Available online at www.sciencedirect.com
ScienceDirect
Metabolism Clinical and Experimental 57 (2008) 221–225
Metabolism
Clinical and Experimental
www.elsevier.com/locate/metabol

Increases in ghrelin and decreases in leptin without altering adiponectin during extreme weight loss in male competitive bodybuilders

Jarek Mäestu[a,*], Jaak Jürimäe[b], Ivo Valter[c], Toivo Jürimäe[b]

[a]*Department of Psychology, Centre of Behavioral and Health Sciences, University of Tartu, 50104 Tartu, Estonia*
[b]*Institute of Sport Pedagogy and Coaching Sciences, Centre of Behavioral and Health Sciences, Faculty of Exercise and Sport Sciences, University of Tartu, 50104 Tartu, Estonia*
[c]*Centre for Clinical and Basic Research, J. Pärna 4, 10128 Tallinn, Estonia*

Received 12 July 2007; accepted 25 September 2007

Abstract

The aim of this study was to investigate responses of ghrelin, leptin, and adiponectin to a weight reduction period of 10 weeks in male subjects with high lean body mass and low body fat values. Fourteen male bodybuilders (7 competitors: 28.3 ± 10.3 years, 175.3 ± 5.4 cm, 82.2 ± 9.3 kg; 7 controls: 22.4 ± 3.0 years, 182.4 ± 6.9 cm, 85.3 ± 10.5 kg) participated in this study. The subjects were tested 3 times: 11 weeks (TEST1), 5 weeks (TEST2), and 3 days (TEST3) before the national championships. Testing procedure included dual-energy x-ray absorptiometry scan; calculation of daily energy intake and expenditure; and venous blood sampling for fasting ghrelin, leptin, and adiponectin. In the competitors' group, a significant ($P < .05$) 4.1-kg loss of body fat was observed that resulted in 6.5% ± 1.5% of the body fat at the end of the study. Ghrelin increased significantly by 20.4% by TEST2. By TEST3, ghrelin was further increased by 6% ($P > .05$). The pattern of leptin was opposite, with a significant 27.7% decrease at TEST2 and no further decrease at TEST3 ($P > .05$). No significant change was observed in adiponectin concentration during the study. In the control group, no significant changes in biochemical parameters were observed. In conclusion, ghrelin concentration significantly increases, but is suppressed in conditions of limited energy availability that is accompanied by significant body mass loss in male subjects with initial low body fat values.
© 2008 Elsevier Inc. All rights reserved.

1. Introduction

Body mass is regulated by a powerful homeostatic system that, in response to weight loss, triggers compensatory changes in appetite and energy expenditure to promote weight regain [1]. There have been several efforts in describing the regulation in the energy homeostasis. Implicit in this regulatory system is the existence of several peripheral factors that communicate the status of body energy stores to the brain including ghrelin, leptin, and adiponectin—hormones that affect energy homeostasis. The research objective is to identify the behavior of these hormones in various energy restriction/abundance situations, as they represent pathways for obvious anti-obesity therapeutics [2].

Leptin is a hormone primarily secreted by the adipose tissue and represents several physiological functions. Probably the most important function is the role of influencing energy balance. Furthermore, leptin is closely correlated with body fat content in sedentary people, but not always in competitive sportsmen [3]. Adiponectin is probably the most abundant adipose tissue–specific factor [4]. Serum concentrations of adiponectin are low in obese people and increase after weight loss. Adiponectin has also been found to affect postprandial fatty acid levels and hepatic glucose output [5]. Ghrelin is a recently described peptide hormone that is secreted by endocrine cells in the gastrointestinal tract. It has been found to regulate feeding behavior by modulating expression levels of orexigenic peptides in the hypothalamus [6] and in the coordination of energy balance and weight regulation [7]. Ghrelin administration increases hunger and stimulates food intake and might work as a hormone signaling the need to conserve energy and is one of the few known circulating orexigens [1].

Recent studies describing ghrelin action after weight loss or exercise treatment have used female subjects with relatively high amount of body fat [8-11]. Hansen et al [9] found that plasma ghrelin concentration increases with

* Corresponding author. Tel.: +372 564 772 36; fax: +372 737 6152.
E-mail address: jarek.maestu@ut.ee (J. Mäestu).

