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Metabolic cross-talk between skeletal muscle and adipose tissue in high-intensity interval training vs. moderate-intensity continuous training by regulation of PGC-1 α

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Abstract

Purpose An imbalance in the production of adipokines and myokines impairs the energy expenditure, increases adipocyte and develops metabolic pathologies. Physical exercise is able to regulate the secretion of myokines and adipokines. The present study considers the metabolic cross talk between skeletal muscle and adipose tissue in high-intensity interval training vs. moderate-intensity continuous training by regulation of PGC-1 α .

Methods A sample of 32 male Wistar rats (8 weeks old with mean weight 250 ± 55 g) were divided into four groups randomly: control of base (CO), control of 8 weeks (CO8w), moderate-intensity continuous training (MICT), and high-intensity interval training (HIIT). The rats were fed with standard chow diet. The CO group was killed at the start of the study and the CO8w group was kept alive for the same time as the experimental groups, but did not participate in any exercise. MICT and HIIT groups for 8 weeks were placed under the moderate-intensity continuous training (15–60 min, with speed of 15–30 m/min) and high-intensity interval training (8–4 intense period for 1 min, with speed of 28–55 m/min, with 3–7 slow-intensity period for 1 min, with a speed of 12–30 m/min) for 8 weeks, respectively. To measure the levels of serum irisin, nesfatin, and resistin the ELISA method was used and real-time PCR method was used to evaluate the relative expression of soleus PGC-1 α gene mRNA.

Results The levels of irisin and nesfatin significantly increased in the HIIT compared with control groups ($p=0.001$). Resistin values in both training groups showed a significant decrease compared to the control groups ($p=0.005$). The level of PGC-1 α gene expression in both HIIT and MICT groups was significantly increased in comparison with the control groups ($p=0.001$).

Discussion The results showed that HIIT and MICT increase the transcription of the PGC-1 α gene and possibly the increased expression of this gene after HIIT and MICT plays a central role in the secretion of skeletal muscle myokines and adipokines of adipose tissue.

Level of evidence No Level of evidence: Animal study.

Keywords High-intensity interval training · Moderate-intensity continuous training · Irisin · Nesfatin · Resistin · PGC-1 α

Introduction

The benefit of exercise is attributed to its anti-inflammatory effects that are achieved by reducing the visceral fat mass, or by inducing an anti-inflammatory environment with any modality of regular exercise [1, 2]. Such effects may be due

to muscle-stimulated peptides called myokines. Myokines have autocrine, paracrine, and endocrine effects. The skeletal muscle upon contraction, releases myokines in an endocrine manner, which has anti-inflammatory effects or special effects on other tissues, especially adipose tissue [1, 2]. Irisin is one such myokine that should be mentioned here [3]. The fibronectin type III domain-containing protein 5 (FNDC5) gene promotes the coding of the irisin protein in the skeletal muscle. Physical activity or peroxisome proliferator-activated receptor-gamma coactivator 1 alpha (PGC-1 α) induces expression of FNDC5 and secretion of irisin from the skeletal muscle in human and animal subjects [4]. The PGC-1 α belongs to a relatively large family of nuclear receptors that

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is associated with a wide range of transcription factors [5]. A coactivator is a protein or a set of proteins that increases the amount of gene expression by binding to an activator or transcription factor that has a DNA-binding domain. Studies have shown that PGC-1 α is increased in response to acute [6] and chronic [7, 8] exercises. This marker is able to modulate the metabolism of muscle and fat tissue through the irisin myokine.

Irisin is a newly identified myokine that is expressed from the skeletal muscle during exercise and promotes the white fat cells to change into brownish or white-brown or phenotypic forms similar to brown fat cells [9]. In human subjects, the plasma levels of irisin increase significantly after 10 weeks of regular endurance training. It is suggested that muscle irisin induced by physical activity is capable of treating metabolic disease, namely human obesity [10]. Several studies have shown that training protocols with high intensity are effective in increasing the amount of irisin in the human bloodstream [11, 12]. The recent discovery of the muscle hormone irisin [9] and its ability to modify adipose tissue metabolism, formed the background for our understanding of muscle–fat cross-talk and metabolic disorders [3].

The function and secretion of irisin as a novel molecular agent of adipose tissue browning as well as its activity can be regulated by adipokines. The adipokines have many physiological functions, including the regulation of energy metabolism [13]. White adipose tissue that exists in the subcutaneous, abdominal, inguinal, perineum, gonads, and pericardial area [14] is capable of storing energy as triglyceride, lipolysis, and adipokine secretion. The way in which adipose tissue secretes adipokines to produce positive and negative signals, and also the effect of the myokine irisin on white adipose tissue, can cause the adipocyte–myokine cycle. Hormones such as leptin, ghrelin, NUCB2/nesfatin-1 and irisin can be synthesized in order to keep the fat distribution in balance in the increased white adipose tissue. Among the many factors that are produced from adipose tissue [13], two adipokines, i.e., nesfatin-1 and resistin can induce positive and negative effects, respectively, for homeostasis, energy expenditure, and pathology.

Nesfatin-1 is a new adipokine that was discovered in 2006, initially attributed to appetite and weight control in rats [15]. Nesfatin-1 and irisin are involved in the regulation of energy homeostasis. Nesfatin-1 is expressed in human adipose tissue and tumor necrosis factor- α (TNF- α), interleukin 6 (IL-6), insulin, dexamethasone, and physical activities can increase the secretion of this adipokine [16]. It has been shown that nesfatin-1 regulates the inflammatory responses and cell apoptosis in rats [17]. Human studies have confirmed that this adipokine has a cardioprotective effect [18]. Studies on the effect of exercise on the nesfatin levels are limited and contradictory.

