

Diagnostics of the Cochlear Amplifier by Means of Distortion Product Otoacoustic Emissions

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Key Words

Distortion product otoacoustic emissions · Cochlear amplifier

Abstract

Distortion product otoacoustic emission (DPOAE) growth functions reflect the active nonlinear cochlear sound processing when using a primary-tone setting which accounts for the different compressions of the two primaries at the DPOAE generation site and hence provide a measure for objectively assessing cochlear sensitivity and compression. DPOAE thresholds can be derived from extrapolated DPOAE input/output (I/O) functions independently of the noise floor and consequently can serve as a unique measure for reading DPOAE measurements. The thus-estimated DPOAE thresholds exhibit a close correspondence to behavior audiometric thresholds and thus can be used for reconstructing an audiogram, i.e., a DPOAE audiogram. The DPOAE I/O functions' slope increases with cochlear hearing loss and thus provides a measure for assessing recruitment. Hence, DPOAE I/O functions can give more information for diagnostic purposes than those of DP grams, transiently evoked OAEs (TEOAEs), or auditory brain stem responses (ABRs). DPOAE audiograms can be applied in pediatric audiology to assess cochlear dysfunction in a couple of minutes. In newborn hearing screening, they are able to detect transitory

sound-conductive hearing loss and thus can help to reduce the rate of false-positive TEOAE responses in the early post-natal period. Since DPOAE I/O functions are correlated with loudness functions, DPOAEs offer the possibility of basic hearing aid adjustments, especially in infants and children. Extrapolated DPOAE I/O functions provide a tool for a fast automated frequency-specific and quantitative evaluation of hearing loss.

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Introduction

Otoacoustic emissions (OAEs) are the by-product of the nonlinear sound amplification process in the cochlea [1, 2], referred to as the cochlear amplifier (CA), and hence can serve as a measure for evaluating cochlear integrity. Transiently evoked OAEs (TEOAEs) represent the sum of the pulse responses of outer hair cells (OHCs) along the cochlea whereas distortion product OAEs (DPOAEs) represent cubic distortions of OHCs when stimulated simultaneously by two tones, f_1 and f_2 . In humans, the $2f_1 - f_2$ distortion component yields the highest amplitude and is therefore primarily used in audiological diagnostics. Whereas TEOAEs more qualitatively assess cochlear function, DPOAEs provide quantitative information about the range and operational characteristics of

the CA, i.e. sensitivity, compression, and frequency selectivity.

DPOAE input/output (I/O) functions (DPOAE level L_{dp} as a function of the primary-tone level L_2 for a selected f_2) reflect CA dynamics at the f_2 place in the cochlea [3–6]. In normal hearing, in response to low-level stimuli, DPOAE level I/O functions exhibit steep slopes, while at high-stimulus levels slopes decrease, thus mirroring the strong amplification at low and decreasing amplification (saturation) at moderate sound levels. However, this is only true when a stimulus setting is used which accounts for the different compressions of the primary tones [7–9]. DPOAE slope, calculated from DPOAE I/O functions, indicates CA compression. When plotted across frequency, a slope profile can be established. In ears with cochlear hearing loss, the slope s of the DPOAE level I/O function increases with increasing hearing loss indicating loss of CA compression [4, 5].

The purpose of this contribution is to present a special parameter setting for eliciting DPOAEs more physiologically as well as a new method for estimating loss of sensitivity and compression of the CA by means of extrapolated DPOAE I/O functions. Finally, some clinical case examples will illustrate the potential of DPOAE I/O functions for getting frequency-specific and quantitative information about cochlear hearing loss.

