Noise Exposure, Self-Reported Speech-in-Noise Perception, and the Auditory Brainstem Response in Normal-Hearing Human Ears

By

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ABSTRACT

Difficulty understanding speech-in-noise (SIN) is a common complaint among many listeners. There is emerging evidence that noise exposure is associated with difficulties in speech discrimination and temporal processing despite normal audiometric thresholds. At present, evidence linking temporary noise-induced hearing loss and selective loss of low spontaneous rate fibers in human ears is limited and inconsistent. Likewise, results of SIN measures in relation to noise-induced cochlear synaptopathy varied across studies.

The goals of this study are to further our understanding of the effects of noise exposure on the auditory system and to investigate novel approaches for detecting early noise-induced auditory damage. Data were collected from 30 normal-hearing subjects (18-35 years old) with varying amounts of noise exposure. Auditory brainstem responses (ABR) were recorded to both a click (measure of auditory nerve function) and speech stimulus (/da/; measure of temporal processing). The speech hearing subscale of the Speech, Spatial and Qualities of Hearing Scale (SSQ) was also administered to quantify individual self-reported SIN abilities.

The data resulted in mixed findings. Overall click-ABR wave I results provided no evidence for noise-induced synaptopathy in this cohort. However, differences in the wave I amplitude between males and females were observed suggesting noise effects may vary between sexes. Transient components of the speech-ABR showed no evidence of neural slowing but revealed enhanced neural responses in individuals with greater amounts of noise exposure. This later finding may be a manifestation of either musical training or increased central neural gain as a result of pathology. Lastly, individuals with greater amounts of noise exposure reported experiencing more difficulties hearing SIN (as per the SSQ) but ABR data did not show the predicted physiologic evidence to explain the self-perceived SIN deficit.

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Dedication

To my mom, Lily, and sisters, Mitzi, Diana, and Alexis, for their love, understanding, and overwhelming support.

To my Cooper who never fails to brighten my day!

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INTRODUCTION

Hearing loss is the third most common public health issue. Permanent hearing loss caused by exposure to excessive noise affects approximately 26 million adults (ages 20 – 69) in America (NIDCD, 2001) and as many as 16% of teens (ages 12 to 19) have reported some hearing loss that could have been caused by loud noise (CDC, 2010). It is widely accepted that permanent threshold shifts after noise exposure (i.e., noise-induced hearing loss) are a result of permanent damage to auditory structures. However, the relationship between the amount of acoustic exposure and the resulting anatomic and physiologic damage is variable, even in highly controlled studies.

The detrimental effects of any type of hearing loss on speech, language, and learning are well documented. Most people with noise-induced hearing loss (NIHL) often complain of having difficulty with speech perception in noise, difficulty with sound localization, increased sensitivity to a range of sounds (i.e., hyperacusis), or persistent ringing or buzzing in the ears (i.e., tinnitus). Difficulty understanding speech-in-noise (SIN) is also a common complaint among many listeners despite having normal audiometric thresholds. It has been reported that as many as 5–15% of adult patients seeking audiological help turn out to have normal hearing thresholds (Cooper and Gates, 1991; Kumar et al., 2007; Hind et al., 2011).

Overexposure to loud sounds can also lead to a temporary threshold shift (TTS). A common perception is that if hearing fully recovers over time, no residual auditory damage exists and that exposure is essentially harmless (Humes et al., 2005). Recent investigations involving animal models have contradicted this assumption and showed an abrupt, permanent loss of up to 50% of afferent nerve terminal connections between inner hair cells and auditory nerve fibers (i.e., cochlear synaptopathy) in the frequency region of maximum TTS while outer hair cells

appear to be undamaged following an exposure to loud sounds (Kujawa and Liberman, 2009, Lin et al., 2011; Furman et al., 2013; Valero et al., 2017). Despite substantial deafferentation, threshold level responses were preserved after recovery while the wave I amplitude of the auditory brainstem response (ABR) at suprathreshold stimulation levels (i.e., high levels of sound) was significantly reduced. The reduced neural response for high-level stimuli with preserved thresholds indicates a specific loss of auditory nerve fiber populations that respond at high levels, the low-spontaneous rate, high-threshold fibers. This finding suggests that suprathreshold responses demonstrated better sensitivity at revealing auditory damage following noise-induced TTS.

At present, evidence linking temporary noise-induced hearing loss and selective loss of low-spontaneous rate fibers in human ears is limited and inconsistent. The perceptual consequences linked to noise-induced cochlear synaptopathy remain unclear. However, there is some evidence that a history of noise exposure is associated with temporal processing deficits even in the absence of any audiometric loss (Kumar, Ameenudin, and Sangamanatha, 2012; Bharadwaj et al., 2015; and Liberman et al., 2016) that may lead to difficulties in hearing speech in noise. Normal perception of the temporal aspects of the stimulus is thought to be crucial for understanding speech in quiet and adverse listening conditions. It has been suggested that these reported SIN performance decrements might arise because noise-induced cochlear synaptopathy selectively damages the subset of auditory nerve fibers with high-thresholds and low-spontaneous rates. By virtue of their relatively high threshold, they do not contribute to threshold detection in quiet and are resistant to continuous noise masking. Therefore, they are key to the coding of transient stimuli in the presence of continuous background noise (Costaloupes et al., 1984).

A small number of studies suggest physiologic evidence of noise-induced cochlear synaptopathy in humans (e.g., Stamper and Johnson, 2015a; Liberman et al., 2016; Bramhall et al., 2017). Stamper and Johnson (2015a) first reported a systematic trend of smaller ABR wave I amplitudes in normal-hearing participants with greater noise-exposure background in response to suprathreshold clicks and 4 kHz tone bursts while other common audiological measures (i.e. Pure Tone Thresholds, DPOAEs, ABR wave V amplitude) did not show any sensitivity to noise exposure. However, it is possible the results were confounded by sex since the majority of their high-noise participants were males, and males are known to have smaller ABR amplitudes than females. In a subsequent letter to the editor, Stamper and Johnson (2015b) analyzed their ABR data recorded at 90 dB nHL for the two sexes independently. The relationship initially observed between wave I amplitude and annual noise exposure estimate persisted for the female subjects, but not for the male subjects. Bramhall et al. (2017) also found reduced ABR wave I amplitudes in veterans with significant firearm use and in non-veterans with history of firearm use at suprathreshold levels (110 dB p-pe SPL) to 4 kHz tone burst. Similar to the Stamper and Johnson (2015) paper, no significant differences in ABR waves III and V amplitudes were found between the groups.

Liberman et al. (2016) compared the amplitude ratio of the presynaptic summating potential (SP) generated primarily by the hair cells and the action potential (AP) generated by auditory nerve fibers in two groups of subjects, those at low-risk for noise induced hearing loss and those at high-risk, in response to suprathreshold click stimuli. Their data showed significantly larger mean SP/AP ratios in their high-risk group relative to the low-risk group. Unlike the two studies above (Stamper and Johnson, 2015a; Bramhall et al., 2017), Liberman et al. did not find a significant difference in the AP amplitude (equivalent to ABR wave I

amplitude) between the two groups but found significantly increased SP amplitude in the high-risk group. In addition, word recognition performance in noise was found to be significantly poorer in their group of participants who are at high-risk of developing noise-induced hearing loss. The high-risk group also performed worse than the control group on measures of perception of time-compressed speech in a reverberant background. Furthermore, their data showed that SIN performance was significantly correlated with the physiologic measure (SP/AP ratio) where word recognition scores decreased with increased SP/AP ratio. While an enlarged SP/AP ratio and poorer speech perception in the high-risk group may be due to underlying pathology such as cochlear synaptopathy, it is not well understood how a loss of cochlear synapses would lead to enhancement of the SP.

Schaette and McAlpine (2011) and Gu et al. (2012) also found significant significantly smaller ABR wave I amplitudes in tinnitus subjects compared to non-tinnitus controls when hearing thresholds were matched. Although the exact biological process of tinnitus is still being investigated, it is a symptom that is commonly reported following exposure to loud noises with or without the presence of hearing loss. At the same time, Gu et al. (2012) reported enhanced waves III and V amplitudes in the tinnitus group while Schaette and McAlpine (2011) found no significant difference in the wave V amplitude between their tinnitus and control groups. It has been suggested that the enhancement or no change in the wave V response amplitude observed in individuals with tinnitus may be due to increased central neural gain to compensate for the reduced input from the auditory nerve as evidenced by the reduced wave I amplitude. However, a recent study by Guest et al. (2017) was not able to replicate the reported relation between the noise exposure and ABR wave I amplitude in their group of young adults with tinnitus. They

propose that tinnitus may not be related to cochlear synaptopathy but rather to other effects of noise exposure.

In contrast to the studies described above showing a link between noise exposure and findings consistent with cochlear synaptopathy, other studies have found no physiologic or perceptual evidence of cochlear synaptopathy in humans. In a large-scale study by Prendergast et al. (2017a), no significant relationship between lifetime noise exposure and ABR wave I amplitude was found. When they analyzed their data by sex, they also reported opposing trends in the wave I amplitude between the females and males similar to the observations of Stamper and Johnson (2015b). The high-noise females showed reduced ABR wave I amplitudes compared to the low-noise females while high-noise males showed enhanced wave I amplitudes compared to the low-noise males, but neither of these relationships were statistically significant. These findings suggest a possible difference in vulnerability to the effects of noise between sexes. In a subsequent study (2017b), Prendergast and colleagues found no relation between the ABR data and measures of temporal processing (i.e., frequency and intensity difference limens, interaural phase discrimination, amplitude modulation detection, digit triplet test, co-ordinate response, localization, and musical consonance) or the self-report assessment of hearing ability (via the Speech, Spatial, and other Qualities Scale; SSQ) regardless of noise exposure. Likewise, Grinn et al. (2017) also found no evidence of auditory deficits as a function of previous recreational noise exposure history, and no permanent changes in audiometric, electrophysiological, or functional measures after new recreational noise exposure.

The mixed findings in electrophysiology (i.e., ABR wave I and electrocochleography) questions the existence of noise-induced cochlear synaptopathy in humans. Likewise, the perceptual consequences remain unclear as results of SIN measures vary across studies. It is

possible that how noise exposure is assessed and/or the approach used to measure its effects are responsible for these mixed findings, thus, the need for alternative assessment tools. While ABR to clicks or tone bursts is extensively used in clinical settings and has proven to be a valuable measure in evaluating auditory function, (Hall, 1992; Hood, 1998), the wide variability in ABR amplitude seen even in normal ears limits the use of this measure in clinical applications (Schwartz et al., 1994). Furthermore, the use of simple stimuli like clicks and tones are not acoustically complex sounds and do not represent day-to-day listening conditions. Perhaps, the use of a more complex stimulus like speech will better represent more real-world listening conditions.

A number of studies have demonstrated that click and speech stimuli impose different encoding demands on the brainstem (e.g., Song et al., 2006; Johnson et al., 2008). The speech-evoked ABR has been used as a 'biomarker' for indexing temporal processing at the level of the brainstem (Johnson et al., 2007). It has been suggested that temporal processing deficits in the central auditory pathway may be implicated in difficulties perceiving SIN (Pichora-Fuller & Souza, 2003). Because the speech-evoked ABR provides an objective means for evaluating the brainstem's ability to accurately encode timing and frequency information, it can be used to diagnose auditory processing deficits despite normal processing of click stimuli. While the speech-evoked ABR is not currently used in clinical audiology, it is gaining popularity in the field of research.

ABR recorded in response to the /da/ syllable results in seven characteristic response waves (peak and troughs) and are labeled V, A, C, D, E, F and O. The response includes both transient (i.e. V, A, C, and O) and sustained (i.e. D, E, and F) features that manifest approximately seven to eight milliseconds after the corresponding acoustic landmark. This delay

is attributed to the neural transmission time between the cochlea and brainstem. The transient response features of the speech-evoked ABR come from the onset and offset of the stimulus while the frequency following response comes from the neural phase-locking to the vowel portion of the stimulus. The transient and sustained components are believed to result from different mechanisms of temporal processing both occurring at the brainstem level (Johnson et al., 2005; Akhoun et al., 2008). The V-A complex is the attributed to the highly synchronized neural response to the onset of the stimulus at the level of lateral lemniscus and inferior colliculus and is analogous to the V-Vn complex of the click-evoked ABR. Wave O is thought to be a response to the cessation or offset of the stimulus.

Studies by Anderson et al. (2011 and 2013) in older adults indicated that features of the speech-evoked ABR are related to SIN perception. They proposed that the neural slowing of the offset response (wave O) can affect precise encoding of temporal speech features that can account for some of the older adult's difficulty with hearing in background noise. The detection of stimulus offsets and onsets is thought to activate the duration-tuned neurons in the inferior colliculus and at higher levels of the auditory system (Faure et al., 2003) and that duration perception results from temporal interaction of excitatory and inhibitory inputs that are offset in time (Sayegh, Aubie, & Faure, 2011). Therefore, duration-tuned neurons may act as spectrotemporal filters (Sayegh, Aubie, & Faure, 2011), providing the precise encoding necessary for understanding SIN. The present study explored the utility of the speech-evoked ABR as an objective measure of temporal processing in young normal-hearing adults with varying history of noise exposure. Here, we examined the peak latency of the onset (wave V) and offset (wave O) responses to the syllable /da/ at suprathreshold levels. We hypothesized that individuals with greater noise exposure will have neural slowing characterized by latency delays

particularly in the offset response at suprathreshold levels indicating poorer temporal processing abilities.

This study also explored the link between noise exposure, evoked potential estimates of neural survival and temporal processing, and SIN deficits in individuals with normal thresholds. Researchers have commonly used behavioral measures to assess SIN perception obtained in clinics and laboratories. While these SIN perception tests remain a valuable tool in audiology clinics, they may not accurately capture real-world SIN performance. To achieve our objective of finding an efficacious measure of real-world SIN performance, we explore the use of the Speech, Spatial, and Qualities of Hearing Questionnaire (SSQ; Gatehouse and Noble, 2004). The SSQ was designed in response to recognized limitations of the traditional audiological battery for predicting listening ability in challenging environments, such as rooms with multiple talkers and other noise sources. It measures a range of hearing disabilities across several domains (i.e. speech hearing, spatial hearing, segregation of sounds, recognition, clarity/naturalness, and listening effort). As we are interested in SIN abilities, we focused our attention on the speech hearing domain. The speech hearing subscale of the SSQ assesses 14 different speech listening environments, including quiet environments and a range of challenging environments with competing noise to approximate overall, day-to-day SIN performance. The SSQ score reflects individual self-perception of ability with higher scores indicating less difficulty. Since its development, the SSQ has been used to document the benefit of unilateral vs. bilateral hearing aids (Mostet al., 2012; Noble & Gatehouse, 2006), cochlear implant algorithms (Vermeire, et al., 2010), the advantages of directional microphones for speech intelligibility in noise (Wilson, McArdle, & Smith, 2007), and the individual self-assessment of speech understanding in noise abilities (Agus et al., 2009; Heifer & Vargo, 2009; Anderson et al., 2013). Anderson et al. (2013)

reported significant correlations between the speech-evoked ABR and speech hearing subscale of the SSQ in the older adults. Specifically, they found that the offset transient response (i.e., wave O) of the speech-evoked ABR predicted more variance in the speech hearing subscale of the SSQ than either the QuickSIN or pure tone hearing thresholds. In this study, we examined the relationship of the speech hearing subscale of the SSQ with noise exposure history in young, normal-hearing adults. Likewise, we explored the contributions of noise exposure history combined with speech- or click-evoked ABR in predicting self-perceived SIN ability in young, normal-hearing adult ears. We predict that individuals with greater noise exposure will report more SIN difficulties. Furthermore, noise exposure history combined with the speech-evoked ABR measure will make significant contributions to the predictions of self-assessed SIN ability via SSQ. Specifically, those individuals with greater noise exposure and neural slowing will have subjective ratings of poorer SIN ability.

In summary, the goal of this study is to gain a better understanding of the auditory mechanisms and perceptual consequences associated with noise exposure in normal-hearing ears. By exploring the neural responses to a speech stimulus at the level of the brainstem and an alternative SIN measure, it may be possible to identify improved methods for detecting early evidence of noise-induced auditory damage to which current clinical protocols are insensitive to.

MATERIALS AND METHODS

This study was conducted under the supervision of Dr. Tiffany A. Johnson in the Auditory Research Laboratory in the Hearing and Speech Department at the University of Kansas Medical Center in Kansas City, Kansas. All subject recruitment, audiological testing and data collection was completed by Nikki A. Go. Approval for the study was granted through the University of Kansas Medical Center Human Subjects Committee (HSC). Refer to Appendix B for the HSC-approved informed consent document.

Subjects

A total of 42 subjects consented to participate in this study. Subjects were primarily recruited from local colleges and universities via flyers, broadcast email or word of mouth. Subjects were required to have normal middle-ear function, normal outer hair cell function, and normal hearing in order to be included in the study.

Special attention was directed at recruiting subjects with a wide range of noise-exposure backgrounds. Similar to Stamper and Johnson (2015a), individuals in music programs were heavily recruited as musicians have been identified as a population that is frequently exposed to high levels of noise (Zhao et al., 2010 and Cook-Cunningham et al., 2012). Likewise, recruitment efforts focused on having an equal distribution of males and females across and at both ends of the range. In addition, subjects for this study were required to be native English speakers. Although the stimulus /dɑ/ used in the speech-ABR is a relatively universal syllable that is included in the phonetic inventories of most European languages (Maddieson, 1984), language-specific variation with respect to some acoustic parameters such as voice onset time (Bijankhan & Nour- bakhsh, 2009) may influence the characteristics of the speech-ABR response waveform.

Of the 42 subjects consented, 12 were excluded from participation. One was excluded due to poor click-ABR morphology, 5 were excluded for failing to meet the audiometric criteria (i.e., high-frequency hearing loss, abnormal tympanogram), two were excluded for failing to meet the noise exposure criteria, one voluntarily withdrew due to scheduling conflict, and one was excluded for failing to attend several appointments. A total of 30 subjects (16 females, 14 males) provided data for analyses. The age of the subjects ranged from 18 to 35 years old with an average of 23.1 years (females = 22.5, males = 23.8).

Subject Sample Size

A power analysis (G*Power) indicated a minimum of 23 subjects were necessary to achieve a power of approximately 80% with a significance level of 0.05 in the upper tail, to detect our hypothesized correlation of 0.5. A total of 30 subjects resulted in a power of 89.7%. We hypothesized an effect size (correlation) for the speech-ABR variables similar to that observed by Stamper & Johnson (2015a) for click ABR variables in the absence of pre-existing data for the speech ABR.

Testing Procedures

Data were collected in two 2-hour testing sessions. The first testing session consisted of consenting procedures, audiometric evaluation, DPOAE testing, detailed case history regarding noise exposure background, completion of the SSQ, and click-ABR testing. The second session consisted of speech-ABR testing. Both testing sessions typically occurred within two weeks of each other.

Audiometric Evaluation

For each subject, behavioral thresholds and middle-ear function of both ears were assessed using standard clinical procedures. Normal hearing was defined as pure-tone behavioral

thresholds of ≤ 20 dB HL (re: American National Standards Institutes 2004) for the octave and inter-octave frequencies between 0.25 and 8 kHz. In addition, subjects were required to have no threshold differences > 15 dB between adjacent test frequencies or air-bone gaps > 10 dB at any test frequency. Pure tone hearing thresholds were measured using ER-3A insert earphones with conventional behavioral audiometric procedures in 5-dB step sizes. Middle-ear function was assessed using a standard clinical tympanometer (GSI Tympstar) with a 226-Hz probe tone. Only ears with normal 226-Hz tympanograms (static admittance of 0.3 to 1.7 mmhos and peak pressure between -100 and +50 daPa; Margolis and Hunter, 1999) at both testing sessions were included. Otoscopic examination was also completed and required to be normal at the beginning of each testing session.

While pure-tone thresholds and middle-ear function were assessed in both ears of each subject, only the right ear was selected as the test ear. Differences between the left and right ear speech-ABR responses have been identified in some studies (Hornickel, et. al., 2009; Ahadi, 2014). Published normative data for the right ear (Vander Werf & Burns, 2011; Johnson et al., 2008; Dhar et al., 2009) are more consistent than those reported for the left ear (Hornickel et al., 2009; Ahadi, 2014). While some wave components recorded from the left ear were found to occur later in time compared to the responses recorded from the right ear, there is no consensus as to which specific components were significantly different between ears.

Assessment of Outer Hair Cell Function

DPOAEs were recorded via an ER-10C (Etymotic Research) probe microphone using custom-designed software (EMAV, Neely & Liu, 1993) at test frequencies 1, 1.5, 2, 3, 4, 6, and 8 kHz. DPOAE stimulus level was calibrated using standard in-situ pressure calibration. DPOAE responses were recorded in response to pairs of primary tones (f1, f2; f1< f2) with fixed

f2/f1 ratio of 1.22. The level of f2 (L2) was fixed at 55 dB SPL, with an L1-L2 difference of 10 dB (Gorga et al., 1997). Subjects were required to have normal DPOAEs. Normal DPOAE responses were defined as having DPOAE levels (in dB SPL) greater than the 90th percentile for hearing impaired ears based on the standard clinical template (Gorga et al., 1997; Appendix C).

Assessment of Noise Exposure Background

The NEQ (Johnson et al, 2017), a self-report questionnaire, was used to quantify individual history of noise exposure and was administered during the first testing session. This questionnaire asks about participation in 11 recreational and occupational activities associated with high noise exposure levels for the previous 12 months. Answers to these questions are used to quantify an estimate of an individual's annual noise exposure (ANE). Appendix D provides details regarding the computation of an individual's ANE from responses on the NEQ. Taking the frequency and duration of participation in each high-noise activity over the previous year, a value ($L_{Aeq8760h}$) quantifying the ANE is obtained. The "L" of the $L_{Aeq8760h}$ represents the sound pressure level in dB, the "A" represents the use of an "A-weighted frequency response, "eq" represents a 3-dB exchange rate for calculation of the time/level relationship, and "8760h" represents the total duration of the noise exposure in hours over one year (365 days per year x 24 hours per day). The NEQ has a theoretical range of 64 to 95.5 $L_{Aeq8760h}$ with higher $L_{Aeq8760h}$ values indicating greater amounts of ANE. Subjects with ANE values of 79 or greater were considered to be at highest risk for developing noise-induced hearing loss (NIHL). This was based on the National Institute for Occupational Safety and Health (NIOSH) occupational noise criterion of 85 $L_{Aeq2000h}$ (8 hours/day × 250 workdays/year) extrapolated to an annual equivalent exposure limit of 78.6 $L_{Aeq8760h}$ by Johnson et al. (2017).

Because the NEQ only quantifies exposures over the past year, a detailed case history of current and past exposures was also taken to ensure that the exposure reported on the questionnaire is representative of their lifetime exposure. Specific questions included 1) Have you ever been exposed to loud sounds that made your ears "ring" or "buzz"? 2) Have you ever been exposed to loud sounds that made your hearing seem muffled for a while? 3) Have you ever been exposed to loud sounds that made your ears hurt, feel "full" or bother you in any other way? 4) How would you describe your current exposure to loud sounds? and 5) How would you describe your past exposure to loud sounds? Only those individuals whose ANE value was judged to represent lifetime noise exposure were included in this study. This is similar to the approach taken by Stamper and Johnson (2015a) to ensure the ANE value is representative of lifetime exposure.

Assessment of Speech-in-Noise Abilities

The SSQ (v. 5.6; Gates & Noble, 2004) was administered to each subject during the first testing session. The SSQ was developed in response to recognized limitations of the traditional audiological battery for predicting listening ability in challenging environments. The questionnaire consists of three subscales: speech hearing, spatial hearing, and other qualities of hearing. The speech hearing subscale of the SSQ assesses 14 different speech listening environments, including quiet environments and a range of challenging environments with competing noise. For the purpose of this study, the speech hearing subscale of the SSQ was used to quantify self-perception of SIN abilities. Subjects were asked to indicate the amount of difficulty experienced in each environment on a scale of 0 to 10, with higher scores reflecting less difficulty. The ratings for each of the 14 different environments were combined to yield an

average score for each subject for the speech hearing subscale of the SSQ. See Appendix E for the detailed SSQ-Speech Hearing subscale and sample computation of the score.

Auditory Brainstem Responses

ABR data were collected using a commercial system (System 3; Tucker-Davis Technologies, Alachua, FL) in a single-walled, sound-attenuated booth. TDT software SigGenRP was used to create the acoustic stimuli and BioSigRP was used to record and analyze ABR responses. Hardware components consisted of an RX6 multifunction processor, RA16 Medusa Base System, PA5 programmable attenuator, and HB7 headphone driver. Stimuli were presented via electrically shielded E-A-R-TONE 3A insert earphones. The responses were collected using a RA4PA 4-channel Medusa preamplifier and a RA4LI 4-channel headstage connected to the Medusa base station by a fiber optic cable. Subjects were reclined comfortably in a chair and encouraged to fall asleep during testing.

Click-ABR was recorded using 100-μsec clicks in alternating polarity with a band pass filter of 100-3000 Hz, amplification of 20, and stimulus rate of 11.3/sec. A vertical one-channel montage was used which requires three electrodes corresponding to the positive (Fpz), negative (right mastoid) and ground electrodes (left mastoid). Two responses with signal averaging of 2000 sweeps were collected at a suprathreshold level, 80 dB nHL. Click-ABR recordings were analyzed within a 20ms epoch and visual monitoring of the raw EEG was used to avoid contamination of the response by excessive myogenic activity. The detection thresholds for the click-ABR stimulus measured from a group of 10 normal-hearing individuals were used to calibrate the stimulus levels in dB nHL. Here, 0 dB nHL = 33 dB ppeSPL for 100μsec clicks.

Speech-ABR was recorded using a 40ms synthesized syllable /da/ (provided by the Auditory Neuroscience Laboratory at Northwestern University, Evanston, Illinois).

with an interstimulus interval of 50ms (10ms pre-stimulus and 40ms post-stimulus) and a bandpass filter of 100-2000 Hz. These recording parameters were based on the recommendations of Skoe and Kraus (2010). The stimulus was presented at 85 and 65 dB SPL at a rate of 8.7/sec. Five blocks of 2000 artifact-free sweeps were collected at each intensity level (i.e. 85 and 65 dB SPL) and were averaged to yield a grand-average response. A vertical two-channel montage was used which required four electrodes corresponding to the positive (channel 1 = Cz; channel 2 = Fpz), negative (right earlobe) and ground electrodes (left earlobe). Speech-ABR recordings were analyzed within a 90 msec epoch and visual monitoring of the raw EEG was used to avoid contamination of the response by myogenic artifacts. In addition, baseline recordings to a crimped sound tube were completed before and after speech-ABR testing to check for the presence of any stimulus or electrical artifact. The output intensity of the speech stimulus was calibrated using the Larson Davis 824 System sound level meter with a 2cc coupler. This was measured directly from the insert earphones at the beginning of each testing session.

For both the click-ABR and speech-ABR, the averaged waveforms (4,000 sweeps for click ABR and 10,000 sweeps for speech ABR) were used for analyses. Two independent judges separately identified individual response peaks related to major acoustic landmarks in the stimuli using visual overlay cursors on a computer screen. This included the peak latency (time relative to stimulus onset), peak to trough amplitudes (magnitude), and inter-peak measurements of the wave components (i.e. click = I and V; /da/ = V, A, and O). The first judge analyzed the waveforms during data collection and therefore was not be blinded to subject information (i.e., noise exposure background). The second judge was blinded to subject information during ABR waveform analyses. Any disagreements between the two judges were resolved by reviewing the data together.

