

## Research Article

# The Role of Cognition in Common Measures of Peripheral Synaptopathy and Hidden Hearing Loss

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**Purpose:** The aim of this study was to quantify the portion of variance in several measures suggested to be indicative of peripheral noise-induced cochlear synaptopathy and hidden hearing disorder that can be attributed to individual cognitive capacity.

**Method:** Regression and relative importance analysis was used to model several behavioral and physiological measures of hearing in 32 adults ranging in age from 20 to 74 years. Predictors for the model were hearing sensitivity and performance on a number of cognitive tasks.

**Results:** There was a significant influence of cognitive capacity on several measures of cochlear synaptopathy and

hidden hearing disorder. These measures include frequency modulation detection threshold, time-compressed word recognition in quiet and reverberation, and the strength of the frequency-following response of the speech-evoked auditory brainstem response.

**Conclusions:** Measures of hearing that involve temporal processing are significantly influenced by cognitive abilities, specifically, short-term and working memory capacity, executive function, and attention. Research using measures of temporal processing to diagnose peripheral disorders, such as noise-induced synaptopathy, need to consider cognitive influence even in a young, healthy population.

Determining the extent of peripheral damage due to noise exposure has become a focal point of recent research (Bramhall et al., 2019; Le Prell, 2019). Animal research has shown a direct relationship between noise exposure and the decoupling of auditory nerve fibers from hair cells—a disorder called *synaptopathy* (Kujawa & Liberman, 2009). The primary finding from this research is that synaptic count is negatively correlated with the amount of noise exposure. *Hidden hearing loss*—a term coined by Schaette and McAlpine (2011)—has been used to describe such a disorder in humans. A partial loss of auditory nerve fibers from noise-induced synaptopathy will result in reduced neural output from the cochlea while maintaining auditory sensitivity (Kujawa & Liberman, 2009). This could theoretically translate to issues in coding temporal fine structure, leading to exacerbated difficulty understanding speech in noisy situations (Bharadwaj, Masud,

Mehraei, Verhulst, & Shinn-Cunningham, 2015). Furthermore, these symptoms could occur in the presence of a normal audiogram. In the search to find noise-induced synaptopathy and hidden hearing disorder in humans, a plethora of physiological and behavioral measures, most of which were inspired by animal studies, have been explored by researchers. Some studies have found a negative relationship between noise exposure history and the amplitude of Wave I of the auditory brainstem response (ABR) in humans (e.g., Bramhall, Konrad-Martin, McMillan, & Griest, 2017; Grose, Buss, & Hall, 2017; Stamper & Johnson, 2015; Valderrama et al., 2018). Most are not finding an association between noise exposure history and speech perception in noisy situations (e.g., Fulbright, Le Prell, Griffiths, & Lobarinas, 2017; Grinn, Wiseman, Baker, & Le Prell, 2017; Grose et al., 2017; Guest, Munro, Prendergast, Millman, & Plack, 2018; Le Prell, Siburt, Lobarinas, Griffiths, & Spankovich, 2018; Yeend, Beach, Sharma, & Dillon, 2017). One issue may be the assumption that all variance in hearing measures that cannot be explained by audiometric thresholds must be due to noise-induced synaptopathy, which is not entirely true (Kohrman, Wan, Cassinotti, & Corfas, 2019).

Changes in central auditory and secondary cortical processes can affect hearing independently of sensitivity.

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The influence of cognitive ability on hearing is well established in the aging population (Baltes & Lindenberger, 1997; Bergman et al., 1976; Humes, 1996; Mayer, Levitt, & Bergman, 1976; Wingfield, 1996). Aging is correlated with reduced processing speed (Fitzgibbons & Gordon-Salant, 1996; Grassi & Borella, 2013; Salthouse, 1996) and working memory capacity (Mishra, Stenfelt, Lunner, Rönnberg, & Rudner, 2014). Impairment of these cognitive processes negatively influences speech recognition performance (Jerger, Jerger, & Pirozzolo, 1991; D. R. Moore et al., 2014), even when hearing sensitivity is within clinically normal limits (Füllgrabe, 2013; Wu & Chiu, 2016). Speech recognition, especially in difficult listening conditions, requires high levels of temporal processing. Temporal processing, in turn, relies on processing speed and working memory (Broadway & Engle, 2011; Füllgrabe, Moore, & Stone, 2015). Therefore, we hypothesize that some of the variance in common current measures of synaptopathy and hidden hearing disorder in humans is due to differences in cognitive function, even though some of the measures are intended to probe the peripheral auditory system.

We test this hypothesis by quantifying the variance explained by cognitive function in several proxy measures of synaptopathy and hidden hearing disorder, including pure-tone thresholds in noise (TIN), frequency modulation detection thresholds, tone burst ABR wave amplitudes, and the strength of frequency-following response (FFR) of the speech-evoked ABR. We also quantified the variance explained by cognitive function in measures of speech perception in three difficult listening conditions: background noise, time compression, and time compression with reverberation. We included a comprehensive assessment of cognition that spanned several cognitive domains, including measures of short-term memory capacity, working memory, selective attention, executive function, and processing speed. The goal of our study was to determine whether some of the variance in suprathreshold measures of peripheral noise-induced cochlear synaptopathy and hidden hearing disorder that is unaccounted for by auditory thresholds can be attributed to cognitive function.

## Method

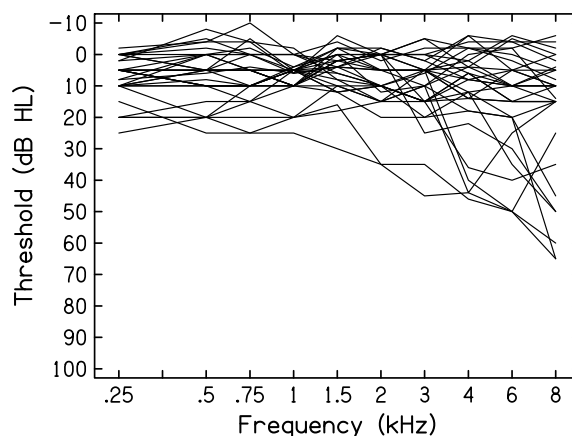
### Participants

This investigation was conducted as part of a larger ongoing study relating noise exposure and behavioral and physiological measures of hearing. Thirty-two adults from the larger study (19 women, 13 men) ranging in age from 20 to 74 years ( $Mdn = 38$ ) volunteered to participate in an additional cognitive testing for this study. All participants for this study met the following inclusion criteria: (a) sensorineural hearing loss of  $\leq 65$  dB HL and normal middle ear function, (b) native English speaker, and (c) had recently completed the Montreal Cognitive Assessment (MoCA).