DPOAE I/O Functions Only Reflect Nonlinear Sound Processing when Using a Special Stimulus Setting

When using a primary-tone setting, which accounts for the different compressions of the primary-tone traveling waves at the f_2 place [7–10], the DPOAE I/O function reflects compressive nonlinear sound processing known from direct measurements of basilar membrane displacements [11]. Due to the steep slope of the traveling wave towards the cochlear apex, the maximum interaction site is close to the f_2 place in the cochlea. Thus, OHCs at the f_2 place contribute most to DPOAE generation. The number of OHCs contributing to DPOAE generation depends on the size of the overlapping region, which is determined by the primary-tone levels L_1 and L_2 , respectively, and the frequency ratio f_2/f_1 of the primary tones f_1 and f_2 . To preserve optimum overlap of the primary-tone traveling waves, the primary-tone level difference has to be increased with decreasing stimulus level resulting in an L_1/L_2 setting described by $L_1 = 0.4L_2 + 39$ [9]. This special L_1/L_2 setting, and not the $L_1 = L_2$ setting, yields compressive DPOAE growth reflecting nonlinear CA sound processing.

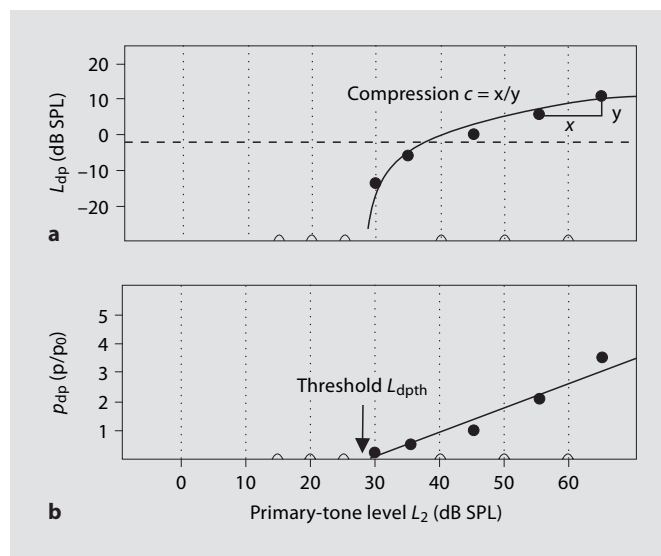
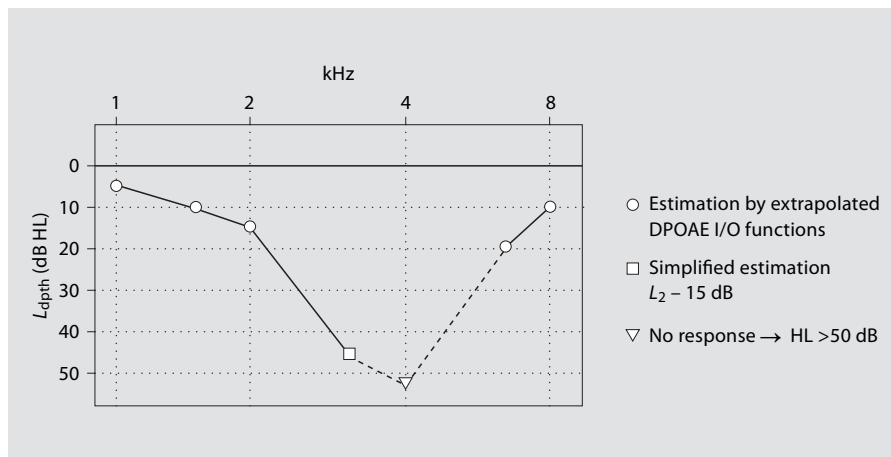


Fig. 1. Threshold estimation by means of extrapolated DPOAE I/O functions. DPOAEs are measured at different primary-tone levels representing an I/O function in the common double-logarithmic plot (a). If the DPOAE pressure p_{dp} instead of the DPOAE level L_{dp} is plotted (b), DPOAEs can easily be fitted by using linear regression analysis. The intersection point of the linear regression line with the primary-tone level axis can then serve as an estimate for the threshold level L_{dp}^{th} . At least 3 valid DPOAE points are necessary for the extrapolation. If there are only one or two valid points in the I/O function, a simplified estimation is done where $L_{dp}^{th} = \text{lowest } L_2 - 15 \text{ dB}$. Cochlear compression c is quantified by calculating the slope s of the I/O function ($s = 1/c$). $p_0 = 20 \mu\text{Pa}$. Semi-circles on the x-axis indicate the L_2 levels at which DPOAEs were not measured.

