Published in final edited form as:

Ear Hear. 2017 ; 38(3): 332–343. doi:10.1097/AUD.0000000000000392.

Effects of Stimulus Polarity and Artifact Reduction Method on the Electrically Evoked Compound Action Potential

Michelle L. Hughes, Jenny L. Goehring, and Jacquelyn L. Baudhuin

Boys Town National Research Hospital, 555 North 30th Street, Omaha, NE, USA 68131

Abstract

Objective—Previous research from our laboratory comparing electrically evoked compound action potential (ECAP) artifact reduction methods has shown larger amplitudes and lower thresholds with cathodic-leading forward masking than with alternating polarity. One interpretation of this result is that the anodic-leading phase used with alternating polarity elicits a less excitatory response (in contrast to results from recent studies with humans), which when averaged with responses to cathodic-leading stimuli, results in smaller amplitudes. Another interpretation is that the latencies of the responses to anodic- and cathodic-leading pulses differ, which when averaged together, result in smaller amplitudes than for either polarity alone due to temporal smearing. The purpose of this study was to separate the effects of stimulus polarity and artifact reduction method to determine the relative effects of each.

Design—This study used a within-subjects design. ECAP growth functions were obtained using cathodic-leading forward masking (CathFM), anodic-leading forward masking (AnodFM), and alternating polarity (AltPol) for 23 CI recipients (N=13 Cochlear and N=10 Advanced Bionics). N1 latency, amplitude, slope of the amplitude-growth function, and threshold were compared across methods. Data were analyzed separately for each manufacturer due to inherent differences between devices.

Results—N1 latencies were significantly shorter for AnodFM than for CathFM and AltPol for both Cochlear and Advanced Bionics participants. Amplitudes were larger for AnodFM than for either CathFM or AltPol for Cochlear recipients; amplitude was not significantly different across methods for Advanced Bionics recipients. Slopes were shallowest for CathFM for Cochlear subjects, but were not significantly different among methods for Advanced Bionics subjects. Thresholds with AltPol were significantly higher than both FM methods for Cochlear recipients; there was no difference in threshold across methods for the Advanced Bionics recipients.

Conclusions—For Cochlear devices, the smaller amplitudes and higher thresholds observed for AltPol appear to be the result of latency differences between polarities. These results suggest that AltPol is not ideal for managing stimulus artifact for ECAP recordings. For the Advanced Bionics group, there were no significant differences among methods for amplitude, slope, or threshold, which suggests that polarity and artifact reduction method have little influence in these devices.

Corresponding author: Michelle L. Hughes, PhD, michelle.hughes@boystown.org, Phone Number: 402-452-5038, Fax Number: 402-452-5028.

Conflicts of Interest: No other conflicts of interest are declared for any of the authors.

Supplemental Digital Content 1.jpg

We postulate that polarity effects are minimized for symmetrical biphasic pulses that lack an interphase gap, such as those used with Advanced Bionics devices; however, this requires further investigation.

Keywords

cochlear implant; electrically evoked compound action potential; artifact reduction; forward masking; alternating polarity; evoked potentials

INTRODUCTION

The electrically evoked compound action potential (ECAP) can be easily measured using clinical software with all three of the major CI manufacturers' devices. There are two primary ways in which the ECAP is separated from the stimulus artifact: (1) alternating the stimulus polarity and then averaging the responses (AltPol) or (2) a forward-masking (FM) subtraction paradigm (e.g., Brown et al., 1990). These two methods are illustrated in Fig. 1 and are described in detail in the Methods section. Both artifact-reduction methods are available in Cochlear's Custom Sound EP software (Cochlear Ltd., Macquarie, New South Wales, Australia); the default method is FM. AltPol is the only method available in Advanced Bionics' SoundWave (Advanced Bionics, Valencia, CA, USA) and MED-EL's Maestro (MED-EL, Innsbruck, Austria) software.

Few studies have compared ECAP responses with AltPol and FM (Frijns et al. 2002; Eisen & Franck 2004; Baudhuin et al. 2016). In a recent comprehensive study from our laboratory, Baudhuin et al. (2016) compared ECAP thresholds, slopes of the amplitude growth function (AGF), and peak-to-peak amplitudes between AltPol and FM in a group of 17 Cochlear recipients (N = 18 ears) with newer-generation devices, using the commercial Custom Sound EP software. The results revealed higher thresholds, steeper slopes, and smaller amplitudes with the AltPol paradigm than with FM. One possible interpretation of this result is that for AltPol, the anodic-leading pulse would have to be *less* excitatory than the cathodic-leading pulse, resulting in smaller averaged amplitudes than for the cathodic-leading FM condition (Hypothesis 1). Another possible interpretation is that the latencies of the responses to anodic- and cathodic-leading pulses differ, which when averaged together using AltPol, result in smaller amplitudes than for either polarity alone (Hypothesis 2). The purpose of this study was to investigate these possibilities by separating the effects of stimulus polarity and artifact reduction to determine the relative effects of each.

Hypothesis 1: Unequal Excitation between Polarities

Earlier studies examining the effectiveness of pulse polarity in animal models have reported different outcomes across species (Miller et al. 1994, 1998, 1999, 2003; Ramekers et al. 2014). For *monophasic* pulses, Miller et al. (1998) found that cathodic stimulation was most effective at eliciting auditory-nerve responses in cats, resulting in lower ECAP thresholds; however, anodic stimulation yielded lower thresholds in guinea pigs. Recent studies with human CI recipients using *pseudomonophasic* pulses suggest that anodic stimulation is more effective than cathodic in eliciting auditory-nerve responses, yielding larger amplitudes for the ECAP (Macherey et al. 2008; Undurraga et al. 2010) and for the electrically evoked

auditory brainstem response (EABR; Undurraga et al. 2013). For *symmetrical biphasic* pulses, Macherey et al. (2008) reported that both leading polarities yielded similar amplitudes. However, Undurraga et al. (2010) found significantly larger ECAP amplitudes for anodic-leading than for cathodic-leading symmetrical biphasic probe pulses using the FM paradigm. The latter result suggests that averaging responses to an anodic-leading pulse (larger ECAP) and a cathodic-leading pulse (smaller ECAP) should yield a *larger* resulting ECAP with AltPol than for cathodic-leading FM alone, which is opposite the results reported by Baudhuin et al. (2016) and Frijns et al. (2002). Collectively, these results contradict the hypothesis that the anodic-leading pulse elicits a *less* excitatory response that reduces the overall amplitude of responses obtained with AltPol.

