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High frequency transient-evoked otoacoustic emission measurements using chirp and click stimuli

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Abstract

Transient-evoked otoacoustic emissions (TEOAEs) at high frequencies are a non-invasive physiological test of basilar membrane mechanics at the basal end, and have clinical potential to detect risk of hearing loss related to outer-hair-cell dysfunction. Using stimuli with constant incident pressure across frequency, TEOAEs were measured in experiment 1 at low frequencies (0.7–8 kHz) and high frequencies (7.1–14.7 kHz) in adults with normal hearing up to 8 kHz and varying hearing levels from 9 to 16 kHz. In combination with click stimuli, chirp stimuli were used with slow, medium and fast sweep rates for which the local frequency increased or decreased with time. Chirp TEOAEs were transformed into equivalent click TEOAEs by inverse filtering out chirp stimulus phase, and analyzed similarly to click TEOAEs. To improve detection above 8 kHz, TEOAEs were measured in experiment 2 with higher-level stimuli and longer averaging times. These changes increased the TEOAE signal-to-noise ratio (SNR) by 10 dB. Slower sweep rates were investigated but the elicited TEOAEs were detected in fewer ears compared to faster rates.

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Declaration of Interest

Douglas Keefe has a commercial interest with Interacoustics A/S in developing devices to measure TEOAEs. There are no other conflicts of interest to declare.

Data Statement

Data are sharable upon request.

Data were acquired in adults and children (age 11–17 y.), including children with cystic fibrosis (CF) treated with ototoxic antibiotics. Test-retest measurements revealed satisfactory repeatability of high-frequency TEOAE SNR (median of 1.3 dB) and coherence synchrony measure, despite small test-retest differences related to changes in forward and reverse transmission in the ear canal. The results suggest the potential use of such tests to screen for sensorineural hearing loss, including ototoxic loss. Experiment 2 was a feasibility study to explore TEOAE test parameters that might be used in a full-scale study to screen CF patients for risk of ototoxic hearing loss.

Keywords

transient-evoked otoacoustic emissions; chirp stimulus; high-frequency hearing loss; ototoxicity; cystic fibrosis

1. Introduction

This study was designed to measure transient-evoked (TE) otoacoustic emissions (OAEs) elicited by click and chirp stimuli in the ear canals of adults and children at frequencies as high as 14.7 kHz, and evaluate their relative accuracy in classifying ears as having normal function or a sensorineural hearing loss (SNHL). TEOAEs are sensitive to outer hair cell dysfunction, which is an important mechanism underlying the presence of SNHL. TEOAEs are low-level sounds measured by a sensitive microphone placed in the ear canal in response to a transient sound stimulus (Kemp, 1978). When presented at low to moderate stimulus levels, TEOAEs are presumed to originate on the basilar membrane predominantly from the region of the tonotopic place (Kemp, 1986), although source regions may also extend more basally. An analogous place mechanism accounts for the generation of a stimulus frequency (SF) OAE within a tonotopic place region. At low stimulus levels, SFOAE and TEOAE generation is theorized to occur within a cochlear tonotopic region having a sufficiently tall and broad activator pattern via a coherent pattern of reflections from randomly distributed inhomogeneities within that region (Shera & Guinan, 1999; Zweig & Shera, 1995). As stimulus level is increased, such OAEs in human ears with normal function show a compressively nonlinear growth of response arising from outer-hair-cell function. Suppression experiments in human ears provide evidence that SFOAEs and TEOAEs are mainly generated near the tonotopic region of the stimulus (Keefe et al., 2008; Zettner & Folsom, 2003). Reflection-based OAEs may also be generated at larger stimulus levels due to nonlinear sources of reflection on the basilar membrane (Talmadge et al., 2000).

Some studies have reported TEOAE results at high frequencies above 8 kHz. A nonlinear TEOAE residual was measured up to 14.7 kHz using a pair of sound sources, each generating a click stimulus (Goodman et al., 2009). A double-evoked measurement procedure enabled latency measurements at times as short as 0.2 ms after the click. Such data were interpreted as indicative of reflection sites at the basal end of the cochlea. These data were used to classify adult ears as having normal function or SNHL at frequencies based on receiver operating characteristic (ROC) curve analyses (Keefe et al., 2011). The mean area under the ROC curve was 0.90 between 1 and 10 kHz, and 0.86 at 12.7 kHz. The latter test may have been less accurate due to reduced forward middle-ear transmission at

higher frequencies, which limited signal excitation within the cochlea generating the TEOAE, and reduced reverse middle-ear transmission, thus limiting TEOAE amplitude in the ear canal.

The click stimuli used to measure TEOAEs can generate system distortion at higher levels due to peak clipping by the sound source. The use of chirp stimuli to measure TEOAEs has the advantage of spreading the stimulus energy out over time so as to reduce the peak levels that generate distortion (Neumann et al., 1994). The stimulus level of a transient may be specified in terms of the total sound exposure level (SEL) of the stimulus summed over all frequencies (or times) or by its peak-to-peak equivalent (pe) SPL. The “SEL spectrum” with mathematical symbol L_S (in dB) is the integrated band sound-pressure level spectrum over the bandwidth of a discrete Fourier transform of sampled data of buffer length N , based on a reference time of 1 s and reference root mean-squared pressure of 0.00002 Pa (Keefe et al., 2016). A key property of L_S is that its value for a buffer containing a transient is independent of buffer duration, which is not the case for the corresponding sound-pressure level spectrum. For the same total SEL, a chirp has a reduced peSPL compared to a click, and may thus be advantageous with respect to click stimuli.

Chirp stimuli used in the present study were based on previous research. Chirp stimuli with energy up to 8 kHz were designed by allpass filtering a click stimulus, and the properties of TEOAEs generated by the click and chirp stimuli were compared (Keefe et al., 2016). The allpass filter had unity gain at all frequencies, so the spectral levels of the clicks and chirps were nearly the same across frequency. Chirps were designed to sweep linearly from low to high frequencies (“positive chirps”) or from high to low frequencies (“negative chirps”). TEOAEs elicited by clicks and positive- and negative-chirp stimuli having approximately the same sound exposure had generally similar response properties. Some dissimilarity was observed, e.g., small differences were observed in TEOAE responses between click and chirp stimuli, and as a function of sweep direction (positive or negative chirp). These differences were related to spatial-temporal differences in the nonlinear mechanics of the basilar membrane resulting from differences in stimulus phase.

For a click stimulus in the ear canal, slightly different frequency components of the traveling wave partially overlap in time and space at the basal end of the basilar membrane.

Depending on the relative amplitudes of these components, a particular component can suppress the amplitude of motion of other components. The underlying mechanism is the presence of two-tone mechanical suppression on the basilar membrane (Ruggero et al., 1992), which implicates the bi-directional and electromechanical properties of outer hair cells. Relative to a click stimulus, the positive chirp increases the spatial-temporal overlap of stimulus energy at nearby locations on the basilar membrane, while the negative chirp decreases this overlap (Keefe et al., 2016). Slightly different frequency components of the traveling wave elicited by a chirp stimulus are better separated with slower sweep rates. Nonlinear temporal interactions between pairs of clicks with relative delays on the order of 1–6 ms are evident in TEOAEs elicited by clicks (Kapadia & Lutman, 2000a; Kapadia & Lutman, 2000b; Kemp & Chum, 1980; Verhulst et al., 2011). This suggests that frequency components within chirp stimuli, which have an overall duration on the order of tens to hundreds of ms, may not show mutual suppression on the basilar membrane when their

relative delay exceeds about 6 ms. For both sweep polarities, chirps with slower sweep rates have smaller amounts of nonlinear interaction on the basilar membrane than chirps with faster sweep rates. This distinction might appear when comparing TEOAEs generated by chirps of varying sweep rates. In TEOAE measurements using chirp stimuli, nonlinear interactions in TEOAEs were larger for positive- than negative-chirp stimuli (Keefe et al., 2016), although that study did not explore the use of chirp stimuli with multiple sweep rates. The present study compared TEOAEs generated by positive- and negative-rate chirps having a range of sweep rates, with a clinical translational focus on selecting stimulus properties to improve the application of TEOAEs to detect SNHL related to outer hair cell dysfunction at high frequencies.

Other studies have described SFOAE and distortion product (DP) OAE results at high frequencies above 8 kHz, e.g., Dewey and Dhar (2017) reported SFOAE and DPOAE data up to 20 kHz in normal-hearing (NH) adult ears, with SFOAE stimuli calibrated to a forward pressure level of 36 dB. SFOAEs were detected on average at 1/3rd-octave frequencies of 10.1 and 12.7 kHz, but not at 16 kHz, although a subset of ears had SFOAEs at frequencies as high as about 15 kHz. The mean spectral envelopes of SFOAE and DPOAE signal levels were similar at frequencies above 2 kHz when DPOAE level was plotted versus the response frequency of $2 f_1 - f_2$, with both spectra showing substantial decline above 7 kHz. Dewey and Dhar recommended the use of higher stimulus levels for high-frequency (HF) SFOAE measurements.

A general outcome of these OAE studies is the increased difficulty of interpreting responses at and above about 10 kHz. Thus, further studies of HF OAEs are warranted. The present study investigated the properties of TEOAEs elicited by stimuli containing energy above 8 kHz in NH adults, and also in pediatric patients with cystic fibrosis (CF) receiving ototoxic medications. This is the first HF TEOAE study to include the use of chirp stimuli. The measurement of HF TEOAEs provided a physiological assessment of outer hair cell function in the more basal region of the basilar membrane, which is of particular relevance in screening programs for ototoxic hearing loss.

The overall duration of each TEOAE measurement across frequency from 0.7 to 14.7 kHz was constrained to six minutes or less in the two experiments that were performed in the present study. This ensured the clinical relevance of the test procedures. The experiments compared TEOAE generation based on click and chirp stimuli, and using chirps with frequency-specific energy whose center frequency either increased or decreased with time. Experiment 1 investigated the use of chirp stimuli to record TEOAEs at frequencies above 8 kHz in NH adults, while Experiment 2 refined the methodology used in the first experiment and included children with CF with a history of potentially ototoxic aminoglycoside treatments.

2. Experiment 1

Experiment 1 addressed the ability of click and chirp stimuli to generate TEOAEs up to kHz in adults with NH up to 8 kHz. The subjects had a range of hearing thresholds at test frequencies between 9 and 16 kHz. The incident pressure level of each stimulus was

controlled to have the same total SEL to facilitate comparisons between TEOAEs generated by click and chirp stimuli. Chirp stimuli better control for system distortion observed at high peak levels of excitation in the use of click stimuli, and thereby can provide higher sound exposure levels than click stimuli to offset the reduction in middle-ear transmission at high frequencies observed in human temporal bone data (Nakajima et al., 2008). The maximum possible stimulus levels in the ear canal are limited by the onset level of probe distortion and the requirement to restrict data collection to comfortable and safe listening levels. In an attempt to better facilitate the translation to clinical utilization, the duration of data collection in Exp. 1 was limited for each TEOAE condition to one minute for each of a low- and high-frequency band of stimulus energy.

2.1 Material and Methods

2.1.1 Subjects and Clinical Procedures—The research plan for using adult human subjects was approved by the Institutional Review Boards at Oregon Health & Science University/Veterans Affairs (Portland, OR) and Boys Town National Research Hospital (Omaha, NE). Following completion of paperwork, each adult participant completed several tests during a single, two-hour session.

All audiometric tests were performed within a sound-attenuated booth. Adult subjects received air-conduction (AC) and bone-conduction (BC) audiometry (GSI 61 audiometer). The AC test frequencies included all half-octave frequencies between 0.25 and 8 kHz using an Eartone ER3A insert earphone (Oaktree), and extended high frequencies at 9, 10, 11.2, 12.5, 14 and 16 kHz using circumaural headphones (Sennheiser, model HDA 200). The BC test frequencies included 0.25, 0.5, 1, 2 and 4 kHz using a BC oscillator (RadioEar, model B71). Subjects also received a clinical 226-Hz admittance tympanometry test (GSI Tympstar). Inclusion criteria for this study were 226-Hz tympanometry within normal limits, AC audiometric thresholds of 20 dB HL or better at all frequencies up to 8 kHz, and air-bone gaps of 10 dB or less at all BC frequencies.

A total of 51 participants met these inclusion criteria for normal hearing (28 female, 23 male), with 98 test ears included in the study (47 left, 51 right). The age range was 19 to 62 y., with mean age of 32.8 y. and standard deviation (SD) of 10.7 y.

2.1.2 TEOAE methods—TEOAE testing was performed at ambient pressure in the ear canal using an Etymotic 10B+ microphone probe assembly, which had a pair of ER2 sound sources and a soft foam eartip for a comfortable leak-free insertion into the ear canal. The computer sound card (CardDeluxe) delivered stimulus signals through each of a pair of digital-to-analog converter outputs driving an ER2 sound source. The microphone output was recorded by an analog-to-digital converter. The sample rate was 44.1 kHz per channel. Data were acquired using custom software.

