LITERATURE REVIEW

The following chapter will discuss the previous researches on the effects of noise stress on:

1- Neurotransmitters.
2- Antioxidant states.
3- Immune system.
4- Organs function.
5- Hormones.

1- Effect on neurotransmitters:

Di G et al. (2013),[31] evaluated the effects of high-speed railway (HSR) noise on behaviors and plasma monoamines. Mice were exposed to previously recorded HSR noise for 53 days (d). The noise was equivalent to continuous SPL of 70 dB. The concentrations of plasma NE, DA and serotonin (5-hydroxytryptamine, 5-HT) were measured. It was found that the concentrations of plasma DA of the exposed group were significantly higher than those of the control group, while the plasma NE and 5-HT concentrations showed no significant difference between the 2 groups. The behavioral tests indicate that 70 dB, HSR noise can result in anxiety-like behaviors in mice. The physiological results showed that plasma DA is more sensitive to HSR noise compared with NE and 5-HT.

Persson-Waye K et al. (2013), [32] studied the effects of noise in intensive care units (ICUs) due to activities of patients, and alarms on sleep of patients. Healthy male participants were exposed to originally recorded ICUs noise. Sleep was registered with polysomnography during 4 nights: one adaptation night, one reference night, and the two exposed nights with similar equivalent sound levels (47dB). Salivery cortisol levels were also measured. The participants answered questionnaires and saliva cortisol was sampled in the morning. During ICU exposure nights, sleep was more fragmented with less slow-wave sleep, more arousals, and more time awake. The effects of reduced maximum sound level were minor. The subjective data supported the polysomnographic findings, though cortisol levels were not significantly affected by the exposure conditions.

Sjödin F et al. (2012), [33] analyzed the presence of stress-related health problems among preschool employees and the way in which these reactions were related to noise and other work parameters. The investigation included 101 employees at 17 preschools. Individual noise recordings and recordings in dining rooms and play halls were made at two departments from each preschool. The adverse effects on the employees were analyzed by use of different validated questionnaires and by saliva cortisol samples. Stress and energy output were pronounced among the employees, and about 30% of the staff experienced strong burnout syndromes. Mental recovery after work was low, indicated by remaining high levels of stress after work. The burnout symptoms were associated with reduced sleep quality and morning sleepiness. Cortisol levels supported the conclusion about pronounced daily stress levels of the preschool employees.

Tamura H et al. (2012), [34] investigated whether chronic exposure to low frequency noise (LFN) at a moderate level of 70 dB affects the vestibule, which is one of the organs responsible for balance in mice. Wild-type mice were exposed for 1 month to LFN (0.1 kHz) and high frequency noise (HFN; 16 kHz) at 70 dB at a distance of approximately 10-

20 cm. Behavior analyses including beam-crossing and footprint analyses showed impairments of balance in LFN-exposed mice but not in non-exposed mice or HFN-exposed mice. Immunohistochemical analysis showed a decreased number of vestibular hair cells and increased levels of oxidative stress in LFN-exposed mice compared to those in non-exposed mice. These results suggested that chronic exposure to LFN at moderate levels causes impaired balance involving morphological impairments of the vestibule with enhanced levels of oxidative stress.

Sprague-Dawley rats were exposed by **Di GQ et al. (2011),**[35] in soundproof chambers to previously recorded aircraft-related noise for 6 d. Noise was arranged according to aircraft flight schedules and was adjusted to its noise of 75 and 80 dB for the 2 experimental groups. The concentrations of plasma NE and the morphologies of neurons and synapses in the temporal lobe were examined. The results showed that the concentration of plasma NE of exposed rats was significantly higher than that of the control group. The neuron and synapsis of the temporal lobe of rats showed signs of damage after aircraft noise of 80 dB exposure for 65 d.

Saremi M et al. (2008), [36] compared the effects of different types of train (freight, automotive, passenger) on arousal from sleep. 20 young (25.8 years (y) ±2.6) and 18 middle-age (52.2 y ±2.5) healthy subjects participated in three whole-night polysomnographic recording including one control night (35 dB), and two noisy nights with equivalent noise levels of 40 or 50 dB, responsiveness increased with sound levels. Awakening (> 10 sec) was produced more frequently by freight train than by automotive and passenger trains.

