

Møller A (ed): Cochlear and Brainstem Implants.
Adv Otorhinolaryngol. Basel, Karger, 2006, vol 64, pp 66–88

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Central Auditory Development in Children with Cochlear Implants: Clinical Implications

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Abstract

A common finding in developmental neurobiology is that stimulation must be delivered to a sensory system within a narrow window of time (a sensitive period) during development in order for that sensory system to develop normally. Experiments with congenitally deaf children have allowed us to establish the existence and time limits of a sensitive period for the development of central auditory pathways in humans. Using the latency of cortical auditory evoked potentials (CAEPs) as a measure we have found that central auditory pathways are maximally plastic for a period of about 3.5 years. If the stimulation is delivered within that period CAEP latencies reach age-normal values within 3–6 months after stimulation. However, if stimulation is withheld for more than 7 years, CAEP latencies decrease significantly over a period of approximately 1 month following the onset of stimulation. They then remain constant or change very slowly over months or years. The lack of development of the central auditory system in congenitally deaf children implanted after 7 years is correlated with relatively poor development of speech and language skills [Geers, this vol, pp 50–65]. Animal models suggest that the primary auditory cortex may be functionally decoupled from higher order auditory cortex due to restricted development of inter- and intracortical connections in late-implanted children [Kral and Tillein, this vol, pp 89–108]. Another aspect of plasticity that works against late-implanted children is the reorganization of higher order cortex by other sensory modalities (e.g. vision). The hypothesis of decoupling of primary auditory cortex from higher order auditory cortex in children deprived of sound for a long time may explain the speech perception and oral language learning difficulties of children who receive an implant after the end of the sensitive period.

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In one of developmental neurobiology's classic experiments, David Hubel and Torsten Wiesel showed, for kittens, that a brief period of visual deprivation

during early infancy can profoundly and irrevocably alter central processes in vision [1]. A vast literature now documents the necessity for early stimulation if central processes in sensory systems are to develop normally. Given these results, infants and children with significant hearing loss are at risk for abnormal development of central auditory pathways. Because normal function of the central pathways is a precondition for normal development of speech and language skills, children with hearing loss are also at risk for abnormal development of these skills. The introduction of cochlear implants (and, more recently, auditory brainstem implants) has made it possible to activate auditory pathways and to avoid the effects of stimulus deprivation on the auditory nervous system.

How long a period of deprivation can be tolerated during infancy before the development of central processes is affected? In kittens, a short period of deprivation following birth can affect the normal development of central processes in audition [Kral and Tillein, this vol, pp 89–108]. It is of considerable interest to know the corresponding period for human infants and children. Infants born deaf and who are fit with a cochlear implant at different ages can be viewed as participants in a naturally occurring deprivation experiment and their development provides a unique window through which we can view the effects of deprivation on the auditory system. We have studied infants fit with cochlear implants for many years. In this paper we review our work, and that of others, which provides (a) a timeline for the deterioration of human central auditory pathways in the absence of stimulation and (b) documentation of the plasticity and development of central pathways once stimulation is initiated by a cochlear implant. The time epochs defined by these studies provide the foundation for a rational discussion of rehabilitation options for children with significant hearing loss.

Cortical Auditory Evoked Potentials as Measures of Central Auditory Development in Children with Cochlear Implants

Auditory evoked potentials can be recorded noninvasively from all levels of the central auditory pathways and can provide objective assessments of the development and functioning of the auditory nervous system in young children. For example, the auditory brainstem response (ABR) reflects activity in the auditory nerve and auditory structures in the brainstem. The middle latency response and cortical auditory evoked potentials (CAEP) reflect functioning of the auditory thalamocortical pathways and the auditory cortex. The P1 component of the CAEP has shown promise as a useful clinical biomarker of central auditory maturation in children with hearing loss and in children fit with a cochlear implant.

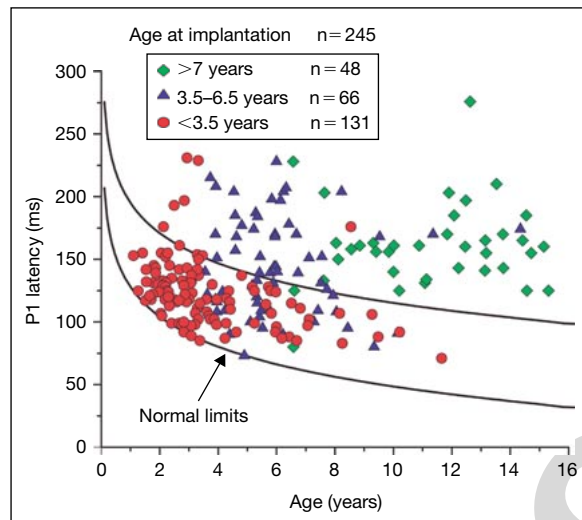


Fig. 1. P1 latencies as a function of chronological age for children with cochlear implants. The solid functions are the 95% confidence limits for normal hearing children [32]. P1 latencies for children implanted before age 3.5 years (early-implanted group) are shown as circles. P1 latencies for children implanted between age 3.5 years and 6.5 years (middle-implanted group) are shown as triangles. P1 latencies for children implanted after age 7 years (late-implanted group) are shown as diamonds.

In our studies, P1 is elicited using a speech stimulus /ba/ (clicks and tonal stimuli are also effective). P1 is an easily identified, robust positivity at a latency of 100–300 ms in young children. P1 is generated by auditory thalamic and cortical sources [2–4]. Ponton and Eggermont [5] suggest that the surface positivity of the P1 response is consistent with ‘a relatively deep sink ([in cortical] layers IV and lower III) and a superficial current return’. The latency of P1 reflects the accumulated sum of delays in synaptic transmission in the ascending auditory pathways including delays in the cerebral cortex [6].

