High-frequency otoacoustic emissions in universal newborn hearing screening

Olubunmi V. Akinpelu, W. Robert J. Funnell and Sam J. Daniel

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Abstract

Objective: Distortion-product otoacoustic emissions (DPOAEs) are currently used in many newborn hearing screening programs as the initial hearing test, typically testing frequencies between 1 and 4 or 6 kHz, but they have been associated with high false-positive rates. The objective was to investigate the possible benefit of high-frequency DPOAEs for reducing false-positive rates.

Methods: 255 healthy newborns (138 males and 117 females) undergoing conventional hearing screening based on DPOAE and automated auditory brainstem response (AABR) testing were recruited. High-frequency DPOAE amplitudes, noise floors and signal-to-noise ratios (SNRs) were measured for f2 frequencies up to 12 kHz.

Results: Of the 255 newborns who participated in this study, 23 (9%) failed the conventional DPOAE test but passed the AABR test, and 8 (3%) failed both tests. For an SNR threshold of 6 dB, high-frequency DPOAE tests at f2 = 4, 6, 8 and 10 kHz resulted in a reduction in the false-positive rate from 9% to 0.4%, or to zero if only three of the four frequencies were required to exceed the threshold. SNRs were lower in newborns with birth weights greater than 4000 g; lower at 2 kHz in newborns with a gestational age of 41 weeks; slightly higher in vaginally-delivered newborns; and higher at 2 kHz with increasing age in the group that failed the conventional DPOAE test but passed AABR.

Conclusion: High-frequency DPOAEs resulted in a reduction in the DPOAE failure rate and the false-positive rate. These findings may be helpful in universal newborn hearing screening programs.

Keywords

High frequency; distortion product otoacoustic emissions; newborn; hearing screening; false positives

1. Introduction

Otoacoustic emission (OAE) testing assesses the function of the cochlear outer hair cells and is used in many newborn hearing screening programs either as the sole test or in combination with automated auditory brainstem response (AABR) testing. Newborn hearing screening with OAEs usually involves testing frequencies from 1 kHz to 4 or 6 kHz.

A major drawback of OAE testing is the associated high false-positive rates [1–3]. OAE false-positive rates have been found to range from 1.2 to 19.5 % [4]. More newborns pass the test if it is performed at later dates [5], but the logistics and cost implications of a return visit to the hospital make this problematic. Other methods that have been used to reduce these false-positive results include repeating the OAE tests before discharge, and performing the AABR test in those who fail the initial OAE test [6].

Retained mesenchyme and amniotic liquid in the middle ear in the newborn period may account for many false-positive results [7–12]. (We use the word “liquid” rather than “fluid” in this paper in order to clearly distinguish it from air, which is also a fluid.) The presence of liquid in the middle ear reduces the middle-ear volume and its compliance [13]. A reduction in middle-ear compliance has greater effects on sound transmission at low frequencies than at high frequencies [14]. Additionally, abnormal middle-ear conditions have been associated with increases in OAE noise floors [15,16], and these increases have been shown to be greater at low frequencies [17]. Therefore, high-frequency OAEs may be better detected than low-frequency OAEs in newborns with middle-ear liquid.

Repeatable high-frequency distortion-product (DP) OAEs (up to 16 kHz) have been measured in human ears [18–20]. The main aim of this study was to evaluate the usefulness of high-frequency DPOAEs in reducing false-positive outcomes associated with conventional DPOAE hearing screening tests. This involved examining OAE amplitudes and noise floors and the OAE pass/fail status at f_2 frequencies from 2 to 12 kHz for different categories of newborns.

2. Materials and methods

Ethics approval was obtained from the Institutional Review Board of the McGill University Health Centre. Newborns were recruited for inclusion on randomly selected days. Prior to testing, parents of the newborns were given written and oral explanations of the study, questions were addressed and informed consents were obtained. The tests were conducted in the normal newborn nursery of the Royal Victoria Hospital (RVH), Montréal. All newborns included were term (from 37 to 41 completed weeks). Newborns were excluded if they had a family history of hearing loss or perinatal medical conditions that could pose a risk to hearing. We excluded newborns with neonatal infections being treated with gentamicin, those with hyperbilirubinemia and those with history suggestive of birth asphyxia.

