Journal of Clinical and Nursing Research, 2024, Volume 8, Issue 8
http://ojs.bbwpublisher.com/index.php/JCNR
Online ISSN: 2208-3693
Print ISSN: 2208-3685

Effects of High-Intensity Intermittent Training on Metabolic Parameters and Irisin Levels in High-Fat-Fed Rats

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Abstract: *Objective:* To investigate the effects of high-intensity intermittent training (HIIT) on preventing significant weight gain and provide scientific theoretical support and practical guidance for reducing the occurrence of obesity. *Methods:* Twenty-four Sprague-Dawley rats were randomly divided into four groups: the control sedentary group (CS), the high-fat sedentary group (HS), the high-fat continuous exercise group (HE), and the high-fat intermittent exercise group (HI). The HE and HI groups underwent five days of continuous low-intensity exercise and eight weeks of high-intensity intermittent exercise. Weekly monitoring included measurements of food intake and body weight. An automatic biochemical analyzer was used to assess blood lipid and glucose levels, while ELISA kits measured serum insulin and irisin content. H&E staining was used to observe adipocyte size. *Results:* In the HS group, body weight, blood lipid levels, blood glucose levels, and adipocyte size significantly increased, while the QUICKI index decreased. In the HI group, body weight, blood lipid levels, blood glucose levels, and adipocyte size decreased, and the QUICKI index increased. The effects of high-intensity intermittent exercise were superior to those of continuous low-intensity exercise. In the HI group, serum irisin levels did not change significantly after exercise, while in the HE group, there was a slight upward trend in irisin levels. *Conclusion:* A high-fat diet induced abnormal metabolism in rats. HIIT effectively prevents metabolic abnormalities induced by a high-fat diet, and its effects are more pronounced than those of low-intensity exercise. HIIT stimulates the secretion of blood irisin, affecting secretion levels, and may represent a novel mechanism for maintaining metabolic homeostasis. This has important implications for controlling significant weight gain.

Keywords: High intensity interval training; Rats; Metabolic characterization; Irisin

Onlinet publication: August 26, 2024

1. Introduction

As changes occur in living environments, diets, and lifestyles, the incidence of obesity and related metabolic diseases is increasing, posing significant threats to health and quality of life. Effectively preventing obesity and reducing risk factors for chronic diseases are key objectives in the prevention of chronic metabolic diseases. These issues are crucial challenges in modern preventive medicine and exercise science.

High-intensity intermittent training (HIIT) offers unique advantages for the early treatment and prevention of metabolic diseases. This type of exercise is time-efficient, yields quick results, and can improve cardiovascular fitness, enhance glucolipid metabolism, and increase oxidative stress. It plays an important role in the intervention of chronic diseases such as cardiovascular diseases and diabetes. Currently, there are few reports on the effects of HIIT on obesity prevention in the context of a high-fat diet and its impact on blood irisin levels [1].

Therefore, this research uses HIIT to intervene in rats fed a high-fat diet, with constant low-intensity exercise as a control. The study analyzes the effects of different exercises on rat metabolism, related indices, and blood irisin levels. It discusses the impact of HIIT on weight control in rats, providing a reference for obesity prevention, weight loss, the formulation of mass fitness exercise prescriptions, and the prevention and treatment of metabolic diseases.

2. Materials and methods

2.1. Experimental animals

The study used 28 specific-pathogen-free (SPF) male Sprague-Dawley (SD) rats, aged 6 weeks and weighing 175.36 ± 10.25 g, purchased from the Southern Medical University Animal Center (license SCX (Guangdong) 2016-0012). Regular feed and high-fat feed for SD rats were provided by the Medical Experimental Center of Guangdong Province. The regular feed was a national standard rodent dry feed. The high-fat feed consisted of 20% sucrose, 15% lard, 1.2% cholesterol, 0.2% sodium bile acid, 10% casein, 0.6% calcium hydrogen phosphate, 0.4% powder, 0.4% premix, and 52.2% feed. The mass ratio of the feed was 19% protein, 18.5% fat, and 50.5% carbohydrates; the heat ratio was 17.5% protein, 37% fat, and 45.5% carbohydrates.

