Cortical Neuroplasticity Across Auditory, Visual, and Somatosensory Modalities in Children with Cochlear Implants

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Abstract

Auditory deprivation, as in hearing loss, appears to tax the brain, resulting in changes in cortical resource allocation. One form of cortical resource allocation in hearing loss is cross-modal reorganization, whereby cortical resources in the deprived modality are recruited and repurposed for processing by other sensory modalities. Cross-modal reorganization has been proposed as a source of variability underlying speech perception in patients receiving cochlear implants (CIs). Previous studies have documented cross-modal recruitment of auditory cortex for visual and somatosensory processing in hearing-impaired children with CIs. However, changes within the auditory modality have not been documented alongside visual and somatosensory cross-modal changes within the same subject group. Thus, the goal of this study was to examine cross modal reorganization across all three sensory modalities within a single group of CI children (n = 10) using high-density EEG. Behavioral correlates of speech perception in background noise were also measured. Amplitude and latency of cortical auditory, visual, and somatosensory evoked potentials were analyzed and source localization was performed to visualize cortical activation patterns within the entire group of CI children, and across groups of CI children exhibiting good vs. poor speech perception. Results suggest widespread changes in cortical resource allocation in CI children in all three sensory modalities. Further, frontal cortex activation was observed in response to auditory and visual stimulation in CI children, suggesting that frontal areas may be recruited as a means to help compensate in speech perception and/or higher-order cognitive processing tasks. CI children with good speech perception did not show recruitment of frontal cortex or cross-modal recruitment by visual processing, while the children with poor speech perception did. Taken together, results of this study reflect

widespread changes in cortical networks in CI children, and it appears that these changes are correlated with functional performance.

Cortical Neuroplasticity Across Auditory, Visual, and Somatosensory Modalities in Children with Cochlear Implants

For the significant portion of the population with a severe or profound hearing loss, the most viable treatment option is a cochlear implant (CI). While treatment with CIs has proven successful, the variability of success among those treated remains high. Research on neural changes associated with hearing loss and its treatment may explain this variability and is therefore critical to improving rehabilitation in the hearing-impaired population. A basic tenet of neuroplasticity is that that the brain will reorganize when it is deprived of sensory input. The present study attempts to understand how treatment of deaf children with CIs affects brain reorganization across sensory modalities: vision, audition (hearing), and somatosensation (touch). Furthermore, in an effort to determine whether the brain's reorganization is associated with better or poorer outcomes with CIs, these neural changes were compared to a behavioral test of speech perception in noise. This comparison helps establish whether the neuroplastic changes occurring are adaptive (helpful in speech perception) or maladaptive (negatively affects speech perception) for children with CIs.

Literature Review

Neural plasticity is a phenomenon that allows us to interact with, adapt to, and learn from environments and experiences. The brain's ability to reorganize when it is deprived of sensory input is just one example of neural plasticity, but has been key to studying the malleability of cortical connections. This phenomenon, known as cross-modal reorganization or cross-modal plasticity, has been demonstrated in studies of the congenitally deaf populations—such studies have shown that the deprived auditory cortex is subject to recruitment by the

visual system for visual perception in both humans and animals (Neville & Lawson, 1987; Sharma & Mitchell, 2013; Finney, Fine, & Dobkins, 2001; Finney, Clementz, Hickok, & Dobkins, 2003; Lomber, Meredith, & Kral, 2010). In addition to recruitment of auditory cortices by vision, deaf populations have also been found to demonstrate recruitment by the somatosensory modality (Levänen and Hamdorf, 2001). Essentially, some higher-order cortical areas that would be used for auditory processing in animals and humans with normal hearing were found to process different stimuli in those who experience hearing loss.

Cortical reorganization that occurs with sensory deprivation affects behavioral outcomes in that cross-modal plasticity tends to be beneficial for the recruiting modality. For example, Lomber et al. (2010) found that congenitally deaf cats had improved visual capabilities such as localization in the periphery and movement detection. However, reversible deactivation of the dorsal and posterior auditory cortices eliminated these superior visual abilities. It was therefore concluded that the supranormal visual performance in the deaf cats was subserved by cross-modal recruitment of deprived auditory cortex. The visual benefits of cross-modal recruitment have also been documented in deaf humans who demonstrate improved visual motion detection (Hauthal, Sandmann, Debener, & Thome, 2013). However, the effects of hearing loss are not limited only to changes in sensory cortices of the brain. In comparison to normal-hearing (NH) controls, adults with mild to moderate hearing loss have shown recruitment of frontal cortices for processing of auditory stimuli (Campbell & Sharma, 2013; Sharma et al., 2016). The activation of the frontal and pre-frontal cortex, areas traditionally associated with executive function and working memory, implies changes in cortical resource allocation due to increased listening effort in age-related hearing loss. Frontal areas may be

recruited as a means to help compensate in speech perception and/or higher-order cognitive processing tasks. Thus, two forms of compensatory neuroplasticity have been demonstrated by populations with hearing loss: cross-modal reorganization and changes in cortical resource allocation such as frontal activation.

While cross-modal plasticity is well-documented in deaf populations, fewer studies have been done on its occurrence in populations who have received treatment for hearing loss. Cochlear implantation remains the leading treatment for people with severe to profound hearing losses; it is estimated that over 400,000 people world-wide have received CIs (NIDCD, 2012). By directly stimulating the auditory nerve, the implant is able to transmit an electrical representation of acoustic signals which the brain interprets and processes as sound. The development of the CI has been key to the scientific exploration of neural plasticity for two reasons: first, it enables the study of neuroplastic changes induced by deprivation, and second, it has allowed the auditory system to become a model system due to convergence between animal and human data (Kral, Hartmann, Tillein, Heid, & Klinke, 2002). Studies have shown that the plasticity induced by cochlear implantation is optimized by early implantation within a critical period (Kral & Sharma, 2012); however, even those implanted within this period show significant variability of language outcomes (Kral, Kronenberger, Pisoni, & O'Donoghue, 2016).

One example of cross-modal reorganization in populations with CIs was documented by Campbell & Sharma in a group of twelve children (2016). Current density reconstruction (CDR) was used to calculate the probable cortical activation sources of children's responses to a visual motion stimulus. The resulting source reconstruction revealed that the NH control group showed activation of visual motion processing areas (cerebellum, striate, extrastriate) while CI

children showed activation of both visual areas and auditory areas (inferior, middle, and superior temporal gyrus). This finding suggests that in children with CIs, auditory cortical areas were recruited by vision via cross-modal plasticity.

Cardon (2015) also provided evidence for recruitment of auditory areas by the somatosensory modality. Similar methodology revealed that, as expected, a vibrotactile stimulus evoked activation of the contralateral somatosensory cortex (pre/post-central gyrus) in NH children. The CI group, however, showed activation of both contralateral somatosensory and contralateral auditory cortices (inferior, middle, and superior temporal gyrus). This finding suggests that the deprived auditory cortical areas were recruited by the somatosensory modality for the processing of a vibrotactile stimulus, another example of cross-modal plasticity in children with CIs.

