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Research paper

Forward and reverse transfer functions of the middle ear based on pressure and velocity DPOAEs with implications for differential hearing diagnosis

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ABSTRACT

Recently it was shown that distortion product otoacoustic emissions (DPOAEs) can be measured as vibration of the human tympanic membrane *in vivo*, and proposed to use these vibration DPOAEs to support a differential diagnosis of middle-ear and cochlear pathologies. Here, we investigate how the reverse transfer function (r-TF), defined as the ratio of DPOAE-velocity of the umbo to DPOAE-pressure in the ear canal, can be used to diagnose the state of the middle ear. Anaesthetized guinea pigs served as the experimental animal. Sound was delivered free-field and the vibration of the umbo measured with a laser Doppler vibrometer (LDV). Sound pressure was measured 2–3 mm from the tympanic membrane with a probe-tube microphone. The forward transfer function (f-TF) of umbo velocity relative to ear-canal pressure was obtained by stimulating with multi-tone pressure. The r-TF was assembled from DPOAE components generated in response to acoustic stimulation with two stimulus tones of frequencies f_1 and f_2; f_2/f_1 was constant at 1.2. The r-TF was plotted as function of DPOAE frequencies; they ranged from 1.7 kHz to 23 kHz. The r-TF showed a characteristic shape with an anti-resonance around 8 kHz as its most salient feature. The data were interpreted with the aid of a middle-ear transmission-line model taken from the literature for the cat and adapted to the guinea pig. Parameters were estimated with a three-step fitting algorithm. Importantly, the r-TF is governed by *only* half of the 15 independent, free parameters of the model. The parameters estimated from the r-TF were used to estimate the other half of the parameters from the f-TF. The use of r-TF data – in addition to f-TF data – allowed robust estimates of the middle-ear parameters to be obtained. The results highlight the potential of using vibration DPOAEs for ascertaining the functionality of the middle ear and, therefore, for supporting a differential diagnosis of middle-ear and cochlear pathologies.

1. Introduction

With the discovery of otoacoustic emissions (OAE) by Kemp (1978) the hope emerged that the functional state of the cochlea could be diagnosed objectively and reliably (Probst et al., 1991; Shera, 2004). Indeed, research on OAE has steadily driven our understanding of cochlear mechanics and especially the so-called cochlear amplifier (Allen and Fahey, 1992; de Boer et al., 2005; Shera and Guinan, 2007; Dong and Olson, 2008). Today, OAEs are used routinely in ENT clinics to assess cochlear status. However, specificity or accuracy of OAE-based diagnosis leaves more to be desired than initially hoped. There are several reasons for this concern. First, OAEs are usually measured in an acoustically sealed ear canal with a measuring microphone coupled to a probe tube with tip located at a distance of about 20 mm from the tympanic membrane. Standing waves in the closed ear canal, particularly evident over such a long (acoustical) distance, can cause measurement errors of 10–20 dB for frequencies more than a few kHz (Siegel, 2002). Errors of such magnitude are of considerable importance because cochlear impairment usually begins at high frequencies. In addition, under sealed conditions, the measured OAE can also be influenced significantly by the acoustic input impedance of the measurement system (Kemp, 1978; Farmer-Fedor and Rabbitt, 2002). Second, the state of the middle ear contributes considerably to the measured OAE, because it is passed twice – in the forward direction by the stimuli and in the reverse direction by

Abbreviations: CAP, compound action potential; CV, coefficient of variation; DPOAE, distortion product otoacoustic emission; EDPT, estimated distortion product threshold; f-TF, forward transfer function, defined as the ratio of umbo velocity to ear-canal pressure when driven in the forward direction by sound; I/O function, input/output function; LDV, laser Doppler vibrometer; OAE, otoacoustic emission; SD, standard deviation; SNR, signal-to-noise ratio; r-TF, reverse transfer function, defined as the ratio of umbo velocity to ear-canal pressure when driven in the reverse direction by OAEs from the cochlea.

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the emitted OAEs. Thus, variation of middle-ear function, due to inter-subject variability or pathology, limits the accuracy of OAE-based diagnostics (Gehr et al., 2004; Kummer et al., 2006; Keefe and Abdala, 2007).

In the clinical routine, use of an OAE relies typically on the measurement of OAE amplitude in response to a predefined stimulus level. In the last few years, extrapolation of input-output (I/O) functions of distortion product otoacoustic emissions (DPOAE) has been introduced to objectively estimate hearing threshold (Boege and Janssen, 2002; Gorga et al., 2003; Schmuziger et al., 2006). For a given frequency of the second primary tone, extrapolation has been of a semi-logarithmic plot of DPOAE amplitudes to 0 Pa to estimate the minimum level of the secondary primary required to yield a DPOAE; this level is called the estimated distortion product threshold (EDPT) and is correlated with hearing threshold. This approach has the advantage that because of the properties of the stimulus paradigm used (Kummer et al., 1998, 2000) and the essentially nonlinear extrapolation procedure (Boege and Janssen, 2002), ideally neither the absolute stimulus levels nor the absolute emission levels contribute directly to the EDPT. Therefore, middle-ear transmission does not affect the accuracy of the EDPT, at least to a first approximation.[1] Indeed, based on the EDPT, hearing threshold can be estimated with reasonable accuracy, achieving standard deviations ranging from 6.6 to 10.9 dB (Boege and Janssen, 2002; Gorga et al., 2003; Turcanu et al., 2009), depending on measurement technique. The premise is that "neural" pathologies are excluded, which in the following should be understood to be located "behind" the cochlear amplifier in the acoustic signal processing chain and, therefore, would preclude, for example, assessing damage of the inner hair cell system (Turcanu et al., 2009). However, even under that premise, EDPTs do not exclusively diagnose cochlea function. While, to a first approximation, the accuracy of the EDPT and, therefore, of the hearing threshold estimate are not affected by middle-ear transmission, their absolute values are definitely influenced. Therefore, considering the diagnostic needs, the situation is still not ideal.

