Effects of combined training on interleukin-7 plasma levels in obese middle-aged men

Efeitos do treinamento combinado sobre as concentrações plasmáticas de interleucina-7 em homens obesos de meia-idade

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ABSTRACT

Introduction: There are divergences about the effects of obesity on plasma concentrations of interleukin-7 (IL-7) and the role of physical exercise as a metabolic regulator of this cytokine. Objective: To compare the plasma concentrations of IL-7 between obese and normal weight individuals, in addition to evaluating the effects of combined training (CT) on concentrations of this cytokine in obese individuals. Methods: Initially, obese group (OG, n = 15) and normal weight group (NWG, n = 8) were compared. Subsequently, the obese individuals participated in a pre-post 16-week experimental period and were randomly distributed into obese CT group (OT, n = 8) and obese control group (OC, n = 7). Physical fitness, body composition, and IL-7 concentrations evaluations were performed. The CT program consisted of strength training and aerobic training in the same session. Results: A significant increase of IL-7 was observed in the OG (27.14 ± 3.64 pg/mL) compared to the NWG (21.26 ± 3.93 pg/mL) (p = 0.01). Although no significant group x time interaction was found, a time effect was observed in the pre-post experimental period on IL-7 concentrations (OC: 18.8%, ES: 1.68; OT: 28.5%, ES: 5.15). In the assessment of the effect size, a greater reduction in OT was observed. Moreover, reductions in weight, body mass index and fat mass were observed in the OT group when compared to CG, accompanied by significant increases in 1 maximum repetition test in the Leg Press and Bench Press, and maximum oxygen consumption. Conclusion: Obese individuals have higher circulating concentrations of IL-7, which suggest that elevated body weight and fat are associated with an increase in this cytokine. Although the effect size for IL-7 was larger in the OT group, probabilistic statistics did not show a significant effect.

Keywords: Combined training; Physical exercise; Interleukin-7; Obesity; Inflammation; Metabolism.

RESUMO

Introdução: Existem divergências sobre os efeitos da obesidade nas concentrações plasmáticas de interleucina-7 (IL-7) e do papel do exercício físico como regulador metabólico dessa citocina. Objetivo: Comparar as concentrações plasmáticas de IL-7 entre indivíduos obesos e com peso normal, além de avaliar os efeitos do treinamento combinado (TC) nas concentrações dessa citocina em indivíduos obesos. Métodos: Inicialmente, foram comparados o grupo obeso (GO, n = 15) e o grupo com peso normal (GNT, n = 8). Posteriormente, os indivíduos obesos participaram de um período experimental de 16 semanas e foram distribuídos aleatoriamente em grupo TC obeso (OT, n = 8) e grupo controle obeso (OC, n = 7). Foram realizadas avaliações de aptidão física, composição corporal e concentrações de IL-7. O programa de TC consistiu em treinamento de força e treinamento aeróbico na mesma sessão. Resultados: Um aumento significativo de IL-7 foi observado no GO em comparação ao GNT (p = 0,01). Embora não tenha sido encontrada interação grupo x tempo significativa, foi observado efeito de tempo no período pré-pós experimental sobre as concetrações de IL-7 (OC: 18,8%, ES: 1,68; OT: 28,5%, ES: 5,15). A avaliação do tamanho do efeito, indicou uma maior redução no OT. Além disso, reduções no peso, índice de massa corporal e massa gorda (kg) foram observadas no grupo OT quando comparado ao GC, acompanhadas por aumentos significativos em no teste de uma repetição máxima no Leg Press e no Supino, e no consumo máximo de oxigênio. Conclusão: Indivíduos obesos apresentam maiores concentrações circulantes de IL-7, o que sugere que o aumento do peso corporal e da gordura corporal está associado a um aumento dessa citocina. Embora o tamanho do efeito para IL-7 tenha sido maior no grupo OT, a estatística probabilística não mostrou um efeito significativo.

Palavras-chave: *Treinamento combinado; Exercício físico; Interleucina-7; Obesidade; Inflamação; Metabolismo.*

Introduction

Obesity is considered a global pandemic that compromises quality of life and can lead to morbidity and mortality[1]. Excess body fat, especially in the visceral region and in ectopic compartments, generates a process of low-grade chronic inflammation[2]. These factors

contribute to the increase in the concentration of circulating cytokines and other inflammatory markers, which can develop to diseases such as type 2 diabetes, atherosclerosis, hypertension, and cancers[3].

Among the various inflammatory markers, interleukin-7 (IL-7) has been gaining prominence for its pleiotropic effects, because despite to being associated with inflammatory induction, it also presents important anti-inflammatory and regulatory effects such as growth, survival, maturation, and development of T cells[4,5].