0026-0495/$ – see front matter © 2008 Elsevier Inc. All rights reserved.
doi:10.1016/j.metabol.2007.09.004

weight loss in obese female subjects and speculated that the increase in ghrelin concentration may be the result of negative energy balance. A 1-year aerobic training program was shown to increase circulating ghrelin concentrations in postmenopausal women with 47% body fat at the beginning of the study [10]. However, in this study, the training program itself, not food restriction, was the main factor of negative energy balance [10]. Contrary to this, neither increase nor decrease was found in ghrelin in response to overfeeding and negative energy balance [12]. It has been suggested that changes in ghrelin appear to be most sensitive to changes in body mass resulting from energy deficit, independent of specific effects of reduced nutritional intake and/or physical exercise [10,11].

To our knowledge, there are no data available in the literature to describe the behavior of ghrelin during body fat decrease from normal to extremely low values. In this situation, the energy stores of the body are more limited compared with subjects with higher body fat values who have mainly been investigated so far. Moreover, there is a lack of data in the literature to describe ghrelin concentrations in male subjects during a short weight intervention period. Therefore, the aim of the present investigation was to investigate ghrelin concentration changes in blood in male subjects with very high lean body mass and low body fat values during a weight reduction period of 11 weeks. We hypothesized a significant increase in ghrelin with concomitant increase in caloric restriction and body mass decrease. In addition, leptin and adiponectin, which also stand for energy homeostasis, were investigated.

2. Materials and methods

Fourteen male bodybuilders (25.4 ± 8.0 years; training experience, 7.8 ± 8.7 years) participated in this study. The subjects were divided into the competitors' (weight reduction) group (n = 7, 28.3 ± 10.3 years, 175.3 ± 5.4 cm, 82.2 ± 9.3 kg, body mass index [BMI] 26.7 ± 2.8 kg/m^2), who were preparing for the competition, and the control group (n = 7, 22.4 ± 3.4 years, 182.4 ± 6.9 cm, 85.3 ± 10.5 kg, BMI 25.6 ± 2.3 kg/m^2), who did not change their training or eating pattern. The inclusion criterion for the study was that the subjects must have been at the level of competitive bodybuilding for at least 3 years. The subjects were not using any drugs during the study period, and they were free of any disease. The bodybuilders were tested against doping during the competitions, and none of them failed; and during the last 2 years, they had not been positive in doping tests. All the procedures and possible risks were described to the subjects before they signed their written consent to participate in the study. This study was approved by the Ethical Committee of the University of Tartu and was in accordance with the Declaration of Helsinki.

The study period was 11 weeks, with the national cup at the end of week 11. The competitors' group was preparing for the championships with the aim of decreasing their body fat content through negative energy balance, obtained by increasing the training volume and decreasing caloric intake. Subjects were tested 3 times: 11 weeks (TEST1), 5 weeks (TEST2), and 3 days (TEST3) before the competitions. During each testing, the testing procedures were identical.

During each testing, subjects filled the consecutive 3-day eating diaries, with the indications of all the consumed food and food supplements. They had to report the diaries of 2 working days and 1 weekend day. The bodybuilders were allowed to maintain their usual diet, that is, similar to the diet that they have found to be most successful during previous weight reduction strategies. Based on this, the daily energy intake was calculated as the average of the 3 days. The daily energy expenditure was calculated according to the method of Bouchard et al [13]. Briefly, a day is divided into 96 periods of 15 minutes each; and the subject had to fill each period with an activity intensity scale from 1 to 9. The scale and corresponding example activities were explained to the subjects before filling the tool.

The measurements were conducted with the Lunar DPX-L total body scanner (Lunar, Madison, WI), which was operated in the medium scan mode (~20 minutes). The calibration of the machine was done daily as suggested by the manufacturer. The subjects were measured while wearing only their underwear and with their arms at the sides and were analyzed for fat and lean body mass.

The fasting blood samples (10 mL) were obtained from the antecubital vein with the subject in the upright position at 7:30 to 8:00 in the morning. The subjects were asked to refrain from physical activity 24 hours before the blood sampling. The plasma was separated and frozen at −20°C for later analysis. Ghrelin and adiponectin were determined in duplicate using commercially available radioimmunoassay kits (Linco Research, St. Charles, MO). The sensitivity of this kit was 93 pg L; and the intra- and interassay coefficients of variation for ghrelin were <10% and <14.7%, respectively. The intra- and interassay variations for adiponectin were <7% and <7%. Leptin was determined in duplicate by radioimmunoassay (Mediagnost, Reuttlinger, Germany). This assay has a detection limit of 0.01 ng/mL, and intra- and interassay coefficient of variation was <5%.

