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Research Paper

Chronic traffic noise stress accelerates brain impairment and cognitive decline in mice

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ABSTRACT

Although traffic noise exposure is a well-known environmental pollutant whose negative health effect has been discussed in different aspects of the human life, only a few animal studies have tackled this issue as a cohort study, which is not feasible to be addressed in human studies. In addition to the deleterious impact of the daytime noise on well-being, chronic nocturnal noise can also disturb sleep and affects physical and mental health, but to date, little research has examined the neurobiological effects light/dark cycles of traffic noise exposure. We investigated the effects of light/dark cycles and sex on the impact of chronic traffic noise exposure on mouse brain structure-function. The mice were randomly assigned to either one of two stress conditions or a control condition. Animals were exposed to traffic noise on either the light-cycle (LC) or dark-cycle (DC) for 30 days. Traffic noise exposure caused the hypothalamic–pituitary–adrenal (HPA) axis hyperactivity, anxiety-like behavior, impairments in learning and memory, dysfunction in balance and motor coordination, and a reduction in variety of brain measures including a brain volume, medial prefrontal cortex (mPFC) area, cortical thickness, hippocampal volume, amygdala area, and the neural density in mPFC and dentate gyrus. All behavioral and brain measures revealed adverse effects of the chronic noise stress irrespective of the LC/DC exposure or sex. Our findings were a re-emphasis on the significance of noise prevention and mitigation strategies for public health.

1. Introduction

Noise is a common environmental pollutant that is more than just a nuisance. It constitutes a danger that is real to people's health by producing both physical, and psychological stress (Ouis, 2001). According to the WHO, more than one million healthy life years are lost annually owing to environmental noise exposure in European A-member states alone. Most of this effect results from noise-induced sleep disturbance and annoyance, increased ischemic heart disease, cognitive impairment, and tinnitus respectively (Basner et al., 2014).

Noise evokes the sympathetic nervous system and induces a stress response. The noise-evoked activity transmits through connections from the auditory thalamus via the central amygdala, lateral and medial hypothalamus to the paraventricular nucleus and the arcuate region, and activates two primary components of endocrine functioning including the hypothalamic–pituitary–adrenal (HPA) axis and the arcuate region (Eggermont, 2014). The HPA axis activation elevates the corticotropin and the corticosterone levels. Inducing the arcuate region increases the synthesis of adrenocorticotropic hormone (ACTH) and beta-endorphins-like substances that are conveyed to extrahypothalamic brain regions. ACTH is an important component of the HPA axis that, along with its precursor corticotropin-releasing hormone (CRH), is produced in response to stress. The long-lasting activation of the HPA axis can lead to a disturbed hormonal balance and even to severe neuropsychiatric disorders (Jafari et al., 2017a).

Noise is a common cause of sleep disturbance because the brain still can process incoming acoustic stimuli. Thus autonomic responses, such as increased heart rate, might also be seen. Furthermore, even a low level of noise that could be disturbing during sleep might not have the same effects in wakefulness. Therefore, despite the suppressive effect of sleep state on the stress system and plasma levels of stress hormones, sleep disturbance triggers higher activation of these stress systems typical to what is seen in the wakeful state (Eggermont, 2014). However, it is not obvious that this increase in nocturnal HPA activation is as large as that is seen in daytime wakefulness. The degree of control during the stressful events is also an effective factor that differs among the stressors and modulates the degree of the HPA axis response to stress (Jafari et al., 2017a). Living or working in noisy environments,

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such as city quarters densely loaded with traffic and/or near highways, results in people being passively subjected to noise disturbances, that are out of an individual's control. Both humans and laboratory animal studies have shown that the sense of control over the stressor in such conditions affects the prefrontal cortex regulation of stress hormones (Arnsten, 2009).

Extensive research has exhibited that chronic stress or prolonged exposure to glucocorticoids negatively affects the rodent hippocampal neuronal morphology, neural proliferation, and volume (Tata and Anderson, 2010; Wilson et al., 2015), medial prefrontal cortex (mPFC) volume and function (Lo Iacono and Carola, 2017; Yang et al., 2016), and cell proliferation (Czeh et al., 2007), cortical thickness (Saleh et al., 2017), and amygdala morphology and function (Guadagno et al., 2018; Wilson et al., 2015). Human studies also suggest the same effects occur in these brain structures and have a relationship with many neuropsychiatric disorders (Ahmed-Leitao et al., 2016; Kim et al., 2015). Among the diverse kinds of stressful events examined in rodents, there are few studies that have tackled the negative effects of traffic noise exposure on brain and behavior. Furthermore, although the adverse effect of noise stress on health and brain function have been widely expressed in both humans and nonhuman animals, there is no prospective cohort study to show whether the nocturnal noise exposure has the same effects as reported for the daytime exposure. The influence of the time of exposure in the daily circadian cycle is important to know because the effect of environmental stress depends on the type, time, and duration of exposure, as well as age, sex, and the test conditions (Weinstock, 2008; Wilson et al., 2015). Given that chronic stress can severely impact neural plasticity in diverse brain areas, especially in limbic structures, i.e., the hippocampal formation, mPFC, and amygdala (Czeh et al., 2007), the present study aimed to investigate structural changes in cortical and limbic brain areas as well as impairments in behavior under chronic traffic noise exposure in either the light cycle (LC) or dark cycle (DC).

