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Comparing evaluation of Physical and psychological stress on plasma level of corticosterone and peptide YY in male and female mice

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ABSTRACT

Now society is faced with a big problem called stress. Stress can increase or decrease the hormones and body composition results in increased susceptibility to most diseases. Identifying compounds that are altered by stress and find out the impact of them in the body, in turn, are able to provide solutions to counter with the stress. This study is considered to impact of two different types of physical and psychological stress on corticosterone and peptide YY for greater recognition of them. Three groups of 12 mice of both sexes were randomly performed, control, group under physical stress and the last group under psychological stress (a hunter). At the end of study period blood samples were collected and plasma levels of corticosterone and peptide YY were measured. In our study, peptide YY levels negatively correlated with plasma corticosterone levels which indicate a stress-lowering effect of this peptide. Mice were under physical stress had significantly higher levels of corticosterone than the control group which it's may indicate the impact of stressful factors. However, the mice that endured psychological stress have significantly higher corticosterone levels compared with the control group and with group under physical stress. As a result, with consider that the stressor factors period are the same for both groups, it can be concluded that the mice under psychological stress could not habituate to stressor factors so adaptation to psychological stress is much harder than getting used to physical stress.

Keywords: Physical stress, Psychological stress, Corticosterone, Peptide YY

INTRODUCTION

Today one of the most important problems in modern societies and the main causes of diseases is plentiful stress. Stress study is important in both fields of safety and health and also to evaluate the performance of people in organizations.

Stress is a state due to physical and psychological pressure to get into the living organism. In another definition, stress is the response of the one to adapt with a foreign state different from the normal situation as well as behavioral and hormonal.

All the results of stress in the body are due to increase or decrease hormones or chemicals in the brain and peripheral circulation system which can cause harmful effects. Evidence suggests that stress can cause immune suppression that this would be a predisposing factor causing many diseases[1,2,3]. Among the compounds that can be measured in plasma during stress conditions include: cortisol, antidiuretic Hormone, oxytocin, prolactin, ghrelin, leptin, orexin, neuropeptide Y (NPY) and some other compounds [4,5,6,7,8]. Glucocorticoids are family of compounds secreted by the cortex of the adrenal gland in response to stress. Cortisol is a steroid hormone from the family that has been introduced as an indicator of stress innumerous studies in humans [9]. Corticosterone is more important in

mice [4]. These hormones cause increase of glucose, suppress the immune system and increase the metabolism of fats, proteins and carbohydrates[9].High levels of cortisol in plasma delays wound healing [10]. Other effects of steroidal corticoids can be noted to being a diuretic, salt reabsorption from the gut and excrete more potassium from the body[11,12]. This hormone prevents secretion of some interleukins, interferon gamma and alpha tumor necrosis factor [13].

Digestive system secretes many different peptide hormones whose effects are different and some of them affect the stress and corticosteroids[8]. Neuropeptide Y family consists of neuropeptide Y, peptide YY and pancreatic peptide [14]. Peptide YY is a compound secreted by the digestive tract that is secreted primarily from the ileum and colon in response to food intake [15, 16].In a study in rats has been reported that peptide YY is also secreted from the islets of Langerhans [17].The major role of this peptide is reducing of appetite [18,19].This peptide acts by affecting the receptors associated with NPY, and causing further movements of the stomach and increased uptake of water and electrolytes in the colon [20].Inhibition of gastric acid secretion and inhibition of colonic motility in mice were carried out by the Y2 receptor of this peptide [16,21,22].It was found that this peptide also imposes a state of loss of appetite through Melanocortin -4 receptors[23]. In a study in mice has been argued that in the absence of genomic peptide YY, depression behaviors were increased but anxiety reactions have not affected [24].This peptide plasma level change has not ever been examined by the effects of physical or psychological stress.

Measuring and discovering compounds that are altered by stress and identifying their effects in the body, in turn, are able to provide solutions to counter with stress. Specific objectives of this study are evaluation the effect of two different types of stress, physical and psychological, on corticosterone and peptide YY and comparing these probably changes between male and female mice.

MATERIAL AND METHODS

Study design: An experimental study was designed for evaluating effects of physical and psychological stress on two compounds in the plasma of male and female mice.

Ethics: The protocol for experiment on animals was approved by the Ethics committee of AJA University of Medical Sciences (Iran).

Grouping: 36 adult mice (Balb/c) of both sexes were purchased from central animal house of faculty of veterinary medicine of Tehran University. All mice were divided randomly into three groups. Each group was contained six females and six males. The mice were kept in the laboratory for adaptation to the environmental condition for two weeks.

Methods

At the beginning of the experiment, every mouse in each group was weighed and their weight recorded. All groups of mice having received the same food and water and they were kept under the same ventilation conditions. The ambient temperature was set to 25 °C and they were having 12 hours of light and 12 hours of dark. The mice were kept in stress boxes daily at a specified time, for 10 days. In our study, physically stressed mice were individually placed in an area that has half centimeter deep water. It should be noted that this group weren't able to see each other. To induce psychological stress, other group is watched a predator (cat) in the environment. At the end of 10 days, the mice were weighed and the weight was recorded. Then all mice anesthetized with the suitable pharmaceutical composition (Ketamine in combination with Xylazine) and blood samples were taken from their hearts. Blood has been spilled into tubes containing EDTA anticoagulant and then they were sent to the laboratory. In the laboratory, plasma was separated from whole blood and was evaluated by commercial ELISA kits. Corticosterone (Corticosterone Elisa Kit, Zellbio, Germany) and peptide YY (Mouse PYY Elisa Kit, Zellbio, Germany) are measured and the results were recorded.

