Effects of Different Physical Exercises on Leptin Concentration in Obese Adolescents

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Key words
- obesity
- adolescents
- leptin
- physical exercise

Abstract

In order to compare the effects of leisure physical activity (LPA), aerobic training (AT) and aerobic plus resistance training (AT+RT) as part of a 6-month interdisciplinary therapy in body composition, insulin resistance and leptin concentrations in obese adolescents, 72 volunteers (n=24 in each group) ages 15–19 years were evaluated. Delta (Δ) body mass (kg) and Δ BMI (kg/m^2) was different between AT and LPA groups and in AT+RT group compared to both LPA and AT groups; Δ body fat mass (kg and %) was different only in AT+RT group compared to both LPA and AT; Δ body lean mass (%) was different only in AT+RT group; Δ body lean mass (kg) was negative only in AT and positive and different from AT in AT+RT group; ΔHOMA-IR did not differ among groups; Δ leptin (ng/ml) was negative and different from LPA for both AT and AT+RT groups. In conclusion, both AT and AT+RT promoted a reduction on leptin levels, however, the adolescents subjected to AT+RT presented better results in body composition than the AT group. These results highlight the importance of associating aerobic and resistance training with nutritional and psychological approaches in the treatment of obese adolescents.

Introduction

The prevalence of obesity is increasing at an alarming rate in children, adolescents and adults worldwide [44]. In Brazil, for example, recent data have shown that this prevalence in boys and girls was 16.1% and 17.5%, respectively [15]. A similar trend was also observed in several parts of the world: in the European countries, the estimated rates ranging from 10% to 12% up to 36% [32] and in Latin American 23% of the children and adolescents are overweight [8, 34].

Obesity results mostly from a disorder of energy balance (increased caloric intake and decreased energy expenditure) and represents a major public health problem for several countries. In addition to this, it is important to note that many epidemiological and clinical studies have confirmed that adverse effects on physical health associated with adult obesity are already being seen in obese adolescents, including metabolic syndrome risk factors (visceral obesity, hypertension, type 2 diabetes, dyslipidemia, nonalcoholic fatty liver diseases, cancer and cardiovascular mortality), asthma and sleep apnea [40].

A large number of neural and hormonal mechanisms that control the energy balance and leptin, an adipokine that is primarily expressed by adipose tissue in response to increased fat storages to induce a state of satiety, are particularly important in this process. It has been demonstrated that most obese individuals, including adolescents, have increased serum leptin concentrations, indicating a resistance to the action of this protein. The reason for the occurrence of such mechanism has been studied. Hypotheses concerning the occurrence of pre-receptor deficient in the receptor and post-receptor of leptin in the hypothalamus culminate in resistance to the effects of the control of food intake assigned to this adipokine. In addition to this, recently the state of hyperleptinemia was associated with a pro-inflammatory condition, promoting atherosclerosis and possible impairing the weight loss. Thus, the reduction in leptin to recommended values in these individuals would promote better control of food intake. In this way, it has recently been shown that this beneficial effect on leptin action in the control of energy balance was obtained only when obese adolescents lost approximately 10% of their initial body weight [11, 17, 35–37, 45, 46].

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Despite major efforts to promote weight reduction, the effective treatment of obesity is still a challenge. Tsiros and colleagues [44] emphasizes that dietary interventions are more effective in achieving weight loss when combined with other strategies, such as increasing physical activity levels and/or psychological interventions to promote behavior changes. In fact, it has previously been shown that the increase in the saturated trans-fat intake was related to an increase in the non-alcoholic fatty liver diseases (NAFLD) in obese adolescents and a reduction in the adiponectin concentration. Moreover, the expansion of visceral adipose tissue may substantially promote an increase in the pro-inflammatory adipokines and a reduction in anti-inflammatory adipokine adiponectin. Together it may increase the prevalence of comorbidities commonly linking obesity, metabolic syndrome, NAFLD, atherosclerosis and others chronic diseases [7,13,14].

