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Cortical Encoding of Pitch Contour Changes in Cochlear Implant Users: A Mismatch Negativity Study

Fawen Zhang[*], **Chelsea Benson**[*], and **Qian-Jie Fu**[†]

[*]Department of Communication Sciences and Disorders, University of Cincinnati, Ohio, USA

[†]House Ear Institute, Los Angeles, CA, USA

Abstract

A better understanding of melodic pitch perception in cochlear implants (CIs) may guide signal processing and/or rehabilitation techniques to improve CI patients' music perception and appreciation. In this study, the mismatch negativity (MMN) in response to infrequent changes in five-tone pitch contours was obtained in CI users and normal hearing (NH) listeners. Melodic contour identification (MCI) was also measured. Results showed that MCI performance was poorer in CI subjects than in NH subjects; The MMNs were missing in all CI subjects for the 1-semitone contours. The MMNs with the 5-semitone contours were observed in a smaller proportion of CI subjects than in NH subjects. Results suggest that encoding of pitch contour changes in CI users appears to be degraded, most likely due to the limited pitch cues provided by the CI and deafness-related compromise of brain substrates.

Keywords

cochlear implant; music perception; pitch contour; mismatch negativity; electrophysiology

Introduction

Cochlear implants (CIs) are biomedical electronic devices that restore hearing to profoundly deaf people. Many CI users are capable of good speech understanding in quiet (Wilson & Dorman, 2008), but most have great difficulty with challenging listening tasks such as speech understanding in noise and music perception. While CI users' musical rhythm perception is comparable to that of normal-hearing (NH) listeners (Kong et al., 2004), perception of musical pitch and timbre is much poorer for CI users than for NH listeners (Gfeller & Lansing, 1991; Gfeller et al., 1997, 2002a; Kong et al., 2004; McDermott, 2004; Galvin et al., 2007).

CI users' music perception is most likely limited by several factors, including the relatively poor spectro-temporal representation with the CI device, the health of the auditory periphery, and central processing deficits associated with long term deafness. Compared to speech perception in quiet, melody perception requires many more spectral channels, especially when other cues such as rhythm or lyrics are unavailable (Friesen et al., 2001; Kong et al., 2004; Shannon et al., 2004). Current CI signal processing also does not preserve spectro-temporal fine structure cues, which while not necessary for speech, are necessary for complex pitch perception (Smith et al., 2002). Even with these CI technology limitations that adversely affect all CI users, there is considerable variability from one CI user to the

Corresponding author: Fawen Zhang, PhD., Department of Communication Sciences and Disorders, University of Cincinnati, Cincinnati, Ohio, USA, Phone: 513-558-8513, Fax: 513-558-8500, Fawen.Zhang@uc.edu.

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next. For instance, Gfeller et al. (2002) reported that the performance in melody recognition in 49 CI participants ranged from 0-43.75% correct. Therefore, the variability of music perception in CI users may also be related to patient-related factors such as the distribution of healthy neurons in the cochlea, the proximity of the implanted electrodes to these elements, etc. This variability may also be due to CI patients' musical experience before and after implantation (Gfeller et al., 2000), or to central processing deficits associated with long-term deafness (Leake et al., 1995; Giraud et al., 2000; Pisoni, 2000; Shibata et al., 2011).

While better CI technology may improve the representation of music, auditory training may allow CI patients to better use the information provided by their device. Auditory training has been shown to improve CI users' timbre perception (Gfeller et al., 2002b) and melodic contour identification (Galvin et al., 2007). Music training may improve attention and working memory for processing relatively small pitch differences, cues that are also important for speech understanding in noise, speech prosody perception, and syntax processing (Jentschke & Koelsch, 2009; Parbery-Clark et al., 2009, 2011). Better understanding of the neural mechanisms of pitch contour processing in CI users would guide both future CI technology as well as rehabilitation techniques. As such, it is important to differentiate the limitation of cues provided by the CI, which is related to the device and the neural interface, and the limitation of the perception of these cues, which is related to experience and cortical processing.

One approach toward understanding differences in peripheral and central processing of melodic pitch would be to use neural imaging combined with behavioral measures. Noninvasive electroencephalographic (EEG) techniques are often used to reflect brain responses of CI users (Ponton, et al., 1999; Groenen, et al., 2001; Purdy, et al., 2001). Compared to other techniques, e.g., magnetoencephalograph (MEG), functional magnetic resonance imaging (fMRI), and positron emission tomography (PET), EEG directly records the electrical responses of neurons elicited by stimuli with a high temporal resolution. The noninvasive nature and the compatibility with the CI device make EEG the most suitable tool with which to examine neural responses in CI users (Debener et al., 2008).

Using EEG techniques, the auditory evoked potentials (AEPs), a series of brain responses representing the summation of synchronized activities from many neurons, can be obtained from electrodes placed at the scalp. Among various AEPs, the mismatch negativity (MMN) is evoked by the infrequent (deviant) stimuli embedded in a series of frequent (standard) stimuli. The MMN can be identified in the difference waveform, which is typically obtained by subtracting the late latency evoked potential (LAEP) elicited by standard stimuli from the LAEP evoked by deviant stimuli. In NH listeners, the MMN occurs in a latency range of approximately 100-250 ms after any discriminable change in the deviants relative to the standard stimuli (Kraus et al., 1995; Ponton & Don, 1995). The MMN does not require subjects' attention and is thought to reflect the automatic (pre-attentive) detection of the sound change in the auditory cortex (Giard et al., 1990; Näätänen, 2010). The MMN has been used in NH listeners to examine music processing. For instance, unexpected note in a melodic contour or rhythmic pattern can evoke the MMN (Tervaniemi et al., 2001; Lopez et al., 2003; Fujioka et al., 2005; Vuust et al., 2011).

The MMN may also be used to explore cortical encoding of changes in pitch contour in CI users. The MMN evoked by changes in music stimuli has been studied in only two studies with CI users. Koelsch et al. (2004) found that MMN amplitudes in response to chords played by deviant instruments were smaller in CI users than in NH listeners. Sandmann et al. (2010) studied auditory discrimination and measured the MMN evoked by a set of clarinet sounds with deviant features in different acoustic dimensions, i.e., frequency, intensity, and duration. Results showed poorer behavioral discrimination performance and reduced MMN amplitudes in CI users than in NH listeners. The MMN amplitude was also found to be inversely correlated to the duration of deafness.

The primary goal of this study is to better understand encoding of pitch contour changes in electric and acoustic hearing. As such, behavioral and electrophysiological measures were collected in CI and NH subjects listening to melodic contours. For the behavioral measures, melodic contour identification (MCI) was measured, using stimuli similar to those used in a previous study (Galvin et al., 2007). Because EEG recording using MMN paradigms is time consuming, EEG recordings were obtained for a subset of the melodic contour stimuli used in the behavioral task. The frequency spacing between successive notes in the contours was varied (1 or 5 semitones) to compare responses to small and large pitch differences. We hypothesized that, due to the limited representation by the CI device and functional deficits in the central nervous system, the MMN would be different for CI users and NH listeners, especially when the spacing in the contours was small. We also predicted that MMN results would be consistent with behaviorally measured MCI performance.

