Abstract

Objectives. This project involves animal and human subjects. In animals, objectives are to extend characterization of neurodegenerative consequences of noise exposure by identification of key events required to produce substantial auditory neuropathy vs. those that do not, develop sensitive metrics of underlying injury that can be applied non-invasively in the human, and probe our hypothesis that terminal retraction interrupts neurotrophic support of neurons by applying drugs that will target this mechanism for prevention or repair. In humans, we will determine whether evidence shows similar response changes from noise compared with changes found in animals, test effectiveness of physiological biomarkers developed in animals, and characterize perceptual functions, like speech understanding in noise and recovery from noise masking, which we have hypothesized to be particularly vulnerable to the neural degeneration.

Plan. Project coordination will be provided by Sharon Kujawa, PhD, at the Massachusetts Eye and Ear Infirmary, in Boston. Animal studies (Aims 1 and 3) will be accomplished entirely in Dr. Kujawa's laboratory and through collaboration with Albert Edge, PhD, also at the Mass Eye and Ear. Human studies (Aim 2) will be done in collaboration with research scientist and clinician Dawn Konrad-Martin, PhD and her colleagues at the Department of Veterans Affairs National Center for Rehabilitative Auditory Research (NCRAR) in Portland, OR. At NCRAR, we will use non-invasive responses to characterize supra-threshold auditory nerve function as we have begun to do in our animal models. Distortion product otoacoustic emission (DPOAE) metrics with optimized sensitivity and behavioral thresholds for pure tones will be recorded in the same ears to assess hair cell functional integrity. In parallel, behavioral/psychoacoustic techniques will be used to characterize speech understanding in quiet and noise and to study recovery from noise masking. Results in humans will be used to determine relationships between noise exposure history, auditory nerve degeneration, and auditory perception.

Methods. The NCRAR portion of this project will investigate auditory function in noise-exposed Veterans recently separated from the military and age-matched individuals with no noise exposure history, all of whom will be under age 40. Military MOS will be considered along with self-report to categorize Veterans as having low or high noise exposure. We will assess discrimination of speech presented at a normal rate and time-compressed, in quiet and in noise. In addition, we will assess suprathreshold compound action potential (CAP) response growth, wave peak ratios and morphology, and sample auditory nerve timing fidelity using a forward masking paradigm. Distortion product otoacoustic emission threshold and saturation levels will be determined from response growth curves to account for noise-related outer hair cell loss that could influence the other measures. Data arising from proposed animal and human studies will be combined with previously published data from human temporal bone studies to generate a predictive model characterizing human spiral ganglion cell loss with age, for ears with high, low and no prior exposure to noise. A similar approach will be used to estimate human OHC loss as a function of noise exposure category.

Clinical Relevance. Evidence from animal studies suggests that noise-induced loss of LS rate fibers reduces the fidelity with which sound frequency and timing cues are encoded within the auditory nerve, particularly at high levels and in background noise where these fibers are selectively operational. Auditory neuropathy also induces plastic changes in the brainstem as an animal ages and these changes are associated with poor auditory temporal processing measured behaviorally. Extrapolating to humans, such deficits likely interfere with the perceptual encoding of speech, which could explain why speech amplified through a hearing aid provides the necessary audibility, but often lacks the clarity needed for its comprehension.

Relevance to VA's Mission. Hearing loss is one of the most common service-related disabilities and can lead to communication difficulties that result in problems with employment, social isolation, depression, and overall reduced quality of life. Information gained from this research will guide future decisions as to safe levels of noise exposure and auditory rehabilitation decisions for Veterans with noise-related hearing loss. If successful, it may lead to effective otoprotection for future war-fighters and thus reduce the burden of hearing loss among Veterans.