IMPACT OF NINE MONTH HEALTH TRAINING AND A SINGLE EXERCISE ON CHANGES IN GHRELIN, LEPTIN AND FREE FATTY ACIDS LEVELS IN WOMEN'S BLOOD

Eugenia Murawska-Ciałowicz,[1, A, B, C, D, E] Iwona Wierzbicka-Damska,[1, B, E]
Ewa Bakońska-Pacoń,[1, B, C] Małgorzata Kałwa,[2, B, C] Piotr Dzięgiel[3, 4, C, E]

[1] Physiology and Biochemistry Department, University School of Physical Education, Wroclaw, Poland
[2] Theory of Sport Department, University School of Physical Education, Wroclaw, Poland
[3] Histology and Embryology Department, Medical University, Wroclaw, Poland
[4] Department of Physiotherapy, University School of Physical Education, Wroclaw, Poland
[A] Study Design; [B] Data Collection; [C] Statistical Analysis; [D] Manuscript Preparation; [E] Funds Collection

Address for correspondence:
Eugenia Murawska-Ciałowicz
University School of Physical Education, Physiology and Biochemistry Department
Paderewskiego Ave. 35; 50-612 Wroclaw, Poland
E-mail: eugenia.murawska-cialowicz@awf.wroc.pl

Abstract. The aim of the research was to assess changes in ghrelin, leptin and free fatty acids (FFA) levels in women's blood after training. The research was carried out in women aged 45.55 ±11.33 years and with the BMI of 26.49 ±4.49. Health training at 50–66% VO_2max took place twice a week for 9 months. In the baseline phase and in the 3rd, 6th and 9th month of the training, body mass and composition were measured, cardiorespiratory fitness was checked after a 10-minute exercise test on a cycloergometer, and fasting levels of ghrelin, leptin and FFA in the serum were assayed and 15 minutes after the exercise test.
Body mass was reduced in the 6th month of the training. Fasting ghrelin level increased because of training, leptin and FFA decreased. After single 10-minute exercises performed every 3 months level of ghrelin and FFA increased while leptin decreased.
An increase in ghrelin level in the blood after the single exercise can be the result of negative energy expenditure. An increase in fasting ghrelin level after training can be one of the adaptive physiological mechanisms connected with energy saving. A mechanism that is switched on as a result of a long-lasting stimulus that leads to energy losses, reduction in body mass and a decrease in leptin level in the blood.

Key words: ghrelin, leptin, free fatty acids, women, health training, single exercise

Introduction

Ghrelin is the orexigenic hormone that regulates processes of hunger and satiety. It stimulates appetite by influencing the hunger centre in the hypothalamus. Its peripheral activity is connected with the control of broadly understood metabolic-energy balance. It intensifies processes leading to hyperglycemia – accelerates

gluconeogenesis and inhibits glycogenesis. It also stimulates growth hormone secretion (Cummings et al. 2001; Tschöp et al. 2000; Varela et al. 2011).

The most important organ producing ghrelin is the stomach, where enteroendocrine X/A – like cells located mainly in the fundus of the stomach are responsible for its synthesis (Date et al. 2002; Kraemer and Castracane 2007). Ghrelin is also synthesized in other parts of the gastrointestinal tract and outside it, e.g. in adrenal glands, the heart, blood vessels, hypothalamus, pituitary, cerebellum and others (Van der Lely et al. 2004).

Ghrelin has two forms: acylated – which contains n-octanoyl modification of the serine 3 residue and des–acylated without the n-octanoyl form. The particle is modified by the enzyme GOAT (ghrelin O-acyltransferase). Acylation augments the particle's lipophilicity and facilitates the hormone's ability to cross the blood-brain barrier and excite specific receptors (Andrews 2011). The biggest concentration of the acylated form is found in the stomach. In the blood, 80–90% of ghrelin circulates as the des-acylated form because the acylated one is quickly captured by the cells with the GHS-R receptor (growth hormone secretagogue receptor) (Toshinai et al. 2006).

Nowadays two subtypes of the receptor are known: GHS-R1a and the GHS-R1b, which belongs to the family of the seven transmembrane G protein-coupled receptors. Acylated ghrelin activates the GHS-R1a in the hypothalamus and releases the growth hormone (Van der Lely et al. 2004). The research showed the presence of the GHS-R receptors in different parts of the central nervous system and in many organs ([Date et al. 2002; Van der Lely et al. 2004; Gnanapavan et al. 2002), which supports the notion of its wide, however not completely explained, biological activity. Ghrelin level in the blood of a grown-up person is not a constant value. It depends, most of all, on nutrition, changes in energy balance, glucose homeostasis and changes in GH secretion. Its secretion is also affected by lifestyle factors such as stress or lack of sleep (Polińska et al. 2011), and is sex-related – it is lower in men than in women. It decreases with age and shows a correlation with testosterone level (Kozakowski et al. 2008). Ghrelin secretion is influenced by the parasympathetic nervous system, by acetylcholine that stimulates the secretion of the hormone (Broglio et al. 2004).