Materials and Methods

Participants

Ten CI subjects (3 females and 7 males; age range: 22-81 years) participated in the study. All CI subjects had at least one year of experience with their device. All CI subjects received their CI in their left ear, except for two binaurally implanted CI users (Sci06 and Sci07). All CI subjects were right-handed, and none had any formal music training (e.g., college level instruction or extended instruction in high school). No CI subjects had any neurological or psychological disease except for Sci06, who took Adderall for attention deficit hyperactivity disorder (ADHD). Relevant CI subject demographics are shown in Table 1.

Ten healthy NH subjects (1 male and 9 females; age range: 20-30 years) also participated in the study. NH subjects had audiometric hearing thresholds < 20 dB HL at octave test frequencies from 250 to 8000 Hz, normal type A tympanometry, and normal acoustic reflex thresholds at 0.5, 1, and 2 kHz. None had formal music training. All NH subjects were right-handed. Because most CI subjects were implanted in the left ear, NH subjects were stimulated in the left ear to obtain control EEG data. All subjects provided written consent, and the research protocol was approved by the Institutional Review Board of the University of Cincinnati.

Stimuli

For behavioral MCI testing, stimuli were similar to those used in Galvin et al. (2007). Nine five-note melodic contours (Rising, Falling, Flat, Rising-falling, Falling-rising, Flat-falling, Flat-rising, Falling-flat, Rising-flat, see Figure 1) were generated in relation to a root note, i.e., the lowest frequency in the contour (A4, 440 Hz), according to $f_n=2^{n/12} f_{ref}$, where f_n is the frequency of the target note, n is the number of semitones relative to the root note and f_{ref} is the frequency of the root note. The spacing between each of the successive notes in the contour was 1 or 5 semitones. The note was a sinewave, and the note duration was 250 ms (10 ms rise/fall time) with no interval between successive notes. The total contour/stimulus duration was 1250 ms. Within each stimulus set, each stimulus was presented two times, for a total of 36 stimuli (9 contours × 2 semitone spacings × 2 repeats).

For EEG measurements, a subset of the MCI behavioral test stimuli was used (see Figure 2). The “STANDARD” stimuli were the Rising and Falling contours with 1- or 5-semitone spacing. The “DEVIANT” stimuli were the Rising-flat and Falling-flat contours with 1- or

5-semitone spacing. The frequencies for each note in the contours used for EEG recording are shown in Table 2.

Procedures Behavioral testing—MCI performance was measured as in Galvin et al. (2007). All subjects (CI and NH) were seated in a comfortable chair within an electrically-shielded and sound-treated room; subjects were 1 m away from the computer monitor and 1 m away from the a loudspeaker used to deliver stimuli. Stimuli were presented at a comfortable listening level (starting at 80 dBA and possible adjustment was allowed for individual subjects). CI subjects were tested using their clinical processors and settings, which were not changed during the behavioral and AEP measures.

During testing, a stimulus was randomly selected from the set and presented to the subject, who responded by clicking on one of the nine response boxes shown on the computer screen, labeled (with text and picture) according to the nine target contours. After responding, a new stimulus was presented 3 s later; no feedback was provided. Subjects were told to guess if they were unsure of the answer. Prior to testing, subjects listened to 5 randomly selected contours to familiarize themselves with the stimuli and test procedures. Behavioral testing was administered in a 15-minute session before the EEG recording to avoid learning effects.

EEG recordings—For CI subjects, stimuli were delivered via a single loudspeaker placed at ear level, 50 cm from the left ear at 90° azimuth. For the two binaural CI users, the right CI was turned off. CI subjects were asked to set their microphone sensitivity and volume so that the listening level was 7 on a 0-10 loudness scaling (Valente et al., 1997; Hoppe et al., 2001). Once set, subjects were not allowed to change these settings. For NH subjects, stimuli were presented via insert earphones to the left ear only at a loudness level of 7. The non-test (right) ear was plugged in all CI and NH subjects.

AEPs were recorded using a 40-channel Neuroscan evoked potential system (Compumedics Neuroscan, Inc., Charlotte, NC), with a link-ear as the reference. Elecrooculogram (EOG) was also recorded to monitor eye movements so that eyeblink artifacts can be removed offline. During the AEP recordings, subjects were asked to relax and ignore the auditory stimuli while reading a self-selected book. Periodic breaks were given to keep the subjects alert during the experiment.

AEPs were separately recorded for four oddball paradigms (STANDARD/DEVIANT): 1) Falling/Falling-flat (1 semitone), 2) Falling/Falling-flat (5 semitones), 3) Rising/Rising-flat (1 semitone), and 4) Rising/Rising-flat (5 semitones). In each oddball paradigm, AEPs were collected in two blocks that each contained 340 STANDARD stimuli and 60 DEVIANT stimuli, with a 5 s silent interval between test blocks. In each block, the STANDARD (probability of occurrence = 85%) and DEVIANT (probability of occurrence = 15%) were presented in a pseudo-random order so that the first 20 stimuli were always the STANDARD and that 3-7 STANDARD stimuli were presented before each DEVIANT stimulus. The inter-contour interval was 900 ms. For each subject, 2 repetitions were recorded for each oddball paradigm, with a sampling rate of 1000 Hz for EEG recording.

Data Analysis—Continuous EEG data were first processed using SCAN software (Compumedics Neuroscan, Inc., Charlotte, NC). Specifically, data were digitally filtered (band-pass filter: 0.1 to 30 Hz). Next, the continuous EEG data were epoched using a 0.6-sec analysis window including 0.1 sec before and 0.5 sec after the onset of the 4th tone in the pitch contour (the first tone with pitch change in the deviant contour compared to the standard contour, Tew et al., 2009). Average activity in the pre-stimulus period of 0.1 sec for the 4th tone was used as the baseline activity. Further EEG data analysis was performed using EEGLAB 6.03 (freely available from http://sccn.ucsd.edu/eeglab) running under Matlab 6.3 (The Mathworks, Natick, MA).

After rejecting approximately 5-10% of epochs that contained unique, non-stereotyped artifacts (ie., artifacts due to muscle movements), the remaining data epochs from the repeated recordings were concatenated into single-trial data sets. Next, an average reference for each of the scalp electrodes was computed (Hagemann et al., 2001; Delorme & Makeig, 2004). EEG data were then decomposed using independent component analysis (ICA). The ICA model decomposed the EEG dataset into mutually independent components, including those from artifactual and neutral EEG sources. ICA has been successfully used in removing the CI artifacts, which can mask neural responses, as well as artifacts from other sources such as eye blinks and muscular activity (Gilley et al., 2006; Bakhos et al., 2012). For each individual data set, ICA derived 40 independent components (ICs). ICs representing artifacts were identified and removed by visual inspection of IC properties including the waveform, 2-D voltage map, and the spectrum (Gilley et al., 2006; Debener et al., 2008). Detailed ICA procedures were provided in our previous papers (Zhang et al., 2009; Zhang et al., 2010). After removing artifacts, the remaining components were then constructed to form the final EEG dataset.