Estimation of Cochlear Hearing Threshold by Means of Extrapolated DPOAE I/O Functions

The relation between OAE level and auditory threshold – or rather the lack of it – is strongly debated. Earlier, it was common to define confidence limits to determine the degree of certainty with which any measured response could be assigned to either normal or impaired hearing [12, 13], or to define a ‘DPOAE detection threshold’ as the stimulus level at which the response equalled the noise present in the instrument [6]. However, since the noise is of technical origin (e.g. microphone noise), the threshold evaluated in this way does not match the behavioral threshold. A more relevant measure is the intersection point between the extrapolated DPOAE I/O function and the primary-tone level axis at which the sound pressure of the response is zero and hence at which OHCs are inactive [10, 14]. A linear dependency

Fig. 2. DPOAE audiogram from an ear with cochlear hearing loss. At 1.5, 2, 3, and 4 kHz, there were more than 3 points in the respective I/O function, so estimation could be done by extrapolation. At 4 kHz, a valid DPOAE response was only present at $L_2 = 60$ and 65 dB SPL. Here, the Cochlea-Scan does a simplified estimation. At 4 kHz, no DPOAEs could be measured and the hearing loss is estimated to be higher than 50 dB.



between the DPOAE sound pressure and the primary-tone sound pressure level is present [10] when using the $L_1 = 0.4L_2 + 39$ paradigm for eliciting DPOAEs [9]. Because of the linear dependency, DPOAE data can easily be fitted (fig. 1) in a semilogarithmic plot by linear regression analysis, where the intersection point of the regression line with the L_2 primary-tone level axis at $p_{dp} = 0$ Pa can thus serve as an estimate of the DPOAE threshold. The estimated DPOAE threshold L_{dpth} is independent of noise and seems to be more closely related to the behavioral threshold than the DPOAE detection threshold [10, 14]. The DPOAE growth rate steepens when the auditory threshold is elevated [4, 5, 10, 14, 15] and differs significantly between hearing loss classes (their width being 10 dB) [16]. The slope of DPOAE I/O functions is reported to be related to the slope of the loudness functions [15, 17]. Thus, the slope s of DPOAE I/O functions is suggested to allow a quantitative assessment of CA compression and hence provide an objective recruitment test.

When converting sound pressure level to hearing level, the estimated threshold can be plotted in an audiogram form. The Cochlea-Scan™ hand-held device (Fischer-Zoth/Natus) estimates the hearing loss at 5 frequencies, i.e. at 1.5, 2, 3, 4, and 6 kHz. Due to the high noise floor level at low frequencies and the problem of standing waves in the outer ear canal at high frequencies, the frequency range had to be restricted (fig. 2). Test-retest stability of the estimated threshold is relatively high with a standard deviation lower than 10 dB (fig. 3).