Changes in ghrelin level in the blood dependent on energy balance made us explain the influence of regular physical activity on the hormone's secretion. Available research in the field does not provide unequivocal information. Some sources show that physical exercise causes a significant increase in circulating ghrelin (Jürime et al. 2007), while in others there is no influence of physical exercise on the hormone's level (Martins et al. 2007), and still some others report that ghrelin level significantly decreases after exertion (Vestergaard et al. 2007).

Such an ambiguous state of knowledge about the subject made us do the research, the aim of which was to assess ghrelin level in the serum of adult women after 9-month health training and a 10-minute single exercise, which was taken to verify the adaptive progress of training.

Material and methods

In our research 75 women, aged 45. 55 ±11.33 years, took part. They started the health training to reduce their body mass and to improve their cardiorespiratory fitness. The excluding criteria were diabetes, thyroid diseases, affecting lipid parameters of the blood, irregular participation in control tests, smoking. During the training period the women did not change their old eating habits. Their diet was assessed quantitatively and qualitatively on the basis of the prepared menus. Before training the average consumption of protein was at the level of 0.88 ±0.18 g/kg body mass (0.92 ±0.13 g/kg after training, n.s.), of fat at the level of 0.86 ±0.3 g/kg of body mass (0.81 ±0.2 g/

kg after training, n.s.), of carbohydrates at the level of 2.75 ±0.64 g/kg of body mass (2.95 ±0.48 g/kg after training, n.s.) and of fibre at the level of 17.51 ±5.38 g/day (21 ±3.20 g/day after training, $p < 0.05$).

All the subjects were informed about the aim of the research, test procedures and the hazard involved. All the subjects started performing tests after signing a written consent, and the study protocol was approved by the Research Ethics Commission of the University of Physical Education in Wroclaw.

Health training

Training sessions were organized twice a week for 9 months. Each exercise unit lasted for 60 minutes. Intensity of the training was at 50–66% VO_2max. It is the intensity typical of a conditioned exercise which enables obtaining energy from fat utilization. Training units were characterized by different efforts undertaken by the subjects. During the first training unit, the method of Total Body Condition was used to build up muscle force, muscle endurance and flexibility of the subjects. In the second one, aerobic capabilities of the body were shaped using mainly the Fat Burning and Low Impact methods. During the training, heart rate was monitored using the Sportest (Polar, Finland).

During the training program, four control tests were carried out. The first one took place before the trainings started, the next ones in the 3rd, 6th and 9th month of the training. Each control test included: anthropological study, a physiological study (single exercise) and biochemical study. The anthropological study involved: measurement of body mass and height, calculation of the BMI value (Body Mass Index), measurement of waist and hip circumference, calculation of the WHR indicator (Waist to Hip Ratio) and measurement of body composition. The assessment of body composition parameters was done by means of spectrometry in near-infrared (Near Infrared Light) using the FUTREX – 6100/XL (Futrex Inc., USA).

A single exercise consisted in a subject performing a 10-minute test on an Excalibur Sport (LODE) cycloergometer at a workload of 100W and a pedaling frequency of 70–80 rpm. During the test, the content of the exhaled air was monitored by a Quark b^2 (Cosmed) ergospirometer and respiratory parameters were measured. Among them, the following were registered: the volume of the oxygen consumption (VO_2), of the CO_2 output (VCO_2), the respiratory exchange ratio (RER), energy expenditure and the metabolic equivalent of task (MET) were calculated. During the test, changes of the heart rate (HR) were recorded, and the VO_2max was determined using the Astrand – Ryhming method on the basis of the steady state HR during exercise test.

Biochemical parameters

Blood samples for the biochemical analysis were taken from the fasting subjects between 8 and 10 a.m. Then, the subjects performed an exercise test, after which, at the 15th minute of the restitution, their blood was taken again. After the serum was obtained, it was stored at –80°C until the biochemical analysis was carried out.

Levels of ghrelin and leptin in the serum were assayed using the radioimmunoassay (RIA) method and ready-made kits. A Human – Ghrelin – RIA Kit (Diasource Europe, Belgium) was used to assay total ghrelin. The results were expressed as pg/ml. Sensitivity of the method was 40 pg/ml. Intra-assay coefficient of variation (CV) was 5,0% and inter-assay CV was 7,3%. A Human Leptin RIA Kit (Linco Research LTD, USA) was used to assay leptin. The reference range for this method for women is 7.4–11.1 ng/L. Sensitivity of the method was 0.5 ng/ml. Inter-assay and intra-assay coefficient of variation was <8.3% and <6.2%, respectively. FFA levels were assayed using the colorimetric method and a NEFA-HR (2) Kit (WAKO Chemicals GmbH, Germany). The reference range for women was 0.1–0.45 mmol/l (2.8–12.7 mg/dl).

Lactate (LA) level was assayed using the colorimetric method and a Lactate Cuvette Test kit (Dr. Lange, Germany). The reference range was 0.6–0.9 mmol/l.

Glucose level was assayed using the colorimetric method, an Olympus AU650 analyzer manufactured by DPC, and a Glucose GOD-POD kit. The reference range was 70–110 mg/dl.

