

# The Comparison of the Effects of Acute Swimming Stress on Plasma Corticosterone and Leptin Concentration in Male and Female Rats

Parvin Zareian, Mohammad Vahid Karimi, and Gita Dorneyani

*Department of Physiology, School of Medicine, Jahrom University of Medical Sciences, Jahrom, Iran*

*Received: 29 Oct. 2009; Received in revised form: 10 Apr. 2010; Accepted: 2 Jun. 2010*

**Abstract-** The aim of this study was to investigate the effect of acute swimming stress on plasma corticosterone and leptin levels in female and male rats. Thirty-seven adult male (n=20) and female (n=20) Sprague Dawley rats (200-250 g weight) were used. The leptin and corticosterone levels were measured following swimming stress (10 minutes) or no stress. Plasma leptin and corticosterone were measured by ELISA system. The plasma leptin and corticosterone levels were significantly increased in female and male rats by swimming stress. Plasma leptin level was not correlated significantly with plasma corticosterone in all groups. There were no sex differences in leptin level among stressed and non stressed rats. The results suggest that changes in plasma leptin level could not be associated with stimulation of corticosterone secretion from adrenal glands and leptin secretion is not sex dependent.

© 2011 Tehran University of Medical Sciences. All rights reserved.

*Acta Medica Iranica* 2011; 49(5): 284-287.

**Keywords:** Stress; Leptin; Corticosterone; Rat

## Introduction

In response to stressful events hypothalamus is activated to secrete corticotrophin releasing factor (CRF) from paraventricular nucleus. CRF can causing the secretion of adrenocorticotrophin (ACTH) from anterior pituitary, in turn, stimulates the release of glucocorticoids from adrenal glands. Activation of HPA axis is responsible for maintenance of homeostasis during stress. Recent investigation demonstrated existence of a classical endocrine loop between HPA axis and adipose tissue. Glucocorticoids can stimulate leptin secretion from adipocyte, where increase in leptin level may exert inhibitory effect upon the HPA axis (1-3). In spite of numerous studies in related to effect of stress on leptin level, most of them have been done in males. It is known females respond differently to stress (4-6) and HPA activity is gender specific (5). According to the above considerations, the aim of this study was to investigate effect of acute stress on leptin level in both sexes (female and male rats). In another study has been shown inverse relationship between corticosterone and leptin in unstressed animal models (7). Therefore, we sought to answer whether there is or not such relationship between two variables in stressed rats.

## Materials and Methods

### Animal

Thirty seven adult (20 male and 20 female) Sprague-Dawley rats (200-250 g weight) were used. The experimentally animals were housed in groups of 3-4 in home cages made of plexiglass material with the floor covered with sawdust. They were maintained under standard condition (temperature  $20 \pm 2$  °C, lights on from 06.00- 18.00 hours) with free access to food and water. The animals were randomly divided into four groups (n=10 for each group): group1, unstressed male rats; group 2, stressed male rats; group 3, unstressed female rats; group 4, stressed female rats.

For inducing swimming stress rats had placed individually in water containing style sink (30 cm height, 60 cm length, 30 cm wide) for 10 min. The temperature of water was + 25 °C. At the end of the swimming period rats were gently dried before blood collecting. On the day of experiment, trunk blood was collected between the hours of 10:00 and 12:00 a.m. and plasma samples were obtained by centrifugation of blood at 3500 for five minutes (twice). Plasma was frozen until the day of the analysis. Measurement of plasma leptin and corticosterone were done with a commercial rat leptin ELISA (Biovender Inc. Czech-

**Corresponding Author:** Parvin Zareian

Department of Physiology, Jahrom University of Medical Sciences, Jahrom, Iran

Tel: +98 21 44670601, 917 1912484, Fax: +98 21 44670601, E-mail: zareian2008@gmail.com

Slovakia) and rat corticosterone ELISA kit (Baldon, Tyne & Wear, NE35 9PD, UK).

