Cortical Processing of Frequency Changes Reflected by the Acoustic Change Complex in Adult Cochlear Implant Users

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Keywords

Acoustic change complex · Cochlear implant · Cortical auditory evoked potential · Frequency change detection · Electroencephalography

Abstract

The purpose of this study was to examine neural substrates of frequency change detection in cochlear implant (CI) recipients using the acoustic change complex (ACC), a type of cortical auditory evoked potential elicited by acoustic changes in an ongoing stimulus. A psychoacoustic test and electroencephalographic recording were administered in 12 postlingually deafened adult CI users. The stimuli were pure tones containing different magnitudes of upward frequency changes. Results showed that the frequency change detection threshold (FCDT) was 3.79% in the CI users, with a large variability. The ACC N1' latency was significantly correlated with the FCDT and the clinically collected speech perception score. The results suggested that the ACC evoked by frequency changes can serve as a useful objective tool in assessing frequency change detection capability and predicting speech perception performance in CI users.

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Introduction

Cochlear implants (CIs) are prosthetic devices that have been widely used to provide hearing sensation in individuals with severe to profound hearing loss. CIs bypass the damaged inner ear and directly stimulate auditory nerve fibers with electrical pulses. Unlike the normal-hearing individuals who have approximately 3,500 inner hair cells and 12,000 outer hair cells to provide fine-grained spectral resolution, CI users rely on the sound information conveyed by the electrical stimulation through up to 22 electrodes. Due to this technical limitation, a CI device can only provide a coarse frequency information of the input signal.

The capability of discerning small frequency changes and fine cues in the spectral dimension plays a crucial role in speech understanding [Oxenham, 2008; Gifford et al., 2014; Won et al., 2014; Kenway et al., 2015]. Numerous studies reported that postlingual CI users demonstrate poor frequency discrimination [Gfeller et al., 2007; Kang et al., 2009; Limb & Roy, 2014; Turgeon et al., 2015]. Moreover, the frequency discrimination performance varies substantially among patients, who typically have heterogeneous demographic variables (e.g., duration of

deafness, age of implantation, the degree of residual hearing etc.). For example, using a pitch direction discrimination task that requires the participant to identify which of the two stimuli was higher in pitch, Kang et al. [2009] reported that normal-hearing (NH) listeners can detect a 1-semitone difference (approx. 6% frequency change) while CI users demonstrated a much poorer frequency discrimination capability with an enormous variance (from 1 to 8 semitones).

It has been well documented that CI users' speech perception performance varies significantly [Leung et al., 2005; Finley et al., 2008; Gfeller et al., 2008; Holden et al., 2013]. Multiple psychoacoustic studies have shown that the speech outcome of CI users is highly associated with the capability of frequency change detection [Litvak et al., 2007; Gifford et al., 2014; Won et al., 2014; Kenway et al., 2015; Sheft et al., 2015; Turgeon et al., 2015; Won et al., 2015]. Detecting frequency changes may play an important role in pitch-based tasks that are typically challenging for CI users, including melody contour identification, talker gender identification, and speech perception in noise [Stickney et al., 2007; Cullington and Zeng, 2011; Gfeller et al., 2012; Zeng et al., 2014].

Understanding the neural substrates of the variability in CI speech perception outcomes is critical for future efforts to improve speech outcomes by reducing the variability; it will also lead to the identification of promising neural responses as diagnostic tools to objectively assess potential benefits (or problems) in difficult-to-test patients. Much evidence has shown that cortical function is more closely related to CI outcomes than the neural responses from a lower level of the auditory system [e.g., the response from the auditory nerve, brainstem, or subcortical levels, Firszt et al., 2002; Lazard et al., 2012; Anderson et al., 2017]. Therefore, there is an enormous need to examine how CI users' auditory brain processes frequency changes in order to understand the large variability in CI speech outcomes.

The cortical auditory evoked potentials (CAEPs) have been widely used to evaluate the neural detection of sound in the central auditory system [Kelly et al., 2005]. CAEPs can be recorded in a passive listening condition that does not require the participant's attention or voluntary responses and thus can serve as a suitable tool for difficult-to-test subjects [Sharma and Dorman, 2006; Small and Werker, 2012]. The CAEPs can be elicited by stimulus onset (onset CAEP), stimulus offset (offset CAEP), and an acoustic change embedded in an ongoing stimulus (acoustic change complex, ACC), with similar waveform morphologies.

