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Do "Optimal" Conditions Improve Distortion Product Otoacoustic Emission Test Performance?

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Abstract

Objectives—To determine whether an "optimal" DPOAE protocol including (1) optimal stimulus levels and primary-frequency ratios for each f_2, (2) simultaneously measuring $2f_2$-f_1 and $2f_1$-f_2 distortion products, (3) controlling source contribution, (4) implementing improved calibration techniques, (5) accounting for the influence of middle-ear reflectance, and (6) applying multivariate analyses to DPOAE data results in improved accuracy in differentiating between normal-hearing and hearing-impaired ears, compared to a standard clinical protocol.

Design—Data were collected for f_2 frequencies ranging from 0.75 to 8 kHz in 28 normal-hearing and 78 hearing-impaired subjects. The protocol included a control condition incorporating standard stimulus levels and primary-frequency ratios calibrated with a standard sound pressure level (SPL) method and three experimental conditions using optimized stimuli calibrated with an alternative forward pressure level (FPL) method. The experimental conditions differed with respect to the level of the reflection-source suppressor tone, and included conditions referred to as the null-suppressor (i.e., no suppressor tone presented), low-level suppressor (i.e., suppressor tone presented at 58 dB SPL), and high-level suppressor (i.e., suppressor tone presented at 68 dB SPL) conditions. The area under receiver operating characteristic (A_{ROC}) curves and sensitivities for fixed specificities (and vice versa) were estimated to evaluate test performance in each condition.

Results—A_{ROC} analyses indicated (1) improved test performance in all conditions using multivariate analyses, (2) improved performance in the null-suppressor and low-suppressor experimental conditions compared to the control condition, and (3) poorer performance below 4 kHz with the high-level suppressor. As expected from A_{ROC}, sensitivities for fixed specificities and specificities for fixed sensitivities were highest for the null-suppressor and low-suppressor conditions and lowest for standard clinical procedures. The influence of $2f_2$-f_1 and reflectance on test performance was negligible.

Conclusions—Predictions of auditory status based on DPOAE measurements in clinical protocols may be improved by the inclusion of (1) optimized stimuli, (2) alternative calibration techniques, (3) low-level suppressors, and (4) multivariate analyses.

INTRODUCTION

The utility of distortion product otoacoustic emissions (DPOAEs) in the objective assessment of cochlear function in humans has been described in many studies (*e.g.*, Nelson and Kimberly, 1992; Gorga *et al.* 1993, 1997; Lonsbury-Martin *et al.*, 1993; Kim *et al.*,

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1996). Peripheral hearing loss caused by damage to the outer hair cells of the cochlea is known to result in a reduction in otoacoustic emissions (Brownell, 1990; Martin *et al.*, 1990). Standard DPOAE protocols accurately differentiate between normal-hearing and hearing-impaired ears at audiometric frequencies from 2 to 6 kHz, and are often used in universal newborn hearing screening (UNHS) programs for this purpose. Unfortunately, DPOAE performance is not perfect in that some ears with normal hearing are misdiagnosed as hearing-impaired while some ears with hearing loss are incorrectly diagnosed as normal-hearing (*e.g.*, Gorga *et al.*, 1993, 1997; Kim *et al.*, 1996). Performance is even worse for frequencies between 0.75 and 1.5 kHz and at 8 kHz.

Several strategies have been used in attempts to improve the sensitivity and specificity of DPOAE measures at all test frequencies. For example, the earliest descriptions of DPOAE test performance used equal-level primaries ($L_1 = L_2$) to elicit the response (Martin *et al.*, 1990). Recognizing that the representation of the two primaries (f_1 and f_2) differ at the place(s) of generation of distortion products (presumably close to the f_2 place), later efforts used unequal primary levels, with L_1 higher than L_2 (Gorga *et al.*, 1993, 1997). Several studies showed that moderate stimulus levels result in better differentiation of normal-hearing and hearing-impaired ears. This occurs because low-level primaries do not elicit responses from all normal-hearing ears (resulting in an increase in false-positive errors) and high-level primaries may increase the likelihood of producing emissions from ears that are hearing-impaired (increasing the false-negative rate) (Whitehead *et al.* 1995; Stover *et al.*, 1996; Johnson *et al.*, 2010). Moderate-level stimuli appear to reduce both the false-positive and false-negative errors.

Kummer *et al.* (1998) developed an approach for setting primary levels that recognized the compressive growth of the response to f_2 close to the f_2 place, which differed from the response to f_1 at the same place. They advocated the use of a primary-level relationship that took this differential growth into account, and proposed an alternative approach in which $L_1 = 0.4\ L_2 + 39$ dB independent of f_2 (Kummer *et al.*, 1998; 2000). In many respects, this recommendation is similar to previous descriptions of "optimal" primary levels based on data from animal studies (Whitehead *et al.* 1992). Recently, Neely *et al.* (2005) found that the primary-level difference that produced the largest response in normal-hearing ears was frequency dependent, in that larger differences in L_1 and L_2 resulted in larger DPOAEs at higher frequencies. Johnson *et al.*, (2006a) described effects for both primary levels and primary-frequency ratios, deriving formulas for ideal primary level [$L_1 = 80 + 0.137 \cdot \log_2(18/f_2) \times (L_2 - 80)$] and frequency ratio [$f_2/f_1 = 1.22 + \log_2(9.6/f_2) \times (L_2/415)^2$] which took frequency into account. The stimuli described by these equations resulted in larger DPOAE levels in normal-hearing subjects than those observed using the primary levels described by Kummer *et al.* Somewhat surprisingly, Johnson *et al.* (2010) found no improvement in test performance when these "optimal" primary-frequency ratios and primary-level differences were used in a group of normal-hearing and hearing-impaired subjects. Although the reason for the lack of improvement was not obvious, it was speculated that the optimal conditions caused an increase in DPOAE level for both normal and impaired ears (at least at some frequencies), resulting in no net increase in the separation of the distribution of responses from the two groups of subjects.

