

Noise Induces Oxidative Stress in Rat

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Aim: Noise is described as disturbing and unwanted sound. In this study, we aimed to investigate the effect of noise on oxidative stress parameters in rat.

Methods: Twenty male Sprague-Dawley rats were used in the study. Noise group (n=10) was exposed to noise for 20 days / 4 hour 100 dB. Control group (n=10) that was not exposed to any noise and was kept from any stress source, was hold in the same conditions. Baseline and after 20th day of the experiment, blood samples of rats were collected and their sera were separated. Malondialdehyde (MDA), nitric oxide (NO) levels and glutathione peroxidase (GSH-Px) activity were analyzed in rat sera.

Results: MDA and NO levels and GSH-Px activities were found to be increased significantly at the end of experiment in the group exposed to noise. No parameters were significantly differed between at baseline and at the end of experiment in the control group.

Conclusion: The present study showing an elevation in MDA level, an indicator of lipid peroxidation, as well as NO level and GSH-Px activity by noise exposure suggests the presence of oxidative stress which may lead to various degrees of damages in the cells, mainly via lipid peroxidation pathway in the noise group. Therefore, these results appear to support the fact that noise might cause damage not only in the ears but also in whole body leading to oxidative stress.

Key words: Noise, oxidative stress, malondialdehyde, nitric oxide, glutathione peroxidase, sera.

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INTRODUCTION

Noise, defined as disturbing and unwanted sound, is perceived as an environmental stressor and nuisance. Noise is a pervasive aspect of many modern communities, work environments. Its damaging effects particularly the productions of free radicals are not limited to the auditory organ. The response to noise may depend on characteristics of the sound, including intensity, frequency, complexity of sound, duration and the meaning of the noise (1-4).

Exposure to noise causes many health problems such as hearing loss, sleep disturbance, and impairs performance as well as effecting cognitive performance. It also increases aggression and reduce the processing of social cues seen as irrelevant to task performance as well as leading to coronary heart disease, hypertension, higher blood pressure, increased mortality risk, serious psychological effects, headache, anxiety, and nausea (1-4). Children chronically exposed

to noise tend to have poorer reading ability and less cognitive capacity to understand (4). Some studies are being conducted on causation of exposure to noise near airports to the higher risk of developing hypertension, cardiovascular diseases and incidence of cancer (5, 6).

Noise exposure of any kind that exceeds 90 dB reported to be a source of stressor (3). A study showed that working and reference memory error increased significantly following the noise-stress exposure, 100 dBA/4h per day for 30 days, when compared to control animals (7). Acute as well as long term exposure to noise can produce excessive free radicals such as superoxide dismutase (SOD), catalase (CAT), glutathione peroxidase (GSH-Px) (8). Oxygen free radicals can attack protein, nucleic acids and lipid membranes thereby disrupting normal cellular functions and integrity (9, 10).

Nervous system is relatively more susceptible to free radical damage (11). Ravindran et al. reported that neurotransmitters in discrete brain regions were found to be increased during noise stress even after 15 days of exposure (3). In addition to generating free radical species, it also leads to increase in radical induced lipid peroxidation end

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Table 1. Malondialdehyde (MDA), nitric oxide (NO) levels and glutathione peroxidase (GSH-Px) activity in rat sera

Groups	n	MDA ($\mu\text{mol/L}$)	NO (mmol/L)	GSH-Px (U/L)
Prior to the experiment				
I Control	10	3.63 \pm 0.59	45.71 \pm 5.98	1298.52 \pm 134.62
II Noise	10	3.69 \pm 0.73*	43.81 \pm 9.98§	1231.15 \pm 129.44£
After the experiment				
III Control	9	4.12 \pm 0.56†	50.03 \pm 5.10‡	1375.46 \pm 134.75Φ
IV Noise	10	5.76 \pm 1.68	179.72 \pm 26.83	1629.35 \pm 183.78

†; III-IV MDA ($p=0.014$), ‡; III-IV NO ($p<0.001$), Φ: III-IV GSH-Px ($p=0.003$)

*; II-IV MDA ($p=0.004$), §; II-IV NO ($p<0.001$), £; II-IV GSH-Px ($p=0.001$)

products such as malondialdehyde (MDA) which is an indicator of lipid peroxidation processes (12).

