Effect of Resistance Training on Appetite Regulation and Level of Related Peptides in Sedentary Healthy Men

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ABSTRACT

Background and Objectives: Resistance training is a key component of exercise recommendations for weight control, yet very little is known about the effects of resistance training on appetite and related peptides. Hence, the aim of the present study was to investigate the effect of 8 weeks of resistance training on appetite and circulating acyl ghrelin, neuropeptide Y (NPY), and orexin in sedentary men.

Methods: This study included 20 sedentary men (mean age: 21.6±3.5 year, body mass index: 23.1±2.7 kg/m²) who were equally divided into a control group and a resistance training group. Participants in the training group performed the whole body exercises three sessions per week with 3-4 sets of 8-10 repetitions at 60-85% one-repetition maximum. Participants in the control group performed no resistance training. Fasting blood samples were taken before starting the study and 72 hours after the last session of resistance training for evaluation of serum acyl ghrelin, NPY, and orexin levels. In addition, perceived appetite was assessed by visual analogue scale while fasting.

Results: Statistical analysis showed that fasting acyl ghrelin and NPY were not changed by resistance training, but serum orexin level elevated by 40% in response to training (P=0.01). Appetite was not significantly different between the two groups at baseline (P=0.9). However, appetite significantly increased after resistance training (P=0.001).

Conclusion: Results of the present study show that the 8-week resistance training increases perceived appetite by orexin promotion in previously sedentary men.

Keywords: Appetite, Ghrelin, NPY, Orexins, Resistance Training.
INTRODUCTION
Some sections of the brain such as hypothalamus act as central regulators of food intake, satiety, and energy homeostasis. However, hormones produced by adipose tissue and stomach influence these centers, leading to stimulation of hunger and feeling of fullness (1). These hormones are involved in metabolism, and change in their levels affect weight and appetite (2). It is well known that physical activity and food intake regulation are the two most important factors involved in body weight control. The brain must alter appetite in order to regulate food intake. Therefore, much effort has been made to understand the intricate interplay between gut hormones and the central nervous system, and the role of these peptides in food intake regulation through appetite modulation (3).

According to previous studies on humans, it is thought that exercise training is an effective method of maintaining body weight in the normal range, which relies not only directly on energy expenditure, but also indirectly on short-term appetite suppression and appetite regulation (4). The effect of resistance training on appetite and the molecular mechanism of this process in sedentary healthy men are not yet clear. There are conflicting reports about the effect of exercise training on peptides that regulate appetite. There are many factors involved in hunger and satiety signals. In this regard, previous studies show that ghrelin, neuropeptide Y (NPY) and orexin have key roles in appetite regulation. Ghrelin is a 28-amino acid peptide hormone, produced predominantly in the ghrelinergic cells of the gastrointestinal tract, representing as the only known orexigenic (appetite-stimulating) gut hormone identified to date (3). Acylation of ghrelin is thought to be essential for appetite regulation because only the acylated form of the hormone can cross the blood-brain barrier (5). Ghrelin stimulates food intake and appetite in lean and obese individuals via NPY (6, 7). NPY is a 36-amino acid neuropeptide produced in various sites including the hypothalamus, acting as a neurotransmitter in the brain. It is thought to have several functions, including increasing food intake and storage of energy as fat (8). Orexin or hypocretin is a recently discovered neuropeptide synthesized mainly by neurons located in the posterolateral hypothalamus. Intracerebroventricular administration of orexin-A stimulates food intake and energy expenditure (9). Tomasik et al. have demonstrated that concentration of orexin-A is significantly correlated with body mass index (BMI) in healthy subjects (10).

To our knowledge, no study has yet investigated the effect of resistance training on plasma ghrelin, NPY and orexin levels, and perceived appetite in sedentary men with normal weight. Therefore, the purpose of the present study was to examine the effects of negative energy balance induced by resistance training on perceived appetite and related peptides in healthy but previously sedentary men.

