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Effects of High-Intensity Training Upon Appetite, Body Mass, Aerobic Capacity, and Metabolic Hormones in Overweight Women

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ABSTRACT

Objective: The purpose of this study was to investigate the effect of high-intensity exercise training on appetite, body mass, maximal aerobic capacity (VO_{2max}), leptin, and acylated ghrelin in overweight women.

Methods: Twenty-five women aged 25-45 years (35.4 ± 6.9 years; 74.2 ± 7.6 kg) were randomly assigned into high-intensity exercise training (n = 15) and control (n = 10) groups. Data assessment included body mass, skinfolds, appetite questionnaire, 1-mile Rockport Walk Test, and blood sample collection. High-intensity exercise training consisted of running an intensity corresponding to 80%-85% maximal heart rate, 3 times/week for 8 weeks.

Results: Estimated maximal aerobic capacity increased in high-intensity exercise training vs. controls (*P* = .01). Body mass, estimated fat percentage, plasma leptin, and acylated ghrelin remained stable. No difference pre- vs. post-intervention in appetite scores was detected between groups (*P* = .33).

Conclusions: In conclusion, high-intensity exercise training was effective to improve aerobic capacity, but did not elicit enough negative energy balance to reduce fat mass or promoting appetite compensatory responses, nor changes in acylated ghrelin and leptin concentrations in overweight women. Further studies with longer duration and greater training volumes are warranted to ratify these findings.

Keywords: Acylated ghrelin, aerobic training, energy balance, leptin, metabolism

Introduction

The regulation of energy balance in humans is complex and ambiguous, including genetic, physiological, and behavioral factors.[1] Appetite is a mental concept used to describe food intake control and is referred to as regulating food-related variables that predict normal eating habits. At the physiological level, appetite and food intake are controlled by the brain and hormones produced by the gastrointestinal tract, pancreas, adrenal glands, and adipose tissue.[2,3]

Two substances play a pivotal role in the regulation of food intake and energy metabolism – ghrelin and leptin. Ghrelin is a peptide mainly derived from the stomach, which circulates in acylated and nonacylated forms.[4,5] The acylated ghrelin is considered to be the active form and increases hunger. On the other hand, leptin is predominantly released by adipose cells and inhibits hunger.[6] Leptin is produced in adipocytes and reduces appetite and weight gain by inhibiting Agouti-related peptide(AgRP)/Neuropeptide Y (NPY) neurons and stimulating neurons that express pro-opiomelanocortin (POMC) and cocaine- and amphetamine-regulated transcript (CART) neurons in the hypothalamic arcuate nucleus. Ghrelin exerts orexigenic effects by binding to growth hormone secretagogue receptor (GHSR) expressed by AgRP/NPY neurons in the hypothalamus and by neurons in the area postrema,[7] which integrates several peripheral signals – as adiposity and caloric intake – and is acknowledged as the main regulator of human appetite.[8]

Ghrelin and leptin levels have been shown to be respectively reduced and increased in metabolic disorders such as obesity, metabolic syndrome, and type 2 diabetes.[9] Ghrelin prevents against energy deficit by enhancing hunger, conserving carbohydrates, and promoting fat oxidation, while leptin has the opposite effect.[6,10,11] In short, the hypothalamic balance between ghrelin and leptin actions controls the amount of needed energy, being a major determinant of body fat accumulation.[6]

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Body and fat mass reduction depend on long-term negative energy balance. In this sense, physical activity seems to be efficacious to regulate the energy balance, ultimately influencing changes in body mass.[12,13] Exercise training helps to prevent overweight and obesity by directly increasing energy expenditure and regulating appetite.[14] However, prior research about the effects of exercise on acylated ghrelin produced conflicting results. While some studies reported an increase in its levels,[15-17] others failed to detect changes.[18,19] Data concerning leptin are also mixed.[20] Moreover, it has been shown that overweight per se affects the response of these metabolic hormones to exercise training.[21] Therefore, additional research is warranted to clarify the role of exercise training in controlling the appetite and metabolism of overweight and individuals with obesity.