### Statistical analysis

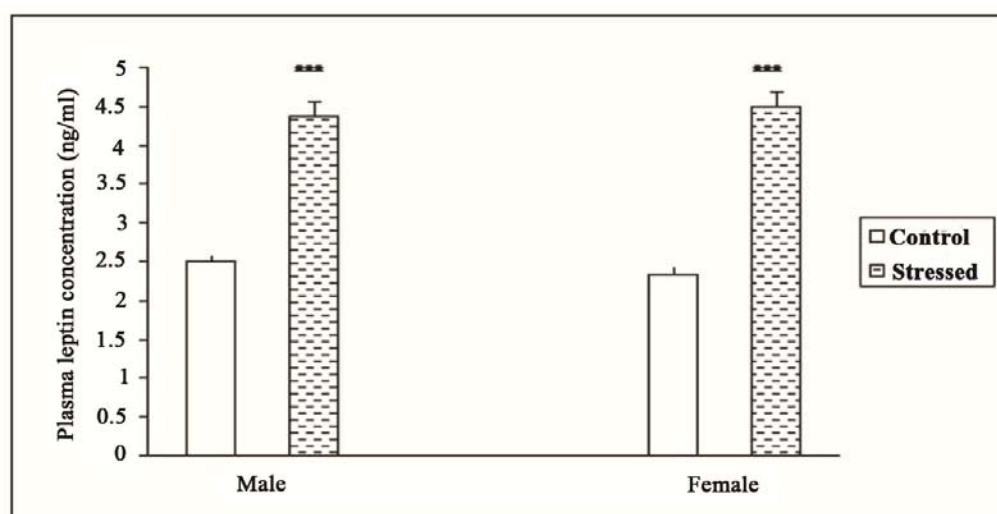
All experiments were conducted in accordance with the guidelines Jahrom University Ethics Committee on the use of laboratory animals.

Data were expressed as Means  $\pm$  S.E.M. To analyze leptin or corticosterone level after stress, student's t-test was used. The correlation between plasma leptin and corticosterone level examined by simple bivariate analysis. Statistical analyses were performed using spss12 software. Threshold of significance was defined at  $P < 0.05$ .

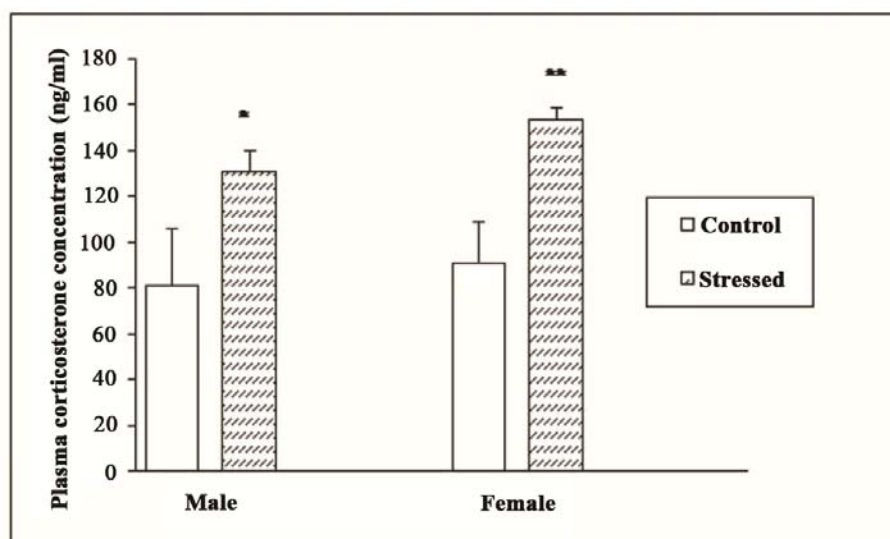
### Results

The effect of acute swimming stress on plasma leptin was shown in fig 1. Stress increased circulation leptin concentration in male and female rats ( $P < 0.001$ ). In addition, stress increased significantly corticosterone concentration in male ( $P < 0.05$ ) and female ( $P < 0.01$ ) rats (Figure 2).