A low-frequency (LF) click stimulus was designed and calibrated in a long tube that provided an effectively anechoic termination to have an approximately constant incident pressure level (Goodman et al., 2009) between 0.5 and 8 kHz. A separate HF click stimulus was designed and calibrated to have an approximately constant incident pressure level between 7.1 and 14.7 kHz. Using a time-domain technique of Agullo et al. (1995), both

stimuli were designed such that the incident sound pressure of the click response approximated the impulse response of a Kaiser window with the same passbands as stated above. The passbands of LF and HF stimuli overlapped such that each stimulus contained stimulus energy over the entire 1/12th octave band centered at 7.55 kHz. The maximum frequency of the HF stimulus was aligned with the upper frequency of the 1/12th octave band centered at 14.3 kHz, which included spectral energy up to kHz. There was a near alignment of the extended high audiometric frequencies listed above with the 1/6th octave center frequencies of the TEOAEs at 9, 10.1, 11.3, 12.7, 14.3 and 16 kHz, although no TEOAE data were analyzed at 16 kHz due to limitations of probe performance above 14.7 kHz. This near alignment allowed the ability to predict hearing loss at each audiometric frequency using a 1/6th octave averaged HF TEOAE response whose bandwidth contained a single audiometric frequency.

LF and HF chirp stimuli were designed by allpass filtering the respective LF and HF click stimuli using a procedure previously used to create LF chirps (Keefe et al., 2016). Three allpass filters were used to generate LF chirps and HF chirps with slow, medium and fast sweep rates (52.8, 188, 317 Hz/ms, respectively). The single chirp sweep rate of 174.6 Hz/ms used by Keefe et al. (2016) was most similar to the medium sweep rate in the present study.

The following procedures summarized below were used to process the TEOAE data. A detailed description of these procedures is available elsewhere (Keefe et al., 2016). A nonlinear TEOAE residual was measured based on averaging responses to multiple presentations of stimulus sets. Each stimulus set included 3 stimuli: the first reference stimulus delivered through one of the ER2 sound sources at a reference level, the second delivered through the other of the ER2 sound sources at 4 times the reference level (or 12 dB higher), and the third delivered simultaneously through both ER2s, which made the composite stimulus in the ear canal about 5 times the reference level (or 14 dB higher). The reference level is defined below. The L_5 and peSPL for each stimulus set were calculated based on the stimulus at the reference level. A TEOAE residual to extract a compressively nonlinear OAE response was calculated using a double-evoked procedure as the sum of the first and second buffers of data minus the third buffer. This calculation removed the linear response.

Data were highpass filtered in real time to reduce physiological and environmental noise using a Kaiser window finite impulse response filter (with response attenuated by 3 dB and 40 dB at 0.66 kHz and 0.4 kHz, respectively). Intermittently noisy responses to each stimulus set were removed from the dataset using a median absolute deviation test. Those data not excluded as artifact were termed valid data. At least 1 minute of valid data was acquired for each analysis. The number (B) of buffers of data that were averaged in at least 1 minute differed across stimulus conditions: click ($B=552$), fast chirp ($B=288$), medium chirp ($B=288$), and slow chirp ($B=120$). Each chirp TEOAE residual was transformed into an equivalent click TEOAE residual by convolution with the inverse of the allpass filter used to generate the chirp from the click stimulus. Multi-window analyses were performed in both time and frequency domains to improve the ability to detect click and chirp TEOAEs. This reduced the TEOAE noise level by about 5–6 dB (Keefe et al., 2016).

All responses were acquired based on a single probe insertion whenever possible. The tester confirmed that no leak was present due to an improper probe seal in the ear canal by viewing the real-time spectrum of a LF test. The lowest-level LF click data were collected at a SEL of 38 dB and peSPL of 72 dB (for the reference click stimulus) for incident pressure level, and the lowest-level HF click data were collected at a SEL of 32 dB and peSPL of 70 dB. These LF and HF responses were denoted as having a relative stimulus level L_{rel} of 0 dB. Each HF stimulus type was calibrated to have the same integrated band sound pressure level L_S (Keefe et al., 2016) in the 1/12th octave frequency bin at 7.55 kHz as the corresponding LF stimulus. This calibrated the incident pressure level to be constant over the combined bandwidths of the LF and HF stimuli. Click TEOAE data were also recorded with LF and HF stimuli at $L_{rel} = 6$ dB. This was 1 dB above the maximum L_{rel} used to avoid any system distortion in the click TEOAE recordings, so click TEOAEs at $L_{rel} = 6$ dB were interpreted with caution. This avoidance of distortion was accomplished for all stimulus types by limiting the maximum stimulus level to at least 9 dB below the maximum stimulus level at which any distortion was observed in the TEOAE residual recording in a long, reflection-less cylindrical tube. This provided 6 dB over which ear-canal standing waves might elevate the microphone pressure via pressure doubling, and an additional 3 dB to control for individual variability in the incident pressure wave in the ear canal due to variations in ear-canal area (Keefe et al., 2016). Any residual system distortion in an ear recording was considered to be acceptably small. A similar process was used to search for distortion using chirp stimuli, although clicks distorted at a lower SEL than the corresponding chirps.

TEOAE data were recorded for 30 different stimulus conditions listed in Table 2, 2 with clicks at L_{rel} of 0 dB, and 28 with chirps. Of the 28 chirp stimulus conditions, 24 included 3 sweep rates (slow, medium, fast), 2 sweep polarities (positive, negative), 2 bandwidths (LF, HF), and 2 stimulus levels (L_{rel} of 0 and 6 dB). TEOAE data were also recorded for 4 chirp stimulus conditions at a stimulus level of $L_{rel} = 12$ dB for: a HF positive chirp with medium sweep rate, LF and HF positive chirps with slow sweep rate, and a HF negative chirp with slow sweep rate. These highest-level chirp stimuli for longer-duration chirps did not show any measurement-system distortion according to the procedures described in the previous paragraph.

The signal-to-noise ratio (SNR) and coherence synchrony measure (CSM) were used to assess the presence and strength of the TEOAE response. Individual sets of buffers with valid data were distributed in equal numbers in each of $K = 24$ sub-averaging buffers for click responses or $K = 12$ sub-averaging buffers for chirp responses. Data were time averaged within each sub-averaging buffer, and data in the multiple buffers were averaged coherently to obtain the mean TEOAE response and incoherently to calculate the TEOAE noise response (Schairer et al., 2003). Coherent averaging is a synchronous averaging of waveform or spectral responses. The use of multiple buffers ($K > 1$) does not influence the coherent average, which depends only on the total number of averages. Incoherent averaging over K buffers is based on the variance of spectral responses at each frequency. The minimum value $K=2$ is used in many evoked OAE studies to estimate the noise level, but this results in substantial fluctuations of noise level across frequency. Using a larger value $K > 2$ decreases the variability of the estimated noise level across frequency, although it does

not decrease the average noise level. The use of $K=24$ for clicks and $K=12$ for chirps resulted in more smoothly varying noise levels across frequency than would be obtained with $K=2$. CSM quantifies the degree of synchrony of the TEOAE across the multiple buffers holding the TEOAE responses. A CSM value of one represents perfect synchrony, and a value of zero represents no synchrony (i.e., noise alone). As a function of frequency, CSM is closer to one if the spectral phasor angles calculated from the complex TEOAE spectra across the K buffers are highly similar to one another (i.e., if they point in a similar direction on the complex plane).

A TEOAE was classified as present based on CSM if the CSM calculated from the data was the same or greater than the critical CSM corresponding to a detection criterion at $p=0.05$. This critical CSM varied with the p value and number of sub-averaging buffers K as (Greenwood & Durand, 1955; Keefe, 2012; Wilkie, 1983),

$$CMS_{crit} = \left[(1 + 2K)^2 - (\ln p + (1 + 2K))^2 \right]^{1/2} / (2K). \quad [1]$$

This critical CSM was 0.352 for click TEOAEs and 0.494 for chirp TEOAEs, with the difference due to the different values of K for clicks and chirps. A TEOAE was classified as present based on SNR if the measured SNR was the same or greater than the critical SNR of

$$SNR_{crit} = 10 \log_{10}(-2 \ln(2p)). \quad [2]$$

at a detection criterion p (Green & McGill, 1970; Keefe, 2012). This corresponds to $SNR_{crit} = 6.6$ dB for $p = 0.05$. The critical SNR is the minimum SNR for correct detection of signal energy in noise with error rate p in a two-alternative forced-choice paradigm (the often-used criterion of 6 dB SNR in OAE studies corresponds to $p=0.068$).

Results in individual ears were smoothed over bands as narrow as $1/24^{\text{th}}$ octave bands (3% change in center frequencies) to resolve more of the TEOAE fine structure while retaining some smoothing across frequency. Group results were smoothed over $1/6^{\text{th}}$ octave bands (12% change in center frequencies) across LFs and HFs.

2.2. Results

2.2.1. Individual-ear data—Individual-ear HF TEOAE results are described in Fig. 1 for an adult test ear (subject A) with NH at all audiometric frequencies between 0.25 and 16 kHz. TEOAE responses were measured using the negative chirp over the HF bandwidth with a medium sweep rate and $L_{ref} = 6$ dB. The mean equivalent-click waveform of the HF TEOAE (residual) in Fig. 1A has a burst of energy between 0.9 and 3 ms, for which 0 ms corresponds to the time at which the peak amplitude of the equivalent-click stimulus occurred. The mean TEOAE waveform is shown on a logarithmic time axis to reveal the short-time portion of the response generated in the basal part of the basilar membrane tuned to higher frequencies. The time-domain CSM in Fig. 1B was larger than the critical CSM (of 0.494), which is evidence that the TEOAE was present between 0.9 and 3 ms. The time-

domain SNR in the same panel exceeded its critical SNR (of 6.6 dB) over similar times (except for several outliers with smaller SNR). CSM and SNR briefly exceeded their critical values at times near 0.3 and 0.6 ms, which provide evidence for the presence of TEOAEs at these early times. TEOAEs were absent after 3.5 ms.

Figure 1C shows the $1/24^{\text{th}}$ octave averaged means of L_S for the TEOAE signal and noise. The fine structure of L_S without any averaging is also plotted. The fine structure was resolved by the $1/24^{\text{th}}$ octave averaging except for a narrow notch into the noise floor just above 8 kHz. The CSM and SNR values in Fig. 1D were generally consistent in classifying the response as present or absent across frequency. The TEOAE was present at frequency bins from 7.55 up to 12.7 kHz except for the bin at 8.2 kHz that included the notch frequency in fine structure.

TEOAE levels (L_S) elicited by LF and HF chirps are shown in Fig. 2 for subject A, along with their respective noise levels. The individual-ear plots are all based on data for subject A in order to communicate the diversity of TEOAE responses obtained for a single subject. Spectral fine structure was largely removed by averaging over each $1/6^{\text{th}}$ octave. Data are shown for the $L_{\text{rel}} = 0$ dB responses for positive (left) and negative chirps (right), and for fast (top), medium (middle) and slow (bottom) sweep rates. Data are shown for both LF and HF responses at 8 kHz, although the LF response was bandlimited to half the $1/6^{\text{th}}$ octave centered at 8 kHz while the HF response was the full-band response. Noise levels were similar for all stimulus conditions. TEOAE levels elicited by positive- and negative-chirp stimuli were generally similar for medium and slow sweep rates. In contrast, larger differences were apparent for the fast sweep rate.

Figure 3 shows the fine structure of three TEOAE levels (L_S) measured for subject A for the following stimulus types: positive chirp with slow sweep rate (top), positive chirp with medium sweep rate (middle), and negative chirp with slow sweep rate (bottom). These were the only stimulus conditions that included L_{rel} of 12 dB for some or all test frequencies (see Table 2). Responses are shown for relative stimulus levels L_{rel} of 0, 6 and 12 dB. The noise levels (dotted lines) are also shown for the $L_{\text{rel}} = 0$ dB measurement. The ability of incoherent averaging with $K > 2$ to reduce the fluctuations in noise level is apparent in the smoothly varying noise levels plotted in Fig. 3 for the responses at each bin frequency in the raw spectral data. A pattern is revealed of increased TEOAE level with increasing stimulus level, although not uniformly so. TEOAEs were absent in this ear at and above 12.7 kHz for all conditions.

A distinctive feature of all TEOAE spectra in Fig. 3 was the alignment of a peak just above 8 kHz, which showed a systematic increase of TEOAE level with stimulus level. This frequency was aligned with the nominal half-wavelength resonance frequency (9 kHz) of the sound stimulus, corresponding to a relative maximum in the microphone pressure at this frequency. As explained in Methods, the incident pressure level was maintained constant in these measurements for a specified value of L_{rel} .

This resonance is partially explained by ear-canal standing wave effects in forward transmission of the stimulus (Souza et al., 2014). The transfer function between pressure

level at the tympanic membrane relative to the probe-microphone pressure level of the stimulus used in a behavioral audiogram has a relative peak at frequencies around the harmonics of the nominal half-wavelength frequency in an ear canal with constant area (Lee et al., 2012), and such a property is common to stimuli used in TEOAE testing. This half-wavelength resonance frequency partially accounts for the boost in TEOAEs just above 8 kHz in this ear. As further described below, the half-wavelength resonance also affected reverse transmission of the TEOAE component from the tympanic membrane back to the probe (Charaziak & Shera, 2017). This elevates the gain in the measured TEOAE in Fig. 3.