Hypothesis 2: Unequal Latency between Polarities

Studies in both animals and humans have shown polarity-dependent effects on ECAP latency. In guinea pigs, Klop et al. (2004) found shorter latencies for cathodic-first than for anodic-first *biphasic* pulses for ECAP recordings made at the round window. Miller et al. (1998) found longer N1 and P2 latencies for *monophasic* cathodic stimulation in both cats and guinea pigs in comparison to anodic stimulation. However, those recordings were made from the nerve trunk, so their results are essentially similar to those reported by Klop et al. (2004). Collectively, these results suggest that the cathodic phase preferentially stimulates peripheral axons, whereas the anodic phase preferentially stimulates the central axons, consistent with the modeling studies of Rattay et al. (2001a). For intracochlear recordings in human CI recipients, who likely have substantial loss of peripheral axons, Macherey et al. (2008) and Undurraga et al. (2010) showed shorter N1 latencies for anodic-leading symmetrical biphasic pulses than for cathodic-leading pulses. They proposed that the anodic phase is primarily the excitatory phase with symmetrical biphasic pulses. Thus, shorter latencies result when the anodic phase is presented first. When the second phase is anodic, the latency shift should roughly equal the duration of the first phase (see Undurraga et al. 2010). Averaging ECAP responses between polarities with offset latencies (as with AltPol) should therefore yield smaller amplitudes than for either polarity alone due to temporal smearing. Taken together, the literature supports Hypothesis 2 as the likely reason for why AltPol yields smaller amplitudes than FM with symmetrical biphasic pulses.

The goal of this study was to separate the effects of stimulus polarity and artifact-reduction method to elucidate the mechanisms contributing to the smaller amplitudes and higher thresholds with AltPol that were observed in Baudhuin et al. (2016). ECAP growth functions were obtained for each subject using AltPol, FM with cathodic-leading pulses for both masker and probe (CathFM; this is the clinical default in Cochlear's Custom Sound), and FM with anodic-leading pulses for both masker and probe (AnodFM). N1 latencies, peak-to-peak amplitudes, AGF slopes, and thresholds were compared across methods. It was hypothesized that N1 latencies would be shortest for AnodFM and longest for CathFM based on results from Macherey et al. (2008) and Undurraga et al. (2010), with AltPol latencies occurring somewhere in between those of the two FM methods due to averaging. ECAP amplitudes were expected to be largest for AnodFM (based on results from Undurraga et al. 2010), followed by CathFM, with AltPol yielding the smallest amplitudes due to averaging waveforms with offset latencies. AGF slopes were expected to be steeper

for AnodFM than CathFM due to larger expected supra-threshold amplitudes for AnodFM (Undurraga et al. 2010) and minimal amplitude differences near threshold (Hughes et al. 2015). AltPol slopes were also expected to be steeper than for CathFM based on our earlier findings in Baudhuin et al. (2016). Last, it was hypothesized that ECAP thresholds would be similar for AnodFM and CathFM because polarity effects have primarily been observed only at suprathreshold levels (Hughes et al. 2015; Macherey et al. 2006). AltPol thresholds were expected to be higher than both FM methods due to the expected latency differences between polarities resulting in smaller amplitudes for the averaged trace.

MATERIALS AND METHODS

Participants

Twenty-three ears (13 Cochlear, 10 Advanced Bionics) in 18 CI recipients were tested. Data for eight of the Cochlear subjects (F1, F2, F5, F10/F11, N5, N6, N9, and N11) were also included in Baudhuin et al. (2016). Demographic information is detailed in Table 1 (subject numbers are ear specific). Eight subjects were implanted bilaterally. For three of those subjects (F1, F5, and C40), only one ear was tested. For the remaining five bilateral recipients (F10/F11, FS19/N11, FS26/N5, C8/C47, C29/C45), both ears were tested. The mean age at implant was 53 years, 6 months (range: 1 year, 10 months to 82 years). The mean duration of CI use at the time of study participation was 5 years, 6 months (range: 4 months to 14 years, 9 months). The mean duration of deafness was 8 years, 6 months (range: 6 months to 25 years). This study was approved by the Boys Town National Research Hospital Institutional Review Board (protocol 03-07-XP).

Equipment and Stimuli

Figure 1 illustrates the AltPol technique (left panel), CathFM (middle panel), and AnodFM (right panel) used for all participants. For AltPol, ECAP responses are obtained for cathodic-leading (C) and anodic-leading (A) pulses and then averaged together $((C+A)/2)$. When the polarity is reversed, the stimulus artifact also reverses, but the ECAP response does not. This method assumes that the ECAP responses to each polarity are identical and that the artifact is symmetrical. For FM, four stimulus frames are delivered ($a-d$). The probe (a) elicits an ECAP response and stimulus artifact. The masker+probe condition (b) forces the neurons into an absolute refractory period resulting in a probe response that should only contain artifact. In this condition, it is important that the masker is higher in level than the probe to ensure that all fibers that could potentially be recruited by the probe are in a refractory state when the probe is delivered. The artifact from condition b is then subtracted from the probe response in a , resulting in a relatively artifact-free ECAP. Two additional stimulus conditions, the masker alone (c) and a switching artifact (d) are applied to remove any residual neural response to the masker pulse and any artifacts associated with switching on the recording amplifier. This method assumes no neural component is present in the probe trace in condition b . In the present study, the switching artifact was subtracted out for the AltPol condition for the Advanced Bionics data $((C+A)-2d)/2$ but not for the Cochlear data, to be consistent with the default settings in the clinical software for both Advanced Bionics and Cochlear¹, and to be consistent with the methods used with the Cochlear subjects in our earlier study (Baudhuin et al. 2016).

For Cochlear recipients, ECAPs were obtained using the commercial Custom Sound EP software (v. 4.0–4.1; Cochlear Ltd., Macquarie, NSW, Australia) via a programming pod connected to a laboratory Freedom processor. Stimuli consisted of 25- μ sec/phase charge-balanced biphasic pulses with a 7- μ sec interphase gap (clinical default). All stimuli were delivered in monopolar mode, referenced to the extracochlear electrode, MP1. The software default delivers a cathodic-leading biphasic pulse. To reverse the stimulus polarity, MP1 was used as the active electrode, with the intracochlear electrode used as the return. Intracochlear electrode 11 was used for stimulation in all Cochlear participants except for N5. For N5, electrode 18 was used due to suspected insulation damage (Cullington 2013) affecting some of the mid-array electrodes. ECAPs were recorded from two electrode positions apical² to the stimulating electrode (e13), referenced to the extracochlear electrode on the body of the implant, MP2. Default stimulus and recording parameters that were used included an 80-Hz probe rate, 50-dB gain, 122- μ sec recording delay (optimized individually as needed to avoid amplifier saturation), and 100 averages with a 1.6-msec time window and 20-kHz sampling rate. All remaining parameters were set to the software defaults. For the FM conditions (CathFM and AnodFM), the masker-probe interval was 400 μ sec, and the masker level was 10 CL above each respective probe level in the AGF.

For Advanced Bionics recipients, ECAPs were obtained using the Bionic Ear Data Collection System (BEDCS, v. 1.18.295; Advanced Bionics, Valencia, CA) via a CPI-II interface connected to a laboratory Platinum Series Processor. Stimuli consisted of 32- μ sec/phase charge-balanced biphasic pulses with no interphase gap. All stimuli were delivered in monopolar mode, referenced to the extracochlear electrode on the body of the implant. Intracochlear electrode 9 was used for stimulation in all Advanced Bionics participants. ECAPs were recorded from two electrode positions³ apical to the stimulating electrode (e7), referenced to the extracochlear electrode on the body of the implant (for CII recipients) or the extracochlear ring electrode (for HiRes 90K recipients). Other stimulus and recording parameters that were used included a probe rate of approximately 20 Hz, gain of 1000 (linear multiplier; equal to 60 dB) and 100 averages over a 2-ms time window. Waveforms were sampled at 56 kHz and smoothed using a 2-point boxcar filter (built-in function within BEDCS). The acquisition bandwidth was approximately 26 kHz. Because BEDCS begins recording prior to the last pulse, there is no recording delay parameter in the software. For FM, there is a delay preceding the probe in the probe-alone frame that equals the duration of the masker pulse and the masker-probe interval to ensure that the probe-alone frame lines up in time with the masker+probe frame. This resulted in a time-delayed waveform relative to the AltPol waveforms. As a result, the latency data for the two FM methods were corrected by subtracting the masker-probe interval (400 μ sec) and the total masker pulse duration (64 μ sec). For the FM conditions (CathFM and AnodFM), the masker level was set 1.57 dB above each probe level (this is approximately equivalent to the 10-CL masker-probe offset

¹The switching artifact (“d” trace) is measured in Custom Sound EP with alternating polarity, but is not applied in the software default settings. Effects of the “d” trace subtraction are discussed further in Figure 9.