For example, some studies have shown that two types of exercise including one session of endurance training [19] and one session of aerobic exercise in elderly people [20] had an insignificant effect on the plasma levels of nesfatin. But other studies stated that 20 weeks of resistance training could significantly increase the level of plasma nesfatin-1 in adults [21]. The effect of exercise on irisin and nesfatin-1 hormones has been shown in the regulation of energy homeostasis [22]. Most studies considered separate reviews of these factors with different training modalities. Ahmadizad et al. considered the effect of 6 weeks of HIIT and MIT on levels of nesfatin in 30 inactive obese men. They showed that HIIT caused a significant increase in nesfatin-1 compared to the control group ($p < 0.05$). Finally, HIIT exercises increased the survival levels of nesfatin-1 after detraining [23].

In contrast to irisin and nesfatin-1, resistin is a member of the protein family found in inflammatory zone (FIZZ), belonging to the group of hormones associated with adipose tissue (adipokine) [24, 25]. In rodents, high plasma levels of resistin with a diet-induced obesity model were associated with insulin resistance increase [26]. The relationship between obesity and increased plasma resistin has been confirmed [24]. It has been shown that resistin plays a role in metabolism and physiology with inflammation [27], endothelial dysfunction [28], cardiomyocyte function [29], and cholesterol metabolism [30]. In skeletal muscle cells, chronic incubation with resistin reduced the consumption and metabolism of fatty acids by reducing the content of FAT/CD36 levels of cellular and acetyl-co-carboxylase levels [31]. Resistin also reduces glucose-stimulated insulin, its oxidation, and glycogen synthesis in an AMPK-dependent manner by altering the insulin receptor and Akt activity and reducing the displacement of glucose transporter type 4 (GLUT-4) [32]. All of this reflects the potential role of resistin in obesity and glucose homeostasis disorder in contrast to irisin and nesfatin-1, which as an adipokine expresses the effects at both the autocrine and endocrine levels. The goal of performing aerobic exercises and HIIT are to reduce and improve the metabolism of muscle and fat tissue. Hence, exercising can neutralize the adverse effects of the resistin adipokine. PGC-1 α regulates genes in response to nutritional and physiological conditions [33]. Physical activity by increasing the muscle PGC-1 α can modulate the muscle genes and adipose tissue. Several studies have examined the positive effects of various exercise training modalities on the increase of irisin myokine and nesfatin adipokine, and the reduction of resistin adipokine. Yet, no study has investigated the cross-talk between these markers with a focus on PGC-1 α . Thus, the aim of this study was to consider the metabolic cross talk between skeletal muscle and adipose tissue in high-intensity interval training vs. moderate-intensity continuous training by regulation of PGC-1 α .

Methods

An experimental laboratory study was conducted wherein male Wistar rats weighing 250–300 g were used (8 weeks age). The sample consisted of 32 male rats divided into main groups of control and training. The study protocol conformed to the Declaration of Helsinki and was approved by the Ethical Committee supervising procedures on experimental animals at Baqiyatallah University of Medical Sciences (Ethical cod#IR.BMSU.REC.1396.818). The experiment was conducted at the Baqiyatallah University of Medical Sciences. The animals were randomly grouped with a 12:12 h light cycle, temperature of 22 ± 2 °C, relative humidity of 55%. The rats were maintained under standard conditions and fed standard rat chow with water ad libitum. Prior to the experiment, they were randomly grouped and interventions were performed on them. The experiments were conducted in accordance to the Iranian Society for the Protection of Animals used for laboratory purposes. The site of the rats' holding and training was at the animal's house of the University of Medical Sciences, Baqiyatallah (AS). The animals were grouped and placed in cages made of transparent polyethylene with metal and doors, marked appropriately to tell them apart. Drinking water was supplied in special plastic containers placed on the cages' door and during the research; the rats were given ad libitum access to water and food. In each cage, four rats were kept. The rats were divided into two main groups of control and exercise training. The control group was divided into two subgroups of control (CO) and control group for 8 weeks (CO8w). The CO group was killed at the start of the study and the CO8w group was kept alive for the same period as the experimental groups, i.e., 8 weeks. They did not participate in any exercise program, but to create the same environmental conditions five times, they were immobilized on the treadmill for 10–15 min per session. The exercise group was divided into two groups: moderate-intensity continuous training (MICT) and high-intensity interval training (HIIT). Then, after about 48 h from the last training session and 12 h of fasting, the rats were anesthetized and surgically operated. Then, using a syringe, 5 cc of blood was taken from the heart of each rat and immediately transferred to the test tube. The soleus muscle tissue of the rats were removed and placed in liquid nitrogen. Then the tissue and serum were stored in a freezer at a temperature of -80 °C.

