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Research Paper

Medial olivocochlear efferent reflex inhibition of human cochlear nerve responses

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ABSTRACT

Inhibition of cochlear amplifier gain by the medial olivocochlear (MOC) efferent system has several putative roles: aiding listening in noise, protection against damage from acoustic overexposure, and slowing age-induced hearing loss. The human MOC reflex has been studied almost exclusively by measuring changes in otoacoustic emissions. However, to help understand how the MOC system influences what we hear, it is important to have measurements of the MOC effect on the total output of the organ of Corti, i.e., on cochlear nerve responses that couple sounds to the brain. In this work we measured the inhibition produced by the MOC reflex on the amplitude of cochlear nerve compound action potentials (CAPs) in response to moderate level (52–60 dB peSPL) clicks from five, young, normal hearing, awake, alert, human adults. MOC activity was elicited by 65 dB SPL, contralateral broadband noise (CAS). Using tympanic membrane electrodes, approximately 10 h of data collection were needed from each subject to yield reliable measurements of the MOC reflex inhibition on CAP amplitudes from one click level. The CAS produced a 16% reduction of CAP amplitude, equivalent to a 1.98 dB effective attenuation (averaged over five subjects). Based on previous reports of efferent effects as functions of level and frequency, it is possible that much larger effective attenuations would be observed at lower sound levels or with clicks of higher frequency content. For a preliminary comparison, we also measured MOC reflex inhibition of DPOAEs evoked from the same ears with f_2's near 4 kHz. The resulting effective attenuations on DPOAEs were, on average, less than half the effective attenuations on CAPs.

1. Introduction

To enhance the sensitivity and frequency selectivity of hearing, sound-evoked cochlear mechanical vibrations are amplified within the cochlea. This “cochlear amplification” is under central control via the medial olivocochlear (MOC) efferent system. MOC efferent fibers synapse on, and inhibit, outer hair cell responses thereby reducing cochlear-amplifier gain. In humans, MOC inhibition has mostly been studied with measurements of otoacoustic emissions (OAEs) (see Guinan, 2006; for review). OAEs provide an indirect measure of MOC effects on cochlear mechanics but do not reveal the MOC effects on the cochlear neural responses that mediate hearing. Several reports presented measurements of MOC effects on cochlear neural responses in humans (Folsom and Owsley, 1987; Kawase and Takasaka, 1995; Chabert et al., 2002). However, each of these reports has issues that prevent it from giving a clear picture of MOC effects on cochlear neural output in awake, alert, normal-hearing humans. Indirect measurements of MOC inhibition have been made psychophysically (e.g., Kawase et al., 2000; Aguilar et al., 2013; Wicher and Moore, 2014; Strickland, 2001, 2004, 2008; Wojtczak et al., 2014; Jennings et al., 2009; Roverud and Strickland, 2010; Yasin et al., 2014). But, psychophysical measurements are confounded by the possibility that the MOC reflex, the sound used to elicit MOC reflex, or the attention required for the psychophysical measurements, may change signal processing in the brain as well as in the cochlea (Keefe et al., 2009; Wittekindt et al., 2014). To understand the roles of the MOC reflex in human hearing, it is necessary to know the extent to which the MOC reflex inhibits responses from the cochlear nerve and to do this direct

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measurements of cochlear-nerve responses are needed.

Here we set out to obtain statistically significant measurements of human cochlear-nerve compound action potentials (CAP) responses without and with MOC activity elicited by contralateral noise. CAP responses from a single click level were measured from auditory-brainstem response (ABR) wave I recorded with a tympanic membrane electrode. To achieve adequate accuracy, this required extensive measurements done over five two-hour sessions for each subject. After the CAP data had been obtained, we did a brief set of measurements of MOC effects on distortion-product OAEs (DPOAEs) from the same ears as a preliminary step in a secondary goal of comparing MOC effects on CAPs and OAEs.

2. Methods

2.1. Methods overview

CAP measurements were made from the first negative peak in the ABR waveform recorded with an electrode placed on the tympanic membrane (Lichtenhan and Chertoff, 2008; Chertoff et al., 2010). The MOC reflex was activated by contralateral acoustic stimulation (CAS) that was alternated on and off across runs. In five subjects, the MOC-induced change on CAPs was measured at one sound level as the percentage change in CAP amplitude from the no-CAS to the with-CAS condition. We refer to these five subjects as "CAS-on-CAP subjects". In each of these subjects CAP measurements were averaged over multiple (five) two-hour visits to the lab to achieve an adequate signal-to-noise ratio. The percent change in the CAP amplitude was translated into effective attenuation using the slope of the change in CAP amplitude with sound level averaged from 19 subjects and, in three of the five CAS-on-CAP subjects, using the slope from the individual ears. Effective attenuation is the amount that the probe sound level would have to be raised with MOC inhibition to obtain the same response amplitude that was obtained without MOC inhibition. Effective attenuation is a constant-response metric that allows changes in different measured quantities to be compared along the same sound-level axis. In contrast, the percentage change metric is greatly affected by nonlinearities such as those in the inner hair cell to auditory-nerve synapse. Thus, for comparing changes in CAPs and OAEs, effective attenuation is the preferred metric.