Data Analysis

Simple linear regression was used to explore and describe the unknown relationship of ANE values (independent variable) with each of the following dependent variables: SSQ-Speech Hearing score and specific speech-evoked ABR transient components (waves V and O). Likewise, simple linear regression was used to determine if the previously reported associations between the ANE (independent variable) and select click-evoked ABR wave components (dependent variable) were replicated in this cohort of young, normal-hearing adults. In order for a linear regression model to be an appropriate statistical analysis approach, four assumptions must be met. The first assumption is that a linear relationship exists between the dependent and independent variables. This assumption was verified by visually inspecting scatter plots and residual plots of ABR data and SSQ-Speech Hearing scores as a function of annual noise exposure value. Second, individual samples are required to be uncorrelated in order to demonstrate independence from each other. No individual subject influenced another subject's data; the subjects were enrolled at random. Thirdly, homoscedasticity, or equal variance, is required across all values of the independent variable (i.e., ANE). This assumption was assessed by visually inspecting the residual plots of the ABR and SSQ-Speech Hearing data as a function of noise exposure background and verifying that the spread of the data was uniform. Lastly, normality of the error distribution is required. To determine this, a normal probability plot of the residuals was inspected and was required to fall along a diagonal line.

The data presented here did not violate any assumptions of linear regression analysis. However, some extreme observations (i.e., outliers) were noted in the data. While all data points were valid observations, it was necessary to determine if the exclusion of the outliers changed the conclusions of the data analysis. To do this, studentized residuals were obtained for each

linear regression analysis. The magnitude of the residuals was inspected to see if large values existed (greater than 2 or less than -2). Regression analyses were repeated without the inclusion of the potentially influential observation. Excluding these potentially influential outliers did not change the study conclusions and, therefore, no observations were removed from the data set.

To determine the contributions of the ANE and ABR (speech- or click-evoked) data in predicting self-perceived SIN abilities, the multiple linear regression technique was employed. The assumptions for the multiple linear regression model are the same as simple linear regression with the addition of one more assumption. In multiple linear regression analysis, the two (or more) independent variables must not be correlated with each other (collinearity). To determine if collinearity existed, the Variance Inflation Factor (VIF) was inspected and must be close to 1. All of the assumptions were met for conditions where multiple linear regression analyses were conducted.

RESULTS

The goal of this study was to explore the link between auditory evoked potential estimates of neural survival and temporal processing or SIN deficits in young, normal-hearing adults with varying noise exposure backgrounds. Click-evoked ABR amplitudes were used to evaluate auditory nerve function and speech-evoked ABR latencies were used to evaluate temporal processing. The SSQ-Speech Hearing scores were used to quantify self-reported SIN abilities. These measures were compared to the amount of voluntary noise exposure.

NEQ Data

Individual noise exposure background was quantified using the NEQ. Shown in Fig. 1 is a histogram of the ANE values obtained across all 30 subjects. The NEQ has a theoretical range of 64 to 95.5 $L_{Aeq8760h}$ where higher values indicate greater amount of noise exposure. According to Johnson et al. (2017), $L_{Aeq8760h} \geq 79$ is considered high where these individuals were judged to be at highest risk for noise-induced hearing loss. The subjects tested here ranged from 64 to 86.9 $L_{Aeq8760h}$. This demonstrates that the ANE values in the present study span a wide range and indicate variation in noise exposure background across subjects.

The motivation for recruiting equal number of males and females is to control for the confounding variable of sex in our data. Here, we analyze the distribution of the ANE values between males and females (displayed in Fig. 2). The ANE values ranged from 64 to 86.75 $L_{Aeq8760h}$ (median = 74.33) for the females while the ANE values ranged from 65.98 to 85.43 $L_{Aeq8760h}$ (median = 74.95) for the males. The Mann-Whitney rank sum test was used to compare the distribution of ANE values across the categories of sex. The result indicated the ANE values for our male and female subjects are not significantly different ($p = 0.918$).

Click-ABR Data

Since the physiologic evidence of cochlear synaptopathy reported in animal studies was characterized by reduced ABR wave I amplitude, previous investigations in human ears have focused on examining ABRs to clicks or tone bursts. In an attempt to replicate the findings reported by Stamper and Johnson (2015a), click-evoked ABR data also were collected in the present study. A single-channel, mastoid recording of the ABR was obtained from all subjects at a stimulus level of 80 dB nHL. Figure 3 shows an example of ABR waveforms from one subject collected in response to a click stimulus at 80 dB nHL. Two repetitions of the individual waveform are shown in the top row while the averaged waveform is shown in the bottom row. The peaks and troughs of wave I and V for each subject were picked on the averaged waveform.

Table 1 provides the individual peak latencies and peak amplitudes of the click-ABR responses obtained in the present study as well as the means and standard deviations which are in agreement with ABR data available in the literature for normal-hearing ears (e.g., Hall, 2007).

Figure 4 shows the click- ABR wave I (top row) and wave V (bottom row) peak amplitudes as a function of ANE values of the 30 subjects at 80 dB nHL. The simple linear regression analysis revealed no statistically significant relationship between the ANE values and the wave I peak amplitude ($p = 0.264$). This is in contrast to the data from previous human studies (e.g. Stamper & Johnson, 2015a; Bramhall et al, 2017) where significantly smaller suprathreshold wave I amplitude were reported for individuals with greater amounts of noise exposure compared to those with less noise exposure. Likewise, no significant relationship was seen between ANE values and wave V peak amplitude ($p=0.567$; $r^2 = 0.012$). This lack of relationship between ANE and ABR variables was also observed with the peak latencies of waves I ($p = 0.668$; $r^2 = 0.007$) and V ($p = 0.363$; $r^2 = 0.007$), data shown in Fig. 5.

It has been known that there are differences in the click-ABR response characteristics between males and females. The ABR responses from males are known to have delayed peak latencies and smaller peak amplitudes compared to the ABR response from females (Jerger & Hall, 1980). For this group of subjects, the described sex differences for peak latencies and peak amplitudes for waves I and V can be observed in Figures 6 & 7, respectively. Here, our male subjects generally have longer peak latencies and smaller peak amplitudes than our females. All male-female differences except for wave I latency were found to be statistically significant ($p \leq 0.05$) using the Kruskal-Wallis test. This result is consistent with the literature and therefore affirms the importance of controlling for this variable in this study.

When Stamper and Johnson (2015b) and Prendergast et al. (2017a) analyzed their ABR data according to categories of sex, they both observed reduced ABR wave I amplitudes in high-noise females but enhanced wave I amplitudes in high-noise males compared to the low-noise counterparts. In light of the sex differences reported in these two studies, analyses of click-ABR data for each category of sex were also conducted in the present study. Individual linear regression analysis for each category of sex (shown in Fig. 8) revealed differences in the patterns of wave I amplitude in relation to ANE values between the females and males. Here, the data from female subjects showed non-significant association to ANE values (females: $p=0.264$, $r^2 = 0.088$), consistent with the findings for the entire subject sample. Meanwhile, the male subjects show an opposite trend of increasing wave I amplitude with increasing ANE values (top right panel), which was found to be borderline significant ($p = 0.071$, $r^2 = 0.246$). It should be noted that the sample size for each group (females = 16 and males = 14) is small and that the present study is not statistically powered to detect such an effect for each sex. However, the finding that is most likely to be significant with more power is the finding for males. The enhanced wave I

amplitude in males suggest that the impact of noise exposure on auditory nerve may vary between sexes. No such trends were observed with the peak amplitude of wave V (bottom panels of Fig. 8; females: $p = 0.803$, $r^2 = 0.005$; males: $p = 0.422$, $r^2 = 0.054$) or with the peak latencies of waves I and V (Fig. 9).

Contrary to the reported animal findings, our overall click-ABR data provided no physiologic evidence of cochlear synaptopathy, characterized by reduced wave I amplitude, in this group of noise-exposed young adults. However, when the analyses were restricted to each category of sex, the male subjects with greater noise exposure showed borderline significant enhanced wave I amplitude. Further investigations in a larger number of males and females are therefore needed to determine the specific effects of noise exposure between sexes.

Speech-ABR Data

This study explored a novel objective measure of temporal processing in the form of the speech-ABR. A 2-channel ABR recording to a synthesized /da/ syllable was obtained from all subjects at stimulus levels of 85 and 65 dB SPL. One channel utilized the customary vertex electrode and the other channel utilized a forehead electrode. Figure 10 shows an example of averaged ABR waveforms (10,000 sweeps) from one subject collected from each channel. While we were able to record speech-ABRs successfully from both channels, response waveforms obtained via the vertex electrode in general had sharper and clearer peaks and troughs (i.e., less noise) than the response waveforms obtained via the forehead electrode (see Fig. 10). This allowed for an easier and more accurate identification of the peak components in the response waveforms. Likewise, all previous speech-ABR studies recorded from the vertex. For consistency, only speech-ABR data from the vertex recording were included in the data analyses in the present study. A sample of speech-ABR waveforms from one subject collected at stimulus

levels of 85 and 65 dB SPL are displayed in Figures 11 and 12, respectively. Five repetitions of the individual waveforms are shown in the top row while the averaged waveform is shown in the bottom row. Similar to the click-ABR, the peaks and troughs of wave components V and O for each subject were picked on the averaged waveform.

Table 2 provides the individual peak latencies and peak amplitudes of the speech-ABR responses as well as the means and standard deviations obtained at 85 and 65 dB SPL which are in agreement with the published norms for young adults by Vander Werff & Burns (2011).

The accurate neural timing of the offset and onset response is thought to be important for SIN perception. Neural slowing characterized by delayed peak latencies, particularly of the offset response, may lead to SIN difficulties (Anderson et al., 2013), which is a common complaint even by normal-hearing listeners. Here, we examined the relationship between the ANE values and the latencies of the speech-ABR wave components V (onset response; top row) and O (offset response; bottom row) when recorded at stimulus levels of 85 (right column) and 65 (left column) dB SPL (shown in Figure 13). Linear regression analysis revealed that there is no statistically significant association between the ANE values and the peak latency of the onset response in the speech-evoked ABR, wave V, whether recorded at 85 ($p = 0.388$; $r^2 = 0.0267$) or 65 ($p = 0.323$; $r^2 = 0.035$) dB SPL. This lack of relationship was also seen between the ANE values and the latency of the offset response in the speech-ABR, wave O, at both stimulus levels (i.e., 85 dB SPL: $p = 0.453$; $r^2 = 0.020$ and 65 dB SPL: $p = 0.814$; $r^2 = 0.002$). These results provide no evidence of neural slowing in individuals with greater noise exposure.

Given the negative findings with the peak latencies, the magnitude of the transient response features was also analyzed. Here, we examined the relationship between the ANE values and the peak amplitudes of the onset (wave V) and offset (wave O) response in the

speech-evoked ABR (see Figure 14). Unexpected trends were observed between ANE and the amplitudes of waves V (top panels) and O (bottom panels). When the /da/ syllable was presented at 85 dB SPL (left column), the peak amplitudes of both waves V ($p = 0.001$; $r^2 = 0.3067$) and O ($p = 0.038$; $r^2 = 0.145$) were significantly associated with ANE. Individuals with greater ANE tend to have larger amplitudes. The direction of the association was opposite to what was expected. Likewise, at stimulus level of 65 dB SPL (right column), the same significant trend was also observed in wave V amplitude ($p = 0.018$; $r^2 = 0.185$) but not in wave O ($p = 0.714$; $r^2 = 0.005$).

In summary, individuals with greater ANE showed no significant delays in peak latencies of the onset (wave V) and offset (wave O) responses but had significantly larger peak amplitudes (more consistently in wave V) compared to individuals with less ANE.

In the interest of the differing trends observed between sexes with the click-ABR wave I amplitude, we conducted further analyses to the speech-ABR data for each sex category. Figure 15 shows the speech-ABR peak latencies of waves V latencies as a function of ANE values when /da/ was presented at 85 (top row) and 65 (bottom row) dB SPL. No significant trends were observed in the peak latencies of waves V of both males (right column) and females (left column) for either stimulus level in relation to ANE. Likewise, the same non-significant trends were observed for the peak latencies of wave O (Fig. 16).

Figure 17 shows the speech-ABR peak amplitudes of wave V as a function of ANE values at stimulus levels of 85 (top row) and 65 (bottom row) dB SPL. The female subjects (left column) showed a statistically significant trend of larger wave V amplitude in individuals with higher ANE values at both stimulus levels (85 dB SPL: $p = 0.008$; $r^2 = 0.402$ and 65 dB SPL: $p = 0.045$; $r^2 = 0.257$). While a similar trend persisted in the male subjects (right column), the

relationships were only borderline significant ($p \leq 0.1$) at both stimulus levels (85 dB SPL: $p = 0.078$; $r^2 = 0.236$ and 65 dB SPL: $p = 0.104$; $r^2 = 0.205$).

The same analysis was conducted for the wave O amplitude of the speech ABR (as shown in Fig. 18). At stimulus level of 85 dB SPL, only the males showed borderline significant enhanced amplitudes with greater ANE (males: $p= 0.061$, $r^2 = 0.263$; females: $p = 0.212$, $r^2 = 0.109$). However, no such trends were seen in either sex (males: $p= 0.252$, $r2 = 0.108$; females: $p = 0.915$, $r^2 = 0.001$) at the lower stimulus level of 65 dB SPL (bottom panels). As previously stated, the small sample size for each group (females = 16 and males = 14) should be taken into consideration when interpreting these results.

Overall, the speech-ABR data revealed no evidence of expected neural slowing (characterized by delayed peak latencies) with increased ANE. However, an unexpected statistically significant increase in amplitudes (seen more consistently in the onset response, wave V) was observed as ANE increased. When the analysis was restricted to each category of sex, this later finding of significantly enhanced speech-ABR amplitude in individuals with greater ANE was observed more consistently in males and at a stimulus level of 85 dB SPL.

SSQ-Speech Hearing Data

With the objective of finding an efficacious measure of real-world SIN performance, individual SIN abilities were assessed using the self-report speech hearing subscale of the SSQ as opposed to a standardized SIN test. Figure 19 shows a histogram of the speech hearing scores across all 30 subjects where higher values indicate less difficulty. Study participants were asked to rank their self-perceived ability from a scale of 0 to 10. The maximum value of 10 indicates that no difficulty is experienced at all with what is described in the question. Decreasing values indicate increasing difficulty with 0 indicating complete disability. Likewise, we also examined

the distribution of speech-hearing scores between the male and female subjects. The speech hearing scores for males ranged from 6.8 to 10 (median = 8.19) while female scores ranged from 6.5 to 9.8 (median = 8.68) as illustrated in a boxplot in Fig. 20. The Kruskal-Wallis test indicated no significant differences in the distribution of speech-hearing scores across the male and female categories (p = 0.36).

As previously mentioned, the relationship between ANE and self-perceived SIN abilities are unknown. Here, we examined the relationship between ANE and self-perceived SIN abilities. Figure 21 plots the speech hearing score of all subjects as a function of ANE ($L_{Aeq8760h}$). Linear regression analysis revealed a statistically significant relationship (p-value=0.034; r^2 = 0.15) between the SSQ-Speech Hearing score and ANE value. This finding indicates that individuals with more noise exposure reported experiencing greater difficulty hearing speech in the presence of background noise.

In order to determine the link between noise exposure, evoked potential estimates of neural survival and temporal processing, and perceptual deficits in this group of young, normal-hearing adults, multiple regression analyses were conducted. We hypothesized that both the ANE and ABR components to speech or click stimuli will make significant contributions to the prediction of self-perceived SIN abilities quantified by the SSQ-Speech Hearing subscale. The general multiple regression model used is as follows: $\boldsymbol{\gamma_i = \beta_0 + \beta_1 X_{1i} + \beta_2 X_{2i} + \beta_{12} X_1 X_2 + \varepsilon_i}$; where $\boldsymbol{\gamma_i}$ is the estimated speech hearing score, $\boldsymbol{\beta_0}$ is the $\boldsymbol{\gamma}$ intercept, $\boldsymbol{\beta_1 X_{1i}}$ is the estimated regression coefficient for the ANE on speech hearing score, $\boldsymbol{\beta_2 X_{2i}}$ is the regression coefficient of ABR data on speech hearing score, $\boldsymbol{\beta_{12} X_1 X_2}$ is the regression coefficient of the interaction effect between ANE and ABR data the on speech hearing score, and $\boldsymbol{\varepsilon_i}$ is the random error. In the case where no interaction effect was observed between the two

independent variables, the analysis was rerun using a reduced multiple regression model of: $\boldsymbol{\gamma_i = \beta_0 + \beta_1 X_{1i} + \beta_2 X_{2i} + \varepsilon_i}$.

For the click-ABR wave components I and V, no interaction effect was found between the peak latencies or peak amplitudes and ANE ($p > 0.05$). In the reduced multiple regression model, the inclusion of the click-ABR variable (i.e., peak latencies and peak amplitudes of waves I and V) did not add anything statistically meaningful to the regression equation. Please refer to Table 3 for the adjusted and change in coefficient of determination (r^2) and p-value for each model.

The same results were found with the speech-ABR components V and O. No interaction effect was found between the ANE and either the peak latencies or peak amplitudes of waves V and O. Likewise, the inclusion of the speech-ABR data in the regression model did not make a significant contribution to the regression equation (Table 4). Therefore, these "nuisance" variables were removed reducing the further reducing the equation to a simple linear regression model, where ANE alone accounts for 15% of the variance in self-perceived SIN abilities.

The present data resulted in mixed findings. The click-ABR results consistent with noise-induced cochlear synaptopathy were not replicated in this group of young, normal-hearing adults when analysis included all data. However, individual analysis of data according to categories of sex reveal differing trends in the click-ABR wave I amplitude suggesting sex may be an important variable in the susceptibility of an individual to noise-induced auditory damage. The speech-ABR data revealed no evidence of expected neural slowing with increased ANE and an unexpected increase in amplitude as ANE increased. Lastly, individuals with greater amounts of noise exposure reported experiencing more difficulty hearing in noise (as per the SSQ speech-hearing score).

DISCUSSION

In this group of young, normal-hearing adults, individuals with greater noise exposure reported experiencing greater SIN difficulties. However, the evoked potential measures at suprathreshold level did not provide the expected physiologic evidence (i.e., reduced auditory nerve response or neural slowing at higher brainstem level) that would account for the self-perceived SIN deficits. Instead, the data revealed greater neural response amplitude to the transient features of a complex stimulus in all "high-noise" individuals (i.e., ANE $\geq$ 79 $L_{Aeq8760h}$) and to simple stimuli in "high-noise" males.

ABR Wave I Measure

Contrary to previous investigations (Stamper and Johnson, 2015a; Bramhall et al., 2017), our ABR wave I amplitude results provide no evidence for noise-induced cochlear synaptopathy in this group of young, normal-hearing listeners. These inconsistencies may be due to several factors. One possible factor is the insufficient sensitivity of the highly variable ABR amplitude measure to detect subtle injurious effects of noise exposure. While the loss of predominantly low-spontaneous rate fibers was shown to attenuate the auditory nerve (AN) response (Kujawa and Liberman, 2009; Furman et al., 2013), Bourien et al. (2014) reported otherwise. Bourien and colleagues found that the compound action potentials (equivalent to ABR wave I) of gerbils and guinea pigs did not reduce substantially despite great depletion of the low-spontaneous rate fibers via ouabain suggesting that low-spontaneous rate fibers contribute little to the compound action potential (probably because they have delayed, and broadened, first spike distribution). Therefore, if low-spontaneous rate fibers do not contribute to wave I, the sensitivity of this measure is limited relative to the synaptopathy described in the animal literature.

The distribution of fiber types across species may be another factor. Variation in inter-species susceptibility has been demonstrated by Valero et al. (2017), who found that the sound pressure levels of the noise needed to be 20 dB higher to produce a similar degree of cochlear synaptopathy in primates when compared to rodents. Therefore, it is possible that our assumptions of the fiber groups and their relative distributions in humans may be inaccurate. Another possibility is that not all subjects are equally susceptible to noise exposure, and therefore noise exposure would induce cochlear synaptopathy only in certain individuals. It is also plausible that synapses disrupted by noise exposure partially repair, thus leading to partially-recovered wave I amplitudes, as has been reported in guinea pigs (Shi et al., 2013; Song et al., 2016). It could also be possible that noise exposure induces cochlear synaptopathy only in selected portions of the cochlea (Kujawa and Liberman, 2009, 2015; Furman et al., 2013), and therefore, the effect of cochlear synaptopathy is obscured when ABRs are evoked by short-duration clicks, which present energy in a broad range of frequency components.

Sex Differences in the Click-ABR Wave I Amplitude

While the present study was not powered to detect an effect for each sex, differences in the patterns of the click-ABR wave I amplitude in relation to noise exposure between the females and males were observed, where females showed no significant association and males showed a positive linear trend. The opposing trends in the wave I amplitude for each category of sex may well have effaced possible associations with the noise exposure history when data for both sexes were combined. It is also possible that the male-female differences reflect differences in the susceptibility to the effects of noise between the sexes. The reasons for the sex differences cannot be determined in this study and are opposite to what would be predicted from data on male-female differences in susceptibility to noise-induced permanent threshold shifts.

Sex differences have been reported in susceptibility to permanent NIHL in humans (e.g., Berger, Royster and Thomas, 1978; Gallo and Glorig, 1964; Tambs et al., 2006). The retrospective studies of permanent hearing loss, generally caused by long-term occupational exposure, tend to indicate that men are more susceptible than women to hearing loss. In exposures to low frequency continuous noises, males were found to develop much more hearing loss than females. Both Berger et al. (1978) and Gallo and Glorig (1964), found approximately 20 dB more permanent threshold shifts in males than in females after 9 years of industrial noise exposure. These results are consistent with the gender differences observed in studies of temporary threshold shift in humans (e.g., Axelsson and Lindgren, 1981; Dengerink et al., 1984; Petiot and Parrot, 1984; Ward, 1966). In general, experimental studies of temporary threshold shifts (TTS) have found that males exhibit more TTS than females from low-frequency exposures (below 2 kHz), whereas females exhibit more TTS than males from high-frequency exposures (above 2 kHz).

Some studies have proposed that sex hormones may be responsible for the difference in the male-female susceptibility described above. Hormonal influences on cochlear function generally suggest males should be more susceptible to noise-induced damage than females. Animal studies have suggested that males may be more vulnerable to the effects of noise due to the estrogen hormone having a protective effect on the female cochlea especially during young adulthood (Willott and Bross, 2004; Guimaraes et al., 2004). Estrogen receptors have been observed in the mouse auditory system (Stenberg et al., 1999; Nathan et al., 1999), although what role they might play is still unknown. It is thought that estrogen and progesterone modulate the secretion of the inhibitory neurotransmitter, GABA, in the auditory pathway (Nadal et al., 2001). Noise overstimulation causes an excessive release of glutamate (excitatory

neurotransmitter found in the cochlea) that can lead to synaptic damage (excitotoxicity). Estrogen may interact with the surface membrane receptors or ion channels to change the excitability of nerve cells. It is thought to block the glutamate receptor, NMDA 'R', and could be protective against excitotoxicity of glutamate by simply delaying conduction in the auditory pathway (Lee and Marcus, 2001). Ovarian steroids have also been reported to have influence on cochlear blood flow and potentially hearing functions too (Laugel et al., 1987). If estrogen is indeed neuroprotective as suggested, males, therefore, should show increased susceptibility to noise induced pathology and to the extent that reduction in wave I amplitude reflects pathology, However, the findings in the present data are opposite to what would be predicted. Likewise, this does not explain why the males did not show the expected trend of attenuated AN response with increasing noise exposure.

On the other hand, some studies have contradicted the assertion of estrogen having a protective effect. A subsequent study by Willott et al. (2006) examined the effects of exposing gonadectomized and surgically intact mice of both sexes to a high-frequency noise. Their data failed to support the hypothesized protective role of estrogen in the female mice. In fact, they found that the surgically intact females had more severe ABR threshold elevations at higher frequencies than the gonadectomized females and the male counterparts suggesting suggest that ovarian hormones have little effect during adulthood, and may even potentiate noise-induced hearing loss in mice. Interestingly, studies by McFadden et al. (1999, 2000) showed that female chinchillas exposed to noise exhibited more severe threshold elevations at higher frequencies than males, whereas they showed less hearing loss than males at lower frequencies. Taken together, these studies suggest that ovarian hormones may be neurotoxic rather than neuroprotective in relation to noise exposure particularly at the basal region of the cochlea

suggesting females may be more vulnerable to the effects of noise exposure. If estrogen is neurotoxic rather than neuroprotective as suggested, "high-noise" females therefore, should exhibit attenuated wave I than "high-noise" males. While this may explain the findings by Stamper and Johnson (2015b) in their female subjects, the data from the present study did not provide evidence of this.

It is also likely that the method of quantifying noise-exposure could play a role and/or introduce errors leading to sex differences. Although our statistical analysis showed similar distribution of ANE across the categories of sex, it is possible that we did not capture "true low-noise males". We do note that the ANE range for our male subjects is slightly more restricted than for our female subjects at both ends of the spectrum (minimum ANE: males = 66, females = 64; maximum ANE: males = 85, females 87). However, there was no statistical difference between the two groups, even if the extreme values were slightly different. If noise exposure is a factor contributing to a difference in wave I amplitude between males and females, it is not clear why our data showed a trend opposite of what would be expected in male subjects (i.e., larger wave I amplitude in males with greater ANE).

Given the conflicting data from the animal studies, the possibility of hormone effect causing these sex differences in relation to noise exposure is yet to be determined. It is possible that our male–female amplitude difference for wave I is driven by several factors as discussed above. However, it is not clear why these factors would influence the amplitude of wave I but not wave V. These issues have potentially important implications for our understanding of the impact of noise exposure on human ears; therefore, further investigations are needed.

Enhanced Speech-ABR Amplitudes

While our measure of temporal processing (i.e., speech-ABR), did not show evidence of neural slowing with respect to delayed timing of the ABR, it revealed enhanced neural responses to the transient features (i.e., onset and offset) of the speech stimulus in individuals with greater noise exposure. One possibility is that this unexpected finding of enhanced speech-ABR amplitudes may be due to refined neural encoding driven by corticofugal projections.

The absence of latency delays in conjuction with larger amplitudes for the onset and offset components of the speech-ABR in individuals with greater ANE could possibly be a manifestation of the influence of musical training. Upon the review of our data, majority of the individuals with higher ANE (i.e., $\geq$ 79 $L_{Aeq8760h}$) were trained musicians (see Table 6). Musacchia et al. (2007) reported significantly enhanced onset response (wave V latency and amplitude) to /da/ in their group of musicians when compared to non-musicians controls when speech-ABR was recorded in quiet. Similarly, the study by Parbery-Clark et al. (2009) examined the effect of musical training on the neural representation of SIN by comparing speech-ABR in quiet and in noise. While musicians were found to have earlier and larger onset response (i.e., wave V latency and amplitude) to speech in quiet, they were not statistically significant when compared to the non-musicians. The significant enhancement in the neural response was more evident when in background noise suggesting faster and more robust neural encoding of speech in musicians. It is thought that musicians' use of fine-grained acoustic information and experience with parsing simultaneously occurring melodic lines may refine the neural code in a top-down manner (Parbery-Clark et al., 2009). Studies have shown that the auditory cortex sharpens the subcortical sensory representations of sounds through the enhancement of the target signal and the suppression of irrelevant competing background noise via the efferent system (Suga et al., 1997; Zhang et al., 1997; Luo et al, 2008).

This "musician effect" described in the two studies (Musacchia et al. 2007 and Parbery-Clark et al., 2009) provides a possible explanation why our "high-noise" individuals showed enhanced peak amplitudes in the onset response (wave V) when compared to the "low-noise" individuals. However, our data did not show the reported earlier wave V latencies in musicians.

While these two studies (Musacchia et al., 2007 and Parbery-Clark et al, 2009) reported on the effects of musical training on the other components of the speech-ABR (i.e., transition from consonant to vowel and steady state), they did not include the offset response in their data. Given that we observed similar response patterns between the onset and offset components in our data at the higher stimulus level, it is likely that the musical training has the same effect on the speech-ABR offset response.

If the speech-ABR data is indeed influenced by the subjects' musical experience, it is possible that the benefits of musical training may diminish the negative impacts of exposure to high levels of sound. This may explain why our data did not show the expected delay in the peak latencies and unexpected enhanced amplitudes of waves V and O at suprathreshold levels. The effect of musical training in relation to noise exposure has yet to be determined. It may be necessary to either exclude them or place them in a separate category in future studies in order to fully understand the impact of noise exposure on temporal coding abilities without the confounding effect of musical experience.

