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Research Article

Effects of Acute Noise Stress on Cognitive Performance and Lipid Peroxidation in Young Wistar rats

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ABSTRACT

Noise has been reported to have deleterious effect; this effect seems to be gender sensitive. This study evaluated the effects of acute noise on cognitive performance in young females and males Wistar rats. Wistar rats weighing 70 to 120 g were randomly divided into four groups (n = 6). Group 1(Female experimental), Group 2 (Male experimental), Group 3 (Female control), and Group 4 (Male control).The experimental groups were exposed to noise 4 hours daily for 14 days consecutively, and their cognitive abilities tested on day 15.Vital samples; brain and serum were collected for biochemical and histological analysis. The homogenate was used to evaluate the concentration of malondialdehyde (MDA), while serum for corticosterone and H and E stains for cytoarchitectural changes. Mean differences were calculated using two-way analysis of variance (ANOVA) factors; sex and stress. Discrimination index (DI) decreased in females, compared to males in the experimental groups. The mean values of corticosterone and MDA increased in females compared to males in the experimental and control groups. Cytoarchitectural change was not pronounced**.** Acute noise exposure impaired cognitive functions in both young male and female Wistar rats and caused elevated levels of MDA, an indicator of lipid peroxidation. These findings suggested noise stress impaired cognition, and the impact may be more pronounced in female rats compared to males.

Keywords: *Acute, noise stress, cognition, corticosterone, learning, memory*

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INTRODUCTION

The growing rate of urbanisation, industrialization, religious centres, clubs and bars among others have imperatively made noise a daily companion; and is the most common source of environmental stress globally (Barnau and Dollah ,2021) . Noise is considered one of the most dangerous environmental stressors because it causes somatic changes that go unnoticed (Barnau and Dollah, 2021).Previous studies confirm that noise above 90 dB is a harmful stressor, affecting organs like immune and endocrine systems (*Ochayi et. al.*, 2023, Baugher *et. al.*, 2022). When noise levels approach 90 dB, they become a stressor and have an impact on people's physical and mental health (El Morzouki *et. al.*, 2021, Archana and Ravindran, 2019). The body responds to stress by activating the hypothalamic-pituitary-adrenal (HPA) axis; this collaborates with the central nervous system (hippocampus, cognitive centre) and endocrine system by stimulating the pituitary gland that further causes the adrenal gland to release cortisol in mammals and corticosterone in rodents. Corticosterone prepares animals for fight or flight reaction (Jafari *et. al.*, 2019). However, when secreted in excess due to repeated stress exposure, its concentration becomes deleterious with some studies showing it has suppressive effects on immunology, reproductive organ damage (Trang *et. al.*, 2020, Gutteridge, 1995). The deleterious effect is mostly associated with increase in the production of reactive oxygen species (ROS) in tissues, which damages receptor proteins, nucleic acids and lipid membranes, thereby damaging cells and tissues both structurally and functionally(Jafari *et. al.*, 2019,Trang *et. al.*, 2020) and because the brain contains large amount of polyunsaturated fatty acids, it is particularly vulnerable to the damaging effects of free radicals; causing stress - induced degenerative changes (Ann *et. al.*, 2019) that results to disorders such as movement disorders, anxiety disorders, and cognitive impairment (Ben *et. al.*, 2015). Albeit, some studies have suggested that the deleterious effects observed, such as anxiety, memory, and locomotive disturbance associated with stress, are a gender response, since some studies have shown that females are more susceptible to stress (Sarah and Roberts, 2015, Kim *et.al.*, 2023), though with some controversy where other reported study failed to agree with such , especially in young animals (Dhurba, 2018).

This study therefore hypotheses that there are no significant differences in the effect of noise stress on cognitive performance among young male and female Wistar rats. To test this hypothesis, both male and female Wistar rats were exposed to 4 hours of noise stress for 14 days, and their stress levels were evaluated by assessing the concentration of corticosterone and cognitive performance using an object recognition task and a Y-maze.

MATERIALS AND METHODS

Design: This is a randomised controlled study

Animals: Twenty- four young male and female Wistar rats weighing 70 to 120 g were purchased, and they were randomly divided into four groups (n =6). Group 1 (female experimental; exposed to 4 hours of noise stress), Group 2 (male experimental; exposed to 4 hours of noise stress), Group 3 (female control; not exposed to stress), and Group 4 (male control; not exposed to stress). Animals handled according to the International Guiding Principles for Biomedical Research Involving Animal Use and Care. The rats were kept within ambient conditions (temperature: 27 ± ºC, photoperiod: 12 hours on natural light and 12 hours dark, humidity: 40 ± 5%). Animals were fed (Grant cereal LTD, UAC Nigeria plc. Jos, Nigeria, and water was given *ad libitum.*

Procedure: The rats (experimental) were exposed to noise for 4 hours daily for 14 days consecutively.

