# Critical Review: Are Simultaneous Bilateral Cochlear Implants More Effective in Promoting Normal Functioning Bilateral Auditory Pathways in Children than Sequential Bilateral Cochlear Implants?

Edna Lau
M.Cl.Sc (AUD) Candidate
University of Western Ontario: School of Communication Sciences and Disorders

This critical review examines the use of the P1 from cortical evoked auditory potential responses to determine whether children fitted with simultaneous bilateral cochlear implants will develop more efficient or normalized bilateral pathways in their central auditory system than children fitted with sequential bilateral implants. Study designs included: mixed (repeated measures) cohort study (2) and case studies (3). Overall, the research suggests that children fitted early in life with bilateral cochlear implants either simultaneously or sequentially after a short interimplant delay will more likely develop normalized bilateral pathways. This is clinically relevant to parents and audiologists in deciding whether there is a significant benefit to providing a child with implants simultaneously versus sequentially.

## *Introduction*

Binaural listening offers several advantages over monaural hearing such as improved abilities in sound localization, speech perception in quiet and noise, and listening comfort. These improvements are attributed to binaural mechanisms such as binaural summation, binaural redundancy, head diffraction effects, and binaural squelch. Binaural hearing is particularly important for children because they are acquiring speech and language in environments that are seldom quiet one-on-one situations. Children often listen and learn in noisy environments with multiple speakers. Children often listen to the teacher give instructions while involved in an activity, looking at the blackboard, or playing a game. Consequently, bilateral cochlear implants (BCIs) are prescribed as a treatment strategy for young children with bilateral severe to profound sensorineural hearing loss (SNHL) in an attempt to promote binaural processing to assist in sound localization and hearing. Yet it is unclear whether the input provided by BCIs will be integrated in a normal manner along the pathways in the central auditory nervous system (CANS). It has been reported in the literature that BCI users tend to demonstrate significant improvements in speech understanding in noise and sound localization abilities compared to unilateral implant users, however this is dependent on the age at which an individual is fitted with the second implant and the duration of the delay between implantation of the first and second ears. It is common practice to provide a young child with severe to profound SNHL with two cochlear implants simultaneously or at different times during childhood. Otolaryngologists and parents must decide whether early simultaneous bilateral implantation will be more beneficial than sequential bilateral implantation. Factors to consider when considering simultaneous implantation include: additional surgical risks with anesthetics, potential damage to both vestibular systems, and the desire to determine level of performance with a single implant. However an extended period of unilateral cochlear implant use could compromise the ability of the auditory system to process binaural input due to a lack of auditory stimulation to the unaided ear. It is difficult to measure the relative benefit of simultaneous versus sequential bilateral implantation objectively in very young children as these patients are unable to complete behavioral measures such as speech perception in noise. Measurements of cortical auditory evoked potentials (CAEPs) provide an objective and passive method of evaluating benefit from bilateral implantation by assessing the development and plasticity of the CANS pathways. Hence this method can be used to determine whether simultaneous or sequential bilateral implantation is more effective in promoting normal development of pathways responsible for binaural processing in the CANS.

## *Objectives*

The primary objective of this review is to critically assess the existing literature that utilized cortical responses to determine whether the normalization of the binaural pathways in the CANS occurs more rapidly in children fitted simultaneously with BCIs versus those who are fitted sequentially. The second objective is to propose evidence-based practice recommendations for the age of implantation in pediatric bilateral cochlear implant candidates.

## *Methods*

Search Strategy

Computerized databases CINAHL, EMBASE, PubMed, and Scopus were searched using the following search strategy:
[(cochlear implant) AND ((bilateral) OR (binaural)) AND ((simultaneous) OR (sequential)) AND ((child) OR (infant) OR (preschool) OR (school age) OR (pediatrics) OR (children) OR (paediatrics)].

Journal articles were also acquired from the reference lists of relevant articles.

Selection Criteria

Studies selected for inclusion in this critical review were required to investigate the impact of simultaneous and/or sequential bilateral cochlear implantation on the development of the central auditory nervous system (CANS) using CAEP in children. No limits were set on the methodological design of the studies.