The alteration in the levels of plasma corticosterone, and brain NE, after different durations of noise exposure (acute, 1 d; sub-acute, 15 d; chronic, 30 d) has been studied by **Samson J et al. (2007),** [37] to analyze their role in combating time-dependent stress effects of noise. Broadband white noise (100dB) exposure to male Wister albino rats significantly increased the levels of plasma corticosterone, and NE in all 3 duration of noise exposure. The sustained increase observed in their levels in the chronic group suggests that animals are not getting adapted to noise even after 30 d of exposure.

Ravindran R et al. (2005), [38] studied the association between noise exposure and the neurotransmitter (NT) level. The Wistar strain albino rats were exposed to 100 dB broadband white noise, 4 hours (hr) daily for 15 d. The high-pressure liquid chromatographic estimation of NE, epinephrine, DA, and 5-HT in discrete regions of the rat brain indicates that noise stress can alter the brain biogenic amines after 15 d of stress exposure.

2- Effect on antioxidant states:

A group led by **Nawaz SK (2011),** [39] studied the effects oxidative stress due to noise exposure at cell level using model of growing lymphocytes. Group A and Group B were exposed to sound with intensity 110 dB for 4 hr/d and for 8 hr/d respectively. Control group was exposed to sound less than 85 dB. Viable cell count was performed using trypan blue. Catalase (CAT) activity of each group was estimated using ELISA kit. Viable cell count of Group A and Group B was almost same but significantly less than that of control group. CAT activity of lymphocytes in Group B was significantly low as compared to

Group A and controls. There was no significant difference between CAT activity of Group A and control group.

Uran SL et al. (2010), [40] investigated the effect of acute and chronic noise exposures on different behavioral tasks. Levels of oxidative status markers were determined in two areas related to memory processes, the hippocampus and the cerebellum. 15 Wistar rats were exposed to loud noise (95-97 dB, 2hr/d). At 30 d, rats were subjected to different cerebellum and hippocampus-related behavioral tasks. Reactive oxygen species (ROS) levels and antioxidant enzyme activities (CAT and superoxide dismutase "SOD") were also assessed. It was found that impairments in spatial and associative memory in noise-exposed animals. Moreover, a decrease in anxiety levels and an increase in habituation memory were observed. While an increase in cerebellar ROS levels was found early after the first noise exposure, a decrease was found in the cerebellum and the hippocampus at 30 d. The activity of hippocampal CAT was increased early and remained high in acute noise exposure rats, while it was unchanged in the cerebellum.

Demirel R et al. (2009), [41] investigated the effect of noise on oxidative stress parameters. Noise group was exposed to noise for 20 d / 4 hr 100 dB. Control group that was not exposed to any noise and was kept from any stress source, was hold in the same conditions. After 20th d of the experiment; Malondialdehyde (MDA), nitric oxide (NO) levels and glutathione peroxidase (GPx) activity were analyzed in rat sera. It was found that MDA and NO levels and GPx activities were found to be increased significantly at the end of experiment in the group exposed to noise which may lead to various degrees of damages in the cells, mainly via lipid peroxidation (LPO) pathway.

Samson J et al. (2008), [42] determined changes in SOD, CAT, LPO and the auditory brainstem response (ABR) in the cochlea of mice prior to and immediately, 1, 3, 7, 10, 14 and 21 d after noise exposure (4 kHz at the intensity of 110 dB for 4 hr). A significant increase in SOD activity immediately and on 1st d after noise exposure, without a concomitant increase in CAT activity suggested a difference in the time dependent changes in the scavenging enzymes, which facilitates the increase in LPO observed on day 7. The ABR indicated significant noise-induced functional deficits which stabilized in 2 wk with a permanent threshold shift of 15 dB at both 4 kHz and 8 kHz. The antioxidant D-methionine (reversed the noise-induced changes in LPO levels and enzyme activities.

Heinrich UR et al. (2008), [43] identified the effect of ascorbic acid (vitamin C) on tissue-dependent NO content in the inner ear of the guinea pig. Over a period of 7 d, male guinea pigs were supplied with minimum (25 mg/kg body weight/d) and maximum (525 mg/kg body weight/d) ascorbic acid doses, and afterwards exposed to noise (90 dB SPL for 1 hr). The organ of Corti and the lateral wall were incubated differently for 6 hr in culture medium, and the degree of NO production was determined. Ascorbic acid treatment reduced the hearing threshold shift after noise exposure depending on concentration. When the maximum ascorbic acid dose was substituted, NO production was significantly reduced in the lateral wall after noise exposure and slightly reduced in the organ of Corti.