The averaged waveforms in response to the STANDARD and DEVIANT stimuli were separately derived. The responses from 9 electrodes (F3, Fz, F4, C3, Cz, C4, FC3, FCz, and FC4) were averaged to form one waveform. The reasons why responses from these electrodes were combined were: 1) the later derived MMN is largest in the fronto-central area rather than any other regions of the scalp (Lang et al., 1995; Petermann et al., 2009), and 2) the noise in CI data could be reduced after averaging responses from multiple electrodes. This approach of analyzing MMN data has been used in a previous study with CI users (Roman et al., 2005). Thus, there was one waveform for each type of stimuli (STANDARD and DEVIANT) for each subject.

The STANDARD waveform was subtracted from the DEVIANT waveform to derive the difference waveform, for which the MMN was judged to be present or absent (Roman et al., 2005; Nikjeh et al., 2009). The MMN was judged by the first author and it was defined as a visually identified negativity deflecting from the baseline in the difference waveform between approximately 100 and 350 ms after stimulus presentation (Singh et al., 2004). To further judge the presence of the MMN, a point-by-point t-test of the two averaged waveforms (STANDARD and DEVIANT) was performed over the latency range where the MMN was visually identified. The MMN was regarded to be valid if the two waveforms were significantly different. The measures used to evaluate the MMN included the MMN peak latency and amplitude, and the MMN duration (offset-onset). The MMN onset was identified using the difference waveform and was defined as the point at which the DEVIANT waveform became consistently more negative than the STANDARD waveform within the latency range 50–150 ms. The MMN offset was defined as the point at which the DEVIANT and STANDARD waveforms converged within the latency range 150–350 ms. The MMN duration was the time between MMN onset and offset. The peak of the MMN was defined as the most negative point in the MMN duration.

Behavioral data were analyzed using a mixed design repeated measures analysis of variance (RMANOVA) with factors of subject group (NH vs. CI) and pitch interval (1 vs. 5 semitone spacing). Any significant effects were followed by a post-hoc comparison using Bonferroni t-tests. Independent sample t-tests were performed to examine the difference in MMN measures between the NH and CI subject groups. A p-value of 0.05 was used to indicate statistical significance for all analyses.

Results

Behavioral Performance

Figure 3 shows MCI performance on 1- and 5-semitone tasks for CI and NH subjects. The data for this figure only include results obtained from 10 NH and 9 CI users, because the specific data for 1- and 5-semitone spacings from one CI user (Sci02) could not be retrieved from the computer for some unknown reason. MCI performance was poorer for CI subjects than for NH subjects. For CI subjects, median performance was 33.3% correct (range: 11.1-77.8% correct) with 1-semitone spacing and 72.2% correct (range: 27.8-100% correct) with 5-semitone spacing. For NH subjects, median performance was 88.9% correct (range: 27.8-77.8% correct) with 1-semitone spacing and 91.7% correct (range: 50-100% correct) with 5-semitone spacing. Although the relatively poor performance for CI subjects was not surprising, 4 of the NH subjects performed much more poorly (<65% correct across both semitone conditions) than the other six NH subjects (>90% correct across both semitone conditions). This finding will be discussed in greater detail in the Discussion section. A two-way RM ANOVA was performed on the behavioral data, with semitone spacing (1- vs. 5-semitones) and subject group (CI vs. NH) as factors. Significant effects were found for semitone spacing [$F(1,8)=36.43$, $p<0.05$] and subject group [$F(1,8)=6.85$, $p<0.05$], and there was a significant interaction between factors [$F(1,8)=43.60$, $p<0.05$]. Post-hoc Bonferroni t-tests showed that NH performance was significantly better than CI users performance for the 1-semitone spacing ($t=3.94$, $p<0.05$), but not for the 5-semitone spacing ($t=1.18$, $p>0.05$). Performance with the 5-semitone spacing was significantly better than with the 1-semitone spacing in CI users ($t=8.47$, $p<0.05$) but not in NH users ($t=2.12$, $p>0.05$).

Electrophysiological Data

Most NH listeners exhibited LAEPs with good morphologies and present MMNs for contours with 1- and 5-semitone spacing. No CI subjects exhibited MMNs for contours with 1-semitone spacing, and MMNs were present with the 5-semitone spacing for fewer CI subjects, compared to NH listeners. The number of subjects whose MMN was judged to be present is shown in Table 3.

NH listeners were grouped according to mean performance across the 1- and 5-semitone conditions: 1) good performers (n=6) scored >90% correct and 2) poor performers (n=4) scored <65% correct. Figure 4 shows the grand mean LAEP waveforms (DEVIANT and STANDARD) and the difference waveform for the 4 test conditions in for good (n=6) and poor (n=4) NH subjects whose MMNs were judged to be present. Since there were 7 or 8 out of 10 NH subjects who had present MMNs for each condition, each subplot of Figure 4 may not involve the responses from all good or poor performers. Time zero represents the onset of the 4th note in the contour. The MMN measures including the onset time, offset time, and MMN duration (see the top left panel of Fig. 3). The LAEPs and MMNs show larger amplitudes in NH good performers than in NH poor performers. The MMNs are also larger with the 5-semitone spacing than with the 1-semitone spacing. The MMN amplitudes, latencies, and durations were compared between the 1-semitone and 5-semitone conditions across all NH listeners using paired-t tests. Results showed that the MMN was significantly larger in amplitude with the 5-semitone spacing (mean = −0.87 μV, SD = 0.37) than with the 1-semitone spacing (mean = −0.57 μV, SD = 0.43, $t = -6.85$, $p < 0.05$); the MMN latency was significantly shorter with the 5-semitone spacing (mean = 173.04 μV, SD = 18.99) than with the 1-semitone spacing (mean = 189.80 μV, SD = 32.94, $t = 2.45$, $p < 0.05$); there was no significant difference in the duration between the 1- and 5- semitone spacing (mean for 1-semitone = 118.83 ms, SD = 50.17; mean for 5-semitone = 112.71 ms, SD = 40.58, $t = 1.01$, $p > 0.05$).