Data Collection

Results of the literature review yielded the following types of articles congruent with the aforementioned selection criteria: mixed (repeated measures) cohort study (2) and case study (3). There is little variety in the number of research groups represented as 3 out of the 5 articles come from the same research department thereby increasing the potential for bias towards findings presented by these researchers.

### *Results*

Sharma, Gilley, Martin, Roland, Bauer, and Dorman (2007) conducted a mixed (repeated measures) cohort study to determine whether early, simultaneous BCIs promoted faster development of CANS pathways compared to children who were implanted early on in life with sequential BCIs. CAEPs were collected, at various time intervals, from 20 children. The latency and morphology of the P1 response was used as a biomarker of the development and plasticity of CANS. P1 was defined as the first robust positivity in the waveform in the 50-175ms range, or if the peak was broad, at the midpoint. The maturity of CANS pathways is reflected in the systematic decrease in P1 latencies with increasing age. The activity in the auditory cortex is represented by the P1 response as its neural generators are attributed to auditory thalamic and cortical sources. Participants were divided into two groups of 10 according to whether they had been implanted simultaneously or sequentially with BCIs. All subjects presented with severe to profound sensorineural hearing loss (SNHL) and received their bilateral implants prior to 3.5 years of age. Mean age of implantation for the sequential group was: 1.3 and 2.26 years (first and second implant, respectively) and 1.57 years for the simultaneous group. P1 latencies for each ear were measured individually (i.e. CI on other ear was turned off) at implant activation and post implant intervals of 1 week and 1, 3, 5, 8, 11, and 15 months.

During recordings the subject was seated in a sound booth while the stimulus was presented from a loudspeaker positioned at a 45° angle to the side of the subject's implant. The subject's CIs were set to their usual settings. A synthesized speech syllable /ba/ of 90 ms duration was used to elicit the CAEP. Ag/AgCl electrodes and a Synamps EEG amplifier were used to collect the CAEPs. Partially repeated measures analysis of variance (ANOVA) was conducted under a general linear model for unbalanced data. Results revealed no effects between the two implant groups ($F(3.16) = 0.64$, $p = 0.602$). An analysis of all possible pairwise comparisons using Scheffe's correction for multiple comparisons and alpha= 0.05 also revealed no significant differences in P1 latencies between the two implant groups or either test ear at initial activation or at the different post-implantation intervals. Normative data for P1 latency as a function of age in normal hearing (NH) children were derived from a previous study by Sharma and colleagues and used as a comparison. The mean P1 latencies for both implant groups were found to occur outside the 95% confidence intervals for normal development of the P1 response at initial activation, 1 week, and 1 month post-implantation. However P1 latencies and morphology for both implant groups were within normal limits by 3 months post-activation and continued to indicate normal development at the following post-implantation time intervals. The developmental trajectory of the P1 response did not differ significantly for the two groups over the 15 month period. Although not statistically significant, it was observed that the P1 latency for the second implanted ear tended to be less delayed than the first implanted ear within the sequential group. These results suggest the CANS pathways will most likely develop normally in children who are BCI candidates regardless of simultaneous or sequential implantation provided that both ears are implanted prior to 3.5 years of age, although no late implanted participants were included in this study to confirm this. This sensitive period was observed by Sharma and colleagues in previous investigations and is the period of development when the CANS presents with a high degree of plasticity. Bilateral cochlear implantation should occur within the first 3.5 years of life as the CANS is most plastic during this time and will most likely impart the greatest binaural advantage possible for that given child.