In studies about obesity, discrepant results have been found in the relationship between plasma IL-7 values and gene expression in adipocytes. While some studies have demonstrated an increase in circulating IL-7 in pre-diabetic obese women[6] and in gene expression in adipocytes of obese men[7]. Other findings verified the relationship between excess body fat and thymic involution and impaired maturation and consequent reduction of T cells, a process in which IL-7 has a significant role[7,8]. This divergence of results becomes especially significant after acute administration of exogenous IL-7 was able to prevent the accumulation of body fat, reduce markers associated with inflammation, and protect against glucose intolerance in a model of mice obese by a high-fat diet[9], showing its therapeutic potential in the management of metabolic complications related to obesity. However, possible differences in circulating IL-7 concentrations in obese men without diabetes and other comorbidities compared to normal weight individuals are not well known.

Physical exercise has been shown to be an important anti-inflammatory agent and is considered a non-pharmacological treatment for obesity[10,11]. Specifically, muscle contraction performed in an acute session of physical exercise has been shown to promote the survival of naïve T cells[12], as well as increasing circulating concentrations of IL-7 in elderly athletes who practice cycling when compared to sedentary elderly people[13]. Additionally, an increase in IL-7 gene expression was observed in the skeletal muscle of obese rats subjected to a combined training (CT) protocol (with the resistance and aerobic exercises in the same training session), which is recommended for the maintenance and improvement of health[14]. However, it is important to highlight the differences in effects between animal and human models, especially in the context of the time for which effects can be observed. Additionally, although there is evidence that physical exercise can interfere with IL-7 secretion[13], exploration in this context focuses more on acute effects in humans , which raises doubts about the effects of chronic training and its influence on serum levels, especially in a population with excess body fat.

Based on the divergence in circulating concentrations of IL-7 according to body weight, and how physical training can interfere in this context, the present study aims to compare the plasma concentrations of IL-7 between obese and normal weight individuals, in addition to evaluating the effects of CT applied to obese individuals on the concentrations of this cytokine through a randomized and controlled study.

Methods

Subjects and experimental design

This paper presents the results of IL-7 dosages from the research project "Investigation of the effects of combined training on early immunosenescence associated with obesity," which aims to evaluate the responses of CT on cardiovascular, neuromuscular, body composition, biochemical, and molecular variables in obese individuals. The study was approved by the Research Ethics Committee of *Universidade Estadual de Campinas* (CAAE: 16563719.7.0000.5404; Approval number 6.017.319) according to the principles of the Declaration of Helsinki. The volunteers were informed of the purpose of the study and signed the informed consent form.

The inclusion criteria adopted were: men and women in middle age (40 to 60 years) classified as grade 1 obese (body mass index [BMI] between 30.0-35.0 kg/m²) or normal weight (BMI between 18.5-25.0 kg/m²); have a non-active lifestyle; have not regularly participated in training programs or undergone any type of systematic diet over the last 12 months prior to the beginning of the experiment. Particularly in the case of women, the volunteers should be in menopause. The exclusion criteria were: volunteers who demonstrated in the anamnesis, or in the clinical evaluation (general physical, cardiological and ergometric examination) and/or laboratory tests any disease (coronary artery disease, severe arterial hypertension, chronic obstructive pulmonary disease, limiting osteoarticular diseases, type 1 and 2 diabetes) that could affect research results or indicate a risk factor or unwillingness to participate in the proposed physical activities; or those who were taking any medication that could affect their physical responses to the tests or exercise, such as anti-inflammatories; and not having IL-7 data evaluated.

The following discontinuation criteria were also adopted: a) the volunteer's lack of motivation or unavailability to attend the training sessions and/or tests; b) attendance at training sessions of less than 85% and/or more than three consecutive absences; c) other risks to the volunteers that could occur even after clinical clearance.

Volunteers were instructed not to change their medications if used (dosage/types) or their eating pattern during the experimental period. The control group was not submitted to any training protocol and was followed up on monthly by telephone during the experimental period.

Before the study, all subjects (normal weight group - NWG and obese group - OG) carried out an assessment of physical activity levels, anthropometry, body composition, food intake, physical fitness analyses (muscular maximal strength and maximum cardiorespiratory capacity), and blood collection for plasma IL-7 analysis. After the experimental period, obese subjects were randomized into the obese control (OC) and obese training (OT) groups and repeated the initial assessments (except physical activity levels analyses evaluated only in pre moment). In the 8th week of training, the OT participants performed another cardiorespiratory test to readjust the aerobic training loads. Each assessment was performed in a room with an average temperature of 23°C, with the volunteers breathing spontaneously in atmospheric air. The volunteers were familiarized with the location, procedures, tests, and equipment used before the study.

Physical activity questionnaire

The Baecke questionnaire was applied to assess the level of physical activity of the subjects. This is a self-report instrument used to measure an individual's habitual physical activity over the past 12 months. In the period prior to the study, none of the selected volunteers performed systematic physical exercises or sports, and did not engage in significant physical activity in the context of leisure and occupational activities. Thus, all subjects were categorized as sedentary/irregularly active[10].