The MMN was present for CI subjects with the 5-semitone spacing but not with the 1-semitone spacing. Figure 5 shows the grand mean LAEP waveforms (DEVIANT and STANDARD) and the difference waveform for the 5-semitone conditions in CI subjects whose MMNs were judged to be present. The MMN onset and offset time are marked in the plots that show present MMNs. Because no MMNs were present with the 1-semitone spacing, CI data only includes MMNs with the 5-semitone spacing. For those CI users whose MMNs evoked by Falling/Falling-flat (5-semitone) and Rising/Rising-flat (5-semitone) were present, their MMNs did not look obviously different. Therefore, if MMNs were judged to be present for these two stimulus conditions, the MMN was averaged across conditions. Thus, there was one set of values for MMN peak latency, peak amplitude, and duration, respectively for each subject who had a significant MMN. Paired-t tests were performed separately. The MMN with the 5-semitone spacing exhibited smaller amplitudes in CI subjects (mean = −0.57 μV, SD = 0.43), longer latency (median = 195.03 ms), and shorter duration (mean = 101.89 ms, SD = 18.44) than in NH listeners (amplitude mean = −0.87 μV, SD = 0.37; latency median = 171.11 ms; duration mean = 112.71 ms, SD = 40.58), but the difference did not reach the statistical level ($p > 0.05$). The lack of difference between subject groups in the MMN measures was consistent with the lack of difference in MCI performance with the 5-semitone spacing between subject groups.

Despite the generally poorer LAEPs and MMNs in CI subjects compared to NH listeners, the LAEPs and MMN for the top CI performer exhibited good morphologies and comparable amplitudes to the NH good performers. Figure 6 panel A shows LAEPs and MMNs for one NH good performer (SnhBB) and the top CI performer (Sci06). For a convenient comparison, the mean data from NH performers whose MMNs were judged to be present (n=8) were also plotted in panel B. Sci06's performance was 77.8% and 100% with the 1- and 5-semitone spacings, respectively. The LAEPs and the MMNs for the 5-semitone spacing were similar between Sci06 and SnhBB. However, with the 1-semitone spacing, the LAEP exhibited poor morphology and the MMN was absent in Sci06.

The correlation between MMN measures and behavioral results was examined. Figure 7 shows the MMN amplitude, latency, and duration as the function of MCI performance. The relationship between behavioral performance and MMN amplitude in CI users shown on the top left subplot can be described using a linear regression model, with a R^2 of 0.84. This linear regression is statistically signifiant ($p<0.05$). There was no significant relationship between the MMN measures and MCI performance plotted in the other subplots of this figure.

Discussion

This study is the first to compare behavioral measures and AEPs in CI subjects listening to melodic pitch contours. Results showed that MMNs were absent in all CI subjects with the 1-semitone spacing, and present in only a subset of CI subjects with the 5-semitone spacing (albeit with a smaller amplitude than observed with NH subjects). Below we discuss the results in greater detail.

Behavioral Performance

There was a bimodal distribution in in NH subjects' behavioral MCI performance. When averaged across the 1- and 5-semitone conditions, 6 out of 10 NH subjects scored better than 90% correct (“good” performers); the remaining 4 NH subjects scored less than 65% correct (“poor” performers). It is unlikely that the poor performers did not pay adequate attention during MCI testing, as they performed quite well in another behavioral test (timbre perception, not reported in this study) conducted in the same session as the MCI testing. Pitch processing was not likely impaired, given subjects' “normal-hearing” status. Although the NH group did not receive any formal music training, the variability in MCI performance may be attributed to differences in previous informal music listening experience.

MCI performance was generally poorer for CI subjects than for NH subjects, consistent with previous studies (Galvin et al., 2007, 2008, 2009). When averaged across the 1- and 5-semitone conditions, only 3 out of 10 CI subjects scored better than 65% correct (ranging from 72.22 to 88.89%); the remaining 7 CI subjects scored less than 65% correct (ranging from 22.20 to 58.33%). CI performance with the 1-semitone spacing was significantly poorer than NH performance. While there was a difference in median performance with the 5-semitone spacing between CI (72.2% correct) and NH subjects (91.65% correct), the difference was not statistically significant; a larger sample size may reveal a significant difference between subject groups.

Previous studies have suggested the poorer CI performance in melodic pitch perception tasks is largely due to the poorer spectral resolution of the CI device (Kong et al., 2004). Despite this limitation, the top CI subject (Sci06) performed comparably to the median NH score. With 1-semitone spacing, Sci06 scored 77.8% correct, poorer than (but close to) the median NH score of 88.9% correct. With 5-semitone spacing, Sci06 scored 100% correct, better than the median NH score of 91.65% correct. Musical experience after implantation may have contributed to Sci06's “star” performance. Sci06 stated that she frequently listened to music after implantation. Although previous studies have shown that auditory training with music stimuli can improve music perception (Gfeller et al., 2002b; Galvin et al., 2009), it is also possible that Sci06 listens to music more than the others because she receives better acoustic cues and has better perception of melody. While bilateral implantation has been reported to be related to better MCI performance (Veekmans et al., 2009), MCI performance was measured using the left CI only despite that Sci06 wore implants bilaterally. Nevertheless, it is possible that listening experience with bilateral implantation, which may be beneficial for the establishment of musical memory, and personal motivation may have positively affected MCI performance in this CI subject.

EEG results

Previous NH studies have reported that violations of musical expectancy (e.g., a wrong note in a familiar melody, a melody with an unstructured sequence of notes) can produce the MMN (Minati et al., 2008; Tew et al., 2009). The present NH results show that the MMN evoked by changes in pitch contours occur in the latency range of 150-250 ms. The MMN elicited by the change in pitch direction suggests that neuronal populations of the auditory cortex can automatically react to this change, without attention.

The MMN was significantly larger with the 5-semitone spacing than with the 1-semitone spacing. This is consistent with previous findings that the amplitude of the MMN is related to perceptual salience between the DEVIANT and STANDARD and the processing demands to differentiate these stimuli (Tiitinen et al., 1994; Amenedo & Escera, 2000; Titova & Näätänen, 2001). The good NH performers in the MCI task exhibited better waveform morphologies in LAEPs and MMNs than poor NH performers. According to Trainor et al. (2002), the neural encoding of relative pitch within a pitch contour is different from the encoding of the absolute pitch, which relies on the tonotopic organization of the auditory cortex. NH listeners are unlikely to have damaged auditory cortex. Although some previous studies have reported that MMNs are unreliably present across normal hearing listeners even for simpler stimuli (Kraus et al., 1995; Dalebout & Fox, 2000, 2001), the correspondence of poor LAEPs/MMNs and poor behavioral performance in the poor NH performers may suggest that their brain regions that encode relative pitch may be functionally less active than those in good performers.

All CI subjects exhibited absent MMNs for 1-semitone spacing and fewer CI users displayed present MMNs compare to NH listeners for 5-semitone spacing. This may be related to several factors. First, the clinical frequency-to-electrode map is not aligned along the absolute pitch dimension in CIs. As a much wider acoustic frequency range is mapped onto a limited cochlear extent (due to the length of the electrode array and limited insertion depth), there is likely to be a spectral mismatch between acoustic frequency and electrode place (Skinner et al., 2002). This frequency mismatch may interfere with absolute pitch perception by CI users. However, this factor may not explain the poor LAEPs and MMNs in CI subjects, since the ability to accurately perceive absolute pitch is not always a prerequisite for melody recognition.

