Impact of Aging and the Electrode-to-Neural Interface on Temporal Processing Ability in Cochlear-Implant Users: Gap Detection Thresholds

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Abstract

Accurate processing of temporal information is critical to understanding speech through a cochlear implant (CI). This has potential implications for the growing population of CI users who are ≥ 65 years of age because of age-related auditory temporal processing deficits. The goal of this study was to measure temporal processing ability in a gap detection task in younger, middle-aged, and older CI users and to determine the relative contributions of chronological age and peripheral neural survival to performance. Single-electrode gap detection thresholds (GDTs) were measured using direct stimulation at five electrode locations and three electrical stimulation rates. The relationship between peripheral status (e.g., electrode-to-neural interface) and GDTs was assessed by the slope of the electrically evoked compound action potential (ECAP) amplitude growth function. Results showed that ECAP slope was the strongest subject-level predictor of GDTs. Steeper ECAP slopes, which are partially indicative of better peripheral function, were associated with better GDTs in younger participants. However, ECAP slope significantly interacted with stimulation rate and age, suggesting that ECAP slopes were not predictive of GDTs in middle-aged and older participants at some stimulation rates. ECAP slope was also related to age, with middle-aged and older participants exhibiting relatively shallow slopes and smaller ranges of slopes compared with younger participants. This pattern of ECAP results limited the evaluation of the independent effects of aging per se and peripheral status on temporal processing ability.

Cochlear implants (CIs) are a viable treatment option for adults of all ages who do not benefit from traditional hearing aids. Although nearly all CI users obtain significant improvements in their speech recognition performance following implantation, there is a large amount of variability in CI performance across individuals (Blamey et al., 2013; Holden et al., 2013). Some of this variability may be a result of individual differences in temporal processing ability. The signals delivered through a CI are severely degraded in the spectral domain, which requires CI users to rely primarily on cues within the temporal domain to recognize speech (Loizou, 2006;

Shannon et al., 1995). Thus, the ability to accurately process temporal changes within acoustic signals is critical for the perception of speech through a CI (Cazals et al., 1991; Sagi et al., 2009; Tyler et al., 1989). Consequently, CI users experiencing limitations in their

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ability to process temporal changes (e.g., due to age-related changes in temporal processing) may be at a disadvantage compared with younger CI (YCI) users.

Many studies have found that advancing age negatively impacts CI performance using a variety of word and sentence recognition measures (Blamey et al., 2013; Chatelin et al., 2004; Friedland et al., 2010; Sladen & Zappler, 2015; Xie et al., 2019). Sladen and Zappler (2015) measured speech recognition scores on multiple word and sentence tests in quiet and in noise for an older group (mean = 70.7 years) and a younger group (mean = 39.7 years). The groups were matched for duration of deafness (DoD) and length of CI experience. Results showed that the older group performed significantly worse than the younger group on all speech recognition measures. The largest group differences were observed in the speech-in-noise conditions with the worst signal-to-noise ratios (i.e., the most difficult conditions resulting in the poorest performance).

The negative effect of age on CI performance may be partially a result of age-related declines in temporal processing ability. Age-related temporal processing deficits in gap detection ability are well documented in older listeners with normal acoustic hearing and with hearing loss (Snell, 1997; Snell & Frisina, 2000). The gap detection threshold (GDT) is a psychoacoustic measurement that is widely used to quantify temporal acuity (Plomp, 1964; Walton, 2010). The detection of a gap is thought to involve higher level (i.e., central) auditory processes that integrate, or smooth, the temporal characteristics of incoming auditory signals over a short time period or window of between 200 and 300 ms (i.e., temporal integration; Zwislocki, 1960). In the case of a continuous signal with a brief gap inserted, the output of the temporal integration window would contain a dip in amplitude, with the size of the dip dependent on the duration of the gap. This dip in the output of the temporal integrator is theorized to cue the detection of a silent gap in an acoustic signal. In this way, the ability to detect a gap within an otherwise continuous signal is considered to be a measure of the decay of auditory sensation within the central auditory system (Penner, 1977). Support for a central locus of age-related temporal processing deficits in animal models comes from a study by Walton et al. (1998) showing that age-related deficits in temporal gap detection in mice were observed in electrophysiological recordings measured at the inferior colliculus. Support for a central locus of age-related temporal processing deficits in humans is suggested by studies that investigated the independent effects of hearing loss and age on GDTs. These studies found that gap detection ability declined with advancing age independent from peripheral hearing status (Schneider et al., 1994; Snell, 1997). Because older listeners display reduced temporal

resolution beyond what can be explained by age-related changes to the periphery, gap detection ability is often argued to be a measure of central auditory processes independent of peripheral status (Bao et al., 2020). One main purpose of this study was to examine central versus peripheral contributions to temporal processing using CI users, who could also experience age-related declines in auditory temporal acuity that are seen in older acoustic-hearing individuals.

In CI users, the typical filtering performed by the basilar membrane in the cochlea is bypassed and replaced by tonotopically spaced electrode contacts that stimulate the spiral ganglion cells (SGCs) directly. Electrical stimulation also results in increased nerve fiber synchrony and a removal of all basilar membrane filtering (Kiang & Moxon, 1972; Sachs et al., 1983), which could theoretically result in increased temporal acuity compared with normal acoustic-hearing listeners. Furthermore, GDTs can vary across electrode locations within individuals (Bierer et al., 2015), with unique patterns across different listeners. This finding suggests that GDTs in CI users may be related to the local neural population interfacing with a particular electrode location (i.e., the electrode-to-neural interface) rather than tonotopic-specific properties of auditory encoding. Therefore, CI users' temporal acuity is likely dependent on both the quality of the electrode-to-neural interface and resolution within the central auditory system.

