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The relationship between distortion product otoacoustic emissions and audiometric thresholds in the extended high-frequency range

Samantha N. Hauser,[1,a)] Alexandra R. Hustedt-Mai,[1] Anna Wichlinski,[1] and Hari M. Bharadwaj[2]
[1]*Speech, Language, and Hearing Sciences, Purdue University, West Lafayette, Indiana 47901, USA*
[2]*Communication Science and Disorders, University of Pittsburgh, Pittsburgh, Pennsylvania 15260, USA*

ABSTRACT:
Distortion product otoacoustic emissions (DPOAEs) and behavioral audiometry are routinely used for hearing screening and assessment. These measures provide related information about hearing status as both are sensitive to cochlear pathologies. However, DPOAE testing is quicker and does not require a behavioral response. Despite these practical advantages, DPOAE testing is often limited to screening only low- and mid-frequencies. Variation in ear canal acoustics across ears and probe placements has resulted in less reliable measurements of DPOAEs near 4 kHz and above where standing waves commonly occur. Stimulus calibration in forward pressure level and responses in emitted pressure level can reduce measurement variability. Using these calibrations, this study assessed the correlation between audiometry and DPOAEs in the extended high frequencies where stimulus calibrations and responses are most susceptible to the effect of standing waves. Behavioral thresholds and DPOAE amplitudes were negatively correlated, and DPOAE amplitudes in emitted pressure level accounted for twice as much variance as amplitudes in conventional sound pressure level units. Both measures were correlated with age. These data show that extended high-frequency DPOAEs are sensitive to differences in audiometric thresholds and highlight the need to consider calibration techniques in clinical and research applications of DPOAEs.
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I. INTRODUCTION

The extended high-frequency (EHF) region at the base of the cochlea appears highly susceptible to dysfunction. Factors commonly associated with sensorineural hearing loss, such as aging and noise exposure, often affect hearing in the extended high frequencies. For example, many previous studies have shown that EHF hearing begins to decline at around 30 years of age, gradually worsening and extending to lower frequencies with each decade of life (Carcagno and Plack, 2020; Lee *et al.*, 2012; Wang *et al.*, 2021). Some studies have also shown that a history of noise exposure is associated with poorer hearing sensitivity in the extended high frequencies (Liberman *et al.*, 2016), though not all studies of young, noise-exposed adults have replicated this finding (Bharadwaj *et al.*, 2022). In addition to age and noise exposure, ototoxic medications and some systemic illnesses can result in elevated EHF thresholds before audiometric thresholds worsen at lower frequencies (Fausti *et al.*, 1994; Lough and Plack, 2022). A history of ear infections has also been linked to EHF hearing loss, even after active disease has resolved (Hunter *et al.*, 1996). In addition, EHF hearing loss is sometimes found in pediatric populations with otherwise normal hearing sensitivity. In a study of over 500 children aged 7 to 19, approximately 7% showed EHF hearing loss (Mishra *et al.*, 2022).

Good EHF hearing sensitivity is less critical than the mid-frequencies for understanding speech in quiet but likely has important implications for hearing in difficult listening conditions. Speech recognition in noise has been shown to be poorer when the signal is lowpass filtered at 8 kHz (Motlagh Zadeh *et al.*, 2019). Extended high frequencies are also salient cues for localization (Langendijk and Bronkhorst, 2002) and loss of EHF hearing is a significant predictor of self-reported hearing difficulty in noise (Hunter *et al.*, 2020).

Despite the prevalence of EHF hearing loss and its implications for hearing in noise, hearing thresholds are not commonly tested at those frequencies in a standard audiological assessment. Widespread clinical use of EHF audiometric testing is limited in part because it requires specialized headphones with additional calibrations that not all clinics may have. EHF testing also prolongs testing time without a direct impact on hearing aid fitting since traditional hearing devices prioritize amplification of lower frequencies. Even if an audiologist has the clinical time and resources to measure EHF thresholds, behavioral audiometry at any frequency requires patient feedback. Some patient populations—such as infants, young children, and patients who are severely ill during chemotherapy or aminoglycoside

[a)]Email: hauser23@purdue.edu

treatment—may be unable to complete traditional hearing testing regardless of the frequency range being tested. Thus, alternative test procedures are needed.

Otoacoustic emissions (OAEs) have the potential to address these drawbacks of behavioral testing. OAEs are physiological responses to sound generated in the cochlea and are measurable in the ear canal. In a healthy ear, nonlinear interaction between two tones on the basilar membrane results in distortion products (Robles *et al.*, 1991). Active cochlear responses supported by outer hair cell mechanics is thought to give rise to the nonlinearities that create this response, so absent or reduced DPOAEs are interpreted as indicating abnormal outer hair cell function. Because both the stimulus and the response must travel through the outer and middle ear systems, these measurements can also be affected by the acoustics of these systems and conductive hearing losses. So, DPOAEs must be interpreted in the context of other assessments of outer and middle ear health (e.g., otoscopy, tympanometry).

DPOAEs are widely used in the audiology clinic as a quick, non-invasive, measure of cochlear health. They are commonly used for hearing screenings in newborns and in populations that are difficult to test behaviorally (Lonsbury-Martin and Martin, 1990). DPOAEs are often more sensitive to acoustic overexposure (Lapsley Miller *et al.*, 2006) and ototoxic drugs (Stavroulaki *et al.*, 2001) than behavioral audiometry, so they are valuable for monitoring hearing. In fact, high frequency DPOAEs are commonly part of ototoxic monitoring programs given their high sensitivity to ototoxic damage (Reavis *et al.*, 2008). In research settings, DPOAEs are also frequently used to monitor hearing in animal models and to assess the effects of noise, ototoxic drugs, or aging (Whitehead *et al.*, 1992).