2.2. Obesity model rats

Upon purchase, the rats were housed in cages with four rats per cage and allowed to adapt for one week. They were then randomly divided into the normal control group (n = 7), which was fed regular feed, and the obesity model group (n = 21), which was fed a high-fat diet. The rats had free access to food and water. They were kept under a controlled circadian rhythm with 12 hours of light and 12 hours of darkness, at a temperature of 21°C to 25°C and relative humidity of 55.6% ± 4%.

Daily observations included the rats' mental state, activity, fur color, and diet. The bedding was changed every three days, and the cages were cleaned and disinfected. Food intake was weighed daily, and body weight and length were measured every two weeks. After eight weeks of continuous feeding, five rats were randomly selected from the control group to establish the obesity model. Fifteen rats were randomly selected for blood sampling, and their blood lipid levels were measured. Rat body weight and BMI were used to evaluate the obesity model.

2.3. Animals grouping and training program

Successfully modeled rats were randomly divided into four groups, each with seven rats: the control sedentary group (CS), the high-fat sedentary group (HS), the high-fat continuous exercise group (HE), and the high-fat intermittent exercise group (HI).

2.4. Animal sampling

All experimental rats were fasted overnight (12 hours). For the exercise groups, fasting began 12 hours after the last exercise session. The next morning, blood was collected from the tail to measure blood glucose and

insulin levels. The rats were anesthetized by intraperitoneal injection of 10% chloral hydrate (100 g/0.3 mL). Body weight and length were measured, and the rats were fixed for sample collection. Blood samples were collected from the abdominal aorta, and whole blood was centrifuged (4°C, 3000 rpm) to obtain serum. Adipose tissues from the renal area, epididymis, subscapular, and inguinal regions were rapidly separated, weighed, and recorded. The tissues were then placed in liquid nitrogen using sterile foil and moved to a -80°C freezer for cryopreservation and slicing.

3. Results

3.1. Establishment of the rat obesity model

Body weight is the most direct indicator of obesity in rats, and Lee's index is an effective measure of obesity in adult rats. After 8 weeks of diet feeding, the average body weight of rats in the model group was significantly higher than in the control group. **Table 1** shows that the average weight of rats fed a normal diet was 461.73 ± 46.81 g, while rats fed a high-fat diet had an average weight of 578.13 ± 51.64 g, which is 20% higher than the control group rats [2]. In addition, the levels of TC, TG, and LDL-C (**Table 2**) in the model group were significantly higher than in the control group, with a very significant difference ($P < 0.01$). Based on the changes in body weight and blood lipids between the high-fat diet group and the normal diet group, it was confirmed that the rat obesity model was successfully established [3].

Table 1. Changes in body weight, body length, and Lee's index of rats after 8 weeks

Group	*n*	Weight (g)	Body length (cm)	Lee's index (g/cm)
Normal control group	5	464.62 ± 29.78	25.75 ± 0.45	300.72 ± 7.62
Obesity model group	15	577.20 ± 31.35	26.28 ± 0.64	316.93 ± 8.74

Table 2. Changes in lipid levels after successful modeling

Group	*n*	TC	TG	HDL-C	LDL-C
Normal control group	5	1.31 ± 0.33	1.37 ± 0.56	0.46 ± 0.16	0.68 ± 0.28
Obesity model group	15	2.93 ± 0.58	2.19 ± 0.47	0.38 ± 0.12	2.25 ± 0.46

3.2. High-intensity interval training improved the metabolic profile of rats

3.2.1. Comparison of food intake and body weight of rats

Table 3 shows that each rat's food intake remained relatively stable as they grew, with no significant differences in food intake between groups during the training period.

Table 3. Changes in food intake of rats in each group during training

Group	Week 1	Week 2	Week 3	Week 4	Week 5	Week 6	Week 7	Week 8
CS	22.12 ± 1.39	23.12 ± 1.38	23.78 ± 1.06	23.78 ± 1.05	23.42 ± 1.38	22.95 ± 2.58	22.62 ± 2.00	23.28 ± 1.44
HS	22.67 ± 1.08	23.12 ± 1.13	22.62 ± 1.58	22.95 ± 1.10	23.12 ± 0.94	23.28 ± 1.31	23.28 ± 1.28	22.95 ± 1.68
HE	22.67 ± 1.08	23.01 ± 1.18	23.17 ± 1.40	22.82 ± 0.61	21.44 ± 1.09	21.61 ± 1.00	21.62 ± 1.52	21.35 ± 1.25
HI	21.34 ± 1.21	22.35 ± 0.75	22.67 ± 0.56	21.65 ± 0.92	21.94 ± 1.58	22.01 ± 1.26	22.62 ± 1.41	22.52 ± 2.33

