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Research Article

THE IMPACT OF PROLONGED EXPOSURE TO GENERATOR NOISE ON STRESS HORMONES AND IMMUNE FUNCTION IN MALE WISTAR RATS

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Abstract

Noise is an environmental factor that results in the activation of stressful stimuli and is known to activate the peripheral sympathetic nervous system, leading to disruptions of homeostatic activity. The study aims to ascertain the impact of prolonged exposure to generator noise on stress hormones and immune function in Male Wistar rats.Twenty-eight-(28) Male Wistar Rats weighing 120-150g were used in this study and were randomly divided into four (4) groups of seven (7) rats each. Group A served as normal control and received feed and water ad libitum. Group B was exposed to generator noise for 1 hour daily, Group C was exposed to generator noise for 2 hours daily, and Group D was exposed to generator noise for 4 hours daily. Exposure to prolonged generator noise lasted for eight weeks, and exposure was done between the hours of 8 am to 2 pm daily.Data for haematological indices were analysed using SPSS version 25 using ANOVA followed by Post Hoc LSD comparison and values were considered significant at $p<0.05$. The result showed thatCortisol, epinephrine, and CD4+ level showed a significant ($p<0.05$) increase in the treated groups compared to the control. CD8+ level significantly increased in groups C and D compared to the control. The study concluded that generator noise negatively affected cortisol, epinephrine, CD4+ and CD8+ cells in Wistar rats.

Keywords: Generator noise, cortisol, epinephrine, CD4+ and CD8+ cells.

INTRODUCTION

Occupational hazardous factor is one among the environmental stressors that activate neural- hormonal pathways in humans (1), which causes stress related disorders in humans such as tachycardia, hearing impairment, Etc. Environmental noise is a recognised risk factor for healthy individuals, and it is part of the external exposure that results in the loss of healthy lives annually in Western Europe, which is linked to cardiovascular complications such as hypertension, heart failure, myocardial infarction and stroke (2,3). Noise is a non-specific stressor that causes stress reactions, anxiety disorders, insomnia, immune dysregulation syndromes, and hearing impairment (4). Some stress-induced changes are attributed to an autonomic system imbalance and involve hypothalamic-pituitary-adrenal (HPA) axis activation, which is followed by changes in neural-hormonal pathways in humans (1).Cortisol is the most important glucocorticoid that copes with stress (5), which is the final product of the hypothalamus-pituitary-adrenal (HPA) axis (6). After the secretion of cortisol, the hormone is placed on GLUT-4 receptors and does not allow blood sugar to travel into the cells; as a result, blood sugar increases, in which cortisol offsets the action of insulin (7). Epinephrine is a sympathomimetic catecholamine that elicits its pharmacologic effects on alpha and beta-adrenergic receptors using a G protein-linked reaction, which resulted in increased heart rate, myocardial contractility, and renin release via beta-1 receptors (8). Noise as a pollutant has several effects on stress hormones such as corticotrophin releasing hormone (CRH) and adrenocorticotropic hormone (ACTH) specifically in asleep people during the vagotropic night or early morning phase (9). It causes significant changes in the sensitivity of cellular cortisol receptors by increasing the heat-shock proteins, and ultra-structural changes in the tissue of the heart and the adrenal gland (9).The $CD4^+$T cells carry out multiple functions, ranging from activation of the cells of the innate immune system, B-lymphocytes, cytotoxic T cells, as well as non-immune cells, and play crucial role in the suppression of immune reaction (10). The $CD8^+$ cells exert their effects principally by two mechanisms, cytolytic attack on target cells or secretion of interleukins and cytokines. First, when $CD8^+$ cells—by the interaction between the T-cell receptor(TCR) on the $CD8^+$ cells and the peptide on the major histocompatibility complex(MHC) Class I molecule of the target cell—are stimulated to "attack" target cells, they release perforin (11). However, noise related stress could have severe impact on the immune cells, which causes lymphocyte depletion in the thymus and spleen, and causes alterations in circulating leukocyte counts (12). Kui-Cheng and Makoto (13) revealed that acute noise exposure to generator enhances immune function while chronic noise exposure to same showed decrease in $CD4^+$ and $CD8^+$. However, despite reports on noise on stress hormones, there are limited literatures within this region on the impact of generator noise on stress hormones and immune function, therefore, the study investigates it.