Standard audiometry and tympanometry determined inclusion into the study. Pure-tone air-conduction thresholds were obtained (HD 200 over-the-ear headphones, Sennheiser) at octave frequencies (0.25–8 kHz) and interoctave frequencies (0.75, 1.5, 3, and 6 kHz) following the Hughson–Westlake procedure (American Speech-Language-Hearing Association, 1978; GSI AudioStar Pro, Grason-Stadler) in 5-dB steps, with the exception of 1.5 and 4 kHz, which were measured in 2-dB steps. Participants were required to have thresholds of  $\leq 65$  dB HL at all frequencies and no air–bone gap  $> 10$  dB at any octave frequency from 500 to 4000 Hz. Inclusion criteria also included middle ear pressure within the range of  $-100$  to  $+50$  daPa and static compliance between 0.3 and 2.5  $\text{cm}^3$  measured via 226-Hz tympanometry (Otoflex 100, Madsen). Twenty of the 32 participants had clinically normal hearing, that is, audiometric thresholds of  $\leq 15$  dB HL from 0.25 to 8 kHz. Three participants had mild sensorineural hearing loss (i.e., thresholds of  $> 15$  to  $\leq 40$  dB HL for at least one frequency), and nine participants had moderate sensorineural hearing loss (i.e., thresholds of  $> 40$  to  $\leq 65$  dB HL for at least one frequency). We argue for the inclusion of participants with hearing loss in studies pertaining to synaptopathy and hidden hearing loss/disorder because they are likely comorbid with reduced hearing sensitivity, especially in older patients. In this study, we account for the variance explained by thresholds in tests of auditory function. Audiograms of the participants are displayed in Figure 1. Other participant characteristics are shown in Table 1. All additional hearing stimuli were presented monaurally, with the exception of the cognitive measures that were presented free field. If both ears met the inclusion criteria for monaural measures, the better ear was chosen for testing. If both ears had similar audiometric thresholds, the test ear was selected randomly. In total, there were 13 right ears and 19 left ears included in the study.

The MoCA was developed as a screening tool for mild cognitive impairment (Nasreddine et al., 2005), has

**Figure 1.** Audiograms of the participants ( $N = 32$ ). Each line represents data for a participant.



**Table 1.** Characteristics of participants.

Variable	Value
Total Participants	32
Median age (IQR)	38 (18)
Females (%)	19 (60)
Left/right ears	19/13
Median education in years (IQR)	16 (4)
Median MoCA score (IQR)	28 (3)

*Note.* IQR = interquartile range; MoCA = Montreal Cognitive Assessment.

since established normative data around the world, and is commonly used as an estimate of general cognitive function (Rossetti, Lacritz, Munro Cullum, & Weiner, 2011). The MoCA has a maximum score of 30. Normal cognitive function is defined as a score of 26 or higher, mild cognitive impairment is described by a score of 21–25, and scores below 21 are an indication of dementia and Alzheimer's disease. Twenty-eight participants scored within the normal range, and four scored in the mild cognitive impairment range. MoCA score was not used in any of the analyses reported in the results of this study.

### Procedure

Participants completed measures over three visits, completed within 4 months. Total data collection time was approximately 5 hr. All procedures were approved by the institutional review board of the Boys Town National Research Hospital. All participants provided informed consent; participants were paid for their participation.

### Psychoacoustic Tasks

#### Thresholds in Quiet

Audiometric pure-tone thresholds were not used in the regression analysis. Instead, a three-alternative forced choice (3AFC) adaptive procedure was used to determine pure-tone thresholds in quiet (TIQ) at 1.5 and 4 kHz. This method provides a more accurate and reliable measure of threshold than standard audiometry because it mitigates some biases known to occur in the latter, such as the interval bias (entrainment to the stimulus interval) and effects of age (older people are more likely to wait to respond until positive they heard the tone; Gelfand, 1982; Yost, 1978). For a 3AFC trial, three intervals were presented with only one interval containing the stimulus being measured; in this case, two intervals were silent and one interval contained a pure tone (AudioLab MATLAB, developed by Lopez-Poveda). The participant was required to indicate which interval contained the pure tone, and feedback was provided for each response. For each measurement, a 2-up, 1-down adaptive procedure was used to track the 71% point on the psychometric function or threshold.

Stimuli were presented monaurally via ER-3A insert earphones (Etymotic Research) in a soundproof room. The initial stimulus level was 20 dB above the participant's audiometric threshold (in dB SPL) at the stimulus frequency, rounded up to the nearest 10 dB. The procedure had an initial step size of 5 dB, which lasted for three reversals. The step size was then reduced to 2 dB for six reversals, for a total of nine reversals. The final six reversals were used to determine threshold (dB SPL). Participants completed one training run to familiarize with the procedure and then two subsequent trials. Trials were excluded and repeated if the within-trial *SD* was  $\geq 5$  dB and/or if the threshold for the two trials differed by  $> 6$  dB. At least two trials that met the inclusion criteria were averaged to determine threshold.

#### Thresholds in Noise

A 3AFC procedure was also used to measure TIN at 1.5 and 4 kHz. Broadband noise from 0.2 to 8 kHz was set at a constant of 70 dB SPL for both frequencies. If any participants had TIQ higher than 50 dB at either frequency, a second, higher level of TIN was obtained at those frequencies to account for audibility. If TIQ was below 50, the participant was presented stimuli of at least 20 dB SL for TIN. No participants in this study required a higher presentation level. While the noise remained constant, the level of the tone was varied to determine TIN. A TIN trial had a total of 12 reversals, the final eight of which were used to determine threshold. Exclusion of a TIN trial followed the same rules as TIQ.

#### Frequency-Modulation Detection Threshold

A common behavioral measure of temporal processing ability is modulation detection (B. C. J. Moore & Glasberg, 1989). Here, we assessed temporal processing using frequency-modulation detection threshold (FMDT; Johannesen, Pérez-González, Kalluri, Blanco, & Lopez-Poveda, 2016; Strelcyk & Dau, 2009). This procedure measures the minimum excursion in frequency that a listener can detect. FMDT was measured using a 3AFC method, similar to that used for TIQ and TIN. The experiment was identical to that of Johannesen et al. (2016). The stimulus was a pure tone of 1.5 kHz with a duration of 750 ms presented at 70 dB SPL. In one interval, one tone was frequency modulated with a variable maximum frequency excursion. The minimum detectable excursion in hertz was estimated and log-transformed. The tones in all three intervals were also sinusoidally amplitude-modulated with a modulation depth of  $m = 0.333$  or  $20\log_{10}((1 + m)/(1 - m)) = 6$  dB (Johannesen et al., 2016; B. C. J. Moore & Glasberg, 1989). The low-frequency (1500 Hz) carrier and amplitude modulation were intended to prevent the participants from using cues based on changes to excitation patterns in the cochlea (B. C. J. Moore & Sek, 1996). Following Johannesen et al., the initial and final modulation rates were randomized in the interval between 1 and 3 Hz under the constraint that the modulation rate change was always above 1 Hz. The initial step size of the frequency excursion

was  $\log_{10}$  (1.5). This was decreased to  $\log_{10}$  (1.26) after four reversals. The adaptive procedure continued until a total of 12 reversals in frequency excursion had occurred. The mean of the last eight reversals was used to determine FMDT ( $\log_{10}$ Hz). One training run and two additional trials were completed. A trial was excluded and repeated if the *SD* was  $> 0.2$  (Strelcyk & Dau, 2009) and/or if the difference between thresholds for the two trials was  $> 0.3$ . Thresholds from at least two trials, which met the inclusion criteria, were averaged.

