

Contrasting Effects of Pressure Compensation on TEOAE and DPOAE in Children With Negative Middle Ear Pressure

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Abstract

In children with normal cochlear acuity, middle ear fluid often abolishes otoacoustic emissions (OAEs), and negative middle ear pressure (NMEP) reduces them. No convincing evidence of beneficial pressure compensation on distortion product OAE (DPOAE) has yet been presented. Two studies aimed to document effects of NMEP on transient OAE (TEOAE) and DPOAE. In Study 1, TEOAE and DPOAE pass/fail responses were analyzed before and after pressure compensation in 50 consecutive qualifying referrals having NMEP from -100 to -299 daPa. Study 2 concentrated on DPOAE, recording both amplitude (distortion product amplitude) and signal-to-noise ratio (SNR) before and after pressure compensation. Of the 20 participants, 5 had both ears qualifying. An effect of compensation on meeting a pass criterion was present in TEOAE for both left and right ear data in Study 1 but not demonstrable in DPOAE. In Study 2, the distortion product amplitude compensation effect was marginal overall, and depended on recording frequency band. SNR values improved moderately after pressure compensation in the two (overlapping) sets of single-ear data. In the five cases with both ears qualifying, a stronger compensation effect size, over 3 dB, was seen. The absolute dependence of SNR on frequency was also strongly replicated, but in no analysis, the frequency \times compensation interaction was significant. Independent of particular frequency range, the data support a limited SNR improvement in 2 to 3 dB for compensation in DPOAE, with slightly larger effects in ears giving SNRs between 0 dB and +6 dB, where pass/fail cutoffs would generally be located.

Keywords

negative middle ear pressure, transient otoacoustic emissions, distortion product otoacoustic emissions, pressure compensation

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Introduction

Otoacoustic emissions (OAEs) are widely used in establishing anatomical and physiological integrity of the outer hair cells and, in recent years, have become widely applied in hearing screening, clinical diagnostics, and several areas of auditory research. The various categories of OAEs appear to have separate mechanisms of generation despite largely common generator sites. Transient OAEs (TEOAEs) are mainly a reflection due to local amplification of basilar membrane movement by hair cell activity, while distortion product OAEs (DPOAEs) are thought to result from the interplay between nonlinear distortion and coherent reflections (Shera & Guinan, 1999). TEOAEs are recorded by

coherent averaging of transient responses, whereas DPOAEs are recorded as simultaneous intermodulation distortion between two pure tones. Grossly, both types

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of evoked OAEs depend on stimulus level and are affected both by middle ear status and by cochlear sensitivity (Kemp, 1978). Middle ear pathologies affect evoked OAE magnitude in at least two ways, attenuating both forward stimulus transmission from eardrum to hair cells and backward transmission (more details and alternative mechanisms are given later). Copresence of even minor conductive disorders in the middle ear thus introduces major confounding into the clinical use of emissions to assess cochlear function.

The role of pressure (as one aspect of minor middle ear pathology) and its compensation in TEOAE recording in ears with negative middle ear pressure (NMEP) has been studied in adults and children (Hof, Anteunis, Chenault, & van Dijk, 2005; Hof, Dijk, Chenault, & Anteunis, 2005; Trine, Hirsch, & Margolis, 1993). Effects of middle ear pressures (MEPs) on DPOAE, on the other hand, have only so far been reported in adults (Sun & Shaver, 2009; Thompson, Henin, & Long, 2015; Thompson, Long, & Henin, 2013; Zebian et al., 2013). These studies have been focused on NMEPs created artificially by modifying pressure in the ear canal. Compensation effects are smaller in ears with actual NMEP than in ears with artificially induced NMEP (Marshall, Heller, & Westhusin, 1997). In exhaustive literature searches (Cochrane, Embase, and Google Scholar), we found 35 studies combining middle ear dysfunction and DPOAE response in children, but within these, there were only 4 studies on pressure in children (Hof, Anteunis, et al., 2005; Hof et al., 2012; Hof, Dijk, et al., 2005), 3 using TEOAEs, and only 1 using DPOAEs (Karić, Djoković, Dimić, Slavnić, & Savić, 2016). The latter authors included 50 children aged 2 to 15 years and compared amplitude (distortion product amplitude [DPA]) and noise levels before and after pressure compensation; however, they did not report the analysis parameter of signal-to-noise ratio (SNR).

Detailed Acoustical Account of Effects of Middle Ear Problems on OAE Response

Young children have high incidence of acute otitis media, often recurring (RAOM), and of otitis media with effusion (OME); each condition can raise the average air-bone gap (ABG), that is, cause conductive hearing loss (CHL) and accompany abnormal MEP. Definitions and pathogenesis of different otitis media profiles are not the focus of this article (but see Lieberthal et al., 2013; Rosenfeld et al., 2013, 2016). All these entities are characterized by the presence of middle ear effusion at some stage, with NMEP particularly characteristic of early stages of OME. Middle ear effusion further changes the middle ear dynamics, necessarily compromising round-trip transmission, and reduces OAEs; 50% have no measurable DPOAE

(Amedee, 1995). In an experimental study in guinea pigs, Ueda, Nakata, and Hoshino (1998) found in line with physical principles that OAE changed significantly only when fluid filled half of the bulla volume, but it completely disappeared with a filled bulla. OAEs are more likely to be absent in ears with more fluid, and the thicker mucoid middle ear effusion accompanied by higher fluid protein levels (Park et al., 2007; Topolska, Hassman, & Baczek, 2000). However, the effects of NMEP are less obvious. Children with NMEP (C1 and C2 tympanograms) usually have minimal hearing threshold elevation (Fiellau-Nikolajsen & Lous, 1979; Multi-centre Otitis Media Study Group, 2009). Furthermore, in ears with NMEP, the change in OAE is not proportional to the stimulus amplitude change nor to the pressure (Marshall et al., 1997). A slight NMEP, < -100 daPa, causes only very slightly reduced OAE levels or CHL, but a pressure of -200 daPa in general reduces OAE amplitude by about 10 dB (Bray, 1989). The effect of pressure on DPA reduction also seems not to relate closely to the air-conduction threshold, although, as expected, it relates quite closely to the ABG: Kummer, Schuster, Rosanowski, Eysholdt, and Lohscheller (2006) found that presence of 10 dB ABG in adults (normal hearing ears) reduces the prevalence of measurable DPOAEs by 69%.

“Round-Trip” Plurality of Mechanisms Involved in OAE in Ears With Negative Middle Ear Pressure

The pathological substrate, in altering middle ear mechanics, affects ABG and OAEs response via three possible mechanisms: (a) simple reduction in amplitude in forward stimulus transmission to the cochlea; (b) reduction in backward transmission according to middle ear parameter changes (Gorga et al., 2007); (c) a changed relationship between primary tone levels, in turn changing the generated DPA, giving a differing form of the cochlear compression function at differing frequency of primaries. Analyzing the relation of OAEs to MEP in C1 and C2 ears in children is more complex than with experimentally induced ABG in adults, for three main reasons: (a) maturation of the middle ear admittance begins in the first month of life but still has not reached adult state by age 11 (Keefe, Bulen, Arehart, & Burns, 1993; Okabe, Tanaka, Hamada, Miura, & Funai, 1988; Abdala, Keefe, & Oba, 2007); (b) ear canal growth is intensive in the first years of life; and (c) the pathological substrate of mucosal inflammation and Eustachian tube obstruction may cause multiple internal reflections, which can affect DPOAE fine structures (Puria, 2003). However, Gorga et al. (2007) found that the differences in behavioral thresholds between low and high frequencies cannot be completely explained by differences in

energy reflectance because the cochlear dynamic range is not the same for low and high frequencies. High stiffness specifically attenuates low-frequency transmission (Bess & Humes, 2003). If this direct mechanical effect is indeed a major factor in the lower OAE output, then at least for low frequencies, pressure compensation would seem to offer some promise of reducing the false-positive rate in screening applications where obtained DPA or SNR is compared with some pass criterion (Bray, 1989; Trine et al., 1993). Of the Three possible pressure effects listed earlier, most would be applicable to the noise as well as to the DPA, suggesting that the effective SNR in the system would limit any real gain from compensation, despite the apparently enhanced DPA. For good statistical reasons, SNR or DPA can each be used for the decision metric (Brass & Kemp, 1994). This reasoning might contribute to absence of reports of DPOAE compensation effects. Compensation of a negative trans-tympanic pressure differential should in theory increase OAE amplitude, and this has indeed been observed in TEOAE emissions especially in low frequency bands (Hof, Anteunis, et al., 2005; Hof, Dijk, et al., 2005; Naeve, Margolis, Levine, & Fournier, 1992).

