Comparison of behavioral and DPOAE upper frequency limits and DPOAE fine structure in normal-hearing and hearing-impaired subjects

VA RR&D NCRAR

KT Dunckley, KM Deal, E Leigh-Paffenroth, D Konrad-Martin, DJ Lilly, SA Fausti

VA RR&D National Center for Rehabilitative Auditory Research, Portland, Oregon

Introduction

Certain therapeutic drugs can damage the inner ear. Ototoxic drugs typically affect the higher-frequency regions of the cochlea before affecting lower-frequency regions. A behavioral "sensitive range for ototoxicity" has been identified near the upper-frequency limit of hearing as a time-efficient and sensitive early indicator for ototoxic changes [1]. Behavioral testing, however, is not appropriate for sick patients who are unable to respond reliably. Accordingly, an objective estimate of hearing can be an important tool for ototoxicity monitoring.

From the concept of the behavioral sensitive region for ototoxicity (bSRO), came the identification of a similar sensitive region using distortion-product otoacoustic emissions (DPOAE) [2]. Initial DPOAE changes seem to occur near the highest frequency able to elicit a DPOAE, usually within one octave of the bSRO.

Distortion-product otoacoustic emissions can be measured in extremely fine steps over a limited frequency region [3]. Measurements obtained using fine-resolution steps allow assessment of the microstructure (rippling) present in DPOAE responses over a small frequency region, and more precise identification of the highest DPOAE frequency.

The purpose of this study is to determine in ears with normal-hearing and cochlear-hearing losses the relations between: 1) the bSRO, 2) the highest frequency able to elicit a DPOAE, and 3) the frequency regions where fine structure is present. The intent of this study is to develop DPOAE-monitoring protocols for use with patients receiving ototoxic medications.

Methods

Subjects

Eleven subjects with normal-hearing and eleven subjects with cochlear-hearing loss were tested twice within one month. Only the better ear of each subject was evaluated. Normal hearing was defined as pure-tone thresholds at 0.5-1.0 kHz of ≤ 20 dB HL and at 2-8 kHz of ≤ 30 dB SPL. All subjects had normal middle-ear function evaluated with 226-Hz tympanometry.

Audiometrics

- Pure-tone thresholds measured from 0.5-8 kHz in 1/2-octave steps and from 9-20 kHz in 1/6-octave steps.
- Definition of bSRO: The highest frequency at which a response was obtained with a threshold of 100 dB SPL or better along with the six 1/6-octave frequencies below that frequency.
- DPOAE Equipment: EMAV software [4], CardDeluxe sound card housed in a PC, Etymotic Research ER-2 tubephones, and ER-10B+ low-noise microphone.
- Procedures: DPOAEs were collected using a 1/2-octave step sweep at f_2 from 0.7 through14 kHz, and with a 1/48-octave step sweep over a half-octave region, determined by the highest frequency eliciting a response in the 1/2-octave step sweep (refer to Fig. 1). The f_1/f_2 was1.22, and L1 and L2 were 65 dB SPL for all DPOAE recordings.
- DPOAE response criteria: SNR ≥ 10 dB and DPOAE absolute amplitude > -20 dB SPL.
- DPOAE "top frequency" was the highest frequency able to elicit a DPOAE in both sessions on the 1/48-octave step sweep.
- Present fine structure, measured in fine steps, was defined as a 1/2-octave region containing at least 4 peaks, with each peak amplitude at least 3 dB greater than the adjacent valley [3,5,6].

