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NOISE TRAUMA INDUCED PLASTIC CHANGES IN BRAIN REGIONS OUTSIDE THE CLASSICAL AUDITORY PATHWAY

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Abstract—The effects of intense noise exposure on the classical auditory pathway have been extensively investigated; however, little is known about the effects of noise-induced hearing loss on non-classical auditory areas in the brain such as the lateral amygdala (LA) and striatum (Str). To address this issue, we compared the noise-induced changes in spontaneous and tone-evoked responses from multiunit clusters (MUC) in the LA and Str with those seen in auditory cortex (AC) in rats. High-frequency octave band noise (10–20 kHz) and narrow band noise (16–20 kHz) induced permanent threshold shifts at high-frequencies within and above the noise band but not at low frequencies. While the noise trauma significantly elevated spontaneous discharge rate (SR) in the AC, SRs in the LA and Str were only slightly increased across all frequencies. The high-frequency noise trauma affected tone-evoked firing rates in frequency and time-dependent manner and the changes appeared to be related to the severity of noise trauma. In the LA, tone-evoked firing rates were reduced at the high-frequencies (trauma area) whereas firing rates were enhanced at the low-frequencies or at the edge-frequency dependent on severity of hearing loss at the high frequencies. The firing rate temporal profile changed from a broad plateau to one sharp, delayed peak. In the AC, tone-evoked firing rates were depressed at high frequencies and enhanced at the low frequencies while the firing rate temporal profiles became substantially broader. In contrast, firing rates in the Str were generally decreased and firing rate temporal profiles become more phasic and less prolonged. The altered firing rate and pattern at low frequencies induced by high-frequency hearing loss could have perceptual consequences. The tone-evoked hyperactivity in low-frequency MUC could manifest as hyperacusis whereas the discharge pattern changes could affect temporal resolution and integration.

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Abbreviations: ABR, auditory brainstem response; AC, auditory cortex; CF, characteristic frequency; DCN, dorsal cochlear nucleus; FRF, frequency receptive field; IC, inferior colliculus; IHC, inner hair cells; LA, lateral amygdala; MUC, multiunit clusters; NBN, narrowband noise; NIHL, noise-induced hearing loss; OBN, octave band noise; OHC, outer hair cells; PTS, permanent threshold shifts; Str, striatum; SR, spontaneous discharge rate; VCN, ventral cochlear nucleus.

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INTRODUCTION

Intense noise exposures have long been known to induce temporary or permanent noise-induced hearing loss (NIHL) and cochlear damage that reduces neural output of the cochlea. Paradoxically, NIHL often results in enhanced sound-evoked responses in the central auditory pathway indicative of enhanced central gain, a form of homeostatic plasticity that partially compensates or overcompensates for peripheral hearing loss (Salvi et al., 1990, 2000; Syka and Rybalko, 2000; Popelar et al., 2008; Sun et al., 2008). The enhanced sound-evoked activity observed in central auditory structures is often greatest at frequencies below the region of NIHL possibly due to a reduction in lateral inhibition (Salvi et al., 2000). In addition to changes in central gain, NIHL typically results in an increase in spontaneous discharge rates (SRs) in the cochlear nucleus (CN) which in some cases continues rostral up to the auditory cortex (AC) (Eggermont and Komiya, 2000; Kaltenbach and Afman, 2000; Zhang et al., 2006; Dong et al., 2010; Mulders and Robertson, 2013; Luo et al., 2014). Enhanced sound-evoked responses and increased central gain have been linked to hyperacusis or loudness intolerance (Sun et al., 2012) whereas elevated SR in tonotopic regions associated with hearing loss is considered by some as the neural correlate of tinnitus (Chen and Jastreboff, 1995; Kaltenbach and Afman, 2000). NIHL also induces frequency map reorganization in the AC and enhanced inter-neuronal synchrony; these neurophysiological changes have also been linked to tinnitus (Muhlnickel et al., 1998; Seki and Eggermont, 2002; Eggermont, 2006; Norena and Eggermont, 2006).

NIHL also exerts effects beyond the classical auditory pathway. NIHL suppresses neurogenesis in the hippocampus and alters the spatial tuning of hippocampal neurons as animals navigate through a maze (Goble et al., 2009; Kraus et al., 2010; Newman et al., 2015). The amygdala, which attaches emotional significance to sounds, plays a central role in auditory fear conditioning and modulates the acoustic startle reflex (LeDoux, 2000; Kraus and Canlon, 2012). In this context, it is interesting to note that the amplitude of acoustic startle reflex is greatly depressed by unilateral NIHL. Since unilateral ear plugging also suppresses startle reflex amplitude, it seems likely that the sensory or motor

