DISCUSSION

Many studies reported that exposure to noise causes many health problems such as hearing loss, sleep disturbance, and impaired 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 [167-168].

In this work, we have studied the effect of different sources of noise (obtained from factory, traffic and furnace) on some biological, behavioral and histological parameters of mice. All the noise sources were of fixed intensity at 100 dB. Each noise source as a whole (with all its spectrum) was refereed as collection. Each collection noise was analyzed and the predominant frequency was separated. The mice were exposed to collection and predominant noises in two manners either chronic or acute.

We aimed in this work to discriminate between the effect of acute and chronic exposure from one side and the main cause of that effect from the other side whether it is due to the whole noise collection (all frequency spectrums) or mainly because of the predominant frequency in each noise source; we have to discuss that in each parameter.

Starting with the effect of noise on blood glucose level, noise exposure is a stressful condition and stress is known to signal the body to raise blood glucose level in order to generate energy to respond to the stress. But if the body cannot meet this higher demand for blood glucose, hypoglycemia can result. In our study all exposed groups suffered from severe decrease in blood glucose levels compared to control. This hypoglycemia can be partly explained by poor glucose absorption from intestine due to edema and inflammatory changes seen in the histological examination of the intestinal villi in all experimental groups in comparison to control. Such histological changes was also seen by Baldwin AL [169] who subjected the rats to a daily 15-min white noise regime (90 dB) for 3 or 6 weeks and the histological examination of the mice's small intestine showed significantly more eosinophils and degranulated mast cells in the intestinal villi than the quiet rats, In addition, the villi were swollen and the epithelial cells had widened junctions. The noise exposed group also showed significantly more leakage of fluorescent albumin from the mesenteric microvessels. Another suggested explanation to this hypoglycemia in our study is the observed decrease food intake through the exposure period in all groups.

Blood glucose level also decreased in the study held by Simpson GC [170] who used 4 equals male groups, A,B preloaded with glucose, whereas C, D were not, groups A, D exposed to non-stressful white noise (50 dB), while groups B,C exposed to stressful white noise (80 dB), the result showed that stressful noise lead to reduction in high blood glucose level and preloading of glucose lead to attenuation of this reduction, while there are no change in the blood glucose level in unstressed groups. In this study the decrease in blood glucose level was significantly lower after predominant noise exposure than after collection noise exposure, whatever is the noise type or the exposure pattern (chronic or acute) denoting that exposure to fixed highest frequency is more injurious than exposure to different frequencies including this highest noise whatever is the type of noise or the pattern of exposure.

Acute and chronic loud noise exposure generates excessive free radicals and causes disorders involving extra-auditory organs [171]. Oxidative stress is a state where significant imbalance between oxidants and antioxidants occur that leads to damage, dysfunction or cellular death [172]. Under normal conditions, sufficient concentrations of endogenous antioxidants enzymes exist to protect from environmental oxidant attacks. SOD is one of antioxidant enzymes playing a role in removing ROS produced by oxidative stress, while MDA is one of the free radicals production by LPO [173]. In our study both parameters where assessed to measure the oxidative state in brain tissue of experimental animals.

The results showed that all the acute exposed groups have no significant changes in SOD, MDA level in comparison with control. As after single (acute) exposure of noise stress, the endogenous antioxidants have sufficient time to contra the excessive production of ROS that may be caused by noise exposure. On the other hand all the chronic exposed groups had significant decrease in SOD levels in comparison to the control group denoting that chronic exposure to noise can lead to oxidative imbalance in the brain tissue. This was shown in a way that the chronic predominant noise exposure had more significant effect than the chronic collection noise exposure, whatever is the type of noise used. Derekoy et al. [47] also showed the same results,as they exposed rabbits to 100 dB SPL, 1000 Hz for 1 hr then upon estimation of SOD level in these animals it was found that its level was significantly decreased in comparison to control group. Also, Ersoy A et al. [174] found that exposure of rats to 100 dB, 4 hr daily for 20 d led to highly significant decrease in SOD levels in cerebral cortex in the rats' brain which is in great agreement with our results.