Yildirim I et al. (2007), [44] aimed to study effects of noise on hearing, LPO and antioxidant enzymes in textile workers. 30 textile workers exposed to high noise 105 dB in a textile factory, and 30 healthy male volunteers as a control group were included in the study. In both groups, following audiometric tests, blood samples were obtained. In these

blood samples, MDA, SOD and CAT levels were investigated. MDA levels were significantly higher in workers than controls, CAT activity was significantly lower. Also, SOD activity was lower in worker. It was observed that a significant change in hearing threshold of the textile workers compared with that of the control group that there may be a relationship between the oxidative stress and hearing loss.

Samson J et al. (2007), [45] studied The oxidative stress in three discrete brain regions, in wistar strain male albino rats which subjected to three different durations of noise exposures (acute, sub-acute and chronic noise stress) and the in vivo as well as the in vitro antioxidant activity of Ocimum sanctum has been analyzed. Broadband white noise (100 dB) exposure significantly increased the levels of SOD, CAT, GPx, LPO, oxidized glutathione (GSH) and decreased the levels of reduced glutathione (GSSG). However, administration of ethanolic extract of Ocimum sanctum attenuates the alterations induced by noise exposure. The antioxidant activity of Ocimum sanctum is also evident from its effectiveness in scavenging the free radicals in a dose dependent manner in the herbal antioxidant assays.

Manikandan S et al. (2005), [46] evaluated the protective effect of both ethyl acetate and methanolic extract of Acorus calamus against noise stress (30 d, 100 dB/4hr/d) induced changes in the rat brain. the activity of SOD, CAT, GPx and the levels of GSSG, vitamin C, vitamin E, protein thiols and LPO for the evaluation of oxidative stress status in discrete regions of the rat brain like cerebral cortex, cerebellum, ponmedulla, midbrain, hippocampus and hypothalamus had been measured. It was found that during exposure of noisy environment ROS generation led to increase in corticosterone, LPO and SOD, but decrease in CAT, GPx, GSSG, protein thiols, vitamins C and E levels. Both the ethyl acetate and methanolic extract of Acorus calamus protected most of the changes in the rat brain induced by noise-stress.

Dereköy FS et al. (2004), [47] investigated the effects of both noise exposure and ascorbic acid on oxidative status and hearing thresholds of rabbits. 2 groups of rabbits were used in the study. First group were not given any treatment, whereas 500 mg intramuscular ascorbic acid twice daily for 2 1/2 d was given to the rabbits in the second group. Total protein sulfhydryl groups, carbonyl contents, and MDA levels, as well as erythrocyte GSH, SOD, and CAT enzyme levels, were measured in all rabbits. All the rabbits were exposed to noise (100 dB, 1000 Hz, 1 hr). Oxidative parameters before noise exposure were compared; erythrocyte GSH and CAT enzyme levels were detected to be higher in the second group. In the first group of rabbits after noise exposure, total protein sulfhydryl groups were found to be reduced, whereas plasma carbonyl contents and MDA levels were elevated significantly. In this group, erythrocyte GSH, SOD, and CAT enzyme levels were low. In the second group, which was given ascorbic acid, total protein sulfhydryl groups were reduced, whereas plasma carbonyl contents and MDA levels did not change following noise exposure. In the second group, erythrocyte GSH and CAT enzyme levels were reduced, but SOD levels did not change.

Diao MF et al. (2003), [48] aimed at exploring the effect of noise on total antioxidant capacity in serum, NO level in the cochlea and the protective action of alpha-lipoic acid against noise-induced hearing loss. 60 guinea pigs were divided randomly into 3 groups (control group, noise+saline group and noise+alpha-lipoic acid group). Serum and cochlear tissue were treated immediately after noise exposure (115 dB, 5 hr) to determine the level

of total antioxidant capacity and NO, respectively. ABRs were measured before and immediately after exposure. Total antioxidant capacity level of the noise+saline group was significantly lower than that of the control group. Total antioxidant capacity level of the noise+alpha-lipoic acid group was significantly higher than that of the noise+saline group, while there was no significant difference in the levels between the noise+alpha-lipoic acid group and the control group. The NO level of the cochlear tissue in the noise+saline group was significantly higher than that of the control group. Cochlear NO level in the noise+alpha-lipoic acid group was significantly lower than that of the noise+saline group, while there was no significant difference in cochlear NO levels between the noise+alpha-lipoic acid group and the control group.