²Electrode spacing for the Contour Advance array ranges from 0.4 – 0.8 mm, apex to base. The distance between electrodes 11 and 13 is 1.07 mm, center to center (C. van den Honert, personal communication, July 27, 2010). Electrode spacing for the slim straight array (CI422) is 0.95 mm, which translates to 1.9 mm between electrodes 11 and 13, center to center. Note that perimodiolar (Contour) arrays require smaller electrode spacing than straight arrays to maintain a similar radial distance.

³Electrodes for the Advanced Bionics 1j array are spaced 1.1 mm apart, center to center.

used with Cochlear recipients; Cohen 2009). For both Cochlear and Advanced Bionics recipients, stimulus levels for AltPol were equal to the probe levels used for FM.

For all participants, electrode impedances were measured prior to beginning data collection to ensure malfunctioning electrodes (i.e., short or open circuit) were not used for stimulating or recording, and to ensure stimulation stayed within voltage compliance. For Cochlear recipients, impedances were measured in Custom Sound EP, which automatically provides a notification to the user if voltage compliance limits are reached during the ECAP measures. For Advanced Bionics recipients, impedances were measured in the SoundWave commercial programming software (Advanced Bionics, Valencia, CA) and then entered into a voltage compliance calculator that applies Ohm's Law to determine the maximum current level allowed to maintain compliance.

Procedure

For both device types, an ascending procedure was used to obtain starting levels for the AGF using 10 sweeps of the FM stimulus with the masker and probe levels offset as described above. Participants were provided with a visual rating scale ranging from 1 (just noticeable) to 10 (too loud) and were asked to indicate when the stimulus reached ratings of 8 (loud) and 9 (upper loudness limit). To begin the AGF, the masker was set to the current level that equaled an 8 rating, with the probe set 10 CL (Cochlear) or 1.57 dB (Advanced Bionics) below the level of the masker, as described above. For most recipients, 10 CL (or 1.57 dB) below an 8 rating was judged as a rating of 7 (loud but comfortable; see Baudhuin et al., 2016). The masker and probe levels were both systematically reduced (maintaining a constant level offset) until no ECAP response could be visualized (Hughes et al., 2001). The step size was 5 CL for Cochlear (reduced in 2–3-CL steps near threshold). The current steps (CL) for Cochlear are log-based, so a similar log-based step was used for Advanced Bionics recipients using the following formula: $b = a10^{n/20}$, where a is the starting current level, n is the step size factor (–0.45 was typically used), and b is the next current level to be presented (substituted for a on the subsequent iteration).

Data Analysis

For Cochlear participants, N1 and P2 peaks are automatically marked in the Custom Sound EP software. ECAP amplitude is calculated as the difference between these two peaks. All peak markers were visually examined and adjusted as necessary by experienced testers. For Advanced Bionics participants, waveforms were exported from BEDCS into a custom Matlab program to mark the N1 and P2 peaks to derive the peak-to-peak amplitude. For both device types, threshold was the lowest current level that yielded a measurable ECAP response above the noise floor (Glassman & Hughes, 2013). The noise floors for the Cochlear and Advanced Bionics devices in this study were approximately 2–4 μ V (Patrick et al. 2006) and 20–40 μ V (Glassman & Hughes, 2013), respectively⁴.

⁴Although additional filtering could be applied to reduce the noise floor for Advanced Bionics devices, our goal was to examine the effects of polarity and artifact reduction using clinically related parameters.

A within-subjects design was used. Latency, amplitude, AGF slope, and threshold were compared across the three methods, separately for the two manufacturers, using a one-way repeated-measures analysis of variance (RM ANOVA) within SigmaPlot 12.5 (Systat Software, Inc.). Data were analyzed separately for each manufacturer due to inherent differences between devices (e.g., stimuli, array design). For data that were not normally distributed, the non-parametric Friedman ANOVA on ranks was used, and medians are reported in addition to means. Post-hoc analyses were performed using either the Tukey (for non-parametric) or Holm-Sidak (for parametric) tests.

RESULTS

Figure 2 shows example waveforms from a subject with a Cochlear device (top) and a subject with an Advanced Bionics device (bottom). The stimulating electrode and level are indicated in each panel. CathFM, AnodFM, and AltPol waveforms are depicted in black, white, and gray symbols, respectively. For the Cochlear subject (F5), AnodFM yielded the shortest N1 latency (227.8 μ sec) and the largest peak-to-peak amplitude (374.7 μ V). CathFM yielded the longest N1 latency (276.6 μ sec) and the second-largest amplitude (293.9 μ V). The N1 latency for AltPol was the same as for CathFM (276.6 μ sec) and yielded the smallest amplitude (252.0 μ V). Results for the Advanced Bionics subject (C8) were generally similar: AnodFM yielded the shortest N1 latency (292.2 μ sec) and largest peak-to-peak amplitude (204.2 μ V), and CathFM yielded the longest N1 latency (346.1 μ sec) and the second-largest amplitude (153.8 μ V). The N1 latency for AltPol (330.3 μ sec) was intermediate to the latencies for the two FM methods and had the smallest amplitude (139.7 μ V), consistent with Hypothesis 2.

Figure 3 shows representative AGFs from three Cochlear subjects (left column) and three Advanced Bionics subjects (right column) for all three stimulus conditions. In each panel, black circles, white circles, and gray triangles represent AGFs obtained with CathFM, AnodFM, and AltPol, respectively. Subject and electrode numbers are indicated in each panel. For all three Cochlear recipients, ECAP amplitudes were largest for AnodFM. For F16, amplitudes for AnodFM were larger than for the other two methods across the entire AGF; but for N5 and N6, AnodFM amplitudes were only larger at the upper end of the AGF. For F16 and N6, the CathFM and AltPol functions generally overlapped. In contrast, the AltPol function for N5 was smaller than the two FM functions. For the Advanced Bionics subjects, differences across methods were similar to those for the Cochlear subjects, but less pronounced. Amplitudes were largest for AnodFM, but primarily only at the higher levels. For C8, CathFM amplitudes were larger than those for AltPol; for C29, the opposite was true for the mid-level portion of the function; and for C39, both functions overlapped. Across all Cochlear subjects (N=12; excluding FS19 because of limited data points for AltPol; group data not shown), the average ECAP amplitudes at the highest common probe level across methods were 249.7 μ V, 340.6 μ V, and 235.1 μ V for CathFM, AnodFM, and AltPol, respectively. For the Advanced Bionics group (N=9; excluding C29, who was an outlier), the mean ECAP amplitudes at the highest common probe level were 314.4 μ V, 343.3 μ V, and 263.4 μ V for CathFM, AnodFM, and AltPol, respectively. Within each method, there was no significant difference in ECAP amplitude between devices at these highest levels (*t* test, *p* > 0.5).

