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Research paper

Low-frequency modulated quadratic and cubic distortion product otoacoustic emissions in humans

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A B S T R A C T

Previous studies have used low-frequency tones to modulate distortion product otoacoustic emissions (DPOAEs). The cubic DPOAE (CDPOAE) is mostly chosen because amplitudes sufficient for modulation can be evoked with moderate sound pressure levels. Quadratic DPOAEs (QDPOAEs) however, are more sensitive to minute changes of the cochlear operating point (OP) and are better suited to assess changes of the cochlear OP.

Here, we compare the properties of low-frequency (30 Hz, 80–120 dB SPL) modulated CDPOAE and QDPOAEs evoked with $f_2 = 2$ and 5 kHz in human subjects with normal hearing. The modulation depth was quantified with the modulation index (MI), a measure which considers both amplitude and phase.

Modulated CDPOAEs evoked with $f_2 = 2$ kHz have amplitude maxima at the zero crossings and amplitude minima at the extremes of the biasing tone (BT) which correlate positively with the BT level. CDPOAEs evoked with $f_2 = 5$ kHz were recorded during biasing in exactly the same way as described before. At the highest BT levels used (120 dB SPL), very little modulation could be detected. Not only the depth, but also the shape of the QDPOAE modulation pattern is correlated with the BT level. At moderate BT levels (about 90–100 dB SPL) QDPOAEs evoked with $f_2 = 5$ kHz show one amplitude notch around the zero crossing of the positive going flank of the BT (a single modulation pattern). At and above a BT level of about 105 dB SPL, the pattern reverses and shows a double modulation pattern. At the highest BT level used (120 dB SPL), quadratic MIs exceed cubic MIs (2.0 ± 0.5 and 0.97 ± 0.06, respectively).

Patterns of low-frequency modulated QDPOAEs in humans are similar to the modulation seen in animal studies and as predicted by mathematical models. Human low-frequency modulated QDPOAEs are ideally suited to estimate cochlear OP shifts because of their high sensitivity to the OP shift.

1. Introduction

Otoacoustic emissions (OAEs) are sounds produced by active, non-linear processing in the inner ear, which can be measured with a sensitive microphone in the ear canal. There is ample evidence in the literature indicating that OAEs are physiologically vulnerable and can therefore reflect cochlear integrity (see Kemp (2002) for review). At present, OAEs are routinely used for hearing screening, with particular importance in neonates (Janssen et al., 1998, 2006).

OAEs are products of cochlear non-linearities, with their sources predominantly situated in outer hair cells (Bian and Scherrer, 2007; Bian et al., 2002, 2004; Lukashkin and Russell, 1998; Lukashkin and Russell, 2005). One dominant sigmoidal non-linearity lies in the mechano-electrical transducer (MET) transfer function of hair cells and can be approximated by a two-exponential Boltzmann function (Crawford et al., 1989; Frank and Kössl, 1996, 1997; Lukashkin and Russell, 1998; Lukashkin and Russell, 2005). The Boltzmann function (Fig. 1A), as any function with symmetrical and antisymmetrical properties when supplied with the sum of two sinusoids, produces cubic and quadratic two tone distortions (Abel et al., 2009; Frank and Kössl, 1996), among higher order two tone distortions with increasingly smaller amplitudes.

The amplitudes of cubic and quadratic distortions in the Boltzmann simulation depend on the position of the operating point

Abbreviations: BT, biasing tone; CDPOAE, cubic distortion product otoacoustic emission; DPOAE, distortion product otoacoustic emission; FT, Fourier transformation; MET, mechano-electrical transducer; MI, modulation index; OP, operating point; QDPOAE, quadratic distortion product otoacoustic emission; SNR, signal-to-noise ratio.

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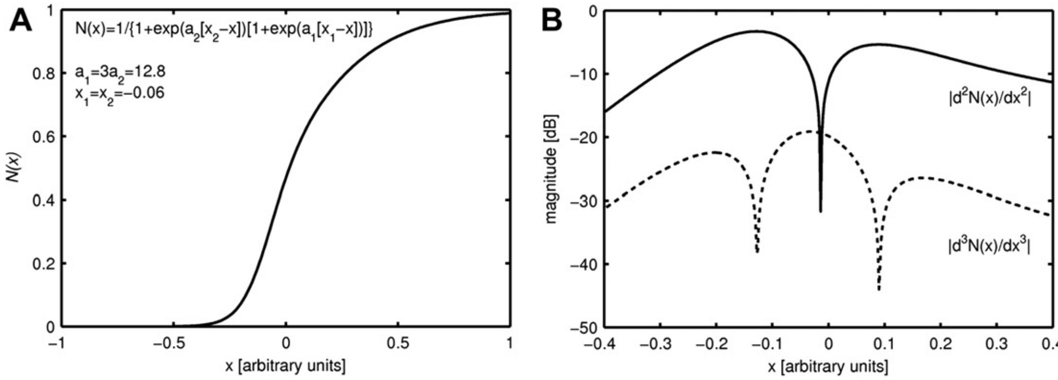

Fig. 1. A: Normalised non-linear transfer function of the mechano-electrical transducer (MET) approximated by a sigmoidal, two-exponential Boltzmann function $N(x)$ (figure inset; Crawford et al., 1989). B: The relation between OP shifts ($\times$) and the magnitude of cubic and quadratic distortions, estimated by the absolute value of the 3rd (dashed line) and 2nd (solid line) derivative, respectively, of a two-exponential Boltzmann function $N(x)$ (see A, figure inset). Note that the 2nd derivative shows a notch when the OP is close to 0 (in a more symmetric position), whereas the 3rd derivative has a maximum at this position.