Scarcity of Publications on Pressure Compensation in DPOAE

No publications have yet reported clear clinical improvements in SNR of DPOAEs on pressure compensation. In addition to the point about SNR as one necessary metric, the relative absence of reported studies on pressure compensation in DPOAEs might include some operation of publication bias following unreported initial null or marginal results. Such a source of bias is likely to be especially high where the objective is to produce a technological solution to a practical problem such as the high OAE screen false-positive rates in absence of the cochlear hearing losses which such screens are intended to identify (Gaffney, Green, & Gaffney, 2010; Kennedy, 2000; Vos, Lagasse, & Levêque, 2014). Contributory explanations for the lack of information could also be great variability of the results/responses between individuals and low reproducibility or an inability to explain influences of middle ear parameters and their compensation in terms of known middle ear or cochlear mechanics.

Aims of Studies

The relative lack of information on pressure and compensation effects in DPOAEs from children's ears with natural NMEP is a lack in both basic science and application. This was the main reason for launching a pair of studies on three main questions: (a) whether pressure compensation implemented in children with a history

of OME/RAOM and Eustachian tube dysfunction would increase the numbers passing a criterion in TEOAE and DPOAE (with possible clinical application in screening and reducing false positives); (b) the gross effect of NMEP compensation on pass/refer criteria in TEOAE versus DPOAE, respectively; (c) in DPOAE, detailed analyses of DPA, noise, and SNR before and after NMEP compensation, to be sure that phenomena were not missed due to incomplete parametrization of the recorded emissions.

Materials and Methods

Children aged 2 to 12 years with a history of RAOM or OME, normal bone and air-conduction thresholds up to 25 dB, and attending the pediatric ENT/audiology outpatient department at a tertiary referral center were participants in two studies. These were consecutive cases seen but subject to meeting entry criteria child and parent cooperation. Children with identified syndromes, craniofacial anomalies, neurodevelopmental problems, tympanic membrane perforation, and history of middle ear surgery were not included. Study 2 proceeded with the same inclusion criteria to better understand DPOAE parameter changes on pressurization. In studies 1 and 2 average ages of participants were 5 years, 1 month and 6 years, 4 months, respectively. The gender distributions were 36 males versus 14 females (Study 1) and 9 males versus 11 females (Study 2); although differing, this was not pursued further because of the lack of material and reliable gender effects in OAE. The test protocol for this work complied with general research practice standards and was passed by the Ethics Committee of the Clinical Centre of Serbia (reference number 415/69).

Equipment

Tympanometry (226 Hz) was performed for recruitment using the Interacoustics AT235. The GN Otometrics EchoMaster-OAE with pressure compensation (55GN Otometrics GmbH & Co. KG, Neckartenzlingen, Germany) was used for TEOAE and DPOAE amplitude, also for SNR and noise recordings. The test was conducted according to standard procedure, in a specially designed and acoustically treated room, but not a sound-isolated booth. The pressure compensation module was used for basic tympanometry examination and pressure compensation, connected to the main auditory module of the EchoMaster-OAE for OAE recordings and to the probe, with the compensating limit between +200 daPa and -200 daPa. The compensation procedure was applied only for ears with NMEP beyond -100 daPa. Tympanometry categories A, C1, C2, and B are interpreted according to MEP and compliance (Fiellau-Nikolajsen & Lous, 1979). Type A ears are not

included in either study, that is, the MEP range between -100 and $+100$ daPa and compliance ≥ 0.2 ml. Type C1 and C2 ears were included, defined, respectively, as MEPs from -101 to -200 daPa and from -201 to -300 daPa, having compliance ≥ 0.2 ml. Children with pressure < -300 daPa and compliance < 0.2 ml are also considered Type B so were not included.

Participants and Procedure

Study 1 Participants

After ENT examination, the 50 children proceeded to tympanometry under the procedure explained earlier. For administrative simplicity, the sequence of OAE conditions was fixed: TEOAEs then DPOAEs. For ears with C1 and C2 tympanometry, the compensation procedure was performed and TEOAEs and DPOAEs tests repeated. Results in Study 1 were analyzed only by pass/fail rate in relation to criteria for TEOAEs and DPOAEs, supplemented by interparameter correlations of percentile pass levels as a form of reliability test.

Study 1 Procedure

Before TEOAE recording, the conventional test probe was run (Kemp, Ryan, & Bray, 1990); stimulus signal and spectrum were observed for presence of oscillations and gaps in which case the probe was changed or cleaned and the test repeated till the signal spectrum became flat and the stimulus spectrum smooth. The target stimulus level for TEOAE recording was set at 80 dB sound pressure level (SPL) and the true stimulus level adjusted to the target level. The number of accepted sweeps was adjusted to 260, and the rejection rate was adjusted to the prevailing noise level. The TEOAEs were recorded in five frequency bands (0.5–1.5 kHz, 1.5–2.5 kHz, 2.5–3.5 kHz, 3.5–4.5 kHz, and 4.5–5.5 kHz). The test pass criterion was set at 60% correlation between the two recording buffers (the stopping criterion in default settings was set at 90%) and the SNR at ≥ 3 dB. Response patterns were then rescored overall according to the number of stimulus frequencies “passed”: full pass (four to five frequency bands passed out of five), partially passed (three of the five frequency bands passed), and fail (less than three frequency bands out of five).

Before DPOAE recording, probe tests were run for fit to the ear canal using an f_1 , f_2 pairing in each frequency range. In the event of amplitude discrepancies across frequency, the probe size was swapped and refitted until the spectra became flat and overlapped for the two frequencies. The noise artifact rejection level was adjusted according to the actual environmental noise, adjusted for each child separately and ranging from 45 to 60 dB SPL. The frequency ratio of the primaries was

$f_2/f_1 = 1.22$, and the sound level of both f_1 and f_2 was set at 70 dB SPL ($L_1 = L_2 = 70$ dB SPL). Given that these participants have pure tone average ≤ 25 dB, stimulus attenuation is not expected to be high, but it could lead to nonoptimal relationship between the levels of the primaries. Forty sweeps per frequency were used, with stopping criterion set at +6 dB SNR. The response was recorded at nine frequencies: 1, 1.3, 1.6, 2.0, 2.5, 3.2, 4.0, 5.0, and 6.0, overlapping with the bands for TEOAEs. Provisionally, a “full pass” criterion was set at SNR > 3 dB for any six or more frequencies, and partial pass was defined as at least five of the nine frequencies passed. The children with pass or partial pass results were finally regrouped for analysis as “pass.”

Study 2 Participants

Study 2 participants were recruited in the same way but separately. The ears with A and B tympanograms were excluded, that is, a child was recruited only if she or he had MEP in the range -101 to -300 daPa (C1 and C2) in one or both ears. Of 30 children initially recruited, 10 were excluded, 9 as incomplete because of lack of cooperation, loud ambient noise or test interruption, and 1 with suspected sensorineural hearing loss. Of the 20 remaining, 5 met the NMEP pressure qualification on both ears.