Changes in the latency of P1 occur throughout infancy and childhood [7–12]. In normal-hearing newborns the mean P1 latency is approximately 300 ms. Over the first 2–3 years of life there is a large decrease in latency (to approximately 125 ms at age 3) and then a smaller decrease into the second decade of life. The mean P1 latency in normal hearing adults (ages 22–25 years) is approximately 60 ms. Ninety-five percent confidence intervals for normal development of P1 latency are described in Sharma et al. [11] and are shown in figure 1. Because P1 latency varies as a function of chronological age, P1 latency can be used to infer the maturational status of auditory pathways in infants and children. Of particular interest are infants and children with significant hearing loss.

Sensitive Periods for the Development of the Human Central Auditory Pathways

Studies of congenitally deaf children fit with cochlear implants at different times during childhood have allowed us to establish the existence and time limits of a sensitive period for the development of the central auditory pathways in humans. Figure 1 shows the latencies of the P1 peak in the CAEP obtained in 245 congenitally deaf children who received electrical stimulation of the auditory nerve through cochlear implants for at least 6 months. P1 latencies are plotted against the 95% confidence intervals of P1 latencies derived from 190 normal-hearing children. Children who were deprived of sound for a long period, greater than 7 years (fig. 1), showed delayed P1 latencies. These data are in keeping with data from animal models [Kral and Tillein, this vol, pp 89–108] and provide clear evidence of the effects of sensory deprivation on the function of the central auditory pathways in humans. About half of the children who experienced fewer years of deprivation, between 3.5–7 years (fig. 1), had normal P1 latencies and almost all children who experienced fewer than 3.5 years of deprivation (fig. 1) showed normal P1 latencies. These results are consistent with those from previous studies [11, 13, 14] and suggest that central auditory pathways are maximally plastic (in response to auditory stimulation) for a period of about 3.5 years in early childhood. If stimulation is delivered within that period, then latency and the morphology of the P1 reach age-normal values within 3–6 months following the onset of stimulation. However, if stimulation is withheld for more than 7 years, children exhibit delayed and abnormal P1 responses, even after years of implant use, suggesting that plasticity of the auditory pathways in response to auditory stimulation is greatly reduced after this age [11].

PET imaging studies have provided important evidence regarding the age cut-offs for the sensitive period. Studies such as those of Lee and colleagues [15–18] found a cut-off of about 4 years and are in good agreement with the electrophysiologic studies [11] described above.

These PET imaging studies made use of recordings of resting glucose-metabolism rates in the auditory cortices of prelingually deafened children and adults before cochlear implantation and related these rates to speech perception scores after implantation. The degree of glucose metabolism preimplantation was taken to be an indicator of the degree to which cross-modal recruitment of the auditory cortex had occurred. Thus, the auditory cortices should be 'silent' (hypometabolic) because of years of auditory deprivation. However, if the cortices had been recruited by other cortical functions, then the cortices would not be hypometabolic. Lee et al. [16] reported that the degree of hypometabolism before implantation (which was greater for younger subjects) was positively correlated with the speech perception scores after implantation. In

general, children who were implanted before age 4 showed the highest degree of hypometabolism in the auditory cortices before implantation and, following implantation, these children had the highest speech perception scores.

The age cut-off (4 years) is consistent with the 3.5 years cut-off for maximal plasticity of the central auditory pathways suggested by Sharma et al. [11]. Lee's data also suggest that following 6.5–7.5 years of deprivation significant cross-modal reorganization occurs in the auditory cortices. This finding is concordant with the Sharma et al. [11] finding of increased P1 latencies following 7 years of auditory deprivation.

Other studies [19, 20] of cochlear implanted children have found similar age cut-offs regarding the sensitive period. Eggermont and Ponton [19] found that the N1 component in the CAEP was absent in cochlear implanted subjects who had been deaf for a period of at least 3 years under the age of 6 years. On the basis of that, Eggermont and Ponton [19] suggested that this period reflects a critical time for cortical maturation and for achieving useful speech perception. Gordon et al. [20] have suggested that the auditory system in children who have experienced longer periods of deprivation (>5 years) have less potential for expression of neural plasticity (as measured by middle latency responses) than in children who have experienced fewer years of deprivation (<5 years).

In general, there are striking similarities between the critical age cut-offs for normal P1 latencies and the age cut-offs for normal development of speech and language skills. Several investigators [21–23] have reported that children implanted under ages 3–4 years show significantly higher speech perception scores and better language skills than children implanted after age 6–7 years. There are similarities between the critical age cut-offs for normal P1 latencies and the age cut-offs for normal development of speech and language skills. Several investigators [21–23] have reported that children implanted under the age of 3–4 years show significantly higher speech perception scores and better language skills than children implanted after 6–7 years. Consistent with these reports, unpublished observations in our laboratory suggest that children who have normal P1 latencies re: age matched, normal-hearing children, show, as a group, better speech perception scores on the multi-syllabic lexical neighborhood test [24] than children with abnormal P1 latencies [25]. However, not all children with normal P1 latencies achieve high scores on tests of speech understanding and not all children with abnormal P1 latencies achieve very poor scores. As Geers [this vol, pp 50–65] reports, many factors influence speech understanding including amount and type of rehabilitation. None-the-less, it is likely that the neural processes that constrain P1 latency have some influence on the complex of auditory functions that underlie speech perception [26–27]. For a review of sensitive periods as they relate to speech perception and language acquisition in children with cochlear implants see Harrison et al. [28].

