Otoacoustic emissions as an indicator of hearing loss

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Otoacoustic emissions (OAE) are generated as a by-product of the nonlinear cochlear amplification process involving the electro-motile properties of the outer hair cells. Most sensorineural hearing losses arise predominantly from reduced cochlear amplification and hence are associated with reduced or absent OAEs. This means that OAE amplitude is a potential indicator of sensorineural hearing loss. However, there is substantial variation in OAE characteristics between individuals with similar hearing threshold, which limits their ability to predict hearing threshold levels (HTL) absolutely. Nonetheless, OAEs are stable within individuals and offer the possibility to predict *changes* in HTL from *changes* in OAE amplitude.

Prediction of changes in HTL requires knowledge of the relationship between OAE amplitude and HTL as well as the test-retest reliability of OAEs. These parameters were established for a range of transiently evoked and distortion product OAE measures (TEOAE and DPOAE) by testing 43 subjects with HTL across a range from normal hearing to mild hearing loss. Results suggested that TEOAE elicited by a maximum length sequence approach would be most sensitive to changes in HTL, having the largest change in amplitude relative to the test-retest reliability. These ideas were further explored by monitoring auditory function in 17 normal hearing subjects over 7 days in whom a reversible hearing loss was induced by administering aspirin at maximum therapeutic dose.

Further ongoing research is evaluating the potential of TEOAEs for monitoring auditory function in people exposed to noise at work. More than 200 new recruits to noisy industry and non-exposed controls have had TEOAEs measured over a 3-year interval to examine whether OAEs are a more sensitive indicator of noise-induced hearing disorder than conventional pure tone audiometry.

Preliminary conclusions suggest that OAEs provide a useful physiological correlate of hearing impairment when used in the context of longitudinal monitoring.

INTRODUCTION

The term hearing loss is used here in the strict sense to describe a change in hearing threshold level (HTL), rather than the loose term that is synonymous with hearing impairment. In particular, the focus is on relatively small changes in HTL that may occur, for example, due to noise exposure of ototoxic drug administration. Conductive hearing loss is outside the scope of this work.

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Mild sensorineural hearing loss is common in the general population and to a reasonable approximation can be considered to be a function of outer hair cell (OHC) loss. The inner hair cells (IHC) are relatively resistant to damage and IHC loss occurs primarily when HTL exceeds approximately 60 dB. Therefore, the model underlying the following analysis is that mild hearing loss is determined solely by loss of OHC function. While it is accepted that this is an approximation, it is held to be a reasonable approximation. Furthermore, the extent to which the experimental evidence is consistent with the model provides an evaluation of the assumed model.

This paper examines the contention that hearing loss can be identified using otoacoustic emissions (OAE) as an indicator, as proposed for example by Probst *et al.* (1991). This would have useful application in developing an objective indicator or screening test for noise-induced hearing loss, or an indicator of ototoxicity in patients undergoing treatment with anti-neoplastic drugs that are known to be ototoxic (Beck *et al.*, 1992).

Generation of otoacoustic emissions

OAEs are fundamentally associated with active cochlear processes that utilise the ability of OHC to inject energy into the motion of the basilar membrane. In the normal cochlea, incoming sound reaches the fluids of the cochlea via the stapes and oval window. In addition to bulk pressure wave created in the virtually incompressible fluids, because of the relatively low impedance of the round window, displacements of the basilar membrane also occur near the base of the cochlea, which in turn initiate a travelling wave on the basilar membrane. The travelling wave progresses rapidly along the cochlear partition where the local natural frequency of the partition is high compared to the stimulus frequency. As the local resonance frequency reduces with distance along the partition, the travelling wave slows down and eventually stalls in the region where the natural frequency equals the stimulus frequency. This process entails an increase in displacement as the travelling wave slows down and the wave energy is concentrated in a smaller region. This amplification is substantially increased by the action of the OHC, which provide positive feedback by adding force in the direction of the partition displacement. This amplification is an active process, consuming metabolic resources and adding up to approximately 60 dB to the displacement amplitude. In other words, the OHC act to increase sensitivity of the ear to low intensity sounds by up to 60 dB. Conversely, reduced OHC activity reduces sensitivity and raises HTL.