Many CI users can obtain GDTs comparable with those obtained by normal acoustic-hearing listeners, but there is substantial individual variability in performance (Dobie & Dillier, 1985; Moore & Glasberg, 1988; Shannon, 1989). Much of the previous literature investigating gap detection ability in CI users evaluated the effect of signal-related factors on GDTs, including presentation level, place of stimulation (electrode location), and the electrical stimulation rate. GDTs vary as a function of presentation level, with poorer GDTs observed for lower presentation levels compared with higher levels (Chatterjee et al., 1998; Moore & Glasberg, 1988; Preece & Tyler, 1989; Shannon, 1989), likely due to the accompanying differences in intensity discrimination thresholds at low presentation levels (Pfingst et al., 1983). As mentioned previously, GDTs can also vary as a function of electrode location within and across individuals with no consistent pattern (e.g., Bierer et al., 2015). Another signal-related factor that can impact GDTs is the electrical stimulation rate, potentially due to the inherent difference in the interpulse interval (IPI) between low- and high-rate stimulation. The IPI is longer in low-rate stimulation and shorter in high-rate stimulation. For lower stimulation rates ≤500 pulses per second (pps), auditory neurons may phase lock to each individual pulse, which is relatively widely spaced from subsequent pulses. This could present a level of uncertainty in

discriminating between the IPI and a short temporal gap between individual pulses, which may cause GDTs to be elevated at low stimulation rates compared with high stimulation rates (Busby & Clark, 1999). Alternatively, the short IPIs that compose high-rate electrical stimulation ($\geq$1000 pps) could potentially limit gap detection ability when the interval approaches the neural refractory period, or the time it takes for a single nerve fiber to recover after firing. This could result in poor transmission of a temporal gap within high-rate stimulation if the fibers that are required to respond to the onset of the signal following the gap are unable to fire because of refractory limitations. It is also possible that the effect of stimulation rate on GDTs could vary as a function of listener age. Degeneration of peripheral auditory neurons, which occurs with advancing age (Makary et al., 2011; Otte et al., 1978), can cause altered temporal discharge patterns at high stimulation rates (Shepherd & Javel, 1997). The disruption in the temporal discharge patterns of auditory neurons at high rates could eliminate the potential benefit from high stimulation rates for detecting a silent gap in older CI (OCI) users. Therefore, the effect of the stimulation rate on GDTs could vary between CI users depending on their age and/or peripheral neural function. In addition to the signal-related factors described earlier, differences in listener-related factors, including the chronological age of the listener and the status of the electrode-to-neural interface, could also impact gap detection ability in CI users and could potentially explain some of the individual variability in performance across listeners.

An estimate of overall peripheral neural survival, or the number of remaining SGCs in the peripheral auditory system, is logically dependent upon a listener's age at onset of hearing loss and DoD. Both of these factors are likely correlated with SGC survival and have also been shown to be predictive of gap detection performance in CI users (Bierer et al., 2015; Busby & Clark, 1999). Busby and Clark (1999) measured GDTs in adolescents and young adult CI users who had early onsets of hearing loss (before 4 years of age). There was a negative correlation between age at onset of profound hearing loss and GDTs, suggesting that participants with the earliest onsets of hearing loss had the poorest gap detection performance. Bierer et al. (2015) showed that individuals with longer DoDs, and presumably poorer neural survival, had poorer GDTs compared with individuals with shorter DoDs. Conversely, Mussoi and Brown (2019) evaluated the effect of age on CI users' temporal resolution, which included psychophysical GDTs, the acoustic change complex in response to gaps, and electrically evoked compound action potential (ECAP) recovery functions. Results showed that the only measure of temporal resolution that was impacted by age was the ECAP recovery function using a pulse train masker. This finding suggested that temporal resolution for detecting silent gaps did not decline as a function of age in their group of CI users.

ECAPs reflect the synchronous firing of SGCs at a specific electrode location in response to electrical stimulation. The input–output functions (amplitude growth functions [AGFs]) of ECAP amplitude (or ABR Wave I) in response to increasing current level are predictive of peripheral neural survival in animal models, with steeper AGFs indicating more surviving SGCs at a particular cochlear location (Hall, 1990; Pfingst et al., 2015; Smith & Simmons, 1983). Each nerve fiber is thought to contribute equally to the response, which represents a "unitary response concept" for SGCs (Goldstein Jr & Kiang, 1958). Thus, the greater the number of SGCs responding to electrical stimuli, the larger the peak-to-peak amplitude of the response, and the steeper the resulting ECAP AGF. In other words, if the peak-to-peak amplitude of the ECAP is limited by a reduction in the number of neurons, an increase in current will not likely result in a large subsequent increase in the peak-to-peak amplitude of the ECAP because there are a limited number of neurons available to contribute to the neural response. However, it should be noted that the slope of the ECAP AGF can be affected by several additional factors independent of neural survival. Factors such as the distance from the electrode to the modiolus, the value of the unitary response from a single neuron, and loudness perception (e.g., central gain), all of which can vary across the electrode array and across individuals, can impact ECAP AGF slopes. While some of these factors can be controlled in animal studies, experiments in human CI recipients must consider the potential impact of these factors on the slope of the AGFs, as well as the impact of peripheral neural survival. In addition to SGC loss, neural degeneration within the peripheral system can alter the temporal discharge patterns of electrically stimulated SGCs, especially at fast stimulation rates (Shepherd & Javel, 1997). Thus, poor neural survival in CI users may limit the ability of the auditory nerve to encode a temporal gap, regardless of age.