The ACC has raised strong interests among researchers in recent years as an objective tool for assessing auditory discrimination capability. The ACC can be elicited by a perceivable change in acoustic features including frequency, intensity, and duration, in ongoing stimuli. The ACC has been studied in non-CI users [Harris et al., 2007; Dimitrijevic et al., 2008; He et al., 2015]. Data in non-CI users have shown that the ACC threshold (the minimum magnitude of acoustic changes required to evoke the ACC) is in agreement with the behavioral auditory discrimination threshold and the ACC amplitude is related to the salience of the perceived acoustic change [He et al., 2012; Liang et al., 2016].

The ACC differs from and has advantages over the mismatch negativity (MMN), another type of auditory evoked response reflecting auditory discrimination [Tremblay et al., 1997; Pakarinen et al., 2007; Sandmann et al., 2010; Itoh et al., 2012]. First, in the stimulus paradigm for the ACC, every trial of the stimuli contributes to the ACC response. In MMN recordings, a large number of standard stimuli is required to embed a sufficient number of deviant stimuli. Thus, the recording time for the ACC is much shorter than that for the MMN. Second, the ACC has a much larger amplitude (higher signal-to-noise ratio) compared to the MMN, which enables the accurate identification of ACC peaks for latency and amplitude calculation [Martin and Boothroyd, 1999]. Third, the MMN is an outcome of waveform subtraction between the response to the deviant stimuli and the response to the standard stimuli, while the ACC is a response directly collected from the participant.

From the several existing ACC studies involving CI users, the findings have not allowed us to draw a conclusion on the correlation between the ACC and the behavioral performance of frequency change detection. For example, one study using synthetic vowels, with a change of the second formant, reported an agreement between the ACC and behavioral discrimination capability based on data from one CI user [Martin, 2007]; another study reported different waveform patterns in the ACC evoked by speech syllables between good and poor performers [Friesen and Tremblay, 2006]. Note that different types of acoustic changes have been used in previous ACC studies [e.g., electrical stimuli delivered via the CI electrode or speech stimuli delivered in the sound field, Friesen and Tremblay, 2006; Martin, 2007; Brown et al., 2008; Kim et al., 2009; Hoppe et al., 2010; Brown et al., 2015; Scheperle and Abbas, 2015]. These stimuli contain changes of sound in multiple dimensions. For instance, the electric stimuli in electrical ACC studies [Brown et

Table 1. Cochlear implant (CI) users' demographics

CI user	Gender	Age, years	Ear	Duration of severe-to-profound deafness, years	Duration of CI use, years	Etiology
SCI44	M	54	L	6	3.00	noise induced
SCI44	M	54	R	3	0.25	noise induced
SCI45	F	48	L	43	6.00	unknown
SCI45	F	48	R	43	6.00	unknown
SCI46	F	64	L	38	1.50	virus infection
SCI47	F	66	R	36	2.50	cochlear otosclerosis
SCI48	F	43	R	41	4.00	meningitis
SCI49	M	62	L	3	4.08	noise exposure
SCI49	M	62	R	3	4.33	presbycusis
SCI50	F	75	R	4	3.00	unknown
SCI50	F	75	L	4	1.58	unknown
SCI51	M	75	R	20	0.92	noise induced
SCI52	F	62	R	10	1.83	genetic
SCI52	F	62	L	10	0.42	genetic
SCI53	M	73	L	12	0.58	presbycusis
SCI54	F	75	R	20	3.42	virus infection
SCI55	F	75	R	41	20.17	congenital
SCI55	F	63	L	41	6.17	congenital

al., 2008; Hoppe et al., 2010] were electrical pulse trains with the first half of each stimulus from one electrode and the other half from a second electrode. Such a stimulus contains the change in stimulation electrode and the change in perceived frequency due to the change in the stimulating electrodes; the speech stimuli in acoustic ACC studies [e.g., vowel /ui/ that has a frequency change in the 2nd formant, Martin, 2007; Brown et al., 2015] contain the changes in spectral envelope, amplitude, and periodicity at the transition in consonant-vowel syllables. Therefore, it is unclear which components of the acoustic change have contributed to the ACCs. It is necessary to further examine the ACC elicited by the change in only frequency dimension and its correlation with the behavioral performance of frequency change detection in CI users.