MATERIAL AND METHODS
This study was performed on 20 sedentary healthy male students (age: 20-25 years) with normal weight (body mass index: 20-25 kg/m²) after obtaining approval from the Ethical Committee of Islamic Azad University (code number: IR.IAU.SARI.REC.1395.2). Informed consent was obtained from all subjects and the study procedures were explained in details. A physical activity questionnaire was provided for the participants to determine eligibility for participation in the study. All participants were untrained with no history of major chronic diseases. Exclusion criteria included cigarette smoking, history of heart disease or diseases known to cause metabolic disturbances such as diabetes, lactose intolerance, and use of any medication that are known to alter metabolism or dietary intake.

After performing baseline testing, the height, weight and body composition of each participant were determined. Weight and height measurements (to the nearest 0.1 kg and 0.1 cm, respectively) were performed using a balance beam scale and stadiometer, respectively. BMI was calculated as weight in kilograms divided by height in meters squared (kg/m²). Body fat percentage was measured by bioelectrical impedance analysis (InBody 3.0, Biospace Co., Ltd).

The participants were matched in terms of BMI, and then divided into a resistance training group (n=10) and a control group (n=10). Basic characteristics of the participants in the two groups are shown in Table 1. The participants in the training group completed 3 sessions of supervised resistance training.
every week for 8 weeks. The control group continued with their normal sedentary routine. The training group completed a range of resistance-based (weight training) exercises for each major muscle group of the body. At first, the participants were allowed to take as much time as they required to recover from each exercise. Then, the participants undertook a supervised resistance-training program for the upper and lower limb for 8 weeks, with three sessions per week. The sessions included chest press, double leg press, seated leg extension, seated leg curl, and seated row. One-minute rest was given between each set. The participants progressed from three sets of 10 repetitions for each exercise at 60% intensity of 1RM to four sets of eight repetitions at 85% intensity of 1RM by the end of the intervention. The 1RM was rested every two weeks and the load was re-adjusted accordingly. Each session was commenced with a 5-min warm-up on a rowing ergometer, followed by completion of the exercises in an alternating manner from upper- to lower-body. A standard 90s recovery was enforced between the sets (12). The conditions in the exercise room remained constant (~21.3 °C, ~25% humidity) during all sessions. It should be noted that all participants completed the 24 sessions.

One day before the first training session and 72 hours after the last training session, desire to eat was recorded by computerized and validated version of 100 mm visual analogue scale (13). For this purpose, the participants were familiarized with the human performance laboratory at 8:00 AM while fasted overnight. After 30 min rest in the laboratory, resting blood samples (3 ml) were collected from an antecubital vein around at 8:30 AM one day before the first exercise session and 72 hours after the last session. All samples were then centrifuged at 1000 g for 15 min at 4 °C. The serum obtained was stored at -80 °C for future analysis. Serum ghrelin, NPY and orexin concentrations were assessed using commercially available enzyme-linked immune sorbent assay kits (Phoenix Pharmaceuticals, Belmont, CA) according to the manufacturer’s instructions. For each hormone, all samples were assayed in the same batch to avoid inter-assay variability. The intra-assay variations were ghel in 3%, NPY 2.8% and Orexin 3.4%.

The data obtained from this study was analyzed using SPSS 16. Descriptive statistics (means ± SEM) were calculated for each dependent variable. Normality of data distribution for all parameters was tested by Shapiro-Wilk's test. Independent and dependent T-tests were used to determine inter-group and intra-group differences, respectively. P-values less than 0.05 were considered statistically significant. The data is presented as mean ± SEM.

RESULTS

There was no statistically significant difference in the basic characteristics of participants at baseline. Level of acyl ghrelin at baseline and after 8 weeks of training did not differ significantly between the two groups (Table 2). In the control group, concentration of acyl ghrelin was 1.4±0.9 ng/ml at baseline and 1.4±1.2 ng/ml after the experiment. Eight weeks of resistance training had no effect on the circulating acyl ghrelin (P=0.7).

Concentration of NPY at baseline and after 8 weeks of training did not differ significantly between the two groups (P=0.3). Concentration of NPY in the resistance-training group was 235±45 ng/ml at baseline and 218±21 ng/ml after the training program. NPY did not change significantly following the resistance training (P=0.7). Concentration of orexin at baseline was significantly different between the two groups (P=0.01). Orexin was not affected significantly in the control group, but increased by 40% after the 8-week resistance training (P=0.01). In addition, there was no significant difference between the groups after the intervention (P=0.1).