Table 1 Moderate-intensity continuous training program (with speed of 15–30 m/min, duration 15–60 min)

| Weeks | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 |
|----------------|----|----|----|----|----|----|----|----|
| Speed (m/min) | 15 | 20 | 20 | 25 | 25 | 30 | 30 | 30 |
| Duration (min) | 15 | 20 | 25 | 30 | 40 | 45 | 50 | 60 |

Exercise training protocol

The animals were trained for 8 weeks after 2 weeks of familiarization (6 sessions). The exercise intensity in the familiarization period was 5, 10, 15 m/min, with duration of 5, 10, 15 min. During the familiarization, rats that did not practice and resisted running was excluded from the exercise. In the training groups, warm-up was performed for 3 min at an intensity of 15–20 m/min and cool-down was done for 2 min at an intensity of 15–20 m/min. The MICT protocol started at speed of 15 m/min (for 15 min). The intensity and duration of training increased more and more so that the rats completed the MICT protocol at the end of eighth week at speed of 30 m/min (for 60 min) (Table 1). Also, the HIIT protocol increased incrementally (both set and speed). Each session after warm-up the rats performed the HIIT protocol with an intense interval followed by a slow interval (active rest) (respectively), to complete the session with the specified number of sets (Table 2). Both protocols performed, 5 sessions per week for 8 weeks. The full schedule of exercise protocols is mentioned in Tables 1 and 2.

The treadmill slope was zero degrees throughout the training. The basis for the intensity of exercise in this study was based on previous studies, which indicated that a speed of 30 m/min results in 70% of the maximum oxygen consumption in rats [34].

Biochemical measurement

For measurement of serum irisin, resistin and nesfatin-1, 5 cc of blood was extracted into a tube. After 15–20 min,

Table 2 High-intensity interval training program (8–4 intense periods for 1 min, with speed of 28–55 m/min, with 3–7 slow-intensity period for 1 min, with a speed of 12–30 m/min)

| Weeks | Intense interval | | Slow interval | |
|-------|------------------|---------------|---------------|---------------|
| | Set (1 min) | Speed (m/min) | Set (1 min) | Speed (m/min) |
| 1 | 4 | 28–30 | 3 | 12–15 |
| 2 | 5 | 30–32 | 4 | 12–15 |
| 3 | 5 | 32–35 | 4 | 12–15 |
| 4 | 6 | 35–40 | 5 | 15–17 |
| 5 | 6 | 41–45 | 5 | 17–20 |
| 6 | 7 | 46–50 | 6 | 20–25 |
| 7 | 7 | 46–50 | 6 | 20–25 |
| 8 | 8 | 50–55 | 7 | 25–30 |

the centrifuge machine was isolated for 15 min at 3000 rpm, it was kept at -20°C for up to the time of measurement in special vials. The serum levels of irisin and nesfatin-1 were measured by ELISA using commercial kits (Bioassay Technology Laboratory, China) with a sensitivity of 0.03 ng/ml for irisin and 16.23 ng/l for nesfatin-1. The serum levels of resistin were measured by ELISA using a commercial kit (Biovendor Research and Diagnostic Products, Czech Republic) with a sensitivity of 0.25 ng/ml.

Measurement mRNA of PGC-1 α gene

The total RNA of the muscle tissue samples was extracted using TRIzol (Invitrogen cat n: 15596-026, USA). The concentration and purity of the RNA obtained by spectrophotometer were evaluated. The cDNA was made using a special kit in two steps. The polymerase chain reaction (PCR) was performed using the SYBR[®] Green I PCR Master Mix kit. Each reaction was done twice. The primer design was extracted from the National Biotechnology Information Center (NCBI) database, and the primer design and control were done using preprimer, Primer3, and oligo online programs. The characteristics of the PGC-1 α gene primers were: F:5/-CACCAAACCCACAGAGAACAG-3/ and R:5/-GGTACTCTGGGGTCAGAG-3/. The 2- $\Delta\Delta\text{CT}$ method was used to evaluate the quantitative expression of the PGC-1 α gene. All analyses were performed separately for the sample groups.

$$\text{Relative fold change in gene expression} = 2^{-\Delta\Delta\text{CT}}$$

$$\Delta\text{CT} = \text{CT target gene} - \text{CT reference gene.}$$

$$\Delta\Delta\text{CT} = \Delta\text{CT test sample} - \Delta\text{CT control sample.}$$

Statistical analysis

Descriptive statistics were used for data categorization. One-way ANOVA was used to analyze the data and to compare the groups (more than two groups). To compare the differences between the groups, post hoc Tukey's test was used. The independent *t* test was used for comparison between groups in dual groups. SPSS Statistics v21 software was used to calculate the data and a statistically significant difference was found at $p < 0.05$.

Results

1. It was found that 8 weeks of training enhanced the plasma levels of irisin. The circulating levels of irisin were higher in the MICT and HIIT group than in the control groups after 8 weeks (Fig. 1). This increase was significant in the HIIT group.
2. The plasma levels of nesfatin-1 were enhanced after 8 weeks of HIIT. Since training may induce brown-

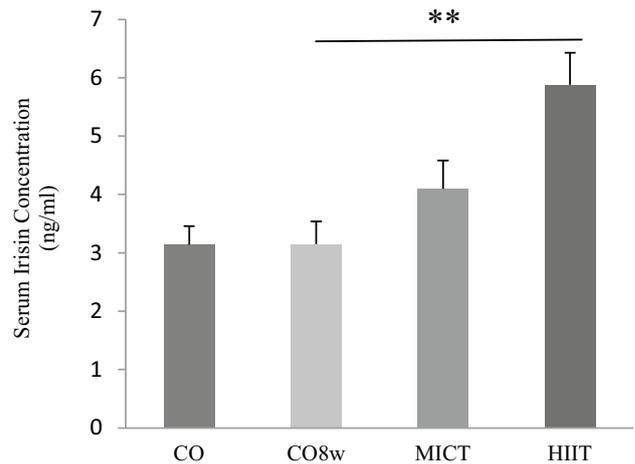


Fig. 1 Serum irisin concentrations in basic-control (CO), 8-week control (CO8w), moderate-intensity continuous training (MICT), and high-intensity interval training (HIIT) groups. The results are expressed as mean \pm SD. * $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$

