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Short-latency transient-evoked otoacoustic emissions as predictors of hearing status and thresholds^{a)}

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Estimating audiometric thresholds using objective measures can be clinically useful when reliable behavioral information cannot be obtained. Transient-evoked otoacoustic emissions (TEOAEs) are effective for determining hearing status (normal hearing vs hearing loss), but previous studies have found them less useful for predicting audiometric thresholds. Recent work has demonstrated the presence of short-latency TEOAE components in normal-hearing ears, which have typically been eliminated from the analyses used in previous studies. The current study investigated the ability of short-latency components to predict hearing status and thresholds from 1–4 kHz. TEOAEs were measured in 77 adult ears with thresholds ranging from normal hearing to moderate sensorineural hearing loss. Emissions were bandpass filtered at center frequencies from 1 to 4 kHz. TEOAE waveforms were analyzed within two time windows that contained either short- or long-latency components. Waveforms were quantified by root-mean-square amplitude. Long-latency components were better overall predictors of hearing status and thresholds, relative to short-latency components. There were no significant improvements in predictions when short-latency components were included with long-latency components in multivariate analyses. The results showed that short-latency TEOAE components, as analyzed in the current study, were less predictive of both hearing status and thresholds from 1–4 kHz than long-latency components.

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I. INTRODUCTION

Behavioral audiometric thresholds (hereafter referred to as “thresholds”) are generally considered the gold standard for assessing the degree of an individual’s hearing loss. Threshold measurement requires subject attention and cooperation, which may be unfeasible in some clinical populations such as infants and young children. In these cases, objective measures can provide useful estimates of thresholds. The auditory brainstem response (ABR) is an objective measure that is highly correlated with thresholds across a range of frequencies (e.g., Gorga *et al.*, 1985; Gorga *et al.*, 2006; van der Drift *et al.*, 1987; Johnson and Brown, 2005). However, older infants and young children typically must be sedated during ABR testing, which requires careful subject monitoring and in some cases may be medically contraindicated. Estimation of thresholds using the ABR most often relies on skilled human interpretation of recorded waveforms. For these reasons, ABR testing can be time consuming and expensive. Additionally, some clinics may not have access to ABR equipment, necessitating referral to a different facility for testing. It is therefore of clinical interest to maximize the accuracy of threshold prediction from other potentially available objective tests, such as otoacoustic emissions (OAEs).

OAEs are objective measures that have found wide application as a hearing screening tool. They are non-invasive, fast to administer, cost-effective, and accessible. Generated as a byproduct of the nonlinear amplification process in cochlear outer hair cells (OHCs) (Brownell, 1990), OAEs are measured using a tiny microphone placed in the ear canal. Transient-evoked (TE) OAEs are one subtype of OAE that are routinely measured in clinical settings. TEOAEs are elicited by brief stimuli such as clicks and provide information about OHC integrity across a broad range of frequencies (for a review, see Probst *et al.*, 1991; Glattko and Robinette, 2007). TEOAE measurement does not require sedation, and interpretation of results is typically straightforward. TEOAEs are useful for screening applications because they can quickly and accurately predict hearing status (i.e., normal hearing vs hearing loss) in a frequency-specific manner across a wide range of frequencies (e.g., Prieve *et al.*, 1993; Hurley and Musiek, 1994; Hussain *et al.*, 1998).

However, previous studies have generally shown that TEOAEs are less effective at predicting thresholds than predicting hearing status (e.g., Collet *et al.*, 1991; Suckfüll *et al.*, 1996; Wagner and Plinkert, 1999; Sisto *et al.*, 2007; but see also Vinck *et al.*, 1998). These studies have typically used analysis methods described by Bray and Kemp (1987) and Kemp *et al.* (1990), in which the first 2.5 ms of TEOAE waveforms were eliminated and an onset ramp was applied from 2.5 to 5.0 ms in order to reduce stimulus artifact. Because the latencies of TEOAEs decrease with increasing frequency, elimination of the first 5 ms would reduce high-frequency TEOAEs. Recent studies have shown that with appropriate measurement paradigms, artifact-free TEOAEs

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up to 16 kHz can be measured by retaining the first several ms of the waveforms (Goodman *et al.*, 2009; Keefe *et al.*, 2011).