Nutritional assessment

Food intake was monitored before and after the experimental period through food records. Volunteers were asked to list all foods and beverages they consumed during the designated days (two non-consecutive weekdays and one weekend day). Total caloric intake, quantity/proportions of macronutrients (carbohydrates, lipids, and proteins) were calculated based on the average of the data from the three FRs, using the Diet Pro Program, Diet Pro, version 5i, Dietpro Store (Viçosa, Minas Gerais, Brazil).

Anthropometry and body composition

To calculate BMI (kg/m²), a scale (FilizolaTM, São Paulo, Brazil) was used to obtain body mass data, and a wooden stadiometer (0.1 cm accuracy) to measure height. The BMI was calculated from these measurements.

To assess body composition data, a whole-body plethysmography system (air displacement plethysmography (BOD POD - Cosmed, Inc., Concord, United States) was used. The assessment was made according to the criteria discussed in the equipment manual and the criteria normally used in this assessment. After determining body density by plethysmography, body composition was measured from these data based on the Siri equation[15].

Maximum muscle strength and cardiorespiratory assessment

To determine the maximum muscular strength of the upper and lower limbs, the one-repetition maximum (1-RM) test was used in the leg press and bench press exercises. Subjects were required to perform 10 repetitions at 50% of 1RM estimated (according to each participant's capacity). After 3 min of rest, subjects were required to perform 3 repetitions at 70% of 1RM estimated. Another 3 min of rest was applied, and then subsequent trials were performed for 1RM with progressively heavier weights until the 1RM was determined within three attempts, with 3–5 min of rest between trials. All subjects were tested at baseline by two separate sessions (test-retest) with 48-h rest between them. To determine the results of the 1RM tests at baseline, we used the value of the highest load obtained after the test-retest[10].

The cardiorespiratory assessment was performed by performing an effort protocol on a treadmill (Quinton, model TM55, Seattle, United States), with continuous collection of expired gases with each breath (CPX Ultima, Medgraphics, Saint Paul, United States). The protocol had an initial warm-up speed of 4 km/h for 2 minutes, with increases of 0.3 km/h every 30 seconds, and a constant incline of 1% until physical exhaustion. Then there was a 4-minute recovery, with the first minute at 5 km/h, decreasing by 1 km/h every minute[10]. A

Polar® interface recorded heart rate during the execution of this protocol and the subjective perception of effort scale (Borg scale) was applied every minute. The average data from the last 30 seconds of the test, ventilation, maximum oxygen consumption (VO_2max.), and speed of physical exhaustion were used to assess cardiorespiratory fitness[10,16].

Blood collection and biochemical analysis

Blood samples (~20 ml) were collected of the antecubital vein in vacuum tubes with anticoagulant (EDTA). The collections were made between 7:00 and 10:00 a.m. All volunteers were instructed: not to perform any activities before collection for 72 hours; fasting for 12 hours; and not to consume alcohol or caffeine 24 hours before collection.

Subsequently, the collected blood samples were subjected to the centrifugation process to separate the blood plasma, which was stored in a freezer at -80° C for later analysis.

Plasma IL-7 concentrations were determined in duplicate using the ELISA (Enzyme-Linked Immunosorbent Assay) method, adhering to the recommendations and specifications of the high-sensitivity kits (Quantikine HS ELISA kits, Catalog No. HS750, R&D Systems, Minneapolis, United States). The kits have a sensitivity of 0.1 pg/mL and an intra- and interassay coefficient of variation of 3.3% and 7.8%, respectively.

Combined training

Strength training (ST) and aerobic training (AT) were performed in the same session by OT. These training sessions were divided into two stages and performed on 3 alternating days throughout the week (Mondays, Wednesdays, and Fridays). During stage 1, participants performed ST through a linear periodization with knee flexion, knee extension, 45º leg press, high pulldown, barbell curl, bench press, shoulder press, and triceps pulley, performed in all sessions; and calf extension/flexion and upper abdominal exercises performed in one or two sessions per week, with an alternation of these two exercises per session. Strength exercises were performed in 3 sets of 10-12 submaximal repetitions (without apparent Valsalva maneuver, apnea, and concentric failure) with a one-minute interval between sets, taking approximately 35 minutes to complete the session. Evaluating the training load in the bench press and leg press with the results of the 1RM test

of these exercises, the load was between 65 to 80% of 1RM. During this phase, the ordering of the exercises was alternated by segment. Subsequently, participants performed 36 minutes of walking/running on the treadmill. The AT had variation in intensity, such as: 4 minutes between 50 and 55% of VO_2max; 14 minutes between 55 and 65% of VO_2max; 14 minutes between 65-75% of VO_2max; and 4 minutes between 50 and 55% of VO_2max[14].