Noise was produced by a loudspeaker (15 W), driven by a white noise generator (0–26 kHz), and installed 10 cm above the cage. The noise level was set at 100 dB uniformly throughout the cage and monitored by a sound-level meter D2023. The noise duration was from 07:30 AM to 11:30 AM daily for 14 days as described by (Marklun and Marklun, 1974, WHO, 2011); while the control groups were exempted from the noise. The cognitive performance was tested using the Novel Object Discrimination Task to evaluate discrimination index and the Y-maze for percentage alternation, on day 15, after which the blood serum was used to assay for corticosterone concentration, and the brain homogenate for lipid peroxidation. The object recognition task was conducted with slight modification of the described by Sarah and Roberts [12], and the mean values of the discrimination index were determined. Also, the Y-maze was used to evaluate the percentage alternation according to the method of (Qixuan *et. al.*, 2021, Hajali *et. al.*, 2012), with a small modification.

This study was performed using the method adopted by (Ochayi *et. al.*, 2023, El-Marzouki *et. al.*,2021) , with little modification. The test was conducted in an open field box (50 × 50 × 40 cm). The test consisted of three phases. Animals were allowed to explore the open field for 5 minutes during the habituation phase, and during the acquisition phase (T1), where 2 identical objects (blue cubes of 4 × 4 × 4 cm) were placed in two corners of the open field of a distance of 10 cm from the sidewall. Rats were placed in the middle of the open field and allowed to explore the 2 objects for 5 minutes, after which they were returned to their home cages. 24 hours after the T1, the test (T2) choice was conducted. During the T2, a new object (red cone) was introduced and mice were exposed to the 2 objects (familiar, F and new, N). The time spent by each rat in exploration of each object during T1 and T2 were recorded using stopwatch.

A recognition index was used to measure memory preference; this is the percentage of time spent exploring the novel object relative to total time spent exploring both objects, it is the main index of retention (El- Mazouki *et. al*., 2021).

Y-*Maze spontaneous alternation test*: Y-maze is shaped like the letter Y, it is used to study how the rodents function with memory and spatial learning through applying various stimuli. The Y-maze consists of a start box (16.5 cm×16.5 cm), stem (arm 1) length is 71.1 cm, goal area (arm 2 and 3) lengths are 45.7 cm, and arm width is 10.2 cm. The stem and start box are separated by a sliding door, and Y-maze is kept in a dimly lit, sound-attenuated room. Behavioural evaluation was performed in three phases: orientation session, learning performance test and retention test as described by (Kim *et. al.*, 2023)**.**

Determination of cortisol levels: The cortisol levels were determined using a commercial kit (Cat. No. MBS263105, Bio resource, USA). And the double ELISA sandwich approach is based on the principles of antigens against double valences based on the manufacturer's instructions (Salimetrics, State College, PA**).**

Hematoxylin and eosin (H & E staining): The tissues were first stained with Harris' hematoxylin solution for 6 hours at 60 – 70ºC. They were then rinsed in clean tap water until it was clear. After being separated three times for 2 hours each and once for ten hours using 10% acetic acid and 85% ethanol in water, the tissues were cleansed with tap water. As part of the bling procedure, the tissues were submerged in a saturated lithium carbonate solution for 12 hours before being rinsed with tap water. The material was then stained using an ethanol solution containing eosin for 48 hours. The tissues were submerged in xylene for 1 hour at 60 – 70º C after being dehydrated twice for 0.5 h with 95% ethanol**.**

Photomicrography: A Biobase Trinocular Head Inverted Biological microscope (2 # Building, No. 9 Guangxing Rd, High – Tech Zone, Jinnan city,Shangdong province, China) together with a scope image 9.0(HIC) cameras with specification (HDCE – 10C) were used to photograph the brain tissues (GO1201253) as adopted by(Cleal *et. al.*, 2020).

Evaluation of the level of lipid peroxidation: *Malondialdehyde (MDA):* This was carried out using a modified spectrophotometry method of thiobarbituric acid (TBA) test. 400 µL of the sample of the homogenate was reacted with 200 µL of trichloroacetic acid (TCA), 20% for deproteination. Then the HC centrifuged at a speed of 5000 rpm for 10 minutes. The supernatant formed was then taken and 400 µL of TCA, 0.6% was added. Then the sample was vortexed and incubated in water heater at 96ºC for 10 minutes, then allowed to cool at room temperature. Then read the absorption at a wavelength of 530 nm. The average normal value for reference is 2.61 µmol. /L.