Gap detection ability, and the impact of signal-related and listener-related variables, has been studied extensively in individuals with CIs, although it is not commonly studied within the context of auditory aging. Despite the evidence suggesting declines in gap detection performance as a function of age for acoustic-hearing listeners, age is rarely evaluated as a potential factor impacting GDTs in CI users. To evaluate the effect of age on gap detection ability, the impact of other listener-related variables, including duration of hearing loss and peripheral neural survival, was also taken into account. In the current study, electrophysiological techniques (ECAPs) were used to probe the electrode-to-neural interface to control

for potential differences in peripheral neural survival between younger and older participants.

The goal of this study was to investigate the effect of age among CI users on gap detection ability at different electrical stimulation rates and to explore the impact of other potential covariates to age (i.e., the electrode-to-neural interface, which is related to peripheral neural survival) on GDTs. It was hypothesized that OCI participants would demonstrate poorer GDTs compared with YCI participants because of age-related auditory temporal processing limitations. OCI participants were also hypothesized to have shallower ECAP AGFs compared with YCI participants potentially due to age-related reductions in SGCs, which in turn could indirectly impact GDTs. Thus, it was also hypothesized that independent effects from central aging and peripheral status on measured GDTs would be observed.

Method

Participants

Thirty CI users were recruited to represent a wide range of ages across the adult life span. Participants' ages ranged from 20 to 83 years (mean = 54.3 ± 19.1 years). Participant demographics are provided in Table 1. All participants passed a cognitive screening for dementia with a score of ≥22 on the Montreal Cognitive Assessment (Nasreddine et al., 2005). A Montreal Cognitive Assessment score of 22 to 25 indicates that an individual is at risk for mild cognitive impairment (Cecato et al., 2016). Being considered at risk for mild cognitive impairment did not preclude anyone from participating in this study because (a) participants' age is of primary importance in this experiment and (b) excluding older potential participants who are considered at risk of cognitive impairment, many of whom were in their 80s, would limit the recruiting potential for older participants. All participants were implanted with Cochlear-brand devices, primarily with perimodiolar electrode arrays, which are intended to sit in close proximity to SGCs and make electrophysiological measurements more feasible. All participants had at least 6 months of CI experience.

Stimuli and Procedure

Gap Detection Thresholds. All stimulus presentation was performed with direct stimulation of the CI electrode array using the Nucleus Implant Communicator (NIC2) and a Cochlear-brand L34 research sound processor. Direct stimulation procedures bypass participants' external sound processors and control stimulation to the electrode array using a computer. This method allows for precise stimulation at the single-electrode level. Experimental stimuli were 300-ms constant-amplitude pulse trains with a 25-μs phase duration and an 8-μs interphase gap. Monopolar stimulation was used. GDTs were measured for five single electrodes (4 [basal], 8, 12, 16, and 20 [apical]) at three stimulation rates (500, 1000, and 4000 pps) using a three-interval, two-alternative forced-choice adaptive procedure (Levitt, 1971). The three-down, one-up adaptive procedure, which targeted a 79.4% threshold level, was terminated after 10 reversals with the GDT calculated as the geometric mean of the last six reversals. The initial gap duration was 100 ms and decreased by a factor of five until the first two reversals, after which the gap duration was decreased by a factor of two. This procedure was repeated at least three times for each condition on each electrode, and more trials were tested if the GDT between trials varied by more than 2 ms. The final GDT for each electrode was an average of the results of all three runs. The gaps were inserted into the pulse-train stimuli by deleting a number of individual pulses from the middle of the target stimulus to create silent gaps of varying duration. Direct stimulation best practices were followed to perform the experiments (Litovsky et al., 2017). The pulse-train stimuli were presented at the most comfortable level (MCL) for each electrode as reported by the participant. MCL was measured using standard CI mapping procedures for each test electrode for every stimulation rate. No feedback was provided to participants during the adaptive procedure. The presentation of stimuli was blocked for different stimulation-rate conditions; the order of the electrodes tested in each rate block was randomized. The order of the conditions and electrodes tested was randomized across participants.

ECAP AGFs. To isolate age-related changes in temporal processing ability due to reduced neural survival or a poor electrode-to-neural interface, ECAP AGFs were measured at the same five electrode locations that were tested in the behavioral measurements using research processors and Custom Sound EP software provided by Cochlear Ltd. ECAP measurements used the forward-masking procedure (Abbas et al., 1999) with an 80-pps probe rate, 50-μs phase duration, and a 7-μs interphase gap. Measurements taken from the CI24M and CI24R electrode arrays used a 55-μs recording delay and 60 dB recording gain. Measurements from the CI24RE and more recent arrays used a 122-μs delay and 50 dB gain. The delay and gain parameters represent the default recording parameters for the different electrode arrays; all stimulation parameters (probe and masker parameters) for the ECAP measurements were consistent across all electrode types. The masker pulse had the same stimulation parameters as the probe pulse with a +10 clinical unit (CU) offset in input level (the masker pulse was 10 CUs higher than the probe pulse). This

Table 1. Participant Demographics.