Another possibility is that the enhanced speech-ABR responses observed in our data may be a manifestation of pathology resulting in increased central neural gain to compensate for the reduced input from the auditory nerve consistent with noise-induced cochlear synaptopathy. There is evidence of increased spontaneous neuronal activity in the inferior colliculus of gerbils (Vale & Sanes, 2002) and guinea pigs (Mulders and Robertson, 2009) as a consequence of

hearing loss. The inferior colliculus receives multiple inhibitory and excitatory projections through the lateral lemniscus and contralateral inferior colliculus pathways (Adams, 1979; Nordeen et al., 1983; Coleman & Clerici, 1987; Smith, 1992; Oliver et al., 1994; Wagner, 1996; Lo et al., 1998; Moore et al., 1998; Vale & Sanes, 2000). It has been shown that activity deprivation as a result of hearing loss or deafness leads to 1) increased spontaneous and evoked excitation in the inferior colliculus, 2) decreased spontaneous and evoked inhibition in the inferior colliculus (Vale and Sales, 2002), and 3) intrinsic excitability of cortical neurons is increased (Desai et al., 1999). These changes could lead to hyper-excitable neuronal networks that amplify spontaneous cortical activity (Houweling et al., 2005).

Gu et al. (2012) reported reduced ABR wave I but enhanced waves III and V amplitudes to clicks in their subjects with tinnitus. They proposed that central hyperactivity elevate input to the inferior colliculi (wave V) to compensate for reduced input from the AN (wave I). Therefore, it is possible that enhancement of the speech-ABR wave V that is thought to be generated primarily from the lateral lemniscus and inferior colliculus may be an indication of early noise-induced damage in the auditory system in this case.

While literature states that the wave V-A complex (onset response) of the speech-ABR is analogous to the wave V-Vn of the click-ABR, the enhanced neural response in relation to increased noise exposure was not observed in the latter. A number of studies have demonstrated that click and speech stimuli impose different encoding demands on the brainstem. Specifically, children with learning and literacy disorders show abnormal neural encoding of speech in the presence of a normal click-evoked ABRs (Cunningham et al., 2001; Wible et al., 2004, 2005; Banai et al., 2005; Johnson et al., 2005, 2007; Russo et al., 2005; Song et al., 2006). This underscores an important neural encoding discrepancy between click and speech stimuli, despite

similar generation sites. It is possible that the differences in acoustical features of the stimuli may be responsible for the inconsistent findings in our click- and speech-evoked ABR data in relation to noise exposure. Speech stimuli have a longer rise time and are acoustically more complex compared to clicks. The click stimulus is a short, non-periodic sound containing a broad range of frequencies, whereas consonant–vowel speech syllables such as /da/ begin with relatively low-amplitude transient onset features followed by a sustained periodic signal, the vowel, which is considerably louder with respect to the consonant. Another possible factor is the environmental relevance and exposure of these two stimuli in humans. Speech is more prevalent and relevant in our day-to-day activities than clicks. There is evidence that brainstem encoding of sound has been shown to be shaped by lifelong linguistic and musical experience (Krishnan et al., 2004, 2005; Musacchia et al., 2007; Wong et al., 2007) and the reverse hierarchy theory suggests that learning modifies the neural circuitry starting at the highest level and gradually refining lower areas when more fine-grained sensory information is required (Ahissar and Hochstein, 2004). This suggests that the use of speech stimulus may be a more sensitive ABR measure and provide important and relevant neurophysiological information that cannot be obtained from non-speech stimuli. Therefore, the speech-ABR test may be a valuable tool in detecting early damages to the auditory pathway in relation to noise exposure, but further investigations are needed.

Self-Perceived SIN Ability

We chose to use the SSQ rather than a more direct measure of SIN perception, such as the QuickSIN, because we wanted to approximate overall, day-to-day SIN performance, as opposed to a one-time test in the laboratory. Likewise, it addresses individual self-perception of ability, which is what generally motivates someone to seek help for hearing difficulties. As predicted, our data showed significant relationship between ANE and the SSQ-speech hearing

subscale. Individuals with greater noise exposure reported greater SIN difficulties compared to those with less or minimal noise exposure. Prendergast et al. (2017b) examined the relationship of the SSQ-speech hearing subscale with lifetime noise exposure in their study participants and found no significant association between the two. It is possible that our differing method of quantifying individual noise exposure may account for the contrasting results with the NEQ seemingly a better predictor of self-perceived SIN ability.

The lack of relationship between the click-ABR data and SSQ-speech hearing score is consistent with the findings of Prendergast et al. (2017b). Furthermore, the addition of the click-ABR data to the ANE value did not strengthen the regression model for predicting self-perceived SIN ability. These findings suggest that the sensitivity of the click-ABR is insufficient for identifying neural deficits related to SIN difficulties.

While the speech-ABR is thought to be a more sensitive measure for detecting temporal processing deficits implicated in SIN difficulties, our data failed to show a relationship between the transient speech-ABR components and the SSQ. The associations observed between ANE and the amplitudes of these components in some stimulus conditions indicate enhanced neural encoding of temporal cues in individuals with greater ANE which does not translate to increased SIN difficulty. As discussed in the above paragraphs, musical experience may have potentially influenced the outcome of our analyses. Therefore, future investigations controlling for this confounding variable are needed to investigate the relationship between speech-ABR and SSQ-speech hearing subscale in young, noise-exposed, normal-hearing listeners.

Despite the statistically significant relationship between the ANE and the SSQ-speech hearing score, ANE alone explains a small proportion of the total variation (15%) in the SSQ-speech hearing score of our study participants. It is possible that personality characteristics and

lifestyle biases likely affect individual answers on the SSQ. Musicians and other individuals who engage in noisy activities may answer questions differently compared to those who have a quieter lifestyle. Therefore, individual response biases likely contributed to the variability in SSQ.

While some of our study participants were students from the audiology or speech and language programs, they would not be familiar with or exposed to the SSQ as it is not a commonly used tool in most clinical sites. It should also be noted that our subjects were not recruited based on their hearing difficulties and, therefore, are not typical for patients of an audiologic clinic who are seeking treatment or advice for hearing problems. Nevertheless, some of our participants were motivated to participate in the study because they had noticed some trouble when listening in noise and wanted to participate in a research study before seeking clinical consultation.

Given our results, the SSQ proves to be an effective measure of real-world SIN abilities in young, noise-exposed normal-hearing individuals. It can be a valuable tool in addition to the standardized behavioral tests for assessing individual SIN difficulties both in clinic and in research. The extension of this analysis to a clinical population of normal-hearing individuals seeking audiological help due to SIN difficulties in a future study may be beneficial.

CONCLUSIONS

The goal of this study is to explore the link between noise exposure, evoked potential estimates of neural survival and temporal processing, and SIN deficits in normal-hearing listeners. The overall click-ABR wave I results provide no evidence for noise-induced synaptopathy in this group of subjects. However, differences in the wave I amplitude between categories of sex were observed suggesting varying noise effects between males and females. Transient components of the speech-ABR showed no evidence of neural slowing but revealed enhanced neural responses in individuals with greater amounts of noise exposure. The latter finding may be due to either "musician effect" or increased central neural gain as a result of a pathology. While individuals with more noise exposure reported experiencing greater difficulty hearing speech in the presence of background noise, suprathreshold evoked potential data failed to provide neurophysiologic link that would explain the reported SIN deficit.

The results of the present study have raised more questions that warrant further investigation. Pursuing research exploring the impact of noise exposure on males vs. females and musicians vs. non-musicians with normal hearing may be necessary. Knowing the specific effects of noise exposure on each of these groups will help with the identification of a more appropriate assessment approach that may detect early auditory noise damage. In addition, the full potential of the speech-ABR measure needs further exploration. The present study has only collected speech-ABRs in quiet. Speech-ABRs to masked and binaural conditions in noise-exposed normal-hearing listeners have yet to be examined; therefore, more work in this area is needed. Lastly, extending these analyses to a clinical population of normal-hearing individuals seeking audiological help due to SIN difficulties may be beneficial.

References

Adams, J.C. (1979). Ascending projections to the inferior colliculus. *J. Comp. Neurol*., 183, 519–538.

Agus, T.R., Akeroyd, M.A., Noble, W., Bhullar, N. (2009). An analysis of the masking of speech by competing speech using self-report data. *J Acoust Soc Am*, 125:23–26.

Ahadi, M., Pourbakht, A., & Jafari, A., Jalaei, S. (2014). Effects of stimulus presentation mode and subcortical laterality in speech-evoked auditory brainstem responses. *International Journal of Audiology*, 53, 243-249.

Ahissar, M., Hochstein, S. (2004). The reverse hierarchy theory of visual perceptual learning. *Trends in Cognitive Sciences,* 8: 457–46.

Akhoun, I., Moulin, A., Jeanvoine, A., Ménard, M.,; Buret, F., Vollaire, C., Scorretti, R., Veuillet, E.,Berger-Vachon, C., Collet, L., Thai-Van, H. (2008). Speech auditory brainstem response (speech abr) characteristics depending on recording conditions, and hearing status: An experimental parametric study. *J Neurosci Methods*, 2175:196–205.

Anderson, S., Parbery-Clark, A., White-Schwoch, T., & Kraus, N. (2013). Auditory Brainstem Response to Complex Sounds Predicts Self-Reported Speech-in-Noise Performance. *Journal of Speech, Language, and Hearing Research : JSLHR*, *56*(1), 31–43.

Anderson, S., Parbery-Clark, A., Yi, H., Kraus, N. (2011.) A neural basis of speech-in-noise perception in older adults. *Ear Hear*, 32(6): 750-757.

ANSI (2004) Specifications for Audiometers, *ANSI Report No. S3.6-2004*. American National Standards Institute, New York.

Axelsson, A., Lindgren, F. (1981). Pop music and hearing. *Ear Hear*, 2:64–9.

Banai, K., Abrams, D., Kraus, N. (2007). Speech evoked brainstem responses and sensory-based accounts of learning disability. *International Journal of Audiology,* 46: 524-532.

Banai, K., Hornicke,l J., Skoe, E., Nicol, T., Zecker, S., Kraus, N. (2009). Reading and subcortical auditory function. *Cereb Cortex*, 10:2699-2707.

Banai, K., Nicol, T., Zecker, S., Kraus, N. (2005) Brainstem timing: implications for cortical processing and literacy. *Journal of Neuroscience,* 25(43): 9850-9857.

Berger, E., Royster, L., Thomas, W. (1978). Presumed noise-induced permanent threshold shift resulting from exposure to an A-weighted Leq of 89 dB. *J Acoust Soc Am*, 64:192-7.

Bharadwaj, H.M., Masud, S., Mehraei, G., Verhulst, S., Shinn-Cunningham, B.G. (2015). Individual differences reveal correlates of hidden hearing deficits. *J. Neurosci*., 35, 2161-2172.

Biacabe, B., Chevallier, J.M., Avan, P., Bonfils, P. (2001). Functional anatomy of auditory brainstem nuclei: Application to the anatomical basis of brainstem auditory evoked potentials. *Auris, nasus, larynx*. 28. 85-94.

Bijankhan, M. & Nourbakhsh, M.. (2009). Voice onset time in Persian initial and intervocalic stop production. *Journal of the International Phonetic Association,* 39. 335 - 364.

Boston, J. R. & Møller, A. R. (1983). Brainstem auditory-evoked potentials. *CRC Critical Reviews in Biomedical Engineering,* 13(2), 97-123.

Bourien, J., Tang, Y., Batrel, C., Huet, A., Lenoir, M., Ladrech, S., Desmadryl, G., Nouvian, R., Puel, J.L., Wang, J. (2014). Contribution of auditory nerve fibers to compound action potential of the auditory nerve. *J. Neurophysiol*., 112, 1025-1039.

Bramhall, N.F., Konrad-Martin, D., McMillan, G.P., Griest, S.E. (2017). Auditory brainstem response altered in humans with noise exposure despite normal outer hair cell function. *Ear Hear*., 38, 1-12.

Centers for Disease Control and Prevention, (2010). Adolescent School Health, Noise-Induced Hearing Loss, http://www.cdc.gov/healthyyouth/noise/.

Cook-Cunningham, S.L., Grady, M.L. & Nelson, H. (2012). Hearing dose and perceptions of hearing and singing effort among university choir singers in varied rehearsal and performance settings. *Int J Res Choral Singing*, 4(1), 19-35.

Cooper, J.C., Gates, G.A. (1991). Hearing in the elderly—the Framingham cohort, 1983–1985: part II. Prevalence of central auditory processing disorders. *Ear Hear*., 12(5):304–311.

Costalupes, J.A., Young, E.D., Gibson, D.J. (1984). Effects of continuous noise backgrounds on rate response of auditory nerve fibers in cat. *J Neurophysiol*., 51(6):1326–44.

Chandrasekaran, B., Kraus, N. (2009). The scalp-recorded brainstem response to speech: neural origins *Psychophysiology*.

Coleman, J.R. & Clerici, W.J. (1987). Sources of projections to subdivisions of the inferior colliculus in the rat. *J. Comp. Neurol*., 262, 215–226.

Cunningham, J., Nicol, T., Zecker, S,G, Bradlow, A., Kraus, N. (2001). Neurobiologic responses to speech in noise in children with learning problems: deficits and strategies for improvement. *Clinical Neurophysiology*, 112: 758-767.

Dhar, S., Abel, R., Hornickel, J., Nicol, T., Skoe, E., Zhao, W., Kraus, N. (2009). Exploring the relationship between physiological measures of cochlear and brainstem function. *Clinical Neurophysiology*, 120: 959-966.

Dengerink, H.A., Trueblood, G.W., Dengerink, J.E. (1984). The effects of smoking and environmental temperature on temporary threshold shifts . *Audiology* 23 :401-410.

Desai, N.S., Rutherford, L.C., Turrigiano, G.G. (1999). Plasticity in the intrinsic excitability of cortical pyramidal neurons. *Nat Neurosci* 2:515–520.

Don, M. & Eggermont, J.J. (1978). Analysis of the click-evoked brainstem potentials in man using high-pass noise masking. *J Acoust Soc Am,* 63(4), 1084-92.

Faure, P.A., Fremouw, T., Casseday, J.H., Covey, E. (2003). Temporal masking reveals properties of sound evoked inhibition in duration-tuned neurons of the inferior colliculus. *J. Neurosci*., 23:3052–3065.

Fernandez, K.A., Jeffers, P.W., Lall, K., Liberman, M.C., Kujawa, S.G. (2014) Aging after noise exposure: acceleration of cochlear synaptopathy in "recovered" ears. *J Neurosci*.,13; 35(19):7509-20.

Furman, A.C., Kujawa, S.G. & Liberman, M.C. (2013) Noise-induced cochlear neuropathy is selective for fibers with low spontaneous rates. *J Neurophysiol*., 110(3), 577-86.

Gallo, R., Glorig, A. (1964). Permanent threshold shift changes produced by noise exposure and aging. *Am Ind Hyg Assoc J*, 25:237-45.

Galvin, K., Noble, W. (2013). Adaptation of the speech, spatial, and qualities of hearing scale for use with children, parents, and teachers. *Cochlear Implants International*. 14.

Gatehouse, S., Noble, W. (2004). The speech, spatial and qualities of hearing scale (SSQ). *International Journal of Audiology*, 43, 85–99.

Gorga, M.P., Neely, S.T., Orlich, B., Hoover, B., Redner, J. & Peters, J. (1997). From laboratory to clinic: A large scale study of distortion product otoacoustic emissions in ears with normal hearing and ears with hearing loss. *Ear Hear*, 18, 440–55.

Grinn, S.K., Wiseman, K.B., Baker, J.A., Prell, L.,G.,C. (2017). Hidden hearing loss? No effect of common recreational noise exposure on cochlear nerve response amplitude in humans. *Front. Neurosci*. 11.

Gu, J.W., Herrmann, B.S., Levine, R.A., Melcher, J.R. (2012). Brainstem auditory evoked potentials suggest a role for the ventral cochlear nucleus in tinnitus. *J. Assoc. Res. Otolaryngol.,* 13, 819-833.

Guest, H., Munro, K.J., Prendergast, G., Howe, S., Plack, C.J. (2017). Tinnitus with a normal audiogram: Relation to noise exposure but no evidence for cochlear synaptopathy. *Hear. Res.,* 344, 265-274.

Guimaraes, P., Zhu, X., Cannon, T., Kim, S.H., Frisina, R.D. (2004). Sex Differences in Distortion Product Otoacoustic Emissions as a Function of Age in CBA Mice. *Hear Res.,* 192:83–89.

Hall, J (1992) Handbook of Auditory Evoked Responses. Boston. Allyn and Bacon.

Hall, J. (2007) ABR analysis and interpretation In: *New Handbook of Auditory Evoked Responses* (ed J. Hall). pp. 171-211. Pearson Education, Inc., Boston.

Heifer, K.S., Vargo, M. (2009). Speech recognition and temporal processing in middle-aged women. *Journal of the American Academy of Audiology*. 20:264–271.

Hickox, A. E., & Liberman, M. C. (2014). Is noise-induced cochlear neuropathy key to the generation of hyperacusis or tinnitus? *Journal of Neurophysiology*, 111, 552–564.

Hind, S.E., Haines-Bazrafshan, R., Benton, C.L., Brassington, W., Towle, B., Moore, D.R. (2011). Prevalence of clinical referrals having hearing thresholds within normal limits. *Int J Audiol*, 50:708–716.

Hood, L. J. (1998). Clinical applications of the Auditory Brainstem Response. Clifton, Park, Thompson Delmar Learning.

Hornickel, J., Skoe, E., Kraus, N. (2009). Subcortical Laterality of Speech Encoding. *Audiology & Neurology*, 12(1), 198-207.

Houweling A.R., Bazhenov, M., Timofeev, I., Steriade M, Sejnowski, T.J. (2005). Homeostatic synaptic plasticity can explain post-traumatic epileptogenesis in chronically isolated neocortex. *Cereb Cortex*, 15:834–845.

Humes, L.E., Joellenbeck, L.M. & Durch, J.S. (2005). Noise and Military Service: Implications for Hearing Loss and Tinnitus. National Academies Press, Washington DC.

Jerger, J., Hall, J. (1980). Effects of age and sex on auditory brainstem response. *Arch. Otolaryngol.*, 106, 387-391.

Johnson, K.L., Nicol, T.G. & Kraus, N. (2005). Brainstem response to speech: A biological marker of auditory processing. *Ear Hear*, 26, 424 - 434.

Johnson, K.L., Nicol, T.G., Zecker, S.G., Bradlow, A., Skoe, E., Kraus, N. (2008). Brainstem encoding of voiced consonant-vowel stop syllables. *Clinical Neurophysiology*, 119: 2623-2635.

Johnson, K. L., Nicol, T. G., Zecker, S. G., & Kraus, N. (2007). Auditory brainstem correlates of perceptual timing deficits. *Journal of Cognitive Neuroscience*, 19(3), 376-385.

Johnson, T.A., Cooper, S., Stamper, G.C., Chertoff, M. (2017). Noise Exposure Questionnaire (NEQ): A tool for quantifying annual noise exposure. *J. Am. Acad. Audiol*, 28, 14-35.

Krishnan, A., Xu, Y., Gandour, J., Gandour, J., Cariani, P. (2004). Human frequency-following response: representation of pitch contours in Chinese tones. *Hear. Res*., 189, 1-12.

Krishnan, A., Xu, Y., Gandour, J., Gandour, J., Cariani, P. (2005). Encoding of pitch in the human brainstem is sensitive to language experience. *Cognitive Brain Research*, 25(1), 161-168.

Kumar, G., Amen, F., & Roy, D. (2007). Normal hearing tests: is a further appointment really necessary? *Journal of the Royal Society of Medicine*, 100(2), 66.

Kumar, U. A., Ameenudin, S., & Sangamanatha, A. V. (2012). Temporal and speech processing skills in normal hearing individuals exposed to occupational noise. *Noise and Health*, 14, 100–105.

Kujawa, S.G. & Liberman, M.C. (2009). Adding insult to injury: Cochlear nerve degeneration after "temporary" noise-induced hearing loss. *J Neurosci*,, 29(45), 14077-85.

Kujawa, S.G., Liberman, M.C. (2015). Synaptopathy in the noise-exposed and aging cochlea: primary neural degeneration in acquired sensorineural hearing loss. *Hear. Res*., 330, 191-199.

Laugel, G.R., Dengerink, H.A., Wright, J.W. (1987). Ovarian steroid and vasoconstrictor effects on cochlear blood flow. *Hear Res*., 31:245–251.

Lee, J.H., Marcu,s D.C. (2001). Estrogen acutely inhibits ion transport by isolated stria vascularis. Hear Res 158:123–130.

Liberman, M.C., Epstein, M.J., Cleveland, S.S., Wang, H., Maison, S.F. (2016). Toward a differential diagnosis of hidden hearing loss in humans. *PLoS One* 19, 0162726.

Lim, D.J. & Dunn, D.E. (1979). Anatomic correlates of noise induced hearing loss. *Otolaryngol Clin North Am*, 12(3), 493-513. 45.

Lin, H.W., Furman, A.C., Kujawa, S.G. & Liberman, M.C. (2011). Primary neural degeneration in the guinea pig cochlea after reversible noise-induced threshold shift. *J Assoc Res Otolaryngol*, 12(5), 605-16.

Luo F., Wang Q., Kashani A., Yan, J. (2008). Corticofugal modulation of initial sound processing in the brain. *J Neurosci*., 28:11615–11621.

Maddieson, I. (1984). Patterns of Sounds. Cambridge [Cambridgeshire], MY: Cambridge University Press.

Margolis, R.H. & Hunter, L.L. (1999). Tympanometry: Basic Principles and Clinical Applications. In: *Contemporary Perspectives in Hearing Assessment* (eds F.E. Musiek & W.F. Rintelmann). pp. 89-130. Allyn & Bacon, Needham Heights.

McFadden, S.L., Henselman, L.W., Zheng, X. (1999). Sex differences in auditory sensitivity of chinchillas before and after exposure to impulse noise. *Ear Hear*, 20:164-74.

McFadden, S.L., Zheng, X.Y., Ding, D.L. (2000). Conditioning-induced protection from impulse noise in female and male chinchillas. *J Acoust Soc Amer* 107:2162–2168.

Mohrle, D., Ni, K., Varakina, K., Bing, D., Lee, S.C., Zimmermann, U., Knipper, M., Rüttiger, L. (2016). Loss of auditory sensitivity from inner hair cell synaptopathy can be centrally compensated in the young but not old brain. *Neurobiol. Aging*, 44, 173-184.

Møller, A.R. (1994). Neural generators of auditory evoked potentials. In: Principles & Applications in Auditory Evoked Potentials (ed J.T. Jacobson). pp. 23-46. Allyn and Bacon, Needham Heights.

Most, T., Adi-Bensaid, L., Shpak, T., Sharkiya, S., Luntz, M. (2012). Everyday hearing functioning in unilateral versus bilateral hearing aid users. *American Journal of Otolaryngology*. 3:205–211.

Mulders, W.H., Robertson, D. (2009). Hyperactivity in the auditory midbrain after acoustic trauma: dependence on cochlear activity. *Neuroscience*, 164:733–746.

Musacchia, G., Sams, M., Skoe, E., Kraus, N. (2007). Musicians have enhanced subcortical auditory and audiovisual processing of speech and music. *Proceedings of the National Academy of Science*. 104(40): 15894-15898.

Nadal, A., & Diaz, M., Valverde, M. (2002). The Estrogen Trinity: Membrane, Cytosolic, and Nuclear Effects. News in physiological sciences : an international journal of physiology produced jointly by the *International Union of Physiological Sciences and the American Physiological Society*. 16. 251-5.

Nathan, C.A., Kim, T.S., Harris, J.P., Koutnouyan, H.A., Ryan, A.F.(1999). Absence of mRNA encoding estrogen receptor in the rat cochlea. *Acta Otolaryngol.,* 119:853–857.

National Institute for Occupational Safety and Health (NIOSH). (1998). Criteria for a recommended standard: Occupational noise exposure. *U.S. Department of Health and Human Services, Centers for Disease Control and Prevention*, Cincinnati.

National Institute on Deafness and Other Communication Disorders (NIDCD). (2001) Fact Sheet: Work Related Hearing Loss. *National Institute on Deafness and Other Communication Disorders, Health and Human Services*, Washington, DC.

Neely, S.T. & Liu, Z. (1993). EMAV: Otoacoustic Emission Averager (version 3.28). Boys Town National Research Hospital, Omaha.

Neitzel, R., Seixas, N., Olson, J., Daniell, W. & Goldman B. (2004a). Nonoccupational noise: exposures associated with routine activities. *J Acoust Soc Am,* 115(1), 237-45. 47

Neitzel, R., Seixas, N., Goldman, B. & Daniell W. (2004b). Contributions of non-occupational activities to total noise exposure of construction workers. *Ann Occup Hyg,* 48(5), 463-73.

Noble W, Gatehouse S. (2006). Effects of bilateral versus unilateral hearing aid fitting on abilities measuredby the Speech, Spatial, and Qualities of Hearing Scale (SSQ). *International Journal of Audiology*, 45:172–181.

Noble, W., Jensen, N. S., Naylor, G., Bhullar, N., & Akeroyd, M. A. (2013). A short form of the Speech, Spatial and Qualities of Hearing scale suitable for clinical use: The SSQ12. *International Journal of Audiology*, 52(6), 409–412.

Nordeen, K.W., Killackey, H.P. & Kitzes, L.M. (1983). Ascending auditory projections to the inferior colliculus in the adult gerbil, Meriones unguiculatus. *J. Comp. Neurol*., 214, 131–143.

Oliver, D.L., Winer, J.A., Beckius, G.E. & Saint Marie, R.L. (1994). Morphology of GABAergic neurons in the inferior colliculus of the cat. *J. Comp. Neurol*., 340, 27–42.

Petiot, J.C., Parrot, J.E. (1984). Effects of ovarian and contraceptive cycles on absolute thresholds, auditory fatigue and recovery from temporary threshold shifts at 4 and 6 kHz. *Audiology*, 23 :581-598 .

Pichora-Fuller, M.K., & Souza, P. (2003). Effects of aging on auditory processing of speech. *International Journal of Audiology*, 42 (Supp 2), S11–S16.

Prendergast, G., Guest, H., Munro, K.J., Kluk, K., Leger, A., Hall, D.A., Heinz, M.G., Plack, C.J. (2017a). Effects of noise exposure on young adults with normal audiograms I: Electrophysiology. Hear. Res. Adv. *J.HeaRes*., 10.028

Prendergast, G., Millman, R.E., Guest, H., Munro, K.J., Kluk, K., Dewey, R.S., Hall, D.A., Heinz, M.G., Plack, C.J. (2017b). Effects of noise exposure on young adults with normal audiograms II: Behavioral measures. *Hear. Res*., 356, 74-86.

Russo, N., Bradlow, A., Skoe, E., Trommer, B., Nicol, T., Zecker, S., Kraus, N. (2008). Deficient brainstem encoding of pitch in children with autism spectrum disorders. *Clinical Neurophysiology*. 119(8): 1720-1731.

Russo, N., Nicol, T., Musacchia, G., Kraus, N. (2004). Brainstem responses to speech syllables. *Clinical Neurophysiology*. 115: 2021-2030.

Russo, N., Nicol, T., Zecker, S., Hayes, E., Kraus, N. (2005). Auditory training improves neural timing in the human brainstem. *Behavioral Brain Research*, 156: 95-103.

Sayegh, R., Aubiem B., Faure, P. (2011). Duration tuning in the auditory midbrain of echolocating and nonecholocating vertebrates. *Journal of Comparative Physiology A: Neuro-ethology, Sensory,Neural, and Behavioral Physiology*, 197:571–583.

Schaette, R., McAlpine, D. (2011). Tinnitus with a normal audiogram: physiological evidence for hidden hearing loss and computational model. *J Neurosci* , 31: 13452–13457.