The amplification by the OHC is nonlinear, affecting primarily sounds at low and moderate intensities. At higher intensities, the force generation of the OHC saturates and becomes relatively unimportant compared to the stimulus energy directly from the travelling wave.

OAEs arise from either or both of two mechanisms in addition to active cochlear amplification: linear reflection and nonlinear distortion. The prevalent theory explaining reflection involves scattering at sites of random inhomogeneity and constructive interference of those components that coincide with the filtering characteristics of the travelling wave (Shera and Guinan, 1999). These coherent reflection components may travel back along the basilar membrane as a reverse travelling wave, ultimately resulting in pressure fluctuations in the ear canal where they are recorded as OAEs. Brief stimuli such as clicks or tone bursts evoke transient evoked otoacoustic emissions (TEOAE) primarily via this mechanism of coherent linear reflection[1]. Note that TEOAEs require the presence of both reflection sites and active amplification: if either is absent there will be no TEOAEs. The pattern of TEOAEs may be complicated further by additional reflections occurring at the oval window and intermodulation of frequency components due to the nonlinearity of basilar membrane motion.

When a stimulus contains more than one frequency, for example two tones, nonlinear distortion due to active cochlear amplification will create distortion products (intermodulation) in the region of overlap of the travelling waves of the different frequencies. For two tones at frequencies F1 and F2 (F2 > F1), the most prominent distortion product is at the frequency 2F1−F2, particularly for frequency ratios (F2/F1) in the region of 1.2. These distortion products initiate a new travelling wave that travels from the overlap region in both directions. The reverse travelling wave leads directly to a recordable distortion product otoacoustic emission (DPOAE) in the ear canal. The forward travelling wave behaves exactly like a stimulus at the same frequency and in the case of the 2F1−F2 component has a peak at a position apical to the overlap region. This secondary travelling wave will create a further DPOAE component via the mechanism of coherent reflection, as for TEOAEs. Therefore, the entire DPOAE will be the vector sum of the two components generated by the distortion and reflection processes. Depending on the frequencies involved, the vector summation may entail constructive or destructive interference. As frequency varies, this may lead to patterns like standing waves, which are referred to as fine structure[2]. As for TEOAEs, additional refection at the oval window may complicate the pattern of DPOAEs.

Measurement of otoacoustic emissions

OAEs are usually measured using a small probe sealed into the ear canal with a disposable plastic ear tip. The probe contains a miniature microphone and one or two miniature earphones. The earphones generate the evoking stimuli and the microphone signal is amplified to produce a recordable response. The most common stimulus for TEOAEs is a broadband click. Because of the low amplitude of the TEOAE, synchronous averaging of responses to several hundreds of clicks is required to achieve adequate SNR. Figure 1 illustrates TEOAE recordings for clicks at peak-equivalent sound pressure levels (pe SPL) from 35-70 dB in 5-dB steps.

The figure shows TEOAEs recordable from the full range of stimuli from 35-70 dB pe SPL. The validity of the recording is demonstrated by the high correlation between the two replications in each panel. Note that the amplitude of the TEOAE grows by a factor of only about 10 (or 20 dB) for a stimulus increase of 35 dB, illustrating the com-

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[1] Despite the reflection mechanism being fundamentally linear, TEOAEs display nonlinear growth with increasing stimulus intensity due to the nonlinearity of basilar membrane motion.

[2] Fine structure also occurs as a consequence of the coherent reflection mechanism, affecting the reflection component of DPOAEs.

pressive nonlinearity of cochlear amplification. The amplitude of the TEOAE is typically characterised by taking the RMS amplitude of the response components that are common to both replications, which in Fig.1 is 28 dB for the top left panel. Note that while the waveform of the TEOAE shown in Fig. 1 is fairly consistent across stimulus levels for the individual, other ears would have quite different waveforms. Each ear has an idiosyncratic TEOAE waveform that cannot be predicted from other measures at the current state of knowledge.