Figure 4 illustrates how the data were derived for the group latency and amplitude comparisons across methods. The same analysis was performed as in Baudhuin et al. (2016), except that each group of growth functions per electrode were first normalized to the highest amplitude in the set. This was done to control for large amplitude differences across subjects⁵. The normalized amplitudes were compared across methods using the same range of current levels that yielded non-zero values across all three methods; this was necessary because the thresholds and slopes generally differed across methods. Figure 4 shows the AGFs for the three methods for subject F5, electrode 11. The vertical dashed line at 185 CL indicates the lowest level that yielded non-zero amplitudes across the three artifact-reduction methods. The arrows indicate the range of current levels that were used for the group latency and amplitude comparisons.

Figure 5 shows box-and-whisker plots for the N1 latency data across methods for Cochlear (top row, N = 12) and Advanced Bionics recipients (bottom row, N = 10). One Cochlear recipient (FS19) was excluded from the group analyses because the AGF for AltPol was only comprised of two data points. Boxes and whiskers represent the 25th/75th and 10th/90th percentiles, respectively. Dashed and solid horizontal lines represent means and medians, respectively, and filled circles represent the 5th and 95th percentile (outliers). For the data in the left panels ('Average'), mean latencies were first calculated for each subject's AGF across the common range of current levels (as depicted in Figure 4) so that each subject contributed a single data point for each method. Although reduced stimulus level prolongs latency to a greater extent for acoustic evoked potentials than for electrically evoked potentials, level-dependent latency effects were evident for some participants. The middle and right panels therefore show latency data for the lowest and highest common CLs, respectively. Group mean latencies (in μsec) for each condition are indicated at the top of each graph above each box plot. For the Cochlear group, the RM ANOVA showed a significant main effect of method for the average across CLs ($F_{(2, 11)} = 20.54, p < 0.001$), lowest common CL ($F_{(2, 11)} = 18.69, p < 0.001$), and highest common CL ($F_{(2, 11)} = 7.69, p = 0.003$). For the Advanced Bionics group, there was also a significant main effect of method for the average across CLs ($F_{(2, 9)} = 24.40, p < 0.001$), lowest common CL ($F_{(2, 9)} = 5.49, p = 0.014$), and highest common CL ($F_{(2, 9)} = 7.93, p = 0.003$). Post-hoc comparisons (Holm-Sidak) that were statistically significant are indicated with arrows and respective p values in each panel of Fig. 5. In general, AnodFM yielded the shortest latencies, consistent with the hypothesis.

Figure 6 shows box-and-whisker plots for the normalized ECAP amplitude data across methods (plotted as in Fig. 5). For Cochlear subjects, the RM ANOVA showed a significant main effect of method for the average amplitude across CLs ($F_{(2, 11)} = 10.63, p < 0.001$), lowest common CL ($X^2_{(2, 11)} = 17.17, p < 0.001$; non-parametric Friedman's RM ANOVA) and highest common CL ($F_{(2, 11)} = 11.97, p < 0.001$). Group mean normalized amplitudes for each condition are indicated at the top of each graph above each box plot. Median

⁵For example, compare the maximum amplitudes for C29 and C8 in Figure 3 – the amplitudes for C29 were an order of magnitude larger than those for C8, which would bias the mean amplitude differences between methods if the absolute amplitudes were used. A subset of ECAP waveforms for C29 (CathFM) is shown in the Supplemental Digital Content (see Figure, SDC1) to demonstrate that the waveforms were not contaminated by artifact.

normalized amplitudes for the lowest common CL for Cochlear subjects (non-parametric comparisons) were 0.15, 0.19, and 0.04 for CathFM, AnodFM, and AltPol, respectively. Post-hoc comparisons (Holm-Sidak for average across CLs and highest common CL; Tukey for lowest common CL) that were statistically significant are indicated with arrows and respective p values in each panel. In general, AnodFM yielded the largest amplitudes for Cochlear subjects. For Advanced Bionics subjects, there was no significant difference for any of the amplitude comparisons across method for the average ($F_{(2, 9)} = 0.06$, $p = 0.95$), lowest ($F_{(2, 9)} = 0.74$, $p = 0.49$), or highest CL ($F_{(2, 9)} = 0.31$, $p = 0.74$).

Figure 7 shows box-and-whisker plots for the slopes of the ECAP AGFs calculated using the normalized amplitude data. For Cochlear subjects (top panel), there was a statistically significant effect of slope ($X^2_{(2, 11)} = 8.17$, $p = 0.02$; non-parametric Friedman's RM ANOVA), with CathFM having the shallowest slope, as expected. Mean slopes are shown on each box plot; median slopes were 0.023, 0.025, and 0.025 for CathFM, AnodFM, and AltPol, respectively. Post-hoc analysis (Tukey) showed a significant difference between AnodFM and CathFM only. For the Advanced Bionics participants (bottom panel), the RM ANOVA showed no significant difference in slope across methods ($F_{(2, 9)} = 0.69$, $p = 0.5$). Mean slopes are shown on each box plot. Note that the range of slopes differ between devices because the units of measure differ between manufacturers: Cochlear slopes were calculated using CL units and Advanced Bionics slopes were calculated using μA to make the across-method comparisons more clinically meaningful within each device type.

Figure 8 shows box-and-whisker plots for the threshold data across methods. Although FS19 only had two data points for the AltPol AGF (which precluded inclusion in the group amplitude and slope analyses), his threshold data were included in Fig. 8. For Cochlear subjects (top panel), the RM ANOVA showed a statistically significant difference in threshold across methods ($F_{(2, 12)} = 12.14$, $p < 0.001$). Mean thresholds (in CL) are indicated on each box in the figure. Post-hoc comparisons (Holm-Sidak) that were statistically significant are indicated with arrows and respective p values. In general, thresholds were similar for both FM methods and highest for AltPol, consistent with the hypothesis. For Advanced Bionics recipients, there was no significant difference in threshold across methods ($X^2_{(2, 9)} = 5.09$, $p = 0.08$; non-parametric Friedman's RM ANOVA), which was not consistent with the hypothesis. Mean thresholds are shown on each box; medians were 366.7, 396.4, and 377.4 μA for CathFM, AnodFM, and AltPol, respectively.

DISCUSSION

The primary goal of this study was to separate the effects of stimulus polarity and artifact-reduction method to determine how amplitude and latency contribute to previously reported differences in ECAP waveforms between CathFM and AltPol methods. Specifically, Baudhuin et al. (2016) showed that AltPol yielded smaller amplitudes, steeper slopes of the AGF, and higher thresholds than CathFM for a group of 18 ears with Cochlear devices. The two potential hypotheses posed in the present study were: (1) the anodic-leading phase elicits a less excitatory response than the cathodic-leading phase, which when averaged together, results in smaller overall amplitudes than for CathFM; and (2) the latencies of the responses to anodic- and cathodic-leading pulses differ, which when averaged together,

result in smaller amplitudes than for either polarity alone. Results from recent studies (Macherey et al. 2008; Undurraga et al. 2010) suggested that the first hypothesis was likely not viable; therefore, the second hypothesis was adopted as the likely reason for the results reported in Baudhuin et al. (2016). In general, the results from the present study supported the second hypothesis.