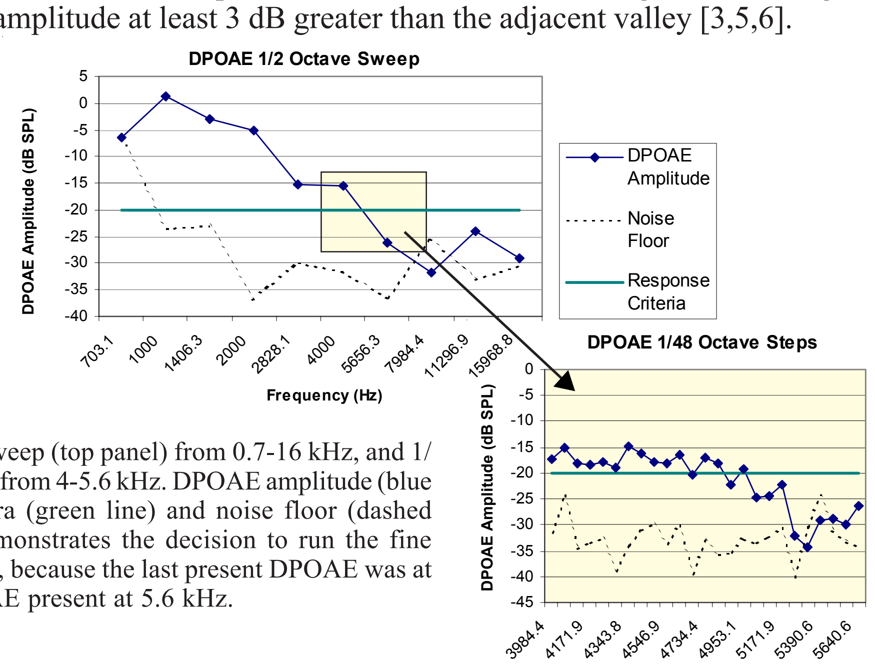

Fig 1. Example of 1/2-octave sweep (top panel) from 0.7-16 kHz, and 1/48-octave sweep (bottom panel) from 4-5.6 kHz. DPOAE amplitude (blue line), absolute amplitude critera (green line) and noise floor (dashed line) are plotted. This plot demonstrates the decision to run the fine structure sweep from 4-5.6 kHz, because the last present DPOAE was at 4 kHz, and there was no DPOAE present at 5.6 kHz.

Results

Audiometric Results

Behavioral thresholds in normal ears rose steeply from 10 to 20 kHz. Impaired ears showed greater inter-subject variability compared to normal ears, with no measurable responses above 16 kHz. Behavioral SROs were identified from 8-18 and 2.8-14 kHz for normal and impaired ears, respectively.

DPOAE Results

Top frequency Identified by 1/2- vs. 1/48-octave Sweep

The 1/2-octave sweep identified the same top frequency as the 1/48-octave sweep in only 19% of cases. In most cases (81%), the top frequency revealed by the 1/2-octave sweep was comparatively lower. The mean difference between these top frequency estimates was 2415 Hz (109-8303 Hz range).

Fine Structure Analysis

DPOAE results obtained using the 1/2-octave sweep were used to determine the region tested with the 1/48-octave sweep. Individual 1/48-octave sweeps were analyzed for fine structure, and four patterns in normal ears were identified: a) fine structure present with high DPOAE amplitudes, b) fine structure present with relatively low DPOAE amplitudes Fig. 2), c) fine structure absent with high DPOAE amplitudes over the measured half-octave frequency region (Fig. 3), and d) fine structure absent with DPOAE amplitudes rolling off from high to low (Fig. 4). These last three patterns were measured in impaired ears, as well as the following additional patterns: e) absent emissions/emissions not repeatable in both sessions, f) reverse roll-over, with rising DPOAE amplitudes as frequency increased (reflecting a "notch" in the behavioral audiogram), g) lack of repeatable fine structure in both sessions, h) fine structure present in both sessions, but with disparate amplitudes between sessions, and i) fine structure absent, low DPOAE amplitudes in both sessions.

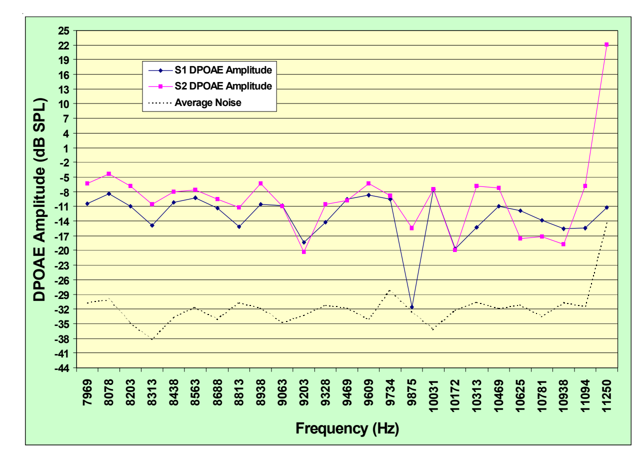

Fig 2. Example of 1/48-octave sweep from 8 to 11 kHz in a normal ear. Session 1 (S1) and session 2 (S2) DPOAE amplitudes are indicted in blue and pink lines, respectively. The S1 and S2 noise floor measurements were averaged (dashed line). Fine structure is present in both sessions, with relatively low DPOAE amplitudes.