Figure 1 shows that rats in Groups CS and HS exhibited a gradual increase in weight from the first to the eighth week. In contrast, rats in Groups HE and HI experienced weight loss starting from the third week as the training cycle progressed, with Group HI showing a more pronounced decline than Group HE. As shown in **Table 4**, there was no significant statistical difference in the weight gain of rats in each group during the first three weeks. By the fourth week, rats in Group CS had significantly higher weight gain than those in groups HE and HI ($P < 0.05$), and weight gain in Group HS was significantly higher than in Group HI ($P < 0.05$). Weight gain in Group CS was lower than in Group HE ($P < 0.05$).

In the fifth week, Groups HE and HI experienced negative weight growth, showing a significant statistical difference compared to Groups CS and HS ($P < 0.01$). In the sixth week, weight gain in Groups CS and HS was significantly higher than in Groups HE and HI, but weight gain in Group CS was significantly higher than in Group HS ($P < 0.01$). Groups HE and HI continued to lose weight, with Group HI losing more weight than Group HE, and the weight loss between the two groups was significantly different ($P < 0.01$).

In the seventh week, weight gain in Groups CS and HS was significantly higher than in Groups HE and HI ($P < 0.01$), with Group CS showing slightly higher weight gain than Group HS ($P < 0.05$). Both groups HE and HI experienced negative weight growth. In the eighth week, weight gain in Groups CS and HS remained significantly higher than in Groups HE and HI ($P < 0.01$), with Group CS showing significantly higher weight gain than Group HS ($P < 0.01$). Rats in Groups HE and HI continued to lose weight, with Group HI experiencing more pronounced weight loss than Group HE ($P < 0.01$).

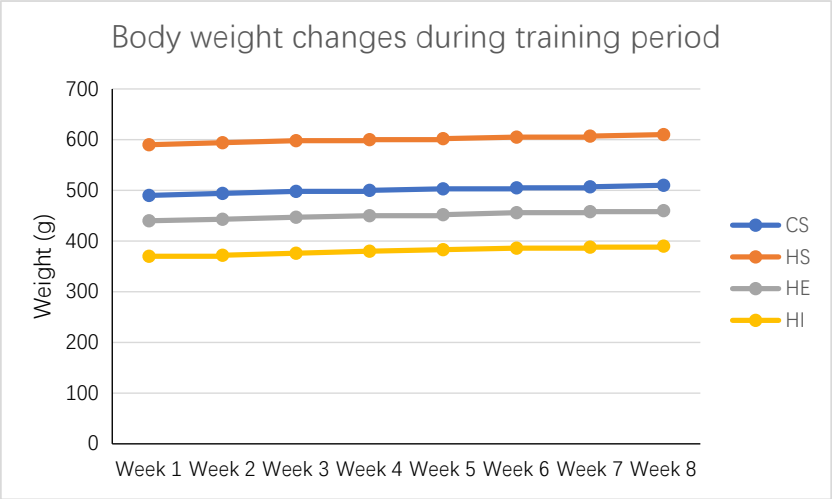

Figure 1. Changes in body weight of rats during the training period

Table 4. Changes in weight gain of rats in each group during training

Group	1st	2nd	3rd	4th	5th	6th	7th
CS	11.83 ± 11.53	18.10 ± 18.55	30.98 ± 24.34†	24.67 ± 9.91††	18.63 ± 4.84$^{\#\#\dagger\dagger}$	90.63 ± 21.24$^{\#\dagger\dagger}$	108.03 ± 28.70$^{\#\#\dagger\dagger}$
HS	11.83 ± 11.53	18.10 ± 18.55	28.14 ± 20.38	19.50 ± 7.61††	9.00 ± 6.10**††	58.57 ± 22.04*††	62.81 ± 22.95**††
HE	34.86 ± 35.41	9.93 ± 10.02	4.08 ± 14.61*	-11.46 ± 5.80$^{\# \#}$	3.19 ± 6.16**$^{\#\#}$	23.07 ± 17.69**$^{\#\#}$	-29.48 ± 27.17**$^{\#\#}$
HI	10.61 ± 14.67	5.64 ± 16.99	0.55 ± 20.82*$^{\#}$	-11.46 ± 5.80**$^{\# \#}$	16.06 ± 4.61**$^{\#\#\dagger\dagger}$	-40.63 ± 21.46**$^{\#\#}$	-63.73 ± 21.83**$^{\#\#\dagger}$

