Research Paper

Associations between speech recognition at high levels, the middle ear muscle reflex and noise exposure in individuals with normal audiograms

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ABSTRACT

It has been hypothesized that noise-induced cochlear synaptopathy in humans may result in functional deficits such as a weakened middle ear muscle reflex (MEMR) and degraded speech perception in complex environments. Although relationships between noise-induced synaptic loss and the MEMR have been demonstrated in animals, effects of noise exposure on the MEMR have not been observed in humans. The hypothesized relationship between noise exposure and speech perception has also been difficult to demonstrate conclusively. Given that the MEMR is engaged at high sound levels, relationships between speech recognition in complex listening environments and noise exposure might be more evident at high speech presentation levels. In this exploratory study with 41 audiometrically normal listeners, a combination of behavioral and physiologic measures thought to be sensitive to synaptopathy were used to determine potential links with speech recognition at high presentation levels. We found decreasing speech recognition as a function of presentation level (from 74 to 104 dBA), which was associated with reduced MEMR magnitude. We also found that reduced MEMR magnitude was associated with higher estimated lifetime noise exposure. Together, these results suggest that the MEMR may be sensitive to noise-induced synaptopathy in humans, and this may underlie functional speech recognition deficits at high sound levels.

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1. Introduction

Mounting evidence from animal studies demonstrates that noise exposure can lead to cochlear synaptopathy, a loss of connections between inner hair cells and auditory nerve fibers, in the absence of permanent threshold shift (e.g. Kujawa and Liberman, 2009; Lin et al., 2011; Parthasarathy and Kujawa, 2018; Valero et al., 2017). In humans, synaptopathy cannot be detected using standard audiometric testing (Lobarinas et al., 2013; Schuknecht and Gacek, 1993), and to date, no other physiologic or behavioral measures have been proven reliable enough to diagnose synaptopathy in vivo (Bharadwaj et al., 2019; Bramhall et al., 2019; Le Prell, 2019). There is therefore a strong need for new approaches to investigating synaptopathy in humans.

Part of the challenge of finding reliable measures of synaptopathy in humans has been the degrees of inconsistency in results across studies. For example, reductions in wave I amplitudes of the auditory brainstem response (ABR) have been shown in animals to be strongly associated with noise exposure (Furman et al., 2013; Kujawa and Liberman, 2009; Lin et al., 2011), but in humans, the results are mixed. Some studies have shown relationships between noise exposure and ABR measures (Bramhall et al., 2017; Stamper and Johnson, 2015b; Stamper and Johnson, 2015a; Valderrama et al., 2018), but many studies have shown no relationship (Fulbright et al., 2017; Grose et al., 2017; Guest et al., 2017a; Prendergast et al., 2017a, 2018; Ridley et al., 2018; Skoe and Tufts, 2018; Spankovich et al., 2017). Inconsistent relationships with noise exposure have also been observed for electrocochleography (Grinn et al., 2017; Liberman et al., 2016; Mepani et al., 2020;
Prendergast et al., 2018) and the envelope-following response (Bharadwaj et al., 2015; Guest et al., 2017b). In addition, non-associations with noise exposure have been reported for a variety of psychoacoustic tasks such as temporal summation, temporal/spectral/amplitude modulation detection, interaural phase difference (IPD) discrimination, frequency/intensity resolution, localization, and loudness scaling (cf. Fulbright et al., 2017; Grose et al., 2017; Prendergast et al., 2017b; Ridley et al., 2018; Yeend et al., 2017). Relationships between speech perception at conversational levels and noise exposure have also been mixed. Most studies have shown no significant relationships (Fulbright et al., 2017; Grinn et al., 2017; Grose et al., 2017; Guest et al., 2018a, 2019; Prendergast et al., 2017b; Yeend et al., 2017), although Liberman et al. (2016) reported poorer recognition of time-compressed reverberant speech for listeners with elevated noise exposure risk.

One physiologic measure that has shown promise for the detection of synaptopathy is the middle ear muscle reflex (MEMR). Animal studies by Valero and colleagues (2016; 2018) found significantly reduced wideband MEMR magnitudes and elevated MEMR thresholds in noise-exposed mice compared to controls. In particular, they found strong correlations between percent synapse loss and MEMR threshold/magnitude for the spectral regions most damaged by noise exposure (Valero et al., 2018). In humans, reduced MEMR strength has been shown to be related to other potential correlates of synaptopathy, such as tinnitus due to noise exposure (Wojtczak et al., 2017) and speech perception in noise and in reverberation tested at conversational levels (Mepani et al., 2020). Importantly, these studies all used wideband MEMR measurement techniques. On the contrary, Guest et al. (2019) used standard clinical MEMR measures and found no significant associations with spatial speech perception, self-reported tinnitus, or lifetime noise exposure estimates. It remains to be clarified whether the differences in MEMR measures could account for these discrepant findings.