Secondly, perception of relative pitch, a prerequisite for melodic contour perception, was degraded in CI subjects relative to NH subjects. Due to the limited number of electrodes and the lack of temporal fine structure cues, relative pitch perception is likely to be distorted. While crude spectro-temporal cues may be sufficient for speech understanding in quiet, they do not support the complex pitch perception required for music perception (Smith et al., 2002; Shannon et al., 2004). Current CI technology does not well encode small changes in relative pitch (1 semitone). Larger changes in relative pitch (5 semitones) may be sufficiently coded and perceived by some CI users, as shown in the present results.

Thirdly, long-term deafness can cause neural damage along the auditory pathway, and other sensory inputs may encroach upon cortical areas normally dedicated to auditory processing (i.e., crossmodal plasticity; Rouger et al., 2011). This may result in less recruitment of the auditory cortex in CI subjects than in NH listeners when processing sounds. Previous studies have shown smaller activation of the auditory cortex in response to speech stimuli in CI users than in NH listeners (Fujiki et al., 1999; Tobey et al., 2004). The limited auditory cortex recruitment may be a greater factor when processing more complex stimuli or performing more difficult perceptual tasks. Using PET technique, Limb et al. (2010) reported less activation in the auditory cortex during melody perception (the most difficult task for many CI users) than during speech perception or musical rhythm perception.

Fourthly, the working memory and cognitive abilities related to MMN generation may be compromised in CI subjects. Pisoni and colleagues reported poor performance in pediatric CI subjects for speech perception and for tasks involving working memory (digit span recall; Pisoni, 2000; Pisoni & Cleary, 2003). Other researchers reported that working memory and cognitive measures are among the predictors of implant outcome in adult CI users (Knutson et al., 1991; Gfeller et al., 2008). Because the generation of the MMN requires working memory that allows for the comparison of the neural representation of the STANDARD and DEVIANT stimuli (Cowan et al., 1993), the reduced working memory in CI user could result in poor MMNs.

Finally, the smaller/absent MMNs in CI subjects may be partially attributed to age effects. The age range was 22-81 yr for the CI group and 20-30 yr for the NH group. Ageing has been shown to degrade sensory and perceptual function, and older listeners exhibit decreased temporal processing, working memory, and cognitive abilities, compared to younger listeners (Gordon-Salant & Fitzgibbons, 1997, 1999); similar findings have been reported for CI users (Schvartz et al., 2008). Thus, aging can contribute to a reduced MMN (Cooper et al., 2006).

It is interesting to note that the top performing CI subject in the MCI task (Sci06) displayed LAEPs and MMNs with the 5-semitone spacing that were similar to those for the good NH performer (SnhBB). With 1-semitone spacing, however, the LAEPs for Sci06 showed poor morphologies and the MMN was missing. This suggests that the spectral resolution of the CI may be insufficient to code small pitch changes but good enough to code large pitch changes. The MMNs were smaller and MCI performance was poorer with the 5-semitone spacing for CI subjects (Median=72.2% correct) than for NH listeners (Median=91.65% correct). While the MCI performance difference was not statistically significant (a greater sample size may reveal significant performance differences between groups), the poorer CI performance may be due to deafness-related neural deficits, inappropriate interface between electrodes and neural substrates, degraded working memory and auditory attention, and ageing.

Implications and Future work

The present data supports the notion that CI users' music perception is presumably limited by both the peripheral representation and central processing. While pitch contrasts may be weak in CI users (as reflected by the absent/smaller MMNs), auditory training may help re-shape sensitivity to these pitch contrasts. Tremblay and colleagues (Tremblay et al., 1998; Tremblay et al., 2001) reported that, for NH listeners, improved speech performance after training of voice onset time was associated with increased amplitude of the N1-P2 and MMN. This indicates that cortical representation and pre-attentive sound encoding can be enhanced by training. Fu and Galvin (2008) reported that, for a single CI subject, electrode discrimination training generalized to better phoneme recognition. Auditory training has been reported to improve CI users' music perception (Galvin et al., 2007; 2009; Gfeller et al., 2002b) as well as speech understanding (Fu et al., 2004; Fu and Galvin, 2007, 2008). It is possible that these training benefits are associated with improved processing at both the pre-attentive and attentive level. Prior MMN studies with NH listeners (Tremblay et al., 1998) showed that, during auditory training, changes in the MMN can be observed before the improvements in behavioral performance. Therefore, the MMN may be a useful objective tool to monitor brain plasticity during auditory training. For music perception in particular, the MMN may be used to: 1) assess neurophysiologic processing of pitch contours and melodies, 2) assess deficits in the central auditory system for sensory encoding, and 3) explore the effects of music training on brain plasticity in CI users.

Despite the potential utility of MMN as a clinical tool, it is noteworthy that the MMN has limitations. First, the MMN is small auditory evoked potential, which makes reliable interpretation difficult. It can coarsely separate individuals into good and poor performers at the group level, it is a poor predictor at the individual subject level; Second, the MMN is a response derived using a subtraction procedure, which adds additional noise to the waveforms that are already noisier in CI users than in NH listeners due to stimulus artifact and/or less synchronized neural response in CI users; Third, it is time consuming to record the MMN since a large number of stimulus trials must be presented.

The MMN examined in this study only reflects the automatic detection of changes in pitch contour at the pre-attentive level, which is thought to be more bottom-up memory-driven than top-down attentional processing (Berti et al., 2004). However, it is unclear whether CI users' pitch contour processing is more bottom-up or top-down, given the performance difference when sufficient auditory cues are provided (e.g., the 5-semitones spacing condition). It is possible that sound discrimination at the auditory cortex and pre-attentive level is better in some CI users, which results in better perceptual performance. It is also possible that top CI performers (e.g., Sci06) may have greater attention and cognitive capability, which drive better neural responses at the cortical and pre-attentive level. Neural mechanisms involved in melody perception may be further revealed by combining AEPs that reflect higher-level processing (e.g., P300). Finally, it would be interesting to see whether music training can improve MCI performance, and whether these changes would be reflected in the MMN.

Based on the limitations of MMN measures and limitations of this study, we will do the following in future studies: 1) use age-matched control subjects to rule out age effects, 2) implement a multi-feature MMN paradigm used in previous studies (Pakarinen et al., 2007; Pakarinen et al., 2010) instead of the traditional paradigm used in this study to include more systematic pitch changes so that more information will be derived to examine the processing of pitch contour changes in CI users.