Statistical analyses were performed using SPSS for Windows, version 13.0 (SPSS, Chicago, IL). Means and SDs were determined. Friedman analyses of variance by ranks were used to examine changes. The Wilcoxon matched-pairs signed rank test was used where post hoc analysis was relevant. Comparison between groups was made using Mann-Whitney *U* test. Kendall rank correlation coefficients were used to evaluate associations among different variables of interest. The level of significance was set at $P < .05$.

3. Results

There were no significant differences in the anthropometric or biochemical parameters between the competitors and the control group at the beginning of the study (Table 1,

Table 1
Changes (mean ± SD) in body compositional parameters during the 10-week weight loss in competitors and controls

	Group	TEST1	TEST2	TEST3
Body mass (kg)	COMP	82.9 ± 9.3	81.2 ± 9.0 [a]	78.8 ± 8.4 [a,b]
	C	85.3 ± 10.5	84.7 ± 9.3	84.7 ± 9.4
BMI (kg/m^2)	COMP	26.7 ± 2.8	26.4 ± 2.7 [a]	25.6 ± 2.3 [a,b]
	C	25.6 ± 2.2	25.4 ± 1.9	25.3 ± 2.1
Body fat %	COMP	9.6 ± 2.3	8.0 ± 2.2 [a]	6.5 ± 1.5 [a,b]
	C	11.9 ± 3.4	11.1 ± 2.3 *	11.8 ± 3.0 *
FFM (kg)	COMP	72.9 ± 8.4	72.9 ± 8.4	72.5 ± 8.1
	C	70.5 ± 8.6	72.6 ± 7.6	72.2 ± 7.8

COMP indicates competitors; C, controls; FFM, fat-free mass.
[a] Significantly different from TEST1.
[b] Significantly different from TEST2.
* Significantly different from competitors' group ($P < .05$).

Table 2). The competitors' group was in the negative energy balance of −199.2 ± 115.9 kcal/d at TEST1, −536.3 ± 298.8 kcal/d at TEST2, and −978.4 ± 625.2 kcal/d just a few days before competition during TEST3. None of the competitors showed a positive energy balance during the study period. The differences between energy balance at different testings were significant ($r = 0.018$-0.043, $P < .05$). The control group was in slight negative energy balance at TEST1 (−72.2 ± 49.0 kcal/d), in small positive balance at TEST2 (24.0 ± 94.1), and again in slight negative balance at TEST3 (−66.3 ± 49.9). There were no significant differences in the energy balance across the testings in the control group. Competitors were able to decrease their mean body mass values by 4.1 kg ($P < .05$) during the 11-week preparation for competition (Table 1), which resulted also in significant decreases in body fat mass values, whereas no changes in body compositional or biochemical parameters over the 11-week period were found in the control group.

The average consumption of food components was not different between the groups and was an average of 28% proteins, 15% lipids, and 57% carbohydrates. The total training time during 10 weeks was higher ($P < .05$) in the competitors' group during all 3 testing times. The initial training load for competitors was 615.7 ± 55.6 min/wk and was significantly increased to 842.9 ± 346.5 min/wk, whereas the training load for controls did not change over time and was 424.3 ± 164.6 min/wk on the average.

Ghrelin increased significantly by 20.4% by TEST2 in the competitors group (Table 2). By TEST3, ghrelin was further increased by 6% ($P > .05$). The pattern of leptin was opposite, with a significant 27.7% decrease at TEST2 and no further change in leptin concentration at TEST3 ($P > .05$), whereas no change was observed in the concentration for adiponectin (Table 2).

There was a significant relationship between the energy expenditure and training volume during all 3 testing times ($r = 0.52$-0.73, $P < .05$). Leptin was correlated with body fat percentage in the competitors' group only at TEST1 ($r = 0.964$, $P < .05$), whereas it was significant in the control group during all testing sessions ($r = 0.72$-0.80, $P < .05$). There were no other significant correlations between body compositional and biochemical parameters in both studied groups. During competitions, 3 of the bodybuilders ranked first, 3 ranked second, and 1 ranked fourth.

4. Discussion

Competitive bodybuilding is a unique sport where the performance level is significantly related to muscular size and definition [14]. The latter can be achieved with the reduction of body fat mass through the negative energy balance achieved by increasing energy expenditure (training volume) and restricting daily caloric intake. Competitive bodybuilding therefore provides a good opportunity to study the peripheral hormonal signals that reflect body energy status during low and very low body fat values.