The logic underlying a potential association between reduced MEMR and synaptopathy involves the functional role of low spontaneous rate (SR) auditory nerve fibers in the MEMR. Because the afferent portion of the MEMR circuit is thought to be dominated by low-SR fibers (Kobler et al., 1992; Liberman and Kiang, 1984), the MEMR should be sensitive to loss of these fibers. Further, low-SR fibers have been shown to be particularly susceptible to damage from noise exposure (Furman et al., 2013; Song et al., 2016), and these fibers may be most affected by synaptopathy (Furman et al., 2013). Although low-SR fibers have generally been thought to be responsible for the neural encoding of sound at high sound pressure levels (Liberman, 1978), the extent to which they code speech information at high levels in the human auditory system is subject to debate (Carney, 2018; Prendergast et al., 2019). However, even if they were not directly involved in speech coding, they might still play an important role in coding speech information at non-conversational levels with high fidelity (Carney, 2018), or through their control of the MEMR.

The MEMR, which becomes active only at higher sound levels, has been suggested to improve speech recognition at higher-than-conversational levels by reducing upward spread of masking (Borg and Zakrisson, 1974; Liberman and Guinan, 1998; Pang and Guinan, 1997). Patients without a functional MEMR can show speech rollover, i.e., decreasing speech recognition with increasing speech level in quiet (Borg and Zakrisson, 1974; Liberman and Guinan, 1998; Pang and Guinan, 1997) and in noise (Alken et al., 2013; Chadwell and Groseberg, 1979). A link between the MEMR and speech rollover has also been observed in normally hearing individuals (Dorman et al., 1986, 1987). In addition, individuals with normal audiograms who report hearing difficulties may primarily experience these difficulties in loud, noisy environments such as clubs and bars (Guest et al., 2018a), where sound levels can easily exceed 90 dB A-weighted (dBA) and often surpass 100 dBA (Keppler et al., 2015; Spira-Cohen et al., 2017). Taken together, these findings suggest that effects of synaptopathy on speech perception might be more apparent at high speech levels than at conversational levels where most testing has occurred.

The purpose of the present study was to explore the potential predictors of and the relationships between two primary outcome measures: level-dependent speech intelligibility (rollover) and the wideband MEMR. To sample from a candidate synaptopathy population, we recruited adult patients from the Heuser Hearing Institute (Louisville, KY, USA) who had sought care for suspected hearing loss, but upon evaluation, were found to have normal audiograms. We also tested a group of listeners who did not self-report hearing difficulties to compare to the help-seeking group. Overall, the sample had a range of noise exposure histories and tinnitus presentations but was intentionally limited to individuals of ages <55 years. All participants completed a test battery of physiologic, objective, and subjective measures believed to be associated with synaptopathy, in particular speech recognition at high presentation levels, the wideband MEMR, and estimates of lifetime noise exposure. We then performed analyses of covariance (ANCOVAs) to explore predictors of the speech recognition and MEMR outcome measures. In addition, we explored potential predictors of IPD discrimination. To reduce the likelihood of false discovery, no dependent variables other than speech recognition, the MEMR, and IPD discrimination were modeled in this study.

## 2. Methods

### 2.1. Participants

Forty-three adults (ages: 21–54 years) were recruited for this study. Twenty-three of the participants had previously sought help for self-reported hearing difficulties at the Heuser Hearing Institute but were found to have normal audiograms. One individual reported a diagnosed perilymph fistula. Another individual reported a diagnosis of hypothyroidism, which is associated with strong acoustic reflexes and tinnitus (Brandy and Lynn, 1995). Their data were excluded from data analysis, resulting in 21 participants in the help-seeking group. The other 20 participants were normal-hearing individuals recruited from the community who had never sought help for hearing difficulties. All testing procedures used in this study were approved by the University of Louisville Institutional Review Board, and were in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for experiments involving humans. Written consent was obtained for all participants.

Pure-tone air conduction thresholds were measured at each standard octave and inter-octave frequency from 125 to 8000 Hz and at 10,000, 12,500, and 14,000 Hz using a Grason-Stadler Inc. Audiostar audiometer and Sennheiser HDA 200 headphones. All pure-tone thresholds were <20 dB HL from 125 to 8000 Hz except for participants 20 and 29 who had 25–dB HL thresholds at 8000 Hz in one ear, and participant 32 who had 25 dB HL thresholds at 8000 Hz in both ears. None of the participants had an asymmetry between ears greater than 10 dB at two or more consecutive test frequencies. Bone conduction thresholds were measured at octave frequencies from 500 to 4000 Hz via a RadioEar B-71 bone oscillator. None of the participants had air-bone gaps greater than 10 dB at any of the test frequencies.

Distortion product otoacoustic emissions (DPOAEs) were measured using an Interacoustics Titan device version 4 (Middelfart, Denmark). DPOAEs were measured from 2000 Hz to 6000 Hz using an f2/f1 ratio of 1.22 at 65/55 dB SPL. Distortion...
product level and noise level were averaged for 8 s at each test frequency. All participants had robust DPOAEs with SNRs greater than 6 dB at all test frequencies.