Conclusions

The primary goals of this study were to use the MMN to examine cortical encoding of changes in pitch contour and NH and CI listeners, and to compare electrophysiological and behavioral measures within and across these subjects groups. The behavioral performance was significantly poorer in CI subjects than in NH subjects when the frequency interval between successive notes in the pitch contour was small (1-semitone spacing), but not when the interval was large (5-semitone spacing). The MMN was absent for all CI subjects with the 1-semitone spacing, and present in only a subset of CI subjects with the 5-semitone spacing; in contrast, the MMN was present in most NH subjects with the 1-semitone spacing and the 5-semitone spacing. The present data suggest that the poor melodic pitch perception by CI users may be due to both the lack of detailed auditory cues as well as central auditory processing deficits.

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List of Abbreviations

AEP	Auditory Evoked Potential
CI	Cochlear Implant
EEG	Electroencephalography
EOG	Electrooculogram
ERP	Event-Related Potential
ICA	Independent Component Analysis
LAEP	Late Auditory Evoked Potential
MMN	Mismatch Negativity
NH	Normal Hearing
RM ANOVA	Repeated-Measures Analysis of Variance

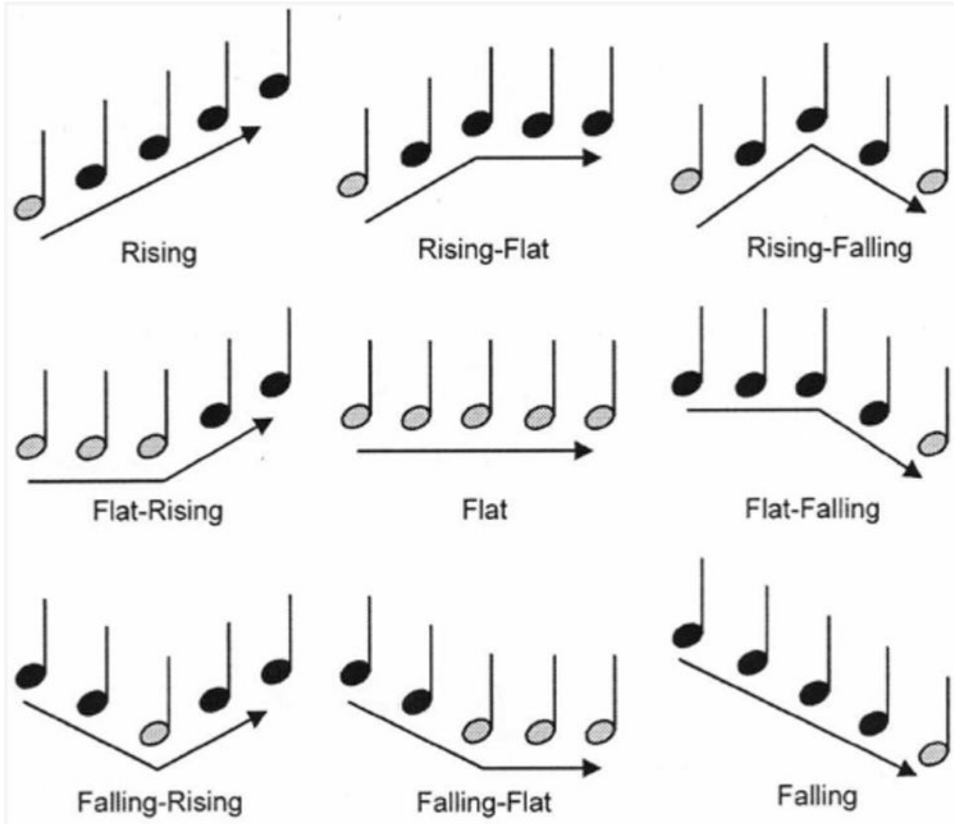

Figure 1.
The five-note pitch contours used for MCI test. The frequency interval between successive notes in the pitch contours was 1 or 5 semitones. The shaded notes represent the root note in each contour.

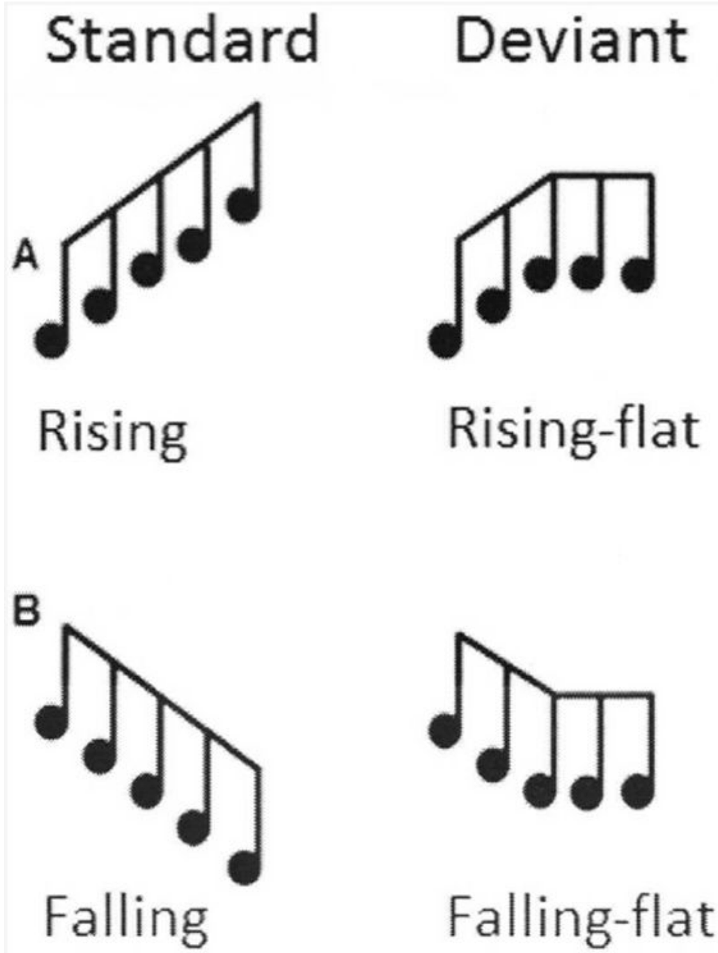

Figure 2.
The five-note pitch contours used for EEG recording. The frequency interval between successive notes in the pitch contours was 1 or 5 semitones.