Device Differences

The present study was motivated by the results from our earlier study (Baudhuin et al. 2016), which was only conducted with recipients of Cochlear devices. It was therefore important to extend the results of our earlier study to include data for Advanced Bionics recipients because, to date, comprehensive comparisons between artifact reduction methods have not been reported for this group. Only two studies (Frijns et al. 2002; Eisen & Franck 2004) have compared artifact reduction methods for Advanced Bionics recipients, and both only reported results for four subjects. Further, comparisons were generally reported descriptively rather than statistically and were not the primary focus of either study. It was not our intent to explicitly compare outcomes between devices in the present study because we had no *a priori* expectations for differences in outcomes between device manufacturers. As a result, we opted for a within-subjects design to compare polarity and artifact-reduction methods within each device type using stimulus parameters aligned with those used in the respective clinical software, which are not the same across manufacturers.

Results from the Cochlear subjects in the present study were generally consistent with our earlier findings (Baudhuin et al. 2016; note there was some overlap of subjects between the two studies). Results from the Advanced Bionics subjects, however, did not reveal significant differences in amplitude, slope, or threshold between artifact-reduction methods. It is possible that the conflicting outcomes between devices in the present study are due to stimulus differences and/or differences in electrode array placement that are inherent to each device. These differences are discussed in greater detail in the sections that follow.

Another factor to consider is the difference in duration of deafness between the two groups. The mean durations of deafness prior to implantation for the Cochlear and Advanced Bionics groups were 5.3 and 12.7 years, respectively. Although the means appear to be quite different between groups, statistical analysis revealed no significant differences in median duration of deafness (Mann-Whitney $U = 33.0$, $p = 0.05$; non-parametric Rank Sum Test due to unequal variance). Still, it is important to point out that longer durations of deafness are associated with poorer neural survival (e.g., Nadol et al. 1989). Models of the healthy human auditory nerve (Rattay et al. 2001a) suggest that both polarities are effective at stimulating the peripheral axons, but anodic stimulation more effectively activates the central axon when peripheral processes are degenerated. As a result, we would expect lesser polarity effects for shorter durations of deafness (better neural survival) and greater polarity effects for longer durations of deafness (poorer neural survival). The opposite trend was found in the present study, which suggests that either the difference in deafness duration between groups was not large enough to matter, or some other factor is responsible for the different outcomes between groups.

Hypothesis 1: Unequal Excitation between Polarities

The first potential hypothesis was that the anodic-leading pulse would have to be *less* excitatory (i.e., yield smaller amplitudes) than the cathodic-leading pulse, resulting in smaller averaged amplitudes for AltPol than for the traditional cathodic-leading FM condition. Results from this study (see Fig. 6) did not support Hypothesis 1, as anticipated from recent physiological studies in human CI recipients using various pulse designs (Macherey et al. 2008; Undurraga et al. 2010; Undurraga et al. 2013). For Cochlear devices, the anodic-leading pulse typically yielded *larger* amplitudes than the cathodic-leading pulse, consistent with an earlier study with Advanced Bionics recipients by Undurraga et al. (2010). This alone should cause AltPol ECAPs to be *larger* than CathFM due to averaging with the larger ECAPs obtained with the anodic-leading pulses. However, this was not the case. Unlike the Cochlear data, the Advanced Bionics data in the present study did not consistently show larger amplitudes for AnodFM than for CathFM, which was consistent with Macherey et al. (2008). However, the AnodFM amplitudes were not significantly *smaller* than those for CathFM for Advanced Bionics recipients, which also refuted Hypothesis 1.

Hypothesis 2: Unequal Latency between Polarities

The second potential hypothesis was that the latency difference between polarities yields a temporally smeared waveform when averaged together, resulting in smaller amplitudes and higher thresholds with AltPol compared with FM. Specifically, N1 latencies were expected to be shortest for AnodFM and longest for CathFM. As hypothesized, the shortest N1 latencies occurred for AnodFM for both device groups (see Fig. 5), consistent with prior evidence suggesting that ECAP responses to biphasic pulses are elicited primarily by the anodic phase (Macherey et al. 2008; Undurraga et al. 2010). This trend held for high stimulus levels (Fig. 5, right column), low levels (Fig. 5, middle column), and the average across a common range of levels (Fig. 5, left column). Because CathFM latencies have been shown to be longer than AnodFM, latencies for AltPol were expected to occur between those for the two FM methods due to averaging responses for the two polarities. In most cases, however, there was no significant difference in N1 latency between CathFM and AltPol (see Fig. 5; the exception was for the lowest common CL in Cochlear subjects). The lack of a significant difference between AltPol and CathFM latencies could be due to limited resolution of the sampling rates used to record the ECAPs. For Cochlear devices, the sampling rate is approximately 20,000 samples/sec (48.8- μ sec sample period); in Advanced Bionics devices, it is 56,000 samples/sec (18- μ sec sample period). The difference in average latency between AnodFM and CathFM was approximately 50 μ sec ($\sim$ 1 sample) for Cochlear subjects and 34 μ sec ($\sim$ 2 samples) for Advanced Bionics subjects, which minimizes the chance that a statistically significant intermediate latency value could occur for AltPol. Only one condition – the lowest common CL for Cochlear subjects – yielded a significant difference in latency between AltPol and CathFM. In that case, the latency for AltPol was significantly *longer* than for CathFM, rather than between the latencies of the two FM methods as hypothesized. The reason for this finding remains unclear.

Amplitudes

Although the latency differences across artifact-reduction methods exhibited similar trends between Advanced Bionics and Cochlear groups, the amplitude and threshold trends differed between devices. ECAP amplitudes were expected to be largest for AnodFM (based on results from Undurraga et al. 2010), followed by CathFM, with AltPol yielding the smallest amplitudes due to averaging waveforms with offset latencies. This expected trend was observed for the Cochlear data at high and low levels, as well as for the average across levels (Fig. 6, top row). For the data averaged across levels, all comparisons were statistically significant. For the high and low stimulus levels, AltPol yielded the smallest mean amplitudes, although the differences between CathFM and AltPol were not statistically significant. For Advanced Bionics recipients, however, there were no significant amplitude differences among methods for any of the level comparisons. This difference between devices might be due to interphase gap effects. Cochlear devices utilize an interphase gap, whereas Advanced Bionics devices do not. The interphase gap allows auditory neurons more time to initiate an action potential before the charge is removed by the opposing phase (Shepherd & Javel 1999; McKay & Henshall 2003; Ramekers et al. 2014). Thus, the longer the interphase gap, the greater the effect of the leading phase. The lack of an interphase gap (as in the Advanced Bionics devices) might reduce the impact of which polarity is presented first, and might also reduce temporal smearing associated with averaging polarity-dependent latency differences. Although it could be argued that a longer phase duration (Advanced Bionics) might show *more* effect of the leading phase than a shorter phase duration (Cochlear), it is important to understand that the neural membrane is a leaky integrator. This is why short-duration pulses are more effective than longer-duration pulses for equal charge (Loeb et al. 1983). We would therefore expect the shorter-duration pulse, in conjunction with an interphase gap, to exhibit a greater effect of the leading phase compared with a 32- μ sec/phase pulse with no interphase gap, even though in both cases the opposing (second) phase occurs 32 μ sec after the onset of the first phase. This idea is supported by the latency data in Fig. 5, where the latency differences between methods were smaller for the Advanced Bionics data than for the Cochlear data. Smaller latency differences between anodic-leading and cathodic-leading stimuli should reduce temporal smearing that will occur with averaging for AltPol, minimizing potential amplitude differences between FM and AltPol methods. The amplitude data for AB subjects in the present study are consistent with findings reported by Macherey et al. (2008), who also found similar ECAP amplitudes between cathodic-leading and anodic-leading symmetrical biphasic probes that had no interphase gap ($N = 6$ Advanced Bionics subjects). It should be noted, however, that Undurraga et al. (2010) found significantly larger ECAP amplitudes (0.5 dB on average) for anodic-leading probes than for cathodic-leading probes in four Advanced Bionics subjects, despite using the same stimuli as in Macherey et al. (2008).

