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Article

Effects of Cardiovagal Training on Autonomic Function, Inflammatory Markers and Insulin Levels in Adults with Obesity

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Abstract: Obesity is linked to an inflammatory process, with adipocyte release triggering insulin resistance (IR) and autonomic imbalance. A cardiovagal trainning protocol has shown favorable results in autonomic balance and decrease of inflammatory markers. The aim of this study was to analyze the autonomic behavior related to inflammatory and metabolic parameters in obese people after a cardiovagal exercise protocol. Twenty people with obesity, were distributed by their HOMA-IR value: obese without IR (n/IR) (n=8) and obese with IR (y/IR) (n=12). The cardiovagal training program was carried out in both groups for 8 weeks at a frequency of 5 times per week. A blood sample was obtained to determine insulin, leptin, TNF alpha and IL6 levels, in addition to determining the HOMA-IR index and autonomic function was measured by heart rate variability. Changes were recorded in the OB-IR group, a decrease in inflammatory markers, glycemia and a reduction of sympathetic activity after the cardiovagal training intervention. In addition, significant differences between the y/IR and n/IR groups were shown in insulin, leptin, TNFa and IL6 values. It can be concluded that after 4 weeks of intervention with a cardiovagal trainning protocol, parasympathetic modulation increased and inflammatory markers decreased in obese subjects.

Keywords: obesity; high-intensity interval training; heart rate variability; inflammatory markers; insulin resistance; autonomic function.

1. Introduction

The great changes of lifestyle in the world population toward more sedentary behaviours have been influenced by the industrialisation and automation of society. This has triggered a progressive increase of metabolic diseases [1], with an increasing trend in the young adult population [2].

Abdominal obesity is considered to be a metabolic disorder associated with a greater rate of cardiovascular disease, insulin resistance (IR), type 2 diabetes, and alterations in the functioning of the autonomic nervous system (ANS) [3,4]. In this sense, the neural mechanisms that have been involved in the etiopathogeny of obesity and IR could be partially explained by sympathovagal imbalance, due to the fact that high sympathetic activity plays a fundamental role in this complex relationship [5].

Sedentary lifestyles, unbalanced diets and a genetic predisposition are important factors that underlie obesity; however, the evidence also indicates that the sympathetic nervous system (SNS) plays an important role in the development and progression of such

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condition [6,7]. In this line, the ANS participates in the control of the cardiovascular, respiratory, immune and endocrine systems [8,9]. Moreover, the activity of the ANS, through the sympathetic fibres that innervate the adipose tissue, stimulates the lipolysis of the latter and the vasoconstriction of the peripheral arterioles, which has been associated with the deterioration of glucose uptake by skeletal muscles [10].

One of the intervention strategies for the management of autonomic imbalance in people with obesity is the control of eating habits and physical exercise with the aim of losing weight, since weight loss is associated with an inhibition of sympathetic activity [6,11–13].

In this line, performing physical exercise regularly is associated with adaptations that favour vagal activation and reduce the sympathetic load at rest [10,14]. This modification in ANS balance has been associated with a decrease in the chronic inflammatory response, reducing the synthesis and release of pro-inflammatory cytokines [6,15,16].

One of the intervention methods through physical exercise is high-intensity interval training (HIIT), which has been described as an effective tool to modify the autonomic balance, increasing vagal activation and favouring a regression of the sympathetic activity [17–19]. From this training method, a new exercise strategy emerged, known as "vagal training", which is defined as an exercise protocol based on sudden intensity changes (low to high) [20]. This is mainly justified by the baroreceptor-modulated response linked to the high blood volume, which would trigger a great post-high-intensity cardiac ejection power [21,22].

The aim of this study was to analyse the effect of a vagal exercise protocol on the inflammatory and autonomic response and compare the responses among obese people with and without IR. We proposed the hypothesis that vagal training is associated with a decrease in the inflammatory markers and with an increase in the vagal response in people with obesity.

