Optimizing the Measurement of 0.5-kHz Cubic Distortion Product Otoacoustic Emission

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Cite this article as: Yu Y, Liu J, Antisdel J, et al. Optimizing the measurement of 0.5-kHz cubic distortion product otoacoustic emission. J Int Adv Otol. 2022;18(6):471-477.

BACKGROUND: The measurement of low-frequency cubic distortion product otoacoustic emission, for example, 0.5-kHz cubic distortion product otoacoustic emission, is often severely affected by background noise, and currently 0.5-kHz cubic distortion product otoacoustic emission is not commonly applicable in clinical setting.

METHODS: The fundamental part of current study was the optimization of recording technology to reduce noise interference with the measurement of 0.5-kHz cubic distortion product otoacoustic emission and to establish the response patterns of cubic distortion product otoacoustic emission across speech frequencies from 0.5 to 8kHz in the presence of normal hearing and noise-induced hearing loss.

RESULTS: After a series of optimization, a clinically applicable technology of measuring 0.5-kHz cubic distortion product otoacoustic emission was successfully completed via animal model. Cubic distortion product otoacoustic emission was recorded in 6 guinea pigs across speech frequencies from 0.5 to 8kHz before and after exposure to white bandnoise between 0.5 and 2 kHz. After noise exposure, significant reduction in the signal-to-noise ratio of cubic distortion product otoacoustic emission was found at 0.5 and 2 kHz, indicating our recording technology was sensitive and accurate. Other interesting finding was the reduction in cubic distortion product otoacoustic emission-signal-to-noise ratio at 4 and 6 kHz although the reduction was not statistically significant probably because of short exposure time. The result implied that the damaging effect induced by low-frequency noise exposure might spread upward to high-frequency region.

CONCLUSIONS: Our recording technology was stable and reliable and had the great potentiality to be used in clinical setting.

KEYWORDS: 0.5-kHz cDPOAE, low-frequency noise exposure, noise-induced hearing loss (NIHL)

INTRODUCTION
Noise-induced hearing loss (NIHL) is becoming increasingly common in our community. Distortion product otoacoustic emissions (DPOAEs) are often adopted in clinical setting to evaluate hearing functions. Distortion product otoacoustic emissions depend on the electro-mechanical activity of outer hair cells (OHCs). When ear receives 2 simultaneous pure-tone stimuli (primary tone-burst F1 and secondary tone-burst F2), OHCs generate a few nonlinear DPOAEs.1 The frequencies of the first and the second primary tones are defined as f1 and f2, respectively, (with f1 < f2). The frequencies of DPOAEs (f0n) are mathematically associated with primary-tone
frequencies. Of all the nonlinear DPOAEs, the one with the biggest magnitude is called cubic DPOAE (cDPOAE) whose frequency is calculated as $f_{2} = 2f_{1} - f_{2}$. The magnitude of cDPOAE is often defined as signal-to-noise ratio (SNR). At present, 0.5-kHz cDPOAE signal-to-noise ratio (SNR) was very small because of noise interruption. There were only a few reports about the measurement of 0.5-kHz cDPOAE, and SNR was not commonly available in clinics.

Cubic DPOAE is an objective test of cochlear function, and the response pattern of cDPOAE provides an overview of hearing function from low to high frequency. However, when $f_{2}$ is lower than or equal to 0.5 kHz, for example, 0.5-kHz cDPOAE is often interrupted by background noise; here, 0.5 kHz indicates the frequency of the secondary primary tone-burst ($f_{2}$). At present, 0.5-kHz cDPOAE and the response pattern of cDPOAE are not commonly available in clinics.

There were only a few reports about the measurement of 0.5-kHz cDPOAE, and SNR was very small because of noise interruption. The measurement of 0.55-kHz cDPOAE was attempted in human, and if $\text{SNR} \geq 6 \text{ dB sound pressure level (SPL)}$ was taken as acceptable criteria, successful recording rate was very low as a result of noise disturbance. So noise interference is an issue in the measurement of 0.5-kHz cDPOAE which needs to be addressed urgently.

Our first research goal was to optimize recording technology to control and reduce background noise so that 0.5-kHz cDPOAE could be recorded successfully. The second research goal was to establish the response pattern of cDPOAE across speech frequencies from 0.5 to 8 kHz in the presence of normal hearing and NIHL.

