

## Effect of Noise and Crowding Related Stress on Serum Level of TSH and Thyroid Hormones in Female Albino Rats.

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### Abstract

**Background:** Noise and crowding are the most stressful factors for human beings.

This study is aimed to clarify their effect on some thyroid hormones and the amelioration effect of sulpirid .

**Material and Methods:** Thirty six female rats were divided into four groups (6/each):

1-control, 2-treated with sulpiride drug, 3- rat exposed to noise (90db/3hper day for 45 days) 4-Noise plus drug, 5 – rat exposed to crowded exposure and 6- crowded plus drug.

**Results:** Noise and crowding stresses caused a significant increase only of T3 and T4 while there was a significant decrease in TSH. Sulpiride drug was ameliorated these parameters.

**Key words:** Noise, Crowding, Sulpiride drug, Grave's disease Albino rats, Physiological parameters.

### Introduction

Environmental factors including infection, smoking and stress such as crowdedness and noise are considered to be of the putative environmental causes of Grave's disease. Genetic and environmental factors other than stress are relevant to the development and course of the disease, because the difference of stressful life events, which are recorder more frequently in Grave's patients in many cases (1).

Although Graves' disease has a well-known familial tendency, heredity does not explain everything (2, 3, 4). A study of twins, who are not always concordant for the disease, suggests that genetic factors explain 79% of the incidence of the disease, while environmental factors are responsible for 21% of the cases (5). A recent study shows that the risk of having Graves' disease is multiplied by 5 if there is one affected member in the family, by 310 if there are two affected members in the family, and by 16 if one twin is affected. The risk is higher in men than in women. The finding that the risk is increased among spouses by 2.75 highlights the role of the environment (6).

**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.

**Noise** stress is a part of everyone's life every day. Noise is a kind of stress which is defined as unwanted sound. Noise is pervasive aspect of many modern community and work environments. Numerous studies have indicated a connection between stress and autoimmunity and that stress may trigger or worsen autoimmune disease (7, 8, 9,10).

Antidepressant drugs are the most successful drugs in patients with clear vegetative characteristics including psychomotor retardation, 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 (11).

Sulpiride is the most favorite drug which used to tolerate stress symptom (12). People who expose to stress take one or some drugs to avoid the effect of stress. So the present study deals with the possible protective effect of one of the antidepressant drugs (sulpiride) against crowded in female albino rats.

### Material and Methods

#### 1-Experimental animals:

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

#### 2-Sulpiride administration:

The drug was administered orally by gastric tube at a dose of 0.28mg/100g body weight/day for 40 days. The dose for the rat was calculated

according to the Paget's formula on the basis of the human dose (13).

### 3- Application of Noise

Noise was applied by 5 different sources of enharmonic and high intensity music.

### 4- Application of crowding

Each 6 rats were but 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 (without any treatment for 45 days-in a cage (20 × 30 × 20).

#### Group 2:

Rats were treated with the sulpiride drug at a dose of 0.28mg/100mg body weigh/day for 45 days.

#### Group 3:

Rats were exposed to noise only for 45 day ( over 90 dB), 3hr. /day.

#### Group 4:

Rats were exposed to noise and treated with the drug for 45days.

#### Group 5:

Rats were exposed to crowding only for 45 days.

#### Group 6:

Rats were exposed to crowding and treated with the drug for 45days.

Serum Triiodothyronine, T3, Thyroxin (T4) was estimated according to method described by Fisher (14) and thyrotropin (TSH) detected by Keffer (15).

#### 6-Data analysis:

The obtained results were statistically analyzed by using the student t-test according to the method of Snedecor and Cochran. (16),  $P \leq 0.05$  considered significant while  $P \leq 0.01$  highly significant.

## Results

**Table (1): Percentage of TSH, T3, T4 change in female albino rats after exposure to stresses (noise or crowding) and treatment with the Sulpiride**

Group Parameter		Control	drug	Noise alone	Noise + drug	crowding	Crowding +drug
T3 (mg/dl)	Mean	89.95	90.6	153.9	108.6	155.36	113.13
	SE±	4.26	2.83	0.62	3.11	1.45	1.31
	P		NS	<0.01	<0.01	<0.01	<0.01
	% OF change		0.72	71.09	20.73	72.71	25.76
T4 (mg/dl)	Mean	11.9	9.95	118.78	88.1	118.8	85.2
	SE±	0.34	0.74	1.1	0.84	0.89	0.76
	P		NS	<0.01	<0.01	<0.01	<0.01
	% OF Change		16.3-	898	640.3	898.3	615.9
TSH (mIU/L)	Mean	3.8	3.7	1.1	2.2	1.9	2.5
	SE±	0.26	0.24	0.02	0.03	0.83	0.03
	P		NS	<0.01	<0.01	<0.01	<0.01
	% OF Change		2.6-	-71.05	-42.1	-50	-34.2

Table (1) showed highly significant increase ( $P \leq 0.01$ ) of T3 levels in rats exposed to stresses (noise and crowding) in comparison with control group. Sulpiride supplementation in rats exposed to noise decreased from 71.09 to 20.73% and rats exposed to crowding decline from 72.71 to 25.76% which clarify the good effect of sulpiride on rats exposed to stress.