Note: Weight increase each week is calculated as the difference in weight from the previous week; * indicates $P < 0.05$ compared with Group CS; ** indicates $P < 0.01$ compared with Group CS; $^{\#}$ indicates $P < 0.05$ compared with Group HS; $^{\#\#}$ indicates $P < 0.01$ compared with Group CS; † indicates $P < 0.05$ compared with Group HE; †† indicates $P < 0.01$ compared with Group HE.

3.2.2. Fat weight of rats with H&E staining observations

As shown in **Figure 2**, the epididymal fat pad weight ($P < 0.05$), perirenal fat ($P < 0.01$), inguinal fat ($P < 0.05$), and total adipose tissue weight ($P < 0.01$) were significantly higher in Group HS than in Group HI. The fat pad weight (renal and groin fat) in Group HE was significantly lower than in Groups CS and HI ($P < 0.05$). There was no significant statistical difference in fat pad weight between Groups HE and HI.

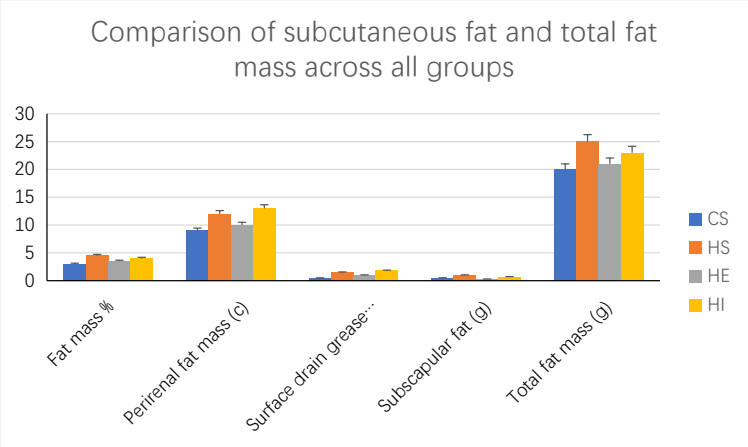

Figure 2. Comparison of subcutaneous and total fat mass across rat groups

Figures 3 and **4** illustrate that in the H&E staining of inguinal fat, Groups CS and HS had fewer but larger adipocytes (significantly larger than those in Group HI, $P < 0.01$), with large intracellular lipid droplets and indistinct cell walls, showing signs of fusion at the boundary intersections. In contrast, adipocytes in Groups HE and HI were smaller (much smaller than in Group HS, $P < 0.01$) and more uniform in size, with clearly visible cell walls and no large cell fusion. The number of adipocytes was significantly lower in Groups HE and HI than in Groups CS and HS ($P < 0.05$).