Schwartz, D. M., Morris, M. D., & Jacobson, J.T. (1994). The normal auditory brainstem response and its variants. In J. T. Jacobson (Ed.), *Principles and applications in auditory evoked potentials* (pp. 123–154).

Shi, L., Liu, L., He, T., Guo, X., Yu, Z., Yin, S., Wang, J., (2013). Ribbon synapse plasticity in the cochleae of guinea pigs after noise-induced silent damage. *PLoS One*, 8, 81566.

Skoe E., Kraus N. (2010) Auditory brainstem response to complex sounds: a tutorial. *Ear Hear*., 31(3): 302-324

Smith, P.H. (1992). Anatomy and physiology of multipolar-cells in the rat inferior collicular cortex using the in vitro brain slice techniques. *J. Neurosci*., 12, 3700–3715.

Song, J.H., Banai, K., Russo, N.M., Kraus, N. (2006). On the relationship between speech and nonspeech evoked auditory brainstem responses. *Audiology and Neuro-Otology*, 11: 233-241.

Song, J., Skoe, E., Banai, K., Kraus, N. (2011). Perception of speech in noise: neural correlates. *Journal of Cognitive Neuroscience*, 23(9): 2268–2279.

Song, Q., Shen, P., Li, X., Shi, L., Liu, L., Wang, J., Yu, Z., Stephen, K., Aiken, S., Yin, S., Wang, J. (2016). Coding deficits in hidden hearing loss induced by noise: the nature and impacts. *Sci. Rep*., 6, 25200.

Stamper, G.C., Johnson, T.A. (2015a). Auditory function in normal-hearing, noise exposed human ears. *Ear. Hear*., 36, 172-184.

Stamper, G.C., Johnson, T.A. (2015b). Letter to the Editor: Examination of Potential Sex Influences in Stamper, G.C., Johnson, T.A., 2015a. Auditory function in normal-hearing, noise-exposed human ears, Ear. Hear., 36, 172-184. *Ear. Hear*., 36, 738-740.

Stapells, D.R. (2000). Threshold estimation by the tone-evoked auditory brainstem response: a literature meta-analysis. *Journal of Speech-Language Pathology and Audiology*, 24(2), 74-83.

Stenberg, A.E., Wang, H., Sahlin, L., Hultcrantz, M. (1999). Mapping of estrogen receptors alpha and beta in the inner ear of mouse and rat. *Hear Res,* 136:29–34.

Suga N., Zhang Y., Yan J. (1997). Sharpening of frequency tuning by inhibition in the thalamic auditory nucleus of the mustached bat. *J Neurophysiol,* 77:2098 –2114.

Taberner, A.M., Liberman, M.C. (2005). Response properties of single auditory nerve fibers in the mouse. *J. Neurophysiol,*. 93, 557-569.

Tambs, K., Hoffman, H., Borchgrevink, H., Holmen, J., Engdahl., B. (2006). Hearing loss induced by occupational and impulse noise: Results on threshold shifts by frequencies, age and gender from the Nord-Trøndelag Hearing Loss Study. *International Journal of Audiology*, 45:5, 309-317

Vale, C. & Sanes, D.H. (2000). Afferent regulation of inhibitory synaptic transmission in the developing auditory midbrain. *J. Neurosci*., 20, 1912–1921.

Vale, C., Sanes, D.H. (2002). The effect of bilateral deafness on excitatory and inhibitory synaptic strength in the inferior colliculus. *Eur J Neurosci*., 16:2394 –2404.

Valero, M.D., Burton, J.A., Hauser, S.N., Hackett, T.A., Ramachandran, R., Liberman, M.C. (2017). Noise-induced cochlear synaptopathy in rhesus monkeys (Macaca mulatta). *Hear. Res.*, 353, 213-223.

Vander Werff, K.R. & Burns, K.S. (2011). Brainstem responses to speech in younger and older adults. *Ear Hear.*, 32(2), 168-180

Vermeire K, Kleine Punte A, Van de Heyning P. (2010). Better speech recognition in noise with the fine structure processing coding strategy. *Journal of Otolaryngology and Related Specialties,* 72:305–311.

Wagner, T. (1996). Lemniscal input to identified neurons of the central nucleus of mouse inferior colliculus: an intracellular brain slice study. *Eur. J. Neurosci*., 8, 1231–1239.

Ward, W.D. (1966). Temporary threshold shift in males and females. *J Acoust Soc Am.,* 40:478-85.

Wible, B., Nicol, T., Kraus, N. (2004). Atypical brainstem representation of onset and formant structure of speech sounds in children with language-based learning problems. *Biological Psychology,* 67: 299-317.

Wible, B., Nicol, T., Kraus, N. (2005). Correlation between brainstem and cortical auditory processes in normal and language-impaired children. *Brain,* 128: 417-423.

Willott JF, Bross LS. (2004). Effects of prolonged exposure to an augmented acoustic environment on the auditory system of middle-aged C57BL/6J mice: cochlear and central histology and sex differences. *J Comp Neurol* ., 472:358–370.

Willott, J.F., VandenBosche, J., Shimizu, T., Ding, D.L., Salvi, R. (2006). Effects of exposing gonadectomized and intact c57bl/6j mice to a high-frequency augmented acoustic environment: auditory brainstem response thresholds and cytocochleograms. *Hear Res.*, 221(1-2), 73–81.

Wilson, R.H., McArdle, R.A., Smith, S.L. (2007). An evaluation of the BKB-SIN, HINT, QuickSIN, and WIN materials on listeners with normal hearing and listeners with hearing loss. *Journal of Speech, Language, and Hearing Research*, 50:844–856.

Wong, P.C.M., Skoe, E., Russo, N.M., Dees, T., Kraus, N. (2007). Musical experience shapes human brainstem encoding of linguistic pitch patterns. *Nature Neuroscience,* 10:420-422.

Zhang, Y., Suga, N., Yan, J. (1997) Corticofugal modulation of frequency processing in bat auditory system. *Nature,* 387:900–903

Zhao, F., Manchaiah, V.K., French, D. & Price, S.M. (2010) Music exposure and hearing disorders: an overview. *Int J Audiol,* 49(1), 54-64.

APPENDIX A

LITERATURE REVIEW

Introduction

Hearing loss is the third most common public health issue. Permanent hearing loss caused by exposure to excessive noise affects approximately 26 million adults (ages 20 – 69) in America (NIDCD, 2001) and as many as 16% of teens (ages 12 to 19) have reported some hearing loss that could have been caused by loud noise (CDC, 2010). It is widely accepted that permanent threshold shifts after noise exposure are a result of permanent damage to auditory structures. However, the relationship between the amount of acoustic exposure and the resulting anatomic and physiologic damage is variable, even in highly controlled studies. In addition, most people with noise-induced hearing loss (NIHL) also suffer from temporal processing deficits (e.g., difficulty with speech perception in noise and localization) and tinnitus. In clinical practice, an increasing number of normal-hearing listeners complain about experiencing similar hearing deficits as those described above. It has been reported that as many as 5–15% of adult patients seeking audiological help turn out to have normal hearing thresholds (Cooper and Gates, 1991; Kumar et al., 2007; Hind et al., 2011). Overexposure to loud sounds can also lead to a temporary threshold shift (TTS). A common perception is that if hearing fully recovers over time, no residual auditory damage exists and that exposure is essentially harmless (Humes et al., 2005). Recent investigations involving animal models have contradicted this assumption and showed the occurrence of cochlear synaptopathy due to noise exposure in the absence of permanent change in hearing thresholds.

This literature review will first focus on research related to noise-induced cochlear synaptopathy demonstrated in animal models and recent investigations in human ears including reported link to speech-in-noise deficits. This will be followed by a review of research utilizing electrophysiological techniques namely, the auditory brainstem response (ABR), with greater

focus on the novel approach of using a speech stimulus that may identify early damages in the auditory system. Finally, a summary of studies investigating the use of self-report questionnaires like the Noise Exposure Questionnaire (NEQ) and Speech, Spatial, and Other Qualities Scale (SSQ) will be provided.

Evidence of Noise-Induced Cochlear Synaptopathy in Animals

Kujawa and Liberman (2009) demonstrated the occurrence of cochlear synaptopathy in mice after a 2-hour exposure to a 100 dB SPL noise (8-16 kHz). Results of this experiment showed an abrupt, permanent loss of up to 50% of afferent nerve terminal connections between inner hair cells and auditory nerve fibers in the frequency region of maximum TTS (basal region of the cochlea) while outer hair cells appeared undamaged upon anatomical assessment. Despite substantial deafferentation, threshold level responses were preserved after recovery while the wave I amplitude of the auditory brainstem response at high stimulation levels (i.e., suprathreshold levels) was significantly reduced. The reduced neural response for high-level stimuli with preserved thresholds indicates a specific loss of auditory nerve fiber populations that respond at high levels, the low-spontaneous rate, high-threshold fibers. This finding suggests that suprathreshold responses demonstrated better sensitivity at revealing auditory damage in temporary noise-induced hearing loss. Noise-induced cochlear synaptopathy has also been demonstrated in a range of rodents (e.g., guinea pig, Lin et al., 2011 and Furman et al., 2013; chinchilla, Liu et al., 2012 and Song et al., 2016; rat, Möhrle et al., 2016) and recently in rhesus monkey (Valero et al., 2017). However, not all exposures that produce TTS are synaptopathic (Hickox and Liberman, 2015). It is not clear what specific factors distinguish TTS episodes that yield permanent damage from those that do not. However, when permanent anatomical damage is present (i.e., synaptopathy), the animal studies suggest that the use of suprathreshold stimuli

may provide evidence of early-onset noise-induced auditory damage that is not yet evident in threshold assessment. Likewise, vulnerability to cochlear synaptopathy varies between species as demonstrated by the variation in intensity level and duration of exposure used in the studies cited above to produce TTS that are synaptopathic. The study by Valero et al. (2017) using rhesus monkeys required a longer duration of high noise exposure (4 hours) whereas studies using rodents (e.g., Kujawa and Liberman, 2009; Lin et al., 2011; Furman et al., 2013; Liu et al., 2012; Song et al., 2016; and Möhrle et al., 2016) only required exposures of 2 hours. This indicates that non-human primates may be less vulnerable to noise damage than rodents; therefore, cochlear synaptopathy described in these animal studies may not translate directly to human pathology. This highlights the need for investigations of noise-induced cochlear synaptopathy in human ears.

Physiologic Evidence of Noise-Induced Cochlear Synaptopathy in Humans

At present, physiologic evidence of noise-induced cochlear synaptopathy in human ears is limited and inconsistent. Stamper and Johnson (2015a) first reported evidence of noise-induced cochlear synaptopathy in human ears. They recruited 30 volunteers (20 females and 10 males) with varying noise exposure backgrounds quantified by a self-report questionnaire, NEQ. They found a systematic trend of smaller ABR wave I amplitudes in normal-hearing human ears with greater amounts of noise exposure history in response to suprathreshold clicks and 4 kHz tone bursts while other common audiological measures such as pure tone thresholds, DPOAEs, and ABR wave V amplitudes did not show any sensitivity to noise exposure. However, it is possible the results were confounded by sex since the majority of their high-noise participants were males, and males are known to have smaller ABR amplitudes than females. In a subsequent letter to the editor, Stamper and Johnson (2015b) analyzed their ABR data recorded at 90 dB

nHL for the two sexes independently. The relationship initially observed between wave I amplitude and the annual noise exposure estimate persisted for the female subjects, but not for the male subjects.

A recent study by Bramhall et al. (2017) also reported evidence of cochlear synaptopathy in firearm users. They recruited both veterans and non-veterans (ages 19 to 35) with normal pure tone thresholds from 250 to 8000 Hz and normally functioning middle ear and outer hair cells (DPOAEs at 1, 3, 4, and 6 kHz). The subjects were grouped into 4 categories: 1) veterans with significant firearm use, 2) veterans with less firearm use, 3) non-veterans with history of firearm use, and 4) non-veterans with no firearm use. Here, they found reduced ABR wave I amplitudes at suprathreshold levels (110 dB p-pe SPL) in veterans with significant firearm use and in non-veterans with a history of firearm use not only to the 4 kHz tone burst but also to the other test frequencies (i.e., 1, 3, and 6 kHz). It is thought that exposure to high-intensity level broadband noise sources, such as an impulse noise or blasts, may be more likely to cause synaptic damage throughout the cochlea than noise exposures confined to an octave band. Similar to the Stamper and Johnson (2015) paper, Bramhall et al. found no significant differences in waves III and V amplitudes of the ABR between the groups.

Liberman et al. (2016) also reported evidence of cochlear synaptopathy in their group of young adults. They collected data from 34 college students who were grouped into those at low-risk and those at high-risk for developing noise damage based on their self-report of noise exposure and use of hearing protection. However, they did not disclose what noise exposure criteria they used for categorizing their subjects into low- and high-risk groups. In this study, they compared the amplitude ratio of the presynaptic summating potential (SP) generated primarily by the hair cells and the action potential (AP) generated by auditory nerve fibers

between the two groups (i.e., low- and high risk) in response to a 94.5 dB nHL click stimulus. Here, the high-risk group had significantly larger mean SP/AP ratio than the low-risk group. Unlike the two studies above (Stamper and Johnson, 2015; Bramhall et al., 2017), the authors of this study did not find a significant difference in the AP amplitude (equivalent to ABR wave I amplitude) between the two groups but found a significantly increased SP amplitude in the high-risk group. They speculated that this enhancement may be due to 1) a loss of one of the two components contributing to the SP (e.g., loss of the excitatory post synaptic cochlear nerve potential under the inner hair cells) or 2) attenuation of the middle ear muscle reflex. Likewise, the high-risk group showed elevated thresholds at high frequencies (10,000 to 16,000 Hz) compared to the low-risk group but no significant difference in the mean DPOAEs.

In contrast to the human studies discussed above, a large-scale study by Prendergast et al. (2017) reported no significant relationship between lifetime noise exposure and ABR wave I amplitude in their cohort of 126 normal-hearing, young adults. Here, they estimated lifetime noise exposure using a questionnaire developed to assess the effectiveness of the UK noise at work regulations (Lutman et al., 2008) that considers both social and occupational noise exposures. ABR was recorded in response to a 100 μsec click high-pass filtered at 1.5 kHz and presented at 100 dB peSPL. Similar to Stamper and Johnson (2015b), they also reported opposing trends in the wave I amplitude between the females and males. The high-noise females showed reduced ABR wave I amplitudes compared to the low-noise females, while high-noise males showed enhanced wave I amplitudes compared to the low-noise males, although neither relationship was statistically significant. Elevated 16 kHz pure tone thresholds were also observed in the high noise females but not in males. This suggests a possible difference in vulnerability to the effects of noise between sexes that may warrant further investigation.

While there is no evidence yet of a direct link between tinnitus and noise exposure, tinnitus is a common symptom reported by those individuals with noise-induced hearing loss. Significant differences in ABR wave I amplitudes in tinnitus subjects versus non-tinnitus controls when hearing thresholds were matched. (Schaette and McAlpine, 2011 and Gu et al., 2012). At the same time, Gu et al. (2012) reported enhanced waves III and V amplitudes in the tinnitus group while Schaette and McAlpine (2011) found no significant difference in the wave V amplitude between their tinnitus and control groups. It has been suggested that the enhancement or no change in the wave V response amplitude observed in individuals with tinnitus may be due to increased central neural gain to compensate for the reduced input from the auditory nerve as evidenced by the reduced wave I amplitude. In contrast, Guest et al. (2017) were not able to replicate the reported relation between the lifetime noise exposure and ABR wave I amplitude in their group of young adults with tinnitus. In addition to the ABR measure, they also recorded the envelope following response (EFR) to a 4000 Hz carrier with 100 Hz modulator at 75 dB SPL. Again, no significant relationship was found between the lifetime noise exposure and EFR. Based on their findings, they propose that tinnitus may not be related to cochlear synaptopathy but rather to other effects of noise exposure.

Speech-in-Noise Deficit and Noise-Induced Cochlear Synaptopathy

The perceptual consequences of noise-induced cochlear synaptopathy remain unclear. However, there is some evidence that a history of noise exposure is associated with temporal processing deficits even in the absence of any audiometric loss (e.g., Kumar, Ameenudin, and Sangamanatha, 2012; Bharadwaj et al., 2015; and Liberman et al., 2016) that may lead to difficulties in hearing speech in noise and/or sound localization.

Kumar et al. (2012) investigated the effects of occupational noise on temporal processing abilities and speech perception in noise of 28 train drivers that were divided into 3 age groups (30-40 =13; 41-50= 9; and 51-60 = 6) and compared them to their age-matched non-exposed counterparts (n= 30 per age group). All subjects had normal pure tone thresholds (defined as ≤ 25 dB HL) in the octave frequencies from 250 to 8000 Hz. A variety of psychophysical tests (i.e., gap detection in noise, amplitude modulation detection, and duration pattern) were utilized to assess temporal processing skills with the addition of speech recognition in multi-talker babble to assess speech-in-noise performance. Their results showed that the noise-exposed individuals generally had significantly poorer modulation detection thresholds, duration pattern scores, and speech-in-noise scores. Although gap detection thresholds and modulation detection thresholds for low modulation frequencies were not statistically different between the noise‑exposed and non‑exposed groups, the mean modulation and gap detection thresholds were slightly lower in the noise-exposed group. Furthermore, they found that temporal processing skills, specifically, gap detection thresholds, modulation detection thresholds at 200 Hz modulation frequency, and duration pattern scores were significantly associated with the speech-in-noise performance and accounts for 26% of the variability in speech-in-noise scores.

Bharadwaj et al. (2015) used both electrophysiological (i.e., envelope following responses, cortical EEG - N100, and spatial attention) and behavioral (i.e., amplitude modulation detection and envelope interaural time difference discrimination tasks) measures to assess the temporal processing abilities at suprathreshold levels in 26 normal-hearing participants aged 21 to 39 years. They found that, while individual temporal processing skills varied among their participants in both types of measures, these measures correlated significantly with each other. Their results showed that those with poor subcortical encoding showed poor cortical sensitivity

to changes in interaural time differences and performed poorly in the spatial attention task. These temporal processing skills are important for sound localization and analyzing complex acoustic scenes like speech-in-noise. On the other hand, none of these measures correlated with the audiogram, DPOAE, or psychophysical tuning curves (measures of cochlear mechanical function) suggesting that these deficits likely originate at the level of the cochlear nerve consistent with the auditory mechanism of noise-induced cochlear synaptopathy described in the animal models.

Liberman et al. (2016) also found word recognition performance was significantly poorer in their high-risk group when NU-6 words were presented at 35 dB HL in the presence of ipsilateral white noise at 0 and 5 dB signal-to-noise ratios. The same results were found when the NU-6 words were time compressed (45% or 65%) with the addition of 0.3 sec reverberation time. Furthermore, their word recognition performance for all non-quiet conditions significantly correlated with the physiologic measure (SP/AP ratio) where word recognition scores decrease with increase in SP/AP ratio.

Conversely, Prendergast et al. (2017b), in a subsequent study, found no relation between the psychophysical (i.e., frequency and intensity difference limens, interaural phase discrimination, amplitude modulation detection, digit triplet test, co-ordinate response, localization, and musical consonance) or the self-report assessment of hearing ability (via the Speech, Spatial, and other Qualities Scale; SSQ) and electrophysiological (i.e., ABR and FFR) measures. Likewise, they found no significant difference with the performances in the behavioral tasks between the high- and low-noise groups.

Overall, the inconsistent findings in the current literature on human ears suggest that perhaps not all noise exposures result in cochlear synaptopathy in humans. It remains unclear

what of the exposure to a loud noise (e.g., type of noise, noise dose level, etc.) will render synaptopathy in human ears. Likewise, the conflicting findings highlight the need for a more robust and sensitive tool that can help identify early noise-induced damages in the human auditory system.

Auditory Brainstem Responses

The auditory brainstem response (ABR) test is a non-invasive neurophysiological test used to assess the functionality of the central auditory pathway, which includes structures from the auditory nerve to the brainstem. In clinical assessment, it is commonly used in the screening and diagnosis of hearing loss especially in infants and young children. The ABR is an evoked potential created by ongoing activity of the structures along the central auditory pathway. This can be recorded by placing surface electrodes on the scalp and/or skin of an individual in response to a simple (e.g., clicks and tone bursts) or complex (e.g., speech) acoustic stimulus. The resulting output is a series of waves that occur within milliseconds of the stimulus presentation. The waves are interpreted based on their timing and magnitude. The timing measures such as absolute latency (the time between the stimulus presentation and a particular peak), interpeak interval (the time between peaks), and interaural latency (the difference in absolute latency between ears) reflects the synchronicity with which the brainstem nuclei respond to the stimulus. The magnitude or amplitude measure such as peak-to-trough, peak-to-peak, and root-mean-square amplitude reflects the robustness of the brainstem response to the stimulus.

Click-Evoked ABR

The ABR recorded in response to a click or tone burst results in a series of five to seven waves that occur within 10 milliseconds following the stimulus onset. The positive vertex waves

(i.e., peaks) are labeled I to VII, with each one generally corresponding to a specific point of activity along the central auditory pathway. There has been some disagreement about which brain structures generate which waves, but one of the more common interpretations attributes Wave I to the distal portion of the auditory nerve, Wave II to the proximal portion of the auditory nerve, Wave III to the cochlear nucleus, Wave IV to the superior olivary nucleus, and Wave V to the lateral lemniscus as it enters the inferior colliculus (Møller, 1994; Hall 2007). Although they are not commonly used clinically, it is thought that Waves VI and VII are attributed to the medial geniculate body of the thalamus (Biacabe et al., 2001). When the ABR is used to test hearing acuity, the stimulus needs to be at an intensity that creates a barely-detectable response (threshold). Because wave V is the most robust and is seen at the lowest intensity, it is the wave of choice to determine auditory threshold (Boston & Møller, 1983). In addition, ABR threshold has been found to be correlated with behavioral hearing thresholds (Gorga et al., 1993; Stapells, 2000). When the ABR is used to test auditory system integrity, the latencies of the different peaks are analyzed, as well as waveform changes. The wave amplitude may also be analyzed but the wide variability in amplitude seen even in normal ears limits the use of this measure clinically (Schwartz et al., 1994). However, researchers have recognized the value of examining the wave amplitude in providing important information about possible anatomical changes in the auditory system particularly in noise and tinnitus studies. Kujawa et al. (2009) first reported reduced wave I amplitudes in their synaptopathic, noise-exposed mice. Schaette and McAlpine (2011) also reported reduced wave I amplitude with no change in wave V amplitude in normal-hearing individuals with tinnitus. Recent investigations of noise-induced cochlear synaptopathy in human ears (e.g., Stamper and Johnson, 2015; Bramhall et al., 2017; Prendergast et al., 2017, etc.) have since primarily focused on examining the amplitude of wave I.

Speech-Evoked ABR

While click-ABR is extensively used in clinical settings and has proven to be a valuable measure in evaluating auditory function, (Hall, 1992; Hood, 1998), clicks and tones are not acoustically complex sounds and do not represent day-to-day listening conditions. A number of studies have demonstrated that click and speech stimuli impose different encoding demands on the brainstem (Song et al., 2006; Johnson et al., 2008). While speech-evoked ABR is not currently used in clinical audiology, it is gaining popularity in the field of research. It has been hailed as a 'biomarker' for indexing temporal processing at the level of the brainstem (Johnson et al., 2007). It has been suggested that temporal processing deficits in the central auditory pathway may be implicated in difficulties perceiving speech-in-noise (Pichora-Fuller & Souza, 2003), which is the commonly encountered complaint even among normal-hearing adults. Because the brainstem response to speech provides objective information about how the sound structure of speech syllables is encoded by the auditory system, it can be used to diagnose auditory processing deficits despite normal processing of click stimuli. Several stop consonant-vowel (CV) syllables (e.g., /ga/, /ba/, and /da/) have been used to examine how the temporal and spectral features of sounds are preserved in the ABR (Johnson et al., 2008). The CV syllable /da/ is the most commonly used stimulus in studying various populations including musicians (Parbery-Clark et al., 2009), children with dyslexia, specific language impairment, and autism spectrum disorders (Cunningham et al., 2001; Banai et al., 2005; Banai and Kraus, 2008; Russo et al., 2004; Hornickel et al., 2009;), and adults with sensorineural hearing loss (Anderson et al, 2013). It has also been used to evaluate the effects of auditory training (Russo et al., 2008 and Song et al., 2008).

The 40-msec synthesized /da/ was created using a Klatt cascade/parallel formant synthesizer at a sampling rate of 10 kHz. It is composed of an onset burst frication at third, fourth and fifth formants (F_3, F_4, and F_5, respectively) during the first 10 msec, followed by 30-msec F_1 and F_2 transitions ceasing immediately before the steady-state portion of the vowel (Johnson et al., 2005). The stimulus /da/ is typically delivered at suprathreshold levels within the "conversational" range of 60 to 85 dB SPL via electrically shielded insert earphones (Skoe and Kraus, 2010). This stimulus has been used successfully in different recording conditions: monaural (e.g., Cunningham et al., 2001; Vander Werff and Burns, 2011; Anderson et al., 2013), binaural (e.g, Parbery-Clark et al., 2009 and Anderson et al., 2013), left ear and right ear (e.g. Hornickel et al., 2009), and audiovisual and auditory-only (Musacchia et al., 2006, 2007, 2008) stimulations. In addition, ABR to /da/ in the presence of background noise has also been used in several studies (e.g., Cunningham et al., 2001; Russo et al., 2004, 2005, 2008; Parbery-Clark et al., 2009; and Song et al., 2011).

In order to optimally record speech-evoked ABRs, Skoe and Kraus (2010) have provided a summary of recommended recording parameters. ABR to /da/ is typically recorded using alternating stimulus polarity to extract the neural response from the cochlear microphonic and eliminate stimulus artifact. A vertical montage for electrode placement is used to optimally record more rostral brainstem responses: Cz (positive), earlobe/s (negative/s), and forehead (ground). The earlobe is preferred over the mastoid when recording speech-evoked ABRs as it causes fewer artifacts from skull vibration. A high sampling rate of 6000-20,000 Hz is also recommended for better temporal precision. Similar to the click-evoked ABR, the band-pass filters for speech-evoked ABRs fall in the range of 100 to 2000 or 3000 Hz to maximize the detection of the high-frequency transient peaks. To obtain a robust and reliable speech-evoked

ABR, a greater number of sweeps (6000-10,000 total sweeps) is required. A longer inter-stimulus interval (ISI) is required that consists of 1) a pre-stimulus time of 10-50 msec (baseline) to facilitate determining whether a particular response peak is above the noise floor and 2) a post-stimulus time of 10-50 msec where neural activity should return to baseline with the offset of stimulus and also provides information re: the neural noise floor. Due to the duration of the /da/ stimulus and ISI, a longer averaging window is required, which will lead to a slower presentation rate compared to that of the click-evoked ABR.

Speech-evoked ABRs may be recorded in active and passive test conditions. Most studies have either encouraged their participants to fall asleep, watch a movie, or read a book (e.g., Johnson et al., 2007, Anderson et al., 2013) but it has also been recorded while subject performs a task (e.g., Musacchia et al., 2007). ABR recorded in response to the synthesized syllable /da/ results in seven characteristic response peaks and troughs and are labeled V, A, C, D, E, F and O. The response includes both transient (i.e. V, A, C, and O) and sustained (i.e. D, E, and F) features. The transient and sustained components are believed to result from different mechanisms of temporal processing both occurring at the brainstem level (Johnson et al., 2005; Akhoun et al., 2008). The V-A complex is the attributed to the highly synchronized neural response to the onset of the stimulus at the level of lateral lemniscus and inferior colliculus and is analogous to the V-Vn complex of the click-evoked ABR. Wave C is attributed to the transition between onset burst and more periodic portion of the stimulus. Wave O is thought to be a response to the cessation or offset of the stimulus. The sustained components D, E, and F form the frequency following response (FFR) to the voiced portion of the stimulus that is phase-locked to the period of the fundamental frequency (F_0) of the stimulus. These characteristic response peaks and troughs manifest approximately seven to eight milliseconds after the corresponding

acoustic landmark. This delay is attributed to the neural transmission time between the cochlea and brainstem.