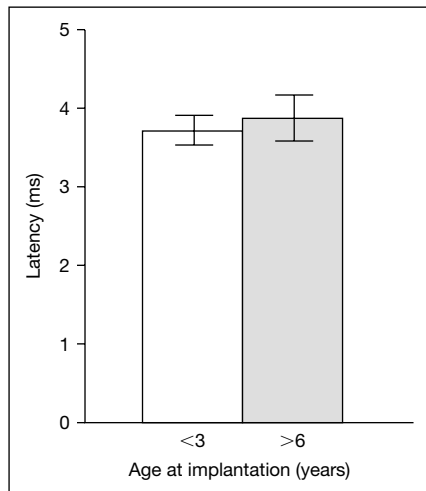


Fig. 2. EABR wave V latency for early-implanted children (<3 years) and late-implanted children (>6 years).

In summary, electrophysiologic and functional brain imaging (PET) data in humans suggest that there is a sensitive period of about 3.5–4.0 years in early development during which the plasticity of the central auditory nervous system is greatest and auditory stimulation delivered during this time is most effective in eliciting expression of neural plasticity. If more than 7 years of deprivation precede the onset of stimulation, then that stimulation is delivered to an already reorganized auditory nervous system.

There is no evidence, so far, from studies of children fit with a cochlear implant that suggest the existence of sensitive periods regarding expression of neural plasticity at the level of the auditory brainstem. Gordon et al. [29] reported rapid development of the ABR response after cochlear implantation regardless of the age at which children were implanted. Data from our laboratory (fig. 2) show no difference in the latency of peak V of the ABR from children who were implanted before the age of 3 years compared with that of children implanted at 6 years or older. Children who were implanted between 2–3 years of age had normal P1 latencies for their age, whereas children who were implanted after 6 years of age had abnormal P1 latencies compared to age-matched normal-hearing children [30]. All the children in this study had at least 1 year of experience with an implant. Critically, even though the P1 latencies were normal for one group and abnormal for the other group, the ABR wave V latencies did not differ between the two groups.

The ABR findings described above (fig. 2) are not consistent with recent data from animal studies that suggest rapid alteration of synaptic terminals in the brainstem nuclei following early deprivation [31, 32]. It may be that measures of latency and morphology of the ABR are not appropriate to assess the

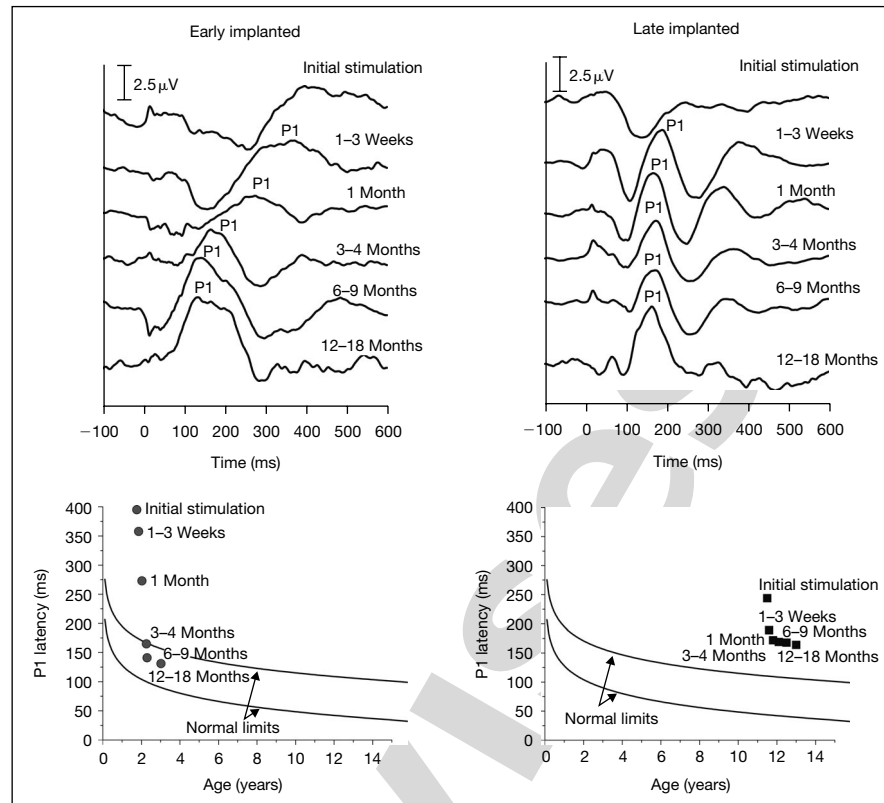


Fig. 3. Grand average waveforms and mean developmental trajectories of P1 latency for early- and late-implanted children. The normal limits are 95% confidence intervals.

effects of deprivation of auditory input at lower levels of the auditory pathway. Another possibility is that lower levels of the human pathway are less sensitive to deprivation than homologous pathways in the congenitally deaf white cat.

Longitudinal Development of the Central Auditory Pathways after Implantation

The brief sensitive period for central auditory development suggests that central auditory development following the onset of electrical stimulation should unfold in a different manner in early- and late-implanted children. This hypothesis is supported by the data shown in figure 3. The morphology of the CAEP and latency change in children implanted before and after the sensitive

period are markedly different [20, 33]. At the time of initial stimulation, the CAEP waveform from early- and late-implanted children is dominated by a large early negativity, which is strikingly similar to the long-latency negative potential reported in studies of preterm infants before 25 weeks postconception [34, 35]. This similarity suggests that CAEP morphology and latency obtained at the time of implantation are signs of an unstimulated auditory pathway. Alternately, the early negativity may reflect involvement of nonprimary auditory pathways in the generation of the CAEP when the primary auditory pathways are suppressed [36].

In early-implanted children (fig. 3) there is a large and rapid decrease in P1 latency and significant changes in CAEP morphology in the weeks and months following implantation. Within 6–8 months of implant use, P1 latency and CAEP morphology reach age-normal values (other investigators [19] have presented different interpretations of the rate of development of the P1). The neurophysiologic mechanisms underpinning these rapid changes in P1 latency and morphology are not clear. Animal models suggest that the changes may be related to two factors: overcoming desynchronization between neurons in different cortical layers of the cortex and increasing the activity within the different layers [33, 37].