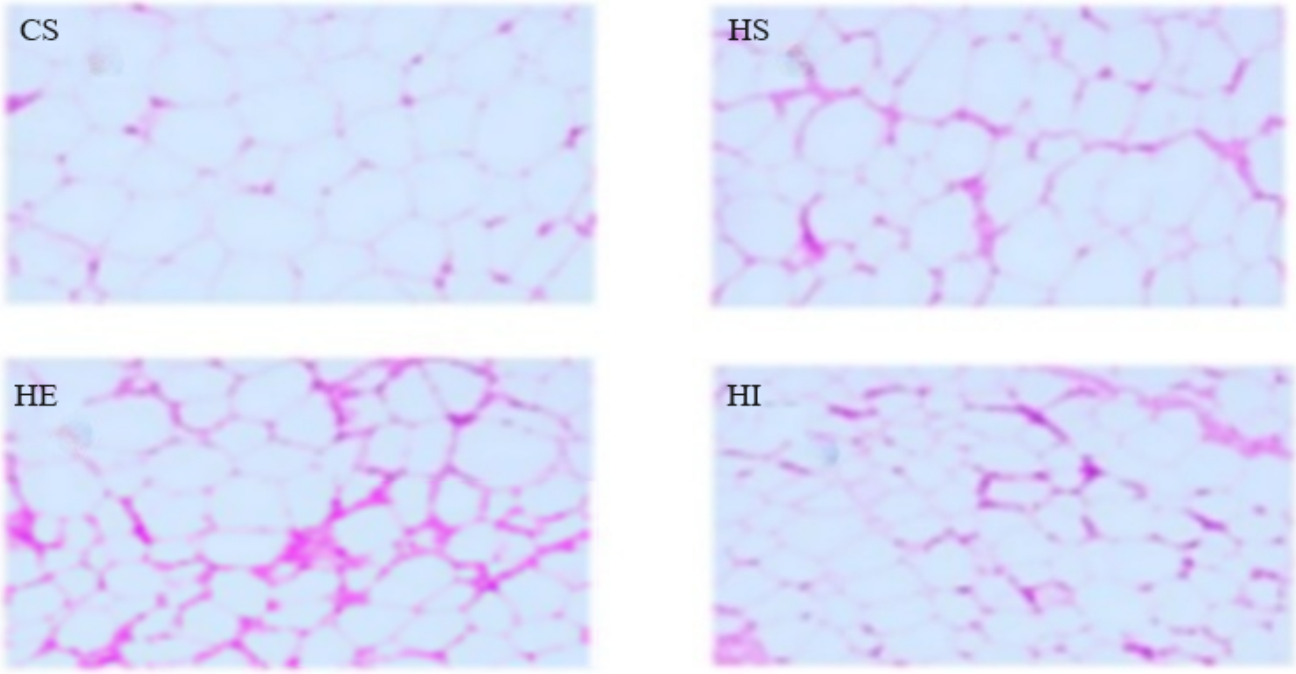

Figure 3. H&E staining of rat fat tissue (×200 magnification, scale of 50 microns)

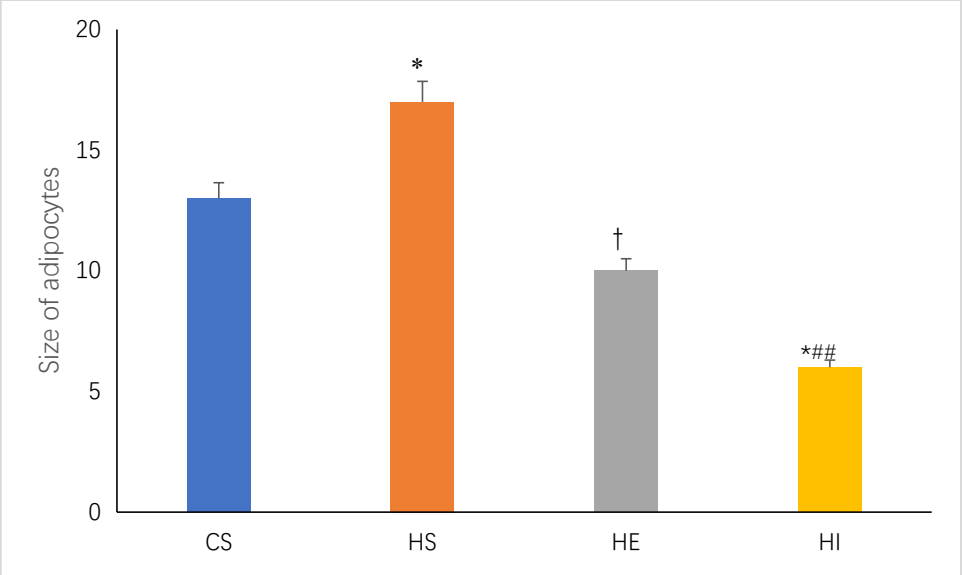

Figure 4. The average size of adipocytes across rat groups

4. Discussion

4.1. Impact analysis of HIIT on metabolic characterization in rats

There were significant differences in body composition, blood glucose, and blood lipid profiles between the high-fat-fed rats and the exercise group [4]. The high-fat-fed rats had increased body weight, visceral fat accumulation, and increased adipocyte volume [5]. The levels of blood lipids (TC, TG, LDL-C) and blood glucose were increased, and insulin sensitivity was decreased [6]. The results of this study were consistent with previous reports. HIIT had the greatest effect on body composition and blood lipid profile in rats. This study mainly discusses the effect of HIIT on reducing weight in rats, successfully establishing a high-fat control obesity model, and providing an important basis for further research on exercise intervention for obesity [7].

