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Research Paper

Low-frequency bias tone suppression of auditory-nerve responses to low-level clicks and tones

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ABSTRACT

We used low-frequency "bias" tones (BT's) to explore whether click and tone responses are affected in the same way by cochlear active processes. In nonlinear systems the responses to clicks are not always simply related to the responses to tones. Cochlear amplifier gain depends on the incremental slope of the outer-hair-cell (OHC) stereocilia mechano-electric transduction (MET) function. BTs transiently change the operating-point of OHC MET channels and can suppress cochlear-amplifier gain by pushing OHC METs into low-slope saturation regions. BT effects on single auditory-nerve (AN) fibers have been studied on tone responses but not on click responses. We recorded from AN fibers in anesthetized cats and compared tone and click responses using 50 Hz BTs at 70–120 dB SPL to manipulate OHC stereocilia position. BTs can also excite and thereby obscure the BT suppression. We measured AN-fiber response synchrony to BTs alone so that we could exclude suppression measurements when the BT synchrony might obscure the suppression. BT suppression of low-level tone and click responses followed the traditional pattern of twice-a-BT-cycle suppression with more suppression at one phase than the other. The major suppression phases of most fibers were tightly grouped with little difference between click and tone suppressions, which is consistent with low-level click and tone responses being amplified in the same way. The data are also consistent with the operating point of the OHC MET function varying smoothly from symmetric in the base to offset in the apex, and, in contrast, with the IHC MET function being offset throughout the cochlea. As previously reported, bias-tones presented alone excited AN fibers at one or more phases, a phenomena termed "peak splitting" with most BT excitation phases ~¼ cycle before or after the major suppression phase. We explain peak splitting as being due to distortion in multiple fluid drives to inner-hair-cell stereocilia.

1. Introduction

The current conception of cochlear mechanics attributes the high sensitivity and frequency selectivity of the cochlea to amplification of cochlear mechanical responses by outer hair cells (OHCs). Movement of the basilar membrane (BM) results in deflections of OHC stereocilia and mechano-electric transduction (MET) in these stereocilia gives rise to current flow that changes OHC voltage and drives OHC somatic motility. If the resulting OHC motion is in the right phase relative to BM motion, it injects energy on a cycle-by-cycle basis into the traveling wave and amplifies the cochlear mechanical response. This process is termed "cochlear amplification." OHC-stereocilia MET functions have saturating nonlinearities. Large stereocilia deflections into low-slope regions of the OHC MET functions reduces cochlear amplification. As sound level is increased, the oscillatory deflections of OHC stereocilia spend more time in low-slope regions, which reduces overall cochlear-amplifier gain. This reduction in gain as sound level is increased produces the compressive amplitude vs. sound-level functions of BM motion.

One line of evidence for the above scenario comes from the effect of very-low-frequency "bias" tones on cochlear responses. If the bias-tone level is high enough, the response to it can transiently push OHC stereocilia into low-slope "saturation" regions of the OHC MET function. If a low-frequency bias tone is presented

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simultaneously with a probe tone that is of higher frequency and receives cochlear amplification, then during the part of the bias-tone cycle when the OHC stereocilia are in a low-slope MET region, OHC deflections from the probe tone produce smaller changes in probe-frequency OHC current than the OHC current changes without the bias tone. The net effect is that the bias tone decreases cochlear amplification of the probe-tone response whenever the bias tone moves OHC stereocilia into low-slope regions at the high-deflection edges of the OHC MET function. If the OHC MET function is asymmetric, one low-slope MET edge is reached at a lower sound level than the other, which results in one gain reduction per bias-tone cycle. At higher bias-tone levels, the stereocilia deflections reach the low-slope regions on both ends of the MET function and there are two gain reductions per cycle. Many experiments have produced evidence consistent with this scenario (Sachs and Hubbard, 1981; Sellick et al., 1982; Javel et al., 1983; Patuzzi et al., 1984a,b; Rhode and Cooper, 1993; Cooper, 1996; Cai and Geisler, 1996a, 1996b; Rhode, 2007).

The cochlea is a nonlinear system and the effect of the bias tone is one manifestation of this nonlinearity. There have been many tests of bias-tone effects on tone responses (referenced above), but there are no data on bias tone effects on auditory-nerve (AN) fiber responses to clicks. In a nonlinear system, click responses cannot always be predicted from tone responses. Although a variety of measurements show a concordance between cochlear tone and click responses (e.g. Recio et al., 1998; Kalluri and Shera, 2007) not all such measurements concur. In AN-fiber responses to clicks, Lin and Guinan (2004) found that the decaying oscillations in click skirts (the longest latency part of the click response) were sometimes not at the tone characteristic frequency (CF) even when tone and click oscillatory amplitudes were similar. This suggests that there may be differences between cochlear mechanical operation for click and tone responses. In another line of experiments, Sininger and Cone-Wesson (2004) reported that otoacoustic emissions (OAEs) evoked by tones (distortion product OAEs (DPOAEs)) were larger than OAEs from clicks (CEOAEs) in the left ear, but the opposite was true in the right ear. Although this result has been questioned (Keefe et al., 2008), it is consistent with there being differences in the cochlear mechanisms for click and tone responses.

