Purinergic signalling via ATP-gated ion channels mitigates noise-induced hearing loss

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We tested the hypothesis that activation of $P2X_2$ receptor-mediated signal transduction in the cochlea mitigates noise-induced hearing loss (NIHL). ATP-gated ion channels assembled from $P2X_2$ receptor subunits are expressed by the cochlear sensory hair cells, associated epithelial supporting and secretory cells, and by the spiral ganglion neurons. These sites of expression may be activated by noise-induced release of ATP to affect sound transduction, cochlear electrochemical homeostasis, and auditory neuron excitability (see Housley, Bringmann & Reichenbach, 2009, for a review). This $P2X_2$ receptor signalling is up-regulated by sustained exposure to high noise levels (Wang *et al.*, 2003), suggesting a potential relationship. Wildtype (WT) and $P2X_2$ receptor knockout (KO) mice (C57BL/6J background strain) were exposed to two noise conditions: acute - high level noise, and long-term – medium level (environmental) noise. In the case of the acute study (30 minutes, 95 dB SPL, 1 octave (8 – 16 kHz) white noise), hearing sensitivity was measured by auditory brainstem response (ABR) before, immediately after, and then two weeks after the noise exposure, to determine temporary (TTS) and permanent (PTS) threshold shifts.* The WT and KO mice groups had comparable TTS within the noise band, however, the KO mice sustained high frequency PTS. In the second study, WT and KO mice were born into either an acoustically attenuated "quiet" environmental chamber, or an environmental chamber providing exposure to moderate ambient noise (75 dB white noise). After four months, both WT and KO mice in the "noise chamber" had significantly worse hearing than the mice in the "quiet chamber". However, as seen in the acute noise study, hearing loss in the KO mice extended to higher frequencies than in the WT mice.

Conclusion: In the absence of $P2X_2$ receptor signalling (KO mice), NIHL in the cochlea is exacerbated for both high-level, short-term noise exposure and long-term moderate noise levels. Thus $P2X_2$ receptor signalling is oto-protective, providing intrinsic reduction of high-frequency NIHL.

*The mice were anaesthetized using ketamine (40 mg/kg); xylazine (8 mg/kg); acepromazine (0.5 mg/kg) (i.p.) during the ABR measurements following a protocol approved by the UNSW Animal Care and Ethics Committee.

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Supported by the National Health & Medical Research Council (Australia).