Another factor potentially affecting DPOAE test performance relates to source contribution. DPOAEs, as measured at the plane of the probe tip in the ear canal, arise primarily from the interaction of two sources: the distortion source, located near the f_2 place and thought to be the main generator, and the coherent-reflection source resulting from a linear reflection from the characteristic place for the DPOAE frequency along the basilar membrane (*e.g.*, Heitmann *et al.*, 1998; Shera and Guinan, 1999). The phase relationship of the two emission sources varies as a function of frequency, resulting in a pattern of constructive and destructive interference known as "fine-structure" which can be observed in plots of DPOAE level as a function of frequency, especially when frequency is incremented in small steps (Talmadge *et al.*, 1999). This interaction between distortion and reflection sources may cause changes in measured DPOAE level that affect test performance. Specifically, destructive interaction might result in a reduction in DPOAE level in a normal ear, causing it to be misdiagnosed as hearing impaired, while constructive interaction might increase the magnitude of the measured response in an ear with (mild or moderate) hearing loss, resulting in a diagnosis of normal hearing. Fine structure is reduced when a suppressor tone, f_3, with a frequency slightly lower than that of the $2f_1$-f_2 frequency, is presented simultaneously with the primaries (Heitmann et al, 1998; Talmadge *et al.* 1999). However, Johnson *et al.* (2007), using stimulus conditions that reduce fine structure based on work in subjects with normal hearing (Johnson *et al.* 2006b), failed to demonstrate an improvement in test performance when a suppressor tone was presented, compared to the performance achieved when there was no suppressor tone.

Poorer DPOAE test performance, especially for lower frequencies, might relate to the distortion product that typically is measured during clinical assessments. The $2f_1$-f_2 DPOAE emission is measured to predict auditory status, as it is typically the highest level distortion product in humans. However, the $2f_1$-f_2 emission occurs at a frequency approximately ½ octave below f_2, where the noise floor surrounding the emission may be higher (*e.g.*, Gorga *et al.* 1993). The poor signal-to-noise ratio (SNR) might make it more difficult to measure responses in ears with normal hearing, thus driving up the false-positive rate. There are other distortion products produced as a result of the presentation of two primaries, one of which occurs at a frequency that is about ½ octave above f_1 (namely $2f_2$-f_1) where noise levels typically are lower. There has been some interest in using both the $2f_2$-f_1 and $2f_1$-f_2 emissions to determine auditory status (Gorga *et al.*, 2000; Fitzgerald and Prieve, 2005); however, the results from these two studies differ. In one case, multivariate analyses incorporating both emissions resulted in slight improvements in DPOAE test performance (Gorga *et al.* 2000), although in the other case, no significant improvement in test performance was observed when the levels of the two emissions were combined or with the application of logistic regression analysis (Fitzgerald and Prieve, 2005).

Stimulus calibration prior to DPOAE measurements also might influence DPOAE test performance. Typically, stimulus sound pressure level (SPL) is measured at the plane of the probe, and is assumed to represent the level of the stimulus at the eardrum. However, standing waves introduce errors in SPL calibrations at and above 3 kHz (Siegel, 1994; Siegel and Hirohata, 1994; Neely and Gorga, 1998, Dreisbach and Siegel, 2001; Scheperle *et al.*, 2008). Thus, the level at the eardrum may be higher than the level at the probe or (less frequently) the level at the eardrum might be lower than the level estimated at the plane of the probe. Given the influences of stimulus level on test performance (Whitehead *et al.*, 1992; Stover *et al.*, 1996; Johnson *et al.* 2010), calibration errors might affect the accuracy with which auditory status is determined from DPOAE measurements. Several alternative calibration methods have been described that are unaffected by standing waves (Neely and Gorga, 1998; Scheperle *et al.*, 2009), and thus might result in improvements in DPOAE test performance. Burke *et al.* (2010) showed that using alternative calibration methods that are not susceptible to standing-wave errors (*e.g.* forward pressure level, FPL) can improve DPOAE test performance, but the effect was restricted to 8 kHz, where test performance was poorest when stimuli were calibrated in SPL. At lower frequencies, differences were observed related to calibration procedure, but the effects were small and not always as predicted.

Middle-ear transfer of energy may have an influence on the accuracy with which auditory status is predicted from DPOAE measurements. The true input level of the primaries at the plane of the tympanic membrane and the level of the emission as recorded at the plane of the probe microphone depend on the forward and reverse transmission characteristics of the middle ear (Keefe *et al.*, 2000). Keefe *et al.* (2003) described the relationship between high-frequency (2–8 kHz) reflectance properties of the ear and the level of recorded emissions in neonates. They found that a significant percentage of the variance in OAE levels (up to 28%) could be accounted for by middle-ear transmission characteristics, with OAE levels decreasing with increasing high-frequency energy reflectance. Evidence suggests that the typically greater DPOAE levels observed in infants arise from differences in ear-canal area which affect reverse middle-ear transmittance properties (Keefe and Abdala, 2007). Sanford *et al.* (2009) observed greater reflectance in neonatal ears that failed a DPOAE-based UNHS test, compared to infants who passed the same test. Given that reflectance can be measured at atmospheric pressure using the same probe assembly that is used to measure OAEs (Sanford *et al.*, 2009), it might be advantageous to use reflectance measures to assist in the classification of cochlear status based on DPOAE measurements. To date, however, there are no studies on test performance in children and adults that incorporate measures of middle-ear energy reflectance with DPOAE measurements.