Exercise training bouts performed with high vs. low intensity spend more energy in shorter periods and may increase the post-exercise fat oxidation.[22] This helps explaining why exercise training routines focusing on continuous activities performed with low intensity (as walking or jogging) have produced frustrating results in terms of weight loss. In addition, the influence of exercise training upon cardiorespiratory fitness and cardiovascular risk seems to be optimized by increased intensity.[23]

In brief, the accumulated evidence suggests that physical training with increased intensity has greater potential to reduce body fat and body mass.[24,25] People with obesity could therefore benefit from exercise training routines with high intensity, provided they are compatible with their functional capacity. However, this is still uncommon and further studies on the effects of high-intensity training in overweight and obese individuals are needed.[25] Potential mechanisms of weight reduction include the modulation of appetite and metabolism, which are regulated by acylated ghrelin and leptin levels. There is a lack of information regarding the response of these hormones to exercise training bouts performed with high intensity, particularly in individuals with overweight.

Additionally, women appear to exhibit lower weight loss in response to exercise compared to men. Thus, either a gender difference exists in regard to exercise-related changes in the energy balance or women would compensate for exercise to a greater extent in comparison with men. Sex differences in body fat loss due to aerobic exercise may result, at least in part, from changes in key circulating hormones (e.g., acylated ghrelin, leptin) that moderate the energy balance.[26] It would be therefore of interest to investigate the effects of different modalities and intensities of exercise training upon those hormones in overweight females.

Given these gaps in the literature, the purpose of the present controlled trial was to investigate the effects of 8 weeks of high-intensity exercise training upon appetite, body mass, aerobic capacity, and metabolic hormones (acylated ghrelin and leptin) in overweight women. We have hypothesized that high-intensity exercise training (HIET) would be capable to provoke favorable changes in all these outcomes.

MAIN POINTS

- Physical training with increased intensity has greater potential to reduce body fat and body mass. People with overweight could therefore benefit of exercise training routines with high intensity, provided they are compatible with their functional capacity.
- High-intensity exercise training was effective to improve aerobic capacity, but did not elicit enough negative energy balance to reduce fat mass or promote appetite compensatory responses.
- High-intensity exercise training intervention induced no change in appetite nor in plasma concentration of metabolic hormones (leptin and ghrelin).

Materials and Methods

Participants

Participants were women under 25-45 years old exhibiting body mass index (BMI) >25 kg/m^2. Exclusion criteria were (a) inconstant weight (variation ≥2 kg) or participation in weight management programs (dieting, regular exercise, etc.) within the last 6 months; (b) smoking or any drug addiction; (c) cardiovascular, kidney, or metabolic disease (high blood pressure, high blood sugar, high serum triglycerides, and low serum high-density lipoprotein). After advertisement, 80 individuals volunteered and 25 were considered eligible for the study (35.4 ± 6.9 years; 74.2 ± 7.6 kg).

All of them had regular menstruals and were not in the bleeding phase at the time of blood sampling. After selection, participants were randomly assigned into 2 groups: control (n = 10; 38.6 ± 7.7 years; 74.5 ± 10.3 kg) and HIET (n = 15; 32.6 ± 5.0 years; 74.0 ± 4.9 kg). For ethical reasons, women allocated to the control group were invited to participate in the HIET routine after the experiment. All individuals provided written consent to participate in the research, and the study was approved by the medical ethics committee of the Islamic Azad University (No: IR-IAU1399-16).