Because of cochlear round-trip travel times, latencies of TEOAEs from 1 to 4 kHz are generally expected to occur after 5 ms (e.g., Tognola *et al.*, 1997; Sisto and Moleti, 2007). However, some studies have demonstrated that TEOAEs with energy in the 1–4 kHz range are obtainable within the first 5 ms following stimulus onset (e.g., Kruglov *et al.*, 1997; Withnell *et al.*, 2008; Goodman *et al.*, 2009; Goodman *et al.*, 2011; Sisto *et al.*, 2013). This indicates that short-latency portions of mid-frequency (1–4 kHz) TEOAEs have been reduced or eliminated in the analyses used by most previous TEOAE studies. In this paper, *short-latency* (SL) refers to TEOAEs with latencies that are shorter than expected, while *long-latency* (LL) refers to TEOAEs with latencies that are expected. The time frames delineating SL and LL TEOAEs are quantified precisely in Sec. II. Multiple TEOAE components are exhibited as SL and LL peaks across time when envelopes of TEOAE waveforms from 1 to 4 kHz are analyzed (Goodman *et al.*, 2009; Goodman *et al.*, 2011; Moleti *et al.*, 2012). The latencies and growth rates of LL peaks are consistent with generation by a linear coherent reflection mechanism (Shera and Guinan, 1999; Kalluri and Shera, 2007). The growth rates of SL peaks are less compressive relative to LL peaks, which may indicate that the two are generated either by different mechanisms, or at different cochlear locations, or both. Proposed generation mechanisms of SL components include nonlinear distortion (Withnell *et al.*, 2008; Goodman *et al.*, 2009; Moleti *et al.*, 2012) and linear coherent reflection at a location near, but slightly basal, to the traveling wave peak (Goodman *et al.*, 2011; Sisto *et al.*, 2013). A fast compression wave in the cochlear fluid (e.g., Ren, 2004) is also a possible mechanism. While the underlying generation mechanisms remain an area of investigation, it is also of interest to explore the clinical utility of SL components.

To the authors' knowledge, no studies have directly investigated the clinical utility of SL TEOAE components. TEOAEs appear to be composed of both SL and LL components, regardless of frequency (Goodman *et al.*, 2009). At high frequencies (≥ 5 kHz), SL and LL components both occur within the first 5 ms of the TEOAE waveform. By including the first 5 ms but not explicitly separating SL and LL components, some studies have indirectly investigated SL components (e.g., Goodman *et al.*, 2009; Keefe *et al.*, 2011). Keefe *et al.* (2011) showed accurate classification of hearing status from 1 to 10 kHz when including TEOAEs in the first 5 ms in analyses. They attributed the test performance at higher frequencies (≥ 5 kHz) to the inclusion of the first 5 ms of TEOAE waveforms; however, the relative contribution of SL and LL components to test performance was not specifically examined. Additionally, the ability to predict thresholds was not examined. While assessment of hearing at high frequencies can be useful for clinical purposes such as monitoring for ototoxicity and noise-induced hearing loss, hearing in the 1–4 kHz frequency range is critical for speech perception. Therefore, it is of clinical value to understand how to maximize predictions of hearing status and thresholds in the 1–4 kHz range using TEOAEs.

The purpose of the current study was to investigate the contribution of SL TEOAE components to predictions of hearing status and thresholds from 1 to 4 kHz. Because the generation of OAEs in humans is generally dependent on OHC integrity, it was hypothesized that SL components would contain useful information regarding OHC integrity, which is related to hearing status and thresholds. Because previous OAE studies have generally found improved predictions when using multivariate analyses relative to univariate analyses (e.g., Suckfüll *et al.*, 1996; Vinck *et al.*, 1998; Dorn *et al.* 1999), it was further hypothesized that predictions would improve when including SL and LL components in multivariate analyses.

II. METHODS

A. Subjects

Forty-eight adults ages 18 to 65 yr were recruited. Potential subjects were screened using a brief case history, otoscopy, 226 Hz tympanometry, and conventional audiometry. All testing took place in a double-walled sound booth. Using a clinical audiometer (GSI 61, Grason-Stadler), pure tone air- and bone-conduction thresholds were measured in 5-dB steps at five audiometric frequencies: 1, 1.5, 2, 3, and 4 kHz. Inclusion criteria consisted of having at least one air-conduction threshold ≤ 60 dB hearing level (HL, ANSI, 1996), air-bone gaps ≤ 10 dB at all frequencies, an unremarkable otoscopic examination, tympanometric results within normal clinical limits, and no reported history of middle ear surgery or retrocochlear pathology. Data from ears with thresholds > 60 dB HL between 1 and 4 kHz were excluded from analysis *at that frequency* for three reasons. First, pilot data showed that ears with severe and profound sensorineural hearing loss had TEOAE amplitudes that did not exceed the system distortion measured in an ear simulator (IEC 711, G.R.A.S. Sound & Vibration A/S). Second, physiologic data have suggested a lack of functioning outer hair cells when thresholds exceeded 60 dB (Stebbins *et al.*, 1979). Third, previous studies using OAEs to predict thresholds have used similar threshold exclusion criteria (Suckfüll *et al.*, 1996; Gorga *et al.*, 2003; Ellison and Keefe, 2005; Rogers *et al.*, 2010). The experimental protocol was approved by the Institutional Review Board at the University of Iowa, and written informed consent was obtained from all subjects.

A total of 77 ears (41 left ears, 36 right ears) from 46 subjects (24 males, 22 females) met the inclusion criteria. The mean subject age was 45.5 yr (SD = 14.9 yr, range = 20–65 yr). The distributions of thresholds at each frequency are shown by box and whisker plots in Fig. 1. Most subjects with hearing loss had sloping audiometric configurations, so their thresholds tended to increase with increasing frequency.

B. TEOAE measurement and extraction

Stimulus generation and response acquisition were performed using a desktop computer running custom software written in MATLAB (version 7.8.0 R2009a, The MathWorks, Inc.) and the software utility Playrec (Humphrey, 2008).