In this study, we examined how auditory cortex process frequency changes in CI users and how the neural measures correlate with the frequency change detection capability using pure tones containing only frequency changes. The use of pure tones as opposed to complex tones is due to the following reason: a pure tone stimulates one electrode or two electrodes, while a complex tone stimulates several electrodes. Therefore, a pure tone allows for a better detection of frequency changes based on a single excitation site than a complex tone does. Previous studies showed that the performance of melody rec-

ognition with a pure tone is significantly better than with complex tones, suggesting that current CIs cannot code the complex pitch [Singh et al., 2009]. Our primary goals were: (1) to characterize the ACC features in CI users and (2) to determine whether ACC measures can be used to predict the frequency change detection threshold in CI users. Additionally, we explored the correlation between the ACC measures and the speech perception performance collected clinically.

Materials and Methods

Subjects

Twelve postlingually deafened CI users (7 females and 5 males; 43–75 years old, with the mean age of 63 years) participated in this study. All participants were right-handed, native English speakers without any neurological disorder history. The CI users wore the devices from Cochlear (Sydney, Australia), and they all had severe-to-profound sensorineural hearing loss bilaterally prior to implantation. In the 12 CI subjects, 7 had bilateral CIs, 4 had bimodal devices (a CI in one ear and a hearing aid in the other), and one had a unilateral CI. All subjects have been using the CI for their daily communication. Each CI ear was tested individually. One bilateral CI user was tested with only one CI ear because the other CI ear was not able to detect the maximum magnitude of frequency changes in the psychoacoustic test. Therefore, a total of 18 CI ears underwent both psychoacoustic and electroencephalographic (EEG) tests. Individual CI subject's demographic information is provided in Table 1. All participants gave informed written con-

sent prior to their participation. This study was approved by the Institutional Review Board of the University of Cincinnati. The authors did not have any conflicts of interest.

Stimuli

Stimuli for Psychoacoustic Tests

A tone of 1 s duration at a base frequency of 160 Hz was used as the standard tone. The target tones were the same as the standard tone except that the target tones contained upward frequency changes at 500 ms after the tone onset, with the magnitude of frequency change varying from 0.05 to 65%. These tones were generated using Audacity 1.2.5 (<http://audacity.sourceforge.net>) at a sample rate of 44.1 kHz. To avoid an abrupt onset and offset of the 1-s tones, the amplitude was reduced to zero over 10 ms. These tones contained upward frequency changes at 500 ms after the tone onset. The frequency change occurred for an integer number of cycles of the base frequency and the change occurred at 0 phase (zero crossing). Therefore, the onset cue of the frequency change was removed, and it did not produce audible transients [Dimitrijevic et al., 2008]. The amplitudes of all stimuli were normalized. The stimuli were calibrated using a Brüel & Kjær (Investigator 2260) sound level meter set on linear frequency and slow time weighting with a 2-cm³ coupler.

Stimuli for EEG Recording

Tones of 1 s duration at base frequencies of 160 Hz and 1,200 Hz that contained 3 types of frequency change (0, 5, and 50%) were used to evoke the event-related-potentials (ERPs). We used the above two different base frequencies because 160 Hz is in the frequency range of the fundamental frequency (F0), while 1,200 Hz is in the frequency range of the 2nd formant of vowels. The F0 and 2nd formant frequency are important spectral cues in speech processing [Blamey et al., 1987; Stickney et al., 2007]. Examining the ACC at these two base frequencies would help understand how the auditory cortex processes the frequency change near the F0 and the 2nd formant of vowels. A total of 6 stimuli (3 types of frequency changes $\times$ 2 base frequencies) were used for the EEG recording. The interstimulus interval was 0.8 s.

Procedure

All participants underwent a psychoacoustic test of frequency change detection and EEG recording. Stimuli were presented in the sound field via a single loudspeaker placed at ear level, 50 cm in front of the participant. The stimuli were presented at an intensity corresponding to the loudness level 7 (most comfortable level) on a 0- to 10-point (inaudible to too loud) numerical scale [Hoppe et al., 2001] to the tested CI ear. This stimulus presentation approach has been widely used in CI users. The device (either the CI or hearing aid) in the nontest ear was tuned off and the nontest ear was blocked with an earplug.

Psychoacoustic Test of Frequency Change Detection

An adaptive, 2-alternative forced-choice procedure with an up-down stepping rule using APEX software [Francart et al., 2008] was employed to measure the minimum frequency change the participant was able to detect. In each trial, a target stimulus and a standard stimulus were included. The standard stimulus was the tone without frequency change, and the target stimulus was the tone with a frequency change. The order of standard and target stimulus was randomized and the interval between the stimuli in

a trial was 0.5 s. The initial frequency change between the standard and target was 5% from 10 to 65%, 0.5% from 0.5 to 10%, and 0.05% from 0.05 to 0.5%. The participant was instructed to choose the target signal by pressing the button on the computer screen and was given a visual feedback regarding the response. Each run generated a total of 5 reversals. The asymptotic amount of frequency change (the average of the last 3 trials) was used as the frequency change detection threshold (FCDT).