Johnson et al., 2007 first described how perceptual temporal resolution deficits affect the neural encoding of speech at the level of the brainstem. They found that language based learning-impaired individuals with poor backward masking threshold (i.e., pronounced difficulty detecting rapid changes in sound over time or poor temporal resolution) showed neurophysiological timing deficits that are specific to certain, but not all, acoustic of speech. Learning-impaired children with poor behavioral temporal processing showed imprecise brainstem encoding of filter cues (consonant and vowel identity) in speech (as evidenced by abnormal latencies of waves A, C, and O) with normal encoding of acoustic cues related to speaker identity and prosody (reflected by normal latencies of waves D, E, an F). These findings suggest that children with poor temporal resolution do not have an overall neural processing deficit, but rather a deficit specific to the encoding of certain acoustic cues in speech. Thus, speech-ABRs are considered to be a biological marker for auditory temporal processing ability.

Normative data for identifying the characteristic response peaks recorded from the right ear has been established for normally developing children of different age groups (Johnson et al., 2008) and normal-hearing young and older adults (Dhar et al., 2009, Hornickel et al, 2009, Vander Werff and Burns, 2011). The published norms for the adults are fairly consistent across the different studies. However, normative data for the left ear has yet to be established. Left- and right-ear stimulations produce similar but not identical speech-evoked ABRs (Akhoun et al., 2008). Currently, only two studies have identified response latency and amplitude differences between the two ears. Hornickel et al (2009) reported significantly longer peak latencies for the sustained components (waves D and F) collected from the left ear of native English speakers.

Ahadi et al. (2014) in their cohort of native Persian speakers reported longer peak latencies in waves A and E in the left ear. The inconsistencies in the reported differences by the two studies may be attributed to language differences. Although the /da/ syllable is included in the phonetic inventories of the Persian and English language, Ahadi et al. argued that the voice onset time is slightly longer in the Persian language. However, both studies have consistently demonstrated longer response latencies to select components when recorded from the left ear suggesting possible right-ear advantage at the level of the brainstem. Both studies also found generally smaller peak amplitudes in the left ear responses but none were statistically significant.

There are several methods that have been used to analyzing speech-evoked ABRs. Similar to the click-evoked ABRs, identification of the individual peak latency and amplitude can be used to characterize the transient features of the response. The sustained features of the response may be analyzed using a variety of methods with each method providing different information. The RMS amplitude, a global measure of the magnitude, can be used to calculate signal-to-noise ratio of the response. The Fourier analysis, a frequency domain representation, can provide neural phase-locking information at specific frequencies. Cross-correlation analysis compares the timing and morphology of two signals (i.e., stimulus-to-response or quiet-to-noise).

Speech-evoked ABR has potential for both research and clinical applications. It can be recorded using the same acquisition procedures used in click-evoked ABRs and may provide valuable neural coding information that click-ABRs are not sensitive to. The ABR to /da/ has been extensively studied. However, the majority of the literature comes from one laboratory. Further explorations and investigations from other research laboratories are needed to establish the reliability and validity of the speech-evoked ABR before it can be incorporated in clinical

protocols. Likewise, normative data is yet to be established for left ear responses if there are indeed significant differences between the right- and left-ear speech-evoked ABR responses.

Noise Exposure Questionnaire

Various questionnaires have been developed and used in an attempt to quantify individual noise exposure background. Likewise, each questionnaire has its own method of calculating noise dose levels. Therefore, the definition of "high noise exposure" for each study also varies. As with all questionnaires, it is subject to recall bias. While dosimeters directly measure the dose of noise exposure, they can be expensive and impractical when conducting studies in the general population. Improper use of these devices also leads to inaccuracies in the measurements therefore, distorting the data. For these reasons, many of the previous investigations rely on the use of questionnaires to quantify individual noise exposure history.

The Noise Exposure Questionnaire (NEQ; Johnson et al., 2017) is a task-based questionnaire intended for use in the general population to quantify noise exposure history from both occupational and non-occupation exposures. The questionnaire consists of 11 detailed questions about participation in loud, noisy activities. It queries episodic and routine exposures as well as frequency and duration of each exposure. A respondent is asked to recall participation in specific noisy activities during the past 12 months. A one-year time period was chosen to capture seasonal and infrequent activities. Based on the responses, a value can be calculated that estimates the individual's annual noise exposure (ANE).

The ANE is expressed in $L_{Aeq8760h}$, where the "L" represents sound pressure level in dB, the "A" represents the use of an A-weighted frequency response, the "eq" represents a 3-dB exchange rate for calculation of the time/level relationship, and the "8760h" represents the total duration of the noise exposure in hours (24 hours/day x 365 days/year). Episodic and routine

exposures are calculated separately and then combined to produce an overall estimate of ANE based on the approach used by Neitzel et al. (2004a & b). The NEQ excludes firearm use in the computation of the ANE value as there is currently no accepted protocol for integrating impulse-noise exposures with continuous noise exposures. Firearm exposures are described separately instead.

The NEQ has a theoretical range of 64 to 95.5 $L_{Aeq8760h}$ with higher $L_{Aeq8760h}$ values indicating greater amounts of ANE. Subjects with ANE values of 79 or greater were considered to be at highest risk for developing noise-induced hearing loss (NIHL). This was based on the National Institute for Occupational Safety and Health (NIOSH) occupational noise criterion of 85 $L_{Aeq2000h}$ (8 hours/day × 250 workdays/year) extrapolated to an annual equivalent exposure limit of 78.6 $L_{Aeq8760h}$. Refer to Appendix D for the detailed computation of the ANE.

The NEQ can be a valuable tool in the clinic for identifying individuals at high risk for noise-induced hearing loss. This allows for hearing conservation activities to be more focused on those who are most in need of those services. The use of the NEQ can also extended to the field of research. It has been used by several investigators in conducting noise studies (e.g., Stamper and Johnson, 2015 and Grinn et al., 2017).

Speech, Spatial, and Qualities of Hearing Scale

The Speech, Spatial, and Qualities of Hearing Scale (SSQ) was developed by Gatehouse and Noble in 2004. It was designed in response to recognized limitations of the traditional audiological battery for predicting listening ability in challenging environments, such as rooms with multiple talkers and other noise sources. It measures a range of hearing disabilities across several domains (i.e. speech hearing, spatial hearing, segregation of sounds, recognition, clarity/naturalness, and listening effort). The questionnaire consists of three subscales: speech

hearing, spatial hearing, and other qualities of hearing. The speech hearing subscale of the SSQ assesses 14 different speech listening environments, including quiet environments and a range of challenging environments with competing noise. The second subscale spatial hearing, contains 17 items that addresses directional and distance judgments as well as movement. The third section of the SSQ, or 'other qualities', has 18 items that address the issues of segregation of sounds, recognition, clarity/naturalness, and listening effort.

Respondents are asked to rate their abilities and experiences with hearing and listening in different situations by placing a mark anywhere on a scale that runs from 0 to 10. Putting a mark at '10' means that the respondent would be perfectly able to do or experience what is described in the question. Putting a mark at '0' means that they would be quite unable to do or experience what is described. Essentially, the lower the rating is, the greater the difficulty or disability. An average score for each subscale can be calculated by combining the ratings for each item in that subscale. The SSQ score reflects individual self-perception of ability with higher scores indicating less difficulty. Appendix E contains the detailed computation of the score for this subscale.

Since its development, the SSQ has been used to document the benefit of unilateral vs. bilateral hearing aids (Mostet al., 2012; Noble & Gatehouse, 2006), cochlear implant algorithms (Vermeire, et al., 2010), the advantages of directional microphones for speech intelligibility in noise (Wilson, McArdle, & Smith, 2007), and the individual self-assessment of speech understanding in noise abilities (Agus et al., 2009; Heifer & Vargo, 2009; Anderson et al., 2013). Abbreviated (e.g., SSQ12; Noble et al., 2013) and adapted (e.g. for parents; Galvin et al., 2007) versions of the scale have also been developed for clinical and clinical research-related applications.

The SSQ was designed to provide insight into many functions and capacities that are simply not measurable in the laboratory or clinical populations. It can be used as a complementary tool to behavioral or experimental measures of hearing ability.

APPENDIX B

RESEARCH CONSENT FORM

RESEARCH CONSENT FORM

Noise Exposure, Self-Reported Speech-in-Noise Perception, and the Auditory Brainstem Response in Normal-Hearing Human Ears

You are being asked to join a research study. You are being asked to take part in this study because you have normal hearing and either have a little or a large amount of exposure to loud sound(s). You do not have to participate in this research study. The main purpose of research is to create new knowledge for the benefit of future patients and society in general. Research studies may or may not benefit the people who participate.

Research is voluntary, and you may change your mind at any time. There will be no penalty to you if you decide not to participate, or if you start the study and decide to stop early. Either way, you can still get medical care and services at the University of Kansas Medical Center (KUMC).

This consent form explains what you have to do if you are in the study. It also describes the possible risks and benefits. Please read the form carefully and ask as many questions as you need to, before deciding about this research. You can ask questions now or anytime during the study. The researchers will tell you if they receive any new information that might cause you to change your mind about participating.

This research study will take place at the University of Kansas Medical Center (KUMC) under the direction of Tiffany Johnson, Ph.D. as the principal investigator, and Nikki Go, Ph.D. candidate, as a secondary investigator. About 40 people will be in the study at KUMC.

BACKGROUND

Frequent exposure to loud sound can cause damage to the ear and can lead to a hearing loss. However, recent research has given us new information about how loud sounds affect the ear. New studies have questioned the amount of noise that is harmful and suggest it might be less than previously thought. The new studies also suggest that the techniques we use in the clinical setting to test for damage from loud sounds in the ear might not be sensitive enough to identify early damage. Two clinical tests will be used to help us determine how well your ears are working: otoacoustic emissions and the auditory brainstem response.

- Otoacoustic emissions are quiet sounds that we record in the ear canal. They are produced by the inner part of the ear in response to sound and can help us to know if a person has normal hearing or hearing loss.

- The auditory brainstem response is a measure of the brain's electrical activity as it processes sound. The response is produced by neural activity in the auditory nerve and the brain and can help us know if a person has normal hearing or hearing loss.

Neither of these tests are experimental, but new studies suggest that testing with a broader range of loudness levels and the use of a more complex sound during these tests than has previously been used might help identify damage from loud sounds before a hearing loss develops.

PURPOSE

By doing this study, the researchers hope to identify methods of detecting auditory damage from exposure to loud noise before a hearing loss develops.

PROCEDURES

If you are eligible and decide to participate in this study, your participation will last approximately 1-5 hours, spread over 2 testing sessions.

Your participation will involve different activities across the 2 sessions.

Day 1): During the first test session, your participation will consist of the following activities:

- A standard hearing test. This test tells us how soft a sound you can hear. During this test, we will first look in your ears using a light called an otoscope. You then will be asked to wear headphones and to respond by either pressing a button or by raising your hand when you hear a tone. This test will take 10-15 minutes to complete.

- A standard tympanogram. This tests checks how well your middle ear is working. During this test, a small rubber tip will be placed in your ear canal. You will hear a low-pitched sound and will feel slight pressure changes in your ear canal. This test will take no more than 5 minutes to complete.

- A standard otoacoustic emission test called a DpGram. This test checks how well your inner ear is working. During the DpGram test, we will place a soft, foam eartip in your ear and you will sit quietly in a comfortable chair. During the DpGram test, you will hear tones that have several different pitches and we will record the otoacoustic emissions that your ear produces. The DpGram test will take no more than 10 minutes.

- A noise-exposure questionnaire. You will be asked a series of questions related to your involvement in common activities where you may have been exposed to loud sounds. You will take this questionnaire on a computer. You will either take it alone or with the assistance of one of the researchers. This questionnaire will take 10-15 minutes to complete.

These tests are used to verify that you meet the study-related hearing requirements and can participate in the research. If you do not have normal hearing, your participation will be complete at this time. You will be counseled regarding the outcome of your hearing test and will receive information regarding any further testing that is recommended. If you have normal hearing, you will be invited to continue in the research. If you choose to continue, you will undergo additional testing.

- A speech-in-noise performance questionnaire. You will be asked a series of questions related to your day-to-day ability to hear speech in different background conditions. The questionnaire will be in traditional paper form. You will either take it alone or with the assistance of one of the researchers. This questionnaire will take 10-15 minutes to complete.

The total test time for the first day will be up to 1.5 hours.

Day 2): You will return within a week or two following your first testing session for your second testing session.

On this day we will again complete the middle-ear test (the tympanogram). After the tympanogram, we will proceed directly to auditory brainstem response testing.

- Auditory Brainstem Response testing. For this test, you will sit quietly in a comfortable recliner and can sleep. Your forehead and the area behind each ear will be gently scrubbed with a gel and stickers called surface electrodes will be placed on the skin. A soft, foam ear tip will be placed in your ear canal and you will hear sounds presented through the ear tip. The sounds will change in loudness and some will be clicks and some will be a speech syllable. The sounds will never get loud enough to hurt or cause harm to your hearing. The total test time for auditory brainstem response testing will be up to 3 hours.

You will be offered (and can request) breaks during testing and you should tell us if you feel the sounds are louder than is comfortable for you.

The total test time for the second day will be up to 3.5 hours.

RISKS

The sounds that will be played to your ear will vary in loudness. You will feel slight pressure in your ear during the testing. If any of the sounds are bothering you, please tell us to turn off the sound.

Your skin needs to be cleaned using a mild abrasive scrub in order to place the electrodes. You should let us know if it is irritating your skin too much.

You may feel restless during the test sessions. We will offer you a break during each session and you may ask us to take a break at any time.

There may be other risks of the study that are not yet known.

BENEFITS

You will not directly benefit from this study. You will receive a hearing test during the study. Researchers hope that the information from this research study may be useful in improving our ability to identify early damage to the ear caused by loud noise.

ALTERNATIVES

Participation in this study is voluntary. Deciding not to participate will have no effect on the care or services you receive at the University of Kansas Medical Center.

COSTS
There is no cost for being in the study.

PAYMENT TO SUBJECTS
You will be paid $12/hour for your participation in this study. A total amount of up to $60.00 will be paid if you complete the entire study. If you travelled from Lawrence to participate in this study, you will receive an extra payment of $24/visit, for up to $48 additional compensation. You will receive payment in the form of a check and will receive it within 30 days after your final study visit. If you choose to withdraw before the end of the study, you will be paid for the visits you have completed.

The KUMC Research Institute will be given your name, address, social security number, and the title of this study to allow them to write checks for your study payments. Study payments are taxable income. A Form 1099 will be sent to you and to the Internal Revenue Service if your payments are $600 or more in a calendar year.

IN THE EVENT OF INJURY
If you have discomfort or other problems during this study, you should immediately contact Dr. Johnson or Dr. Go at 913-588-5929. If it is after 5:00 p.m., a holiday or a weekend, you should leave a message at the same number. A member of the research team will decide what type of treatment, if any, is best for you at that time.

INSTITUTIONAL CONTACT
If you think you have been harmed as a result of participating in research at the University of Kansas Medical Center (KUMC), you should contact the Director, Human Research Protection Program, Mail Stop #1032, University of Kansas Medical Center, 3901 Rainbow Blvd., Kansas City, KS 66160. Their phone number is 913-588-1240.

CONFIDENTIALITY AND PRIVACY AUTHORIZATION
The researchers will protect your information, as required by law. Absolute confidentiality cannot be guaranteed because persons outside the study team may need to look at your study records. Your health information is protected by a federal privacy law called HIPAA. By signing this consent form, you are giving permission for KUMC to use and share your health information. If you decide not to sign the form, you cannot be in the study.

The researchers will only use and share information that is needed for the study. To do the study, they will collect health information from the study activities. You may be identified by information such as name, address, phone, date of birth, social security number, or other identifiers. Your health information will be used at KUMC by Dr. Johnson, members of the research team, the KUMC Research Institute and officials at KUMC who oversee research, including members of the KUMC Human Subjects Committee and other committees and offices that review and monitor research studies. All study information that is sent outside KU Medical Center will have your name and other identifying characteristics removed, so that your identity will not be known. Because identifiers will be removed, your health information will not be re-disclosed by outside persons or groups and will not lose its federal privacy protection.

Your permission to use and share your health information will not expire unless you cancel it. Any research information that is placed in your medical record will be kept indefinitely.

The researchers may publish the results of the study. If they do, they will only discuss group results. Your name will not be used in any publication or presentation about the study.

QUESTIONS

Before you sign this form, Dr. Tiffany Johnson or other members of the study team should answer all your questions. You can talk to the researchers if you have any more questions, suggestions, concerns or complaints after signing this form. If you have any questions about your rights as a research subject, or if you want to talk with someone who is not involved in the study, you may call the Human Subjects Committee at (913) 588-1240. You may also write the Human Subjects Committee at Mail Stop #1032, University of Kansas Medical Center, 3901 Rainbow Blvd., Kansas City, KS 66160.

SUBJECT RIGHTS AND WITHDRAWAL FROM THE STUDY

You may stop being in the study at any time. Your decision to stop will not prevent you from getting treatment or services at KUMC. The entire study may be discontinued for any reason without your consent by the investigator conducting the study.

You have the right to cancel your permission for researchers to use your health information. If you want to cancel your permission, please write to Dr. Tiffany Johnson. The mailing address is Tiffany Johnson, Ph.D., University of Kansas Medical Center, 3901 Rainbow Boulevard, Mail Stop 3039, Kansas City, KS 66160. If you cancel permission to use your health information, you will be withdrawn from the study. The research team will stop collecting any additional information about you. The research team may use and share information that was gathered before they received your cancellation.

CONSENT

Dr. Johnson, or the research team, has given you information about this research study. They have explained what will be done and how long it will take. They explained any inconvenience, discomfort or risks that may be experienced during this study.

By signing this form, you say that you freely and voluntarily consent to participate in this research study. You have read the information and had your questions answered.

You will be given a signed copy of the consent form to keep for your records.

_____

Print Participant's Name

_____ _____ _____

Signature of Participant Time Date

_____

Print Name of Person Obtaining Consent

_____ _____

Signature of Person Obtaining Consent Date

APPENDIX C

DISTORTION PRODUCT OTOACOUSTIC EMISSIONS

CLINICAL TEMPLATE

Otoacoustic emissions (OAEs) are low-level sounds caused by the motion of the cochlear sensory hair cells as a response to auditory stimulation. They are considered to reflect the outer hair cell activity of the cochlea, which in turn is recognized as the site most affected by noise exposure. Distortion product OAEs (DPOAEs), generated by a two-tone complex, have become a commonly used clinical tool for assessing cochlear status, specifically outer hair cell function. DPOAEs were recorded from each study participant to assess outer hair cell function using clinical stimulus parameters. Participants in the present study were required to have normal DPOAEs. Here, normal DPOAE responses were defined as having DPOAE levels (in dB SPL) greater than the 90th percentile for hearing impaired ears based on the standard clinical template (DPGram; Gorga et al., 1997). The corresponding dB SPL values at the 90th percentile for hearing impaired ears (red curve) are shown below.

DPOAE Levels (dB SPL)							
Hz	1000	1500	2000	3000	4000	6000	8000
90th (Impaired)	4.40	0.43	-3.50	-5.55	-4.42	-6.88	-12.85

APPENDIX D

THE NOISE EXPOSURE QUESTIONNAIRE (NEQ)

AND

COMPUTATION OF ANNUAL NOISE EXPOSURE

The noise exposure questionnaire (NEQ; Johnson 2017) was used to assess individual annual noise exposure of the study participants. The questionnaire contains 11 questions on categories of noisy activities like power tools, heavy equipment/machinery, commercial sporting/entertainment events, motorized vehicles (e.g., motorcycles, speed boats, etc.), small/private aircraft, firearm use, musical instrument playing, music listening via personal earphones, music listening via audio speakers, and occupational exposure (summer and school year). It queries episodic and routine exposures as well as frequency and duration of each exposure. A respondent is asked to recall participation in specific noisy activities during the past 12 months. Based on the responses, a value can be calculated that estimates the individual's annual noise exposure (ANE).

The ANE is expressed in $L_{Aeq8760h}$, where the "L" represents sound pressure level in dB, the "A" represents the use of an A-weighted frequency response, the "eq" represents a 3-dB exchange rate for calculation of the time/level relationship, and the "8760h" represents the total duration of the noise exposure in hours (24 hours/day x 365 days/year). The questionnaire was administered using an electronic format (Microsoft Access) for ease of use. A Word document version of the questionnaire can be found at the end of this appendix. The electronic NEQ took study participants approximately 5 minutes to complete. Following completion of the NEQ, answers were exported to a Microsoft Excel file to facilitate computation.

NEQ Computation

Episodic and routine exposures are calculated separately and then combined to produce an overall estimate of ANE. The NEQ excludes firearm use in the computation of the ANE value as there is currently no accepted protocol for integrating impulse-noise exposures with continuous noise exposures. Firearm exposures are described separately instead.

The $L_{Aeq8760h}$ is calculated using the equation [10 x $\log_{10}$(D/100)] + 79. "D" here is the noise dose for an individual subject given a 79 dBA recommended exposure limit for 8760 hours and a 3 dB exchange rate. The 79 dBA exposure limit is based on NIOSH recommended annual limits for noise exposure. A dose of over 100% can be interpreted as exceeding NIOSH recommendations of what is considered a safe listening environment.

The "D" for each of the episodic activity is computed using the equation, [C/T] x 100. "C" in this equation refers to the number of hours/year reported by the subject for the activity. It is calculated by multiplying the frequency of participation and duration values. The frequency of participation responses on the NEQ are assigned numerical values (i.e., 'daily = 200, 'weekly' = 50, 'monthly'=12, 'every few months' = 1, and 'never' = 0). Similarly, duration values are as follows: '8 hours or more' = 8, '4 to 8 hours' = 6, '1 to 4 hours' = 3, and 'less than 1 hour' = 1. For questions relating to occupational noise exposure (questions 10 and 11), the subject is asked to report on average how many hours a week they worked during the summer (question 10) or the school year (question 11). These responses are multiplied by 10 (10 weeks per year) if it is a summer job and by 40 (40 weeks per year) if it is a school year job. The "C" for routine exposures is calculated by subtracting the combined episodic values across all episodic exposures from 8760. The "T" represents the number of hours/year at which the activity is considered hazardous based on the recommended exposure limit over a 1 year time period and is calculated using the equation, $8760/2^{(L-79/3)}$. Here, "L" is the continuous equivalent sound level in dB L_{Aeq} derived from scientific literature for that specific noise exposure type (e.g., power tools, small/private aircraft, etc.). The "L" for each of the noisy activities categories (excluding firearm use) are as follows: power tools, 94 dB L_{Aeq}; heavy equipment/machinery, 97 dB L_{Aeq}; commercial sporting/entertainment events, 94 dB L_{Aeq}; motorized vehicles, 98 dB L_{Aeq}; 68

small/private aircraft, 91 dB L_{Aeq}; musical instrument playing, 87 dB L_{Aeq}; music listening via personal earphones, 76 dB L_{Aeq}; music listening via audio speakers, 78 dB L_{Aeq}; occupational exposure, 90 dB L_{Aeq}. The "L" of routine activities was defined as 64 dB $L_{Aeq8760h}$, which was obtained from studies by Neitzel et al., (2004a, 2004b).

Sample Computation

Activity	**Question**	**Response**	**C (hours)**	**L (LAeq)**	**T (hours)**	**D (%)**
Power tools	1a	Every few months (1)	3	94	273.75	1.096%
	1b	1 hour up to 4 hours (3)				
Heavy equipment & machinery	2a	Weekly (50)	150	97	136.88	109.589%
	2b	1 hour up to 4 hours (3)				
Commercial sporting & entertainment events	3a	Monthly (12)	36	94	273.75	13.151%
	3b	1 hour up to 4 hours (3)				
Motorized vehicles	4a	Never (0)	0	98	108.64	0.00%
	4b	n/a				
Small/private aircraft	5a	Never (0)	0	91	547.50	0.00%
	5b	n/a				
Musical instrument playing	7a	Every few months (1)	1	87	1379.61	0.072%
	7b	Less than 1 hour (1)				
Music listening via personal earphones	8a	Daily (200)	600	76	17520	3.425%
	8b	1 hour up to 4 hours (3)				
Music listening via audio speakers	9a	Daily (200)	600	78	11036.91	5.436%
	9b	1 hour up to 4 hours (3)				
Occupational exposure	10	Yes (3 hrs)	30	90	689.81	4.349%
	11	No				
Routine activities			7340	64	280320	2.618%
Total Dose						139.736%
$L_{Aeq8760h}$						**80.453**

The NEQ has a theoretical range of 64 to 95.5 $L_{Aeq8760h}$ with higher $L_{Aeq8760h}$ values indicating greater amounts of ANE. Subjects with ANE values of 79 or greater were considered to be at highest risk for developing noise-induced hearing loss (NIHL). This was based on the National Institute for Occupational Safety and Health (NIOSH) occupational noise criterion of 85 $L_{Aeq2000h}$ (8 hours/day × 250 workdays/year) extrapolated to an annual equivalent exposure limit of 78.6 $L_{Aeq8760h}$.

Noise Exposure Questionnaire

Name:_____Date: _____

INSTRUCTIONS:

Please answer the following questions about yourself, your hearing, and any noise you may have been around during the past year. Write an answer in the blank [_] or check [√] the best answer to each question.

Please answer these questions about any loud sounds.