Though DPOAEs and the audiogram are both sensitive to hearing loss and outer hair cell dysfunction, previous comparisons between DPOAE amplitudes and audiometry have only found moderate correlations (depending on frequency) between the two measurements (Gorga *et al.*, 1997). While part of the discrepancy between the measurements likely results from differences in the physiological processes they reflect, extraneous factors related to the acoustic constraints inherent of OAE measurements also contribute (Heitmann *et al.*, 1996). DPOAEs are generated by a combination of two basic mechanisms: nonlinear distortion and linear reflection (Shera and Guinan, 1999). Interactions between the linear reflection and non-linear distortion components of the emission results in peaks and valleys of the response (Mauermann *et al.*, 1999; Talmadge *et al.*, 1999). While this fine structure is clearly visible when using swept tone stimuli, it is less readily apparent when using the discrete tone stimuli common in most clinical applications (Shaffer *et al.*, 2003). Because the two components of the emission have different phase delays, the fine structure can be mitigated by analyzing swept DPOAEs recordings using a time-frequency window to effectively separate just the distortion component and provide a more easily interpretable estimate of DPOAE amplitudes (Abdala *et al.*, 2015). Clinical DPOAE measurements that sparsely sample the frequency range at discrete points inherently capture a mix of reflection and distortion emissions and do not have enough information to disambiguate the two.

From a purely measurement perspective, calibration-related inaccuracies of stimuli levels have made it difficult to obtain repeatable measurements of high frequency otoacoustic emissions (Heitmann *et al.*, 1996). In clinical otoacoustic emission systems, ear canal acoustics are assessed by an in-ear calibration prior to testing. A calibration stimulus is played, and the sound levels in the ear are measured by the microphone in the probe used to record the emissions. The sound level at the probe is taken as a near approximation of the sound level at the tympanic membrane. While this estimation holds for low- and mid-frequencies, the difference between levels measured at the entrance of the ear canal and at the tympanic membrane can vary significantly for higher frequencies. At the probe, sound levels result from the superposition of both the forward-traveling sound wave and the waves reflected by the tympanic membrane, creating standing waves. The resulting peaks and valleys in the frequency response underestimate the sound levels reaching the eardrum at some frequencies and overestimate the levels at others, adjusting stimulus levels erroneously to compensate. The specific frequencies affected, and the degree to which this affects the sound level reaching the eardrum, vary with probe placement (i.e., insertion depth) and individual ear anatomy (Charaziak and Shera, 2017; Maxim *et al.*, 2019). Variation across tests—both during repeated measurements of the same ear and across ears—can lead to as much as 20 dB differences in the level of the stimulus that reaches the tympanic membrane (Souza *et al.*, 2014).

Although the inaccuracies resulting from standing waves in ear-level calibrations have long been acknowledged, the implementation of a practical solution is still relatively new for otoacoustic emissions. One such technique estimates the Thevenin-equivalent impedance and sound pressure from the probe (Scheperle *et al.*, 2008) to separate the forward-traveling and reflected waves in the ear canal and estimate their levels independently, reducing the effect of standing waves. When using this technique, stimulus levels are measured in dB forward pressure level (FPL). FPL calibrations help control the stimulus levels reaching the tympanic membrane, but the emission amplitude recorded at the entrance to the ear canal will also be affected by reflections. Separating the forward- and backward-traveling waves also makes calculation of the emission's sound level leaving the ear straightforward, so the level of the emission can be converted from sound pressure level (SPL) at the microphone to dB emitted pressure level (EPL) which approximates the level of sound at the tympanic membrane traveling toward the microphone (Keefe, 1997; Charaziak and Shera, 2017).

Because the acoustic issues that FPL and EPL calibration methods handle are sensitive to the depth of the probe in the ear, these methods should improve intrasubject variability by removing the effect of probe placement.

Experimental studies have confirmed this prediction, finding that OAE amplitudes are less dependent on probe position when stimuli are calibrated in FPL than with SPL (Scheperle *et al.*, 2008) and that EPL correction further improves reliability (Charaziak and Shera, 2017). Maxim *et al.* (2019) directly compared these calibration methods and found improved test-retest repeatability of OAE amplitudes using FPL/EPL calibrations compared to SPL/SPL and FPL/SPL. FPL and other depth-compensation calibration methods also can improve test-retest repeatability of audiometric thresholds (Lee *et al.*, 2012; Souza *et al.*, 2014). The improvements are generally greatest in the high frequencies (>4 kHz) where the effect of standing waves is most prominent.

Given the clinical value of testing in the extended high-frequencies, and the benefits of DPOAEs over traditional behavioral audiometry, we investigated whether FPL and EPL calibration, methods that control for additional sources of extraneous noise in DPOAE measurements, improve DPOAE estimates of behavioral thresholds in adults. We also explored the effect of age on EHF measurements as both otoacoustic emissions and behavioral thresholds in the standard hearing range are known to covary with age (Lee *et al.*, 2012; Oeken *et al.*, 2000).

II. MATERIALS AND METHODS

A. Participants

This study included 166 participants (61 male), aged 18 to 60 years (mean = 32.3 years, SD = 13.4 years) from Purdue University and the Greater Lafayette, Indiana region. They were recruited as part of a larger study of individual differences in physiological markers of cochlear synaptopathy in the normal hearing population (Bharadwaj *et al.*, 2022). All participants had normal hearing sensitivity in at least one ear from 250 to 8000 Hz, defined as thresholds less than or equal to 25 dB HL. For subjects who met this threshold criteria in both ears, responses were averaged across ears. All subjects reported no history of neurological disorders or ear pathology. All procedures were approved by the Purdue University IRB (No. 1609018209), and participants were compensated for their time.