Related to physical activity, many treatment centers focus on aerobic training, which enhances cardiorespiratory fitness and has some impact on body composition [49]. Resistance training, however, can potentially also play a central role in obesity treatment because of its relationship to increased energy expenditure during and after exercise and to enhanced lean body mass, which impacts joint stability and basal energy expenditure, and counterbalances the muscular catabolism triggered by caloric restriction [31,44,49]. In this context, it has been postulated that aerobic training associated with resistance training is more efficient than aerobic training alone to treat diabetes and obesity in adults [47].

In previous studies we have demonstrated that aerobic training reduces leptin concentrations in obese adolescents [9,37]. However, investigations that compare aerobic training with aerobic plus resistance training in body composition and leptin levels remain scarce. In this context, the primary aim of this study was to compare the effects of leisure physical activity, aerobic training and aerobic plus resistance training as part of an interdisciplinary therapy in body composition, insulin resistance and leptin concentrations in obese adolescents.

Methods

Study subjects

A total of 132 adolescents were selected to participate of the present study. They were selected from GEO (Interdisciplinary Obesity Program) of the Universidade Federal de São Paulo-UNIFESP in recent years. The GEO project has been conducted every year since 2004 in São Paulo, Brazil. At the beginning of each year, the project is advertised in newspapers and magazines from São Paulo to recruit adolescents. Of these 132 participants, we excluded those who did not complete therapy for reasons such as having found work, changes in school hours, lack of motivation and lack of funds for transportation, as well as patients who did not perform all necessary examinations for this study in 3 stages of evaluation. A total of 72 obese adolescents was then evaluated in this study. Obese adolescents (BMI >95th percentile of the CDC reference growth charts) [10], ages 15–19 years (16.46±1.51 years; Z-score 0.28±1.00), who reported not having had experience in exercise training before the study, including 50 girls and 22 boys, were recruited for a short-term (6 months) weight loss intervention study. The inclusion criteria for the postpubertal stage were based on Tanner (stage 5) for boys and girls [42]. The non-inclusion criteria were: endocrine diseases, chronic alcohol consumption, pregnancy and previous use of drugs which may affect appetite regulation, such as anabolic-androgenic steroids or psychotropics. Informed parental consent and adolescents' assent to participate as volunteers in an interdisciplinary weight loss program were obtained. This study was conducted in accordance with the principles of Helsinki Declaration and was formally approved by the ethics committee of the Universidade Federal de São Paulo – Escola Paulista de Medicina (Number: 0135/04) and registered in the Clinical Trial: Clinicaltrials.govNCT 0135/7883.This study meets the ethical standards of the journal [25].

Subjects were randomized into 3 groups: 1) aerobic plus resistance training (AT+RT: n=24; 9 boys and 15 girls); 2) aerobic training (AT: n=24; 7 boys and 17 girls) and 3) leisure physical activity (LPA: n=24; 6 boys and 18 girls). All subjects reported not having had experience in exercise training before the study. Volunteers were instructed to not participate in any physical activity the day before the experiments (pre- and post-training). All subjects were completely familiarized with all testing procedures before the experiment to reduce the influence of any learning effects solely due to the mechanics of performing the test protocol. After evaluations, but before the periodization, AT+RT and AT groups performed 2 weeks of training for adaptation, totaling 6 months of protocol.

Anthropometric measurements and body composition

Subjects were weighed wearing light clothing and barefoot on a Filizola scale to the nearest 0.1 kg. Height was measured to the nearest 0.5 cm by using a wall-mounted stadiometer (Sanny, model ES 2030). BMI was calculated as body weight divided by height squared (wt/ht^2). Body composition was measured by plethysmography in the BOD POD body composition system (version 1.69; Life Measurement Instruments, Concord, CA) [19]. All volunteers were encouraged to adopt a balanced diet throughout treatment, including before and after assessments. Adolescents were instructed to not consume foods with caffeine prior to the body composition assessment.