2. Materials and Methods

2.1. Participants

The study sample consisted of 20 people of both sexes (12 men and 8 women), aged 24.1 ± 2.15 years, who presented obesity, determined by body mass index (BMI) ≥30 (31.59 ± 1.14 kg/m^2). The participants were distributed into two groups, categorised by their HOMA-IR value: the group of obese without IR (n/IR) (n=8) included the participants with a HOMA-IR value under 2.5, whereas the group of obese with IR (y/IR) (n=12) included those with a HOMA-IR value above 2.5 (Table 1).

All participants were physically inactive (<150 minutes of moderate or vigorous physical activity per week). The exclusion criteria were: (i) blood pressure (BP) ≥130/85 mmHg, (ii) being diagnosed with some skeletal muscle, pulmonary or neurological disease that prevented them from performing the protocol of exercises, and (iii) being under treatment with some drug that affects the autonomic function. All participants signed the informed consent form, and the rules of the Declaration of Helsinki were followed throughout the study. The procedures were evaluated and authorised by the Ethics Committee of Santo Tomás University (Santiago de Chile, Chile) (CEC UST N°51/2019).

2.2. Procedures

The study was carried out in the Physiology Laboratory of Santo Tomás University (Santiago de Chile, Chile). The participants were recruited by non-probability convenience sampling. Heart rate variability (HRV) and blood markers were measured between 8 and 10 a.m., two days before and two days after the HIIT intervention (Table 2).

Anthropometric variables. To calculate the BMI and categorise the obesity level, the height and weight of the participants were measured [23]. Waist circumference (WC) was

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recorded using an anthropometric tape (SECA – 203®, precision of 0.1 cm) (Table 1), considering the middle point between the anterior superior iliac crest and the last rib as the anatomical reference [24].

Autonomic function variables. HRV was measured using a heart-rate chest strap (Polar, model H7®), recording the R-R intervals of the QRS complex. The data recording for the evaluation of HRV was conducted with the participants at rest, in the supine decubitus position, for 10 minutes (the first 5 minutes for the stabilisation of the HR and the last 5 minutes for the data recording). The room temperature (22-24°C) and the noise during data recording were controlled (table 2). The data were extracted and analysed using the Kubios HRV 2.2 software (Department of Applied Physics, University of Eastern Finland, Kuopio, Finland).

Blood samples. These were obtained with the participants fasting before and immediately after the intervention by a qualified nurse, through antecubital fossa venipuncture. Blood samples (5 ml) were gathered for the determination of glucose, insulin and the following inflammatory markers: interleukin-6 (IL-6), interleukin-10 (IL-10), tumour necrosis factor alpha (TNF-α), leptin, and adiponectin (Table 2). The levels of glycemia and insulin were quantified using a clinical chemistry analyser equipment SIEMENS ADVIA 2400®. HOMA-IR was calculated with the following equation: *([fasting insulin «Uu/mL» x fasting glucose «mg/dL»] / 405)* [25]. This is the most reliable and frequently used method in clinical trials to evaluate changes in IR [26,27]. The value of 2.5 was considered as cut-off point to associate it with a state of IR [28,29].

The inflammatory markers were measured through ELISA (enzyme-linked immunosorbent assay) using a visible spectrophotometry equipment Iris - HI801 (HANNA INSTRUMENTS®). Moreover, the adiponectin/leptin variable was also calculated, which is associated with the function of the adipose tissue, being a biomarker of IR and a risk factor of cardiometabolic diseases [30].

2.3. Intervention

A vagal training protocol was applied for 8 weeks, at a frequency of 5 times per week, using a cycle ergometer without external resistance (Monark®, model Ergomedic 874E) and ergonomically adjusted to each participant. The training consisted of two phases: 1) the individual remained sitting for 55 seconds without pedaling (passive phase), and 2) the individual pedaled at maximum intensity for five seconds (active phase). The protocol consisted of 10 repetitions, with a total duration of 10 minutes. In the active phase, the individual was encouraged to carry it out at maximum intensity. As a safety and control measure during the execution of the exercise protocol, HR, BP and perceived effort were evaluated through the Borg scale. The criteria to interrupt the training protocol were the following: 1) Borg scale >15 (out of 20), 2) HR > 80% HRmax, and 3) systolic BP >160 mmHG, diastolic BP >100 mmHg. The test was performed indoors and it was controlled and supervised by the researchers (Figure 1).