The existing literature would suggest that vision, audition, and somatosensation are flexible, interrelated processes where a change in input in one modality will result in the potential reorganization of the brain for neuronal processing of the other two. The above studies of both Campbell & Sharma and Cardon have each surveyed cross-modal recruitment by a single modality (vision and somatosensation, respectively) but have failed to assess the brain's responses across visual, somatosensory, and auditory modalities within the same group of CI subjects. Through neurophysiological testing of auditory, visual, and somatosensory processing and comparative behavioral assessments, the present study attempts to draw conclusions about how cross-modal plasticity occurs among all three modalities for ten children with CIs.

Methods

Participants

As shown in Table 1, ten children with CIs were retrospectively included in this study. Their ages at the time of data collection ranged from 5.84–15.43 years with an average age of 10.61 years (SD = ±3.33 years). Eight of the ten subjects had bilateral CIs; two children had a CI on one side and a hearing aid on the opposite side. The average age of implantation for the first CI was 2.89 years (SD = ±2.59 years) while the average age of implantation for the second CI was 6.34 years (SD = ±3.68 years). Testing occurred at least 1.5 years after cochlear implantation of the first ear.

Table 1. Subject Demographic Characteristics

Subject Code	Age (Years)	Age at first CI (Years)	Age at Second CI (Years)	First CI Ear	Duration of First CI Experience (Years)	Duration of Second CI Experience (Years)
CI15	12.39	1.00	3.33	R	11.39	9.06
CIgd1	13.13	0.50	8.09	R	12.63	5.04
CI7	15.43	1.41	9.26	R	14.02	6.17
CI3	9.4	1.99	4.36	R	7.41	5.04
CI12	6.89	2.28	2.9	L	4.61	3.99
CI13	5.84	4.33	Hearing aid	R	1.51	N/A
CIavg2	11.41	1.61	6.61	R	9.8	4.8
CI5*	13.79	8.42	13.18	R	5.37	0.61
CI6*	11.42	6.14	Hearing aid	L	5.28	N/A
CI4	6.44	1.23	2.98	L	5.21	3.46

*Subjects had progressive hearing losses associated with diagnoses of enlarged vestibular aqueduct syndrome (EVAS).

All testing took place at the University of Colorado at Boulder in the Speech, Language, and Hearing Sciences Department in the Brain & Behavior Laboratory. The study was performed under the approval of University of Colorado Institutional Review Board. Written consent was obtained from parents of children participating in the research study along with verbal and/or

written assent from the child. Participants were recruited via advertisements in the community and local audiologists' offices. The subjects' parents reported normal to corrected vision. No neurological conditions were reported.

High-Density EEG Recording

Cortical auditory, visual, and somatosensory evoked potentials (CAEPS, CVEPs, and CSEPs) were recorded using a high-density, 128-channel electrode recording net (Electrical Geodesic, Inc.). A sampling rate of 1 kHz was used with an online band-pass filter set at 0.1-200 Hz. All testing was performed with the subjects positioned in a chair in an electromagnetically shielded sound booth. Stimuli were presented via E-Prime® 2.0 software, compatible with Net Station 4 software (Electrical Geodesics, Inc.). For the auditory and somatosensory stimuli, subjects were asked to ignore the stimuli while watching a movie with subtitles on and the sound off to ensure they remained awake and alert (Sharma et al., 2005). CI children removed the external processors of their CIs during the visual and somatosensory testing.

Auditory stimuli. CAEPs were elicited in response to a speech syllable, /ba/, comprised of spectral energy occurring mainly in the low-mid frequency region (0.5–2 kHz) (Sharma, Dorman, & Spahr, 2002). The speech stimulus was 90 ms in duration and presented with an inter-stimulus interval (ISI) of 610 ms. 1600 presentations of the stimulus were recorded for each subject resulting in a recording session of approximately 20 minutes. The stimulus was presented via a speaker located at an angle of 0° azimuth at a level of 65 dB HL. The children were tested binaurally with their CIs and/or hearing aid on and set to typical settings.

Visual stimuli. The visual stimulus was a high-contrast sinusoidal concentric grating that transitioned continuously from a circle pattern to a star pattern. The transition from the circle

to the star gives the percept of apparent motion. The stimulus was presented on a 26-inch flat screen LCD television positioned approximately 42 inches from the subject. This circle and star were each present for 600 ms. Each stimulus was presented 150 times for a total of 300 epochs in a recording session that lasted approximately 3 minutes (Doucet, Bergeron, Lassonde, Ferron, & Lepore, 2006; Bertrand et al., 2012).

Somatosensory stimuli. The somatosensory stimulus used to evoke CSEPs consisted of a 250 Hz vibrotactile stimulus applied to the index finger via a standard clinical bone oscillator (RadioEar Inc., B71 Bone Transducer) at a level of 55 dB HL. These stimuli had a duration of 90 ms, with 10 ms onset and offset linear ramps. Approximately 1000 instances of the vibrotactile stimulus were presented to the subjects (Cardon, 2015). Any auditory artifact of the 250 Hz stimulus was masked with the presentation of continuous white noise at 50 dB HL via a loudspeaker located 45° azimuth to the subject. The participant ensured that the stimulus was felt and not heard.

EEG Post-Processing

While the data collection for this study was retrospective, data analysis was performed prospectively. Raw CAEP, CVEP, and CSEP data were 1 Hz high-pass filtered offline and segmented accordingly for each sensory stimulus using Net Station 4 software. Data were then exported into Matlab using the EEGLAB toolbox (MathWorks, Inc., 2014). Baseline correction was performed with respect to a 100 ms pre-stimulus interval. Epoch rejection and bad channel rejection were performed. Data were re-referenced to a common average reference before being downsampled to 250 Hz to reduce processing time. A spherical interpolation algorithm was used to interpolate rejected channels.

Regions of interest (ROI) were identified for the CAEP, CVEP, and CSEP data based on previous studies (Campbell and Sharma 2016; Cardon 2015). These ROIs were averaged to allow computing of latencies and amplitudes of each waveform component for CAEP, CVEP, and CSEP data.

Current Density Reconstruction

EEGLAB was used to perform independent components analysis (ICA) was performed on each of the post-processed CAEP, CVEP, and CSEP recordings from each subject. ICA uses a statistical procedure to identify spatially and temporally independent components underlying the evoked potential. ICA was first used to remove CI artifact according to procedures described in Gilley et al. (2006). Next, ICA was used to prune for each component of the cortical evoked potential waveforms by selecting the ICA components that accounted for the greatest percent variance for each CAEP (P1, N1, P2), CVEP (P1, N1, P2), and CSEP (P50, N70, P100, N140) component. These pruned data sets, separated by type of component, were then exported into Curry 7 Neuroimaging Suite (Compumedics Neuroscan). This software was used to perform CDR for each component of the CAEP, CVEP, and CSEP waveform. CDR depicts brain areas that are statistically likely to be the source of post-synaptic electrical activity. This was achieved using standardized low-resolution electromagnetic tomography (sLORETA) which estimates cortical sources by measuring the likelihood of a source in each location of the brain. A standardized head model was created using Boundary Element Method (BEM) geometry which considers the average conductivities of three layers (scalp, skull, and brain) within the head (Fuchs, Kastner, Wagner, Hawes, & Ebersole, 2002). This head model was created using developmental white matter averages in children based on research done by Wilke, Krageloh-

Mann, and Holland (2007). The resulting CDRs are represented via a graded color scale image superimposed on an average child MRI collected by the Montreal Neurological Institute (MNI). The scale represents an F-statistic which measures the likelihood of a source in each location standardized by EEG source variance and EEG noise variance.