Study 2 Procedure

Only DPOAEs were recorded for Study 2, but other aspects of general procedure were as for Study 1. There was no preemptive scoring of band pass/fail. The data reduction for Study 2 used all nine frequencies, but to achieve some leverage on frequency along with aggregate reliability, these were divided into three frequency bands in which responses were then averaged: low (1.0, 1.3, and 1.6 kHz), middle (2.0, 2.5, and 3.2 kHz), and high (4.0, 5.0, and 6.0 kHz). The need for some leverage on frequency arises because (a) the pressure difference increases stiffness of the middle ear (and hence the CHL) and thus opposes low-frequency transmission so a distinction at least into high and low is needed; (b) high background noise level could obscure or mask the effect of compensation, especially when using SNR and given that noise is greatest in the low frequency bands; (c) presence of any middle ear effusion could influence high-frequency DPA. The design variables of chief interest were thus compensation (C), frequency band (F), and the interaction between frequency and compensation ($F \times C$).

The unilateral data were analyzed in two versions in which the five bilaterally qualifying cases had their left then right ear used. Thus, the principle was honored to use as much of the data as feasible to maximize power

and generality, without fallaciously conflating degrees of freedom (*df*) by using more than one ear from some participants in any single analysis. Two supplementary analyses strengthened conclusions. The first focused on 5 binaurally qualifying cases (so separating individual differences from replicate error variance) and the second restricted data analyses to ears with compliance above 0.3 ml, this leaving 14 cases. The suggested cutoff is a balanced choice to leave a sufficient sample size. A higher cutoff would enhance the difference sought but reduces relevant sample size, hence the reliability of finding. For the chief analysis, there were enough *df* to also adjust for compliance (taken from the uncompensated condition, and itself first preadjusted for the slight effect of pressure on compliance).

Statistical Techniques

Study 1 provided descriptives for the one ear used of each participant (measure of variability, central tendency, and relative numbers). In order to evaluate the effect of pressure compensation in TEOAE and DPOAE, the simple McNemar Test for Significance of Changes, before versus after pressure compensation, was performed for hypothesis testing (Fisher Exact Probability test, *t* test, and McNemar Test for Significance of Changes, before vs. after pressure compensation). The initial preliminary pass and partial pass categories were combined to give a 1 *df* contrast with “fails,” for simplicity and stability given the moderate sample size (*n* = 50). The dependence of TEOAE and DPOAE responses for each ear was tested in relation to compliance (value ≤0.2ml vs. higher) using the Fisher Exact test. A simple index of steepness of the gradient in effect of baseline pressure around criterion is offered by the difference in average pressure values between groups with present

and absent TEOAEs and DPOAEs; this was accompanied by two-tailed unrelated sample *t* tests.

To compare responses as effect sizes before versus after pressure compensation in Study 2, analysis of covariance (SPSS-22) was used, distinguishing within-subject variables of frequency band (*F*) and compensation (*C*); the analyses was additionally adjusted, for baseline compliance (itself preadjusted for baseline pressure where significant); more details are in individual tables and footnotes. Partial eta squared (η_p^2) was adopted as a simple measure of effect size, applicable to both categorical and continuous independent variables, reflecting their contribution to total variance in the dependent variable. Correlations gave a prerequisite check on reliability. Disaggregation of data into responses below and above the suggested cutoff values for paired (related-sample) *t* tests on the compensation effect documented the dependence of compensation effect on general signal quality.

Results

Study 1 Results

Preliminaries. All ears with tympanometry Category A “passed” TEOAE as defined, and all ears with B failed. The distributions for tympanometry categories were for the left ear: A (2), C1 (4), C2 (20), and B (24) and for the right ear: A (5), C1 (13), C2 (23), and B (9). Tympanometry Category B was more often present in the left (24) than in the right ear (9). In the left ear, TEOAE was passed in 15 and failed in 35 ears. In the right ear, TEOAE passed in 22 and failed in 28 (Table 1: Fisher Exact *p* for laterality, two-tailed = .214; *n.s.*). After pressure compensation, OAE pass/fail numbers were then compared with the uncompensated ones. In

Table 1. Pass/Fail Rates for 50 Ears in Study 1 on TEOAE and DPOAE, With Category Mean Pressures (daPa) of the Tympanograms and Effects of Compensation on Pass or Fail.

	Left ear (<i>n</i> = 50)		Right ear (<i>n</i> = 50)	
	Pass	Fail	Pass	Fail
TEOAE				
Uncompensated (<i>n</i>)	15	35	22	28
Pressure in daPa (<i>SD</i>)	-197 (73)	-277 (21)	-175 (71)	-277 (21)
Compensated (<i>n</i>)	21	29	29	21
DPOAE				
Uncompensated (<i>n</i>)	24	26	35	15
Pressure in daPa (<i>SD</i>)	-226 (70)	-283 (10)	-200 (76)	-253 (71)
Compensated (<i>n</i>)	24	26	37	13

Note. *SDs* were calculated in floating point but rounded to nearest integer as milliliter units are so small. Significance statistics for associations of pass/fail with pressure, and compliance, and for compensation effects are given in text. *SD* = standard deviation; DPOAE = distortion product otoacoustic emission; TEOAE = transient otoacoustic emission.

Table 1, the top and bottom rows of each field in italic give passes and fails, while the middle rows give the initial (baseline) pressure data of the passing and failing ears (and standard deviation [*SDs*]). These uncompensated pressure values of passing versus failing ears summarize pressure effects where they matter most. Differences were all in the direction expected from compensation; left 80 daPa (unrelated *t* test with equal variances $t = 3.341$; $p = .002$) and right 102 daPa (unequal variances, $t = 4.075$; $p = .001$). In absolute terms, left ears passing seemed to tolerate more NMEP than right, but the difference in 22 daPa here is too small to be significant. Having compliance ≤ 2 ml was also much more common in the TEOAE failing than passing ears (not tabulated; Fisher Exact test: left $p = .0002$, right $p = .0027$). Given that no Type B passed on either side, it follows that compliance ≥ 2 ml is generally necessary for a TEOAE pass, so this offers one general qualification criterion for attempting measurements or applying compensation, placing the effective borderline evidently slightly higher, as revisited in Study 2.

Compensation effect on TEOAE pass rate. Compensation of MEP as negative as -200 daPa showed improvement in the pass rates (left ear six more passes, right eight more, but this latter figure was reduced to seven, as in one ear the compensation paradoxically caused loss of TEOAEs; last row of upper field in Table 1). The numbers passing TEOAE thus increase by $+12\%$ to $+14\%$ absolute for the whole sample on compensation, a relative increase in the number of initially passed ears in the left and right ears, respectively, by 40% and almost 32% , not a trivial percentage. Thus, via qualifying NMEP cases, we confirm that the potential for compensation in TEOAE within individual case assessment is significant in our sample with our scoring conventions (McNemar Test for Significance of Changes, left ear $p = .031$; right ear $p = .039$; Table 1).

Compensation effect on DPOAE pass rate. The pressure differences between initially failing/passing categories by DPOAE subgroups were less than those seen with TEOAE (left 57 daPa; right 53 daPa, Table 1), indicating less pressure susceptibility, so predicting less ability to compensate. As the particular failing ears differed between OAE modalities, there is no straightforward statistical test for this difference of differences. However, the absolute condition *SDs* of 10 to 70 daPa, together with the ear asymmetry, suggest that the possibly lesser susceptibility of DPOAEs to pressure would best be approached more directly in a further study with continuous signal parameters as variates. In contrast to the TEOAE findings, pressure compensation did not significantly improve DPOAE pass rate with the procedure and criteria used in Study 1; only two further right ears

and no further left ones passed DPOAE after pressure compensation (McNemar Test for Significance of Changes, left ear $p = 1.0$; right ear $p = .5$; lower half of Table 1).

