

Speech Perception Ability in Noise is Correlated with Auditory Brainstem Response Wave I Amplitude

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Abstract

Background: Difficulty understanding speech in background noise is a common complaint of individuals with sensorineural hearing loss. Recent animal studies suggest this difficulty may be due, in part, to spiral ganglion cell degeneration related to aging or noise exposure. Although auditory brainstem response (ABR) thresholds and standard clinical audiometric tests are minimally affected by neuronal degeneration, the amplitude of wave I of the ABR is correlated to spiral ganglion cell density.

Purpose: This study hypothesized that wave I amplitude was correlated to speech-in-noise performance. To test this, the relationships between wave I amplitude, age, and speech perception ability were analyzed in human participants.

Research Design: This is a correlational study.

Study Sample: A total of 101 ears from 57 adults ranging in age from 19 to 90 yr with a pure-tone average of 45 dB HL or better were examined in this study. Only individuals with no history of neurological disease and ears without any evidence of conductive involvement were included.

Data Collection and Analysis: Speech perception was measured in quiet using NU-6 word lists and in background noise using the QuickSIN. Ear canal electrodes were used to obtain ABR waveforms from each ear and the amplitude of wave I was measured as the absolute difference in voltage between the peak of the wave and the following trough. Speech perception performance in quiet and in background noise were both modeled using a linear mixed model with the covariates age, four-frequency pure-tone average ($_4f$ PTA), wave I amplitude, and the interaction between $_4f$ PTA and wave I amplitude. ABR wave I amplitudes were modeled using a linear mixed model with age and $_4f$ PTA as the covariates. The correlation between the right and left ears of the same participant were modeled using random effects.

Results: The results indicate that reduced ABR wave I amplitudes are (1) related to increased age, (2) associated with decreased speech-in-noise performance, with the greatest effects in individuals with poorer pure-tone thresholds, and (3) not correlated to speech perception in quiet.

Conclusions: Reduced ABR wave I amplitude, an indicator of cochlear neuronal degeneration, is associated with decreased speech perception ability in noise, with a more pronounced effect in ears with poorer pure-tone thresholds, but does not appear to contribute to decreased speech perception in quiet.

Key Words: Auditory brainstem response, auditory nerve, sensorineural hearing loss, cochlear neuronal degeneration, speech perception, speech-in-noise

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Abbreviations: ABR = auditory brainstem response; DPOAE = distortion product otoacoustic emissions; $_4$ fPTA = four-frequency pure-tone average (average of pure-tone thresholds at 0.5, 1, 2, and 4 kHz); SNR = signal-to-noise ratio; SR = spontaneous rate

INTRODUCTION

Even when wearing hearing aids, individuals with hearing loss often have difficulty understanding speech-in-noise because amplifying sound improves the audibility, but not the clarity, of speech. Recent animal studies suggest that partial loss of spiral ganglion neurons may explain why some individuals have more difficulty understanding aided speech than would be expected based on their pure-tone audiogram. Because partial neuronal loss is not accurately measured by standard audiometric tests, if this type of loss is shown to negatively impact auditory perception in humans, it will be important to develop noninvasive clinical measures to assess spiral ganglion cell loss.

Animal studies show that moderate noise exposure can cause permanent loss of spiral ganglion neurons even when hair cell function recovers (Kujawa and Liberman, 2009; Lin et al, 2011). In both mice and guinea pigs, initial synaptic degeneration is evident by 24 hr after noise exposure and is followed by degeneration of spiral ganglion cell bodies that occurs over the course of several months to years, depending on the species. Even after up to a 50% loss of spiral ganglion cells, there are no permanent changes in distortion product otoacoustic emission (DPOAE) and auditory brainstem response (ABR) thresholds (Kujawa and Liberman, 2009; Lin et al, 2011; Furman et al, 2013). A similar pattern of synaptic degeneration followed by loss of spiral ganglion cells is seen in aging mice, with significant synaptic losses occurring before changes in DPOAE or ABR thresholds or decreases in hair cell number (Sergeyenko et al, 2013).

Previous studies in mice, gerbils, and guinea pigs show that the amplitude of wave I of the ABR is correlated with the number of surviving spiral ganglion neurons, with smaller amplitudes indicating greater neuronal loss (Kujawa and Liberman, 2009; Earl and Chertoff, 2010; Lin et al, 2011). This reduction in wave I amplitude is observed even in the absence of any permanent shift in DPOAE or ABR thresholds (Kujawa and Liberman, 2009; Lin et al, 2011; Furman et al, 2013). Wave I of the ABR is a far-field response produced by the summed activity of spiral ganglion nerve fibers (Hashimoto et al, 1981; Møller and Jannetta, 1981; Melcher and Kiang, 1996). A reduction in ABR wave I amplitude with age has been demonstrated in humans (Konrad-Martin et al, 2012) and is consistent with a human temporal bone study showing a 30% loss of spiral ganglion cells over a lifespan of 90–100 yr (Makary et al, 2011).

