Effects of Acute and Chronic Noise Stress on Depressive- and Anxiety-like Behaviors in Mice

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Abstract

**Objective:** Noise is an inescapable stressor of modern life and a substantial number of population are exposed to noise produced by urban traffic, air crafts, and the industrial environment. The noise stress causes central nervous system dysfunction and altered brain neurotransmission and hormone levels that potentially result in psychological and behavioral changes. In this study, we investigated the impact of acute and chronic noise stress at levels of 90 and 110 dB on different behavioral tasks.

**Materials and Methods:** Sixty male BALB/c mice were randomly divided into 6 groups: control-acute, acute-noise 90 dB, acute-noise 110 dB, control-chronic, chronic-noise 90 dB, and chronic-noise 110 dB groups. Mice in acute- and chronic-noise groups were exposed to 2 h/day of 90 or 110 dB white noise for 1 day and 12 weeks, respectively. In order to evaluate depressive- and anxiety-like behaviors mice were subjected to tail suspension and elevated pulse maze tests, while locomotor activity was assessed by the open field test.

**Results:** In this study, acute and chronic noise at 90 and 110 dB increased depressive-like behavior. The acute noise at 110 dB and chronic noises at both 90 and 110 dB induced anxiety-like behaviors. Moreover, a significant reduction in locomotor activity in open field test was observed following acute 110 dB and chronic 90 and 110 dB noises.

**Conclusion:** In summary, the current study shows that noise stress at levels above 90 dB causes short- and long-term behavioral changes including depressive and anxiety-like symptoms as well as low locomotor activity.

**Keywords:** Chronic noise stress, acute noise stress, depressive-like behavior, anxiety-like behavior

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Introduction

Sound is a type of mechanical wave and is considered as an invaluable tool for communication, whereas, undesirable and hurtful levels of sound are known as noise. With fast industrialization and modernization, noise pollution in the workplace and industry has become an unavoidable public health problem [1]. Noise is an environmental stressor at levels exceeded 90 dB leading to many detrimental auditory and non-auditory effects [2, 3]. The long-term exposure to noise stress results in exhaustion, annoyance, arousal response followed by sleep disturbance and reduction in social contacts [4]. To date, many pre-clinical studies demonstrated detrimental effects of noise stress on brain function. Impaired cognitive functions such as memory and learning have been reported following noise exposure [5]. Moreover, chronic exposure to noise stress at the level of 100 dB leads to oxidative stress in various rat brain regions [6].

From the psychological point of view, release of stress hormones and mood disturbance as well as anxiety responses have been reported following exposure to the noise stress [7]. Studies have showed that noise stress changes the brain neurotransmitter levels, produces atrophy of dendrites, and elevates plasma corticosterone levels [8]. Besides these neurochemical data, behavioral evidence from animal studies has been also revealed...
harmful effects of noise stress on psychological symptoms [9, 10]. Given this, due to the increase in number of noise producing stressors in the daily life, the evaluation of impacts of noise stress on different aspects of mental health is warranted.

The goal of this study was to determine effects of acute and chronic noise stress at two different sound levels, 90 and 110 dB, on depressive- and anxiety-like behaviors in male mice.

**Materials and Methods**

**Animal use and experimental grouping**

Sixty adult male BALB/c mice, weighing 28-30 g were obtained from animal center of Tabriz University of Medical Sciences (TUOMS). Mice were socially housed in standard cages (five in each cage) and kept on a 12-h light, 12-h dark cycle with standard laboratory chow and tapwater ad libitum. All experimental procedures were carried out under guidelines of TUOMS for care and use of laboratory animals. After ten days of acclimatization, mice were randomly assigned to control-acute, acute noise stress 90 dB (ANS90), acute noise stress 110 dB (ANS110), control-chronic, chronic noise stress 90 dB (CNS90) and chronic noise stress 110 dB (CNS110) groups. For all experimental procedures, 8-10 mice were used.