Study 2 Results

Preliminaries. The DPA (dB SPL), SNR (dB), and noise (dB SPL) before and after pressure compensation at nine frequencies were first split into even versus odd positions in ascending order; averages of the five odd and four even values thus permitted a reliability (split-half) test of individual differences in response. For the two recorded variables (averaged DPA and noise), this correlation was run on the uncompensated and compensated conditions, combined across individuals. Although particular frequencies do not all contain totally identical information, these correlations attest replicability because even and odd frequencies convey similar information by pooling across any systematic effect of frequency. The Pearson correlation of 0.8945 for DPA and 0.915 for noise and confirm that individuals' DPOAE responsiveness levels do differ systematically and that such data are reliable. The data properties for noise are determined once DPA and SNR are given because of the simple subtractive relation between them, so the third correlation of any third pairing would not be independent or further informative.

To avoid data exclusion and possible bias in choice of data from the five children having two ears qualifying, we collated two versions of which one uses the five left ears and the other uses the right; thus, the data for the two versions overlap by $15/20 = 75\%$. There is an absolute level difference between DPA and SNR, largest at low frequencies (~ 10 dB), due to the predominantly low-frequency spectrum of the noise entering DPA but subtracted out in SNR. Patterns of results were simple and highly similar between versions both for DPA and for SNR as signal parameters, thus legitimating report of left ear only data for descriptive simplicity from these five cases in other analyses above and below.

Figure 1 gives an overall visual appreciation of Study 2 results via cumulative frequency distributions for DPA and SNR averaging three frequencies within the three main frequency bands and also across the uncompensated and compensated conditions (for their separation, see Table 2). At the left for a very low SNR ratio, there are few cases; but as the value considered is increased, the number included rises, most steeply at middling parameter values, as is usual for probabilistic data. Finally, only few further cases are added for further step rises in the value considered at the top right. Low-frequency noise in DPOAE accounts for the low first correlation value in Figure 1. The enhancement from subtracting noise out in the expression for SNR disappears in the

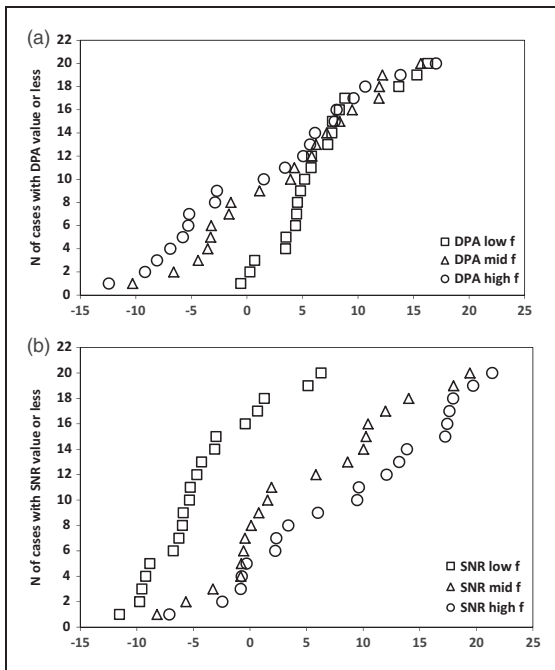


Figure 1. Cumulative frequency distributions on 20 ears with NMEP for DPA (Panel a) and SNR (Panel b) in dB, for three bands of DPOAE primary frequency. (a) Mean in dB over 3 frequencies in band and 2 compensation conditions; (b) Mean in dB over 3 frequencies in band and 2 compensation conditions. DPA = distortion product amplitude; SNR = signal-to-noise ratio.

data for high-frequency primaries. The most important of the six curves for application is the one for SNR from the high-frequency band, which is approximately linear, rather than markedly sigmoid. One extra ear passing here thus suggests an extra 5% would pass in a population, around almost any cutoff that might be imposed on this curve. Over the 25 dB SNR range seen from -3 to $+22$ dB, the pass rate in qualifying ears increases by approximately $100\%/25\text{ dB} = 4\%$ per dB of obtained SNR, before we consider pressure compensation. The general need to maximize SNR via instrumentation, recording conditions, and test duration hardly needs to be emphasized, but the absence of any natural cutoff in the data (so making imposed cutoff values widely tradable against such technical considerations, and against the economics of referral and retesting) underlines the need for explicit justification of any cutoff value to be used for “pass.”

Figure 2 displays SNR as a function of an untransformed and a transformed value of the baseline NMEP. The transform is obtained by fitting both a linear and a quadratic component, then making the x -axis the predicted value for SNR. The comparison graphically aids appreciation of the limited role of mechanical status of the middle ear for DPOAE, via the reduction in SNR at the very highest negative pressures, at which its effects become less amenable to compensation. Due to somewhat variable data, the nature of the transition phase close to -300 daPa is more clearly seen by using the transformed version and the gain in quality of fit is

Table 2. Main Results Summary on 20 Cases (25 Qualifying Ears) in Study 2 as Mean and Variability of DPA and SNR in dB, Adjusted for the Slight Compliance Differences at Baseline.

		Left else right ear ($n = 20$)			Right else left ear ($n = 20$)				
		Mean	SD	95% CI	Mean	SD	95% CI		
DPA									
Uncompensated	Low	5.34	1.39	2.43	8.25	5.59	1.14	3.20	7.98
	Mid	2.08	1.32	-0.69	4.85	2.48	1.43	-0.53	5.48
	High	0.63	1.51	2.54	3.79	0.15	1.96	-3.96	4.26
Compensated	Low	7.41	1.05	5.21	9.61	8.10	1.20	5.58	10.62
	Mid	4.28	1.88	0.33	8.24	4.36	2.08	0.00	8.72
	High	2.42	2.16	-2.12	6.96	2.04	2.35	-2.88	6.97
SNR									
Uncompensated	Low	-5.72	0.97	-7.76	-3.69	-5.03	1.07	-7.28	-2.77
	Mid	3.18	1.44	0.16	6.20	4.38	1.69	0.84	7.93
	High	7.44	1.69	3.88	10.99	7.14	2.17	2.59	11.69
Compensated	Low	-2.94	1.36	-5.81	-0.08	-1.84	1.58	-5.16	1.49
	Mid	6.13	1.93	2.07	10.19	6.66	2.05	2.35	10.98
	High	9.77	2.26	5.03	14.51	9.63	2.38	4.62	14.63

Note. To use all data validly, the left and right half fields overlap by 75% in data (ears) used. DPA = distortion product amplitude; SNR = signal-to-noise ratio; SD = standard deviation; CI = confidence interval.