In this study, ABR wave I amplitude was used as a noninvasive measure of spiral ganglion neuronal survival in human participants to examine the impact of spiral gan-

glion cell loss on speech perception performance in quiet and in background noise. The results show a reduction in speech-in-noise perception ability for smaller wave I amplitudes that is dependent on pure-tone average, with a stronger relationship between wave I amplitude and speech-in-noise performance in individuals with poorer thresholds. This suggests that spiral ganglion fiber loss has a negative impact on speech perception in noise and the effect is more pronounced in individuals with elevated pure-tone thresholds. In contrast, reduced wave I amplitude was not correlated with speech perception performance in quiet.

MATERIALS AND METHODS

Participants

Fifty-seven English-speaking adults (35 females and 22 males) age 19–90 yr (mean 48.6 yr) with a four-frequency pure-tone average ($_4$ fPTA, average of pure-tone thresholds at 500, 1000, 2000, and 4000 Hz) ranging from –1.25 to 38.75 dB HL (mean 16.26 dB HL) participated in this study. Both the right and left ears from 44 participants were included in the analysis. Only a single ear met the inclusion criteria in the remaining 13 participants. Individuals with a history of acoustic neuroma or neurodegenerative disease were excluded from the study as well as participants who could not successfully repeat the sentences from the QuickSIN test (Killion et al, 2004) at a 25-dB signal-to-noise ratio (SNR). Pure-tone air conduction thresholds from all the ears included in the study are plotted in Figure 1.

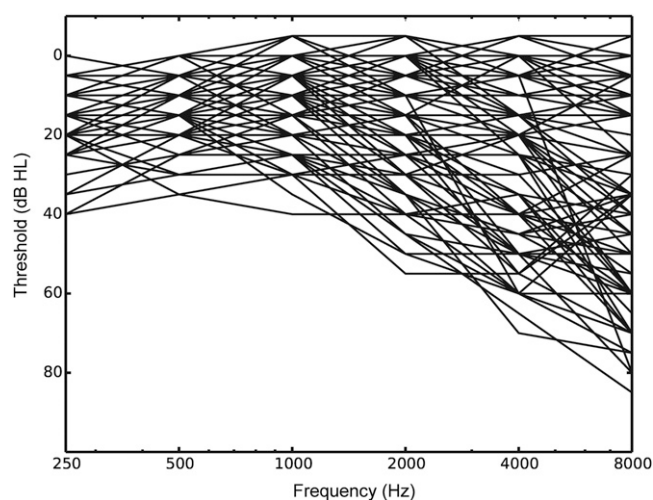


Figure 1. Pure-tone thresholds of all ears included in the study. Overlay of the pure-tone thresholds from 250 to 8000 Hz of all the ears meeting the study criteria that were included in the analysis. Frequency in Hz is shown on the x-axis and intensity in dB HL on the y-axis.

Procedures

All study procedures were performed at St. Elizabeth's Medical Center in Brighton, MA and approved by the St. Elizabeth's Institutional Review Board. All participants in the study provided informed consent. An audiological evaluation including tympanometry, air and bone conduction thresholds, speech reception threshold, and speech perception in quiet using NU-6 word lists was completed for each participant. For the majority of ears, speech perception testing was completed at 50 dB HL or 40 dB above the speech reception threshold, whichever was greater. However, a higher intensity presentation level was used for 14 ears with sloping pure-tone thresholds to provide increased audibility in the high frequencies. Ears exhibiting tympanometric peak pressures < -100 decapascal, static admittance < 0.3 mmho, or air-bone gaps > 15 dB were excluded from the study. ABR waveforms were generated with the Bio-logic Navigator Pro auditory evoked potentials system using gold foil ear canal electrodes (Etymotic Research, Inc.) coupled with Bio-logic 580-SINER-012 (a.k.a. Trip-tode) insert earphones. These electrodes were used rather than tympanic membrane electrodes, which may have resulted in greater peak amplitudes, because they are relatively more comfortable for the patient, are standard equipment used in most clinics in the United States, and their use resulted in reliable and reproducible waveforms. An 80-dBnHL alternating polarity 4000-Hz tone-burst stimulus (Blackman ramp with a four cycle rise and fall) was presented at a repetition rate of 13.3/sec with a 10–1500 Hz filter and an amplifier gain of 50,000 and digitized in a 10.66-msec time window. A 4000-Hz stimulus was chosen to correspond to the frequency region that most typically demonstrates noise-related damage. ABR waveforms were analyzed by an experienced audiologist. Wave I was identified as a peak occurring at ~ 2 –2.5 msec

after stimulus onset and the amplitude was measured with the Bio-logic Auditory Evoked Potential software (version 6.2.0) as the difference in voltage between the peak of wave I and the following trough (Figure 2). At least three waveforms were generated for each ear and the average amplitude was obtained from the two most similar waveforms. The mean difference between these two averaged waveforms was $0.034 \mu\text{V}$ with a standard deviation of $0.031 \mu\text{V}$ and range of 0 – $0.14 \mu\text{V}$. Ten ears from 13 participants were eliminated from the study because wave I could not be identified in these ears. Ears with no identifiable wave I had a mean 4_fPTA of 33.85 dB HL (range 20–46.25 dB HL), a mean pure-tone threshold at 4000 Hz of 56.54 dB HL (range 45–80 dB HL), and mean age of 65.46 yr (range 51–90 yr). The difficulty detecting wave I in these ears was likely due to the high degree of hearing loss, particularly at 4000 Hz, although it is possible that wave I might have been detectable in these ears if a tympanic membrane electrode was used. In total, 101 ears qualified for inclusion in the study (41 from males, 60 from females). Speech-in-noise performance was measured using the QuickSIN (Killion et al, 2004). As recommended by the test developer, sentences were presented at 70 dB HL in the presence of multitalker babble varying in SNR from 0 to 25 dB. Participants were familiarized with the task using one practice list and then presented with two scored lists for each ear. Scores are reported as SNR loss, with larger positive numbers indicating poorer performance.