In stage 2, ST was maintained as in E1, however, with a decrease in volume and an increase in intensity, being 8-10 submaximal repetitions (70 to 80% of 1RM) and a 1 minute and 15-second rest between sets. Following the same duration of E1 per session. During this phase, the exercises were organized by performing the largest muscle groups and then the smallest. For AT, there was no change in training volume, only a progressive increase in intensity that followed the patterns of 4 minutes between 55 and 60% of VO_2max; 14 minutes at 60 and 70% of VO_2max; 14 minutes at 70 and 80% of VO_2max; and 4 minutes between 55 and 60% of VO_2max[14].

To control the intensity of AT, the calculation/transformation of VO2max values was used as a basis for the heart rate and speed established on the treadmill. In addition, maximum repetition tests were performed in the last session of each week to adjust the ST according to previously adopted procedures[10,11].

Statistical analysis

The Kolmogorov-Smirnov test was applied to identify data normality. To verify possible differences between OG and NWG, the independent Student's t-test was used. To compare pre-experimental period values and delta percentage change (Δ%) of OT and OC the independent Student's t-test, also was applied.

To compare pre-and post-experimental period effects (OC and OT groups), analysis of variance (ANOVA) for repeated measures was applied to determine significant differences between time*groups/treatment, followed by Tukey's post hoc (when applicable).

Pearson's correlation coefficient tests were performed to evaluate the correlation of plasma IL-7 (baseline NWG and OG, and Δ% of OT group) with anthropometric, body composition, physical fitness, and nutritional variables. Finally, we also calculated the "d" effect size for IL-7 (in cross-sectional and experimental period). Data are presented as mean ± standard deviation, and the significance level used was p ≤ 0.05. All

analyses were performed using Statistica 6.0 software.

Results

Cross-sectional results (NWG vs. OG)

A total of 23 volunteers completed the cross-sectional study. In the baseline comparison, 8 subjects composed the NWG; (2 women and 6 men), and 15 the OG (4 women and 11 men).

The characterization and comparison data of NWG and OG are presented in Tables 1 and Figure 1. The NWG shows lower weight, BMI, fat mass (kg and %), lean mass (kg), and lipid intake. The NWG also presents a higher protein consumption and lean mass percentage when compared to the OG (Table 1).

Regarding the plasma concentrations of IL-7 between the NWG and OG, higher levels were observed in IL-7 levels of obese (NWG = 21.26 ± 3.93 pg/mL; OG = 27.14 ± 3.64 pg/mL; p = 0.01) (Figure 1). The effect size of this difference between groups was ES = 1.54, which shows a large magnitude of difference between the groups.

Experimental períod results – Obese Combined Training Group (OT) vs. Obese Group (OG)

After baseline comparisons, the OG was divided for the experimental period into an OT (n = 8; 2 women and 6 men) and an OC (n = 7; 2 women and 5 men).

The pre- and post-clinical data of the OT and OC groups are presented in Table 2 and Figure 2. The OT group presented an increase in 1RM Leg Press (Tukey
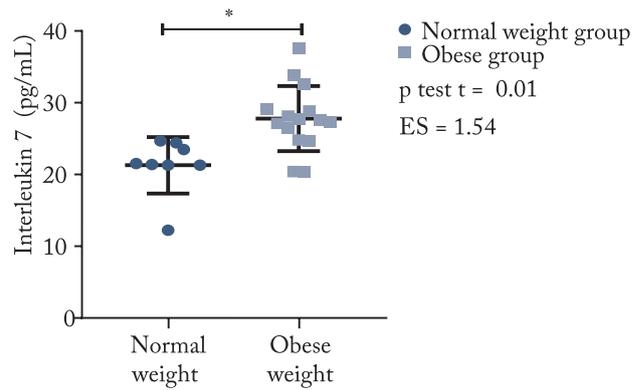

Figure 1 – Comparison of plasma interleukin-7 between normal weight and obese groups
Normal weight Group n = 8. Obese Group n = 15. *difference between groups by an independent t-test. Values presented as Mean ± Standard deviation. * p ≤ 0.05.

p< 0.001), 1 RM Bench Press (Tukey p< 0.001), and VO_2max (Tukey p< 0.02). The OT also showed a tendency to decrease weight (Tukey p = 0.07) and BMI (Tukey p = 0.06). When comparing the Δ% of OC and OT, differences were observed in weight (OC = 0.73% vs. OT = -2.22%, p = 0.02), BMI (OC = 0.73% vs. OT = -2.22%, p = 0.02), fat mass (OC = -0.68% vs. OT = -11.10%, p = 0.04), 1RM leg press (OC = 6.67% vs. OT = 37.88%, p = 0.001), 1 RM bench press (OC = 1.43% vs. OT = 35.17%, p = 0.0001) and VO_2 (OC = -11.76% vs. OT = 16.07%, p = 0.0001).