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MATERIALS AND METHODS

Location of the Study: The study was carried out in the Department of Human Physiology, Faculty of Basic Medical Sciences, College of health Sciences, Nnamdi Azikiwe University, Nnewi Campus.

Ethical Approval: Ethical consideration was obtained from Faculty of Basic Medical Sciences, College of Health Sciences, Nnamdi Azikiwe University. Rats handling and

treatments was conformed to guidelines of the National Institute of Health (NIH publication, 1985) for laboratory animal care and use.

Materials: Twenty-eight-(28) Male wistar rats, Sumec Firman Fuel Generator (2900) (SPG-2900, China), Noise Meter, Distilled water, Standard Plastic Cages and water can, Cotton wool (KENS LINT, Benin City, Nigeria), Latex Medical Hand gloves (Supermax Gloves, Selangor, Malaysia), Chloroform, and Vital top feed grower (JOS, Nigeria). Dissecting kits, Microhematocrit Centrifuge (SH120), Plain sample bottle, Spectrophotometer (Model 721), and Enzyme Immunoassay (ELISA) kits IBL-America (IB89154) and (IB79311) for cortisol and epinephrine, and Heparinized Capillary Tube.

Experimental Animals: Twenty-eight-(28) Male Wistar Rats weighing 120-150g were used in this study and was housed in the animal house, College of Health Sciences, Nnewi Campus, Nnamdi Azikiwe University, Anambra State. Animals were kept in standard cages at a room temperature of 27±2°C. The animals were maintained with normal laboratory chow (Grower feed) and water *ad libitium*. They were acclimatized for a period of two weeks and before the prolonged exposure to generator noise that lasted for a period of 8 weeks. The animals were kept on 12hours light and dark cycles.

Experimental Design: The experimental animals were randomly divided into four (4) groups of seven (7) animals each. Group A serve as normal control and received feed and water *ad libitum*. Group B was exposed to generator noise for 1-hour daily. Group C was exposed to generator noise for 2-hours daily. Group D was exposed to generator noise for 4-hours daily. Exposure to prolonged generator noise lasted for a period of 8 weeks, and exposure was done between the hours of 8am to 2pm daily. The noise meter was used to measure the sound decibels of the Sumec Fuel generator and noise greater than 90 is considered noise pollutant and detrimental to health.

Noise Exposure: The noise was produced from Sumec Fuel generator 2900 and produced a sound level of 90 dB as indicated by the noise meter as described by Zheng & Ariizumi, (13). Experimental animals were kept at 3 meters away from the source of the noise.

Sample Collection: The animals were anaesthetized with Chloroform in an enclosed container, after 24 hours of the last exposure to generator noise; ocular puncture was done according to the method of Parasuraman *et al.* (14) to collect blood samples. The blood was obtained through the orbital sinus using a heparinized capillary tube for hematological indices was put into an EDTA container, and blood for cortisol, epinephrine, was $CD4^+$ and $CD8^+$ cells was put in a plain container and allowed to cool for 10 minutes before it was centrifuged using a centrifuged and serum was retrieved using micropipette and placed in a plain container for serum cortisol, epinephrine, $CD4^+$ and $CD8^+$ cells assay.

Cortisol and Epinephrine: Serum cortisol and epinephrine level were assayed using Enzyme Immunoassay (ELISA) technique supplied by IBL-America (IB89154) for epinephrine and IB79311 for cortisol as described by the manufacturer's manual.

