NeuroImage 107 (2015) 1–9

Contents lists available at ScienceDirect

NeuroImage

journal homepage: www.elsevier.com/locate/ynimg

Long-term, passive exposure to non-traumatic acoustic noise induces neural adaptation in the adult rat medial geniculate body and auditory cortex

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ARTICLE INFO

Article history:
Accepted 22 November 2014
Available online 3 December 2014

Keywords:
Functional magnetic resonance imaging
Auditory system
Acoustic exposure
Rat

ABSTRACT

Exposure to loud sounds can lead to permanent hearing loss, i.e., the elevation of hearing thresholds. Exposure at more moderate sound pressure levels (SPLs) (non-traumatic and within occupational limits) may not elevate thresholds, but could in the long-term be detrimental to speech intelligibility by altering its spectrotemporal representation in the central auditory system. In support of this, electrophysiological and behavioral changes following long-term, passive (no conditioned learning) exposure at moderate SPLs have recently been observed in adult animals. To assess the potential effects of moderately loud noise on the entire auditory brain, we employed functional magnetic resonance imaging (fMRI) to study noise-exposed adult rats. We find that passive, pulsed broadband noise exposure for two months at 65 dB SPL leads to a decrease of the sound-evoked blood oxygenation level-dependent fMRI signal in the thalamic medial geniculate body (MGB) and in the auditory cortex (AC). This points to the thalamo-cortex as the site of the neural adaptation to the moderately noisy environment. The signal reduction is statistically significant during 10 Hz pulsed acoustic stimulation (MGB: $p < 0.05$, AC: $p < 10^{-4}$), but not during 5 Hz stimulation. This indicates that noise exposure has a greater effect on the processing of higher pulse rate sounds. This study has enhanced our understanding of functional changes following exposure by mapping changes across the entire auditory brain. These findings have important implications for speech processing, which depends on accurate processing of sounds with a wide spectrum of pulse rates.

Introduction

Exposure to high sound pressure levels (SPLs) can permanently damage the sensory apparatus of the inner ear (Liberman and Kiang, 1978). The resulting hearing loss (i.e., increase of the minimum detectible SPL, or hearing threshold) can produce extensive reorganization of the central auditory system (Gold and Bajo, 2014). For example, following a high-frequency hearing loss, neurons in the auditory cortex (AC) that were formerly sensitive to high frequencies become sensitive to neighboring mid-frequencies (Rajan et al., 1993; Robertson and Irvine, 1989), i.e., the mid-frequencies become "over-represented" as a consequence of the high-frequency hearing loss. Some of these central effects of deafness can be reversed following the restoration of hearing, as in cochlear implantation (Pantev et al., 2006; Seghier et al., 2005). Exposure to somewhat lower SPLs may lead to only temporary elevations of hearing thresholds, followed by recovery. Such exposures are presently permitted by occupational noise standards (NIOSH, 1998; OSHA, 2002). However, recent studies found that such exposures can result in a permanent loss of inner hair cell synaptic terminals and degeneration of auditory nerve fibers, even if hearing thresholds are (initially) only temporarily affected (Kujawa and Liberman, 2009; Wang and Ren, 2012). In light of these findings, there is a serious need to further assess the potential impact of acoustic exposures that do not permanently elevate hearing thresholds.

Traditionally, research on more moderate acoustic exposures (well within present occupational limits) has focused on the more plastic developing brain (Hensch, 2004). In mature subjects, after "critical" or "sensitive" developmental periods have closed, conventional wisdom held that moderate-level acoustic exposure could not, under passive

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http://dx.doi.org/10.1016/j.neuroimage.2014.11.048
1053-8119/

conditions (not paired with conditioned learning or stimulated neuromodulator release from the forebrain), have any long-term impact on the auditory brain (Pienkowski and Eggermont, 2011). However, the impact of long-term, passive exposure at moderate SPL in adulthood has recently gained renewed attention (Brattico et al., 2005; Gourévitch et al., 2014; Kujala et al., 2004; Noreña et al., 2006; Pienkowski and Eggermont, 2009, 2010a, 2010b; Pienkowski et al., 2011, 2013; Zhou and Merzenich, 2012; Zhou et al., 2011). Eggermont et al. exposed adult cats for several weeks to months to various types of noise at levels of 68–80 dB SPL (Noreña et al., 2006; Pienkowski and Eggermont, 2009, 2010a, 2010b; Pienkowski et al., 2011, 2013). The general finding was that the auditory cortical representation of sound frequencies within the noise band was profoundly suppressed, and the representation of frequencies outside of the noise band was enhanced. This is reminiscent of the effects of restricted hearing loss (Rajan et al., 1993; Robertson and Irvine, 1989), although the moderate-level exposures produced no observable signs of cochlear damage. Zhou and Merzenich extended this work to show that moderate exposure of adult rats led to behavioral deficits on an auditory temporal discrimination task (Zhou and Merzenich, 2012). Prior to this animal work, Kujala et al. had observed impaired syllable discrimination (as assessed electrophysiologically, using the mismatch negativity response) in eight shipyard workers and two preschool teachers (23– 36 years old), with an average six years of moderate occupational noise exposure but no elevation of hearing threshold (Kujala et al., 2004). Brattico et al. extended this work by comparing the effects of moderate occupational exposure on the cortical representation of speech and non-speech sounds (Brattico et al., 2005).