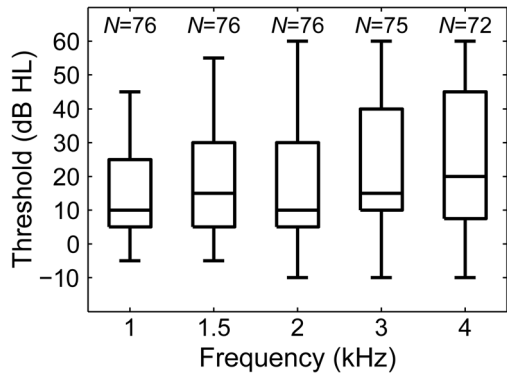


FIG. 1. Box and whisker plots of thresholds from 1 to 4 kHz. Boxes represent the upper quartiles, medians, and lower quartiles. Whiskers represent the maximum and minimum values. The total number of ears meeting the threshold inclusion criteria (≤ 60 dB HL) at each frequency is shown above each plot.

Stimuli were routed to an OAE probe microphone system (ER-10C, Etymotic Research) via a 24-bit sound card (Lynx L22, Lynx Studio Technologies) and a power amplifier (GFA-5002, Adcom). Recordings were routed from the microphone to the sound card, digitized at a sampling rate of 44.1 kHz, and saved to disk for offline analysis. During recording, subjects sat in a recliner inside the sound booth and watched a closed-captioned DVD movie with no sound.

Transient stimuli with a bandwidth of 1–4 kHz were presented at a rate of 33.3/s. The stimuli were presented using a nonlinear double-evoked paradigm (Keefe, 1998). This paradigm uses a series of three stimulus presentations to obtain each TEOAE waveform. The transient stimulus was first presented at 75 dB peak-equivalent sound pressure level (peSPL) from channel one of the loudspeaker assembly. The transient stimulus was then presented at 87 dB peSPL from channel two. Finally, the transient stimuli were presented simultaneously using the channels and levels previously indicated. The TEOAE waveform was obtained by adding the responses to the first two presentations and subtracting the response to the third. This process cancels the stimuli and leaves the nonlinearly growing portion of the TEOAE. The stimulus levels were chosen based on previous work examining SL TEOAEs and hearing status (Goodman *et al.*, 2009; Keefe *et al.*, 2011). Stimulus sound pressure levels were calibrated *in situ*. Synchronous TEOAE recordings ($N = 2048$) were obtained from each ear. Artifact rejection was performed during recording, as well as *post hoc*, using methods described in Goodman *et al.* (2009).

TEOAE waveforms were filtered with overlapping, 1/3-octave wide, finite impulse response filters with center frequencies (1, 1.6, 2, 3.2, and 4 kHz), close to standard audiometric frequencies. Prior to filtering, waveform onsets and offsets were ramped using raised-cosine windows with durations of 1.25 and 2.5 cycles of the filter center frequency, respectively. The number of filter coefficients ranged from 512 at 1 kHz to 128 at 4 kHz. Appropriate filter group delay corrections were applied. The time axes of the filtered TEOAE waveforms were set so that time zero corresponded to the location of the stimulus peak. In order to ensure responses free of system distortion artifact, the

waveform amplitudes from 0 to 0.75 ms were set to 0. This duration was chosen empirically based on recordings measured in an ear simulator.

Bandpass filtered TEOAEs were analyzed using two time windows that included either SL or LL components. The long-latency window used onset and offset times based on the 95% confidence intervals for the expected stimulus frequency (SF) OAE latencies in humans reported by Shera *et al.* (2002). These times were chosen under the assumption that LL TEOAEs and SFOAEs are generated by linear coherent reflection (Kalluri and Shera, 2007) and should therefore have similar latencies. The confidence intervals reported by Shera *et al.* (2002) were widened by a factor of 1.25 to account for potential differences due to higher stimulus levels (Schairer *et al.*, 2006). The short-latency window began at 0.75 ms and ended at the onset of the LL window. The time locations of the SL and LL windows at all frequencies are listed in Table I. The SL windows were earlier in time than the range of TEOAE latencies from 1 to 4 kHz reported by previous studies using approximately similar stimulus levels (see Fig. 7 of Tognola *et al.*, 1997; Fig. 1 of Sisto and Moleti, 2007), further suggesting that the SL windows encompassed TEOAEs with latencies that were earlier than expected. Previous TEOAE analysis methods (Bray and Kemp, 1987; Kemp *et al.*, 1990) have zeroed-out the amplitudes of the first 2.5 ms and applied an onset ramp 2.5 ms in duration. Therefore, the current method retained more of the SL portions of waveforms, especially at frequencies above 1 kHz. Representative examples of band-pass filtered TEOAE waveforms from three ears and the locations of the SL and LL analysis windows at 1, 2, and 4 kHz are shown in Fig. 2.

TEOAE signal and noise levels were calculated for the filtered waveforms. The recordings were separated into two buffers, with one buffer containing odd-numbered recordings and the other buffer containing even-numbered recordings. The time-domain signal was calculated as the mean of the two buffers and the noise was calculated as the mean of the difference of the two buffers (Kemp *et al.*, 1990). The root-mean-square (RMS) amplitude was calculated in dB sound pressure level (SPL) for the signal and noise. Some studies have obtained the best results using signal-to-noise ratio (SNR) as the predictor variable, including a minimum SNR criterion for the emission to be considered present (e.g., > 6 dB). However, in the current study, RMS amplitude was found to be a better predictor. Additionally, no minimum SNR criterion was implemented in the current study because analyses revealed a linear relationship

TABLE I. Time locations of the short- and long-latency windows at each filter center frequency. The long-latency window times were based on the 95% confidence intervals (widened by a factor of 1.25) for expected SFOAE latencies in humans (Shera *et al.*, 2002).

