JOURNAL OF
OTOLOGY

PERIPHERAL HEARING LOSS CAUSES HYPEREXCITABILITY OF THE INFERIOR COLLICULUS

Sun Wei

Abstract

Growing evidence has been found to suggest that early development of the central auditory system is dependent on acoustic stimuli. Peripheral damage caused by noise exposure and ototoxic drugs can induce functional and anatomical changes along the auditory pathways. The inferior colliculus (IC) is a unique structure in the auditory system located between the primary auditory nuclei of the brainstem and the thalamus. Damage to the IC inhibitory circuitry may affect central auditory processing and sound perception. Here, we review some of the striking electrophysiological changes in the IC that occur after noise exposure and ototoxic drug treatment. A common occurrence that emerges in the IC after peripheral damage is hyperexcitability of sound-evoked response. The hyperexcitability of the IC is likely related with reduced inhibitory response that requires normal peripheral inputs. Early age hearing loss can result in a long lasting increased susceptibility to audiogenic seizure which is related to hyperactivity in the IC evoked by loud sounds. Our studies suggest that hearing loss can cause increased IC neuron responsiveness which may be related to tinnitus, hyperacusis, and audiogenic seizure.

Key words: Inferior colliculus, noise exposure, salicylate, audiogenic seizure, tinnitus, hyperacusis

Introduction

The inferior colliculus (IC), a complex neural circuit in the auditory brainstem, plays an important role in sound processing. Damage to the IC inhibitory circuitry likely contributes to different hearing disorders including tinnitus and hyperacusis[1,6]. Previous studies in our lab have demonstrated that restricted cochlear lesions can cause massive functional changes in the IC. Hyperexcitability in a region of the IC may be triggered by noise exposure[12] or ototoxic drugs[18]. These changes may be related with inhibitory circuitry reduction or synaptic efficiency increase. In the following sections, we will summarize the IC function changes caused by peripheral damages due to noise exposure, carboplatin treatment, and early age hearing loss.

It has been proposed that peripheral hearing loss would reduce the local inhibition of the central auditory system, resulting in increased central neural responsiveness[8]. Since the central auditory system is enriched with inhibitory circuitry, damage in the cochlea can cause an increase, rather than a decrease, in the central auditory response, presumably due to reduction of the central inhibition. Aging and noise induced hearing loss often cause lesion to a small area such as the basal turn of the cochlea, which corresponds to a high frequency region. The cochlear damage in these regions may cause an increased gain in high frequency response. This also affects the tonotopic map of auditory cortex (AC) which may be a central source of tinnitus. The fact that perceived pitch of tinnitus is commonly equal to the frequency on the lower edge of the damaged frequency regions supports this theory. The tonotopic map changes may be caused by the uniformity of the inhibitory field in the central auditory system, such as the IC and the AC.

Noise Exposure Caused IC Function Changes

Peripheral damage caused by noise exposure can cause elevated responses in the auditory midbrain. Using chronically implanted recording electrodes on the round window, the cochlear nucleus (CN), and the IC, Salvi et al found that the input/output function of compound action potential (CAP) recorded from the round

Affiliation:
Center for Hearing & Deafness, Department of Communicative Disorders and Sciences, State University of New York at Buffalo, Buffalo, NY 14214

Corresponding authors:
Sun Wei , Email: weisun@buffalo.edu

window in awake chinchillas shifted to the right by 10-15 dB one day after noise exposure (2.8 kHz tone presented for 2 hours at 105 dB SPL), reflecting a slight loss in sensitivity (Figure 1A)[17]. The amplitude of CAP also showed a significant reduction at moderate to high intensities consistent with the loss in sensitivity. The IC response to low intensity acoustic stimuli also reduced significantly after noise exposure. However, the IC response at the level above the threshold maintained the same or even increased (Figure 1B). The result suggests that noise exposure may impair inhibition from the damaged region. Wang et al. tested the acute change in IC neural response caused by noise exposure (narrow band noise) in anesthetized chinchillas[24]. They found that the excitatory response area of many neurons expanded to lower frequencies (Figure 1C) and the firing rate of those neurons tuned to low frequencies significantly increased after noise exposure (Figure 1D). The results suggested that neurons tuned to high frequencies became sensitive to low frequency acoustic stimuli after noise exposure. This change may be caused by damage to side-band inhibition in the IC[18]. Damage of side-band inhibition may increase the evoked potential amplitude of the IC at low frequency by increasing the number of neurons responding to these low frequency stimuli. This phenomenon suggests that peripheral damage not only reduces sound sensitivity to noise exposed frequencies, but may also cause increased sound sensitivity to frequencies at the lower edge of the damaged frequency range.