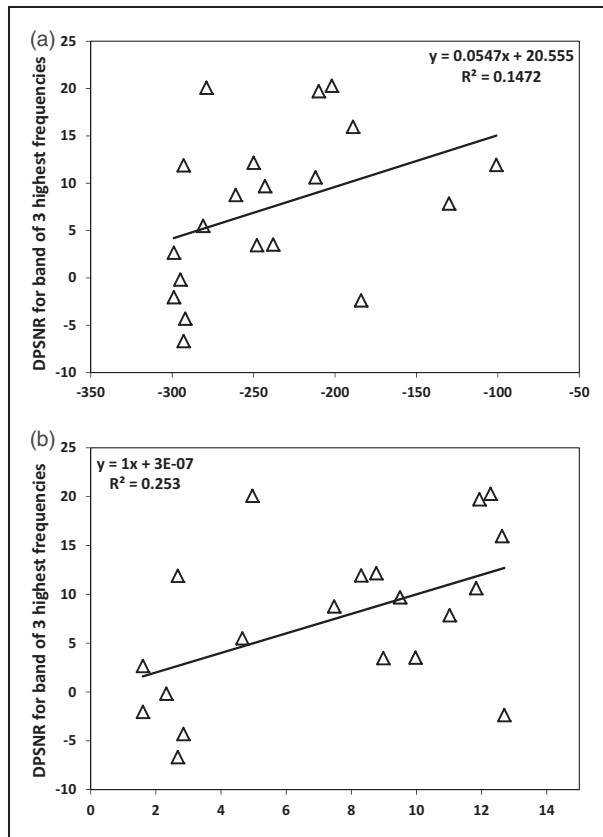


Figure 2. Non-linear relation between unilateral DP SNR and middle ear pressure, confirmed by the improvement in fit (RSQ for linear fit rising from .147 to .253) between the untransformed (a) and transformed (b) versions. (a) Untransformed MEP; (b) Transformed MEP. DPSNR = distortion product signal to noise ratio; MEP = middle ear pressure.

moderate [Rsq (the correlation squared) rising from .147 to .253]. However, the same variability limits the scope for specifying some particular pressure value less negative than -299 daPa at which it would be efficient to suspend compensation. For amplitude, the corresponding transformation also raised RSQ absolutely and relatively less, from .237 to .318, though on the stronger basic relationship seen, for the less performance-related signal parameter. In this respect, SNR is less subjected to baseline mechanical differences.

Chief analysis of effects of interest on DPA and SNR. Table 2 gives descriptives of the compliance-adjusted condition means of DPA and SNR for distortion product primary frequency, with compensation for 20 qualifying ears in two versions; from the five children giving data on both ears, the left panel uses only their left ears, and the right panel uses the right ears. The between-subjects compliance is itself lightly preadjusted for uncompensated pressure, by expressing as the residual from a prior regression, which avoids the above transformation

issue. The compliance adjustment contributes to a slightly better SNR model by reducing error for the left panel, adjustment term $F(1,18) = 5.956$: $p = .025$; $\eta_p^2 = .249$, but not significantly so for the right panel, adjustment term $F(1,18) = 1.395$: $p = .253$; $\eta_p^2 = .072$. To avoid overfitting, such adjustment was omitted in the later smaller N analyses. This slight ear pattern discrepancy is probably simply due to the relative incidence/severity of problems in the two ears. This inconsistent effect of adjustment for baseline compliance confirms the suggestion in Figure 2 that for SNR in DPOAEs, the baseline individual ear mechanical effects other than pressure are marginal, so barely worth adjusting for.

In DPA, there were marginal trends for compensation, and significant trends for frequency, but no significant $F \times C$ interaction (minimum p was .749 from four analyses, that is, two linearities by two sampling versions). In the analysis of noise corresponding to main Table 2, the overall effect of compensation on noise was not significant in either version, $F(1,18) = 1.153$, $p = .297$, $\eta_p^2 = .060$; $F(1,18) = 0.598$, $p = .449$, $\eta_p^2 = .032$, and nor was any other term.

Detailed reporting hereafter is focused on SNR because of the direct relationship of SNR to system performance and the high variability in DPA. For transparency in significance testing, this is reported separately for the two ear versions, although we do not of course claim that their evidence accumulates independently. For frequency, both linear and quadratic components were estimated, leaving 1 df for each, and both were usually significant, with the more significant one being specified and quoted here for simplicity. Thus, all F values have 1 df . Frequency was pervasively significant, F linear (1, 18) = 72.605; $p < .0005$; $\eta_p^2 = .801$; F linear (1, 18) = 38.722; $p < .0005$; $\eta_p^2 = .683$. While there is no single convention for labeling ranges of η_p^2 as to general magnitude, these effect sizes are very large. Compensation was also pervasively significant, $F(1,18) = 6.171$: $p = .023$; $\eta_p^2 = .255$; $F(1,18) = 7.654$: $p = .013$; $\eta_p^2 = .298$. The $F \times C$ interaction was never significant, with minimum p of .676. In physical magnitude rather than statistical terms, the mean pressure compensation effect for these qualifying type C ears is about 2 to 3 dB. The DPA and SNR results argue for using high or mid plus high-frequency DPOAE primaries generally, and the absence of $F \times C$ interaction leaves that argument unaltered.

Shaping of results by compliance range restriction. In the light of Study 1 findings, the qualifying compliance cutoff was raised to ≥ 3 ml, now giving 13 or 14 qualifying cases, respectively, according to the declared composition of left and right ear data. Again, compensation and frequency were always significant, but their interaction never was. For the effect of chief interest, compensation,

the estimates in dB of effect are generated by SPSS repeated-measures analysis of variance for each frequency; as p varies with N , there emerges a trade-off between magnitude and standard error. For succinct summary of magnitude, only η_p^2 values are suitable to reflect the effect of this compliance censoring on effect magnitude. In the censored subset, for the version preferring left ear data, the η_p^2 for compensation rose to .398 (cf. .255 uncompensated); in the right ear data, it rose to .437 (cf. .298). This confirms that restriction to more serious cases with respect to compliance, within the overall pressure range, increases (as expected) the gain from compensation.

Data from five binaurally qualifying cases. There are a number of possible bases for the two ears of the same individual being more similar than unrelated ears of different individuals, even after taking pressure and compliance into account. The overlapping versions in Table 2 already use all relevant data, but focusing on two-eared cases offers a chance to document the extent of this similarity and to inspect and reduce error. There is no reason why the frequency effect should differ in participants with two qualifying ears and indeed the η_p^2 of .730 for frequency lies between those ($\sim .8$, $\sim .6$) seen in the main analysis. However, the reduction in the residual error with repeated-measures permitted compensation to be shown as significant on the small sample of five participants, $F(1,4) = 10.803$; $p = .030$; $\eta_p^2 = .730$. This contrast in strength of findings relative to the larger single-ear analysis cannot practicably be controlled for possible sample differences in the history or relative severity (e.g., other ear status), and such factors are indeed likely to be involved. It is not impossible that in the case of substantial NMEP in both ears of the same participant, the size of compensation effect could be larger, but pending controlled replication on a larger sample, possible explanations are beyond present scope. More importantly, the sheer magnitude of the jump from η_p^2 values under .3 in the main analyses to .730 here confirms the intrinsically greater power from error reduction when the two ears within participants are

analyzed, a point explored in more detail in the Discussion section.

Subsets of data sensitive to small differences. Censoring criteria that might define data subsets most sensitive to small influences remain of general interest, although where the criterion is imposed in the same domain as the measured variate (e.g., SNR), cautious interpretation is needed. Rather than a single a priori cutoff (e.g., in SNR as for a clinical pass-fail), we envisage a qualifying range, where all the continuous data above the postulated cutoff would be used for optimum decision. However, in doing this, the data below the selected range would have to be discarded, with some inevitable restriction of generality. This refers to a scientific study, not to passing an individual case. Given that the SNR value has better replicability and more direct decision relevance than DPA, we would expect it to perform better in such a sensitized analysis, but we have evenhandedly examined DPA also as measure.

For an existence proof (i.e., answering whether DPOAEs can show gain from pressure compensation), we next limited analyses to a subset where gain from pressure compensation is known to be more sensitive. We considered two possible cutoffs where such data pre-selection might assist decisions: SNR ≥ 0 dB as a low and ≥ 6 dB as a high inclusion criterion (Table 3). To avoid artifactual reversion (“regression”) to the mean, we applied this inclusion criterion to the average of the two conditions (uncompensated and compensated). Descriptively, these two qualification criteria produced fairly similar results for the cases included above their respective criterion values, but the statistical significance is inevitably less convincing for the +6 dB SNR qualification because such a small proportion of the data remain. The range SNR ≥ 0 dB is thus favored, which includes the often-used individual case pass/fail criterion of ≥ 3 dB SNR (Brass & Kemp, 1994; Sun & Shaver, 2009). However, data below a conventional criterion can still be informative, an option which counting *passes* does not have. Here, a cutoff at ≥ 0 dB makes the pressure compensation effect very highly significant

Table 3. Effect of SNR Range Restriction on Extracted Compensation Effect, Above Versus Below Cutoff.