Frequency (kHz)	Short-latency (ms)	Long-latency (ms)
1	0.75–7.84	7.84–15.25
1.5	0.75–5.90	5.90–12.15
2	0.75–4.83	4.83–10.34
3	0.75–3.63	3.63–8.24
4	0.75–2.97	2.97–7.02

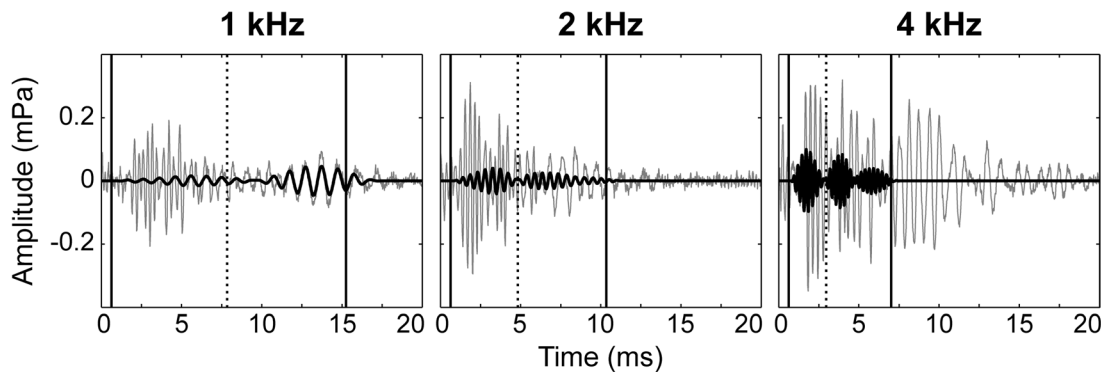


FIG. 2. Mean TEOAE waveforms bandpass filtered at 1, 2, and 4 kHz. The filter center frequencies are indicated at the top of each panel. Unfiltered waveforms are shown as thin gray tracings. Band-pass filtered waveforms are shown as thick black tracings. Data in each panel were obtained from a different normal-hearing ear. Time zero is relative to the location of the stimulus peak. The solid vertical lines represent the beginning and end of the SL and LL windows, respectively. The dotted vertical line represents the boundary between the two windows.

between TEOAE amplitude and thresholds across the range of thresholds included at all frequencies. For all analyses presented in this paper, RMS amplitudes in the SL and LL windows were used as the predictors.

C. Prediction of hearing status and thresholds

Prior to examining threshold predictions, the ability of SL and LL components to predict hearing status (normal hearing vs hearing loss) was assessed using receiver operator characteristic (ROC) analyses. ROC analysis has been implemented in many previous studies using OAEs as predictors of hearing status (e.g., Prieve *et al.*, 1993; Hurley and Musiek, 1994; Dorn *et al.*, 1999; Keefe *et al.*, 2011). ROC analysis is used to determine the ability of a variable to predict a binary outcome. In this case, the variable was amplitude (SL and LL amplitudes were assessed individually) and the outcome was normal hearing (thresholds ≤ 20 dB HL) or hearing loss (thresholds > 20 dB HL). The hit rate (number of ears with hearing loss correctly identified as having hearing loss) and false alarm rate (number of ears with normal hearing incorrectly identified as having hearing loss) were calculated for different criterion values of amplitude that classified the hearing status of an ear. The results were quantified by the area under the ROC curve (AROC). A larger AROC value indicates a more accurate prediction of audiometric status, with values of 0.5 corresponding to chance performance and 1 corresponding to perfect performance. AROC values were obtained for SL and LL amplitudes at each frequency. Standard errors of the AROC values were computed using methods described by Hanley and McNeil (1982).

Results of the ROC analyses (described in the next section) indicated that both SL and LL amplitudes were able to predict hearing status. Therefore, predictions of thresholds were examined using linear regression analyses, where SL and/or LL amplitudes were the predictor variables and threshold was the response variable. Slopes of the regression lines were examined for statistical significance ($\alpha = 0.05$) to determine if there was a linear relationship between amplitudes and thresholds. Prediction accuracy was quantified by the coefficient of determination (R^2) and standard error (in dB) resulting from the linear regression analysis.

Univariate predictions were first investigated, where predictions using SL and LL amplitudes were assessed individually. Two types of analyses were used for the univariate predictions. *On-frequency* analyses involved using amplitudes of TEOAEs filtered at a given frequency to predict thresholds at the same frequency, while *off-frequency* analyses involved using amplitudes of TEOAEs filtered at a given frequency to predict thresholds at a different frequency. It was of interest to examine off-frequency analyses because previous work has found that TEOAEs at a given frequency can be predictive of thresholds at a different frequency (Collet *et al.*, 1991). Multivariate linear regression analyses were also performed at each frequency to determine if the accuracy of threshold predictions improved by including SL and LL amplitudes together.