Furthermore, Manikandan et al. [175] had found increased MDA levels in different areas of the brain after 30 days of 100 dB white noise exposure. Also Srikumar et al. [176] in their study found increased levels of MDA in the serum, thymus gland, and spleen tissue after a 15-d exposure to white noise. Similarly, high levels of LPO have been indicated in other studies as an indirect sign of increased ROS production in the serum and different areas of the brain in chronic noise exposure mainly in the cerebellum and brainstem [41]. This might be attributed to the fact that noise enters the brain from the brainstem, where auditory nuclei are located.

Regarding WBCs count which was assessed in this study, results showed significant decrease in total WBCs counts in all experimental groups in comparison to control group; in such a way that the decrease was more significant in the predominant frequency exposed groups than the collection frequencies exposed groups whatever is the noise type or the pattern of exposure. This decrease in the WBCs counts may be due to the effect of oxidative stress on the bone marrow mesenchymal stem cells (MSCs) as donated by some researches [177, 178]. Lu WY and Zhao MF who denoted that oxidative stress can induce the senescence and apoptosis of MSCs via phosphatidylinositol 3-kinase/protein kinase B (PI3K/AKT) and p53 pathways, and inhibit the proliferation and differentiation of MSCs through apurinic/apyrimidinic endonuclease/redox factor 1 (APE/REF-1) and extracellular signal-regulated kinase (ERK) pathways. This result is similar to previous studies, Archana R and Namasivayam A [80] who dealt with acute exposure of rats to 100 dB for 4 hours and found significant reduction in both total white blood cells and differential count, but they related their results to the measured excessive release of corticosteroid. In our study, we did not find significant variation in differential count which is in agreement with Van Raaij et al. [179] who showed that no variation in differential count after noise stress. In contrast Bedanova I et al. [180] examined the responses of peripheral blood leukocytes to chronic

noise exposure (70 and 80 dB) in broilers from day 1 or day 7 of fattening. This noise treatment resulted in a significant elevation of basophil granulocytes. But, there was a significantly smaller total number of leukocytes and significantly smaller differential counts of lymphocytes and basophils in broilers treated with noise from day 7 than in broilers treated with noise from day. Differential counts of eosinophils and monocytes were not affected by the time of exposure to noise. The discrepancy between these results and our results in the differential WBCs count may be due to different animal models as well as the different noise intensity used.

Serotonin (5-HT) is synthesized from tryptophan and metabolized to 5-hydroxyindoleactic acid (5-HIAA). Stress can alter 5-HT, tryptophan, and 5- HIAA concentrations in the central nervous system and in the periphery [181]. Studies[22,38,182] investigating the effects of noise on the 5-HT levels showed that varying noise intensity and exposure duration led to different impacts on 5-HT levels. In this study, we find a non significant effect of noise either chronic or acute on 5-HT levels in brain. These findings are in agreement with Di G et al. [31] who indicated that high speed railway noise of 70 dB had a little influence on the mice plasma 5-HT levels.

It is widely accepted that noise is a stressful environmental stimulus and stress has been previously shown to impair cognition such as the acquisition of memory, consolidation, and recall [183, 184]. Exposure to noise stress in the present study also impaired recognition memory donated by the calculated recognition index (RI) of the NOR task. The mice in the chronic noise-exposed group showed a significant decrease in RI in comparison to the control group, which means a decrease in time spent exploring the novel object in comparison to the familiar one and hence exhibited a marked impairment in recognition memory. While no changes in RI were found in all acute groups. Neurobiological studies on cognition show that the hippocampus is the key region critically involved in memory formation [185] and a primary target of stress hormones [186]. Furthermore, stress has also been shown to suppress neurogenesis [187]. The impaired memory function exhibited by noise-exposed mice in the present study may be attributed to noise stress-induced hippocampal damage [188] as proved by the histological brain examination that showed that many vacuolation and astrocytosis as well as condensed chromatin denoting the presence of apoptosis. This damage may be attributed to the shown oxidative stress in brain tissue especially that there was a positive correlation between RI and SOD and the negative correlation between RI and MDA in chronic exposed groups. This indicates the direct effect of oxidative stress on the recognition memory of these animals. Soujanya S et al. [189] stated that condensed chromatin and vacuolation in brain histopatholgy indicates the increase in free radicals production in the brain cells. Another possible cause for impaired recognition memory in these animals is the hypoglycemic state that may affect the performance of such mice. Haider S et al. [190] found that exposure of rats to 100 dB 4 hr daily for 15 d led to significant decreased recognition index of rats exposed to noise as compared to the control and exhibited a significant decrement in spatial memory.