Examination of the CAEP indicates that the pattern of central auditory development is different in late-implanted children (fig. 3) than in early-implanted children. The early negativity linked to auditory deprivation occurs at a shorter latency in late-implanted children than early-implanted children. Also, P1 latency, when assessed immediately following implant activation, is shorter in late-implanted children than in early-implanted children. Both observations suggest that there is some intrinsic development of the central auditory pathways even in the absence of stimulation.

Late-implanted children commonly show a polyphasic waveform morphology of the CAEP, which may persist for a year following the onset of electrical stimulation. Gradually between the 12th and 18th month after implantation, the morphology of the waveform assumes the unimodal shape of a typical P1 component. However, P1 latencies decrease significantly only over a period of approximately 1 month following the onset of stimulation and then remain constant or change very slowly over months and years. This pattern is in contrast to the rapid change in latency in early-implanted children (compare the bottom panels in fig. 3).

Given the difference in the morphology of the CAEP waveform between the early- and late-implanted children, it is possible that the peak that we describe as the P1 does not have the same generator for the early- and late-implanted groups. We are currently examining this possibility using multi-channel recordings. So far in our studies we have found it useful to label the first, large, positive

component P1 as this allows us to quantitatively compare the development of cortical activity for early- and late-implanted children following the onset of electrical stimulation.

Cortical Mechanisms Underlying the Sensitive Period

Congenitally deaf cats can be used as a model system to study cortical activity after the end of the sensitive period. In kittens, the sensitive period for development of central auditory pathways lasts up to 5 months of age [38]. When electrical stimulation is started after 4 months of deafness there is a delay in the activation of supragranular layers of the cortex and a near absence of activity at longer latencies and in infragranular layers (layers V and VI) [39]. The near absence of outward currents in layers IV and III of congenitally deaf cats suggests incomplete development of inhibitory synapses and an abnormal information flow from layer IV to supragranular layers. This abnormal pattern of activity within the auditory cortex is likely to be the basis for the abnormalities in morphology and latency of the recorded CAEP that we have observed in children implanted after the end of the sensitive period. Because the higher order auditory cortex projects back to the primary auditory cortex (A1) mainly to the infragranular layers, the absence of activity in infragranular layers suggests a decoupling of A1 from higher order auditory cortices [Kral and Tillein, this vol, pp 89–108]. Such a decoupling would allow other sensory input to predominate in the higher order auditory cortex in children deprived of sound for a long period. Decoupling of the primary cortex from higher order auditory cortices may aid in the recruitment of the higher order auditory cortex by other modalities (such as vision) [15, 16, 40]. Decoupling between primary and higher-order language cortex in children deprived of sound for a long period may also account for the speech perception and oral language difficulties of children who receive an implant after the end of the sensitive period.

We are currently investigating the functional (behavioral) consequences of a possible decoupling between primary auditory and higher-order cortices. One hypothesis we are exploring is that decoupling would result in abnormal development and integration of audiovisual or other forms of multi-sensory input. A recent study [41] that used the McGurk effect [42] to study audiovisual integration in implanted children found that that the this effect was experienced by children who received an implant by age 30 months but not by later-implanted children. (The McGurk effect is an auditory-visual illusion in which ‘seeing’ the lips move for ‘box’, for example, causes a clear ‘fox’ to be heard as ‘box’ or a visual /ba/ and auditory /ga/ to be heard as /da/.) The outcome of this study suggests that early-implanted children develop normal multi-sensory (auditory-visual)

integration. In contrast, children who receive implants at a later age experience deficits in multi-sensory integration.

The Effect of Prior Hearing Experience on Central Auditory Development after Cochlear Implantation

Age at implantation is not the only variable that influences outcomes after cochlear implantation. As shown in figure 1, there is a 'middle' age range (between 4–7 years), where roughly half the children show normal P1 latencies and the other half show delayed P1 latencies. Critically, there were several children in the latter half of the 4–7 year age range who had age-appropriate latencies. Oh et al. [17] using PET also found variable outcomes in children implanted between ages 4–7 years. This suggests that reorganization of auditory cortices is driven by both the duration of deprivation and another (or other) factor(s).

An obvious candidate for another factor is hearing experience. Studies that have provided evidence for a sensitive period have used primarily congenitally deaf animals and human participants. However, many children who receive cochlear implants have noncongenital hearing losses and have 'heard' to different extents before implantation. It is possible that children who had normal hearing prior to becoming deaf from meningitis and children with progressive hearing losses (who initially benefited from amplification) may demonstrate normal central-auditory development even after implantation at a late age. Studies of a population of noncongenitally deafened, cochlear implanted individuals who acquired hearing loss at different times in life provide an opportunity to investigate the extent to which hearing experience prior to cochlear implantation preserves the plasticity of central auditory pathways.

In an unpublished study we analyzed the latency of P1 in 15 children who acquired deafness after meningitis, and who then received cochlear implants at ages ranging from 1.99 to 14.63 years. We found that the majority (7/10) of children, who received their implants under the age of 6 years, had normal P1 latencies and none (0/5) of the children who were implanted after age 6 years had normal P1 latencies. On average, these children had normal hearing for 22.5 months prior to being diagnosed with meningitis. Children were tested after an average of 3.5 years of implant usage. In one case, a child, who had heard for 3 years, showed abnormal P1 latencies after she was implanted at age 7.5 years. These results suggest that a period of normal hearing early in life is not sufficient to preserve the plasticity of central pathways throughout childhood. These results are consistent with studies of speech and language development in children who had normal hearing and who acquired deafness due to meningitis in early childhood [43].