Each baby was first tested by an audiology technician with the conventional DPOAE EroScan screening device (MAICO Diagnostics, Eden Prairie, MN) used by the RVH newborn hearing screening program. The probe consisted of two primary tones, f_1 and f_2, with $f_1/f_2 = 1.22$ and with the primary levels L1 and L2 being 65 and 55 dB SPL respectively. The $2f_1{-}f_2$ DP was measured. The EroScan device used a fixed averaging time (four seconds) as a stopping rule. This test (referred to throughout as the initial or conventional test) used f_2 frequencies of 1.5, 2, 3, 4, 5 and 6 kHz. The criterion for passing was a signal-to-noise ratio (SNR) of 6 dB or more in at least 4 of the 6 f_2 frequencies tested. Newborns who failed this initial test were referred immediately for the second-stage screening with AABR using ABaer (Bio-logic, Mundelein, IL). This machine used a 100-microsecond click stimulus at 35 dB SPL intensity. It automatically evaluated the response with a point-optimized variance-ratio (POVR) signal-detection algorithm. A pass or refer was recommended based on the comparison of the POVR with a preset criterion. The test was terminated when one of the following happened: a POVR score of 3.5 was achieved after a minimum of 1536 stimuli had been averaged; a total of 6144 stimuli were averaged and the POVR score reached a value of 3.1 or higher; or the POVR score did not reach a value of 3.1 at the end of two sets of 6144 stimuli.

The newborns (regardless of their pass or fail status at the initial test) were also tested with the OtoRead DPOAE device (Interacoustics, Middelfart, Denmark) for f_2 frequencies of 2, 4, 6, 8, 10 and 12 kHz within an hour of the initial test. For this second DPOAE measurement (referred to below as the high-frequency test) the noise floor and DPOAE amplitudes were retrieved for analysis in addition to the SNR. To allow for comparison of the high-frequency outcomes with those of the conventional OAE test, we accepted the same SNR value of 6 dB above the noise floor as a pass criterion for each f_2 frequency we tested. The OtoRead device had the same probe specifications, preset protocols, stimuli and stopping rules as the EroScan device. The EroScan DPOAE device was configured to give only a pass/fail result at the end of the hearing screening, so separate DPOAE and noise-floor data were not available. For the OtoRead device, the DP levels were less than or equal to the noise levels at all f_2 frequencies when measurements were taken with a 5-ml coupler.

Recordings were done with the DPOAE probe inserted as deeply as possible in the canal while making sure that the baby was not in discomfort. A complete DPOAE test with either the OtoRead or the EroScan instrument began with a calibration phase in which responses from a sequence of calibration tones (at the same f_1 and f_2 as the first DPOAE to be measured) were used to determine the voltages needed to obtain the desired sound pressures. Once the calibration had been done successfully, the actual test was done. This consisted of measuring the responses obtained for the various pairs of test frequencies. For each f_2 the OAE signal was taken to be the power in the DP ($2f_1{-}f_2$) frequency bin; the noise floor was estimated by averaging the power in the four bins closest to the DP bin (i.e., two on either side); and the SNR was the ratio of the two.

