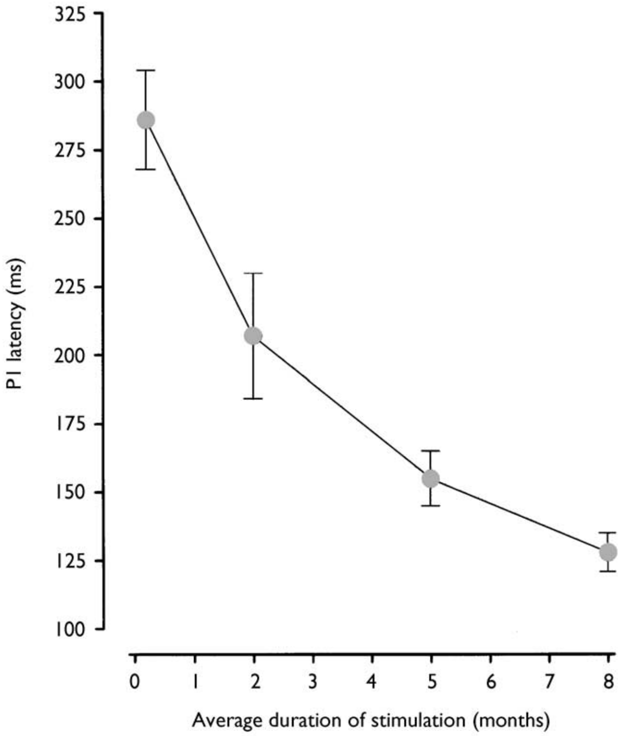

Fig. 2. Changes in P1 latency as a function of duration of stimulation with the cochlear implant.

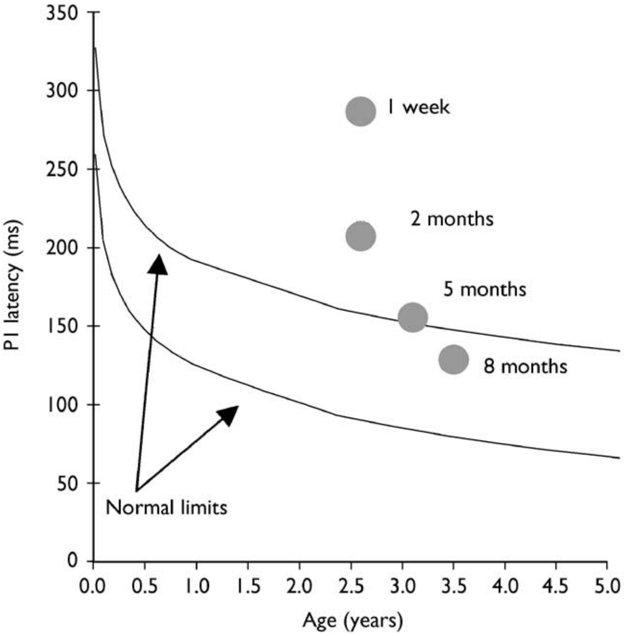

Fig. 3. 95% confidence interval for the normal development of P1 latencies from Sharma *et al.* [14]. Superimposed are the mean P1 latencies (circles) from four groups of implanted children as a function of their chronological age and based on average duration of stimulation with the cochlear implant (1 week, 2 months, 5 months and 8 months).

the P1 response appeared more robust and was shorter in latency. With a still longer duration of stimulation of 5 months, the initial negativity essentially disappeared and the P1 latency was shorter. Finally, after 8 months of stimulation with the implant, P1 latency was still shorter and the waveform morphology resembled that of age-matched normal-hearing controls [13,14].

Mean P1 latencies for the four groups are shown in Fig. 2. A One-way ANOVA revealed a significant main effect of duration of stimulation with the implant on the P1 latency ($F = 20.39$, $p = 0.000005$).

Figure 3 shows the 95% confidence interval for normal development of P1 latencies from ages 0.1 to 5 years derived from 124 normal-hearing subjects [14]. The mean P1 latency data as a function of chronological age for the four groups are superimposed on the 95% confidence intervals. After 1 week of stimulation with the implant, P1 latencies were similar to those of normal-hearing newborns. The rate of development of P1 latencies for implanted children was greater than for age-matched normal-hearing children, and by 8 months of stimulation implanted children showed age-appropriate P1 latencies.

DISCUSSION

Our results show that in congenitally deaf, early-implanted children the cortical auditory evoked response waveform undergoes dramatic changes in the first 6–8 months following implantation. An early negativity seen in children with little auditory experience diminishes in amplitude and latency with more auditory experience. P1 latency decreases rapidly with increasing auditory experience reaching age-appropriate values within 8 months post-implantation. Immediately post-implantation, P1 latencies of our 3-year-old implanted children were similar to those of normal-hearing newborns. Subsequently, the rate of development of P1 latencies over the first 8 months was more rapid than for age-matched normal-hearing controls.

The precise neurophysiological mechanisms for the rapid development of P1 latencies after early implantation are not clear at this time. Kral *et al.* [19] have shown that congenitally deaf cats show a restricted (atypical) pattern of activation of the primary auditory cortex compared with normal-hearing cats. Perhaps early stimulation with a cochlear implant initiates a more widespread (typical) sequence of activation of different cortical layers resulting in robust cortical responses and shorter response latencies over time.

Our findings are consistent with recent results from the visual system. Maurer *et al.* [7] assessed visual acuity in human infants who were congenitally deprived of patterned visual input by cataracts. The cataracts were removed at 1 week to 9 months of age. Maurer *et al.* found the initial acuity levels after cataract removal were at newborn levels and that acuity improved rapidly, with some improvement apparent after as little as 1 h of visual input. Critically, the rate of development of visual acuity following cataract removal was significantly greater than that found for age-matched children with normal vision.

CONCLUSION

We have found a high degree of plasticity in the central auditory pathways of congenitally deaf children who were fitted with a cochlear implant early in childhood. We infer the presence of plasticity from the rapid alterations in morphology and decreases in the latency of cortical auditory-evoked potential components within the first 8 months following implantation. The rate of development of P1 response latencies in early-implanted children is greater than for age-matched normal-hearing controls and results in age-appropriate latencies within 8 months following initiation of implant use.

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