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Research Report

Noise exposure of immature rats can induce different age-dependent extra-auditory alterations that can be partially restored by rearing animals in an enriched environment

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ARTICLE INFO

Article history:
Accepted 27 January 2016
Available online 3 February 2016

Keywords:
Noise
Enriched environment
Developing rats
Behavior

ABSTRACT

It has been previously shown that different extra-auditory alterations can be induced in animals exposed to noise at 15 days. However, data regarding exposure of younger animals, that do not have a functional auditory system, have not been obtained yet. Besides, the possibility to find a helpful strategy to restore these changes has not been explored so far. Therefore, the aims of the present work were to test age-related differences in diverse hippocampal-dependent behavioral measurements that might be affected in noise-exposed rats, as well as to evaluate the effectiveness of a potential neuroprotective strategy, the enriched environment (EE), on noise-induced behavioral alterations. Male Wistar rats of 7 and 15 days were exposed to moderate levels of noise for two hours. At weaning, animals were separated and reared either in standard or in EE cages for one week. At 28 days of age, different hippocampal-dependent behavioral assessments were performed. Results show that rats exposed to noise at 7 and 15 days were differentially affected. Moreover, EE was effective in restoring all altered variables when animals were exposed at 7 days, while a few were restored in rats exposed at 15 days. The present findings suggest that noise exposure was capable to trigger significant hippocampal-related behavioral alterations that were differentially affected, depending on the age of exposure. In addition, it could be proposed that hearing structures did not seem to be necessarily involved in the generation of noise-induced hippocampal-related behaviors, as they were observed even in animals with an immature auditory pathway. Finally, it could be hypothesized that the differential restoration achieved by EE rearing might also depend on the degree of maturation at the time of exposure and the variable evaluated, being younger animals more susceptible to environmental manipulations.

Abbreviations: HC, Hippocampus; Noise7d/Noise15d, Rats exposed to noise at 7 or 15 days of age; Ct7d/Ct15d, Control rats of Noise7d/15d, respectively; CNS, Central Nervous System; PND, Postnatal Day; EE, Enriched environment cages; St, Standard cages; OF, Open Field; EPM, Elevated plus maze; IA, Inhibitory avoidance

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http://dx.doi.org/10.1016/j.brainres.2016.01.050
0006-8993/

1. Introduction

Noise can be defined as an unpleasant sound, in general of high intensity. As a result of exposure to noise, physiological functions such as those involving structures of the auditory and non-auditory systems might be damaged (Gannouni et al., 2013).

Noise is formed by a wide range of frequencies and differs from natural sounds or music. Prolonged noise exposure at high intensities can interfere with the performance of humans` work activities and might produce temporary or permanent damage to the auditory system, which can lead to significant hearing loss (Frenzilli et al., 2004; Gourévitch et al., 2014).

People working in heavy manufacturing (>105 dBA for 1 h) or those that handle firearms (>130 dBA for a few seconds) are commonly affected by permanent hearing loss. Likewise, a temporary hearing loss for a few hours is often experienced by people attending concerts or nightclubs, where elevated noise levels ranging between 90 dBA and 105 dBA for 2 hours or more can be usually found (Trapanotto et al., 2004). In contrast, safer noise levels, below 80 dBA, have been considered harmless for the auditory system (NIOSH, 1998).

Luckily, the environmental noise experienced during daily life such as traffic noise is, in general, of mild intensity. Nevertheless, the negative effects that might be induced by continuous noise exposure of moderate intensity on the auditory and non-auditory systems are largely unknown. Moreover, although the effects of noise in living organisms are typically reversible in the short term, some can cause long-lasting or even permanent damage (Manikandan et al., 2006; Goble et al., 2009; Pienkowski and Eggermont, 2012). However, the consequences of noise impact are largely underestimated by the public health setting, and little is known about possible strategies for counteracting noise-induce damage.

Unfortunately, noise is potentially hazardous for millions of people working in noisy places. However, people that live in a noisy environment without being exposed to noise in their daily work-related activities, may also be at risk (Gourévitch et al., 2014). Importantly, little attention has been paid in the study of noise-induced extra-auditory effects. For this reason, scarce publications can be found on this subject (Lenzi et al., 2003; Turner et al., 2005; Rabat, 2007). Further, few data are available using developing animals exposed to noise.

Previous results from our laboratory and from others (Manikandan et al., 2006; Uran et al., 2010, 2012; Cui et al., 2013) showed that the Central Nervous System (CNS) might be one extra-auditory target for noise-induced damage. In particular, much remains unknown regarding the effect of noise on CNS structures, beyond the classical auditory pathway. Specifically, several behavioral and biochemical alterations were observed in noise-exposed animals. Interestingly, it has been shown that chronic and/or intense exposure to noise can impair hippocampal-dependent memory (Manikandan, et al., 2006; Rabat, 2007; Uran et al., 2010, 2012, 2014) and reduce the number of hippocampal neurons and their ramifications (Jáuregui-Huerta et al., 2011). As an acoustic stimulus, noise can be transmitted through the lemniscal ascending path via the inferior colliculus, then to the auditory cortex and finally to the CA3 region of the hippocampus (HC), suggesting that hippocampal function may be affected by noise exposure (Xi et al., 1994; Sakurai, 2002; Kraus et al., 2010; Cheng et al., 2011). However, it should not be discarded that noise might directly affect HC as suggested by Säljö et al (2011), who concluded that the scalp, skull bone and cerebrospinal fluid, which separate the brain from the surrounding air, do not constitute an appreciable protection for the brain against noise, allowing the impact of noise vibrations that might produce undesirable alterations.

During early mammalian life, the CNS undergoes progressive structural and functional development and may be more susceptible to potential damage induced by a variety of environmental factors like noise. In fact, developing brain is considered more plastic than the adult brain; therefore, disruption of the normal developmental time-course can be induced after a relatively short noise exposure period and with more lasting effects when compared with noise-exposed adult individuals (Wang, 2004; Kujawa and Liberman, 2006).

Interestingly, it is known that the critical period in the development of rat auditory system extends from about postnatal days 11–13 (De Villers-Sidani et al., 2008). Therefore, it could be of interest to investigate if rats of 7 days, that do not have a functional auditory pathway yet, can anyway be affected by noise exposure.

Since different tissues could be affected by the vibration provoked by noise, it should not be discarded that noise might impact the HC through a direct mechanism, besides the already known indirect pathway (Säljö et al., 2011).

Finally, the possibility of restoring noise-induced damage has not been evaluated in our experimental model yet. A non-pharmacological neuroprotective strategy, the enriched environment (EE, Laviola et al., 2008; Petrosini et al., 2009), has shown to be an effective protective tool against different CNS injuries (Lores-Arnaiz et al., 2006; Baldini et al., 2013). It consists in accommodating the animals in cages larger than the standard, which contains different toys, ramps and wheels. Unfortunately, few reports about the success of enriched environment strategy as an approach to counteract the effects of different injuries in developing animals, including noise, have been published (Baldini et al., 2013; Jiang et al., 2015).

Thus, the aims of the present work were to test the existence of age-related differences in extra-auditory hippocampal-dependent behavioral measurements that might be affected in noise-exposed rats as well as to evaluate the effectiveness of a non-pharmacological potential neuroprotective strategy, the EE, on noise-induced behavioral alterations.

2. Results

2.1. *Open field (OF) parameters*

2.1.1. *Vertical exploration (rearing and climbing in the first session)*

Two way ANOVA analysis shows significant differences in the time spent rearing and climbing in the first session of the OF,