Int. J. Devl Neuroscience 37 (2014) 41–51

Contents lists available at ScienceDirect

International Journal of Developmental Neuroscience

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

Long-term recovery from hippocampal-related behavioral and biochemical abnormalities induced by noise exposure during brain development. Evaluation of auditory pathway integrity

S.L. Uran[a], M.E. Gómez-Casati[b,c], L.R. Guelman[a,*]

[a] 1ª Cátedra de Farmacología, Facultad de Medicina, UBA, CEFYBO-CONICET, Buenos Aires, Argentina
[b] Instituto de Investigaciones en Ingeniería Genética y Biologia Molecular INGEBI-CONICET, Buenos Aires, Argentina
[c] 3ª Cátedra de Farmacología, Facultad de Medicina, UBA, Buenos Aires, Argentina

ARTICLE INFO

Article history:
Received 1 April 2014
Received in revised form 30 May 2014
Accepted 1 June 2014

Keywords:
Noise
Hippocampus
Developing CNS
Auditory pathway

ABSTRACT

Sound is an important part of man's contact with the environment and has served as critical means for survival throughout his evolution. As a result of exposure to noise, physiological functions such as those involving structures of the auditory and non-auditory systems might be damaged.

We have previously reported that noise-exposed developing rats elicited hippocampal-related histological, biochemical and behavioral changes. However, no data about the time lapse of these changes were reported. Moreover, measurements of auditory pathway function were not performed in exposed animals. Therefore, with the present work, we aim to test the onset and the persistence of the different extra-auditory abnormalities observed in noise-exposed rats and to evaluate auditory pathway integrity.

Male Wistar rats of 15 days were exposed to moderate noise levels (95–97 dB SPL, 2 h a day) during one day (acute noise exposure, ANE) or during 15 days (sub-acute noise exposure, SANE). Hippocampal biochemical determinations as well as short (ST) and long term (LT) behavioral assessments were performed. In addition, histological and functional evaluations of the auditory pathway were carried out in exposed animals.

Our results show that hippocampal-related behavioral and biochemical changes (impairments in habituation, recognition and associative memories as well as distortion of anxiety-related behavior, decreases in reactive oxygen species (ROS) levels and increases in antioxidant enzymes activities) induced by noise exposure were almost completely restored by PND 90. In addition, auditory evaluation shows that increased cochlear thresholds observed in exposed rats were re-established at PND 90, although with a remarkable supra-threshold amplitude reduction.

These data suggest that noise-induced hippocampal and auditory-related alterations are mostly transient and that the effects of noise on the hippocampus might be, at least in part, mediated by the damage on the auditory pathway. However, we cannot exclude that a different mechanism might be responsible for the observed hippocampal-related changes.

1. Introduction

Sound above a certain range of sound-pressure level (SPL), referred to as "unwanted sound" or noise, can produce hearing loss as well as different types of extra-auditory alterations (Trapanotto et al., 2004; Fonseca et al., 2012). Although usually the effects of noise on living organisms are reversible in the short term, some can cause long-lasting or even permanent damage. However, the consequences of noisy stimuli coming from the environment on auditory and extra-auditory structures are largely underestimated in the public health setting.

Different extra-auditory alterations can be found in the literature. It has been reported that noise can produce serious

Abbreviations: HC, hippocampus; ANE, acute noise exposure; SANE, sub-acute noise exposure; Ct, control; CNS, Central Nervous System; PNS, Peripheral Nervous System; PND, postnatal day; ROS, reactive oxygen species; Cat, catalase; SOD, superoxide dismutase; OF, open field; OR, object recognition; ST, short term; LT, long term; IHC, inner hair cell; OHC, outer hair cell; ABRs, auditory brainstem responses; DPOAEs, distortion product otoacoustic emissions.

* Corresponding author at: Paraguay 2155, piso 15, 1121, Buenos Aires, Argentina. Tel.: +54 11 5950 9500x2204.
E-mail addresses: lguelman@fmed.uba.ar, lguelman2001@yahoo.com.ar (L.R. Guelman).

http://dx.doi.org/10.1016/j.ijdevneu.2014.06.002
0736-5748/

behavioral disturbances in eating (Krebs et al., 1996) and sleep (Rabat et al., 2004). Besides, a variety of CNS-related symptoms, including emotional stress, increase in social conflicts and general psychiatric disorders (Rabat, 2007) were observed after noise exposure, together with an increase in aggressive behavior and anxiety (Stansfeld and Matheson, 2003).

Previous results from our laboratory (Uran et al., 2010, 2012) and from others (Manikandan et al., 2006; Cui et al., 2009, 2013) demonstrated that the Central Nervous System (CNS) might be a target for noise exposure damage. Specifically, several behavioral and biochemical extra-auditory abnormalities were observed in noise-exposed animals. Manikandan et al. (2006) and Cui et al. (2009, 2013) showed a deficit in spatial memory in noise-exposed animals. In our previous work, we found alterations in a CNS structure, the hippocampus (HC), that include an oxidative imbalance at PND 30 (decrease in hippocampal ROS levels, increase of antioxidant enzymes Cat and SOD activities) together with several behavioral abnormalities (including deficits in habituation, associative and recognition memories, mainly at LT in SANE rats, as well as a decrease in anxiety-like behaviors) and histological changes (increase in the number of pyknotic cells in all hippocampal layers, see Uran et al., 2010, 2012).