Statistical analysis
The mean differences were calculated using two-way analysis of variance (ANOVA) factors: sex and stress. Individual group means were compared by Turkey's; the statistical package used is Graph Pad Prism 8.0 (San Diego, California, USA). The data from this study are expressed in mean (± SD). And values of P<0.05 are considered statistically significant.

RESULTS

Figure 1 shows a consistent decrease in the mean values of DI in females (0.07±0.3004), compared to males (0.63±0.1277) in the experimental groups. While among the control groups DI in females (1.090±0.3504) shows an increase in mean DI compared to the males (0.6625±0.2247); though, the difference in means was not statistically significant (P=0.1089) with F (DFn, DFd) F (3, 12) = 2.502 (32.75±3.065) Although, the difference i (P=0.5417) with F (DFn, DFd) F (3, 12) =0.7526 for females and males respectively.

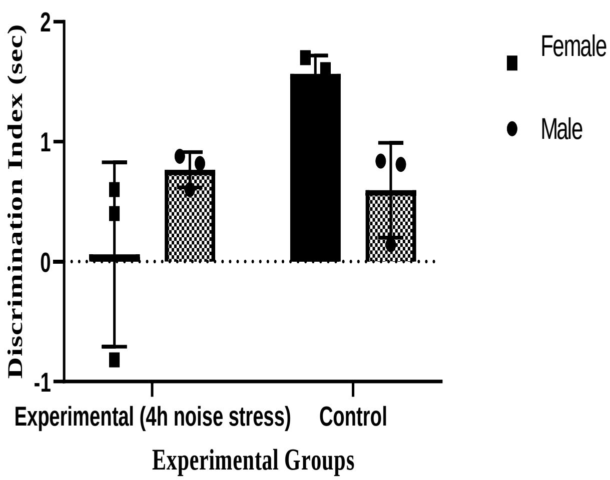

Figure 1
Mean discrimination index of experimental and control male and female Wistar rats exposed to noise stress. Data are expressed in mean ± SEM.

Figure 2, shows a consistent decrease in the mean values of percentage alternation in females (26.05±11.50), compared to males (52.0±22.17) in the experimental groups. While among the control groups percentage alternation in females (35.0±3.851) shows an increase in mean percentage alternation compared to the males (32.75±3.065). Although, the difference in means was not statistically significant (P=0.5417) with F (DFn, DFd) F (3, 12) =0.7526.

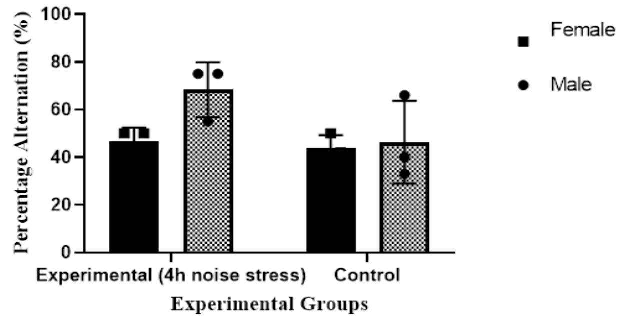

Figure 2
Mean values of percentage alteration in females compared males in the experimental groups. Data is expressed as means ± S.E.M

Figure 3, shows a consistent increase in the mean values of corticosterone levels in females (27.73±2.123), compared to males (17.83±5.343) in the experimental groups. While among the control groups, corticosterone in females (22.82±1.387) shows an increase in mean percentage alternation compared to the males (24.92±0.6249). Although, the difference in means was not statistically significant (p=0.1964) with F (DFn, DFd) F (3, 8) =1.975.

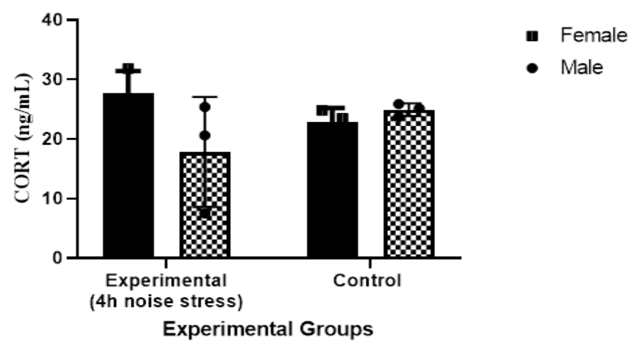

Figure 3:
Mean values of corticosterone levels in females compared to males in the experimental groups. Values are means ± SEM.

