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Acute and chronic responses of metabolic myokine to different intensities of exercise in sedentary young women

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ABSTRACT

Introduction: Irisin is a myokine secreted from the muscle in response to exercise. The aim of this study was to investigate the acute and chronic effect of resistance training in sedentary young women.
Material and methods: In this study, 21 sedentary young women with range of 20–30 years and BMI 22–25 kg/m^2 were selected by convenience sampling. Then, the volunteers were randomly assigned into two groups. The selected training was comprised of 8 weeks, 3 times a week. Blood samples were obtained at baseline, after one session and 48 h at the end of the study. For all statistical comparisons, the level of significance was considered $P < 0.05$.
Result: The results of this study showed that the levels of Irisin, body mass index, and body fat percentage in the low-intensity training group were not significant ($P > 0.05$). Moreover, no significant changes were shown in body mass index and body fat percentage in high-intensity training ($P > 0.05$). In contrast, the levels of Irisin in high-intensity training decreased significantly ($p = 0.034$). In low-intensity RT group and high-intensity RT group, no significant changes were observed in serum Irisin after 1 session.
Discussion: These results suggest that one period and one session of resistance training with low intensity and one session of resistance training with high intensity did not change serum Irisin levels significantly; in addition, after one period of weight training with high intensity, serum level of Irisin decreased in young women with a body mass index between 22 and 25 kg per square meter.

1. Introduction

The subject of adjusting weight, homeostasis and energy balance, appetite, food intake behavior, and energy expenditure has been the basic, favorite subject for researchers (Hosoda et al., 2002). The regulation and energy balance apparently seem easy; however, they have a complex process. The change of energy balance process towards positive or negative balance can cause hazardous consequences such as obesity, diabetes, cardiovascular diseases, wasting, and anorexia (Woods et al., 2004). Conventionally, the hypothalamus was thought to be important in feeding behavior, and it has appeared as the most important area to adjust food intake and body weight homeostasis in the brain. In addition to this traditional center, the other factors except hypothalamus have an impact on the regulation of energy balance (Zhang et al., 2005; Green et al., 2007; Nogueiras et al., 2007). On the other hand, the energy condition of peripheral tissues, changed by various metabolic factors and physical activity, result in the alteration of the environmental massages, such as the hormones secreted from peripheral tissues. There are different theories regarding the molecular mechanism and adaptation of the fat tissue changes caused by exercise, one of which recognizes the muscle tissue as an endocrine organ that releases myokines into the circulation during or immediately after physical activity (Huh et al., 2012), which adjust physiological and metabolic pathways (Kobayashi et al., 2012). The discovery of myokines has emphasized the role of muscle as a source of hormones that communicate information and interact with other tissues, including fat, liver, and pancreas to alter metabolism (Huh et al., 2012; Kumahara et al., 2004; Sato et al., 1984). In a recent study, Boströmet et al (Boström et al., 2012) reported that PGC1α[1] expression in the skeletal muscle stimulates increased expression of FNDC5, a membrane protein that

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[1] Peroxisome proliferator-activated receptor gamma coactivator-1α (PGC-1 α).