Finally, test performance may be affected by the approach that is taken to analyze DPOAE data. Typically, predictions of auditory status are based on simple univariate procedures, in which either DPOAE level (L_d) or SNR at $2f_1$-f_2 is used to determine cochlear status. Multivariate analyses, which incorporate several factors as decision variables in classifying ears as either normal hearing or hearing impaired, have been shown to result in improvements in test performance, especially for frequencies at which univariate analyses result in poor performance (Dorn *et al.*, 1999; Gorga *et al.*, 1999, 2005). Although relatively simple to implement, it remains the case that multivariate analyses have not been incorporated into clinical assessments. One possible factor contributing to this may relate to the idiosyncratic nature of multivariate solutions. Further studies to validate the approach, therefore, may be needed prior to their acceptance in the clinic.

The purpose of the present study is to combine several techniques that have been used in efforts to improve DPOAE test performance. Specifically, DPOAE data were collected with "optimal" primary-level and primary-frequency ratios, using calibration procedures unaffected by standing waves, measuring two DPOAEs simultaneously, controlling for source contribution, and incorporating measurements of middle-ear reflectance, all of which were combined in a multivariate analytical framework. The test performance achieved under these conditions was compared to the results achieved when traditional stimulus conditions were used, only one DPOAE was measured, and data were analyzed with a univariate or a multivariate approach. The hypothesis is that measurements and analyses using several factors will result in improved test performance compared to what is achieved with simpler conditions in common clinical use.

METHODS

Instrumentation

An ER-10C probe microphone (Etymōtic Research, Elk Grove Village, IL) was used for presentation of stimuli, calibration, and recording of responses. Stimuli were generated with a 24-bit sound card (CardDeluxe, Digital Audio Labs, Chanhassen, MN) at a 32-kHz sampling rate. A custom-software system (EMAV Version 3.07; Neely and Liu, 1994) was used to (1) calibrate the probe source, (2) present stimuli (including primary and suppressor stimuli), (3) measure DPOAEs, and (4) measure reflectance of the ear.

Calibration

For the control condition, calibration was completed in the ear canal, using a standard sound pressure level (SPL) method and wideband chirp stimulus. The experimental conditions implemented an FPL technique to estimate the Thévenin source acoustic properties of the probe microphone and, in turn, isolate the incident from reflected components of the calibration signal pressure wave (Neely and Gorga, 1998; Scheperle *et al.*, 2008). FPL calibration was performed daily using cavities (acoustic loads) warmed to approximate body temperature (95–105°F) and with resonant peaks occurring at approximately 2, 3, 4, 6 and 8 kHz (Burke *et al.*, 2010).

Subjects

Data were collected from 28 normal-hearing and 78 hearing-impaired subjects ranging in age from 11 to 75 years. Whenever possible, data were collected from both ears of each subject, resulting in data from 147 ears with hearing loss and 51 ears with normal hearing. Audiometric thresholds were obtained by conventional audiometry, in 5-dB increments, using either insert (ER-3A) or supra-aural (TDH-50P) headphones. Normal hearing was defined as audiometric thresholds ≤ 20 dB HL (ANSI, 2004) for frequencies of 0.75, 1, 1.5, 2, 3, 4, 6, and 8 kHz, while hearing loss was defined as thresholds exceeding this level at one or more of those frequencies. Only hearing-impaired subjects with confirmed sensorineural hearing loss, defined as having air-bone gaps of < 15 dB for frequencies 0.5, 1.0, 2.0, and 4.0 kHz, were eligible for inclusion. During data analyses, the assignment to hearing category (normal or impaired) was made on a frequency-by-frequency basis. The distribution of ears across hearing-loss categories is provided in Table 1.

Prior to DPOAE data collection, middle-ear status was assessed using tympanometry with a 226-Hz probe tone. In order to qualify for inclusion, the following tympanometric criteria had to be met: peak-compensated, static acoustic admittance of 0.3–2.5 mmho and tympanometric peak pressure between −100 to +50 daPa. Otoscopic examination also was completed as a way to further assess ear-canal and middle-ear status. Subjects were seated in a comfortable reclining chair in a sound-attenuating booth, and were allowed to watch closed-captioned videos with the sound turned off. The work described in this paper was conducted under an approved Institutional Review Board protocol. Following the acquisition of informed consent, audiometric, tympanometric and otoscopic assessments, data collection commenced, which required approximately 40 minutes per ear.

Procedures

The protocol consisted of a control condition and three experimental conditions. In the control condition, DPOAEs were measured at octave and interoctave frequencies from 0.75 to 8 kHz with L_2 = 50 dB SPL, L_1 = 59 dB SPL, and the f_2/f_1 fixed at 1.22. The primary-frequency ratio was chosen based on previous work (*e.g.*, Gaskill and Brown, 1990) and was the same for all test frequencies, while L_1 was set according to the formula described by Kummer *et al.* (1998). In the experimental conditions, L_2 was also set to 50 dB SPL and L_1 was determined for the same frequencies that were tested under the standard protocol using a modified version of the formula derived by Johnson *et al.*, 2006a:

$$L_1 = 80 + 0.1 \cdot \log_2(64/f_2) \cdot (L_2 - 80)$$

The f_2/f_1 was determined for those same frequencies also using a formula derived by Johnson *et al.*, 2006a:

$$f_2/f_1 = 1.22 + \log_2(9.6/f_2) \cdot (L_2/415)^2$$

These stimulus conditions were chosen because they have been found to result in the largest DPOAEs for subjects with normal hearing (Neely *et al.*, 2005; Johnson *et al.*, 2006a). Two of the three experimental conditions included simultaneous presentation of a suppressor tone 16 Hz lower than the $2f_1$-f_2 distortion-product frequency. Suppressor levels of 58 and 68 dB SPL were selected to bracket the range shown to reduce fine structure and, therefore, presumably reduce contributions from the reflection source (Johnson *et al.*, 2006b). Though Johnson *et al.* (2007) demonstrated no improvements in DPOAE test performance with simultaneous suppression, experimental suppressor conditions were included in the present study to determine possible interaction effects with other factors, such as calibration method. Simultaneous measurement of the $2f_1$-f_2 and $2f_2$-f_1 distortion products and ear-canal reflectance at f_1 and f_2 were obtained in all conditions, although the contribution of these variables was only considered in the analysis of the experimental conditions.

During data collection for each frequency and condition, DPOAE data were alternately stored in two separate buffers. The level of the DPOAE, L_d, was estimated from the level in the frequency bin containing the emissions of interest, namely $2f_1$-f_2 or $2f_2$-f_1, after summing the contents of the two buffers. Frequency resolution for each bin was approximately 4 Hz. Estimates of the noise floor were derived by subtracting the contents of the two buffers and then using the bin containing the DPOAE and the two closest frequency bins above and below it, for a total of five bins. Measurement-based stopping criteria were used during data collection such that measurements terminated for any condition when (1) the noise floor ≤ −25 dB SPL, (2) the SNR exceeded 60 dB, or (3) 32 seconds of artifact-free averaging passed. These rules were chosen so that the test never stopped on SNR, stopped mainly on the noise-floor criterion (for higher f_2 frequencies), but also stopped on averaging time (for lower f_2 frequencies). Test time could have been extended so that all measurement stopped when the noise-floor criterion was met. However, this would have resulted in excessive test time for some subjects and some conditions, and would not be representative of test conditions that could be used clinically.

Analysis

Multivariate logistic-regression analyses were used to describe the relative contribution of the experimental variables to the distribution of responses from normal-hearing and hearing-impaired ears. These analyses produced a logit function (LF) for each audiometric frequency and were completed independently for each experimental condition. LF coefficients for those variables which contributed positively to DPOAE test performance in the null experimental condition are listed in Table 2. In the control condition, LF coefficients derived from previous work (Dorn *et al.* 1999; Gorga *et al.* 2005) were applied to the DPOAE data.

Receiver operating characteristic (ROC) curves were then constructed for the control and experimental conditions and area under these curves (A_{ROC}) was estimated to evaluate test performance. In addition, test performance was evaluated using standard univariate analyses (SNR and DPOAE level at $2f_1$-f_2). Finally, test performance was assessed by determining the sensitivity for fixed specificities and vice versa.

RESULTS

Results of the A_{ROC} analyses, shown in Fig. 1, revealed improved test performance in all conditions using the multivariate approach (compare A_{ROC} in the top panel to A_{ROC} in the two lower panels). These results are consistent with previous findings that demonstrated improved performance when multivariate analyses are applied (Dorn *et al.* 1999; Gorga *et al.*, 2005). Greater A_{ROC} values were observed below 2 and at 8 kHz in the null-suppressor (circles) and low-suppressor (upright triangles) conditions compared to the control condition (squares). This was true using DPOAE level (L_d) and SNR criteria (compare circles and upright triangles to squares in the middle and bottom panels), and the case in which multivariate analyses (LF) were applied to both data sets (compare circles and upright triangles to squares in the top panel). The fact that test performance improved in the null-suppressor and low-suppressor conditions for univariate analyses (SNR and L_d) indicates that there was an influence of calibration method (SPL vs. FPL), optimized stimuli, and low-level suppression on test performance. Little effect of low-level suppression (to reduce the reflection source) on A_{ROC} was found in comparison to the null-suppressor condition when multivariate analyses were applied. Small improvements in test performance were observed for the low-level suppressor condition, compared to the null-suppressor condition, when univariate analyses were applied, but only at low frequencies (compare circles and upright triangles in middle and bottom panels). A decline in A_{ROC} relative to the null- and low-level suppressor conditions was observed in the low frequencies when a high-level suppressor was presented (inverted triangles). Application of multivariate analyses improved the situation, but not to the same extent as it was improved for null-suppressor and low-suppressor conditions.

Figure 2 shows specificity at each audiometric frequency for fixed sensitivities of 90% (left column) and 95% (right column) for each analysis method, the results for which are shown in separate rows. As expected from previously reported data and the results shown in Fig. 1, the greatest specificity was found when using multivariate analyses, regardless of condition. Specificity was greater at 2 and 8 kHz with a fixed sensitivity of 95% in the null-suppressor and low-level suppressor conditions compared to the control condition. The differences in specificity between the null-suppressor and the low-level suppressor conditions were negligible for multivariate analyses, but the low-level suppressor condition resulted in higher specificities when univariate analyses (SNR or L_d) were used. The reasons for the improvements for these two conditions, which mostly had lower specificities compared to when multivariate analyses were used, are not obvious. Consistent with the A_{ROC} shown in Fig. 1, decreased specificity below 2 kHz was found with high-level suppression, most notably when sensitivity is fixed at 95%.