B. Behavioral audiometry

All testing took place in an electrically shielded, sound-attenuating booth. Otoscopy confirmed ear canals were clear of obstructing cerumen. As normal hearing sensitivity in the standard clinical range was a requirement for the broader study, all participants completed behavioral audiometry before further testing. Audiometry was completed using the GSI Audio Star Pro (Eden Prairie, MN) with Sennheiser HDA 200 high-frequency circumaural headphones, which have shown to have good test-retest reliability (Frank, 2001). Thresholds at 0.25, 0.5, 1, 2, 3, 4, 6, 8, 10, 12.5, 14, and 16 kHz were determined using pulsed tones and the modified Hughson-Westlake procedure. Participants were asked to report detection of a tone by pushing a button. Thresholds were measured in dB HL with stimulus levels calibrated to ANSI S3.6 standards and normed in accordance with ISO389 Part 1. High-frequency (3–8 kHz) and EHF (greater than 8 kHz, i.e., 10–16 kHz) pure tone averages were calculated for each subject. For frequencies where no response could be obtained at the limits of the audiometer, the threshold for that frequency was omitted from the average.

C. Compensation for individual ear canal acoustics

Additional corrections to compensate for the acoustics of an individual's ear canal and probe placement were made for DPOAE measurements but not for behavioral audiometry. As in Bharadwaj *et al.* (2022), the Thevenin-equivalent source pressure and impedance across frequency of the probe was estimated with the built-in ER-10X calibrator (Etymotic Research, Elk Grove Village, IL). The probe was coupled to loads where the impedance can be calculated (i.e., an 8 mm diameter brass tube with five length settings) from physical principles. A "calibration error" was derived based on the deviation between the measured and calculated load impedance of each length of tube (Scheperle *et al.*, 2011). Typical errors for the data collected in this study were less than 0.05. Errors of less than 1 were considered good calibration and required before moving to ear calibration.

Following probe calibration, the probe was coupled to an appropriately sized ear tip and placed securely in the subject's ear canal. Repeated 90-dB peSPL clicks with a flat incident power spectrum in the 0–10 kHz range were presented to estimate immittance properties of the subject's ear and derive the appropriate voltage to FPL transfer function for a given probe fit. Low-frequency absorbance was required to be less than 29% and the admittance phase was greater than 44° to ensure the probe was adequately sealed in the ear canal before DPOAE measurements were made (Groon *et al.*, 2015). DPOAE levels were converted from dB SPL to dB EPL using the individualized transfer function derived from each participant's in-ear calibration as in Charaziak and Shera (2017). The values required to convert the emission level from dB SPL to dB EPL (i.e., ear canal reflectance, pressure reflectance of the probe, and one-way ear canal delay by frequency) were obtained during the initial ear calibration.

D. Distortion product otoacoustic emissions

Participants watched a captioned and muted movie of their choosing while seated comfortably in the sound-treated booth. Following in-ear calibration of the probe, primary tones were swept downward logarithmically at a rate of one-third octave/s with a frequency ratio of $f1 = f2/1.225$. Two stimulus sweeps with overlap in frequencies were presented. For the first, f2 ranged from 16 to 4 kHz; for the second, f2 ranged from 8 to 2 kHz. We found excellent agreement in DPOAE amplitudes from the two sweeps in the overlapping frequency range. The frequencies of the primary tones were held constant for 0.5 s at the beginning and end of each sweep. Stimuli were presented at f1 = 66 and f2 = 56 dB FPL. Twenty-five trials of each sweep were presented. The first trial and all trials with energy greater than two times the mean absolute deviation above the median were not included in the final averaged response. A least squares approach was used to calculate the magnitude of the primary distortion product at 2f1 − f2 after averaging the response across trials with a 0.5 s windows to extract only the distortion-component of the emission (Abdala *et al.*, 2015). DPOAE levels were summarized by averaging emissions for a high (3–8 kHz) and extended high (9–16 kHz) frequency range of f2. Most analyses included all data, regardless of signal-to-noise ratio (SNR); however, some analyses were limited to a subset of data in which the average DPOAE amplitude in SPL was at least 6 dB greater than the average noise floor SPL in the same frequency range. As noted in Charaziak and Shera, expressing the OAE in EPL units does not affect the SNR as it is a scale factor applied on a per-frequency basis. Furthermore, because the noise in OAE measurements comes from extraneous contributions such as physiological and room noise and does not originate at the eardrum, there are no principled ways to transform noise levels to EPL units. Whether the full data or SNR-filtered data were used is indicated with each result.

III. RESULTS

Individual differences in ear canal acoustics were greatest at frequencies near 4 kHz and above (Fig. 1). There are peaks in variability around 4 and 8 kHz, which correspond to the quarter-wave (open triangle) and half-wave (filled triangle) resonance frequencies, respectively, of the typical human ear canal. Sound levels are much less variable below 3 kHz, where the standard deviation was less than 5 dB.

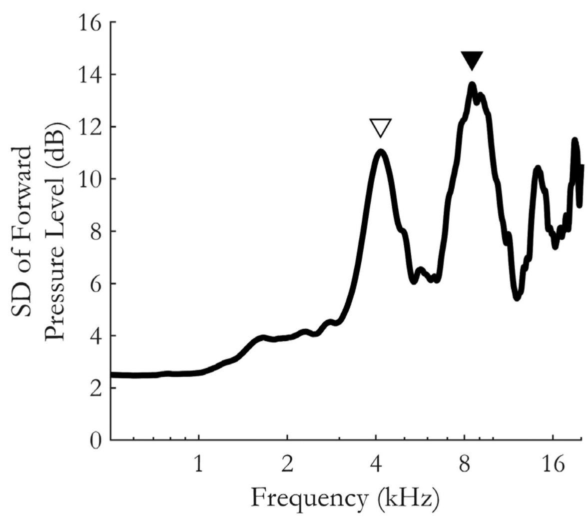

FIG. 1. Standard deviation (SD) of in-ear calibrated forward pressure level with constant voltage stimulation (n = 166). Standard deviation increases with increasing frequency with local maxima near 4 and 8 kHz. These peaks reflect the average quarter-wavelength resonance (unfilled triangle) and the half-wavelength resonance (filled triangle).

