Effect of Noise and Crowding Related Stress on Serum Level of Cortisol 
ACTH, Epinephrine and Insulin in Female Albino Rats. 
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Abstract

Background: Noise and crowding are the most stressful factors for human beings. Study aimed to clarify their effect on cortisol, ACTH, epinephrine, insulin and the amelioration effect of Sulpiride.

Material and Methods: Thirty six female rats were divided into six groups (6/each): 1- Rats served as control, 2- Rats treated with Sulpiride drug, 3- Rats exposed to noise (90db, 3hr. per day) for 45 days, 4- Rats exposed to noise and treated with sulpiride drug, 5- Rats exposed to crowding, 6- Rats exposed to noise and treated with Sulpiride drug.

Results: Noise and crowding stresses caused a significant increase of cortisol, ACTH and epinephrine while there was a significant decrease in insulin hormone. Sulpiride drug ameliorated these parameters.

Conclusion: it is useful to use Sulpiride drug with people who are exposing to noise and crowding stress.

Keywords: Noise, Crowding, Sulpiride drug, Physiological parameters, Cortisol, ACTH, Epinephrine, Insulin.

INTERODUCTION

Stress can be defined as a state of threatened balance, induced by external stressor and appear as the display of somatic and psychic reaction, struggling to regain homeostasis (1) among stressful stimuli, crowding and noise.

Noise is an environmental pollutant capable of causing hearing impairment (2), behavioral, mental and widespread disturbances at several levels in human organs and apparatus due to chemical and physiological modification of endocrine (3).

Crowding stress is a type of psychosocial stress induced by an increased density of population. Population density may be raised either by increasing the number of species living in the same area and/or by reducing their living space (4).

Antidepressant drugs are the most successful drugs in patients with clear vegetative characteristics including psychomotor retardation, stress, sleep disturbance, poor appetite and weight loss. However, a variety of different chemical structures have been found to have antidepressant activity. Their number is constantly growing, but as yet no group has been found to have a clear therapeutic advantage over the others (5).

Sulpiride is the most favorite drug which used to tolerate stress symptom (6). People who expose to stress take one or some drugs to avoid its effect. So, the present study deals with the possible protective effect of one of the antidepressant drugs (Sulpiride) against noise and crowding stresses in female albino rats.

Aim of the work: during all the day time Cairo is extra crowded and noise city, where it suffer from movement of huge number of especially in the morning about 30,000,000 persons in the morning. Also it is suffer from a very loud noise. This study amid at clarifying the effect of each stress on some hormonal pattern. The question arise here, could Sulpiride drug (which is a favorable and widely used drug) completely ameliorate stress effects or it would be worsen?

Material and Methods

Thirty six normal white female albino rats weighing 150±30 g were purchased from the Farm of the National Organization for Control and Research. They were kept under observation for one week before the beginning of the experiment acclimation period. The chosen animals were housed in cages and kept under to artificial light for 14 hr. and 10 rodent hr. complete darkness at normal atmospheric temperature. All animals were fed on standard
rodent diet contained protein, fibers, fats, ash, carbohydrates and supplied with vitamins and minerals mixture. The animals had free access to water.

1- Sulpiride administration:
The drug was administered orally by gastric tube at a dose of 0.28mg/100gm. body weight/day for 45 days. The dose for the rat was calculated according to the Paget’s formula on the basis of the human dose (7).

2- Application of Noise:
Noise was applied by 5 different sources of enharmonic and high intensity music.

3- Application of crowding:
A group of 6 rats were put in a cage (20 × 15 × 20 cm).

5- Animal groups:
Thirty six female albino rats were divided into six main groups each group contained six rats.

Group 1:
Normal rats served as control group untreated for a duration of 45days in a cage (20 × 30 × 20).

Group 2:
Rats were treated with the Sulpiride drug at a dose of 0.28mg/100mg. body weight/day for a duration of 45days.

Group 3:
Rats were exposed to noise (90db, 3hr. per day) for a duration of 45days.

Group 4:
Rats were exposed to noise and treated with the drug for a duration of 45days.

Group 5:
Rats were exposed to crowding only for a duration of 45days.