The Sharma et al. (2007) investigation was motivated by the case study administered by Sharma, Dorman, and Kral (2005) as well as the retrospective case series carried out by Bauer, Sharma, Martin, and Dorman (2006). Sharma et al. (2005) measured P1 latencies in two subjects who had been fitted with BCIs sequentially. Subject one received her implants early in life (first implant: 1.07 years of age, second: 2.07 years). Subject two was categorized as late-implant as she received her first implant at 2.08 years of age and the second at age 10.10 years. Both subjects had been diagnosed with profound SNHL by 1 year of age. The materials and procedure used for measuring CAEPs were identical to that outlined in the Sharma et al. (2007) study. The early implanted subject showed rapid normalization of P1 latency and waveform morphology for both the first and second implants (i.e. P1 latencies were within normal limits by 3 and 1 month(s) post-activation for the first and second CIs respectively. The late implanted child displayed P1 latencies within normal limits for the first implant however abnormal waveform morphology and delayed P1 latencies, even with 9 months of bilateral implant experience, were observed for the second implant.

Bauer et al. (2006) collected CAEPs from 4 children who received BCIs by 2 years of age to determine the impact of bilateral implantation on the maturation of CANS pathways. Two subjects were fitted with BCIs simultaneously and two were fitted sequentially. All subjects presented with congenital severe to profound SNHL. CAEPS were recorded using the same methods and materials as outlined by Sharma et al. (2007). P1 latencies were plotted against the 95% confidence intervals for the P1 response of NH children. P1 latencies from both ears in the 2 simultaneously implanted subjects reached normal limits within 1 month post-stimulation. Those who had been implanted sequentially displayed P1 latencies from the first implant that reached normal limits within 3 to 6 months post-stimulation while the second implant reached normal P1 latencies after 1 month of implant use. Initial activation of the second implant yielded P1 latencies that were less delayed than the first. When tested at 2 and 3.5 years of age both sequential subjects displayed P1 latencies that continued to show normal development. Results imply there is a high degree of plasticity of the auditory pathways in the CANS after early bilateral implantation and support early bilateral implantation to maintain the integrity of CANS development.

Key, Porter, and Bradham (2010) presented a case study in which event-related potentials (ERP) were recorded in a 6 year old child to examine changes in auditory processing in response to single syllable and word stimuli. The child was identified with profound SNHL by 12 months of age. The first implant (Nucleus 24) was received in the right ear at age 28 months and the second (Cochlear Freedom) at age 6.8 years. Revision surgery of the first implant occurred at 3.6 years. The child was hearing age matched to 5 NH subjects between 3 to 6 years of age to more effectively estimate the potential range of auditory processing abilities. ERPs were recorded using 128 Ag/AgCl electrodes at pre-activation and 2, 4, and 6 months postactivation of the second implant in response to a speech perception task and a word recognition task using a match/mismatch visual paradigm. Auditory stimuli were presented at 75 dB SPL (A) from a speaker positioned above the child's head with CIs set to typical user settings. Speech-sound stimuli included computer generated four consonant-vowel syllables (/ba/, /bu/, /ga/, /gu/) and words (bird, bus, car, cat, dog, duck). ERPs from the BCIs were compared to those from the unilateral recordings taken pre-activation of the second CI and those from the NH subjects. It was observed that by 6 months postactivation of the second CI, the P1-N1-P2 complex in response to single syllable stimuli was similar to that of the NH subjects despite this ear being deprived of auditory stimulation for almost 7 years. However, the P1-N1-P2 complex measured prior to activation of the second CI was immature and differed in morphology from the NH subjects. ERPs measured while the subject was fitted with a unilateral CI showed word processing abilities that were not as efficient as NH children as indicated by the absence of the left anterior N400 and posterior P500 responses. Yet, 6 months post activation of the second CI, these responses were observed and the ERP waveforms were almost identical to those of the NH children, hence implying an improvement in word processing, comprehension, and utilization abilities. Results suggest BCIs improve auditory processing, due to possibility of increased binaural cues, beyond that offered by a unilateral CI and in this case despite a long interimplant delay (4.4 years).

