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Journal of Otology 9 (2014) 111–116

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Acoustic trauma-induced auditory cortex enhancement and tinnitus

Erin Laundrie, Wei Sun*

Department of Communicative Disorders and Sciences, State University of New York at Buffalo, 122 Cary Hall, 3435 Main Street, Buffalo, NY 14214, USA

Received 16 October 2014; accepted 17 November 2014

Abstract

There is growing evidence suggests that noise-induced cochlear damage may lead to hyperexcitability in the central auditory system (CAS) which may give rise to tinnitus. However, the correlation between the onset of the neurophysiological changes in the CAS and the onset of tinnitus has not been well studied. To investigate this relationship, chronic electrodes were implanted into the auditory cortex (AC) and sound evoked activities were measured from awake rats before and after noise exposure. The auditory brainstem response (ABR) was used to assess the degree of noise-induced hearing loss. Tinnitus was evaluated by measuring gap-induced prepulse inhibition (gap-PPI). Rats were exposed monaurally to a high-intensity narrowband noise centered at 12 kHz at a level of 120 dB SPL for 1 h. After the noise exposure, all the rats developed either permanent (>2 weeks) or temporary (<3 days) hearing loss in the exposed ear(s). The AC amplitudes increased significantly 4 h after the noise exposure. Most of the exposed rats also showed decreased gap-PPI. The post-exposure AC enhancement showed a positive correlation with the amount of hearing loss. The onset of tinnitus-like behavior was happened after the onset of AC enhancement.

Keywords: Auditory cortex; Tinnitus; Startle reflex; Hyperacusis; Noise exposure

1. Introduction

Tinnitus is a phantom perception of sound in the absence of external stimuli. Fifteen to seventeen percent of the population is affected by subjective tinnitus and approximately 2% experience severe or disabling tinnitus (Axelsson and Ringdahl, 1989; Cooper, 1994). Although the underlying physiology of tinnitus is unknown, acoustic overstimulation (Atherley et al., 1968; Axelsson and Hamernik, 1987) and ototoxic drugs (Day et al., 1989; Sun et al., 2009; Yang et al., 2007) are common inducers of tinnitus. Since acoustic overstimulation is one of the most commonly cited causes of tinnitus, aside from aging, many animal studies have used intense noise exposure to explore the behavioral manifestation and the mechanisms of tinnitus (Kaltenbach, 2000).

As it has been demonstrated repeatedly, tinnitus is likely a result of irregular neural activity emerging from a given level in the auditory pathway (Norena and Eggermont, 2005). The level in the auditory system where tinnitus arises remains obscure. Some authors have suggested that the aberrant neural signal may be generated at the peripheral level (Jastreboff, 1990), while other authors have proposed a central origin of tinnitus (Eggermont and Roberts, 2004; Roberts et al., 2010; Salvi et al., 2000). The peripheral damage, however, cannot fully explain the audiological symptoms associated with noise-induced hearing loss, e.g. tinnitus, reduced speech intelligibility and hyperacusis

There is growing evidence suggests that noise-induced peripheral damage may cause a plasticity change in the central auditory system (CAS), which may give rise to tinnitus. However, the correlations of neurophysiological changes in CAS and onset of tinnitus are not well understood. Central

* Corresponding author. Tel.: +1 716 8295307.
E-mail address: weisun@buffalo.edu (W. Sun).
Peer review under responsibility of PLA General Hospital Department of Otolaryngology Head and Neck Surgery.

http://dx.doi.org/10.1016/j.joto.2014.11.001

auditory plasticity changes have been observed following peripheral damage induced by salicylate (Sun et al., 2009), cisplatin (Salvi et al., 2000) and noise exposure (Sun et al., 2012; Syka, 2002). Both monaural and binaural noise exposure often enhanced the amplitude of the auditory cortex (AC) responses in awake rats. Even though there has been a correlation between noise exposure and increased AC amplitude as well as noise exposure and tinnitus behavior, the correlations of neurophysiological changes in CAS and onset of tinnitus remain unclear.