DURING THE PAST YEAR (12 months):

1.	Outside of a paid job, how often did you use power tools, chainsaws, or other shop tools? ☐ Never ☐ Every few months ☐ Monthly ☐ Weekly ☐ Daily If you used power tools, on average, how many hours did each time/session last? ☐ 8 hours or more ☐ 4 hours up to 8 hours ☐ 1 hour up to 4 hours ☐ Less than 1 hour If you used power tools, how often did you wear earplugs or earmuffs during this activity? ☐ Never ☐ Sometimes ☐ Always
2.	Outside of a paid job, how often did you drive heavy equipment or use loud machinery (such as tractors, trucks, or farming or lawn equipment like mowers/leaf blowers)? ☐ Never ☐ Every few months ☐ Monthly ☐ Weekly ☐ Daily If you drove/used loud machinery, on average, how many hours did each time/session last? ☐ 8 hours or more ☐ 4 hours up to 8 hours ☐ 1 hour up to 4 hours ☐ Less than 1 hour If you drove/used machinery, how often did you wear earplugs or earmuffs during this activity? ☐ Never ☐ Sometimes ☐ Always
3.	How often did you attend car/truck races, commercial/high school sporting events, music concerts/dances or any other events with amplified public announcement (PA)/music systems? ☐ Never ☐ Every few months ☐ Monthly ☐ Weekly ☐ Daily If you attended these events, on average, how many hours did each time/session last? ☐ 8 hours or more ☐ 4 hours up to 8 hours ☐ 1 hour up to 4 hours ☐ Less than 1 hour If you attended these events, how often did you wear earplugs or earmuffs during this activity? ☐ Never ☐ Sometimes ☐ Always
4.	How often did you ride/operate motorized vehicles such as motorcycles, jet skis, speed boats, snowmobiles, or four-wheelers? ☐ Never ☐ Every few months ☐ Monthly ☐ Weekly ☐ Daily If you rode motorized vehicles, on average, how many hours did each time/session last? ☐ 8 hours or more ☐ 4 hours up to 8 hours ☐ 1 hour up to 4 hours ☐ Less than 1 hour If you rode motorized vehicles, how often did you wear earplugs or earmuffs during this activity? ☐ Never ☐ Sometimes ☐ Always

Please continue answering these questions about any loud sounds. **DURING THE PAST YEAR (12 months):**	
5.	How often did you ride in or pilot small aircraft/private airplanes? ☐ Never ☐ Every few months ☐ Monthly ☐ Weekly ☐ Daily If you flew airplanes, on average, how many hours did each time/session last? ☐ 8 hours or more ☐ 4 hours up to 8 hours ☐ 1 hour up to 4 hours ☐ Less than 1 hour If you flew airplanes, how often did you wear earplugs or earmuffs during this activity? ☐ Never ☐ Sometimes ☐ Always
6.	How often were you around or did you shoot firearms such as rifles, pistols, shotguns, etc.? ☐ Never ☐ Every few months ☐ Monthly ☐ Weekly ☐ Daily If you were around/shot firearms, on average, how many shots did you fire each time/session? _____shotgun/rifle shots per session _____pistol shots per session If you were around/shot firearms, how often did you wear earplugs or earmuffs while shooting? ☐ Never ☐ Sometimes ☐ Always
7.	How often did you play a musical instrument? ☐ Never ☐ Every few months ☐ Monthly ☐ Weekly ☐ Daily If you played, please tell us what musical instrument: _____ If you played a musical instrument, on average, how many hours did each time/session last? ☐ 8 hours or more ☐ 4 hours up to 8 hours ☐ 1 hour up to 4 hours ☐ Less than 1 hour If you played a musical instrument, how often did you wear earplugs or earmuffs while playing? ☐ Never ☐ Sometimes ☐ Always
8.	How often did you listen to music, radio programs, etc. using personal headsets or earphones? ☐ Never ☐ Every few months ☐ Monthly ☐ Weekly ☐ Daily If you listened through earphones, on average, how many hours did each time/session last? ☐ 8 hours or more ☐ 4 hours up to 8 hours ☐ 1 hour up to 4 hours ☐ Less than 1 hour
9.	Other than music concerts and headset use (already covered in questions 3 and 8), how often did you listen to music, radio programs, etc. from audio speakers in a car or at home? ☐ Never ☐ Every few months ☐ Monthly ☐ Weekly ☐ Daily If you listened via speakers, on average, how many hours did each time/session last? ☐ 8 hours or more ☐ 4 hours up to 8 hours ☐ 1 hour up to 4 hours ☐ Less than 1 hour

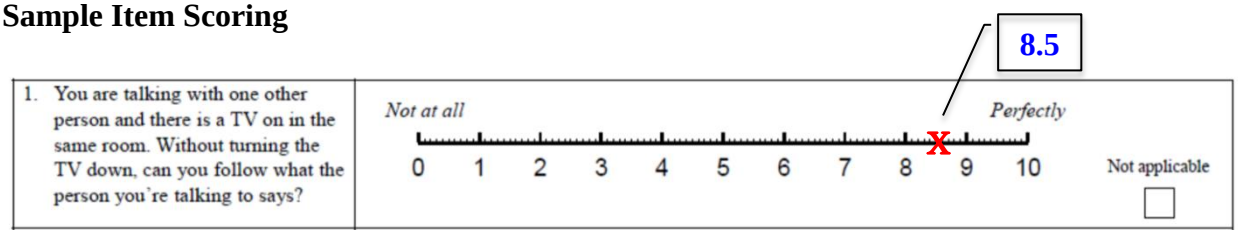
APPENDIX E

SPEECH, SPATIAL, AND QUALITIES OF HEARING SCALE (SSQ) COMPUTATION

The speech hearing subscale of the SSQ (v. 5.6; Gates & Noble, 2004) was used to assess self-perceived speech-in-noise abilities of the study participants. The speech hearing subscale of the SSQ assesses 14 different speech listening environments, including quiet environments and a range of challenging environments with competing noise. The study participants were instructed to rate their abilities and experiences with hearing and listening in different situations by placing an 'X' mark anywhere on a scale that runs from 0 to 10. Putting a mark at '10' means that the respondent would be perfectly able to do or experience what is described in the question. Putting a mark at '0' means that they would be quite unable to do or experience what is described. If a question described a situation that does not apply to the study participant, they are instructed to put an 'X' in the "not applicable" box.

The SSQ was administered in paper form in the laboratory. The speech-hearing subscale took study participants approximately 5-10 minutes to complete. A copy of the speech-hearing subscale can be found at the end of this appendix. Each rating was judged by the principal investigator based on where the intersection of the 'X' mark was placed. This was done consistently for all subjects. Computation of scores were manually completed and entered into an excel spreadsheet. The ratings for each item are combined to yield an averaged score with a theoretical range from 0 to 10. This score reflects individual self-perception of ability with higher scores indicating less difficulty.

Sample Item Scoring



APPENDIX F

FIGURES AND TABLES

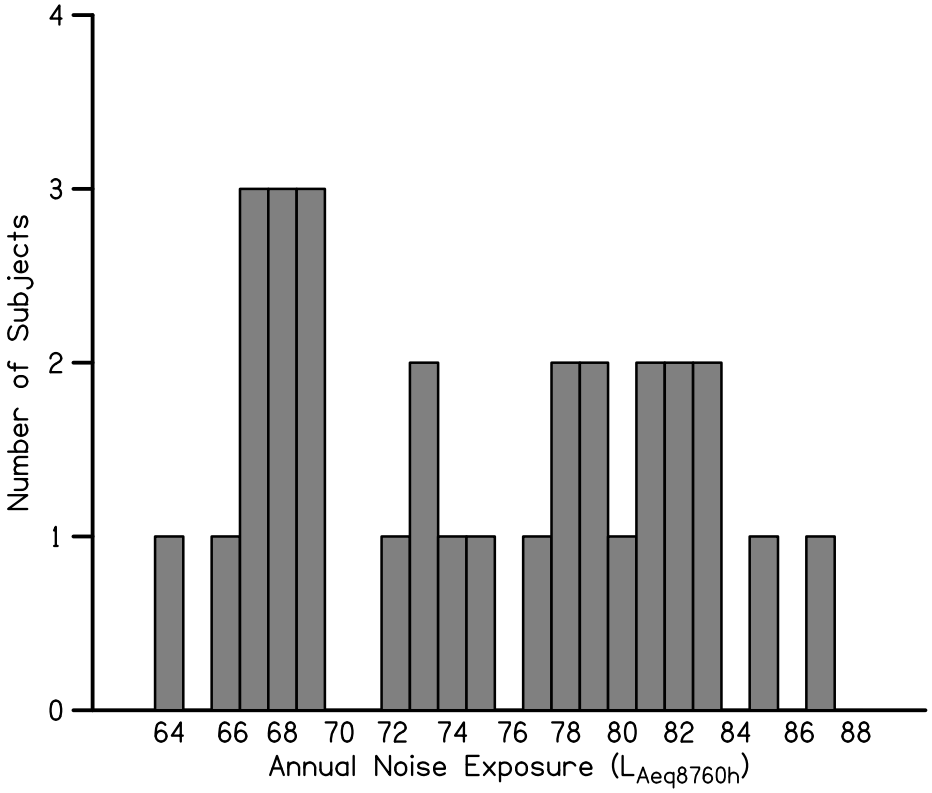


Fig. 1: Histogram of annual noise exposure values ($L_{Aeq8760h}$) obtained via the Noise Exposure Questionnaire (Johnson et al., 2017) from 30 study participants.

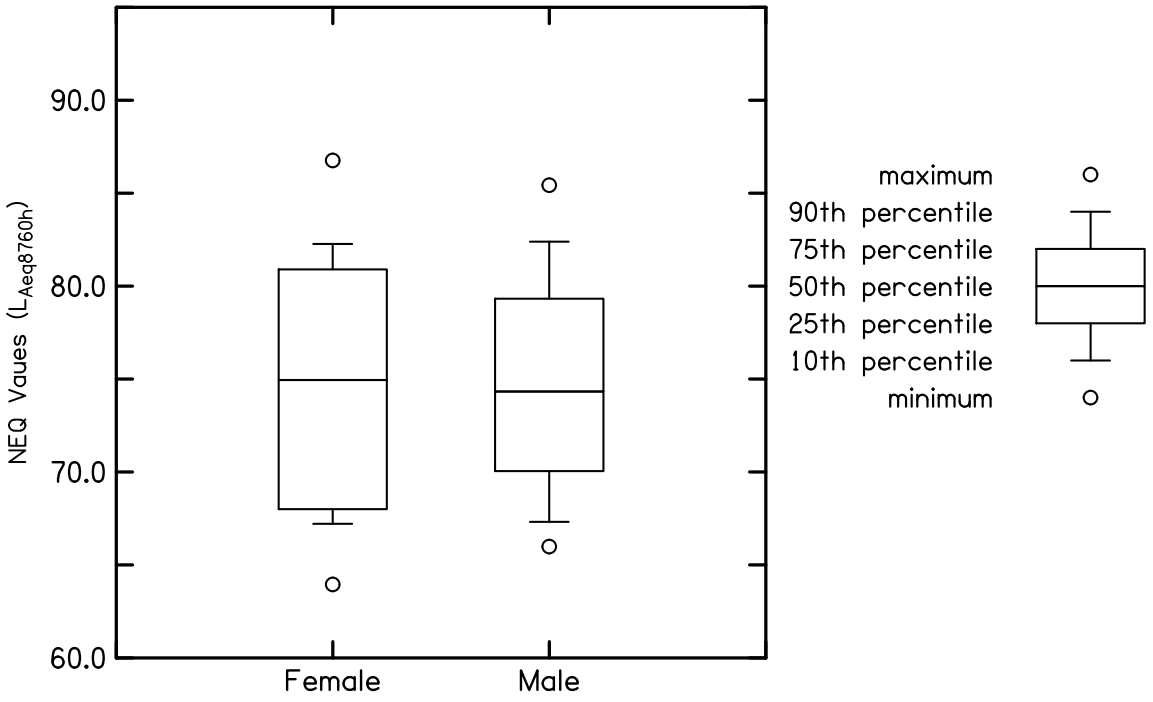


Fig. 2: Distribution of annual noise exposure values ($L_{Aeq8760h}$) as quantified by the Noise Exposure Questionnaire between female (n=16) and male (n=14) study participants.

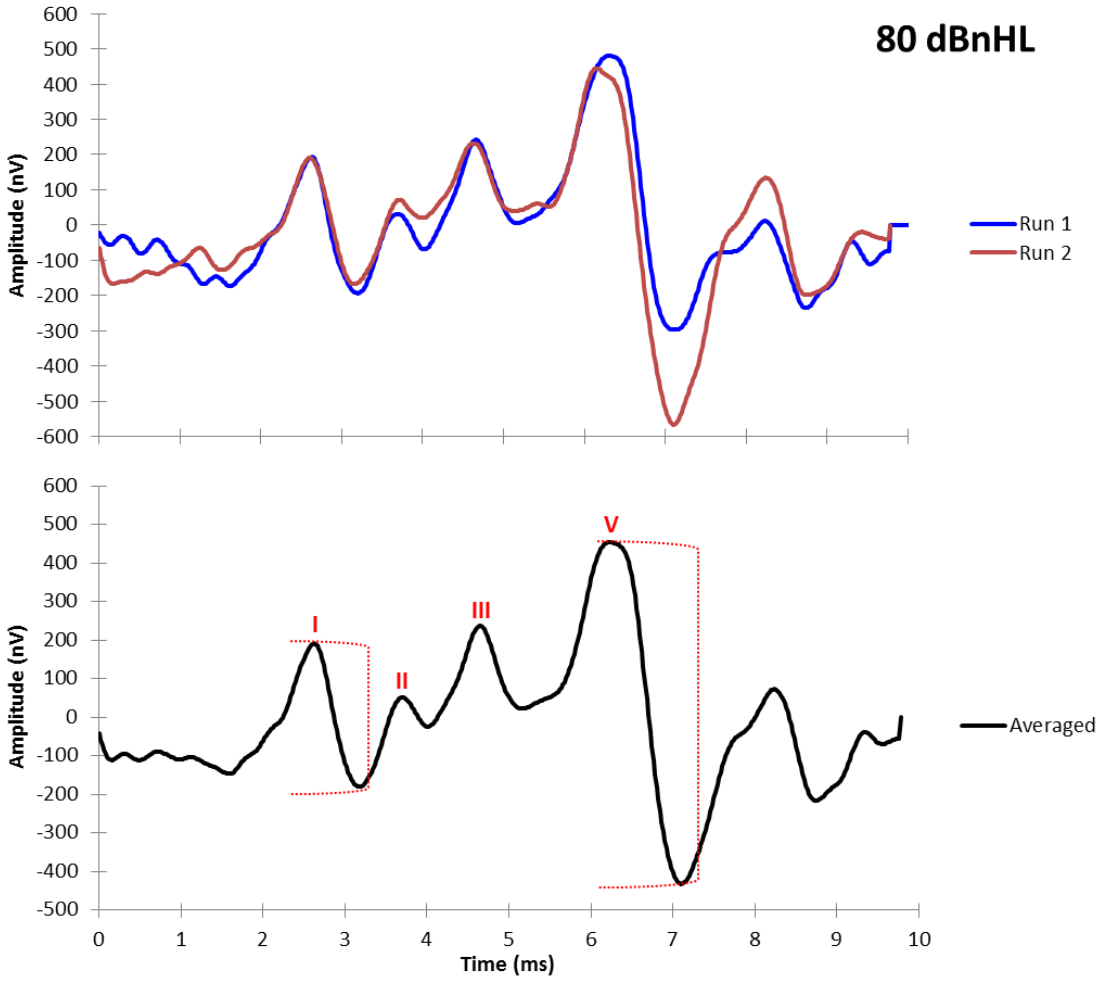


Fig. 3: Example ABR waveforms recorded with a mastoid electrode in response to a click stimulus presented at 80 dB nHL from one subject. Individual waveforms (blue and red = 2000 sweeps each) are shown in the top panel and averaged waveform (black = total of 4000 sweeps) is shown in the bottom panel. The time scale is 10 msec. Red brackets show the peak to trough amplitude measured for waves I and V.

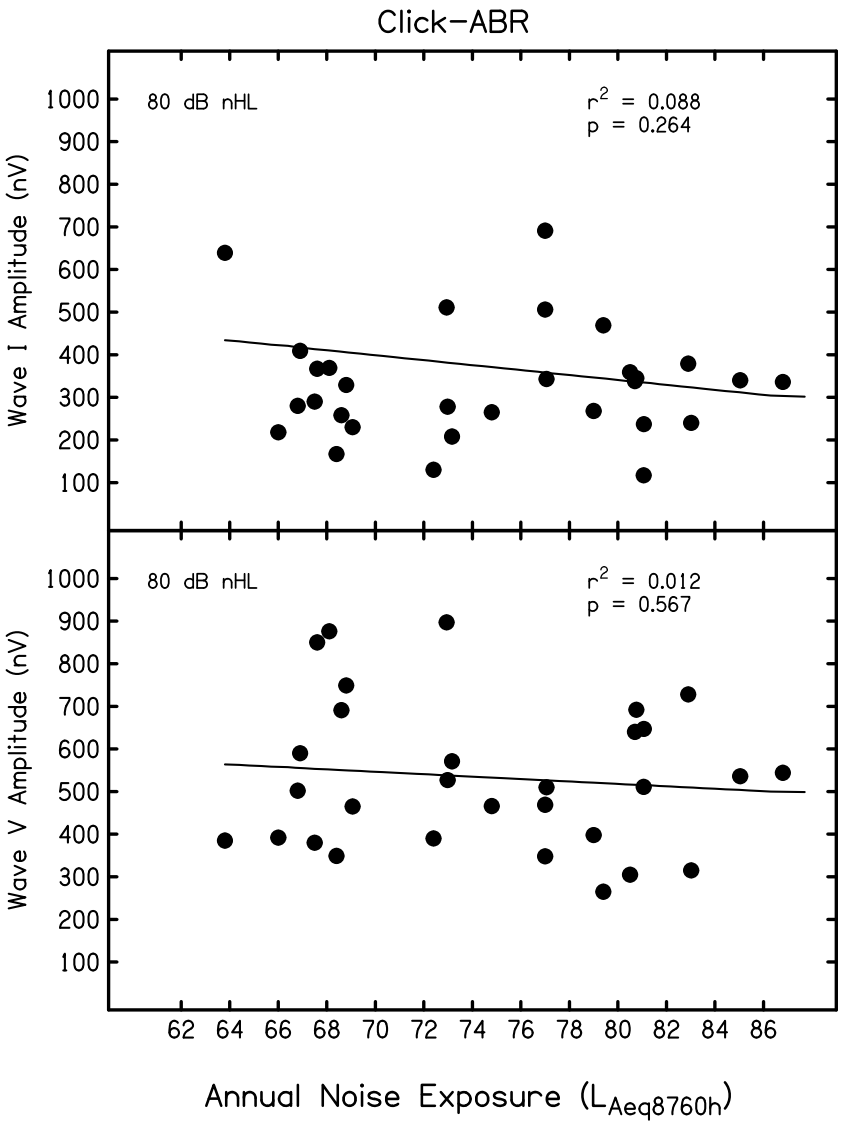


Fig. 4: Click-ABR amplitudes of waves I (top row) and wave V (bottom row) as a function of ANE at stimulus level of 80 dB nHL (n = 30). Within each panel, symbols (filled circles) represent individual data. Linear regression analysis was completed for each wave component and the resulting regression line, p-value and r^2 (coefficient of determination) are shown.

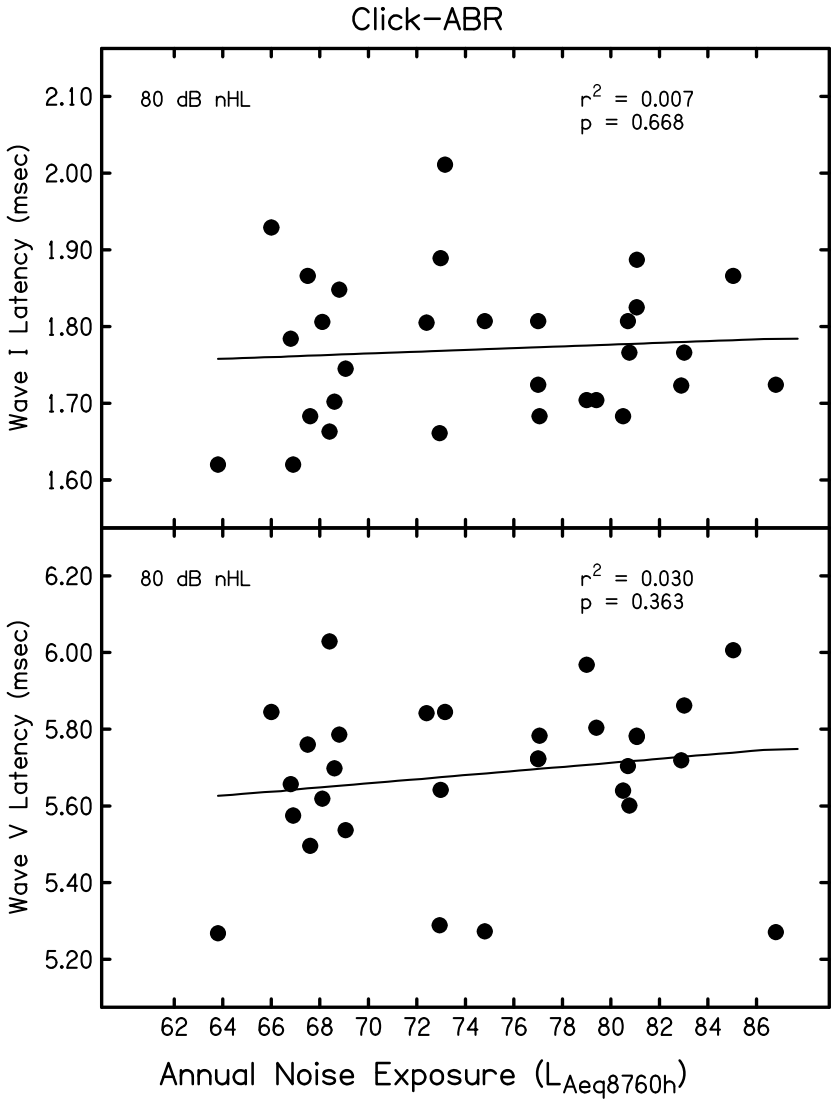


Fig. 5: Click-ABR latencies of waves I (top row) and wave V (bottom row) as a function of ANE at stimulus level of 80 dB nHL (n = 30). Data are shown following the conventions used in Figure 4.

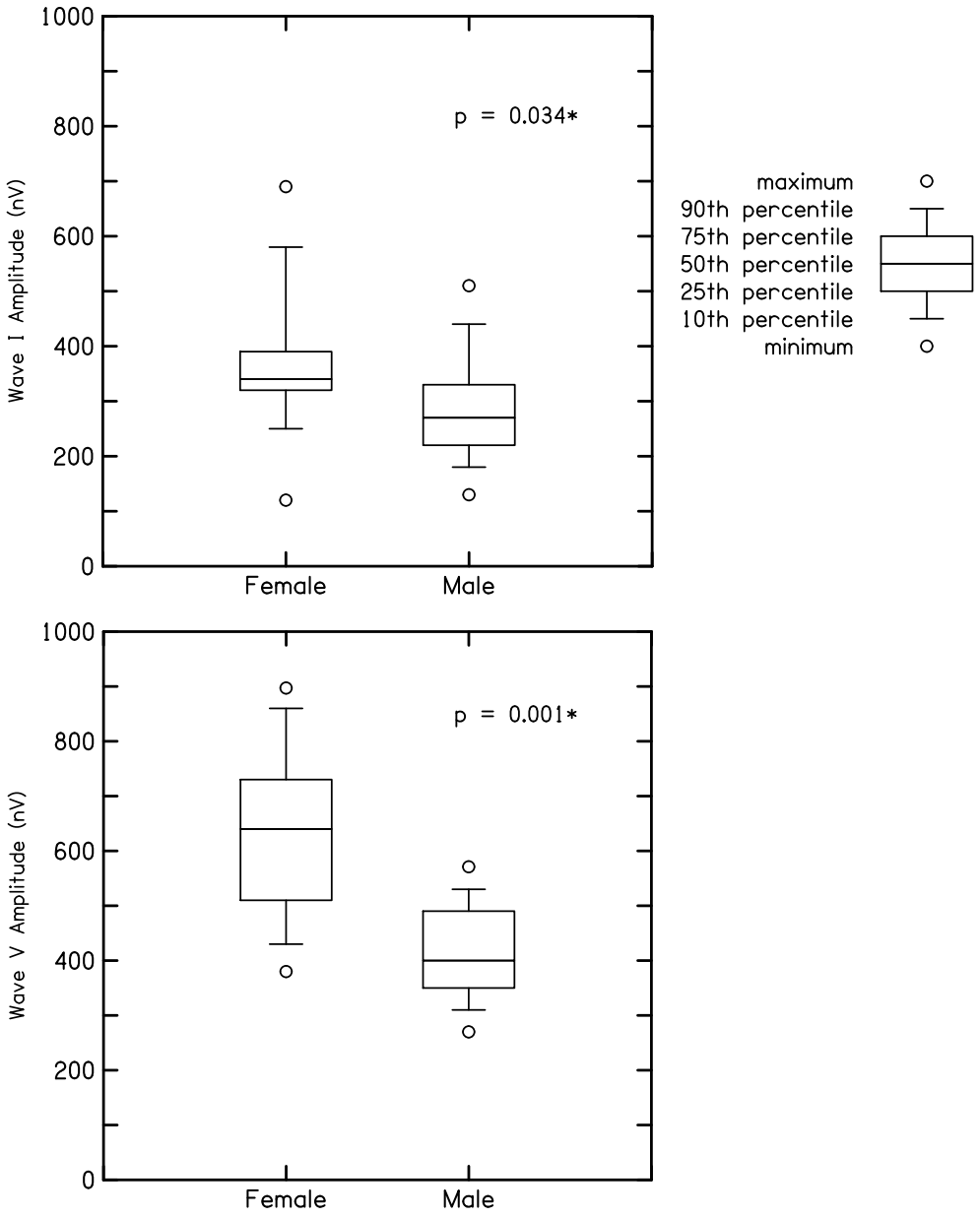


Fig. 6: Distribution of the response amplitude for waves I (top panel) and V (bottom panel) to 80 dB nHL clicks via mastoid recording between female (n=16) and male (n=14) study participants. The amplitude distribution of waves I and V significantly differs between the males and females (Kruskal-Wallis test). The asterisk (*) symbol indicates a p-value ≤ 0.05)

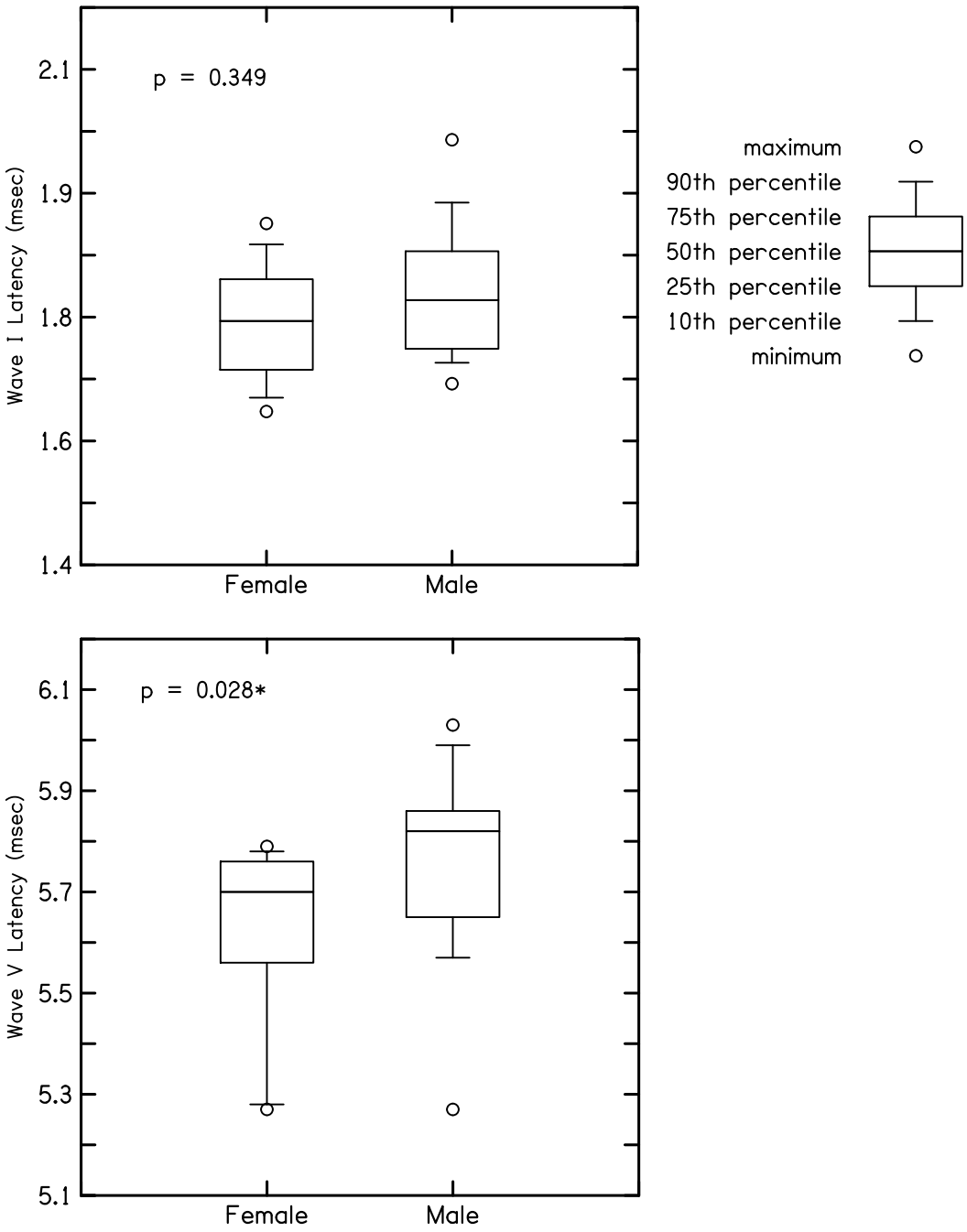


Fig. 7: Distribution of the peak latencies for waves I (top panel) and V (bottom panel) to 80 dB nHL clicks via mastoid recording between female (n=16) and male (n=14) study participants. Only the latency distribution of wave V significantly differs between the males and females based on the Kruskal-Wallis test.