circuits that regulate the startle reflex requires information from both ears (Kraus et al., 2010; Lobarinas et al., 2013). The Str, which is involved in motor planning and movements, receives auditory inputs and can modulate the startle reflex (Bordi and LeDoux, 1992; Kodsi and Swerdlow, 1995). Sound-evoked neural activity in the Str is also greatly enhanced by sodium salicylate, an ototoxic drug that induces tinnitus and hyperacusis (Chen et al., 2014b). Although the neural correlates of tinnitus and hyperacusis have been extensively studied in the classical auditory pathway, there is growing awareness that non-classical auditory areas such as the amygdala and Str may contribute directly or indirectly to these aberrant perceptions (Jastreboff, 2007; Rauschecker et al., 2010; Chen et al., 2012). Some clinical reports suggest that the amygdala and Str are involved in tinnitus and hyperacusis (De Ridder et al., 2006; Cheung and Larson, 2010). The lateral amygdala (LA) and striatum (Str) have extensive connections with the classical auditory pathway (Romanski et al., 1993; Budinger et al., 2008) and respond robustly to acoustic stimulation (Bordi et al., 1993; Romanski et al., 1993; Quirk et al., 1995; Cromwell et al., 2007; Chen et al., 2012). Therefore the response properties of neurons in the LA and Str are likely to be altered by NIHL. Although the effects of acoustic trauma have been explored at many different sites in the classical auditory pathways, the effects of NIHL on non-classical auditory centers are poorly understood. To address this issue, we studied the effects of high-frequency NIHL on the sound-evoked responses and SR in the LA and Str of the rat and compared the results to similar data obtained from primary and secondary AC.

EXPERIMENTAL PROCEDURES

Subjects

Sprague–Dawley rats (2 months of age) were acquired from Charles River Laboratories Inc. (Wilmington, MA, USA) and housed in the Laboratory Animal Facility (LAF) of the University at Buffalo and given free access to food and water. The colony room was maintained at 22 °C with a 12-h light–dark cycle. All procedures regarding the use and handling of animals were reviewed and approved by the Institutional Animal Care and Use Committee (IACUC) at the University at Buffalo.

Noise exposure

NIHL was induced with either an octave band noise (OBN, 10–20 kHz) or a narrowband noise (NBN, 16–20 kHz). At three months of age, the rats were exposed to the NBN (24 h/day for 8 days, 7 rats) or to the OBN (24 h/day for 35 days, 4 rats) at an overall intensity level of 104-dB SPL. The rationale for using these two exposures is that they are identical to those being used in ongoing behavioral studies designed to obtain behavioral measures of hearing loss, hyperacusis and tinnitus. The advantage of using long-duration exposures is that all animals develop the similar asymptotic threshold shift after they have been in the noise for > 24 h (Carder and Miller, 1972; Salvi et al., 1978; Chen et al., 2014a). These long-duration exposures reduce between subject variability in the amount of hearing loss and cochlear pathology compared to intense, short-duration (e.g. 1–3 h) exposures. Control rats (n = 9) were housed in the colony room without intense noise exposure. The two exposures also allowed us to evaluate the effect of the bandwidth of the hearing loss on the electrophysiological results.

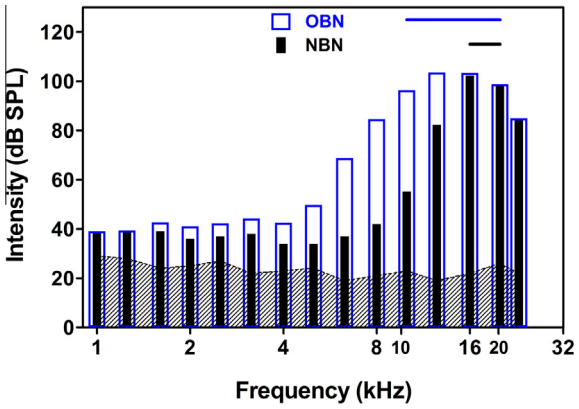

Fig. 1. Blue open bars and black-filled bars show the dB SPL measured in one-third octave bands for the 10–20 kHz OBN and 16–20 kHz NBN. The dashed line and hatched area show the background noise in the colony. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

The OBN and NBN stimuli were generated using a TDT RP2 Real-time signal processor (TDT, Gainesville, FL, USA), amplified by AMP 300 power amplifier (AudioSource Inc., Portland, OR, USA) and delivered to a speaker (Vifa D25AG35 1″ Dome Tweeter, Madisound Speaker Components, Inc., Middleton, WI, USA). Each rat was housed in a single cage (28 × 25.4 × 20.3 cm) equipped with a speaker located on the top of the cage. The rats were awake during the exposure and both ears were exposed to the OBN or NBN. The rats had free access to food and water, moved freely in the cage during the binaural exposure. The noise intensity level in the cage was calibrated with a sound-level meter (Larson Davis System 824) with a free-field ø″ microphone (model 2540, Larson Davis). The overall intensity and intensity in one-third octave bands were measured. Fig. 1 presents spectra of the OBN (blue open bars) and the NBN (black-filled bars).

Measurement of noise-induced hearing loss (NIHL)

The auditory brainstem response (ABR) was used to estimate the magnitude of the NIHL. The ABRs were recorded pre- and one month post-exposure and the pre-post threshold differences were used to calculate the NIHL or permanent threshold shifts (PTS). Rats were anesthetized initially with 4% isoflurane in O_2 at a flow rate of 0.5 L/min and then maintained at 1.5% isoflurane. Needle electrodes (Grass Technologies) were placed at the vertex (active), posterior bulla