Melkonian MM. (1993), [49] used alpha-Tocopherol acetate as a repeated treatment within a year of weavers working under highly uncomfortable conditions (the level of noise up to 90 dB), was shown to exhibit the regulating effect on the rate of LPO and on content of alpha-tocopherol and cholesterol in blood plasma and erythrocyte membranes. The vitamin decreased distinctly the atherogenicity coefficient; these data suggest that treatment with tocopherol is essential for prophylaxis of noise-produced impairments.

3- Effect on immune system:

Pascuan CG et al. (2014), [50] investigated the effect of chronic (2 wk) noise (95-97dB) exposure on immune responses in BALB/c and C57 mice. The effect of chronic restraint-applied for the same time-on immune response was also analyzed. It was found that chronic noise impaired immune-related end-points in vivo and ex-vivo depending on the strain used. Noise, but not restraint, affected C57Bl/6 mouse T-cell-dependent antibody production and ex-vivo stimulated T-cell proliferation, but had no effect on these parameters in BALB/c mice or their cells. Further, noise exposure induced a decrease in corticosterone and catecholamines levels in BALB/c mice. In contrast, no differences were seen in these parameters for those BALB/c mice under restraint or for that matter C57Bl/6 mice exposed to restraint or noise.

Akan Z et al. (2011), [51] focused on measurements of noise pollution levels in Van Ferit Melen airport and effect of noise pollution over the immunoglobulin (Ig) A, G, and M changes among airport workers. It was seen that apron and terminal workers were exposed to high noise (>80 dB) without any protective precautions. IgA values of apron terminal and control group workers were approximately the same in the morning and increased in a linear manner during the day. IgG and IgM values of apron, terminal, and control group workers were approximately same in the morning. Apron and terminal workers IgG and IgM levels were increased until noon and then decreased until evening as compare to control group. These findings suggested that the noise pollution in the Van Ferit Melen airport could lead to hearing loss and changes in blood serum Ig levels of airport workers.

Zheng KC et al. (2007), [52] determined the effect of acute or chronic noise stress on both cellular and humoral immune responses and oxidative status. BALB/c mice were exposed to 90 dB white noise 5 hr/d for either 3 d or 4 wk. Hormone levels, splenic lymphocyte proliferation, lymphocyte subsets in spleen and thymus, serum antibody and oxidative status were determined. A 3-d exposure to noise stress resulted in increased hormone levels, splenic lymphoproliferation and serum IgM. On the other hand, a 4-wk exposure to noise stress caused a reduction of splenic lymphoproliferation, splenic CD4(+)

cells and serum IgG, but hormone levels and urinary 8-hydroxy-2'deoxyguanosine were increased. These results imply that acute exposure to noise stress may enhance immune responses, whereas chronic exposure to noise stress may suppress both cellular and humoral immune functions. The effect of noise stress on immune functions may be related to neuroendocrine modulation and oxidative imbalance as well.

The effect of acute noise induced changes on the immune functions of albino rats was studied by **Archana R et al. (2000)**.[53] Cell mediated immunity was assessed by Leukocyte migration inhibition index and humoral immunity by estimating antibody titre. The organ weight of spleen, thymus, adrenal and lymph node was noted, the cell count of spleen and thymus was enumerated and plasma corticosterone level was estimated. A significant increase in the plasma corticosterone level, thymus weight and cell count along with significant decrease in the antibody titre, spleen weight and cell count was observed in noise stressed animals. No significant changes were observed in the migration inhibition index and organ weight of adrenal and lymph node in these animals.

Aguas AP et al. (1999), [54] studied the effect of LFN exposure on mice splenic lymphocytes. Flow cytometry analysis of spleen lymphocytes was performed in BALB/c mice that had been exposed to occupationally simulated large pressure amplitude and low frequency noise ($\geq$ 90dB, $\leq$ 500 Hz) (8 hr x d, 5 d x wk) for a total of 1272 hr (approximately 8 months). The following surface phenotypes of splenic lymphocytes were quantified: IgM, CD4+, and CD8+. Quantification of splenic lymphocytes from non-exposed, age-matched, control BALB/c mice was also performed. Noise-exposed BALB/c mice had decreased T cells, involving both helper (CD4+) and cytotoxic (CD8+) lymphocytes, and also of IgM+ B lymphocytes.