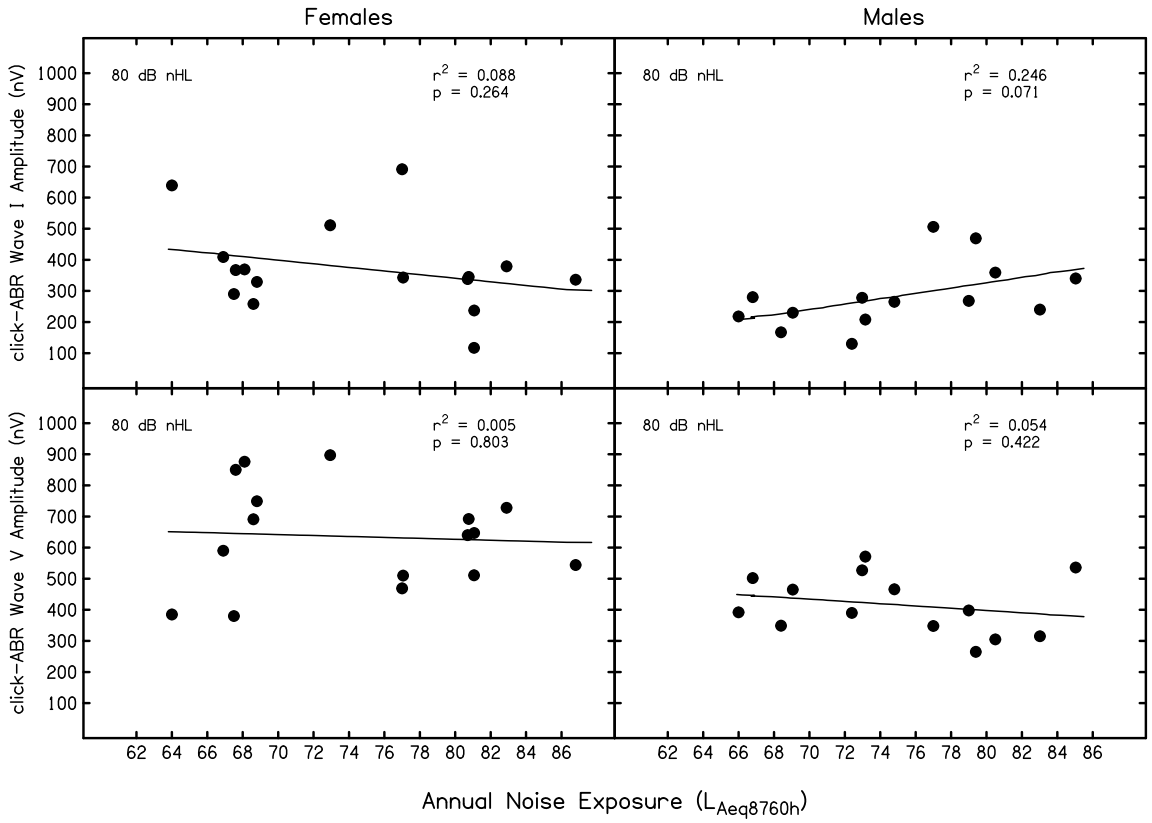


Fig. 8: Click-ABR amplitudes of waves I (top row) and wave V (bottom row) as a function of ANE at stimulus level of 80 dB nHL. Within each panel, symbols (filled circles) represent individual data. Linear regression analysis was completed for each category of sex: 16 females (left column) and 14 males (right column). The resulting regression line, p-value and r^2 (coefficient of determination) are shown.

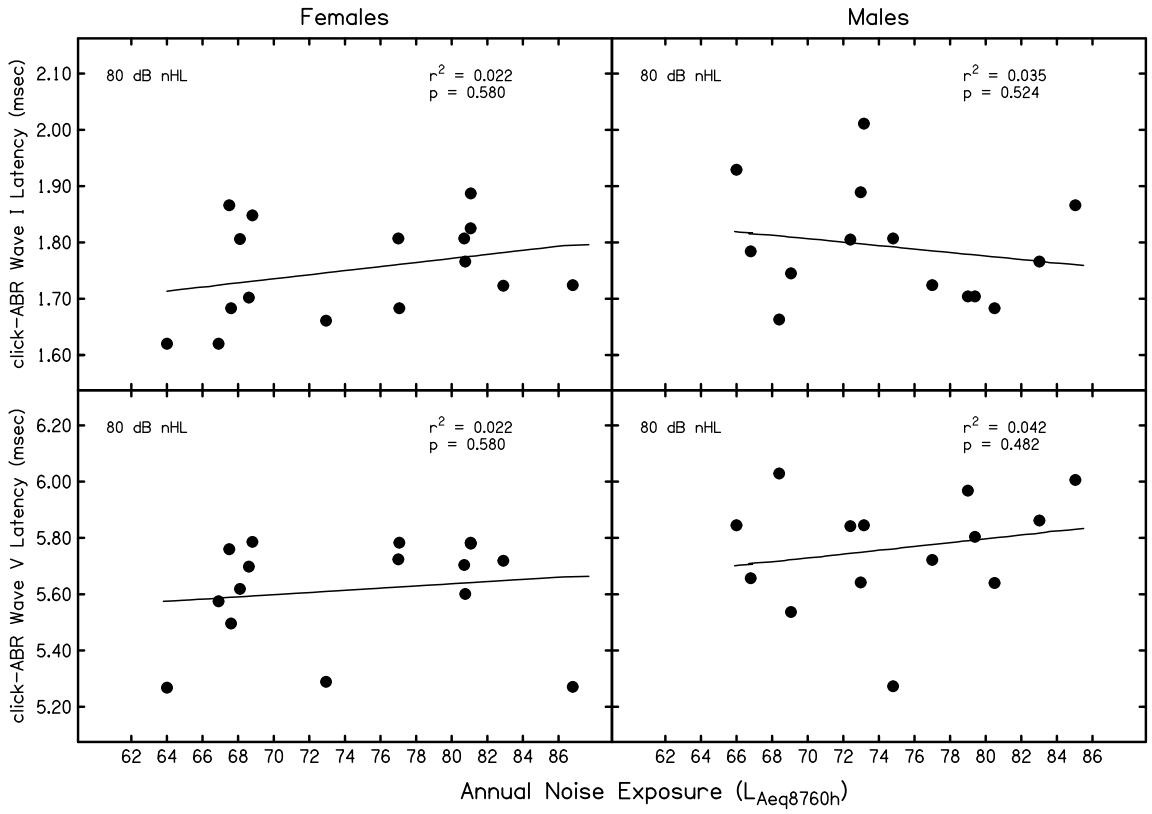


Fig. 9: Click-ABR latencies of waves I (top row) and wave V (bottom row) as a function of ANE at stimulus level of 80 dB nHL. Data are shown following the conventions used in figure 8.

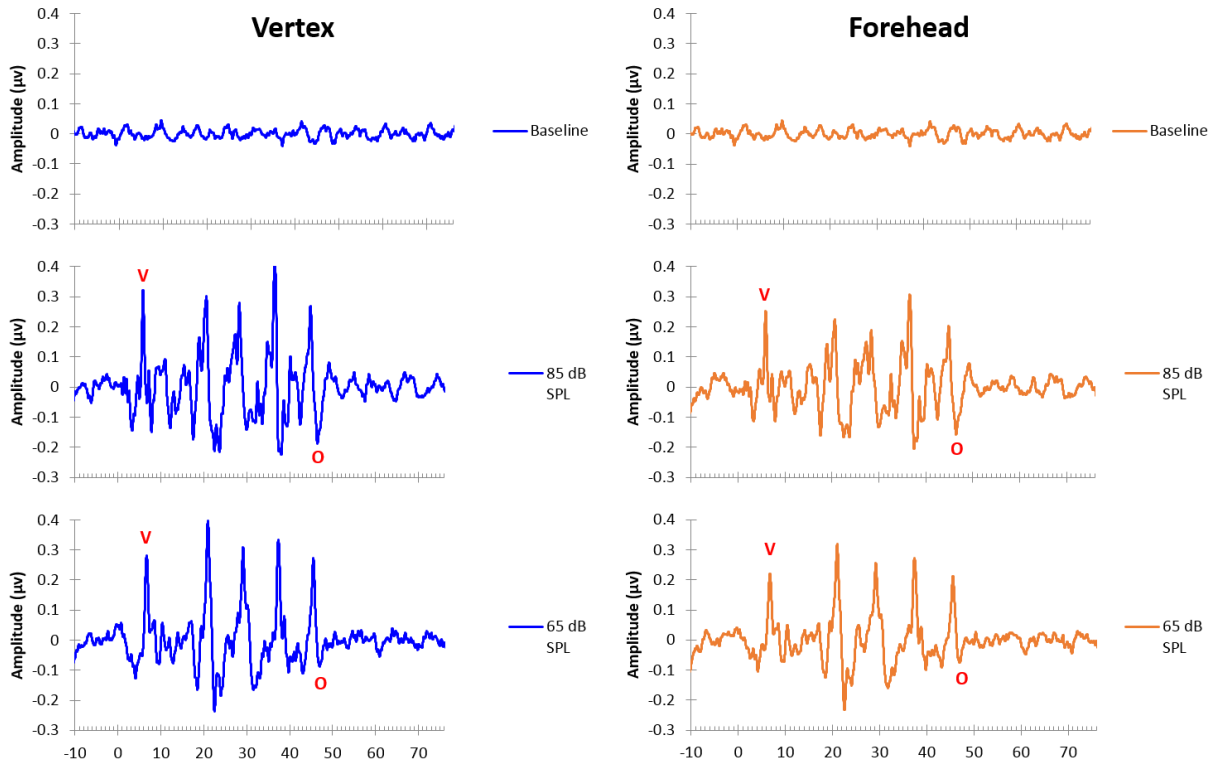


Fig. 10: Sample of speech-ABR waveforms recorded from the vertex (left column) and forehead (right column) obtained from one study participant. The displayed waveforms are averages of 10,000 sweeps for the following test conditions: crimped sound tube (top row), stimulus level at 85 (middle row), and 65 dB SPL (bottom row).

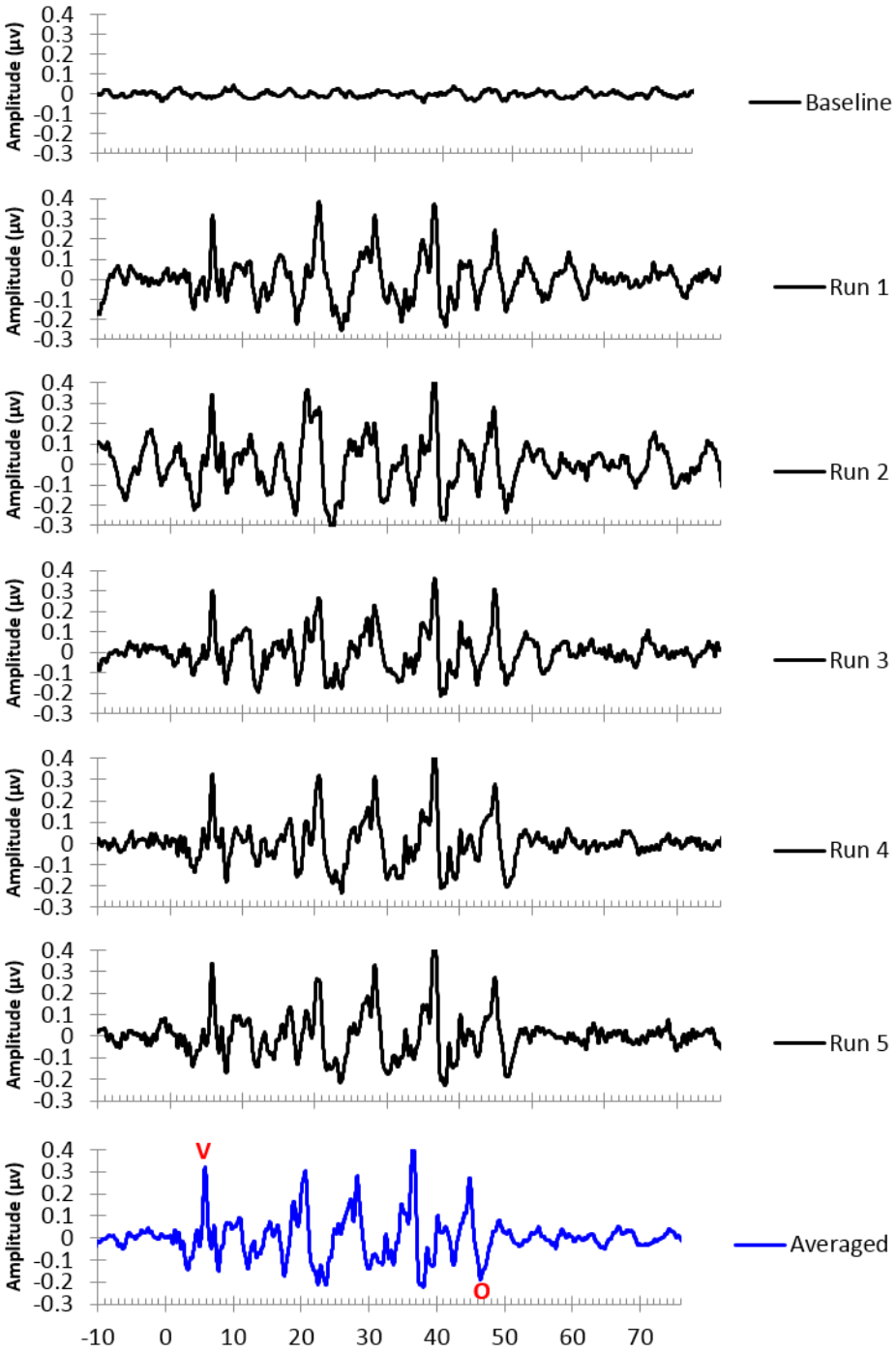


Fig. 11: An example of speech-ABR waveforms recorded from one subject at 85 dB SPL. The averaged baseline recording (10,000 sweeps) was recorded prior to collection of speech-ABR data with a crimped sound tube of the insert earphone. Five blocks of 2000 sweeps (runs 1 to 5) were recorded then averaged (blue) where identification of peak components are completed.

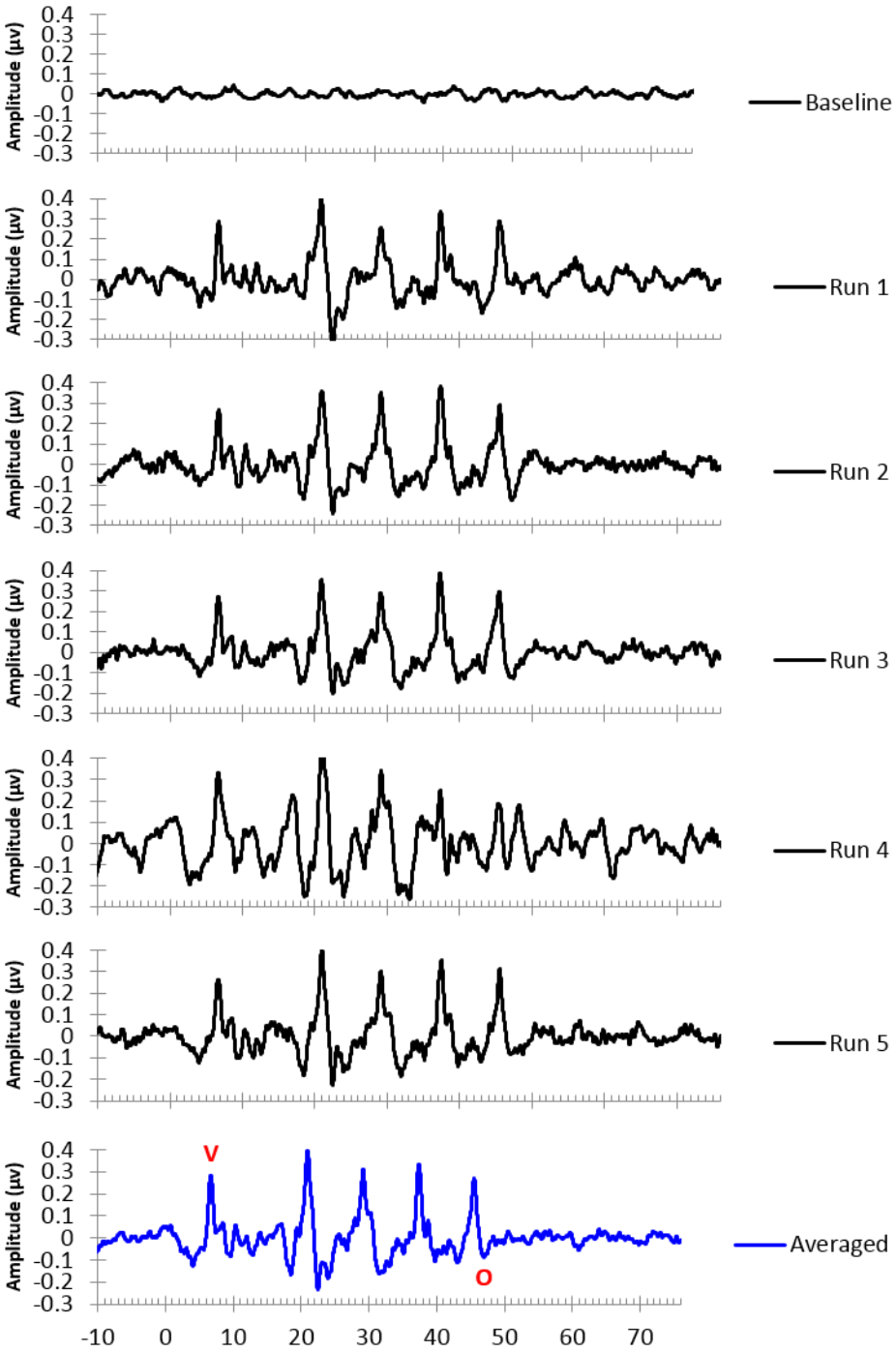


Fig. 12: An example of speech-ABR waveforms recorded at 65 dB SPL from the same study participant. Data are shown following conventions used in Figure 11.

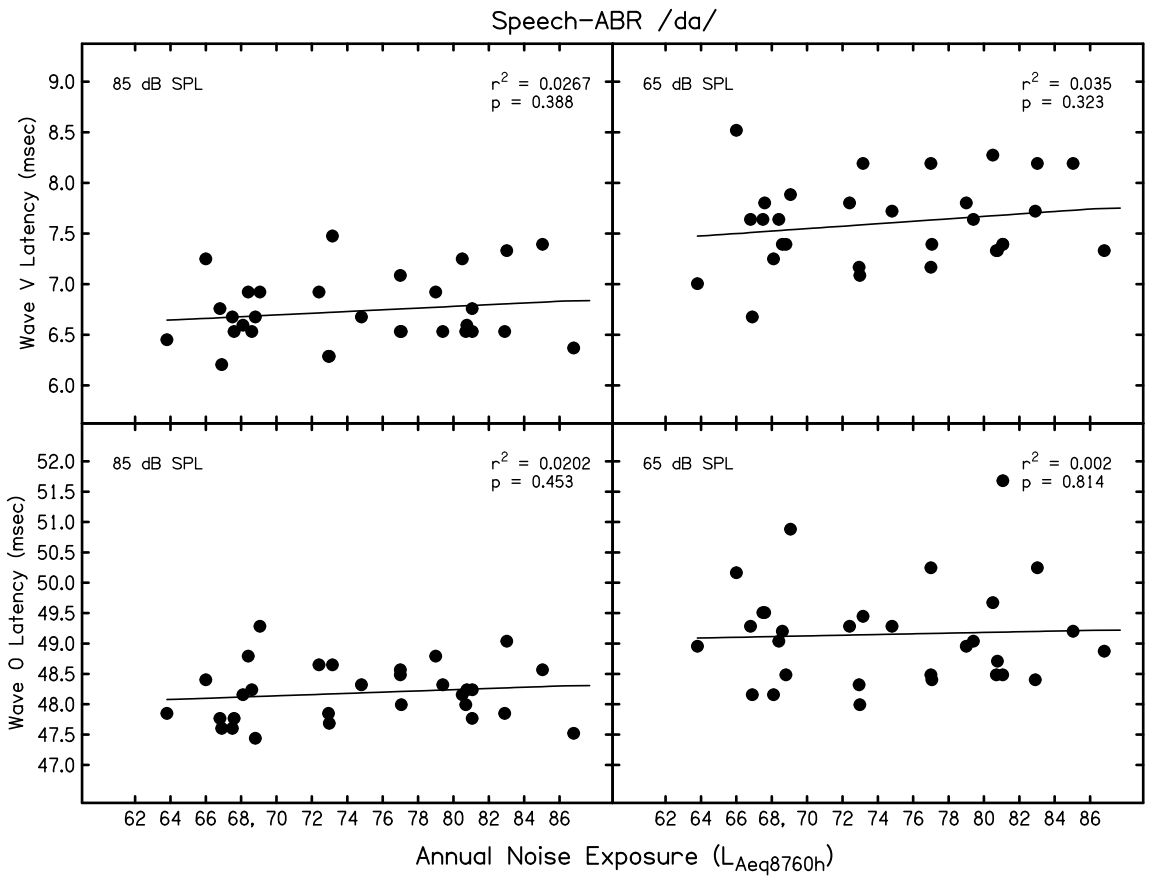


Fig. 13: Latencies of speech -ABR onset response wave V (top row) and offset response wave O (bottom row) to syllable /da/ as a function of ANE when presented at 85 (left column) and 65 (right column) dB SPL. Again, symbols (filled circles) represent individual data and the resulting regression line, p-value and r^2 are shown.

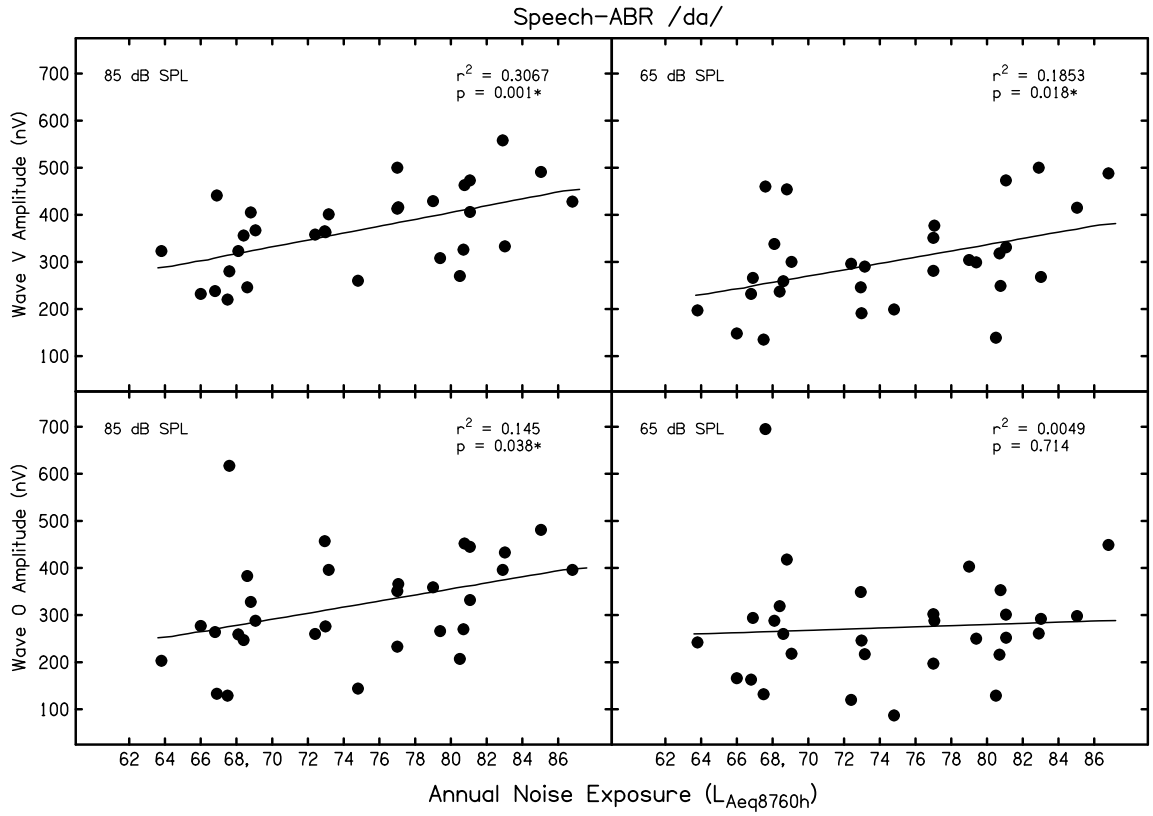


Fig. 14: Amplitudes of speech-ABR onset response wave V (top row) and offset response wave O (bottom row) to syllable /da/ as a function of ANE when presented at 85 (left column) and 65 (right column) dB SPL. Data are shown following the conventions used in figure 13. The asterisk symbol (*) indicates a p-value ≤ 0.05.

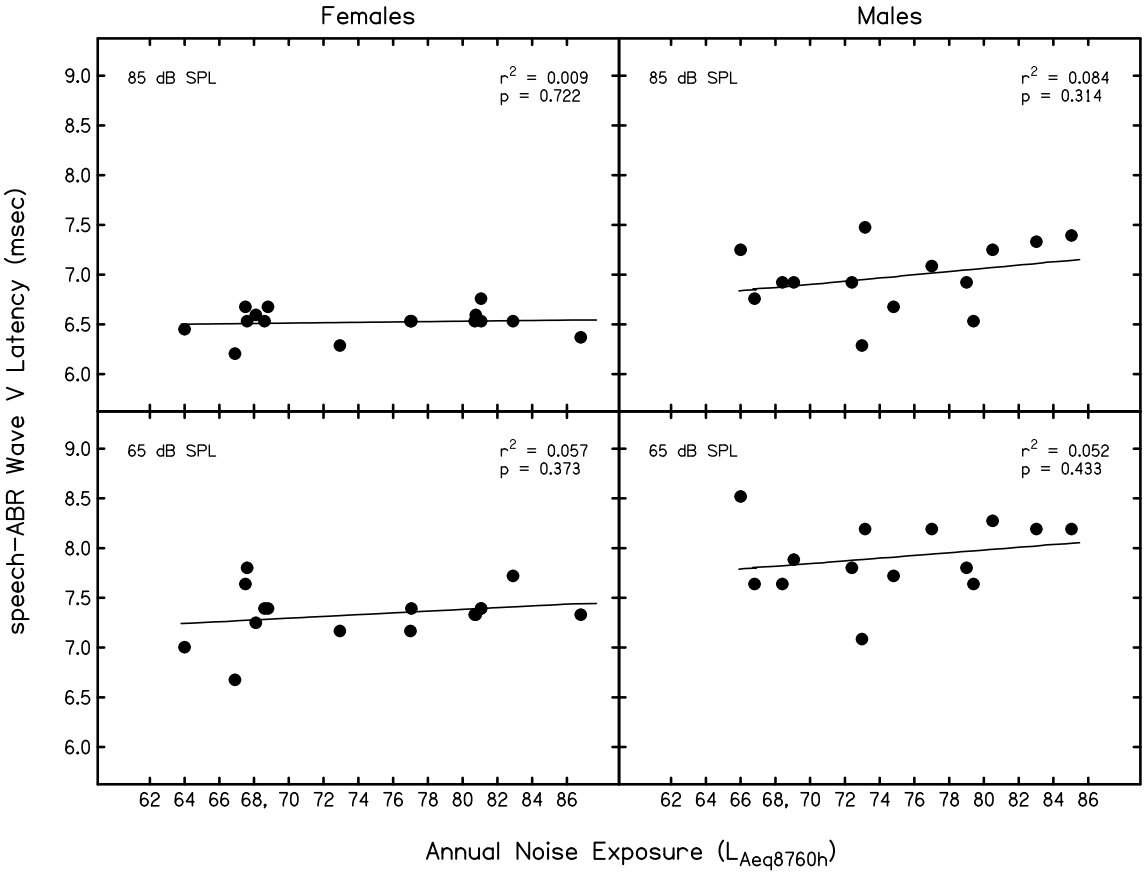


Fig. 15: Latency of speech-ABR onset response (wave V) as a function of ANE when presented at 85 (top row) and 65 (bottom row) dB SPL. Linear regression analysis was completed for each category of sex: 16 females (left column) and 14 males (right column). Filled circles represent individual data and the resulting regression line, p-value and r^2 are shown for each panel.