Serum analysis

Blood samples were collected in the outpatient clinic around 8 h after an overnight fast. After collection, the blood was centrifuged for 10 min at 5000 rpm and stored at 70 °C for future analysis. The materials used for collection were disposable and adequately labeled. Blood was collected by a skilled and qualified technician. Insulin resistance was assessed by homeostasis model assessment of insulin resistance index (HOMA-IR). HOMA-IR was calculated as the product of blood glucose (fasting blood glucose) and the immunoreactive insulin (I): (fasting blood glucose (mg/dl)×I(mU/l))/405. The HOMA-IR data were analyzed according to reference values reported by Keskin et al. The HOMA-IR cutoff point for insulin resistance adopted for adolescents was 3.16 [30]. The leptin concentrations were measured using a commercially available enzyme-linked immunosorbent assay (ELISA) kit from Phoenix Pharmaceuticals, Inc. (Belmont, CA, USA), according to the manufacturer's instructions. The evaluations and data collection were made at baseline and 6 months after interdisciplinary therapy, both after an overnight fast in the Sleep Institute. For this study, the leptin reference values were described by Gutin et al. [24] and Dâmaso et al. [11].

Research design

The interdisciplinary obesity intervention consisted of physical training (aerobic plus resistance training or aerobic training alone or leisure physical activity) associated with clinical, nutritional and psychological therapy. The use of interdisciplinary therapy has been suggested by the World Health Organization [50]. All measurements were performed at baseline and after 6 months of therapy.

Exercise protocol

Aerobic training (AT)

During 6 months of therapy, the obese adolescents followed a personalized aerobic training program lasting 60-min per session and performed 3 times a week (180-min/week) under the supervision of a sports physiologist. The aerobic training mode was running performed on a motor-driven treadmill (Life Fitness, Model TR 9700HR) or pedaling at the cardiac frequency intensity of the ventilatory threshold I (±4 bpm), according to the results of an initial oxygen uptake test for aerobic exercises (cycle-ergometer or treadmill). The physiologists controlled the cardiac frequency, which was measured with a cardiometer at intervals of 5 min during all training sessions (Polar Model FS1 dark blue). The exercise program was based on the 2001 recommendations provided by the American College of Sports Medicine (ACSM) [28] and adapted by Foschini and colleagues [20].

Aerobic plus resistance training (AT + RT)

The program aerobic plus resistance training was performed 3 times per week for 6 months, including 30 min of aerobic training plus 30 min of resistance training per session (180-min/week). The volunteers were instructed to invert the order of the exercises at each training session: in one session the adolescent started the training session with aerobic exercises and in the subsequent session the same adolescent started with the resistance training.

The aerobic training was identical to that previously described. Resistance training was divided following the recommendations of ACSM [28]. It used exercises for the main muscular groups: bench press, leg press, sit-ups, lat pull-down, hamstring curls, lower back, military press, calf raises, arm curls, triceps push-down. The exercise program was based on the 2001 recommendations provided by the American College of Sports Medicine (ACSM) [28] and adapted by Foschini and colleagues [20].

The first 2 weeks of the resistance training had as main purpose the learning of the movements (3 sets of 15–20RM for each exercise). Training loads were successively adjusted, with volume and intensity being inversely modified and the number of repetitions being decreased to between 6 and 20 repetitions for 3 sets. The rest interval between series and exercises were: 15–20RM = 45 s; 10–12RM = 1 min and 6–8RM = 1.5 min. The training loads were adjusted in each training session and evaluated according to the increase in participants' strength. Thus, the training was conducted with maximal repetitions (RM).

Leisure physical activity (LPA)

The adolescents had 3 sessions per week during the intervention. Each session lasted for 60 min and included, alternatively, recreational team sports (soccer, handball, basketball, etc.), gymnastics and walking performed in groups. Information about lifestyle changes related to activity was also provided and spontaneous physical activity (walking, stair climbing, etc.) was encouraged. This methodology, as previously described, has been used in obese adolescents [43]. In the 3 kinds of exercises all sessions were supervised individually by an experienced physiologist.

Psychological therapy

Psychological therapy was established by validated questionnaires, taking into account some of the psychological problems caused by obesity, as described in the literature, including depression, eating disorders, anxiety, decreased self-esteem and body-image disorders. During the interdisciplinary therapy, the adolescents received psychological orientation for 1 h in a weekly group session. The psychologist discussed: body image and eating disorders, such as bulimia and anorexia nervosa, and binge eating disorders as well as their signs, symptoms, and consequences for health; the relationship between feelings and food; familiar problems, such as alcoholism and other issues. Individualized psychological therapy was recommended when weight problems or poor-dietary habits were found.