EEG Recording

Participants wore a 40-channel Neuroscan quick-cap (NuAmps, Compumedics Neuroscan Inc., Charlotte, NC, USA) for the EEG recording. The cap was placed according to the International 10-20 system. Electro-ocular activity was monitored so that eye movement artifacts could be identified and rejected during the offline analysis. Electrodes located directly over or closely surrounding the implant transmission coil were not used. Electrode impedances for the remaining electrodes were kept at or below 5 k Ω during EEG recordings using the SCAN software (version 4.3, Compumedics Neuroscan Inc., Charlotte, NC, USA) with a band-pass filter setting from 0.1 to 100 Hz and an analog-to-digital converter sampling rate of 1,000 Hz.

CI users were presented with 400 trials for each type of the stimuli. Previous study showed that 400 trials were adequate for obtaining an ideal signal-to-noise ratio in the recording of cortical evoked potentials in CI users [Han et al., 2016]. During testing, participants were instructed to avoid excessive eye and body movements. Participants read self-selected magazines to keep alert and were asked to ignore the acoustic stimuli. The total recording time was approximately 1.4 h for each CI ear.

EEG Data Processing

Electrophysiological data were initially processed using Scan software (Compumedics Neuroscan Inc., Charlotte, NC, USA). Continuous EEG data were digitally filtered using a band-pass filter (0.1–30 Hz). Then the data were segmented into epochs over a window of 1,100 ms (including a 100-ms prestimulus duration). Following segmentation, the baseline was corrected by subtracting the mean amplitude in the 100-ms prestimulus time window. Data were then imported into the EEGLAB toolbox [Delorme and Makeig, 2004] in MATLAB (Mathworks Inc.) for further analysis. The data were re-referenced to the common average reference. Bad channels near the CI coil that were not injected with recording gel (up to 3 channels for unilateral CI users and 6 channels for bilateral CI users) were removed and interpolated. Visual inspection of the epochs which contained nonstereotyped artifacts were discarded. There were at least 200 epochs left for each participant.

Independent component analysis [Delorme and Makeig, 2004] was performed for the identification and removal of stereotyped artifacts including CI artifacts. The success of artifact removal, using the independent component analysis method, is demonstrated in Figure 1 and detailed information can be found in the EEGLAB manual and our previous published papers [Delorme and Makeig, 2004; Zhang et al., 2009]. After the independent components related to artifacts were linearly subtracted from the EEG data, the remaining independent components were used to reconstruct the data set. Then data epochs were averaged separately for each of the 6 types of stimuli (2 base frequencies $\times$ 3 types of frequency changes) in each participant.

Fig. 1. The example of event-related potential waveforms at Cz evoked by a tone with 0% (black line), 5% (green line), and 50% (red line) frequency change. The waveforms before artifact removal (**a**) and after artifact removal (**b**) are displayed.

We performed further waveform analysis on the responses from the electrode Cz where the response amplitudes were the largest. The presence of the onset CAEP and ACC response was determined based on criteria: (i) an expected wave morphology within the expected time window for the specific response based on mutual agreement between two researchers [He et al., 2015] and (ii) a visual difference in the waveforms between the frequency change conditions versus no change condition when evaluating the ACC. Then, the wave peaks of the onset CAEP and ACC response were identified. In the onset CAEP, the response peaks were labeled using standard nomenclature of N1 and P2. The ACC response peaks were labeled using N1' and P2' (Fig. 1). For each averaged response, the N1 was identified as the maximum negative peak in the latency range of 100–200 ms, and P2 was identified as the maximum positive peak in 150–300 ms after stimulus onset [Näätänen and Picton, 1987; Budd et al., 1998]. The N1' and P2' peaks of the ACC were identified in a latency range of 600–700 ms and 650–800 ms, respectively, after the stimulus onset (or 100–200 and 150–300 ms after the starting point of the frequency change, respectively).

The measures used for statistical analysis include: N1 and P2 peak latencies (the time interval between the peaks and the stimulus onset), N1-P2 peak-to-peak amplitude (the voltage difference between N1 and P2) for the onset CAEP and the corresponding measures (N1' and P2' peak latencies and N1'-P2' amplitude) for the ACC responses.