Our primary goal was to determine whether the cochlear-amplifier processes that enhance low-level responses are affected by bias tones in similar ways for tone and click responses. This was done by measuring bias-tone effects on AN single-fiber tone and click responses. Previous reports of bias-tone effects on AN single-fiber tone responses relied on visual inspection of AN response histograms to determine the presence of bias-tone synchrony and the phase of maximal suppression. A secondary goal of our work was to develop and use objective, quantitative methods for determining the presence of suppression and the phase of maximal suppression.

2. Materials and methods

2.1. Methods overview and rationale

Bias-Tone (BT) effects were measured by presenting the BT simultaneously with either clicks or tones, and determining AN single-fiber click and tone responses at different times during the BT period. The BT itself may excite AN responses when it is high enough in sound level, and these BT excitatory responses may obscure BT suppression of click or tone responses. Thus, an initial task was to determine the sound level at which the BT itself excites responses, and then to exclude such BT levels from further consideration. The rationale for this is that the bias-tone effects of interest are the BT effects on OHCs that change the cochlear amplification of click and tone responses. Deflections of OHCs stereocilia are directly coupled to displacements at the top of the organ of Corti because OHC stereocilia are imbedded in the tectorial membrane (TM). In contrast, inner-hair-cell (IHC) stereocilia are freestanding. For low-frequency stimulation (such as BTs), IHCs are sensitive to the velocity of the fluid flow in the sub-tectorial space (Sellick and Russell, 1980; Freeman and Weiss, 1990; Guinan, 2012). As a result, for low-frequency BTs (which produce low-velocity responses), the mechanical drive to IHCs is greatly reduced compared to the mechanical drive to OHCs. Thus, there can be BT levels at which the BT significantly deflects OHC stereocilia while at the same time the BT produces minimal deflections of IHC stereocilia. A major task of our methods is to distinguish when this is true vs. when the BT significantly affects the IHC receptor potential and thus affects the AN firing pattern.

2.2. Animal preparation

We report here on recordings made from 92 single AN fibers from 14 anesthetized cats using methods approved by the Massachusetts Eye and Ear Infirmary animal care committee. The surgical approach and methods for animal anesthesia, monitoring animal health during experiments and recording from AN fibers were similar to those described previously (Stankovic and Guinan, 1999; Lin and Guinan, 2000; Guinan et al., 2005). Briefly, animals were anesthetized with Nembutal in urethane. Booster doses were given as indicated by toe-pinch reflex, heart rate and breathing rate. The rectal temperature was maintained at ~38 °C and fluid balance was maintained by dripping lactated ringers into a leg vein. On both sides, the ear-canals were truncated for insertion of acoustic assemblies and the bulla cavities were exposed to reveal the round windows. A silver electrode near each round window was used to measure cochlear compound action potentials (CAPs). An automated tone-pip audiogram was run from 2 to 32 kHz at octave intervals using a CAP criterion of 10 μV pp. Tone pip audiograms were run approximately every hour, and also after obtaining a useful, high-quality data series in order to ensure that the cochlea was in good health. For units with CFs >2 kHz, all tone-pip thresholds (evaluated at unit CF by interpolation of the audiogram data versus frequency) were within 20 dB of the tone-pip-threshold curve made from good animals. For units with CFs <2 kHz, all but 4 units had thresholds at 2 kHz and above that were within 20 dB of the good-threshold curve and the remaining 4 units were within 27 dB at 2 kHz and within 20 dB above 2 kHz. A posterior craniotomy was followed by aspiration and retraction of cerebellar tissue to expose the AN. Single AN fibers were recorded from using electrolyte-filled pipette electrodes (10–20 MΩ impedance) inserted into the visually-identified AN.

Upon isolating an AN fiber, a threshold tuning curve (TC) was obtained, the characteristic frequency (CF) was determined, and the spontaneous rate (SR) was measured from a 20 s recording with no stimulus. Next AN responses to the BT were obtained using the “BT-alone” paradigm. From these responses we determined BT levels at which the BT alone produced a response that indicated this BT level might obscure suppression. BT effects vary from fiber to fiber, so the BT-alone paradigm was run on every fiber. After this, the BT was paired with clicks or tones at CF using the “BT-on-clicks” or BT-on-tone” paradigms. Click and tone thresholds are required for these paradigms, so before running them, we obtained click and tone thresholds. Due to limited contact time for most AN fibers, not all of the paradigms were run on every fiber.