Participant	Age	Gender	Age at HL onset	Duration of HL	Etiology	Device
CCG	20	M	0	19	Unknown	CI422
CDE	23	M	0	12	Connexin 26	CI24RE(CA)
CAR	24	M	4	14	Hereditary	CI24RE(CA)
CBX	27	F	0	22	Waardenburg syndrome (type 2)	CI24RE(CA)
CDA	27	F	0	20	Connexin 26	CI512(CA)
CAT	29	M	10	9	Hereditary	CI24RE(CA)
CDF	30	F	0	16	Hereditary	CI24RE(CA)
CBP	37	F	5	15	Hereditary	CI24M
CCS	41	M	1	37	Meningitis	CI422
CBW	45	M	26	5	COGAN syndrome	CI24R(CS)
CAP	50	F	38	1	Hereditary	CI24RE(CA)
CAS	54	F	41	3	Hereditary	CI24RE(CA)
CAW	54	M	0	47	Unknown	CI24RE(CA)
CCF	55	F	48	5	Unknown	CI422
CAQ	58	F	22	29	Unknown	CI24RE(CA)
CBK	58	F	20	31	Unknown	CI24RE(CA)
CBF	59	M	5	47	Hereditary	CI24RE(CA)
CBG	64	F	4	53	Rh incompatibility	CI512(CA)
CAJ	65	F	0	47	Unknown	CI24M
CBR	65	F	0	57	Unknown	CI24RE(CA)
CCR	69	F	2	60	Measles	CI24RE(CA)
CAK	70	M	57	2	Unknown	CI24R(CS)
CAF	71	F	5	49	Unknown	CI24RE(CA)
CAM	72	F	40	24	Unknown	CI24RE(CA)
CAO	72	F	3	63	Rheumatic fever	CI512(CA)
CBT	75	F	50	20	Unknown	CI24RE(CA)
CCA	76	M	70	1	Ototoxicity	CI512(CA)
CAD	77	M	55	10	Unknown	CI24RE(CA)
CBC	79	F	35	41	Unknown	CI24RE(CA)
CBB	83	M	77	2	Aging	CI24RE(CA)

Note. HL=hearing loss; duration of HL = number of years that hearing loss of any degree was experienced prior to implantation.

procedure takes advantage of the refractory properties of auditory nerve fibers to measure the relatively small neural response without signal artifact. ECAP stimulation parameters were the same for all electrode locations and all participants. The presentation levels for ECAP measurements started below the threshold level for each electrode and increased in 5 CU steps up to the maximum comfort level. Participants were instructed to inform the tester when the loudness reached a level at which any further increase would cause the stimulus to be uncomfortable. ECAP AGFs were measured once on each test electrode. Linear ECAP slope was computed by transforming the input values from the logarithmic CU scale to a linear charge scale (nC). Linear input values in nC were used to calculate the slope of the linear input–output function for each electrode.

Statistical Analysis

A three-level linear mixed-effects (LME) model was used to examine the effects of stimulation rate, chronological age, age at onset of hearing loss, duration of hearing loss, and ECAP AGF slope on GDTs. The model-building approach followed the recommendations by Hox et al. (2017). First, an intercept-only model was used as a benchmark. Second, the stimulation rate variable (three levels: $-1 = 500$ pps, $0 = 1000$ pps [reference level], $1 = 4000$ pps) and electrode location variable (5 levels: 4, 8, 12 [reference level], 16, and 20) were added as level-1 predictors to the fixed effects structure. The improvement in model fit with the addition of the fixed effect variables was compared with the intercept-only model with a χ^2 significance test (α level = .05). Next, the main effects and interactions for all level-2 predictors (age group, age at onset, duration of hearing loss, and ECAP slope) were added to the fixed effects. Values for continuous level-2 predictors were transformed into standardized values (z scores) before being entered into the model. Thus, results for continuous level-2 predictors (i.e., ECAP slopes) represent changes to GDTs with increasing or decreasing a particular variable on a standard deviation (SD) scale. Nonsignificant level-2

predictors were then removed to create the most parsimonious fixed effects structure.

The random effects were structured to represent a three-level model in which the multiple electrode locations were nested within subject. Because each subject was tested at five electrode locations, measurements at the electrode level are not independent of one another. Therefore, by specifying that electrodes were nested within subjects, ECAP slopes could be added to the model as a level-2 predictor. In this way, ECAP slopes for individual electrodes were recognized as an attribute of that electrode within its respective subject.

Next, random slope variation for the level-1 predictor (stimulation rate) was added to the model. Cross-level interactions (interactions between fixed level-1 and level-2 predictors) were then added to the fixed effects structure. To appropriately interpret these interactions, both the main effect and any lower-level interaction term remained in the model regardless of significance. Lastly, the model residuals were checked to verify the goodness of fit and that LME assumptions were met. When GDTs were analyzed on a linear scale, the variance of the residuals was not normally distributed across all fitted values, suggesting that the assumption of homoscedasticity had been violated. To make the measured GDT values appropriate for a linear mixed model approach, GDTs were log-transformed and reanalyzed using the same model building procedure as described earlier.

Results

Average GDTs obtained at each stimulation rate for three age groups are shown in Figure 1. The age groups shown in Figure 1 were separated by commonly used categorical age limits. Thus, the YCI group represented the 10 participants who were ≤45 years of age, the middle-aged CI (MCI) group represented the 10 participants who were between 46 and 64 years of age, and the OCI group represented the 10 participants who were ≥65 years of age. Although the average group data plotted in Figure 1 showed age effects, the main effect of age was not statistically significant when accounting for the effect of ECAP slope on GDTs. The results of the final LME model, which accounted for the effect of ECAP slope as well as the interactions between ECAP slope, age-group, and stimulation rate, are shown in Table 2.