The data were analyzed using two-way mixed analysis of variance (ANOVA) that independently examined the effects of several independent variables on the dependent variable DPOAE SNR (measured in dB) over six f_2 frequencies (2, 4, 6, 8, 10 and 12 kHz). The independent variables included: (i) outcomes on the initial OAE and AABR tests (newborns who passed the initial OAE test, newborns who failed the initial OAE test but passed the AABR test, and newborns who failed the initial OAE test and also failed the AABR test); (ii) age at screening (12–24, 25–36 and 37–48 hours); (iii) birth weight (less than 2499, 2500–2999, 3000–3499, 3500–3999, and 4000 g or more); (iv) gestational age (37, 38, 39, 40 and 41 weeks); (v) sex (male or female); (vi) side tested (left or right); and (vii) mode of delivery (by Caesarean section or vaginally). Post-hoc tests were done using *t*-tests. Chi-squared tests of independence were performed to examine the relationship between the pass/fail status on our high-frequency test and the f_2 frequency tested; Fisher's exact test was used when a cell had fewer than 5 participants. Lastly, the effects of noise-floor levels on the performance on the high-frequency test at the different frequencies were evaluated.

3. Results

3.1. Overview

There were 255 newborns included in the study, of whom 138 (54%) were males and 117 (46%) females. There were 160 (63%) delivered vaginally and 95 (37%) by Caesarean section. The initial OAE tests were done within 24 hours of birth in 84 cases (33%), and after 24 hours but before discharge from the hospital in 171 (67%). The birth weights ranged between 2390 and 5290 grams, and all newborns were delivered at or after 37 completed weeks of gestation. The initial test was passed by 224 (88%) newborns; 23 (9%) failed the initial test but passed the AABR test, four cases being unilateral failures; and 8 (3%) failed both the initial OAE test and the AABR test, all of them bilaterally.

Table 1 contains the high-frequency OAE SNR means and standard deviations for the different f_2 frequencies for all newborns, whether or not they passed the initial screening test, according to the sex, mode of delivery, birth weight and gestational age. Figure 1 shows the SNRs with males and females shown separately. The mean SNRs were somewhat higher for females than for males ($F(1,253) = 5.03$, $p = 0.03$, $\eta^2 = 0.02$). The SNRs were robust for f_2 frequencies 2 to 10 kHz. There was a slight progressive increase in the mean SNR from about 16 dB at 2 kHz to 18 dB at 8 kHz followed by a sharp drop-off to about 13 dB at 10 kHz and only about 5 dB at 12 kHz. An SNR value of at least 6 dB was present at 12 kHz in 99 (39%) of all the newborns.

The SNRs were slightly but not significantly higher on average for the left ears than for the right ears ($F(1,490) = 0.35$, $p = 0.56$, $\eta^2 = 0.001$).

3.2. Effects of birth weight and mode of delivery

Figure 2 shows the SNR values grouped by birth weight. A significant main effect was observed for the birth weights of the newborns ($F(4,249) = 4.3$, $p = 0$ .002, $\eta^2 = 0.07$), and there was also a significant birth-weight-by-frequency interaction effect ($F(20,1245) = 1.71$, $p = 0.03$, $\eta^2 = 0.03$). Post-hoc comparison of the birth-weight main effect, using between-group *t*-tests, showed that newborns with birth weights in the range 2500 to 2999 g had on average significantly greater OAE SNRs than those with weights in the range 3500 and above ($t = 3.2$, $p = 0.002$, $d = 0.79$). SNR values were significantly higher for small babies (birth weights between 2500 and 2999 g) than for babies weighing 3500 g or more ($t = 3.60$, $p < 0.001$, $d = 0.63$). In addition, babies with birth weights ranging from 3000 to 3499 g had significantly higher SNR values than babies whose birth weights were from 3500 to 3999 g ($t = 3.43$, $p = 0.001$, $d = 0.92$).

Newborns delivered by Caesarean section had slightly lower SNR values than those who were born vaginally, but this difference did not reach statistical significance ($F(1,253) = 0.75$, $p = 0.39$, $\eta^2 = 0.003$).

3.3. Effects of gestational and postnatal ages

There were no statistically significant differences in the SNR values for either the main effect of gestational age ($F(4,250) = 0.69$, $p = 0.60$, $\eta^2 = 0.011$) or the gestational-age-by-frequency interaction effect ($F(4,250) = 1.09$, $p = 0.36$, $\eta^2 = 0.017$). However, the SNR values appeared to be highest for babies born at 37 weeks and lowest for babies born at 41 weeks.

