**Title**: Plasticity of the Older Ear and Brain: Neurobiological Mechanisms and Neuroscientific Underpinnings of Age-Related Hearing and Speech Communication Problems.

**Abstract**:

Age-related functional decline of the nervous system is readily observed, has been well-studied, and yet mechanistically, is little understood. The auditory system has one of the most prevalent age-related functional declines. Age-related hearing loss (ARHL), also known as presbycusis, is a progressive, bilateral sensorineural loss that is associated with decreased hearing sensitivity, decreased ability to understand speech, especially in a noisy environment, and impaired sound localization. ARHL is a complex disorder involving both peripheral and central mechanisms. Within the inner ear, the dysfunction and degeneration of sensory and non-sensory structures are prominent features of ARHL. Although substantial progress has been made in determining the genetic and cellular functions of the inner ear disrupted by ARHL, comparatively little is known about the underlying causes. Noise exposure impacts the onset and progression of ARHL. It has been known for some time that high levels of noise cause sensory and non-sensory cell degeneration. Recent studies confirm that even moderate levels of noise may lead to synaptopathy and neuronal degeneration. Investigations into aging within the inner ear increasingly suggest that ARHL is a multifactorial process that involves molecular, cellular and functional changes in the stria vascularis, sensory hair cells, cochlear blood flow, and neuronal connections. It is intriguing to think that some of the prominent features of ARHL may be the result of an intrinsic attempt to repair age-related damage caused by recapitulating early cochlear development. Age-related changes eventual lead to increased activation of macrophages, atrophy of the stria vascularis, and loss of both sensory hair cells and neurons likely due to oxidative stress. Our investigations have focused on the age-related changes occurring in sensory cells, particularly the outer hair cells, and in the age-related plasticity of neuronal connections. The outer hair cells are one of the most prominent targets of noise and aging defects. Loss of outer hair cells leads to elevated hearing thresholds, along with loss of cochlear frequency tuning. Since outer hair cell function depends heavily on the tight regulation of $Ca^{2+}$, we have investigated whether changes in $Ca^{2+}$ buffering play a role in ARHL. Furthermore, changes in neuronal connectivity may be induced by the lack of hair cell activity.