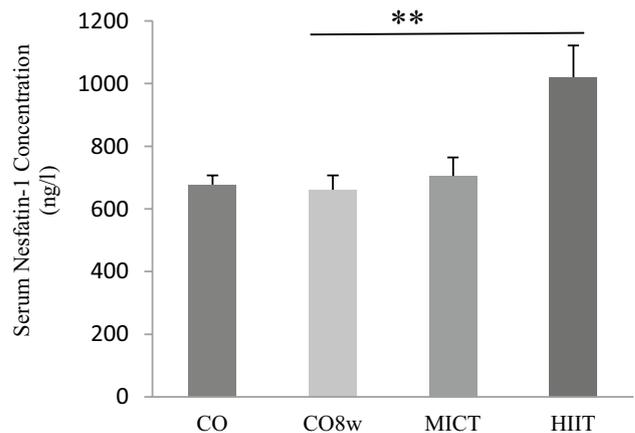


Fig. 2 Serum nesfatin-1 concentrations in basic-control (CO), 8-week control (CO8w), moderate-intensity continuous training (MICT), and high-intensity interval training (HIIT) groups. The results are expressed as mean \pm SD. * $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$

ing of subcutaneous fat in rodents, we investigated the effect of training on nesfatin-1 adipokine in the rats. The serum levels of nesfatin-1 were higher in the training groups compared with the control group after 8 weeks (Fig. 2). The levels of nesfatin-1 were not significantly enhanced in response to MICT training; however, in the HIIT group this increase was significant.

3. The plasma levels of resistin decreased after 8 weeks of HIIT. The levels of plasma resistin with HIIT and MICT exercise significantly decreased compared to the control group, this decrease was higher in the MICT group (Fig. 3).
4. The expression of PGC-1 α mRNA in the rat skeletal muscle was also investigated. It was found that the total

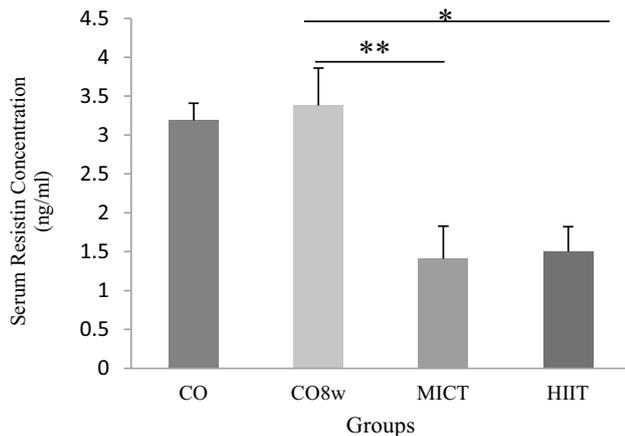


Fig. 3 Serum resistin concentrations in basic-control (CO), 8-week control (CO8w), moderate-intensity continuous training (MICT), and high-intensity interval training (HIIT) groups. The results are expressed as mean \pm SD. * $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$

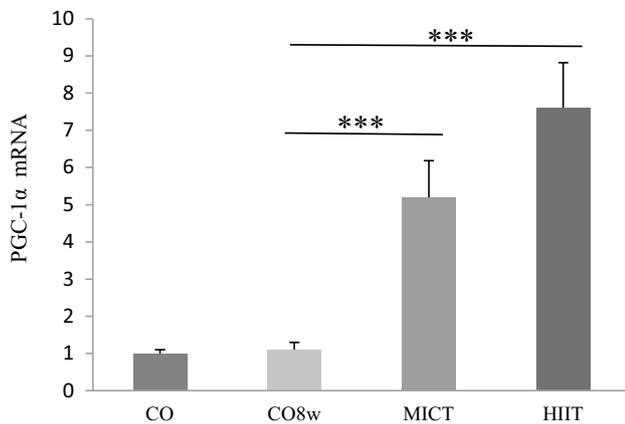


Fig. 4 The real-time PCR of skeletal muscle tissue PGC-1 α relative mRNA expression in basic-control (CO), 8-week control (CO8w), moderate-intensity continuous training (MICT), and high-intensity interval training (HIIT) groups. The results are expressed as mean \pm SD. * $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$

PGC-1 α mRNA is a constitutive expression in the skeletal muscle influenced by two modalities of MICT and HIIT exercises (Fig. 4). This data illustrates that mRNA levels of PGC-1 α gene in both MICT and HIIT exercises showed a significant increase compared to the control group. The increase was slightly higher in the group HIIT.