Study Design

The first visit occurred 2 weeks before the beginning of the exercise program. The participants underwent body mass, height, skinfolds, waist-to-hip ratio (WHR), and aerobic capacity assessments. On the second visit, after 8-hour fasting, the participants answered an appetite perception questionnaire and a venous blood sample was taken. Subsequently, the participants were randomly assigned to experimental and control groups. Those in HIET group attended to training sessions 3 times/week during 8 weeks, while controls were instructed to keep their daily routine. During the 8 weeks of intervention, HIET and control groups were instructed not to change their diet, and 3 days before the first and second blood sample tests the amount of their energy intake was determined by 24-hour dietary recall. This measurement was done by researchers and face-to-face by recording food consumption images. Three-day averages of energy intakes were analyzed by specific software (Nutritionist 4, First Databank Inc., Hearst Corp., San Bruno, Calif, USA). The last visit occurred within 70 to 72 hours after the end of the training intervention. All measurements performed at baseline were repeated after the 6-week intervention, following exactly the same procedures.

Fat Percentage, Energy Expenditure, and Aerobic Capacity Assessment

Skinfolds were measured to estimate fat percentage (Saehan^{TM}, SH5020, South Korea) using the Jackson-Pollock 3-point method and the Siri equation, as described elsewhere.[27,28] Each site was visually

Table 1. High-Intensity Exercise Training (HIET) Protocol

Week	1	2	3	4	5	6	7	8
Intensity (% max heart rate)	80-85	80-85	80-85	80-85	80-85	80-85	80-85	80-85
Rest time (min)	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5
Number of bouts	10	12	14	16	18	20	22	24
Warm up (min)	10	10	10	10	10	10	10	10
Cool down (min)	5	5	5	5	5	5	5	5
Total workout (min)	33.5	37.5	41.5	45.5	49.5	53.5	56.5	60

located and marked so that consecutive measurements were at identical sites. Each measurement was repeated until 3 identical readings (variation <10%) were performed at all sites. The average of 3 values was calculated for subsequent analysis. The sum of 3 skinfolds was used to estimate body density. The participants completed a 24-hour physical activity recording form[29] during 7 days before the beginning of the exercise program and after 8 weeks of intervention, in order to determine the individual increase in caloric expenditure. The 1-mile Rockport Walk Test (RWT) (1609 m) was used to estimate the maximum aerobic power,[30] as described elsewhere. The heart rate was continuously measured during the test using a cardiotachometer (Polar™ F11, Kempele, Finland).

Appetite and Biochemical Assessment

Participants were asked not to exercise for 72 hours and fast for at least 8 hours before the first blood sampling. On the blood sampling day, they completed an appetite questionnaire (visual analogue scales, VAS) including 2 items[31]: (1) How much hungry are you? (2) How much full are you? The scale is graded from 0 to 150 mm and divided into 5 modes that determine the severity of individual mental emotions. The VAS is most often composed of lines with words anchored at each end, describing the extreme sensations (e.g.; "I have never been more hungry" and "I am not hungry at all"). The individuals were asked to make a mark across the line the point corresponding to their feelings. The final score was obtained by measuring the distance from the left end of the line to the mark.[31] This VAS exhibits a good degree of within-subject reliability and validity, being validated against the scale developed by Stubbs et al.[32] It appears that VAS best applies to within-subject repeated-measures designs since the effect of different treatments can be compared under similar circumstances.

Then, individuals remained at rest in a sitting position and 5 mL of blood was taken from their antebrachial vein. Aprotinin and ethylenediaminetetraacetic acid (EDTA) were used, respectively, as the protector and the separated plasma. The plasma was stored at −80°C for further analysis to determine the concentration of acylated ghrelin and leptin. The Human Acylated Ghrelin ELISA Kit (Eastbiopharm, Hangzhou, China) was used to measure acylated ghrelin with a sensitivity of 2.6 ng/mL and 10% intragroup variation coefficient. The Human Leptin ELISA Kit (Eastbiopharm Company, Hangzhou, China) was used to measure leptin with a sensitivity of 1.2 ng/mL and 10% intragroup variation coefficient. After the 8-week intervention, the participants repeated the appetite questionnaire and blood collection.