The average GDT (intercept coefficient) was 3.75 ms (log-transformed value = 1.32), which represents the average threshold measured at the reference stimulation rate of 1000 pps at Electrode 12, for a participant in the YCI group with an average ECAP slope. There was a significant main effect of stimulation rate on GDTs. Compared with the reference rate (1000 pps), GDTs measured at 500 pps significantly increased (worsened) by approximately 13% ($p < .001$). When measured at
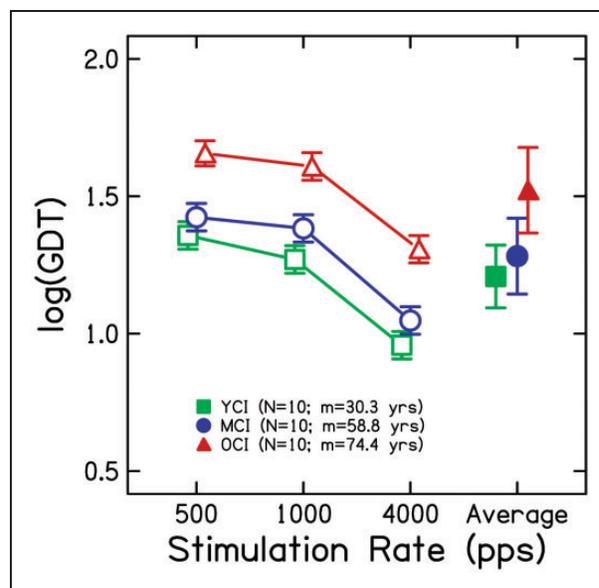
Figure 1. GDTs (Log-Transformed) for Each Age Group Plotted as a Function of Electrical Stimulation Rate. Green squares represent YCI group. Blue circles represent MCI group. Red triangles represent OCI group. Filled symbols represent group averages across all stimulation rates. Error bars = ±1 standard error. GDT = gap detection threshold; YCI = younger cochlear implant; MCI = middle-aged cochlear implant; OCI = older cochlear implant.

4000 pps, GDTs significantly decreased (improved) by approximately 26% compared with the reference rate ($p < .001$). This pattern suggests a significant improvement in GDTs with increasing stimulation rate. There was also a significant main effect of ECAP slope. With every 1 SD increase in ECAP slope, GDTs for the YCI group decreased (improved) significantly by approximately 12% ($p = .036$) at the reference rate. Thus, electrodes that exhibited steeper ECAP AGFs had generally better GDTs, at least in the YCI group.

There were significant three-way interactions of 500 pps × ECAP slope × MCI group and 500 pps × ECAP slope × OCI group. These interactions are highlighted in Panels D and G of Figure 2 for the MCI and OCI groups, respectively, in comparison with Panel B for the YCI (reference) group. GDTs (log-transformed) for each electrode from each participant are plotted at each stimulation rate. These three-way interactions suggested that the association of better GDTs with a steep ECAP slope does not hold in the MCI and OCI groups. In other words, the relationship between GDTs and ECAP slope was weakened in older participants. These interactions, however, could be driven by a reduction in the variability in ECAP slope values for participants in the MCI and OCI groups, which were generally shallower in comparison with participants in the YCI group.

Table 2. Final LME Model for GDTs (Log-Transformed).

Fixed effects	Coefficient estimate	SE	t	p
Intercept	**1.32**	**0.14**	**9.65**	**<.001**
Rate:				
500 pps	**0.13**	**0.06**	**2.04**	**.049**
1000 pps	Reference			
4000 pps	**−0.31**	**0.07**	**−4.32**	**<.001**
Electrode:				
4	**0.26**	**0.06**	**4.31**	**<.001**
8	0.04	0.06	0.68	.497
12	Reference			
16	−0.07	0.06	−1.12	.264
20	−0.06	0.06	−1.05	.294
ECAP slope (standardized)	**−0.12**	**0.06**	**−2.12**	**.036**
Age-group:				
YCI	Reference			
MCI	−0.02	0.19	−0.11	.910
OCI	0.08	0.19	0.40	.695
Interactions				
500 pps × MCI	0.04	0.09	0.48	.637
4000 pps × MCI	0.01	0.10	0.12	.907
500 pps × OCI	0.09	0.09	1.00	.325
4000 pps × OCI	0.11	0.11	1.02	.317
500 pps × ECAP	0.02	0.04	0.47	.638
4000 pps × ECAP	0.01	0.04	0.26	.799
ECAP × MCI	0.22	0.12	1.87	.064
ECAP × OCI	−0.12	0.13	−0.92	.360
500 pps × ECAP × YCI	0.02	0.04	0.47	.638
4000 pps × ECAP × YCI	0.01	0.04	0.26	.799
500 pps × ECAP × MCI	**0.29**	**0.08**	**3.45**	**<.001**
4000 pps × ECAP × MCI	0.06	0.09	0.67	.501
500 pps × ECAP × OCI	**0.34**	**0.08**	**4.27**	**<.001**
4000 pps × ECAP × OCI	0.17	0.09	1.92	.060

Random effects	Variance			SD
Subject (intercept)	0.139			.373
500 pps	0.017			.133
1000 pps	Reference			
4000 pps	0.026			.163
Subject/electrode (intercept)	0.057			.239
500 pps	0.031			.176
1000 pps	Reference			
4000 pps	0.038			.195
Residual	0.027			.16

Note. ECAP = electrically evoked compound action potential; YCI = younger cochlear implant; MCI = middle-aged cochlear implant; OCI = older cochlear implant; pps = pulses per second.
Bold text indicates significance at the p < .05 level.