4- Effect on organs function:

Lercher P et al. (2014), [55] investigated the effect of environmental noise on human in cross sectional study. They randomly sampled participants from circular areas around 31 noise measurement sites from four noise exposure strata (35-44, 45-54, 55-64, >64 dB). Repeated blood pressure measurements were available. Standardized information on socio-demographics, housing, life style and health was obtained. Reported hypotension or hypotension medication past year was the main outcome studied. Exposure-effect relationships were modeled with multiple non-linear logistic regression techniques using separate noise estimations for total, highway and rail exposure. Reported hypotension was significantly associated with rail and total noise exposure and strongly modified by weather sensitivity. Reported hypotension medication showed associations of similar size with rail and total noise exposure without effect modification by weather sensitivity. This study confirms a potential new noise effect pathway and discusses potential patho-physiological routes of actions.

Xue L et al. (2014), [56] investigated the pathological damage HFN exposure on the brain, heart, liver, and spleen of female rats. Rats in the experimental group were exposed to continuous HFN for 2 wk (3 hr/d). The most prominent histopathologic changes in the brain tissue structures of the experimental group included loose disorder, hyperemia, edema, blood vessels expand without degeneration or necrosis. There were dilatation and congestion of central vein, hepatic sinus, and interlobular veins of liver tissue. There was hyperemia in spleen, but the structure was clear. There was extravasated blood, and the

splenic sinuses were highly expanded by a blood clot. There was dilation and congestion in myocardial interstitial vascular, and there was mild degeneration and hyperemia in myocardial cells. No hemorrhage and myocardial necrosis were observed. High-frequency stable noise can cause pathological damage in brain, liver, spleen, and heart tissues of female rat at a various degree.

Choi CH et al. (2014), [57] examined the therapeutic effects of orally administrated antioxidant drugs on acute noise induced hearing loss. 30 rodents were exposed to a 105 dB noise centered at 4 kHz for 6 hr and randomly assigned to a control group (saline only) The drugs were orally administrated beginning 4 hr after noise exposure and then administered twice daily for the next two days. ABRs threshold shifts and the percentage of missing outer hair cell were determined. The oral administration significantly reduced permanent hearing threshold shift, and the percentage of missing outer hair cell in a dose-dependent manner.

Zamanian Z et al. (2013), [58] aimed to investigate the effect of noise exposure on BP and HR of steel industry workers. 50 workers were selected from a steel company, and exposed to 85, 95, and 105 dB noise levels for 5 minutes. The participants' BP and HR were measured both before and after the exposure. It had been found that no significant difference in BP and HR before and after the exposure. However, the workers' SBP had increased compared to before the exposure; ofcourse, the difference was not statistically significant. Also, the subjects' heart rate had reduced in comparison to before the exposure.

The association between road traffic noise exposure and BP among children was studied by **Liu C et al. (2013)**.[59] BP in 605 children aged 10 y was measured. Demographic and health information was collected by parent completed questionnaires. Road traffic noise levels were assessed. Minimum and maximum levels within a 50 m buffer around child's home address were derived. Generalized additive models were applied to explore effect of noise levels on SBP and DBP. The orientation of child's bedroom window was considered in sensitivity analyses. DBP was significantly associated with the minimum level of noise during 24 hr and night time. Specifically, DBP increased by 0.67 and 0.89 mmHg for every 5 dB increase. DBP of children whose bedroom window faced the street was 1.37 mmHg higher than those whose bedroom window did not, these children showed statistically significant increased SBP for compared to children whose bedroom window did not face the street.

Attarchi M et al. (2012), [60] aimed to assess the relationship between shift working and occupational exposure to noise with BP. The study was carried out in a rubber manufacturing company. All 331 under study workers were divided into 4 groups according to work shift and noise exposure severity, from non-noise exposed day time workers (Group 1) to noise exposed shift workers (Group 4). Finally, SBP and DBP levels were compared among these four groups. The results of this study showed that there was a significant difference between average SBP and DBP and HTN frequency in the four groups. The highest rate of HTN and mean SBP and DBP were observed among shift workers who were exposed to noise higher than permissible limit (Group 4). Also the results of logistic regression analysis showed that there was a significant relationship between simultaneous exposures to noise more than the permitted limit and shift work with HTN.

Chang TY et al. (2012), [61] investigated the association between noise exposure at different frequencies and the prevalence of HTN in 188 screw-manufacturing workers. Participants were divided into one high-noise-exposure group (≥80 dB; n=68) and 2 reference groups, including 68 low-noise-exposure workers (75.8±3.2 dB) and 52 office workers (61.5±0.5 dB). Male workers exposed to noise levels at high frequencies of 2000, 4000 or 8000 Hz had a higher but non-significant risk of HTN. Those exposed to ≥80 dBA for 2-4 y, 4-6 y and more than 6 y had a 4.43-fold, 1.21-fold and 0.95-fold risk of HTN, respectively, compared with reference workers. A significant association was only observed in male workers exposed to ≥70 dBA at 4000Hz for 2-4 y and was not found at other frequencies for any periods.