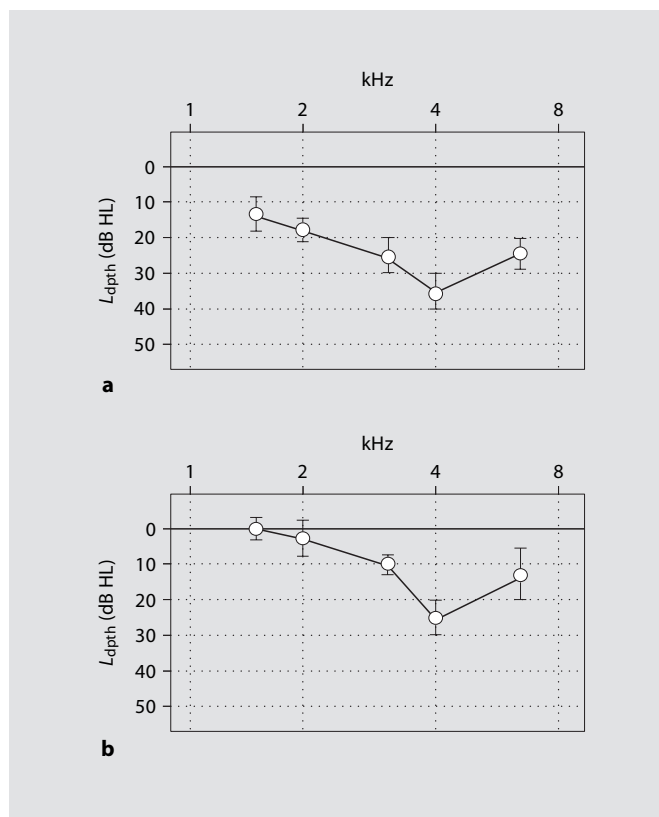


Fig. 3. Test-retest stability of a DPOAE audiogram. **a** Nine measurements were performed in an adult patient. The sound probe insertion was changed at each measurement. SD amounted to about 5 dB at each test frequency. **b** Minimum and maximum hearing thresholds obtained in a newborn at the neonatal care unit did not differ more than 10 dB except at 6 kHz.

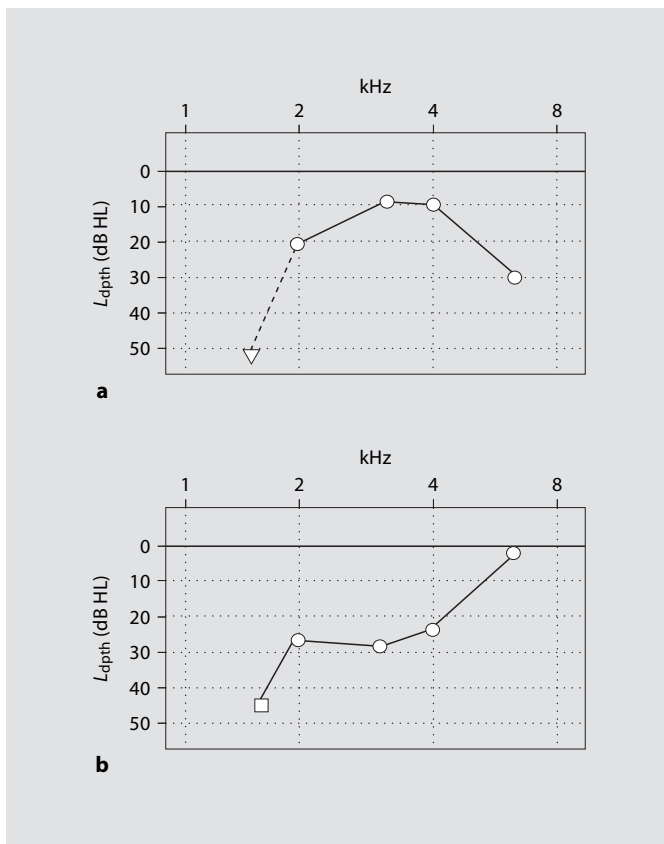


Fig. 4. DPOAE audiograms from two 1-day-old newborns where a sound-conductive hearing loss is likely. In one of them (a), both amniotic fluid and eustachian tube dysfunction, and in the other (b), only amniotic fluid may be the reason for the hearing loss.

Clinical Applications of DPOAE I/O Functions

Like tympanometry, which examines the status of the middle ear, OAEs are a fast and easy-to-handle method for examining cochlear function objectively. Due to the simple handling, OAEs are the first choice in newborn hearing screening. In pediatric audiology, especially DPOAE audiograms can provide frequency-specific and quantitative information about the hearing loss within a couple of minutes only.

Automated Hearing Threshold Estimation in Newborns

TEOAEs and DPOAEs are widely regarded as being suitable for screening in newborns and infants, as they are not present in the case of OHC dysfunction [18–21]. A major disadvantage of using OAEs in screening proto-