The negative effect of noise on organisms and biological systems has been studied hitherto on the basis of hearing loss. However, it might exert its effects on the systemic basis such as increasing free radicals, thereby causing oxidative stress. Therefore, in the present study, we aimed to investigate the effect of noise on oxidative stress parameters in rat sera.

MATERIAL AND METHODS

Twenty male Sprague-Dawley, weighing between 200–220g, rats were used in this study. All animals were maintained under standard laboratory conditions housed 2 per cage (55cm \times 33cm \times 20cm) and were allowed free access to food and water.

Experimental group ($n=10$) was exposed to noise for 20 days. Control group ($n=10$) was held in the same experimental conditions without any noise exposure for the same duration. Rats were housed in rooms with controlled lightning (12 h light/dark). Appropriate ethical clearance was obtained for this work from the Institutional Animal Ethical Committee.

Noise stress induction procedure

Noise group were subjected to 100 dB SPL broadband white noise, 4 h daily for 20

days based on the established protocols in the literature with a slight modification (3, 7). Noise was produced by one loudspeakers (15W), driven by a white-noise generator (80–9000 Hz), and installed 30 cm above the cage.

The noise level was set at 100 dB SPL uniformly throughout the cage and monitored by a digital sound level meter Extech instruments 407727 (S/N: 9113496; China).

To avoid the influence of handling-stress on evaluation of effects due to noise exposure, control rats were kept in the above-described cage during the corresponding period of time, without noise stimulation.

Data collection

Blood samples from rat tails were collected prior to and at the end of the experiment and its sera were centrifuged at 3000 g for 5 min. The sera samples were stored at $-25\text{ }^{\circ}\text{C}$ until analysis.

Malondialdehyde (MDA) and nitric oxide (NO) levels, and glutathione peroxidase (GSH-Px) activity were measured spectrophotometrically as described previously (13-15).

Statistical analysis

Results of all parameters were expressed as mean \pm standard deviation for each group. Shapiro-Wilks test were performed to check the normality of the data before running

statistical tests. The results were evaluated statistically using paired samples t-test and independent samples t-test. A p-value less than 0.05 was considered to be statistically significant.

RESULTS

Table 1 shows the levels of MDA and NO and activity of GSH-Px at the beginning and at the end of the experiment in two groups. The baseline levels of the parameters were similar and not significantly different between the control and study group exposed to noise (Table 1).

The GSH-Px activity and levels of MDA and NO were not significantly different between at baseline and at the end of experiment in control group (Table 1, $p=0.241$, 0.138 and 0.266 , respectively).

MDA levels (as $\mu\text{mol/L}$) significantly increased from 3.69 ± 0.73 to 5.76 ± 1.68 in the noise group (Table 1). The increase of MDA levels in the noise group was also significantly higher when compared with the increase of MDA levels in the control group after the experiment ($p=0.014$).

NO levels did not significantly change at the end of the experiment in the control group ($p=0.266$). On the other hand, NO increased about 4 fold from 43.81 ± 9.98 to 179.72 ± 26.83 (mmol/L) in the study group ($p<0.001$). Likewise, there was a statistically significant ($p<0.001$) increase in NO in the study group when compared to that of control group (Table 1).

The baseline GSH-Px activities of the control and study groups were 1298.52 ± 134.62 (U/L) and 1231.15 ± 129.44 , respectively. The GSH-Px activity increased 32.3% in the study group ($p=0.001$) when compared to the baseline value. The activity change was also significantly higher than that of control group at the end of the experiment ($p=0.003$).