Table 1 lists the participants’ demographic and audiologic information. Individuals in the help-seeking group and non-help-seeking group were on average 36.0 and 35.5 years old, respectively. The difference was not significant based on a permutation test (p = .85, Efron and Tibshirani, 1993). Gender distributions did not differ significantly either (p > .9, Pearson’s Chi-squared test with simulated p-value). However, the frequency-four pure-tone average (PTA; 0.5, 1, 2, and 4 kHz) differed significantly between the groups (p = .01): The help-seeking individuals had on average 3.3 dB higher PTAs than the non-help-seeking individuals. The extended high-frequency pure-tone average (HFPTA; 10, 12.5, and 14 kHz) did not differ between groups (p = .78).

2.2. Tests and procedures

Ipsilateral and contralateral wideband MEMRs were measured using the Interacoustics Titan device. The measurement protocol was implemented in MATLAB software version 2018a (The MathWorks Inc., Natick, MA, USA) and interfaced with the Titan device via the Interacoustics Research Platform. The MEMR was measured at tympanometric peak pressure. The probe signal was a series of five 105-dB-ppSPL clicks with four ipsilateral or contralateral elicitor noise bursts between each click (Keefe et al., 2010, 2017). The clicks were separated by 186 ms, and the duration of each noise burst was 116 ms. The noise was broadband (100–4000 Hz) with the ipsilateral and contralateral spectra following the transfer functions of the ipsilateral probe and contralateral EARtone 3A earphones, respectively (see Appendix A). The noise was presented at 75, 90 and 105 dB SPL as measured in an IEC 60318-4 (2010) ear simulator (GRAS RA04045) in a KEMAR manikin (GRAS 458BB-7, Burkhard and Sachs, 1975) with anthropometric pinnae (GRAS KB5000). This corresponded to 67, 82, and 97 dBA diffuse-field level for the ipsilateral noise and 65, 80, and 95 dBA for the contralateral noise (diffuse-field levels were used in the calculation of noise exposure in this study, OSHA, 2014). Responses were averaged across four runs of clicks and noise, and absorbance was calculated in 1/5-octave bands (Rosowski et al., 2013). The MEMR magnitude was defined as the maximum difference in absorbance between the first click (baseline) and the final click across the 14 bands from 250 to 1516 Hz.

Table 1

| ID  | Group | Age (years) | Gender | PTA (dB HL) | HFPTA (dB HL) | Tinnitus | NESI | SSQ |
|-----|-------|-------------|--------|-------------|---------------|----------|------|-----|
| 1   | NHS   | 23          | female | 6.25        | 1.67          | no       | 0.58 | 9.36|
| 2   | NHS   | 24          | female | -5.63       | 2.50          | no       | 0.15 | 8.86|
| 3   | NHS   | 26          | female | -5.63       | 0.83          | no       | 19.5 | 9.18|
| 4   | NHS   | 27          | female | 0           | -6.67         | no       | 0.73 | 7.79|
| 5   | NHS   | 28          | male   | -6.25       | -6.67         | yes      | 1.92 | 8.43|
| 6   | NHS   | 30          | female | -1.88       | -5.00         | yes      | 9.18 | 8.79|
| 7   | NHS   | 31          | female | -3.75       | 4.17          | yes      | 1.74 | 9.00|
| 8   | NHS   | 32          | male   | 0           | 13.3          | yes      | 3.41 | 8.93|
| 9   | NHS   | 33          | female | 0.63        | 5.83          | yes      | 2.20 | 7.71|
| 10  | NHS   | 34          | female | 1.25        | -4.17         | no       | 5.79 | 6.93|
| 11  | NHS   | 35          | female | 3.13        | 4.17          | no       | 6.45 | 4.86|
| 12  | NHS   | 36          | female | -3.13       | 0.83          | no       | 1.00 | 8.07|
| 13  | NHS   | 37          | male   | 2.50        | 11.7          | no       | 10.7 | 9.43|
| 14  | NHS   | 38          | female | 10.0        | 30.8          | no       | 53.4 | 5.50|
| 15  | NHS   | 39          | female | -3.13       | 8.33          | no       | 4.21 | 8.02|
| 16  | NHS   | 40          | male   | 7.50        | 45.8          | no       | 7.25 | 8.71|
| 17  | NHS   | 41          | female | 4.38        | 17.5          | no       | 9.84 | 8.86|
| 18  | NHS   | 42          | female | 1.25        | 26.7          | yes      | 0.85 | 9.29|
| 19  | NHS   | 43          | male   | 6.25        | 60.8          | no       | 1.49 | 9.21|
| 20  | NHS   | 44          | female | 1.25        | 1.67          | no       | 0.33 | 9.14|
| 21  | HS    | 21          | male   | -2.50       | 13.3          | yes      | 0.73 | 6.07|
| 22  | HS    | 22          | male   | 5.63        | -11.7         | no       | 8.07 | 4.21|
| 23  | HS    | 23          | male   | 7.50        | 11.7          | no       | 186.4 | 3.50|
| 24  | HS    | 24          | male   | 5.63        | -0.83         | no       | 11.0 | 7.07|
| 25  | HS    | 25          | female | 2.50        | 5.83          | no       | 3.92 | 5.93|
| 26  | HS    | 26          | female | 1.25        | -5.00         | yes      | 10.2 | 4.00|
| 27  | HS    | 27          | female | 9.38        | 1.67          | no       | 24.3 | 3.31|
| 28  | HS    | 28          | female | 8.13        | 17.5          | yes      | 49.5 | 1.50|
| 29  | HS    | 29          | female | 1.88        | 6.67          | yes      | 15.7 | 5.79|
| 30  | HS    | 30          | female | 0.63        | -3.33         | yes      | 5.83 | 4.57|
| 31  | HS    | 31          | female | 6.25        | 26.7          | yes      | 5.31 | 4.36|
| 32  | HS    | 32          | male   | -1.25       | 10.0          | yes      | 5.22 | 6.09|
| 33  | HS    | 33          | female | 6.88        | 35.8          | yes      | 74.2 | 4.00|
| 34  | HS    | 34          | female | 1.88        | 35.8          | no       | 2.57 | 4.61|
| 35  | HS    | 35          | female | 5.00        | 21.7          | yes      | 153.7 | 7.29|
| 36  | HS    | 36          | female | 5.63        | 31.3          | no       | 1.50 | 3.57|
| 37  | HS    | 37          | female | 6.88        | 5.83          | no       | 22.5 | 7.79|
| 38  | HS    | 38          | female | 5.63        | 14.2          | no       | 117.5 | 5.07|
| 39  | HS    | 39          | female | 0           | 9.17          | yes      | 0.96 | 5.50|
| 40  | HS    | 40          | female | 9.38        | 17.5          | no       | 6.22 | 7.00|
| 41  | HS    | 41          | female | 5.02        | 7.50          | yes      | 3.38 | 8.19|