Another potential reason for the difference in results between devices is the design and subsequent placement of the electrode array. The majority of the Cochlear participants (10/13) had perimodiolar arrays, whereas all of the Advanced Bionics recipients had straight arrays (only one, C40, had an electrode positioner). Modeling data from Rattay et al. (2001b) suggests limited polarity effects for the “long dendrite” model, whereas larger polarity effects are evident for the “short dendrite” model. The short dendrite model could be

used to reflect closer electrode-nerve proximity (i.e., a perimodiolar array as used with the majority of Cochlear subjects), whereas the long dendrite model could reflect farther electrode-nerve positioning (straight arrays, as those used with the Advanced Bionics subjects). Straight arrays, which occupy a mid-scalar to lateral-wall position, might therefore yield limited polarity effects compared to perimodiolar arrays.

Last, the probe rate differed between devices. Cochlear recipients used the software default rate of 80 Hz, whereas Advanced Bionics recipients were tested with a probe rate of 20 Hz (it was not possible to increase the probe rate in BEDCS to match the default rate used by Cochlear). One potential concern is that the faster rate used for Cochlear recipients could induce some adaptation of the ECAP responses (Schmidt Clay & Brown, 2007). Faster stimulation rates can increase temporal jitter and subsequently reduce ECAP amplitude. If adaptation occurs, we would expect it to occur similarly across all three methods, although we are not aware of any studies that have explicitly examined adaptation for different polarities. Regardless, if adaptation occurred, we might expect the differences across conditions for Cochlear subjects (faster rate) to be smaller than for AB subjects (slower rate), which was opposite the findings in this study. Therefore, it does not appear that the faster probe rate used for Cochlear subjects obfuscated the polarity effects that were observed.

Slopes

We anticipated that the CathFM slopes would be shallowest across the three methods. AnodFM slopes were expected to be steeper than for CathFM due to larger amplitudes (particularly at higher current levels) for AnodFM (Undurraga et al. 2010) and minimal amplitude differences near threshold (Hughes et al. 2015; see also Macherey et al. 2006 for similar findings with behavioral measures). Slopes for AltPol were also expected to be steeper than for CathFM based on results from Baudhuin et al. (2016), where thresholds were higher with AltPol. This hypothesis was generally supported for Cochlear devices in the present study (see Fig. 7). Although the difference between CathFM and AltPol was not statistically significant, it was in the predicted direction. The hypothesis was not supported for the Advanced Bionics devices. This was likely due to the lack of significant amplitude and threshold differences across methods.

Thresholds

Last, we expected ECAP thresholds to be similar for AnodFM and CathFM because polarity effects have primarily been observed only at suprathreshold levels (Hughes et al. 2015; Macherey et al. 2006). AltPol thresholds were expected to be higher than for both FM methods due to the anticipated latency differences between polarities yielding smaller amplitudes for the averaged trace. This hypothesis was supported for Cochlear subjects, but not for Advanced Bionics subjects. As noted above, although the latency differences among methods were significant for Advanced Bionics devices, the average latency differences were smaller overall than those for Cochlear devices. This, coupled with no significant amplitude or slope differences across methods, yielded no difference in threshold across methods.

General Issues Surrounding Artifact-Reduction Methods

Each of the two artifact-reduction methods described here makes certain assumptions. When these assumptions are violated, the method will not yield accurate results. For AltPol, the following assumptions are made: (1) the ECAP responses to each polarity are equal in amplitude and latency, and (2) the stimulus artifact is symmetric for each polarity. For FM, it is assumed that the masker is fully effective, yielding no response to the probe in the masker-plus-probe condition. Factors that might influence the effectiveness of the masker include: (1) a masker level that is not sufficiently high to fully drive all fibers that might be recruited by the probe into a refractory period, or (2) a masker-probe interval that is too short or too long, yielding a partial response to the probe in the masked condition that is subsequently subtracted from the probe-alone trace. If all the assumptions for both methods are correct, then we would expect that averaging the ECAPs obtained in response to both FM methods (CathFM and AnodFM) should exactly equal that obtained in using AltPol (Klop et al. 2004). Figure 9 shows three individual examples of this comparison. For the two Cochlear subjects (left and middle panels), the AltPol waveform is shown with and without (thin and thick solid lines, respectively) subtraction of the switching artifact (“d” trace). As can be seen from the figure, the additional subtraction of the switching artifact results in a slight vertical shift of the waveform, with little effect on latency or amplitude. The more important point, however, is that the average of the two FM traces (thin line with symbols) is generally larger in amplitude than for AltPol, which suggests that one or more of the assumptions listed above are violated. Klop et al. (2004) demonstrated that amplifier saturation can leave residual charge at the electrode-tissue interface, which can contaminate the ECAP response in guinea pigs. When they applied an artifact subtraction prior to the input of the amplifier, they were able to obtain similar results between AltPol and the average of the two FM methods. If the amplifier saturation is not symmetrical and the time course of the residual charge extends into the ECAP recording, the collective effects might differ across repeated sweeps that alternate in polarity versus those that are obtained with a consistent polarity. Clearly, the mechanisms underlying the differences between AltPol and FM require further investigation.

CONCLUSIONS

Taken together, the results from the present study suggest that the smaller amplitudes and higher thresholds obtained with AltPol versus CathFM in our earlier study (Baudhuin et al. 2016) are primarily due to latency differences, not polarity-dependent amplitude differences. These results suggest that AltPol is not ideal for managing stimulus artifact for ECAP recordings with Cochlear devices (note that CathFM is the default method in their software). However, averaging the responses to both FM methods does not appear to yield equivalent waveforms to those obtained with AltPol, suggesting one or more assumptions required for either method might be violated. There were no significant differences among methods for amplitude, slope, or threshold for Advanced Bionics recipients, which suggests that polarity and artifact-reduction method have little influence in these devices. We postulate that polarity effects are minimized for symmetric biphasic pulses that lack an interphase gap; we are currently investigating the combined effects of polarity and interphase gap on ECAP AGFs (Glickman et al., 2016).

