Dynamic regulation of the cochlea amplifier in response to contralateral noise

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Contralateral suppression (CS), the reduction in hearing sensitivity in one ear when sound is delivered to the opposite ear, is a well described within auditory neuroscience research. We know that the reduction in hearing sensitivity arises from inhibition of auditory transduction in the cochlear outer hair cells (OHCs) mediated by the medial olivocochlear (MOC) efferent pathway. Contralateral sound stimulation activates MOC neurons in the superior olivary complex in the brainstem. This MOC activation then causes hyperpolarization of OHCs in the other cochlea via unique $\alpha 9$ / $\alpha 10$ nicotinic acetylcholine receptor synapses, leading to increased thresholds. Sensory input from either type I spiral ganglion neurons (SGN) which make up 95% of the cochlear sensory fibres and synapse with inner hair cells, or type II SGN (the remaining 5%), innervating the OHCs must be involved in mediating this MOC activation. There is, however, still the major unanswered question of how sensory input drives CS.

Our experiments have studied the frequency dependence of CS in WT mice as well as utilizing a peripherin ($Pph^{-/-}$) knockout mouse model to investigate the potential contribution of type II SGN to CS. Pph is a type III intermediate filament expressed by type II SGN but not type I SGN, and development of these neurons has been shown to be affected by loss of Pph expression (Barclay *et al.*, 2011). We therefore tested whether type II SGN innervation of OHC was affected in $Pph^{-/-}$ mice, and if so, whether this was associated with altered CS. Using CtBP2 / Ribeye immunofluorescence to identify the ribbon synapses, OHC innervation (number and position) was compared between $Pph^{-/-}$ and WT control mice (C129/Bl6).

The position of CtBP2-immunolabeled afferent synapses relative to the centre of the OHC nucleus was analysed using confocal microscopy of mid-modiolar cochlea cryosections. Sections were from adult (4 months old) $Pph^{-/-}$ and WT mice and these were batch processed for immunolabeling and microscopy. This analysis revealed displacement of synapses towards the apex of the cell on the $Pph^{-/-}$ OHCs. Quadratic (f2-f1) Distortion Product Otoacoustic Emissions (DPOAEs) have been shown to be sensitive to CS induced attenuation (Abel *et al.*, 2009). We therefore observed changes in the ipsilateral quadratic DPOAEs of $Pph^{-/-}$ and WT mice, in response to sound delivered to the contralateral ear. These experiments demonstrated that while the quadratic DPOAE were of equivalent amplitude in $Pph^{-/-}$ and WT mice, they were significantly less attenuated by CS in $Pph^{-/-}$ animals. These results support the hypothesis that the sensory signal driving the MOC pathway to the OHCs of the opposite cochlea has a significant contribution from the type II SGN.

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