Figure 3 shows sensitivity at fixed specificities of 90% (left column) and 95% (right column) for all four test conditions following the convention used in Fig. 2. As in previous examples, the best performance (greatest sensitivity) in each condition was found using the multivariate approach. Sensitivity was greater below 2 kHz and at 8 kHz in the null-suppressor and low-level suppressor conditions compared to the standard control condition. As expected from previous results, the null-suppressor and both suppressor conditions achieved higher sensitivities for univariate conditions, compared to the control condition. These effects were not uniform across frequency, with some variability in which experimental conditions produced the highest sengsitivity, especially at 0.75 and 8 kHz. However, the highest sensitivity was achieved in the null-suppressor condition when multivariate analyses were applied to the data. Decreased sensitivity below 2 kHz was found with high-level suppression when univariate analyses were applied to the data, with the effect most notable when specificity was fixed at 95%. In contrast, both suppressor conditions resulted in higher sensitivities, compared to the null condition, when univariate analyses were applied at 8 kHz.

Figure 4 shows the influence of $2f_2\text{-}f_1$ and reflectance (R1/R2) on A_{ROC}. Note the expanded Y-axis scale, ranging from 0.96 to 0.99. This scale was necessary in order to assess the size of the effect of removing these variables from the analyses. Removing reflectance (R1/R2) from the multivariate analysis had a negligible effect. Removing $2f_2$-f_1 resulted in at most a 0.005 decrease in A_{ROC} at audiometric frequencies 1.5 and 2 kHz. Removing both reflectance estimates and data for the $2f_2$-f_1 distortion product had the largest and most consistent effect across frequency, but even then, the maximum decrease in A_{ROC} was 0.005 at 2 kHz.

DISCUSSION

The purpose of this study was to determine whether an "optimal" protocol which (1) used optimal stimulus levels and primary-frequency ratios for each f_2, (2) simultaneously measured $2f_2$-f_1 and $2f_1$-f_2 emissions, (3) controlled source contribution, (4) implemented improved calibration techniques, (5) accounted for the influence of middle-ear reflectance, and (6) applied multivariate analyses to DPOAE data resulted in improved accuracy in differentiating between normal-hearing and hearing-impaired ears, compared to a standard clinical protocol.

The results of this study confirm and extend the findings of other studies (Dorn *et al.* 1999, Gorga *et al.* 2005) regarding the superiority of multivariate analyses of DPOAE data. A_{ROC} was greatest when previously derived coefficients from a multivariate analysis were applied to the control condition or when newly derived coefficients from a logistic regression analysis were applied to the experimental conditions (Fig. 1), especially at the frequencies where standard univariate analyses of L_d or SNR at $2f_1$-f_2 show the poorest performance, specifically at 8 kHz and at 1.5 kHz and below. Although not studied in the present experiment, another factor in the poorer performance at 8 kHz for each analysis method may be the output limitations of the ER-10C transducer at this frequency.

FPL calibration and group-optimized stimulus levels, implemented in the experimental conditions, were found to increase A_{ROC} over the control condition (Fig. 1) independent of the analysis method. Our results confirmed that accurate estimates of the level of the stimulus at the plane of the probe with FPL calibration, when combined with group-optimized stimulus levels, can help to improve DPOAE test performance, although others have only found improvements at 8 kHz (Burke *et al.*, 2010). The relative contribution of either stimulus optimization or calibration method to test performance could not be determined because test conditions were not included in which these two variables were separated.

The impacts of playing a suppressor tone just below the distortion-product frequency were mixed. Mostly, the inclusion of a low-level suppressor resulted in outcomes that were close to those observed in the null-suppressor condition, but the pattern was variable. Test performance with low-level suppression was slightly better, slightly worse or the same as it was for the null-suppressor condition. These small differences were even less obvious when multivariate analyses were used. Suppressor tones have been found to reduce fine structure in recorded DPOAEs (*e.g.*, Heitmann *et al.* 1998, Johnson *et al.* 2006b). However, in agreement with the findings of Johnson *et al.* (2007), no consistent improvement in test accuracy was observed with the inclusion of a suppressor tone in the stimulus complex. It is possible that the suppressor levels used in the present study did not reduce or suppress the reflection source in some subjects. The levels that were used were chosen on the basis of previous work in an entirely different group of subjects (Johnson *et al.*, 2007). However, determining suppressor levels in individual subjects would be prohibitive and perhaps impossible during clinical applications. Given that the inclusion of a suppressor creates a more complex stimulus, perhaps it is unnecessary to include a low-level suppressor when attempting to identify ears with hearing loss. In contrast, inclusion of a high-level suppressor almost invariably reduced test accuracy, just as it did previously (Johnson *et al.*, 2007). This finding indicates that the inclusion of a high-level suppressor would be detrimental for clinical purposes.

Little or no advantage was gained by (1) measurement of middle-ear reflectance or (2) inclusion of the $2f_2$-f_1 distortion product in the multivariate analysis. A lack of significant contribution of middle-ear reflectance measurements at the two primary frequencies (Fig. 4) suggests no benefit to their inclusion in clinical DPOAE protocols. This finding is not inconsistent with the results from other studies showing the influence of middle-ear status on DPOAE test results (Keefe *et al.*, 2000, 2003; Sanford *et al.*, 2009). Those previous studies were conducted in neonates, whose middle-ear status likely differed from the status in the present group of older subjects, who were included only if there was no evidence of middle-ear dysfunction. That the addition of the $2f_2$-f_1 DPOAE in the multivariate analysis contributed little to improving test performance (Fig. 4) contradicts some previous studies (Gorga *et al.*, 2000) which showed a small effect of including both DPOAEs in the analyses. The results, however, are consistent with the findings of others (Fitzgerald and Prieve, 2005) who found no such advantage.