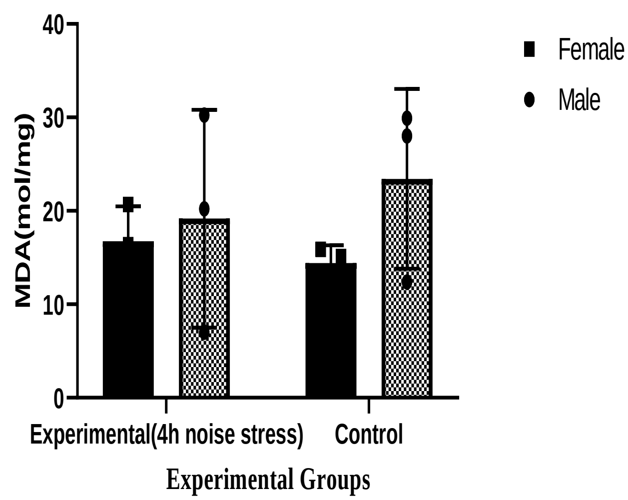

Figure 4
Mean MDA level of experimental and control male and female Wistar rats. Data are expressed in mean ±SEM.

Figure 4 shows the mean values of MDA level in females (16.75±3.16), and indicated a consistent decrease in value compared to males (19.17±6.3) in the experimental groups. However, among the control groups, MDA in females (14.43±.09) shows a decrease in mean MDA compared to the males (23.43±5.56) even though, the difference in means was not statistically significant(P=0.5671) with F (DFn, DFd) F (3,8) = 0.7209

Histology: The micrographs of histological studies is shown in plates 1-4. In the control groups (CGP1 and CGP2), the hippocampal tissue showed normal cytoarchitecture with normal pyramidal cells. However, in the experimental groups (EGP1 and EGP2), there was evidence of degeneration, necrosis and cytoplasmic vacuolation of sporadic pyramidal necrosis, as well as the presence of inflammatory cells.

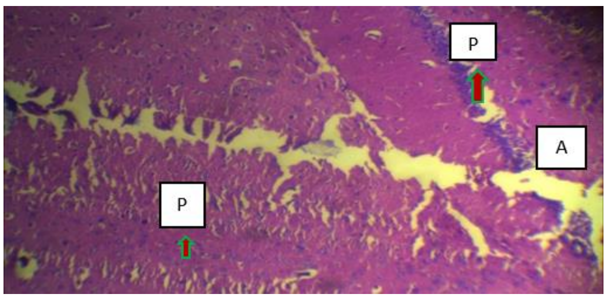

Plate 1:
Photomicrograph of a section of hippocampus (Group 1), showing normal cytoarchitecture with normal pyramidal cells stained with H/E X100

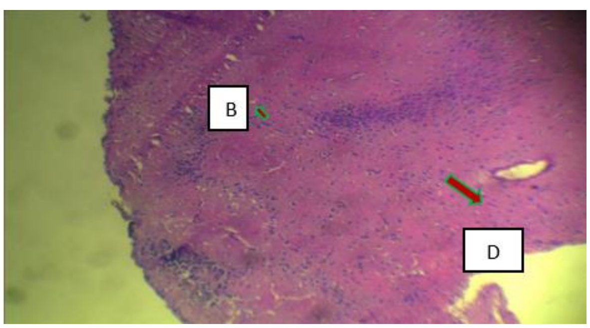

Plate 2:
Photomicrograph of a section of hippocampus (Group 2), showing degeneration/ necrosis of sporadic pyramidal neuron (arrow) stained with H/E X100

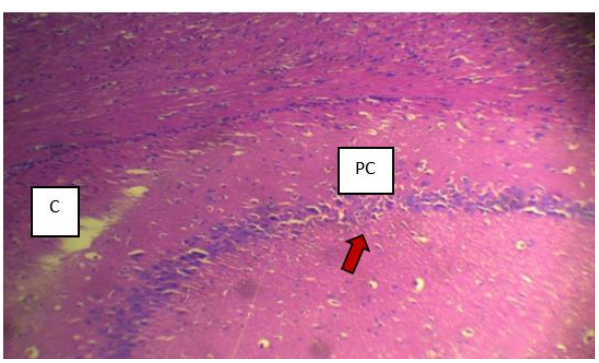

Plate 3.
Photomicrograph of a section of hippocampus (Group 3), showing normal cytoarchitecture with normal pyramidal cells stained with H/E X100