Statistical Analysis

For behavioral testing, the dependent variable is the FCDT. For EEG testing, the dependent variables include: (1) the measures in the onset CAEP (N1 latency, P2 latency, and N1-P2 amplitude); (2) the measures in the ACC (N1' latency, P2' latency, and N1'-P2' amplitude). The mean values and standard errors of amplitude and latency measures for each type of stimuli were obtained. Repeated

measures analysis of variance (ANOVA) procedures were performed to examine the difference between the ACC and onset CAEP for different base frequencies. The Pearson product-moment correlation analysis was performed to examine correlations between FCDT and the ACC measures as well as the correlation between speech perception performance and the ACC measures. Statistical analysis was performed with SPSS 13.0. A *p* value of 0.05 was used as the significance level for all analyses.

Results

Electrophysiology Results

Figure 2 shows the individual ERPs evoked by tones containing no change (solid line), 5% change (dashed line), and 50% change (dotted line) in 3 CI users whose FCDT was good (1.17%), moderate (2.17%), and poor (9.33%), respectively. There were two types of responses in the ERP waveforms. One is onset CAEP, characterized as the N1-P2 complex with peak latencies of approximately 100–300 ms after the onset of stimuli; the other is the ACC, labeled as N1'-P2' complex, with the latency at approximately 600–800 ms after stimulus onset or 100–300 ms after the occurrence of the frequency change. As seen in this figure, the ACC is smaller for moderate and poor performers than for the good performer. Compared to the ACC, the onset CAEP does not appear to indicate the FCDT of the participant.

Fig. 2. Individual event-related potentials evoked by 160-Hz tones containing no change (solid line), 5% change (dashed line), and 50% change (dotted line) in 3 CI users whose FCDT was good (1.17%; **a**), moderate (2.17%; **b**), and poor (9.33%; **c**), respectively.

Figure 3 shows the grand mean of the ERPs evoked by tones of 160 Hz (left plots) and 1,200 Hz (right plots) containing no change (solid line), 5% change (dashed line), and 50% change (dotted line) in CI users. This figure shows that, while the onset CAEPs evoked by the tones without and with frequency changes are similar, the ACC only exists when there is a frequency change and the ACC amplitude is larger for the 50% frequency change than for the 5% change. The trend is the same for both 160 Hz and 1,200 Hz base frequency, although the same percentage of frequency change in the latter evoked bigger ACCs.

The ACC exists in 61–78% of CI ears for the 5% change depending on the base frequency and 100% for the 50% change. Table 2 shows the means and standard deviations

of the peak amplitudes and latencies in the onset CAEP and the ACC evoked by tones with the 50% frequency change. Note that the ACC N1' and P2' latencies were adjusted by subtracting the prefrequency change duration of 500 ms for comparison purposes. It can be seen that the ACC peak latencies are longer than those of the onset CAEP peaks.

A series of 2-way repeated ANOVAs were conducted to examine the effects of base frequency (within-subject factors) and the response type (onset CAEP vs. ACC) for different measures (peak latency and amplitude). The statistical results showed that there was a difference between 160 and 1,200 Hz ($F(1, 71) = 17.9, p < 0.01$) as well as a difference between onset CAEP and ACC ($F(1, 71) =$

Fig. 3. Group average waveforms in CI users evoked by tones (160 Hz in **a** and 1,200 Hz in **b**) with 0% (solid line), 5% (dash line), and 50% change (dotted line).

Table 2. Latencies and amplitudes (means $\pm$ SD) of the responses elicited by tones with 50% change

Tone	Onset CAEP			ACC response		
	latency, ms		amplitude, μ V	latency, ms		amplitude, μ V
	N1	P2		N1'	P2'	
160 Hz	138 (18.9)	233.8 (20.2)	1.8 (0.8)	157.2 (19.2)	250.8 (24.5)	1.62 (1.0)
1,200 Hz	129.6 (15.3)	227.4 (35.1)	2.0 (1.0)	135.4 (21.4)	245.4 (22.4)	1.9 (1.1)