As the subjects had normal hearing sensitivity in the standard clinical frequency range (0.25–8 kHz), most participants were expected to have present DPOAEs in the high-frequency range (3–8 kHz). Our results were consistent with this expectation—high-frequency DPOAEs were at least 6 dB above the noise floor for 163 of 166 subjects at frequencies from 3 to 8 kHz, albeit spanning a wide range of amplitudes (–18.86–13.62 dB EPL). Hearing thresholds were not controlled in the EHF range, hence a larger range of DPOAE amplitudes was observed for these frequencies (–36.53–1.64 dB EPL). The median DPOAE and noise floor for all subjects is plotted in Fig. 2. The surrounding gray areas capture the data within the 5th and 95th percentiles of the data.

A. DPOAE relationship to audiometry

In the EHF range, DPOAE amplitudes were negatively correlated with audiometric thresholds. Significant correlations between DPOAE amplitudes and audiometric thresholds were present whether the emission was measured in SPL (Fig. 3(A); $r = -0.326$, $p < 0.001$) or EPL (Fig. 3(B); $r = -0.466$, $p < 0.001$). We then asked whether DPOAEs measured in EPL units accounted for more of the variance in audiometric data compared to DPOAEs expressed in SPL units at the OAE microphone. To avoid making distributional assumptions, we performed a permutation test comparing the difference in R^2 between EPL and SPL units to an approximated null distribution where the EPL and SPL labels were shuffled 1×10^6 times. We found that the R^2 value with EPL units ($R^2 = 0.217$) is significantly higher than SPL ($R^2 = 0.106$), accounting for twice as much variance, though at the edge of statistical significance under conventional criteria ($p = 0.041$). Since all DPOAEs were collected only with FPL-calibrated stimuli, this dataset only allowed for analysis of the effect of converting DPOAE

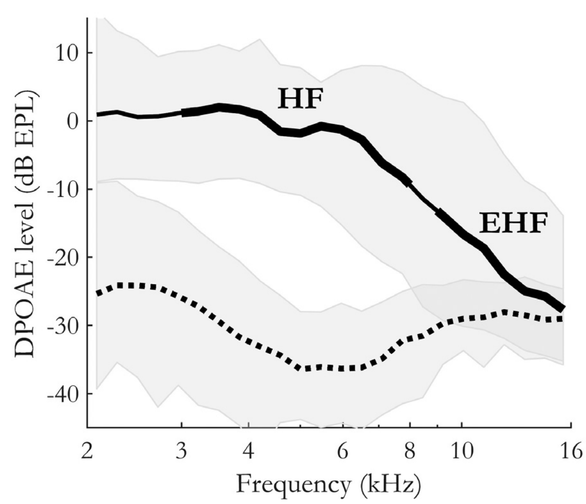

FIG. 2. Median DPOAE (solid) and noise floor (dotted) across all 166 subjects. Bolded sections represent the two primary frequency ranges evaluated in this study—the high frequency (HF, 3–8 kHz) and EHF range (9–16 kHz). Grey areas represent the data within the 5th and 95th percentiles of the dataset.

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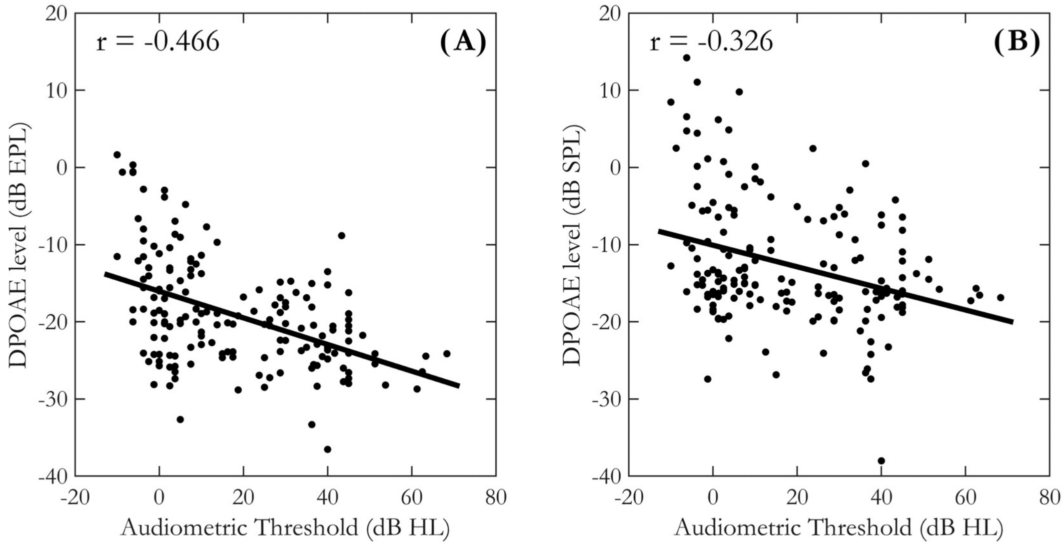

FIG. 3. Audiometric thresholds averaged across frequencies above 8 kHz compared to average DPOAE amplitudes in the same frequency range for all participants (n = 166). (A) shows the relationship when DPOAE amplitude is in EPL units and (B) shows the relationship when DPOAE amplitude is in SPL units.

amplitude from SPL to EPL units, not the effect of calibrating the stimulus in SPL compared to FPL, which is also likely to contribute to the strength of this correlation.

Although the EPL calibration method increased the correlation between DPOAE amplitudes and audiometric thresholds, DPOAE amplitudes varied among individuals, even when behavioral hearing thresholds were similar. For example, participants with EHF audiometric thresholds near zero had DPOAE amplitudes spanning a 30 dB range.