Speech Perception in Noise

The subjects' ability to perceive speech in background noise was assessed via a clinical assessment of sentence-level speech perception in background noise (BKB-SIN) (Bench, Kowal, & Bamford, 1979; Etymotic Research, 2005). Target sentence lists were presented at 65 dB HL via a speaker located at 0° Azimuth to the subject with their CIs and/or hearing aids and set to typical settings. The participants were asked to repeat sentences with increasing background noise, a process which decreased the signal-to-noise ratio (SNR) from 25 dB SNR (least challenging) to 0 dB SNR (most challenging). The subjects' responses were scored based on the correct identification of key words for each sentence. The subjects received a dB SNR score corresponding to the level at which they could correctly repeat 50% of the key words. Lower scores on the test indicate a better performance. The scores collected for two sentence lists were then averaged to obtain the score for each participant. Age corrections were applied to each participant's score to normalize for comparison across subjects. The CI children were divided into two groups based on their performance on the test: a group that performed exceptionally (BKB < 6 dB SNR) and an average-performing group (BKB > 6 dB SNR). A cutoff of 6 dB SNR between groups was chosen based on outcomes for hearing impaired children—children with scores above 6 dB SNR tend to struggle more in real-life noisy situation such as in the classroom (Etymotic Research, 2005).

Results

Current Density Reconstruction

Unlike previous studies by Campbell & Sharma (2016) and Cardon (2015), in which cross-modal reorganization by only the visual modality and only the somatosensory modality, respectively, were documented in different groups of CI children, this current study examines simultaneous changes across auditory, visual, and somatosensory cortical resource allocation in the same group of CI children. In addition, this study aimed to examine differences in cortical activation patterns in CI children who exhibited good versus poor speech perception abilities in an effort to determine whether these changes in cortical resource allocation may be functionally related to speech perception. CDRs were computed for each component of the CAEP, CVEP, and CSEP group waveforms. The CDR activations are represented by the graded color scale (F-distribution) superimposed on an average MRI.

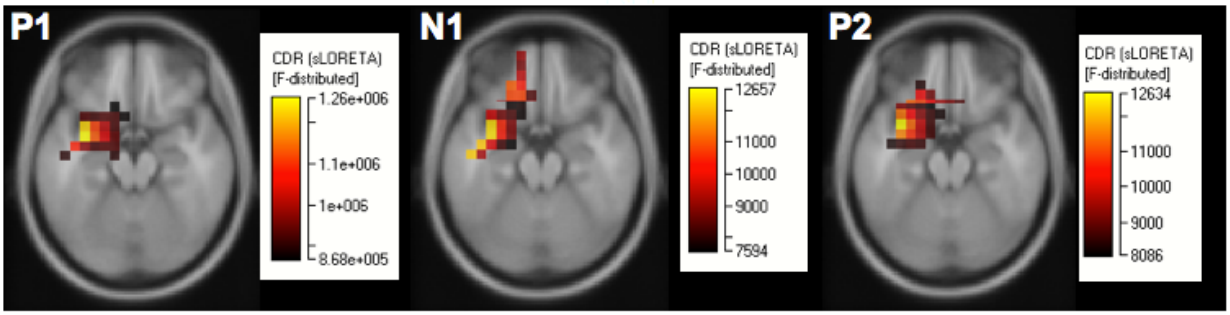

Figure 1. Cortical Auditory Evoked Potentials (CAEPs) in Children with CIs (n=10)

Figure 1 depicts CAEP source reconstructions for the group of CI children in response to the auditory stimulus. As shown in this figure, the auditory speech stimuli elicited activation of left temporal cortex (middle temporal gyrus, superior temporal gyrus, inferior temporal gyrus, parahippocampal gyrus) and frontal cortex (inferior frontal gyrus, superior frontal gyrus, medial frontal gyrus) for all CAEP components (see Appendix A for all activated cortical areas). Frontal

cortex activation was visibly larger for the higher-order CAEP components (N1, P2). Activation of left temporal cortical regions is likely due to the use of a speech syllable stimulus (Stefanatos, Joe, Aguirre, Detre, & Wetmore, 2008; Campbell & Sharma, 2013). Recruitment of frontal cortical regions for auditory processing is consistent with previous studies in hearing impaired populations and has been considered an indication of effortful listening (Campbell & Sharma, 2013; Glick & Sharma, 2017; Sharma et al., 2016; Peelle, Johnsrude, & Davis, 2010; Peelle, Troiani, Wingfield, & Grossman, 2010; Peelle, Troiani, Grossman, & Wingfield, 2011).

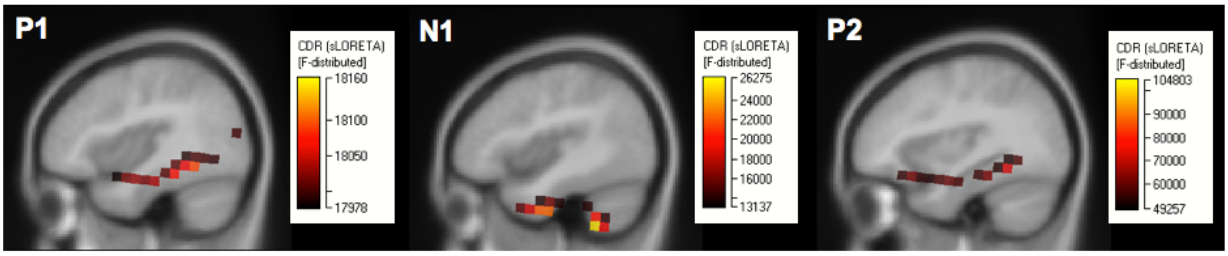

Figure 2. Cortical Visual Evoked Potentials (CVEPs) in Children with CIs (n=10)

Figure 2 shows CVEP source reconstructions for the group of CI children in response to the visual motion stimulus. For all CVEP components, the CI children exhibit activation of left or right occipital and cerebellar cortical regions (fusiform gyrus, middle occipital gyrus, lingual gyrus, culmen; see Appendix B) typically associated with the encoding of visual motion stimuli (Doucet et al., 2006; Sharma, Campbell, & Cardon, 2015). In addition, the CI children show recruitment of temporal cortical regions (middle temporal gyrus, inferior temporal gyrus, superior temporal gyrus), suggestive of cross-modal reorganization. These results are consistent with those of Campbell and Sharma (2016) where CI and NH children showed activation of visual cortical areas but only CI children showed additional activation of auditory areas.