No significant differences in SNR values were observed with respect to age at screening. Neither the main effect ($F(1,241) = 0.42$, $p = 0.66$, $\eta^2 = 0.003$) nor the age-by-frequency interaction effect ($F(2,241) = 1.0$, $p = 0.37$, $\eta^2 = 0.008$) reached significance. However, when other variables (birth weight, gestational age, mode of birth delivery) were taken into consideration, the age at screening had a significant effect ($\chi^2(6, N = 23) = 18.2$, $p = 0.006$) only at 2 kHz for the group of newborns who failed the initial OAE test but passed the AABR test; at other f_2 frequencies there were no significant effects.

3.4. Effects of results at initial screening

Figure 3 shows the SNR results of the high-frequency OAE test grouped according to whether the newborns (i) passed the initial OAE test, (ii) failed the initial OAE test but passed the AABR test, or (iii) failed both the initial OAE test and the AABR test. Based on our SNR cut-off value of 6 dB at individual f_2 frequencies, all of the newborns who passed the initial OAE test also passed the high-frequency OAE test at all f_2 frequencies except 12 kHz, where only 95 out of 224 had an SNR of at least 6 dB. Of the 31 (12%) who failed the initial OAE screening test, 23 passed the second-stage screening with AABR; all of these 23 newborns also had sufficiently high SNRs to pass the high-frequency OAE test at f_2 frequencies of 4, 6 and 8 kHz, and all but one passed at 10 kHz. The newborns who failed both the initial OAE test and AABR also failed the high-frequency OAE test at all f_2 frequencies with the exception of one newborn who passed only at 8 kHz. The failure rate and the false-positive rate for the initial OAE test were 12% (31/255) and 9% (23/247) respectively. Requiring an SNR of 6 dB or more at all of 4, 6, 8 and 10 kHz for a pass, our high-frequency OAE test led to a reduction of the OAE failure rate from 12% to 3.5% (9/255), and a reduction of the false-positive rate from 9% to 0.4% (1/247). If the SNR was required to exceed the threshold only at three of the four frequencies, the OAE failure rate would be slightly lower (8/255) and the false-positive rate would be zero. The mean SNR values were statistically different for the three groups for f_2 frequencies 2, 4, 6, 8 and 10 kHz ($p < 0.05$).

Figure 4 shows the OAE amplitudes and noise floors for the newborns grouped according to their pass or fail status at the initial OAE screening test. The OAE amplitudes were higher in the newborns who had a pass status than in those who had a fail status ($t(253) \geq 2.767$, $p < 0.05$) except at 2 and 12 kHz ($t(253) \leq 1.77$, $p \geq 0.08$). The noise floor at 2 kHz was significantly higher in the group of newborns who failed the initial OAE screening test than in those who passed it ($t(253) = 5.822$, $p = 0.02$), but at f_2 frequencies above 2 kHz the noise floors were similar for both groups ($t(253) \leq 1.8$, $p \geq 0.396$). The noise floors were not significantly different between sexes, nor for different gestational ages or birth weights.

4. Discussion

OAEs were consistently present at 2, 4, 6, 8 and 10 kHz in all the newborns that passed the initial (conventional) OAE screening test but they were not always present at 12 kHz. The SNRs generally became smaller at 10 and 12 kHz, consistent with findings in young adults [19,20]. High-frequency hearing is usually better in younger people, including infants [21–23], but the relatively low OAE levels that we report, especially at 12 kHz, may be because high-frequency OAEs are still developing in the perinatal period [24].

Our high-frequency OAEs were slightly greater for the female newborns but the noise floors were not statistically different between the two sexes. OAE differences with sex have been described previously [25–30] but the causes are uncertain. We found no significant differences between right and left ears, but some differences have been found previously [31,25].

