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Rat hippocampal alterations could underlie behavioral abnormalities induced by exposure to moderate noise levels

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ABSTRACT

Noise exposure is known to affect auditory structures in living organisms. However, it should not be ignored that many of the effects of noise are extra-auditory. Previous findings of our laboratory demonstrated that noise was able to induce behavioral alterations that are mainly related to the cerebellum (CE) and the hippocampus (HC). Therefore, the aim of this work was to reveal new data about the vulnerability of developing rat HC to moderate noise levels through the assessment of potential histological changes and hippocampal-related behavioral alterations. Male Wistar rats were exposed to noise (95–97 dB SPL, 2 h daily) either for 1 day (acute noise exposure, ANE) or between postnatal days 15 and 30 (sub-acute noise exposure, SANE). Hippocampal histological evaluation as well as short (ST) and long term (LT) habituation and recognition memory assessments were performed. Results showed a mild disruption in the different hippocampal regions after ANE and SANE schemes, along with significant behavioral abnormalities. These data suggest that exposure of developing rats to noise levels of moderate intensity is able to trigger changes in the HC, an extra-auditory structure of the Central Nervous System (CNS), that could underlie the observed behavioral effects.

1. Introduction

During daily life, people are exposed to potentially harmful noise levels coming from work environment, urban traffic, household appliances and/or discotheques (Frenzilli et al., 2004). For these reasons, exposure to loud noise levels represents a problem in all regions of the world. In the United States of America, for example, more than 30 million workers are daily exposed to hazardous noise (NIOSH, 1998). It is estimated that 16% of disabling hearing loss observed in adults worldwide is due to occupational noise (Kopke et al., 2007).

Although it is known that auditory structures of living organisms can be affected by noise exposure (Cappaert et al., 2000; Hu and Zheng, 2008), it should not be ignored that many of the effects are extra-auditory (Lenzi et al., 2003; Rabat, 2007;

Abbreviations: HC, hippocampus; ANE, acute noise exposure; SANE, sub-acute noise exposure; Ct, Control; CNS, Central Nervous System; PND, postnatal day; OF, open field; OR, object recognition; ST, short term; LT, long term

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Uran et al., 2010; Chengzhi et al., 2011). It has been reported that noise can produce severe behavioral disruptions in eating (Krebs et al., 1996) and sleep (Rabat et al., 2004). In addition, CNS-related signs such as emotional stress, enhancement of social conflicts and multiple psychiatric disorders (Rabat, 2007) were observed after noise exposure, along with increases in aggressive behavior and anxiety (Stansfeld and Matheson, 2003). Moreover, animal experiments demonstrated that different schemes of acute and chronic noise exposures can induce temporary or permanent changes in learning and memory processes, both in developing and mature specimens (Ising and Braun, 2000; Prior, 2002; Manikandan et al., 2006; Goble et al., 2009; Uran et al., 2010; Chengzhi et al., 2011). It is to be noted that the level of environmental noise generally experienced by humans is of moderate intensity and its effects on brain function are largely unknown.

It is important to highlight that developing animals might be more vulnerable to noise than adults, given that mammalian CNS undergoes a progressive structural and functional growth during early life stages (Cheng et al., 2011). Consequently, it seems that plastic changes induced by noise are not limited to the auditory pathway (Kaltenbach, 2000; Kaltenbach and Zhang, 2007; Kujawa and Liberman, 2009) but would extend to other parts of the CNS, such as the HC. It has been suggested that, in addition to its involvement in learning and memory processes (Eichenbaum, 2004; Goble et al., 2009), HC might also act in response to auditory stimuli (Sakurai, 2002), as 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 HC (Moller and Rollins, 2001; Kim et al., 2008; Gao et al., 2009). Therefore, it could be hypothesized that hippocampal functioning may be affected by noise exposure through an indirect mechanism. Previous findings of our laboratory demonstrated that noise was able to induce behavioral alterations, mainly related to the CE and the HC (Uran et al., 2010). Hippocampal-dependent behavioral alterations included decreased anxiety levels as well as impairments in associative memory and habituation "within session". Therefore, to confirm if HC is one of the targets of noise-induced damage, it is essential to investigate whether exposure to moderate noise levels can affect other hippocampal-related tasks and to establish a relationship with possible hippocampal histological alterations.