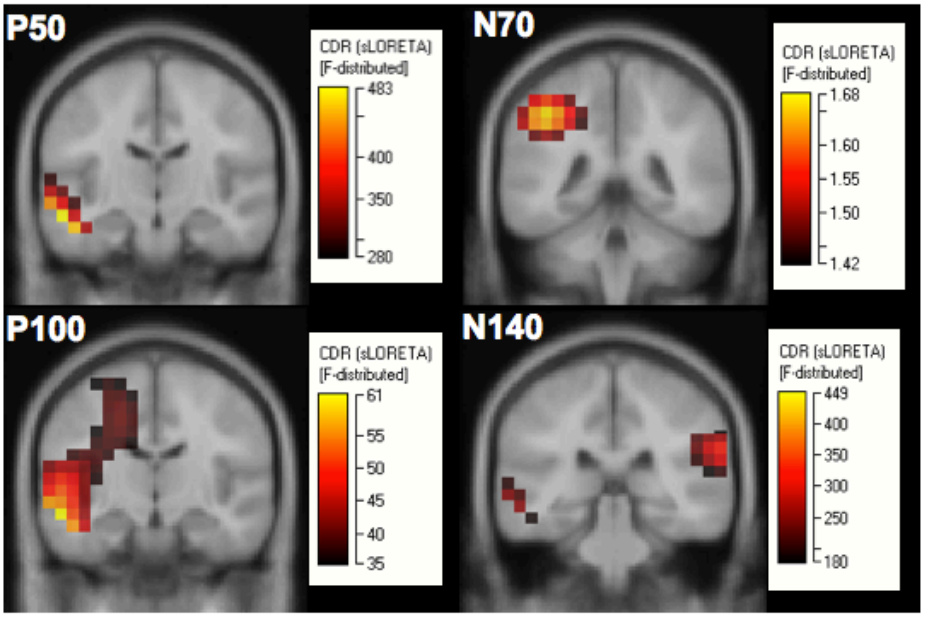

Figure 3. Cortical Somatosensory Evoked Potentials (CSEPs) in Children with CIs (n=10)

Figure 3 depicts CSEP source reconstructions for the group of CI children in response to the vibrotactile stimulus. For the N70, P100, and N140 components, the somatosensory stimulus elicited responses in left or right parietal cortex (precentral gyrus, postcentral gyrus, inferior parietal lobule; see Appendix C), consistent of normal processing of these stimuli (Sharma et al., 2015; Cardon, 2015). In addition, the CI children exhibit activation of left or right temporal cortex for the P50, P100, and N140 CSEP components (inferior temporal gyrus, superior temporal gyrus, middle temporal gyrus, transverse temporal gyrus). These results are consistent with those of Cardon (2015) where CI and NH children showed activation of somatosensory cortical areas but only CI children showed activation of additional auditory areas.

The CI children were also divided into two groups based on their auditory-only speech perception performance using a clinical test of speech understanding in background noise (BKB-SIN). Three children from the 2016 Campbell & Sharma study were added to the group with

poor speech-in-noise performance in order to increase the sample size for this comparison. The speech-in-noise scores of two the groups were statistically different as demonstrated by a one-tailed t-test ($p = .002$). CDRs were computed for the CAEP, CVEP, and CSEP waveforms for the group of children demonstrating good speech perception ($n = 5$, BKBSIN score < 6 dB SNR, mean BKBSIN score = 3.94 dB SNR, SD = 2.07 dB SNR) and the group of CI children demonstrating poor speech perception ($n = 8$, BKBSIN score > 6 dB SNR, mean BKBSIN score = 11.33 dB SNR, SD = 5.20 dB SNR). No differences were observed in CAEP or CSEP cortical source activation patterns between the two groups. However, differences were observed in CVEP cortical source activation patterns between the two groups. Figure 4 depicts CVEP source reconstructions for the good vs. poor performers.

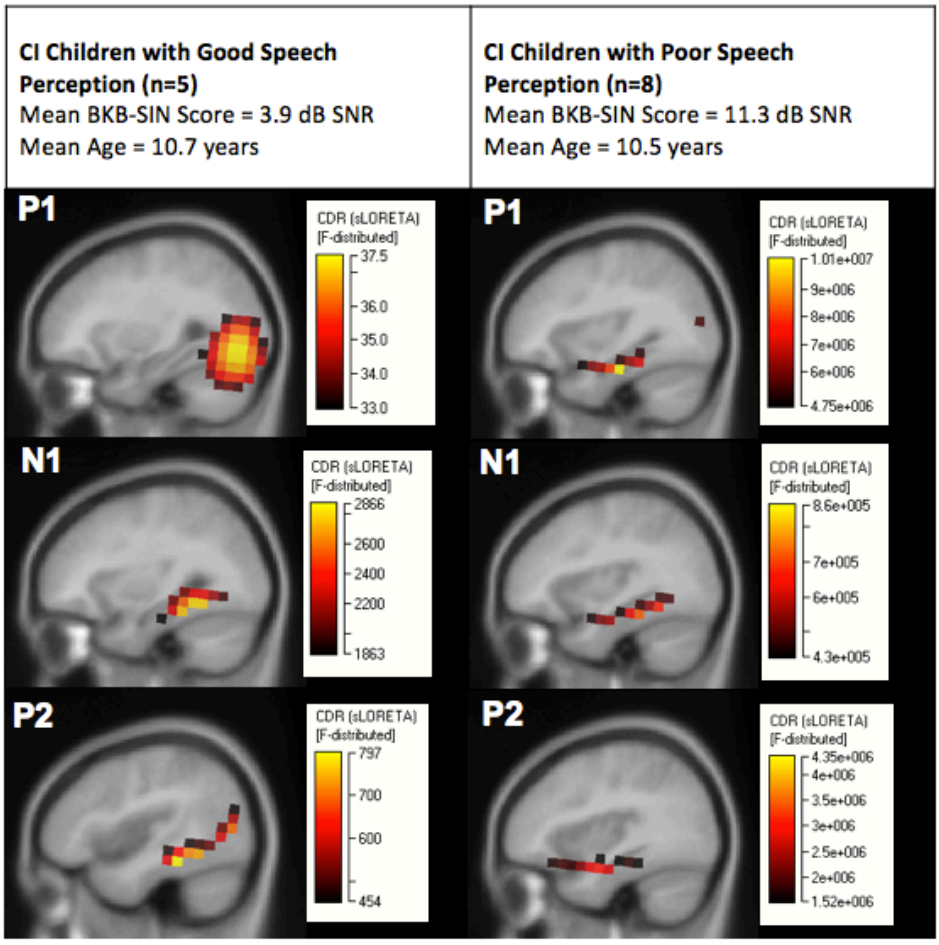

Figure 4. Cortical Visual Evoked Potentials (CVEPs) in CI Children with Good and Poor Speech Perception

As seen in Figure 4, the CI children with good speech perception show activation of only occipital cortical regions for all CVEP components (inferior occipital gyrus, middle occipital gyrus, fusiform gyrus; see Appendix D). In contrast, the CI children exhibiting poor speech perception demonstrate activation of occipital cortical regions (middle occipital gyrus, fusiform gyrus), auditory cortical regions (middle temporal gyrus, inferior temporal gyrus, superior temporal gyrus, parahippocampal gyrus), and frontal cortical regions (inferior frontal gyrus) for all CVEP components.