Guinea pig had been used to investigate the effect of noise exposure on hearing function. Cubic DPOAE recorded in guinea pig was usually greater than that measured in human; however, the difference was less obvious and predictable when the levels of primary tone-bursts were in the range of low to moderate SPL which were similar to that used in clinical setting. Thus, guinea pig model is appropriate for human cochlear investigation.

**METHODS**

**Animals**

Six guinea pigs with normal hearing as estimated by the presence of Preyer’s reflex were used in our study. Animals were ~2 months old and weighed from 250 to 300 g. The animals were from the same strain, and they were genetically identical. All animal procedures were reviewed and approved by University Animal Care and Use Committee. The protocol number is 201. All experimental methods were performed in accordance with the relevant guideline and regulation.

Otoscopy was performed under surgical microscope to ensure ear canal clean of debris and cerumen that could obstruct probe tube and interfere with the measurement of cDPOAE. Tympanic membrane was also examined to make sure that the membrane color and shape were normal.

**Instruments**

The lab computer used in experiment had an embedded controller (National instrument, NI, PXI-8108 Core 2 Duo 2.53 GHz Controller, etc.), a 16-bit digital input/output board (NI, PXI-6221), and a 24-bit digital input/output board (NI, PXI-4461). The instruments used to deliver stimuli included a 2-channel audio amplifier (Tucker-Davis Technologies Stereo Amp & Power Supply), 2-channel equalizer, and 2-speaker acoustic system. A stainless steel nosepiece transmitted the stimuli generated by speakers into animal ear canal. The instruments used to collect cDPOAE included a probe-tube microphone (Knowles Electret Condenser, FG-23329-P07), a Mic. Bias Box, and a Mic. Amplifier (Etymotic ER10C).

Band-pass filter was set in Labview Signal Express (National Instruments, version 8.5) and was used to generate white band noise between 0.5 and 2 kHz. The noise level was set at 5 Vrms (root mean square voltage) so that the noise output was equal to 120 dB SPL.

**Calibration**

The system was calibrated to ensure that auditory stimuli presented to animal ear were at the set level. System calibration included 3 parts, the calibration of reference microphone, the calibration of probe tube, and in-ear calibration. The reference microphone was a Larson-Davis 1/4”microphone (#377B10) which had a very flat frequency response (LD2530: $\pm 1 \text{ dB 0.02-50 kHz}$, $\pm 3 \text{ dB 0.02-100 kHz}$).

The sensitivity of reference microphone was determined by calibration with a pistonphone. In brief, the levels of pistonphone output (dB SPL) and gain of B&K microphone amplifier (dB) were selected, the sampling rate and number of spectrum averages at 20 kHz and 1, respectively, were set, and the calibration was run. In the calibration procedure, there was no need to specify the frequency of the pistonphone tone because it was automatically detected from the measured power spectrum. Since the SNR of the measurement was very high, it was only necessary to average one response.
The calibration of probe tube was conducted within acoustic assembly to calculate the relationship between the SPL at the end of probe tube and the voltage output of acoustic assembly microphone. This calibration was made by measuring the SPL near the tip of probe tube with reference microphone while simultaneously measuring the voltage output of acoustic assembly microphone. The probe-tube calibration was performed by holding reference microphone at a very short distance from the end of probe tube using a calibration coupler. The probe tube calibration used the ratio of the output of acoustic assembly microphone to the output of reference microphone, so the SPL of acoustic stimuli used for calibration was cancelled out.

In brief, in probe-tube calibration, a chirp (a brief sound that contained all frequencies throughout the range to be calibrated) was produced as stimulus by one of the earphone speakers. The stimulus frequency resolution step of calibration was set to 50 Hz, calibration sampling rate was 100 kHz, attenuation of calibration stimulus from full scale was 30 dB, and the number of averages of response signals was 256. The outputs of acoustic assembly microphone and reference microphone were measured simultaneously. Then, calibration software could compute the ratio of the voltage output of acoustic assembly microphone to the SPL at the end of probe tube.

