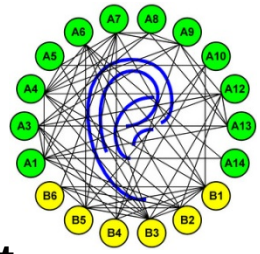
Sonderforschungsbereich/Transregio 31 “Das aktive Gehör”

E I N L A D U N G

zum Vortrag im Rahmen des Seminars des SFB/TRR 31



Freitag, 18. November 2011, 13:00 Uhr c.t.

im Raum W2 1-143 der Universität Oldenburg
und Raum H28 / R 2.31 med. Campus Magdeburg,
(per Videoübertragung)

“Exploring the molecular machinery of the cochlear amplifier through exploiting genetically modified mice”

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The remarkable power amplifier of the cochlea boosts low-level and compresses high-level vibrations of the basilar membrane. By contributing maximally at the characteristic frequency of each point along its length, the amplifier ensures the exquisite sensitivity, frequency tuning and enormous dynamic range of the mammalian cochlea.

The motor protein prestin in the outer hair cell lateral membrane is a prime candidate for the cochlear power amplifier. The other contender for this role is the ubiquitous calcium-mediated motility of the hair cell stereocilia, which has been demonstrated in vitro and is based on fast adaptation of the mechanoelectrical transduction channels. We measured acoustically and electrically elicited basilar membrane displacements from the cochleae of wild-type and Tecta $^{\Delta ENT/\Delta ENT}$ mice, in which stereocilia are unable to contribute to amplification near threshold. Electrically elicited responses from Tecta $^{\Delta ENT/\Delta ENT}$ mice were markedly similar to acoustically and electrically elicited responses from wild-type mice. We concluded that somatic, and not stereocilia, motility is the basis of cochlear amplification.

Absence of prestin from outer hair cells results in a 40-60 dB reduction in cochlear neural sensitivity but sound-evoked basilar membrane vibrations in the high frequency region of prestin$^{-/-}$ mice cochleae are, surprisingly, as sensitive as those of their wild type siblings. The basilar membrane vibrations of prestin$^{-/-}$ mice are, however, broadly tuned to a frequency ~ a half octave below the characteristic frequency of wild type mice at similar basilar membrane locations. The peak sensitivity of wild type basilar membrane tuning curves matches the neural thresholds. In contrast, prestin$^{-/-}$ basilar membrane tuning curves at their best frequency are > 50 dB more sensitive than the neural responses. We propose the absence of prestin from outer hair cells changes the passive impedance of the cochlear partition reducing its stiffness and that prestin influences the dynamic properties of the cochlear partition to permit transmission of its vibrations into neural excitation. Prestin is crucial for defining sharp and sensitive cochlear frequency tuning by reducing the sensitivity of the low-frequency tail of the tuning curve although this necessitates a cochlear amplifier to determine the narrowly tuned tip.

We further hypothesised that Prestin evolved for amplifying and mechanically coupling the tuned vibrations of the basilar membrane to the organ of Corti. This extrinsic mechanical tuning greatly extends the auditory frequency range of mammals beyond those of other vertebrates with intrinsically tuned hair cells. Electrical and mechanical measurements from cochleae of mice with prestin specific mutations support this hypothesis.