Analysis

To investigate the effects of age on wave I amplitude and the relationship between wave I amplitude and speech perception in both quiet and in noise, statistical models were used to account for 4_fPTA and age or 4_fPTA and wave I amplitude interactions. Specifically, linear mixed models were fit to the data using the *nlme* package (version 3.1-109) in R (version 3.0.1, 2013-05-16) (R Development Core Team, 2014; Pinheiro et al, 2014). Linear mixed models are a type of regression analysis that allows for control of within-participant variation and interactions between predictor variables. For all models, random effects were used to account for possible correlations in measurements from the two ears of the same participant (such correlations may arise, for example, from cognitive effects that affect processing from both ears equally). χ^2 tests were employed to assess whether including the interaction term ($4_f\text{PTA} \times \text{age}$ or $4_f\text{PTA} \times \text{wave I amplitude}$) significantly improved the model fit compared to a model containing only the main effects without an interaction term. Statistics were then computed on the best-fitting models to determine which of the predictor variables (such as age and 4_fPTA) had a significant influence on the dependent variable (such as wave I amplitude) using Wald *F*-tests and the denominator degrees of freedom reported by *nlme*.

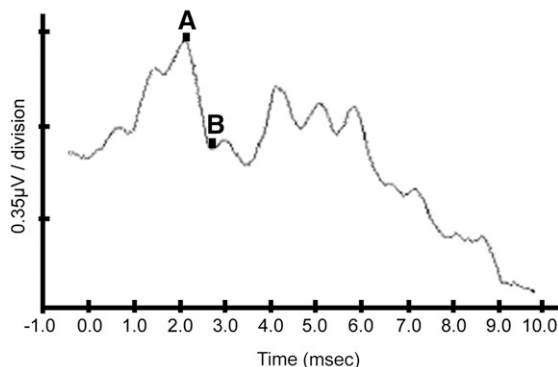


Figure 2. Sample ABR waveform. A sample ABR waveform from a 35-yr-old participant with normal pure-tone thresholds. Wave I amplitude was defined as the difference in voltage between the peak of wave I (A) and the following trough (B).

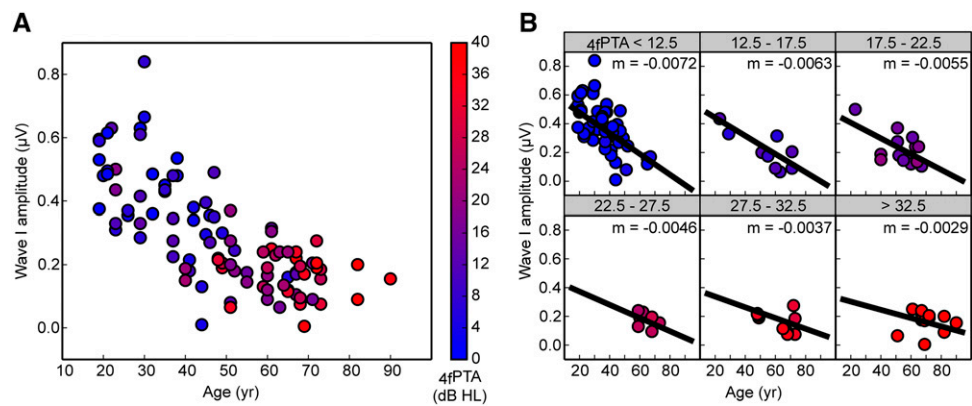


Figure 3. Wave I amplitude decreases with age. Each point represents the raw data from a single ear, with the color of the point indicating the $4f$ PTA of that ear. (A) Age is plotted versus wave I amplitude, showing a decrease in wave I amplitude with age. The data are split into six groups based on $4f$ PTA to illustrate how the relationship between age and wave I amplitude changes with $4f$ PTA. (B) The range of $4f$ PTAs included in each group is indicated at the top of the panel. The solid line in each panel shows the linear mixed model fit based on the complete data set. To compute the slope, $4f$ PTA was set to the center of the $4f$ PTA range for that panel (indicated above each panel). The slope (m) of the line is indicated in the upper right corner of the panel. This model includes the $4f$ PTA \times age interaction, which can be visualized by the change in the slope of the relationship between age and wave I amplitude as $4f$ PTA increases. Wave I amplitude decreases with age, with the steepest slopes in the ears with the best pure-tone thresholds. (This figure appears in color in the online version of this article.)

RESULTS

Wave I Amplitude Decreases with Age

Figure 3A shows the relationship between age and wave I amplitude, with each point representing the data from a single ear. This plot shows a decrease in wave I amplitude with advancing age. $4f$ PTA is represented by the color of the point and illustrates how the relationship between age and wave I amplitude changes with $4f$ PTA. Ears with a better $4f$ PTA (blue) exhibit a steeper relationship between age and wave I amplitude than ears with a poorer $4f$ PTA (red).