Finally, in-ear calibration was performed right before the measurement of cDPOAE. In brief, chirp was always selected as calibration stimulus, frequency resolution step of calibration was set to 50 Hz, calibration sampling rate was set to 10 kHz, attenuation of calibration stimulus from full scale was set to 30 dB, the number of average of response signal was set to 128 and then the in-ear calibration was run. In-ear calibration involved computing the ratio of the voltage applied to earphone speakers to the SPL at the end of probe tube (near animal tympanic membrane).

Measurement of Cubic Distortion Product Otoacoustic Emission

Eaton-Peabody Laboratories Cochlear Function Test Suite (CFTS) was used to record cDPOAE. Cochlear Function Test Suite was a free software provided by the Massachusetts Eye and Ear Infirmary (USA). The experimental procedure was similar to that in previous reports.27,28

Cubic DPOAE was measured before and after band noise exposure at f1 of 0.5, 2, 4, 6, and 8 kHz, respectively, as these frequencies were in the range of human speech. Animals were exposed to white band noise at 120 dB SPL for 2 hours. In each animal, the average of 2 ears’ measurements was adopted as the final level in statistical analysis.

Surgical-plane anesthesia was reached with intramuscular injection of a mixture of ketamine and dex-domitor (ketamine 40 mg/kg and dex-domitor 0.15 mg/kg). If needed, a maintenance dose of the mixture was given every 1 hour. Animal was placed on its side into a customized foam bed to make sure that animal position was stable during recording procedure. And the foam bed was placed on a warm water pad to maintain the animal’s temperature at 37°C. During the experiment, the animal’s temperature was monitored with a digital rectal probe thermometer.

Optimization of the Measurement of 0.5-kHz Cubic Distortion Product Otoacoustic Emission

Background noise usually included 3 sources: instrumental, environmental noise, plus the one coming from subject itself. Because of the stationary property of instrumental and environmental noise, increasing synchronous averaging times could improve SNR.29 Thus, increasing averaging times was adopted in our study to minimize the disturbance of instrumental and environmental noise, but the averaging times in our experiment were only 8, as increasing averaging times were time-consuming and could cause discomfort to subject. Our averaging times are acceptable in clinical setting.

Three methods were adopted to reduce environmental noise: a sound-proof box with an appropriate noise-rejection threshold, a rubber immittance tip fitted onto the nosepiece of acoustic assembly, and the shielding of acoustic assembly. Cubic DPOAE was recorded inside the sound-proof box. The level of environmental noise inside the sound-proof box during recording procedure was estimated at about 11-dB SPL. A rubber immittance tip was fitted onto the nosepiece of acoustic assembly. The tip was like a sealing ring used to seal ear canal and reduce environmental noise. Acoustic assembly was painted with CuPro-Pro-Cote conductive copper-bearing paint for 3 times, and these paints were electromagnetic shielding which could prevent acoustic assembly from picking up environmental noise.

However, it was difficult to deal with the noise coming from subject itself. Subject-noise, for example, respiratory sound, cardiovascular murmur, swallowing, snoring, and teeth grinding, were usually of low frequency. The measurement of low-frequency cDPOAE, such as 0.5-kHz cDPOAE, was mostly interfered by subject noise.30-32

Fortunately, low-frequency noise could be controlled and reduced by digital filtering technique.31,33 Based upon this concept, an optimal pass-filter technique was adopted in our research to reduce the low-frequency noise coming from the subject itself and to maximize 0.5-kHz cDPOAE-SNR. And this digital filtering technique was our important optimization method to reduce subject noise.

In brief, cDPOAE was recorded by probe-tube microphone. The microphone’s output was amplified by ER10C (Etymotic Research) which was then connected to the lab computer. Digital pass filter was setup by LabView Signal Express, raw signal of cDPOAE was put through the filter to remove unwanted noise, and then the "pure=" signal was analyzed by CFTS. In this way, low-frequency noise coming from animal itself were controlled and reduced, and 0.5-kHz cDPOAE-SNR was optimized and maximized. Other optimization methods included the adjustment of input/output parameters, for example, the f1/f2 ratio was set at 1.22 to evoke the most robust cDPOAE.