Table 1 lists the participants’ demographic and audiologic information. Individuals in the help-seeking group and non-help-seeking group were on average 36.0 and 35.5 years old, respectively. The difference was not significant based on a permutation test (p = .85, Efron and Tibshirani, 1993). Gender distributions did not differ significantly either (p > .9, Pearson’s Chi-squared test with simulated p-value). However, the frequency-four pure-tone average (PTA; 0.5, 1, 2, and 4 kHz) differed significantly between the groups (p = .01): The help-seeking individuals had on average 3.3 dB higher PTAs than the non-help-seeking individuals. The extended high-frequency pure-tone average (HFPTA; 10, 12.5, and 14 kHz) did not differ between groups (p = .78).
ABRs were measured twice in each ear using a Vivosonic Integrity V500 (Toronto, ON, Canada) device. Two thousand sweeps were averaged in response to an 85 dB nHL click of alternating polarity presented at a rate of 11.1 clicks (100 μs in duration) per second via an ER-3A insert earphone. ABR wave I peaks were selected by the first author (an ASHA certified audiologist). Amplitudes were measured from peak to trough and averaged across two repetitions. No contralateral masking was presented, and no artifact rejection was used. Filter settings were set to 100 Hz high-pass and 1500 Hz low-pass filters with a 12 dB/octave rolloff for the high-pass filter and a 24 dB/octave rolloff for the low-pass filter. The single-channel electrode montage was set to: high forehead (non-inverting), low forehead (ground), and ipsilateral mastoid (inverting). Electrode sites were scrubbed using an alcohol wipe and inverting), low forehead (ground), and ipsilateral mastoid (inverting). A single-channel electrode montage was set to: high forehead (non-inverting), low forehead (ground), and ipsilateral mastoid (inverting). Electrode sites were scrubbed using an alcohol wipe and inverting), low forehead (ground), and ipsilateral mastoid (inverting).

Correct-response feedback was provided throughout all training cues, followed by the measurement run consisting of 60 trials. Training run with IPD cues replaced by interaural level difference (ILD) JNDs. The ILD JND task was the same two-interval task with eyes closed. Participants were asked before the test session whether they perceived tinnitus in the sound booth. They were specifically asked to look for ringing, buzzing or roaring in one or both of their ears. All participants who reported perceiving tinnitus described it as a continuous percept (see Table 1).

The Trail Making Tests part A and B (Reitan, 1955) were administered using the same touchscreen version as described by Strelcyk et al. (2019). The Trail Making Test part A (TMA) involved tapping 25 numbers in sequence (1–2–3–4 and so on), whereas the Trail Making Test part B (TMB) involved tapping 25 alternating numbers and letters in sequence (1–A–2–B and so on). The test scores were the times required to complete the trails. TMA indexed processing speed, visual search, and motor skills (Bowie and Harvey, 2006). In addition to these, TMB captured executive control abilities (Arbuthnott and Frank, 2000; Sanchez-Cubillo et al., 2009).

Because high presentation levels were used in this study, total noise exposure was calculated to ensure that our participants would not be overexposed. We used the National Institute of Occupational Safety and Health equation to calculate a time-weighted average in dBA (NIOSH, 1998). The recommended daily exposure limit is 85 dBA, and the calculated time-weighted average for all of our stimuli was 77 dBA. Participants were also advised at the end of the test session to limit their noise exposure for the rest of the day.

All audio testing was performed in a double-walled sound booth, and non-audio testing was conducted in a quiet room. Testing was completed in a single test session that lasted for about 2–2.5 h. All participants were paid $20 per hour for their participation.

