Abstract: 58O

Maintenance of hearing sensitivity in an ultraquiet environment requires olivocochlear efferent feedback

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Hearing sensitivity and frequency selectivity depend on the sound-induced vibrations of the cochlear organ of corti through a unique type of sensory cell called outer hair cells (OHC). These cells can shorten and lengthen in response to sound, and this electromotility contributes to the amplification of sound and increased hearing sensitivity in quiet to moderately loud sound levels. This so called 'cochlear amplifier' augments cochlear vibrations in specific sections of the cochlea and thereby enhances the sound transduction at the inner hair cells (IHC). Regulation of the level of IHC sound transduction between the two ears involves a sensorimotor reflex mediated by olivocochlear efferent projections that dynamically suppress the cochlear amplifier. This is evident as 'contralateral suppression' where noise in one ear reduces cochlear amplifier-mediated otoacoustic emissions in the other ear. We previously showed that a major sensory driver for this contralateral suppression is the type II spiral ganglion afferent innervation to the cochlear outer hair cells (based on the loss of contralateral suppression in mice null for the gene encoding the type III intermediate filament peripherin (*Prph*$^{(-/-)}$)) (Froud et al., 2015). Furthermore, in a recent study, we showed that high-intensity, broadband noise (108 dB SPL, 1 hr) produced permanent high frequency (24-32 kHz) hearing loss in *Prph*$^{(-/-)}$ mice consistent with the attenuated contralateral suppression seen in *Prph*$^{(-/-)}$ mice (Cederholm et al., 2022). In the current study, we sought to investigate the effect of sustained moderate noise. Wild-type (n=11-13) and *Prph*$^{(-/-)}$ (n=10-13) mice (129/C57Bl/6J background) were born in environmental chambers with either continuous noise (74 dB SPL, 8-16 kHz noise-band) or a highly attenuated sound environment (~ 7 dB SPL, 500 Hz – 40 kHz (quiet). Hearing thresholds were measured at 2, 4 and 6 months of age using auditory brainstem response (ABR) and distortion product otoacoustic emission (DPOAE) measurements in mice anaesthetised (i.p.) with a cocktail of ketamine (40 mg/kg), xylazine (8 mg/kg), acepromazine (0.5 mg/kg); the latter being able to directly measure OHC electromechanical transduction. We observed permanent high-frequency (24-32 kHz) hearing loss at 2 months of age in *Prph*$^{(-/-)}$ mice born and kept in the quite environment (Two-way repeated measures ANOVA; *Prph*$^{(-/-)}$ noise *vs* quiet, 24-32 kHz, $p<0.001$) as evident from their DPOAE measurements. This was sustained at 4 and 6 months of age. ABR measurements showed no change at 2 months, however, high-frequency hearing loss developed over time in the *Prph*$^{(-/-)}$ mice born in the quiet environment (6 months; Two-way repeated measures ANOVA on Ranks; *Prph*$^{(-/-)}$ noise *vs* quiet, 24-32 kHz, $p<0.001$). The findings at 2 months were corroborated in a subsequent study. Our findings suggest that the olivocochlear efferents have a role in protecting hearing loss in sustained ultra-quiet conditions when the cochlear amplifier is maximally sensitive. Further, independent of the olivocochlear reflex, sustained sound provides otoprotection (conditioning). Funded by NHMRC APP1052463. Approved by the UNSW Sydney Animal Care and Ethics Committee.

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