More than half of participants with normal behavioral hearing thresholds (<25 dB HL) in the EHF range had DPOAE amplitudes at least 6 dB above the noise floor, but the SNR of the DPOAE in the extended high frequencies decreased with increasing degree of hearing loss (Fig. 4). Audiometric thresholds and SNR were significantly correlated ($r = -0.406$, $p < 0.001$). 107 of 166 ears had an average extended high frequency DPOAE amplitude at least 6 dB above the noise floor.

We then assessed whether the correlations between audiometric thresholds and DPOAE amplitudes held when the 59 participants with an EHF SNR below 6 dB were excluded (Fig. 5). Correlations were not significantly different after removal of the low-SNR points. As before (Fig. 3), R^2 was higher with EPL ($R^2 = 0.224$) than SPL ($R^2 = 0.091$) for the SNR-filtered data. The difference in R^2 remained statistically significant ($p = 0.044$) using the same permutation test used to assess the R^2 difference in the full dataset.

Thus far, we have assessed the relationship between average audiometric thresholds and average DPOAE amplitudes, but single frequency points more comparable to the discrete-tone testing used clinically can be extracted from the results obtained using a swept-tone paradigm. So, rather than looking across an average frequency range, we compared DPOAE amplitudes in dB EPL at two EHF points. Figure 6 shows the correlation between audiometric thresholds and DPOAE level at 10 kHz [Figs. 6(A), 6(B)] and 12.5 kHz [Figs. 6(C), 6(D)]. Low-SNR (<6 dB) points were excluded in Figs. 6(B) and 6(D). Consistent with the average EHF data, DPOAE amplitudes decreased with an increasing degree of hearing loss. All correlations were significant, though slightly stronger when including all points regardless of SNR [(A) 10 kHz all points: $r = -0.323$, $p < 0.001$; (B) 10 kHz, >6 SNR: $r = -0.292$, $p = 0.001$; (C) 12.5 kHz all points: $r = -0.4$, $p < 0.001$; (D) 12.5 kHz, >6 SNR: $r = -0.391$, $p = 0.001$). The number of ears meeting the SNR criteria was fewer for 12.5 than 10 kHz.

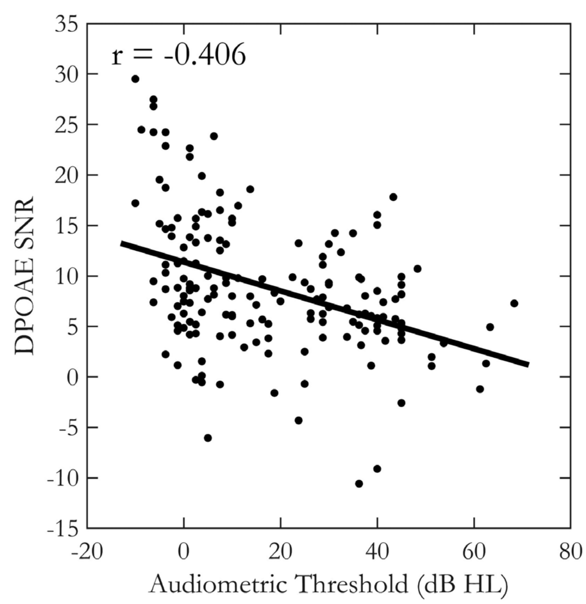

FIG. 4. Audiometric thresholds correlate with the SNR of the DPOAE in the EHF range. SNR was calculated as the average DPOAE level minus the average noise floor in the same frequency range.

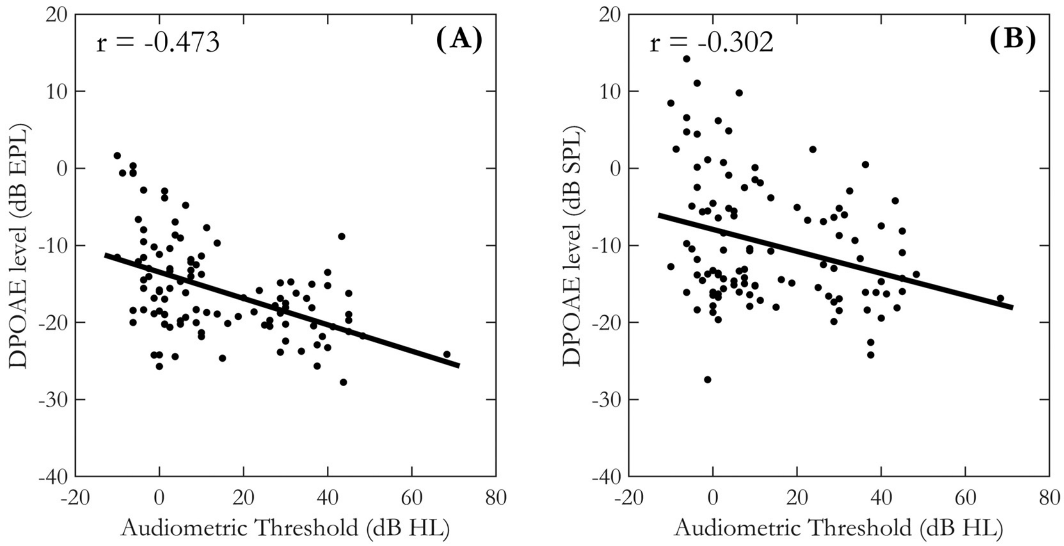

FIG. 5. Same comparisons of as in Fig. 3 but only points from participants with an SNR exceeding a 6 dB criterion were plotted (n = 107). (A) DPOAE amplitudes are presented in dB EPL and (B) presented DPOAE amplitudes in dB SPL.