Sørensen M et al. (2011), [62] studied the effect of exposure to road traffic and railway noise and associations with BP and self-reported HTN. 57,053 participants aged 50-64 y were involved in this study. SBP and DBP were measured. Incident HTN during a mean follow-up of 5.3 y was assessed by questionnaire. Residential long-term road traffic noise was estimated for 1- and 5-y periods preceding diagnosis of HTN. Residential exposure to railway noise was estimated at enrollment. It was found that a 0.26 mm Hg higher SBP per 10 dB increase in 1-y mean road traffic noise levels. Road traffic noise was not associated with DBP or HTN. Exposure to railway noise above 60 dB was associated with 8% higher risk for HTN.

Haralabidis AS et al. (2011),[63] studied the association between exposure to transportation noise and BP reduction during nighttime sleep. 24-hr ambulatory BP measurements at 15-min intervals were carried out on 149 persons living near 4 major European airports. Noise indicators included total and source-specific equivalent indoor noise, total number of noise events, annoyance scores for aircraft and road traffic nighttime noise. Long-term noise exposure was also determined. The pooled estimates showed that the only noise indicator associated consistently with a decrease in BP dipping is road traffic noise. The effect showed that a 5 dB increase in measured road traffic noise during the study night is associated with 0.8% (-1.55, -0.05) less dipping in DBP. Noise from aircraft was not associated with a decrease in dipping, where the aircraft noise was higher. Noise from indoor sources did not affect BP dipping.

Goyal S et al. (2010), [64] studied the effect of noise stress on autonomic function tests. The study was carried out in 200 male volunteers. They were divided into 2 groups. The study group was exposed to noise levels of more than 80 dB for more than 8 hr /d for a period of 6 months, working in the steel and hammer industry, whereas the control group was working under normal conditions. Various autonomic function tests were carried out in both the groups. HR and BP were recorded. The tests depicted significant increase in the mean resting HR and the HR response to standing, the valsalva ratio, the % change in diastolic BP response to standing and valsalva maneuver, the SBP and DBP in study group as compared to the control group. The significant higher results in study group may be attributed to increased sympathetic activity.

Lee JH et al. (2009),[65] identified the effects of chronic noise exposure on BP. 530 male workers at a metal manufacturing factory were enrolled in the study. They were monitored with an annual health check-ups for nine consecutive years from 1991 to 1999. The subjects were divided into 4 groups which were determined by noise level categories according to the exposure of noise intensity; I: office workers who were exposed to <60 dB

at work; II: worksite technical supporters or inspectors who were intermittently exposed to noise and were not using hearing protection devices; III: worksite workers exposed to a noise below 85 dB and used one type of hearing protection device, earplug or earmuff; IV: worksite workers who were exposed to a noise level of 85 dB or higher in average and used both earplug and earmuff. After controlling the possible confounders, such as baseline age, smoking, alcohol intake, exercise, family history of HTN, SBP, or DBP, and changes in body mass index, the mean values for the SBP over the duration of this study were measured 3.8, 2.0, and 1.7 mmHg higher in groups IV, III, and II, respectively, in comparison to that of the I group. There was no significant difference in DBP among the groups.

Erken G et al. (2008), [66] aimed at investigating the effects of classical and rock music on hemorheological parameters in rats. 28 rats were divided into 4 groups: the control, noise-applied, and the classical music- and rock music-applied groups. Taped classical or rock music were played repeatedly for 1 hr/d for 2 wk and 95-dB machine sound was applied to the noise-applied rats during the same period. RBCs deformability and aggregation were measured. Red blood cell (RBC) deformability was found to be increased in the classical music group. Exposure to both classical and rock music resulted in a decrement in erythrocyte aggregation, but the decline in RBCs aggregation was of a higher degree of significance in the classical music group. Exposure to noise did not have any effect on the parameters studied.

Baldwin AL et al. (2007), [67] studied the effect of noise on microvascular integrity in laboratory rats. Rats were exposed to daily 15-min episodes of 90-dB noise to determine whether similar effects occurred and whether vitamin E with a-lipoic acid or Traumeel (a homeopathic anti-inflammatory-analgesic) reduced these effects. All groups exposed to excess noise had significantly more leaks per venule length and greater leak area per venule length than did the quiet group. However, the number and area of leaks in the rats that received Traumeel or vitamin E were significantly smaller than those in rats exposed to noise only. In addition, mast cell degranulation was significantly lower in rats given Traumeel.