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

Source of Funding: Michelle Hughes is a member of the Ear and Hearing editorial board.

This research was supported by the National Institutes of Health (NIH), the National Institute on Deafness and Other Communication Disorders (NIDCD), grants R01 DC009595 and P30 DC04662. The content of this project is solely the responsibility of the authors and does not necessarily represent the official views of the NIDCD or the NIH. Portions of this study were presented at the 8th International Symposium on Objective Measures in Auditory Implants meeting in Toronto, Canada, October 15–18, 2014. The authors thank Kirsten Euscher for assistance with data collection, Rachel Scheperle for assistance with data collection and analysis, and Leo Litvak (Advanced Bionics) and Bas Van Dijk (Cochlear) for technical assistance.

REFERENCES

- Baudhuin JL, Hughes ML, Goehring JL. A comparison of alternating polarity and forward masking artifact-reduction methods to resolve the electrically evoked compound action potential. *Ear Hear.* 2016 (*in press*).
- Brown CJ, Abbas PJ, Gantz BJ. Electrically evoked whole-nerve action potentials: Data from human cochlear implant users. *J Acoust Soc Am.* 1990; 88(3):1385–1391. [PubMed: 2229673]
- Cohen LT. Practical model description of peripheral neural excitation in cochlear implant recipients: 1. Growth of loudness and ECAP amplitude with current. *Hear Res.* 2009; 247:87–99. [PubMed: 19063956]
- Cullington HE. Managing cochlear implant patients with suspected insulation damage. *Ear Hear.* 2013; 34(4):515–521. [PubMed: 23411657]
- Eisen MD, Franck KH. Electrically evoked compound action potential amplitude growth functions and HiResolution programming levels in pediatric CII implant subjects. *Ear Hear.* 2004; 25:528–538. [PubMed: 15604914]
- Frijns JHM, Briare JJ, de Laat JAPM, et al. Initial evaluation of the Clarion CII cochlear implant: Speech perception and Neural Response Imaging. *Ear Hear.* 2002; 23:184–197. [PubMed: 12072611]
- Glassman EK, Hughes ML. Determining electrically evoked compound action potential thresholds: A comparison of computer versus human analysis methods. *Ear Hear.* 2013; 34:96–109. [PubMed: 22885406]
- Glickman, E., Hughes, M., Goehring, J., Miller, M. Effects of interphase gap and polarity in cochlear implants; Abstracts of the 2016 American Auditory Society Scientific & Technology Meeting; 2016. from https://aas.memberclicks.net/assets/final_16_posters.pdf
- Hughes, ML., Scheperle, RA., Goehring, JL. What can ECAP polarity sensitivity tell us about auditory nerve survival?. Abstracts of the 2015 Conference on Implantable Auditory Prostheses; July 12–17, 2015; Lake Tahoe, CA. 2015. p. 16
- Hughes ML, Vander Werff KR, Brown CJ, et al. A longitudinal study of electrode impedance, the electrically evoked compound action potential, and behavioral measures in Nucleus 24 cochlear implant users. *Ear Hear.* 2001; 22:471–486. [PubMed: 11770670]
- Klop WMC, Hartlooper A, Briare JJ, Frijns JHM. A new method for dealing with the stimulus artefact in electrically evoked compound action potential measurements. *Acta Otolaryngol.* 2004; 124:137–143. [PubMed: 15072415]
- Loeb GE, White MW, Jenkins WM. Biophysical considerations in electrical stimulation of the auditory nervous system. *Ann NY Acad Sci.* 1983; 405:123–136. [PubMed: 6575638]
- Macherey O, Carlyon RP, van Wieringen A, et al. Higher sensitivity of human auditory nerve fibers to positive electrical currents. *J Assoc Res Otolaryngol.* 2008; 9:241–251. [PubMed: 18288537]
- Macherey O, van Wieringen A, Carlyon RP, et al. Asymmetric pulses in cochlear implants: effects of pulse shape, polarity, and rate. *J Assoc Res Otolaryngol.* 2006; 7:253–266. [PubMed: 16715356]

- McKay CM, Henshall KR. The perceptual effects of interphase gap duration in cochlear implant stimulation. *Hear Res.* 2003; 181:94–99. [PubMed: 12855367]
- Miller CA, Abbas PJ, Robinson BK. The use of long-duration current pulses to assess nerve survival. *Hear Res.* 1994; 78:11–26. [PubMed: 7961173]
- Miller CA, Abbas PJ, Rubinstein JT, et al. Electrically evoked compound action potentials of guinea pig and cat: Responses to monopolar, monophasic stimulation. *Hear Res.* 1998; 119:142–154. [PubMed: 9641327]
- Miller CA, Abbas PJ, Robinson BK, et al. Electrically evoked single-fiber action potentials from cat: responses to monopolar, monophasic stimulation. *Hear Res.* 1999; 130:197–218. [PubMed: 10320109]
- Miller CA, Abbas PJ, Nourski KV, et al. Electrode configuration influences action potential initiation site and ensemble stochastic response properties. *Hear Res.* 2003; 175:200–214. [PubMed: 12527139]
- Nadol JB, Young Y-S, Glynn RJ. Survival of spiral ganglion cells in profound sensorineural hearing loss: Implications for cochlear implantation. *Ann Otol Rhinol Laryngol.* 1989; 98(6):411–416. [PubMed: 2729822]
- Patrick JF, Busby PA, Gibson PA. The development of the Nucleus® Freedom™ cochlear implant system. *Trends Amplif.* 2006; 10(4):175–200. [PubMed: 17172547]
- Ramekers D, Versnel H, Strahl SB, et al. Auditory-nerve responses to varied inter-phase gap and phase duration of the electric pulse stimulus as predictors for neuronal degeneration. *J Assoc Res Otolaryngol.* 2014; 15:187–202. [PubMed: 24469861]
- Rattay F, Lutter P, Felix H. A model of the electrically excited human cochlear neuron. I. Contribution of neural substructures to the generation and propagation of spikes. *Hear Res.* 2001a; 153:43–63. [PubMed: 11223296]
- Rattay F, Leao RN, Felix H. A model of the electrically excited human cochlear neuron. II. Influence of the three-dimensional cochlear structure on neural excitability. *Hear Res.* 2001b; 153:64–79. [PubMed: 11223297]
- Shepherd RK, Javel E. Electrical stimulation of the auditory nerve: II. Effect of stimulus waveshape on single fibre response properties. *Hear Res.* 1999; 130:171–188. [PubMed: 10320107]
- Schmidt Clay K, Brown CJ. Adaptation of the electrically evoked compound action potential (ECAP) recorded from Nucleus CI24 cochlear implant users. *Ear Hear.* 2007; 28:850–861. [PubMed: 17982371]
- Undurraga JA, van Wieringen A, Carlyon RP, et al. Polarity effects on neural responses of the electrically stimulated auditory nerve at different cochlear sites. *Hear Res.* 2010; 269:146–161. [PubMed: 20600739]
- Undurraga JA, Carlyon RP, Wouters J, et al. The polarity sensitivity of the electrically stimulated human auditory nerve measured at the level of the brainstem. *J Assoc Res Otolaryngol.* 2013; 14:359–377. [PubMed: 23479187]

Fig. 1.