Calculation of Cubic Distortion Product Otoacoustic Emission-Signal-to-Noise Ratio

The level of F2 stimulus ranged from 40- to 60-dB SPL. When F2 level was <60-dB SPL, the recorded cDPOAE was considered as real response from OHCs, when F2 level was >60-dB SPL, the recorded signal was taken as artifact. When F2 level reached 60-dB SPL (F1 = F2 + 10 = 70-dB SPL), amplitude of cDPOAE plateaued. Cubic DPOAE-SNR was calculated as cDPOAE plateau value minus noise-floor level.14

Statistical Analysis

Based on G-Power analysis, when the sample size was 6, the effect size was in the range of 0.8-0.9, thus sufficient statistical power was
available to detect the difference between and within groups if such difference existed. Also, it was common to have a sample size of 6 ears in previous animal experiments.35,36-38

Repeated measure of analysis of variance along with Bonferroni correction was used to compare cDPOAE-SNR before and after noise exposure, with \( P < .05 \) adopted as an indication of statistical significance.

RESULTS

Successful Recording of 0.5-kHz Cubic Distortion Product Otoacoustic Emission After Optimization

Cubic DPOAE measured at \( f_2 \) of 0.5 kHz was expressed as 0.5-kHz cDPOAE; however, \( f_{DP} \) of cDPOAE itself was 0.34 kHz. Many cut-off values of low- and high-frequency pass filter were attempted covering the range from 0 to 0.68 kHz. For each value of low-frequency pass filter, high-frequency pass filters were varied so that a better and strong cDPOAE signal could be achieved. After a series of experiments, it was found out that when low-frequency pass filter was set at 0.17 kHz and high-frequency pass filter was set at 0.51 kHz, the magnitude of 0.5-kHz cDPOAE was maximal. Our technique was optimal in the sense that the pass filters were set according to the value of \( f_{DP} \), low-frequency pass filter was set at \( f_{DP} - \frac{1}{2} f_{DP} \) and high-frequency pass filter was set at \( f_{DP} + \frac{1}{2} f_{DP} \).

Figure 1 and 2 show the measurements of 0.5-kHz cDPOAE before and after optimization, respectively. Before optimization, 0.5-kHz cDPOAE-SNR was unstable, and in some animals, 0.5-kHz cDPOAE could not be recorded at all. After optimization, 0.5-kHz cDPOAE-SNR was greatly improved. The SNR in Figure 2 was more obvious and stable than that in Figure 1.

Research Goal 2—Establishment of Response Patterns of Cubic Distortion Product Otoacoustic Emission in the Presence of Normal Hearing and Noise-Induced Hearing Loss

The overall response of an auditory test across all tested frequencies is called response pattern. In Figure 3, cDPOAE-SNR was plotted as function of \( f_2 \) of 0.5, 2, 4, 6, and 8 kHz to establish the response pattern of cDPOAE.

The response pattern of cDPOAE before noise exposure showed that the lowest SNR of cDPOAE was at 0.5 kHz and the highest was at 6 kHz. With the increment of \( f_2 \), cDPOAE-SNR had a tendency to increase. After noise exposure, reduction in SNR was observed at 0.5 and 2 kHz as compared to that before noise exposure. The response pattern before noise exposure reflected the standard characteristics of normal cochlea, and the change in response pattern after exposure provided a general estimation of hearing loss across all tested frequencies.

Figure 3 shows the difference in cDPOAE-SNR before and after noise exposure, indicating that band-noise exposure could cause significant reduction in cDPOAE-SNR at 0.5 and 2 kHz, \( P < .05 \); this implied our recording technology is sensitive and accurate.

Another interesting finding was that exposure to white band noise between 0.5 and 2 kHz could produce hearing losses at higher frequencies, such as at 4 and 6 kHz; however, the reduction in cDPOAE-SNR at 4 and 6 kHz was not statistically significant, probably because of short exposure time.

Figure 1. The recording of 0.5-kHz cDPOAE before optimization. In figure 1 and 2, the left part showed the parameters of stimulus and averaging times. The middle section was spectrum display, the top graph was full spectrum, the bottom was a small range centered on the frequency of 2\( f_1 - f_2 \). The right panel showed the measured SPL of F1, F2, F1-F2, 2F1-F2 noise floor, F2-F1, F2-F1 noise floor as function of F2 stimulus level. In figure 1, when F2 stimulus level was equal to or lower than 60 SPL, the cDPOAE was overwhelmed by background noise, the SNR was very low and meaningless; please note that when F2 stimulus level was higher than 60 SPL, cDPOAE was considered as artifact. cDPOAE, cubic distortion product otoacoustic emission; SPL, sound pressure level.
DISCUSSION