Table (1) showed highly significant ( $P \leq 0.01$ ) increase of T4 level in rats exposed to stresses (noise and crowding) in comparison with control group. Sulpiride supplementation in rat exposed to noise decreased from 898 to 640% and rat exposed to crowding decline from 898 to 615.9% which clarify the good effect of sulpiride on rat exposed to stress. However, TSH level in rats exposed to stress showed highly significant decrease in comparison with control group. Sulpiride supplementation in rats exposed to noise increase from -71.05 to -42.1% while, the rats exposed to crowding increased from -50 to -34.2%.

## Discussion

Stress affects the immune system either directly or indirectly through the nervous and endocrine systems. The immune modulation may contribute to the development of autoimmunity as well as the susceptibility to autoimmune disease in genetically predisposed individuals. Crowding and noise stress can be one of the environmental factors which effects thyroid autoimmunity (17).

Weetman (18) suggested that, the best circumstantial evidence for the effect of stress on autoimmune thyroid disease is the well-known relationship between the onset of Grave's hyperthyroidism and major stress. Furthermore, most of the recent case-control studies support stress as a factor in the onset and clinical course of Graves' disease.

The present study on rats showed a significant increase in T3, T4 and a significant decrease in TSH after exposure to chronic crowding and noise stress.

Numerous studies have indicated a connection between stress and autoimmunity and that stress may trigger or worsen autoimmune disease, also demonstrated that, psychological and physiological stressors induce various immunological changes (19, 20, 21, 22). Exposed to stress led to overproduction of the thyroid hormones T3, T4 and it is the most commonly caused of the development of Grave's disease, an autoimmune disease in which antibodies are produced which stimulate the thyroid to secrete excessive quantities of thyroid hormones (23).

The association of stress with Grave's disease is probably affect the immune response to TSH receptor through the modulation of hormones, neurotransmitters and cytokines. Graves' disease is still considered a predominantly Th2 autoimmune disease (24, 25, 26).

The lymphocytic infiltrate contains Th2 lymphocytes. The disease can result in the production of stimulating anti-TSH receptor antibodies causing goiter and hyperthyroidism.

The previous authors reported that Graves' disease was considered for some time as an only Th2 disease, it is now admitted that auto antibodies against TSH receptor could also be Th1-dependent antibodies.

In a harmony with our results, the results by Pearce (27) which clarify the interaction between stress and Graves' disease, which induced by thyroid stimulating auto antibodies.

Psychological stress suggested as a risk factor for Graves' disease, although the mechanism by which stress induces disease remains unknown. Stress hormones acting on antigen-presenting immune cells, may influence the differentiation of bipotential helper T-cells away from a Th1 phenotype towards a Th2 phenotype. These results of suppression of cellular immunity and in potentiating of humoral immunity. Thyroid autoimmunity is clinically expressed as Hashimoto's thyroiditis or as Graves' disease (28, 29). The different phenotypic expressions of thyroid autoimmunity are largely dependent on the balance of Th1 versus Th2 immune response. Predominance of Th2-mediated immune response may induce antigen specific B lymphocytes to produce anti-TSH receptor (TSHr) antibodies causing Graves' disease (30, 31).

It should be noted that, the issue of environment and autoimmune disease remains one of the hot areas in autoimmunity and frequently discussed not only with respect to susceptibility, but also found in the majority of epidemiologic analyses. The treatment of autoimmune diseases should consider stress management and behavioral intervention (32, 33).

Stressed rats treated with sulpiride drug led to amelioration in T3 and T4 because of using antidepressant drug (Sulpiride). Stress increased lipid peroxidation, which resulted from increased free radical generation in Grave's disease. Dose of Sulpiride and treatment duration have been chosen on the basis of previous studies performed by Wang (34). He found that, the long-term administration of sulpiride at the daily dose

4mg/kg is effective in animal models of depression.

Sulpiride, a atypical (1-4) neuroleptic from the group of banzamides, is a selective dopaminergic receptor, namely a 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 (34).

In the present results, we suggested that sulpiride nearly inhibited the effect of stress, so the functions of the affected glands were improved. This led to the improvement of the hormonal disruption which induced by stress.

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