### Speech Perception

Word recognition scores for each participant were assessed in four listening conditions: (a) speech in quiet, (b) speech in the presence of speech-shaped noise, (c) speech that had been time compressed by 45%, and (d) speech that had been time compressed by 45% and a reverberation time of 0.3 s (Noffsinger, Wilson, & Musiek 1994). The stimuli were four 50-word lists spoken by a male talker (Northwestern University Auditory Test No. 6; Auditec, Inc.). The words were presented monaurally via ER-3A insert earphones (Etymotic Research) in a soundproof room at 65 dB SPL for participants with a pure-tone average (PTA) at 1, 2, and 4 kHz of  $\leq 35$  dB SPL. For six participants with a PTA of  $> 35$  dB SPL, words were presented at 30 dB SL rounded up to the nearest 5 dB for all conditions to ensure that stimuli were audible. Given the difficulty of some of the listening conditions, the first five words were considered training to familiarize participants with the condition. Performance in each condition was calculated from the total number of words correct of the final 45 words in each list.

### Electrophysiology

#### ABR Waves I and V

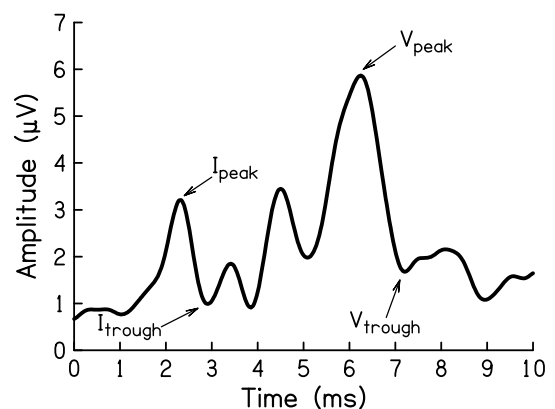
Tone burst-elicited ABR waveforms were recorded at 1.5 and 4 kHz using custom-designed software (Cochlear Response Version 1.0, Boys Town National Research Hospital) on a computer equipped with a 24-bit soundcard (Babyface, RME). Electroencephalographic (EEG) responses were acquired using surface electrodes placed on the forehead (Fpz, ground), ear canal (inverting reference; ER3-26A gold foil tippers), and vertex (Cz, noninverting active electrode). Electrode impedances were  $\leq 5$  k $\Omega$  in all cases. One-millisecond Blackman-gated tones at 1.5 and 4 kHz were presented monaurally, in alternating polarity, at a rate of 11/s to an ER-3A insert earphone (Etymotic Research) coupled to the soundcard. The 1-ms stimulus duration resulted in large Wave I amplitudes in a previous study (Ridley, Kopun, Neely, Gorga, & Rasetshwane, 2018). The stimulus level used in this study was 110 dB peak-equivalent (pe)SPL. High levels were chosen to maximize the number of ABR waves observed in participants, especially those with hearing loss (Ridley et al., 2018). The EEG signal was amplified ( $\times 100,000$ ), filtered (0.01–1.5 kHz; Opti-Amp 8001; Intelligent Hearing Systems), and directed to the computer via the soundcard for averaging. Responses were

separated by even and odd recordings and stored in two buffers, which were averaged for the final waveform (total averages = 1,500 artifact-free responses). Artifact rejection was based on the peak absolute differences between the buffers and was set at a maximum of  $\pm 20$   $\mu$ V. Two examiners independently identified peaks and troughs of Waves I and V. The software allowed for a resolution of 0.02  $\mu$ V for amplitude and 0.02 ms for latency. The amplitudes of Waves I and V were calculated as the difference between the positive peak and the following trough. Figure 2 plots an exemplar ABR and peaks picked. Latencies were used to clarify disagreements between examiners and were not used for any other analyses. The processing delay of the soundcard was taken into account when analyzing the data for latency. Disagreements occurred in six of the total 64 waveforms (9%) and were arbitrated by a third examiner. The wave V/I amplitude ratio was used in the model to reduce the confounds of age and sex on ABR wave amplitudes.

#### Speech ABR

The ABR to a speech stimulus was recorded immediately following the tone burst-elicited ABR. A 170-ms synthetic /da/ was chosen as the stimulus because it has been used extensively in complex ABR research (see Skoe & Kraus, 2010). The stimulus used in this study was developed by the Auditory Neuroscience Laboratory at Northwestern University as part of their Brainstem toolbox. The /da/ is a six-formant syllable synthesized at a rate of 20 kHz. The duration is 170 ms, with a voicing onset at 10 ms (100-Hz fundamental frequency). Additional details of the formant frequencies and transitions can be found in the study of Song, Nicol, and Kraus (2011). The stimulus was played at a level of 90 dB SPL at a rate of 4/s. The EEG was bandpass filtered at cutoff frequencies of 0.1–3 kHz, and the processing delay of the soundcard was taken into account when analyzing the data. The analyses performed on the speech ABR were directed at the response of the

**Figure 2.** A 4-kHz auditory brainstem response waveform from a participant with clinically normal audiometric hearing. Location of peaks and troughs for Waves I and V are indicated.





periodic (vowel) portion of the stimulus; therefore, the response to the initial transient portion of the stimulus and formant transition portion was removed, and analyses were performed over the portion of the response that was delayed 60–170 ms relative to onset of the stimulus (Song et al., 2011). Two metrics were derived from the speech ABR: (a) stimulus-to-response (STR) correlations—an assessment of how closely the response represents the stimulus in the time domain—and (b) the FFR—a measure of the strength of the spectral components of the response regarding noise floor. Figure 3 shows a representative speech ABR waveform. To calculate STR, the stimulus is time-shifted to align with the peaks and troughs of the response and then correlated. The left panel of Figure 3 shows the stimulus and response before being aligned. The right panel displays the spectrum of the steady-state portion of the stimulus (gray) and response (blue). The response peaks occur at the harmonics of the stimulus. FFR-to-noise ratio is calculated as the energy of these harmonics regarding non harmonic energy.