In summary, our findings provide evidence in favor of adopting optimized stimulus parameters, multivariate analyses, and FPL calibration in clinical DPOAE test protocols. These variables resulted in the largest improvements in test performance as assessed by A_{ROC}, specificities for fixed sensitivities, and sensitivities for fixed specificities. Support for low-level suppression in DPOAE protocols was equivocal. The inclusion of other variables had little or no impact on test performance and in some cases (high-suppressor condition) actually caused a decrease in test performance. The use of optimized stimulus parameters and multivariate analyses would result in no additional test time in the clinic and no more complicated stimulus paradigm than the one in current clinical use. However, FPL calibrations require additional efforts over current calibration procedures, due to the need to determine the Thévenin-equivalent acoustic-source properties. Even so, the additional time required for these calibrations may be warranted if they result in fewer calibration errors and better test performance when combined with optimized stimuli and multivariate analyses.

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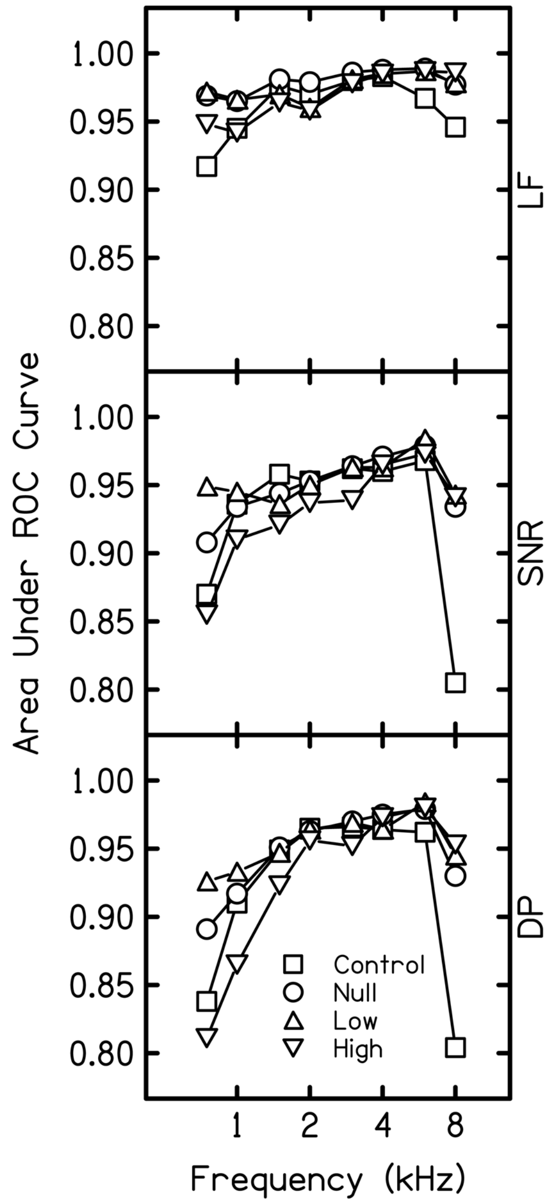

Figure 1.

A_{ROC} for control and experimental conditions. The upper panel shows A_{ROC} using multivariate logistic regression analysis (LF), the middle panel shows A_{ROC} using univariate analysis of SNR at $2f_1$-f_2 (SNR), and the bottom panel shows A_{ROC} using univariate analysis of distortion product level at $2f_1$-f_2 (DP). Squares represent results for the control condition, circles represent the null-suppressor condition, upright triangles represent the low-suppressor condition, and inverted triangles represent the high-suppressor condition.

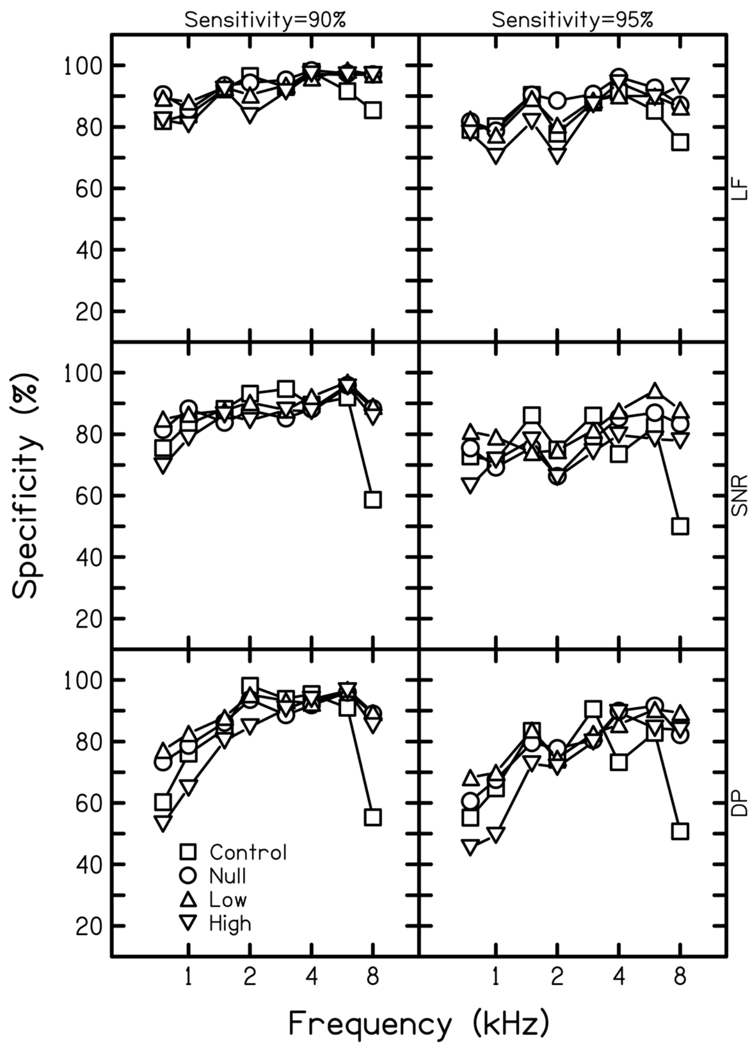

Figure 2.