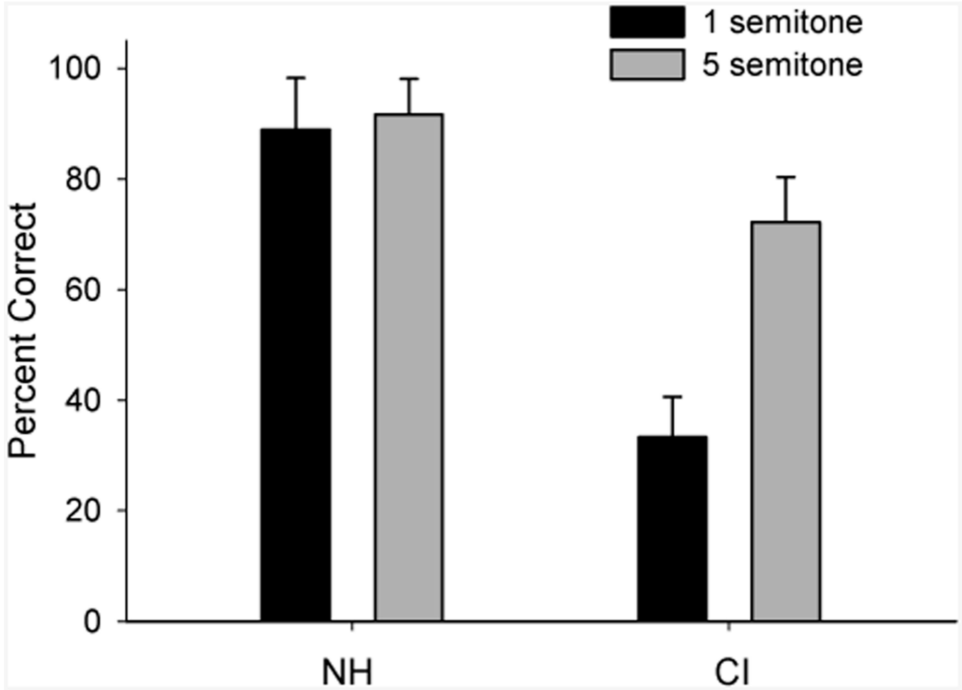

Figure 3.
Behavioral MCI performance for NH and CI subjects. The error bar indicates one standard error.

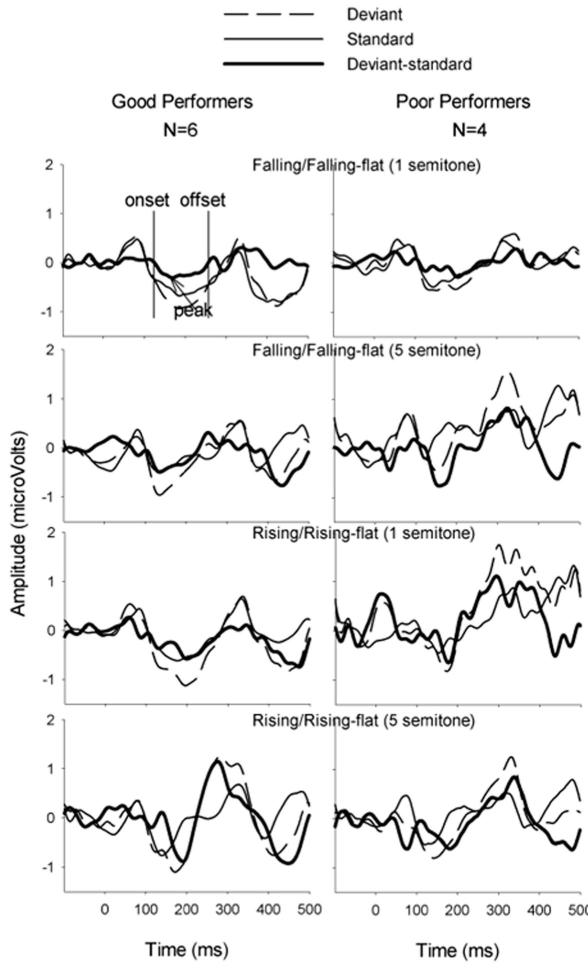

Figure 4.

Grand average LAEPs for good (n=6) and poor NH performers (n=4) whose MMNs were judged to be present. The STANDARD waveforms, the DEVIANT waveforms, and the difference waveforms (DEVIANT–STANDARD) are shown. Time zero represents the onset of the 4^{th} note. Data from nine electrodes in the fronto-central area were averaged for each waveform. MMN markers including the onset time, offset time, and duration are shown in the top left plot.

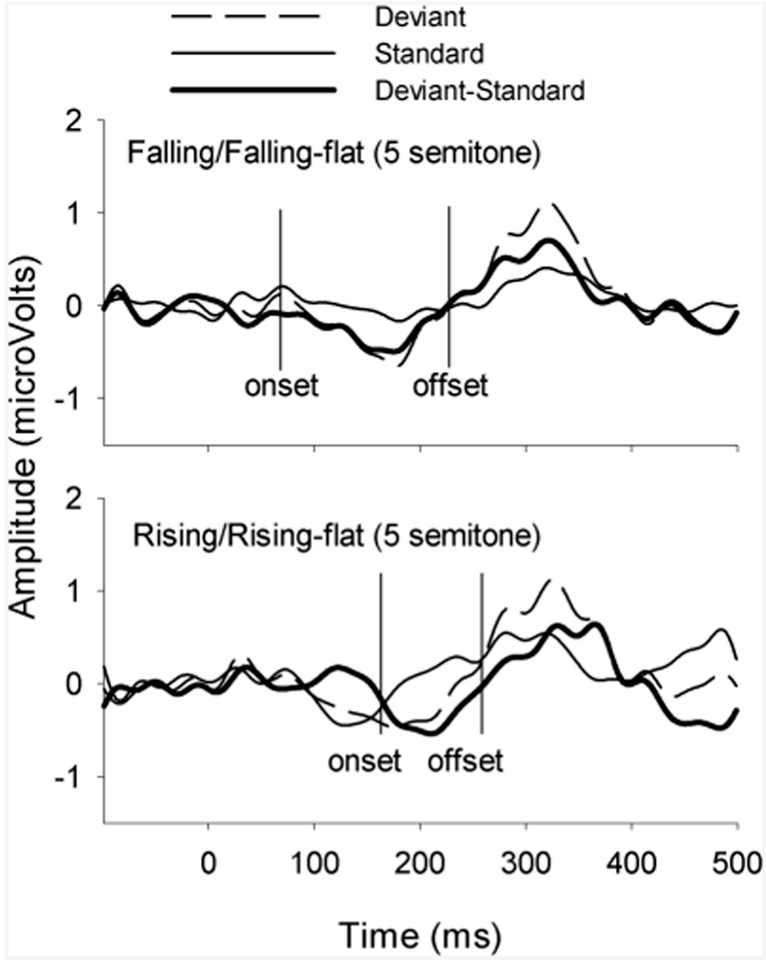

Figure 5.
Similar plot as Figure 3, but for CI users whose MMNs were judged to be present for 5-semitone spacing (n = 3 for Falling/Falling-flat condition and n = 6 for Rising/Rising-flat condition).