Waveform Latency and Amplitude Analysis

An age-controlled, partial correlations analysis was performed using a multiple comparisons correction (Benjamini & Hochberg, 1995) at the q = 0.1 level to explore the relationships between the data sets under study. Decreased latencies and increased amplitudes reflect more efficient processing in the recruiting modality and have been considered markers of cross-modal reorganization (Sharma et al., 2015). The statistical relationships between evoked potential components and BKB-SIN scores suggest a relationship between cross-modal recruitment and CI outcomes. As shown in Figure 5, a significant negative relationship between the CVEP N1 latency in the right temporal ROI and the BKB-SIN score emerged (r = -0.764; p = 0.01). Decreased N1 latency was correlated with worse speech perception. This replicates the findings of Campbell & Sharma in the similar group of CI children (2016) suggesting that greater cross-modal recruitment is associated with worse CI outcomes.

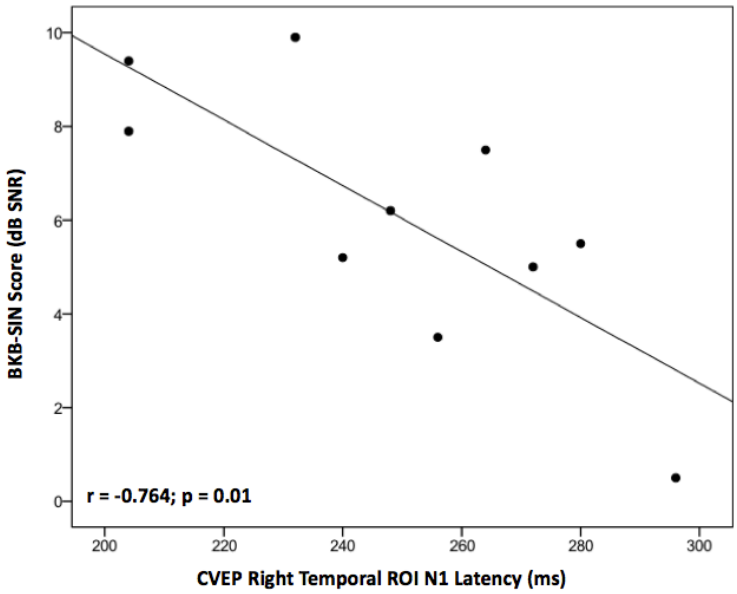

Figure 5. Scatter Plot Illustrating the Correlation Between BKB-SIN Score and CVEP N1 Latency in the Right Temporal ROI in Children with CIs

As seen in Figure 6, a negative relationship was significant between the CSEP P50 component in the right temporal ROI and the BKB-SIN score (r = -0.726; p = 0.018). This finding is in agreement with that of Cardon (2015) showing that decreased P50 latency is associated with worse speech perception. Both of the above correlations suggests that cross-modal recruitment of the auditory cortex by vision and somatosensation (as indicated by decreased latency of CVEP and CSEP components) may have negative impacts on speech perception.

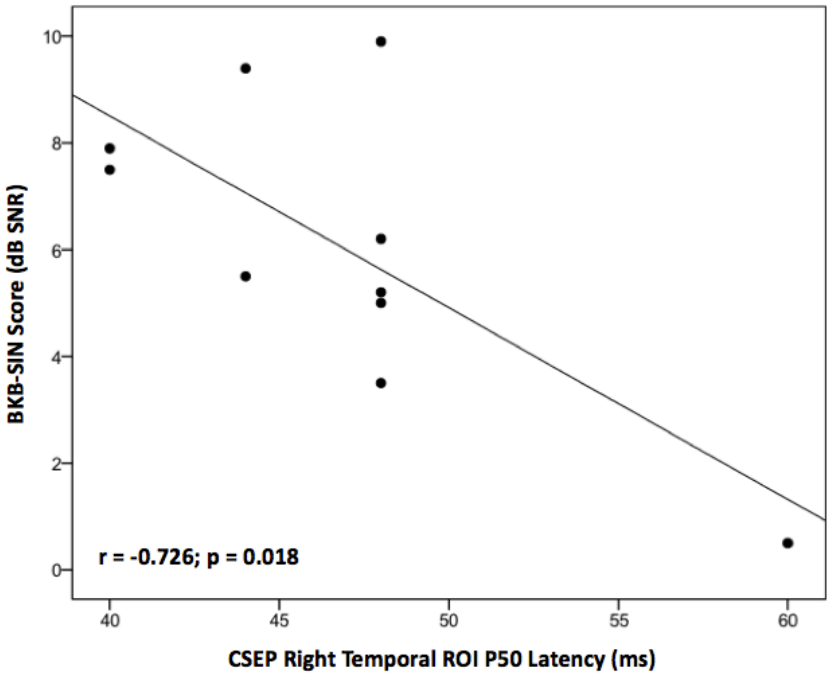

Figure 6. Scatter Plot Illustrating the Correlation Between BKB-SIN Score and CSEP P50 Latency in the Right Temporal ROI in Children with CIs

The same statistical methodology was used to explore the relationship between the latencies and amplitudes of CAEPs, CVEPs, and CSEPs. As shown in Figure 7, a significant relationship emerged between the latencies of the CSEP N140a in the right temporal ROI and the CVEP N1 latency in the same ROI (r = 0.882; p = 0.009). This correlation may reflect the fact that a majority of the subjects were implanted first on the right side, leaving the less-stimulated

(i.e., ipsilateral) right temporal cortex vulnerable to recruitment by both visual and somatosensory modalities (Levänen & Hamdorf, 2001; Cardon, 2015).

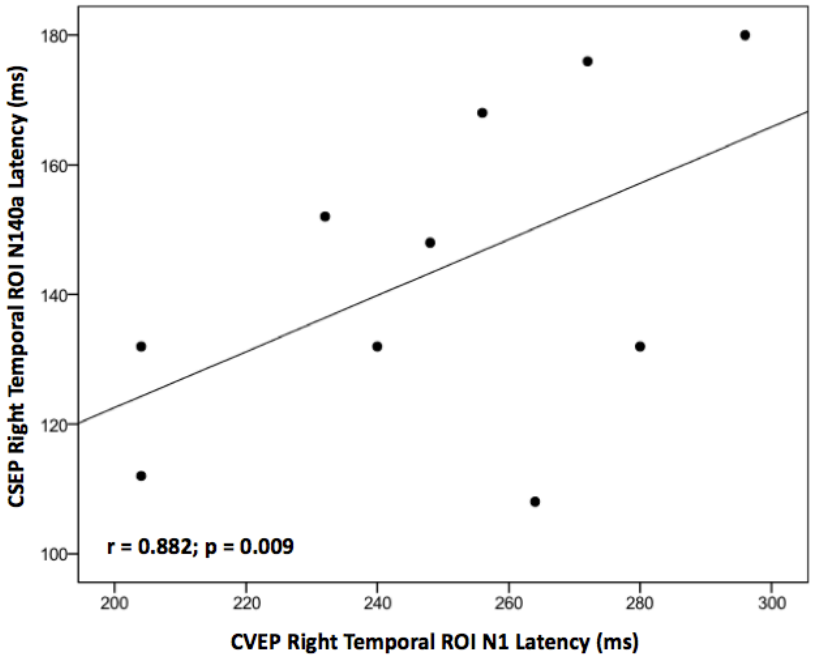

Figure 7. Scatter Plot Illustrating the Correlation Between CSEP N140a Latency and CVEP N1 Latency in the Right Temporal ROI in Children with CIs