The plasma concentrations of IL-7 in the pre- and post-intervention moments of the OT and OC groups are shown in Figure 2-A. Although no significant

Table 1 – Characterization of the groups at the pre-intervention stage

Variable	Normal weight group (n = 8)	Obese group (n = 15)	p value
Age (years)	52.25 ± 4.20	51.66 ± 4.35	0.75
Weight (kg)	67.81 ± 8.51	94.80 ± 14.32 *	< 0.001
Height (meters)	1.70 ± 0.06	1.69 ± 0.12	0.91
Body mass index (m/kg²)	23.38 ± 1.53	32.85 ± 1.62 *	< 0.001
Carbohydrate intake (g/day)	45.46 ± 2.07	42.99 ± 6.51	0.38
Lipid intake (g/day)	27.97 ± 4.06	35.42 ± 4.54 *	< 0.001
Protein intake (g/day)	26.56 ± 4.14	21.51 ± 5.54 *	0.05
Total calorie intake (kcal/day)	1669.24 ± 333.97	1760.87 ± 539.18	0.66
1 Repetition Maximum Leg Press (kg)	191.25 ± 36.42	226.00 ± 58.92	0.14
1 Repetition Maximum Bench Press (kg)	31.00 ± 12.56	35.83 ± 12.30	0.38
Maximum oxygen consumption (ml/kg/min)	30.50 ± 4.70	25.77 ± 5.20 *	0.04
Lean mass (kg)	51.72 ± 8.19	59.02 ± 10.67 *	< 0.01
Lean mass (%)	74.82 ± 6.93	62.37 ± 6.01 *	< 0.001
Fat mass (kg)	17.28 ± 4.84	35.39 ± 7.42 *	< 0.001
Fat mass (%)	25.17 ± 6.93	37.68 ± 5.90*	< 0.001

Normal weight Group n = 8. Obese Group n = 15. Values presented as Mean ± Standard deviation. * = p ≤ 0.05

Table 2 – Pre and post values of anthropometric variables, body composition, physical fitness and eating behavior of the obese control and training groups

Variable	Obese Training Group (n = 8)			Obese Control Group (n = 7)			ANOVA group* time
	Pre	Post	Δ%	Pre	Post	Δ%	
Age (years)	51.94 ± 2.84	-	-	52.00 ± 4.93	-	-	-
Height (meters)	1.69 ± 0.08	-	-	1.67 ± 0.12	-	-	-
Weight (kg)	98.12 ± 16.33	95.90 ± 16.01	-2.2 ± 2.7 &	91.01 ± 11.65	91.60 ± 11.09	0.7 ± 1.3	0.03
Body mass index (m/kg²)	33.14 ± 1.67	32.40 ± 1.78	-2.2 ± 2.7 &	32.53 ± 1.62	32.76 ± 1.59	0.7 ± 1.3	0.02
Carbohydrate intake (g/day)	43.79 ± 7.35	46.03 ± 10.79	4.8 ± 4.8	42.06 ± 6.60	47.68 ± 7.27	7.4 ± 15.8	0.80
Lipid intake (g/day)	35.13 ± 5.07	34.88 ± 8.06	-0.2 ± 19.8	35.90 ± 4.79	31.25 ± 5.11	-12.4 ± 14.9	0.35
Protein intake (g/day)	21.06 ± 5.97	19.07 ± 4.38	-6.5 ± 18.1	22.04 ± 6.17	21.05 ± 6.00	-8.6 ± 44.1	0.78
Total calorie intake (kcal/day)	1720.00 ± 656.83	1776.76 ± 513.89	6.9 ± 18.0	1808.66 ± 467.63	1731.72 ± 288.21	-5.8 ± 18.2	0.29
1 Repetition maximum Leg Press (kg)	223.75 ± 46.88	306.87 ± 61.92 *	37.9 ± 15.6 &	228.57 ± 74.31	243.57 ± 86.92	6.7 ± 15.0	0.001
1 Repetition maximum Bench Press (kg)	35.10 ± 12.97	47.70 ± 16.84*	35.2 ± 18.0 &	36.78 ± 12.44	37.42 ± 13.61	1.4 ± 7.9	0.001
Maximum oxygen consumption (ml/kg/min)	25.34 ± 4.17	29.04 ± 2.90*	16.1 ± 12.0 &	26.27 ± 6.50	22.67 ± 4.24	-11.8 ± 11.9	< 0.001
Lean mass (kg)	59.32 ± 10.82	61.38 ± 11.82	3.5 ± 9.2	58.67 ± 11.36	58.92 ± 11.09	0.5 ± 3.6	0.42
Lean mass (%)	60.71 ± 6.81	64.07 ± 10.02	5.4 ± 9.3	64.27 ± 4.72	64.45 ± 5.10	0.3 ± 2.3	0.20
Fat mass (kg)	38.42 ± 9.23	34.58 ± 11.61	-11.1 ± 17.4&	31.93 ± 1.76	31.75 ± 2.76	-0.7 ± 3.6	0.10
Fat mass (%)	39.26 ± 6.81	35.78 ± 9.99	-9.5 ± 17.6	35.87 ± 4.48	35.54 ± 5.10	-1.0 ± 4.6	0.13

