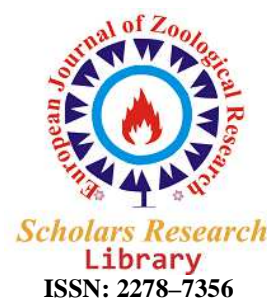




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An Investigation of Serum lipid profile in Chronic Mild Stress Rat Model of Depression

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ABSTRACT

The aim of the present study was to investigate the effects of CMS (chronic mild stress) on serum lipids, which may be in interaction with stress or depressive disorders. Forty to forty-five-day-old laboratory rats were assigned to two groups; control (n: 10) and CMS (subjected to CMS procedure, n: 30). Rats in the control group were reared in single cages without any environmental stress. Rats in CMS were entered the CMS procedure. This protocol consisted of mild unpredictable stressors (intermittent illumination, stroboscopic light, grouping, food or water deprivation, exposure to an empty water bottle, solid cage, cage tilting, etc.). Later, CMS protocol sucrose preference (SP) test was used for the identification of depressed animals. Rats with SP lower than 65% were defined as depressed animals. Blood serum was taken from two groups (control and CMS) for the determination of blood lipids by Elisa kits. The analyzed data showed that serum lipids including total cholesterol, triglyceride, HDL-cholesterol and LDL-cholesterol didn't lead to a significant difference between two experimental groups. We concluded that CMS-induced depression cannot affect serum lipid profile in rat model. Further studies with different protocol of depression are required for the identification of possible relations of depression and lipid metabolism.

Key words: Chronic mild stress, Depression, Lipid metabolism, Sucrose Preference test.

INTRODUCTION

Research concerning depression has largely prescribed anti-depressant medicines as well as different levels of effective hormones being studied. However, studies with adverse effects of depression on lipid metabolism are limited [1].

Also, these studies have focused mainly on major depression cases [2] not chronic or depression resulting from mild environmental stresses. So, studies on plasma lipid indices of various models of depression are necessary.

Among trusty models of depression, chronic mild stress (CMS) model of depression in rodents has been proposed to model some of the environmental factors that contribute to the introduction of depressive disorders in humans [3, 4]. In the present protocol (CMS), sequential exposure to a variety of mild stressors causes behavioral deficits in different paradigms that measure sensitivity to rewards. Thus, CMS suppresses the consumption of and preference to palatable sweet solution such as sucrose or saccharin [5], and the rewarding properties of food pellets, sweet solutions, and amphetamine as assessed by the place preference conditioning procedure. There is a controversy on the correlation of depression and plasma lipids. In this regards, some of the studies have stated that low total

cholesterol (TC) can be the sign of depressive changes in the body [6, 7] and there is no any correlation between TC and depression or depressive changes in other studies [8, 9].

So, the aim of the present study was to investigate the effects of CMS on serum lipids, which may be in interaction with stress or depressive disorders.

MATERIALS AND METHODS

Animals

Forty to forty-five 40-45 - old Male Wistar rats were kept in the laboratory animal room for 1 week pre-experimental adaptation period. Animals were weighted and assigned to two groups; control (n: 10) and CMS (subjected to CMS procedure, n: 30). Animals in the control group were reared in single cages without any environmental stresses while animals in CMS were entered into the CMS procedure (table 1). Exception for limitations of CMS procedure, the food and water were available ad libitum for all animals. Other environmental conditions including light/dark cycle (12h: 12h), light intensity, and ventilation were the same for both groups. Experiments were performed in accordance with the guide for the Care and Use of Laboratory Animals (National Institutes of Health Publication No. 85-23, revised 1985).

CMS procedure

CMS was used to achieve depressive-like symptoms in Wistar rats [4, 5]. It was designed to maximize the randomness of the stressors. The protocol was carried out for 4 weeks as described in Table 1.

This protocol consisted of mild unpredictable stressors which including intermittent illumination, stroboscopic light (300 flashes/min), grouping, food or water deprivation, exposure to an empty water bottle immediately following a period of water deprivation, solid cage (300 ml water spilled into bedding), and 45° cage tilting. Grouping indicates housing a rat in pairs with different partners while an individual rat alternately becomes a resident or an intruder. Details of the CMS procedure are presented in table 1.