Previous studies have found that ghrelin increases during body mass loss and that the loss of body mass is the most potential determinant of the increase in ghrelin concentration [9,11]. An additional hypothesis proposed by Hansen et al [9] was that energy deficit caused by food restriction and physical exercise is probably the stimulus for the increase in ghrelin concentration. Whereas previous studies have used relatively sedentary people [9-11], our study with competitive bodybuilders demonstrated that ghrelin concentration increases in well-trained athletes already with relatively low values of body fat mass, but reaches a plateau beyond which there is no further increase in ghrelin with further body mass loss.

Table 2
Changes (mean ± SD) in blood biochemical parameters during the 10-week weight loss period in bodybuilders and controls

	Group	TEST1	TEST2	TEST3
Ghrelin (pg/mL)	COMP	1148.4 ± 475.4	1424.6 ± 704.0 [a]	1521.09 ± 753.5 [a]
	C	932.6 ± 194.0	807.7 ± 86.7 *	862.6 ± 137.6 *
Leptin (ng/mL)	COMP	1.1 ± 0.6	0.7 ± 0.1 [a]	0.7 ± 0.1 [a]
	C	1.5 ± 0.7	1.4 ± 0,4 *	1.5 ± 0.5 *
Adiponectin (ng/mL)	COMP	8.0 ± 3.2	7.1 ± 1.6	8.2 ± 3.2
	C	6.3 ± 2.8	6.6 ± 1.7	7.1 ± 2.5

[a] Significantly different from TEST1.
* Significantly different from competitors' group ($P < .05$).

In contrast to these findings, Ravussin et al [12] found that neither positive nor negative energy balance had a significant effect on ghrelin concentration during a prolonged study. However, this 100-day period might have been too long to detect significant changes in ghrelin concentration; therefore, the possibility remains that manipulations with energy status might have had significant impact on ghrelin concentration but it could have been missed due to the effect of accustomization. Therefore, the impact of negative energy balance on ghrelin concentration at the end of the study was smaller. This speculation is somewhat supported by the results obtained in this study. In the present study, the energy deficit at about 536.3 kcal/d during TEST2 in the competitors' group was already sufficient to cause a significant increase in ghrelin concentration, whereas no further increase in ghrelin was observed with the energy deficit reaching −978.4 ± 625.2 kcal/day at TEST3. Therefore, we speculate that the importance of the negative energy balance or body weight loss on ghrelin concentration decreases in extreme situations. The subjects in this study were competitive bodybuilders with body fat percentage of 9.6 ± 2.3 at the beginning of the study and 6.5 ± 1.5 at the end, indicating that total body energy stores were quite limited and that there is no extra accumulated energy available for them. The other possible explanation might be that ghrelin mechanisms have reached the limits, and the negative energy balance of more than 900 kcal/d and significant weight loss of 2.4 kg in 5 weeks (between TEST2 and TEST3) were not sufficient to further the significant ghrelin increase. Furthermore, the same but opposite pattern was observed in leptin: a significant decrease by TEST2 that is in accordance with previous results that an imposed energy deficit causes a rapid initial decrease in circulating leptin levels that becomes more marked with progressive body fat loss [15]. Because leptin is secreted by adipose tissue, it has been suggested that it is the key signal reflecting adipose stores; but because ghrelin is regulated acutely like a satiety factor, leptin levels are not regulated by meals, but by actual change in adipose mass [16]. However, no further changes in leptin were observed from TEST2 to TEST3 despite increased energy deficit and body fat loss, which would also suggest that a functional limit of leptin levels exists. Further studies on leptin and ghrelin during conditions of extremely low energy status in humans are clearly needed.

An interesting finding of this study was that no change in adiponectin concentration was observed despite significant weight and fat mass loss. It has been reported that serum adiponectin concentrations increase in obese subjects during weight reduction period, [17]. One possible explanation might be that adiponectin is secreted also by visceral fat depot that is considered metabolically more active than subcutaneous fat depot [18]. The weight management during low body fat values could have less impact on visceral fat than on subcutaneous fat depot.

There are some limitations in our study. Firstly, it is known that food consumption and frequency questionnaires are imprecise and typically underestimate food consumption because subjects tend to underreport. However, because food consumption is of very high importance during competitive bodybuilding not only during weight management but also during hypertrophy stages and all the athletes were keeping food diaries already before the study, there is no need to believe that they did not report all that they consumed and that their diet changed significantly during the time between different testings. Second is the suitability of indirect calculation of the energy expenditure calculation during the study. We agree that those results can be viewed with caution because the method was not initially developed for bodybuilders. However, as the calculated energy expenditure was significantly related to increased training volume (r = 0.52-0.73, $P < .05$), it can be viewed as the indicator of the shift to increased energy expenditure from TEST1 to TEST3.