Values presented as Mean ± Standard deviation. * $p \leq 0.05$ in the comparison between the pre and post moments by the Tukey post hoc.
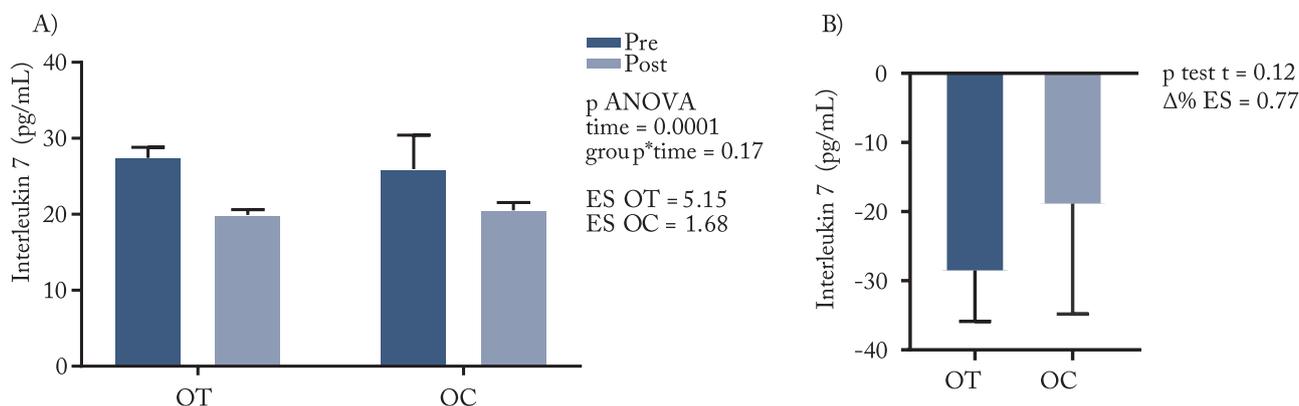

Figure 2 – Behavior of plasma interleukin-7 in the pre and post-experimental period of the obese control group and obese training group groups A- Pre-post results. B- Δ% results. OT: Obese training group n = 8. OC: Obese control group n = 7. Values presented as Mean ± Standard deviation.

group x time interaction was found in the ANOVA ($p = 0.67$), a time effect was observed in the pre-post experimental period on IL-7 concentrations (OC = pre 25.95 ± 4.45, post 20.52 ± 1.02 pg/mL; OT= pre 27.41 ± 1.93, post 19.90 ± 0.72 pg/mL; $p < 0.0001$). In the effect size of the pre-post values of each group, the OT presents an ES = 5.15 and the OC an ES = 1.68. No significant differences were observed between the Δ% of the groups (OC = -18.82% vs OT = -28.50%, $p = 0.12$) (Figure 2-B). In the effect size of the percentage deltas, an ES = 0.77 was observed, which is considered a medium/large magnitude of difference.

Regarding the analysis of correlations in pre- moment with all subjects together, a positive correlation was found between IL-7 with body weight ($r = 0.66$; $p = 0.01$; figure 3-A), BMI ($r = 0.65$; $p = 0.01$; figure 3-B), and fat mass ($r = 0.48$; $p = 0.03$; figure 3-C). No significant correlations were observed between the Δ% of the OT.