We also investigated whether high-frequency DPOAEs were predictive of EHF hearing loss, as prior studies have found (Lough and Plack, 2022). To see whether DPOAE amplitudes in one frequency range were indicative of change in higher frequency regions, we compared EHF audiometry to high-frequency DPOAE amplitudes (Fig. 7). DPOAE amplitudes in the high-frequency range proved to be lower as EHF hearing thresholds worsened ($r = -0.277$,

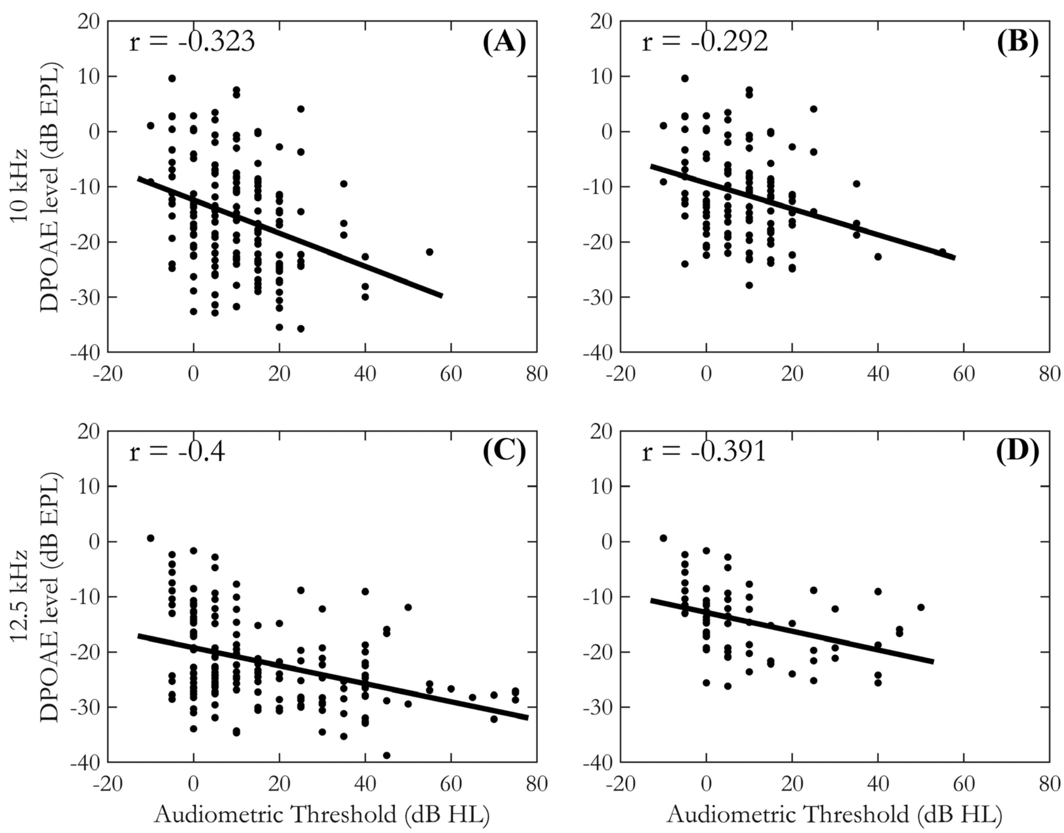

FIG. 6. Comparison of audiometric thresholds with DPOAE amplitudes (dB EPL) at single frequency points in the EHF range. (A) Comparison at 10 kHz with all points regardless of SNR included (n = 166) and (B) comparison at 10 kHz of only points with at least a 6 dB SNR at that frequency (n = 122). (C) Comparison at 12.5 kHz with all points regardless of SNR included (n = 166) and (D) comparison at 12.5 kHz of only points with at least a 6 dB SNR at that frequency (n = 67).

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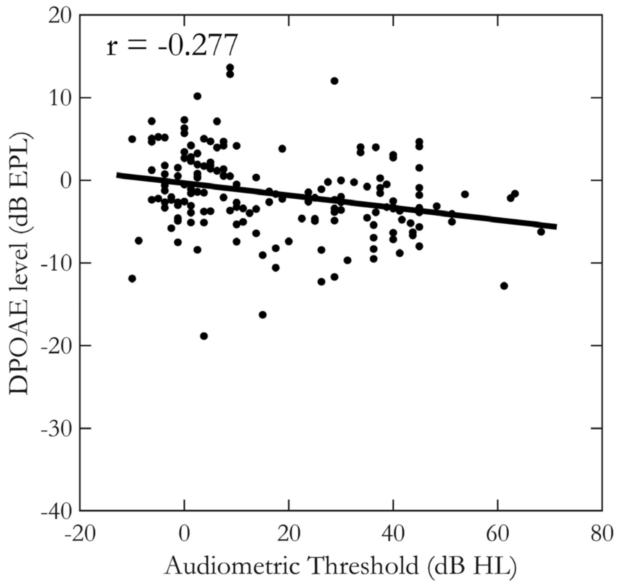

FIG. 7. High frequency (3–8 kHz) DPOAE amplitudes are negatively correlated with EHF (10–16 kHz) audiometric thresholds.

$p < 0.001$). Consistent with these prior studies, our results indicate that DPOAEs from 3 to 8 kHz may be sensitive to EHF hearing loss and thus serve as an early indicator of hearing loss in this EHF range.

B. Correlations with age

As expected, age was significantly correlated with EHF audiometric thresholds [Fig. 8(A); $r = 0.852$, $p < 0.001$]. Audiometric thresholds in the EHF range worsened with age, despite all subjects having normal hearing through 8 kHz. In our cohort, nearly every participant over the age of 40 had elevated EHF thresholds. Similarly, as age increased, EHF DPOAE amplitudes declined significantly ($r = -0.371$, $p < 0.001$). Although audiometric thresholds and DPOAE amplitudes in the extended high both covary with age, DPOAE amplitudes in dB EPL are still predictive of audiometric thresholds after controlling for age (Table I). A type II ANOVA revealed both age and DPOAE amplitude to be significant predictors of audiometric thresholds in the EHF range, suggesting DPOAE amplitude uniquely contributes to predicting thresholds even after accounting for age.