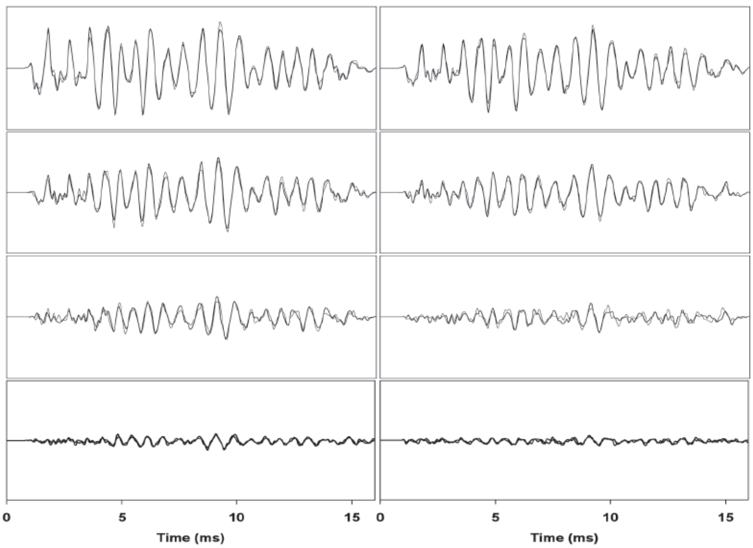

Fig. 1: TEOAE recordings for clicks at various levels in steps of 5 dB. Top left to bottom right: 70, 65, 60, 55, 50, 45, 40, 35 dB. The duration of recording is 16 ms and the click occurs at 2 ms before the start on the window; gain is reduced by a factor of 1000 until 1 ms into the window. Each panel contains two superimposed replications. The vertical scale is identical for all panels.

DPOAEs are recorded by presenting two continuous tones at frequencies F1 and F1 and levels L1 and L2. The ear canal pressure contains both the stimuli and the DPOAE, which can be separated by filtering in the frequency domain. SNR is maximised by filtering a sufficiently long recording to obtain fine spectral resolution or by synchronous averaging techniques. The amplitude of the DPOAE is taken as the SPL of the spectral line corresponding to the DPOAE (most commonly 2F1−F2) and background noise levels is estimated from the SPL of adjacent spectral lines.

Relationship between OAE and HTL

Virtually all otologically normal ears with normal hearing thresholds display OAEs (Kapadia and Lutman, 1997). As HTL increases, the probability of recording an OAE decreases, such that TEAOEs are generally absent when HTL exceeds 35 dB (Bonfils *et al.*, 1988). DPOAEs may be recorded in ears with somewhat greater HTL as long as the stimulus intensity is sufficient. They have been shows to be useful for separating normal and impaired ears (Prieve *et al*, 1993). These characteristics of OAEs make them particularly suitable as an indicator of normal, or near-normal, hearing and have led to widespread adoption of OAEs for neonatal hearing screening.

The relationship between the amplitude of OAEs and the magnitude of HTL has been less well studied (e.g. Gorga *et al.*, 1993). Such studies illustrate that there is a great deal of overlap between the amplitudes of OAEs in groups of individuals with different HTL. It is clear that HTL cannot be predicted accurately from OAEs, due to the idiosyncratic nature of OAEs. However, OAEs are very stable for a particular ear, which suggests that *changes* in OAEs may form the basis for reliable prediction of *changes* in HTL. Evidence on changes in OAEs can only be obtained by longitudinal studies, examples of which are limited. DPOAEs have been shown to be affected by temporary noise damage (temporary threshold shift, TTS) and have also been shown to be sensitive to noise (Hotz *et al.*, 1993; Engdahl *et al.*, 1996). However, there are many different OAE techniques and measures that could be employed and only a few arbitrary combinations have been used. Of particular interest, Marshall and Heller (1996) have suggested that using lower stimulus intensities would give greater sensitivity while most studies have used higher intensities.