To determine the effect of $4f$ PTA on the relationship between age and ABR wave I amplitude, wave I amplitude was fit using a linear mixed model with age, $4f$ PTA, and the interaction between age and $4f$ PTA (age \times $4f$ PTA) as predictor variables. Using this approach, the mean wave I amplitude can be estimated for any combination of age and $4f$ PTA using the equation

Mean wave I amplitude = $b_0 + b_1 \times (\text{age}) + b_2 \times (4f\text{PTA}) + b_3 \times (\text{age}) \times (4f\text{PTA})$

where b_0 , b_1 , b_2 , and b_3 are coefficients for the intercept, age, $4f$ PTA and age \times $4f$ PTA, respectively. Coefficients

based on the fitted data are listed in Table 1 in the column labeled “coefficient.” For example, by entering the coefficients into the equation shown above, the expected wave I amplitude for a 30-yr-old with a $4f$ PTA of 20 dB HL can be estimated as $0.72597 - 0.00892 \times 30 - 0.01044 \times 20 + 0.00017 \times 30 \times 20$, which equals 0.35 μ V.

To test whether the interaction between age and $4f$ PTA (age \times $4f$ PTA) significantly improved the fit of the model to the data, a model containing only the main effects (i.e., age and $4f$ PTA) was compared to the full model that included both the main effects and the age \times $4f$ PTA interaction. A χ^2 test ($\chi^2 = 6.46$, $df = 1$, $p = 0.011$) indicated that the model containing the interaction between age and $4f$ PTA showed a significantly better fit to the data. The age \times $4f$ PTA interaction term allows the model to compensate for the influence of pure-tone threshold on the relationship between age and wave I amplitude. In this model, the age \times $4f$ PTA interaction was found to have a significant effect on wave I amplitude (Wald F -test, $df = 42$, p value = 0.01), with a stronger effect of age on wave I amplitude in ears with better hearing. To determine whether gender had a significant effect on wave I amplitude, gender was included as a predictor variable in a preliminary version of the model. However, because the p value for gender of 0.94 suggested that gender had little effect on wave I amplitude, it was removed to simplify the final model.

Table 1. Regression Coefficients for the Linear Mixed Model of ABR Wave I Amplitude

| | Predictor | Coefficient | Standard Error | p Value |
|------------------|-----------------------|-------------------------------------|----------------|-----------|
| Wave I amplitude | Intercept | 0.72597 (μ V) | 0.05853 | <0.01 |
| | Age | -0.00892 (μ V/year) | 0.00145 | <0.01 |
| | $4f$ PTA | -0.01044 (μ V/dB) | 0.00391 | 0.01 |
| | Age \times $4f$ PTA | 0.00017 (μ V/[dB \times yr]) | 0.00007 | 0.01 |

The linear mixed model includes two different independent variables; age and $_{4f}$ PTA. To facilitate visualization of how the relationship between age and wave I amplitude changes with $_{4f}$ PTA, in Figure 3B the data from Figure 3A is split into six groups based on $_{4f}$ PTA and plotted in separate panels. The solid line in each panel shows the linear mixed model fit to the data. Although only a subset of the data are shown in each panel, the model fit shown in the panel is based on the complete data set. The model illustrates the relationship between age and wave I amplitude as a function of $_{4f}$ PTA. The slope of the model fit decreases as $_{4f}$ PTA increases, demonstrating the importance of the age \times $_{4f}$ PTA interaction. This interaction suggests that elevated pure-tone thresholds alter the relationship between age and wave I amplitude, resulting in a weaker effect of age on wave I amplitude than is observed in ears with better thresholds. This is likely due to attenuation of the stimulus used to generate wave I, which is a consequence of elevated pure-tone thresholds. Wave I amplitude decreases systematically with age, as seen in previous studies (Konrad-Martin et al, 2012). These results are consistent with both animal and human temporal bone data showing an inverse relationship between the number of spiral ganglion neurons and age (Schmiedt et al, 1996; Makary et al, 2011), and suggest that ABR wave I amplitude can be used as an indirect measure of neuronal survival.

Lower Wave I Amplitude Correlates with Decreased Speech-in-Noise Performance

Figure 4A shows the relationship between ABR wave I amplitude and QuickSIN score, with each point represent-

ing the data from a single ear. This plot shows decreased QuickSIN performance for smaller wave I amplitudes. The color of each point corresponds to the $_{4f}$ PTA of that ear and illustrates how the relationship between wave I amplitude and QuickSIN score changes with $_{4f}$ PTA. Ears with a poorer $_{4f}$ PTA (red) show a steeper relationship between wave I amplitude and QuickSIN score than ears with a better $_{4f}$ PTA (blue).