Statistical analyses

The computer program Statistica PL Stat Soft version 10.0 (Cracow, Poland) was used for statistical analysis. In all tests the statistically significant level was $p < 0.05$. All values are expressed as means ±SD. The following tests were used to analyze the results. Normality of distribution was examined with the Shapiro-Wilk test. If a variable was characterized by normal distribution, for further calculations one-way analysis of variance (ANOVA) was applied and it was preceded by Levene's test of homogeneity of variance. If the null hypothesis of equal variances was rejected ($p = 0.05$ or less), for further analysis the Duncan's post-hoc test was used. When a variable did not have a normal distribution, the assessment of differences between the variable's values in further examinations was made using the non-parametric ANOVA test (the Friedman test), which is equivalent to a one-way repeated measures analysis of variance. When the null hypothesis was rejected, for further analysis, the Wilcoxon's test as a post-hoc test was used. To assess the statistical dependence of the variables, Spearman's rank correlation coefficient was calculated.

Results

The 9-month training modified the anthropological, physiological and biochemical parameters that the authors measured.

The mean energy expenditure during the single training session was 254.3 kcal. Nine month training led to the reduction in body mass and the BMI of the subjects, even though body mass reduction happened only after 6 months of training. No changes in lean body mass (LBM) were noticed, but total fat mass decreased. Thickness of the skin-fat fold measured on the abdomen was also reduced. Its significant change in relation to the baseline value also took place only in the 6th month of the training. The value of the WHR indicator remained the same because waist and hip circumferences decreased, too (Table 1).

There was a significant improvement in the subjects' cardiorespiratory fitness, which was seen in a gradual increase in the value of VO_2max. Maximal oxygen intake increased, as did the anthropological parameters, only in the 6^{h} month of the training (on average by 16%). In the 9th month of the training the value of VO_2max was different on average by 25% in relation to the baseline value.

The result of an improvement in cardiorespiratory fitness was seen in the lowering physiological cost of a 10-minute exercise test performed every three months. A decrease in the value of the HR and MET during steady state was observed, there was also a decrease in energy expenditure (EE) during a 10-minute exercise (Table 1). Both the MET and the HR reached their highest values in the first (baseline) and third (6th month) examination and their lowest in the fourth (9th month) examination. Even though cardiorespiratory fitness was improved, physiological and energy cost of exercise tests was reduced, according to ACSM (Garber et al. 2011) physiological cost of work was high in the first 3 examinations. In the 4th one, it decreased to moderate.

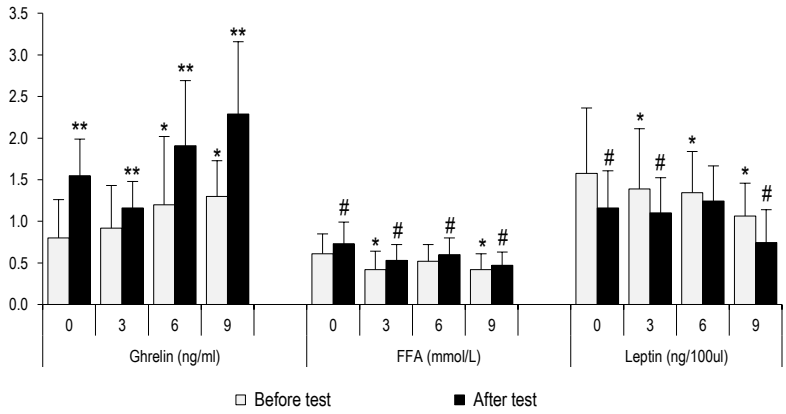
The dynamics of changes in biochemical parameters was the following.

Table 1. Values of chosen anthropological and physiological parameters in successive examinations

		Baseline	3 month	6 month	9 month
Body mass [kg]		72.51 ±12.73	72.06 ±10.09	68.34 ±8.99*	65.33 ±9.56*
BMI [kg/m^2]		26.49 ±4.49	26.43 ±3.63	25.69 ±3.88*	25.50 ±3.66*
FAT [kg]		27.38 ±8.58	26.60 ±6.66	23.08 ±6.72#	20.54 ±6.52#
% FAT		37.70 ±5.82	36.91 ±5.25	33.77 ±5.64#	31.44 ±5.46#
LBM		45.85 ±4.92	45.46 ±4.72	45.26 ±3.88	44.79 ±3.99
Abdominal fat fold [mm]		32.15 ±9.95	31.31 ±9.37	27.99 ±8.27*	28.53 ±9.97*
Waist circumference [cm]		86.74 ±12.61	84.07 ±9.75*	80.46 ±8.20#	82.81 ±7.43#
Hip circumference [cm]		106.06 ±9.30	104.30 ±6.59*	102.26 ±5.13*	103.24 ±5.0*
WHR		0.82 ±0.06	0.81 ±0.06	0.78 ±0.05*	0.80 ±0.05
VO_2max [ml × kg^{-1} × min^{-1}]		27.04 ±7.94	28.60 ±8.20	31.65 ±9.75*	33.49 ±9.41#
HR steady state [bpm]		157.9 ±13.60	152.5 ±13.91*	148.8 ±14.83*	146.6 ±14.30#
MET steady state [ml × kg^{-1} × min^{-1}]		6.92 ±0.80	7.19 ±1.34	6.75 ±0.81	6.15 ±1.03#
EE/min [kcal]		8.04 ±1.05	8.62 ±1.60	8.11 ±0.77	7.62 ±0.72
EE/test [kcal]		90.28 ±20.66	94.24 ±18.16	88.63 ±10.17	74.78 ±12.79#
Test intensity	% VO_2max	85%	87%	72%	63%
	% HR_{max}	84%	81%	79%	67%

*p < 0.05; #p < 0.01 as compared to the baseline.