### Measures of Cognitive Function

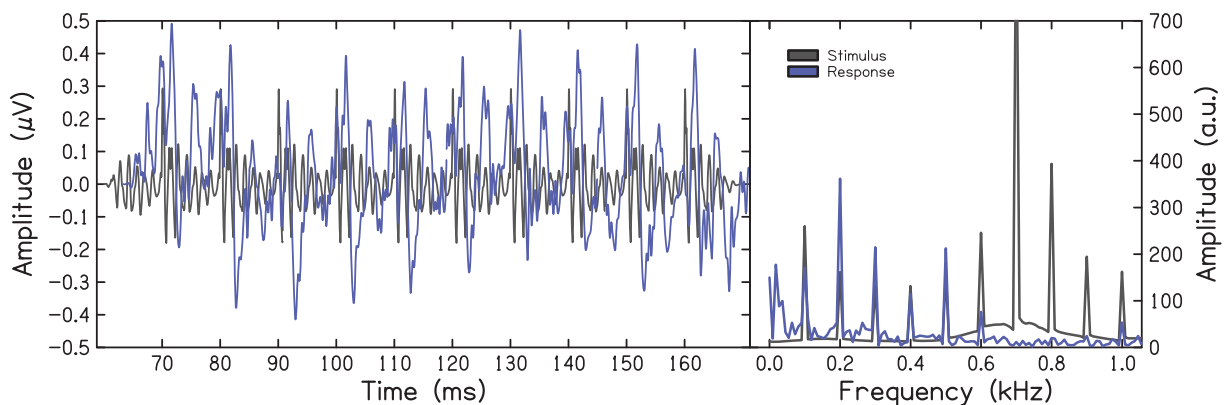
Seven tasks spanning several cognitive domains were investigated, including tasks of short-term memory capacity, working memory, selective attention, executive function, and processing speed. All tasks except digit span (described later) were taken from the NIH Toolbox. The NIH Toolbox is the result of a collaborative, multi-institutional effort to develop a set of normed assessments of neurological function. The Cognition Battery is a set of tests that have been validated and normed across the adult population (Heaton et al., 2014; Weintraub et al., 2014). Fully corrected *t* scores of each test, which accounted for age, education, and race/ethnicity (Casaletto et al., 2015), were used as predictor variables in the analysis of this study. NIH Toolbox assessments were administered on an iPad, including the

standard instruction as dictated by the NIH Toolbox Cognition manual. The digit span tasks were taken from the Wechsler Adult Intelligence Scale–Third Edition (Wechsler, 1997). All audio instruction and testing were presented in an open sound field at 80 dB SPL as measured at ear level by a sound-level meter (System 824 and Sound-Track LxT1, Larson Davis). This presentation level was > 30 dB SL of participants' PTA. All tasks besides digit span were presented in an audiovisual modality to reduce any effect of hearing loss on performance, and audiometric thresholds did not correlate with performance on any measure.

### Short-Term Memory

Short-term memory is a cognitive domain that involves the temporary storage of new information. Two tasks were chosen to assess this domain: the Picture Sequence Memory Test (PSMT; Dikmen et al., 2014) and the Digits Span Forward (DSF; Wechsler, 1997). At the start of each PSMT trial, blank boxes appeared around the perimeter of the screen representing the number of items to be presented on that trial. Then, a sequence of activity-related pictures appeared, one at a time, in the center of the screen paired with a spoken phrase matching the activity (e.g., “ride a bike”). After each picture was presented, it moved to the next open spatial location around the screen's perimeter. Once all pictures were presented, they were scattered to a random location in the center of the screen. The task objective was to move the pictures to the original spatial location replicating the presented sequence. A practice sequence (four pictures) with verbal and text instructions preceded two performance trials of 12 and 15 pictures. Performance was scored based on correct adjacent pairs of pictures. For the DSF, digit sequences of increasing length (from two to nine digits) were presented verbally at one digit per second. The objective was to verbally recall the

**Figure 3.** The speech-evoked auditory brainstem response /da/ stimulus (gray) and representative response from a participant with clinically normal audiometric hearing (blue). The left panel displays the steady-state portion of the response in the time domain. To calculate stimulus to response, the stimulus is time-shifted to align with the peaks and troughs of the response and then correlated. The left panel shows the stimulus and response before being aligned. The right panel displays the spectrum of the steady-state portion of the stimulus (gray) and response (blue). The response peaks occur at the harmonics of the stimulus. Frequency-following response is calculated as the energy of these harmonics regarding non harmonic energy.



digits in order. Two trials for each sequence length were presented until two incorrect recalls; after which, the test was stopped. The DSF score corresponded to the maximum sequence length where both sequences were correctly recalled.

### Working Memory

Working memory is essentially an active form of short-term memory in which stored information undergoes processing or manipulation (Baddeley, 1992). Two tasks were chosen to assess working memory capacity: the List Sorting Working Memory (LSWM) test (Tulsky et al., 2014) and the Digits Span Backward (DSB) test (Wechsler, 1997). The LSWM test requires participants to store and order information. Participants were presented with a series of familiar items (food or animals) in a combined audio-visual format. The objective was to remember each item, mentally reorder the items from smallest to largest, and recall the items in this order once the sequence was presented. Two practice sequences with two and three items preceded the trial sequences. Two trial sequences of increasing length (two to seven items) were presented until the participant provided incorrect responses on two trials of the same length. Two versions of this task were completed: one version presented food and animal items in separate sequences, and the second presented food and animal items together requiring the participant to first sort the items into categories before reordering by size. The LSWM score was based on a sum of the total correctly recalled lists across both versions. DSB is identical to DSF except that participants are instructed to recall the digits in reverse order. The DSB score corresponded to the maximum sequence length where both sequences were correctly recalled.

### Executive Function and Attention

Executive function is the ability to plan, organize, and monitor the execution of behaviors (Diamond, 2013). Attention refers to the capacity to manage environmental stimuli. The Dimensional Change Card Sort (DCCS; Zelazo, 2006) was chosen as a test of executive function, and the Flanker Inhibitory Control and Attention test (Flanker; Eriksen & Eriksen, 1974) was chosen as a test of both executive function and selective attention. In the Flanker, participants were required to respond to information provided in a central visual target, which was surrounded by uninformative flanking stimuli. Specifically, participants were presented with a row of arrows. The participant was to touch the button that matched the direction of the middle arrow (left or right). In some presentations, the flanking arrows were pointed in the same direction as the target (congruent), and in some presentations, the flanking arrows were pointed in the opposite direction (incongruent). Thus, the incongruent conditions required participants to attend to the central arrow while ignoring, or inhibiting, conflicting information from the surrounding arrows. In the DCCS test, participants were required to sort target stimuli by either color or shape and switch quickly between the two dimensions. Scores for both the Flanker and DCCS were

calculated according to the classical test theory or the sum of an accuracy score and incongruent stimuli reaction time score, with higher accuracy and lower reaction times resulting in a higher overall score for the task. If accuracy levels were  $\leq 80\%$ , the final raw score was the accuracy score alone. If accuracy levels were  $> 80\%$ , reaction time score and accuracy score were combined (Slotkin, Kallen, Griffith, & Magasi, 2012).