III. RESULTS

A. Prediction of hearing status

Figure 3 shows the results of the ROC analyses at each audiometric frequency. The AROC values and standard errors are plotted for SL and LL amplitudes. All AROC values were greater than 0.5, demonstrating that predictions were better than chance performance in all cases. There was

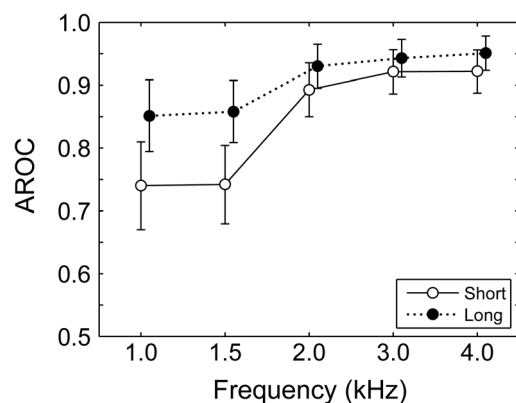


FIG. 3. Predictions of hearing status, quantified by the AROC, as a function of audiometric frequency. Separate AROC values were obtained using SL (open circles) and LL amplitude (filled circles). Error bars indicate ± 1 standard error.

TABLE II. Univariate threshold prediction results. Each cell shows the R^2 values from linear regression analyses using short- and long-latency amplitudes. The slopes of all regression lines were significantly different from zero ($p < 0.05$). The gray shaded boxes indicate on-frequency analyses (see text for details). The purpose of this table is to show which TEOAE frequency best predicts a given audiometric frequency. Comparisons should be made horizontally across columns to determine the TEOAE frequency that best predicts a given audiometric frequency.

Audiometric Frequency (kHz)	Short-latency Frequency (kHz)					Long-latency Frequency (kHz)				
	1	1.5	2	3	4	1	1.5	2	3	4
1	0.32	0.30	0.30	0.12	0.12	0.54	0.43	0.43	0.18	0.18
1.5	0.30	0.34	0.33	0.20	0.16	0.50	0.52	0.54	0.25	0.23
2	0.37	0.40	0.50	0.29	0.23	0.51	0.54	0.68	0.39	0.37
3	0.35	0.38	0.53	0.59	0.53	0.31	0.37	0.49	0.72	0.67
4	0.25	0.33	0.43	0.56	0.58	0.23	0.33	0.45	0.59	0.73

a trend of increasing predictive accuracy with increasing frequency for SL and LL amplitudes. From 1 to 1.5 kHz, AROC values were 0.74 for SL amplitude and 0.85–0.86 for LL amplitude, with little or no overlap between standard errors. This suggests that LL amplitudes were more accurate predictors at these frequencies. From 2 to 4 kHz, AROC values ranged from 0.89 to 0.92 for SL amplitude and from 0.93 to 0.95 for LL amplitude, with more overlap between standard errors. This suggests similar predictive accuracy between SL and LL amplitudes from 2 to 4 kHz. With the exception of AROC values obtained at 1–1.5 kHz using SL amplitude, the results are similar to those reported by previous studies (see Fig. 5 of Keefe *et al.*, 2011). The high test performance of both SL and LL amplitudes indicated that investigation of threshold predictions was warranted.

B. Prediction of thresholds

The results of univariate predictions of thresholds for the on- and off-frequency analyses are shown in Table II. R-squared values are shown in each cell. On-frequency analyses are indicated by the gray shaded regions. In all cases, the slopes of the regression lines were statistically significant ($p < 0.05$), indicating a linear relationship between thresholds and amplitudes. At a given audiometric frequency, the on-frequency analysis resulted in a better prediction than the off-frequency analyses. This was the case for both SL and LL amplitudes. The only exception was the prediction of the 1.5 kHz threshold, where LL amplitude at 2 kHz was a slightly better predictor than at 1.5 kHz.

Scatter plots of thresholds as a function of SL and LL amplitudes (on-frequency) are shown in Fig. 4. Predictions tended to improve with increasing frequency, as evidenced by increasing R^2 values. The slopes of all regression lines were significantly different from zero ($p < 0.05$). At all frequencies, LL amplitudes were better predictors than the corresponding SL amplitudes, as evidenced by higher R^2 values and lower standard errors.

Although SL amplitudes were less accurate predictors, they were still statistically significant predictors, and it was of interest to determine if they could be combined with LL amplitudes in a way that would improve threshold predictions. Therefore, SL and LL amplitudes (on-frequency) were included in multivariate linear regression analyses. Results showed minimal change in R^2 values between the univariate LL predictions and multivariate predictions, and the regression

coefficients for SL amplitude in the multivariate analyses were not statistically significant ($p > 0.05$). The differences in R^2 values between the three on-frequency analyses (SL univariate, LL univariate, and multivariate) were evaluated statistically using a bootstrap procedure (random resampling