We found that newborns with a gestational age of 37 weeks had the highest SNR values; those at 41 weeks had the lowest SNR values, albeit still sufficient for a pass. These findings are not in complete agreement with some previous results [32,33].

In our study, newborns delivered by Caesarean section had slightly (but statistically significantly) lower SNR values than those born vaginally, consistent with a previous report [34]. This difference might result from enhanced middle-ear drainage.

We also observed that, among those delivered by Caesarean section, newborns who weighed more than 3500 g had lower SNR values than those born at the same gestational ages but weighing less. SNR values at 8, 10 and 12 kHz decreased with increasing birth weight. The role of birth weight in newborn hearing screening has scarcely been studied [35–37].

The initial OAE test for our newborn population had a failure rate of 12% and a false-positive rate of 9%, taking the AABR result as the truth. Additional testing at 4, 6, 8 and 10 kHz in this study resulted in significant reductions in the OAE failure and false-positive rates. A possible explanation for this is the fact that stiffness-dominated lower frequencies are more affected by conditions that increase the stiffness of the middle ear, such as liquid in the middle ear [14]. In newborns who failed the initial OAE test but passed the AABR (representing the false-positive group), the outcome at 2 kHz was more likely to be a pass as the age at screening increased. This supports the observation that the performance at low frequencies is affected by transient conditions.

We found a significant difference in the noise floor at 2 kHz between newborns who passed and those who failed the initial OAE test. Noise floors are important determinants of the SNR, which is the basis of the pass criterion in most OAE devices. Conditions that increase the impedance of the middle ear are likely to also result in higher noise floors, especially at low frequencies [17]. It is plausible that the observed increase in the noise floor at 2 kHz is associated with middle-ear liquid.

Compared with AABR testing, OAE testing has the disadvantage of not detecting auditory neuropathies. Nonetheless, OAEs are still often used for newborn hearing screening, if only as an initial test and for non-high-risk newborns [e.g., 38,39], so reduction of the high false-positive rates of OAE screening is important.

One limitation of our study is that we compared our high-frequency OAE test with AABR, another screening test, rather than with diagnostic testing. A second limitation is that our study had to make use of a different device for the initial screening than for the high-frequency OAE test, although the probe specifications and the protocols were the same for the two devices. In addition, only babies who failed the conventional OAE tests underwent the AABR test, so the sensitivity and specificity of the high-frequency OAE test could not be ascertained.

5. Conclusion

High-frequency OAE measurements resulted in a reduction in the OAE failure rate and false-positive rate. This could lead to reductions in the cost and total time needed for hearing screening, and in parental stress and unnecessary follow-ups.

Acknowledgments

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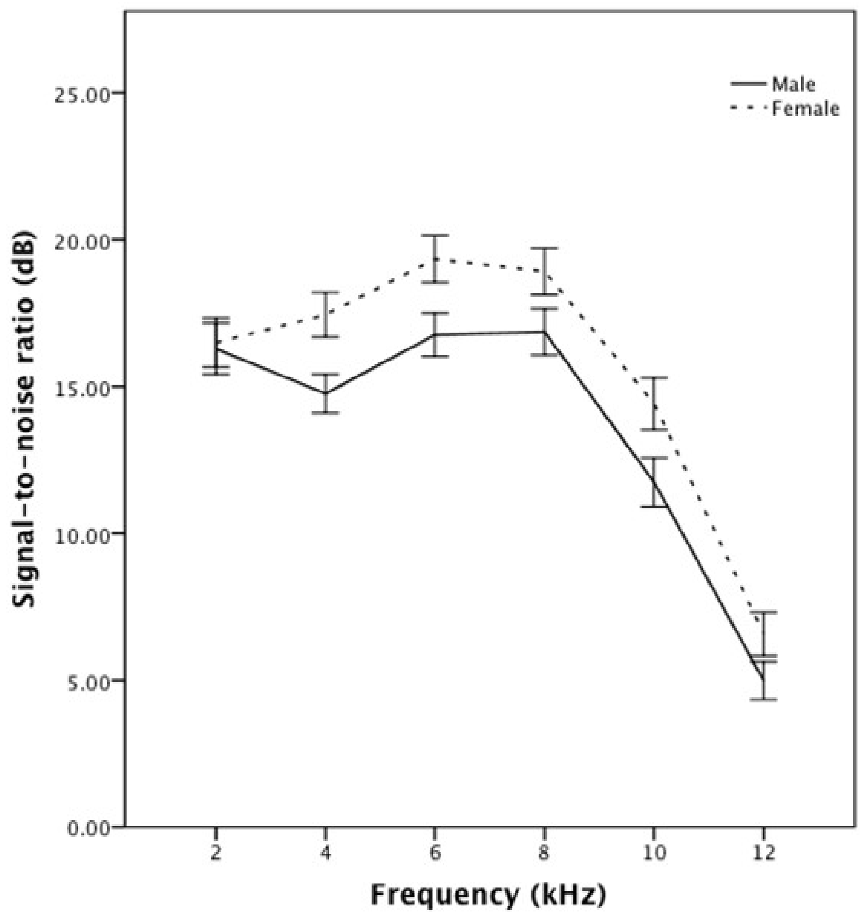