Specificity at fixed sensitivities of 90% and 95% for each condition. Results using multivariate logistic regression analysis (LF) are shown in the top row, followed by univariate analysis of SNR at $2f_1$-f_2 (SNR) and univariate analysis of distortion product level at $2f_1$-f_2 (DP) methods, in descending order. Squares represent specificity for the control condition, circles represent the null-suppressor condition, upright triangles represent the low-suppressor condition, and inverted triangles represent the high-suppressor condition.

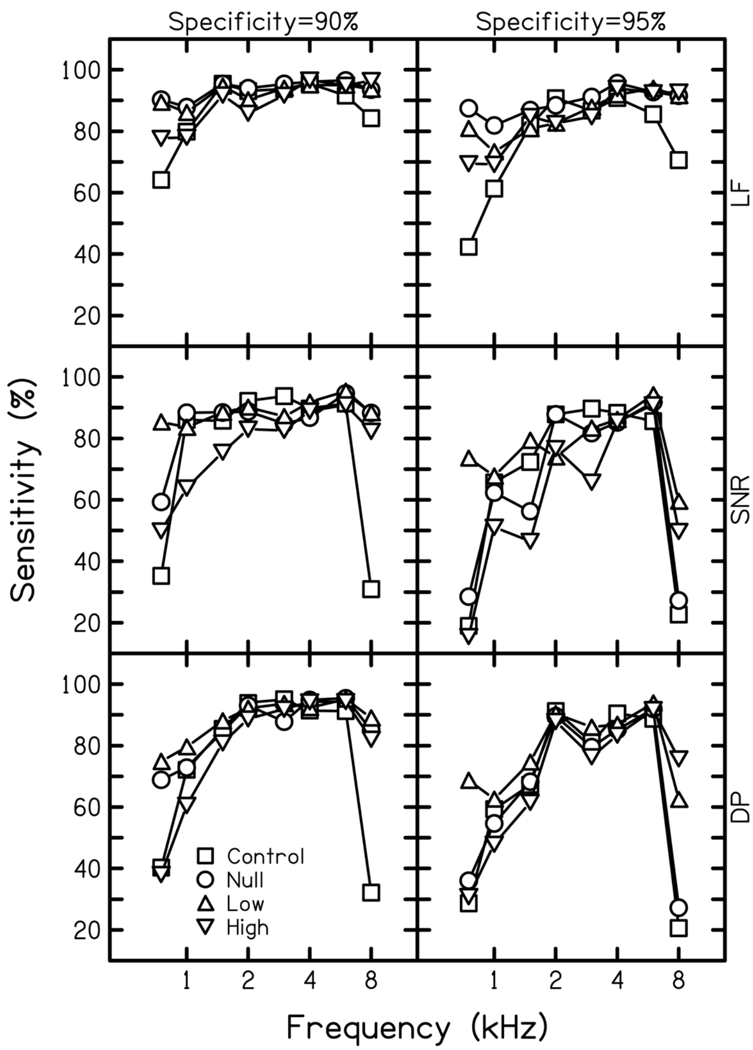

Figure 3.

Sensitivity at fixed specificities of 90% and 95% for each condition. Results using multivariate logistic regression analysis (LF) are shown in the top row, followed by univariate analysis of SNR at $2f_1$-f_2 (SNR) and univariate analysis of distortion product level at $2f_1$-f_2 (DP) methods, in descending order. Squares represent sensitivity for the control condition, circles represent the null-suppressor condition, upright triangles represent the low-suppressor condition, and inverted triangles represent the high-suppressor condition.