Cutoff value	SNR < 0	SNR ≥ 0	SNR < 6	SNR ≥ 6
N of cases	9	11	13	7
DPA	-1.78 ($t = 0.828$, $p = .432$)	5.13 ($t = 5.277$, $p = .000$)	0.29 ($t = 0.164$, $p = 0.873$)	5.25 ($t = 3.668$, $p = .010$)
SNR	0.34 ($t = 0.283$, $p = .785$)	4.61 ($t = 3.396$, $p = .007$)	1.70 ($t = 1.522$, $p = .154$)	4.53 ($t = 2.280$, $p = .063$)

Note. Parameters are averaged over all 9 frequencies, so involve 18 data points per participant. Unrelated t test values and p values implement a validation paradigm for delimiting the SNR able best to show the expected and obtained compensation. In the subset of data above 0 dB SNR, the low effective noise level can be seen as the compensation effect in SNR being not much less than the effect in DPA and further restriction to cases with highest SNR becomes pointless. DPA = distortion product amplitude; SNR = signal-to-noise ratio.

both for DPA and for SNR (respectively, $t=5.27$, $p < .001$; $t=3.396$, $p = .007$). Thus, restriction to bilateral NMEP and restriction to higher SNRs both serve to establish significant compensation in DPOAE in ways consistent with theoretical constraint but in doing so imply restricted applicability.

Discussion and Implications

Our practical goal was to assess what role compensating for NMEPs might have in screening and assessment of cochlear disorders with OAEs. Given the apparent absence of gain in pass rate on compensation with DPOAEs from Study 1 and a similar silence in the literature, Study 2 unleashed an analytically more powerful approach to measurement, plus consistency checks from three different slices through the data. It showed that there is gain from compensation in DPOAE, but by only ~ 2 to 3 dB SNR, unless further targeting is imposed, an apparently modest gain.

Role of Pressure and Compensation in DPOAE

Our results are broadly consistent with previous studies showing gain from pressure compensation with TEOAEs (e.g., Hof, Anteunis, et al., 2005; Hof, Dijk et al., 2005). Our Study 1 showed clearly that in pass/fail terms, TEOAEs benefited from pressure compensation, except at the very highest negative pressures. This seems to overrule studies not finding compensation gain even with TEOAEs, for example, Marshall et al. (1997). Strength of DPOAE here was minimally affected by NMEP or its compensation, demanding an explanation of the gross difference in pressure and compensation effects between DPOAEs and TEOAEs.

Recent DPOAE research shows that differences in level and frequency of the primaries both influence the magnitude of response recorded. Consequently, minor changes in air-conduction threshold, even in the presence of normal hearing acuity, can reduce the DPA, by changing primary level separation. Various formulae for optimum L1 to L2 separation have been suggested (Brown & Gaskill, 1990; Kummer, Janssen, & Arnold, 1998; Marcrum, Kummer, Kreitmayer, & Steffens, 2016; Neely, Johnson, & Gorga, 2005; Whitehead, McCoy, Lonsbury-Martin, & Martin, 1995). One of these proposed for the frequency range 1 to 6 kHz is that L1 should be changed by 0.4 dB for each dB change in L2 (formula: $L1 = 0.4 L2 + 39$ dB; Kummer et al., 1998). Those experimental results were obtained in healthy adults with normal MEP, so application to children with NMEP should be cautious. Minor low-frequency CHL in children with C1 and C2 tympanograms, even in the presence of hearing thresholds < 20 dB, could shift

the relative effective levels of primaries at the hair cells away from optimum. This shift would be pressure-dependent, both for the well understood middle ear mechanical effect (stiffness bass cut) and for the less understood changes in cochlear compression. Overall, the round-trip outer plus-middle ear signal attenuation in normal adults for DPOAEs is thought to range from -39 to -17 dB at 1 to 3.3 kHz (Naghbolhosseini & Long, 2017); these values could be expected to be higher in NMEP and further to depend on frequency band. The actual value carries implications for separation of the presentation level from the noise floor.

In Study 2, we found that the SNR parameter of DPOAE does gain from pressure compensation, with apparently no frequency-specific effect (nonsignificant $F \times C$ interaction). This was despite the aforementioned possible influence of pressure on effective relative levels of the primaries or differing cochlear compression between low and high frequencies (Gorga et al., 2007). According to that study, minor changes in DP primary levels could strongly influence DP generation. Compensating NMEP improves trans-tympanic transmission, but the NMEP still exists, so abnormal trans-labyrinth transmission could result from the remaining outward stapes displacement (Bray, 1989), possibly altering relative levels of the primaries in DPOAE. Given these multiple effects, some in part cancelling, we should not expect to find any particular pattern of frequency dependency in the effect of compensation; indeed, we found no interaction, only the overall known effect of frequency, as largely shaped in SNR by the noise spectrum.

Pressure compensation does give minor improvement for SNR in DPOAEs, but at highest NMEPs, it is too small to show as statistically significant. Similarly, Sun and Shaver (2009) showed compensation in adults but only for slighter NMEPs. Also, here as with Sun and Shaver, the internal noise level did not change on pressure compensation. However, there were several differences between our Study 2 and theirs: (a) their low-frequency band was considerably lower than ours: 0.5, 0.6, 1.0, and 1.5 kHz (vs. 1.0, 1.3, 1.6, and 2.0 kHz); (b) all our included participants had NMEP more negative than -100 daPa. Most crucially, (c) our NMEPs were not artificially induced but contained the associated middle ear effects from presumed Eustachian tube dysfunction, so our study adds generality, along with clinical applicability for hearing assessment in NMEP.

Several factors could contribute to restricting pressure compensation effects in DPOAE recordings: (a) presence of middle ear fluid in C2 ears, which could be the source of frictional energy dissipation and internal reflections, even if the effect of pressure is equalized; (b) incomplete compensation may actually be achieved for NMEPs more negative than -200 daPa (although no residual

canal pressure here remained more negative than -99 daPa); and (c) the different role of NMEP on distortion compared with its role on the reflective component could contribute to a limited role for compensation. Although the trans-tympanic pressure difference is corrected in compensation, an abnormal pressure difference still exists at the oval window. Our results on DPA and noise changes on pressure compensation were only partly similar to those of Karić et al. (2016) on 50 child participants; they found modest enhancement of DPA in low frequency bands (1.0, 1.6, and 2.0 kHz) but surprisingly increased noise in mid-frequency bands (2–4 kHz) which we did not. The fact that the SNR parameter was not reported, and the modest sample size limits the value of further comparison.

Practical Implications of Restricting Baseline Compliance or SNR Range

Individual baseline compliance is not completely irrelevant to DPOAE recorded levels; however, in preliminary analyses of the uncompensated condition, and in adjustment of the main results for both compensated and uncompensated, it had only a weak and inconsistent effect. Restricting inclusions to those with compliance ≥ 0.3 ml increased the estimated effect of compensation, implying some gain from such adjustments with large data sets, and suggesting for practice possible restriction of compensation to such cases, where it can make most difference.