Gordon, Wong, and Papsin (2010) measured cortical responses from 10 children: 2 NH, one implanted simultaneously with BCIs, and 7 implanted sequentially. The sequential subjects were organized into two groups according to the length of their interimplant delay: short (2 subjects) or long (5 subjects). The interimplant delay of the short group was 7-8 months whereas the long group ranged from 2.6-5.8 years. The simultaneous subject received BCIs at age 1.1 year. The sequential group received their first implant between the ages of 0.9-4.1 years and second, 1.1-9.7 years. All of the implanted children had 3-4 years of BCI experience and early onset deafness with auditory thresholds (either aided or unaided) poorer than 40 dB HL. All children in the sequential group received their first CI in the right ear and the second in the left. N24 devices, with full insertion, were used. Cortical activity was recorded via encephalography (EEG) using 64 cephalic electrodes. Cortical responses were recorded individually for each ear. The SPEAR 3 system and processor was used to present the stimuli. EEGs were evoked in the same manner for the NH subjects. A beamforming analysis method developed by Gordon and colleagues was used to generate spatial patterns of the cortical activity associated with the dominant positive peak (at 50 to 130 ms) in the BCI subjects and the P1 in NH children. Cortical locations that yielded the greatest beamformer activation or amount of activity were evaluated. The interhemispheric amplitude difference (IHAD) between activity generated in the left and right auditory cortices was calculated using this equation: $- (L – R) / (L + R) \times 100\%$. L corresponds to the left hemisphere dipole moment and R for that of the right hemisphere. Spatial patterns of cortical activity identified the primary/secondary auditory cortex as the location of the main source of neural activity in response to stimuli presented to either the right or left ears in the NH subjects. The simultaneous BCI subject and the short delay group displayed results similar to that of the NH subjects. Whereas in the long delay group stimulation of the second implant (left ear) generated spatial patterns depicting abnormal localization of neural activity in the ipsilateral parietal cortex as well as activity in the primary/secondary auditory cortex in the right hemisphere. However stimulation of the first or more experienced CI yielded activity localized to the primary and secondary auditory cortices. Calculation of IHAD values found that the NH, simultaneous, and short delay subjects displayed lateralization of activity predominantly to the right hemisphere in the auditory cortex when the left ear was stimulated. When the right ear of these subjects was stimulated, symmetrical cortical activity between the two hemispheres or lateralization to the left hemisphere of the auditory cortex was observed. When either the right or left CI was stimulated in the long delay group four of the five subjects displayed activity predominantly in the left hemisphere. The fifth subject in this group displayed atypical results as lateralization would occur mainly in the hemisphere ipsilateral to the stimulus.

### *Discussion*

The goal of this study was to evaluate the degree and quality of reported evidence on the P1 CAEP measurements of simultaneous versus sequential bilateral cochlear implantation within the pediatric population and thereby formulate recommendations about future patient management. There are a limited number of studies that currently exist in the literature addressing this topic. Two of the articles assessed are of high quality evidence levels (Level 2a/2b) whereas the majority (3 articles) of the studies reviewed are deemed to be of low level evidence (level 4) because of the limited number of available subjects, the heterogeneity of the target population, and the logistical and ethical problems associated with attempting to conduct randomized, controlled trials to achieve level 1 type of evidence.