### Processing Speed

Processing speed is the amount of time required to complete a task and is associated with many other areas of cognition, including working memory, attention, and executive function. The Pattern Comparison Processing Speed (PCPS) Test (Carlozzi, Beaumont, Tulsky, & Gershon, 2015) was used to measure processing speed. The PCPS is a simple task requiring participants to judge whether two visual patterns were the “same” or “not the same.” Scores reflected the number of correct judgments made in 90 s.

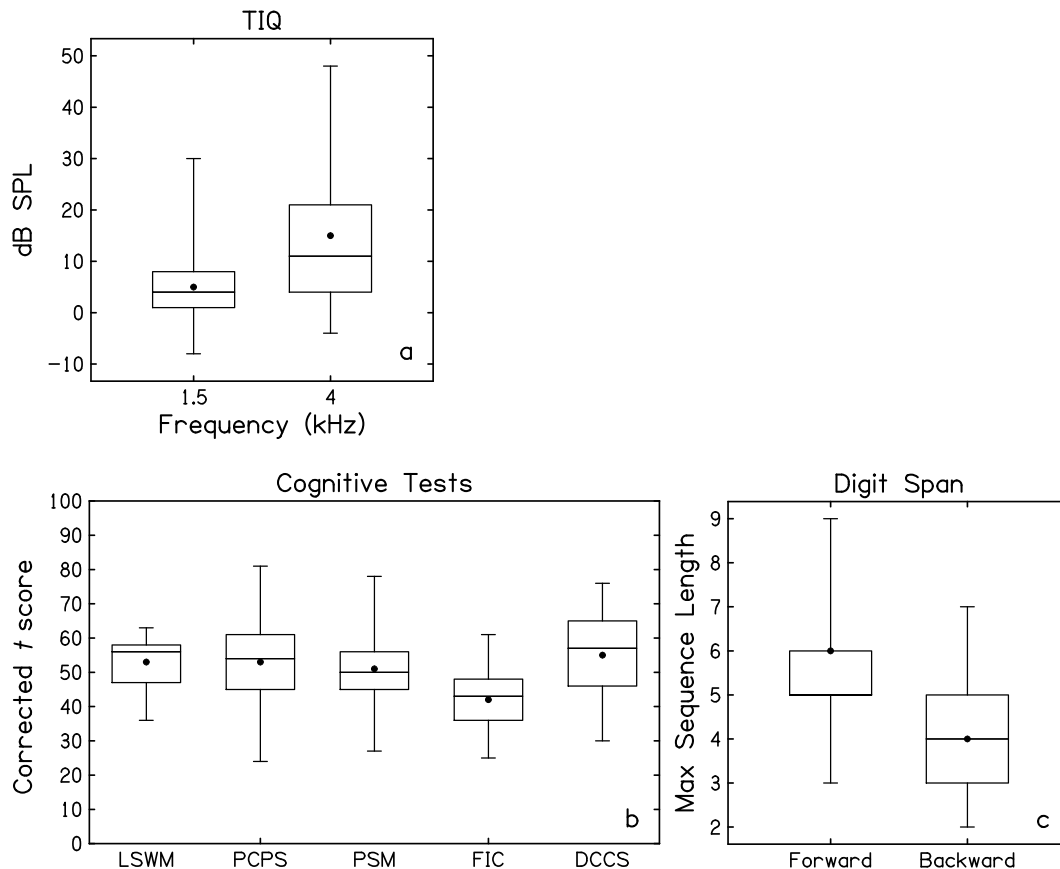
### Analysis

Regression models were created to explain the variability within hearing measures. The outcome variables were (a) tone burst ABR Wave V to Wave I amplitude ratio; (b) FFR-to-noise ratio of the speech-evoked ABR; (c) speech recognition performance in noise, time-compressed speech, and time-compressed speech with reverberation; (d) pure-tone TIN; and (e) FMDT. Predictor variables were pure-tone TIQ and  $t$  scores of the cognitive tasks (PSMT, DSF, LSWM, DSB, DCCS, Flanker, PCPS).  $T$  scores met the criteria for normality, and all other numeric data were centered. Statistical analysis was performed in R (R Core Team, 2018) using ordinary least squares regression (Hebbali, 2018). All possible models using combinations of TIQ and the cognition variables were compared to find the best fit model. Best fit was determined by a combination of  $R^2$ , adjusted  $R^2$ , Akaike information criteria, and Sawa’s Bayesian information criteria.

Collinearity of the predictor variables was reduced by removing redundant variables when possible. However, some correlated variables such as tasks of processing speed and working memory were purposefully left in the model to account for all potential cognitive relationships with hearing measures.

To accurately break down the variance explained by each predictor variable in a set of potentially correlated variables, an assessment of relative importance was implemented on the predictor variables for each model (*relaimpo*; Grömping, 2015). Relative importance can be defined as the proportionate contribution each predictor makes to  $R^2$ , considering both a direct effect and its effect when combined with other variables in the regression equation (Johnson & LeBreton, 2004). This approach is based on sequential sums of squares but accounts for the dependence on ordering, which is biased by correlated predictors, by averaging over orderings.

**Figure 4.** Distributions ( $N = 32$ ) of predictor variables: thresholds in quiet (TIQ) and the cognitive measures. Cognitive tests taken from the NIH Toolbox are  $t$  scores corrected for age, education, and race/ethnicity. Digit span is measured as the maximum sequence length at which all items are recalled correctly. The lower and upper margins of the boxes represent the 25th and 75th percentiles, respectively. The lower and upper whiskers represent the minimum and maximum observations, respectively. The line within the box represents the median, and the filled circles, represent the mean. LSWM = List Sorting Working Memory; PCPS = Pattern Comparison Processing Speed; PSM = picture sequence memory; FIC = Flanker Inhibitory Control; DCCS = Dimensional Change Card Sort.



