Contents lists available at ScienceDirect

Hearing Research

journal homepage: www.elsevier.com/locate/heares

Research paper

Low-frequency sound exposure causes reversible long-term changes of cochlear transfer characteristics

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ARTICLE INFO

ABSTRACT

Intense, low-frequency sound presented to the mammalian cochlea induces temporary changes of cochlear sensitivity, for which the term 'Bounce' phenomenon has been coined. Typical manifestations are slow oscillations of hearing thresholds or the level of otoacoustic emissions. It has been suggested that these alterations are caused by changes of the mechano-electrical transducer transfer function of outer hair cells (OHCs). Shape estimates of this transfer function can be derived from low-frequency-biased distortion product otoacoustic emissions (DPOAE).

Here, we tracked the transfer function estimates before and after triggering a cochlear Bounce. Specifically, cubic DPOAEs, modulated by a low-frequency biasing tone, were followed over time before and after induction of the cochlear Bounce. Most subjects showed slow, biphasic changes of the transfer function estimates after low-frequency sound exposure relative to the preceding control period. Our data show that the operating point changes biphasically on the transfer function with an initial shift away from the inflection point followed by a shift towards the inflection point before returning to baseline values. Changes in transfer function and operating point lasted for about 180 s. Our results are consistent with the hypothesis that intense, low-frequency sound disturbs regulatory mechanisms in OHCs. The homeostatic readjustment of these mechanisms after low-frequency offset is reflected in slow oscillations of the estimated transfer functions.

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1. Introduction

Intense low-frequency (LF) sound causes slowly oscillating fluctuations of cochlear sensitivity occurring after stimulation offset. This was first noticed in early experiments with human subjects where the hearing threshold was tracked after loud LF sound exposure as a function of time. A period of brief threshold desensitisation was followed by a temporary sensitisation, for which the term 'Bounce' phenomenon was coined (Hirsh and Ward, 1952; Hirsh and Bilger, 1955). Biophysical measurements of evoked

and spontaneous otoacoustic emissions (OAE) in humans and animals revealed a similar trend and showed that OAE levels oscillate with a pattern resembling a very slow, damped, sinusoidal oscillation (Drexl et al., 2014; Kemp, 1986; Kemp and Brill, 2009; Kevanishvili et al., 2006; Kirk and Patuzzi, 1997; Kirk et al., 1997; Kugler et al., 2014). This indicates that the Bounce phenomenon is not a neural phenomenon, but rather a reflection of LF-induced changes in cochlear physiology. In addition, results from animal experiments showed that the Bounce phenomenon can still be detected in measures of cochlear sensitivity, despite temporary blockage of auditory nerve and middle ear muscle activity (Kirk and Patuzzi, 1997; Kirk et al., 1997). Hence, the Bounce phenomenon is clearly of cochlear origin. As a hypothesis, the LF-induced changes of cochlear sensitivity could be interpreted as operating point (OP) changes along the mechano-electrical transducer (MET) transfer function of outer hair cells (OHCs) (Drexl et al., 2014). Changes of the OP (e.g. by changes of the average deflection angle of the OHC

stereocilia, or the opening probability of the mechano-electrical transduction channels) lead to changes of cochlear gain and compression. Such changes can directly affect cochlear physiological measures, e.g. cochlear potentials or OAEs, but will consequently also affect neural and perceptual measures of auditory function (Drexl et al., 2014; Hirsh and Ward, 1952; Hirsh and Bilger, 1955). In animal models, it was shown that the MET transfer functions of OHCs after LF exposure are different from pre-exposure (Kirk et al., 1997), but MET transfer function changes have never been tracked during the Bounce phenomenon in humans.

Direct measurements of cochlear transfer functions are not possible in humans, but indirect measures are available (Bian and Scherrer, 2007). Stimulating the cochlea with intense LF sounds leads to slow, cyclic movements of the cochlear partition. It has been suggested that as a result, the OP slowly shifts along the sigmoidal transfer function of the MET (Abel et al., 2009; Bian and Scherrer, 2007, 2002; Brown and Gibson, 2011; Brown et al., 2009; Frank and Kossl, 1996, 1997; Lukashkin and Russell, 2005), coupled to the phase of the low-frequency biasing tone (BT). When distortion product otoacoustic emissions (DPOAEs) are measured during this procedure, DPOAE levels will be affected by the slowly varying OP which results in typical LF- modulated DPOAEs patterns. As an alternative explanation, Brown and Gibson (2011) suggested that the sensitivity to the primary tones might change during the biasing.

Based on the assumption that DPOAE generation is dominated by one single, saturating non-linearity, the underlying transfer function of the modulation patterns can be extracted (Bian et al., 2002). DPOAEs measured in the ear canal are likely to be the result of a vector summation of emissions originating from more than one source in the cochlea (Lukashkin and Russell, 2005). Nonetheless, 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 disturb such patterns (Lukashkin and Russell, 2005), but it has been shown that DPOAE amplitude modulation patterns can be accurately predicted by a single, saturating non-linearity (Bian and Scherrer, 2007, 2002; Brown and Gibson, 2011; Brown et al., 2009; Drexl et al., 2012; Lukashkin and Russell, 2005). Therefore, it can be assumed that DPOAEs measured in the ear canal, at least for the parameters used in this study, are dominated by one single, saturating non-linearity such as the sigmoidal MET transfer function, which is the model we chose for this paper.