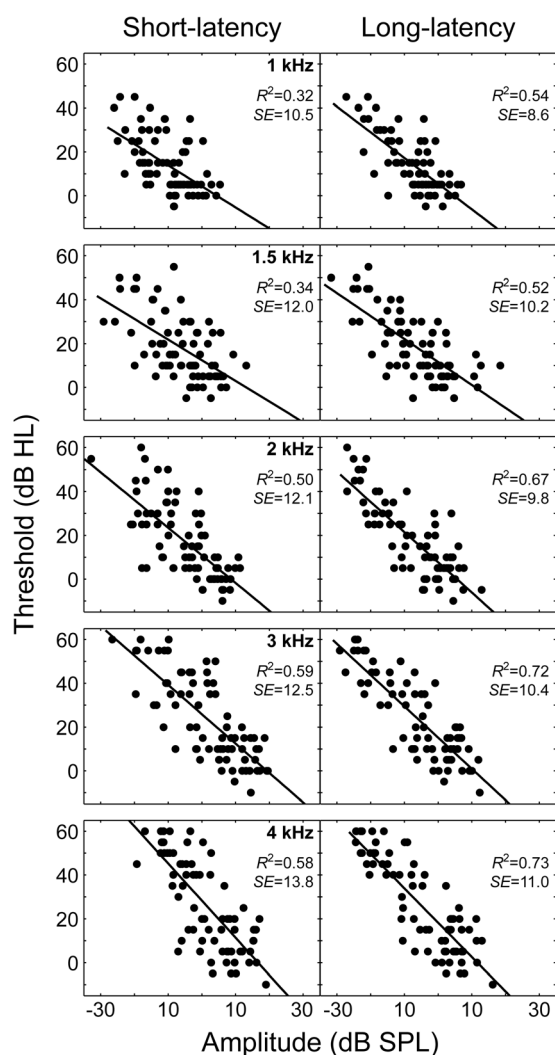


FIG. 4. Scatterplots of thresholds as a function of amplitudes of SL and LL components. Each row shows a different audiometric frequency, as indicated in the upper right-hand corner of each panel in the left column. Columns show SL and LL amplitudes, respectively, using on-frequency analyses (see text for details). Solid black lines represent least-squares fits to the data using linear regression analyses. R^2 and standard error (SE, in dB) values are shown in each panel.

with replacement, $N = 10\,000$ iterations). The means and 95% confidence intervals for each distribution are shown in Fig. 5. Non-overlapping confidence intervals indicate statistically significant differences in distributions, while overlapping confidence intervals may or may not suggest significant differences in distributions. Figure 5 shows some overlap in confidence intervals for the SL univariate and LL univariate results and essentially complete overlap between the LL univariate and multivariate results. Pairwise differences in R^2 values between the three distributions were computed, yielding three distributions of R^2 differences. The 95% confidence intervals of these distributions were used to determine statistical significance of differences in R^2 values. At all frequencies, the R^2 values obtained using the LL univariate results and the multivariate results were significantly higher than those obtained for the SL univariate results ($p < 0.05$). The R^2 values for the LL univariate results and the multivariate results were not significantly different ($p > 0.05$). The bootstrapping results provide further support for the finding that LL amplitude was a better predictor of thresholds than SL amplitude, and that SL amplitude did not provide additional information regarding thresholds.

IV. DISCUSSION

Previous studies of TEOAEs as predictors of thresholds have typically eliminated responses within the first 5 ms, thereby eliminating most SL components from 1 to 4 kHz. The purpose of this study was to determine if SL components were useful predictors of hearing status and thresholds. ROC analyses revealed that SL components from 2 to 4 kHz (but not from 1 to 1.5 kHz) predicted hearing status with similar accuracy to LL components and to the results reported in previous TEOAE studies (see Fig. 5 of Keefe *et al.*, 2011). In contrast, linear regression analyses predicting thresholds revealed that SL components were less accurate predictors than LL components at all frequencies. Additionally, SL components did not improve the accuracy of predictions when included in multivariate analyses,

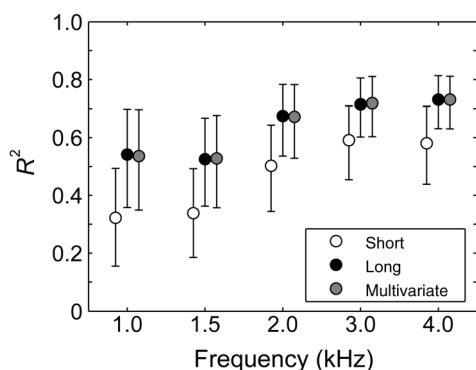


FIG. 5. Comparison of prediction accuracy as assessed by R^2 values. Circles represent the mean R^2 (univariate cases) and adjusted R^2 (multivariate cases) values. Error bars show bootstrapped 95% confidence intervals. Univariate results using SL and LL amplitudes (on-frequency) are shown as white and black circles, respectively. Multivariate results (on-frequency) are shown as gray circles. At all frequencies, univariate predictions using SL amplitudes resulted in significantly lower R^2 values than LL univariate and multivariate results ($p < 0.05$). There were no significant differences between LL univariate and multivariate results ($p > 0.05$).

relative to the predictions using LL components alone. It therefore appears that SL components, as analyzed in the current study, do not provide additional information regarding thresholds.

