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Research article

Auditory central gain compensates for changes in cochlear output after prolonged low-level noise exposure

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ABSTRACT

Remarkably, the central auditory system can modify the strength of its sound-evoked neural response based on prior acoustic experiences, a phenomenon referred to as central gain. Gain changes are well documented following traumatic noise exposure, but much less is known about central gain dynamics following prolonged exposure to low-level noise, a common acoustic experience in many urban and work environments. We recently reported that the neural output of the cochlea is reduced, while gain was enhanced in the inferior colliculus (IC) following a 5-week exposure to 75 dB noise. To determine if similar effects were present at even lower intensities, we exposed rats to a 65 dB noise expecting to see little to no change in the cochlea or IC. The exposure had little effect on distortion product otoacoustic emissions and did not cause any hair cell loss. However, the amplitude of the CAP, which reflects the neural output of cochlea, was depressed by 50–75%. Surprisingly, neural responses from the IC were enhanced up to 70%, mainly at frequencies within the noise exposure band. One-week post-exposure, CAP amplitudes returned to normal at frequencies within or above the exposure band, whereas responses evoked by frequencies below the exposure band were enhanced by more than 80%. In contrast, IC responses below the exposure frequency were depressed 10–20% whereas responses within the exposure frequency band were enhanced 10–20%. Thus, the central auditory system dynamically up- and down-regulates its gain to maintain supra-threshold neural responses within a narrow homeostatic range; a function that likely contributes to the prevention of sounds from being perceived as muffled or too loud.

1. Introduction

Human exposure to low and moderate level noise has steadily increased over the years, especially for urban dwellers [4,10,15,22,39]. Remarkably, the auditory system can acclimate to prolonged changes in the acoustic environment by adjusting its neural representation of loudness [11,24]. Growing evidence suggests these adaptive changes emanate from a neural mechanism responsible for the control of central gain, whereby central auditory nuclei enhance or suppress gain to adjust for changes in the neural output from the cochlea [2,9,31]. While enhanced central gain following exposure to traumatic noise and ototoxic drugs is well established [2,31], research is only beginning to explore central gain changes associated with prolonged exposure to continuous low-level sounds; a pervasive condition in modern societies.

Continuous exposure to low-level noise can have an unexpectedly large effect on both the peripheral and central auditory systems. In mice, exposure to a continuous moderately loud (84 dB SPL) octave band noise for one week damages synapses (synaptopathy) between inner hair cells (IHCs) and type I cochlear nerve fibers [19]. Synaptopathy and selective damage to auditory nerve fibers can lead to enhanced central gain in the auditory cortex [5,20]. In contrast, reports using an exposure consisting of tone-pips (68–72 dB) to create an enriched acoustic environment depressed sound evoked responses in the auditory cortex without causing hearing loss [26]. Recently, we reported that a continuous low-level, octave band noise (10–20 kHz, 75 dB SPL), an intensity level similar to highway traffic noise, significantly reduced the amplitude of rat cochlear compound action potentials (CAPs), but elevated sound-evoked activity in the inferior colliculus (IC), indicating enhanced central gain [33]. Interestingly, at one-week post-exposure, CAP amplitudes were slightly enhanced, and sound-evoked IC responses partially recovered toward normal levels [33]. These observations suggest that continuous exposure to low-level noise may provoke a sequence of cochlear mediated central gain changes in response to prolonged changes in acoustic experience.

In light of our recent findings, we questioned if exposure to an even lower-level noise (65 dB SPL), comparable to levels in urban and work

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environments could produce similar potent effects on cochlear and IC physiology. To test this hypothesis, we exposed Sprague-Dawley rats to a continuous 65 dB noise for 5 weeks, an intensity level similar to an air conditioning window unit, then measured cochlear function with distortion product otoacoustic emissions (DPOAEs) and the cochlear compound action potentials (CAP) and also evaluated central auditory function by measuring sound-evoked local field potentials (LFPs) from the IC. Measurements were made immediately after the 5-week exposure to assess acute change and at one-week post-exposure to determine if changes were temporary or permanent.

2. Methods

2.1. Subjects

Twenty-five Sprague-Dawley rats (3–4 months old, 300–400 g, Charles River) were used in the study. Cochlear CAPs and IC LFPs were obtained from 17 animals that were randomly assigned to one of three groups: 1) controls (n = 6), 2) low-level noise (LLN, n = 6) and 3) one-week post noise exposure (1WPE, n = 5). DPOAE measures were obtained from eight rats before the LLN exposure, after 5 weeks in LLN, and 1WPE. Animals were housed one per cage, provided free access to food and water, and kept on a 12/12 h light-dark cycle. All procedures were approved by the Institutional Animal Car and Use Committee (IACUC) at the University at Buffalo in accordance with NIH guidelines.

2.2. Noise exposure

Animals were exposed to a 10–20 kHz octave-band noise presented at a total integrated intensity level of 65 dB SPL. The noise was generated and presented in an identical manner to our previously published study [33]. Briefly, the noise was generated using a Tucker Davis Technology RP2 real-time processor, sent to a power amplifier, then routed to a loudspeaker suspended with wire mesh above the animal's cage. The noise was calibrated from the center of the cage using a sound level meter (Larson Davis System 824). Neurophysiologic responses were obtained from the IC immediately after animals were removed from the noise, or 1-week post exposure, and CAP data were obtained within 8 h of animals being removed from the noise, or 1-week post exposure.