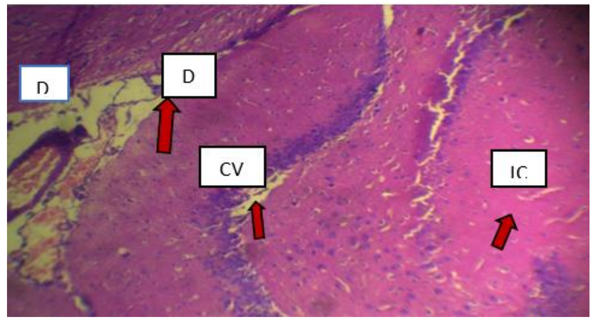

Plate 4.
Photomicrograph of a section of hippocampus (Group 4), showing degeneration and necrosis of pyramidal cells stained with H/E X100

DISCUSSION

Noise is an omnipresence phenomenon characterised with deleterious effects on the brain (Archana and Ravindran, 2019); and the world health organisation declared noise as one of the most hazardous factors of modern societies (WHO, 2001). This study investigated the effect of noise on cognition with emphasis on gender. The results obtained from this study show a consistent decrease in the mean discrimination index (DI) values in female Wistar rats exposed to noise compared to male rats in the experimental groups. The negative value observed in the experimental female Wistar rats is an indicator of cognitive decline. This agrees with previous studies that showed female rats are more susceptible to the negative consequences of noise stress (Baugher *et. al.*, 2022). No impairment was observed among the control groups of both male and female Wistar rats.

Our data on the effects of acute noise stress on spatial working memory in animal models, as shown in the mean percentage alternation on the Y-maze, indicate that the percentage alternation decreases in the female experiment compared to the male experiment. The decrease in the percentage alternation as seen in the experimental female indicates cognitive impairment in the Y-maze apparatus, this agrees with previous studies that show stress induces gender-based-deficit.9 The hippocampus plays an essential role in spatial memory for humans and rodents. The hippocampus is also connected to the hypothalamic-pituitary-adrenal (HPA) axis and is particularly susceptible to stress. (Trang *et. al*., 2020, Kim *et. al*., 2023)

With noise stress, the HPA axis is hyper-activated, releasing adrenocorticotropic hormone (ACTH) and corticosterone level (Kinlein *et. al*., 2019) , Dhurba ,2018).The results obtained from our study indicated a consistent increase in the mean values of corticosterone levels in female Wistar rats exposed to noise compared to male rats in the experimental groups. Conversely, among the control groups, the mean corticosterone level in females is slightly higher compared to males. The increase in corticosterone observed in this study agrees with some previous studies (Gabriella *et. al*., 2023, Stafford *et. al*., 2020). Lipid peroxidation is a process through which free radicals break down lipid molecules, which are major components of cell membrane. Malondialdehyde (MDA) is an indicator of lipid peroxidation process which involves the formation of free radical species. Our study showed MDA levels consistently decreased significantly in female rats exposed to 100 dB, 4 h/daily consecutively for 14 days when compared to male rats given the same treatment; while in control females ,there is decrease in MDA levels compared to male controls, even though not statistically significant. Data on rats not exposed to noise (controls) showed higher MDA levels in females compared to male rats. Similar findings were also reported in noise exposed textile workers when compared to control groups not exposed to noise (Hajali *et. al.*, 2012).

Noise exposure firstly increases levels of ROS such as superoxide radicals, hydroxyl radicals and hydrogen peroxidase; secondly, activities of antioxidant and related enzymes increases in order to eliminate the overproduced ROS due to noise stress (Reha et. al., 2009).

In our histological studies, section obtained from the brain of acute noise stress exposed rats exhibited degenerative necrosis of pyramidal cells and showed some vacuoles in both female and male experiments. Degeneration of pyramidal cells, and significantly reduced hippocampal volume in rats exposed to noise stress have earlier been reported (Madriyel *et. al.*, 2001). The hippocampal cells express the glucocorticoid receptors, and they are the principal target sites for glucocorticoid which are adrenocortical hormones secreted during stress **(**Faezeh *et. al*., 2008). Activation of GC receptors leads to overproduction of ROS (Stafford *et. al.*, 2020); and increased oxidative damage to the protein due to inhibiting activities of mitochondrial complex and antioxidant enzymes, SOD (Stafford *et. al.*, 2020, Edward *et. al*., 2013). This may support the histological changes observed in our study.

In conclusion, the study provides evidence that acute noise exposure can have a negative impact on the cognitive abilities of rats; and this effect is not substantial across genders. Albeit, it is skewed more towards the female Wistar rats, showing a decline in cognitive performance as seen in the values of DI and PA and also an increase in corticosterone compared to the male rats when exposed to noise stress for 4 hours daily for 14 days.

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