DISCUSSION

Reactive oxygen species (ROS), also known as free oxygen radicals, are normal byproducts of cellular aerobic metabolism, these unstable molecules can impair cellular lipids, proteins and nucleic acids in DNA if the balance of corresponding antioxidants is disrupted (16). Acute and chronic loud noise exposure generates excessive free radicals and causes disorders involving extra-auditory organs such as nervous, endocrine, and cardiovascular systems (8).

Oxidative stress is a state where significant imbalance between oxidants and antioxidants

occurs that leads to damage, dysfunction or cellular death (17, 18). Under normal conditions, sufficient concentrations of endogenous antioxidants as well as redundant protective systems exist to protect from environmental oxidant attacks. However, repeated exposure to environmental oxidants such as air pollution, smoking, disease states, or blast overpressure (blast) exposure, can result in accelerated rate of antioxidant depletion tipping the balance from sufficiency to deficiency producing oxidative stress (17).

Lipid peroxidation is a process through which reactive oxygen species and free radicals break down lipid molecules. Lipids are a major component of the cell membrane. Thus, ROS and free radicals can break down cell membranes through lipid peroxidation, leading to cell death (19). MDA is an indicator of lipid peroxidation processes which involve the formation of free radical species (20). In this study, MDA levels were found to be increased significantly at the end of experiment in the noise group. Similarly, Derekoy et al found that MDA levels were increased in rabbits after exposed to 100 dB SPL (sound pressure level) broadband noise for 1 h (12). A Study on textile workers demonstrated that MDA levels were significantly higher in workers compared to the controls (21). Yıldırım et al have showed that noise both causes hearing loss and increases oxidative stress suggesting that there may be a relationship between the oxidative stress and hearing loss.

Noise exposure firstly increases levels of ROS such as superoxide radicals, hydroxyl radicals and hydrogen peroxide. Secondly activity of antioxidants and related enzymes increases in order to eliminate the overproduced ROS due to noise (22). The antioxidative enzyme, glutathione peroxidase, catalyzes the conversion of H_2O_2 to water by using reduced glutathione (GSH) and reduced NADPH as cofactors (23). It has been suggested that glutathione S-transferase which is present in the mammalian cochlea may play a protective role in humans against hair cell damage due to noise or aging (24). GSH-Px activities decreased in the rat brain after 30 d noise exposure (8). Noise induced hearing loss involves a decrease in GSH-Px activity and a subsequent loss of outer hair cells (25). The significantly decreased CAT and GSH-Px activities were observed in the rat brain after 30 days of noise exposure (8). In this study, GSH-Px activities were found to be increased significantly at the end of experiment in noise

group. The difference between our data and the one reported by others could be attributed to the duration and/or the severity of the noise applied as well as the tissue studied.

Nitric oxide (NO) is generated continuously in the living body, and acts as important physiological mediator. NO is a free radical with a diversity of cellular origins and potential functions. Oxidative stress is implicated in the signal transduction pathways for nitric oxide synthase (iNOS) induction (26). NO has chemical properties that make it uniquely suitable as an intracellular and intercellular messenger. It is produced by the activity of nitric oxide synthases, which are present in peripheral tissues and in neurons (23). High-energy impulse noise suggest that a role for endogenous NO in the injury (17). In this study, NO levels were found to be increased significantly at the end of experiment in the noise group. This increase in NO level may be due to the oxidative stress caused noise exposure.

In conclusion, elevation of MDA level, an indicator of lipid peroxidation, by noise exposure indicates that there is oxidative stress in the group exposed to noise in the present study. NO levels and GSH-Px activities were increased by noise exposure in noise group. Therefore, these results appear to support the fact that noise might cause damage not only in the ears but also in whole body leading to oxidative stress. Further studies are needed to clarify how MDA, NO and GSH-Px changes caused by noise exposure may affect various degrees of damages in the cells.

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