Figure 8 demonstrates that CAEP amplitudes for the N1 and P2 components in the frontal ROI were significantly positively correlated with the CSEP N140b amplitude in the left temporal ROI ($r = 0.833$, $p = 0.005$; $r = 0.85$, $p = 0.004$). This finding suggests that greater frontal activation (possibly reflecting increased listening effort), as demonstrated by increased frontal amplitudes for CAEPs, increased with cross-modal activation of the temporal cortex by a somatosensory stimulus.

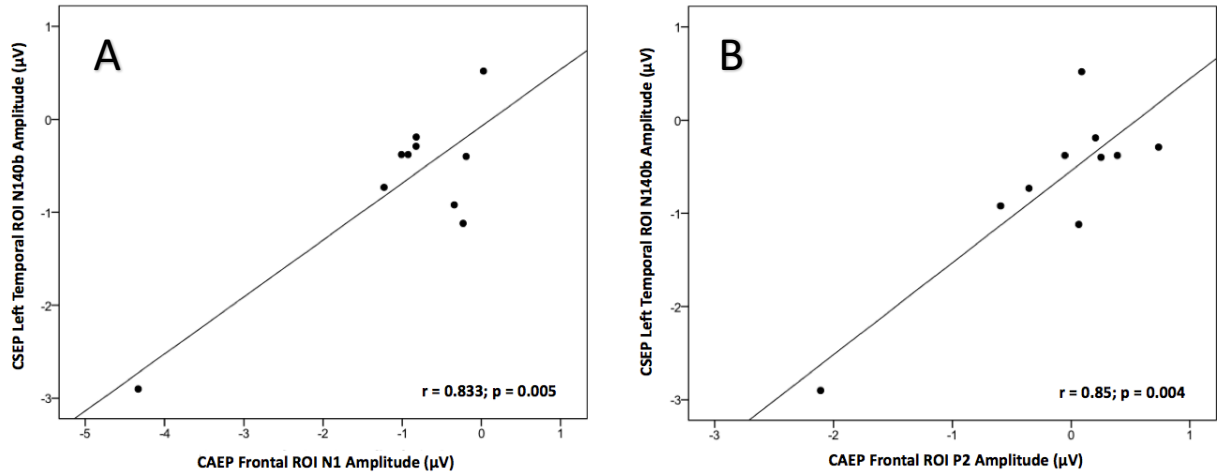

Figure 8. Scatter Plots Illustrating the Correlation between CSEP N140b Amplitude in the Left Temporal ROI with CAEP N1 Amplitude (Panel A) and CAEP P2 Amplitude (Panel B) in the Frontal ROI

Discussion

In this study, we examined the cortical reorganization that occurs with cochlear implantation by analyzing the responses of ten CI children to auditory, visual, and somatosensory stimulation. Latency and amplitude analysis of cortical evoked potential waveforms and their correlation to speech perception in background noise allowed for further examination of how these cortical changes affect behavioral outcomes in CI children. The results of the study showed activation of temporal areas by visual and somatosensory stimuli, suggestive of cross-modal reorganization by both vision and somatosensation. Auditory stimulation resulted in activation of frontal areas (associated with effortful listening) in addition to the expected temporal (auditory) cortical areas. Further, a comparison of sources of CVEPs between the CI children who performed well at speech perception and those who performed poorly revealed increased cross-modal and frontal activation in the poor-performing group. This result may suggest that the cross-modal reorganization is reflective of an increased dependence on visual processing for children who gain less benefit from their CIs.

Finally, several significant correlations were computed relating the latencies and amplitudes of CAEP, CVEP, and CSEP components. A relationship was found between the latencies of visual and somatosensory waveform components in the temporal region, suggesting that the cross-modal recruitment by vision and somatosensation may be interrelated. Amplitude of the CAEP N1 and P2 components in the frontal ROI was positively correlated with the amplitude of the CSEP 140b component in the temporal ROI, which indicates a possible relationship between cross-modal recruitment by somatosensation and frontal activation in auditory stimulation. Negative correlations between speech perception and CVEP and CSEP latencies in the temporal ROI replicate the findings of previous studies which interpret these results as an indication that cross-modal reorganization is a source of variability in speech perception outcomes for children with CIs.

Visual Cross-Modal Recruitment

In NH children, stimulation with a visual motion stimulus results in activation of visual areas such as the occipital cortex and cerebellum (Campbell & Sharma, 2016). Evidence of cross-modal recruitment of the temporal cortex for visual processing is well-documented in animals and humans with congenital or pre-lingual onset deafness (Neville & Lawson, 1987; Buckley & Tobey, 2010; Dewy & Hartley, 2015; Doucet et al., 2006; Finney et al., 2003; Finney et al., 2001; Lee et al., 2001, 2007; Lomber et al., 2010). In this study, we saw activation of temporal (auditory) areas in response to visual motion stimuli suggestive of cross-modal plasticity. Thus, cross-modal recruitment of temporal cortex for visual processing appears to persist even after cochlear implantation in this group of deaf children.

In previous studies, decreased cortical evoked potential latencies and increased cortical evoked potential amplitude have been used as markers of cross-modal reorganization (Doucet et al., 2006; Buckley & Tobey, 2010). By means of this assumption, a faster CVEP N1 response in the temporal ROI may be indicative of greater synaptic strength and efficiency involved in visual cross-modal reorganization (Clemo, Lomber, & Meredith, 2014). The negative correlation between BKB-SIN performance and the CVEP latency (Figure 5) suggests that children with worse speech perception showed earlier latencies (indicative of greater cross-modal recruitment by, and dependence on, vision), consistent with Campbell & Sharma (2016).

Unlike the previous study by Campbell & Sharma (2016), in which only visual and cortical regions were activated for NH and CI children, this sub-group of CI children shows additional recruitment of frontal cortices (inferior frontal gyrus) for the P1 and P2 CVEP components. This is a novel finding which has been observed in case studies of hearing impaired subjects in our laboratory including adults and children with single-sided deafness, but has never been documented in CI children (Glick & Sharma, in preparation). Frontal and pre-frontal activation is commonly reported in subjects with hearing loss during difficult listening situations (Peelle et al., 2010a,b; Campbell & Sharma, 2013). Frontal activation during visual stimulation may indicate a change in default resting state networks in that children with cochlear implants are experiencing difficulty in listening all through the day and are compensating by increased dependence on vision and recruitment of frontal networks.