The desire to eat decreased in the control group (0.04%, P=0.1). However, the desire to eat increased significantly in response to exercise training in the training group (24%, P=0.001). While the desire to eat was not significantly different between the groups at baseline (P=0.9), it was significantly increased in the training group after the experiment (P=0.02).
increase in peptide YY. In this regards, Balaguera-Cortes et al. observed reduced active ghrelin and elevated pancreatic polypeptide (PP) and insulin levels after acute resistance exercise (18). However, it is not known whether such alterations in response to acute exercise could contribute to long-term appetite regulation. In a partial agreement with previous studies, our data demonstrated that 8 weeks of low to moderate intensity aerobic training increases appetite (19). Foster et al. have reported that acyl ghrelin does not change in response to training (20). The mentioned study showed that circulating total ghrelin level increases commensurately with weight loss, while fasting ghrelin concentrations appeared to be unaffected by exercise training in the absence of concurrent weight loss. However, it is important to note that body fat percentage did not change following the training program in our study. Therefore, the change of acyl ghrelin in response to training could be due to weight loss. In this regard, Leidy et al. reported a significant increase in total ghrelin level of women with healthy weight who had lost weight over three months by combination of reduced food intake and exercise. However, this was achieved not due to the effects of physical exercise because total ghrelin levels

### DISCUSSION
Inactive lifestyle impairs appetite regulation, whereas exercise training affects nutrition, behavior and energy homeostasis. Resistance training is an essential part of any weight management program. The effectiveness of resistance training in the absence of dietary restriction for weight control of sedentary adults has been controversial. However, there is little information available on the effect of resistance training on appetite regulation and gut hormones in sedentary men. Acyl ghrelin, NPY and orexin may provide a better understanding of how resistance training contributes to weight management and health promotion (14). The molecular mechanisms of appetite regulation in response to resistance training in sedentary men are not completely understood (12, 15).

Our results show that eight weeks of resistance training with no diet restriction increased perceived appetite in sedentary men by orexin promotion, but had no effects on circulating acyl ghrelin and NPY. Several studies have investigated the acute effects of resistance training on appetite-regulating hormones, and the majority of these studies have focused on ghrelin and leptin (16, 17). Current data suggest that short-term suppression of appetite following a single exercise session may be affected by decrease in acyl ghrelin and increase in peptide YY. In this regards, Balaguera-Cortes et al. observed reduced active ghrelin and elevated pancreatic polypeptide (PP) and insulin levels after acute resistance exercise (18). However, it is not known whether such alterations in response to acute exercise could contribute to long-term appetite regulation. In a partial agreement with previous studies, our data demonstrated that 8 weeks of low to moderate intensity aerobic training increases appetite (19). Foster et al. have reported that acyl ghrelin does not change in response to training (20). The mentioned study showed that circulating total ghrelin level increases commensurately with weight loss, while fasting ghrelin concentrations appeared to be unaffected by exercise training in the absence of concurrent weight loss. However, it is important to note that body fat percentage did not change following the training program in our study. Therefore, the change of acyl ghrelin in response to training could be due to weight loss. In this regard, Leidy et al. reported a significant increase in total ghrelin level of women with healthy weight who had lost weight over three months by combination of reduced food intake and exercise. However, this was achieved not due to the effects of physical exercise because total ghrelin levels

### Table 1- Basic characteristics of the two study groups

<table>
<thead>
<tr>
<th>Variables</th>
<th>Control Group</th>
<th>Training Group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (Year)</td>
<td>22.2±2</td>
<td>21.1±1</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>172.7±9.8</td>
<td>175.4±11.3</td>
</tr>
<tr>
<td>Weight (Kg)</td>
<td>64.8±4.9</td>
<td>68.1±2.1</td>
</tr>
<tr>
<td>Pre-intervention body fat (%)</td>
<td>15.7±4.88</td>
<td>19.1±3.3</td>
</tr>
<tr>
<td>Post-intervention body fat (%)</td>
<td>14.6±3.6</td>
<td>16.9±5.1</td>
</tr>
<tr>
<td>Waist-to-hip ratio</td>
<td>0.83±0.4</td>
<td>0.84±0.4</td>
</tr>
<tr>
<td>BMI(Kg/m²)</td>
<td>22.9±2.1</td>
<td>23.3±1.2</td>
</tr>
</tbody>
</table>