Fasting ghrelin level as a result of the research program increased after the 9 months of training by 62.5% on average. An increase in the level of the hormone in the blood was observed already after 3 months of the training (on average by 15%). In the 6th month of the training the increase was 50% in relation to the baseline value (Figure 1).



* p < 0.001 as compared to the baseline; ** p < 0.01 and # p < 0.05 as compared with the value before exercise test.

Figure 1. Changes in fasting levels of ghrelin and FFA before and after exercise tests, in the baseline, 3rd, 6th and 9th month of health training

Ghrelin level after exercise test in each examination increased in relation to the fasting value measured before the test. In the first (baseline) examination, its concentration after exercise was higher by 93%, in the 2nd one (after

3 months) by 26%, in the 3rd one (after 6 months) ghrelin level after exercise increased by 59%, while in the 4th examination (after 9 months) by 76%.

Fasting leptin level after 9 months of the training decreased by 32% (Figure 1). Lowered fasting level were already noted 3 months after the beginning of the training, on average by 12%, and in the 6th month of the training on average by 18.5% in relation to the baseline value.

The 10-minute exercise test caused a significant reduction in leptin level in the blood. Before the beginning of training (baseline) after a 10-minute test leptin level decreased on average by 26% in relation to the fasting value before the test. In the 3rd month of the training after a 10-minute test leptin level was lower, on average by 21% than before the test, in the 6th months by 20%, and in the 9th month by 30%.

FFA level as a result of training decreased by 31%, on average (Figure 1). A decrease by 31% in relation to the baseline was already noted in the 3rd month of the training. After 6 months FFA level slightly increased but it was still lower than the baseline value (on average by 15%).

The single exercise in each examination led to an increase in FFA level in the subjects' blood. On average by 20% in the baseline, by 26% after 3 months of the training, by 15% after 6 months of the training and by 12% in the 9th month of the training.

Fasting glucose levels did not change significantly within the 9 months of the training, but the exercise test caused a slight increase in glucose level.

LA level after exercise tests increased significantly, reaching the level indicating crossing the anaerobic threshold, which suggests that a 10-minute exercise was performed by the energy obtained from anaerobic sources. The assumption was supported by the value of the RER reaching in each examinations the value of more than 1.0 (data not shown).

Discussion

Ghrelin, which was assayed in our research, is a parameter whose fasting level, like the dynamics of post-exercise changes, depends on many factors, including the type of, intensity and duration of exercise, a subject's physical performance, body mass or health (King et al. 2013; Shiiya et al. 2011; Stokes et al. 2010; Erdmann et al. 2007).

In our research we noticed an increase in fasting ghrelin level after 9 months of the training. The increase was already observed in the 3rd month of the training. The training led to a reduction in the subjects' body mass, but it was noted from the 6th month of the training. On the basis of our research, it can be concluded that ghrelin is a sensitive indicator of changes in body mass (Leidy et al. 2004). A similar direction of changes of the hormone after a year's training in post-menopausal overweight women was observed by Foster-Schubert et al. (2005).

In our research, we also found out that a single, 10-minute exercise in the form of work on a cycloergometer caused an increase in the hormone's level in the blood in all 4 examinations. It proves that an organism that is regularly and for a long time stimulated to physical exercise and to energy expenditure intensifies compensatory mechanisms, connected with energy saving. Thanks to these mechanisms, the organism tries to maintain energy balance by slowing down or inhibiting catabolic processes (Hagobian et al. 2009). One of the mechanisms seems to be an increase in fasting ghrelin level in response to training. It might be thought so, because in our subjects we observed a significant decrease in fasting leptin level in the blood after the training completion and after 10-minute exercises in each control examination.

Leptin acts in opposition to ghrelin. It causes an anorexigenic effect through its auto- and paracrine influences. The central activity location of both the hormones is the hypothalamic arcuate nucleus (ARC), where there are neurons secreting neuropeptide Y (NPY)/agouti-related protein (AgRP) and pro-opiomelanocortin (POMC)/ cocaine- and amphetamine-regulated transcript (CART), which are under the regulatory influence of both leptin and ghrelin (Nogueiras et al. 2007; Nogueiras et al. 2008). Contrary to ghrelin, leptin inhibits the neurons secreting NPY/ AgRP and stimulates the neurons POMC/CART, which physiologically results in reductions in food intake and an increase in energy expenditure (Rak-Mardyla 2013). As a result of a prolonged increased energy expenditure, there is an increase in secretion of NPY, whose secretion can be increased by ghrelin. An increased level of the hormone in the blood after a 4-week training was observed by Rämson et al. (2012). An increase in NPY level as a result of aerobic exercise was also noted by Broom et al. (2009). Zajadacz et al. (2009) noticed a significant increase in NPY secretion after a 20-minute exercise at the intensity above the lactate threshold. In the research done by team of Zajadacz (2009), the intensity of work was similar to the intensity observed in our tests.