**Noise exposure**

The white noise (20–20,000 Hz) was generated using computer software (NCH Tone Generator3.26) and delivered to a loudspeaker, which had been located at 30 cm from the animals cage. The noise intensity was monitored by a sound level meter (Smart Tools co., Ltd., Japan). Animals in acute-noise groups were treated with exposure to 90 or 110 dB sound levels 2 h/day, for one day. Mice in chronic-noise groups were exposed to the same procedures for 12 weeks. Besides, mice in the control-acute and control-chronic groups underwent identical noise procedure (for 1-day or 12-weeks, respectively) except that the noise exposure apparatus was not turned on.

**Behavioral assessments**

Immediately after the noise exposure, mice in acute-noise groups were subjected to the behavioral tests, namely, tail suspension test (TST), elevated plus maze (EPM) test, and open field (OF) test. However, mice in chronic-noise groups were tested in the same procedures one day after the end of noise exposure.

**Tail suspension test**

The TST is a behavioral model and one of the most commonly used tests to evaluate depressive-like behavior in mice [11, 12]. Apparatus of this study consisted of a wooden box (60 × 30 × 40 cm) with a metal hook located at the center of the ceiling. Each mouse was suspended by the tail with adhesive tape and immobility time was recorded manually during the 6 min of test period. An experienced observer who was blind to the experiments nature conducted the behavioral scoring.

**Elevated plus maze test**

The EPM test evaluates anxiety-like behavior in rodents, and was conducted with the previously- explained protocol [13]. In this study the EPM was a plus shaped apparatus and consisted of two (30×5×15 cm) enclosed arms and a central platform (5×5 cm), elevated 40 cm above the floor. The apparatus was positioned in the center of room and a camera located above the apparatus recorded 5 min of test period. The percentage of time spent in open arms (%OAT), the percentage of entries to open arm (%OAE) and the total arm entries (TAE) were reordered. The maze was cleansed with a 70% ethanol solution between each trial.

**Open field test**

Mice were placed individually in the center of the OF arena (33×33×33cm). The activity of mice during 5 min of test was videotaped from above and behavioral data were extracted using a video tracking program Etho Vision™ (Noldus, The Netherlands). The parameters of interest were the total and center distances moved (cm) and velocity (cm/s). After each trial, the arena was cleansed with a 70% ethanol solution.

**Statistical analysis**

The data were analyzed using SPSS statistics 16.0 software. Differences between groups were carried out by one-way ANOVA followed by Tukey’s post hoc test. All data are expressed as means±SEM. Differences were considered as significant if p<0.05.

**Results**

**Tail suspension test**

**Acute noise**

Tukey’s post-hoc comparison showed a significant increase in the immobility time in ANS90 and ANS110 groups with respect to control-acute group (for both p<0.05) (Figure 1A).

**Chronic noise**

There was a significant difference among experimental groups as determined by a one-way ANOVA in the TST (p<0.001). Immobility time in the CNS90 (p<0.01) and CNS110 (p<0.01) groups was significantly higher than in the control-chronic group (Figure 1B).

**Elevated plus maze test**

**Acute noise**

Neither the ANS90 group nor the ANS110 groups showed a significant decrease from the control-acute group for the parameters of %OAE and TAE (Figure 2A and C). However, 1-day noise stress exposure at 110 dB significantly decreased %OAT (p<0.05) compared to the control-acute group (Figure 2B).

**Chronic noise**

Tukey’s post-hoc comparison showed significant decrease in the %OAE for CNS90 (p<0.01) and CNS110 (p<0.01) groups compared to the control-chronic group (Figure 3A). Data from %OAT also showed a significant decrease in both CNS90 (p<0.01) and CNS110 (p<0.01) groups (Figure 3B). However, there were no significant differences for TAE among noise stress groups and control-chronic group (Figure 3C).
Open field test

Acute noise
As shown in Fig. 4A-C, none of the noise stress groups showed significant differences in the parameters of total distance and velocity as compared with the control-acute group. However, significant reduction in the central moved distance for ANS110 animals was observed ($p<0.05$).