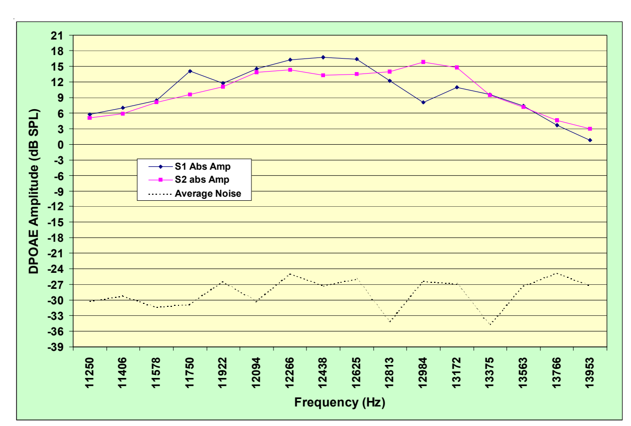

Fig 3. Example of 1/48-octave sweep from 11 to 14 kHz in a normal ear. Format same as Fig. 2. Despite the presence of large DPOAE amplitudes, no fine structure is observed in this graph.

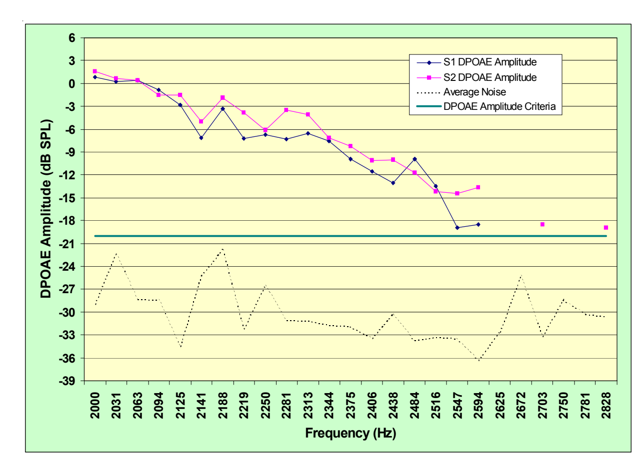

Fig 4. Example of 1/48-octave sweep from 2 to 2.8 kHz in a cochlear hearing loss. Format same as Figs. 2 and 3. Absolute amplitude criteria of -20 dB SPL is plotted in green. Data not meeting response criteria were not plotted, hence absent points at frequencies greater than 2600 Hz. There is no fine structure present in this region for either session. This graph illustrates "roll-off", referring to a region with robust DPOAEs rolling off into a region with absent DPOAEs.

Relationship of bSRO, Top Frequency, and Fine Structure

Normal ears:

- Figure 5 shows an example of a normal ear in which the top frequency and fine structure are within the bSRO.
- 11/11 normal ears had a DPOAE *top frequency* within the bSRO frequency region.
- 6/11 normal ears had present DPOAE *fine structure* within the bSRO frequency region.

Impaired ears:

- Figure 6 shows an example of an impaired ear in which the top frequency and fine structure are below the bSRO.
- 11/11 impaired ears had measurable DPOAE responses.
- 4/11 impaired ears had a DPOAE *top frequency* within the bSRO frequency region.
- 2/11 impaired ears had present DPOAE *fine structure* within the bSRO frequency region and 3 impaired ears had present fine structure in frequency regions below the bSRO.