Previous studies on the effects on the mature auditory brain of persistent exposure to moderate-level noise have employed primarily electrophysiological testing. However, electrophysiology does not allow easy study of functional changes across the entire central auditory system, and is limited to poorly localized far-field recordings in human subjects. To advance this direction of research, including opening avenues for future measurements in humans, we here employ functional magnetic resonance imaging (fMRI) to simultaneously examine the entire central auditory system of moderate noise-exposed rats.

Blood oxygenation level dependent (BOLD) fMRI is a noninvasive neuroimaging technique (Ogawa et al., 1990) that offers a whole brain field of view with relatively high spatial resolution. fMRI has been applied extensively to study the auditory system (Binder et al., 1996; De Martino et al., 2013; Saenz and Langers, 2014), helping to show that music and language training alter response patterns in the hippocampus, AC, and other cortical and subcortical regions (Angulo-Perkins et al., 2014; Callan et al., 2003; Herdener et al., 2010; Rauschecker et al., 2008; Wang et al., 2003). fMRI has also been used to confirm that the AC of cochlear implant users is activated by electrical stimulation (Seghier et al., 2005), and that hearing loss and tinnitus alter auditory system responses (Adjamian et al., 2009; Bilecen et al., 2000; Langguth et al., 2012; Melcher et al., 2000; Middleton and Tzounopoulos, 2012). fMRI has been applied in animal models (Bach et al., 2013; Baumann et al., 2011; Brown et al., 2014; Jin and Kim, 2008; Van Ruijssevelt et al., 2013), including rats (Pawela et al., 2008; Sicard et al., 2003; Smith et al., 2002; Van Camp et al., 2006). We and others have recently developed rat auditory fMRI capabilities (Cheung et al., 2012a,2012b; Gao et al., 2014; Lau et al., 2013; Yu et al., 2009; Zhang et al., 2013).

In this study, adult rats were passively exposed for two months to pulsed noise at 65 dB SPL. Following the cessation of exposure, control (unexposed) and exposed subjects underwent fMRI with acoustic stimulation pulsed at two different rates. Region of interest analysis was performed on fMRI signals measured from the contralateral superior olivary complex, lateral lemniscus, inferior colliculus, medial geniculate body, and auditory cortex of the central auditory system. The amplitudes of fMRI signals from the different brain structures, subject groups, and stimulation rates were compared.

Methods

Animals and housing

All aspects of this study were approved by the Committee on Research Practices of the Hong Kong University of Science and Technology and the Committee on the Use of Live Animals in Teaching and Research of the University of Hong Kong. Normal female Sprague–Dawley rats (three months of age, $N = 24$) were used in this study. Twelve were randomly assigned to receive continuous acoustic exposure while the remaining 12 were assigned to standard housing. Exposed and control subjects were housed in separate rooms. Background noise in the rooms was less than 40 dB total sound pressure level (SPL). All subjects were housed in pairs, exposed to 12 hour light/dark cycles, and received standard food and water ad libitum. Acoustic exposure began when subjects were three months old. During this time, control subjects continued to be housed in standard acoustic conditions.

Acoustic exposure

The acoustic exposure consisted of 50 ms pulses of broadband noise, low-pass filtered at 30 kHz, and presented at 65 dB total SPL. Total $\mathrm{SPL} = 10\log\left(\sum_{k=1}^{n} 10^{SPL(k)/10}\right)$, where SPL(k) was the SPL at each frequency. Five pulses were presented per second and repeated 24 hours/day for two months. Pulses were generated using wide bandwidth speakers (MF1, Tucker-Davis Technologies, USA) and played to the subjects inside their cages. The power spectrum of the acoustic exposure was recorded inside a cage with a calibrated reference microphone (M50, Earthworks, USA) to verify output (Fig. 1). The microphone had flat and known response properties up to 50 kHz. This rat acoustic exposure model was chosen because it had been used in comparable behavioral and electrophysiological studies and demonstrated not to elevate auditory brainstem response thresholds (Zhou and Merzenich, 2012).

Magnetic resonance imaging

Functional magnetic resonance imaging (fMRI) was performed at five months of age. Each subject was anesthetized with 3 % isoflurane (mixed with room air) and anesthesia was maintained with 1 % isoflurane throughout the course of setup and scanning. The subject was placed in the prone position on a body holder with a head motion restricting nose cone and tooth bar. A surface coil was placed over the head. A custom-made sound transmission tube was inserted into

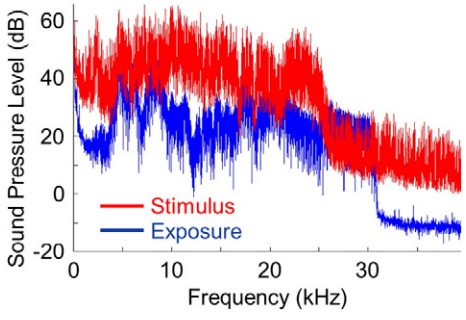

Fig. 1. Power spectra of the acoustic exposure (blue) and stimulus (red) recorded with a reference microphone (M50, Earthworks, USA). The exposure spectrum was recorded inside the cage and the stimulus spectrum was recorded at the tip of the sound transmission tube that entered the ear. The acoustic exposure was low pass filtered at 30 kHz and the acoustic stimulus was low pass filtered at 25 kHz. The total sound pressure level (SPL) of the exposure was 65 dB and the total SPL of the stimulus was 85 dB. A broadband stimulus was employed to excite more neurons in the central auditory system, which leads to higher functional magnetic resonance imaging (fMRI) signals compared with tone stimuli. Note that 0 dB SPL is a standard reference point set to the threshold of human hearing at 1 kHz and a negative SPL does not mean the sound has less than zero energy.