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is cleaved and secreted as a novel myokine, Irisin (Tanisawa et al., 2014). Irisin is a newly discovered exercise-induced myokine (Polyzos et al., 2014), secreted by myocytes, which is believed to mediate the beneficial effects of exercise on metabolism (Boström et al., 2012). It is regulated by PPARγ[2] coactivator 1 alpha (PGC1α) and is identical in mice and humans. its administration results in «browning» or «beigeing» of white adipose tissue thereby increasing the thermogenesis-related energy expenditure and improving systemic metabolism (Polyzos et al., 2014); moreover, it reduces body weight and improves diet-induced insulin resistance (Boström et al., 2012). Exercise and energy expenditure induce the transcriptional regulator PGC1α in the skeletal myocyte, which in turn drives the production of the membrane protein FNDC5.[3] The circulating factor Irisin, cleaved from FNDC5, including mitochondrial biogenesis and the expression of uncoupling protein 1 (UCP1), leads to mitochondrial heat production and energy expenditure (Kelly, 2012). Irisin is transcribed from the FNDC5 gene and transferred to the cell membrane, where it is proteolytically cleaved on the extracellular surface of the muscle cells and released into plasma (Boström et al., 2012). Chronic training is shown to enhance Irisin production in mice although conflicting results have emerged in humans (Huh et al., 2012; Boström et al., 2012; Timmons et al., 2012). In contrast, Bostrom et al (Boström et al., 2012) showed a twofold increase of circulating Irisin after 10 weeks of endurance training; Huh et al. and Pekkala et al (Huh et al., 2012; Pekkala et al., 2013) found no increase in Irisin after 8 weeks of intermittent sprint running or after 21 weeks of combined endurance and strength training, respectively. Timmons et al (Timmons et al., 2012) demonstrated an induction of muscle FNDC5 in older, but not younger, highly active subjects. However, the study of Timmons et al. has been criticized for including exercise interventions without induction of PGC1α expression in muscles (Timmons et al., 2012). Thus, an exercise intervention study with chronically increased muscle PGC1α expression would potentially clarify the relation between FNDC5 mRNA in muscle and Irisin concentration in plasma. However, Raschke et al. observed no effect of recombinant FNDC5 or Irisin on the brightening of cultured, primary, human adipocytes (Raschke et al., 2013). A potential effect of Irisin to induce browning of white adipose tissue in response to chronic training has not been examined in humans (Norheim et al., 2014). Moreover, exercise training results in adaptive structural and metabolic changes in skeletal muscles, including a change in the type of muscle fiber, mitochondrial biogenesis, and angiogenesis and browning of subcutaneous (Kelly, 2012; Xu et al., 2011). Because of its effect, Irisin is emerging as an appealing therapeutic target for metabolic diseases and other disorders known to improve with exercise (Polyzos et al., 2014). Therefore, the purpose of this study was to determine the effects of acute and chronic resistance training with different intensities on serum Irisin levels in sedentary young women.

2. Material and methods

2.1. Subjects

This research was semi-experimental with two phases which were performed before and after one session and before and after 8 weeks in two experimental groups. A total of 21 sedentary young women over 20 years (mean age 24.42 ± 2.95 years, mean % body fat 34.51 ± 4.33% and mean body mass index 23.77 ± 1.54 kg/m2) were recruited in this study. All of the volunteers were participants who had completed the exercise program, including acute and chronic trainings, during 8 weeks.

Based on the demographic and medical records questionnaires, the subjects did not do regular exercise over the last six months and did not have a history of Coronary artery diseases, kidney failure, and hypothyroidism. Furthermore, calorie intake was estimated using the dietary questionnaire in order to control the energy balance in each week. Based on the collected data, daily received calories of subjects varied between 1600 and 1900 kcal.

2.2. Measurement of anthropometric characteristics

BMI and body fat percentages were measured using body composition analyzer device (Inbody-720 Body Composition Analyzer, Japan) while height was measured with a stadiometer (SECA, Germany).

2.3. 1 RM testing

In this study, prior to the 1 RM testing session, subjects were given three familiarization sessions to ensure proper lifting techniques and testing procedures. During these sessions, the load was gradually increased to allow the estimation of a proper starting point for the test session. Prior to performing the actual 1 RM tests, subjects were given a 10-min low-intensity warm-up and 3-min rest between test efforts. They were instructed to refrain from food intake 2 h prior to the test session but were allowed to drink water.

2.4. Resistance training protocol

Twenty one young, sedentary women were assigned to an 8-week high and low intensity resistance training program in a circular shape, involving 3 training sessions per week. Based on the equation of one repetition maximum (1 RM), the training program for both groups was isocaloric. In each training session, subjects were given a 10-min general and specific warm-up (low speed running, Stretching exercises, and weightlifting movements with light weight) and 10-min cool-down exercise. The training protocol consisted of four lower body exercises (Leg Extension, Leg flexion, squat, and standing calf raise) and three upper body exercises (High Pull, Elbow Flexion, and Elbow Extension) performed at both low intensity (40%–60%1 RM and 20–30 repetition in each station) and high intensity (70%–90% 1 RM and 5–15 repetition in each station). In low-intensity exercise group (n = 11), the time of activity in each training station was 45 s. There was a resting period of 30 s between training stations and 2 min between the seven-station training rounds. In high-intensity exercise group (n = 10), the time of activity in each training station was 20 s. There was a resting period of 30 s between training stations and 2 min between the seven-station training rounds. Moreover, the number of training rounds was three. To observe the principle of overload and the regulation of practice pressure, Borg questionnaires were completed by the individuals at the end of the third session of each week. The following equation was used to determine the progressive increase in overload at each station of resistance training in the first week and at the end of the fourth and sixth weeks.