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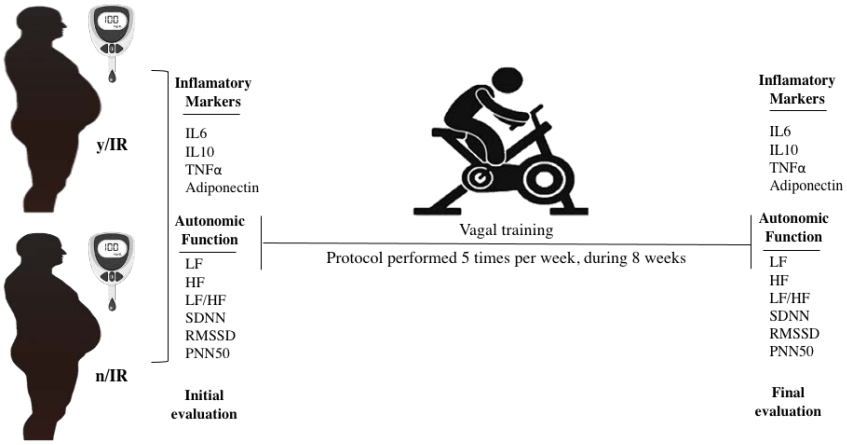

Figure 1. Training and testing exercises. n/IR (obese without insulin resistance group); y/IR (obese with insulin resistance group); IL (interleukins) TNF-α (tumour necrosis factor alfa); LF (low frequency); HF (high frequency); LF/HF (ratio of LF-to-HF power); SDNN (standard deviation of NN intervals); RMSSD (root mean square of successive RR interval differences); PNN50 (percentage of successive RR intervals that differ by more than 50 ms).

2.4. Statistical analysis

IBM SPSS 26® software (SPSS Inc. Chicago, IL, USA) was used for the statistical analysis. For the descriptive statistics, mean and standard error were calculated. To estimate the reliability of means, a 95% confidence interval was calculated. Regarding inferential analysis to study the intragroup pre–post differences, Student's t-test for related samples or Wilcoxon test was conducted depending on the Shapiro–Wilk normality test (normality). The comparison between groups was performed using Student's t-test or Mann–Whitney U-test, depending on the normality and homoscedasticity (Levene tests). Cohen's d effect size was also calculated, considering values of $d < 0.3$ as small, $d = 0.3–0.5$ as moderate, $d = 0.5–0.7$ as large, $d = 0.7–0.9$ as very large, and $d > 0.9$ as extremely large. Statistical significance was set at $p < 0.05$.

3. Results

Table 1 presents the descriptive data of the study population.

Table 1. Anthropometric characteristics and insulin resistance markers of the participants.

Variables.	n/IR (n=8) (Mean ± SD)	y/IR (n=12) (Mean ± SD)	p-value*	Effect Size§
Age (years)	24.6 ± 2.13	23.7 ± 2.18	0.387	0.41
Weight (kg)	92.25 ± 4.65	95.75 ± 5.66	0.164	0.66
Height (m)	1.71 ± 0.04	1.74 ± 0.04	0.164	0.75
BMI (kg/m2)	31.50 ± 1.08	31.67 ± 1.21	0.739	0.14
WC (cm)	112.25 ± 3.24	121.92 ± 4.14	0.000	2.54
Insulin (uU/mL)	10.35 ± 0.93	12.84 ± 1.23	0.000	1.60
Glucose (mg/dL)	89.25 ± 3.81	101.83 ± 8.14	0.001	1.86
HOMA_IR	2.27 ± 0.12	3.21 ± 0.16	0.000	6.46

n/IR (obese without insulin resistance); y/IR (obese with insulin resistance); BMI (body mass index); WC (waist circumference). * p-value: t-test or Mann–Whitney U-test according to normality and homoscedasticity. §Cohen's d (< 0.20, trivial; d = 0.2–0.6, small; d = 0.6–1.2, moderate; d = 1.2–2, large; d = 2–4, very large and d > 4, extremely large).