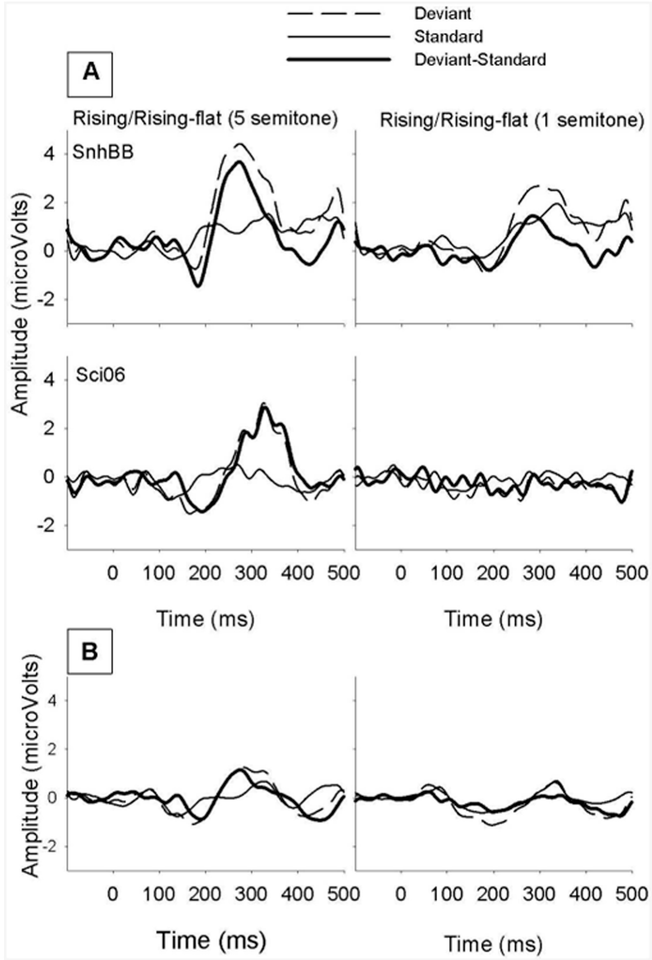

Figure 6.

Subplot A shows LAEPs with 1-semitone and 5-semitone spacing in one good NH subject (SnhBB) and the top-performing CI subject (Sci06). Subplot B displays the mean data for NH performers whose MMNs were judged to be present (n=8) for better visual comparison.

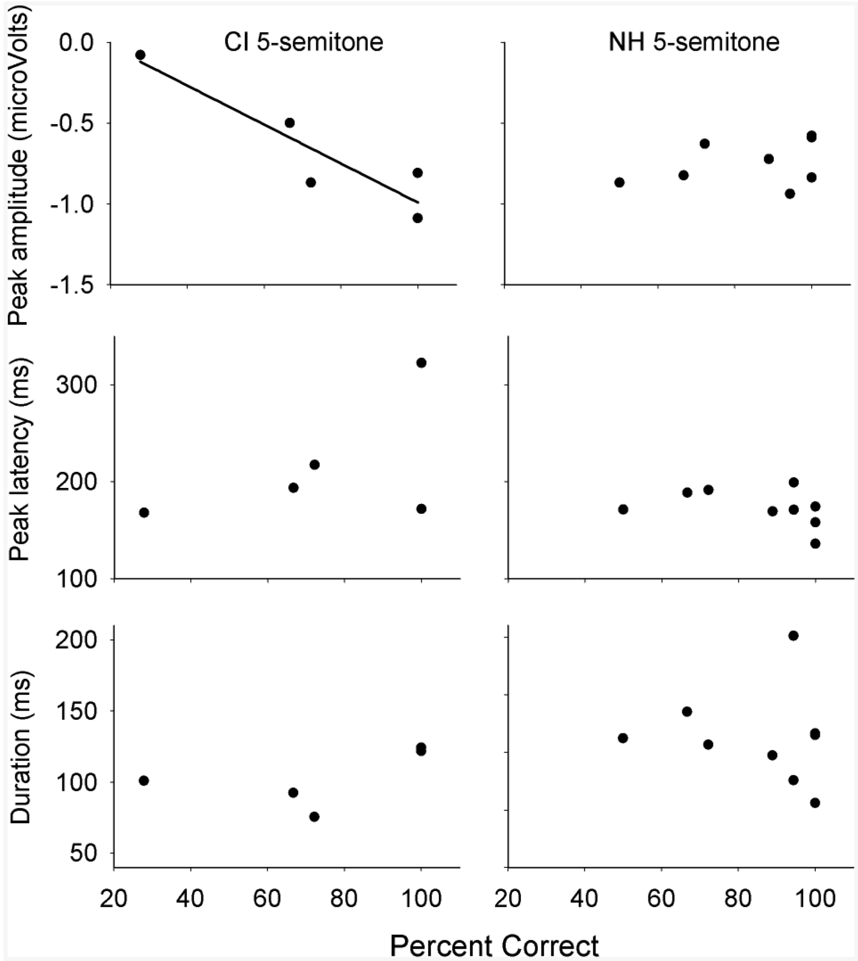

Figure 7.
The MMN measures (peak amplitude, peak latency, and duration) as the function of behavioral performance in CI users (left subplots) and NH listeners (right subplots) for 5-semitone spacing. The correlation between MMN peak amplitude and percent correct in CI users can be described by a linear regression model with a R^2 at 0.84 (top left subplot, $p<0.05$). The line indicates the regression line.

Table 1

CI subject demographics.

Subject	Gender	Age (years)	Duration of deafness (years)	Ear Implanted	Duration of CI use (years)	CI Device	Speech strategy
Sci01	M	72	43	L	2.5	Nucleus Freedom	ACE
Sci02	M	52	48	L	2.5	Nucleus Freedom	ACE
Sci03	F	59	50	L	5	Nucleus Freedom	ACE
Sci04	M	51	40	L	4.5	Nucleus Freedom	ACE
Sci05	M	36	35	L	2	Nucleus Freedom	ACE
Sci06	F	22	19	B	1.5	Nucleus Freedom	ACE
Sci07	F	42	33	B	2.5	Nucleus Freedom	ACE
Sci08	M	81	30	L	3	Nucleus Freedom	ACE
Sci09	M	64	15	L	1	Nucleus Freedom	ACE
Sci10	M	57	15	L	4.5	Advanced Bionics	HiRes

M = male. F = female. L = left. B = both.

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Table 2

Frequencies for of each tone in the pitch contours used for EEG recording. The shaded areas indicate the deviant stimuli, and the bold numbers indicate the frequencies in the deviant that differed from the counterpart in the standard.

	Frequency (Hz) of each note in contour				
	1	**2**	**3**	**4**	**5**
Falling (1 semitone)	554	523	494	466	440
Falling-flat (1 semitone)	554	523	494	**494**	**494**
Rising (1 semitone)	440	466	494	523	554
Rising-flat (1 semitone)	440	466	494	**494**	**494**
Falling (5 semitone)	1397	1047	784	587	440
Falling-flat (5 semitone)	1397	1047	784	**784**	**784**
Rising (5 semitone)	440	587	784	1047	1397
Rising-flat (5 semitone)	440	587	784	**784**	**784**

Table 3

The number of subjects whose MMNs were judged to be present.

	Falling/Falling-flat (1-semitone)	Falling/Falling-flat (5-semitone)	Rising/Rising-flat (1-semitone)	Rising/Rising-flat (5-semitone)
CI	0	3	0	6
NH	7	8	7	8