Patuzzi (2011) suggested that the manifestations of the Bounce can be explained by slow shifts of the OP on the MET function. Here, we show changes of DPOAE modulation patterns and derived estimated MET transfer functions during the Bounce phenomenon.

It must be pointed out that the current experimental paradigm incorporates a potential interference of our experimental manipulation with the measure we use to quantify the effect of that manipulation. Specifically, intense LF sounds are required both to elicit the Bounce and to estimate the MET transfer functions. Indeed, our results indicate that repeated estimates of the MET transfer function changes the transfer function itself due to the fact that the LF sound that is required to estimate the transfer function induces a (smaller magnitude) Bounce itself.

2. Methods

2.1. Stimulus generation and data acquisition

Human subjects were seated in a comfortable recliner situated in a sound-attenuated booth during all experimental procedures and were advised to remain still and quiet during measurements. OAEs were recorded with an ER-10C DPOAE probe system

(Etymōtic Research Inc., Elk Grove Village, IL, USA). Signal generation and data acquisition was carried out with a RME Fireface UC 24-bit external sound card (RME, Audio AG, Haimhausen, Germany), operated with a sampling rate of 44.1 kHz and a buffer size of 512 bits. The recorded signal was amplified 30 dB by the preamplifier of the external soundcard. The external sound card was controlled by scripts written in MatLab 7.5 (MathWorks, Natick, MA, USA) and run on an ASUS G60 VX laptop (ASUSTeK Computer Inc., Taipei, Taiwan). The SoundMexPro sound application (HörTech, Oldenburg, Germany) was employed to use low-latency multi-channel ASIO interfacing in the MatLab environment. Foam ear tips supplied by Etymōtic Research (Etymōtic Research Inc., Elk Grove Village, IL, USA) were used to seal the probe into the ear canal of the subjects. The ear tips were modified to accommodate the LF-tone supply channel, which was produced by an NSW1-205-8A 1" loudspeaker (Aura Sound Inc., Santa Fe Springs, CA, USA). This loudspeaker was coupled to a 50 cm long polyethylene tube (inner diameter 1 mm) fed through the ear tip and was driven by a RB-960BX power amplifier (Rotel, Worthing, UK).

DPOAE modulation patterns were measured with two primary tones to evoke a cubic ($2f_1$-f_2) DPOAE and a LF tone to bias the DPOAE.

One acquisition period for a transfer function estimate lasted 6 s during which all three tones were continuously presented with raised-cosine on- and offset gates of 100 ms. Acquisition periods were concatenated with only very short gaps of 0.7 s. The two DPOAE primary tones, f_1 and f_2, had sound levels of 50 and 60 dB SPL and frequencies of 1639 and 2000 Hz (ratio 1.22), respectively. The BT had a sound level of 110 dB SPL and a frequency of 30 Hz.

In the experimental condition, DPOAE modulation patterns were recorded immediately before (25 recordings with a duration of 6 s each, pre-exposure period) and immediately after (45 recordings, post-exposure period) presentation of a continuous, intense, LF sound (90s, 30 Hz, 120 dB SPL), resulting in total recording duration of about 560 s. In the control condition, the same sequence of stimuli was used, but the LF sound was replaced by an equal-length period of silence and, consequently, the periods before and after the gap will be referred to as the pre-gap- and post–gap period, respectively, in the following. This control condition tested whether the BT alone was able to induce the Bounce phenomenon.

2.2. Analysis

The LF-biased cubic DPOAE ($2f_1$-f_2) is an amplitude-modulated signal. Therefore, the DPOAE frequency can be regarded as the carrier frequency of this signal flanked by modulation sidebands at the DPOAE frequency ± integer multiples of the BT frequency (Marquardt et al., 2007). The DPOAE spectral line and the first- and second-order sidebands were extracted from the complex spectrum. The inclusion of higher-order sidebands yielded no additional information and added only noise to the signal. Data from an acquisition interval were only accepted when the magnitudes of these five spectral lines were at least 3 dB above the noise floor. Inverse Fourier transformation and a subsequent Hilbert Transform resulted in the time-variant amplitude of the DPOAE as a function of the BT phase (Bian and Scherrer, 2007; Drexl et al., 2012; Hensel et al., 2007; Marquardt et al., 2007).

As DPOAE modulation patterns in humans over a full BT cycle tend to be slightly asymmetric, DPOAE amplitude modulation patterns corresponding to the rising or falling half-cycle of the BT had to be used separately for fitting. As the results obtained from both half cycles were qualitatively very similar (representative examples are shown in Fig. 5), only the results based on the modulation patterns corresponding to one half cycle (the rising half) of