3. Results and discussion

3.1. Group differences

Table 2 lists the prevalence of tinnitus and average test results for the SSQ, ABR wave I amplitude, MEMR magnitude, IPD JND, NESI, TMA and TMB time for each participant group. The group averages were calculated as arithmetic means for SSQ and ABR wave I amplitude and as geometric means for MEMR magnitude, IPD JND, NESI, TMA and TMB time. Although more help-seeking than non-help-seeking individuals reported tinnitus, the prevalence of tinnitus did not differ significantly between the groups.
Permutation tests (Efron and Tibshirani, 1993) showed significantly lower SSQ scores for the help-seeking group than for the non-help-seeking group. The mean SSQ score of 8.2 for the non-help-seeking group fell at the 60th percentile of a set of normative SSQ data from 233 young normal-hearing listeners (Zahorik and Rothpletz, 2014). This suggests that the non-help-seeking group’s SSQ scores were consistent with norms. The mean SSQ score of 5.3 for the help-seeking group fell in the 4th percentile of the normative data (Zahorik and Rothpletz, 2014) confirming that the help-seeking group had substantial self-reported difficulties in speech perception. Furthermore, the help-seeking group showed weaker MEMR magnitudes (here, magnitudes were averaged across ears, ipsilateral and contralateral elicitors, and elicitor levels) and larger IPD JNDS than the non-help-seeking group. These two group differences, however, were not significant after multiple testing correction (Benjamini and Yekutieli, 2001). NESI scores were marginally higher in the help-seeking than non-help-seeking group (p = .053). ABR wave I amplitudes (averaged across ears) and Trail Making times did not differ between the groups.

### 3.2. CNC recognition

Fig. 1 shows CNC recognition scores as a function of level for the two participant groups. Plotted scores were corrected for CNC list effects using the predicted list random effects from the final model described below and averaged across left and right ears. While CNC scores varied widely across individuals, average CNC scores decreased similarly for both groups with increasing presentation level.

In order to determine significant predictors of CNC recognition, ANCOVAs were performed on the CNC scores using generalized linear mixed-effects models with binomial distributions and logit link functions (Bates et al., 2019). Participant and CNC list number were entered as random effects. Model selection was performed in forward selection, entering one variable at a time until no variable remained with a p-value of less than 0.05. The tested covariates were: participant group, gender, age (left vs. right), ear, PTA, HFPTA, tinnitus, ABR wave I amplitude, ipsilateral and contralateral MEMR magnitude (averaged across elicitor level), IPD JND, NESI, TMA time, and CNC level (as a factor). In the order of inclusion, the significant predictors in the final model were CNC level [$\chi^2(2) = 213.6, p < .0001$] and ipsilateral MEMR magnitude [$\chi^2(1) = 7.03, p = .008$]. The interaction of CNC level and MEMR magnitude was also significant [$\chi^2(2) = 11.7, p = .003$]. As shown in Fig. 2, CNC scores improved with increasing MEMR magnitude, but this relationship interacted strongly with CNC level. To interpret this interaction, we evaluated the significance of the simple effect of MEMR magnitude at each level for the final model. The corresponding p-value is shown in the lower right corner of each panel in Fig. 2. Note, for visualization purposes Fig. 2 shows linear regression lines on the percent correct scale rather than the log odds scale used in the model. However, the graph would look very similar if plotted on a log odds scale, due to the near linearity of the logit transformation in the range from 20 to 80 percent correct. The final model explained 36% of the variance (proportion of generalized variance explained by the fixed effects, $R^2_F$, Jaeger, 2017; jaeger et al., 2017). CNC level and the interaction of MEMR magnitude with CNC level remained significant (p ≤ .003) when participant group, age and PTA, which were not significant (p > .2), were added to the final model. Standardized residuals were normally distributed by inspection of a Quantile-Quantile plot (Hartig, 2019).

These results demonstrate a positive relationship between MEMR magnitude and speech recognition performance, and this relationship strengthened with increasing level. Importantly, these effects remained even after controlling for the residual effects of participant group (help-seeking vs. non-help-seeking), age, and PTA. The demonstrated relationship between MEMR magnitude and speech recognition performance is generally consistent with results for time-compressed speech in reverberation and speech in noise reported by Mepani et al. (2020), although that study only tested at a single fixed level of 75 dB SPL and did not control for the potential effects of PTA in their results. In contrast, Guest et al. (2019) did not observe a significant relationship between MEMR and anechoic, spatial speech recognition in competing speech for individuals with normal audiograms. However, the MEMR testing in that study was only conducted at a single probe frequency. MEMR threshold varies by probe frequency, and the maximum change in the middle-ear transfer function may not be captured by a 226 Hz probe tone (Bharadwaj et al., 2018, Fig. 5; Schairer et al., 2013). In contrast, the wideband MEMR measure used by Mepani et al. (2020) and in this study surveyed the MEMR simultaneously across several octaves, enabling the measurement of MEMR magnitude at each participant’s frequency of maximum

### Table 2

Summary measures for non-help-seeking and help-seeking groups. The tinnitus measure represents individual counts. The SSQ score (speech subscale) and the ABR wave I amplitude (averaged across ears) are arithmetic means. The MEMR magnitude (averaged across ears, ipsilateral and contralateral elicitors, and all three elicitor levels), IPD JND, NESI units of lifetime noise exposure, TMA and TMB time are geometric means. The stated p-values represent tests for group differences and were not corrected for multiple testing.