Statistics

Data obtained from study groups, Including control, physical stress and psychological stress as well as groups of male mice compared to females, were analyzed using PASW Statistic Software version 18 through unilateral statistical analysis of variances (ANOVA) and post hoc Duncan test at the 0.05 significant levels. Spearman correlations between data have been reported on the significant level of0.05. All data were reported as mean ± standard deviation.

RESULTS

Mice that were kept under physical stress have significantly higher corticosterone levels compared to those of controls (Table 1).Also, mice that endured psychological stress significantly higher corticosterone levels compared to the control and physically stressed groups (Table 1).

Table 1. Comparison the effects of physical and psychological stress on plasma levels of corticosterone and peptide YY with the control group (Mean±SD)

	Control	Physical stress	Psychological stress
Corticosterone(ng/ml)	102.00±13.18[a]	140.25±23.96[b]	293.66±65.15[c]
Peptide YY(pg/ul)	3.87±0.49[a]	3.62±0.51[a]	3.46±0.51[a]

Numbers in a row that are marked with different indices have significant differences (P <0.05).

In the control group, there were no significant differences between male and female mice in plasma levels of corticosterone and also peptide YY (Table 2).

Table 2.Comparison the plasma levels of corticosterone and peptide YY between male and female mice in the control group (Mean±SD)

	Control	
	Male	Female
Corticosterone(ng/ml)	103.33±12.72[a]	100.66±14.70[a]
Peptide YY(pg/ul)	3.71±0.54[a]	4.03±0.42[a]

Numbers in a row that are marked with different indices have significant differences (P <0.05).

In the physically stressed group, there were no significant differences between male and female mice in plasma levels of corticosterone and also peptide YY (Table 3).

Table 3. Comparison the plasma levels of corticosterone and peptide YY between male and female mice in the physically stressed group (Mean±SD)

	Physical stress	
	Male	Female
Corticosterone(ng/ml)	140.16±25.19[a]	140.33±25.06[a]
Peptide YY(pg/ul)	3.83±0.47[a]	3.41±0.50[a]

Numbers in a row that are marked with different indices have significant differences (P <0.05).

Our results showed that plasma corticosterone levels in female mice were significantly higher than in male mice in the psychologically stressed group (Table 4).

Table 4. Comparison the plasma levels of corticosterone and peptide YY between male and female mice in the psychologically stressed group (Mean±SD)

	Psychological stress	
	Male	Female
Corticosterone(ng/ml)	243.33±35.99[a]	344.00±44.31[b]
Peptide YY(pg/ul)	3.53±0.47[a]	3.40±0.59[a]

Numbers in a row that are marked with different indices have significant differences (P <0.05).

Spearman correlation was calculated between PYY and corticosterone, and it exhibited significantly negative correlation between them (P<0.5). The coefficient of it was -0.36 (P=0.03). It should be noted all reported data are based on the difference between the standard deviation of the mean (Mean ± SD).

DISCUSSION AND CONCLUSION

Peptide YY is one of the L-shaped cells of the intestine that secreted in response to receiving the meal and it will be reduced during hunger [15,16].In addition to its main secretion in the gastrointestinal tract, in some studies has also seen its secretion at the brain stem [25].This peptide has common receptors with Neuropeptide Y including; Y1, Y2 and Y5, but after secretion has been broken to the circulation form PYY_{3-36} and this action increases the tendency to Y2 receptor in the peptide[26, 27]. Amygdala object that is a key local of the brain associated with behavioral responses to stress [7] includes a lot of Y1, Y2, Y4 and Y5 receptors [28,29,30,31,32].Studies have shown that this peptide applies appetite lowering effect through Y2 receptor in the vagal afferent nerves [18,19, 33] and also

through hypothalamus [34].Although in our study there was not meaningfull changed of peptide YY plasma levels by physical and psychological stress, however its negative correlation with the level of corticosterone may indicate a stress lowering effect in the peptide. This result corresponded to the study of Forbes *et al.* about another member of these peptides family. They observed that neuropeptide Y through Y1 and Y2 receptors inhibits circulating release of corticosteroids in mice[8].After food intake the body was driven into a state of euphoria and pleasure that this mode was seen due to administration of peptide YY in another study [35].In addition, the peptide has the ability to cross the blood-brain barrier [36]that these effects could be the reasons for prescribing and use of it for other studies in the field of stress.

In our study, plasma levels of peptide YY were not significantly changed in any of the control, physically stressed and psychologically stressed between male and female mice. Plasma corticosterone levels were significantly higher in female mice than in male mice in the group under psychological stress that these findings correspond with the study of Kant et al.In a study on laboratory rats, they found that during stress condition the plasma levels of corticosterone increased faster in females than in males [37].

Exposing animals frequently to a stressor can results in one of two states; (1) animals were habituate with the condition and the stress response reduced, and (2) animals were sensitized and the additional response to stress or was assumed. For example, scientists observed partially reduced corticosterone-releasing response to mild stress [38] while another study did not showed an adaptation in response to the stronger stressor [4].In addition, another study suggested that the type, severity and duration of stress can be used to determine the habituating with the stressor[39].During acute stress plasma corticosterone level rises quickly, but in the case of repeated stimulations, plasma levels of this compound was closed to the normal levels due to negative feedback mechanisms[40].In our study mice were kept under physical stress having significantly higher levels of corticosterone than the control group that this may indicate the impact of stressful factors. However, the mice that endured psychological stress were having significantly higher plasma corticosterone levels than the control and also physically stressed groups. As it is mentioned above, mild stress leads to habituating of the animals, but the animals are not habituates against any strong stressor [39,41].In our study, because the times of experimental stressors are the same for both groups, it can be concluded that mice whose are under psychological stress could not adapt to stressor. Further experimental studies needed for investigating other compounds involved in stress process, and how we can face with stressful conditions.

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