AIM OF EXPERIMENTAL WORK

The overall aim of the experimental work described here was to evaluate the potential of OAE measures to be used as an indicator of hearing loss occurring within individuals (Hall, 2005). The rationale of the initial evaluation involved assessing the magnitude of change in OAE that could be expected for a specified change in HTL and the stability that could be expected over time. A suitable measure would be highly repeatable and have an expected magnitude of change greater than the uncertainty associated with repeat measurement. To be practically useful, these characteristics would have to be an improvement upon simply measuring HTL directly. Therefore, comparisons were made between OAEs and audiometry.

Further evaluation involved a longitudinal study where temporary changes in hearing were induced by administration of aspirin and changes in OAE and HTL were recorded daily. Finally, a large longitudinal study of new recruits to noisy industry is underway to evaluate the use of a selected OAE measure in practice.

There are a multitude of possible OAE measures that could potentially be used as indicators of hearing loss. Initial selection of measures relied on the expectation that using low stimulus intensities would yield measures that were more sensitive to minor cochlear damage. A counter argument is that low stimulus intensities yield small OAEs that are difficult to record against background noise and will hence lack stability and reliability. Therefore, a range of intensities was used to seek the best compromise.

Prolonging the recording duration for measures of both OAE and HTL can increase reliability of measurement. In order to make fair comparisons and to work towards a practical method, the durations required to obtain the various measures were equalised.

METHODS

Two types of TEOAE were investigated and required two different sets of measurement apparatus. Conventional TEOAEs were recorded using the Otodynamics ILO 288 Echoport system with software version 4.2. This delivers clicks at a rate of approximately 50/s. Stimulus levels of 40, 50, 60, 70, 80 and 90 dB were used with a time window of 20 ms. The linear recording mode was used in preference to the default nonlinear mode of the instrument, in order to extract the amplitude of the TEOAE independent of the compressive nonlinearity of the individual ear. Amplitudes were obtained for the unfiltered broadband TEOAE and for filtered waveforms in 1/6-octave bands centred on 3 and 4 kHz. Also derived nonlinear components were calculated by re-scaling responses in proportion to stimulus intensity and subtracting pairs 10 dB apart. This removed parts of the response that scaled linearly with intensity.

In addition to conventional TEOAEs, maximum length sequence (MLS) TEOAEs (Thornton, 1993) were recorded using prototype apparatus produced by Natus. MLS TEOAEs allow clicks to be delivered at high rates where stimulus and response overlap in time. The nature of the MLS click pattern allows the overlapped responses to be deconvolved to give the TEOAE. The increase in stimulation rate means that more responses can be averaged in a given time, which leads to an improvement in SNR. Stimulus levels of 40, 50, 60, 70 and 80 dB, and click rates of 50, 500 and 5000/s, were used. Measures used for analysis were SNR in 1-kHz-wide bands centred on 3 and 4 kHz.

DPOAE were recorded using custom apparatus consisting of an Etymotic ER-10B microphone probe and Etymotic ER-2 insert earphones connected to data capture apparatus on a personal computer. Software employed signal-averaging techniques that allowed DPOAEs to be recorded with a noise floor of approximately −30 dB SPL. Frequency ratio was fixed at 1.22 for all testing and recordings were referenced to F2. L1 was always 10 dB greater than L2. DPOAEs were recorded by sweeping F2 in steps of 48 Hz over intervals 200 Hz wide, centred on 3, 4 and 6 kHz. This approach allowed the DPOAE amplitude to be averaged over a range of frequency to smooth out any fine structure. Stimulus levels (L2) were 20, 30, 40,50, 60, 70 and 80 dB.

Self-recording audiometry was performed using a swept-frequency technique at intervals of 50 Hz over the range 2.5-6.5 kHz. This approach allowed averaging over restricted frequency ranges to smooth out fine structure in the audiogram.