In the cochlea, noise-induced injury typically includes structural damage to hair cells and supporting cells as well as swollen postsynaptic terminals of the spiral ganglion neurons (Saunders et al., 1985). It has become increasingly evident that even occasional exposure to loud sounds in occupational or recreational settings can cause irreversible damage to the cochlea, although the resulting partial loss of hearing sensitivity could disappear within hours or days after exposure (Bohne, 1977; Hamernik et al., 1984; Hu and Zheng, 2008; Pienkowski and Eggermont, 2012). Conversely, recent work has revealed that exposure to moderate noise levels, causing transient threshold elevation, can cause degeneration of afferent terminals, without loss of hair cells (Kujawa and Liberman, 2009; Chen et al., 2012; Maison et al., 2013).

Therefore, as different functions might be affected without causing evident auditory damage, studying the effect of moderate noise levels on extra-auditory structures acquires relevance. Moreover, long-term reversal of moderate noise-induced damage could take place.

Unfortunately, few data are available concerning the different extra-auditory effects that result after exposure to noise of various intensities (Uran et al., 2010, 2012; Cui et al., 2013). In particular, much is still unknown about the effect of noise on extra-auditory regions of the CNS, outside the classical auditory pathway. Since the HC is able to respond to auditory stimuli through a non-classical pathway (Xi et al., 1994; Sakurai, 2002), this structure could be indirectly affected by noise (Kraus et al., 2010). Alternatively, since different tissues might be affected by the vibration provoked by noise, it should not be discarded that noise might impact the HC through a direct mechanism. Recently, Säljö et al. (2011) 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. In consequence, the transmission of sound into the brain appears to be highly efficient. Interestingly, soldiers and other personnel exposed to extremely high-level noise (170 dB SPL, such as blast waves or explosions) often suffer cognitive and memory impairments. Similarly, rats exposed to shock waves at 10 kPa (174 dB SPL) showed poor cognitive function on the Morris water maze test, which seems to be most likely the result of a direct injury to the brain caused by acoustic overpressure (Säljö et al., 2002).

The developing brain is in general considered more plastic than the adult brain. Disruption of normal developmental trajectory can be affected with a relatively short sound exposure period and with more lasting effects when compared with exposure of adult individuals.

Different structures within the Peripheral Nervous System (PNS) and the CNS have overlapping developmental periods, such as the rat auditory system (from PND 11 to PND 13, de Villers-Sidani et al., 2008) and the HC (from GD 18 to PND 15, Winer and Lee, 2007; Munoz-Lopez et al., 2010). For this reason, it resulted interesting to analyze what happens to both structures when a developing animal is exposed to a harmful agent at this critical developmental period (Winer and Lee, 2007; de Villers-Sidani et al., 2008; Munoz-Lopez et al., 2010). Therefore, since the maturation process of rat' HC occurs within a few weeks after birth, early chronic or intense exposure to noxious events might affect hippocampal development.

In particular, the HC has been proposed to be a potential extra-auditory target for the deleterious effects of noise. It has been shown that chronic and/or intense exposure to noise has the ability to impair hippocampus-dependent memory (Rabat, 2007; Manikandan et al., 2006; Uran et al., 2010, 2012) and to reduce the number of hippocampal neurons and their ramifications (Jáuregui-Huerta et al., 2011).

Even though we have previously reported that developing rats exposed to acute (ANE) or sub-acute (SANE) moderate white noise levels elicited changes in the HC that take place after several weeks, no data concerning the early changes that could be triggered by noise were reported. Besides, the occurrence of a long-term recovery from the disturbances induced after noise exposure has not been explored yet. Since noise exposure started after the beginning of rat hearing, verification of auditory pathway function was necessary to discard possible effects of noise on auditory structures that might influence the extra-auditory effects. With the present work, the onset and persistence of the different extra-auditory abnormalities observed in noise-exposed rats were tested. In addition, auditory pathway integrity through histological and functional studies was evaluated.

2. Materials and methods

2.1. Animals

Healthy male and female albino Wistar rats were obtained from the animal facilities of the Biochemistry and Pharmacy School, University of Buenos Aires, Argentina. A total of 20 females and 10 males were used for mating procedures. Pregnant rats were isolated and left undisturbed until delivery. The day of birth was designated as postnatal day (PND) 0. Only male rats were used for the different experimental procedures.

One hundred and eighty five PND 15 rats were used for the experiments, randomly assigned into three groups: control (Ct), acute noise exposed (ANE) and sub-acute noise exposed (SANE). In each experimental group, 4–7 animals were used for each parameter measured. Therefore, a subset of rats ($n = 121$) was exposed to noise (71 to ANE and 50 to SANE) and another subset – the Ct, sham-exposed rats ($n = 64$) – was placed in the same box as noise-exposed rats, but without being exposed.

Animals were handled and sacrificed according to the Institutional Committee for the Use and Care of Laboratory Animal rules (CICUAL, School of Medicine, University of Buenos Aires, Argentina) and this Committee, under resolution 503/10, approved our experimental protocol. The CICUAL adheres to the rules of the "Guide for the Care and Use of Laboratory Animals" (NIH) (2011 revision) and to the EC Directive 86/609/EEC (2010 revision) for animal experiments.

To avoid circadian rhythm alterations, noise exposures were performed in the intermediate phase of the light cycle, between 10 A.M. and 2 P.M. Moreover, behavioral tests were performed at the same time in each session. Behavioral tests were performed at PND 30 or 90.

2.2. Noise exposure

Animals were kept in their home wire-mesh cages (40 cm × 25 cm × 16 cm), so that they were not handled throughout all noise exposure periods. The cages were introduced in an "ad hoc" wooden sound chamber of 1 m × 1 m × 1 m fitted with a ventilated top as reported by Cui et al. (2009). 2–4 rats per cage were exposed simultaneously.

Computer software (TrueRTA) was chosen to produce white noise, using a bandwidth from 20 Hz to 20,000 Hz in octave bands. For sound amplification, we used an active 2 way monitor (SKP, SK150A, 40 W RMS per channel) located 30 cm above the