In this study, the total plasma ghrelin was measured and not the acylated and desacyl ghrelin separately. The acylated form is thought to be essential for ghrelin biological activity [19]. Recently, Mackelvie et al [20] demonstrated that short aerobic exercise program has no effect on total ghrelin response to a liquid meal, whereas increase was shown in the acylated form. However, there are no data showing that significant increases in total ghrelin do not increase acylated ghrelin in humans. It has also been found that total ghrelin and acylated ghrelin are positively correlated [21] and that both forms of the hormone potentially play role in energy balance [20]. Future studies are needed here to clarify the responses of total ghrelin and its acylated and desacyl forms in various conditions.

Most recent studies published so far would suggest that negative energy balance as a result of short-term exercise may not be enough to alter ghrelin concentration, despite increased growth hormone concentrations [22-24]. However, a recent study in our laboratory has shown that high-intensity intermittent rowing (estimated energy expenditure of approximately 400 kcal in 20 minutes) could increase postexercise ghrelin concentrations [25], whereas at 30 minutes postexercise, ghrelin concentrations were already decreased. These findings may indicate that in conditions with substantially high energy expenditure rate during relatively long periods, exercise could alter ghrelin concentrations. Christ et al [26] found that low-fat diet (0.5 g/kg lipids/body mass) resulted in significant increase in ghrelin concentration and a decrease in leptin compared with high-fat diet (3.5 g/kg lipids/body mass). This study supports the hypothesis that if the body energy reserves are more limited, short-term exercise of high energy expenditure may alter ghrelin levels [27]. In our study, the bodybuilders consumed about 1 g/kg lipids/body mass during the study period. Therefore, exercise training in these conditions per se would have had an impact on ghrelin concentration. However, there are no data in the literature to describe how long the effect of short-term exercise on ghrelin concentration is. However, because the aim of this study was to describe the changes in ghrelin concentration during conditions of limited energy

availability, the impact of possible training effect was not an issue. In addition, the ghrelin concentration in controls did not change over the study period, indicating no or insignificant effect of training itself.

There is also some evidence that ghrelin antagonizes leptin action at the hypothalamic level [28]. The results of the present study did not confirm the exact role of ghrelin during conditions with low body fat percentage in male subjects because the design of our study did not allow us to measure ghrelin and leptin further to investigate whether the ghrelin system/mechanism can really reach its limits or whether the concentration of ghrelin may further increase.

In conclusion, ghrelin concentrations significantly increase in the condition of negative energy balance that is accompanied by significant body mass loss in male subjects with initial low body fat values. However, despite continual negative energy balance and significant body mass loss, ghrelin concentrations reached a plateau beyond which there is no further increase in ghrelin.

Acknowledgment

This study was supported by the Estonian Science Foundation grant 6671. The authors of this study would like to thank the medical staff of the Centre of Clinical and Basic Research and the Tartu University Hospital.