Group 6:
Rats were exposed to crowding and treated with the drug a duration of 45days.

6- Data analysis:
The obtained data were statistically analyzed by using the student t-test according to the method of Snedecor and Cochran (12). P ≤ 0.05 considered significant while P ≤ 0.01 highly significant.

Results
Table (1): Percentage of change of cortisol, ACTH, epinephrine and insulin in female albino rats after exposure to the stressors (noise or crowding) and treated with the Sulpiride.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Group</th>
<th>Control</th>
<th>Drug</th>
<th>Noise</th>
<th>Noise + Drug</th>
<th>Crowding</th>
<th>Crowding + Drug</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cortisol (μg/dL)</td>
<td>Mean</td>
<td>101.7</td>
<td>94.8</td>
<td>149.1</td>
<td>119.8</td>
<td>134</td>
<td>120</td>
</tr>
<tr>
<td></td>
<td>SE±</td>
<td>1.3</td>
<td>1.98</td>
<td>1.2</td>
<td>1.6</td>
<td>1.9</td>
<td>1.3</td>
</tr>
<tr>
<td></td>
<td>P</td>
<td>N.s</td>
<td>&lt;0.01</td>
<td>&lt;0.05</td>
<td>&lt;0.01</td>
<td>&lt;0.05</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td></td>
<td>% of change</td>
<td>-6.8</td>
<td>46.6</td>
<td>17.7</td>
<td>31.7</td>
<td>17.9</td>
<td></td>
</tr>
<tr>
<td>ACTH (pg/mL)</td>
<td>Mean</td>
<td>39.6</td>
<td>39.1</td>
<td>62</td>
<td>47.3</td>
<td>59.3</td>
<td>49.5</td>
</tr>
<tr>
<td></td>
<td>SE±</td>
<td>3.1</td>
<td>0.6</td>
<td>2.3</td>
<td>0.8</td>
<td>3</td>
<td>1.34</td>
</tr>
<tr>
<td></td>
<td>P</td>
<td>N.S</td>
<td>&lt;0.01</td>
<td>&lt;0.05</td>
<td>&lt;0.01</td>
<td>&lt;0.05</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td></td>
<td>% of change</td>
<td>-1.2</td>
<td>56.5</td>
<td>19.4</td>
<td>49.7</td>
<td>25</td>
<td></td>
</tr>
<tr>
<td>Epinephrine (pg/mL)</td>
<td>Mean</td>
<td>17.35</td>
<td>20</td>
<td>30.3</td>
<td>24.5</td>
<td>32.3</td>
<td>25.5</td>
</tr>
<tr>
<td></td>
<td>SE±</td>
<td>0.86</td>
<td>0.6</td>
<td>1.37</td>
<td>1.4</td>
<td>1.37</td>
<td>0.6</td>
</tr>
<tr>
<td></td>
<td>P</td>
<td>N.S</td>
<td>&lt;0.01</td>
<td>&lt;0.05</td>
<td>0.01&lt;</td>
<td>0.05</td>
<td></td>
</tr>
<tr>
<td></td>
<td>% of change</td>
<td>15.2</td>
<td>74.6</td>
<td>41.2</td>
<td>86.1</td>
<td>46.9</td>
<td></td>
</tr>
<tr>
<td>Insulin (μIU/mL)</td>
<td>Mean</td>
<td>21.93</td>
<td>22.55</td>
<td>13.5</td>
<td>15.1</td>
<td>12.1</td>
<td>16.3</td>
</tr>
<tr>
<td></td>
<td>SE±</td>
<td>0.7</td>
<td>0.22</td>
<td>0.3</td>
<td>0.2</td>
<td>0.31</td>
<td>0.21</td>
</tr>
<tr>
<td></td>
<td>% of change</td>
<td>2.8</td>
<td>-38.4</td>
<td>-31.1</td>
<td>-44.8</td>
<td>-25.6</td>
<td></td>
</tr>
</tbody>
</table>

Table (1) showed a highly significant increase (P ≤ 0.01) of cortisol, ACTH and epinephrine levels in rats exposed to the stressors (noise and crowding) in comparison with those of control group. But Exposure of rats to noise, crowding exposure and treated groups with Sulpiride showed less significant increase (P ≤ 0.05) when compared with control.
However serum insulin level in rats exposed to stress showed a highly significant decrease in comparison with that of control group. Sulpiride supplementation to rats exposed to noise showed an increase in the hormone level from -38.4 to -31.1% while, the rats exposed to crowding and treated with Sulpiride exhibited improvement in insulin level to be 25.6% instead of -44%.  