11.21, $p < 0.01$) for the N1 (N1') peak latency. There was no interaction between base frequency and response type ($F(1, 71) = 2.45$, $p > 0.05$). The results showed that the N1 (N1') latency was significantly longer for 160 Hz than for 1,200 Hz and the ACC N1' latency was significantly greater than the onset CAEP N1 latency; there was a difference between onset CAEP and ACC ($F(1, 71) = 10.82$, $p < 0.01$) for the P2 (P2') peak latency. There was no significant effect of base frequency on the P2 (P2') peak latency ($F(1, 71) = 1.75$, $p > 0.05$) and no interaction between base frequency and response type ($F(1, 71) = 0.004$, $p > 0.05$). The results suggested that ACC P2' latency was significantly longer than the onset CAEP P2 latency. There was no effect of base frequency ($F(1, 71) = 2.03$, $p > 0.05$) and response type ($F(1, 71) = 1.05$, $p > 0.05$) as well as their interaction ($F(1, 71) = 0.07$, $p > 0.05$) on the N1P2 (N1'P2')

amplitude. In summary, the peak latencies of the ACC were significantly longer than those of the onset CAEP. The N1 (N1') latency was significantly longer for 160 Hz than for 1,200 Hz.

Correlations between ACC Measures and Psychoacoustic FCDT

The CI group has a mean FCDT of 3.79%. The variability in the CI group is substantial, ranging from 0.67 to 9.66. The ACC responses were correlated with behavioral performance of frequency change detection, evidenced by the results of the following analyses. The first analysis was based on the ACC data evoked by 5% change. The ACCs were missing in some CI subjects when evoked by 5% frequency changes. Therefore, the CI users were separated into two subgroups: CI users without the ACC and

Fig. 4. Mean FCDTs in 2 subgroups of CI ears (CI ears without ACCs and CI ears with present ACC evoked by the 5% frequency change). Error bars indicate the standard error.

CI users with the ACC for the 5% change. Figure 4 shows mean values of the FCDT in the two subgroups. The mean FCDT was 5.34 and 3.09%, respectively, in CI users without the ACC and CI users with present ACCs.

A *t* test was performed to determine whether there was a significant difference in the FCDT between the CI subgroup with present ACC and the CI subgroup (mean = 3.09%, SD = 1.86) without ACC for the 5% change (mean = 5.34%, SD = 3.27). The results showed that the difference between these two subgroups of CI users did not reach statistical significance ($t = -1.87$, $p = 0.08$). The fact that the CI subgroup with present ACCs had an FCDT smaller than 5% and the CI subgroup with absent ACCs had an FCDT greater than 5% suggested that ACC measures for the 5% change were in agreement with behavioral measures.

The second analysis was based on the ACC data evoked by the 50% change. Pearson's product moment correlation analysis was used to evaluate the correlation between FCDTs and the ACC measures for the 50% frequency change. Figure 5 shows that there was a significant correlation between N1' latency and FCDTs ($R^2 = 0.23$, $p < 0.05$). The significant positive correlation between N1' latency and FCDT ($p < 0.05$) seems to be driven by the two subjects who have FCDTs around 9–10%. Future studies with a larger sample size will help determine whether this correlation exists. Although there was a trend that CI users with smaller N1'-P2' amplitudes and longer P2' latency were more likely to have a larger FCDT (poor per-

Fig. 5. The FCDT as the function of ACC N1' latency in CI users. The solid line shows linear regression fit to the data. The stimulus used to evoke the ACC was a 160-Hz tone containing 50% frequency change.

formance), this correlation was not statistically significant (not shown).

ACC Measures versus Speech Perception Outcomes in CI Users

The speech perception data collected by an audiologist, one of the co-authors, at the latest clinical follow-up (within 6 months from our experiment) in the Department of Otolaryngology, Head and Neck Surgery at the University of Cincinnati were used to examine the correlation between ACC and speech perception performance. Although both consonant-nucleus-consonant (CNC) monosyllabic word and AzBio sentences (presented at the most comfortable level) were used for clinical assessment, the CNC score was found to be significantly correlated with the ACC N1' latency. Figure 6 shows the correlation between ACC N1' latency and the CNC score ($R^2 = 0.36$, $p < 0.05$). The CNC scores from 15 individual CI ears were included in this figure. The CNC scores from 3 other CI ears were either unavailable or not meeting the criterion for the clinical testing time.

Discussion

This study used tones containing frequency changes for psychoacoustic tests of frequency change detection and to evoke ACC responses in postlingually deafened CI users. The ACC shows longer peak latencies compared to

Fig. 6. ACC N1' latency as the function of CNC score in CI users. The solid line shows linear regression fit to the data. The stimulus used to evoke the ACC was a 160-Hz tone containing 50% frequency change.

Fig. 7. The FCDT as the function of the duration of deafness in CI users. The solid line shows linear regression fit to the data.

the onset CAEP. There is an effect of the base frequency in the ACC N1' latency measurement. The ACC is in agreement with the FCDT results and is correlated with the CNC score.