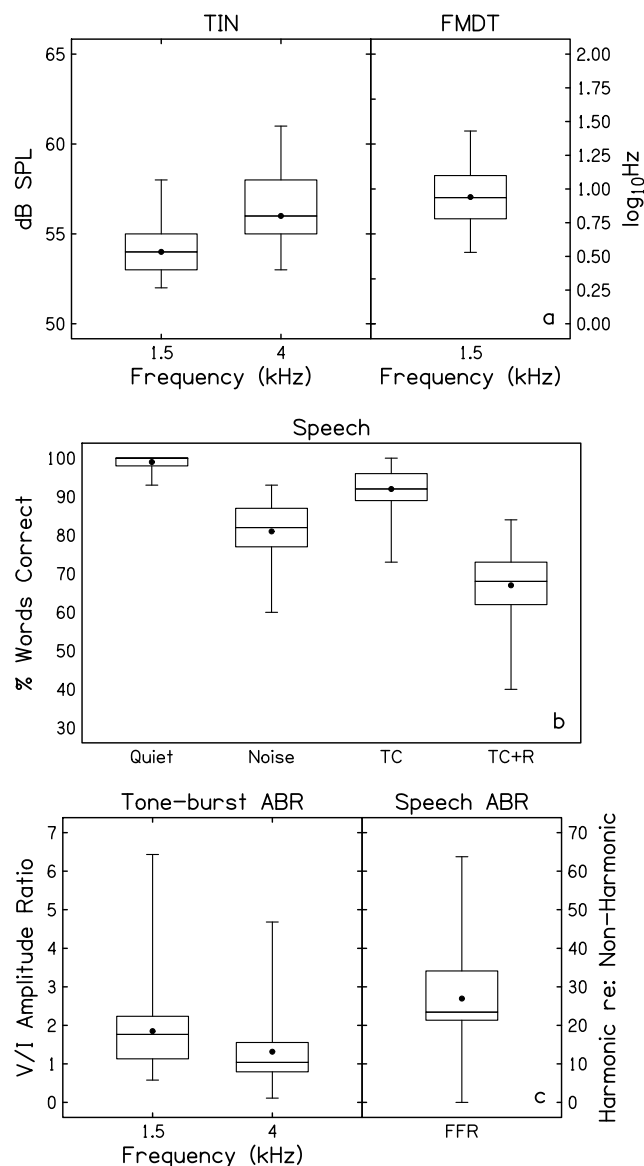
## Results

The distributions of hearing measures are presented in Figures 4 and 5. Mean TIQ for 1.5 and 4 kHz were 5 and 15 dB SPL, respectively (see Figure 4). Using American National Standards Institute standard reference-equivalent thresholds for ER-3A headphones, the means were 7 and 20.5 dB HL for 1.5 and 4 kHz, respectively (Frank & Vavrek, 1992). The larger TIQ at 4 kHz compared to 1.5 kHz was expected and reflects sloping hearing loss configuration that is typical of most adults. The two TIQ frequencies contributed redundant information to the models of hearing; therefore, to avoid overfitting, only TIQ at 4 kHz was used as a predictor, except for FMDT where TIQ at 1.5 kHz was used to match the stimulus frequency of the FMDT task. There were no correlations between TIQ and the cognitive scores. The composite of the cognitive  $t$  scores followed a normal  $t$  distribution ( $\mu = 51$ ,  $\sigma = 11$ ; see Figure 4) based on the NIH norms ( $\mu = 50$ ,  $\sigma = 10$ ). TIN at 1.5 and 4 kHz had mean thresholds of 54 and

56 dB SPL, respectively (see Figure 5a, left). FMDT had a mean threshold of  $0.94 \log_{10}\text{Hz}$  (see Figure 5a, right), falling within the range of  $0.7\text{--}2 \log_{10}\text{Hz}$  reported in Johansen et al. (2016). Speech recognition performance (see Figure 5b) had means of 99% correct for speech in quiet, 81% correct for speech in background noise, 92% correct for time-compressed speech, and 67% for time-compressed speech with reverberation. Mean ABR Wave I amplitudes were 0.77 and  $0.92 \mu\text{V}$  for 1.5 and 4 kHz, respectively. Mean ABR Wave V amplitudes were 1.20 and  $0.98 \mu\text{V}$  for 1.5 and 4 kHz, respectively. ABR amplitude ratios of Wave V/I to 1.5 and 4 kHz tones had means of 1.85 and 1.32, respectively (see Figure 5c, left). The mean FFR-to-noise ratio, or harmonic-to-nonharmonic magnitude ratio, was 27 (see Figure 5c, right).

Predictors included in the best fitting model of each hearing measure and the breakdown of variance explained can be found in Table 2. The variance explained by TIQ and the combined significant cognitive tasks are displayed in Figures 6–8 for each hearing measure that was modeled.

**Figure 5.** Distributions ( $N = 32$ ) of the outcome hearing measures. The lower and upper margins of the boxes represent the 25th and 75th percentiles, respectively. The lower and upper whiskers represent the minimum and maximum observations, respectively. The line within the box represents the median, and the filled circles represent the mean. TIN = thresholds in noise; FMDT = frequency modulation detection threshold; TC = time-compressed speech; TC+R = time-compressed speech with reverberation; ABR = auditory brainstem response; FFR = frequency-following response.



## Psychoacoustics Tasks

No statistically significant model was achieved for TIN at the lower frequency (1.5 kHz), though a model was fit to TIN at 4 kHz. The best fitting model for TIN at 4 kHz included TIQ at 4 kHz, the two tasks of short-term memory (PSMT and DSF), the two working memory tasks (DSB and LSWM), and PCPS processing speed task. Together, these predictors accounted for 45% of the variance

in TIN,  $F(6, 25) = 3.47$ ,  $p = .0125$ . TIQ at 4 kHz alone accounted for 28% of the variance, and the cognitive factors combined accounted for 17% (see Figure 6).

The best fitting model of FMDT included TIQ at 1.5 kHz, DSF (a measure of short-term memory), and LSWM (a measure a working memory) and accounted for 44% of the variance,  $F(4, 27) = 7.59$ ,  $p = .0003$ . TIQ at 1.5 kHz only accounted for 2%, and the DSF and LSWM cognitive tasks combined accounted for 41% of the variance (see Figure 6).

## Speech Recognition

Performance on speech in quiet was at or near ceiling; therefore, no model was generated. TIQ at 4 kHz was the only significant variable in a model of speech recognition in speech-shaped noise and accounted for 22% of the variance in performance,  $F(1, 30) = 8.47$ ,  $p = .0067$ . For time-compressed speech, TIQ at 4 kHz (24%) and the LSWM task (16%) together accounted for 40% of the variance in performance,  $F(3, 28) = 8.22$ ,  $p = .0004$  (see Figure 7). Performance on time-compressed speech with reverberation required TIQ at 4 kHz, LSWM, and the addition of the DCCS executive function task that combined accounted for 60% of the variance,  $F(4, 27) = 10.15$ ,  $p < .0001$ . TIQ at 4 kHz alone accounted for 38% of the variance, and the LSWM and DCCS cognitive tasks accounted for 22% (see Figure 7).

## Electrophysiology

Models of ABR Wave V/I amplitude ratios at both frequencies and the STR of the speech-evoked ABR fit poorly and did not reach statistical significance. The best fit model of the FFR-to-noise ratio of the speech-evoked ABR included TIQ at 4 kHz, LSWM, and Flanker task of attention and accounted for 36% of the variance,  $F(2, 27) = 6.82$ ,  $p = .004$ . TIQ at 4 kHz accounted for 4%, and the LSWM and Flanker cognitive tasks accounted for 32% (see Figure 8).