Change in SBP over an 8-y period was explored in groups defined according to exposure to shift work, occupational noise, and physical workload by **Virkkunen H et al. (2007)**.[68] The impact of baseline SBP and its increase in relation to coronary heart disease risk due to these exposures was also studied. Shiftwork status was obtained from a questionnaire, and other exposures were determined with the Finnish job-exposure matrix. SBP was measured, and coronary heart disease end points were obtained. During the SBP follow-up, the steepest SBP gradient was found for physical workload only and physical workload combined with noise; shift work alone or combined with noise primarily entailed a lower mean SBP level than no such exposure. However, the shift workers had a relative risk of 1.71 even without an increase in SBP, but, with a baseline SBP of ≥140 mmHg and an additional increase, their relative risk rose to 4.62 when they were compared with day workers with an SBP of <140 mmHg and no increase.

Castle JS et al. (2007), [69] evaluated the effect of age and acoustic stress on gastric myoelectrical activity (GMA) and autonomic nervous system function. Twenty-one men subjects were recruited and exposed, in random order, to 3 auditory stimuli (Hospital noise, conversation babble and traffic noise). All periods lasted 20 min and were interspersed

with a 10 min of recovery. GMA was obtained using a Synectics Microdigitrapper. Autonomic nerve function was assessed by monitoring BP and HR using an automatic recording device. It was found that GMA changes with age. Loud noise can alter GMA, especially in younger individuals. The data indicate that even short-term exposure to noise may alter the contractility of the stomach.

Pei Z et al. (2007), [70] investigated the effects of infrasound exposure of 5 Hz at 130 dB on cardiac ultrastructure and function in rats. Rats were exposed for 2 hr/d for up to 14 d, and time-dependent increases in SBP and DBP were reported along with cellular and molecular changes in cardiac cells.

Frenzilli G (2004), [71] investigated the effects of noise exposure on DNA integrity in rat adrenal gland evaluated by the comet assay. The exposure to loud noise (100 dB) for 12 hr caused a significant increase of DNA damage in the adrenal gland.

Lenzi P et al. (2003), [72] evaluated the effect of noise exposure on DNA integrity and ultrastructure of rat cardiomyocytes. The exposure to loud noise (100 dB) for 12 hr caused a significant increase of DNA damage, accompanied by swelling of mitochondrial membranes, dilution of the matrix, and cristolysis.

Pellegrini A et al. (1998), [73] showed the effect of repeated stress (1 hr of daily immobilization for seven consecutive days) on the adrenal cortex of young adult male albino rats which was evaluated by morphohistochemical methods and plasma assays; at the same time, testes and major salivary glands, as steroid-producing and depending organs, respectively, were examined. Morphological and histochemical changes were found in the adrenal cortex, testis and submaxillary gland, though varying in degree and extent depending on the gland examined. Corticosterone and progesterone plasma levels increased, in agreement with the lipid depletion observed in the zona fasciculata, while testosterone and androstenedione decreased. The study thus proves that repeated stress, even of temporary duration, is able to influence directly or indirectly the morphofunctional state of the three examined glands, suggesting a functional linkage.

Pellegrini A et al. (1997), [74] examined the effect of varying duration of noise exposure on rat adrenal gland. Animals were exposed to noise for 1, 6 and 12 hr continuously and the sections obtained from exposed rats were compared to those from corresponding controls. No significant ultrastructural changes were found in the zona glomerulosa, while mitochondria of the zona fasciculata showed matrix dilution and cristolysis after 1 and 12 hr of noise stress. At all exposure times examined, the zona reticularis exhibited areas of diluted cytoplasm, disarranged endoplasmic reticulum, membrane vestigia and some altered mitochondria. Diluted cytoplasmic areas appeared in noradrenaline and adrenaline-storing cells after 6 and 12 hr of exposure, respectively.

The effect of sound stress on the circulating level of thymulin and on the cellularity of the thymus gland was studied by **Folch H et al. (1991)**.[75] The experiments were done in mice exposed to a noise level of 100 dB for a period of 1 hr. Following the noise exposure, the animals were bled at different times for thymulin titration, or killed in order to evaluate the number of cells and the weight of each thymus. It was found that young mice exposed to the stressor stimulus show an increase in serum thymulin titre, and an increment in thymus weight and in thymocyte number compared to control.