There was no significant difference in leptin level between non-stressed female and male rats. In addition, there was no significant difference in leptin level between stressed female and male rats. Plasma leptin level was not correlated significantly with plasma corticosterone in all groups.



**Figure 1.** The effect of acute swimming stress on plasma leptin concentration in male and female rats. (Data are represented as Mean  $\pm$  S.E.M) \*\*\*  $P < 0.001$



**Figure 2.** The effect of acute swimming stress on plasma corticosterone concentration in rats. (Data are represented as Mean  $\pm$  S.E.M) \* $P < 0.05$ , \*\* $P < 0.01$

## Discussion

The present results show that acute swimming stress increases level of leptin and corticosterone in female and male rats. Increase in corticosterone level confirmed stress exposure. The data from this study are in consistent with similar other researches (8,1,9). Stress activate sympathetic system and hypothalamo-hypophyseal- adrenal axis (10,11). There is evidence which suggests, stimulation of sympathetic system inhibits leptin secretion from adipocyte tissue (12) and glucocorticoids (13,14) and possibly ACTH (14) stimulates leptin biosynthesis and secretion. In our study, we did not observe any correlation between plasma concentration of leptin and corticosterone. It is consistent with some previous reports (15, 16). Ceballos and colleagues reported that correlation between leptin and corticosterone were strain specific (17), but it is reasonable to speculate that the swimming stress in rats resulted in enhanced leptin levels as stress related hormone. Several studies support this speculation (16,18,19).

There is evidence for gender difference in the HPA axis responses to stress. In response to alcohol intact female rats secret significantly more ACTH and corticosterone than intact males (20). Also Rivier observed in response to shock intact females secret significantly less ACTH than intact females (5). In present study, stressed female rats displayed higher corticosterone secretion levels than stressed male rats. But this difference was not significant between two groups.

It seems gender difference in HPA axis response were not always present and it depends to kind of stress (21, 22) or even the stress intensities (23). Male rats release more ACTH than female rats in response to alcohol (3g /kg) (5) but after the injection of smaller doses of alcohol (0.2-1.8 g/kg) female rats release more ACTH and corticosterone in response to alcohol (20). In another study have been shown, psychosocial stress induced significant increase in salivary free cortisol with no significant differences between men and women (22).

To date, a few studies assess whether gender-associated differences exist in plasma leptin level (24,25,17). These researches have shown leptin level in female rats is more (17) or less (24,25) than male rats. But our data did not show sex differences in plasma leptin level between male and female rats. In this regard, many more studies will be necessary to confirm whether leptin secretion by adipose tissue is gender-dependent.