Procedure for serum cortisol: Pipette 20 µl of each calibrator, control and specimen sample into correspondingly labelled wells in duplicate. Pipette 100 µl of the conjugate working solution into each well (A multichannel pipette is recommended). Incubate on a plate shaker (approximately 200rpm) for 45 minutes at room temperature. Wash the wells 3 times with 300 µl of diluted wash buffer per well and tap the plate firmly against absorbent paper to ensure that it is dry (The use of a washer is recommended). Pipette 150 µl of TMB substrate into each well at timed intervals. Incubate on a plate shaker for 15-20 minutes at room temperature (or until calibrator A attains dark blue colour for desired OD). Pipette 50 µl of stopping solution into each well at the same timed intervals as in step 7. Read the plate on a microwell plate reader at 450nm within 20 minutes after addition of the stopping solution.

Procedure for serum epinephrine: Pipette 90 µL of standards, controls and samples from the Enzyme Plate into the respective pre-coated Mikrotiter Strips. Pipette 50 µL of the respective Antiserum into all wells. Cover the plate with Adhesive Foil. Incubate for 1 min at RT (20-25°C) on a shaker. Incubate for 15 – 20 hours (overnight) at 2 – 8 °C. Remove the foil and discard or aspirate the contents of the wells and wash each well 4 times thoroughly with 300 µL Wash Buffer. Blot dry by tapping the inverted plate on absorbent material. Pipette 100 µL of Enzyme Conjugate into all wells. Cover the plate with Adhesive Foil and incubate 30 min at RT (20-25°C) on a shaker (approx. 600 rpm). Remove the foil and discard or aspirate the contents of the wells and wash each well 4 times thoroughly with 300 µl Wash Buffer. Blot dry by tapping the inverted plate on absorbent material. Pipette 100 µL of Substrate into all wells. Incubate 20-30 min at RT (20-25°C) on a shaker (approx. 600 rpm). Note: Avoid exposure to direct sun light! Pipette 100 µL of Stop Solution into all wells. Read the absorbance of the solution in the wells within 10 minutes, using a microplate reader set to 450 nm and a reference wavelength between 620 nm and 650 nm.

Measurement of CD4+ and CD8+ cells: The CD4+ and CD8+ kits were provided from Elabscience Company, Bulgaria. CD4+ and CD8+ levels in serum of experimental animals were measured using ELISA device (Human Reader Company, Germany) according to instructions of the manufacturer.

Statistical Analysis: Data obtained was analyzed using One Way Analysis of Variance (ANOVA), followed with post Hoc LSD to determine the level of significance between the control and experimental groups. The values were expressed as Mean ± Standard Error of Mean (Mean±SEM) and the difference was considered statistically significant at $p<0.05$. All statistical analysis was performed using statistical package for social sciences (SPSS) version 25.

RESULTS

Table 1 result showed a significant increase in the serum cortisol levels in groups exposed to noise at 1-hour, 2-hours, and 4-hours ($p=0.02$, $p=0.01$, $p=0.01$) compared to control. Epinephrine results showed a significant increase in groups exposed to noise at 1-hour, 2-hours, and 4-hours ($p=0.01$, $p=0.03$, $p=0.01$) compared to control.

Table 2 result showed a significant increase in the $CD4^+$ count levels in group exposed to noise at 1-hour, 2-hours, and 4-hours ($p=0.02$, $p=0.01$, $p=0.00$) compared to control. The

$CD8^+$ count result showed a non-significant increase in-group exposed to noise at 1-hour (*p=0.17*), while groups exposed to noise at 2-hours, and 4-hours indicated a significant increase (*p=0.01, p=0.04*) compared to group control.