Training Protocol

The HIET consisted of 33- to 53-minute exercise bouts during which the participants performed 18-38 minutes of 30-second bouts of fast running forward/backward with intensity corresponding to 80%-85% of maximum heart rate (220-age), interspersed with 90-second intervals. Exercise sessions took place 3 times/week always in the morning (2 hours after breakfast), in order to minimize the circadian influence upon hormonal responses. Table 1 details the characteristics of the HIET protocol throughout the 8-week intervention. The control group maintained their daily routine activities with no regular exercise training at all.

Statistical Analysis

Data normality was confirmed by the Shapiro-Wilk test, and therefore, data are presented as mean ± standard deviation. The effects of intervention on continuous variables were compared by 2-way analysis of variance with repeated measures, followed by Tukey's post hoc verifications in the event of significant *F* ratios. In all cases, the significant level was set at $P \leq .05$ and calculations were performed using the Statistical Package for Social Sciences 18.0 software (SPSS Inc.; Chicago, IL, USA).

Results

Table 2 presents the characteristics of HIET and control groups at baseline and after intervention. No difference across groups was detected at baseline for any of the observed variables. After training, HIET exhibited a significant increase in estimated aerobic capacity vs. controls ($P = .01$).

Table 3 exhibits data for plasma levels of the observed metabolic hormones. No difference within or between groups was detected for either leptin ($P = .62$) or acylated ghrelin ($P = .06$). Moreover, no significant difference in fasting appetite level was found between groups ($P = .33$). During the research protocol, there was a significant increase in daily energy expenditure in HIET versus controls

Table 2. Anthropometric and Physiological Outcomes in High-Intensity Exercise Training (HIET) and Control Groups Before and After Intervention (Mean ± SD)

Variable	HIET (n = 10) (Pre)	Control (n = 10) (Pre)	HIET (n = 10) (Post)	Control (n = 10) (Post)
Body mass (kg)	74.02 ± 4.90	74.45 ± 10.29	71.58 ± 5.10	73.30 ± 4.84
Body fat (%)	39.71 ± 4.24	38.89 ± 3.02	39.43 ± 1.74	38.48 ± 3.93
WHR	0.86 ± 0.06	0.82 ± 0.07	0.88 ± 0.07	0.82 ± 0.08
BMI (kg/m^2)	28.99 ± 1.73	28.97 ± 3.44	28.59 ± 2.09	29.05 ± 3.28
Estimated VO_2max (mL kg^{-1} min^{-1})	33.62 ± 2.41	30.07 ± 3.91	36.34 ± 5.58 *†	27.39 ± 6.82

BMI, body mass index; WHR, waist-to-hip ratio; SD, standard deviation.
*$P \leq .05$ for training effects; †Significantly different from control group ($P \leq .05$).

Table 3. Plasma Leptin and Acylated Ghrelin Concentrations at Baseline and After 8-Week Intervention (Mean ± SD)

Variable	Group	Pre	Post
Leptin (ng/mL)	Control group	517.44±102.57	429.67±92.67
	HIET group	892.00±115.59	881.40±102.78
Acylated ghrelin (pg/mL)	Control group	711.11±109.17	663.11±84.65
	HIET group	805.40±104.59	883.10±116.14

HIET: high-intensity exercise training.
All within-between groups comparisons $P > .05$.

(2267.25 ± 151.18 vs. 2042.89 ± 113.81 kcal, $P = .01$), but not in caloric intake (1821.23 ± 582.14 vs. 1707.03 ± 190.70 kcal, $P = .58$).

Discussion

The present study investigated whether HIET was capable to provoke changes in appetite, body mass, maximal aerobic capacity, leptin, and acylated ghrelin in overweight women. Our findings indicated that body mass, estimated fat percentage, WHR, and BMI did not change versus controls after 8-week HIET intervention. On the other hand, the aerobic capacity estimated by the distance within RWT significantly improved. Although daily energy expenditure has increased in HIET versus controls, the caloric intake remained stable. Accordingly, the intervention induced no change in appetite nor in plasma concentration of metabolic hormones (leptin and ghrelin).