$$1RM = W/[1.0278 - (0.0278.r)]$$

2.5. Collection and analysis of blood samples

Blood samples were taken before and after one session resistance training along with before and after 8 weeks of resistance

[2] Peroxisome proliferator-activated receptor(PPAR-γ).
[3] Fibronectin type III domain-containing protein 5 precursor(FNDC5).

training. The procedure was performed by standard antecubital venous puncture. Blood samples were collected after 12 h fasting, and then the samples were clotted for 2 h at room temperature before centrifugation for 15 min at 1000 × g. Serum was stored at −20 °C for 2 months until the time of analysis. Serum Irisin concentrations were determined with a commercially available ELISA kit (CSB-EQ027943HU, CASABIO, and Japan) according to the manufacturer's instructions.

2.6. Statistical analysis

All statistical analyses were performed with SPSS version 16. The average and standard deviations of data were calculated after checking the normal distribution using Shapiro-wilk test and Homogeneity of variance method and then examined by comparison of means within and between means groups. Paired-Samples t-test and Independent t-test were used respectively. Statistical significance was assigned at $P < 0.05$ for all analysis (see Table 1).

3. Result

3.1. Acute and chronic effects of resistance training on serum Irisin

The results of the present study reveal that baseline serum Irisin concentration was not significantly different among groups ($p = 0.61$). Serum ELISA analysis show that in low-intensity RT group, no significant changes are observed in serum Irisin after 8 weeks ($p = 0.97$) (sedentary young women, $n = 11$; Table 2, Fig 1) while in high-intensity RT group, serum Irisin reduced significantly after 8 weeks ($p = 0.034$) (sedentary young women, $n = 10$; Table 2, Fig 1).

In low-intensity RT group and high-intensity RT group, no significant changes were observed in serum Irisin after 1 session ($p = 0.21$, $p = 0.35$ respectively) (Table 3, Fig 1). After 1 session and 8 weeks, the variance between groups in Irisin variables was not significant ($p = 0.67$, $p = 0.73$ respectively; Table 2, Table 3, Fig 1).

3.2. Body composition

There were no significant baseline differences between low and high-intensity RT for BMI and PBF ($p = 0.69$, $p = 0.88$ respectively). None of the parameters developed differently over time after low-intensity RT ($p = 0.35$, $p = 0.37$, respectively) and after high-intensity RT ($p = 0.54$, $p = 0.68$, respectively). There were no significant differences in the changes in anthropometric data between groups ($p = 0.27$, $p = 0.80$, respectively, LRT: $N = 11$, HRT: $N = 10$) (Table 2, Fig 2, Fig 3).

Table 1
Characteristics of the subjects.

	LRT	HRT	P[a]
Irisin (ng/ml)	86.9 ± 39.0	78.1 ± 39.7	0.61
BMI (kg/m2)	23.8 ± 1.58	23.6 ± 1.57	0.69
PBF (%)	35.5 ± 5.71	33.3 ± 1.66	0.88
Age (years)	25.27 ± 3.34	23.50 ± 2.27	0.17
Height (cm)	161.18 ± 8.03	161.90 ± 6.83	0.82
Body weight (kg)	6212 ± 730	5680 ± 12.17	0.97

Data are presented as mean ± standard error of the mean (SEM) or absolute numbers.
Data were analyzed by Student's t-test (for normally distributed variables).
[a] Low intensity resistance training vs. high intensity resistance training.

Table 2
The anthropometric and serum Irisin concentration before and after 8 weeks of resistance training.