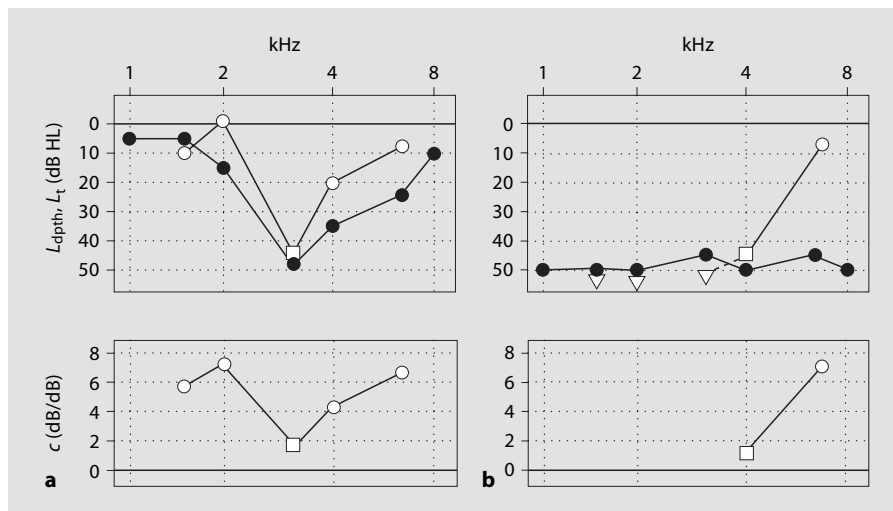
cols is a lower validity as compared to auditory brain stem response (ABR) methods [20, 22]. This is especially true in populations with a high prevalence of slight threshold elevation due to a temporary sound-conductive hearing loss, as it is found in neonates in the first 36 h of life due to eustachian tube dysfunction or amniotic fluid in the tympanic cavity. To avoid high referral rates, OAE referrals are usually followed up with an ABR screening before diagnostic assessment, i.e., two-stage screening [21, 23]. DPOAE audiograms may be an alternative means for revealing a transitory hearing loss in the early postnatal period or detecting a persisting cochlear hearing loss. Figure 4 shows DPOAE audiograms obtained in two 1-day-old babies at the neonatal care unit. Figure 4a indicates both a low- and a high-frequency hearing loss. In this baby, eustachian tube dysfunction (where middle ear stiffness is increased and therefore low frequencies are affected) and amniotic fluid (where middle ear mass is increased and therefore high frequencies are affected) may be the reason for the hearing loss. In the other baby (fig. 4b), only low frequencies are affected indicating eustachian tube dysfunction.

DPOAE audiograms can be applied in babies immediately after automated TEOAE or ABR testing to reveal a transitory sound-conductive hearing loss or detect a persisting cochlear hearing loss. DPOAE audiograms should be generally applied in babies at risk where a hearing loss is likely. In follow-up diagnostics, DPOAE audiograms can serve as an advanced tool for bridging the gap between screening and audiological testing.

Automated Hearing Threshold Estimation in Pediatric Audiology

DPOAE audiograms are an alternate method to behavioral audiometry or frequency-specific evoked response audiometry [tone burst ABR, auditory steady-state response (ASSR)] in case pure-tone audiometry cannot be performed or does not reflect the real hearing threshold. In contrast to TEOAEs, common DPOAEs, and click-evoked ABRs, which only qualitatively describe the hearing loss, DPOAE audiograms are able to quantitatively assess cochlear hearing thresholds at distinct test frequencies. DPOAE audiograms can assess the hearing loss at 5 frequencies in a couple of minutes. This is an essential advantage over tone burst ABR or ASSR. It should be emphasized that predicting the hearing loss at 5 frequencies by tone burst ABR or ASSR takes more than half an hour. Figure 5 illustrates the capability of DPOAE audiograms to detect a persisting cochlear hearing loss. Conditioned behavioral threshold in a 5-year-old boy is closely related

Fig. 5. Conditioned behavioral thresholds (filled circles), DPOAE audiograms (white circles), and compression profiles (bottom) from a 5-year-old boy (a) and from a 6-month-old infant (b). In the 5-year-old boy, behavioral and estimated thresholds are closely related, whereas in the 6-month-old baby, there is a high discrepancy between the two measures. In both ears, a medio-cochlear hearing loss is likely since the compression profile indicates compression loss in the mid-frequency region. L_t = Behavioral threshold; L_{dpth} = estimated threshold.