TABLE I. Results of type II ANOVA reveal a main effect of both age and DPOAE amplitude on audiometric thresholds in the EHF range.

	Sum of squares	DF	F	p-value
Age (Years)	31605.0	1	351.13	<0.001
DPOAE amplitude (dB EPL)	1546.4	1	17.18	<0.001
Residual	14671.4	163		

IV. DISCUSSION

Change in EHF thresholds is often an early indicator of cochlear pathology, but hearing in this range is not commonly assessed in the audiology clinic due to equipment and time limitations. If the methodological limitations that introduce extraneous sources of variability obscuring the relationship between DPOAE amplitudes and audiometric thresholds are overcome, DPOAEs would be an ideal tool to assess EHF hearing as they can quickly be measured without a behavioral response from the listener.

Here, we tested whether FPL and EPL calibration methods, which account for individual variation in stimulus levels at the eardrum, improve our ability to use DPOAEs to estimate behavioral thresholds in the EHF range. Our results demonstrated a strong correlation between audiometric thresholds and DPOAE amplitudes in the EHF range which was somewhat strengthened by converting DPOAE amplitudes from SPL to EPL units. This relationship between DPOAE amplitudes and audiometric thresholds was similar when only evaluating ears which met our +6 dB SNR

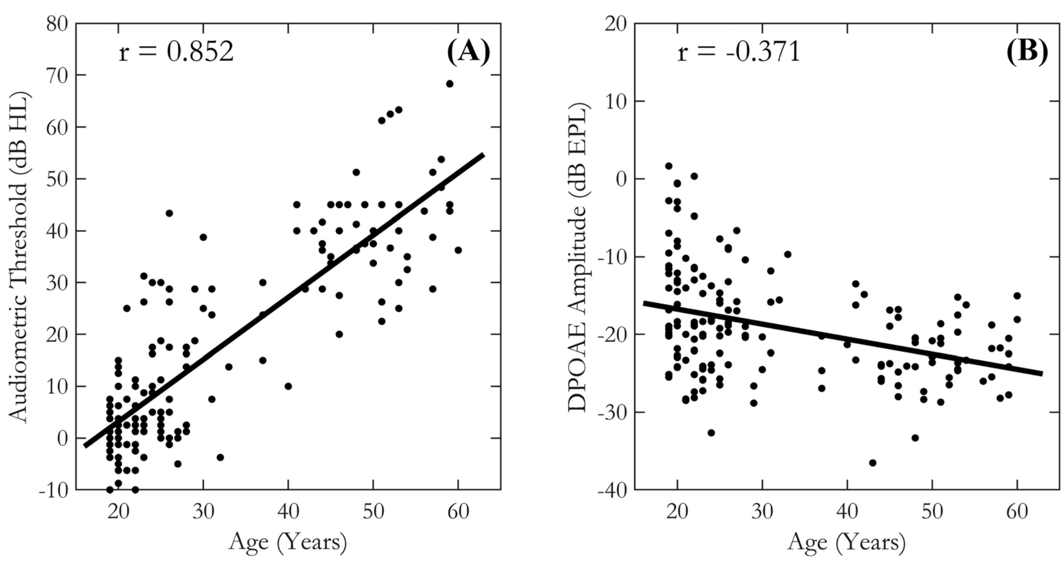

FIG. 8. Age is correlated with both audiometric thresholds (A) and DPOAE amplitudes (B) in the EHF range.

criterion. Furthermore, we found that both behavioral thresholds and DPOAE amplitudes were highly correlated with age in the EHF range, even when hearing was normal at frequencies from 250 through 8000 Hz.

A. Methodological considerations for DPOAEs

EHF testing is especially sensitive to the acoustics of the ear canal, and this has made DPOAE measurements that use SPL stimulus calibrations less reliable at frequencies near 4 kHz and above. Studies have shown that FPL calibrations improve the reliability of DPOAE measurements over the standard SPL calibration (Maxim *et al.*, 2019) and the results of this study suggest that use of FPL/EPL may help to expand the clinical use of DPOAEs to estimate hearing thresholds. With stimuli calibrated in FPL, which already reduces the variance between tests, measuring the DPOAE in EPL improves the correlation between audiometric thresholds and DPOAE amplitudes. Handling calibration of not only stimulus levels but the level of the emission appropriately further reduced undesirable measurement noise to improve the diagnostic utility of DPOAEs.

A second potential source of variability, the interaction of distortion and reflection components, was not investigated in this study. Because our analyses focused primarily on the average DPOAE amplitude across a few frequency points, we did not see an impact of using only the distortion component of the DPOAE compared to the mixture of distortion and linear coherent reflection. The fine structure of the response is present in our data when using a smaller analyses window in the least squares fitting procedure, but those fluctuations largely are canceled out by averaging across frequency. Comparison of DPOAE amplitudes from the composite DPOAE did not change the results or the relationship with audiometric thresholds presented here.

This study utilized only one set of parameters, but L1 and L2, the level ratio, and the frequency ratio have all been shown to influence the DPOAE amplitude. The optimal frequency ratio for DPOAE varies as a function of frequency and level ratio (Abdala, 1996; Johnson *et al.*, 2006), and it is possible that the optimal ratio in the extended high frequency range may not be $f2/f1 = 1.225$ as tested in this study. The optimal frequency ratio arises from the characteristics of cochlear tuning on the basilar membrane which varies as a function of frequency, implying that extended high frequency emissions could be greater with a different frequency ratio or level combination. Recent work from Stiepan and Dhar (2025) shows that a frequency ratio of 1.14 to 1.16 would be more appropriate for measurement of extended high frequency DPOAEs. However, the frequency ratio chosen for this study, 1.225, is similar to the ratios chosen in prior studies of EHF OAEs [∼1.2, e.g., Dreisbach *et al.* (2006) and Portugal *et al.* (2024)].