Prelabeling low SNR values as provisional fail (e.g., using SNR ≥ 0 dB cutoff) is a statistical rather than physical form of censoring. Like a raised compliance qualification, it would also restrict the scope of cases to which compensation could be usefully applied in practice. Scientifically, such censoring did permit a clearer compensation effect in both DPA and SNR to be shown, so helping to keep compensation in DPOAEs on the research agenda. That agenda can now move back to larger more applied evaluation studies taking into account the applicability and process efficiency of conditional testing. Even for DPOAEs, pressure compensation of NMEP could still be useful in small subsets of children where it makes a difference, such as those with compliance > 0.3 ml or SNR ≥ 0 to 3 dB.

For practice, the particular clinical goals will determine the scope for technical sophistications such as pressure compensation or data subset selection, when deciding on further testing or referral. For example, if ruling out binaural cochlear loss is the overarching aim, the role for compensation would depend on the family's likelihood of later attendance (when Eustachian tube dysfunction might have resolved). Where not likely, immediate pressure compensation may play a useful role. If the estimate in Figure 1 of the slope of the

prototypic pass/fail cumulative probability generalizes, then a 3 dB compensation effect would shift the pass rate, hence the number of retests or referrals by about $4 \times 3 = 12\%$. This is a preliminary figure and would require a larger sample to estimate accurately. It is also only one component of the (smaller) gain to be seen on the total caseload because it applies only to those with NMEP problems. Thus, pressure compensation in DPOAE exists, but it may be insufficiently large to recommend routinely. The implication seems to be that in the absence of a qualifying response in DPOAE in a case with NMEP, selective pressurization could still be used conditionally for reducing false positives in hearing screening, although it will not handle every case of conductive loss.

Study Limitations and Future Recommendations

The obvious limitation to the studies was absence of a soundproof booth and hence suboptimal noise levels, entailing some discard of potential participants especially in Study 1, and contributing to the low-frequency noise and hence SNR parameter strength in Study 2. This was shown, and for interpretation was overcome, by showing coherence of results across designed conditions and by focussing on data with higher SNR. The ear probe calibration was done using traditional methods and not the currently recommended depth calibration with removal of standing wave effects. The latter could influence DPA and hence SNR variability in the higher frequencies. No studies in this largely experimental literature have used samples large enough to generalizably or precisely project the health-care system gain from technical improvements in OAEs, for example, via prevalences of tympanogram types and their degrees of compensability. The present sample sizes were adequate to demonstrate basic phenomena such as compensation gain for DPOAE and to assist design of such larger studies, as needed to project system improvement. In the analyses with binaurally qualifying participants, it was shown that being able to consider the two ears as replicates greatly improved statistical power by comparison with having to take the variation across individuals as the estimate of error. Given the linearity of the SNR function in Figure 1, this translates into an effective improvement in SNR. The need to assess individual ears in clinical practice limits the immediate practical gain from doing this on a binaural bases. But in a field where many studies remain to be done (such as comparing the general importance of pressure match and optimum relative level of primaries), the demonstration of the power gain from having replicates in each cell defining the conditions of interest is salutary. Other bases for repeated-measures designs could be randomly sampled replicate

measurement or seeking generalization across fixed experimental conditions not expected to differ. Whether for research or clinical work, a future improvement in DPOAE testing strategy would be the allocation of testing time to such replicate runs at the more responsive higher frequencies of primaries, rather than covering the full frequency range. Finally, although the number of participants that would pass at criterion SNR (or DPA) is a proxy for screen sensitivity in application, it is a fairly crude one. For a single technique with a single receiver operating characteristic, a demonstration of improved specificity might prompt fears of inevitably degraded sensitivity; such fears are unnecessary here because the addition of a technique represents a jump to a different, more favorable receiver operating characteristic not a slide along a single one. Nevertheless, there is a need for larger scale data estimating screen sensitivity and specificity more precisely.

Conclusions

MEP has a moderate to large effect on recorded TEOAEs, so having pressure compensation available for NMEP is in general worthwhile for obtaining reliable inner-ear responses with TEOAE. In contrast, the DPOAE is less influenced by natural variations in pressure, and compliance, or by compensation. However, with suitable analysis in qualifying cases, a general gain of about 2 to 3 dB in SNR is found from compensation of NMEP for DPOAE—small but nontrivial. This can be increased if further case restriction is introduced by censoring, according to baseline compliance or targeting the marginal SNR range. Until the exact clinical scope for pressure compensation with DPOAE has been determined in larger studies which stratify the caseload including case-type frequency projections, the clinical goal of saving “false-positives” in the form of retesting or unnecessary onward referrals of children would be better served by the use of TEOAE, with pressure compensation where available.

Authors' Note

S. A. F and M. P. H. designed the methodology and statistical strategy, interpreted results and implications, and prepared the manuscript. Data were collected by S. A. F. Statistical analyses were done by H. S. and G. T.

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References

- Abdala, C., Keefe, D., & Oba, S. (2007). Distortion product otoacoustic emission suppression tuning and acoustic admittance in human infants: Birth through 6 months. *The Journal of the Acoustical Society of America*, *121*(6), 3617–3627. doi:10.1121/1.2734481
- Amedee, R. (1995). The effects of chronic otitis media with effusion on the measurement of transiently evoked otoacoustic emissions. *The Laryngoscope*, *105*(6), 589–595. doi:10.1288/00005537-199506000-00006
- Bess, F., & Humes, L. (2003). *Audiology: The fundamentals* (3rd ed.). Philadelphia, PA: Lippincott Williams & Wilkins.
- Brass, D., & Kemp, D. (1994). Quantitative assessment of methods for the detection of otoacoustic emissions. *Ear and Hearing*, *15*(5), 378–389. doi:10.1097/00003446-199410000-00005
- Bray, P. (1989). *A study of the properties of click-evoked otoacoustic emissions and development of a clinical otoacoustic hearing test instrument* (PhD thesis). University of London, London, UK.
- Brown, A., & Gaskill, S. (1990). Measurement of acoustic distortion reveals underlying similarities between human and rodent mechanical responses. *The Journal of the Acoustical Society of America*, *88*(2), 840–849. doi:10.1121/1.399733
- Fiellau-Nikolajsen, M., & Lous, J. (1979). Prospective tympanometry in 3-year-old children: A study of the spontaneous course of tympanometry types in a nonselected population. *Archives of Otolaryngology—Head and Neck Surgery*, *105*(8), 461–466. doi:10.1001/archotol.1979.00790200023005
- Gaffney, M., Green, D., & Gaffney, C. (2010). Newborn hearing screening and follow-up: Are children receiving recommended services? *Public Health Reports*, *125*(2), 199–207. doi:10.1177/003335491012500208
- Gorga, M., Neely, S., Dierking, D., Kopun, J., Jolkowski, K., Groenenboom, K., . . . Stiegemann, B. (2007). Low-frequency and high-frequency cochlear nonlinearity in humans. *The Journal of the Acoustical Society of America*, *122*(3), 1671–1680. doi:10.1121/1.2751265
- Hof, J., Anteunis, L., Chenault, M., & van Dijk, P. (2005). Otoacoustic emissions at compensated middle ear pressure in children. *International Journal of Audiology*, *44*(6), 317–320. doi:10.1080/14992020500057822
- Hof, J., de Kleine, E., Avan, P., Anteunis, L., Koopmans, P., & van Dijk, P. (2012). Compensating for deviant middle ear pressure in otoacoustic emission measurements, data, and comparison to a middle ear model. *Otology & Neurotology*, *33*(4), 504–511. doi:10.1097/mao.0b013e3182536d9f