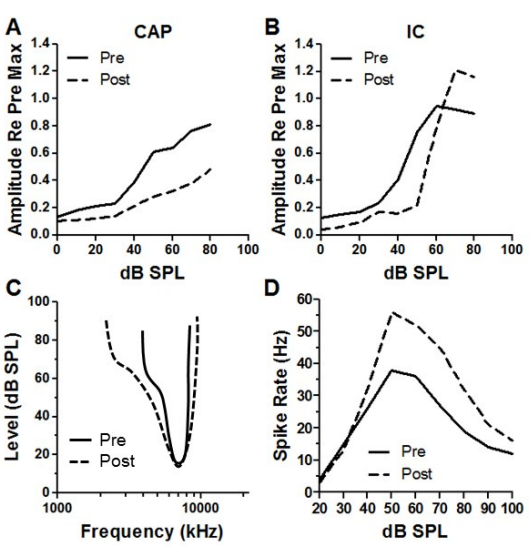

Figure 1. Noise exposure caused functional changes in the cochlea and the inferior colliculus (IC). (A) Rightward shift of the input/output function of the compound action potential (CAP) recorded from the round window of chinchillas caused by noise exposure. This reflects a slight loss in sensitivity. (B) Significant reduction of the IC response to low intensity acoustic stimuli caused by noise exposure. However, the IC response at the level above the threshold showed an increased response. (C) Expansion of the excitatory response area of the IC towards the lower frequencies and increased firing rates (D) caused by noise exposure

Recently, Ben Scholl et al. reported that acute acoustic trauma could induce an imbalance of excitation and inhibition in auditory cortical neurons[19]. They found that noise exposure caused a decrease of synaptic inhibition in the auditory cortex at low frequency ranges and an increase of synaptic inhibition at high frequency ranges. This study indicated that acoustic trauma might cause an asymmetrical damage in the inhibitory field in the auditory cortex. Noise exposure may impair side-band inhibition from the damage region at the lower frequencies of tested neurons.Since the lack of side-band inhibition had been hypothesized as a cause of the increased IC neuronal response, we tested the input-output function of the IC neuron located at different sides of the hearing loss regions to reveal how impairment of side-band inhibition affects the input-output function of the IC neurons. Interestingly, we found that high frequency noise exposure caused an expansion of the tuning curve towards lower frequencies, but not higher frequencies (Figure 2). However, the spontaneous activity in high frequency region showed a significant increase (Figure 2, arrows). These results suggest that noise trauma induced a decrease in synaptic inhibition at the low frequency range, not in the high frequency range. A recent study found that trauma-evoked tinnitus developed in the frequency range bordering the low frequency slope of the induced noise trauma[14]. This result supports the theory of lateral inhibition as the physiological basis of tinnitus. The spontaneous activity change caused by noise exposure in the high frequency range may be related with tinnitus perception after noise exposure[13, 16].

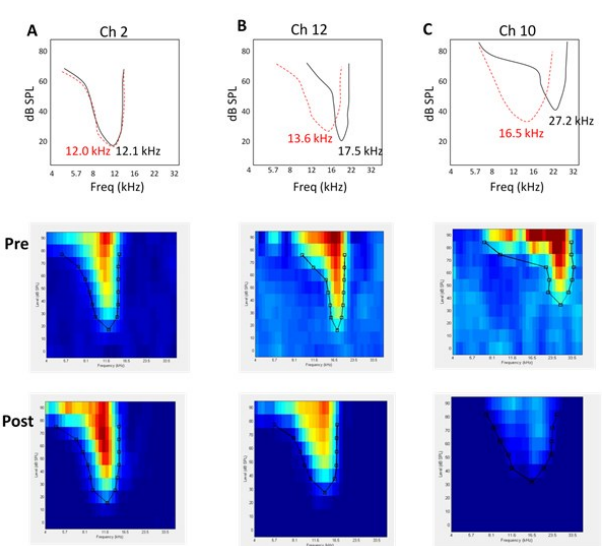

Figure 2. Tuning curves (the first row) and the excitatory frequency responses (the second and third rows) of inferior colliculus (IC) neurons in mice. (A) The characteristic frequency (CF) and mini-