On the other hand there are some studies which found no effect of noise on cognitive functions as Uygur E et al. [191] research that studied the effect of chronic white noise (100 dB) stress exposure on rats using 8-arm radial maze and forced swimming test, there were no significant differences among groups for cognition and behavior in their study.

This may be due to the protocol used in their study, where these two tests were employed for investigating spatial learning and long term memory, while in our study assessment was for the short term working memory

Again, the affection of memory in chronic exposed groups was in a manner that the predominant frequency exposure groups were significantly more affected than the collection frequencies exposed ones in all used noise types.

The presence of background noise systemically affects the auditory system. Latency shifts may reflect a decrease in neural synchronization and/or a decrease in the number of neurons firing, causing responses to be both smaller in amplitude and delayed (Burkard and Sims). [192] The addition of background noise to an auditory signal delays brainstem response timing. This effect has been extensively documented using manual peak selection. Peak picking, however, is impractical for large-scale studies of spectrotemporally complex stimuli, and leaves open the question of whether noise-induced delays are frequency-dependent or occur across the frequency spectrum.

Our results indicate that all the predominant frequency groups are more affected than the collection group. Our results can be explained by the experiment performed by Tierney A. et al. [193] which studied the effects of background noise on the brainstem response to speech by analyzing both shifts in peak latencies and shifts in phase. There was a significant phase shift between the quiet and the noise condition in the phase of the noise condition lagged compared to the quiet condition. Next, they examined whether the phase shifts were uniform across the frequency spectrum or whether they were frequency-dependent. The phase shift in the formant transition was not uniform across frequencies, but differed significantly between the four frequency ranges analyzed. Finally, they investigated whether phase shifts and peak latency shifts were correlated, and if so, whether this relationship depended on the frequency range in which phase shifts were analyzed. Peak latency shifts were highly correlated with phase shifts in both the transition and the steady-state portions of the response. In the transition, latency shifts correlated with phase shifts between at certain frequency range while were not significantly correlated with phase shifts in any other frequency bands. They concluded that shifts in neural response timing would also be reflected in frequency-specific phase shifts. This noise-induced delay is not uniform such that some frequency bands show greater shifts than others. Most importantly, phase shifts occurring in specific frequency bands correlate strongly with shifts in the latencies of the predominant peaks in the auditory brainstem response, while other frequency bands do not correlate with latency shifts.

SUMMARY AND CONCLUSIONS

I. Summary:

Sound is of great value to living beings for communication. It warns of danger and appropriately arouses and activates us. Sound is a pressure wave traveling in a medium. We normally consider the medium to be air, but sound travels through liquids and solids as well. The audible range is 20-20,000 cycles per second (Hertz).

Sound those are unwanted, unpleasant or harmful become noise. Stress has become an integral part of human life in this modern era. Among the innumerable stressors to which mankind is exposed, noise happens to be a commonly encountered stressor throughout the world.

During daily life, people are exposed to potentially harmful noise levels coming from work environment, urban traffic, and household appliances. Noise exposure is known to affect auditory structures in living organisms. However, it should not be ignored that many of the effects of noise are extra-auditory. The effects of noise vary depending on the characteristics of noise, such as intensity and frequency, exposure time and form, individual age, sex and health condition.