## Discussion

The aim of this study was to assess the dependence on cognitive capacity of the hearing measures that are currently being used in attempts to find a direct relationship between noise exposure and peripheral cochlear synaptopathy. It is important to take into account other factors that could explain the variance seen in these hearing measures. We hypothesized that cognition played a role in these hearing measures that, if true, needs to be considered when defining hidden hearing disorder. We prefer cognitive decline to be excluded from the definition of hidden hearing disorder because it is not specific to the auditory system. Therefore, tests of peripheral function that have little or no contribution from cognitive factors would be preferable because any such dependence either confounds the test result or



**Table 2.** Variance (95% confidence interval) accounted for by pure-tone thresholds and cognitive performance.

Variable	Task	Psychoacoustics		Speech recognition			sABR
		TIN	FMDT	Noise	TC	TCR	FFR
Hearing sensitivity	TIQ	.28 [.03, .51]	.02 [0, .24]	.22	.24 [.02, .65]	.38 [.11, .58]	.04 [0, .20]
Short-term memory	PSMT	.04 [.01, .16]				.02 [.01, .09]	
	DSF	.04 [.01, .21]	.17 [.01, .42]				
Working memory	DSB	.02 [.01, .16]					
	LSWM	.04 [.01, .21]	.24 [.07, .44]		.16 [.02, .45]	.12 [.02, .32]	.17 [.01, .40]
Executive function and attention	DCCS					.08 [.01, .21]	
	FIC						.15 [.01, .41]
Processing speed	PCPS	.03 [.01, .22]					
	Total $R^2$	.45	.44	.22	.40	.60	.36

*Note.* Empty cells indicate predictors not included in the model. sABR = speech-evoked auditory brainstem response; TIN = thresholds in noise; FMDT = frequency modulation detection threshold; TC = time-compressed words; TCR = time-compressed words with reverberation; FFR = frequency-following response; TIQ = thresholds in quiet; PSMT = Picture Sequence Memory Test; DSF = Digit Span Forward; DSB = Digit Span Backward; LSWM = List Sorting Working Memory; DCCS = Dimensional Change Card Sort; FIC = Flanker Inhibitory Control; PCPS = Pattern Comparison Processing Speed.

must be independently quantified in order to assess its contribution.

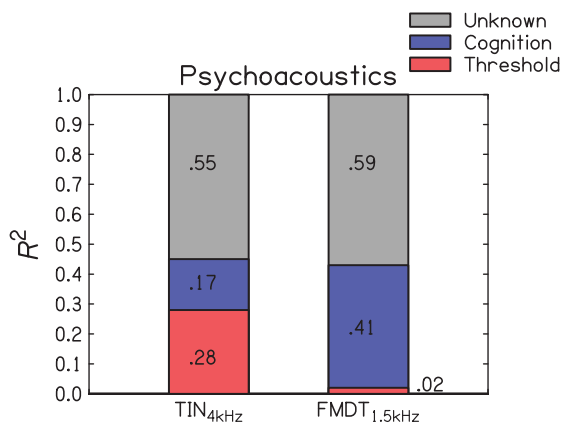
Several cognitive domains were assessed in a group of adults varying in age and hearing sensitivity. Performance on several cognitive tasks were corrected for age, race/ethnicity, and education, with the exception of digit span, which was extraneous to the NIH Toolbox battery, and were uncorrelated with TIQ. Significant models that included TIQ and cognitive performance as predictors were determined for TIN at 4 kHz, FMDT, speech recognition in speech-shaped noise, time-compressed speech recognition, time-compressed speech recognition in reverberation, and the FFR of the speech-evoked ABR. No significant models were generated for TIN at 1.5 kHz, ABR Wave V/I amplitude ratio, and the STR of the speech-evoked ABR.

For the significant models, the variance explained by each predictor, independent of the other predictors, was calculated via relative importance analysis.

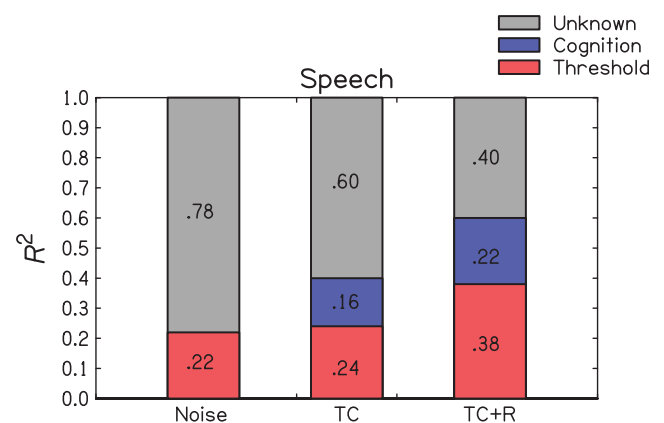
The variance explained by TIQ in TIN at 4 kHz was expected because hearing sensitivity of a pure tone will influence the threshold of a pure tone in noise. Indeed, there was a large correlation between TIQ and TIN. Short-term memory, working memory, and processing speed combined also explained some of the variance in TIN, with each task making a comparable 2%–4% contribution.

The impact of larger memory capacity in lowering FMDT scores was by far the most interesting finding. Together, short-term and working memory capacity accounted for almost all of the variance explained by the model, with working memory alone accounting for 24% of the overall

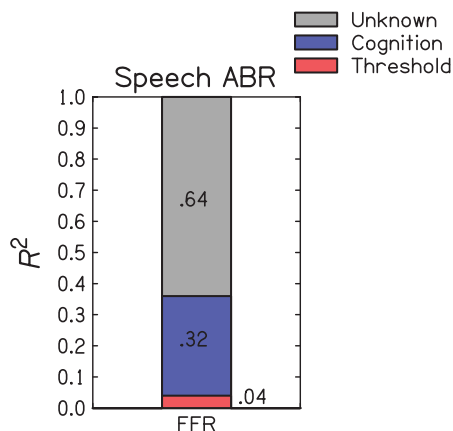
**Figure 6.** Proportion of variance of the psychoacoustics tasks explained by thresholds in quiet (red) and statistically significant cognitive tasks (blue) out of the total possible variance ( $R^2 = 1$ ). The gray area represents the remaining variance not explained by threshold or cognitive tasks. TIN<sub>4 kHz</sub> = thresholds in noise for a 4-kHz tone; FMDT<sub>1.5 kHz</sub> = frequency modulation detection threshold of a 1.5-kHz tone.



**Figure 7.** Proportion of variance of performance on speech recognition tasks explained by thresholds in quiet (red) and statistically significant cognitive tasks (blue) out of the total possible variance ( $R^2 = 1$ ). The gray area represents the remaining variance not explained by threshold or cognitive tasks. TC = time-compressed speech; TC+R = time-compressed speech with reverberation.