Ghrelin level increases before meals and it lowers maximally 60–120 minutes after the meal, which proves that ghrelin is secreted in energetically adverse conditions (Tschöp et al. 2001). What is more, an increased secretion of the hormone noted during starvation, in hypoglycemia and in negative energy balance proves that when energy sources are used up, which is a condition typical of physical exercise, among others, ghrelin level increases, both in short-term and long-term (regularly stimulated by training) energy loss.

Energy expenditure connected with training in our research was more than 500kcal/week, and in a 10-minute test less than 100 kcal. In our opinion, the values were high enough for overweight women to activate compensatory mechanisms.

An increase in ghrelin level in the blood leads to an increase in the RER, which slows down the rate of lipolysis to increase catabolism of carbohydrates (Theander-Carrillo et al. 2006), which might also explain the observed increase in fasting ghrelin level in response to a training cycle and a single exercise. In response to a long-term stimulus, such as training, ghrelin might exert a protective influence on saving energy and slowing lipolysis. In our research, during training session the value of RER was lower than 1.0, at the level indicating the domination of lipids as an energy source, while during exercise tests its value was 1.0, which indicates the dominant role of carbohydrates in exercise energetics. It can be assumed that independently of the type of energy substrates, in exercise of different intensity and duration, an increase in ghrelin level will be an adaptive response.

The results similar to ours were observed by Jürimäe et al. (2007), who claim that both short maximal anaerobic exercise and aerobic exercise at 50% VO_2max lead to an increase in ghrelin secretion.

In conditions of short-term energy imbalance, when ATP level decreases and AMP increases, AMPK (AMP-activated protein kinase) is activated. It is a very sensitive intracellular energy sensor which protects cells from excessive energy loss and that promotes processes enabling the production of ATP at the cellular level and in the whole organism. It is possible by the activation of catabolic processes that provide energy and the switching off of biosynthetic pathways, through their influence on the hypothalamus, among others (Carling et al. 2008; Hardie et al. 2012).

In the case of lipid metabolism, AMPK inhibits acetyl-CoA carboxylase (ACC) by blocking the synthesis of fatty acids, but activates malonyl-CoA decarboxylase, lowering the level of malonylo-CoA. Thus, it fosters processes of fatty acids oxidation. It is supposed that short-term activity of ghrelin in the hypothalamus through AMPK can inhibit

the synthesis of fatty acids (Lopez et al. 2008; Lopez at al. 2008a; Lopez et al. 2010; Schneeberger and Claret 2012; Sangiao-Alvarellos et al. 2010).

In our research, we observed a decrease in fasting FFA level in the 3rd month of the research and then stabilization that was maintained till the end of the 9th month of the training. An increase in ghrelin level appearing as a result of a decrease in adipose tissue mass, might have a preventative effect and protect the organism from excessive energy loss and a further loss of body mass. In research carried out on animals, it was proved that a prolonged intracerebroventricular infusion of ghrelin caused a significant increase in the level of mRNA enzymes participating in reactions of fat accumulation, among others, lipoprotein lipase (LPL), ACC, fatty acid synthase (FAS) and stearoyl-CoA desaturase-1 (SCD1), leading to a decrease in the level of mRNA enzyme fostering lipid oxidation – carnitine palmitoyl transferase-1α (CPT-1α). In brown adipose tissue, it also inhibits the expression of the mitochondrial protein connected with thermogenesis – uncoupling protein-1 (UCP-1) (Theander-Carrillo et al. 2006). A significant loss of body mass in patients suffering from anorexia leads to an almost three-fold increase in ghrelin level in the plasma in relation to healthy people (Ariyasu et al. 2001). As mentioned before, the role of ghrelin is to accumulate energy sources, try to maintain positive energy balance, and foster the growth of subcutaneous and visceral adipose tissue. Thus, it seems obvious that a decrease in body mass and in fat mass observed in our subjects causes an increase in ghrelin level in the blood.

Ghrelin released by the stomach activates orexigenic signals. As mentioned before, its central activity mechanism depends on the activation of the pathway CaMKK/AMPK/CPT1/UCP2 (calmodulin-dependent protein kinase/ AMP-dependent kinase/ carnitine palmitoyl transferase-1/ uncoupled protein-2) to maintain the proper level of excitation of the right hypothalamic neurons and of secretion of neuropeptide Y (Andrews 2011; Hardie et al. 2012; Scerif et al. 2012). Tsubone et al. (2005) claim that during prolonged fasting and energy losses ghrelin favours anabolic processes. It stimulates lipogenesis, excites UCP-2 in white adipose tissue and helps change negative energy balance into neutral. Velasquez et al. (2011) suppose that Sirtuin 1/p53 pathway plays an important role in ghrelin's orexigenic activity.