2. Materials and methods

2.1. Animals

All experiments were carried out in accordance with the Canadian Council of Animal Care and approved by the University of Lethbridge Animal Care Committee. All C57BL/6NJ mice were group-housed (2–3 per cage) in standard cages given access to food and water ad libitum, and were maintained on a 12:12-h light:dark cycle (on 7:30 am and off 7:30 pm) under normal light condition (200 Lux) in a temperature-controlled room (21 °C) with $< 58 \pm 2$ dB room noise level. All testing and training were performed during the light phase of the cycle at the same time of day. When the mice reached to eight weeks of age they were randomly assigned to four groups consisting of two stress groups; i.e., traffic noise exposure either in the LC or the DC (16 mice per group, n = 32), and two control groups (16 mice per group, n = 32). Sixteen animals containing eight males and eight females were included in each chronic noise exposure (CNE) group, as well as in the control groups corresponded to every stress group (Fig. 1). The experimenter was blind to the experimental groups in all behavioral and brain measures.

2.1.1. Chronic noise stress group

The CNE was a broadband traffic noise recorded for 8 h in a high-traffic road in the capital of Iran (Tehran) by a standard recorder (Sony Icdbx140). Given that the maximum recommended noise dose exposure level to prevent hearing risk is < 85 dB for eight hours per day (Sayapathi et al., 2014), and because the high levels of road traffic noise reported are 70–80 dB (Basner et al., 2014; Brown et al., 2015), the equivalent continuous sound level (LAeq using the A-weighting setting) of 75 dB SPL was applied for the CNE (min = 70.8 dB, max = 79.1 dB, peak = 81.3 dB, frequency spectrum = 65–9200 Hz). A speaker, which emitted the noise was placed in the cage. The sound pressure level was monitored (Tektronix RM3000, Digital Phosphor Oscilloscope) daily inside the cage without an animal. The mice in groups of two to three in their standard cage were moved to a testing room specified for the CNE and exposed to the same audio file of traffic noise 8 h per day either at 8:00 am −16:00 pm for the LC group or 8:00 pm-4:00 am for the DC group for 30 days.

2.1.2. Control group

There were two sets of control animals: one served as a control for the LC group, and another was a control for the DC group. For every group, the mice in their standard cage were moved to a testing room specified for the control animals. A silent speaker was placed in the cage. The mice were left undisturbed for 8 h starting at 8:00 am or 8:00 pm for 30 days. In the control groups, no stress was given.

2.2. Plasma corticosterone assay

In our study, the stressed animals were exposed to 8 h chronic noise exposure either at 8:00 am-16:00 pm for the LC group or at 8:00 pm-4:00 am for the DC group. To meet the protocol for measuring corticosterone levels twice, a day before and a day after the CNE for the stressed group and the corresponding days for the control groups (Fig. 1), as well as to preclude the effect of circadian pattern on corticosterone levels (Barriga et al., 2001; Malisch et al., 2008), blood was taken from the submandibular vein 1) at 7:30 to 8:30 am one day before starting the CNE and 2) at similar time a day after finishing the CNE. The second blood collection corresponded with 15.30–16.30 h after the last noise exposure in LC group and 27.30–28.30 h after the last noise exposure in DC group. Approximately 0.1 ml of submandibular blood was collected in heparin-coated tubes (Golde et al., 2005). The tubes were centrifuged at 6000 rpm at 4 °C for 15 min to collect the plasma. Collected plasma samples then were stored at −80 °C until further analysis. A commercially available enzyme-linked immunosorbent assay (ELISA) kit from Abcam (ab108821) was used to quantify the levels of corticosterone in the plasma (ng/ml). The optical density of corticosterone was read at 450 nm wavelength using a microplate reader (Synergy HT BioTek®). The concentration of corticosterone in samples was calculated using KC4 Bio-Tek® Microplate Data Collection and Analysis software. To reduce intra-plate variability, the coefficient of variation for all samples was determined using the same standards and controls across all plates (Jafari et al., 2017b; Jafari et al., 2017c).

2.3. Behavioral tests

Several behavioral tests were performed after the CNE to measure the effect of CNE on cognitive and motor performance of the mice. Tests of pre-pulse inhibition (PPI) of the acoustic startle reflex (ASR), novel object recognition (NOR), elevated plus-maze (EPM), rotarod (RR), balance beam test (BBT), and the Morris water task (MWT), were conducted respectively in separate days, with an alternating order of animals, by the same examiner in the mornings at 8-11 am (Fig. 1).

2.3.1. PPI of the ASR test

The test was performed for all animals a day before starting the CNE and a day after the second blood collection. Each mouse was placed in a plastic cylinder situated on a plate with a pressure sensor in an acoustic chamber (PANLAB Harvard Apparatus). Any animal motion was detected by the sensor which measured its amplitude and stored data on a computer hard drive. Software generated a sequence of stimulus trials including a startle stimulus, a pre-pulse stimulus, and a startle stimulus paired with a pre-pulse stimulus in a white background noise of 65 dB. The ASR stimulus was an 8 kHz tone frequency with 115 dB intensity, 40 ms duration, and a 1 ms rise/fall time. The prepulse stimulus was also an 8 kHz tone frequency with 80 dB intensity, 20 ms duration, and a 1 ms rise/fall time which was presented 100 ms before the startle stimulus. The testing session was started with an acclimation period