2.2.2. Group data—Group LF and HF TEOAE results were analyzed with 1/6th octave averaging in adult ears with NH at all frequencies. There were 96 ears with NH at frequencies up to 8 kHz and complete data sets, but fewer ears with NH at higher frequencies. The fewest number of ears with NH was 74 ears at 14.7 kHz. The distribution statistics for the stimulus peSPL and SEL are listed in Table 2 for all stimulus conditions at which TEOAE data were acquired. The values of the mean and SD were calculated for the 96 ears with NH at frequencies up to 8 kHz. Because the peSPL and SEL of the stimuli are measured across the entire frequency range, ears with SNHL at one or more frequencies above 8 kHz were retained in this stimulus analysis.

Results were measured for all stimulus types at a relative level of 0 dB. At LFs, the mean peSPL ranged from 80.3 dB for the click down to 62.0 dB for the slow negative chirp, while the mean SEL ranged over a much smaller range from 46.3 to 47.1 dB for all stimuli. The mean magnitude difference in the LF peSPL between positive and negative chirp polarities ranged from 0.1 to 0.4 dB, while that for the LF SEL ranged from 0.0 to 0.1 dB. At HFs, the mean peSPL ranged from 82.2 dB for the click down to 60.7 dB for the slow negative chirp, while the mean SEL ranged over a much smaller range from 46.4 to 47.3 dB for all stimuli. The mean magnitude difference in the HF peSPL between positive and negative chirp polarities did not exceed 0.2 dB, while that for the HF SEL did not exceed 0.1 dB.

The near invariance of SEL across stimulus conditions was part of the stimulus design procedure, which generated stimuli with equal SEL of incident pressure in the anechoic tube. Standing wave effects in individual ears were present in a similar manner across all stimulus conditions. The measured peSPL between LF and HF stimuli at the same relative level were not expected to be equal, as the HF stimulus was calibrated to have the same integrated 1/12th octave band sound-pressure level spectrum at 7.55 kHz. The mean SELs for LF and HF stimuli were similar to one another inasmuch as the stimulus bandwidths were similar.

At higher relative levels of 6 and 12 dB, the results in Table 2 were unremarkable compared with the results at the relative level of 0 dB. When the relative level was increased from 6 to 12 dB, the peSPL and SEL of a linear system would be expected to increase by 6 dB (subject to random measurement errors). This pattern was largely observed in the tabulated data. Aside from effects of noise and the compressive growth of the TEOAE, the stimulus levels were approximately linear in relation to the applied voltage inputs to the sound sources.

Box and whisker plots of NH group data are shown in Fig. 4 for TEOAEs elicited at $L_{rel} = 0$ dB using click and chirp stimuli. Only those ears were included that had NH at the closest audiometric frequency. The box and whiskers plot of L_S in Fig. 4 (top) shows the distribution of TEOAE levels elicited by the click stimulus. Relative to the noise level (dashed line), the median TEOAE level was classified as present based on the SNR criterion (of 6.6 dB) at all frequencies except 12.7 kHz at which the median SNR was 5.0 dB. The 75th percentiles of TEOAE level were classified as present at all frequencies. For both TEOAE signal and noise levels, the median L_S in Fig. 4 (top) at 8 kHz was slightly larger than the corresponding median at other nearby frequencies. This may have resulted from the fact that the average half-wavelength resonance frequency for this group was also close to 8 kHz. Outliers were grouped into two classes. The larger class had TEOAE levels on the order of the median noise level plotted in the panel. These levels were likely substantially influenced by noise, and would likely correspond to absent emissions. The smaller class (with 6 outliers overall) had levels exceeding the 75th percentile by more than 1.5 IQR. It is unknown whether these outliers were indicative of an ear with exceptionally large TEOAE levels or a condition in which some intermittent artifact was present.

The middle and bottom panels of Fig. 4 show median and IQR differences in TEOAE level between pairs of stimulus conditions. Outliers were present but are not plotted so as to more easily view the range of IQRs across several comparisons. The slow sweep rate chirps were expected to produce the largest differences in TEOAEs relative to the use of clicks, and this was confirmed by the results in NH ears. The middle panel of Fig. 4 shows the difference

L_S in TEOAE level between responses acquired using the positive chirp with slow sweep rate relative to the click stimulus. The median TEOAE level was slightly lower for the positive chirp than the click at all test frequencies, and ranged from -3.3 dB at 1.6 kHz to -0.8 dB at 12.7 kHz with a grand median of -2.2 dB. Although not shown, the magnitudes of TEOAE L_S of the chirp relative to the click level were less for the medium and fast sweep rate conditions. These TEOAE level differences are evidence of spatial-temporal differences in the nonlinear mechanics of the basilar membrane resulting from differences in stimulus phase.

The bottom panel of Fig. 4 shows the difference L_S in TEOAE level between responses in NH ears acquired using the positive chirp relative to the negative chirp stimulus at the fast sweep rate. The median L_S of the TEOAE ranged from -0.2 dB at 0.89 kHz to 2.2 dB at 2.8 kHz with a grand median of 1.0 dB. Thus, the TEOAE levels were nearly independent of the polarity of the fast-swept chirp stimulus. Compared to the median L_S of TEOAEs acquired using medium and slow chirps (not shown), the magnitude of L_S was largest for the fast sweep rate condition shown in this panel. This is consistent with theoretical expectations (Keefe et al., 2016), as the degree of spatial-temporal overlap for the fast chirp on the basilar membrane would be larger than for the medium and slow chirps.

Figure 5 illustrates the effect of relative stimulus level L_{rel} on the difference L_S in TEOAE level in NH ears observed between positive- and negative-chirp TEOAEs for the stimulus conditions with slow sweep rate. At $L_{rel} = 6$ dB (Fig. 5, left), the median L_S was close to zero dB so that L_S was nearly the same for the positive- and negative-chirp TEOAEs. This was similar to the null results at $L_{rel} = 0$ dB for the slow sweep rate chirp

(Fig. 4, bottom). Both positive- and negative-chirp data were acquired only at HFs at $L_{rel} = 12$ dB, and the median L_S (Fig. 5, right) was again close to zero dB. Thus, the median and IQR of the HF TEOAE levels were essentially the same for positive- and negative-chirp stimulus conditions at the slow sweep rate.

The median CSM and SNR in ears with NH at each frequency are shown in each panel of Fig. 6 for the TEOAE elicited by the click stimulus at L_{rel} of 0 dB for comparison with chirp TEOAEs. The median CSM and SNR in the same group of NH ears are shown for the positive chirp stimulus conditions with slow, medium and fast sweep rates, and for L_{rel} of 0, 6 and 12 dB (the latter condition at any frequency at which data were acquired, see also Table 2). The critical SNR and critical CSM lines are also displayed. In general, each TEOAE was classified as present at lower frequencies and absent at higher frequencies. For example, the TEOAE for the medium sweep rate condition with L_{rel} of 6 dB (in middle panels) was classified present up to kHz for both SNR and CSM, and absent at higher frequencies. The CSM and SNR were generally similar between the positive and negative chirp conditions that were examined, so only the positive chirp data are shown as they were obtained for more stimulus conditions. For SNR, the performance was similar for the click and chirp conditions at L_{rel} of 0 dB, except that the click SNR was larger for the slow sweep rate (Fig. 6B).

The CSM data are more complicated to examine as the critical CSM values differed for clicks and chirps. At L_{rel} of 0 dB, the CSM intersected the critical CSM value at the same frequency for the medium and fast sweep rate chirps as for the click (Figs. 6C, 6E), so that the ability to detect TEOAEs in this group based on CSM was similar. As with SNR, the click CSM was present up to a higher frequency (8 kHz) in Fig. 6A than for the slow sweep rate chirp (that was present up to 5 kHz). The chirp TEOAE CSM and SNR increased with increasing stimulus level at the larger L_{rel} of 6 and 12 dB, and their ability to classify NH ears as having a present TEOAE was better at HFs than for the click condition. The best performance at HFs for both CSM and SNR was the medium sweep rate chirp at L_{rel} of 12 dB. However, no corresponding data were obtained at this level for the fast sweep rate condition. The relatively better performance of the clicks and chirps with faster sweep rates is mainly due to the greater amount of averaging possible in a fixed measurement duration compared to chirps with slower sweep rate (see Table 1).

The presentation of chirps at larger SELs compared to clicks also improved performance. The ability of positive-chirp TEOAEs to classify an ear as NH or having a SNHL was investigated using an on-frequency predictor at the $1/6^{\text{th}}$ octave average including each audiometric frequency above 8 kHz. Ears with audiometric thresholds of 20 dB HL or better were classified as NH, and otherwise were classified as SNHL. The best results presented here were obtained for the positive chirp stimuli presented at $L_{rel} = 12$ dB with a medium sweep rate (no data were acquired for the corresponding negative chirp condition).

Scatter-plot results of TEOAE CSM versus AC audiometric threshold are shown in 98 ears for this stimulus condition in Fig. 7 for each audiometric frequency between 8 and 14 kHz. Specificities were larger at lower frequencies, i.e., 79% at 8 kHz, 78% at 9 kHz and 74% at 10 kHz. In contrast, specificities at higher frequencies ranged from 64% at 11.2 kHz down to

38% at 14 kHz. The corresponding sensitivities varied within a narrow range from 67% to 80% at frequencies between 9 and 14 kHz, with an average sensitivity of 76%. Results were generally similar for TEOAE SNR (not shown), although SNR was slightly less accurate at classification than CSM. It is evident in Fig. 7 that a few test ears with SNHL had robust TEOAEs between 10 and 14 kHz (i.e., those data in the upper right quadrant of each panel). Such ears may have had normal outer hair cell function at the basal end of the cochlea in conjunction with some other pathology related to inner hair cell or auditory-nerve function. Random errors in the HF TEOAE measurements or the HF audiogram might have played a role (HF audiometry is discussed in more detail in the Discussion at the end of Exp. 2). The present data set is insufficient to unravel these unknowns, although it suggests a possible role for combining audiometric with HF OAE testing to help interpret the type of SNHL, whether due to outer or inner hair cell dysfunction or a neural deficit.

2.3. Discussion

Click- and chirp-evoked TEOAEs were compared (Fig. 4, middle) based on the same incident pressure level ($L_{rel} = 0$ dB) across stimulus type and stimulus frequency. Other results in Fig. 4 (bottom) showed a slight sensitivity to the chirp polarity and sweep rate on the order of 0–2 dB in median TEOAE levels. This is sufficiently small to recommend the use of chirp stimuli of varying durations and of either polarity to measure TEOAEs.

The generation mechanisms underlying TEOAEs and SFOAEs are considered to be similar (Shera & Guinan, 1999; Kalluri & Shera, 2007) so that their resulting spectral shapes would be expected to be similar (when stimulus conditions are appropriately equalized). In practice, stimulus conditions differ across studies. At stimulus levels sufficiently high to enable the detection of TEOAEs above 8 kHz, 1/3rd octave-averaged click TEOAE levels in NH adults had a relative maximum at 8 kHz with reduced levels by about 7 dB at 10.1 and 12.7 kHz (Goodman et al., 2009). In contrast, Dewey and Dhar (2017) described that SFOAE levels declined substantially above 7 kHz, e.g., they were about 20 dB down at 9 kHz. The chirp and click TEOAE spectral envelopes in the present study were more similar at HFs to the click TEOAEs of Goodman et al. than the more attenuated SFOAEs of Dewey and Dhar. This degree of dissimilarity is likely related to the differing stimulus conditions and measurement procedures.

For DPOAEs and SFOAEs measured in the same group of ears, Dewey and Dhar observed that the spectral levels of DPOAEs plotted as a function of the distortion product frequency ($2f_1 - f_2$, or $0.724 f_2$) also declined substantially above 7 kHz for which the corresponding f_2 corner frequency was 9.7 kHz. They concluded that the similarity of SFOAE and DPOAE at high response frequencies suggests that middle-ear function limits reverse propagation of the evoked OAE back to the ear-canal microphone. This spectral pattern was similar to a model prediction (Keefe, 2015) of the reverse middle-ear pressure reflectance magnitude. This model was developed based on human temporal-bone measurements up to 8 kHz (Nakajima et al., 2008; Puria, 2003). The predicted reverse middle-ear reflectance magnitude had relatively low values below 7 kHz (e.g., ranging from 0.07 to 0.28 between 2 and 5.7 kHz) and much higher values above 7 kHz (e.g., increasing to a maximum of 0.64 at 8 kHz). This suggests that a reverse-directed SFOAE or TEOAE would be attenuated at 8 kHz, and a

reverse-directed DPOAE would be attenuated at a f_2 frequency of 11 kHz. The maximum frequency at which TEOAEs were measured in the present study was 14.7 kHz, which would correspond to a f_2 frequency of 20.3 kHz in a DPOAE. If reverse middle-ear transmission is indeed reduced at 8 kHz, then it may be beneficial in clinical applications to retain the boost in forward level associated with the half-wavelength frequency near 8 kHz to offset the reverse attenuation of the TEOAE. More research is needed to evaluate that conjecture. More generally, additional research is needed to compare evoked OAEs from multiple emission types to better understand the intertwined influences of cochlear and middle-ear function, including effects of aging (Abdala et al., 2018).