2.3. Compound action potential (CAP)

Details of our methods for acquiring and analyzing the CAP can be found in previous publications [33,34]. Briefly, animals were placed in a customized head-holder, the right bulla was exposed and a small fistula was made to access the cochlear round window. A silver ball electrode was placed on the round window and a reference electrode was inserted into the neck muscles. Tone bursts were generated using a Tucker Davis Technologies (TDT) real-time processor (RP2.1, System 3) and presented via an ACO ½" microphone driven in reverse. Stimulus intensity was decreased in 10 dB steps from 80 to 0 dB SPL using a TDT PA5 programmable attenuator. The cochlear response within a 20 ms time window was amplified (1000x) with a WPI DAM50 differential amplifier and filtered online (0.1 −10,000 Hz). The voltage difference between N1 and P1 was measured and used to compute CAP amplitude. CAP amplitudes were tested for significance using a two-way ANOVA and Bonferroni post-hoc analysis.

2.4. Distortion product otoacoustic emissions

Our methods for collecting and analyzing DPOAEs have been described in detail in previous publication [34,35]. Briefly, DPOAEs were measured with the Smart Distortion Product Otoacoustic Emission System (version 4.53, Intelligent Hearing System, Miami, FL), using two primary tones (f1 and f2) with an f2/f1 ratio of 1.2. The f1 intensity (L1) was presented at an intensity 10 dB higher than the intensity of f2 (L2). L1 was decreased from 80 to 25 dB SPL in 5-dB steps. The DPOAE signal-to-noise ratio (SNR) was plotted as function of L1 intensity and DPOAE input/output (I/O) functions were analyzed for significance using a two-way ANOVA and Bonferroni post-hoc analysis.

2.5. Cochleograms

Our methods for assessing inner hair cell (IHC) and outer hair cell (OHC) loss are described in detail in previous publications [6,33]. After decapitation, and cochleae removal, the oval windows were opened and a small fistula was placed at the apex of the cochlea. Cochleae were perfused with succinate dehydrogenase (SDH) incubation solution (0.05 M sodium succinate, 0.05 M phosphate buffer and 0.05% tetranitroblue tetrazolium) then immersed in a SDH solution for 1 h (37 °C). Cochlea were then fixed in 10% formalin for 2 days then decalcified in 7% ethylenediamine tetracetic acid (EDTA) for 3 days. The organ of Corti was carefully microdissected out as a surface preparation, mounted in glycerin on glass slides and SDH-labeled hair cells examined along the entire length of the cochlea using a light microscope (400X). Percent hair cell loss was obtained by comparing the hair cell counts from animals in the LLN group to counts in the control group (Fig. 1B).

2.6. IC local field potentials

Details of our electrophysiological techniques have been described in previous publications [7,33]. Rats were anesthetized with ketamine (60 mg/kg, i.p.) and xylazine (6 mg/kg, i.p.) and secured in a stereotaxic apparatus. The dorsal surface of the skull was exposed and using stereotaxic coordinates [43], a craniotomy was made over the left IC. The dura was removed and a linear 16-channel silicon microelectrode (A-1 × 16–10 mm 100–177, NeuroNexus Technologies) was advanced into the IC using a hydraulic microdrive (FHC Inc., Bowdoin, ME). Several electrode penetrations were performed in order to obtain neural responses across the entire tonotopic area of the IC. Tone bursts were presented to the right ear at a rate of ~3/s through a loud speaker (FT28D, Fostex). LFPs were obtained with a resolution of 40.96 μs using a TDT RA16PA preamplifier and RX5 base station controlled with a custom MATLAB software. LFPs were extracted by low-pass filtering (2–300 Hz) and responses were down-sampled online at 610 Hz. LFPs were averaged 100 times and the root mean square (RMS) voltage was measured over a 50 ms time window following stimulus onset.

3. Results

3.1. DPOAEs and hair cells

DPOAEs, arising from the nonlinear electromotile response of OHCs, are a reliable measure of OHC function [41]. To determine if the 65 dB SPL LLN affected OHC function, we measured DPOAE I/O functions immediately after the LLN, and at 1WPE and compared the results to pre-exposure amplitudes. Fig. 1A shows the DPOAE I/O functions for 4, 8, 16, and 24 kHz. DPOAE I/O functions immediately after the LLN exposure were nearly the same as baseline except for slight, yet significant reductions ($p < 0.05$) at several frequency/intensity combinations (8 kHz/35 dB, 16 kHz/35 dB and 24 kHz/35 dB). At 1WPE, DPOAE amplitudes were nearly the same as baseline except for slight, but significant ($p < 0.05$) changes at a few frequency/intensity combinations (8 kHz/40 dB, 16 kHz/30 &35 dB and 24 kHz/35 dB). Notably, most of these significant changes occurred at SNRs below 0 dB, meaning the DPOAE was already below the noise floor. Therefore, the results suggest that OHC function was essentially unchanged after the LLN exposure. Fig. 1B shows the mean cochleograms for the Control and LLN groups (n = 3/group). Neither group showed evidence of OHC or IHC loss consistent with the DPOAE data.