with the DPOAE audiogram (fig. 5a). Compression c calculated by the slope s of the DPOAE I/O function (fig. 1) is high in the range of normal hearing at the low and the high test frequencies. However, at the mid-frequencies, compression decreased, revealing OHC dysfunction in the medio-cochlear region which is typical of a congenital hearing loss. In a 6-month-old infant, the DPOAE audiogram indicated normal hearing at high and a hearing loss at mid-frequencies (fig. 5 b). Also here, compression was high at 6 kHz where hearing was estimated to be normal but low at 4 kHz where the estimated threshold was elevated. In this case, medio-cochlear OHC dysfunction is also likely. So compression c is suggested to be able to provide quantitative information about the compression loss of the CA.

Quantitative Evaluation of Hearing Loss and Recruitment for Providing Hearing Aid Fitting Parameters

Especially for hearing aid adjustment in children, a quantitative evaluation of the hearing loss and recruitment (compression loss) is necessary. With the help of the DPOAE audiogram and the DPOAE slope profile characteristic quantities of the cochlear-impaired ear and hence parameters for a noncooperative hearing aid adjustment situation are provided [17]. Gain functions derived from DPOAE I/O functions have the ability to serve as a fitting parameter in dynamic compression hearing aids for compensating loss of cochlear sensitivity and compression.

Early Detection and Monitoring Cochlear Dysfunction

DPOAEs are stable through time and hence are capable of detecting beginning OHC impairment and moni-

toring recovery from OHC impairment. Sound overexposure, and therapeutic drugs (antibiotic and antitumor chemotherapeutic agents) are reported to induce an irreversible hearing loss that typically affects the highest frequencies first, with hearing loss systematically progressing to the lower frequencies [24]. Early detection of ototoxicity is important for providing effective management options such as substitution of medications, change of dosage, and mode of administration [25]. Early detection of noise-induced hearing loss in subjects with job-related sound exposure in a potentially hazardous sound pressure level range can protect from severe hearing problems. Because TEOAEs are less effective above 4 kHz, DPOAEs are better suited for detecting and monitoring OHC dysfunction due to sound overexposure or ototoxic drugs. Moreover, DPOAEs have an additional advantage over TEOAEs, in that they can give information about the compression of the CA. If OHC function is disturbed during the toxic process or during noise overexposure, then not only DPOAE level but also DPOAE growth should be altered. Since DPOAE functions are able to assess both loss of sensitivity and loss of compression of the CA, it is suited for monitoring cochlear dysfunction during ototoxic drug administration or noise overexposure.

Discussion and Conclusions

The CA is an essential sound processing element in that the auditory end organ considerably enhances sensitivity and frequency selectivity. Being a by-product of co-

chlear amplification, OAEs directly reflect CA function. DPOAEs, when elicited by stimulus features, which account for the different compressions of the two primary tones at the DPOAE generation site, mirror the nonlinear basilar membrane motion found in animal studies. DPOAE I/O functions provide information about CA sensitivity and compression. OHCs – the motor elements of the CA – are most sensitive to extrinsic and intrinsic contaminants and can be irreversibly impaired. OAEs are a noninvasive tool for assessing OHC dysfunction. The main OAE applications in clinical diagnostics are newborn hearing screening, topological diagnostics, quantitative evaluation of hearing loss and recruitment, detecting the beginning stages of cochlear impairment during noise exposure or ototoxic drug administration, and monitoring cochlear function during recovery from co-

chlear dysfunction. Since OAEs describe detailed characteristics of the impaired ear, hearing aid adjustment can be improved by OAE measurements, especially in infants in which subjective audiometric tests fail to quantitatively determine cochlear dysfunction. In pediatric audiometry, DPOAE audiograms can assess cochlear hearing loss more precisely than behavioral tests, especially in infants where the conditioned free-field audiogram does not reflect the real threshold. Moreover, unilateral hearing loss can be detected. DPOAE audiograms are an automated measuring procedure with simple handling and short measuring time. No sedative is necessary in most cases. Assessment of hearing loss is possible up to 50 dB HL. Therefore, higher hearing losses have to be detected using tone burst ABR or ASSR. However, the incidence of a hearing loss higher than 50 dB is low.

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