Somatosensory Cross-Modal Recruitment

In NH populations, vibrotactile stimuli evoke responses in contralateral somatosensory cortices (pre/post-central gyrus) (Cardon, 2015; Sharma et al., 2016). In this study, in CI

children, a vibrotactile stimulus evoked responses in both the expected parietal (somatosensory) areas and temporal (auditory) areas, suggestive of cross-modal sensory reorganization (Figure 3). This finding replicates those documented by Cardon (2015) in CI children and in congenitally deaf adults (Levänen & Hamdorf, 2001; Levänen et al., 1998). While the source reconstruction for CVEPs showed activation of frontal cortical areas, this result was not seen for the cortical potentials evoked by somatosensory stimulation. Interestingly, despite the frontal activation shown by CDR for the visual stimulus, the CVEP latencies or amplitudes did not significantly correlate with CAEP latencies or amplitudes, while those of the somatosensory modality did (Figure 8). While the implications of this finding are not entirely clear, it is possible that the proximity of the frontal cortex to somatosensory areas may facilitate the amplitude correlations found in this study.

The results of Cardon (2015) are also echoed by the negative correlation between performance on speech-in-noise testing to CSEP P50 latency in the right temporal ROI. As was discussed for the BKB-SIN correlation with CVEP N1 latency, decreased latency is often used as a marker for increased cross-modal reorganization. The results of the current study support the same conclusion that the degree of cross-modal reorganization is related to negative speech perception outcomes in CI children.

By studying cross-modal reorganization by vision to that by somatosensation within the same group of children with CIs, a positive correlation between CSEP N140a latency and CVEP N1 latency in the right temporal ROI was found to be significant, suggesting that cross-modal recruitment by vision and somatosensation may be related (Figure 7). While the temporal cortex in CI children has been shown to be subject to recruitment by both vision and

somatosensation, their interrelation in the same group of subjects has not been previously documented. The positive correlation between CSEP and CVEP latencies may reflect the fact that a majority of the subjects were implanted first on the right side, leaving the less-stimulated (i.e., ipsilateral) right temporal cortex vulnerable to recruitment by both visual and somatosensory modalities (Levänen & Hamdorf, 2001; Cardon, 2015).

Auditory Stimulation

Gilley, Sharma, & Dorman (2008) found that in NH children, a passive speech stimulus activates temporal cortices bilaterally. However, the same study found that CI children show activation only of the temporal cortex contralateral to the ear of implantation. Even though the children in the current study had either bilateral CIs or a CI and a hearing aid, the majority of them were implanted in the right ear first (see Table 1). Because sLORETA shows only the dominant source of cortical activation, the lateralization of temporal activation to the left hemisphere (Figure 1) is in accordance with the above studies of Gilley & Sharma and their respective colleagues (2008; 2016). The use of a speech stimulus is further explanation for this lateralization, as speech is processed in the left hemisphere for the majority of the population (Stefanatos et al., 2008). The discussion above also supports the fact that significant correlations were found for CVEP and CSEP activation in the right temporal cortex, as it is less stimulated for these children and thus more susceptible to recruitment by vision and somatosensation.

Involvement of Frontal Areas

In addition to the expected temporal activation, the auditory stimulus evoked activation of frontal cortices, as shown by Figure 1. This finding is consistent with previous studies that

have documented frontal activation in adults with hearing loss (Campbell & Sharma, 2013). Frontal cortices were activated to a further extent for the higher-order CAEP waveform components (N1, P2). This result is expected given the fact that these components are associated with more complex processing of the auditory stimulus. It therefore follows that increased listening effort may be taking place for these CI children, and that frontal areas may constitute part of the cortical source for these components. The amplitudes of the CAEP N1 and P2 components in the frontal ROI were found to correlate with the amplitude of the CSEP N140b component in the right temporal ROI (Figure 8). While evidence of frontal recruitment by the somatosensory modality was not demonstrated via CDR, this relationship between CSEP amplitudes in auditory regions and CAEP amplitudes in the frontal ROI may suggest a relationship between cortical reorganization by the somatosensory modality and increased listening effort.

Interestingly, as previously described, the frontal cortex was also found to be a cortical source for processing of the visual motion stimulus (Figure 2). As indicated above, the effect of cochlear implantation on frontal activation by vision suggests a change in the default sensory network in the CI population and requires further study on how cochlear implantation affects the brain's resting state. Additionally, this evidence of frontal recruitment by vision may be representative of an adaptive mechanism where the frontal cortex is utilized in conjunction with increased dependence on visual processing when listening is effortful as it tends to be for children listening through a cochlear implant. In keeping with this, it is interesting to note that children with good speech perception scores did not show frontal activation during visual stimulation (Figure 4). However, there was no correlation found between CAEP waveform

components in the frontal ROI and CVEP waveform components in the temporal ROI, suggesting that there may be different mechanisms underlying compensatory changes by vision in comparison to those occurring for somatosensation. While frontal activation by visual stimuli has not been previously documented in the CI population, this finding is supported by unpublished findings in our lab which show that frontal CVEP activation increases with the severity of hearing loss (Campbell & Sharma, in preparation). This may be explained by the fact that people tend to rely more on visual cues as their hearing loss progresses and listening becomes more effortful.

Overall, recruitment of the frontal cortex by both auditory and visual modalities is suggestive of broad changes in cortical resource allocation in children with CIs which may be reflective of mediation of sensory processes via top-down modulatory control (Campbell & Sharma, 2013; Peelle et al., 2011; Sharma et al., 2016; Cardin, 2016). Future studies should examine compensatory recruitment of visual and frontal areas using more complex and attention regulated stimuli.

Performance on the Speech-in-Noise Task

The comparison between cortical activation for the CVEP for good and poor groups shows increased cross-modal reorganization for the poor performing group, both of auditory and frontal cortical areas (Figure 4). Thus, it is possible that the recruitment of temporal and frontal cortical regions by vision in the poor performing group may be functionally correlated to an increased reliance on visual cues for speech perception (Stropahl et al., 2015). For example, regardless of age of implantation, CI children exhibit greater dependency on visual cues for the McGurk effect compared to age-matched, NH children (Schorr, Fox, van Wassenhove, &

Knudsen, 2007). Further, late-implanted CI children have been shown to achieve higher levels of visual-only speech perception (lip reading abilities) and greater benefit from visual cues in an auditory and visual speechreading task compared to early-implanted CI children (Bergeson, Pisoni, & Davis, 2005).

Statistical analyses comparing speech perception and visual and somatosensory latencies within the temporal ROI (Figure 5, Figure 6) suggest an inverse relationship between cortical reorganization and speech perception. That is, decreased CVEP and CSEP latencies (suggestive of increased cross-modal recruitment) correlate with poorer performance on speech-in-noise testing. This reflects previous findings that adults with CIs who demonstrate visual cross-modal organization show deficits in speech perception performance (Buckley & Tobey, 2011; Lazard, Innes-Brown, & Barone, 2014).