It is clear from Figure 2 that most of the participants who displayed relatively steep ECAP slopes (values >0 on the x axis) belonged to the YCI group. Figure 3 shows ECAP slopes (µV/nC) plotted as a function of chronological age. In general, ECAP slopes declined (became more shallow) with increasing age. In addition, there was substantial overlap in ECAP slope values across the MCI and the OCI groups, with the majority of those values falling below the mean ECAP slope. The YCI group, however, had a much larger range of slope values, with the majority falling above the mean. When ECAP slope values were transformed to z scores (standardized) for statistical analysis purposes, the YCI group had eight instances in which the slope was ≥2 SD above the mean. The proportion of standardized ECAP slopes falling *above* zero (the mean) in each group were 75.5% for YCI, 26.1% for MCI, and only 12.5% for OCI.

Lastly, there was a significant main effect of electrode location for Electrode 4, suggesting that GDTs
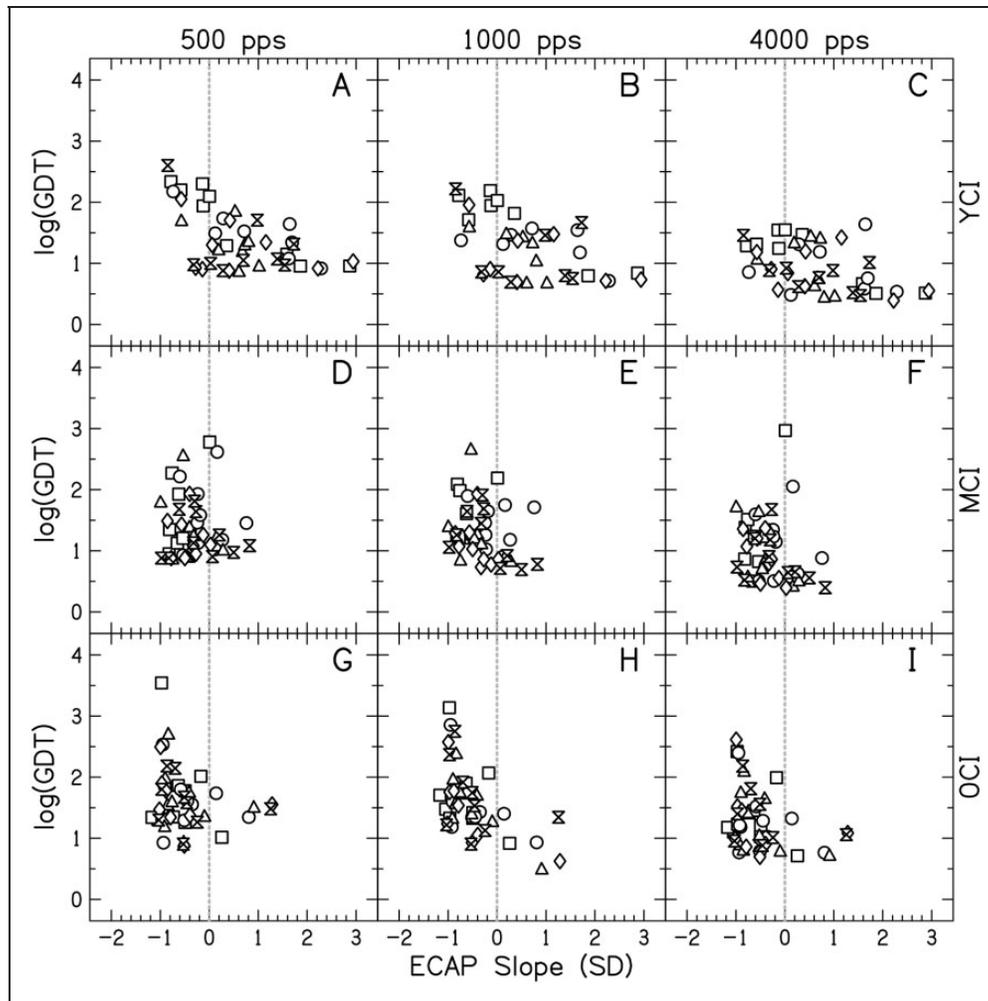
Figure 2. GDTs (Log-Transformed) Plotted as a Function of ECAP Slope for the Three Stimulation Rate Conditions (Columns).
Participants were separated into three age groups (rows) to highlight the interactions between rate, ECAP slope, and age. YCI group
($N = 10$) represents participants ≤ 45 years of age. MCI group ($N = 10$) represents participants between the ages of 46 and 65 years. OCI
group ($N = 10$) represents participants ≥ 66 years of age.
GDT = gap detection threshold; ECAP = electrically evoked compound action potential; OCI = older cochlear implant; MCI = middle-
aged cochlear implant; YCI = younger cochlear implant.

measured on Electrode 4 were approximately 30%
higher (worse) compared with Electrode 12 (reference;
$p < .001$). Post hoc comparisons between Electrode 4
and the other electrode locations revealed that GDTs
measured on Electrode 4 were significantly higher
(between 19 and 28% higher) compared with all other
electrodes. There were no significant interactions
between electrode location and any other variables.