5- Effect on hormones:

Saki G et al. (2013), [76] evaluated the effects of administration of Vitamins C and E on fertilization capacity in rats exposed to noise stress. 40 adult male rats were randomly divided into 5 equal groups. Group 1 as controls who were not exposed to noise and groups 2-5 exposed to noise with 90-120 dB intensity and 300-350 Hz frequency from 7 pm to 7 am for 50 d. Group 2 exposed to noise and did not receive Vitamins. Group 3 received vitamin C, Group 4 received Vitamin E. Group 5 received Vitamins C and E concomitantly. After 50 d, serum Follicle-stimulating hormone (FSH), Luteinizing hormone (LH) and testosterone were measured. Then each rat was left with three female rats for mating. Pregnant females were sacrificed on the 19th d of pregnancy and evaluated for the presence and number of viable, dead and absorbed fetuses. The level of FSH, LH and testosterone significantly decreased in rats exposed to noise. By administration of Vitamins in groups 3-5, it was observed that the level of hormones significantly increased in compared to group 2. The fertilization capacity of male rats in groups 3-5 significantly increased in compared to group 2. The data in this study strongly suggests a negative role for noise stress on level of FSH, LH and testosterone level and also fertilization capacity of male rats.

Fouladi DB et al. (2012), [77] assessed the relationship between industrial noise exposure and salivary cortisol concentrations, and the possibility of using salivary cortisol as a possible marker of noise-induced stress. 80 male participants working in 4 different parts (painting, assembling lines, casting, and packaging) of a household manufacturing company was included in this study. Morning and evening saliva samples were collected at 7.00 am and 4.00 pm, respectively. Noise exposure levels were assessed by sound level meter and noise dosimeter. All measurements occurred in two days: One in leisure day and other in working day. On the leisure day, morning salivary cortisol was significantly higher than evening cortisol. Also, on the working day, morning salivary cortisol was significantly higher than evening cortisol. No significant difference was obtained for morning cortisol levels between leisure day and working day samples. But, for evening cortisol concentrations, a strong significant difference was noted leisure day and working day. The evening cortisol in the working day correlated significantly with noise exposure > 80 dB.

Rasmussen S et al. (2009), [78] analyzed the effects of construction noise on mouse gestation and neonatal growth. Female Swiss Webster mice were individually implanted with 15 B6CBAF1/J embryos and then exposed to 70 and 90 dB concrete saw cutting noise samples at defined time points during gestation. In addition, groups of mice with litters were exposed to noise at 70, 80, or 90 dB for 1 hr daily during the first week after parturition. Litter size, birth weight, incidence of stillborn pups, and rate of neonatal weight gain were analyzed. Noise decreased reproductive efficiency by decreasing live birth rates and increasing the number of stillborn pups.

Effects of various periods of acoustic noise on the dynamics of insular indices and associated biochemical parameters were studied in 22 male volunteers aged 20-25 by **Petrova TV et al. (2000),** [79]. Experimental and literary data was suggested that acoustic noise can increase insulin in blood and cause, during prolonged chronic exposure, development of insulin resistance. At the same time, in individuals with signs of insulin resistance or hyperinsulinemia tolerance for the factors of flying activity was reduced;

thus, insulin resistance may be considered a premorbid background for metabolic shifts and symptoms of stressogenic illnesses in a delayed period.

The effect of acute noise stress on albino rats was studied by **Archana R et al. (1999),**[80] by estimating the plasma corticosterone level, total and differential WBCs count. Neutrophil function was assessed. The total leukocyte count was significantly decreased. No significant changes were observed in the differential count of the leukocytes. A significant increase in the plasma corticosterone level.

Armario A et al. (1985),[81] studied the relations between chronic noise stress and insulin secretion. The effect of chronic noise, followed by acute noise, on basal glucose and insulin levels was studied in adult male rats. Chronic noise did not modify basal levels of either measured variable before or after the exposure of rats to acute stress. Acute noise decreased serum glucose and insulin levels, although hypoglycemia was transient.

Rai RM et al. (1981), [82] studied the biochemical effects of chronic exposure to noise in man. Biochemical parameters in 75 normal healthy male subjects exposed to intense noise of 88-107 dB (6-8 hr/d) for 10 to 15 y during their work situation have been monitored and compared with 35 normal unexposed subjects. Levels of free cholesterol, gamma-globulin, and cortisol were found to be significantly higher in the exposed subjects. Significant changes in free cholesterol also altered the ratio of free to esterified cholesterol significantly. The value of the A/G ratio was also lower in the exposed group. Uric acid did not show any change.