Discussion

The main findings show that obese individuals have higher plasma concentrations of IL-7 when compared to normal weight individuals of similar ages, which, to- gether with the observed correlations and baseline differ-
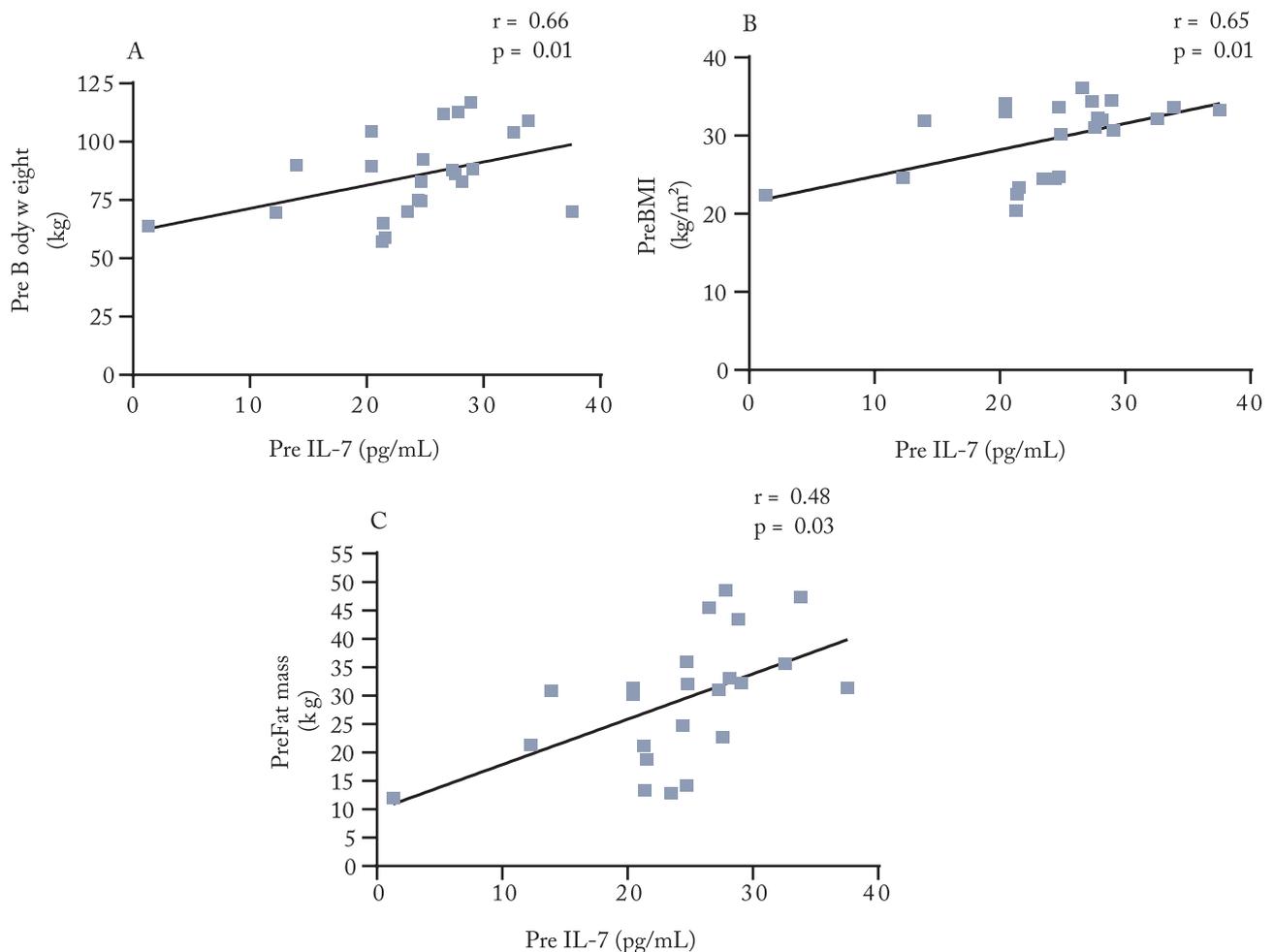
Figure 3 – Significant correlation.
A – Pre-moment interleukin-7 with body weight; B- Pre-moment interleukin-7 with Body mass index; C- Pre-moment interleukin-7 with fat mass.

ences between OG and NWG, suggest that excess body fat is associated with increased plasma concentrations of this cytokine. Additionally, CT can improve body composition and physical fitness in middle-aged obese individuals, although it is not possible to state that it induced decreases in plasma IL-7 concentrations by probabilistic statistics. However, the effect size analysis suggests that CT tends to induce a threefold greater magnitude of IL-7 decrease in OT when compared to OG.

The behavior of IL-7 has been shown to be quite complex in research with humans. Some studies that compared obese and eutrophic individuals observed that this cytokine was increased in the circulation of individuals with morbid obesity[17-19]. These findings are similar to the present results of higher circulating concentrations of IL-7 in obese individuals, reinforcing the hypothesis that obesity may have an influence on increasing this cytokine in an attempt to reestablish homeostasis and counterbalance the inflammation gener-

ated by excess body fat. Furthermore, we observed positive correlations between IL-7 and body weight, BMI, and fat mass, which shows the importance and influence of the relationship between weight control and body composition on the concentration of this cytokine.

However, other studies observe different results, with a decrease in circulating IL-7 in a group of obese elderly diabetics when compared to a eutrophic middle-aged group[20], and in young obese women without comorbidities when evaluated with middle-aged eutrophic women[21]. Certain studies have not yet observed differences between middle-aged women with metabolic syndrome compared to healthy overweight women[22] and among overweight and normal weight young women[23]. Differences between populations may have influenced these results, such as the discrepant ages of obese diabetic elderly individuals when compared to a eutrophic middle-aged group[20], or even high adiposity in both groups in the case of women with metabolic syndrome com-

pared to women without metabolic syndrome, with both groups being characterized as overweight[22].