The primary limitation of the results of Exp. 1 was that TEOAEs were not detected between 11.2–14.3 kHz in many ears with NH, as shown in Fig. 6 and quantified by the specificities in Fig. 7. This limitation applied to TEOAEs recorded using clicks and positive/negative chirps. This limitation arose, in part, from a relatively short recording time of 1 minute, and from a limitation of the maximum stimulus level ($L_{rel} = 12$ dB). The latter limit avoided any distortion associated with these chirp stimuli that occurred at a smaller L_{rel} in the LF stimuli compared to the HF stimuli. This HF decline in specificity paralleled results from other HF TEOAE and SFOAE studies (Goodman et al., 2009; Dewey and Dhar, 2017). Experiment 1 provided evidence that TEOAEs were more difficult to measure above 10 kHz, and that this difficulty was not resolved by simply substituting chirp for click stimuli with the same total SEL. The group results on CSM and SNR in Fig. 6 showed that TEOAEs remained difficult to measure above 10 kHz when using chirps that were 6 dB higher in SEL than any of the click stimuli. The best results occurred in Fig. 6 for TEOAEs recorded using the positive chirp stimuli with medium sweep rate at a relative level of 12 dB, for which TEOAEs were present based on the median CSM and SNR up to 11.3 kHz but absent at 12.7 and 14.3 kHz. These findings suggest that higher stimulus levels at HFs and longer averaging times may be helpful in detecting HF TEOAEs.

3. Experiment 2

The goals of Exp. 2 included a preliminary assessment of TEOAEs recorded with chirp stimuli that have even slower sweep rates than those used in Exp. 1, and a change in procedure to increase the averaging time of LF TEOAEs from 1 to 2 minutes, and of HF TEOAEs from 1 to 4 minutes. The longer averaging time for HF responses would hopefully address the difficulty of detecting HF TEOAEs found in Exp. 1, while remaining sufficiently short for potential clinical use. Experiment 2 mainly focused on the use of chirp stimuli that could be presented without system distortion at higher relative levels than was possible with click stimuli. Including chirps with slower sweep rates traversed the qualitative divide between sweep rates used in swept-tone studies of SFOAEs (Chen et al., 2014; Kalluri & Shera, 2013) and the relatively faster sweep rates typically used with chirp OAE measurements. Experiment 2 used a smaller set of test ears than Exp. 1, although both adult and child subjects were tested. A further goal of Exp. 2 was to measure TEOAEs using a higher stimulus level at HFs compared to that at LFs. This was adopted to partially address the high-frequency attenuation of forward transmission from the ear canal to the cochlea.

Another goal of Exp. 2 was to evaluate the feasibility of measuring TEOAEs in children with CF for use as a physiological test to diagnose ototoxic SNHL. CF is an autosomal recessive genetic disorder associated with infections that threaten and reduce the quality of life. Such infections residing in the lung are managed using aminoglycoside (e.g., tobramycin or amikacin) and/or glycopeptide antibiotics (e.g., vancomycin). The drugs are typically administered using an intravenous or inhaled application. These antibiotics are ototoxic, i.e., they degrade auditory function in the inner ear and often result in a permanent SNHL. The cumulative intravenous dose of these antibiotics in CF patients has a negative effect on hearing sensitivity, after controlling for age and gender effects (Garinis et al., 2017a). The damage from these ototoxic drugs appears first at the basal end of the cochlea tuned to high frequencies, and includes damage to outer hair cells whose functioning is assessed via OAEs. Previous work demonstrated the potential value of TEOAEs to detect ototoxic SNHL in CF patients (Garinis et al., 2017b), but the upper TEOAE test frequency in that study was 8 kHz. This suggests the use of HF TEOAEs above 8 kHz as a potentially more sensitive diagnostic test for early identification of ototoxicity in CF patients.

3.1 Material and Methods

3.1.1 Subjects and Clinical Procedures—The research plan for using human subjects was approved by the Institutional Review Boards at Cincinnati Children's Hospital Medical Center (Cincinnati, OH) and Oregon Health & Science University/Veterans Affairs (Portland, OR). Each participant signed informed consent documents to participate in this study, and completed testing during a single, two-hour session.

Clinical tests were as described for Exp. 1. Inclusion criteria in a NH group in Exp. 2 were 226-Hz tympanometry within normal limits, and AC audiograms of 15 dB HL or better at all frequencies up to 16 kHz. The above clinical tests were used for adults and children, except that the extended high frequencies used with children were at 10, 12.5, 14 and 16 kHz compared to those used with adults at 9, 10, 11.2, 12.5, 14 and 16 kHz. The AC inclusion criteria in Exp. 2 for NH of hearing within 15 dB HL were more stringent than the inclusion criteria in Exp. 1 of hearing within 20 dB HL. TEOAEs were measured in both ears of some NH adult subjects, for which each ear was tested in a separate visit. The inclusion criterion for the test ear on the second visit was 226-Hz tympanometry within normal limits. Audiometry was conducted on both ears on the initial visit.

A total of 9 adult participants (4 female, 5 male) met these NH inclusion criteria for at least one ear, with 11 NH test ears included in the study (3 left and 8 right). The age range was 23 to 38 y., with mean age of 32.3 y. and SD of 4.8 y. The mean age was similar to the adults in Exp. 1 with a much smaller SD. Four adult ears with 226-Hz tympanometry within normal limits were retested at approximately one month after the initial test to establish test-retest reliability.

A total of 6 child control participants without CF met these NH inclusion criteria (3 female, 3 male), with 6 test ears included in the study (3 left, 3 right). The age range was 11.3 to y., with mean age of 14.0 y. and SD of 2.1 y. A total of 4 female child participants with CF participated in the study, with 1 having NH and the other 3 having SNHL (as described below in more detail). One ear of each CF patient was tested (3 left, 1 right). The CF age

range was 16.7 to 17.6 y., with mean age of 17.3 y. and SD of 0.4 y. Thus, the age ranges of the control and CF child groups were generally similar with slightly older CF subjects.

Information is provided about the CF subjects and their previous history of ototoxic medications and onset of hearing loss. This is relevant to the question of the degree of confidence that any observed hearing loss is ototoxic. All measured hearing loss occurred at high frequencies, which is consistent with ototoxicity as the cause of the hearing loss. The four CF subjects (test ear) are denoted as CF1003 (left), CF1016 (left), CF1023 (right) and CF1051 (left). All subjects had received ototoxic medications to remediate symptoms of CF prior to enrollment in the study.

CF1003 had normal hearing except at 14–16 kHz, at which hearing levels in the test ear were 35–45 dB. Hearing loss worsened in the opposite ear at 14 kHz on later study visits. The subject had 673 doses of intravenous (IV) Vancomycin and 279 doses of IV Tobramycin from 2012–2017, mainly before entry into the study in late 2016.

CF1016 entered study in early 2017. Audiograms were initially measured with an existing SNHL at 10–16 kHz that did not change on three subsequent visits. The subject received 104 doses of IV Tobramycin starting in 2014 and continuing through 2017.

CF1023 entered study in mid-2017 and received audiograms on two visits with SNHL at 14 kHz in the test ear on each visit. The subject received 27 IV Tobramycin doses between 2015 and 2017.

CF1051 entered study in early 2018 and was tested once. Audiometry was normal up to 16 kHz in both ears. The subject received 61 IV Tobramycin doses between 2012 and 2018.

3.1.2. TEOAE methods—TEOAE testing was performed at ambient pressure in the ear canal using the same probe as in Exp. 1, i.e., the Etymotic 10B+ microphone probe assembly with a pair of ER2 sound sources. A different computer sound card was used (RME Babyface Pro) that enabled the use of chirps with longer durations. The TEOAE methods were the same as those in Exp. 1, except for modifications described in the remainder of this section.

Both click and chirp stimuli were used with an emphasis on the chirp stimuli, which were all positive chirps (sweeping from low to high frequencies). The chirp sweep rates included the fast, medium and slow rates used in Exp. 1, an extra (X) slow rate, and an extra, extra (XX) slow rate. Only one stimulus polarity condition was used in Exp. 2 to reduce the overall number of tests and because the results from Exp. 1 showed only small differences in TEOAEs between positive- and negative-chirp conditions. The decision to use positive-chirp stimuli in Exp. 2 was due to the fact that the preliminary software and testing for absence of distortion was only completed for the positive chirps at the onset of the study. The sweep rates for each chirp stimulus are listed in Table 1. The corresponding buffer duration for each stimulus type is also listed in the table. Each stimulus was sufficiently long to contain the swept stimulus over the analysis band, a TEOAE waveform ending as much as 25 ms after the effective end of the stimulus, and an additional period of silence. These sweep rates and

buffer durations were the same for LF and HF stimuli. This was possible because the bandwidths of LF and HF stimuli were similar (0.5–8 kHz versus 7.1–14.7 kHz).

In Exp. 1, the LF and HF stimuli had been presented at the same set of relative stimulus levels to support spectral measurements of TEOAEs across the combined frequency range at a constant incident sound pressure level, but the stimulus levels were insufficient in Exp. 1 to elicit HF TEOAEs in many NH ears. Thus, the stimulus levels used in Exp. 2 for chirps were in pairs that were 6 dB larger for the HF stimuli than for the corresponding LF stimuli. The relative stimulus levels for clicks were $L_{rel} = 0$ dB for the LF stimuli and $L_{rel} = 5$ dB for the HF stimuli. The latter level was 5 dB rather than 6 dB larger, because a slight amount of distortion was considered possible at $L_{rel} = 6$ dB.

TEOAE data were recorded for 16 different chirp stimulus conditions in Exp. 2 (see Table 3). For LF stimuli, chirp TEOAEs were recorded at $L_{rel} = 0$ dB for all 5 sweep rates to enable comparison of TEOAEs with constant incident sound pressure levels. Chirp TEOAEs were also recorded for 3 LF stimuli at $L_{rel} = 12$ dB for the slow, X slow, and XX slow sweep rates. The X and XX slow sweep rates reduced peak levels, and thus it was possible to apply more gain to these stimuli without producing measurement-system distortion. For HF stimuli, chirp TEOAEs were recorded at $L_{rel} = 6$ dB for all 5 sweep rates, and at $L_{rel} = 18$ dB for the slow, X slow, and XX slow sweep rates. Table 1 shows the number of stimulus buffers B in 4-minute recordings of HF TEOAE data, which ranged from $B=2206$ for the click, $B=1148$ for the fast and medium chirps, and $B=40$ for the XX slow chirps. The corresponding numbers of stimulus buffers in the 2-minute recordings of LF TEOAE data were half the numbers listed in the table.

In Exp. 2, the intermediate step (used in Exp. 1) of time-averaging responses over a set of sub-averaging buffers was omitted, so $K=B$. This increased the calculation time of the incoherent average used to estimate the TEOAE noise level, but the benefit was to reduce the variability of estimating this noise level by increasing K (see related discussion in section 2.1.2). Reducing random variability of the noise was desirable to better interpret TEOAE responses with relatively small SNRs. After removing intermittently noisy responses, all remaining buffers of data were averaged coherently to obtain the mean TEOAE response and incoherently to calculate the TEOAE noise response. For example, the number of buffers in the HF TEOAE measurement using the medium chirp was $B=1148$, so the incoherent spectral averaging was performed on each of these buffers of data.

The TEOAE SNR and CSM were used to assess the presence and strength of the TEOAE response at each frequency and time value, but were calculated over the K data buffers. The critical CSM was calculated using Eq. (1) with the number of averaging buffers K equal to the appropriate value from Table 1 ($K=B$ in Exp. 2). For example, the critical CSM for TEOAEs measured using the medium chirp was 0.0511 at HF, based on $K=1148$ with 4 minutes of data, and 0.0722 at LF, based on $K=574$ with 2 minutes of data. The critical SNR was 6.6 dB, the same as in Exp. 1.

TEOAE group delay (GD) was calculated as the phase gradient of the TEOAE pressure residual at each spectral frequency for which CSM exceeded its critical value. A signal-

processing rationale for investigating GD is that TEOAE level discards phase information whereas GD describes the phase gradient of the TEOAE spectrum. Another rationale for investigating GD is that it is theorized to be a measure of the frequency selectivity of cochlear tuning at low to moderate stimulus levels (Shera et al., 2002). The GD was smoothed over each $1/6^{\text{th}}$ octave band by weighting its value at each spectral frequency within the band by the squared magnitude of the TEOAE at that frequency. These procedures were sufficient to provide individual-ear estimates of GD, and are described elsewhere in more detail (Keefe, 2012; Keefe et al., 2016).

Cochlear mechanics in the mammalian ear is compressive at the moderate stimulus levels typical of TEOAE measurements. In response to an increase in stimulus amplitude x , the TEOAE amplitude was assumed to grow compressively as x^v with a positive growth exponent value v bounded above by 1. More complex models of response growth are available (Schairer et al., 2003), but were not used inasmuch as TEOAE data in Exp. 2 were acquired at only two stimulus levels. The growth exponent was calculated based on the TEOAE levels recorded at these two stimulus levels differing by 12 dB. In addition to the basic interest in understanding OAE response growth, there is interest in the potential clinical use of TEOAE response growth. One application might be in longitudinal monitoring of TEOAE properties in individuals selected from a high-risk occupational noise group or in a group exposed to ototoxic medications. These types of cochlear damage may linearize the mechanics of the basilar membrane at moderate stimulus levels, thereby increasing the growth exponent of a detected TEOAE. Such a change would be an addition to any reduction in TEOAE level arising from such damage.

3.2. Results

3.2.1. Individual results in adult ears—Illustrative results of the TEOAE spectra and GD are shown in Fig. 8 for adult subject C. Results for TEOAE GD in an individual ear are presented because few studies have examined GD in an individual ear, particularly at HF.