Previous studies using animal models have allowed researchers to study the physiology of tinnitus. Sun et al. revealed that salicylate-induced tinnitus paralleled a substantial increase in the AC amplitude in the first few hours following the 250 mg/kg salicylate injection before recovering toward the baseline within a day or so (Sun et al., 2009). Even though acoustic-trauma evoked tinnitus is one of the most commonly reported causes of tinnitus, it is unknown to what extent the AC response of an awake rat will be affected by acoustic trauma-induced tinnitus. We hypothesize that an increase in AC response will be related to tinnitus behavior. To test this hypothesis, we investigated the influence of monaural noise exposure on the AC amplitudes by using a chronically implanted silver ball electrode of awake rats before and after treatment with a 120 dB SPL narrowband noise centered at 12 kHz for 1 h. We also monitored tinnitus behavior by measuring the startle reflex before and after the monaural noise exposure.

2. Materials and methods

2.1. Animals

Three Harlan Sprague-Dawley male rats (3–4 months old) were used for testing. The rats did not have any diet restrictions. All rats were exposed to 120 dB SPL monaural narrowband noise centered at 12 kHz (1 kHz bandwidth) for 1 h following a series of reliable AC baseline and ABR measures. Following the noise exposure, AC responses were obtained at 1 h, 4 h, 1 day, 2 days, 1 week and 2 weeks. Startle reflex testing was administered pre noise exposure until a stable baseline was obtained. Startle reflex testing was also administered 2–4 h, 1 day, 2 days, 1 week and 2 weeks following noise exposure.

2.2. Auditory brainstem response (ABR) recording

Hearing thresholds were obtained from each subject as measured by ABR under isoflurane anesthesia (1–2%). The ABR recordings were measured using a surgically implanted chronic electrode connected to a preamplifier (RA16LA, TDT) using a low noise cable. The preamplifier was then connected to a digital signal processing module (RX5-2, Pentusa Base Station, TDT) before being processed with software (BioSigRP) with a band pass filter set at 100–3000 Hz. The sound stimulus was a tone-burst (5 ms duration; 1 ms rise/fall time) at 6, 12, 16 and 20 kHz generated by TDT hardware with a repetition rate of 21 times/second. Sound stimuli were presented through a high frequency super tweeter (FT28D, Fostex) and the sound level was calibrated using a sound level meter (Larson Davis Sound Level Meter, model 824, ½ inch condenser microphone). ABR was obtained in both ears 5–6 h following noise exposure and on a daily basis until the rat had recovered to its full potential.

2.3. AC recording

Rats were anesthetized using 1–2% isoflurane. A silver ball electrode was implanted into the right AC, cemented in place, and the wound was sutured around the electrode connector. The rats were allowed 2 weeks to recover before testing began.

Sound stimuli were generated using TDT hardware (RP2 D/A converted, PA5 attenuator, HB7 headphone amplifier) connected to a loudspeaker. The electrode was connected to a low impedance amplifier (RA16PA Medusa Preamp, TDT) and signals were sampled using an RA16 Medusa Base Station (TDT). Stimulus generation and data acquisition was accomplished using TDT software (BioSigRP).

The awake rats were tested in a custom testing apparatus to restrict rat's movement during the test. Before the test, rats were placed in the testing apparatus for 1–2 h per day for 2–3 days to let the rats get used to the testing environment. The sound level was calibrated. Local field potentials were recorded before and after noise exposure. Tone-bursts centered at 6, 12, 16 and 20 kHz were used to elicit AC responses.

2.4. Acoustic startle reflex

All startle reflex testing was performed in a sound attenuating box. Each box contained a startle reflex platform and a high frequency speaker (FT28D, Fostex) located 20 cm above the rat. All rats were placed in a wire mesh cage (15–20 cm long × 7 cm wide × 5.5 cm high) mounted on an acrylic glass base to restrict their movement. The cage rested on top of a piezoelectric transducer (Radio Shack 273-066) within the calibrated sound field

Sound stimuli were generated by a RP2 Real-Time Processor (TDT) from custom software created in MatLab 6.0. The rat's body movement elicited from the startle stimuli was measured by the sensitive piezoelectric transducer connected to an A/D converter on an Real-Time Processor (TDT). The output was sent to a low-pass filter set at 1000 Hz (LPF-300, World Precision Instruments). The root mean square (RMS) amplitude was measured over 100 ms response following the onset of the startle stimulus using custom software. The startle eliciting stimulus consisted of a broadband noise burst presented at 105 dB SPL (0.5–30 kHz, 20 ms duration, 0.1 ms rise/fall time).

Acoustic startle reflexes were measured on all three rats before and after noise exposure using two testing procedures: gap-induced prepulse inhibition (gap-PPI) and noise burst prepulse inhibition of startle reflex (NB-PPI). For the gap-PPI, the startle reflex was measured in the presence of continuous