Nutritional therapy

Energy intake was set at the levels recommended by the dietary reference for subjects with low levels of physical activity of the same age and gender, following a balanced diet [27]. No drugs or antioxidants were recommended. Once a week, adolescents had a dietetics lessons (providing information on food pyramid; diet record assessment; weight loss diets and miracle diets; food labels, dietetics, fat-free and low-calorie foods; fats (kinds, sources and substitute foods); fast food calories and nutritional composition; good nutritional choices for special occasions; healthy sandwiches; shakes and products to promote the weight loss; functional foods; making decisions on food choices). All patients received individual nutritional counseling during the intervention program.

At the beginning of the study and 6 months into the program, a 3-day dietary record was collected. Since most obese people under-report their food consumption, each adolescent was asked to record their diet with the help of their parents [26]. The degree of under-reporting may be substantial, but this is a validated method to assess dietary consumption [41]. Portions were measured in terms of familiar volumes and sizes. The dietician taught the parents and the adolescents how to record food consumption. These dietary data were transferred to a computer by the same dietician and the nutrient composition was analyzed by a PC program developed at the Universidade Federal de São Paulo – Escola Paulista de Medicina (Nutwin software, for windows, 1.5 version, 2002) that uses data from western and local food tables. In addition, the parents were encouraged by a dietitian to call if they needed additional information. All volunteers were encouraged to adopt a balanced diet throughout treatment, including before and after assessments.

Clinical therapy

To accomplish the health and clinical parameters, obese adolescents of all groups analyzed visited the endocrinologist once each month. Medical follow-up and treatment is based on patient's characteristics, family history, physical examination and intervention in response to unhealthy problems developed over the course of the therapy.

Statistical analysis

All data were analyzed using STATISTICA version 7 for Windows, with the significance level set at 5%. Data are expressed as the

mean ± SD. Distributional assumptions were verified by Kolmogorov-Smirnov test. Comparisons between measures at baseline and after weight-loss intervention in each group and among groups were made using an analysis of variance (ANOVA) for repeated measures and Tukey's post hoc test. One-way ANOVA and Tukey's post hoc test were used to compare deltas (Δ) among groups. Dependent variables were transformed into Z scores to check outliers.

Results

At the beginning of therapy, 72 obese adolescents were enrolled in the program. The subjects were paired according to gender and BMI and then were randomized in 3 groups (LPA, AT and AT + RT), since the values between boys and girls were not different. Each group was composed of 24 volunteers: 9 boys and 15 girls in aerobic plus resistance training group (AT + RT), 7 boys and 17 girls in aerobic training group (AT) and 6 boys and 18 girls in leisure physical activity group (LPA). The results of anthropometric measurements and body composition are presented in **Table 1**. There were no observed differences for body mass (kg), height (cm), body mass index (BMI, kg/m^2), body fat mass (kg and %) and body lean mass (kg and %) at baseline. Body mass (kg), BMI (kg/m^2) and body fat mass (kg) decreased only in AT and AT + RT group after intervention. Body fat mass (%) and body lean mass (%) improved only in AT + RT group. Body lean mass (kg) decreased in AT group. However, body lean mass (%) did not change in this group after intervention.

The results of glucose (μU/ml), insulin (μU/ml), HOMA-IR and leptin levels (ng/ml) are presented in **Table 2**. No statistical differences were observed among groups at baseline and after intervention for glucose (μU/ml), insulin (μU/ml) and HOMA-IR (**Table 2**). AT group presented reduced leptin concentration compared to LPA group at baseline. Only AT and AT + RT groups exhibited significantly decreased leptin concentration after 6 months of intervention. Both AT and AT + RT groups presented lower leptin values compared to LPA group after intervention (**Table 2**).