The effect of stimulus sweep rate is shown on the TEOAE spectra of subject C, which are plotted in the left column of Fig. 8. Each plot combines LF spectra (for stimulus level $L_{rel} = 0$ dB) and HF spectra (for stimulus level $L_{rel} = 6$ dB). These overlapped between 7.1 and 8 kHz. The LF spectrum at 7.1 kHz and the HF spectrum at 8 kHz are the preferred responses since each is an average of TEOAE data over a full $1/6^{\text{th}}$ octave. The SNR may be inferred in each left panel as the difference between TEOAE signal and level plots (group SNR results are described below). The SNR was largest at HF for the medium sweep rate, and next largest at the fast and slow sweep rates. TEOAE were absent at 10 kHz at the X and XX slow sweep rates (based on the SNR criterion), while they were present at all frequencies up to 14.3 kHz at the fast, medium and slow sweep rates. This is mainly because of the much larger number (B) of averaging buffers at these relatively faster sweep rates (see Table 1). The noise reduction (in dB) varies with B as $10\log_{10} B$ with 0 dB for no averaging ($B=1$) and larger noise reductions as B increases, as listed in Table 1. It was not possible to obtain HF click data at $L_{rel} = 6$ dB with the selected criterion to avoid system distortion, so that the greatest noise reduction in chirps was obtained using fast and medium sweep rates.

The fine structure of each TEOAE spectrum (left column, Fig. 8) varied with sweep rate. The 1/6th octave averaging sufficed to smooth out most of the fine structure differences. Excessive variability in the HF fine structure for the X and XX slow sweep TEOAEs was driven by noise. The TEOAE was classified as present at all test frequencies for this ear based on both SNR and CSM criteria.

The smoothed GD of the TEOAE data of Subject C also varied with sweep rate (see right column of Fig. 8). The GD data were only calculated for TEOAE frequency bins within each 1/6th octave at which the CSM exceeded the critical CSM. This criterion was satisfied to calculate GD at HF's up to 14.3 kHz for the fast, medium and slow sweep rates, but only up to 10 kHz for the XX slow sweep rate. The dashed line shows the GD for a scale-symmetric cochlea, which varies inversely with frequency and which is selected to have a GD of 11 ms at 1 kHz typical of a NH human adult ear. The extent to which GD lies above this dashed line shows a relative increase from scale symmetry, which is theorized to be related to increased frequency selectivity of cochlear tuning (Shera et al., 2002). For the click and the faster sweep rates, the GD values in this ear were below this scaling line at frequencies up to 1 kHz, close to the scaling line between 1.2 and 4 kHz, and above the scaling line at some higher frequencies, especially at and above 10 kHz. This frequency variability in GD in this ear relative to the GD of a scale-symmetric cochlea is consistent with group results for SFOAEs (Shera & Guinan, 2003) and TEOAEs (Keefe et al., 2012). There was considerable HF variability in GD for the medium chirp with the largest SNR (row 3). Residual differences in the TEOAE fine spectral structure and GD across sweep rates in Fig. 8 is evidence for effects of temporal-spatial nonlinearities in cochlear response.

3.2.2 Group results in ears of adults—The distribution statistics for the stimulus peSPL and SEL in adult ears are listed in Table 3 for all stimulus conditions in Exp. 2. Values of the mean and SD were calculated for 11 ears with NH at frequencies up to 16 kHz. The mean peSPL was largest for the LF click condition and decreased with decreasing sweep rates for the LF chirp conditions over a range of 27.9 dB, at which the mean SEL varied only for a range of 2.6 dB. The mean peSPL and SEL had similar trends at HF's. At levels of L_{rel} that were 12 dB higher than the corresponding lower-level conditions, the mean peSPL and SEL increased by amounts that ranged from 0.1–1.6 dB less than 12 dB in the LF and HF chirp conditions. For example, the mean HF peSPL for adults in the slow chirp condition was 68.2 dB at L_{rel} of 0 dB and 79.9 dB at L_{rel} of 12 dB, which was a change in peSPL of 11.7 dB or 0.3 dB less than the change in L_{rel} . This reduction compared to a 12-dB increase in L_{rel} was larger at LF's. This small discrepancy may have resulted from a larger contribution of noise to the lower-level stimulus conditions, especially at the XX slow sweep rate with the fewest averages. Overall, these results show the linearity of stimulus levels at the lower and higher L_{rel} values, and the expected reduction in the chirp peSPL as the sweep rate decreased.

Group TEOAE results in NH adults are shown in the top row for the median CSM (Fig. 9A) and median SNR (Fig. 9B) measured at L_{rel} of 0 dB at LF's and 6 dB at HF's (except for L_{rel} of 5 dB for the HF clicks). The median TEOAE SNR was classified as present based on the criterion SNR at all test frequencies for the click, and for chirps with fast, medium and slow sweep rates (Fig. 9B). The median TEOAE SNR at this L_{rel} was classified as

absent at higher frequencies for the chirps with X slow and XX slow sweep rates. The critical CSM values for classifying the TEOAE as present or absent based on CSM are plotted in Fig. 9A for each stimulus condition. The critical CSM varied with the total number of buffers (see Table 1), so that the interpretation of CSM across stimulus conditions is more complicated than for SNR. Notwithstanding that fact, the median TEOAE CSM at this L_{rel} was classified as present based on the appropriate criterion CSM at all test frequencies for the click and the chirps with fast, medium and slow sweep rates. The median CSM classified the TEOAE as absent for the X slow and XX slow sweep rates. The “best” performing TEOAE test was defined as that test with the largest median of the 25th percentiles of SNR across HFs, and was calculated to be the medium sweep-rate chirp condition. The fast sweep-rate chirp performed nearly as well on both SNR and CSM, while the click performed nearly as well on SNR but not CSM. The IQR is shown as a fill pattern in Fig. 9A–B for the best, i.e., the medium sweep-rate, test. The key property is that its 25th percentile of SNR and CSM exceeded their respective criterion values at all test frequencies. This is improved performance relative to the TEOAE results for NH adults in Exp. 1 (see Fig. 6).

Group TEOAE results in NH adults are shown in row 2 for the median CSM (Fig. 9C) and median SNR (Fig. 9D) measured at L_{rel} of 12 dB at LFs and 18 dB at HFs. The slow sweep-rate chirp condition performed much better than the X slow and XX slow sweep-rate conditions at this stimulus level for both SNR and CSM. The IQR is shown as a fill pattern in these panels for the best, i.e., slow sweep-rate, condition. The median CSM and SNR were classified as present for this condition at all frequencies, and similarly for the 25th percentiles of CSM and SNR except for near misses at 14.3 kHz in both responses. The responses at the lower stimulus level in Figs. 9A–B suggest that the medium and fast sweep-rate chirps might have performed better than the slow sweep-rate chirp, although no data were acquired for these faster sweeps (see Table 3).

3.2.3. Group results in ears of children—The distribution statistics for the stimulus peSPL and SEL in ears of children are listed in Table 3 for all stimulus conditions. Values of the mean and SD were calculated for 6 ears with NH at frequencies up to 16 kHz. Overall, these results in children were similar to those listed in Table 3 for adults. Nevertheless, the mean peSPL and SEL were about 1 dB larger for children than adults, which may either be due to differences in the sound sources between the pair of testing sites used for adults and children, or else a small maturational effect in the acoustic functioning of the ear canal and middle ear. The SDs of peSPL and SEL were slightly larger in children than adults, which is consistent with increased noise levels in children.

Group TEOAE results in NH children are shown in row 3 of Fig. 9 for the median CSM (Fig. 9E) and median SNR (Fig. 9F) measured at L_{rel} of 0 dB at LFs and 6 dB at HFs (except for L_{rel} of 5 dB for HF clicks). Consistent with adult data, the median TEOAE SNR was classified as present based on the criterion SNR at all test frequencies for the click and for the chirps with fast, medium and slow sweep rates (Fig. 9F). The best performing test on SNR was the fast sweep-rate chirp TEOAE (although the medium sweep-rate chirp performed nearly as well and was the best on CSM). The median TEOAE CSM at this L_{rel} was classified as present based on the criterion CSM at all test frequencies for the click, and

for the chirps with slow sweep rate, except that CSM classified the click TEOAE as absent at 12.7 kHz. The IQRs of CSM and SNR for the fast chirp condition are shown as fill patterns in Figs. 9E–F, respectively. The 25th percentiles of CSM and SNR for the fast chirp condition were classified as having TEOAEs present at all frequencies up to 11.3 kHz, and both were classified as absent at 12.7 and kHz. The X slow and XX slow chirp conditions led to TEOAEs classified as absent at mid-to-high frequencies for both CSM and SNR.

Group TEOAE results in NH children are shown in the bottom row for the median CSM (Fig. 9G) and median SNR (Fig. 9H) measured at a L_{rel} of 12 dB at LFs and 18 dB at HF. The slow sweep-rate chirp condition again performed much better than the X slow and XX slow conditions. The IQR is shown as a fill pattern in these panels for this slow sweep-rate condition. The median CSM and SNR were classified as present for this condition at all frequencies except kHz. The 25th percentiles of both CSM and SNR classified the TEOAE as present at all frequencies up to 10.1 kHz, and absent at 12.7 and 14.3 kHz.

Audiometric and TEOAE data are shown in Fig. 10 for the control group of six test ears of children (NH without CF) and the four CF ears for both LF (left column) and HF (right column) data. The LF audiogram (Fig. 10A) shows the gray fill pattern for the control group of children with NH. The LF TEOAE data for the control group are shown using box and whiskers plots. The 25th percentiles of CSM (Fig. 10B) and SNR (Fig. 10C) exceeded or equaled their critical values at frequencies up through 5.7 kHz, consistent with their specificities of 75% or more. The TEOAE spectral levels (L_S) of the control group of children (Fig. 10D) were similar to the NH adults (Fig. 4, top panel).

The LF audiograms of the four CF ears were in the normal range (Fig. 10A), although a slight hearing loss was observed for CF1016 and CF1023 at 0.5 kHz, and for CF1016 between 2 and 3 kHz. The LF CSM (Fig. 10B) and LF SNR (Fig. 10C) of ears CF1016 and CF1023 were reduced compared to the corresponding IQR of the control group at frequencies between 0.7 and kHz. Ear CF1016 with slight hearing loss at 2 and 3 kHz had low CSM and SNR between 2.8 and 5.7 kHz. The L_S of CF1003 (best hearing thresholds in subset of CF ears) was in the control range between 0.7 and 5.7 kHz, while L_S of CF1016 and CF1051 were below the control range between 0.7 and 4 kHz.

The LF CSM and SNR in 3 of the 4 CF ears were highly consistent with one another in terms of classifying TEOAEs as present or absent (Fig. 10B–C), and their values in three of the four CF ears were reduced between 0.7 and 2 kHz compared to the NH control group. CF ear CF1016 had a LF hearing loss at 2 and 2.8 kHz, compared to a borderline CSM and SNR values at 2.8 kHz and absent values at 4 kHz. The fourth CF ear (CF1051) had a normal LF audiogram but lower values of CSM and SNR than the control group, including absent TEOAEs based on CSM at 0.7 and 1 kHz (Fig. 10B).

The HF audiograms and TEOAEs are described in more detail. The HF audiograms (Fig. 10E) are again represented by a gray fill pattern of NH for the control group. For controls, the median HF CSM (Fig. 10F) and SNR (Fig. 10G) exceeded their critical values at all HF, and the 25th percentile of HF CSM exceeded the critical CSM up to 11.3 kHz and was

equal at 12.7 kHz. The 25th percentile of HF SNR also exceeded the critical SNR up to 11.3 kHz, but not at 12.7 and 14.3 kHz.

The four CF ears had differing HF audiometric patterns with ear CF1051 having NH at all frequencies up to 16 kHz (Fig. 10E). Ear CF1023 was in the normal range except for a slight hearing loss at 14.0 kHz. Ears CF1003 and CF1016 had larger HF losses, with CF1003 normal up to 12.5 kHz and CF1016 normal up to 8 kHz. Their HF losses were consistent with a typical pattern of ototoxic SNHL, although more data would be needed to analyze the relationship over time between cumulative dosage of antibiotics and audiometric thresholds.

For CF1003 at extended HFs where there is NH (8, 10 and 12.5 kHz), the TEOAE was classified as present based on both CSM and SNR at 8, 9, 10.1, and 11.3 kHz, and absent at 12.7 kHz. CF1003 had an audiometric loss at 14.0 kHz, for which CSM and SNR at 14.3 kHz each classified the TEOAE as absent (Figs. 10G–H). There is close agreement for CF1003 between the audiogram and TEOAE responses.

For CF1016 at extended HFs where there is NH (8 kHz), the TEOAE was classified as present based on both CSM and SNR at 8 and 9 kHz (Figs. 10F–G). HF hearing loss occurred for CF1016 at 10, 12.5 and 14 kHz (Fig. 10E). The CSM and SNR for CF1016 classified the TEOAE as absent at 10.1, 11.3 (except borderline present for CSM) and 12.7 kHz. Their TEOAE values at 9 kHz were below the respective TEOAE values of any NH ear. Both CSM and SNR classified the TEOAE as present at 14.3 kHz, even though the largest measured hearing loss of 60 dB HL occurred at 14.0 kHz (Fig. 10E). With this exception, the HF TEOAE classification of the predicted frequencies of NH and SNHL for CF1016 agreed with the partitioning of the measured audiogram into regions of NH and SNHL.