		Before (M ± SD)	After (M ± SD)	p-value[a]	p-value[b]
Irisin (ng/ml)	LRT	86.9 ± 39.0	65.7 ± 41.2	0.97	0.73
	HRT	78.1 ± 39.7	51.3 ± 19.0	0.034[c]	
BMI (kg/m2)	LRT	23.8 ± 1.58	24.0 ± 1.76	0.35	0.27
	HRT	23.6 ± 1.57	23.5 ± 1.58	0.54	
PBF (%)	LRT	35.5 ± 5.71	35.9 ± 6.08	0.37	0.80
	HRT	33.3 ± 1.66	33.5 ± 1.90	0.68	

Data are presented as mean ± standard error of the mean (SEM) or absolute numbers.
Abbreviations: LRT, low -intensity resistance training; HRT, high-intensity resistance training; BMI, body mass index; PBF, percent body fat.
[a] Within group comparison.
[b] Between groups comparison.
[c] Significant correlation ($p < 0/05$).

4. Discussion

Irisin is a newly defined myokine that increases energy expenditure by stimulating the expression of UCP1 and hence the browning of white adipose tissue (Medicine ACoS, 2009). A potential limitation of all studies on Irisin in humans is that the kinetics of circulating Irisin concentration following acute and chronic exercise is unknown (Scharhag-Rosenberger et al., 2014). Consequently, Irisin was proposed to mediate some of the health-promoting effects of physical activity (Hofmann et al., 2013). In the present study, serum Irisin level did not significantly change after the 8 weeks of LRT, Which was consistent with others. In another study, Scharhag-Rosenberger et al. concluded that serum Irisin concentration did not significantly change in RT after 6 months (Scharhag-Rosenberger et al., 2014). According to the similarity of body mass range of participants, between the present study and other researches in this context, lack of changes in serum Irisin levels is approved. Irisin is a product of FNDC5 expressed in skeletal muscle. Irisin plasma levels are associated with muscle mass (Huh et al., 2012; Stengel et al., 2013). However, it is important to highlight that our subjects were normal weight according to BMI. In addition, the total muscle mass might be too low in our subjects to detect differences in the levels of serum Irisin. Moreover, Stengel et al. reported that obese patients had higher circulating Irisin compared to normal weight and anorexic patients (Stengel et al., 2013). Obese subjects present higher muscle mass compared to subjects of normal weight, and this factor may explain the higher levels of Irisin in these subjects (Timmons et al., 2012). In addition, since Irisin has been shown to initiate the browning of white adipose tissue and thereby eliciting an additional energy dissipating effect (Boström et al., 2012; Wu et al., 2012), the existence of a reasonable amount of beige adipocytes would be crucial to mediate these effects. Hofman et al. observed no correlation between Irisin and activity parameters in anorexic patients (Hofmann et al., 2013). Timmons et al. reported that after exercise in a population of younger adults, they failed to detect a strong increase of the Irisin precursor, FNDC5, whereas only in a subgroup of older subjects, after exercise, an increase of FNDC5 mRNA expression was observed (Timmons et al., 2012). With respect to the age range of participant in this study, the results could underline the hypothesis that exercise-related effects on Irisin expression are associated with age. Raschke et al. noted that they did not observe significant effects on FNDC5 mRNA expression in muscle biopsies after eleven weeks of endurance and resistance training. Nonetheless, they observed the differentiation of white fat cells into brown fat cells in subjects. Because no adipose tissue biopsies were taken in the present study, it cannot be ruled out that a “browning” of white adipocytes