**Figure 8.** Proportion of variance of performance on ABR measures explained by thresholds in quiet (red) and statistically significant cognitive tasks (blue) out of the total possible variance ( $R^2 = 1$ ). The gray area represents the remaining variance not explained by threshold or cognitive tasks. ABR = auditory brainstem response; FFR = frequency-following response.



variance in FMDT. The memory component of both TIN and FMDT could be explained in two ways. First, working memory could be important for temporal processing. As FMDT is a much more demanding temporal processing task than TIN, it might require more working memory resources. Studies have shown significant contributions of age-related cognitive decline—particularly in working memory, processing speed, and attention—to temporal processing (e.g., Buss, Hall, & Grose, 2004; 2013 Füllgrabe et al., 2015; Grose & Mamo, 2010; Grose, Mamo, & Hall, 2009; He, Mills, Ahlstrom, & Dubno, 2008; Neher, Lunner, Hopkins, & Moore, 2012). Another explanation could be the FMDT task itself places a greater demand on working memory. Both TIN and FMDT were measured using a 3AFC task. This paradigm requires the participant to listen to three intervals before deciding which interval contained the target sound. For the TIN task, the participant was only waiting for the interval that contained a tone, as the others did not. In other words, each interval could be considered an independent judgment of tone “presence/absence” followed by retention of only the appropriate interval. Thus, the acts of processing and storage are not simultaneous. This small amount of storage and recall capacity is well within most adult’s expected limits (Cowan, 2000; Miller, 1956). In contrast, FMDT demands simultaneous storage and processing. All three intervals in the FMDT task contained amplitude-modulated tones but in one interval; the tone was also frequency modulated. Participants were instructed on what differentiated the frequency-modulated tone from the others, but as modulation depth decreases, it is increasingly difficult to hear clear frequency modulation. We posit that, eventually, the task devolves into an odd-one-out task, where participants are listening for the interval that is different from the other two. This type of task requires the storage of the information in all

three intervals and processing of this information before a recall is made. This, in fact, is the definition of a working memory task. If this is indeed the case, this particular method for the FMDT threshold may not be an appropriate diagnostic measure of a peripheral pathology because it involves central processing.

The dependence of speech recognition tasks on cognitive ability was expected. Speech recall in difficult conditions, such as a noisy background, would likely require some amount of working memory. Interestingly, no cognitive measure was a significant predictor of speech recognition in speech-shaped noise. The reason for this may be that the stimuli were monosyllabic words (as opposed to sentences), reducing storage demands. Significant amounts of variance on the time-compressed words were explained by working memory capacity. The increased temporal processing demand of added reverberation resulted in variance accounted for by additional memory and executive function and attention. This may be more evidence that temporal processing tasks do require more attention, storage capacity, and processing ability, similar to FMDT. These findings confirm results of Yeend, Beach, and Sharma (2019), who showed working memory accounted for significant variance in the Speech, Spatial, and Qualities of Hearing Scale and a speech-in-noise task involving spatial cues, in a population of young adults with clinically normal hearing. These trends are also seen in the aging population, in studies that found that older people perform more poorly on speech recognition tasks involving time compression and reverberation (e.g., Golomb, Peelle, & Wingfield, 2007; Gordon-Salant & Cole, 2016; Gordon-Salant & Fitzgibbons, 1993).

Further evidence for a large cognitive component in temporal processing is the variance in the speech-evoked FFR-to-noise ratio. The ABR is a passive task; in fact, many of our participants slept during this measure. Yet, the ability of the ear to encode the frequency information in the stimulus was predicted by performance on deliberate tasks of working memory and attention. This finding is corroborated by brain imaging studies showing a significant cortical contribution to the FFR (Coffey, Herholz, Chepesiuk, Baillet, & Zatorre, 2016; Coffey, Musacchia, & Zatorre, 2017). Other studies show that FFRs at 80–140 Hz are sensitive to musical training (Musacchia, Sams, Skoe, & Kraus, 2007) and language experience (Krishnan, Gandour, & Bidelman, 2010).

The results of this study add to the growing consensus that we should recognize and assess the influence of cognitive factors in our tests of peripheral pathology (Musiek, Chermak, Bamio, & Shinn, 2018; Smith, Pichora-Fuller, & Alexander, 2016; Yeend et al., 2019). These cognitive factors may be important for processing the information presented in the task or may be required by the task itself. Assessment of cognitive abilities alongside other hearing measures are especially important for aging participants but may be important to measure in young, healthy adult participants as well. Eighty-eight percent of the participants in this study had MoCA scores within normal limits and were highly educated (14 of the 32 participants held a master’s

or doctorate degree) and relatively young ( $Mdn = 38$  years) compared to other studies of hearing loss. Although overall performance on the cognitive tasks was quite high, small between-subjects variances in performance were able to explain significant differences on the hearing tests.

### Limitations

The primary limitation of this study was the small sample size and the diversity of ages within the group. Significant models were generated for most hearing measures, but no predictor was related to TIN at 1.5 kHz or tone burst ABR Wave V–I amplitude ratio. This could be due to underpowering. Though the effect of age on cognitive scores was controlled by using corrected  $t$  scores, age has a complex relationship with both cochlear health and cognitive function that is not accounted for in this study. Another limitation of this study was the use of only two standard pure-tone threshold frequencies (1.5 and 4 kHz) in the model. Though audiometric thresholds through 8 kHz were obtained in each participant, we chose a more accurate method of obtaining TIQ at 1.5 and 4 kHz for the analysis. A 3AFC procedure was deliberately chosen to reduce age-related bias and improve reliability. To represent low-frequency hearing, which codes for many speech sounds, 1.5 kHz was chosen. Four kilohertz was chosen as the common locus of increased thresholds due to noise exposure.

### Future Directions

This is not the first study to encourage cognitive measures as part of the test battery for hearing pathologies. There has been a push from hearing scientists to include measures of working memory and listening effort in the audiology clinic. The Framework for Understanding Effortful Listening is a report from experts in cognition and hearing to provide audiologists with an understanding of the mechanisms underlying cognitive capacity and its role in peripheral hearing loss and methods to assess cognition in both clinical and research environments (Pichora-Fuller et al., 2016). Audiologists and hearing scientists alike should consider including measures of cognition in their assessments of hidden and unhidden hearing loss.

### Conclusions

Our conclusions are as follows:

1. Measures of auditory function that involve temporal processing, such as frequency-modulation detection, the frequency-following response, time-compressed speech, and reverberation, are significantly influenced by cognitive abilities, specifically short-term and working memory capacity, executive function, and attention.
2. Research using measures of temporal processing to diagnose peripheral disorders, such as noise-induced synaptopathy, need to account for cognitive influence even in a young, healthy population.

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