Frequency Discrimination in Postlingual CI Users

Numerous studies have reported that postlingual CI users have significantly poorer frequency discrimination ability than NH listeners [Gfeller et al., 2007; Kang et al., 2009; Limb and Roy, 2014; Turgeon et al., 2015]. Several factors have been reported to negatively affect the ability to discriminate frequencies in CI users. First, the auditory system of CI users typically suffers from pervasive neural degeneration due to long-term deafness before the implantation. This inadequate peripheral input to the auditory cortex results in weaker cortical responses to sound, which in turn leads to poorer frequency discrimination capability compared to their NH peers. Second, the spectral cues of the sound transmitted by CI devices are degraded. In CI hearing, the perception of frequency change is achieved by the change of the electrical stimulation rate and the change of the location of the stimulated electrodes. The poor spectral resolution is the result of the small number of electrodes (6–22), the interference between adjacent electrodes when several electrodes are activated concurrently, and a possible mismatch between the acoustic input and electrode location in the cochlea [Oxenham et al., 2004; Fu and Nogaki, 2005]. Third, the auditory cortex reorganization (intra- and cross-modal reorganization as the result of long-term deafness) may

be so resistant to change that it cannot be reversed in some CI users even after years of CI use [Hung et al., 2010; Sandmann et al., 2012; also see review by Anderson et al., 2017].

In this study, the results support the poor capability of frequency discrimination in CI users. The FCDT of CI users was 3.79%, with a range from 0.67 to 9.66% in the CI ears. An ad hoc analysis of the correlation between the FCDT and the duration of deafness was conducted. Figure 7 shows that the FCDT is significantly correlated with the duration of deafness, suggesting that the degree of deafness-related neural deficit is a significant factor for the variance in the FCDT.

These FCDT results are consistent with those reported in previous studies [Gfeller et al., 2007; Kang et al., 2009; Limb and Roy, 2014; Kenway et al., 2015; Turgeon et al., 2015]. Goldsworthy [2015] reported that CI users' pitch discrimination thresholds for pure tones (0.5, 1, and 2 kHz) ranged between 1.5 and 9.9%, while the thresholds for complex tones (with fundamental frequencies at 110, 220, 440 Hz) ranged between 2.6 and 28.5%. Gfeller et al. [2002] reported that NH listeners' mean discrimination threshold for complex tones (F0 between 73 and 553 Hz) was 1.12 semitones (range of 1–2 semitones), while CI users had a mean threshold of 7.56 semitones (range of 1–24 semitones). Note that the exact values of frequency discrimination may vary among these studies, possibly due to: (1) the various degrees of heterogeneity in demographic variables of the CI subjects recruited, (2) the difference in the psychoacoustic tasks used (pitch discrimi-

nation, pitch ranking, frequency change detection etc.), (3) the difference in the stimulus type used (pure tone vs. complex tone, acoustic vs. electric stimuli), and (4) the difference in the base frequency.

Previous evidence showed that CI users with poorer auditory frequency discrimination also have poorer speech recognition compared to CI users with better frequency discrimination ability [Kenway et al., 2015; Turgeon et al., 2015]. The capability of spectral ripple discrimination was more significantly correlated with the identification of formant transitions and word recognition than the capability of temporal discrimination [Winn et al., 2016]. Frequency perception deficiency is a major reason causing poor performance in speech perception in CI users [Finley et al., 2008; Zeng et al., 2014; Kenway et al., 2015].

ACC Is an Objective Tool for Assessing Frequency Change Detection Capability and Speech Perception Score in CI Users

In this study, the correlation between the ACC measures and FCDT is reflected in the following observations. First, the subgroup of CI users with missing ACCs evoked by the 5% change exhibited FCDTs greater than 5% while the subgroup of CI users with present ACCs had an FCDT of less than 5%. Second, the ACC is larger with a more salient frequency change (50 vs. 5% change). Third, there was a significant positive correlation between ACC N1' latency and FCDT ($p < 0.05$). There was also a trend that other ACC components are correlated with the FCDT: individuals with lower FCDTs (better performance) had a shorter P2' latency and a bigger N1'P2 amplitude (not shown). These correlations were not statistically significant, however, possibly due to the small sample size and large intersubject variability.

The correlation between behavioral measured auditory discrimination ability and ACC measures has been reported in several ACC studies. Hoppe et al. [2010] reported that the ACC N1' latency of the electrically evoked ACC response was significantly correlated with the perceptual difference between two electrodes. The findings in the current study further supported that ACC measures can serve as an objective indicator of frequency change detection capacity in CI users.