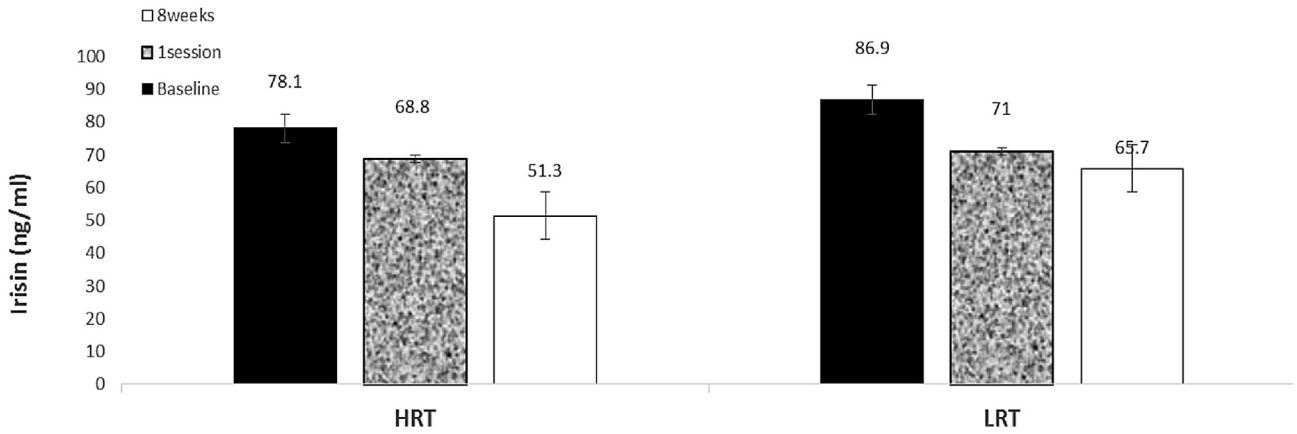

Fig. 1. Change in circulating Irisin of sedentary young women before and after 1 session and 8weeks of resistance training with high and low intensites. Data are shown as mean ± SE. P < 0.05.

Table 3
Irisin concentration (LRT: N = 11, HRT: N = 10) before and after 1 session of resistance training.

		Before (M ± SD)	After (M ± SD)	p-value[a]	p-value[b]
Irisin (ng/ml)	LRT	86.9 ± 39.0	71.0 ± 47.2	0.21	0.67
	HRT	78.1 ± 39.7	68.8 ± 31.1	0.35	

Data are presented as mean ± standard error of the mean (SEM) or absolute numbers.
Abbreviations: LRT, low -intensity resistance training; HRT, high-intensity resistance training.
*Significant correlation (p < 0/05).
[a] Within group comparison.
[b] Between groups comparison.

occurred despite no change in circulating Irisin (Hecksteden, 2014). The reason for different effects of chronic training on Irisin concentration may be explained by the study of Raschke et al. They suggested that the human FNDC5 gene differs from other species by a mutation in the start codon (ATA in humans and ATG in mice). This sequence, which may result in a lower translation efficiency, could explain difficulties in translating animal data to humans (Raschke et al., 2013). The findings from the present study are consistent with those reported in the literature. It was observed that the serum Irisin was acutely decreased after 8 weeks HRT. Moreover, Norheim et al. demonstrated that while both PGC1α and FNDC5 mRNA expressions increased in skeletal muscles in response to 12 weeks of training, the plasma concentration of Irisin was reduced (Norheim et al., 2014). Huh et al. also demonstrated reduced plasma level of Irisin after 8 weeks of intermittent sprint running (Huh et al., 2012). It has been suggested that the lack of PGC1α induction in some of the exercise studies may explain the conflicting results (Pekkala et al., 2013). In addition, the measurement method of Irisin could contribute to the lacking correlation of physical activity and circulating Irisin (Erickson, 2013). While these studies have similarities with our study, there are studies that obtained different results from ours (Aydin et al., 2013). Bostrom et al. showed increased levels of Irisin after 10 weeks of endurance training (Raschke et al., 2013; Erickson, 2013). Pekkala et al. did not find elevated Irisin concentration at different time points after a single heavy-exercise bout and 3 h after a low-intensity endurance exercise bout. Another study has also reported that acute strength training for up to 30 min did not increase serum levels of Irisin (Pekkala et al., 2013). Nonetheless, other investigations have reported opposing findings. Norheim et al. observed that the plasma concentration of Irisin acutely increased after 45 min ergometer cycling (~1.2-fold) and then decreased after 2 h rest (Norheim et al., 2014). Tsuchiya et al. determined circulating Irisin responses following a single bout of running at different intensities. Compared with pre-exercise levels, the Irisin concentrations rose at 6 h and 19 h after high-intensity exercise but significantly declined after low-intensity exercise (Tsuchiya et al., 2014). Daskalopoulou et al. found that Circulating Irisin levels acutely increased in response to exercise with a greater increase after maximal Workload (Daskalopoulou et al., 2014). According to different characteristics of the participants in our study, we can explain the