Schematic illustrating the three stimulus conditions used in this study. Left panel: Alternating polarity averages responses to a cathodic-leading (C) and an anodic-leading (A) symmetrical biphasic pulse to eliminate artifact. Note the polarity of the artifact (gray dashed curve) inverts with inverted stimulus polarity, whereas the ECAP waveform does not invert. Middle panel: The standard forward-masking subtraction method with cathodic-leading biphasic pulses for both the masker and probe. Right panel: The forward-masking subtraction method with anodic-leading biphasic pulses for both the masker and probe. MPI, masker-probe interval; ECAP, electrically evoked compound action potential.

Fig. 2.

Example ECAP waveforms for each artifact-reduction method. CathFM, AnodFM, and AltPol waveforms are displayed in black, white, and gray symbols, respectively. The top panel shows the resulting ECAP from each artifact-reduction method for Cochlear subject F5, electrode 11, at 200 CL. The bottom panel shows the waveforms for each method for Advanced Bionics subject C8, electrode 9, at a current level of 903 μA . ECAP, electrically evoked compound action potential; CathFM, cathodic-leading forward masking; AnodFM, anodic-leading forward masking; AltPol, alternating polarity.

Fig. 3.

Individual amplitude growth functions displaying ECAP amplitude as a function of probe current level (CL or μA) from three Cochlear subjects (left column) and three Advanced Bionics subjects (right column) for all three artifact-reduction methods. Black, white, and gray symbols represent functions obtained with CathFM, AnodFM, and AltPol, respectively. Subject and electrode numbers are indicated in the bottom right corner of each panel. ECAP, electrically evoked compound action potential; CathFM, cathodic-leading forward masking; AnodFM, anodic-leading forward masking; AltPol, alternating polarity.

Fig. 4.

Illustration of how the data were derived for the group comparisons. Only the current levels that yielded non-zero amplitudes across the three artifact-reduction methods were included (indicated by the arrows in the plot). In this example for subject F5, electrode 11, the vertical dashed line at 185 CL indicates the lowest level that yielded non-zero amplitudes across the three artifact-reduction methods.

Fig. 5.

Box-and-whisker plots showing N1 latency (µsec) across methods for Cochlear (top row) and Advanced Bionics recipients (bottom row). The left column shows the average latency across levels, as described in Fig. 4. The middle column shows latency data for the lowest common current level (CL) that yielded a non-zero ECAP amplitude, and the right column shows latency data for the highest common CL. Boxes and whiskers represent the 25th/75th and 10th/90th percentiles, respectively. Dashed and solid horizontal lines represent means and medians, respectively. Filled circles represent the 5th and 95th percentile (outliers). Means for each method are listed at the top of each plot. ECAP, electrically evoked compound action potential; CathFM, cathodic-leading forward masking; AnodFM, anodic-leading forward masking; AltPol, alternating polarity.

Fig. 6.

Box-and-whisker plots displaying normalized amplitude (μV) across methods for Cochlear (top) and Advanced Bionics participants (bottom). Data are plotted as in Figure 5. Means for each method are listed at the top of each plot. CathFM, cathodic-leading forward masking; AnodFM, anodic-leading forward masking; AltPol, alternating polarity.

Fig. 7.

Box-and-whisker plots for slopes of the normalized amplitude growth functions across artifact-reduction methods for Cochlear (top) and Advanced Bionics (bottom). Means are shown on each box. CathFM, cathodic-leading forward masking; AnodFM, anodic-leading forward masking; AltPol, alternating polarity.

Fig. 8.

Box-and-whisker plots for ECAP threshold across artifact-reduction methods for Cochlear (top) and Advanced Bionics (bottom). Means are shown on each box. CathFM, cathodic-leading forward masking; AnodFM, anodic-leading forward masking; AltPol, alternating polarity.

Fig. 9.

Three individual examples of ECAP waveforms obtained with alternating polarity (AltPol; thick solid line) and the average of the two forward-masking (FM) methods (thin line with gray circles). Data are from two Cochlear recipients (left and middle panels) and one Advanced Bionics recipient (right panel). Because the switching artifact (“d” trace) is not applied by default in Cochlear’s clinical Custom Sound EP software for AltPol, those data are shown with and without the “d” trace subtraction. Data for AltPol in the Advanced Bionics recipient has the “d” subtraction applied, as is done in the clinical software.

Table 1

Participant demographics. Ages and durations are in years and months (y; m). For Cochlear devices, the CI24RE (CA) and CI512 have the perimodiolar electrode array, and the CI422 has a straight array. For Advanced Bionics devices, the CII and 90K have straight arrays (+p, with positioner).

Subject	Device	Ear	Age at CI	Dur. CI Use	Dur. Deafness	Etiology/Onset
F1*	CI24RE(CA)	L	60; 7	7; 10	11; 0	Unknown/Progressive
F2	CI24RE(CA)	R	60; 2	6; 8	10; 0	Unknown/Progressive
F5*	CI24RE(CA)	R	48; 3	5; 7	7; 0	Unknown/Sudden from established HL
F10 ^A	CI24RE(CA)	R	8; 3	8; 4	8; 3	Waardenburg Syndrome
F11 ^A	CI24RE(CA)	L	1; 10	14; 9	1; 10	Waardenburg Syndrome
F16	CI24RE(CA)	R	57; 7	2; 2	4; 0	Unknown/Congenital
FS19 ^B	CI422	R	68; 11	1; 2	2; 0	Unknown-Noise Exposure/Progressive
FS20	CI422	R	70; 3	1; 5	2; 0	Unknown-Familial/Progressive
FS26 ^C	CI422	L	54; 3	0; 4	5; 0	Unknown/Sudden SNHL
N5 ^C	CI512	R	50; 9	3; 4	1; 0	Unknown/Sudden SNHL
N6	CI512	R	82; 0	4; 10	4; 0	Unknown/Progressive
N9	CI512	R	80; 0	2; 10	7; 0	Unknown-Noise Exposure/Progressive
N11 ^B	CI512	L	67; 6	2; 8	6; 0	Unknown-Noise Exposure/Progressive
C3	90K 1J	R	18; 8	10; 4	16; 7	Unknown/Congenital
C8 ^D	CII HiFocus	L	55; 7	10; 8	3; 0	Unknown/Progressive
C26	90K 1J	R	67; 6	5; 11	14; 0	Unknown/Progressive
C29 ^E	90K 1J	R	30; 11	6; 6	20; 11	Meningitis
C39	90K 1J	L	63; 0	5; 2	0; 6	Unknown/Sudden SNHL
C40*	CII HiFocus+p	L	59; 5	12; 9	21; 0	Genetic
C42	90K 1J	R	70; 11	1; 1	2; 0	Unknown-Familial/Progressive
C45 ^E	90K 1J	L	35; 1	2; 4	25; 0	Meningitis
C46	90K 1J	L	63; 11	6; 11	13; 0	Unknown/Progressive
C47 ^D	90K 1J	R	65; 11	0; 6	10; 6	Unknown/Progressive

Author Manuscript

Author Manuscript

Author Manuscript

Author Manuscript

* Bilaterally implanted; only the ear listed was tested in this study.

A,B,C,D,E Bilaterally implanted; both ears were tested. Paired letters indicate both ears from the same subject.