Significance of the Optimization of Recording Technology

Because of noise interruption, it was difficult to record low-frequency cDPOAE, or cDPOAE-SNR was very small and unstable. The level of background noise is high at low \( f_2 \), and the noise level tends to decrease with the increment of \( f_2 \). For example, when \( f_2 \) is equal to or below 1 kHz, the noise level is about at least 18 dB higher than that when \( f_2 \) is 8.0 kHz.\(^{39-41}\) Thus, the diagnostic value of cDPOAE was poor when \( f_2 \) is equal to or below 1 kHz; in clinical setting, cDPOAE is useful only when \( f_2 \) ranges from 2 to 8 kHz.\(^{42}\)

And the performance of cDPOAE was poor at low frequency in terms of the correlation between cDPOAE and behavioral hearing threshold (BHT). Larger discrepancy of the correlation was noted at low frequency as compared to that at high frequency.\(^{43}\) The correlation between cDPOAE and BHT at high frequency was strong. On the other hand, the association between cDPOAE and BHT at low frequency was weak and not reliable.\(^{16,44}\) In a word, BHT could be predicted by cDPOAE at high frequency but could not be predicted by cDPOAE at low frequency. At present, 0.5-kHz cDPOAE is not commonly available for patients.

Before our optimization, the characteristics of cDPOAE have not been thoroughly examined across the speech frequency range.

Figure 2. The recording of 0.5-kHz cDPOAE after optimization. The cDPOAE-SNR increased gradually with the growth of \( f_2 \) stimulus level and reached the maximum plateau when \( f_2 \) stimulus level was 60 SPL. The comparison between figure 1 and 2 showed that background noise reduced and SNR became distinct and stable after optimization. cDPOAE, cubic distortion product otoacoustic emission; SNR, signal-to-noise ratio; SPL, sound pressure level.

Figure 3. The response pattern of cDPOAE before and after noise exposure. The response pattern before noise exposure showed the lowest cDPOAE-SNR was at 0.5 kHz, the highest was at 6 kHz, and with the increment of tested frequency, cDPOAE-SNR had a tendency to increase, the response pattern before noise exposure may represent the standard characteristics of normal cDPOAE. The response pattern after noise exposure showed, significant reduction in the cDPOAE-SNR was observed at 0.5 and 2-kHz; reduction was also observed at 4 and 6 kHz, but not statistically significant.
(including 0.5 kHz) due to the fact that the measurement of low-frequency cDPOAE is often deteriorated by background noise. The significance of current study was that stable 0.5-kHz cDPOAE can be successfully measured after our optimization of recording technology, and the technology used in the study can provide valuable information for its future clinical application.

The Mechanism About the Reduction in Cubic Distortion Product Otoacoustic Emission-Signal-to-Noise Ratio After Noise Exposures

Cubic DPOAE is generated by OHCs. It is expected that cDPOAE-SNR will decrease after noise exposure; however, the mechanism underlying the reduction in cDPOAE-SNR is complex. Exposure to noise of high SPL could induce damage and or death of OHCs, so the number of functioning OHCs became smaller after exposure, and cDPOAE-SNR fell down correspondingly. On the other hand, the remaining functioning OHCs might be less efficient in energy transduction with respect to the transformation between mechanical and electrical energy, and less efficient in energy transduction of OHCs could also lead to the reduction in cDPOAE-SNR.41,46

Some research indicated that noise exposure could cause abnormal change in potassium gating system, also resulting in less-efficient energy transduction of OHCs.46,47 However, the detailed mechanism about noise-induced damage of OHCs remains unclear.

Response pattern of Cubic Distortion Product Otoacoustic Emission

Response pattern of cDPOAE was the plot of cDPOAE-SNR as function of tested f2. From the response pattern of cDPOAE before noise exposure, it was noted that cDPOAE-SNR had a tendency to rise when the tested frequencies increased. There might be 2 explanations for this finding; the first explanation was that low-frequency cDPOAE-SNR was easily interrupted by severe background noise so that the cDPOAE-SNR was small, whereas the interruption was mild at high frequency, and the cDPOAE-SNR became large. The second explanation was that the auditory acuity of guinea pig was better at high frequency than that at low frequency. In guinea pig, the most appropriate frequency range of hearing was between 4 and 20 kHz; thus, the cDPOAE-SNR recorded at appropriate frequency range (above 4 kHz) was larger than that recorded at the less appropriate frequency range (e.g., 0.5 kHz).48

The response pattern of cDPOAE provided an overview of OHCs function across the tested frequencies. The comparison of response patterns before and after noise exposures could be very useful for the estimation of hearing loss.