Bauer et al. (2006) examination of P1 CAEP latencies for BCI children for whom both ears were implanted simultaneously or sequentially before 2 years of age showed that both groups of subjects developed normal P1 latencies and morphology, although the sequentially implanted subjects displayed less rapid normalization of P1 latencies after the second CI was activated. These findings support those obtained from the longitudinal comparative study by Sharma et al. (2007) which examined the effect of simultaneous versus sequential bilateral cochlear implantation prior to the critical age for CANS development and plasticity (3.5 years of age). Results from this study indicated by 3.5 months post-implantation the mean P1 latencies and morphology were within normal limits for both the simultaneous and sequential subject groups. No significant differences in P1 latencies or morphology were found between the two groups. The case study presented by Key et al. (2010) shows that early implantation of the first ear (3 years of age) and acquisition of the second CI at 6.8 years of age still yielded normal P1 latencies and morphology by 6 months post-activation of the second CI. These studies imply that bilateral stimulation during critical periods of development is important for optimizing auditory functioning in children with BCIs. This belief is further reinforced by the passive paradigm administered by Key et al. (2010). As a unilateral CI user the participant was able to process word-level stimuli but not as efficiently as the NH subjects. Yet at 6 months post-activation of the second CI word comprehension and utilization of this information matched those of the NH subjects thereby suggesting improvements in auditory processing exceeding what was achievable by a single implant. This is in contrast to Sharma et al. (2005) case study of an older child receiving a second sequential BCI later in development (10 years of age), who demonstrated limited plasticity in the second ear as indicated by delays in P1 latency and abnormal morphology of the CAEP responses. Poorer behavioral outcomes on assessments of speech perception have been associated with children who have received sequential BCIs late in life. Peters et al. (2007) measured speech perception in a group of 30 children implanted bilaterally and sequentially. All subjects received their first implant prior to 5 years of age and were organized into 3 groups according to the age of second implantation: 3-5 years, 5-8 years, and 8-13 years. Overall significant improvements in speech intelligibility in quiet and noise were demonstrated with binaural input. However speech perception scores of the second implanted ear (unilateral input) for children in the 8-13 years group were found to be significantly poorer compared to those displayed by their first implanted ear and by the children implanted sequentially at a younger age. The results from Peters et al. (2007) and Sharma et al. (2005) imply that normal development and function of CANS pathways linked to the second CI ear will be negatively impacted if auditory stimulation of that ear is delayed for 7 or more years. Sharma et al. (2002) found that children who had been deprived of auditory stimulation for 7 or more years prior to unilateral implantation generally displayed abnormal P1 latencies to speech stimuli thereby suggesting abnormally functioning auditory pathways and reduction in plasticity of the CANS after this age and duration of auditory deprivation. Therefore lack of stimulation early in life will likely hinder the integration of the neural pathways responsible for binaural hearing in the CANS. Research from Peters et al. (2007) and Sharma et al. (2005) imply that long periods of stimulation from a unilateral implant are not sufficient to preserve the plasticity of those auditory pathways ispilateral to that implant thereby preventing that primary cortex from developing normal connections to the higher-order auditory and language cortex. Sharma et al. (2005) hypothesizes that this decoupling will leave this higher-order cortex vulnerable to cross-modal reorganization by the visual or somatosensory modalities however, early binaural stimulation may preserve this plasticity. Yet the Key et al. (2010) study indicates that although one ear had been unaided for an extended period of time an improvement in binaural auditory processing may still be achievable. A future large scale replication study comparing evoked related potentials of early and late simultaneous bilateral cochlear implantation relative to sequential BCI in the pediatric population is necessary to provide a more definitive answer to this postulation.

According to Gordon et al. (2010) the spatial patterns of cortical activity obtained from localizing the source location of the P1 in BCI users demonstrate that BCIs are capable of promoting normal functioning bilateral auditory pathways in young children with minimal interimplant delays. This study confirmed evidence provided in the literature that, depending on the ear being stimulated and the type of stimulus, the contralateral cortical hemisphere will tend to response more dominantly. When stimuli are presented to the opposite ear the cortical lateralization will also switch hemispheres. The literature also reports a specialization of the auditory cortices in each hemisphere. The left hemisphere is better at processing temporal information while the right has greater spectral processing abilities. Speech stimuli activate the left hemisphere more so than the right and non-speech stimuli such as pure tones will generate greater activity in the right cortical hemisphere. In the Gordon et al. (2010) study cortical lateralization to the right hemisphere occurred when pure tone stimuli were presented to the left ear of the NH subjects. When this stimulus was presented to the right ear the cortical activity shifted to the left cortical hemisphere or was symmetrical between the two hemispheres. The simultaneously implanted child and the two short delayed sequentially implanted children all received both CIs before 2 years of age. These 3 subjects showed results that were the same as the NH subjects. However 4 out the 5 children that had been sequentially implanted with long interimplant delays and at older ages displayed abnormal P1 source localization to the left parietal cortex in response to stimulation from the left CI, the second implanted ear, and lateralization to the left cortical hemisphere to either right or left stimuli. Parietal activity has been reported by Gilley et al. (2008) in children who have experienced long durations of auditory deprivation prior to unilateral implantation and is likely due to reorganization in the auditory cortex. Therefore, these findings suggest the auditory pathways in children who receive BCIs after a long interimplant delay, or prolonged period of auditory deprivation in the second ear, will likely be abnormally organized compared to the more normally organized auditory pathways in children who receive both BCIs early in life (< 2 years of age) simultaneously or sequentially after a short interimplant delay. A replication study of the Gordon et al. (2010) research using a larger sample population and a comparison between spatial patterns generated by speech and non-speech stimuli is necessary to confirm this study's findings. In addition binaural function in children who receive their second CI after a long period of experience with a unilateral implant should be explored.