The correlation between ACC response and speech performance is uncertain with the current CI studies. Friesen and Tremblay [2006] reported the CI users with good syllable identification scores showed a different ACC evoked by speech token change pattern compared to those with poor scores. Scheperle and Abbas [2015]

reported that spectral ACC (evoked by ripple noise stimuli presented directly via the CI processor) was significantly correlated with speech perception in noise. Some other investigators reported no correlation between the ACC response and speech performance [Brown et al., 2015]. The above discrepancy reported in previous studies may be related to different stimuli used (electric vs. acoustic stimuli). In this study, the stimuli for both psychoacoustic tests and ACC recordings were pure tones containing frequency changes, with the onset amplitude cues of the frequency change removed [Dimitrijevic et al., 2008]. The ACC is evoked by the change of frequency only. The finding that the ACC is correlated with both behaviorally measured frequency change detection ability and CNC scores indicates that the ACC can be used as an objective tool to predict CI outcomes.

Previous ACC studies have suggested that the ACC can be used as a promising tool to objectively assess auditory discrimination for several reasons: (1) the EEG recording is noninvasive and the ACC is a preattentive response, which made it suitable for the hard-to-detect population who cannot reliably perform behavioral tasks [He et al., 2015], (2) the ACC's feature change can reflect the change of stimulus properties [Friesen and Tremblay, 2006], and (3) the ACC shows excellent test-retest reliability [Tremblay et al., 2003].

Cortical Responses to Frequency Changes Differ between Low and High Base Frequencies

The current study showed that the ACC response exhibited longer latencies for the 160-Hz base frequency than for the 1,200-Hz one. In acoustic hearing, it takes a longer time for low-frequency sounds to be transmitted in the peripheral auditory system (e.g., a longer traveling wave time along the basilar membrane for low frequencies). The time delay for low-frequency sounds also exists at the cortical processing stage, where the subcortical temporal codes need to be transformed into central rate codes [Dimitrijevic et al., 2008].

In the current study, the traveling wave time difference does not exist since the CI bypasses the damaged cochlea and directly stimulates the auditory nerve fibers, yet the response time for processing frequency changes at the low base frequency is longer than that at the high base frequency. We speculated that these neural timing differences between low and high frequencies were due to the difference in the temporal window of integration [Dimitrijevic et al., 2008]. The low-frequency sound has a longer duration for each cycle. To get a necessary number of cycles for frequency change detection, the integra-

tion window needs to be longer for low frequencies than for high frequencies. Thus, the ACC displayed longer latencies for the 160-Hz than for the 1,200-Hz base frequency.

An alternative explanation for the latency difference in the ACC evoked by frequency changes at 160 and 1,200 Hz may be related to the different cues perceived by the participants at these two base frequencies. At the CI speech-processing stage, the acoustic signal is separated based on its frequency components and then filtered through a number of contiguous band-pass filters before further processing. In Cochlear devices, the first cutoff frequency band is higher than 160 Hz, and therefore the 160 Hz is located at the filter slope of the first band. The detection of a frequency change from 160 Hz relies on the different intensities in the CI output and thus temporal rate cues (different intensities result in different neural activation patterns and neural timing [Eggermont, 2001]). On the other hand, the 1,200 Hz is assigned to a middle electrode, and thus the frequency change from 1,200 Hz would be perceived mainly based on the electrode place cue [Pretorius and Hanekom, 2008]. It is possible that the cue for frequency change detection at 1,200 Hz is more obvious than the cue at 160 Hz, resulting in a larger ACC amplitude and a shorter peak latency (Fig. 2; Table 2).

Limitations and Future Studies

One limitation of this study is that the participants in this study have heterogeneous demographic features. Specifically, bilateral, bimodal, and unilateral CI users were included. Future studies will separately recruit patients of each category. Moreover, because the position of the reference frequency relative to the frequency response of filters in the CI users' clinical map would affect the

frequency discrimination threshold [Pretorius and Hanekom, 2008], future study will explore which frequency position will result in the best behavioral-neurophysiological relationships.

Conclusion

This study found that the features of the onset CAEP and the ACC have differences, indicating different neural substrates for coding acoustic onset and frequency changes. The ACC measures are correlated with the behavioral frequency change detection in CI users. The ACC is also related to the clinically collected CNC score of the CI users. The ACC can be used as an objective tool for assessing frequency discrimination and predicting speech perception performance.

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