Several potential explanations for why SL components were less accurate predictors of thresholds than LL components were investigated. First, it was possible that the SNRs of SL components were lower than LL components. If this was the case, SL components would have more variability and would be expected to correlate less highly with thresholds. Figure 6 shows the mean SNRs of SL and LL components at each frequency. The mean SNRs were not significantly different from 1 to 2 kHz ($p > 0.05$), while the SL components had significantly higher mean SNRs from 3 to 4 kHz ($p > 0.05$). As expected, noise amplitudes were the same in the short- and long-latency time windows, indicating that SL components were equal to or higher in amplitude than LL components. These findings suggest that relative SNR does not explain the difference in predictive ability between SL and LL components.

Another factor that potentially influenced the accuracy of predictions using SL components may have been the prevalence of sloping hearing losses in the group of subjects tested. Subjects with sloping hearing loss would be expected to have greater OHC damage in basal locations. Therefore, depending on where the SL components were generated, sloping hearing losses may have influenced the results. This was examined by re-computing the regression analyses using a subset of ears that had thresholds ≤ 30 dB HL at all frequencies. Results (not shown) indicated that predictions using SL and LL components both decreased in accuracy overall, but LL components remained better predictors at all frequencies. This suggests that the presence of sloping hearing loss did not have a large effect on threshold predictions using SL components.

It is also possible that variables other than RMS amplitude better characterize the relationship between SL components and thresholds. In the current study, variables such as SNR and peak amplitude were examined but were found to have similar or poorer test performance relative to RMS amplitude. Another potential characterization that was not examined in the current study is the amplitude growth of SL

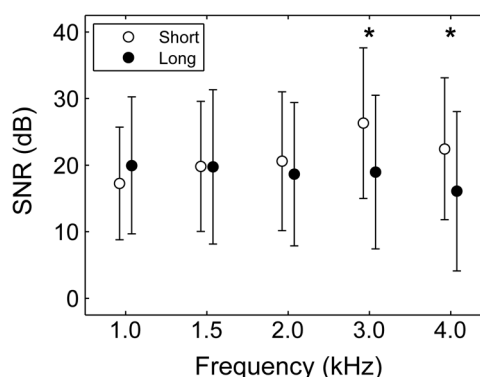


FIG. 6. SNRs of SL and LL components as a function of audiometric frequency. Circles represent mean values. Error bars represent ± 1 standard deviation. Asterisks indicate statistically significant differences between mean SNRs of SL and LL components at a given frequency ($p < 0.05$).

components, which has been described in normal-hearing ears (Goodman *et al.*, 2009; Goodman *et al.*, 2011; Sisto *et al.*, 2013). Growth functions of distortion-product (DP) OAEs have been used to predict thresholds in ears with hearing loss with promising results (Boege and Janssen, 2002; Gorga *et al.*, 2003; Rogers *et al.*, 2010). A similar approach could be investigated with SL TEOAE components.

Finally, it is possible that SL components from 1 to 4 kHz correlate better with high frequency thresholds (>4 kHz) due to the generation mechanisms and/or cochlear locations. In this study, predictions were restricted to the 1–4 kHz range due to the band-limited nature of the stimulus. This frequency range was chosen due to its importance for speech understanding and because it is routinely measured in clinical settings. The ability of SL components at a given frequency to predict a threshold at higher and lower frequencies (within the 1–4 kHz region) was examined over a limited range in the off-frequency analyses (see Table II). SL components were most accurate when predicting thresholds at the same frequency, becoming less accurate at higher and lower frequencies. These results suggest that prediction accuracy using SL components would decrease at frequencies even further removed (i.e., >4 kHz).

The univariate predictions using LL components were more accurate than most univariate predictions reported by previous TEOAE studies, as assessed by R^2 values (Table III). Potential methodological factors explaining the improved predictions include differences in the number of synchronous averages, stimulus bandwidth and level, emission extraction method, and time-domain analysis windows. Subject characteristics may have also accounted for the improved predictions. Regardless of the reason, the correspondence between TEOAEs and thresholds seen in the current study appears reasonable given that the inclusion criteria likely ensured that most subjects' hearing losses were OHC-related.

Although previous studies have shown improved predictions of hearing status and thresholds when using multivariate analyses (e.g., Suckfüll *et al.*, 1996; Vinck *et al.*, 1998;

Dorn *et al.*, 1999), this was not the case in the current study. It should be noted that the variables included in multivariate analyses have differed between studies (e.g., TEOAE amplitude and SNR, TEOAE and DPOAE amplitudes, results from multiple levels). It is possible that predictions using TEOAEs could be improved using a different combination of variables in multivariate analyses. The purpose of the current study was to investigate the contribution of SL components to prediction, rather than to find the best possible combination of predictors to maximize R^2 values. Future studies could also examine a larger number of potential variables to determine which contribute to improved predictions.