If one were able to estimate middle-ear transmission in the forward direction with sufficient accuracy, a reliable cochlear diagnosis would be within reach because the middle-ear loss component could be subtracted from the threshold loss estimated from the DPOAEs to yield the cochlear loss (but excluding purely "neural" losses). Recently, we have shown using an LDV with sub-picometre sensitivity that DPOAEs can also be measured as vibration of the umbo in humans (Dalhoff et al., 2007) and animals (Turcanu et al., 2009). Here, we investigate the possibility of using umbo *vibration* DPOAEs to estimate middle-ear transmission in individuals. To this end, a middle-ear model was fitted to measurements of the forward transfer function (f-TF) of umbo velocity relative to stimulus sound pressure and to the corresponding reverse transfer function (r-TF), evaluated as the velocity DPOAE relative to the pressure DPOAE. While the complete middle-ear transfer function influencing hearing threshold should be evaluated strictly between ear-canal pressure and vestibule fluid pressure (or, alternatively, stapes velocity), knowledge of these two transfer functions should considerably assist in estimating the parameters governing middle-ear transfer. We make this assertion because in the sense of the number of middle-ear modeling parameters, the umbo may be viewed as lying somewhere midway between ear-canal pressure and stapes velocity. In this sense, in most sophisticated lumped-element models, as well as in a more recent hybrid model of the middle ear, the number of independent parameters between ear-canal pressure and umbo velocity is approximately half of the number of parameters between ear-canal pressure and stapes velocity[2] [10 versus 18 in Goode et al. (1994) and seven versus 15 in Puria and Allen (1998)]. Here, we show that use of the r-TF, derived from vibration measurements of DPOAEs on the umbo, allows robust estimates of model parameters of an individual middle ear and discuss how this information might be used for differential diagnosis of middle-ear and cochlear pathologies.

Different aspects of this work were presented in preliminary form at the 31st ARO Midwinter Research Meeting, Phoenix, in 2008 (Dalhoff et al., 2008) and the Mechanics of Hearing Meeting, Keele, in 2009 (Dalhoff et al., 2009).

2. Material and methods

2.1. Animals

Twelve normal hearing guinea pigs from our breeding house are included in the analysis; body weight was 350–650 g. Normal hearing was defined by (i) presence of Preyer's reflex, (ii) otoscopic examination of the tympanic membrane, (iii) normal compound action potential (CAP) frequency threshold curve (FTC) for tone-pip stimulation, and (iv) normal umbo velocity response (f-TF) for multi-tone stimulation. CAP FTC and f-TF were considered normal if values were within mean $\pm$ 2 SD for all frequencies in the range of 0.5–20 kHz as based on results in Turcanu et al. (2009). The surgical preparation has been described in detail in Turcanu et al. (2009). Briefly, animals were anaesthesized with a mixture of ketamine hydrochloride (50 mg/kg) and xylazine (8 mg/kg). The pinna flange and cartilaginous ear canal were resected to the osseous part of the external auditory canal. Rectal temperature was feedback controlled with a heating pad (38.5 $\pm$ 0.5 °C). The animal's head was fixed with a head-holder and the bulla opened to place a silver electrode on the promotorium for recording the CAP. To preserve the transfer function of the middle ear, the bulla was then closed with dental cement and ventilated by a long thin silicone tube (ID = 0.50 mm, OD = 0.95 mm, length = 70 mm). The side of the microphone probe tube (ID = 0.58 mm, OD = 0.95 mm) was glued onto the wall of the remnant ear canal with Histoacryl®. The insertion depth of the tip was 1.5 mm.

The experiments were approved by the Committee for Animals Experiments of the regional council (Regierungspräsidium) of Tübingen.

2.2. Stimulation and measurement

Acoustic stimulation was delivered free field by two DT 48 earphones (Beyer Dynamic, Heilbronn, Germany). Sound pressure was measured using a probe-tube microphone (ER-7C; Etymotic Research, Elk Grove, IL, USA). Further details are given in Turcanu et al. (2009).

Vibration of the umbo in response to acoustic stimuli was measured with a self-made LDV tailored to measure sub-picometre amplitudes in the presence of relatively large endogenous

[1] If middle-ear transmission is too abnormal, the stimulus paradigm is no longer optimal (Kummer et al., 2006), which will ultimately lead to reduction of estimation accuracy.

[2] These numbers are obtained without counting transformers. The three parameters "behind the footplate"; that is, the compliances of the annular ligament and round window, the cochlear input resistance and the stapes mass, are not counted because they do not load stapes velocity in the reverse direction. This is analogous to the decision to count the elements starting from the middle-ear cavity parameters and not to include parameters describing the load seen by the ear-canal pressure at the tympanic membrane in the reverse direction; that is, the ear-canal impedance and the radiation impedance. Counted are parameters for human – including the incudo-malleolar joint and taking five parameters for the middle-ear cavities.