Delta (Δ) values of all variables analyzed are presented in **Table 3**. Δ body mass (kg) and Δ BMI (kg/m^2) were negative in all groups, indicating the decrease of these parameters after intervention compared to baseline values. However, this change was different between AT and LPA groups and in AT + RT group compared to both LPA and AT groups. For Δ body fat mass (kg and %) the negative value observed was different only in AT + RT group compared to both LPA and AT, while the positive value for Δ body lean mass (%) was different only in AT + RT group compared to the others groups. Related to Δ body lean mass (kg), a decrease in body lean mass (kg) was observed in AT group after intervention compared to LPA and an increase was observed in AT + RT group compared to AT group. Finally, Δ glucose (μU/ml), Δ insulin (μU/ml) and ΔHOMA-IR did not differ among groups, while Δ leptin (ng/ml) was positive for LPA group and negative for both AT and AT + RT groups, indicating the decrease of leptin after intervention only with AT and AT + RT therapy. Additionally, this change was different between AT and AT + RT groups compared to LPA, but was not different between AT and AT + RT groups. Changes in leptin and HOMA-IR [Delta (%)] are presented in **Fig. 1**. Δ leptin (%) was positive for LPA group but negative for AT and AT + RT groups, and this change was different for AT and AT + RT groups compared to LPA but not different between AT and AT + RT groups. Δ HOMA-IR (%) was negative for all groups, but these changes were not different.

Table 1 Anthropometric data of obese adolescentes before and after weight loss interventions.

	Leisure physical activity (LPA)		Aerobic training (AT)		Aerobic + resistance training (AT + RT)	
	Baseline	After intervention	Baseline	After intervention	Baseline	After intervention
body mass (kg)	95.67 ± 13.51	95.14 ± 14.25	96.11 ± 12.69	90.46 ± 10.81[a]	97.22 ± 13.06	89.12 ± 12.13[a]
height (cm)	1.66 ± 0.09	1.66 ± 0.09	1.66 ± 0.08	1.66 ± 0.08	1.66 ± 0.08	1.67 ± 0.08[a]
BMI (kg/m^2)	34.57 ± 3.84	34.33 ± 4.2	35.06 ± 3.90	33.22 ± 3.70[a]	35.10 ± 4.67	31.82 ± 3.90[a]
BMI (Z-score)	−0.083 ± 0.936	0.300 ± 1.046[a]	0.037 ± 0.950	0.024 ± 0.919	0.046 ± 1.140	−0.324 ± 0.971[a]
body fat mass (%)	44.11 ± 6.00	43.25 ± 6.98	41.79 ± 6.59	41.07 ± 8.15	45.57 ± 6.04	38.68 ± 6.27[a]
body lean mass (%)	55.89 ± 6.74	56.75 ± 6.98	58.21 ± 6.59	58.93 ± 8.15	54.43 ± 6.04	61.32 ± 6.27[a]
body fat mass (kg)	42.20 ± 7.79	41.15 ± 9.25	40.17 ± 7.78	37.15 ± 9.50[a]	44.31 ± 9.80	34.48 ± 8.31[a]
body lean mass (kg)	53.47 ± 10.08	53.99 ± 10.31	55.94 ± 10.82	53.31 ± 8.17[a]	52.91 ± 7.27	54.64 ± 8.04

BMI: body mass index

Values expressed by mean ± SD

[a] comparison of baseline vs. after intervention, $p < 0.05$

Table 2 HOMA-IR and leptin levels of obese adolescents before and after weight loss interventions.

	Leisure physical activity (LPA)		Aerobic training (AT)		Aerobic + resistance training (AT + RT) group	
	Baseline	After intervention	Baseline	After intervention	Baseline	After intervention
glucose (μU/ml)	5.06 ± 0.32	4.97 ± 0.35	5.01 ± 0.34	4.97 ± 0.42	4.97 ± 0.39	4.96 ± 0.32
insulin (μU/ml)	15.44 ± 6.78	14.01 ± 5.61	19.07 ± 11.53	17.55 ± 9.21	15.03 ± 5.09	11.41 ± 5.42
HOMA-IR	3.47 ± 1.56	3.14 ± 1.41	4.29 ± 2.75	3.97 ± 2.41	3.32 ± 1.17	2.54 ± 1.28
leptin (ng/ml)	46.09 ± 19.07	48.55 ± 22.29	25.28 ± 19.47[b]	16.66 ± 18.01[a,b]	38.15 ± 16.08	24.81 ± 14.69[a,c]
leptin (Z-score)	0.480 ± 0.955	0.812 ± 0.976	−0.562 ± 0.975[b]	−0.584 ± 0.789[b]	0.083 ± 0.805	−0.227 ± 0.643 [c]