References

[1] Cummings DE, Schwartz MW. Genetics and pathophysiology of human obesity. Annu Rev Med 2003;54:453-71.
[2] Cummings DE. Ghrelin and the short- and long-term regulation of appetite and body weight. Physiol Behav 2006;30:71-84.
[3] Jürimäe J, Mäestu J, Jürimäe T. Leptin as a marker of training stress in highly trained male rowers? Eur J Appl Physiol 2003;90:533-8.
[4] Vendrell J, Broch M, Vilarrasa N, Molina A, Gómes JM, Gutiérrez C, et al. Resistin, adiponectin, ghrelin, leptin, and proinflammatory cytokines: relationships in obesity. Obes Res 2004;12:962-71.
[5] Berg AH, Combs TP, Scherer PE. ACRP30/adiponectin: an adipokine regulating glucose and lipid metabolism. Trends Endocrinol Metab 2002;3:84-9.
[6] Kojima M, Hosoda H, Date Y, Nakazato M, Matsuo M, Kangawa K. Ghrelin is a growth-hormone–releasing acylated peptide from stomach. Nature 1999;402:656-60.
[7] Wren AM, Seal LJ, Cohen MA, et al. Ghrelin enhances appetite and increases food intake in humans. J Clin Endocrinol Metab 2001;86:4992-5.
[8] St-Pierre DH, Karels AD, Cianflone K, et al. Relationship between ghrelin and energy expenditure in healthy young women. J Clin Endocrinol Metab 2004;89:5993-7.
[9] Hansen TK, Dall R, Hosoda H, et al. Weight loss increases circulating levels of ghrelin in human obesity. Clin Endocrinol 2002;56:203-6.
[10] Foster-Schubert KE, McTiernan A, Scott Frayo R, et al. Human plasma ghrelin levels increase during one-year exercise program. J Clin Endocrinol Metab 2005;90:820-5.
[11] Leidy HJ, Gardner JK, Frye BR, et al. Circulating ghrelin is sensitive to changes in body weight during a diet and exercise program in normal weight young women. J Clin Endocrinol Metab 2004;89:2659-64.
[12] Ravussin E, Tschop M, Morales S, Bouchard C, Heiman ML. Plasma ghrelin concentration and negative energy balance studies in twins. J Clin Endocrinol Metab 2001;86:4547-51.
[13] Bouchard C, Tremblay A, Leblanc C, Lortie G, Savard R, Thériault G. A method to assess energy expenditure in children and adults. Am J Clin Nutr 1983;37:461-7.
[14] Huygens W, Claessens AL, Thomis M, et al. Body composition estimations by BIA versus anthropometric equations in body builders and other power athletes. J Sports Med Phys Fitness 2002;42:45-55.
[15] Larsson H, Helmstahl S, Berglund G, Ahren B. Evidence for leptin regulation of food intake in humans. J Clin Endocrinol Metab 1998;83:4382-5.
[16] Hovarth TL, Diano S, Sotonyi P, Heiman M, Tschop M. Minireview: ghrelin and the regulation of energy balance—a hypothalamic perspective. Endocrinology 2001;42:4163-9.
[17] Yang WS, Lee WJ, Funahashi T, et al. Weight reduction increases plasma levels of an adipose-derived anti-inflammatory protein, adiponectin. J Clin Endocrinol Metab 2001;86:3815-9.
[18] Fredriksson J, Carlsson E, Orho-Melander M, Groop L, Ridderstråle M. A polymorphism in the adiponectin gene influences adiponectin expression levels in visceral fat in obese subjects. Int J Obes 2006;30:226-32.
[19] Muccioli G, Tschop M, Papotti M, Deghenghi R, Heiman M, Ghio E. Neuroendocrine and peripheral activities of ghrelin: implications in metabolism and obesity. Eur J Pharmacol 2002;440:235-54.
[20] MacKelvie KJ, Meneilly GS, Elahi D, Wong ACK, Barr SI, Chanoine JP. Regulation of appetite in lean and obese adolescents following exercise: role of acylated and desacyl ghrelin. J Clin Endocrinol Metab 2007;2:648-54.
[21] Marzullo P, Verti B, Savia G, et al. The relationship between active ghrelin levels and human obesity involves alterations in resting energy expenditure. J Clin Endocrinol Metab 2004;89:936-9.
[22] Jurimae J, Hofmann P, Jurimae T, et al. Plasma ghrelin responses to acute sculling exercises in elite male rowers. Eur J Appl Physiol 2007;99:467-74.
[23] Kraemer RR, Durand RJ, Acevedo EO, et al. Rigorous running increases growth hormone and insulin-like growth factor–I without altering ghrelin. Exp Biol Med 2004;229:240-6.
[24] Schmidt A, Maier C, Schaller G, et al. Acute exercise has no effect on ghrelin plasma concentrations. Horm Metab Res 2004;36:174-7.
[25] Jürimäe J, Jürimäe T, Purge P. Plasma ghrelin is altered after maximal exercise in male rowers. Exp Biol Med 2007;232:904-9.
[26] Christ ER, Zehner M, Boesch C, et al. The effect of increased lipid intake on hormonal responses during aerobic exercise in endurance-trained men. Eur J Endocrinol 2006;154:397-403.
[27] Tschop M, Smiley DL, Heiman ML. Ghrelin induces adiposity in rodents. Nature 2000;407:908-13.
[28] Shintani M, Ogawa Y, Ebihara K, et al. Ghrelin, an endogenous growth hormone secretagogue, is a novel orexigenic peptide that antagonizes leptin action through the activation of hypothalamic neuropeptide Y/Y1 receptor pathway. Diabetes 2001;50:227-32.