In another unpublished study, we analyzed P1 latencies from 23 children who had a diagnosis of progressive hearing loss prior to implantation. The majority (16/23) of these children showed a normal P1 CAEP, regardless of the age at which they were implanted. On average, these children had pure tone average (PTA) thresholds of 48 dB HL before implantation. In one case, a child who was implanted as late as age 10 years had normal P1 latencies after implantation. It is noteworthy that she had aided thresholds of 28 dB HL for the better part of her childhood. These data suggest that the quality of hearing experience prior to implantation can alter central auditory development after implantation. Stimulation can preserve the plasticity of the central auditory pathways beyond the sensitive period and lead to a good outcome (in terms of speech and language development) even when implantation takes place after age 7 years.

Nonauditory factors that affect success in speech and language development following implantation have been identified. One is increased metabolic activity in the frontoparietal regions that are important for executive and visuospatial functions [16]. Performance on motor development, visual-motor integration and auditory-visual comprehension tasks is also positively correlated with postimplantation speech and language outcomes [44, 45]. On the other hand, increased metabolic activity in the ventral visual pathway, the 'what' pathway, before implantation is correlated with poor outcomes after implantation [16].

Long-Term Development of the Central Auditory Pathways after Early Implantation

When children are implanted early in childhood, central auditory development (as reflected by the morphology of the CAEP and the latency of P1) becomes age-appropriate within 3–6 months after implantation. It is reasonable to ask whether development continues to be normal over time. In normal-hearing listeners evoked potential latencies and morphologies change during at least the first 20 years of life [7, 9, 46]. We have studied the development of auditory functions for a longer period after implantation using recordings of the CAEP in early-implanted children to find out if the CAEP continues to have normal latencies and normal morphologies throughout their childhood years.

Figure 4 shows changes in the morphology of the CAEP which occur in normal-hearing children during their preschool, school-age and teenage years. From birth to age 3 years, the CAEP waveform (elicited at rates of 1 or 2 stimuli/s) is dominated by the P1 component. At age 3–6 years, a small invagination of the P1 component appears, indicating the emergence of the N1 component. As time passes, the N1 component becomes robust and is reliably detected in

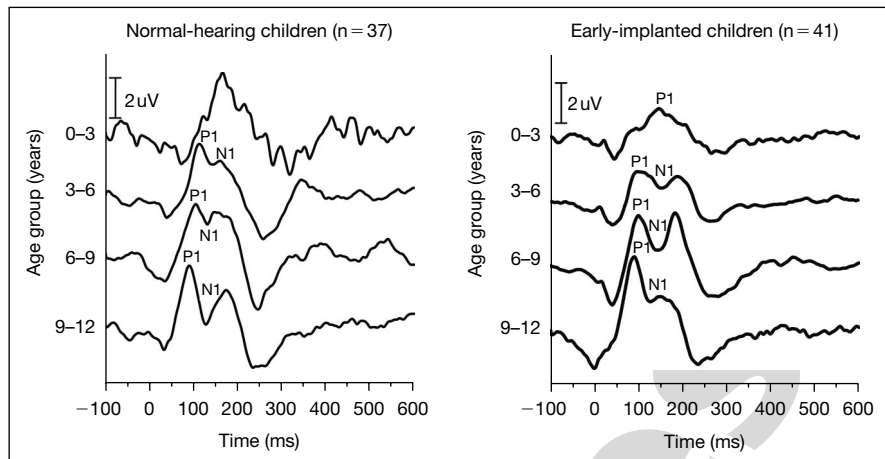


Fig. 4. Grand average waveforms for early- and late-implemented children as a function of chronological age.

the CAEP waveform by age 9 years. As children enter their teenage years and into young adulthood, the relative amplitude of the P1 and N1 components shifts and the N1 component begins to dominate the CAEP waveform. As shown in figure 4 the CAEP in early-implemented children has a normal pattern of age-dependent emergence of the N1 component [12, 19]. We take that as an indication that, in children implanted early in childhood, central auditory pathways continue to develop normally over time.

Central Auditory Development after Bilateral Implantation

Bilateral cochlear implantation is becoming increasingly common in clinical pediatric practice. ‘Binaural benefits’ include improved performance in noise, binaural summation, binaural squelch, and localization of sound. These benefits are well documented in adults fitted with a cochlear implant, and similar advantages are found in children [47–52]. It is reasonable to speculate that bilateral implantation may ameliorate the effects of auditory deprivation faster and in a more comprehensive manner than unilateral implantation.

As documented earlier in this chapter, we have found that P1 latency and morphology of the CAEP are sensitive indicators of the maturational status of the central auditory pathways. Preliminary data [53] suggest that changes in latency and morphology also offer a window on the benefits of bilateral

implantation. After simultaneous, early, bilateral cochlear implantation, the latency of P1 reaches normal limits sooner (within 1–3 months) than after unilateral implantation (3–6 months). Simultaneous stimulation from the two ears appears to create a convergence of the input at the level of the auditory cortex (and lower levels) that promotes normal development of central pathways.

Not all children receive bilateral implants during the same operation. Consider the case of children implanted early who receive sequential implants before the age of 3–4 years. P1 latencies from a second implanted ear are less delayed when that implant is activated than latencies from the first implanted ear. In addition, the latencies reach normal values sooner than the first implanted ear. This is likely conditioned by a starting point for latency that is close to the upper edge of normal latencies.

Children who receive their second implant after the age of 5–7 years (regardless of the age at which they received their first implant) show delayed and abnormal P1 responses even after 2–3 years of experience with the second implant. These data are consistent with speech perception performance in the same children showing that the best speech perception outcome is achieved when the second ear is stimulated by age 3–5 years. Speech perception performance is intermediate when the second implant is introduced between ages 5–7 years, and children who receive their second implant after age 12 year have poor speech perception, despite having excellent speech understanding with their first implant [54]. We infer that even early implantation and long-term implant use in one ear is inadequate to preserve the plasticity of the auditory pathways that serve the opposite ear. Just as with a unilateral implant, there is a sensitive period, or window of opportunity, which exists for children to develop functional bilateral central auditory pathways and acquire effective binaural integration. As our studies with bilaterally implanted children continue, we expect to delineate in further detail the age cut-offs for the sensitive period for bilateral implantation.