Table 1. Time and length (h) of stressors used in the CMS procedure

Stressor/ timing	Saturday	Sunday	Monday	Tuesday	Wednesday	Thursday	Friday
Intermittent lighting (light/dark)	00:00-14:00 (1 time/ 2 h)	-	-	-	-	-	-
Strobe light	-	-	00:00-12:00	-	-	-	-
Cage tilt 45°	-	13:00-23:00	-	-	-	13:00-23:00	00:00-12:00
Solid cages	-	-	12:00-24:00	-	-	-	13:00-23:00
Feed/ Water deprivation	-	00:00-10:00	-	10:00-24:00	-	00:00-12:00	-
Empty water bottle	-	10:00-12:00	-	-	-	-	-
Paired housing	-	-	-	-	10:00- 24:00	-	-

Sucrose preference test

Sucrose preference (SP) test is a measure to evaluate anhedonic effect of CMS [5] and efficiency of protocol to induce depression. In this test, animals were trained to consume a 1% sucrose solution following 18 h of food/water deprivation at week three. Sucrose intake measure with weight losses of sucrose contained bottle at the end of the test for 24 h during a no-stress period. Rats with lower than 65% SP (net sucrose consumption/ [sucrose consumption+ water consumption] × 100 %) were defined as depressed animals [10-12].

Blood sampling and analysis

Healthy animals (control) and depressed animals recognized by SP test were subjected to blood sampling for the identification of effects of CMS on serum variables. Blood samples taken from orbital sinus were centrifuged at 1,200 x g for 7 min at 18° C, and serum was prepared for determination of serum lipids including TC, triglyceride, HDL-Cholesterol (HDL) and LDL-Cholesterol (LDL) with an auto analyzer (Alcyon 300; Abbott Park, IL, US) and Elisa commercial kits.

The present experiment was arranged with two treatments and four replicates for each. Data were analyzed with SAS (SAS Inst. Inc., Cary, NC, US) and the differences between treatments were assessed by unpaired t-test, and P<0.05 was considered to be significant.

RESULTS

According to table 2, there was not a statistically significant difference between control and CMS groups for serum lipid indices (TC, triglyceride, HDL and LDL).

Table2. Serum lipid profile in rats subjected to CMS procedure

Variable Group	Total cholesterol (TC) mg/dl	Triglyceride mg/dl	HDL mg/dl	LDL mg/dl
Control	79.75	66.25	21.57	42.88
CMS (depressed)	78.50	64.75	20.60	46.48
P value	0.7719	0.5041	0.1812	0.7876
SEM*	2.913	1.493	0.529	10.486

*standard error of the mean.

DISCUSSION

Reports on depression, especially in cases resistant to anti-depressants (such as fluoxetine) indicate that TC and triglyceride can be in high level compared with healthy condition [13]. In this study, hyper-cholesterolemia was suggested as an efficient factor in resistance to treatment of major depression.

In an epidemiological study in Nigeria, depressed individuals had normal TC and higher triglyceride levels. Also, in other indices of plasma lipid profile (such as HDL or LDL), there was not any significant difference between healthy and depressed individuals [1]. So, Onuegbu *et al.*, [1] suggested that changes in plasma lipids couldn't be a sign of depression.

Martinac *et al.*, [14], in their study on lipid profile of depressed individuals and different cases of depression suggested that TC and triglyceride are somewhat unchanged in depression condition, but when the depressed cases were grouped via their body mass index, TC can be changed in depressed individuals. In Huanget *et al.*, [15], there was not any considerable change for TC concentration among different cases of psychological and depression-like disorders while triglyceride had minor decreases in depressed individuals when compared with healthy range.

Regarding published reports on serum lipid profile in depression [1, 14, 15], a considerable dissension is shown. In the present study (table 2), there was not any significant difference between experimental groups for TC, triglyceride, HDL or LDL. In table 2, whereas the decreases in triglyceride level of animals following chronic mild stresses are not significant, but it is in agreement with Huang *et al.*, [15] reports for TC and triglyceride. On the other hand, findings of present study are in accordance with Onuegbu *et al.*, [1] results, which show that a change in serum lipids cannot be a sign for depression.

It is concluded that chronic mild stress induced depression cannot affect serum lipid profile in rat model.

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