Although the univariate threshold predictions were generally improved in the current study relative to previous TEOAE studies, stronger correlations between ABR measurements and thresholds have been reported in the literature, with R^2 values for ABR results ranging from 0.86 to 0.89 in the 2–4 kHz region (van der Drift *et al.*, 1987; Johnson and Brown, 2005; Gorga *et al.*, 2006). It does not appear that TEOAEs, as analyzed in the current study, provide the predictive accuracy needed in clinical settings. Although one published TEOAE study reported predictive accuracy comparable to ABR results using multivariate analyses (Vinck *et al.*, 1998), similar results have not been reported elsewhere, and there may be concerns regarding over-fitting due to a large number of predictor variables used in the model. Encouraging results using DPOAEs were reported recently by Rogers *et al.* (2010), with R^2 values from 0.79 to 0.86 and standard errors less than 10 dB at some frequencies. Further work is needed to determine if the accuracy of threshold predictions using TEOAEs and/or DPOAEs can be improved to the point where they can be used clinically for predicting thresholds with similar accuracy to the ABR. It should also be considered that though OAEs may still be able to predict thresholds through a moderate hearing loss range, ABRs have the ability to predict thresholds up to and including severe hearing losses.

A potential limitation of the current study was the relatively small sample size compared to previous TEOAE studies (see Table III). In addition, fewer ears had hearing loss in the lower frequencies relative to the higher frequencies, which may have resulted in the poorer predictions found at lower frequencies relative to higher frequencies. Most subjects had sloping hearing losses, and it was difficult to recruit subjects that had moderate hearing loss in the lower frequencies without having severe or profound hearing loss in the higher frequencies. This resulted in a smaller range of thresholds over which to predict in the lower frequencies. Future studies should equate the distribution of thresholds across different frequencies when possible.

The current study appears to provide only limited insight into the potential generation mechanisms of SL components. Recent work has suggested that SL components may be generated by reflection near, but basal, to the traveling wave peak in the case of TEOAEs (Goodman *et al.*, 2011; Moleti *et al.*, 2012; Sisto *et al.*, 2013) and SFOAEs (Choi *et al.*, 2008; Moleti *et al.*, 2012). If lower-frequency SL components were predictive of higher-frequency thresholds, this could suggest that SL components were generated

TABLE III. Comparison of threshold prediction accuracy across TEOAE studies. All results are for univariate predictions only. The number of ears tested (N) and R^2 values for prediction results for five audiometric frequencies are shown. Correlation coefficients, if reported as such, were converted to R^2 values. The results shown in bold are from the current study using LL amplitude. The results shown for Vinck *et al.* (1998) were obtained using 86 dB SPL clicks, and the values are approximated because the results were reported graphically (see their top panel of Fig. 5). Dashes indicate that predictions were not reported at that frequency.

Study	N	Audiometric Frequency (kHz)				
		1	1.5	2	3	4
Current study	77	0.54	0.52	0.67	0.72	0.73
Keppler <i>et al.</i> (2010)	71	0.05	0.12	0.17	0.07	0.01
Sisto <i>et al.</i> (2007)	160	0.17	-	0.27	0.09	0.06
Wagner and Plinkert (1999)	193	0.09	-	0.21	0.23	0.01
Vinck <i>et al.</i> (1998)	589	0.48	-	0.52	-	0.64
Kowalska and Sulkowski (1997)	244	0.20	-	0.23	-	0.15
Suckfüll <i>et al.</i> (1996)	102	0.28	-	0.40	0.42	0.46
Collet <i>et al.</i> (1991)	150	0.05	-	0.14	-	0.18

at more basal locations than LL components. However, the on-frequency analyses resulted in the best predictions at all frequencies. Further examination also found that thresholds at a given frequency were correlated with thresholds at other frequencies, with a similar pattern of correlations emerging as that seen in Table II. This suggests that the off-frequency prediction results may simply be mirroring the correlations seen between thresholds and should not be interpreted as evidence for a particular generation mechanism. The band-limited nature of the stimulus in the current study (1–4 kHz) may argue against a cubic ($2f_1-f_2$) distortion mechanism as the generator of the higher-frequency SL components. In order to produce a cubic distortion product at 4 kHz, the primary frequencies f_1 and f_2 would be 5.1 and 6.3 kHz, respectively. These frequencies were outside the passband of the transient stimulus, resulting in extremely low levels of stimulus energy at these frequencies. Nevertheless, very robust SL components were seen at 4 kHz. This finding would not necessarily preclude generation by other distortion products or by cubic distortion in the middle range of frequencies tested, however. Another potential generation mechanism is a fast compression wave generated in the cochlear fluid (e.g., Ren, 2004). This could explain the observed latencies of SL components. However, recent evidence has suggested that a fast compression wave mechanism is not the primary way in which OAEs are generated in humans (Moleti and Sisto, 2007; Shera et al., 2007). As continuing research further elucidates the generation mechanisms and locations of SL components, issues of the clinical usefulness of SL components of TEOAEs may be re-examined.

V. CONCLUSIONS

SL and LL TEOAE components both predicted hearing status and audiometric thresholds from 1 to 4 kHz. Significantly better threshold predictions resulted when using LL components as predictors, relative to SL components. Multivariate analyses that included both SL and LL components did not significantly improve predictions relative to univariate analyses using LL components alone. Univariate predictions using LL components were more accurate than most previous univariate predictions of thresholds using TEOAEs, possibly due to differences in methodology and/or subject characteristics. However, the current predictions were still less accurate than predictions obtained from ABR measurements. The results suggest that SL TEOAE components, as analyzed in the current study, do not provide additional information about hearing status and behavioral thresholds relative to the information provided by LL components. Further work is needed to determine if TEOAEs can be used as estimators of thresholds in a clinically feasible way.

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