*P1 as a Biomarker for the Maturational Status of
Central Auditory Pathways*

Our work has established the existence of a short period in early childhood during which stimulation must be delivered to the auditory system in one way or another in order to achieve normal development of central auditory pathways in infants and children. It follows that hearing aids and cochlear implants should be fitted as early as possible, with dispatch rather than with delay, during infancy or early childhood. It also follows that the children receiving hearing aids or implants will be preverbal. There is therefore a need for an objective

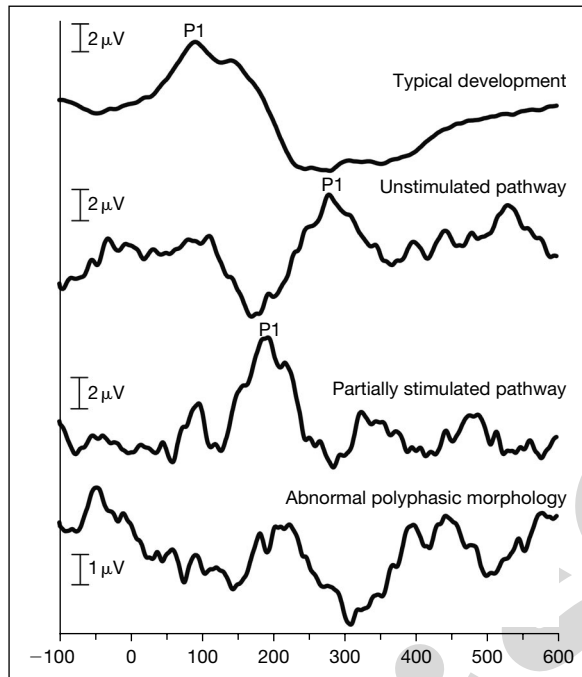


Fig. 5. Examples of P1 waveforms for a hearing child (top), a young child with a congenital, profound hearing loss (second from top), a young child with a mild-moderate hearing loss (third from top), and an older child with a profound hearing loss (bottom).

measure, a biomarker, which can be used to assess whether the hearing aid or cochlear implant provides sufficient stimulation to allow normal development of the function of central auditory pathways. We have found P1 latency and the morphology of the CAEP to fulfill that requirement [33].

Landmarks of Deprivation and Plasticity in the CAEP Waveform

Our longitudinal studies of hearing-impaired children have revealed abnormalities in the CAEP waveform that are reasonably easy to identify. As shown in figure 5, the waveform of the CAEP obtained from young, normal-hearing child is dominated by a large initial positivity (P1). In contrast, initial waveforms following the onset of stimulation (by either a hearing aid or cochlear implant) from children with a severe-to-profound hearing loss are dominated by an initial large negativity. We consider this negativity to be the hallmark of an unstimulated, or little stimulated, central auditory pathway. On the other hand, for children who have a less severe degree of hearing impairment, that is children in whom the auditory pathways have been stimulated to some extent, the

waveform is dominated by a P1 response, albeit with a longer latency (fig. 5). In older (>5–7 years of age) deaf children and in the nonimplanted ears of older, unilaterally implanted children, the CAEP waveforms often have a polyphasic morphology (fig. 5). We believe that the polyphasic morphology is characteristic of a central auditory system that has developed abnormally due to deprivation. Finally, there are children from whom we cannot elicit a response because of the severity of their hearing loss.

The morphology of the CAEP described above typically reflects the maturational status of the central pathways prior to intervention. After infants and young hearing-impaired children are appropriately stimulated with either acoustic or electrical stimulation, distinct changes in CAEP waveform morphology and latency occur indicating progress in central auditory development. Over weeks and months following initial stimulation, the latency of the initial negativity in the CAEP decreases and the positive component (i.e. the P1) becomes more clearly identifiable. The latency of the P1 decreases significantly with age, typically reaching normal values within 3–6 months after stimulation (fig. 3). In children who receive a first or second cochlear implant at a late age (>5–7 years), the CAEP waveform often retains its polyphasic nature in the months following initial stimulation. In these children, the P1 may show small changes in latency in the initial months following stimulation. However, very little or no change in latency occurs over the next several years (fig. 3).

Using these distinct and repeatable patterns of the CAEP and the latency of P1, we have studied the development of the central auditory pathways in over 200 hearing-impaired children who were fitted with hearing aids and/or cochlear implants. In the next section, we present four cases to demonstrate the use of the P1 of the CAEP combined with traditional behavioral measures of audiological and speech-language assessment in clinical decision-making.

Case Descriptions

Case 1

The patient was a male child who was born prematurely and perinatally contracted meningitis. He was treated with ototoxic medications and remained in the Neonatal Intensive Care Unit for several weeks. He was diagnosed with a severe to profound bilateral hearing loss at the age 1 month and was fit with hearing aids at 6 months of age. When tested in a sound field, his unaided PTA was 100 dB and his aided PTA was 75 dB. CAEP recordings were obtained at 16 months and 19 months after hearing aid fitting. As seen in figure 6, P1 latencies did not change during this period of hearing aid usage and remained delayed. These results suggest that the auditory stimulation provided by the hearing aid