Chronic noise
Post hoc analysis revealed that 12 weeks of 90 dB ($p<0.001$) or 110 dB ($p<0.001$) noise stress caused a significant decrease in both total and central moved distance of animals compared with the control-chronic group (Figure 5A and C). However, no significant effect on velocity value was observed with both noise stress groups when compared to the control-chronic group (Figure 5B).

Discussion
The imbalance of brain monoamine neurotransmitters including serotonin and dopamine is considered to involve in the pathophysiology of depression. Decreased serotonin synthesis by serotonergic neurons is associated with appearance of hopelessness, sleep disturbances, and suicidal tendency [14]. Dopamine is also involved in reward-related behaviors and its decline leads to a low sense of pleasure [15]. Studies in animal models showed that decrease in the release of serotonin and
Figure 3. The effect of chronic noise stress on (A) %OAE, (B) %OAT, and (C) TAE in elevated plus maze test. Data are represented as means±SEM. **p<0.01.

Figure 4. The effect of acute noise stress on (A) total moved distance, (B) velocity, and (C) central moved distance in open field test. Data are represented as means±SEM. *p<0.05.
dopamine results in immobility behavior in the TST [16, 17]. In this study, noise stress resulted in increase in immobility time in the TST, which is in line with the previous reports in which exposure to sub-chronic noise and loud tones of noise produced depressive-like behavior in the rodent TST and forced swimming test [9,10]. In this respect, Naqvi et al. [9] showed that 15 days of noise exposure (4 h per day, at 100 dB) to rat significantly increases immobility behavior of animals in the TST. Given this, observed despair and longer immobility activity in the current study could be due to the change in serotonin and dopamine concentrations following noise exposure. Besides, reduced muscle movement and exhaustion following exposure to chronic noise have been reported, which could be related to the disappointment and immobility behavior in the TST [7].

In the EPM test, acute exposure to 110 dB noise resulted in decrease in %OAT, while chronic exposure at levels of 90 or 110 dB notably decreased both spending time on or entering into the open arms. These results indicate that, although chronic noise stress causes obvious anxiety-like behaviors, even 2 h of exposure to noise also induces anxiety. Our result is in consistency with the EPM data from different studies in rat [9, 18]. In this regard, decreased spent time in the open arms of EPM test has been reported following 100 dB sub-chronic noise stress[9]. The hypothalamic pituitary–adrenal (HPA) axis is considered as the main hormone system, playing a key role in the maintenance of homeostatic balance in reaction to stressful insults [19]. In this respect, evidence suggests that noise stress causes HPA axis activation and consequent increase in the blood glucocorticoids which ultimately results in anxiety-like behavior [20, 21].

Our data from OF test demonstrated that acute noise stress at 110 dB resulted in decrease in the central moved distance, whereas chronic exposure at levels of 90 or 110 dB markedly decreased both total and central moved distance. These data suggest that noise stress affects the locomotor activity. Our data is in agreement with other studies in which noise at levels above 100 dB decreases locomotor activity in OF test [9, 22]. Berezhnoy et al. [22] exposed rats to the acute noise stress at 110 dB, and results showed a significant reduction of locomotor activity. A study by Naqvi et al. [9] also revealed an impact of sub-chronic noise stress at 100 dB on the decrease in the animals' locomotor activity. Among the various brain neurotransmitters, dopamine is linked to movement and locomotor activity [23]. On the other hand, studies show that noise exposure could reduce brain's dopamine levels [24]. Based on this, it seems that decreased locomotor activity in this study is due to a decrease in brain dopamine levels. Furthermore, increase in corticotrophin releasing factor following stress could also be responsible for the appearance of low motor activity [25].

In conclusion, noise is a displeasing and inescapable stressor, affecting neurotransmitters and hormone systems and inducing changes of various neurophysiological responses. Considering the results of current study, it could be concluded that observed behavioral deficits following acute and chronic noise stress at levels above 90 dB might be associated with an imbalance of brain dopaminergic and serotonergic systems, which potentially results in depression and anxiety.
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Conflict of Interest

The authors have declared that there is no conflict of interest.

References