Discussion

This study investigated the effects of chronological age and
peripheral neural survival (estimated by ECAP slope) on
gap detection ability measured at different electrical stim-
ulation rates in adult CI users. The average measured GDT
was 3.1 ms in the YCI group, 3.7 ms in the MCI group, and

5.4 ms in the OCI group. These results are within the range
of GDTs that could be expected from a group of acoustic-
hearing listeners with a similar range of ages (Plomp, 1964;
Schneider et al., 1994), as well as from a group of CI users
(Shannon, 1989). Participants in the YCI group with elec-
trodes that exhibited steeper ECAP slopes had better
GDTs in general, but this ECAP effect was not observed
for the MCI and OCI groups at all stimulation rates. In
other words, the association of better GDTs with steeper
ECAP slopes was diminished with advancing age. The
results of this study suggest that there are both peripheral
and central influences on gap detection ability in CI users.
The effect of chronological age above and beyond the
impact of peripheral neural survival remains unclear due
to an apparent decline in ECAP slope concomitant with
advancing age.
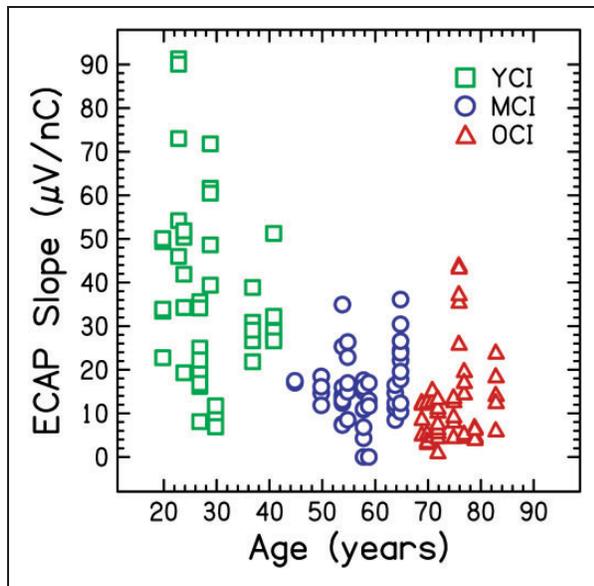
Figure 3. ECAP Slope Values (Expressed in μV/nC) Plotted as a Function of Chronological Age. Green symbols represent the YCI group ($N = 10$). Blue symbols represent the MCI group ($N = 10$). Red symbols represent the OCI group ($N = 10$). Each point on the figure represents an ECAP slope collected from a single electrode; thus, there are five data points per participant, one from each electrode location.
ECAP = electrically evoked compound action potential; YCI = younger cochlear implant; MCI = middle-aged cochlear implant; OCI = older cochlear implant.

Signal-Related Factors: Electrode Location and Stimulation Rate

As expected, GDTs varied across electrode locations within individuals. This result is consistent with previous studies that measured GDTs at multiple electrode locations along the array (Bierer et al., 2015; Garadat & Pfingst, 2011), suggesting a variation in temporal processing ability at different cochlear positions within the same CI user. The current results, however, revealed that GDTs obtained from the most basal electrode (Electrode 4) were higher (worse) compared with the other more apical electrodes. Measurements obtained from basal electrodes can be unpredictable and often relatively poor compared with other electrode locations in the context of single-electrode psychoacoustic experiments (e.g., McDermott & McKay, 1994). Clinical mapping procedures for establishing comfortable loudness levels for basal electrodes can also be challenging. In addition, SGC degeneration in individuals with hearing loss is more severe in the basal half of the cochlea (Zimmermann et al., 1995). Variables such as these, which may be specific to the basal portion of the cochlea, could result in poorer GDTs, either because of relatively poor peripheral neural survival in that location, or

because of potentially questionable MCLs that were established during mapping. Many participants expressed their dislike for listening to single-electrode stimulation at Electrode 4, which they described as very high pitched. However, there was no consistent pattern for the effect of electrode location on participants' MCL.

Results showed a significant improvement in GDTs with increasing the stimulation rate (Figure 1 and Table 2). On average, GDTs improved by more than 2 ms using a 4000-pps signal compared with a 500-pps signal. A primary difference between high- and low-rate electrical stimulation is the IPI, which defines the time interval between individual biphasic pulses. At 500 pps, the IPI is 2 ms. At 4000 pps, the IPI is reduced to only 0.25 ms. The presence of a longer IPI could introduce a level of uncertainty for discriminating a short temporal gap inserted into an otherwise continuous pulse train from the intervals between consecutive pulses. Shorter IPIs could also contribute to a "smoother" percept for pulsatile stimulation rather than a "rough" percept with longer IPIs (Busby & Clark, 1999), resulting in a more salient gap. This result is somewhat inconsistent with previous psychoacoustic studies that evaluated the effect of electrical stimulation rate on gap detection ability. Busby and Clark (1999) measured GDTs in a group of prelingually deafened CI users to investigate the effects of signal-related factors (including stimulation rate) and listener-related factors (including DoD and duration of CI use). On the group level, there was no significant effect of stimulation rate on GDTs; however, 2 of the 15 participants tested showed significant improvements at the highest stimulation rate of 1000 pps compared with the lower rates (200 and 500 pps). In the current study, GDTs significantly decreased with each increase in stimulation rate (from 500 to 1000 pps, and from 1000 to 4000 pps). Therefore, it is possible that stimulation rate could have impacted results in the Busby and Clark study if a higher rate (i.e., 4000 pps) was tested, or if more participants were included in their data set. In addition, participants in the Busby and Clark study were recruited based on onset of hearing loss to include only implantees with prelingual hearing loss. The current study, however, recruited participants based on chronological age. As a result, participants in the Busby and Clark study were younger (between 10 and 21 years of age who were implanted as children) compared with those in the current study. This creates potential confounds in participants' etiologies and age at implantation in comparison with the current study, which recruited participants with a variety of ages at which hearing loss was acquired. In addition, because loudness balancing was not performed across stimulation rates, it is possible that slight differences in loudness

across rates could have contributed to the difference in GDTs for varying stimulation rates.