To account for the effects of $_{4f}$ PTA, speech-in-noise performance as measured by the QuickSIN was fit using a linear mixed model with $_{4f}$ PTA, wave I amplitude, age, and the interaction between $_{4f}$ PTA and wave I amplitude ($_{4f}$ PTA \times wave I amplitude) as predictor variables. Mean QuickSIN score can be estimated for any combination of $_{4f}$ PTA, wave I amplitude, and age by using the equation

$$\begin{aligned} \text{Mean QuickSIN} = & b_0 + b_1 \times (_{4f}\text{PTA}) + b_2 \\ & \times (\text{wave I amplitude}) + b_3 \times (\text{age}) \\ & + b_4 \times (_{4f}\text{PTA}) \times (\text{wave I amplitude}) \end{aligned}$$

where b_0 , b_1 , b_2 , b_3 , and b_4 are coefficients for the intercept, $_{4f}$ PTA, wave I amplitude, age, and $_{4f}$ PTA \times wave I amplitude, respectively. The values of the coefficients are listed in Table 2 in the column labeled "coefficient."

The interaction between $_{4f}$ PTA and wave I amplitude was included in the model to account for the possibility that the effect of neuronal loss on speech perception in noise may be compounded by elevated pure-tone thresholds. To evaluate the goodness of fit, a model containing only the main effects (i.e., age, $_{4f}$ PTA, and wave I amplitude) was compared to the full model that included the $_{4f}$ PTA \times wave I amplitude interaction. A χ^2 test ($\chi^2 = 6.87$, $df = 1$, $p = 0.009$) showed that the interaction

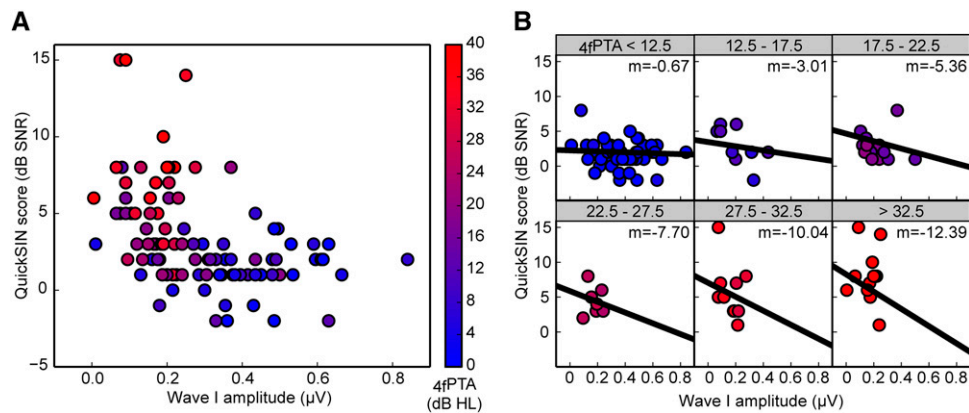


Figure 4. QuickSIN score is inversely related to wave I amplitude. Each point represents the raw data from a single ear, with the color of the point indicating the $_{4f}$ PTA of that ear. Higher positive numbers indicate poorer performance on the QuickSIN. (A) Wave I amplitude is plotted versus QuickSIN score, with a decrease in QuickSIN performance observed for smaller wave I amplitudes. (B) The data are split into six groups based on $_{4f}$ PTA to illustrate how the relationship between wave I amplitude and QuickSIN score changes with $_{4f}$ PTA. The range of $_{4f}$ PTAs included in each group is indicated at the top of the panel. The solid line in each panel shows the linear mixed model fit based on the entire data set. To compute the slope, $_{4f}$ PTA was set to the center of the $_{4f}$ PTA range for that panel (indicated above each panel) and age was set to the average of all ears. The slope (m) of the line is indicated in the upper right corner of the panel. This model includes the $_{4f}$ PTA \times wave I amplitude interaction, which is illustrated by the change in the slope of the relationship between wave I amplitude and QuickSIN score as $_{4f}$ PTA increases. Smaller wave I amplitudes are correlated with poorer QuickSIN scores, with the greatest effect in ears with the poorest thresholds. (This figure appears in color in the online version of this article.)

Table 2. Regression Coefficients for the Linear Mixed Model of QuickSIN Performance

| | Predictor | Coefficient | Standard Error | <i>p</i> Value |
|----------------|--|---|----------------|----------------|
| QuickSIN score | Intercept | -1.52767 (dB SNR loss) | 1.73324 | 0.38 |
| | $_4\text{fPTA}$ | 0.24011 (dB SNR loss/dB) | 0.05344 | <0.01 |
| | Wave I amplitude | 4.01200 (dB SNR loss/ μV) | 2.96006 | 0.18 |
| | Age | 0.02854 (dB SNR loss/year) | 0.02729 | 0.30 |
| | $_4\text{fPTA} \times \text{Wave I amplitude}$ | -0.46866 (dB SNR loss/(dB $\times \mu\text{V}$)) | 0.18105 | 0.01 |

term significantly improved the fit of the model to the data.

The effect of interaction between $_4\text{fPTA}$ and wave I amplitude on QuickSIN score was significant (Wald *F*-test, $df = 41$, $p = 0.013$), indicating that the relationship between wave I amplitude and speech perception in background noise is influenced by the degree of pure-tone threshold elevation.