Values expressed by mean ± SD

[a] comparison of baseline vs. after intervention, $p < 0.05$

[b] difference between LPA and AT at the same time, $p < 0.05$

[c] difference between LPA and AT + RT at the same time, $p < 0.05$

Leptin values between 1 and 20 ng/ml for males and between 4.9 and 24 ng/ml for females described by Gutin et al. [27]; HOMA-IR (< 3.16) [32]

	Leisure physical activity (LPA)	Aerobic training (AT)	Aerobic + resistance training (AT + RT)
Δ body mass (kg)	−0.53 ± 2.74	−5.14 ± 4.54[a]	−8.14 ± 4.17[b,c]
Δ BMI (kg/m²)	−0.24 ± 0.98	−1.85 ± 1.60[a]	−3.28 ± 1.56[b,c]
Δ body fat mass (%)	−1.03 ± 2.37	−1.18 ± 3.83	−6.80 ± 3.03[b,c]
Δ body lean mass (%)	1.86 ± 5.35	1.18 ± 5.06	6.80 ± 3.03[b,c]
Δ body fat mass (kg)	−1.04 ± 2.88	−3.02 ± 4.53	−9.83 ± 4.49[b,c]
Δ body lean mass (kg)	0.53 ± 2.15	−2.62 ± 3.71[a]	1.73 ± 2.02[c]
Δ glucose (uU/ml)	−0.09 ± 0.30	−0.05 ± 0.33	−0.01 ± 0.38
Δ insulin (uU/ml)	−1.43 ± 6.07	−1.53 ± 6.77	−3.63 ± 6.15
Δ HOMA-IR	−0.33 ± 1.39	−0.32 ± 1.55	−0.78 ± 1.44
Δ leptin (ng/ml)	2.46 ± 11.00	−8.62 ± 15.38[a]	−13.34 ± 10.76[b]

Table 3 Delta values of variables analyzed.

BMI: body mass index
Values expressed by mean ± SD
[a] comparison of LPA vs. AT, $p < 0.05$
[b] comparison of LPA vs. AT + RT, $p < 0.05$
[c] comparison of AT vs. AT + RT, $p < 0.05$

Discussion

As it was demonstrated in the results, the groups of obese adolescents subjected to aerobic (AT) and aerobic plus resistance training (AT + RT), 3 times a week, 1 h per day, for 6 months, presented reduced body mass and body mass index at the end of the experimental period (**Table 1**). In addition, both therapeutic approaches resulted in diminished proportion of body fat mass and increased proportion of body lean mass. These data can be better analysed when the absolute masses (in kg) are considered. We found reduction of body fat mass in both AT and AT + RT groups (**Table 1**). This finding is in agreement with Davis and colleagues [12], who demonstrated a better result in the absolute body fat mass in overweight Latin American adolescents subjected to a nutritional therapy and a combination of aerobic and strength training. However, only aerobic combined strength training was sufficient for maintaining lean body mass. This data reinforces that strength training has a central role in the treatment of obese adolescents, stimulating a hypertrophic process in the skeletal muscle [6]. In the present study, the results obtained when deltas (Δ) were analyzed (**Table 3**) showed that aerobic training combined resistance training yielded the best improvement of body composition in obese adolescents. It probably occurred since the AT + RT resulted in a higher energy demand than AT alone as AT was the same in each group. However, it needs to be confirmed in future researches, since we were not able to measure energy expenditure in the present study.