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The descriptive analysis of the initial HRV shows that y/IR presents the highest predominance in the sympathetic autonomic modulation for LF (81.41 ± 11.36 Hz vs 65.78 ± 13.13 Hz) with respect to n/IR (Table 2). Regarding the parasympathetic modulation, n/IR presented lower values than y/IR in all the variables considered: HF (20.47 ± 4.99Hz vs 21.52 ± 4.26 Hz), ratio LF/HF (3.25 ± 0.30 Hz vs 3.93 ± 1.02Hz), SDNN (60.10 ± 20.08 ms vs 61.27 ± 7.07 ms), RMSSD (82.16 ± 25.74 ms vs. 80.60 ±14.07 ms), PNN50 (52.06 ± 15.94 % vs 53.02 ± 6.82 %) (Table 2).

With respect to the initial inflammatory markers, y/IR presented greater values in all the inflammatory markers evaluated with respect to n/IR: IL6 (2.86 ± 0.37 vs 2.06 ± 0.21 pg/mL), IL10 (3.25 ± 0.22 vs 3.14 ± 0.25 pg/mL), TNF-α (3.42 ± 0.19 vs 2.70 ± 0.20 pg/mL) and leptin (35.55 ± 1.63 vs 24.26 ± 1.14 ng/mL) (Table 2). The adiponectin/leptin ratio in y/IR presents lower values than n/IR at the beginning of the intervention (0.13 ± 0.01 vs 0.17 ±0.02); moreover, it was observed that, in both groups, y/IR and n/IR showed an increase in this variable after the intervention (↑31.50% vs ↑24.43%, respectively) (Table 2).

The inflammatory markers of n/IR showed favourable changes after the intervention: IL6 (2.06 ± 0.21 vs 1.73 ± 0.17 pg/mL), IL10 (3.14 ± 0.25 vs 2.78 ± 0.23 pg/mL), TNF-α (2.70 ± 0.20 vs 2.53 ± 0.23 pg/mL), leptin (24.26 ± 1.14 vs 23.16 ± 1.09 ng/mL), adiponectin (4.19 ± 0.27 vs 4.96 ± 0.23 ug/mL) and adiponectin/leptin ratio (0.17 ± 0.02 vs 0.21 ±0.01), with significant changes in all variables (Table 2). In y/IR, there were aksi favourable changes in the post-intervention values: IL6 (2.86 ± 0.37 vs 2.28 ± 0.31 pg/mL), IL10 (3.25 ± 0.22 vs 2.59 ± 0.26 pg/mL), TNF-α (3.42 ± 0.19 vs 2.77 ± 0.26 pg/mL), leptin (35.55 ± 1.63 vs 31.21 ± 2.33 ng/mL), adiponectin (4.51 ± 0.16 vs 5.18 ± 0.19 ug/ml) and adiponectin/leptin ratio (0.13 ± 0.01 vs 0.17 ± 0.02), with significant changes in all the above mentioned variables (Table 2).

Table 2. Pre-post intragroup comparisons.