Listener-Related Factors: Age and ECAP Slope

Age group and ECAP AGF slope were identified as the two listener-related factors that significantly predicted GDTs in this group of CI users (Table 2). In general, steeper (higher) ECAP slope values were associated with better GDTs for participants in the YCI group. Apart from the effect of stimulation rate and electrode location, ECAP slope was the strongest predictor of GDTs. However, the effects of stimulation rate and ECAP slope significantly interacted with the age of the listener.

Results revealed significant three-way interactions between 500 pps $\times$ ECAP slope $\times$ MCI and 500 pps $\times$ ECAP slope $\times$ OCI. Although steep ECAP slopes predicted better GDTs at the reference rate of 1000 pps for participants in the YCI group, this relationship did not hold for the MCI and OCI groups at 500 pps. When age-group was considered, increases in age removed the association of better GDTs with steeper ECAP slopes. This result could be caused by a limited number of participants in the MCI and OCI groups with steep ECAP slopes. Figure 3 shows ECAP slope data for individual participants in each age-group. More than 75% of the standardized ECAP slopes collected from YCI participants fell above zero (the mean ECAP slope for all participants), whereas only 12.5% of OCI participants had ECAP slopes that fell above the mean. This result supports the hypothesis that older participants have shallower ECAP slopes compared with younger participants, presumably because of an age-related reduction in SGCs. However, it is important to note that ECAP AGF slopes can be affected by multiple factors that are independent of neural survival, including peripheral factors (e.g., electrode-to-modiolar distance) as well as central factors (e.g., central gain for loudness perception). Although many of these factors can be carefully controlled in animal models, this is not the case for human experiments.

The current study used ECAP AGF slope to probe the electrode-to-neural interface as it relates to neural survival. This is an imperfect association, however, as there are other factors that may confound the relationship between ECAP slope and peripheral neural survival. In addition, the limited range of ECAP slopes obtained from older and middle-aged participants precluded a thorough analysis of chronological age per se as a *central* effect versus ECAP slope as a *peripheral* effect. The limited range of ECAPs in the two older groups suggests that the process of aging impacts the peripheral auditory system in CI users. The data also suggest that this presumed age-related decline in peripheral neural survival co-occurs with reduced gap detection ability,

which is hypothesized to be a measure of central auditory temporal processing. It is still possible that there is a central contribution of age above and beyond any peripheral contribution, which would be consistent with data from acoustic-hearing listeners and from animal models (e.g., Walton et al., 1998).

Mussoi and Brown (2019) conducted a similar experiment to the current study, which measured GDTs in one younger group ($N = 10$, mean age = 27.8 years, range = 18 to 40 years) and one older group ($N = 10$, mean age = 74.8 years, range = 68 to 82 years) of CI participants. Unlike the current study, the groups were matched for the DoD prior to implantation. Peripheral changes in temporal processing were evaluated with ECAP recovery functions following a single biphasic pulse as well as following a constant-amplitude pulse train. Mussoi and Brown did not find a significant effect of age on GDTs. The only metric that revealed an age effect was the ECAP recovery function following a pulse train masker, indicating that OCI participants had longer neural recovery times compared with younger participants. This result is similar to the current study in that a main effect of peripheral status, or ECAP results, was significant while the effect of age was only significant within the context of stimulation rate and ECAPs. Additional differences in the experimental design and statistical analyses between the Mussoi and Brown study and the current study may have contributed to different conclusions. Mussoi and Brown (2019) obtained measurements from a single, midarray electrode at a single stimulation rate of 400 pps. The current study, however, measured GDTs on five electrode locations, which provided a wider array of responses produced by within-subject variation in the electrode-to-neural interface. The current study also tested three stimulation rates, all of which were higher than the rate used in Mussoi and Brown, which also may have contributed to different results.

The effect of chronological age on CI outcomes is often confounded by differences in the age at onset of hearing loss and the etiology of deafness between age groups. YCI participants tend to have earlier onsets of hearing loss and are more likely to have hearing loss with a genetic component. It is possible that etiology may also play a role in the electrode-to-neural interface. A larger sample of participants would be required to conduct a thorough investigation of the impact of age that is independent from onset and etiology confounds. In addition, ECAP AGFs are just one of many ECAP measurements. Peripheral status can also be estimated by other types of ECAP assessments, including recovery functions, spread of excitation, and rate adaptation. The use of a different metric for estimating peripheral neural survival, either by a different ECAP assessment or by using imaging techniques (e.g., CT scans), may be

more sensitive and could expand the range of responses from an older group.

Conclusions

This study evaluated the effect of age on gap detection ability at a variety of electrical stimulation rates. It was hypothesized that results would show a general age-related decline in central temporal processing ability. Age-related changes in peripheral status or the electrode-to-neural interface were also expected to impact the results for behavioral measures of central temporal processing. Peripheral status, which was inferred from ECAP AGF slopes, significantly impacted gap detection ability, with steeper slopes predicting better GDTs for younger participants. When a signal-related factor (stimulation rate) and an additional listener-related factor (age) were also considered, all three factors significantly predicted gap detection ability. Specifically, the association between better GDTs and steeper ECAP slopes was eliminated for middle-aged and older participants at some stimulation rates. This result is likely due to a limited range of ECAP (mostly shallow) slopes obtained from middle-aged and older participants. The apparent negative impact of age on peripheral auditory status limited the evaluation of the independent effects from *central* aging and *peripheral* aging on auditory temporal processing ability for detecting silent gaps. This is an important area for future research with the objective of quantifying the relative contributions of central versus peripheral factors in auditory aging.

Declaration of Conflicting Interests

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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