Excessive noise has been linked to a variety of health issues, including:

- Hearing loss.
- Mental illness.
- Sleep disturbance.
- Hypertension.
- Cardiovascular diseases.
- Increased plasma corticosterone levels.
- Elevated levels of cholesterol.
- Reduction in body weight.
- Decrease in gastric secretion.
- Changes in immune response and tumor resistance.
- Decrease in reproductive function.

This work aimed to examine the non-auditory effects on mice resulting from the following different sources of noise:

1- Noise comes from blanking press machine at a factory.

2- Noise comes from different kinds of public transportation at crowded traffic sign.

3- Noise comes from baking furnace machine.

The work studied the effect of these noise sources as a collection (all the frequencies included) from one side and separation the predominant frequency for each noise source and use them as a source of exposure from the other side. The exposure system involved both acute and chronic exposure of mice.

In this work the following materials and methods were used:

- The different sources of noise were recorded using microphone attached to laptop, then saved on mp3 device which then connected to loud speaker. All noise sources intensity was adjusted to be 100 dB at the loud speaker using sound level meter device. Computer software were used to analyze each sound source and separate the predominant frequency for each source then tone generator software was used to generate the predominant frequency tone for each source which adjusted also to be 100 dB.

- Anechoic chamber was designed and performed to insulate the sound. Illumination and ventilation were taken into account upon design. All the exposures were performed inside it.

- The animals used were 130 mice divided to 13 groups classified as the following:

  - G0: control exposed (unexposed group).
  - GIa: factory acute collection group exposure.
  - GIIa: traffic acute collection group exposure
  - GIIIa: furnace acute collection group exposure
  - GIaf: factory acute predominant frequency group exposure.
  - GIIaf: traffic acute predominant frequency group exposure.
  - GIIIaf: furnace acute predominant frequency group exposure.
  - GIc: factory chronic collection group exposure.
  - GIIc: traffic chronic collection group exposure.
  - GIIIc: furnace chronic collection group exposure.
  - GIcf: factory chronic predominant frequency group exposure.
  - GIIcf: traffic chronic predominant frequency group exposure.
  - GIIIcf: furnace chronic predominant frequency group exposure.

After the end of the exposure time for all the groups the following parameters were assessed:

- Short memory estimation using recognition index method.
- Blood glucose level.
- Total and differential WBCs count.
- Brain superoxide dismutase activity to indicate the oxidative stress state.
- Brain malondialdhde concentration to assess the lipid peroxidation state in brain cell membrane.
- Brain serotonin concentration to evaluate the neurotransmitter state from brain.
- Histological examination of mice brain and intestine with light microscope at magnification of 40 times for tissue effect study.

The results of the present work are:

1- Very high significant decrease in blood glucose level in all the groups exposed to noise either were acute or chronic compared to control group.
2- Very high significant decrease in total blood WBCs count in all the groups exposed to noise either were acute or chronic compared to control group.

3- Very high significant decrease in brain superoxide dismutase activity in the chronic groups only compared to control group while the changes were non-significant in all the acute groups compared to control group.
4- Very high significant increase in brain malondialdhde concentration in the chronic groups only compared to control group while the changes were non-significant in all the acute groups compared to control group.
5- Non-significant change in brain serotonin concentrations in all the groups exposed to noise either were acute or chronic compared to control group.
6- Very high significant decrease in recognition index in the chronic groups only compared to control group while the changes were non-significant in all the acute groups compared to control group.
7- Very noticeable changes in brain and small intestine histology in all the groups exposed to noise either were acute or chronic compared to control group.

It was measured that the predominant frequency groups were very high significant compared to frequency collection groups in all the measured parameters.

II. Conclusions:

Depending on the present work results, we can conclude that the different sources of noise have direct and clear effect on:

- Blood glucose level.
- Total WBCs count.
- Oxidative stress state.
- Short memory state.
- The histological structure of both brain and small intestine.

The predominant frequency is the major affecter in each noise source on the measured parameters.