### Table 2- Effect of the 8-week resistance training on appetite and circulating related peptides in sedentary men

<table>
<thead>
<tr>
<th>Variables</th>
<th>Pre-intervention</th>
<th>Post-intervention</th>
<th>Pre-intervention</th>
<th>Post-intervention</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acyl-ghrelin (ng/ml)</td>
<td>1.4±0.9</td>
<td>1.4±1.2</td>
<td>1.8±1.3</td>
<td>1.9±1.1</td>
</tr>
<tr>
<td>NPY (ng/l)</td>
<td>207±23</td>
<td>204±31</td>
<td>235±42</td>
<td>218±21</td>
</tr>
<tr>
<td>Orexin (pg/ml)</td>
<td>181±34</td>
<td>199±37</td>
<td>135±57†</td>
<td>190±46†</td>
</tr>
<tr>
<td>Desire to eat score</td>
<td>67.5±7.4</td>
<td>64.8±11.4</td>
<td>61.2±9.6</td>
<td>76.1±5.7†</td>
</tr>
</tbody>
</table>

The data are presented as the mean ± SEM
† P<0.05 VS. Pre
‡ P<0.05 VS. Pre in control group
in weight-stable group was not changed (21). Furthermore, Martins et al. (22) showed a significant reduction in body weight and fasting insulin level and an increase in plasma acyl ghrelin levels and fasting hunger sensations after 12 weeks of aerobic training. According to the mentioned study, ghrelin and leptin are both highly sensitive to changes in body weight (21).

Results of Guelfi et al. (12) about the effect of resistance training on appetite showed that 12 weeks of resistance training does not influence perceived hunger or fullness and related hormones (ghrelin, pancreatic polypeptide, peptide YY and insulin) while fasting in previously sedentary overweight and obese men (12). The inconsistency between these findings and our results could be related to differences in the training protocol and the degree of fat-loss following the training program.

We found that orexin promotion plays an important role in perceived appetite after resistance training. Toshinia et al. reported that centrally administered ghrelin increases feeding through activation of the orexin pathway (23). They also demonstrated the synaptic contact of ghrelin-containing axons with orexin-producing neurons in the rat hypothalamus (23). Our findings suggest that orexin can respond to energy expenditure in a compensatory manner as an endocrine and/or metabolic result of physical exercise. Previous studies have shown that intracerebroventricular administration of orexin A stimulates food intake, which is mediated via the orexin receptor, and subsequently leading to activation of NPY Y1 receptor (24, 25).

Other mechanisms through which exercise training may stimulate satiety that have not been investigated in the present study include an enhanced rate of gastric emptying that allows faster release of satiety signals, or training-induced changes in substrate metabolism (i.e. increased fatty acid oxidation), which may play a role in appetite regulation by affecting hepatic energy status. Moreover, myokines could be involved in the effect of exercise training on appetite regulation. The transient rise in IL-6 observed in response to an acute bout of exercise has been reported to suppress post-exercise energy intake (12). Clearly, further studies should be conducted on the mechanisms through which exercise training affect appetite.

**CONCLUSION**

Exercise can directly affect energy balance by increasing total energy expenditure. It indirectly affects compensatory mechanism of promoting calorie consumption by appetite regulation. In fact, an increase in energy intake could be resulted from changes in the appetite control system toward an orexigenic environment. Currently, little is known about the influence of resistance training on appetite-regulating hormones in sedentary men. Results of the present study show that the 8-week resistance training increases perceived appetite by orexin promotion in previously sedentary men. However, the effects of resistance training on changes in appetite hormones need further investigation.

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**CONFLICT OF INTEREST**

The authors declare that there is no conflict of interest.

**REFERENCES**