A possible reason for the results regarding body mass and estimated fat percentage could be the lack of a significant negative energy balance in the HIET group. It is feasible that subjects have compensated for the increased caloric expenditure by reducing other daily activities.[33] Similar to the present study, Elerian et al[34] showed that there was a significant decrease in the percentage of body fat ($P < .05$) only regarding male group, this was established in a previous study that concluded that female subjects tended to have higher fat mass.[35] Consistent with the findings for body and percent fat mass, women who underwent HIET intervention did not change the waist index or WHR in comparison with controls.

Previous studies have shown the importance of exercise intensity to improve aerobic capacity.[36] The HIET has been extensively acknowledged to induce rapid and broad increases in maximum oxygen uptake,[36-38] by means of central and peripheral adaptations.[36] However, limited research investigated the effects of HIET among sedentary and overweight populations.[39,40] Tjønna (2013) reported a significant increase in VO_{2max} among overweight men after 10 weeks of HIET performed 3 times/week. Our findings concur with this premise, since the estimated VO_{2max} increased by 8.1%, being the sole outcome that significantly improved in our sample of obese and sedentary women.[41,42] Our data suggest that HIET performed 3 times per week would be an efficient method to improve VO_{2max} in overweight, obese, and sedentary women.

Caloric intake after HIET remained unaltered, albeit the increased energy expenditure. This finding concurs with previous studies, particularly in regard to caloric intake.[43,44] Some prior research suggested that the increase in physical activity levels might be concomitant to greater caloric intake and/or lower energy expenditure related to other daily physical activities, which evidently compromises potential weight loss.[33] In the case of individuals with obesity and overweight, exercise-related energy expenditure is often overestimated, with increased reward in terms of food amount and leading to a positive energy balance. Our results did not ratify this premise, since participants seemed not to have compensated for the higher energy expenditure by increasing their caloric intake.

Ghrelin is involved in the onset of hunger and in the long-term regulation of energy balance.[5,15] It has been shown that physical exercise affects the energy balance, as well as the appetite drive via ghrelin.[45] In short, the increase in caloric expenditure due to exercise seems to generate signals to ghrelin-producing cells in the stomach, which are responsible for appetite regulation. Prior studies reported that aerobic exercise might significantly increase the acylated ghrelin production,[15,16,46] with impact on appetite and caloric intake.[15,16] In addition, leptin secreted from the fat tissue consists of a major regulator of food intake and energy expenditure, therefore playing a central role in long-term regulation of energy coherence. Physical exercise has been suggested to reduce leptin levels by reducing fat mass, increasing energy expenditure, and affecting the production of hormones and metabolites related to leptin compatibility.[47]

Our results did not concur with those premises, since we have shown that 8 weeks of HIET were not capable to induce significant changes in the fasting levels of acylated ghrelin or plasma leptin in overweight women. In line with these findings, Guelfi et al[48], Larsen et al[49] and Kim et al[18] could not observe significant changes in ghrelin levels after aerobic training. In the case of the study by Kim et al[18] there was an increase in total ghrelin along with weight loss during the first weeks of intervention, but in the final weeks the body mass has stabilized, while ghrelin returned to baseline levels. The short duration of the present intervention and the lack of weight loss may help to explain why acylated ghrelin remained unaltered after HIET. Larsen et al[49] stated that it was possible that lack of change in acylated ghrelin after exercise could be one reason why exercise didn't induce compensatory appetite and energy intake responses.

In contrast, Tremblay et al[50] showed that high-intensity resistance and endurance exercise attenuate a significant decrease in leptin and a significant increase in ghrelin after 21 days and 3 months. They stated the reason for this is the decrease in the percentage of fat and weight of the subjects. Also, Malin et al[51] showed that interval exercise attenuates the rise in post-prandial acylated ghrelin during short-term caloric restriction in females with obesity when matched on energy availability. Of course, the present study was with calorie restriction. Previous studies have shown that exercise training longer than 12 weeks would be more likely to induce significant decreases in leptin levels than shorter programs.[47] Hopkins et al[52] for instance, applied 12 weeks of aerobic exercise training with moderate-to-high intensity to 46 overweight or obese subjects and reported a decrease in both body mass and leptin levels. In the present study, we tried to compensate for the shorter duration by applying an exercise routine characterized by very vigorous intensity. The overall training volume would be therefore compatible with stimuli applied in longer exercise programs by means of increased intensity. However, our data after 8-week HIET seemed to support the hypothesis that longer aerobic training interventions would be needed to reduce leptin among overweight and obese women, regardless of the exercise intensity. Along with our results, Kishali et al[20] also failed to observe significant changes in leptin after aerobic training performed by young individuals with normal weight during 8 weeks (50%-70% maximum heart rate, 3 days/week).