In Figure 4B, the data from Figure 4A is split into six groups based on $_4\text{fPTA}$ and plotted in separate panels. The solid line in each panel shows the linear mixed model fit based on the complete data set. The linear mixed model illustrates changes to the relationship between wave I amplitude and QuickSIN score as a function of $_4\text{fPTA}$. The slope of the model fit increases as $_4\text{fPTA}$ increases, demonstrating the significance of the wave I amplitude \times $_4\text{fPTA}$ interaction. Larger wave I amplitudes are associated with better QuickSIN scores (lower dB SNR values), with the greatest effect for ears with a poorer $_4\text{fPTA}$. This suggests the relationship between speech-in-noise performance and wave I amplitude is strongest in ears with the poorest hearing.

Wave I Amplitude Shows No Relationship to Speech Perception in Quiet

Figure 5A shows the relationship between wave I amplitude and speech perception performance in quiet, with each point representing the data from a single ear. No apparent relationship is observed between wave I amplitude and speech perception in quiet. The color of each point corresponds to the $_4\text{fPTA}$ of that ear and illustrates how the relationship between wave I amplitude and speech perception in quiet changes with $_4\text{fPTA}$.

Initially, speech perception performance in quiet was fit using a linear mixed model with $_4\text{fPTA}$, wave I amplitude, age, and the interaction between $_4\text{fPTA}$ and wave I amplitude ($_4\text{fPTA} \times \text{wave I amplitude}$) as predictor variables. However, a χ^2 test ($\chi^2 = 0.31$, $df = 1$, $p = 0.57$) indicated that this model did not improve the fit to the data over a model including only the main effects (age, $_4\text{fPTA}$, and wave I amplitude). For all subsequent analyses, only the main effects were included in the model for speech perception in quiet. Using this model, mean speech perception score can be estimated for any combination of

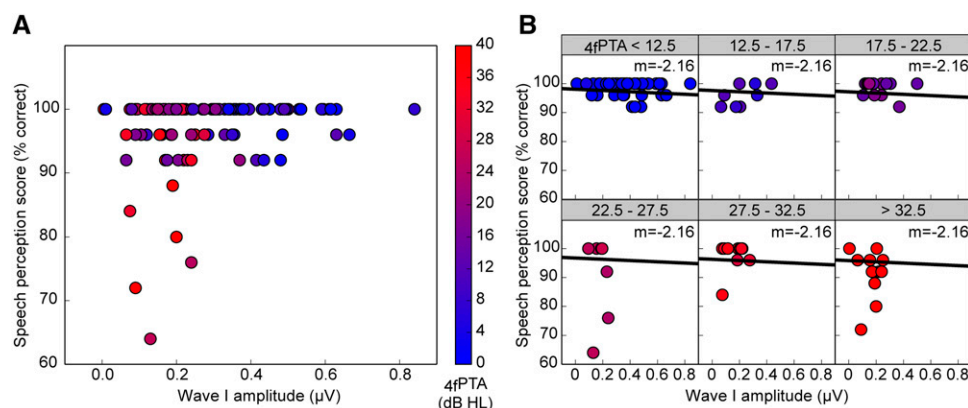


Figure 5. Wave I amplitude is not related to speech perception in quiet. Speech perception in quiet scores is expressed as a percent correct. Each point represents the raw data from a single ear, with the color of the point indicating the $_4\text{fPTA}$ of that ear. (A) Wave I amplitude is plotted versus speech perception performance in quiet, with no clear relationship apparent between them. The data are split into six groups based on $_4\text{fPTA}$ to facilitate comparison with Figures 2 and 3. (B) The range of $_4\text{fPTA}$ s included in each group is indicated at the top of the panel. The solid line in each panel shows the linear mixed model fit based on the complete data set. To compute the slope, $_4\text{fPTA}$ was set to the center of the $_4\text{fPTA}$ range for that panel (indicated above each panel) and age was set to the average of all ears. The slope (*m*) of the line is indicated in the upper right corner of the panel. This model does not include the $_4\text{fPTA} \times \text{wave I amplitude}$ interaction because it was not found to significantly improve the model. The absence of an interaction between wave I amplitude and $_4\text{fPTA}$ can be visualized by the fixed slope of the relationship between wave I amplitude and speech perception score regardless of $_4\text{fPTA}$. The shallow slope illustrates that lack of any significant relationship between wave I amplitude and speech perception performance in quiet. (This figure appears in color in the online version of this article.)

$_{4f}$ PTA, wave I amplitude, and age by using the equation

$$\begin{aligned} \text{Mean Speech Perception Score} = & b_0 + b_1 \times ({}_{4f}\text{PTA}) + b_2 \\ & \times (\text{wave I amplitude}) \\ & + b_3 \times (\text{age}) \end{aligned}$$

where b_0 , b_1 , b_2 , and b_3 are coefficients for the intercept, $_{4f}$ PTA, wave I amplitude, and age, respectively. The values of the coefficients are listed in Table 3 in the column labeled “coefficient.” In contrast to the results observed for speech-in-noise testing, none of the model’s predictors demonstrated a significant effect on speech perception in quiet (Table 3).