RESULTS

OAE amplitude versus HTL

Participants all had normal hearing or a mild hearing loss, and normal tympanometric findings. HTL averaged over 0.5, 1, 2 and 4 kHz measured conventionally was <10 dB (n=22), 11-20 dB (n=13) or 21-30 dB (n=8). Ten of the first group were under 50 years while the remainder were over 50 years. Figs. 2 and 3 illustrate the relationship between HTL at 4 kHz and OAE amplitude for example measures of TEOAE and DPOAE. There is a wide scatter of individual data, showing increasing OAE amplitude associated with decreasing HTL, as expected. Scattergrams in a similar format were obtained for a wide variety of combinations of OAE and HTL measures. Promising measures were deemed to be those with least scatter, or highest correlation coefficient. Regression of the data in Fig. 2 gives a negative slope slightly greater than unity, meaning that differences in HTL are associated with slightly smaller differences in TEOAE amplitude. Conversely, the slope in Fig. 3 is shallower than unity. Overall, promising TEOAE measures had slopes in the region of 1.2, whereas promising DPOAE measures had slopes in the region of 0.75.

Repeatability was measured in the short term (sessions separated by at least 24 hours with a maximum interval of 8 weeks) and medium term (9 months). In general, OAE measures could not be recorded satisfactorily at stimulus levels of 40 and 50 dB. There was no consistent influence of level on repeatability once stimulus levels exceeded 50 dB. Medium-term and short-term repeatability were similar. Table 1 summarises the medium-term repeatability of the of the promising OAE measures, expressed as the standard deviation (SD) on replication.

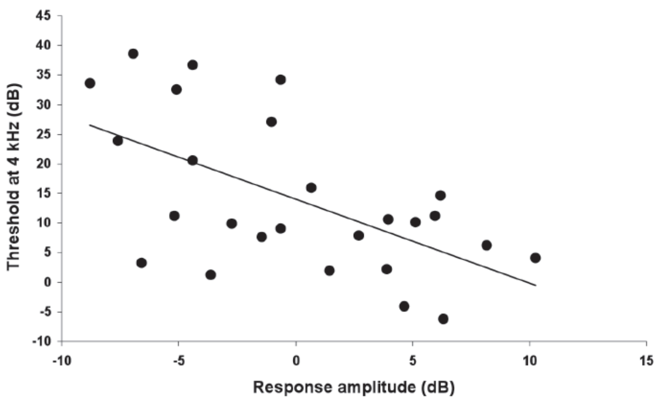

Fig. 2: Individual data showing association between HTL at 4 kHz and conventional TEOAE amplitude in the 1/6-octave band centred on 3 kHz for clicks at 80 dB. Best fit regression line is shown.

Multiplication of the slope value for each measure with the repeatability SD allows the calculation of an index of variability (Marshall and Heller, 1997) that allows the measures to be compared meaningfully. Taking two SD and multiplying by √2 gives an estimate of the magnitude in shift in HTL that could be detected by the measure as a statistically significant change. Table 2 summarises this index for the OAE measures with the lowest values. The table includes audiometry as a reference case, where variability is estimated directly.

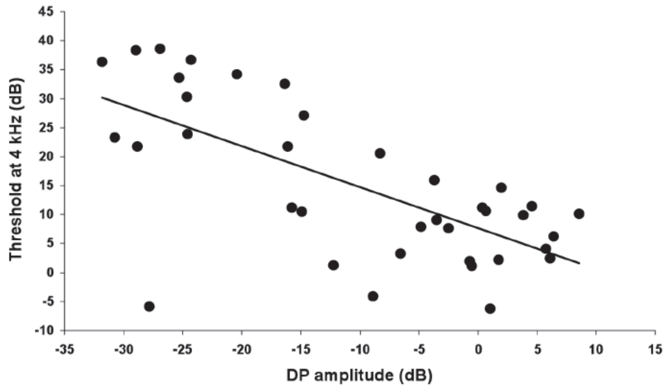

Fig. 3: Individual data showing association between HTL at 4 kHz and DPOAE amplitude for F2 at 4 kHz and L1/L2 at 60/50 dB. Best fit regression line is shown.