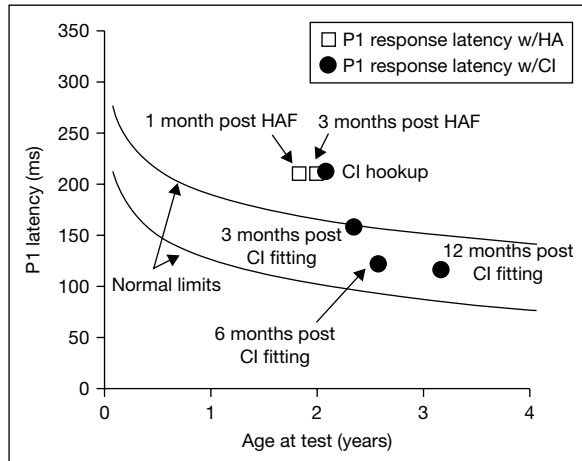


Fig. 6. P1 latency plotted against the 95% confidence intervals (solid lines) for normal development of the P1 response for the patient in case 1. The horizontal scale shows the child's age.

was not sufficient to promote development of the central auditory pathways. The patient met the standard criteria for cochlear implantation and was fitted with a cochlear implant at age 28 months. CAEP recordings were repeated to assess central auditory maturation after implantation. Figure 6 shows P1 latencies at 1 week, 3 months and 24 months after implantation, shown as a function of the child's age. As seen in figure 6, there was a rapid decrease in P1 latency following stimulation with the implant. P1 latency reached normal limits after 3 months of implant use and continued to develop normally when tested 24 months after stimulation. At that time, the patient's speech perception score was 92% using the GASP test. Results of a formal language evaluation conducted at that time indicated progress in acquisition of speech and language.

In this case, the latency of the P1 after 19 months of hearing aid use provided clear evidence that the auditory stimulation provided by the hearing aid was not sufficient for central auditory development. After implantation, the latency of P1 decreased rapidly to within normal limits, indicating that the implant was providing adequate stimulation not provided by the hearing aid. The P1 latency was useful in documenting the lack of adequate stimulation from the hearing aid and the adequate development of the central auditory pathways following electrical stimulation through the cochlear implant. This example illustrates the difference in effectiveness of acoustic and electric stimulation as documented by the rapid decrease in the latency of P1 following the onset of electrical stimulation.

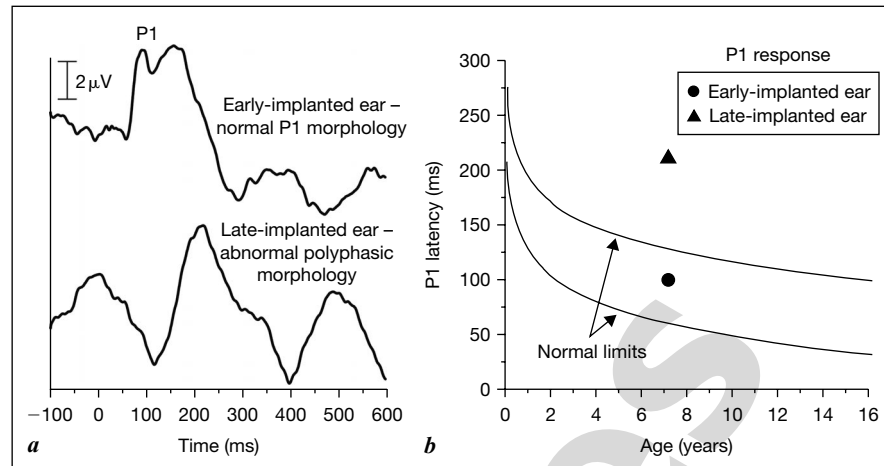


Fig. 7. CAEP waveforms (*a*) and P1 latency (*b*) plotted against 95% confidence intervals for normal development of the P1 response for the patient in case 2.

Case 2

The patient was a female child who was first identified with bilateral severe to profound hearing loss of unknown etiology at 7 months of age. She received a cochlear implant in her right ear at age 1 year 9 months and in her left ear at age 5 years 11 months. She is currently considered a good user with her left implant. When we tested her at age 8 years, her CAEP waveform (in response to right ear stimulation) revealed a P1 response of age-appropriate morphology and latency (fig. 7). Consistent with the normal P1 response, she performed well on the MLNT test of speech perception, obtaining a score of 92%. Implantation of her left ear occurred after the sensitive period. As expected, she had an abnormal response to left ear stimulation with polyphasic CAEP. P1 latency was prolonged even after 2 years of stimulation. Consistent with the abnormal CAEP, she obtained a score of 0% on the MLNT in the left ear.

The CAEP morphology and latency clearly indicated abnormal development of the central auditory pathways that serve the left ear, despite the fact that this child is considered a good user with her right implant. The CAEP findings correctly predicted her poor speech perception performance when using her later implanted ear.

Case 3

The patient was a male child who was first diagnosed with a hearing loss at age 9 years. At that time, behavioral pure-tone audiometry indicated a mild to moderate sensorineural hearing loss in the left ear and a severe to profound

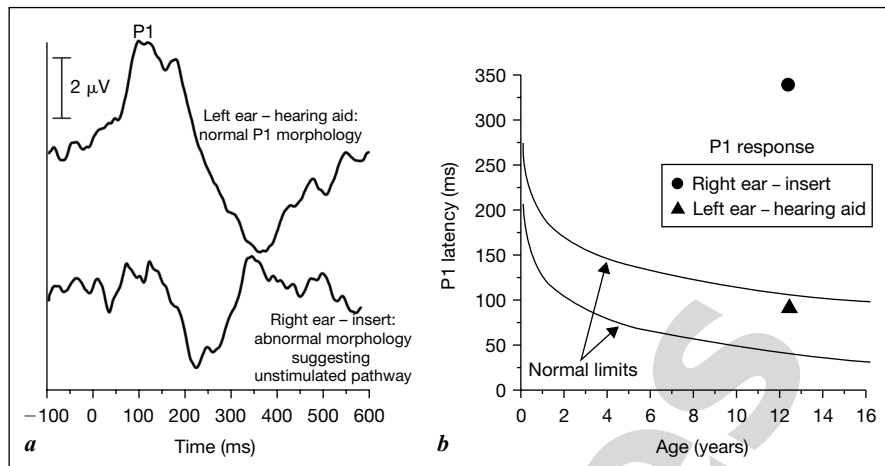


Fig. 8. CAEP waveforms (*a*) and P1 latency (*b*) plotted against 95% confidence intervals for normal development of the latency of P1 for the patient in case 3.

hearing loss in the right ear. Prior to this hearing evaluation, there was no reported history of hearing difficulties. The etiology of the asymmetric hearing loss could not be determined based on the results of genetic testing, imaging or blood tests. In order to determine the best course of intervention, we were asked by the otolaryngologist to determine whether the hearing loss was longstanding or sudden. If the hearing loss was sudden, then a cochlear implant would be considered for the worse ear given that the hearing in the better ear might deteriorate in the future. CAEP testing was performed at age 10 years (fig. 8).