| Measure | Non-help-seeking | Help-seeking | p-value |
|---------|------------------|--------------|---------|
| Tinnitus | 5 yes, 15 no     | 11 yes, 10 no | .11     |
| SSQ score | 8.19             | 5.26         | <.0001  |
| ABR wave I amp. (μV) | 0.27             | 0.24         | .28     |
| MEMR magnitude | 0.053            | 0.034       | .04     |
| IPD JND (degrees) | 9.81             | 14.5         | .02     |
| NESI | 3.38             | 9.49         | .053    |
| TMA time (s) | 25.5             | 25.9         | .85     |
| TMB time (s) | 34.4             | 40.4         | .11     |

![Fig. 1. CNC recognition scores as a function of presentation level. For illustration, scores were averaged across left and right ears for each participant as a function of CNC level (see Table 1 for participant ID). Group means (±1 standard error of the mean) are shown.](image-url)
change in absorbance (Keefe et al., 2010; Schairer et al., 2013). Using this measure, we find that the strength of the relationship between the MEMR and speech recognition performance is strongest at the highest speech presentation level.

### 3.3. MEMR magnitude

As observed above, MEMR magnitude was weaker in help-seeking than in non-help-seeking individuals. Furthermore, ipsilateral MEMR magnitude was a predictor of CNC score. To shed further light on the MEMR, we performed ANCOVAs on general linear mixed-effects models with log-transformed MEMR magnitude as the dependent variable (Pinheiro et al., 2019). Random effects terms were participant and ear nested within participant, and different variances were allowed for each elicitor level. The tested covariates in forward selection were: participant group, gender, age, PTA, tinnitus, ABR wave I amplitude, NESI, side of MEMR elicitor (ipsilateral vs. contralateral), and MEMR elicitor level (as a factor). In the order of inclusion, the significant predictors in the final model were: elicitor level \( [F(2,407) = 347.9, p < .0001] \), elicitor side \( [F(1,407) = 56.3, p < .0001] \), and NESI \( [F(1,39) = 6.24, p = .02] \). The interaction of NESI and elicitor level was also significant, \( [F(2,405) = 10.2, p < .0001] \). MEMR magnitude increased with level and was larger when elicited ipsilaterally than contralaterally, on average by a factor of 1.35. As shown in Fig. 3, MEMR magnitude decreased with increasing lifetime noise exposure particularly at the lower elicitor levels. The \( p \)-value in the lower right corner of each panel reflects the significance of the simple effect of NESI for the final model which controlled for elicitor side. This model explained 35\% of the variance (marginal \( R^2 \)). The above effects of elicitor level, elicitor side, and the interaction of NESI with elicitor level remained significant (\( p < .0001 \)) when participant group, age, and PTA, which were not significant (\( p > .17 \)), were added to the final model. Model residuals were normally distributed by inspection of a Quantile-Quantile plot.

To our knowledge, this is the first demonstration in humans of a significant relationship between noise exposure history and reduced MEMR magnitude. The relationship is highly consistent with animal work showing a direct relationship between noise insult and a reduced MEMR (Valero et al., 2016, 2018). We attribute our ability to detect this relationship primarily to using the wideband MEMR, which has been shown to assess the acoustic reflex with high sensitivity (Keefe et al., 2010; Schairer et al., 2013). Guest et al. (2019) did not find a significant relationship between noise exposure history (in terms of NESI) and the MEMR. It is possible that their single-frequency MEMR measures limited the power to detect such a relationship.

### 3.4. IPD discrimination

IPD discrimination differed between help-seeking and non-help-seeking individuals. In a previous study with 20 older hearing-impaired participants, we observed a significant association between IPD discrimination performance and Trail-Making scores (Strelczyk et al., 2019). However, this had not yet been tested in younger individuals with normal audiograms. We therefore decided to explore predictors of IPD discrimination although IPD discrimination was not a primary measure in this study (CNC recognition and the MEMR were). We performed ANCOVAs on general linear models (Fox et al., 2019) with the log-transformed IPD JND as dependent variable. The tested covariates in forward selection were: participant group, age, PTA (averaged across ears), tinnitus, ABR wave I amplitude (averaged across ears), and MEMR elicitor side (ipsilateral vs. contralateral). The above effects of MEMR elicitor level remained significant (\( p < .0001 \)) when participant group, age, and PTA, which were not significant (\( p > .17 \)), were added to the final model. The final model explained 44\% of the variance (marginal \( R^2 \)). The effects of TMB...
time and PTA remained significant \((p < .01)\) when participant group, which was not significant \((p = .43)\), was added to the final model whereas the effect of age was no longer significant \((p = .06)\). Pearson’s product-moment correlation coefficient between the IPD JND and TMB, which we list here for sake of comparison with previous studies, was \(r = 0.48\).