For CF1023 at extended HFs where there is NH (8, 10 and 12.5 kHz), both CSM and SNR classified the TEOAE as present at 8 and 9 kHz, although at reduced levels compared to the 25th percentiles of NH ears. Both CSM and SNR classified the TEOAE as absent at 10.1, 11.3 and 12.7 kHz. At the single frequency of hearing loss (14 kHz), both CSM and SNR classified the TEOAE as absent at 14.3 kHz. Future research is needed based on longitudinal measurements in CF ears to test whether TEOAE levels are reduced prior to the detection of any SNHL. The agreement is reasonably close for CF1023 between the audiogram and the TEOAE responses at 8, 9 and 14.3 kHz, but the TEOAE would misclassify the ear between 10.1–12.7 kHz.

For CF1051 where there is NH at all HFs (Fig. 10E), CSM classified the TEOAE as present at all frequencies between 8 and 14.3 kHz, while SNR classified the TEOAE as present at all frequencies in this range except 14.3 kHz. The agreement is reasonably close for this CF ear with NH between audiometric and TEOAE data.

In Fig. 10H, the TEOAE spectral levels (L_S) of CF1016 and CF1023 were below the IQR for control ears at frequencies at and above 9 kHz, except that CF1016 was close to the median of control ears at 14.3 kHz. Ear CF1003 was at or below the IQR for control ears at 10.1 kHz and above. Ear CF1051 had L_S in the IQR range of control ears at all test frequencies, consistent with the pattern of NH.

3.2.4. Group repeatability results in four adult ears—The test-retest repeatability of LF and HF TEOAEs was assessed in four adult ears with NH at all frequencies up to 16 kHz. Data were acquired in these ears at two visits approximately one month apart. The repeatability of each TEOAE measure was calculated as the absolute test-retest difference of the measure at each test frequency. McMillan (2014) describes this relationship of the absolute test-retest difference to other measures of reliability. Data were analyzed for the positive chirp stimulus condition at the medium sweep rate. The relative stimulus level L_{rel} was 0 dB for LFs and 6 dB for HFs.

Figure 11A shows repeatability (L_S) of the LF and HF stimuli recorded by the probe microphone. This repeatability is defined as the magnitude difference of the L_S in the initial test and retest. The repeatability was within 3 dB for all ears up to 2 kHz and increased to 8 dB at higher frequencies up to 8 kHz. This stimulus repeatability varied in the range from 0 to 11 dB between 8 and 14.3 kHz. This variability was likely dominated by either differences in the insertion depth of the probe in the two tests, which produced larger differences at higher frequencies due to standing-wave effects in the ear canal, or differences in noise. The four black circles in Fig. 11A indicate data for which the TEOAE was classified as absent based on SNR for one or both tests. The ear test with the largest stimulus level difference of 11 dB at 14.3 kHz corresponded to a test in which the TEOAE was absent on both tests. The median repeatability of stimulus level for data at which the TEOAE was present based on SNR on both tests was 1.5 dB at LFs (0.7–5.7 kHz) and 2.8 dB at HFs (8–14.3 kHz).

Figure 11B shows the corresponding repeatability (L_S) in the TEOAE spectral levels measured in the LF and HF tests. There is a distinct partition with better repeatability in LF TEOAE levels and worse repeatability in HF TEOAE levels. The HF TEOAE level repeatability varied in the range from 0.5 to 15 dB, which exceeded the range of the HF stimulus level variability. The four black circles in Fig. 11B indicate data for which the TEOAE was classified as absent based on SNR for one or both tests. In particular, the ear test with the largest stimulus level magnitude difference of 11 dB at 14.3 kHz and the corresponding largest TEOAE spectrum level magnitude difference of 15 dB corresponded to a test in which the TEOAE was absent on both tests. Thus, this response was contaminated by noise and not interpretable as a test-retest of a TEOAE present on both tests. Otherwise, the largest repeatability in TEOAE spectral levels was 9.5 dB at 8 kHz. The median repeatability of TEOAE spectrum level for data at which the TEOAE was present based on SNR on both tests was 1.1 dB at LFs and 2.0 dB at HFs.

Figure 11C shows the repeatability in the TEOAE SNR. This repeatability was within 6 dB at all frequencies between 0.71 to 14.3 kHz except for one ear with repeatability of 7.6 dB at kHz. The four black circles in Fig. 11C indicate data for which the TEOAE was classified as absent based on SNR for one or both tests. As before, such data were contaminated by noise and not interpretable as a test-retest of a TEOAE present on both tests. The median repeatability of SNR for data at which the TEOAE was present based on SNR on both tests was 2.5 dB at LFs and 1.3 dB at HFs.

Figure 11D shows the repeatability in the TEOAE CSM. Below 4 kHz, the median CSM ranged between 0.45 and 0.7, while the repeatability of CSM in Fig. 11D ranged between 0.01 and 0.18. The four black squares in Fig. 11D indicate data for which the TEOAE was classified as absent based on CSM for one or both tests, while the four black circles in Fig. 11A–C indicate data for which the TEOAE was classified as absent based on SNR for one or both tests. Three of the four black squares occurred for data in Fig. 11D that were also identified with black circles in Figs. 11A–C as having one or both tests having an absent TEOAE based on SNR. A fourth black square signified a TEOAE test frequency that was absent based on CSM but present based on SNR. Thus, the performance of the TEOAE classification tests based on SNR and CSM was similar. The median repeatability of CSM in Fig. 11D for data at which the TEOAE was present based on CSM on both tests was 0.053 at LFs and 0.031 at HFs. These values were smaller than the median CSM in Figs. 10B and 10F, indicating a satisfactory level of repeatability.

For a given test date, it should be noted that the probe would sometimes work its way out of the ear canal over time, resulting in a shallower insertion depth by the end of the test battery. The insertion depth was not quantitatively monitored during data collection. As described in Exp. 1, stimulus repeatability arises only from differences in forward transmission from the probe between the ear canal and the cochlea, while TEOAE repeatability depends on effects associated with both forward and reverse transmission. The median repeatability differences were larger at HFs than LFs for stimulus level and TEOAE spectrum level, but were smaller at HFs than LFs for TEOAE SNR and CSM. The latter relation may be due to the fact that CSM and SNR were larger at LFs than HFs (see Fig. 9), so the test-retest differences in CSM and SNR were also larger at LFs than HFs. It might be helpful in future research to normalize the repeatability of CSM to the mean CSM in test and retest data across frequency, and similarly for other measures of repeatability. In summary, satisfactory repeatability can be achieved at HFs in TEOAE measurements, particularly those based on SNR and CSM.

3.2.5. Group results on level dependence of TEOAEs in children and adult ears—Figure 12 presents results on the level dependence of TEOAEs in adults and children based on tests at two stimulus levels 12 dB apart. These relative levels L_{rel} were 0 and 12 dB for the LF test, and 6 and 18 dB for the HF test. The LF results are shown using $1/2^{\text{th}}$ octave averaging and the HF results using $1/6^{\text{th}}$ octave averaging, with data at 8 kHz used from the HF test. This frequency separation approximated the set of audiometric frequencies.

Results are presented in Fig. 12A for 11 NH adult ears in the form of the growth exponent (ν) of TEOAE spectral level. This is defined as the dimensionless ratio of the TEOAE residual level difference to the stimulus level difference. This exponent would be equal to one for TEOAE residuals that grow linearly with stimulus level (although recalling that the linear-growth component of the TEOAE was removed in calculating this residual), and less than one for TEOAEs with a more compressive growth. The median growth exponent across all adult ears was in the range of 0.4–0.7 at frequencies between 0.7 and 8 kHz, and in the range of 0.8–0.9 at frequencies between 9 and 14.3 kHz. The corresponding IQR of the growth exponent is shown by the shaded region. The median growth exponent was also

calculated and plotted for those ears with TEOAEs present based on SNR at both stimulus levels. The results were similar for both conditions. Growth exponents in the range from 0.44 to 0.61 have been reported (Schairer et al., 2003) for SFOAEs in NH adult ears at moderate frequencies (1–4 kHz) and moderate stimulus levels.

The median and IQR of the growth exponent are shown in Fig. 12B for 6 test ears of children with NH and without CF. The median growth exponent of this child control group for all ears was in the range of the median for the adult group at frequencies up to 7.1 kHz. However, the median growth exponent in this child group trended to smaller values (0.7 down to 0.45) than for adults at frequencies of 9 to 14.3 kHz. The median growth exponent is also shown for those child ears with TEOAEs present based on SNR at both stimulus levels. The median growth exponent in this subgroup of ears was larger than the median growth exponent in all child ears at 2, 12.7 and 14.3 kHz.

Averaged across LFs up to 5.7 kHz in ears with TEOAEs present at both levels, the average growth exponent was 0.56 for adults and 0.55 for children. Averaged across HF between 8 and 14.3 kHz in ears with TEOAEs present at both levels, the average exponent was 0.78 for adults and 0.66 in children, i.e., slightly smaller in children. Progressively fewer test ears had TEOAEs present at both stimulus level for frequencies at higher frequencies above about 10 kHz. This was mainly due to the absence of a TEOAE response at the lower stimulus level. In that regard, it would be helpful in future research to use a smaller difference in stimulus level than 12 dB, so that the TEOAE would more likely be present in more ears at both stimulus levels. A smaller growth exponent is associated with a more compressively nonlinear growth of TEOAE response, which would be consistent with a more compressive nonlinearity in outer hair cell function (Zwicker, 1979). This suggests that outer hair cell functioning was more compressive in this younger group of subjects in the HF range, even though both adult and child groups had NH up to 16 kHz. More research is needed on the age dependence of TEOAE response growth.

3.3. Discussion and Conclusions

The increase in averaging time in Exp. 2 from one to four minutes was helpful in measuring HF TEOAEs. While the slowest (X and XX) chirp sweep rates reduced the peSPL compared to that of the click or of chirps with faster sweep rates, the ability to include more buffers of data in the average at relatively faster chirp sweep rates improved the ability to detect HF TEOAEs. The best overall performance in NH adults or children at the relative stimulus levels of L_{rel} of 0 dB at LFs and 6 dB at HF was obtained with the medium or fast chirp (see Fig. 9). The large number of averaging buffers for the medium and fast chirp responses contributed to this success. The click tests had better performance than the chirp tests at slow, X slow, and XX slow sweep rates.

As listed in Tables 2 & 3, three positive-chirp stimulus conditions were repeated in Exps. 1 and 2: HF medium chirps at L_{rel} of 6 dB, HF fast chirps at L_{rel} of 6 dB, and LF slow chirps at L_{rel} of 12 dB. The magnitude difference of the mean stimulus peSPL between Exps. 1 and 2 was 1.7 dB for the fast HF chirp, 2.9 dB for the medium HF chirp and 0.1 dB for the slow LF chirp. The magnitude difference of the stimulus mean SEL between Exps. 1 and 2 was 1.6 dB for the fast HF chirp, 2.9 dB for the medium HF chirp and 1.3 dB for the

slow LF chirp. These level differences were within the combined SDs of peSPL and SEL for each comparison (combined SD calculated as $\sqrt{SD_1^2 + SD_2^2}$). Some of these measurements were performed at different sites using different equipment, and there was little or no overlap in the subjects in each NH group. Another comparison of interest was the HF slow chirp, which was measured at the L_{rel} of 12 dB in Exp. 1 and 18 dB in Exp. 2, i.e., at a stimulus level that was 6 dB larger than in Exp. 1. The corresponding magnitude differences for this stimulus pair were 7.9 dB for peSPL and 8.2 dB for SEL. These were differences of 1.9 and 2.2 dB, relative to the 6-dB increase L_{rel} , and were within their respective combined SDs.

These pairs of HF chirp tests differed in their measurement duration, which was 1 minute in Exp. 1 and 4 minutes in Exp. 2. The LF slow chirp test duration was 2 minutes in each of Exps. 1 and 2. The (signed) difference SNR in SNR was calculated as the SNR in Exp. 2 minus the SNR in Exp. 1. The mean SNR in the LF slow chirp was averaged over all half-octave frequencies from 0.7 to 5.7 kHz. The mean SNR in each HF chirp comparison was averaged over all $1/6^{\text{th}}$ octave frequencies from 8 to 14.3 kHz.

The mean SNR was improved in Exp. 2 relative to Exp. 1 as follows: 10.2 dB for the HF fast chirp, 9.9 dB for the HF medium chirp, 5.6 dB for the LF slow chirp, and 7.6 dB for the HF slow chirp. The LF slow chirp test had twice the measurement duration in Exp. 2 compared to Exp. 1, which results in a predicted SNR improvement of $10\log_{10} 2$ or 3.0 dB, and the same L_{rel} of 12 dB in both experiments. This is partly explained by the fact that the LF SNR in Exp. 1 was calculated as a mean over $1/2$ octave frequencies, but the SNR at each of these frequencies was averaged over a $1/6^{\text{th}}$ octave frequency bandwidth. Because the bandwidth of the $1/2$ octave is three times the bandwidth of the corresponding $1/6^{\text{th}}$ octave having the same center frequency, then the averaging in Exp. 2 results in a predicted improvement of $10\log_{10} 3$ or 4.8 dB. The total predicted SNR improvement is $3.0 + 4.8 = 7.8$ dB, or 2.2 dB more than the measured mean DSNR of 5.6 dB for the LF slow chirp. At LFs, the NH adult group in Exp. 2 had AC audiograms within 15 dB HL, whereas the NH group in Exp. 1 had AC audiograms within 20 dB HL. It is possible that some of the 2-dB improvement in SNR in Exp. 2 is explained by testing ears with better hearing, and thus having outer hair cells with a more compressively nonlinear function leading to larger TEOAE levels. The difference is otherwise due to measurement variability.