Figure 1. OAE signal-to-noise ratios (SNRs) for f_2 frequencies 2, 4, 6, 8, 10 and 12 kHz, for males and females. Error bars are SEM.

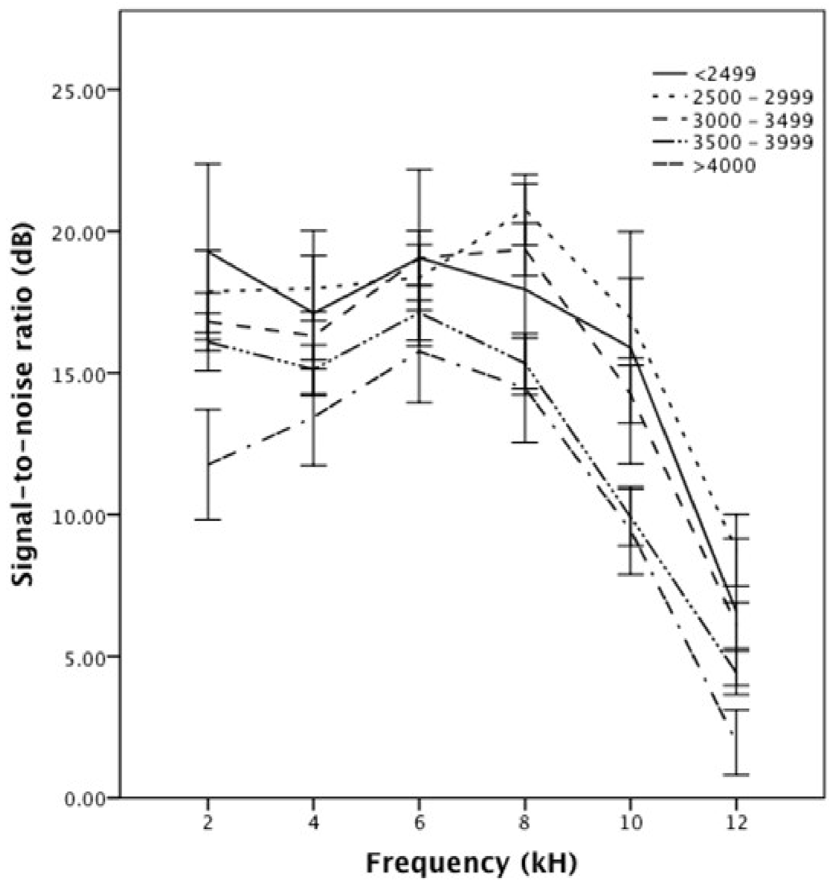

Figure 2. OAE SNRs grouped by birth weight. Error bars are SEM.