The limitation of current study was that no human experiment was carried out. In future, we will do experiment to translate the result of animal study to clinical setting.

Ethics Committee Approval: Ethical committee approval was received from the Ethics Committee of Alberta University (approval no: 201).

Informed Consent: N/A.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept – M.Z., YY; Design – YY, J.L.; Supervision – M.Z.; Funding – M.Z.; Materials – J.L., J.A., X.Z.; Data Collection and/or Processing – C.L., A.R., FM., X.Z.; Analysis and/or Interpretation – J.S., M.C., F.M.; Literature Review – F.M., X.Z.; Writing Manuscript – J.A., C.L., F.M.; Critical Review – J.S., J.A., A.R., X.Z.

Acknowledgments: The authors would like to thank Dr. Lyn Sonnenberg, Dr. Richard Fahlman, Dr. Li Wang, Dr. Ke Liu, Dr. Jingbo Pi, and Dr. Hongbo Liu for their valuable support and inputs.

Declaration of Interests: The authors declare that they have no conflict of interest.

Funding: The project was partly supported by the Natural Sciences and Engineering Research Council of Canada (MZ), CI2P437642-Zhang; the Canada Foundation for Innovation (MZ), CF125761-Zhang; and the Glenrose Rehabilitation Hospital Foundation (MZ), GRHF2010-Zhang.