Table 1 effect of generator noise on cortisol and epinephrine level

	Cortisol level (nmol/L)	Epinephrine level (pg/mL)
	MEAN±SEM	MEAN±SEM
Group A (control)	20.33±1.93	49.00±3.05
Group B (Noise exposure at 1-hr)	33.80±2.57*	75.33±3.17*
Group C (Noise exposure at 2-hr)	35.78±3.56*	83.33±3.38*
Group D (Noise exposure at 4-hr)	35.35±0.15*	87.67±9.93*
F-Ratio	9.44	9.26

Data was analyzed using ANOVA followed by post LSD and values were considered significant at *p<0.05*. SEM: Standard error of mean, significant (*) and not significant (^{NS})

Table 2 effect of generator noise on $CD4^+$ and $CD8^+$ count cells

	$CD4^+$ count (cells/u)	$CD8^+$ count (cells/u)
	MEAN±SEM	MEAN±SEM
Group A (control)	4.33±0.33	16.00±0.57
Group B (Noise exposure at 1-hr)	8.00±2.00*	20.67±2.33^{NS}
Group C (Noise exposure at 2-hr)	8.33±1.52*	27.33±3.17*
Group D (Noise exposure at 4-hr)	9.33±1.52*	23.67±2.02*
F-Ratio	6.37	4.59

Data was analyzed using ANOVA followed by post LSD and values were considered significant at *p<0.05*. SEM: Standard error of mean, significant (*) and not significant (^{NS})

DISCUSSION

Cortisol is a stress hormone and has significant impact on several physiological function both direct and indirect mechanism in eliciting its activities (15). The environmental has several ways of influencing physiological functions through its impact on environmental stressors such as noise pollutant (16). The study findings documented a significant increase in the serum cortisol levels in groups exposed to noise at 1-hour, 2-hours, and 4-hours compared to control. However, the physiology linked to the increased levels of cortisol is associated with oxidative stress from the noise generated from the generator, which has the potency to cause cascade of complex reaction (3). The study has accordance with the works of Spreng, (9), Chamkori *et al.* (17), Farzadinia *et al.* (18), Taban *et al.* (19), Smitha and Mukkadan, (2014), Monsefi *et al.* (20) revealing a significant surge of cortisol levels following noise exposure. However, the study has findings corroborates the reports of Zare *et al.* (21), Abtahi-Eivary *et al.* (22), Ahmadi *et al.* (23), NaderyanFe'li *et al.* (24), Kim *et al.* (25), and Behzad Fouladi *et al.* (26) showing a significant increase in cortisol levels following noise exposure. The study findings revealed that noise generated from generator showed a significant increase in the epinephrine level following noise exposure in the treated groups compared to control. However, the physiology linked to significant increase in the epinephrine level could result from oxidative stress caused by noise, which activates the release of epinephrine through the HPA axis. The study findings are in accordance with the report of Gesi *et al.* (27), Ravindran *et al.* (28), Taban *et al.* (19), Li *et al.* (29), Moslehi and Nabavizadeh Rafsanjani, (30), which revealed significant increase in the epinephrine levels.Multiple immune organs, immune cells, and immune-active substances make up the contents of the immune system, and can identify and eradicate foreign pathogens, senescent cells and tumor cells in the body. However, noise has shown to have an effect on the immune system both innate and specific (31). The study findings showed a significant increase in the $CD4^+$ count levels in group exposed to noise at 1-hour, 2-hours, and 4-hours compared to control. The $CD8^+$ count result showed an insignificant increase in-group exposed to noise at 1-hour, while groups exposed to noise at 2-hours and 4-hours indicated a significant increase compared to group A. The mechanism of action following significant changes in the immune cells of $CD4^+$ and $CD8^+$ is linked to suppression of the activity of the regulatory cells and production of numerous cytokines (32). Zheng &Ariizumi, (13) reported a non-significant change in the $CD8^+$ count following noised exposure, which disagree the study findings in groups exposed to noise at 2-hours and 4-hours, but corroborates the study as well in group exposed to 1-hour.

Conclusion

The study showed that noise had an impact on serum cortisol and epinephrine level, which could have severity on cardiovascular function at the different time exposure of noise. Also, the study indicated that generator noise had an effect on $CD4^+$ and $CD8^+$ cell count negatively, which revealed a decline in function at the different time interval.

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Statement of Competing Interest: The authors have no competing interest.

List of Abbreviations

HPA: Hypothalamic-Pituitary-Adrenal
CRH: Corticotrophin Releasing Hormone
ACTH: Adrenocorticotropic Hormone

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