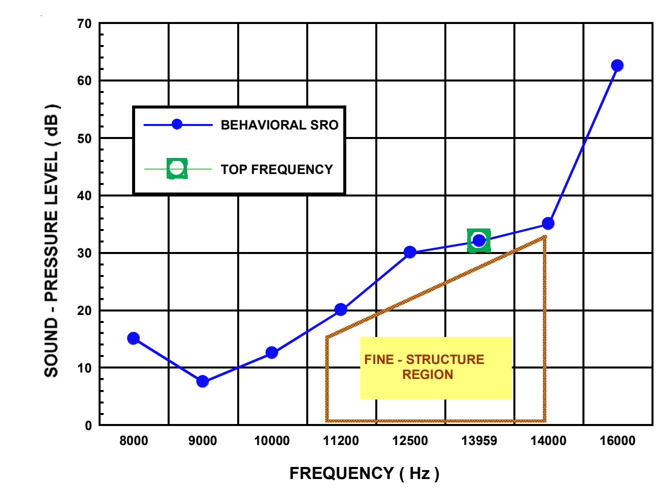

Fig 5. Relationship between the bSRO (blue line), DPOAE top frequency (green box), and fine structure region (outlined in orange). Results are for a normal-hearing subject, where the bSRO, DPOAE top frequency, and present fine structure overlap.

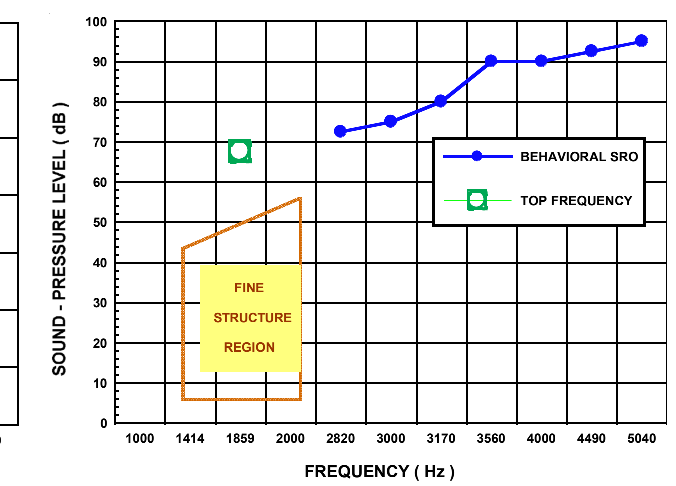

Fig 6. Format is the same as Fig. 5. Results are for a subject with cochlear hearing loss with a DPOAE top frequency and present DPOAE fine structure outside the region of the behavioral SRO.

Discussion

These data describe how characteristics of high-frequency DPOAEs, including fine structure, relate to an individualized bSRO in normal-hearing and hearing-impaired subjects. For ears with normal hearing, there was very good agreement between DPOAE top frequency and the bSRO. In impaired ears these two measures rarely overlapped. However, DPOAE responses were recorded in all impaired ears. Results support the use of fine-resolution DPOAE measurements for monitoring ototoxicity where behavioral testing is inappropriate. Such measurements, based on an individual's pre-treatment data, will more precisely identify the DPOAE top frequency and allow DPOAE measurements closer to the bSRO. Further research is needed to determine whether fine structure, when present in 1/48-octave measurements, is more sensitive to ototoxic change compared to standard DPOAE measurements even for a DPOAE range distant from the bSRO.

References

[1] Fausti SA, Henry JA, Helt WJ, Phillips DS, Frey RH, Noffsinger D, Larson VD, Fowler, CG (1999). An individualized, sensitive frequency range for early detection of ototoxicity. *Ear & Hearing.* 20(6):497-505.

[2] Fausti SA, Phillips D, Helt,W, Gordon,J, Deal KM, (2004). Comparison of objective and behavioral techniques for early detection of ototoxicity. *Unpublished raw data.*

[3] Gaskill SA & Brown AM, (1991). Suppression of human acoustic distortion product: dual origin of 2f1-f2. *J Acoustical Society of America.* 100(5):3268-74.

[4] Neely ST, Liu Z (2001). *EMAV: otoacoustic emissions averager.* Unpublished technical memorandum (17), Boys Town National Research Hospital.

[5] He N & Schmiedt RA (1993). Fine structure of the 2f1-f2 acoustic distortion product: changes with primary level. *J. Acoustical Society of America.* 94(5):2659-2669.

[6] He N & Schmiedt RA (1996). Effects of aging on the fine structure of the 2f1-f2 acoustic distortion product. *J Acoustical Society of America.* 99(2):1002-1015.

Acknowledgments

Work supported by Veterans Affairs Medical Research grant 06-0300. The authors would like to acknowledge Wendy Helt for editorial comments, and Craig Dennis for technical support.