Discussion

The enhanced benefits of exercise are attributed to the increased energy consumption caused by the muscles' contraction, which consequently increases the metabolism in the muscle tissue and the adipose reserve, and thus through the molecular mechanisms can also have anti-inflammatory and protective effects. The purpose of this study was to consider the metabolic interrelationships and cross-talk of signals between the skeletal muscle and adipose tissue through two HIIT and MICT exercise modalities to regulate the expression of PGC-1 α . Physical exercise (especially chronic or with long duration) can enhance the expression of PGC-1 α [35]. In the present study, the levels of PGC-1 α gene in both HIIT and MICT groups were significantly higher than in the control group for 8 weeks (chronic exercise). Various studies have argued that an increased expression of muscle PGC-1 α defends weight loss, inflammation, oxidative stress, and muscle atrophy in the mice. In the current study, through the two training modalities, the increase in this gene showed protective effects in the whole body [36]. It has been shown that a higher expression of PGC-1 α in the Morin mice causes changes in the type of muscle fiber, increased fatty acid oxidation, mitochondrial biogenesis, and angiogenesis [37, 38]. This gene can have autocrine effects because it has been shown that increased expression in muscle PGC-1 α will improve metabolic parameters such as sensitivity and insulin signaling in the same muscle [36]. However, many studies have still not been able to determine how this gene has extensive systematic effects on the overall metabolism of the body. Bostrom et al. determined that this gene (PGC-1 α) could have systematic effects by modulating the muscle secretome [9]. Few studies have been conducted on the effects of different training modalities and the effects of exercise time on the expression of PGC-1 α gene in muscle tissue. The specific PGC-1 α (an initial factor in irisin secretion) increases after 2–3 h of exercise activity [4, 39, 40]. The expression of PGC-1 α increased with acute [6] and severe chronic exercise [8] (consistent with this study), which showed beneficial effects of this gene in Morin model rats [35]. In the present study too, the MICT and chronic HIIT exercise activity significantly increased the expression of this gene.

The contractile muscle secretes the myokines that engage the cross-talk tissues. PGC-1 α induces and produces new myokine irisin due to muscle contraction, which increases the energy consumption without increasing the food intake [9]. Bostrom et al. stated that chronic exercise increases the irisin levels in mice [9]. In the present study, it was found that physical activity increased the levels of irisin in both groups, HIIT and MICT, compared

to the control group, and was significant in the HIIT group. Bostrom et al. [9] showed a twofold significant increase of plasma irisin after 10 weeks of endurance training, whereas in contradiction with this study, Huh et al. and Pekkala et al. [12, 41] showed that there was no increase in irisin after 8 weeks of periodic interval training running and after 21 weeks of endurance and strength training, respectively. The difference in the findings of these studies and the present study can be attributed to the time difference and exercise modality. In relation to the time of exercise, Czarkowska et al. reported that one session of endurance training had no effect on serum levels of the rats' irisin [42]. In this study, two modalities of exercise were performed in chronic form that increased plasma irisin. In contradiction with this study, Fain et al. [43] reported that long-term exercise did not increase either the FNDC5 gene and its protein in skeletal muscle or the serum levels of irisin in healthy pigs. The difference in the findings could be attributed to the type of subject. But the significant increase in the irisin level of the HIIT group compared to the MICT group can be attributed to the greater depletion of cellular energy charge with intense interval training. Huh et al. [12] reported that the level of serum irisin increased after an acute speed training in an untrained human subject, while levels of irisin in subjects training with the same exercise were unchanged. The levels of irisin increase when the ATP level drops. But when the levels of ATP do not change, the amount of irisin remains unchanged. In their study, they expressed an increase in the production of irisin when the concentration of ATP in the muscles decreased. Therefore, the significant increase in the irisin group of the HIIT group can be attributed to the cellular homeostasis with respect to the energy charge and the amount of ATP [12]. It has also been stated in several studies that the high-intensity interval protocol is effective in increasing the amount of irisin in the human blood flow [4, 44]. FNDC5/irisin has been recently postulated as beneficial in the treatment of obesity and increasing energy expenditure. In addition to irisin, nesfatin-1 also plays an important role in regulation of energy homeostasis.

The cross-talk between the muscle tissue and adipose tissue plays a role in regulating the feedback mechanism to increase the PGC-1 α and irisin secretion [45]. Clinical studies showed that the level of serum irisin determined the body weight [46], insulin sensitivity [47], hepatic triglyceride [48], and urea nitrogen and creatinine [49], further proposing that irisin stimulated with PGC-1 α plays a decisive role in reducing the body weight and improving metabolic diseases through its effects on the adipose tissue [9]. The function of nesfatin is responsible for reduction in hunger and satiety, and therefore plays a role in reducing body fat and body weight [15]. The nesfatin-1 levels

are influenced by physical activity too. In this study, the levels of nesfatin-1 in the HIIT group showed a significant increase compared to the control group for 8 weeks, while the increase in nesfatin-1 in the MICT group was not significantly different from the control group for the same period of time. Mohebbi et al. [50] showed a decrease in plasma levels of nesfatin-1 and leptin in a special training session at an anaerobic threshold that remained at a low level for up to 45 min. Finally, they introduced this type of exercise to the anaerobic threshold as an appetite stimulant. The difference in their research findings with the present study is in the choice of the training modality [50]. In agreement with the present study, Ahmadizad et al. [23] examined the effect of 6 weeks of HIIT and MIT (3 days a week with 1 day of inactivity) on levels of nesfatin-1 in 30 obese men. They showed that nesfatin-1 had a significant increase only in the HIIT group compared to the control group ($p < 0.05$). After a period of detraining, the plasma levels of nesfatin-1 in the HIIT group did not return to the earlier training level. As stated, HIIT seems to have an anorectic effect compared to MIT [23]. In this study, the increase of nesfatin-1 and the increase of irisin with PGC-1 α intervention may also be effective in increasing the brown adipose tissue [51]. However, unlike irisin and nesfatin-1, resistin is able to increase the risk of metabolic pathology.