Swept DPOAE methods have been shown to give similar measurements of OAE magnitude and phase as traditional discrete stimuli, at least for slower sweep rates (Long *et al.*, 2008)—allowing for assessment across a larger frequency range with little difference in time burden. Though few studies have evaluated swept DPOAEs in the EHF region, Glavin *et al.* (2023) found a good match between discrete and swept DPOAEs at 10k Hz. The results of the present report are also similar to recent findings from Jedrzejczak *et al.* (2023) which found correlations in the EHF range between DPOAEs and thresholds using discrete tone stimuli. Though swept tone DPOAEs are used in research applications [e.g., Abdala *et al.* (2015)], their analysis is more complex, and norms have not been developed, which limits their current utility in clinical settings. At present, there is also no standardized protocol for swept otoacoustic emissions and their analysis, but adjustments to the least squares fitting parameters can affect the resulting calculation of DPOAE amplitudes. Accordingly, discrete tone DPOAEs are likely to be more readily interpretable in clinical settings until more user-friendly analysis protocols are developed. However, the FPL and EPL calibration techniques are not exclusive to swept DPOAEs and are beneficial regardless of stimulus paradigm.

B. Other sources of variability

Even when controlling stimulus levels, DPOAE amplitudes were highly variable across individual participants with similar hearing thresholds. EHF audiometric thresholds can also be affected by issues related to standing waves in the ear canal. Like the DPOAEs probe, sound levels reaching the eardrum are affected by insertion depth, so thresholds are more variable in the EHF range when using insert earphones (Lapsley Miller *et al.*, 2018). However, the high-frequency headphones used for this study have been shown to have reasonable test-retest reliability. Frank (2001) found that 98% of thresholds obtained with Sennheiser HDA 200 headphones were within 10 dB of the thresholds on subsequent tests. Though this range is accepted clinically, it is another source of noise that may obscure the true relationship between tests. Depth-compensated calibrations such as FPL can also be used for measurement of EHF audiometric thresholds, though test-retest of high frequency thresholds was still ∼10 for at least one study (Lee *et al.*, 2012).

Accurate calibrations for both measures, separation of the distortion and reflection components of the DPOAE, and careful data collection are not likely to result in a perfect correlation between DPOAEs and behavioral thresholds. The audiogram provides a more functional assessment of perception while DPOAEs reflect cochlear function of the outer hair cells. Though cochlear dysfunction is likely to affect both, the pathways they assess differ. However, the more the non-physiologic sources of noise that contaminate diagnostic tests are controlled, the greater confidence we can have that the results reflect the physiologic processes our measures were designed to assess. Diagnostic precision is key to early identification and treatment of hearing loss and, more broadly, will improve understanding of individual differences that matter for hearing outcomes.

C. Relationship with age

Multiple studies have shown that age is a strong predictor of hearing thresholds (Carcagno and Plack, 2020; Grant *et al.*, 2022; Lee *et al.*, 2012; Wang *et al.*, 2021); our results show a similar relationship between age and DPOAE emission amplitudes. Although our cohort was chosen specifically to have normal hearing sensitivity through 8 kHz, nearly half of our subjects had EHF hearing loss, and the proportion of subjects with EHF loss grew with each decade of life. This subclinical hearing loss may have practical implications for speech-in-noise understanding and suggests that EHF audibility may be a potential confound for studies relating age to auditory perception (Lough and Plack, 2022).

D. Potential clinical applications

Future work is needed to implement new calibration strategies like FPL into clinical systems. Translation to the audiology clinic and expanded use in research settings may rely on the development of accessible hardware and software. The equipment used for this study (ER-10X) is expensive and no longer commercially available, but alternative custom calibration tubes can be made (Scheperle *et al.*, 2008). Other strategies have been suggested to improve calibration-related errors (Souza *et al.*, 2014), and complex integrated pressure may be a more practical calibration method to implement than FPL (Nørgaard and Bray, 2023). More studies will be needed to fully optimize calibration, data collection, and data analysis protocols to ensure robust estimates of DPOAEs can be collected efficiently.

If such calibrations can be implemented clinically, one valuable use-case would be ototoxicity monitoring programs. Measuring EHF hearing may allow for earlier identification of hearing loss, leading to better informed individualized treatment plans and clinical recommendations. For example, the American Academy of Audiology recommends that persons undergoing treatment with an ototoxic medication should receive hearing screenings before, during, and after treatment, encouraging the use of high frequency audiometry and OAEs to monitor for hearing loss (Durrant *et al.*, 2009). A change in hearing and its effect on post-treatment quality of life can be considered in conjunction with the medical necessity of the treatment. Just as a change in audiometric thresholds may inform clinical decisions about treatment, decreases in DPOAE amplitude can indicate the need for medication adjustments to ensure hearing is preserved as much as possible.

V. CONCLUSION

Reliable physiological measures in the extended high frequencies are important for identifying hearing loss and improved diagnostic tools are needed for greater personalization of treatment for hearing loss. Critical to optimizing these measures is reducing known sources of variability as much as possible. With FPL/EPL calibration methods, DPOAEs can serve as a valuable tool to assess and monitor EHF hearing as it correlates with behavioral hearing thresholds.

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AUTHOR DECLARATIONS

Conflict of Interest

The authors have no conflicts to disclose.

Ethics Approval

This research was approved by the Purdue Institutional Review Board (No. 1609018209). Informed consent was obtained from all participants.

DATA AVAILABILITY

The data that support the findings of this study were originally collected as part of Bharadwaj *et al.*, 2022 and can be obtained from https://github.com/haribharadwaj/CommunBiol_CrossSpecies_Synaptopathy. This data set is also permanently archived using Zenodo and can be obtained from https://doi.org/10.5281/zenodo.6672827.

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