The HF slow chirp test was performed with a measurement duration of 4 minutes in Exp. 1 compared to a duration of 1 minute in Exp. 1, which would predict a SNR improvement in Exp. 2 of $10\log_{10} 4$ or 6.0 dB. The same averaging bandwidth of $1/6^{\text{th}}$ octave was used in both Exps. 1 and 2. The predicted mean SNR is 6.0 dB, which is 1.6 dB less than the measured mean SNR of 7.6 dB. This difference is not explained by the possibility of better cochlear function in the test ears of Exp. 2, so the difference at both LFs and HF is concluded to be a random effect of measurement variability.

The HF fast and medium chirp tests were performed with a measurement duration of 4 minutes in Exp. 2 and 1 minute in Exp. 1, contributing a SNR improvement of 6.0 dB. Another difference was that L_{rel} was 18 dB in Exp. 2 and 12 dB in Exp. 1. The 6 dB increase in relative level (twice the stimulus amplitude in Exp. 2) would generate a higher-

level TEOAE depending on its growth exponent ν . The average growth exponent of the TEOAE at HFs in the NH adult ears in Fig. 12A was approximately 0.78, for which the predicted SNR improvement would be .. or 4.7 dB. Combining this SNR improvement with the 6.0 dB improvement from the increased averaging time predicts a mean SNR of 10.7 dB, which is 0.5–0.8 dB larger than the measured mean SNR of 10.2 dB for the HF fast chirp and 9.9 dB for the HF medium chirp. These differences of less than 1 dB are concluded to be due to measurement variability, and any error related to the limited accuracy of the response-growth model.

As stated above, the growth exponent data in Fig. 12 is a measure of the growth of the nonlinear TEOAE residual, which is not the same as the growth exponent of the total TEOAE. Thus, the predicted mean DSNR has only an approximate validity according to the following argument. Suppose the total TEOAE generated at stimulus amplitude A is $P_{oae}(A)$. TEOAEs were generated using the double-evoked procedure at the reference amplitude A , and also at larger amplitudes of $4A$ and $5A$ (see section 2.1.2). The measured nonlinear TEOAE residual was calculated as $P_{oae} = P_{oae}(A) + P_{oae}(4A) - P_{oae}(5A)$. A model to approximate the level dependence of the nonlinear TEOAE residual is constructed following that used by Schairer et al. (2003) for SFOAEs. This simple model does not consider the reduction in GD that occurs at higher stimulus amplitudes. TEOAE amplitude growth is known to (at least partially) saturate at larger stimulus amplitudes, so the approximation is made that TEOAEs are in the saturation region for the larger stimulus amplitudes. This implies that $P_{oae}(4A) \approx P_{oae}(5A)$. It follows that the nonlinear TEOAE residual approximately extracts the TEOAE generated at the lower, or reference, amplitude, $P_{oae}(A) \approx P_{oae}(A)$. The total TEOAE $P_{oae}(A)$ is assumed to increase with the reference amplitude with a power-law growth of A^ν , so that $P_{oae}(A) \approx CA^\nu$ with a proportionality constant of C (that may be estimated in terms of the relative level of the TEOAE to the stimulus at each frequency). This is the basis for using the growth exponent data in Fig. 12 in the above prediction of mean SNR for TEOAEs measured using the medium and fast HF chirps.

The conclusion is that the tests in Exp. 2 generated larger TEOAE SNRs at HFs than the corresponding tests in Exp. 1 by approximately 10 dB. After accounting for the averaging bandwidth difference in the LF TEOAEs, the improvement in SNR in Exp. 2 in both LF and HF TEOAEs came from the longer measurement time and increased stimulus level. The amount of improvement was reasonably consistent with numerical predictions.

It is predicted that even better performance might be obtained on TEOAE tests using the medium and fast sweep rate chirps by increasing the level of the HF stimulus above the L_{rel} of 6 dB, but these conditions were not tested in Exp. 2 (see Table 3). It is notable that the best HF TEOAE results in Exp. 1 occurred for the HF medium sweep rate chirp condition with L_{rel} of 12 dB in Exp. 1 (see Fig. 6C–D) although the test in Exp. 1 had fewer averages than those in Exp. 2 (see Fig. 9). More research is needed to study the trade-offs on detecting TEOAEs between measurement time, numbers of buffer averages and the sweep rate for chirp or swept-tone stimuli. This is in the context of limiting the maximum stimulus levels to avoid discomfort in the listening level and to avoid probe distortion.

The Exp. 2 results in 6 NH children and 4 children with CF (see Fig. 10) demonstrated the feasibility of measuring TEOAEs in children and pediatric CF patients. TEOAEs in CF ears had reduced CSM and SNR relative to the 25%-ile of CSM and SNR, respectively, in the NH group. In most comparisons at specific frequencies, CSM and SNR correctly classified the HF TEOAE as present or absent in relation to whether the closest HF audiometric frequencies had NH or hearing loss. However, there were also instances of incorrect classification. These results in a small test set are promising but more extensive studies in pediatric populations with CF are needed.

TEOAEs were measured in the present study using stimuli with approximately constant incident pressure level over frequency. The calibration procedure based on incident pressure level mainly controlled for forward transmission of the stimulus through the ear canal and into the middle ear, although, as explained in Section 2.2.1, this stimulus calibration produced an excess pressure level at the tympanic membrane at the widely spaced resonance frequencies of the ear canal. Other calibration procedures are available that make use of reflectance data measured over the same frequency range as the evoked OAE (Souza et al., 2014; Keefe et al. 2017). No high-frequency reflectance data were acquired in the present study. This stimulus calibration procedure has the advantage of simplicity inasmuch as it does not require any in-the-ear calibration. The reference equivalent threshold sound pressure levels above 8 kHz in the audiometer were based on normative measurements in young adults. Hearing thresholds in pediatric subjects were calibrated in terms of this audiometric standard. In future research, age-matched normal comparisons may be appropriate because hearing thresholds across low and extended high frequencies differ in children (of age 5–19 y.) compared to young adults (of age 20–29 y.) (Rodríguez Valiente et al., 2014).

Test-retest variability was illustrated in Exp. 2 in small-group analyses of stimulus and TEOAE responses (Fig. 11). This variability may arise from variations in probe insertion, although it may also occur due to transient variations in middle-ear transmission arising from fluctuations in middle-ear pressure or other physiological changes.

The TEOAE test-retest variation due to probe insertion may be controlled by measuring transfer relations between the probe microphone and the “TEOAE radiation source” on the tympanic membrane that reverse propagates to the microphone. For a given impulsive stimulus as measured by the probe microphone, this TEOAE radiation source is the initial reverse-directed TEOAE pressure generated at times after the stimulus presentation but in the hypothetical absence of any round-trip reflections of the TEOAE between the tympanic membrane and probe. When measured as a nonlinear TEOAE residual at the microphone location via a double-evoked procedure, this TEOAE radiated source pressure was analyzed using a cylindrical ear-canal model and termed the otoacoustic reflected pressure (Keefe, 1997). A dimensionless, nonlinear otoacoustic transfer function was calculated by dividing otoacoustic reflected pressure of the TEOAE by the incident (forward) pressure of the stimulus. The TEOAE radiation source pressure at the tympanic membrane was termed the emitted pressure by Charaziak and Shera (2017), and expressed as a transfer function with respect to the total TEOAE pressure measured by the probe microphone for the case of a cylindrical ear-canal model. Both descriptions took into account the multiple internal

reflections of this TEOAE radiation source between the probe and the tympanic membrane. The transfer relation between TEOAE microphone pressure and emitted pressure on the tympanic membrane is obtained in this cylindrical ear-canal model by measuring the pressure reflectance at the probe, estimating the cross-sectional area of the ear canal, and estimating the length between the tympanic membrane and probe microphone (Charaziak & Shera, 2017).

The foregoing explains that TEOAE spectral levels (L_5) reported in the present study were not calibrated for reverse ear-canal acoustics, as this transfer function would vary with insertion depth between the tympanic membrane, and thus with the insertion depth of the probe. As described in Exp. 1 for forward transmission of the stimuli, TEOAE measurements based on incident pressure level would increase the pressure levels at the tympanic membrane at ear-canal resonance frequencies such as the $\frac{1}{2}$ and full wavelength resonances in an ear canal with constant cross-sectional area. A more accurate calibration of TEOAEs may be achieved by measurements of TEOAEs and reflectance at all test frequencies, including information on ear-canal area changes. The additional test-retest variability associated with the reflectance measurement must also be considered in combination with the test-retest variability of the TEOAE measurement. Such calibrated measurements have clinical potential to improve estimates of the absolute sound levels of HF TEOAEs. Inclusion of a wideband reflectance test has the further clinical advantage of assessing middle-ear function to complement the information on cochlear and middle-ear function provided by an OAE test.

It is clinically relevant to point out that other frequency-averaged LF and HF TEOAE measures may be affected less by these complexities of forward and reverse transmission, and do not require a concomitant LF and HF reflectance test in order to interpret the measures. These TEOAE measures include SNR, CSM, the growth exponent, and GD to a lesser extent. A relative increase in SNR and CSM would occur near ear-canal resonance frequencies at which there is a boost in the eardrum stimulus pressure level, or by variations in the reverse transfer function between the emitted and microphone pressure of the TEOAE. The boost effects on CSM and SNR at a resonance frequency are attenuated by averaging over a range of frequencies that include frequencies more distant from the resonance frequency. If the insertion location does not vary over a large distance, then the frequencies of the boost effects are not shifted much. The test-retest values of frequency-averaged SNR and CSM would then be repeatable. This is supported by the repeatability data on TEOAE SNR and CSM in Fig. 11. When calculated for ears having TEOAEs present on test and retest, the median HF repeatability was 1.3 dB for SNR compared to a slightly larger median HF repeatability of 2.0 dB for TEOAE spectral level. Measuring the transfer relation between TEOAE microphone pressure and emitted pressure on the tympanic membrane on test and retest may further improve the HF repeatability of TEOAE measurements. The growth exponent, or more generally the complete input-output function, of the TEOAE (or SFOAE), is only weakly affected by forward transmission (i.e., the boost in TEOAE level at the half- and full-wavelength resonance frequencies), and is unaffected by reverse transmission. The latter derives from the property that the linear transfer function describing reverse ear-canal transmission between the eardrum and microphone is the same at each stimulus level that elicits the TEOAE (or SFOAE). The potential clinical benefit of

measuring the TEOAE growth exponent would be compromised if the insertion depth of the probe during a particular test visit changed between multiple tests that differed only in stimulus level. Such a change in insertion depth between the times of a reflectance test and OAE test would also compromise the use of reflectance to interpret the OAE level in the ear canal. These confounds might be addressed in future research by a real-time acoustical assessment of probe insertion depth. A simple test would monitor any change in the half-wavelength frequency of the stimulus eliciting the OAE between any pair of tests that used the same stimulus. Alternatively, reflectance could be measured before and after each OAE test to detect any change in probe position within the ear canal.

For a growth exponent measurement to be clinically useful in TEOAE tests using two stimulus levels, it should be interpreted at a particular frequency only when the TEOAE is classified as present at both levels. This was the case in the group analyses in Fig. 12. The distributions of growth exponents in adults and children with NH were similar overall, although trending to higher median values in adults at 12.7 and 14.3 kHz. More research is needed to investigate the age dependence of the compressive growth of HF TEOAEs.

The contribution to TEOAE GD of the difference in round-trip travel time, which would be attributable to any difference in probe-insertion depth, is also small. The range of smoothed TEOAE GDs in Fig. 8 is about 1–11 ms from 14.3 kHz down to 0.7 kHz. By comparison, the round-trip travel time is approximately 0.1 ms in an adult ear canal with a mid-canal probe placement (Keefe et al., 2015), and its test-retest variability would be much smaller than 0.1 ms. Thus, smoothed GD measurements in individual ears may also contribute to clinical assessments of cochlear function in the absence of a wideband reflectance measurement.

Experiment 2 is the first report of HF TEOAEs in children with CF and children without CF. This study demonstrated the feasibility of test measurements in this age group and patient group, and the initial data from NH children were relatively similar to data from NH adults. Further study with more participants is needed to improve TEOAE measurements at and above 12.7 kHz. With that reservation, the use of HF TEOAEs is a promising additional test for diagnosing ears with a HF SNHL related to outer-hair-cell dysfunction, including SNHL due to ototoxic antibiotics used to treat CF patients.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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List of Abbreviations:

AC air-conduction

BC	bone-conduction
CF	cystic fibrosis
CSM	coherence synchrony measure
DPOAE	distortion product otoacoustic emission
GD	group delay
HF	high-frequency
IQR	inter-quartile range
LF	low-frequency
NH	normal hearing
OAE	otoacoustic emission
peSPL	peak-to-peak equivalent sound pressure level
ROC	receiver operating characteristic
SD	standard deviation
SEL	sound exposure level
SFOAE	stimulus frequency otoacoustic emission
SNHL	sensorineural hearing loss
SNR	signal-to-noise ratio
TEOAE	transient-evoked otoacoustic emission

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Highlights:

- Transient-evoked otoacoustic emissions non-invasively assess outer hair cell function up to 14.7 kHz
- First report of TEOAE measurements in children above 8 kHz
- Chirp stimuli elicit TEOAEs at higher sound exposure levels than possible with click stimuli
- A subset of clinically useful TEOAE measures do not require a reflectance calibration for satisfactory repeatability at high frequencies
- High-frequency TEOAEs show promise to detect ototoxic hearing loss in children and adults

Figure 1.