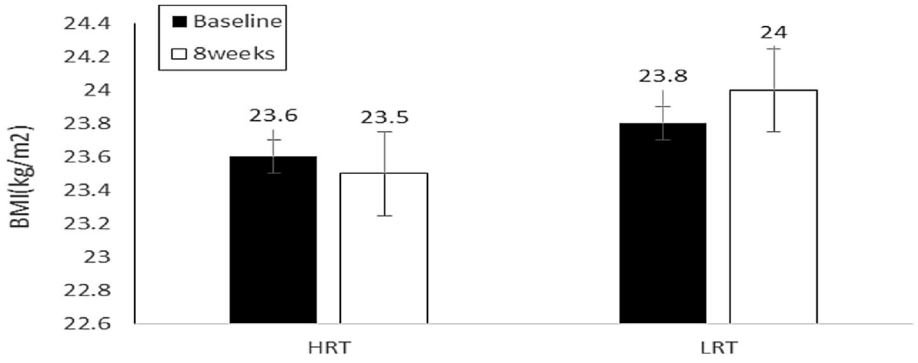

Fig. 2. Change in BMI in sedentary young women before and 8weeks of resistance training with high and low intensites. Data are shown as mean ± SE. P < 0.05. BMI = body mass index.

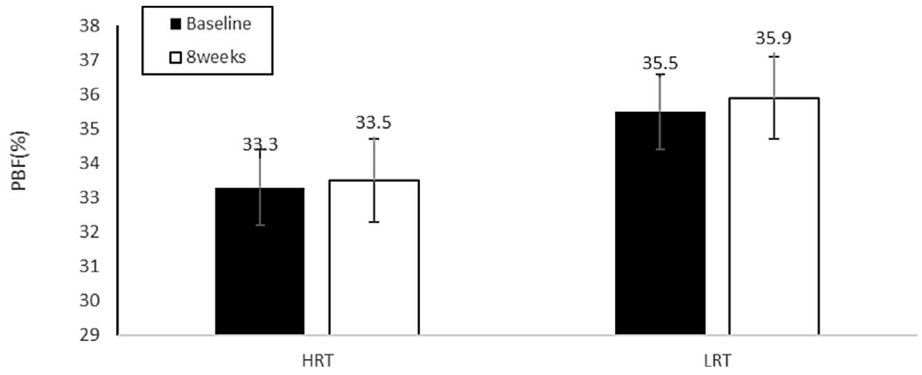

Fig. 3. Change in PBF in sedentary young women before and 8weeks of resistance training with high and low intensites. Data are shown as mean ± SE. $P < 0.05$. PBF = percent body fat.

unchanged levels of serum Irisin. Disparity in the results of the aforementioned studies may be due to individual differences, genetics, diet, differences in type of exercise, intensity and duration of exercise, physical condition of subjects, and the amount of muscle mass of participants in this study, which are all considered limitations of a study. Furthermore, in this study, we did not observe significant changes in body mass index and body fat percentages in both groups after 8 weeks. Dionne et al. investigated the age-related alteration in metabolic variables in response to a 6-month RT program in previously untrained women. For younger women, the RT program increased body weight due to an increase in FFM, and fat mass did not change significantly. On the other hand, older women lost fat mass while no change occurred in their body weight (Dionne et al., 2004). In another study, anthropometric measurements did not significantly change in response to resistance training (Hecksteden, 2014). In contrast to the majority of previous studies, the strength training program did not elicit changes in anthropometric (Dionne et al., 2004; Pratley et al., 1994; Poehlman et al., 2002; Kirk et al., 2009; Byrne and Wilmore, 2001). This might be attributable to the training stimulus. On the other hand, the lack of changes in a subject's body mass index can be interpreted as the Stable body mass index, which can result from simultaneously reducing body fat weight and increasing lean mass weight. In support of this possibility, our results showed that BMI and body fat percentages did not change significantly. It is possible to suggest that there has not been a significant change in lean mass, either.

Ethical consideration

Ethical issues (including plagiarism, informed consent, misconduct, data fabrication and/or falsification, double publication and/or submission, redundancy, etc.) have been completely observed by the authors.

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