In Figure 5B, the data from Figure 5A is split into six groups based on $_{4f}$ PTA and plotted with the linear mixed model fit based on the complete data set. Unlike Figures 3B and 4B, the slope of the model fit does not change with $_{4f}$ PTA because the interaction between $_{4f}$ PTA and wave I amplitude did not have a significant effect on speech perception score and was therefore excluded from the model. No significant relationship was detected between wave I amplitude and speech perception in quiet (Wald F -test, $df = 42$, p value = 0.66). It is possible, these results are due to ceiling effects because the majority of participants scored close to 100% on the speech perception testing, suggesting the test may not have been sufficiently difficult to differentiate between good and poor performers.

Aging is Not Associated with Poorer Speech-in-Noise Performance

Performance on the QuickSIN can be influenced by memory because it requires the test participant to remember the sentence presented long enough to repeat it back. While aging is associated with poorer pure-tone thresholds and reduced ABR wave I amplitude, no significant main effect of age was found on QuickSIN performance (Wald F -test, $df = 55$, p value = 0.3), suggesting that factors such as age-related cognitive decline or memory loss did not have a significant effect on speech perception in noise in our participants. This confirms that the $_{4f}$ PTA-dependent relationship between ABR wave I amplitude and speech-in-noise performance we observed was not an artifact of age-related cognitive changes.

DISCUSSION

Reduced ABR Wave I Amplitude as an Indicator of Neuronal Degeneration

Although true validation of the use of ABR wave I amplitude as a measure of auditory neuronal population size in humans can only be completed in conjunction with temporal bone studies, the relationship between advancing age and decreased ABR wave I amplitude shown here and previously demonstrated by Konrad-Martin et al. (2012) mirrors the reduction in spiral ganglion cell numbers with increasing age that has been observed in human temporal bone studies (Makary et al, 2011). In light of animal studies that show a relationship between ABR wave I amplitude and postmortem spiral ganglion neuron counts (Kujawa and Liberman, 2009; Lin et al, 2011), the present findings make a strong case for the use of ABR wave I amplitude in humans as a measure of spiral ganglion survival. This suggests that ABR measures may be used clinically as a noninvasive assessment of spiral ganglion survival. These measures would be useful for characterizing the impact of spiral ganglion cell loss on auditory perception, monitoring changes in neuronal integrity due to aging or noise exposure, and evaluating agents for prevention of neuronal degeneration.

Selective Effect of Neuronal Loss on Speech Perception in Noise

In humans, each inner hair cell is innervated by roughly 10 spiral ganglion neurons (Nadol, 1983). Spiral ganglion fibers can be functionally classified based on their spontaneous firing rates and response thresholds. Low spontaneous rate (SR) fibers are associated with high absolute thresholds to sound and high SR fibers with low absolute thresholds (Liberman, 1978). The combination of both low- and high-threshold neurons is hypothesized to enable the auditory system to respond to sound over a large range of intensities. This is thought to allow the auditory system to encode the speech signal even in the presence of background noise (Bharadwaj et al, 2014).

In animals, low SR fibers appear to be more vulnerable to noise damage and aging than high SR fibers (Schmiedt et al, 1996; Furman et al, 2013). The lack

Table 3. Regression Coefficients for the Linear Mixed Model of Speech Perception in Quiet

| | Predictor | Coefficient | Standard Error | p Value |
|----------------------------|------------------|-------------------------------|----------------|-----------|
| Speech perception in quiet | Intercept | 102.76996 (% correct) | 3.63421 | <0.01 |
| | $_{4f}$ PTA | −0.08897 (% correct/dB) | 0.07837 | 0.26 |
| | Wave I amplitude | −2.16979 (% correct/ μ V) | 4.89009 | 0.66 |
| | Age | −0.07850 (% correct/yr) | 0.06305 | 0.22 |

of any permanent threshold shift following spiral ganglion neuronal loss suggests that the detection of sound near threshold is unaffected by the loss of low SR fibers, presumably because low intensity sounds are primarily encoded by high SR fibers. However, the responses of high SR fibers become saturated in the presence of noise (Reiss et al, 2011), leaving low SR fibers with the responsibility of encoding the information required to discriminate speech in background noise.

The present analysis showed no significant relationship between ABR wave I amplitude and speech perception in quiet. This suggests that the degree of auditory neuronal degeneration found in the ears included in this study may not have reached the level of severity necessary to impact speech perception in quiet. In a temporal bone study, Otte et al. (1978) found that close to 50% of the spiral ganglion cell population can be lost without having a significant effect on speech perception in quiet.

In contrast to the findings for speech perception in quiet, the present study showed a decline in performance on the QuickSIN as ABR wave I amplitude decreased. The difference in speech perception performance in quiet versus in noise may be explained by selective loss of low SR fibers. If this population of fibers exhibits the same vulnerability in humans as it does in animals, low SR fiber loss could explain why reduced ABR wave I amplitude is associated with poorer speech perception in noise, but has no significant relationship to speech perception performance in quiet. In quiet situations, the high SR fibers should be sufficient for coding the speech signal. However, these fibers may become saturated in the presence of background noise, leaving the low SR fibers to encode the speech signal. Loss of low SR fibers would therefore impair speech perception in noise.

The relationship detected between QuickSIN performance and ABR wave I amplitude was dependent on dPTA , with a stronger effect in ears that had poorer pure-tone thresholds than in ears with very good thresholds. This suggests that when the speech signal is degraded by elevation of pure-tone thresholds, due to factors attributed to outer hair cell loss such as impaired tuning and compression, the loss of neural fibers has a bigger impact on speech-in-noise perception than when a faithful representation of the speech signal reaches the auditory nerve.