Conclusions and Limitations of the Study

This current study documented cross-modal reorganization by visual and somatosensory modalities and intra-modal reorganization within the auditory modality in the same group of children with CIs. The children under study provide evidence of recruitment of auditory cortices for processing of visual and somatosensory stimuli in addition to frontal recruitment by the auditory and visual modalities. Activation of frontal cortices is perhaps associated with increased listening effort and top-down modulatory control. Finally, a comparison of cortical activation by visual stimuli between implanted children with good speech perception and poor speech perception showed that the cross-modal recruitment of auditory and frontal cortices by the visual modality is associated with poorer speech perception. In agreement with previous

studies, this finding reflects that a child's behavioral outcomes with their CI may be related to cross-modal reorganization and changes in cortical resource allocation.

However, the results of the study are not without limitation. Due to the retrospective nature of the study and scope of the thesis project, we were not able to analyze data from a NH control group under the same conditions with which to compare the CDRs or latency and amplitude correlations. However, a point of comparison was provided by similar studies with NH controls which used the same stimuli, methods, analyses and age-ranges as the CI children in this study. Another limitation is that the small sample size of the group under study prevented an evaluation of right vs. left ear implantation, which may have affected lateralization of the CDR. Similarly, the vibrotactile stimulation of right vs. left finger was not considered due to the mixture of children that were implanted first in their right vs. left ear. Nevertheless, the methodology still allowed for the exploration of broad cortical changes occurring within the children under study. The use of a passive stimulus for CAEPs restricted this study from investigating how the attentional difficulty of a listening task affects changes in cortical resource allocation in children with CIs. Further imaging studies (such as fMRI or PET) are therefore needed to better understand how cross-modal reorganization and changes in cortical resource allocation are involved in effortful listening in the CI population. Such studies will also allow for better spatial resolution than EEG and may help investigate targeted cortical areas with more specificity. Finally, future longitudinal studies are necessary to understand the time course and permanence of the cortical changes involved in cochlear implantation and their effects on clinical outcomes.

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Appendix A. Areas of Activation for Cortical Auditory Evoked Potentials (CAEPs) in CI Children

Waveform Component	**Areas of Activation**
P1	Superior temporal gyrus (BR 38, BR 34), inferior temporal gyrus, middle temporal gyrus (BR 21), inferior frontal gyrus (BR 11, BR 47), insula (BR 13) parahippocampal gyrus, sub gyrus
N1	Inferior temporal gyrus (BR 20), superior temporal gyrus (BR 38, 22), middle temporal gyrus (BR 21), inferior frontal gyrus (BR 11, BR 47), medial frontal gyrus, rectal gyrus, superior frontal gyrus, BR 25, amygdala, insula (BR 13)
P2	Superior temporal gyrus (BR 38, BR 34), inferior frontal gyrus (BR 11, BR 47), medial frontal gyrus, BR 25, insula (BR 13), sub gyrus, amygdala, parahippocampal gyrus

Note: Source activations are listed in approximate order by highest F-value.

Appendix B. Areas of Activation for Cortical Visual Evoked Potentials (CVEPs) in CI Children

Waveform Component	**Areas of Activation**
P1	Fusiform gyrus (BR 36), middle occipital gyrus (BR 17), cuneus, culmen, lingual gyrus, superior temporal gyrus (BR 38), middle temporal gyrus (BR 21), parahippocampal gyrus, sub gyrus, inferior frontal gyrus (BR 47), lingual gyrus
N1	Cerebellar tonsil, fusiform gyrus (BR 36), Superior temporal gyrus (BR 38), middle temporal gyrus (BR 21), inferior temporal gyrus (BR 20), uncus
P2	Fusiform gyrus (BR 36), cuneus (BR 18), pre-cuneus, culmen, Inferior frontal gyrus (BR 47), middle temporal gyrus (BR 20), superior temporal gyrus (BR 36), inferior temporal gyrus (BR 37), sub gyrus, parahippocampal gyrus, BR 31

Note: Source activations are listed in approximate order by highest F-value.

Appendix C. Areas of Activation for Cortical Somatosensory Evoked Potentials (CSEPs) in CI Children

Waveform Component	**Areas of Activation**
P50	Inferior temporal gyrus (BR 20), middle temporal gyrus (BR 21), superior temporal gyrus (BR 22)
N70	Pre-central gyrus (BR 4), post-central gyrus (BR 3), BR 7, supra-marginal gyrus (BR 40), inferior parietal lobule, transverse temporal gyrus, cingulate gyrus
P100	Middle temporal gyrus (BR 21), superior temporal gyrus (BR 22), inferior parietal lobule, supra-marginal gyrus (BR 40), transverse temporal gyrus (BR 42) post-central gyrus (BR 3), pre-central gyrus (BR 4), inferior parietal lobule (BR 5), insula (BR 13), sub gyrus, extra nuclear
N140	Supra-marginal gyrus (BR 40) Middle temporal gyrus (BR 21), BR 19, superior temporal gyrus (BR 22), insula (BR 13), inferior parietal lobule (BR 5), post-central gyrus (BR2)

Note: Source activations are listed in approximate order by highest F-value.

Appendix D. Areas of Activation for Cortical Visual Evoked Potentials (CVEPs) in CI Children with Good and Poor Speech Perception

Waveform Component	**Areas of Activation** for **CI Children with Good Speech Perception (n = 5) Mean BKB-SIN Score = 3.9 dB SNR Mean Age = 10.7 years**	**Areas of Activation** for **CI Children with Poor Speech Perception (n = 8) Mean BKB-SIN Score = 11.3 dB SNR Mean Age = 10.5 years**
P1	Middle occipital gyrus, lingual gyrus (BR 18), inferior occipital gyrus, cuneus, culmen, pyramis, tuber, uvula, dentate, declive, BR 19, parahippocampal gyrus	Fusiform gyrus (BR 36), middle temporal gyrus (BR 21), lingual gyrus (BR 18), cuneus, middle occipital gyrus (BR 17), transverse temporal gyrus (BR 42), inferior temporal gyrus (BR 20), superior temporal gyrus (BR 22), sub gyrus, inferior frontal gyrus, insula (BR 13), parahippocampal gyrus
N1	Fusiform gyrus (BR 37), culmen, lingual gyrus, sub gyrus, BR 19, BR 28, parahippocampal gyrus, inferior temporal gyrus (BR 20)	Fusiform gyrus (BR 36, BR 37), middle temporal gyrus (BR 21), BR 19, BR 28, inferior temporal gyrus (BR 20), superior temporal gyrus (BR 38), sub gyrus, parahippocampal gyrus
P2	Fusiform gyrus (BR 36, BR 37), middle occipital gyrus, extra nuclear, BR 19, parahippocampal gyrus, sub gyrus	Middle temporal gyrus (BR 21), Inferior temporal gyrus (BR 20), sub gyrus, superior temporal gyrus (BR 38), Inferior frontal gyrus (BR 47), insula (BR 13), uncus, amygdala, fusiform gyrus (BR 36)

Note: Source activations are listed in approximate order by highest F-value.