Eight-week HIET intervention did not have a significant effect on appetite as well. These data disagree with prior studies suggesting that physical exercise would increase appetite due to a homeostatic compensation of the negative energy balance provoked by increased energy expenditure.[15,48] The mechanisms involved in appetite control are several (gastrointestinal and nervous signals, blood signals from energy stores, hormones, body temperature, mental state, environmental factors, etc.)[21] and their interaction in response to chronic exercise remains unclear. Individual appetite responses to exercise can be therefore widely differentiated.[53]

However, it is possible that our relatively short-term HIET intervention was not enough to induce relevant changes in the energy balance. The fact that a significant change in body mass did not occur reinforces this premise. In line with our results, some previous research also did not observe changes in appetite following physical training with short duration and moderate intensity.[16,54] Kanaley et al[54] examined the effects upon the appetite of 15 days of walking with an intensity of 70%-75% VO_{2peak} in 13 individuals with obesity, while Ueda et al[16] investigated the effect of 12 weeks of aerobic exercise training with 65% maximal heart rate on 20 middle-aged Japanese women.

Some limitations of our study must be acknowledged. Firstly, the relatively small sample may have led to type II errors, particularly in regard to appetite and metabolic hormones. Measuring appetite by means of VAS is also problematic. There are problems inherent to this method, particularly the fact that its completion is typically unsupervised. This may result in incomplete or wrongly marked questions. Moreover, there is a great variation of appetite perception between individuals (vs. actual craving for food), which may also have influenced our results. Another limitation was that 24-hour recalls are particularly prone to error and 3 days intake is not enough number of days to accurately represent energy intake (EI).

Also there is insufficient evidence to suggest women are disadvantaged when using exercise to suppress appetite hormones and perceived hunger after exercise at an intensity of at least 60% VO_2max. It is important to note that both referenced studies comparing men and women controlled for the menstrual phase of the women participating; women participated during the early follicular phase of menstruation (1–4 days after menstruation).[55] It is generally accepted that women tend to increase their energy intake during the luteal phase of menstruation compared to the follicular phase[56]; therefore if not controlled for, menstruation could confound the results of a study comparing appetite hormones in women. In the present study, we tried to make all women in the same follicular phase, but it was not possible to completely control this case, which is one of the limitations of the present study.

Conclusion

In conclusion, HIET was effective to improve the estimated aerobic capacity, but did not elicit enough negative energy balance to reduce fat mass or promote appetite compensatory responses nor changes in acylated ghrelin and leptin concentrations in overweight and obese women. Further studies with longer duration and greater training volume are warranted to ratify these findings. The results of this study are relevant for physical training in the context of weight management programs, particularly within obesity treatment.

Ethics Committee Approval: The study was approved by the medical ethics committee of the Islamic Azad University (No: IR-IAU1399-16).

Informed Consent: Written informed consent was obtained from the patients who participated in this study.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept – M.K., A.N.; Design – M.K., A.N.; Supervision – M.K., A.N.; Resources – M.K., A.N.; Materials – M.K., A.N.; Data Collection and/or Processing – M.K., A.N.; Analysis and/or Interpretation – M.K., A.N.; Literature Search – M.K., A.N.; Writing Manuscript – M.K., A.N.; Critical Review – M.K., A.N.

Declaration of Interests: The authors declare that they have no competing interest.

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