REFERENCES

1. Kemp DT, Brown AM. A comparison of mechanical nonlinearities of man and gerbil from ear canal measurements. In: Klinke R, Hartman R, eds. Hearing–Physiological Bases and Biophysics. Berlin: Springer; 1983: 82-88.
2. Duan M, Qiu J, Laurell G, Olofsson A, Counter SA, Borg E. Dose and time-dependent protection of the antioxidant N-Lacteylcysteine against impulse noise trauma. Hear Res. 2004;192(1-2):1-9. [CrossRef]
3. Healy B. Stop the decibel damage. U.S. News & World Report; 2007; 143(2):58.
4. Poirier AL, Pincemail J, Van Den Ackerveken R, Lefebvre PP, Malgrange B. Oxidative stress in the cochlea: an update. Curr Med Chem. 2010;17(30): 3591-3604. [CrossRef]
5. Kim DO, Molnar CE, Matthews JW. Cochlear mechanics: nonlinear behavior in two-tone responses as reflected in cochlear-nerve-fiber responses and in ear-canal sound pressure. J Acoust Soc Am. 1980;67(5): 1704-1721. [CrossRef]
6. Brown AM, Kemp DT. Suppressibility of the 2f1 – f2 stimulated acoustic emissions in gerbil and man. Hear Res. 1984;13(1):29-37. [CrossRef]
7. Martin GK, Lonsbury-Martin BL, Probst R, Scheinin SA, Coats AC. Acoustic distortion products in rabbit ear canal. II Sites of origin revealed by suppression contours and pure-tone exposures. Hear Res. 1987;28 (2-3):191-208. [CrossRef]
8. Harris FP, Probst R, Xu L. Suppression of the 2f1 – f2 otoacoustic emission in humans. Hear Res. 1992;64(1):133-141. [CrossRef]
9. Lukashkin AN, Russell IJ. Dependence of the DPOAEs amplitude pattern on acoustical biasing of the cochlear partition. Hear Res. 2005;203 (1-2):45-53. [CrossRef]
10. Brown AM, Harris FP, Beveridge HA. Two sources of acoustic distortion products from the human cochlea. J Acoust Soc Am. 1996;100(5): 3260-3267. [CrossRef]
11. Gaskill SA, Brown AM. Suppression of human distortion product: dual origin of 2f1 – f2. J Acoust Soc Am. 1996;100(5):3268-3274. [CrossRef]
12. Talmadge CL, Long GR, Tubis A, Dhar S. Experimental confirmation of the two-source interference model for the fine structure of distortion product otoacoustic emissions. J Acoust Soc Am. 1999;105(1):275-292. [CrossRef]
13. Mauermann M, Uppenkamp S, van Hengel PW, Kollmeier B. Evidence for the distortion product frequency place as a source of distortion product otoacoustic emission (DPOAEs) fine structure in humans. I. Fine structure and higher-order DPOAEs as a function of the frequency ratio f2/f1. J Acoust Soc Am. 1999;106(6):3473-3483. [CrossRef]
14. Shera CA, Guinan JJ Jr. Evoked otoacoustic emissions arise by two fundamentally different mechanisms: a taxonomy for mammalian OAEs. J Acoust Soc Am. 1999;105(2 Pt 1):782-798. [CrossRef]
15. Kiss JG, Töth F, Rovó L, et al. Distortion-product otoacoustic emission (DPOAE) following pure tone and wide-band noise exposures. Scand Audiol Suppl. 2001;52(52):138-140. [CrossRef]
16. Siegel JH. Calibrating otoacoustic emission probes. In: Robinette MS, ed., Principles and Practice of Otoacoustic Emissions: Clinical Applications. 2nd ed. New York; Thieme Medical, 2002:416-441.
17. Gorga MP, Neely ST, Dierking DM, et al. Low-frequency and high-frequency cochlear nonlinearity in humans. J Acoust Soc Am. 2007;122(3):1671. [CrossRef]
18. Beattie RC, Kenworthy OT, Luna CA. Immediate and short-term reliability of distortion-product otoacoustic emissions. Int J Audiol. 2003;42(6):348-354. [CrossRef]
19. Gorga MP, Neely ST, Dierking DM, et al. Low-frequency and high-frequency cochlear nonlinearity in humans. J Acoust Soc Am. 2007;122(3):1671. [CrossRef]
20. Brown AM. Acoustic distortion from rodent ears: a comparison of responses from rats, guinea pigs, and gerbils. Hear Res. 1987;31(1):25-37. [CrossRef]
21. Brown AM, Gaskill SA. Measurement of acoustic distortion reveals underlying similarities between human and rodent mechanical responses. J Acoust Soc Am. 1990;88(2):840-849. [CrossRef]
22. Canlon B, Marklund K, Borg E. Measures of auditory brain-stem responses, distortion product emissions, hair cell loss, and forward masking tuning curves in the waltzing guinea pigs. J Acoust Soc Am. 1993;94(6):3232-3243. [CrossRef]
23. Probst R, Lonsbury-Martin BL, Martin GK. A review of otoacoustic emissions. J Acoust Soc Am. 1999;105(5):2027-2067. [CrossRef]
24. Gaskill SA, Brown AM. The behavior of the acoustic distortion product, 2f1-f2, from the human ear and its relation to auditory sensitivity. J Acoust Soc Am. 1990;88(2):821-839. [CrossRef]
25. Martin GK, Lonsbury-Martin BL, Probst R, Coats AC. Spontaneous otoacoustic emissions in a nonhuman primate. I. Basic features and relations to other emissions. Hear Res. 1988;33(1-2):49-68. [CrossRef]
26. Lasky RE, Snodgrass EB, Laughlin NK, Hecox KE. Distortion product otoacoustic emissions in Macaca mulatta and humans. Hear Res. 1995;89(1-2):35-51. [CrossRef]
27. Park JY, Clark WW, Coticchia JM, Esselman GH, Fredrickson JM. Distortion product otoacoustic emissions in rhesus (Macaca mulatta) monkey ears: normative findings. Hear Res. 1995;86(1-2):147-162. [CrossRef]
28. Harvey RC, Walberg J. Special considerations for anesthesia and analgesia in research animals. In: Short C. E., ed., Principles and Practice of Veterinary Anesthesia. Baltimore: Williams & Wilkins; 1987.
29. Zhang M, Abbas PJ. Effects of middle ear pressure on otoacoustic emission measures. J Acoust Soc Am. 1997;102(2 Pt 1):1032-1037. [CrossRef]
30. Kemp DT, Bray P, Alexander L, Brown AM. Acoustic emission cochleography--practical aspects. Scand Audiol Suppl. 1986;25:71-95.