**Discussion**

Stress is defined as the state in which the brain interprets the quantity of stimulation as excessive or its quality as threatening (13). Stress stimulates several adaptive hormonal responses, prominent among which are the secretion of catecholamines from the adrenal medulla, corticosteroids from the adrenal cortex and adrenocorticotropin from the anterior pituitary (14).

Results of the present study revealed a significant increase in stress hormones (ACTH, cortisol and epinephrine) levels as compared to those of control group.  

When the body is activated by a stressor, the hypothalamus is stimulated by an unknown signal with release of corticotrophin – releasing hormone (CRH) which stimulates the anterior pituitary to secrete adrenocorticotrophic hormone (ACTH) which is considered as the hormone of stress. ACTH stimulates secretion and growth of zona fasciculate and zona reticularis of adrenal gland and stimulates the secretion of cortisol. So, there is an increase in plasma cortisol level and increase in the adrenal weight (14). The hypothalamus also stimulates the adrenal medulla to increase secretion of catecholamine (14). The mechanism by which noise and crowding stresses produced elevation in stress hormones may be explained by activation of sympatho-adreno-medullary (SAM) system with increased secretion of epinephrine and whole body activation that is called fight and flight response. Release of epinephrine from the adrenal medulla and glucocorticoids from the adrenal cortex initiate the biological responses permitting the organism to cope with adverse psychological, physiological and environmental stressors. Following its massive release during stress, epinephrine must be restored to replenish cellular pools and sustain release to maintain the heightened awareness and squeal of responses to re-establish homeostasis and ensure survival (16). Epinephrine is regulated in part through its biosynthesis catalyzed by the final enzyme in the catecholamine pathway, phenylethanolamine N-methyltransferase (PNMT) expression, in turn, is controlled through hormonal and neural stimuli, which exert their effects on gene transcription through protein stability (17). Dirk et al. (18) described the physiological responses to physical or psychological stress as the release of “adrenocorticotropin (ACTH)” from the anterior pituitary, glucocorticoids from the adrenal cortex, epinephrine from the adrenal medulla, and norepinephrine from sympathetic nerves. Together, these hormones enable organisms to biologically adapt to stressors, ranging from mild to severe, thereby ensuring the organism’s survival. In cases of prolonged stress, release of epinephrine evokes compensatory elevation of the catecholamine biosynthetic enzymes, tyrosine hydroxylase (TH), dopamine β-hydroxylase (DBH) and PNMT, to replenish depleted neurotransmitter/neurohormone stores, and the magnitude and temporal pattern of change in hormonal and neural activity elicited by a particular stress may differentially affect these enzymes. Variation in plasma catecholamine levels evoked by a variety of stressors points to this possibility (19).  

In noise and crowding stress groups, these results are in agreement with the findings of Lofgren et al. (20), who reported that, there is an elevation in ACTH and cortisol level in humans and animals that exposed to air craft noise, road traffic noise and density population. Sylvia et al. (21) reported that, exposure of rats to noise and crowding produced increase of ACTH, cortisol and epinephrine level combined with changes of the myocardial ultra-structure.  

These results are also compatible with those of Marks et al. (22) who demonstrated that, noise and crowding stress induced cortisol secretion based upon the existence of much closed connection between sub cortical structure of central nervous system and part of auditory system can activate HPA axis. The increased volumes of cortex, medulla and total adrenal gland in noise and crowding exposed groups may be also correlated to the hyperactivity of HPA axis causing an increase in the activity and secretion of this gland. The hyperactivity of adrenal gland may be dependent on cell hypertrophy (22).
Some stereological studies have shown that after exposure to noise and crowding stress an increase adrenal gland weight and enlargement of the zona fasciculate cells occurred due to a notable increase in the volume of mitochondria and hypertrophy changes in different layers of adrenal cortex (23, 24, 25 and 26). However these results disagreement with Those of Chrousoos (27) who found that, cortisol and epinephrine level decreased in rat after chronic repeated exposure to noise and crowding stresses due to adaptation of HPA axis.