In our research, we noted a negative correlation between ghrelin level and body mass as well as thickness of skin-fat fold measured on the abdomen. Results similar to ours were obtained by Hansen et al. (2002) who noted a mean 12% increase in ghrelin level with a 5% decrease in baseline body mass accompanied by an 8% decrease in total fat mass. A negative correlation between the BMI, total fat mass and the fat mass/lean mass ratio in women was also observed by Makovey et al. (2007). Kelishadi et al. (2008) state that together with a decrease in the value of BMI, there is an increase in the total and des- acylated ghrelin levels, while the level of acylated ghrelin does not change, which might show the organism's way to protect itself from excessive food intake, and through physical activity from an increase in body mass. Broom et al. (2007, 2009) and Marzullo et al. (2008) proved that after an aerobic exercise, the level of acylated ghrelin is suppressed and its level decreases after exertion in both lean and obese people. It is thought that ghrelin-O-acyl transferase enzyme participating in ghrelin acylation is an important factor regulating glucose level. In conditions of caloric restrictions, the ghrelin – GOAT system can play a significant role in maintaining physiological level of glucose through stimulation of growth hormone secretion (Kirchner et al. 2012).

Thus, it seems that, most of all, an organism's metabolic state affects secretion of ghrelin, whose task it is to maintain life-sustaining energy homeostasis. In conditions of caloric restrictions, ghrelin increases glucose level, inhibiting secretion of insulin by the pancreas. This adaptive mechanism is to limit removing glucose from the blood and to maintain and provide a quick supply of energy to working cells (Enriori et al. 2012).

Acknowledgements

The study was supported by Habilitation Grant of The Polish Ministry of Science and Higher Education, number N N404 036738.

References

Andrews Z.B. Central mechanisms involved in the orexigenic actions of ghrelin. Peptides 2011; 32: 2248–2255.

Ariyasu H., Takaya K., Tagami T., Ogawa Y., Hosoda K., Akamizu T., Suda M., Koh T., Natsui K., Toyooka S., Shirakami G., Usui T., Shimatsu A., Doi K., Hosoda H., Kojima M., Kangawa K., Nakao K. Stomach is a major source of circulating ghrelin, and feeding state determines plasma ghrelin-like immunoreactivity levels in humans. J. Clin. Endocrinol. Metab. 2001; 86: 4753–4758.

Broglio F., Gottero C., Van Koetsveld P., Prodam F., Destefanis S., Benso A., Gauna C., Hofland L., Arvat E., van der Lely A.J., Ghigo E. Acetylcholine regulates ghrelin secretion in humans. J. Clin. Endocrinol. Metab. 2004; 89: 2429–2433.

Broom D.R., Batterham R.L., King J.A., Stensel D.J. Influence of resistance and aerobic exercise on hunger, circulating levels of acylated ghrelin, and peptide YY in healthy males. Am. J. Physiol. Regul. Integr. Comp. Physiol. 2009; 296: 29–35.

Broom D.R., Stensel D.J., Bishop N.C., Burns S.F., Miyasashita M. Exercise – induced suppression of acylated ghrelin in humans. J. Appl. Physiol. 2007; 102: 2165–2171.

Carling D., Sanders M.J., Woods A. The regulation of AMP-activated protein kinase by upstream kinases. Int. J. Obes. 2008; 32 (Suppl. 4): S55–S59.

Cummings D.E., Purnell J.Q., Frayo R.S., Schmidova K., Wisse B.E., Weigle D.S. A preprandial rise in plasma ghrelin levels suggests a role in meal initiation in humans. Diabetes 2001; 50: 1714 –1719.

Date Y., Nakazato M., Hashiguchi S., Dezaki K., Mondal M.S., Hosoda H., Kojima M., Kangawa K., Arima T., Matsuo H., Yada T., Matsukura S. Ghrelin is present in pancreatic alpha-cells of humans and rats and stimulates insulin secretion. Diabetes 2002; 51: 124–129.

Enriori P.J., Andrews Z.B., Cowley M.A. Ghrelin: neuropeptide regulator of metabolism. In: Ghrelin in health and disease. Contemporary Endocrinology, eds. R.G. Smith, S.M. Thorner. New York, Humana Press, Springer Science+Business Media, 2012; 10: 111–130.

Erdmann J., Tahbaz R., Lippl F., Wagenpfeil S., Schusdziarra V. Plasma ghrelin levels during exercise – effects of intensity and duration. Reg. Peptides. 2007; 143: 127–135.

Foster-Schubert K.E., McTiernan A., Frayo R.S. Human plasma ghrelin levels increase during a one-year exercise program. J. Clin. Endocrinol. Metab. 2005; 90: 820–825.

Garber C.E., Blissmer B., Deschenes M.R., Franklin B.A., Lamonte M.J., Lee I.M., Nieman D.C., Swain D.P. American College of Sports Medicine position stand. Quantity and quality of exercise for developing and maintaining cardiorespiratory, musculoskeletal, and neuromotor fitness in apparently healthy adults: guidance for prescribing exercise. Med. Sci. Sports Exerc. 2011; 43: 1334–1359.

Gnanapavan S., Kola B., Bustin S.A., Morris D.G., McGee P., Fairclough P., Bhattacharya S., Carpenter R., Grossman A.B., Korbonits M. The tissue distribution of the mRNA of ghrelin and subtypes of its receptor, GHS-R, in humans. J. Clin. Endocrinol. Metab. 2002; 87: 2988–2991.

