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Spatial learning and memory deficits in young adult mice exposed to a brief intense noise at postnatal age

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Abstract

Noise pollution is a major hazardous factor to human health and is likely harmful for vulnerable groups such as pre-term infants under life-support system in an intensive care unit. Previous studies have suggested that noise exposure impairs children's learning ability and cognitive performance and cognitive functions in animal models in which the effect is mainly attributed to the oxidant stress of noise on the cognitive brain. The potential role of noise induced hearing loss (NIHL), rather than the oxidant stress, has also been indicated by a depression of neurogenesis in the hippocampus long after a brief noise exposure, which produces only a tentative oxidant stress. It is not clear if noise exposure and NIHL during early development exerts a long term impact on cognitive function and neurogenesis towards adulthood. In the present study, a brief noise exposure at high sound level was performed in neonatal C57BL/6J mice (15 days after birth) to produce a significant amount of permanent hearing loss as proved 2 months after the noise. At this age, the noise-exposed animals showed deteriorated spatial learning and memory abilities and a reduction of hippocampal neurogenesis as compared with the control. The averaged hearing threshold was found to be strongly correlated with the scores for spatial learning and memory. We consider the effects observed are largely due to the loss of hearing sensitivity, rather than the oxidant stress, due to the long interval between noise exposure and the observations.

Keywords: Noise induced hearing loss; Neonatal mice; Learning; Memory; Neurogenesis

1. Introduction

Hearing loss is one of the most common sensory disorders affecting 10% of the general population (Audiology.org, 2011; ASHA, 2011), and approximately 1.4 per 1000 of newborn babies (CDC, 2014). Noise exposure is one of the major causes for acquired hearing loss in adults (Nelson et al., 2005) and children (Niskar et al., 2001; National Institute on Deafness, 2008; National Institute on Dea, 2007). The damaging effect of noise, however, is not limited in the auditory system, but extended to many other systems (Basner et al., 2014). Recent studies have warned of noise-related impairment of learning ability and cognitive performance (Cheng et al., 2011; Cui et al., 2009; Jauregui-Huerta et al., 2011; Wright et al., 2014). Soldiers who were exposed to excessive noise levels including explosions and blast waves revealed severe noise induced hearing loss (NIHL) and tinnitus (Helfer et al., 2011; Cave et al., 2007), as well as cognitive deficits and memory impairment (Belanger et al., 2009).

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The mechanisms underlying cognitive function decline after noise exposure are not entirely clear. However, animal studies have provided clues as to what might be happening. Noise exposure is likely to impair cognitive functions through two different but closely related approaches. One is related to the oxidative reaction initiated by noise exposure. Increased oxidative stress has been reported in many studies as the cause of neuronal degeneration seen in many auditory nuclei as well as in the brain regions critical for cognitive functions (Cheng et al., 2011; Cui et al., 2009; Chengzhi et al., 2011; Hirano et al., 2006). The other approach is the due to the change of auditory input to the cognitive brain after hearing loss induced by noise. This approach is not investigated intensively in the past, but the possibility has been supported by the connection between the auditory brain and cognitive brain (Kraus et al., 2012) and demonstrated by the hippocampal degeneration and deteriorated spatial memory in C57BL/6J mice with age related hearing loss (Yu et al., 2011) and the suppression of hippocampal neurogenesis in the rat after noise-induced unilateral hearing loss (Kraus et al., 2010).

Most of the studies reviewed above are performed on adult subjects. However, the impact of noise exposure during early development on cognitive functions has been suggested by some studies (Xu et al., 2010; Kim et al., 2006). It is important to determine if noise exposure and NIHL at an early stage of an individual's development can produce a long term effect on cognitive function. Exposure to harmful noise exposure is a true risk for new born babies, especially those who are preterm and immature at birth and have to rely on life support systems in an intensive care unit, where the noise level can go beyond 100 dBA (Slevin et al., 2000; Chang et al., 2001; Blackburn, 1998; Lahav et al., 2014). Noise exposure at such levels for a significant period of time is expected to cause oxidative stress and/or NIHL, which may then affect the physical and neurobehavioral development of those babies, resulting in cognitive deficits as they mature (Blackburn, 1998). Exposure to environmental noise has been reported to impair the cognitive function in children (Stansfeld et al., 2005). Animal studies have also demonstrated that hearing impairment during early development can produce long term impacts on behavior and cognitive functions (Jauregui-Huerta et al., 2011; Sun et al., 2011), suggesting that the auditory system and brain are more vulnerable during neonatal age.

Using small rodents (such as rats and mice) to address the developmental impact of noise-induced stress and NIHL on cognitive function is attractive due in part to at least two major reasons. Firstly, this approach allows certain observations, such as neuronal morphology, that are not ethical to perform in human subjects. Secondly, the auditory organs of those rodents are not mature at birth and therefore will mimic the development of preterm human babies (Walters et al., 2013; Kikkawa et al., 2012; Ahituv et al., 2000; Freeman et al., 1999; Sohmer et al., 1995).

In the present study, we observed the impact of a brief noise exposure given at 15 postnatal days (P15d) on the learning/memory function of C57BL/6J mice in young adulthood (2.5 months of age). The noise exposure was at a high level (123 dB SPL) and produced a permanent hearing loss of moderate degree. The changes in hippocampus related learning and memory functions were correlated with the degree of hearing loss.

2. Materials and methods

2.1. Subjects and experimental outline

Pregnant C57BL/6J mice were obtained from the Experimental Animal Center of Jiangsu University, Nanjing, Jiangsu, China. A total of 42 neonatal mice were recruited from 8 litters and were randomly divided into 2 groups with equal sample size ($n = 21$ in each): the control and the noise groups. At P15d, the animals in the noise group were exposed to a broadband (white) noise at 123 dB SPL for 2 h, while the animals in the control group accepted the sham exposure (environmental change). All baby mice were taken back to their mothers after treatment. Two months after the noise exposure (at the age of 2.5 months), all animals were examined for hearing threshold by frequency specific auditory brainstem response (ABR). The capabilities of spatial learning and memory were measured by means of a Morris water maze test prior to the ABR test to avoid the stress impact of anesthesia during ABR. Immediately after the functional test, the hippocampus were harvested for the observation of neurogenesis. All animal procedures were approved by the University Committee for Laboratory Animals of Southeast University, China (Permit number: SCXK2011-0003).

2.2. Noise exposure

The animals in the noise group were treated with an exposure to a broadband noise at 123 dB SPL for 2 h when they were awake. They were unrestrained in a cage 60 cm below the horns of two loudspeakers; one was a low frequency woofer and the other was a high frequency tweeter. Electrical Gaussian noise was delivered to the speakers after power amplification. The acoustic spectrum of the sound was distributed mainly below 20 kHz as reported previously (Wang et al., 2011). The noise level was monitored using a ¼-inch microphone linked to a sound level meter (microphone: 2520, sound level meter: 824, from Larson Davis, Depew, NY, USA).

2.3. ABR test

For ABR recordings, the animal was anesthetized with pentobarbital (80 mg/kg, i.p.) and the body temperature maintained at 37.5–38 °C with a thermostatic heating pad. Three subdermal needle electrodes were used to record ABRs. The non-inverting electrode was inserted at the vertex in the middle point between the two eyes, the reference and the grounding electrodes were on the two earlobes.

TDT hardware and software (BioSig and SigGen) were used for stimulus generation and bio-signal acquisition. The stimuli were played through a broadband speaker (MF1 from TDT, USA), which was placed 10 cm in front of the animal's head. The evoked responses were amplified 20 times and