It is to be emphasized that the growing number of adolescents attending discotheques, in addition to the popular use of portable devices at loud intensities among young people, makes the present paper clinically relevant. Importantly, at 15 days of age (the age at which rats were exposed to noise in this work), rat brain development can be comparable to that of a human toddler. Moreover, at 30 days (the age at which noise effects were evaluated in the present work), it would be comparable to an adolescent brain (Chengzhi et al., 2011).

Therefore, the aim of this work was to reveal new data about the vulnerability of developing rat HC to moderate noise levels through the assessment of potential histological changes and hippocampal-related behavioral alterations.

These data were obtained by testing rats' memory in different hippocampal-dependent tasks, such as habituation memory retention in an open field (OF) device (Vianna et al., 2000) and recognition memory in an object recognition (OR) device (Bevins and Besheer, 2006), both examined at ST (1 h intertrial interval) and at LT (24 h intertrial interval). Animals were evaluated at different post-exposure intervals. Finally, potential hippocampal histological alterations were assessed to test the hypothesis that a plethora of behavioral changes could be underlain by histological changes.

2. Results

2.1. *Behavioral findings at ST*

Results showed a significant decrease in the number of lines crossed in the second session of the OF task at ST in all groups of rats tested at PND 30 (two way ANOVA: between sessions factor: $F_{1,41}=28.17$, $p<0.001$), although a more significant decrease was observed in Ct rats when compared with noise-exposed animals (first session vs. second session: Ct, $p<0.001$; ANE, $p<0.05$; SANE, $p<0.05$, Fig. 2a).

Since OF assessments were performed at 30 days, regardless of the scheme of noise-exposure used, the time elapsed between the completion of noise exposure and the beginning of the behavioral assessment was different in each scheme (it was 15 days in ANE rats and 0 day in SANE rats). Since these discrepancies may produce dissimilar results, SANE rats were also evaluated at PND 45, e.g., 15 days after the end of noise exposure (identical to the length of the interval set for ANE rats), to avoid a potential effect of time on OF performance. Statistical results of lines crossed in the OF task obtained from SANE rats evaluated at PND 45 resulted similar to those observed in SANE animals tested at PND 30 (two way ANOVA: between sessions factor, $F_{1,25}=49.25$, $p<0.001$; first session vs. second session: Ct, $p<0.001$; noise, $p<0.05$, Fig. 2b).

When animals were tested at ST in the OR task at PND 30, Ct and ANE animals showed an increase in exploration time of the novel (*N*) when compared with the familiar (*F*) object, whereas exploration time of each object was similar in SANE

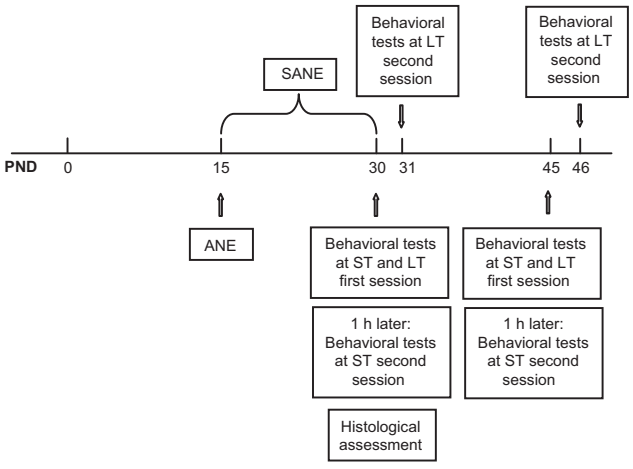

Fig. 1 – Ct: control rats; ANE: acute noise exposed rats; SANE: sub-acute noise exposed rats.ST: short term (1 h intertrial interval); LT: long term (24 h intertrial interval). PND: postnatal day.