Hagobian T.A., Sharoff C.G., Stephens B.R., Wade G.N., Silva J.E., Chipkin S.R., Braun B. Effects of exercise on energy-regulating hormones and appetite in men and women. Am. J. Physiol. Regul. Integr. Comp. Physiol. 2009; 296: 233–242.

Hansen T.K., Dall R., Hosoda H., Kojima M., Kangawa K., Christiansen J.S., Jørgensen J.O. Weight loss increases circulating levels of ghrelin in human obesity. Clin. Endocrinol. 2002; 56: 203–206.

Hardie D.G., Ross F.A., Hawley S.A. AMPK: a nutrient and energy sensor that maintains energy homeostasis. Nature Rev. Mol. Cell Biol. 2012; 13, 251–262.

Jürimäe J., Jürimäe T., Purge P. Plasma ghrelin is altered after maximal exercise in elite male rowers. Exp. Biol. Med. 2007; 232: 904–909.

Kelishadi R., Hashemipourt M., Mohammadifard N., Alikhassy H., Adeli K. Short- and long-term relationship of serum ghrelin with changes in body composition and the metabolic syndrome in prepubescent obese children following two different weight loss programmes. Clin. Endocrinol. 2008; 69: 721–729.

King J.A., Wasse L.K., Stensel D.J., Nimmo M.A. Exercise and ghrelin. A narrative overview of research. Appetite 2013; 68: 83–91.

Kirchner H., Tschöp M., Tong J. GOAT and the regulation of energy and glucose homeostasis. In: Ghrelin in health and disease. Contemporary Endocrinology, eds. R.G. Smith, S.M. Thorner. New York, Humana Press, Springer Science+Business Media, 2012; 10: 131–147.

Kozakowski J., Rabijewski M., Zgliczyński W. Ghrelin – growth hormone releasing and orexigenic hormone in men declines with age, insulin and with decrease in testosterone concentration. Neuro. Endocrinol. Lett. 2008; 29: 100–106.

Kraemer R.R., Castracane V.D. Exercise and humoral mediators of peripheral energy balance: ghrelin and adiponectin. Exp Biol Med (Maywood) 2007; 232: 184–194.

Leidy H.J., Gardner J.K., Frye B.R., Snook M.L., Schuchert M.K., Richard E.L., Williams N.I. 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: 2659–2664.

Lopez M., Lage R., Saha A.K., Pérez-Tilve D., Vázquez M.J., Varela L., Sangiao-Alvarellos S., Tovar S., Raghay K., Rodríguez--Cuenca S., Deoliveira R.M., Castañeda T., Datta R., Dong J.Z., Culler M., Sleeman M.W., Alvarez C.V., Gallego R., Lelliott C.J., Carling D., Tschöp M.H., Diéguez C., Vidal-Puig A. Hypothalamic fatty acid metabolism mediates the orexigenic action of ghrelin. Cell Metabol. 2008; 7: 389–399.

Lopez M., Saha A.K., Dieguez C., Vidal-Puig A. The AMPK – malonyl-CoA – CPT1 axis in the control of hypothalamic neuronal function – reply. Cell Metabol. 2008a; 8: 176.

Lopez M., Varela L., Vazquez M.J., Rodríguez-Cuenca S., González C.R., Velagapudi V.R., Morgan D.A., Schoenmakers E., Agassandian K., Lage R., Martínez de Morentin P.B., Tovar S., Nogueiras R., Carling D., Lelliott C., Gallego R., Orešič M., Chatterjee K., Saha A.K., Rahmouni K., Diéguez C., Vidal-Puig A. Hypothalamic AMPK and fatty acid metabolism mediate thyroid regulation of energy balance. Nature Med. 2010; 16: 1001–1008.

Makovey J., Naganathant V., Seibel M., Sambrook P. Gender differences in plasma ghrelin and its relations to body composition and bone- an opposite-sex twin study. Clin. Endocrinol. 2007; 66: 530–537.

Martins C., Morgan L.M., Bloom S.R., Robertson M.D. Effects of exercise on gut peptides, energy intake and appetite. J. Endocrinol. 2007; 193: 251–258.

Marzullo P., Salvadori A., Brunani A. Acylated ghrelin decreases during acute exercise in the lean and obese state. Clin. Endocrinol. 2008; 69: 970–971.

Nogueiras R., Tschöp M.H., Zigman J.M. Central nervous system regulation of energy metabolism: ghrelin versus leptin. Ann. NY Acad. Sci. 2008; 1126: 14–29.

Nogueiras R., Wiedmer P., Perez-Tilve D., Veyrat-Durebex C., Keogh J.M., Sutton G.M., Pfluger P.T., Castaneda T.R., Neschen S., Hofmann S.M., Howles P.N., Morgan D.A., Benoit S.C., Szanto I, Schrott B., Schürmann A., Joost H.G., Hammond C., Hui D.Y., Woods S.C., Rahmouni K., Butler A.A., Farooqi I.S., O'Rahilly S., Rohner-Jeanrenaud F., Tschöp M.H. The central melanocortin system directly controls peripheral lipid metabolism. J. Clin. Invest. 2007; 117: 3475–3488.