- Hof, J., Dijk, P., Chenault, M., & Anteunis, L. (2005). A two-step scenario for hearing assessment with otoacoustic emissions at compensated middle ear pressure (in children 1–7 years old). *International Journal of Pediatric Otorhinolaryngology*, *69*(5), 649–655. doi:10.1016/j.ijporl.2004.12.010
- Karić, A., Djoković, S., Dimić, N., Slavnić, S., & Savić, R. (2016). The influence of pressure compensation in the middle ear on the detection of distortion product otoacoustic emissions. *Specijalna Edukacija i Rehabilitacija*, *15*(1), 43–62. doi:10.5937/specedreh15-10090
- Keefe, D., Bulen, J., Arehart, K., & Burns, E. (1993). Ear-canal impedance and reflection coefficient in human infants and adults. *The Journal of the Acoustical Society of America*, *94*(5), 2617–2638. doi:10.1121/1.407347
- Kemp, D. (1978). Stimulated acoustic emissions from within the human auditory system. *Journal of the Acoustical Society of America*, *64*(5), 1386–1391. doi:10.1121/1.382104
- Kemp, D., Ryan, S., & Bray, P. (1990). A guide to the effective use of otoacoustic emissions. *Ear and Hearing*, *11*(2), 93–105. doi:10.1097/00003446-199004000-00004
- Kennedy, C. (2000). Neonatal screening for hearing impairment. *Archives of Disease in Childhood*, *83*(5), 377–383. doi:10.1136/ad.83.5.377
- Kummer, P., Janssen, T., & Arnold, W. (1998). The level and growth behaviour of the 2f₁–f₂ distortion product otoacoustic emission and its relationship to auditory sensitivity in normal hearing and cochlear hearing loss. *The Journal of the Acoustical Society of America*, *103*(6), 3431–3444. doi:10.1121/1.423054
- Kummer, P., Schuster, E., Rosanowski, F., Eysholdt, U., & Lohscheller, J. (2006). The influence of conductive hearing loss on DPOAE-threshold. The effect of an individually optimized stimulation. *HNO*, *54*(6), 457–467. doi:10.1007/s00106-005-1341-z
- Lieberthal, A. S., Carroll, A. E., Chonmaitree, T., Ganiats, T. G., Hoberman, A., Jackson, M. A., ... Schwartz, R. H. (2013). Clinical practice guideline: The diagnosis and management of acute otitis media. *Pediatrics*, *131*(3), e964–e999. doi:10.1542/peds.2013-3791
- Marcum, S., Kummer, P., Kreitmayer, C., & Steffens, T. (2016). Average optimal DPOAE primary tone levels in normal-hearing adults. *International Journal of Audiology*, *55*(6), 325–332. doi:10.3109/14992027.2016.1143979
- Marshall, L., Heller, L., & Westhusin, L. (1997). Effect of negative middle-ear pressure on transient-evoked otoacoustic emissions. *Ear and Hearing*, *18*(3), 218–226. doi:10.1097/00003446-199706000-00005
- Multi-centre Otitis Media Study Group. Air-conduction estimated from tympanometry (ACET) 1: Relationship to measured hearing in OME. *International Journal of Pediatric Otorhinolaryngology*, *73*(1), 21–42. doi:10.1016/j.ijporl.2008.09.014
- Naeve, S., Margolis, R., Levine, S., & Fournier, E. (1992). Effect of ear-canal air pressure on evoked otoacoustic emissions. *The Journal of the Acoustical Society of America*, *91*(4), 2091–2095. doi:10.1121/1.403695
- Naghbolhosseini, M., & Long, G. (2016). Estimation of round-trip outer-middle ear gain using DPOAEs. *Journal of the Association for Research in Otolaryngology*, *18*(1), 121–138. doi:10.1007/s10162-016-0592-6
- Neely, S., Johnson, T., & Gorga, M. (2005). Distortion-product otoacoustic emission measured with continuously varying stimulus level. *The Journal of the Acoustical Society of America*, *117*(3), 1248–1259. doi:10.1121/1.1853253
- Okabe, K., Tanaka, S., Hamada, H., Miura, T., & Funai, H. (1988). Acoustic impedance measurement on normal ears of children. *Journal of the Acoustical Society of Japan (E)*, *9*(6), 287–294. doi:10.1250/ast.9.287
- Park, S., Park, K., Park, S., Jeon, E., Chang, K., & Yeo, S. (2007). Clinical and biochemical factors that affect DPOAE expressions in children with middle ear effusion. *Otolaryngology—Head and Neck Surgery*, *136*(1), 23–26. doi:10.1016/j.otohns.2006.08.011
- Puria, S. (2003). Measurements of human middle ear forward and reverse acoustics: Implications for otoacoustic emissions. *The Journal of the Acoustical Society of America*, *113*(5), 2773–2789. doi:10.1121/1.1564018
- Rosenfeld, R., Schwartz, S., Pynnonen, M., Tunkel, D., Hussey, H., Fichera, J., ... Haynes, D. S. (2013). Clinical practice guideline: Tympanostomy tubes in children. *Otolaryngology—Head and Neck Surgery*, *149*(1_suppl), S1–S35. doi:10.1177/0194599813487302
- Rosenfeld, R., Shin, J., Schwartz, S., Coggins, R., Gagnon, L., Hackell, J., ... Poe, D. S. (2016). Clinical practice guideline: Otitis media with effusion (update). *Otolaryngology—Head and Neck Surgery*, *154*(1_suppl), S1–S41. doi:10.1177/0194599815623467
- Shera, C., & Guinan, J. (1999). Evoked otoacoustic emissions arise by two fundamentally different mechanisms: A taxonomy for mammalian OAEs. *The Journal of the Acoustical Society of America*, *105*(2), 782–798. doi:10.1121/1.426948
- Sun, X., & Shaver, M. (2009). Effects of negative middle ear pressure on distortion product otoacoustic emissions and application of a compensation procedure in humans. *Ear and Hearing*, *30*(2), 191–202. doi:10.1097/aud.0b013e31819769e1
- Thompson, S., Henin, S., & Long, G. (2015). Negative middle ear pressure and composite and component distortion product otoacoustic emissions. *Ear and Hearing*, *36*(6), 695–704. doi:10.1097/aud.0000000000000185
- Thompson, S., Long, G., & Henin, S. (2013). Total and component distortion product otoacoustic emission analysis in persons with induced negative middle ear pressure. *The Journal of the Acoustical Society of America*, *133*(5), 3425–3425. doi:10.1121/1.4806014
- Topolska, M., Hassman, E., & Baczek, M. (2000). The effects of chronic otitis media with effusion on the measurement of distortion products of otoacoustic emissions: Presurgical and postsurgical examination. *Clinical Otolaryngology*, *25*(4), 315–320. doi:10.1046/j.1365-2273.2000.00377.x
- Trine, M., Hirsch, J., & Margolis, R. (1993). The effect of middle ear pressure on transient evoked otoacoustic

- emissions. *Ear and Hearing*, 14(6), 401–407. doi:10.1097/00003446-199312000-00005
- Ueda, H., Nakata, S., & Hoshino, M. (1998). Effects of effusion in the middle ear and perforation of the tympanic membrane on otoacoustic emissions in guinea pigs. *Hearing Research*, 122(1–2), 41–46. doi:10.1016/s0378-5955(98)00084-7
- Vos, B., Lagasse, R., & Levêque, A. (2014). Main outcomes of a newborn hearing screening program in Belgium over six years. *International Journal of Pediatric Otorhinolaryngology*, 78(9), 1496–1502. doi:10.1016/j.ijporl.2014.06.019
- Whitehead, M., McCoy, M., Lonsbury-Martin, B., & Martin, G. (1995). Dependence of distortion-product otoacoustic emissions on primary levels in normal and impaired ears. I. Effects of decreasing L2 below L1. *The Journal of the Acoustical Society of America*, 97(4), 2346–2358. doi:10.1121/1.411959
- Zebian, M., Schirkonyer, V., Hensel, J., Vollbort, S., Fedtke, T., & Janssen, T. (2013). Distortion product otoacoustic emissions upon ear canal pressurization. *The Journal of the Acoustical Society of America*, 133(4), EL331–EL337. doi:10.1121/1.4795290