OAE measure	Rate (clicks/s)	Frequency (kHz)	Stimulus level (dB SPL)		
			60	70	80
DPOAE		3 (average)	5.8	5.4	
		4	4.6	4.7	
		4 (average)	5.5	6.1	
TEOAE		Broadband	2.0	2.1	2.5
		3	1.5	1.1	1.7
		4	1.5	1.2	2.1
		3-4 (average)	1.0	1.7	1.4
MLS TEOAE	50	Broadband	2.8	2.8	3.6
		3	1.4	0.9	1.0
		4	1.5	1.0	1.9
	500	Broadband	2.2	2.5	2.8
		3	1.2	1.2	1.1
		4	1.1	1.3	2.3
	5000	Broadband	1.5	1.7	2.6
		3	1.5	1.2	1.4
		4	1.5	1.8	

Note: average in frequency column for DPOAE means average across 200-Hz-wide frequency band. For TEOAE average means average of two frequency measures.

Table 1:. Summary of medium-term replication SD for promising OAE measures.

Rank	OAE measure				HTL frequency for slope (kHz)	Significant change in OAE (dB)	Equivalent change in HTL (dB)
1	MLS	3 kHz	80 dB	50/s	4	2.9	3.2
2	MLS	3 kHz	70 dB	5000/s	4 average	3.3	4.2
3	MLS	3 kHz	80 dB	5000/s	3	3.9	4.3
4	MLS	BB	60 dB	5000/s	3	4.2	5.6
5	MLS	3 kHz	80 dB	5000/s	4 average	3.9	6.1
6	TEOAE	3 kHz	60 dB		3	5.6	6.2
7	MLS	3 kHz	80 dB	5000/s	4	3.9	6.5
8	TEOAE	3 kHz	80 dB		4	4.8	6.6
9	DPOAE	4 kHz (average)	50/40 dB		3	11.3	6.8
10	TEOAE	3 kHz	80 dB		4 average	4.3	7.0
Audiom.					3	8.8	8.8
					4	11.6	11.6

Note: MLS indicates MLS TEOAE. BB indicated broadband.

Table 2: OAE measures ranked in order of index of variability.

The table shows measures with an index of variability better than audiometry. With the self-recording audiometry technique used here, a change of approximately 10 dB is required to be statistically significant. However, for the better OAE measures, a change of approximately 5 dB is significant. The MLS TEOAE measures are ranked in the first five places, followed by the conventional TEOAE measure. DPOAE measures appear to be less effective than TEOAE. TEOAE measures at 3 kHz appear to be most effective to detect changes at 3 and 4 kHz.

Changes in OAE and HTL with aspirin ingestion

The aim of this experiment was to induce small changes in cochlear function by administration of aspirin (salicylate), which affects the motility of the outer hair cells (Cazals, 2000). The TTS induced by aspirin shares the characteristics of permanent sensory hearing impairment (McFadden *et al,* 1984). OAE and HTL measures were obtained before, during and after aspirin ingestion to assess the extent to which OAE changes reflected changes in HTL. The OAE measures were selected from those used in the cross-sectional study above.

Seventeen participants took 11.7 g of aspirin over a period of 72 hours spanning four calendar days (975 mg twice on the first day, four times each on the second and third days and twice on the fourth). Salicylate concentration in the blood was monitored on days 3-5 and generally increased over the dosage period. Maximum concentration ranged from 0.5 to 1.5 mmol/l across subjects (mean value 0.89 mmol/l).

Mean change in HTL was greatest at 4 kHz where it reached approximately 8 dB at day 5. The largest shift recorded in any individual was 21.5 dB. The OAE measures also showed significant changes with aspirin ingestion on average. There were examples where the time courses of both OAE and HTL measures were very similar, as illustrated in Fig 4. There was a tendency for the OAE measures to change more than HTL, as indicated in the example.