In contrast to the role of PGC-1 α , resistin in the muscle tissue reduces the glucose-induced insulin, its oxidation, and AMPK-dependent glycogen synthesis by altering the insulin receptor and Akt activity and decreasing the displacement of GLUT4 [52]. All of this reflects the potential role of resistin in obesity and glucose homeostasis disorders, for which physical exercise is able to modify the plasma levels of this adipokine. In this study, the plasma levels of resistin with HIIT and MICT significantly decreased compared to the control group. This decrease was higher in MICT group. Studies on the effect of physical exercise on levels of resistin are limited. Contrary to the current study, Giannopoulou et al. stated that changes in the levels of resistin and insulin resistance were not observed after 14 weeks of aerobic training [53]. The lack or low decreasing level of resistin in aerobic exercise groups (low intensity) can be due to the lower weight loss attained by these exercises, since in the absence of weight loss, exercise cannot improve the resistin profile [54]. In line with the results of this study, Jones et al. showed that increasing the duration of aerobic exercise can result in variations of resistin levels. After 8 months of aerobic training, there was a significant reduction in serum resistin and no change in the insulin resistance in obese adolescents [55]. Prestes et al. reported a significant reduction in serum resistin with 16 weeks of resistance training [56]. Research concerned with the evaluation of HIIT exercise in relation to changes in resistin levels is limited. However, based on the ability of these exercises (HIIT) to reduce body weight

due to the training system and the widespread metabolism change, it is expected that a reduction in resistin levels will be noticeable.

This study was limited by the amount of food consumed as well as the control of genetic factors with other epigenetic changes that could affect the results of the research. These variables were outside the researcher's control.

The effects of physical exercise on the expression of the PGC-1 α gene in terms of improved performance and improved pathological conditions is evaluated [57]. Increasing the expression of this gene in muscle tissue with irisin upregulation can have endocrine effects on adipose tissue and adipokines as well. The function of some adipokines is consistent with myokines that is to enhance the protective effects of exercise. As a result, in consideration of pathological damage and the development of therapeutic approaches, attention should be given to metabolic interrelationships and the cross-talk of signals between muscle tissue and adipose tissue. One of the important points in this study was that the positive markers (PGC-1 α , irisin, and nesfatin-1) affecting pathological conditions and metabolism showed a greater and significant increase in the HIIT group, while the negative marker (resistin) affecting the pathological conditions and body metabolism showed a significant decrease in the MICT group.

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Compliance with ethical standards

Conflict of interest The authors state that there is no conflict of interests in the present research study.

Ethical approval The study protocol conformed to the Declaration of Helsinki and was approved by the Ethical Committee supervising procedures on experimental animals at Baqiyatallah University of Medical Sciences (Ethical cod#IR.BMSU.REC.1396.818).

Informed consent Informed consent was obtained from all individual participants included in the study.