Polińska B., Matowicka- Karna J., Kemona H. Role of ghrelin in organism. Adv. Hyg. Exp. Med. 2011; 65: 1–7.

Rak-Mardyla A. Ghrelin role in hypothalamus – pituitary – varian axis. J. Physiol. Pharmacol. 2013; 64: 695–704.

Rämson R., Jürimäe J., Jürimäe T., Mäestu J. The effect of 4-week training period on plasma neuropeptide Y, leptin and ghrelin responses in male rowers. Eur. J. Appl. Physiol. 2012; 112, 1873–1880.

Sangiao-Alvarellos S., Varela L., Vazquez M.J., Da Boit K., Saha A.K., Cordido F., Diéguez C., López M. Influence of ghrelin and GH deficiency on AMPK and hypothalamic lipid metabolism. J. Neuroendocrinol. 2010; 22: 543–556.

Scerif M., Kola B., Korbonits M. Ghrelin regulation of AMPK in the hypothalamus and peripheral tissues. In: Ghrelin in health and disease. Contemporary Endocrinology, eds. R.G. Smith, S.M. Thorner. New York, Humana Press, Springer Science+Business Media, 2012; 10: 91–110.

Schneeberger M., Claret M. Recent insights into the role of hypothalamic AMPK signaling cascade upon metabolic control. Front. Neurosci. 2012; 6: 185.

Shiiya T., Ueno H., Toshinai K., Kawagoe T., Naito S., Tobina T., Nishida Y., Shindo M., Kangawa K., Tanaka H., Nakazato M. Significant lowering of plasma ghrelin but not des-acyl ghrelin in response to acute exercise in men. Endocrin. J. 2011; 58: 335–342.

Stokes K.A., Sykes D., Gilbert K.L., Chen J.W., Frystyk J. Brief, high intensity exercise alters serum ghrelin and growth hormone concentrations but not IGF-I, IGF-II or IGF-I bioactivity. Growth Horm. IGF Res. 2010; 20: 289–294.

Theander-Carrillo C., Wiedmer P., Cettour-Rose P., Nogueiras R., Perez-Tilve D., Pfluger P., Castaneda T.R., Muzzin P., Schürmann A., Szanto I., Tschöp M.H., Rohner-Jeanrenaud F. Ghrelin action in the brain controls adipocyte metabolism. Clin. Invest. 2006; 116: 1983–1993.

Toshinai K., Yamaguchi H., Sun Y., Smith R.G., Yamanaka A., Sakurai T., Date Y., Mondal M.S., Shimbara T., Kawagoe T., Murakami N., Miyazato M., Kangawa K., Nakazato M. Des-acyl ghrelin induces food intake by a mechanism independent of the growth hormone secretagogue receptor. Endocrinol. 2006; 147: 2306–2314.

Tschöp M., Smiley D.L., Heiman M.L. Ghrelin induces adiposity in rodents. Nature 2000; 407: 908–913.

Tschöp M., Weyer C., Tataranni P.A., Devanarayan V., Ravussin E., Heiman M.L. Circulating ghrelin levels are decreased in human obesity. Diabetes 2001; 50: 707–709.

Tsubone T., Masaki T., Katsuragi I., Tanaka K., Kakuma T., Yoshimatsu H. Ghrelin regulates adiposity in white adipose tissue and UCP1 mRNA expression in brown adipose tissue in mice. Reg. Peptides 2005; 130: 97–103.

Van der Lely A.J., Tschöp M., Heiman M.L., Ghigo E. Biological, physiological, pathophysiological, and pharmacological aspects of ghrelin. Endocr. Rev. 2004; 25: 426–457.

Varela L., Vázquez M.J., Cordido F., Nogueiras R., Vidal-Puig A., Diéguez C., López M. Ghrelin and lipid metabolism: key partners in energy balance. J. Mol. Endocrinol. 2011; 46: R43–R63.

Velásquez D.A., Martínez G., Romero A. The central sirtuin 1/p53 pathway is essential for the orexigenic action of ghrelin. Diabetes 2011; 60: 1177–1185.

Vestergaard E.T., Dall R., Lange K.H.W., Kjaer M., Christiansen J.S., Jorgensen J.O.L. The ghrelin response to exercise before and after growth hormone administration. J Clin Endocrinol Metab. 2007; 92: 297–303.

Zajadacz B., Skarpańska-Stejnborn A., Brzenczek-Owczarzak W., Juszkiewicz A., Naczk M., Adach Z. The influence of physical exercise on alterations in concentrations of neuropeptyde Y, leptin and other selected hormonal and metabolic parameters in sports people. Biol. Sport 2009; 26: 309–324.

Cite this article as: Murawska-Ciałowicz E., Wierzbicka-Damska I., Bakońska-Pacoń E., Kałwa M., Dzięgiel P. Impact of Nine Month Health Training and a Single Exercise on Changes in Ghrelin, Leptin and Free Fatty Acids Levels in Women's Blood. Central European Journal of Sport Sciences and Medicine. 2015; 9 (1): 5–15.