## Age-related reduction in frequency-following responses as a potential marker of cochlear neural degeneration

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## Abstract

Healthy aging may be associated with neural degeneration in the cochlea even before clinical hearing loss emerges. Reduction in frequency-following responses (FFRs) to tonal carriers in older clinically normal-hearing listeners has previously been reported, and has been argued to reflect an age-dependent decline in temporal processing in the central auditory system. Alternatively, age-dependent loss of auditory nerve fibers (ANFs) may have little effect on audiometric sensitivity and yet compromises the precision of neural phase-locking relying on joint activity across populations of fibers. This peripheral loss may, in turn, contribute to reduced neural synchrony in the brainstem as reflected in the FFR. Here, we combined human electrophysiology and auditory nerve (AN) modelling to investigate whether age-related changes in the FFR would be consistent with peripheral neural degeneration. FFRs elicited by pure tones and frequency sweeps at carrier frequencies between 200 and 1200 Hz were obtained in older (ages 48-76) and younger (ages 20-30) listeners, both groups having clinically normal audiometric thresholds up to 6 kHz. The same stimuli were presented to a computational model of the AN in which age-related loss of hair cells or ANFs was modelled using human histopathological data. In the older human listeners, the measured FFRs to both sweeps and pure tones were found to be reduced across the carrier frequencies examined. These FFR reductions were consistent with model simulations of age-related ANF loss. In model simulations, the phase-locked response produced by the population of remaining fibers decreased proportionally with increasing loss of the ANFs. Basal-turn loss of inner hair cells also reduced synchronous activity at lower frequencies, albeit to a lesser degree. Model simulations of age-related threshold elevation further indicated that outer hair cell dysfunction had no negative effect on phase-locked AN responses. These results are consistent with a peripheral source of the FFR reductions observed in older normal-hearing listeners, and indicate that FFRs at lower carrier frequencies may potentially be a sensitive marker of peripheral neural degeneration. We are currently recording electrocochleographic (ECochG) responses using tympanic membrane electrodes to further explore age-related neural degeneration at the level of the cochlea.

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