References

- Pedersen BK (2011) Muscles and their myokines. *J Exp Biol* 214(2):337–346
- Pedersen BK (2011) Exercise-induced myokines and their role in chronic diseases. *Brain Behav Immun* 25(5):811–816
- Pedersen BK, Febbraio MA (2012) Muscles, exercise and obesity: skeletal muscle as a secretory organ. *Nat Rev Endocrinol* 8(8):457–465
- Norheim F, Langleite TM, Hjorth M, Holen T, Kielland A, Stadheim HK et al (2014) The effects of acute and chronic exercise on PGC-1 α , irisin and browning of subcutaneous adipose tissue in humans. *FEBS J* 281(3):739–749
- Liang H, Ward WF (2006) PGC-1 α : a key regulator of energy metabolism. *Adv Physiol Educ* 30(4):145–151
- Pilegaard H, Saltin B, Neuffer PD (2003) Exercise induces transient transcriptional activation of the PGC-1 α gene in human skeletal muscle. *J Physiol* 546(3):851–858
- Ruas JL, White JP, Rao RR, Kleiner S, Brannan KT, Harrison BC et al (2012) A PGC-1 α isoform induced by resistance training regulates skeletal muscle hypertrophy. *Cell* 151(6):1319–1331
- Short KR, Vittone JL, Bigelow ML, Proctor DN, Rizza RA, Coenen-Schimke JM et al (2003) Impact of aerobic exercise training on age-related changes in insulin sensitivity and muscle oxidative capacity. *Diabetes* 52(8):1888–1896
- Boström P, Wu J, Jedrychowski MP, Korde A, Ye L, Lo JC et al (2012) A PGC1- α -dependent myokine that drives brown-fat-like development of white fat and thermogenesis. *Nature* 481(7382):463–468
- Wada K, Nakajima A, Blumberg RS (2001) PPAR γ and inflammatory bowel disease: a new therapeutic target for ulcerative colitis and Crohn's disease. *Trends Mol Med* 7(8):329–331
- Boström PA, Fernández-Real JM, Mantzoros C (2014) Irisin in humans: recent advances and questions for future research. *Metab Clin Exp* 63(2):178–180
- Huh JY, Panagiotou G, Mougios V, Brinkoetter M, Vamvini MT, Schneider BE et al (2012) FNDC5 and irisin in humans: I. Predictors of circulating concentrations in serum and plasma and II. mRNA expression and circulating concentrations in response to weight loss and exercise. *Metabolism* 61(12):1725–1738
- Rodríguez A, Ezquerro S, Méndez-Giménez L, Becerril S, Frühbeck G (2015) Revisiting the adipocyte: a model for integration of cytokine signaling in the regulation of energy metabolism. *Am J Physiol Endocrinol Metab* 309(8):E691–E714
- Cinti S (2012) The adipose organ at a glance. *Dis Models Mech* 5(5):588–594
- Oh S, Shimizu H, Satoh T, Okada S, Adachi S, Inoue K et al (2006) Identification of nesfatin-1 as a satiety molecule in the hypothalamus. *Nature* 443(7112):709–712
- Ramanjaneya M, Chen J, Brown JE, Tripathi G, Hallschmid M, Patel S et al (2010) Identification of nesfatin-1 in human and murine adipose tissue: a novel depot-specific adipokine with increased levels in obesity. *Endocrinology* 151(7):3169–3180
- Tang C-H, Fu X-J, Xu X-L, Wei X-J, Pan H-S (2012) The anti-inflammatory and anti-apoptotic effects of nesfatin-1 in the traumatic rat brain. *Peptides* 36(1):39–45
- Angelone T, Filice E, Pasqua T, Amodio N, Galluccio M, Montesanti G et al (2013) Nesfatin-1 as a novel cardiac peptide: identification, functional characterization, and protection against ischemia/reperfusion injury. *Cell Mol Life Sci* 70(3):495–509
- Ghanbari-Niaki A, Kraemer RR, Soltani R (2010) Plasma nesfatin-1 and glucoregulatory hormone responses to two different anaerobic exercise sessions. *Eur J Appl Physiol* 110(4):863–868
- Bashiri J, Gholami F, Rahbaran A, Tarmahi V (2012) Effect of single bout of aerobic exercise on serum nesfatin-1 levels in non-athlete elderly men. *Med J Tabriz Univ Med Sci* 34(4):25–30
- Tavassoli H, Tofghi A, Hedayati M (2014) Appetite and exercise influence of 12 weeks of circuit resistance training on the nesfatin-1 to acylated ghrelin ratio of plasma in overweight adolescents. *Iran J Endocrinol Metab* 15(6):519–526
- Bajer B, Vlcek M, Galusova A, Imrich R, Penesova A (2015) Exercise associated hormonal signals as powerful determinants of an effective fat mass loss. *Endocr Regul* 49(3):151–163
- Ahmadizad S, Avansar AS, Ebrahim K, Avandi M, Ghasemikaram M (2015) The effects of short-term high-intensity interval training vs. moderate-intensity continuous training on plasma levels of nesfatin-1 and inflammatory markers. *Horm Mol Biol Clin Investig* 21(3):165–173