Given the mild degree of hearing loss in the left ear, as expected the patient had a CAEP with a robust P1 with normal latency and morphology. Right ear stimulation revealed a CAEP waveform dominated by an initial, large negativity and a delayed P1 component. A CAEP with this morphology is associated with an unstimulated central auditory pathway typically seen in congenitally deaf children. Based on the CAEP, we concluded that the central auditory pathways that serve the right ear did not show age-appropriate development and that the hearing loss in the right ear was likely a long longstanding one. The patient has been fitted with hearing aids and we continue to monitor his progress using behavioral and CAEP testing.

Case 4

The patient was a 3-year-old male child who had significant medical complications as a neonate including RH incompatibility, diagnosis of the CHARGE

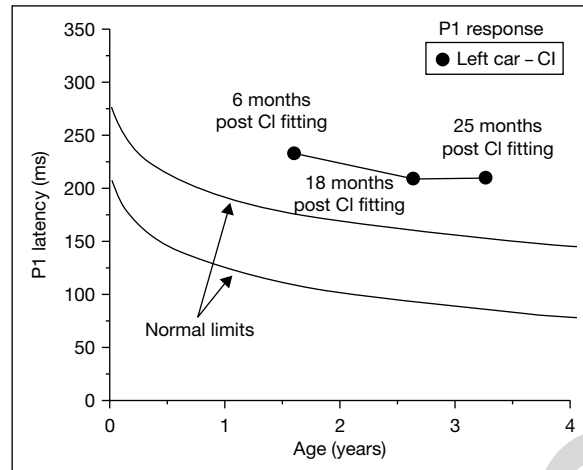


Fig. 9. P1 latency plotted against the 95% confidence intervals (solid lines) for normal development of the P1 response for the patient in case 4.

syndrome, malformed cochleas bilaterally, left facial palsy and swallowing difficulties.

Hearing testing at the age of 1 month using ABR revealed a bilateral, profound, sensorineural hearing loss. Following an unsuccessful hearing aid trial, he was fitted with a cochlear implant at 1.5 years of age. CAEP testing at 6, 18 and 24 months after stimulation with the implant revealed P1 latencies (fig. 9) with only minimal improvement after implantation period and remained prolonged at 24 months after stimulation. The prolonged latency of P1 indicated a lack of normal central auditory pathway development consistent with the finding that the child did not respond to auditory stimuli and did not make progress in oral speech and language development. The child, however, showed progress in acquisition of manual communication. This case demonstrates that not all children implanted within the sensitive period will achieve normal development of the central pathways. For that reason the CAEP provides a useful way to monitor changes in (or lack of) central auditory development of multiply handicapped children who receive cochlear implants. The parents of the patient were considering a second implant. The CAEP results provided an objective analysis of the prognosis, thereby allowing the parents to make an informed choice as they pursued their options.

Our initial clinical results are promising with respect to the use of P1 latency as a measure of central auditory development in children who receive intervention with a hearing aid or a cochlear implant [55]. However, there are

factors we need to consider before the measurement of P1 latencies can gain widespread clinical use. These include the effects of audibility, reduced spectral information, frequency response of the hearing aid, and implant mapping parameters on P1 latencies. We are in the process of evaluating these and other factors that may affect the measurement of P1 latencies in the hearing-impaired population. Preliminary results reveal only minimal effects of mapping changes and sensation levels on P1 latency. Finally, we are developing techniques to minimize the occurrence of an electrical artifact generated from the implanted electrode array that appears in the scalp-recorded EEG and interferes with P1 identification [56].

Summary

Studies of congenitally deaf children fitted with cochlear implants, utilizing behavioral tests, recordings of the CAEP and brain imaging, have established the existence and time limits of a sensitive period for the functional development of central auditory pathways. Based on the results of these experiments, the optimal time to implant a young congenitally deaf child is in the first 3.5 years of life when the central auditory pathways are maximally plastic. This is also the time period when introduction of a second implant is most likely to generate a good outcome. If stimulation is withheld for 7 years or longer, the plasticity of the central auditory pathways is greatly reduced. The loss of central auditory plasticity in congenitally deaf children after age 7 years is correlated with relatively poor development of oral speech and language skills [Geers, this vol, pp 50–65]. Animal models suggest that the primary auditory cortex may be functionally decoupled from the higher order auditory cortices, due to restricted development of functional inter- and intracortical connections after the sensitive period [Kral and Tillein, this vol, pp 89–108]. The decoupling may result in recruitment of higher order auditory cortex by other modalities (e.g. vision) as suggested by brain imaging and consistent with the lack of auditory-visual integration seen in later-implanted children. The hypothesis of a decoupling of primary auditory cortex from higher order language centers in children deprived of sound for a long period may explain the speech perception and oral learning difficulties of children who receive an implant after the end of the sensitive period.

Acknowledgements

We would like to thank Phillip Gilley for his assistance with the figures. Kathryn Martin collected the data for many of the experiments. Justin Langran, Rachel Potts and Katrina Agung assisted with various aspects of manuscript preparation.

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