Our models to predict CNC recognition performance and MEMR magnitude (our primary outcome measures) showed non-relationships with IPD. Nevertheless, the observed association between IPD JND and TMB is noteworthy since it was previously observed for older individuals with normal pure-tone thresholds (Füllgrabe et al., 2015) and older hearing-impaired individuals (Strelcyk et al., 2019). The present results extend this finding to young and middle-aged adults with normal audiograms. It is possible that this association between IPD discrimination and non-auditory cognitive performance is attributable to a modality-general spatial processing deficit or individual differences in global processing speed as discussed by Strelcyk et al. (2019).

### 3.5. Mediation analysis

A mediation analysis was conducted to test for linkages between the primary measured variables in this study. Mediation analyses have commonly been used in the social sciences to examine potential causal relationships among variables (Baron and Kenny, 1986). In the simplest case, mediation analysis allows for determining whether an independent variable asserts its effects on a dependent variable directly or indirectly through a third mediating variable. Here, since CNC recognition was predicted by MEMR magnitude, which was, in turn, predicted by NESI, it is possible that MEMR magnitude mediated effects of NESI on CNC recognition. Fig. 5 shows the hypothesized relationships between these variables. We tested this mediational hypothesis by estimating a series of regression models following steps outlined by Baron and Kenny (1986). First, the independent variable, NESI, significantly predicted the mediator, ipsilateral MEMR magnitude averaged across elicitor levels (path a, Fig. 5), \([F(1,39) = 11.8, p = .001]\). Second, NESI significantly predicted CNC scores at the highest CNC level of 104 dBA (path b, Fig. 5), \([\chi^2(1) = 4.73, p = .03]\), but not at the lower CNC levels \([74, 89, 90, 104\text{ dBA}; p = .12, .16]\). Therefore, in the third model, both NESI and ipsilateral MEMR magnitude averaged across elicitor levels were included as
predictors of CNC scores at the highest CNC level. While MEMR magnitude was significant (path c, Fig. 5), $\chi^2(1) = 8.62, p = .003$, the effect of NESI on CNC recognition was no longer significant (path b, Fig. 5) $\chi^2(1) = 1.21, p = .27$. In other words, NESI had no effect on CNC recognition when MEMR magnitude was controlled. Thus, MEMR magnitude perfectly mediated the effects of NESI on CNC recognition at the highest CNC level. Further, although the causal structure of the mediating relationship can only be hypothesized based on our data, the fact that there is a plausible and consistent temporal order to the relationships strengthens the causal hypotheses (Cole and Maxwell, 2003). Noise exposure history precedes both the MEMR and CNC performance in time, and the MEMR precedes CNC performance, but on a much shorter time scale. How these relationships may relate to cochlear synaptopathy will be discussed in the following section.

4. General discussion

The main findings from this study are that on a group level a) human performance on a speech recognition task, particularly at high levels (104 dBA), can be predicted by MEMR magnitude, and b) MEMR magnitude can be predicted by noise exposure history. Specifically, reduced wideband reflex magnitude was associated with poorer speech recognition, and greater noise exposure history was associated with reduced wideband reflex magnitude. To our knowledge, this is the first study to demonstrate this series of effects together in the same groups of listeners. Further, results of a mediation analysis suggest that noise exposure history does not directly impact speech recognition at high levels, but instead leads to reduced MEMR magnitude which in turn is associated with poorer speech recognition at high levels.

Although this study provides no direct measures of cochlear synaptopathy, our conceptual framework provides support for the effects of synaptopathy within relationships among our measured constructs. Based on the logic that noise exposure may differentially damage the low-SR auditory nerve fibers involved in the circuit that controls the MEMR, a reduced MEMR has been suggested as a marker of synaptopathy in humans (Mepani et al., 2020; Wojtczak et al., 2017). We therefore hypothesize that cochlear synaptopathy encompasses the MEMR within our proposed causal model (Fig. 5).

Examining the three paths in our model lends further support for the placement of synaptopathy within the model.

a) The relationship between noise exposure and the MEMR has been well-established in animal studies (Valero et al., 2016, 2018) and is evident in the data reported here (Fig. 3).

b) The demonstrated non-direct relationship between noise exposure and CNC performance (i.e. relationship mediated by the MEMR) is consistent with the known wide ranges of individual susceptibility to noise exposure. Recent work by Brungart et al. (2019) confirms this heterogeneity of noise susceptibility, and is consistent with the idea of “tough” and “tender” ears (Cody and Robertson, 1983; Maison and Liberman, 2000).

c) The relationship between a reduced MEMR, suspected synaptopathy, and reduced speech recognition is consistent with results from Mepani et al. (2020). This relationship may result from a combination of effects, however. One option, $c_3$, is that synaptopathy leads to a reduced MEMR, which in turn affects speech recognition. This is because lower MEMR magnitude results in reduced attenuation of speech and/or noise signals at low frequencies, which can lead to increased upward spread of masking affecting higher frequency regions critical for good speech recognition (Borg and Zakrisson, 1974; Liberman and Guinan, 1998; Pang and Guinan, 1997). Another possibility, $c_2$, is that synaptic loss limits the information-carrying capacity required for good speech recognition. In this case, synaptic loss would be a common cause for both a reduced MEMR and degraded speech recognition. A third possibility is that some combination of effects $c_1$ and $c_2$ exists. Mepani et al. (2020) leaned toward the $c_2$ hypothesis, given that their electrocochleography measures seemed to have similar predictive strength to the MEMR. In our data, the fact that the relationship between the MEMR and speech recognition strengthened at high presentation levels might seem to support the $c_1$ hypothesis. However, $c_2$ or a combination of both $c_1$ and $c_2$ cannot be ruled out. After all, speech recognition at high levels may especially challenge the information-carrying capacity of a system damaged by synaptopathy.