During the CAS-on-CAP subjects' sixth visit to the lab, we measured their middle-ear-muscle reflex (MEMR) thresholds and made DPOAE measurements with and without CAS from which we calculated MOC-reflex-induced DPOAE effective attenuations.

Stimulus calibration, stimulus generation, and data acquisition were performed with a National Instruments PXI-1031 chassis and the Eaton-Peabody Laboratories Cochlear Function Test Suite (http://www.masseyeandear.org/research/otolaryngology/investigators/laboratories/eaton-peabody-laboratories/epl-engineering-resources/). Custom written software in MATLAB (MathWorks) was used for offline analyses. All procedures were approved by the Institutional Review Board of Washington University in St. Louis.

2.2. CAP measurements with and without CAS

Hearing sensitivity of prospective subjects was assessed with a 20 dB HL hearing screening at 0.5, 1, 2, and 4 kHz using a calibrated audiometer (Earscan, Micro Audiometrics Corp.). Subjects were accepted only if they could hear the 20 dB HL tones. CAP amplitudes measurements were made with an electrode placed on the right tympanic membrane (non-inverting; Lilly TM-Wick Electrode, Intelligent Hearing Systems), and surface electrodes placed on their high forehead (inverting) and contralateral mastoid (ground). Following an extensive pilot study, we learned that our subject recruitment must screen for an ability to remain exceptionally still with the tympanic membrane electrode in place, an ability to stay awake and mentally alert while comfortably reclined in a dark room, and the discipline to return for multiple two-hour sessions. Only five subjects (four females and one male, 18–25 years old) were able to complete these experiments. Since sleep has been reported to reduce MOC effects (Froehlich et al., 1993), the experimenter kept subjects awake and aroused by asking questions between runs, instructing the subject to silently formulate answers during the run, and then asking the subject to speak their answers to the experimenter at the end of each run (communicating using a battery powered baby monitoring system). This is referred to as "tasking". Subjects sat reclined in a double-walled sound-treated room for all measurements.

Alternating condensation and rarefaction clicks were presented at 11.1/sec through a free-field loudspeaker (A'Diva Ti, Anthony Gallo Acoustics) powered by an amplifier (CT475 Drivecore, Crown). We avoided high-rate clicks because they produce CAP adaptation. If MOC inhibition reduces the firing rate of an adapted synapse, the adaptation will decrease which increases the CAP amplitude and partially erases the MOC-induced reduction in the response. Thus, the click repetition rate was kept low to avoid CAP adaptation and allow accurate measurement of the MOC effect. A measuring device ensured that the distance between the loudspeaker and ears did not vary. The loudspeaker was placed such that the click arrived at the ear canal 4 ms after the electric pulse to the loudspeaker, which resulted in a 4 ms baseline measurement before any possible CAP response. The clicks were monitored with a ½″ microphone (Larson-Davis model 378B02) strapped to the subject's head and positioned near the entrance of the ipsilateral ear canal. The loudspeaker produced clicks with a quick decay and very little ringing (Fig. 1).

CAPs and associated acoustic click sound pressure waveforms were simultaneously measured over response epochs of 15 ms, sampled at 25 kHz, and saved to disk. CAPs were band pass filtered at 0.1–3 kHz (GRASS P511, Astro-Med, Inc.) and amplified 10,000 times. CAP artifact rejection thresholds on individual traces ranged from 15 to 45 μV and were adjusted according to each subject's noise level. Separate averages were kept for positive and negative clicks; averaging the two together yielded the CAP, and subtracting the negative-click average from the positive-click average yielded

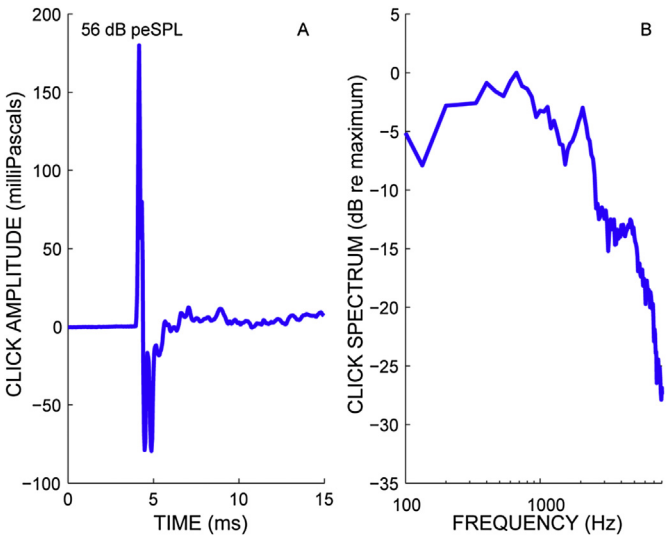

Fig. 1. The average waveform (A) and spectrum (B) of the click stimulus.

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