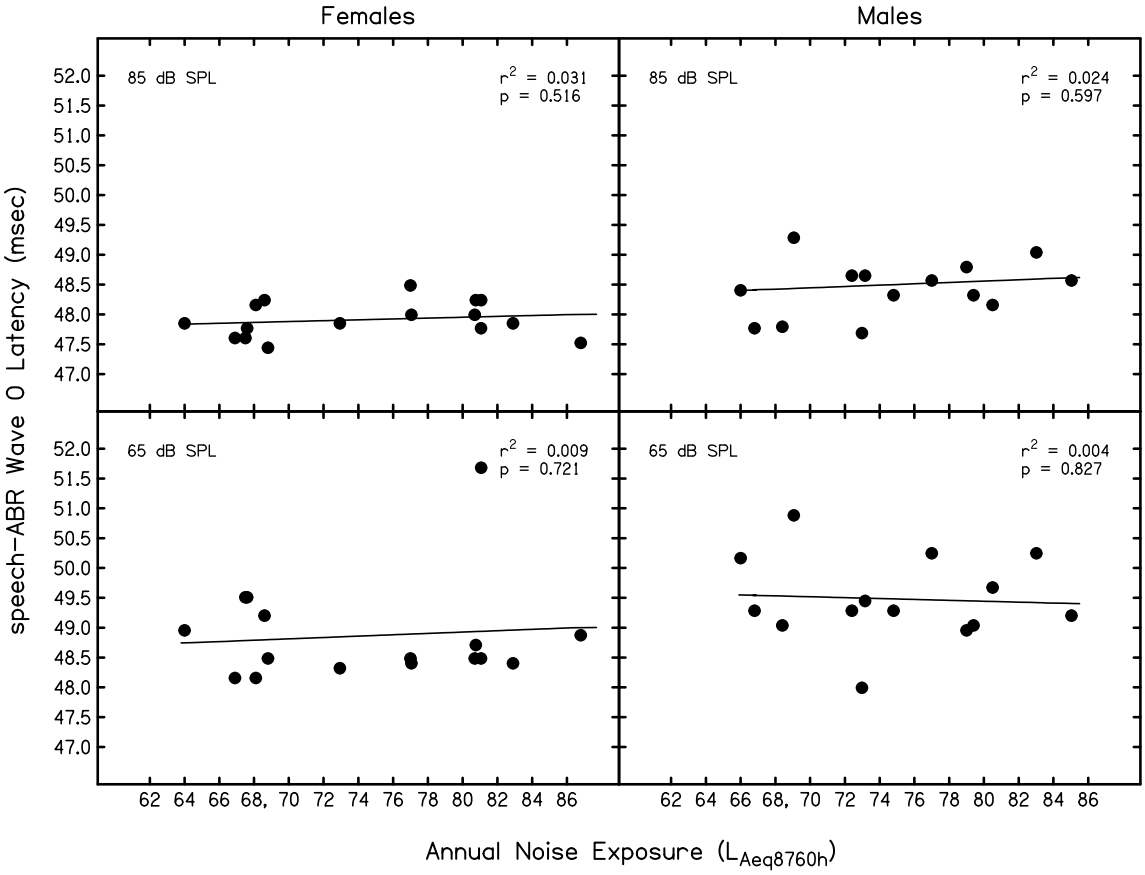


Fig. 16: Latency of speech-ABR offset response (wave O) as a function of ANE when presented at 85 (top row) and 65 (bottom row) dB SPL. Data are shown following the conventions used in figure 15.

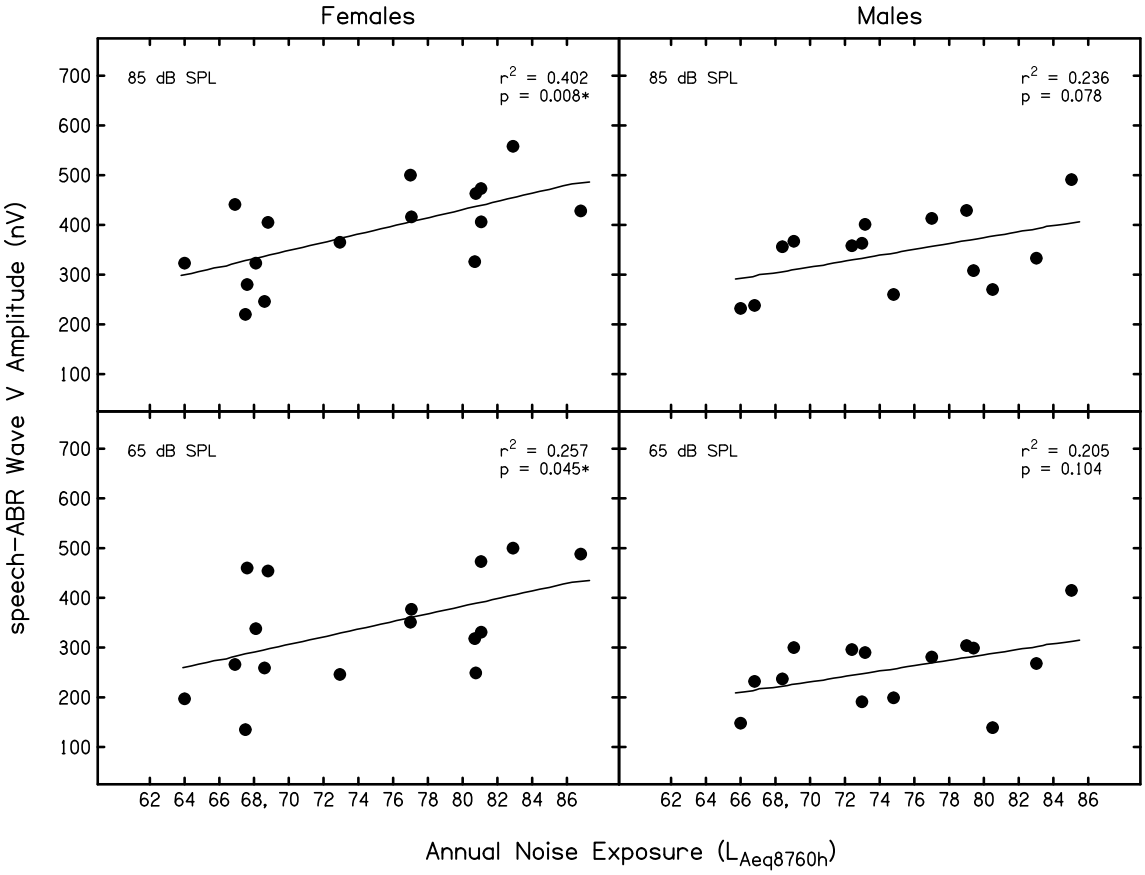


Fig. 17: Speech -ABR wave V amplitude as a function of ANE when presented at 85 (top row) and 65 (bottom row) dB SPL. Data are shown following the conventions used in figure 15 and 16 with the asterisk (*) indicating a p-value ≤ 0.05.

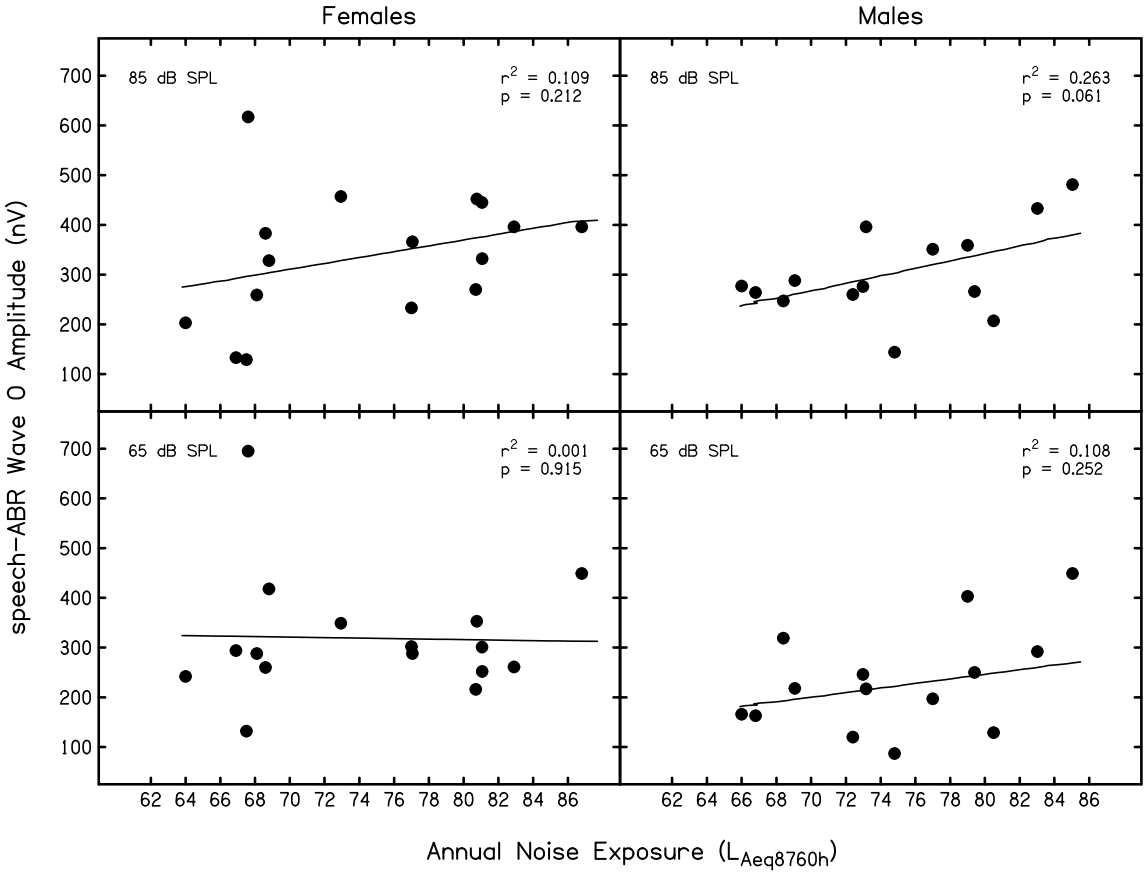


Fig. 18: Speech-ABR wave O latency as a function of ANE when presented at 85 (top row) and 65 (bottom row) dB SPL. Data are shown following the conventions used in figure 15, 16, and17. No significant trends were observed between males (right column) and females (left).

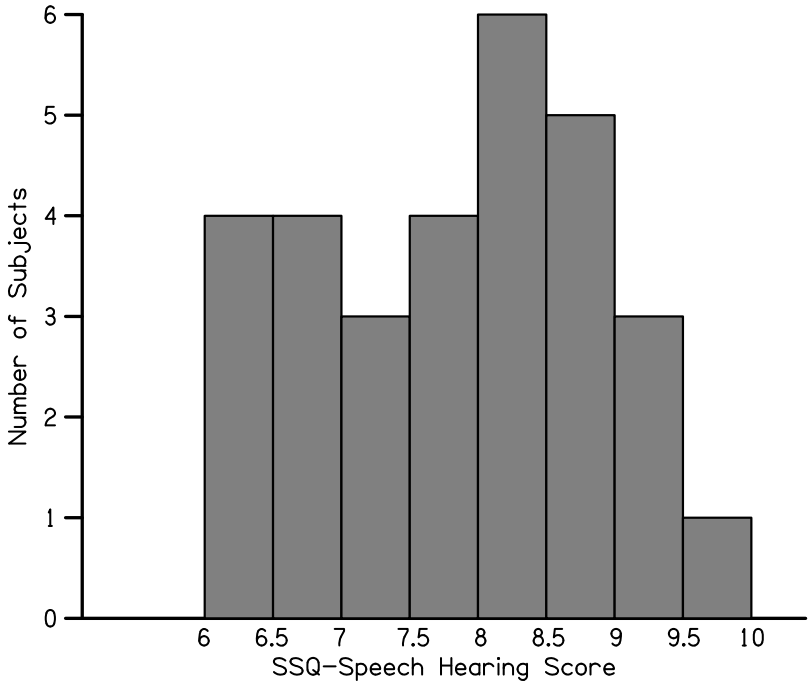


Fig. 19: Histogram of speech-hearing scores obtained via the Speech, Spatial, and Qualities of Hearing Scale (Gates and Noble, 2004) from 30 study participants.

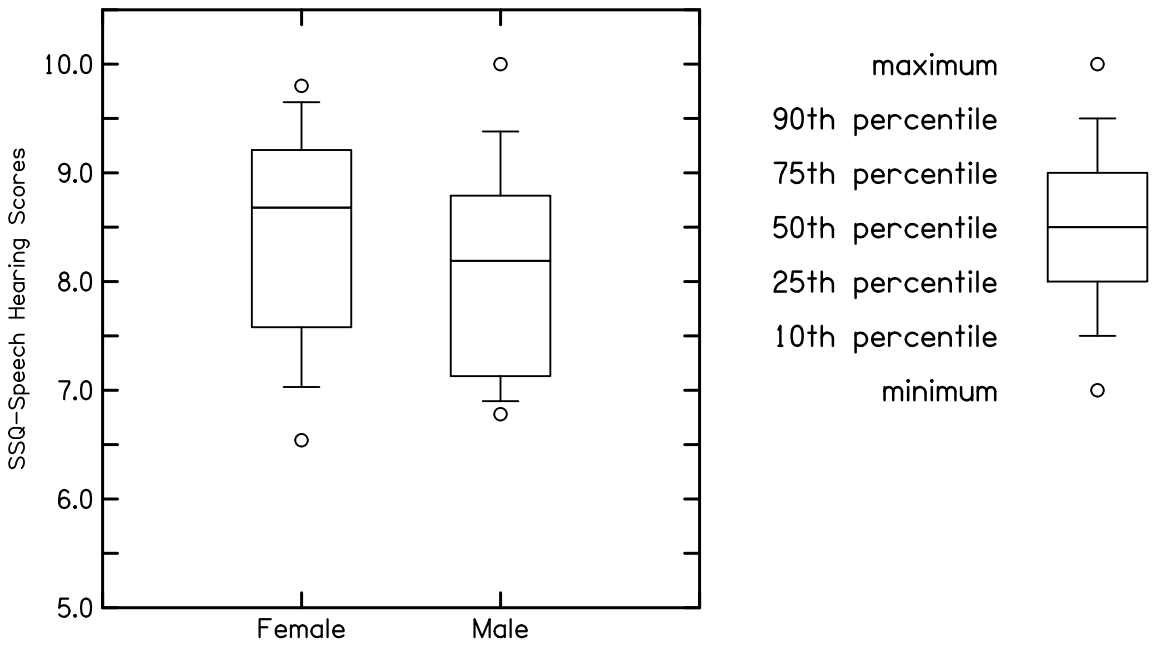


Fig. 20: Distribution of self-perceived speech hearing scores as quantified by the Speech, Spatial, and Qualities of Hearing Scale (SSQ; Gates and Noble, 2004) between female (n=16) and male (n=14) study participants. Data are shown following the conventions used in figure 2. No statistically significant differences were found in the distribution of speech-hearing scores across the males and females (Kruskal-Wallis Test, $p = 0.36$).

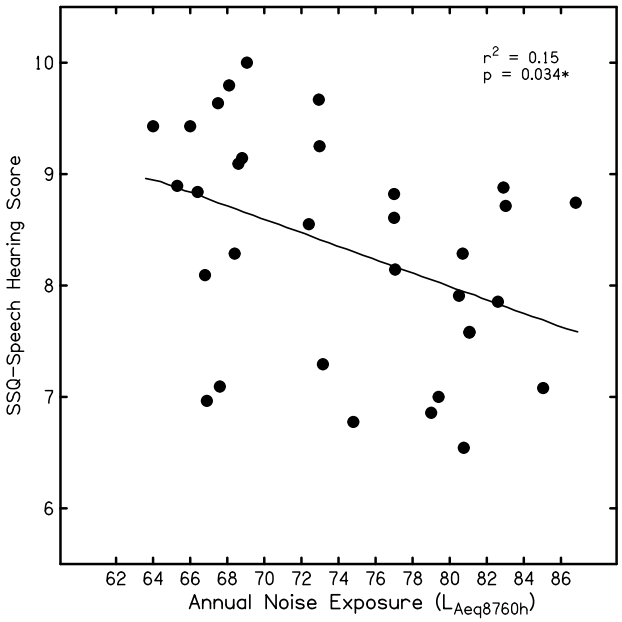


Fig. 21: Self-perceived speech hearing scores (as per the SSQ) as a function of ANE (n = 30). Symbols (filled circles) represent individual data and the resulting regression line, p-value and r^2 (coefficient of determination) are shown. The asterisk symbol (*) indicates a p-value ≤ 0.05.

Table 1. Individual characteristics and click-ABR data at 80 dB nHL of 30 study participants.

Subject ID	Age	Sex	NEQ ANE ($L_{Aeq8760h}$)	SSQ Speech Hearing Score	WAVE I Peak Latency *(msec)*	WAVE I Peak Amplitude *(μV)*	WAVE V Peak Latency *(msec)*	WAVE V Peak Amplitude *(μV)*
1	22	F	68	9.80	1.81	0.37	5.62	0.88
2	28	F	67	9.64	1.87	0.29	5.76	0.38
3	24	F	67	6.96	1.62	0.41	5.58	0.59
4	19	F	81	6.54	1.77	0.35	5.60	0.69
5	27	M	74	7.29	2.01	0.21	5.85	0.57
6	22	F	64	9.43	1.62	0.64	5.27	0.39
7	22	M	68	8.29	1.66	0.17	6.03	0.35
8	22	F	73	9.67	1.66	0.51	5.29	0.90
9	18	F	82	7.58	1.89	0.24	5.78	0.65
10	22	F	77	8.61	1.81	0.69	5.72	0.47
11	27	F	68	7.09	1.68	0.37	5.50	0.85
12	22	M	75	6.78	1.81	0.27	5.27	0.47
13	24	F	69	9.09	1.70	0.26	5.70	0.69
14	32	F	69	9.14	1.85	0.33	5.79	0.75
15	21	M	83	8.71	1.77	0.24	5.86	0.32
16	18	F	82	7.58	1.83	0.12	5.78	0.51
17	19	F	83	8.88	1.72	0.38	5.72	0.73
18	19	M	79	6.86	1.70	0.27	5.97	0.40
19	25	M	72	8.55	1.81	0.13	5.84	0.39
20	26	M	73	9.25	1.89	0.28	5.64	0.53
21	21	M	85	7.08	1.87	0.34	6.01	0.54
22	25	M	80	7.91	1.68	0.36	5.64	0.31
23	24	F	87	8.74	1.72	0.34	5.27	0.54
24	28	M	66	9.43	1.93	0.22	5.85	0.39
25	18	F	81	8.29	1.81	0.34	5.70	0.64
26	25	M	67	8.09	1.78	0.28	5.66	0.50
27	23	M	78	8.82	1.72	0.51	5.72	0.35
28	21	F	78	8.14	1.68	0.34	5.78	0.51
29	20	M	79	7.00	1.70	0.47	5.80	0.27
30	29	M	69	10.00	1.75	0.23	5.54	0.47
Mean	23.10		74.76	8.31	1.77	0.33	*5.68*	0.53
(SD)	*(± 3.58)*		*(± 6.63)*	*(± 1.03)*	*(± 0.09)*	*(± 0.13)*	*(± 0.21)*	*(± 0.17)*

Table 2. Individual speech-ABR data of 30 study participants.

				85 dB SPL				65 dB SPL			
				Peak Latency *(msec)*		Peak Amplitude *(μV)*		Peak Latency *(msec)*		Peak Amplitude *(μV)*	
ID	Sex	NEQ ($L_{Aeq8760h}$)	Speech Hearing Score (SSQ)	V	O	V	O	V	O	V	O
S1	F	68	9.80	6.59	48.16	0.32	0.26	7.25	48.16	0.34	0.29
S2	F	67	9.64	6.68	47.60	0.22	0.13	7.64	49.51	0.14	0.13
S3	F	67	6.96	6.21	47.60	0.44	0.13	6.68	48.16	0.27	0.29
S4	F	81	6.54	6.59	48.24	0.46	0.45	7.33	48.71	0.25	0.35
S5	M	74	7.29	7.48	48.65	0.40	0.40	8.19	49.45	0.29	0.22
S6	F	64	9.43	6.45	47.85	0.32	0.20	7.00	48.96	0.20	0.24
S7	M	68	8.29	6.92	48.79	0.36	0.25	7.64	49.04	0.24	0.32
S8	F	73	9.67	6.29	47.85	0.37	0.46	7.17	48.32	0.25	0.35
S9	F	82	7.58	6.53	48.24	0.41	0.33	7.39	51.68	0.33	0.25
S10	F	77	8.61	6.53	48.49	0.50	0.23	7.17	48.49	0.35	0.30
S11	F	68	7.09	6.53	47.77	0.28	0.62	7.80	49.51	0.46	0.70
S12	M	75	6.78	6.68	48.32	0.26	0.14	7.72	49.28	0.20	0.09
S13	F	69	9.09	6.53	48.24	0.25	0.38	7.39	49.20	0.26	0.26
S14	F	69	9.14	6.68	47.44	0.41	0.33	7.39	48.49	0.45	0.42
S15	M	83	8.71	7.33	49.04	0.33	0.43	8.19	50.25	0.27	0.29
S16	F	82	7.58	6.76	47.77	0.47	0.45	7.39	48.49	0.47	0.30
S17	F	83	8.88	6.53	47.85	0.56	0.40	7.72	48.40	0.50	0.26
S18	M	79	6.86	6.92	48.79	0.43	0.36	7.80	48.96	0.30	0.40
S19	M	72	8.55	6.92	48.65	0.36	0.26	7.80	49.28	0.30	0.12
S20	M	73	9.25	6.29	47.69	0.36	0.28	7.09	47.99	0.19	0.25
S21	M	85	7.08	7.39	48.57	0.49	0.48	8.19	49.20	0.42	0.30
S22	M	80	7.91	7.25	48.16	0.27	0.21	8.27	49.67	0.14	0.13
S23	F	87	8.74	6.37	47.52	0.43	0.40	7.33	48.87	0.49	0.45
S24	M	66	9.43	7.25	48.40	0.23	0.28	8.52	50.17	0.15	0.17
S25	F	81	8.29	6.53	47.99	0.33	0.27	7.33	48.49	0.32	0.22
S26	M	67	8.09	6.76	47.77	0.24	0.26	7.64	49.28	0.23	0.16
S27	M	78	8.82	7.09	48.57	0.41	0.35	8.19	50.25	0.28	0.20
S28	F	78	8.14	6.53	47.99	0.42	0.37	7.39	48.40	0.38	0.29
S29	M	79	7.00	6.53	48.32	0.31	0.27	7.64	49.04	0.30	0.25
S30	M	69	10.00	6.92	49.28	0.37	0.29	7.88	50.88	0.30	0.22
Mean		74.76	8.31	6.74	48.19	0.37	0.32	*7.61*	*49.15*	*0.30*	0.27
(SD)		*(±6.63)*	*(±1.03)*	*(±0.34)*	*(±0.47)*	*(±0.09)*	*(±0.11)*	*(±0.43)*	*(±0.85)*	*(0.10)*	*(±0.12)*

Table 3. Contributions of annual noise exposure and click-evoked ABR data (80 dB nHL) in predicting self-perceived SIN ability (as per the SSQ) in 30 young, normal-hearing adult ears.

Y	=	X_1	+	X_2	
Speech Hearing Score (SSQ)	=	ANE ($L_{Aeq8760h}$)	+	Wave I Latency (msec)	(model p-value)
		adjusted r^2 = .120		r^2 *change* = 0.003	0.11
	=	ANE ($L_{Aeq8760h}$)	+	Wave V Latency (msec)	(model p-value)
		adjusted r^2 = .120		r^2 *change* = 0.015	0.09
	=	ANE ($L_{Aeq8760h}$)	+	Wave I Amplitude (μV)	(model p-value)
		adjusted r^2 = .120		r^2 *change* = 0.014	0.09
	=	ANE ($L_{Aeq8760h}$)	+	WaveV Amplitude (μV)	(model p-value)
		adjusted r^2 = .120		r^2 *change* = 0.002	0.11

Table 4. Contributions of annual noise exposure and speech-evoked ABR data for the stimulus level of **85 dB SPL** in predicting self-perceived SIN ability (as per the SSQ) in 30 young, normal-hearing adult ears.

Y	=	X_1	+	X_2	
Speech Hearing Score (SSQ)	=	ANE ($L_{Aeq8760h}$)	+	Wave V Latency (msec)	(model p-value)
		adjusted r^2 *= .120*		r^2 *change* = 0.002	0.11
	=	ANE *($L_{Aeq8760h}$)*	+	Wave O Latency (msec)	(model p-value)
		adjusted r^2 = .120		r^2 *change* = 0.000	0.11
	=	ANE ($L_{Aeq8760h}$)	+	Wave V Amplitude (μV)	(model p-value)
		adjusted r^2 = .120		r^2 *change* = 0.000	0.11
	=	ANE ($L_{Aeq8760h}$)	+	WaveO Amplitude (μV)	(model p-value)
		adjusted r^2 = .120		r^2 *change* = 0.003	0.11

Table 5. Contributions of annual noise exposure and speech-evoked ABR data for the stimulus level of **65 dB SPL** in predicting self-perceived SIN ability (as per the SSQ) in 30 young, normal-hearing adult ears.

Y	=	X_1	+	X_2	
Speech Hearing Score (SSQ)	=	ANE ($L_{Aeq8760h}$)	+	Wave V Latency (msec)	(model p-value)
		adjusted r^2 *= .120*		r^2 *change* = 0.000	0.11
	=	ANE *($L_{Aeq8760h}$)*	+	Wave O Latency (msec)	(model p-value)
		adjusted r^2 = .120		r^2 *change* = 0.001	0.11
	=	ANE ($L_{Aeq8760h}$)	+	Wave V Amplitude (μV)	(model p-value)
		adjusted r^2 = .120		r^2 *change* = 0.000	0.11
	=	ANE ($L_{Aeq8760h}$)	+	WaveO Amplitude (μV)	(model p-value)
		adjusted r^2 = .120		r^2 *change* = 0.026	0.07

Table 6. Musical background of 30 study participants.

			NEQ		
Subject	Age	Sex	ANE ($L_{Aeq8760h}$)	Musical Training	Musical Instrument
6	22	F	63.95	No	
24	28	M	65.99	Yes	Piano
26	25	M	66.85	Yes	Piano
3	24	F	66.94	No	
2	28	F	67.47	No	
11	27	F	67.65	No	
1	22	F	68.12	No	
7	22	M	68.41	No	
13	24	F	68.62	No	
14	32	F	68.75	No	
30	29	M	69.26	No	
19	25	M	72.41	No	
8	22	F	72.88	No	
20	26	M	72.93	No	
5	27	M	73.85	No	
12	22	M	74.81	Yes	Trombone
10	22	F	77.03	No	
28	21	F	77.58	Yes	Piano
27	23	M	77.59	No	
18	19	M	79.08	Yes	Trombone
29	20	M	79.40	Yes	Trumpet
22	25	M	80.45	Yes	Acoustic guitar
25	18	F	80.66	Yes	Trombone
4	19	F	80.67	Yes	Saxophone
16	18	F	81.56	Yes	French horn, Mellophone
9	18	F	81.67	No	
17	19	F	82.87	Yes	Mellophone, Trumpet
15	21	M	83.23	Yes	Trumpet
21	21	M	85.43	Yes	Guitar, Keyboard
23	24	F	86.76	Yes	String bass, Electric bass, Piano