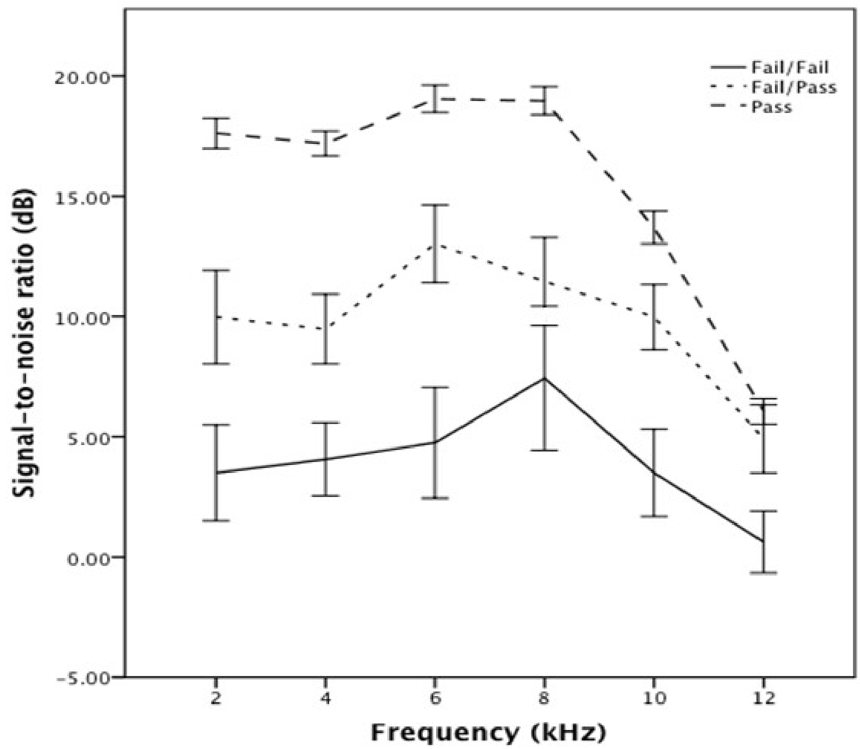

Figure 3. SNRs for the high-frequency OAE measurements grouped according to the performance of the newborn at the initial (conventional) OAE screening test: (i) those who passed the initial OAE test (N=224); (ii) those who failed the initial OAE test but passed the AABR test (N=23); and (iii) those who failed both the initial OAE test and the AABR test (N=8). Error bars are SEM.