Insulin resistance is a hallmark in obesity and could be modulated by interventions directed to its treatment. However, as it is displayed in the results, no intervention resulted in changes in glucose (μU/ml), insulin (μU/ml) and HOMA-IR (**Table 2**). Even when delta (Δ) and changes [delta (%)] were calculated (**Table 3** and **Fig. 1**), this change was not observed. We had demonstrated that 1 year of intervention reduces HOMA-IR values [13], but 3 h per week during 6 months in the present study can be insufficient for improving insulin resistance. Davis and colleagues [12] also did not find improvements in insulin sensitivity in Latin American adolescent girls subjected to nutritional therapy and aerobic plus strength training, 2 h per week for 4 months. Similar result was found by Gutin and colleagues [23]: neither aerobic training (n = 12) nor lifestyle education (n = 10) over 10 weeks improved fasting insulin levels in obese African American girls. In contrast, Goodpaster and colleagues [21] showed that a 16-week aerobic intervention (4–6 d.wk^{-1}) in combination with energy restriction resulted in a 49% increase in insulin sensitivity in 25 obese adults. In another study, Ferguson and colleagues [18] showed that an intensive aerobic training program (5d.wk^{-1} for 4 months; 40-min training sessions) resulted in small, yet significant, improvements in fasting insulin in obese boys and girls (n = 79). The fact that the adolescents in our study were not subjected to energy restriction also helps to explain, at least in part, the HOMA-IR results.

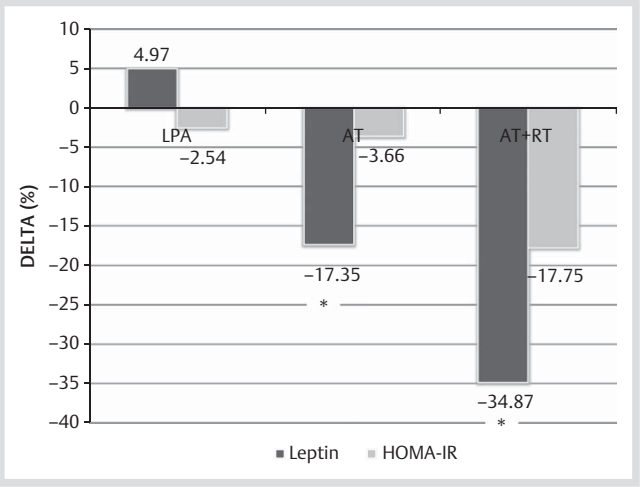

Fig. 1 Changes in leptin and HOMA-IR in obese adolescents after 6 months of weight loss interventions. LPA: leisure physical activity; AT: aerobic training; AT + RT: aerobic + resistance training. *different from LPA group, $p < 0.05$.

Few intervention studies have demonstrated the effects of combined aerobic and strength training to reduce adiposity and insulin resistance in adolescent populations. Byrne and colleagues [6], studying 48 adolescents in 3 groups (aerobic training, strength training and combination of aerobic and strength training), found that the combination of aerobic and strength training resulted in the loss of more fat mass as measured by DXA. However, no assessment of glucose/insulin indices was conducted. Another study [48] found that an 8-week combined training (3 times per week) resulted in significant decreases in trunk and abdominal fat as measured by DXA in 19 obese adolescents, but did not change total adiposity or fasting lipids or glucose. Bell and colleagues [4], on the other hand, showed that

an 8-week combined training in 14 obese children resulted in a 22% increase in insulin sensitivity, as measured by euglycemic-hyperinsulinemic clamp. However, they observed no differences in body composition and did not compare this group to a control group.

Leptin is a protein that is produced and secreted by adipose tissue as the product of Ob gene – the etymology of its name (leptos: slim) has implied the connotation of "slimming". Aside from its effect of inhibiting food intake and increasing energy expenditure at the central level, a state of hyperleptinemia appears to play a pro-inflammatory function [1,5] and may contribute to the development of diabetes mellitus, hypertension and increasing the chances of individuals to develop atherosclerosis [5]. However, the role of leptin in the long-term regulation of body fat via modulation of energy intake and energy expenditure, mostly in obese humans, remains unknown. Yet the failure of elevated leptin levels to suppress feeding and contribute to weight loss in obesity defines leptin resistance, and a number of cellular and molecular mechanisms have been found to attenuate leptin signaling and promote this resistance [38].