For subject A, A: Mean equivalent-click HF TEOAE waveform for negative-chirp stimulus. B: CSM (left axis) and SNR (right axis) vs. time in $1/24^{\text{th}}$ doublings of time, with critical detection values of CSM and SNR as dashed lines. C: Spectral responses for HF TEOAE (mean signal) and noise in $1/24^{\text{th}}$ octave frequency bands, with fine structure in thin black line. D: CSM (left axis) and SNR (right axis) vs. frequency.

Figure 2.

For subject A, mean $1/6^{\text{th}}$ octave averaged TEOAE signal and noise levels are plotted for stimulus condition $L_{\text{ref}} = 0$ dB. Positive-chirp TEOAEs in left column and negative-chirp TEOAEs in right column. Data for sweep rates of fast (top), medium (middle) and slow (bottom).

Figure 3.

For subject A over LF and HF responses, the raw TEOAE spectra for $L_{ref} = 0, 6$ and 12 dB. Positive-chirp TEOAE, slow sweep rate (top), positive-chirp TEOAE, medium sweep rate (middle), negative-chirp TEOAE, slow sweep rate (bottom). Noise spectra in dashed line for $L_{ref} = 0$ dB level.

Figure 4.

Group results for NH adult test ears at $L_{ref}=0$ dB versus $1/6^{\text{th}}$ octave frequency. Top: Group boxplot of click TEOAE signal L_S . Middle: Boxplot of TEOAE level difference L_S of positive-chirp TEOAEs with slow sweep rate relative to click TEOAEs. Bottom: Boxplot of L_S of positive-chirp TEOAEs relative to negative-chirp TEOAEs, with both chirp stimuli having fast sweep rates. Median level is shown in red line within box, which represents the IQR of level. Whiskers extend to the lesser of 1.5 times the IQR and the full range of data, and outliers are shown by red crosses.

Figure 5.

Group results for NH adult test ears using positive chirp stimuli with slow sweep rates versus $1/6^{\text{th}}$ octave frequency. Left: Boxplot of level difference L_S in TEOAEs for L_S of positive-chirp TEOAEs relative to negative-chirp TEOAEs at $L_{\text{ref}} = 6$ dB. Right: same difference measure at $L_{\text{ref}} = 12$ dB. Median level is shown in red line within box, which represents the IQR of level. The whiskers extend to the lesser of 1.5 times the IQR and the full range of data.

Figure 6.

Group results for CSM (panels A, C, E) and SNR (panels (B, D, F) in NH adult ears using click stimulus at $L_{ref}=0$ dB, and positive chirp stimuli at varying levels $L_{ref}=0, 6$, and 12 dB as indicated in the legend in panel C. Panels A and B show TEOAE chirp responses for the slow sweep rate stimulus, panels C and D for medium rate, and panels E and F for fast rate. Click TEOAE results plotted in each panel as baseline.

Figure 7.

Scatter plot of HF TEOAE CSM vs. AC audiometric threshold in 98 adult ears, with CSM data at $1/6^{\text{th}}$ octave centered frequencies closest to each audiometric frequency given in panel. TEOAE CSM measured at $L_{ref}=12$ dB using positive-chirp stimulus of medium sweep rate. Critical CSM for detecting TEOAE shown as horizontal dashed line. Vertical dashed line separates ears into NH and SNHL groups (Terms: Spec is specificity, Sens is sensitivity, NA is not applicable for frequencies with no SNHL ears).

Figure 8.

TEOAE results for adult subject C with NH. Left panels show $1/6^{\text{th}}$ octave averaged TEOAE levels L_S of signal (solid line, circle markers) and noise (dashed line, x markers) versus frequency along with fine structure in TEOAE level (thin black line). Right panels show smoothed GD (open circles), with black dashed line showing a typical GD for a scale-symmetric cochlea (varying inversely with frequency and equal to 11 ms at 1 kHz). LF TEOAEs were recorded with $L_{\text{ref}} = 0$ dB, and HF TEOAEs with $L_{\text{ref}} = 6$ dB. Each row contains data for LF click TEOAE (row 1), and LF and HF chirp TEOAEs of varying sweep rates (rows 2–6).

Figure 9.

Median CSM and SNR of TEOAEs for NH ears plotted in left and right panels, respectively. Group results for adults (11 ears) and children (6 ears) in top and bottom two rows, respectively. TEOAE stimuli selected from clicks and positive chirps of varying sweep rates at pairs of LF and HF stimulus levels. HF chirps were 6 dB higher than LF chirps, and HF clicks 5 dB higher than LF clicks. For LF stimuli at L_{rel} of 0 dB: A. adult CSM, B. adult SNR, E. child CSM, F. child SNR. For LF stimuli at L_{rel} of 12 dB: C. adult CSM, D. adult SNR, G. child CSM, H. child SNR. IQR is plotted as fill pattern for best response. Legend for all panels is in panel G with stimulus conditions including chirp sweep rates: Click, F (fast), M (medium), S (slow), X (X slow), XX (XX slow). Dotted lines show critical SNR (panels B, D, F, H) and critical CSM (panels A, C, E, G), with latter plotted for each stimulus condition using same letter codes as in legend such that F&M denotes fast and medium.

Figure 10.

Audiometric and TEOAE data in 6 NH children (11–16 y.) with no CF, and 4 children with CF (16–17 y.). LF responses in panels A-D versus 1/2th octave frequency. A: audiometry, gray band for NH ears, line curves for CF ears. B: CSM, box plots for NH ears, line curves for CF ears. C: SNR, box plots for NH ears, line curves for CF ears. D: L_S , box plots for NH ears, line curves for CF ears. HF responses in panels E-H correspond to LF responses in panels A-D, respectively, but at 1/6th octave frequencies. Critical CSM and SNR values shown as black dashed lines.

Figure 11.

Magnitude difference in test-retest mean TEOAE data on 4 NH adult ears (no CF) about 1 month apart at 1/2th octave frequencies up to 8 kHz and 1/6th octave frequencies above 8 kHz. The stimulus was a positive chirp with medium sweep rate and L_{rel} of 0 dB for LFs and 6 dB for HFs. A: Stimulus level difference L_S . B: TEOAE level difference L_S . C: Change in SNR of TEOAE. D: Change in CSM of TEOAE. Black circles and black squares show data for which TEOAE was absent on one or both tests based on SNR and CSM, respectively.

Figure 12.

Growth exponent data of TEOAE amplitude using positive chirp stimuli with a slow sweep rate. Each plot shows median and IQR for all ears, and the median for ears with TEOAE present at both stimulus levels along with the number of ears at each frequency with TEOAE present at both levels. A: Adult ears. B: Child ears.

Table 1.

Stimulus and buffer properties

Name	Type	Sweep rate (Hz/ms)	Buffer duration (ms)	Number (<i>B</i>) of Buffers (in 4 min.)	Noise reduction (dB) (in 4 min.)
	Click		36.3	2206	33
Fast	Chirp	317	69.7	1148	31
Medium	Chirp	188	69.7	1148	31
Slow	Chirp	52.8	183.7	436	26
X Slow	Chirp	13.2	666.7	120	21
XX Slow	Chirp	4.17	2000.0	40	16

Table 2.
Measured ear-canal stimulus levels in Exp. 1.

These data were acquired in 96 ears with NH at all frequencies up to 8 kHz. The mean and SD (in parentheses) of peSPL and SEL are listed for each LF and HF stimulus condition at which data were acquired.

Type			L_{rel} (dB)	LF		HF	
	Sweep Rate	Sweep Polarity		peSPL (dB)	SEL (dB)	peSPL (dB)	SEL (dB)
Click			0	80.3 (3.5)	46.3 (3.3)	82.2 (2.8)	47.1 (2.7)
Chirp	Fast	Positive	0	69.2 (3.2)	46.6 (3.3)	68.8 (2.6)	47.3 (2.7)
Chirp	Fast	Negative	0	69.6 (3.2)	46.7 (3.4)	69.0 (2.6)	47.3 (2.7)
Chirp	Medium	Positive	0	67.2 (3.1)	46.8 (3.4)	65.8 (2.6)	46.5 (2.7)
Chirp	Medium	Negative	0	67.5 (3.1)	46.8 (3.3)	65.8 (2.5)	46.4 (2.6)
Chirp	Slow	Positive	0	62.1 (3.0)	47.0 (3.4)	60.8 (2.5)	46.9 (2.6)
Chirp	Slow	Negative	0	62.0 (3.1)	47.1 (3.4)	60.7 (2.5)	46.9 (2.7)
Chirp	Fast	Positive	6	75.1 (2.8)	52.5 (3.2)	74.3 (2.5)	52.8 (2.7)
Chirp	Fast	Negative	6	75.4 (2.9)	52.6 (3.2)	74.4 (2.5)	52.8 (2.7)
Chirp	Medium	Positive	6	73.1 (2.8)	52.6 (3.3)	71.2 (2.5)	51.9 (2.7)
Chirp	Medium	Negative	6	73.3 (2.8)	52.6 (3.3)	71.2 (2.5)	51.9 (2.8)
Chirp	Slow	Positive	6	67.9 (2.7)	52.8 (3.3)	65.9 (2.4)	52.1 (2.8)
Chirp	Slow	Negative	6	67.7(2.8)	52.7 (3.3)	66.0 (2.4)	52.1 (2.8)
Chirp	Medium	Positive	12			77.1 (2.5)	57.8 (2.8)
Chirp	Slow	Positive	12	74.1 (2.9)	58.7 (3.4)	72.0 (2.5)	58.1 (2.8)
Chirp	Slow	Negative	12			71.9 (2.5)	58.1 (2.8)

Table 3.
Measured ear-canal stimulus levels in Exp. 2.

These data were acquired in 11 adult and 6 child ears with NH at all frequencies up to 16 kHz. The mean and SD (in parentheses) of peSPL and SEL are listed for each LF and HF stimulus condition.

Group	Type	Sweep Rate	LF	LF	LF	HF	HF	HF
			L_{rel} (dB)	peSPL (dB)	SEL (dB)	L_{rel} (dB)	peSPL (dB)	SEL (dB)
Adult	Click		0	82.3 (2.4)	48.6 (2.0)	5	84.2 (2.1)	48.4 (2.0)
Adult	Chirp	Fast	0	70.4 (2.1)	48.6 (1.9)	6	76.0 (2.5)	54.5 (1.9)
Adult	Chirp	Medium	0	68.3 (2.1)	48.7 (1.9)	6	74.1 (2.0)	54.8 (1.9)
Adult	Chirp	Slow	0	62.6 (2.0)	48.4 (1.8)	6	68.2 (2.1)	54.4 (2.0)
Adult	Chirp	XSlow	0	55.9 (2.0)	47.5 (1.8)	6	60.1 (2.2)	52.4 (2.1)
Adult	Chirp	XX Slow	0	54.4 (2.3)	50.1 (1.9)	6	56.5 (2.0)	53.5 (2.0)
Adult	Chirp	Slow	12	74.2 (1.8)	60.0 (1.7)	18	79.9 (2.1)	66.3 (2.0)
Adult	Chirp	X Slow	12	67.3 (1.8)	59.0 (1.8)	18	72.0 (2.2)	64.3 (2.0)
Adult	Chirp	XX Slow	12	64.8 (1.8)	61.5 (1.7)	18	68.0 (2.1)	65.3 (2.0)
Child	Click		0	84.0 (3.2)	49.6 (2.7)	5	84.7 (4.2)	49.2 (3.3)
Child	Chirp	Fast	0	71.7 (2.5)	49.8 (2.9)	6	77.3 (2.1)	54.8 (3.6)
Child	Chirp	Medium	0	69.7 (2.5)	49.9 (2.8)	6	75.8 (2.0)	55.5 (3.4)
Child	Chirp	Slow	0	64.4 (2.4)	49.9(3.1)	6	69.8 (2.4)	55.2 (3.5)
Child	Chirp	X Slow	0	57.8 (2.6)	49.3 (3.4)	6	62.1 (2.4)	53.5 (3.6)
Child	Chirp	XX Slow	0	56.4 (1.9)	52.2 (3.5)	6	59.7 (3.4)	54.6 (3.6)
Child	Chirp	Slow	12	75.8 (2.1)	61.7(2.4)	18	82.4(1.6)	67.7 (2.9)
Child	Chirp	X Slow	12	69.1 (2.1)	60.9 (2.2)	18	74.1(1.1)	65.4 (2.8)
Child	Chirp	XX Slow	12	66.7 (2.2)	63.5 (2.3)	18	70.1 (1.4)	66.5 (3.0)