Regarding the results of the experimental period, in the present study, we observed the effectiveness of CT in improving several components of physical fitness and body composition that are normally observed through the practice of this type of training[10,24,25]. For plasma concentrations of IL-7, although a reduction of almost 30% was observed in OT, it is not possible to state that this reduction occurred exclusively due to training, since in the OC group we also observed reductions in this cytokine. This decrease in IL-7 occurring in OC may be explained by the influence of several other factors that can influence inflammatory and immunological responses, such as the seasons, sleep quality and stress control. Improved sleep and reduced stress are factors that beneficially influence the neuroendocrine system, energy expenditure, appetite/hunger, and consequently, metabolism and the immune system[1,2]. Since these factors were not controlled in the study due to its experimental and longitudinal nature, their influence on the results cannot be ruled out. However, the effect size results show that OT shows a greater effect on IL-7, which, together with other benefits influenced by CT, encourages us to speculate that this reduction observed in the OT group is associated with body composition and especially with physical fitness improvements. However, effect size complements, but does not replace, inferential results, and such findings should be interpreted as indicative or exploratory.

Studies that evaluated the effects of physical exercise on the expression of muscle IL-7 observed that both in mice of both sexes that underwent 12 weeks of CT[26], as young men who performed 11 weeks of strenght training[4] showed an increase in the muscular expression of this cytokine, which may characterize it as a myokine. These results of increased expression of muscle IL-7 differ from the indication of a decrease in the average in the OT group, probably due to the fact that we analyzed the concentrations of IL-7 in plasma, and blood factors are affected by various tissues, as well as obesity and low-grade inflammation[2]. Additionally, circulating factors induced by physical exercise, such as myokines, tend to increase during or shortly after the training session[2]. This fact is corroborated by the results of increased IL-7 in the blood of young people after 30 minutes of the last section of 12 weeks of strength training[27]. Since we collected samples 48 hours after the last session of the CT program, a time when there is normally no longer an acute influence of exercise on the secretion of products into the bloodstream, this would explain why our results were divergent.

One result that draws attention when comparing NWG and OG is that we saw no differences in carbohydrate intake and total calories between the groups. However, the anthropometric and body composition differences observed between NWG and OG may be partly justified by the higher lipid consumption of obese individuals. A higher consumption of fat, especially saturated fat, is already well established as an inflammatory inducer. The type of carbohydrate consumption, which, depending on the type has large amounts of fiber, for example, could also influence the intestinal microbiota, inflammation, and body weight[28]. Additionally, the sample size and the way the diet was analyzed in a semi-quantitative manner (although validated and widely used, may present problems) may have influenced the results.

The present study also presents as a limitation the low number of subjects analyzed; however, our cross-sectional results still converge with some of the studies that show lower plasma IL-7 in some populations. Experimental studies with a larger number of subjects analyzed should be carried out to confirm the findings in relation to IL-7. Another limiting factor is that the sample consisted of both men and women, with an imbalance in the number of subjects of each sex within each group. But the fact that the women were in menopause may have minimized these gender differences.

In summary, the results of this study indicate that middle-aged obese insufficiently active individuals have higher circulating concentrations of IL-7 when compared with subjects of normal weight and the same age, suggesting that elevated body weight and fat are associated with an increase in this cytokine. Furthermore, 16 weeks of CT improves cardiorespiratory fitness and maximum strength, as well as reducing weight and body fat. Although the effect size for IL-7 was larger in the OT group, probabilistic statistics did not show a significant effect. Further studies with a larger number of participants should be conducted to evaluate the effects of CT and other types of training on IL-7.

Conflict of interest

The authors declare no conflict of interest.

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Author's contributions

Fatori RF: Conceptualization; Methodology; Validation; Investigation; Data curation; Funding acquisition; Writing – review & editing; Approval of the final version. Bonfante ILP: Validation; Formal analysis; Data curation; Visualization; Funding acquisition; Writing – original draft; Writing – review & editing; Approval of the final version. Ramkrapes APB: Validation; Formal analysis; Writing – review & editing; Approval of the final version. Chacon-Mikahil MPT: Validation; Writing – review & editing; Approval of the final version. Brunelli DT: Conceptualization; Methodology; Validation; Data curation; Funding acquisition; Writing – review & editing; Approval of the final version. Cavaglieri CR: Conceptualization; Methodology; Validation; Data curation; Supervision; Project administration; Visualization; Funding acquisition; Writing – original draft; Writing – review & editing; Approval of the final version.

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After publication the data will be available on demand to authors

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Reviewers' assessment

The authors and/or reviewers did not authorize the publication of either of the two reviews.