In the present study it was shown that leptin levels were reduced by both endurance training and endurance training combined with strength training, demonstrating that both approaches were sufficient for positively modulating this important regulator of body composition. However, leptin levels were much higher in the LPA group at baseline than in the 2 other groups (**Table 2**). The best improvement in the leptin concentration measured following the intervention was confirmed after delta calculation showed that only the AT and AT+RT groups presented significant reduction in the leptin concentration, associated with the decrease in the adipose tissue deposit and body mass only in these groups (**Table 3** and **Fig. 1**). Therefore, we hypothesized that the absence of the effect of leisure physical activity may partly be explained by these aforementioned results, even though the initial BMI was similar among groups. Together, our results reinforce that the state of hyperleptinemia may impair the weight loss process conducted by exercise therapy associated with the interdisciplinary approach. Consistent with these findings, it has previously been shown that baseline leptin level was a negative predictor for percentage of fat loss in obese children and adolescents [11,33]. Moreover, after only a reduction of 10% of the initial body mass, an improvement was observed in the regulation of energy balance, including increased alfa-MSH, an important anorexigenic neuropeptide mediated by leptin in the central nervous system [35].

Although many studies looking at the effect of training on leptin levels have been published with obese adolescents, there is still no consensus in the field. It probably depends on the analyzed conditions from both acute and/or chronic measurements. While some studies showed that leptin concentration measured 24 h after an acute exercise was decreased in diabetic patients [29], a 6-week training did not show any effect on leptin level when this hormone was measured approximately 72 h after the last training session. Since leptin level was measured 24 h after the last training session in the present study, it is possible that the effect seen here is simply the result of the last exercise bout and not the effect of the whole training. Additionally, it is important to note that the results mentioned above were performed after short-term interventions, while in the present study it was analyzed after 6 months of therapy. In scientific literature, Barbeau and colleagues [3] examined the effect of 8 months of 2 intensities of physical training on leptin in obese teenagers and did not show significant group differences in mean change in leptin, although there was great variability in individual response. However, consistent with the present study, Elloumi and colleagues [16] investigated the effects of a 2-month weight loss program on plasma levels of leptin in obese adolescent boys and showed a decrease in plasma leptin in the group subjected to energy restriction and training compared to the energy restriction group. It was corroborated recently by Romeo and colleagues [39] that showed a decrease in serum leptin levels after an intervention consisting of a calorie-restricted diet (10–40%), increased physical activity (at least 60 min/day 5 days a week), psychological therapy and nutritional education for 13 months. The same results have been shown by Gueugnon and colleagues [22] in 32 severely obese adolescents after 1 year in an institution for childhood obesity, i. e., a decrease in leptin levels was demonstrated after 3 months of intervention. These results need to be confirmed in future researches.

Moreover, it is important to state that the adolescents of the leisure physical activity group did not present improvement in the studied variables and this could be related to the decreased values of intensity and volume in this kind of activity [2]. However, future studies should be designed to test the hypothesis that this kind of program result in improvements in psychological aspects in obese adolescents and it is the approach that generates more motivation to the maintenance in the program for long periods of time.

Finally, some limitations of the present study are that we did not measure the baseline physical activity of the subjects as well as energy expenditure in the adolescents from the 3 groups during the physical exercise practices, because there is not a simple and accurate method for this purpose, mainly for leisure physical activity and resistance training. However, we showed that both aerobic and aerobic plus resistance training can be applied in the clinical approach for obesity control in adolescents, mostly in view of its role in the improvement of mechanisms involved in the neuroendocrine regulation of energy balance mediated by leptin.

In conclusion, aerobic plus resistance training, as part of an interdisciplinary therapy, is effective in improving body composition, including a decrease in body fat and increase in lean body mass, and leptin concentration in obese adolescents. However, despite the same improvement in lean body mass not being observed with aerobic training, this group was also able to reduce the leptin concentration after 6 months of intervention. Viewed from a clinical perspective, the data presented in this study highlight the importance of combining aerobic and resistance training with nutritional and psychological approaches in the treatment of obese adolescents.

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