The studies evaluated in this critical review are well formulated using valid methods. The Sharma et al. (2007) and Gordon et al. (2010) were assigned a recommendation of grade B whereas the remaining studies (i.e. case studies) were given a C grade since they were of level 4 evidence. It is important to note that the majority of the journal articles used in this review come from the same research department i.e. Bauer et al. (2006), Sharma et al. (2005), and Sharma et al. (2007). To confirm the validity of the methods used and the results of these studies a replication study conducted by an independent research team is essential. Statistical data was available only for the Sharma et al. (2007) study. The statistical manipulations are valid as researchers used a general linear model for unbalanced data in partially repeated measures ANOVA to account for the inability to collect P1 latency measurements from all subjects at each of the post-implantation intervals specified. Trends presented in this study should still be interpreted with some caution. An increase in power to account for the inadequate sample size of the study is necessary to determine if the patterns observed will reach statistical significance as there may be functional advantages to early simultaneous bilateral cochlear implantation over sequential implantation. Future studies assessing the binaural listening abilities such as speech perception in noise and sound localization are important for determining whether early simultaneous bilateral cochlear implantation offers possible behavioral advantages over sequential bilateral implantation.

## *Clinical Implications*

When taken altogether, the limited research evidence recommends that children be fitted at a very young age, either < 2 years or < 3.5 years of age, with BCIs either simultaneously or sequentially with short interimplant delays to offer the best chance for obtaining normal binaural development within the CANS. A consensus of the upper age limit for fitting children with BCIs has yet to be determined however researchers suggest providing BCIs in children as early as possible. Greater exploration of the appropriate length of the interimplant delay and the child's age at the time of the second cochlear implantation is needed.

## *References*

Bauer, P, Sharma, A., Martin, K., & Dorman, D. (2006). Central auditory development in children with bilateral cochlear implants. *Arch Otolaryngology Head Neck Surgery, 132*, 1133-1136.

Gilley, P., Sharma, A., & Dorman, M. (2008). Cortical reorganization in children with cochlear implants. *Brain Research, 1239,* 56-65.

Gordon, K.A., Wong, D.D., & Papsin, B.C. (2010). Cortical function in children receiving bilateral cochlear implants simultaneously or after a period of interimplant delay. *Otology & Neurotology, 31,*1293-1299.

Key, A., Porter, H., & Bradham, T. (2010). Auditory processing following sequential bilateral cochlear implantation: a pediatric case study using event related potentials. *Journal of the American Academy of Audiology, 21*, 225-238.

Sharma, A., Dorman, M., & Kral, A. (2005). The influence of a sensitive period on central auditory development in children with unilateral and bilateral cochlear implants. *Hearing Research, 203,* 134-143.

Sharma, A, Dorman, M., & Spahr, A. (2002). A sensitive period for the development of the central auditory system in children with cochlear implants: implications for age of implantation. *Ear & Hearing, 23,* 532-539.

Sharma, A., Gilley P., Martin, K., Roland, P., Bauer, P., & Dorman, M. (2007). Simultaneous versus sequential bilateral implantation in young children: effects on central auditory system development and plasticity. *Audiological Medicine, 5,* 218-223.

Peters, R., Litovsky, R., Rarkinson, A., & Lake, J. (2007). Importance of age and postimplantation experience on speech perception measures in children with sequential bilateral cochlear implants. *Otology & Neurotology, 28,* 649-657.