High-intensity intermittent exercise may increase total energy expenditure by inducing strong central and peripheral tissue metabolic stress [8]. Simultaneously, the post-exercise "effect" can enhance the mobilization and utilization of fat and glycogen, promoting a dynamic balance between fat intake and consumption and maintaining the body's homeostasis [4]. Hafstad *et al.* found that high-intensity interval exercise enhanced the respiratory capacity of muscle fiber mitochondria in C57BL/6J mice, promoted substrate oxidation, and enhanced aerobic metabolic capacity [9].

4.2. Analysis of the impact of HIIT on rat blood irisin levels

Irisin is a newly discovered polypeptide factor induced by exercise. It is encoded by the target gene FNDC5, which is activated by peroxisome proliferator-activated receptor-gamma coactivator 1-alpha (PGC-1α) in skeletal muscle. After being modified by the shear of secretory proteins, irisin can promote the conversion of white subcutaneous fat to brown fat, increase energy expenditure, promote weight loss, and improve glucose metabolism. Irisin is also secreted by adipose tissue and functions as both a myokine and an adipokine. Moderately increasing the concentration of irisin in the body can reduce body weight, improve insulin sensitivity, and reduce the incidence of type 2 diabetes.

Studies have found that various methods, such as physical activity and exercise training, can affect FNDC5 and circulating irisin levels in normal individuals or patients [10]. During exercise, muscle contraction increases

PGC-1α and FNDC5 expression, which in turn releases irisin and induces the browning of subcutaneous adipose tissue, subsequently stimulating oxygen consumption and heat production, and reducing body fat. Reisi *et al*. treated rats with 8 weeks of resistance swimming training and found significant increases in UCP1 expression in adipose tissue, FNDC5 expression in muscle, and blood irisin levels [11]. It was observed that the blood irisin concentration in healthy young subjects increased significantly at 54 minutes of 90-minute treadmill aerobic exercise (60% VO_{2max}), but the blood irisin concentration returned to the basal level after 20 minutes of rest immediately after the 90-minute exercise.

In this study, the blood irisin concentration increased slightly in the low-intensity continuous training group, while the circulating irisin concentration did not change significantly in the high-intensity interval training group. Archundia-Herrera *et al.* did not find an increase in plasma irisin concentration after a single session of aerobic exercise or HIIT, but the subjects lost weight and body fat [12], which is consistent with our results. Different studies have not reported an increase in plasma irisin concentration, while others have reported a modest increase in blood irisin after high-intensity exercise. In these studies, irisin was measured immediately after exercise [13]. Studies have shown that during the early stages of high-intensity intermittent exercise, the concentration of irisin suddenly increases, reaching a peak at 45 minutes, and then dropping at 90 minutes. It is speculated that the increase in irisin concentration occurs at the beginning of exercise, and the concentration gradually returns to the original level as exercise continues. As a result, the irisin induced by acute exercise is not associated with the state of motion but is related to the training mode. It can reduce body weight and improve lipid metabolism [14]. The irisin concentration test in this study was conducted 12 hours after exercise. It was hypothesized that the changes in irisin blood concentration following HIIT are not obvious, possibly due to a longer recovery time after exercise. Studies have shown that high-intensity interval training has better effects on glucose and fat metabolism and mobilization during and after exercise. The main reason may be that the high-intensity contraction of skeletal muscle during exercise increases the content of PGC-1α, promotes the expression of FNDC5 [15], increases the browning reaction of subcutaneous white fat, and increases energy expenditure, leading to fat loss and weight reduction.

5. Conclusions

Although HIIT had little effect on circulating irisin levels after exercise, it had a better impact on glucose and fat metabolism and mobilization. The regulation of fat metabolism by HIIT may help maintain metabolic homeostasis, making it a significant and functional approach for weight loss management.

Funding

(1) 2021 Guangdong Province Ordinary University Characteristics Class Project (Natural Science) (Project No. 2021ktscx256)
(2) 2023 Guangdong Science and Technology Innovation Strategy Special Fund Project (Project No. pdjh2023a0896)
(3) Guangdong Sports Vocational and Technical College in 2024 University Curriculum Education Demonstration Projects – Sports Training "Course Education" (Project No. 2024szsftd01)

Disclosure statement

The authors declare no conflict of interest.

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