(OP) on the transfer function. The OP is a location on this function where the transfer characteristics are applied to the input. For cochlear transfer functions, the OP can be seen as the resting position of the organ of Corti or its position during zero crossings of a sinusoidal input (Salt and Hullar, 2010). If the OP is close to the inflection point of the transfer function, cubic distortions will show maximum amplitudes while quadratic distortions are small. Conversely, if the OP is shifted away from the inflection point in either direction, the amplitudes of quadratic distortions will steeply grow larger while the amplitudes of the cubic distortions decrease (see Fig. 1B).

It has been demonstrated experimentally that electrically or acoustically induced shifts of the cochlear OP in humans and animals indeed result in changes of CDPOAEs and QDPOAEs closely resembling the behaviour predicted by the Boltzmann function (Bian, 2004; Bian and Scherrer, 2007; Bian et al., 2002, 2004; Brown and Gibson, 2011; Frank and Kössl, 1996, 1997; Lukashkin and Russell, 2005; Marquardt et al., 2007; Sirjani et al., 2004).

One could ask why it is possible to model the behaviour of low-frequency biased DPOAEs with one single, saturating non-linearity. After all, aside from the generation of DPOAEs at the characteristic frequency place of f_2, where the excitations evoked by the primary tones overlap based on a MET transfer function (Brown and Kemp, 1984; Martin et al., 1987), the cochlea has numerous potential sources of non-linearity in both mechanisms and locations. A recent study by Verpy et al. (2008) showed that non-linear properties of the cochlea are absent in stereocilin-null mutant mice lacking horizontal top connectors of outer hair cells. A second location of generation can contribute to DPOAEs at the characteristic frequency place of the DPOAE frequency (Brown et al., 1996; Kemp, 1980). Therefore, DPOAEs measured in the ear canal might be the result of a vector summation of emissions originating from more than one source in the cochlea (Lukashkin and Russell, 2005). If this would be the case, specific amplitude patterns caused by a single source could not be observed, since phase summation from multiple sources would disrupt such patterns (Lukashkin and Russell, 2005). Nonetheless, it has been shown in both humans and rodents that the modulation patterns of low-frequency biased DPOAEs can be predicted by a single, saturating non-linearity such as the Boltzmann function (Bian and Scherrer, 2007; Bian et al., 2002; Brown and Gibson, 2011; Brown et al., 2009; Lukashkin and Russell, 2005). It has been suggested that this indicates, at least for the parameters used in these experiments, that the DPOAEs measured in the ear canal are dominated by contributions from one source only (Lukashkin and Russell, 2005).

Low-frequency biased CDPOAEs have been used to detect pathological changes of cochlear mechanics, such changes can occur with endolymphatic hydrops associated with Meniere's disease (Brown and Gibson, 2011; Hirschfelder et al., 2005; Rotter et al., 2008; Scholz et al., 1999). The low-frequency BT, when presented at high intensities, will periodically shift the OP of the cochlea depending on the phase of the BT and will therefore produce distinct patterns of DPOAE amplitude modulations. These patterns can be used to quantify the shift of the resting OP (Bian et al., 2002; Brown and Gibson, 2011; Brown et al., 2009).

To date, few publications dealing with low-frequency modulated CDPOAEs in humans exist (Bian and Scherrer, 2007; Brown and Gibson, 2011; Hensel et al., 2007; Hirschfelder et al., 2005; Marquardt et al., 2007; Rotter et al., 2008; Scholz et al., 1999) and, to the best of our knowledge, no reports on low-frequency modulated QDPOAEs in humans have been published.

According to the Boltzmann simulation, QDPOAEs are more suitable to detect minute changes of the OP position, because the relation between the shift of the OP and the quadratic distortion amplitude is much steeper around the point of inflection of the transfer function when compared to the cubic distortions (see Fig. 1B). However, QDPOAEs in humans are more difficult to record with moderate stimulus levels because their amplitudes are small and signal-to-noise ratios are less favourable compared to CDPOAEs.

The aim of this study was therefore to compare the properties of low-frequency modulated CDPOAEs and QDPOAEs in humans and to assess the potential of the use of low-frequency modulated QDPOAEs for the differential diagnosis of cochlear pathologies.

2. Methods

2.1. Subjects

Low-frequency modulated DPOAEs were recorded in 22 subjects with normal hearing (14 females, 8 males, mean age 24) in a sound-attenuated booth. Only subjects with hearing thresholds of less than 10 dB HL in all tested frequencies (250–8000 Hz) were included in the study. No history of chronic middle or inner ear diseases was reported. Subjects were only included if tympanometric assessment gave normal results. Tympanometric results were considered to be normal when the peak admittance was found to be between −150 and +100 daPa with a peak amplitude between 0.2 and 2.5 millimhos. All screened subjects fulfilled these criteria and were eligible for the study. Before