## References

- Hernández C, Simó R, Chacón P, Sabin P, Baena JA, Castellanos JM, Planas M. Influence of surgical stress and parenteral nutrition on serum leptin concentration. *Clin Nutr* 2000;19(1):61-4.
- Evans BA, Agar L, Summers RJ. The role of the sympathetic nervous system in the regulation of leptin synthesis in C57BL/6 mice. *FEBS Lett* 1999;444(2-3):149-54.
- Pralong FP, Gaillard RC. Neuroendocrine effects of leptin. *Pituitary* 2001;4(1-2):25-32.
- Kajantie E, Phillips DI. The effects of sex and hormonal status on the physiological response to acute psychosocial stress. *Psychoneuroendocrinology* 2006;31(2):151-78.
- Rivier C. Gender, sex steroids, corticotropin-releasing factor, nitric oxide, and the HPA response to stress. *Pharmacol Biochem Behav* 1999;64(4):739-51.
- Vendruscolo LF, Pamplona FA, Takahashi RN. Strain and sex differences in the expression of nociceptive behavior and stress-induced analgesia in rats. *Brain Res* 2004;1030(2):277-83.
- Ahima RS, Prabakaran D, Flier JS. Postnatal leptin surge and regulation of circadian rhythm of leptin by feeding. Implications for energy homeostasis and neuroendocrine function. *J Clin Invest* 1998;101(5):1020-7.
- Patterson-Buckendahl P, Pohorecky LA, Kvetnansky R. Differing effects of acute and chronic stressors on plasma osteocalcin and leptin in rats. *Stress* 2007;10(2):163-72.
- Konishi N, Otaka M, Odashima M, Jin M, Wada I, Komatsu K, et al. Systemic stress increases serum leptin level. *J Gastroenterol Hepatol* 2006;21(7):1099-102.
- Sandoval DA, Davis SN. Leptin: metabolic control and regulation. *J Diabetes Complications* 2003;17(2):108-13.
- Gavrilovic L, Dronjak S. Activation of rat pituitary-adrenocortical and sympatho-adrenomedullary system in response to different stressors. *Neuro Endocrinol Lett* 2005;26(5):515-20.
- Schafroth U, Godang K, Ueland T, Bollerslev J. Leptin response to endogenous acute stress is independent of pituitary function. *Eur J Endocrinol* 2001;145(3):295-301.
- Spinedi E, Gaillard RC. A regulatory loop between the hypothalamo-pituitary-adrenal (HPA) axis and circulating leptin: a physiological role of ACTH. *Endocrinology* 1998;139(9):4016-20.
- Martelli F, Kosior-Korzecka U, Ducci M, Buoncristiani P, Bobowiec R. The influence of acth and dexamethasone on leptin and no release from ovine pituitary cells in vitro. *Ann Della Fac Med Veterinaria* 2005;LVIII:27-32.
- Vettor R, Vicennati V, Gambineri A, Pagano C, Calzoni F, Pasquali R. Leptin and the hypothalamic-pituitary-adrenal

- axis activity in women with different obesity phenotypes. *Int J Obes Relat Metab Disord* 1997;21(8):708-11.
16. Perelló M, Chacon F, Cardinali DP, Esquifino AI, Spinedi E. Effect of social isolation on 24-h pattern of stress hormones and leptin in rats. *Life Sci* 2006;78(16):1857-62.
  17. Ceballos RM, Faraday MM, Klein LC. Rat strain and sex differences in leptin responses to immobilization stress. *J Individual Differences* 2006;27(3):136-46.
  18. Bornstein SR. Is leptin a stress related peptide? *Nat Med* 1997;3(9):937.
  19. Ahima RS, Prabakaran D, Mantzoros C, Qu D, Lowell B, Maratos-Flier E, et al. Role of leptin in the neuroendocrine response to fasting. *Nature*;382(6588):250-2.
  20. Rivier C. Female rats release more corticosterone than males in response to alcohol: influence of circulating sex steroids and possible consequences for blood alcohol levels. *Alcohol Clin Exp Res* 1993;17(4):854-9.
  21. Ling S, Jamali F. Effect of cannulation surgery and restraint stress on the plasma corticosterone concentration in the rat: application of an improved corticosterone HPLC assay. *J Pharm Pharm Sci* 2003;6(2):246-51.
  22. Rohleder N, Schommer NC, Hellhammer DH, Engel R, Kirschbaum C. Sex differences in glucocorticoid sensitivity of proinflammatory cytokine production after psychosocial stress. *Psychosom Med* 2001;63(6):966-72.
  23. Burow A, Day HE, Campeau S. A detailed characterization of loud noise stress: Intensity analysis of hypothalamo-pituitary-adrenocortical axis and brain activation. *Brain Res* 2005;1062(1-2):63-73.
  24. Priego T, Sánchez J, Picó C, Palou A. Sex-associated differences in the leptin and ghrelin systems related with the induction of hyperphagia under high-fat diet exposure in rats. *Horm Behav* 2009;55(1):33-40.
  25. Mulet T, Picó C, Oliver P, Palou A. Blood leptin homeostasis: sex-associated differences in circulating leptin levels in rats are independent of tissue leptin expression. *Int J Biochem Cell Biol* 2003;35(1):104-10.