24. Lee SE, Kim H-S (2012) Human resistin in cardiovascular disease. *J Smooth Muscle Res* 48(1):27–35
25. Schwartz DR, Lazar MA (2011) Human resistin: found in translation from mouse to man. *Trends Endocrinol Metab* 22(7):259–265
26. Stepan CM, Bailey ST, Bhat S, Brown EJ, Banerjee RR, Wright CM et al (2001) The hormone resistin links obesity to diabetes. *Nature* 409(6818):307–312
27. Aquilante CL, Kosmiski LA, Knutsen SD, Zineh I (2008) Relationship between plasma resistin concentrations, inflammatory chemokines, and components of the metabolic syndrome in adults. *Metabolism* 57(4):494–501
28. Ntaios G, Gatselis NK, Makaritsis K, Dalekos GN (2013) Adipokines as mediators of endothelial function and atherosclerosis. *Atherosclerosis* 227(2):216–221
29. Kim M, kyun Oh J, Sakata S, Liang I, Park W, Hajjar RJ et al (2008) Role of resistin in cardiac contractility and hypertrophy. *J Mol Cell Cardiol* 45(2):270–280
30. Melone M, Wilsie L, Palyha O, Strack A, Rashid S (2012) Discovery of a new role of human resistin in hepatocyte low-density lipoprotein receptor suppression mediated in part by proprotein convertase subtilisin/kexin type 9. *J Am Coll Cardiol* 59(19):1697–1705
31. Palanivel R, Sweeney G (2005) Regulation of fatty acid uptake and metabolism in L6 skeletal muscle cells by resistin. *FEBS Lett* 579(22):5049–5054
32. Palanivel R, Maida A, Liu Y, Sweeney G (2006) Regulation of insulin signalling, glucose uptake and metabolism in rat skeletal muscle cells upon prolonged exposure to resistin. *Diabetologia* 49(1):183–190
33. Finck BN, Kelly DP (2006) PGC-1 coactivators: inducible regulators of energy metabolism in health and disease. *J Clin Invest* 116(3):615
34. Ghafari Homadini S, Asad MR, Bazgir B, Rahimi M (2017) Effects of high intensity interval training and moderate-intensity continuous training on VEGF gene expression in visceral and subcutaneous adipose tissues of male wistar rats. *Iran J Endocrinol Metab* 19(3):170–176
35. Handschin C, Spiegelman BM (2008) The role of exercise and PGC1 α in inflammation and chronic disease. *Nature* 454(7203):463–469
36. Wenz T, Rossi SG, Rotundo RL, Spiegelman BM, Moraes CT (2009) Increased muscle PGC-1 α expression protects from sarcopenia and metabolic disease during aging. *Proc Natl Acad Sci* 106(48):20405–20410
37. Lin J, Wu H, Tarr PT, Zhang C-Y, Wu Z, Boss O et al (2002) Transcriptional co-activator PGC-1 α drives the formation of slow-twitch muscle fibres. *Nature* 418(6899):797–801
38. Lin J, Handschin C, Spiegelman BM (2005) Metabolic control through the PGC-1 family of transcription coactivators. *Cell Metab* 1(6):361–370
39. Anastasilakis AD, Polyzos SA, Saridakis ZG, Kynigopoulos G, Skouvaklidou EC, Molyvas D et al (2014) Circulating irisin in healthy, young individuals: day-night rhythm, effects of food intake and exercise, and associations with gender, physical activity, diet, and body composition. *J Clin Endocrinol Metab* 99(9):3247–3255
40. Daskalopoulou SS, Cooke AB, Gomez Y-H, Mutter AF, Filippaios A, Mesfum ET et al (2014) Plasma irisin levels progressively increase in response to increasing exercise workloads in young, healthy, active subjects. *Eur J Endocrinol* 171(3):343–352
41. Pekkala S, Wiklund PK, Hulmi JJ, Ahtiainen JP, Horttanainen M, Pöllänen E et al (2013) Are skeletal muscle FNDC5 gene expression and irisin release regulated by exercise and related to health? *J Physiol* 591(21):5393–5400
42. Czarkowska-Paczek B, Zendzian-Piotrowska M, Gala K, Sobol M, Paczek L (2014) One session of exercise or endurance training does not influence serum levels of irisin in rats. *J Physiol Pharmacol* 65(3):449–454
43. Fain JN, Company JM, Booth FW, Laughlin MH, Padilla J, Jenkins NT et al (2013) Exercise training does not increase muscle FNDC5 protein or mRNA expression in pigs. *Metabolism* 62(10):1503–1511
44. Jedrychowski MP, Wrann CD, Paulo JA, Gerber KK, Szpyt J, Robinson MM et al (2015) Detection and quantitation of circulating human irisin by tandem mass spectrometry. *Cell Metab* 22(4):734–740
45. Roca-Rivada A, Castela C, Senin LL, Landrove MO, Baltar J, Crujeiras AB et al (2013) FNDC5/irisin is not only a myokine but also an adipokine. *PLoS One* 8(4):e60563
46. Crujeiras AB, Pardo M, Arturo RR, Santiago NC, Zulet M, Martínez JA et al (2014) Longitudinal variation of circulating irisin after an energy restriction-induced weight loss and following weight regain in obese men and women. *Am J Hum Biol* 26(2):198–207
47. Sesti G, Andreozzi F, Fiorentino T, Mannino G, Sciacqua A, Marini M et al (2014) High circulating irisin levels are associated with insulin resistance and vascular atherosclerosis in a cohort of nondiabetic adult subjects. *Acta Diabetol* 51(5):705–713
48. Zhang H-J, Zhang X-F, Ma Z-M, Pan L-L, Chen Z, Han H-W et al (2013) Irisin is inversely associated with intrahepatic triglyceride contents in obese adults. *J Hepatol* 59(3):557–562
49. Wen M-S, Wang C-Y, Lin S-L, Hung K-C (2013) Decrease in irisin in patients with chronic kidney disease. *PLoS One* 8(5):e64025
50. Mohebbi H, Nourshahi M, Ghasemikaram M, Safarimosavi S (2015) Effects of exercise at individual anaerobic threshold and maximal fat oxidation intensities on plasma levels of nesfatin-1 and metabolic health biomarkers. *J Physiol Biochem* 71(1):79–88
51. Wang Y, Li Z, Zhang X, Xiang X, Li Y, Mulholland MW et al (2016) Nesfatin-1 promotes brown adipocyte phenotype. *Sci Rep* 6:34747
52. Jørgensen SB, Honeyman J, Oakhill JS, Fazakerley D, Stöckli J, Kemp BE et al (2009) Oligomeric resistin impairs insulin and AICAR-stimulated glucose uptake in mouse skeletal muscle by inhibiting GLUT4 translocation. *Am J Physiol Endocrinol Metab* 297(1):E57–E66
53. Giannopoulou I, Fernhall B, Carhart R, Weinstock RS, Baynard T, Figueroa A et al (2005) Effects of diet and/or exercise on the adipocytokine and inflammatory cytokine levels of postmenopausal women with type 2 diabetes. *Metabolism* 54(7):866–875
54. Kelly AS, Steinberger J, Olson TP, Dengel DR (2007) In the absence of weight loss, exercise training does not improve adipokines or oxidative stress in overweight children. *Metabolism* 56(7):1005–1009
55. Jones TE, Basilio J, Brophy P, McCammon M, Hickner R (2009) Long-term exercise training in overweight adolescents improves plasma peptide Y γ and resistin. *Obesity* 17(6):1189–1195
56. Prestes J, Shiguemoto G, Botero JP, Frollini A, Dias R, Leite R et al (2009) Effects of resistance training on resistin, leptin, cytokines, and muscle force in elderly post-menopausal women. *J Sports Sci* 27(14):1607–1615
57. Shirvani H, Aslani J (2017) The effects of high-intensity interval training vs. moderate-intensity continuous training on serum irisin and expression of skeletal muscle PGC-1 α gene in male rats. *Tehran Univ Med J TUMS Publ* 75(7):513–520