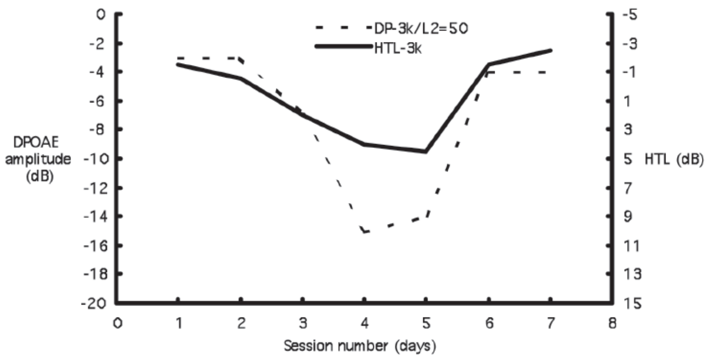

Fig. 4: Individual changes in DPOAE amplitude for F2 = 3 kHz and L2 = 50 dB compared with HTL at 3 kHz as a function of session.

However, this association was not consistent across participants and changes in OAE measure showed only a weak correlation overall with changes in HTL, with correlation coefficients in the region of 0.4. For both TEOAE and DPOAE, greater changes were obtained at lower stimulus intensities than at high stimulus intensities, provided the measure exceeded the noise floor.

The lack of a close relationship between OAE and HTL suggests that the two types of measures reflect somewhat different cochlear processes. This dissociation may be particular to the effects of aspirin. Further research is required to assess whether there is a closer relationship for other forms of sensorineural hearing loss, such as noise induced hearing loss.

Changes in OAE and HTL with noise exposure

A large longitudinal study is currently underway comparing changes in OAE amplitude and HTL in new recruits to noisy industry who are exposed noise levels that may potentially cause noise-induced hearing loss. The magnitude of any noise-induced hearing loss will be small in view of the measures in place to protect hearing, via personal hearing protection. However, it is recognised that real-world attenuation of hearing protection varies substantially from manufacturer's specification in the direction of reduced effectiveness. Moreover, not all workers are conscientious in wearing their protectors. Therefore, slight noise-induced hearing loss may be expected. The study entails annual monitoring of workers over a period of 2-4 years using MLS TEOAEs at stimulus levels of 50, 60 and 70 dB and rates of 50, 500 and 5000 clicks/s. This method was selected on the basis of the studies described above. HTL is also measured at the start and end of the monitoring period.

Interim results from the study are insufficient at present to report on the relationship between changes in OAE and HTL. The study will be completed by the end of 2007.

DISCUSSION

The repeatability of TEOAEs in the present study was better than DPOAEs, despite efforts to maximise SNR in the DPOAE recordings and to counter the effects of fine structure by averaging across a range of frequencies. The replication SD was in the region of 5 dB, which is larger than the short-term repeatability reported by Beattie *et al.* (2003), which approximately 3 dB. More recently, Sockalingham *et al.* (2007) reported similar repeatability to Beattie *et al.* (2003) in children tested on two occasions 13-15 days apart. The shallower slope of HTL change with DP amplitude change, compared to TEOAEs, was not enough to offset the poorer reliability of DPOAEs in the present study and it appears that TEOAEs are the better choice for monitoring potential effects on hearing, such as noise exposure. The cross-sectional results suggest that OAEs should be able to detect changes of approximately half the magnitude that can be detected using self-recording audiometry. Moreover, the requirements for participant cooperation and background noise are less stringent.

The longitudinal results from aspirin administration are mixed. In some cases, HTL changes are mirrored almost exactly by changes in OAE, particularly DPOAE evoked by stimuli at moderate intensities. However, in other cases there was little correspondence. The small shifts in HTL induced by aspirin limited the interpretation of these data. Moreover, aspiring ingestion may cause sensorineural hearing loss with different characteristics from other forms of sensorineural hearing loss, such as noise-induced hearing loss. Other reasons for lack of correspondence between OAEs and HTL may include IHC damage, which would affect HTL but not OAE, differential spread of effects across frequency and variations in reverse travelling wave properties among subjects, which only affect OAEs. Further research is required to explore the ability of OAEs to track changes in HTL due to noise exposure.

It is concluded that OAEs have the potential to act as a sensitive indicator of cochlear hearing loss and also have some practical advantages over pure tone audiometry.

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