Regardless of mechanism, the MEMR and speech recognition are associated, both in our data, and in the data of Mepani et al. (2020). Importantly, our data suggest that the association becomes more evident at higher speech presentation levels, and therefore can be detected statistically with fewer participants (41 in our study versus 165 in Mepani et al., 2020).

Even with the increased sensitivity afforded by testing at high levels, we lack the ability to predict reliably speech outcomes on an individual level. As Mepani et al. (2020) pointed out, group level associations may still have benefits for longitudinal tracking of noise accumulation effects. Additionally, further testing may lead to optimization of test protocols at high levels such that diagnostic potential may be reached at the individual level.

Finally, we note that our recommendations for measuring insult caused by noise exposure explicitly involve additional noise exposure. Although we were careful to stay well below time-weighted average limits set by NIOSH (1998), research in this area will require careful exposure monitoring and ongoing evaluation of recommended noise exposure limits in order to ensure that the research itself does not contribute to noise exposure problems. At the same time, new knowledge regarding the links between noise exposure and synaptopathy has the potential to valuable recommendations for noise exposure limits.
5. Conclusions

Speech recognition tested in reverberation and noise was found to decrease with increasing presentation level in both help-seeking and non-help-seeking groups. Lower recognition scores were associated with reduced MEMR magnitude, and that association was strongest at the highest speech presentation level. Furthermore, reduced MEMR magnitude was associated with higher estimated lifetime noise exposure. Together, these relationships suggest that lifetime noise exposure caused a weaker MEMR, which in turn was associated with degraded speech recognition at high presentation levels. This latter association may result from: 1) a direct causal link between a reduced MEMR and decreased speech recognition; 2) synaptic loss as a common underlying cause that affects both the MEMR and speech recognition; 3) a combination of both causes.

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James Shehorn: Conceptualization, Methodology, Investigation, Data curation, Writing - original draft, Writing - review & editing, Project administration. Olaf Strelcyk: Conceptualization, Methodology, Software, Formal analysis, Resources, Data curation, Writing - original draft, Writing - review & editing, Visualization, Funding acquisition. Pavel Zahorik: Conceptualization, Methodology, Software, Resources, Writing - original draft, Writing - review & editing, Supervision, Project administration, Funding acquisition.

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Appendix A. Elicitor spectra and their influence on MEMR magnitude

Figure A1 shows the ipsilateral (probe) and contralateral (EAR-tone 3A) elicitor spectra as measured in the IEC 60318-4 (2010) ear simulator in the KEMAR manikin with anthropometric pinnae. Both ipsilateral and contralateral elicitors were calibrated to equal levels in the ear simulator and ranged in frequency from 100 to 4000 Hz. Up to 1000 Hz, the ipsilateral elicitor had slightly higher power than the contralateral elicitor, whereas it had slightly lower power above 2000 Hz.

Fig. A1. MEMR elicitor spectra. Power spectral density measured in an IEC 60318-4 (2010) ear simulator.

To investigate the influence of these spectral differences on MEMR magnitude, we created a “contra-matched” ipsilaterial noise elicitor with the same spectrum as the contralateral elicitor (see Figure A1). MEMR measurements for the last 22 participants in the study were performed with this contra-matched ipsilateral elicitor, in addition to the “standard” ipsilateral and contralateral elicitors used for all participants. We modeled the log-transformed MEMR magnitudes observed for these 22 participants using a series of general linear mixed-effects models (Pinheiro et al., 2019). A first model only included MEMR magnitudes measured with the standard ipsilateral and contralateral elicitors, with elicitor level and elicitor side as predictors. MEMR magnitude was significantly larger when elicited ipsilaterally than contralaterally [F(1, 217) = 26.1, p < .0001], on average by a factor of 1.34, which was very similar to the factor of 1.35 observed for the full dataset. In a second model, we replaced the standard ipsilateral MEMR magnitude with the contra-matched ipsilateral MEMR magnitude. This model also showed a significant effect of elicitor side [F(1, 217) = 32.4, p < .0001], with a factor of 1.37 between contra-matched ipsilateral and contralateral MEMR magnitude. Third, we modeled MEMR magnitudes measured with the standard and contra-matched ipsilateral elicitors, with the factor elicitor spectrum replacing the factor elicitor side since contralateral magnitudes were excluded. The effect of elicitor spectrum was not significant [F(1, 217) = 1.04, p = .31]. MEMR magnitudes measured with the standard and contra-matched ipsilateral elicitors differed only by a factor of 0.97. Taken together, the similarity of the effects of elicitor side in the first two models and the absence of an effect of elicitor spectrum in the third model indicate that the differences in the spectra of the ipsilateral and contralateral standard elicitors in this study had negligible effects on MEMR magnitude.

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