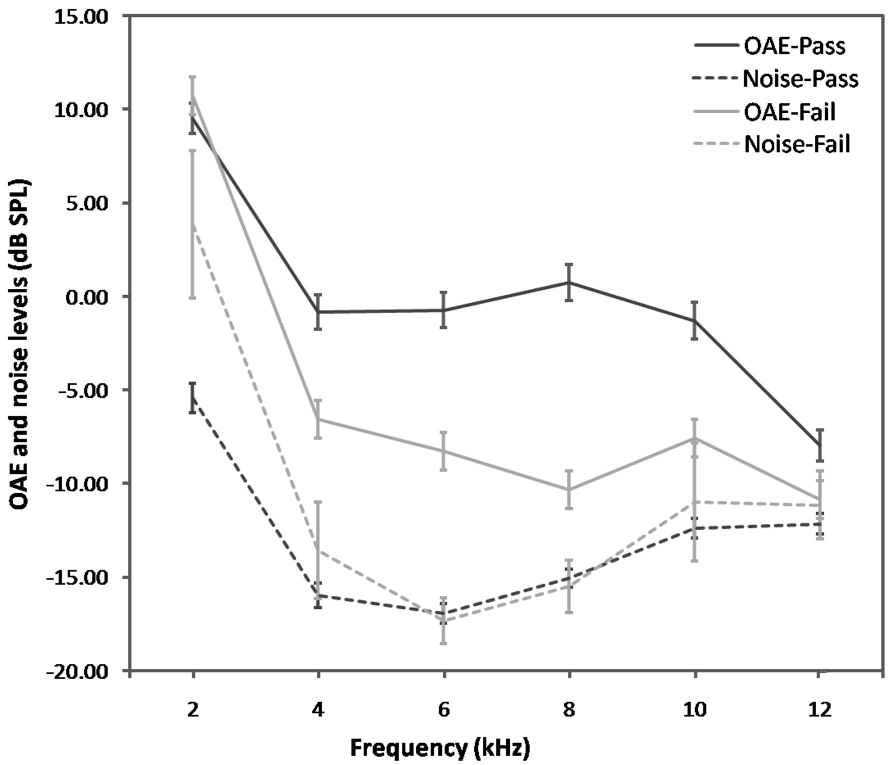

Figure 4. OAE amplitudes and noise floors in the groups of newborns with pass or fail status at the initial (conventional) OAE test. Error bars are SEM.

Table 1: Mean SNR values at the different f_2 frequencies, grouped by sex, mode of delivery, birth weight and gestational age.

Frequency (kHz)	**Sex**						**Mode of delivery**					
	Male (n=138)		Female (n=117)		Total (n=255)		Vaginal (n=160)		Caesarean (n=95)		Total (n=255)	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD
2	16.3	10.2	16.5	9.0	16.4	9.7	16.6	10.0	16.0	9.1	16.4	9.7
4	14.8	7.7	17.4	8.2	16	8.0	16.4	8.1	15.3	7.9	16.0	8.0
6	16.8	8.7	19.3	8.7	17.9	8.8	18.4	8.5	17.2	9.3	18.0	8.8
8	16.9	9.3	18.9	8.6	17.8	9	18.3	8.8	16.9	9.3	17.8	9.0
10	11.7	9.9	14.4	9.6	13	9.8	13.1	9.5	12.7	10.3	13.0	9.8
12	5.0	7.5	6.6	8.0	5.7	7.7	5.7	7.5	5.7	8.2	5.7	7.7

	Birth weight (g)											
	<2500 (n=9)		2500 – 2999 (n=51)		3000 – 3499 (n=83)		3500 – 3999 (n=86)		≥4000 (n=25)		Total (n=254)	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD
2	19.2	9.3	17.9	10.4	16.8	9.3	16.1	9.4	11.8	9.7	16.4	9.7
4	17.1	8.7	18.0	8.2	16.3	7.7	15.1	8.0	13.4	8.5	16.0	8.0
6	19.1	9.3	18.4	8.3	19.1	8.8	17.1	9	15.8	9	17.9	8.8
8	17.9	11.2	20.8	8.9	19.4	8.5	15.3	8.3	14.5	9.6	17.7	8.9
10	15.9	12.3	16.9	10.0	14.3	9.2	9.9	9.3	9.4	7.8	12.9	9.8
12	6.6	7.8	8.7	9.0	6.1	7.3	4.4	7.1	2.0	5.8	5.7	7.7

	Gestational age (weeks)											
	37 (n=35)		38 (n=52)		39 (n=79)		40 (n=64)		41 (n=25)		Total (n=255)	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD
2	17.4	8.5	17.2	9.5	15.9	10.2	17.0	9.7	13.5	10	16.4	9.7
4	17.5	6.7	16.0	6.5	16.0	9.0	15.4	8.6	15.4	8.0	16.0	8.2
6	19.8	7.5	17.0	7.7	17.6	10.0	17.8	8.9	18.8	8.1	18.0	8.8
8	20.7	8.8	16.5	7.8	17.5	9.8	18.0	8.7	16.8	9.5	17.8	9.0
10	15.3	9.1	11.8	9.7	12.6	10.3	13.5	9.7	11.8	9.8	12.9	9.8
12	6.1	7.2	4.1	6.5	6.2	8.2	6.0	8.3	6.5	8.0	5.7	7.7