The time window and recording parameters in these experiments were optimized to capture wave I and, as such, precluded a detailed analysis of wave III–V amplitudes or interwave latencies. It is not only possible, but also likely that primary neuronal degeneration implied by the decreased wave I amplitudes leads to subsequent neuronal degeneration along the ascending auditory pathway (Konrad-Martin et al, 2012). Therefore, we assume that waves III–V would exhibit a similar effect as wave I, but further experiments are required to test this hypothesis.

Clinical Implications

Based upon the results described here, individuals with elevated pure-tone thresholds that exhibit lower wave I amplitudes are more likely to experience increased difficulty with speech understanding in noise. This has implications on hearing aid fitting and counseling. Patients with poor QuickSIN performance potentially related to spiral ganglion cell loss will require more careful hearing aid selection. These individuals will likely benefit from hearing aids with more advanced noise reduction algorithms. In addition, counseling to set realistic expectations will be critical as these patients may not achieve the same level of success with amplification as those with better speech perception in noise. A greater focus on the use of visual cues may also be necessary to optimize communication in this population. The present findings indicate that measurement of speech perception ability in noise before fitting hearing aids will be particularly important for individuals at increased risk of neuronal loss, namely those of advanced age or with a significant noise exposure history.

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REFERENCES

- Bharadwaj HM, Verhulst S, Shaheen L, Liberman MC, Shinn-Cunningham BG. (2014) Cochlear neuropathy and the coding of supra-threshold sound. *Front Syst Neurosci* 8:26.
- Earl BR, Chertoff ME. (2010) Predicting auditory nerve survival using the compound action potential. *Ear Hear* 31(1):7–21.
- Furman AC, Kujawa SG, Liberman MC. (2013) Noise-induced cochlear neuropathy is selective for fibers with low spontaneous rates. *J Neurophysiol* 110(3):577–586.
- Hashimoto I, Ishiyama Y, Yoshimoto T, Nemoto S. (1981) Brainstem auditory-evoked potentials recorded directly from human brain-stem and thalamus. *Brain* 104(Pt 4):841–859.
- Liberman MC. (1978) Auditory-nerve response from cats raised in a low-noise chamber. *J Acoust Soc Am* 63(2):442–455.
- Lin HW, Furman AC, Kujawa SG, Liberman MC. (2011) Primary neural degeneration in the Guinea pig cochlea after reversible noise-induced threshold shift. *J Assoc Res Otolaryngol* 12(5):605–616.
- Killion MC, Niquette PA, Gudmundsen GI, Revit LJ, Banerjee S. (2004) Development of a quick speech-in-noise test for measuring signal-to-noise ratio loss in normal-hearing and hearing-impaired listeners. *J Acoust Soc Am* 116(4):2395–2405.
- Konrad-Martin D, Dille MF, McMillan G, et al. (2012) Age-related changes in the auditory brainstem response. *J Am Acad Audiol* 23(1):18–35, quiz 74–75.
- Kujawa SG, Liberman MC. (2009) Adding insult to injury: cochlear nerve degeneration after “temporary” noise-induced hearing loss. *J Neurosci* 29(45):14077–14085.

- Makary CA, Shin J, Kujawa SG, Liberman MC, Merchant SN. (2011) Age-related primary cochlear neuronal degeneration in human temporal bones. *J Assoc Res Otolaryngol* 12(6):711–717.
- Melcher JR, Kiang NY. (1996) Generators of the brainstem auditory evoked potential in cat. III: Identified cell populations. *Hear Res* 93(1–2):52–71.
- Møller AR, Jannetta PJ. (1981) Compound action potentials recorded intracranially from the auditory nerve in man. *Exp Neurol* 74(3):862–874.
- Nadol JB, Jr. (1983) Serial section reconstruction of the neural poles of hair cells in the human organ of Corti. I. Inner hair cells. *Laryngoscope* 93(5):599–614.
- Otte J, Schunknecht HF, Kerr AG. (1978) Ganglion cell populations in normal and pathological human cochleae. Implications for cochlear implantation. *Laryngoscope* 88(8 Pt 1):1231–1246.
- Pinheiro J, Bates D, DebRoy S, Sarkar D, and R Core Team. (2014) *nlme: Linear and Nonlinear Mixed Effects Models*. R package version 3.1-115; <http://CRAN.R-project.org/package=nlme>.
- R Development Core Team. (2014) *R: A Language and Environment for Statistical Computing*. Vienna, Austria: R Foundation for Statistical Computing.
- Reiss LA, Ramachandran R, May BJ. (2011) Effects of signal level and background noise on spectral representations in the auditory nerve of the domestic cat. *J Assoc Res Otolaryngol* 12(1):71–88.
- Schmiedt RA, Mills JH, Boettcher FA. (1996) Age-related loss of activity of auditory-nerve fibers. *J Neurophysiol* 76(4):2799–2803.
- Sergeyenko Y, Lall K, Liberman MC, Kujawa SG. (2013) Age-related cochlear synaptopathy: an early-onset contributor to auditory functional decline. *J Neurosci* 33(34):13686–13694.