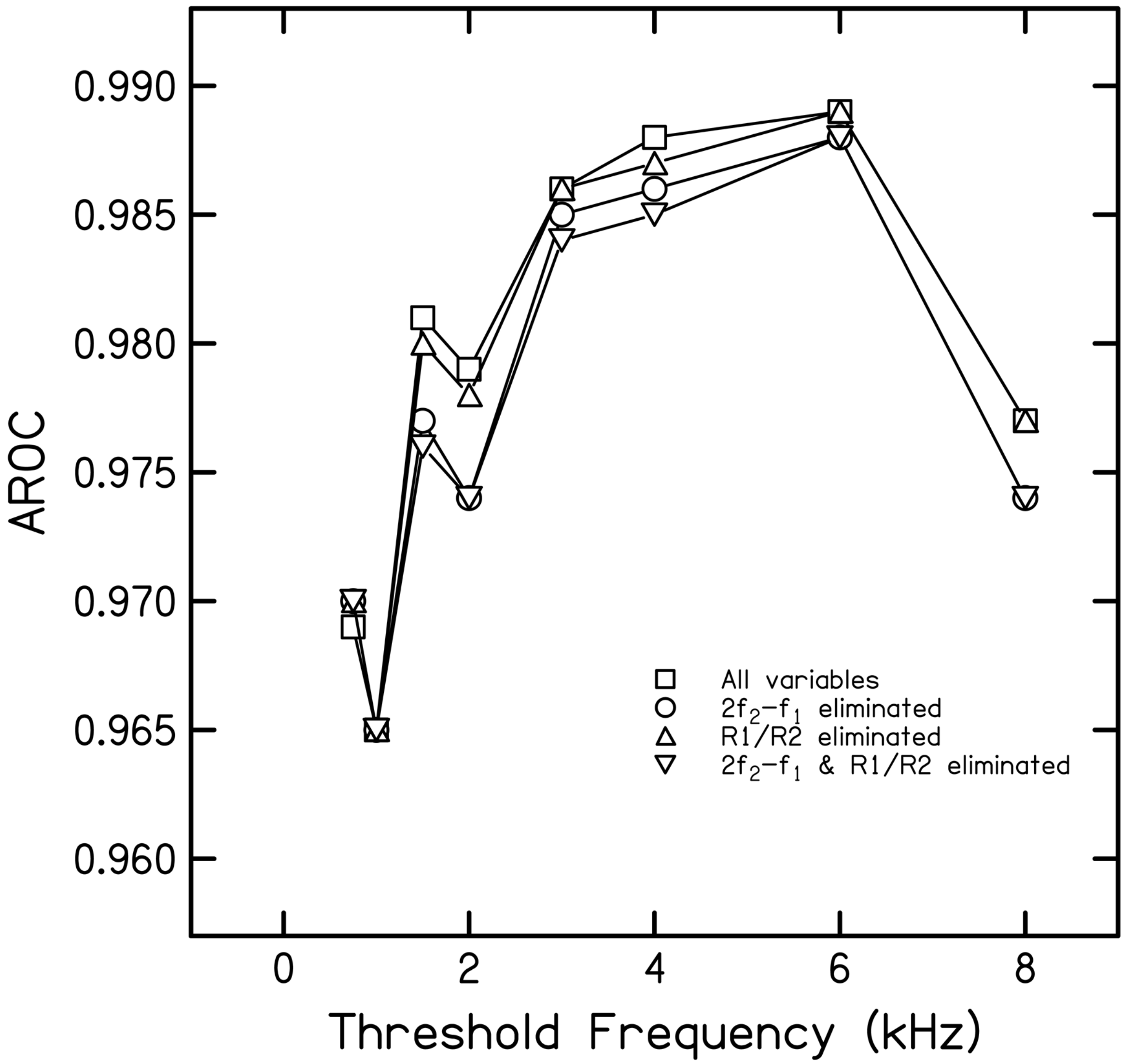

Figure 4.
Influence of $2f_2$-f_1 and reflectance (R1/R2) on A_{ROC}. Squares represent A_{ROC} with all variables included in the LF analysis, circles represent A_{ROC} with $2f_2$-f_1 eliminated from the LF analysis, upright triangles represent A_{ROC} with R1/R2 eliminated, and inverted triangles represent A_{ROC} with both $2f_2$-f_1 and R1/R2 eliminated from the LF analysis.

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Table 1

Number of ears in each hearing loss category by audiometric frequency. Normal hearing was defined as ≤20 dB HL, mild hearing loss as thresholds between 21 and 40 dB HL, moderate between 41 and 60 dB HL, severe between 61 and 80 dB HL, and profound as thresholds greater than 80 dB HL.

	Normal	Mild	Moderate	Severe	Profound
750 Hz	112	38	29	10	9
1000 Hz	112	35	31	10	10
1500 Hz	95	46	34	10	13
2000 Hz	83	43	46	12	14
3000 Hz	76	40	55	13	14
4000 Hz	70	33	56	22	17
6000 Hz	67	33	52	27	19
8000 Hz	68	29	51	32	18

Table 2

Logit function coefficients derived from multivariate analysis of experimental variables. Coefficients are listed for noise and DP level at $2f_1$-f_2 in the null-suppressor condition. Coefficients for $2f_2$-f_1 and R1/R2 are omitted.

	750	1000	1500	2000	3000	4000	6000	8000
Predictor								
Ldp750	0.112	0.086	−0.004	0.008	0.026	0.009	−0.003	0.042
Ldp1000	0.136	0.108	0.022	0.002	−0.053	−0.037	−0.055	0.031
Ldp1500	0.072	0.078	0.148	0.087	0.045	0.019	0.015	0.019
Ldp2000	0.044	0.066	0.161	0.164	0.063	0.012	0.015	−0.005
Ldp3000	−0.022	0.007	0.021	0.100	0.137	0.079	0.058	0.022
Ldp4000	−0.034	−0.029	−0.072	−0.067	0.016	0.077	0.017	0.039
Ldp6000	0.030	0.015	0.008	0.064	0.099	0.079	0.132	0.082
Ldp8000	0.089	0.057	0.118	0.051	0.069	0.062	0.167	0.117
Ndp750	−0.046	−0.035	−0.031	−0.010	0.008	0.005	0.017	0.003
Ndp1000	−0.040	−0.031	−0.027	−0.014	−0.031	−0.019	0.007	0.008
Ndp1500	−0.080	−0.052	−0.014	−0.006	−0.008	−0.004	0.018	0.005
Ndp2000	−0.057	−0.036	−0.021	−0.004	−0.014	−0.009	0.013	0.009
Ndp3000	−0.017	−0.010	−0.014	0.001	−0.006	−0.006	−0.003	−0.001
Ndp4000	−0.008	−0.006	−0.009	−0.002	0.008	0.005	0.004	0.001
Ndp6000	−0.002	−0.002	−0.003	−0.006	0.000	0.002	0.001	0.001
Ndp8000	0.000	0.000	−0.002	0.000	0.000	−0.001	−0.002	−0.002