More over, the present results also disagreement with those of Animesh et al. (28) who reported that, plasma cortisol and glucose concentration returned to values approximately similar to those prior to stress on the 30th day of the experiment, reflecting possible adaptation of the animals to stress.

The hypothalamus –pituitary –adrenal (HPA) axis; its response to a stimulus is sustained for an appropriate time, and is turned off when the stressor is efficiently inactivated and when stressor inactivation is inefficient, the HPA axis becomes desensitized through its normal adaptation to repeated stressors of the same type and this results in inadequate secretion of cortisol (29).

The results of the present study revealed a significant decrease in the insulin level as compared to control group. Exposure of rats to noise and crowding stress showed activation of (HPA) with subsequent release of adrenocorticotropic hormone, cortisol and catecholamines leading to increase glucose level and decreased insulin level (30). Significantly higher plasma cortisol level could increase responsiveness of pancreatic cell to glucose of low insulin level (31).

These results are also in agreement with those of Julia et al. (32) who reported that, plasma cortisol is the stress hormone that affects the way of the body processes insulin. This steroid hormone makes muscle and fat cells resistant to insulin and increases the production of glucose. The body depends on insulin to regulate glucose levels in blood. Insulin works by processing glucose into energy in cells. Diabetes is a condition that affects of ability to produce or process insulin. The increase in glucose due to stressful situations can alter the amount of insulin necessary to provide healthy blood-sugar levels, meaning individuals with diabetes may experience glucose spikes during periods of stress (33).

Sissel et al. (34) reported that, hyperglycemia may also be decreased insulin secretion which may be due to noise or crowding stress or due to the associated food intake.

The hyperglycemia effect of stress may be also due to sympatho adrenal stimulation which may cause a concomitant increase in glucagons level (35). Stress hyperglycemia and decreased insulin may be also due to stimulation of hypothalamic noradrenergic activity and hepatic glucose output. So, if the central noradrenergic activity had been inhibited, the stress hyperglycemia also inhibited (36). Stressed rats treated with Sulpiride drug led to some extent an amelioration in ACTH, cortisol, epinephrine and insulin because antidepressant effect of Stress increased lipid peroxidation, which resulted from increased free radical generation. Dose of Sulpiride and treatment duration have been chosen on the basis of previous studies performed by Wang (37) who found that, the long–term administration of Sulpiride at the daily dose 4mg/kg is effective in animal models of depression.

The mechanism by which Sulpiride decreases stress hormones is by lowering responsiveness of HPA axis, which is up regulated by stress and contributes to the alleviation (38). Sulpiride improves the quality of life for patient receiving palliative care, enhancing a sense of comfort and help one to cope with stress; it may also evoke stress, anxiety and intolerance (39).

Sulpiride; a atypical (1–4) neuroleptic from the group of banzamides, is a selective dopaminergic receptor, namely D2 and D3 receptor antagonis. Sulpiride selectively blocks the above–mentioned types of dopaminergic receptors. It is an exception ally hydrophilic drug and not lipophilic as most drugs of this type are. It causes no strong extra pyramidal symptoms which could result from D2 receptor blocked in the corpus striatum and which are the equivalent of catalepsia in animals (40).

According to above mentioned results it is possible to conclude that Sulpiride a administration to stressed animals nearly inhibited the effect of stress, so the functions of the affected glands were nearly improved. This led to the improvement of the hormonal disruption which induced by stress. More studies must be done or other types of
antidepressant drugs, and variable stress factors in order to justify the possible ameliorative effects of antidepressant drugs against the screening risks of exposure to environmental stressors which induce several diseases in the body due to the induction of hormonal imbalance stress and combination of different stresses.

Reference
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