		n/IR					y/IR				
		Pre (Mean ± SD)	**Post (Mean ± SD)**	**Change %**	**p-value***	**Effect size §**	Pre (Mean ± SD)	Post (Mean ± SD)	Change %	p-value*	Effect size§
Inflammatory Markers	IL6 (pg/mL)	2.06 ± 0.21	1.73 ± 0.17	↓ 16.03	0.001	1.94	2.86 ± 0.37	2.28 ± 0.31	↓ 20.38	<0.001	1.87
	IL10 (pg/mL)	3.14 ± 0.25	2.78 ± 0.23	↓ 11.41	0.001	1.56	3.25 ± 0.22	2.59 ± 0.26	↓ 20.30	<0.001	2.53
	TNF-α (pg/mL)	2.70 ± 0.20	2.53 ± 0.23	↓ 6.51	0.004	0.73	3.42 ± 0.19	2.77 ± 0.26	↓ 19.11	<0.001	2.5
	Leptin (ng/ml)	24.26 ± 1.14	23.16 ± 1.09	↓ 4.50	0.003	1.0	35.55 ± 1.63	31.21 ± 2.33	↓ 12.16	<0.001	1.86
	Adiponectin (ug/dL)	4.19 ± 0.27	4.96 ± 0.23	↑ 18.71	<0.001	3.34	4.51 ± 0.16	5.18 ± 0.19	↑ 15.00	<0.001	3.52
	Adip/Leptin	0.17 ± 0.02	0.21 ± 0.01	↑ 24.43	<0.001	4.0	0.13 ± 0.01	0.17 ± 0.02	↑ 31.50	<0.001	2.0
Heart rate variability	SDNN	60.10 ± 20.08	65.25 ± 20.96	↑ 9.07	0.004	0.24	61.27 ± 7.07	80.14 ± 9.41	↑ 31.30	<0.001	2.0
	RMSSD	82.16 ± 25.74	91.52 ± 26.09	↑ 12.4	<0.001	0.35	80.60 ± 14.07	100.43 ± 18.49	↑ 25.67	<0.001	1.07
	PNN50	52.06 ± 15.94	55.49 ± 16.52	↑ 6.76	0.002	0.20	53.02 ± 6.82	66.98 ± 6.92	↑ 27.34	<0.001	2.01
	LF	65.78 ± 13.13	56.29 ± 13.30	↓ 14.78	0.002	0.71	81.41 ± 11.36	70.27 ± 12.26	↓ 14.05	<0.001	0.90
	HF	20.47 ± 4.99	23.21 ± 5.72	↑ 13.29	<0.001	0.47	21.52 ± 4.26	31.61 ± 7.26	↑ 48.03	<0.001	1.38
	LF/HF	3.25 ± 0.30	2.44 ± 0.29	↓ 24.7	<0.001	2.79	3.93 ± 1.02	2.35 ± 0.77	↓ 40.06	<0.001	2.05

n/IR Group (obese without insulin resistance); y/IR Group (obese with insulin resistance). Change % (percentage change between n/IR and y/IR pre and post intervention)IL (interleukins) TNF-α (Tumour Necrosis Factor alfa); LF (low frequency); HF (high frequency); LF/HF (ratio of LF-to-HF power); SDNN (standard deviation of NN intervals); RMSSD (root mean square of successive RR interval differences); PNN50 (percentage of successive RR intervals that differ by more than 50 ms). * p-value: t-test or Wilcoxon according to normality. §Cohen's d (< 0.20, trivial; d = 0.2–0.6, small; d = 0.6–1.2, moderate; d = 1.2–2, large; d = 2–4, very large)

In n/IR, HRV showed favourable changes: SDNN (60.10 ± 20.08 vs 65.25 ± 20.93 ms), RMSSD (82.16 ± 25.74 vs 91.52 ± 26.09 ms), PNN50 (52.06 ± 15.94 vs 55.49 ± 16.52 %), LF (67.78 ± 13.13 Hz vs 56.29 ± 13.30 Hz), HF (20.47 ± 4.99 vs 23.21 ± 5.72 Hz), and LF/HF ratio

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(3.25 ± 0.30 vs 2.44 ± 0.29 Hz), with significant changes in the variables RMSSD, HF and LF/HF ratio (Table 2). Similarly, in y/IR, there were also favourable changes in the post-intervention values: SDNN (61.27 ± 7.07 vs 80.14 ± 9.41 ms), RMSSD (80.60 ± 14.07 vs 100.43 ± 18.49 ms), PNN50 (53.02 ± 6.82 vs 66.98 ± 6.92 %), LF (81.41 ± 11.36 Hz vs 70.27 ± 12.26 Hz), HF (21.52 ± 4.26 vs 31.61 ± 7.26 Hz), and LF/HF ratio (3.93 ± 1.02 vs 2.35 ± 0.77 Hz). All changes were statistically significant (Table 2).

Figures 2 and 3 compare the differences between groups in the pre-post changes for the inflammatory markers and HRV, respectively. Regarding the inflammatory markers, there were significant differences in the change percentages between the two groups. In y/IR, there were greater changes in the levels of IL6 (0.25 pg/mL), IL10 (0.30 pg/mL), and TNF-α (0.48 pg/mL). Leptin presented a greater decrease (3.24 ng/mL) with respect to n/IR. The change differences between groups showed important modifications in the inflammatory markers: IL-6 (p=0.002), IL-10 (p=0.002), TNF-α (p=0.001) and leptin (p=0.001).

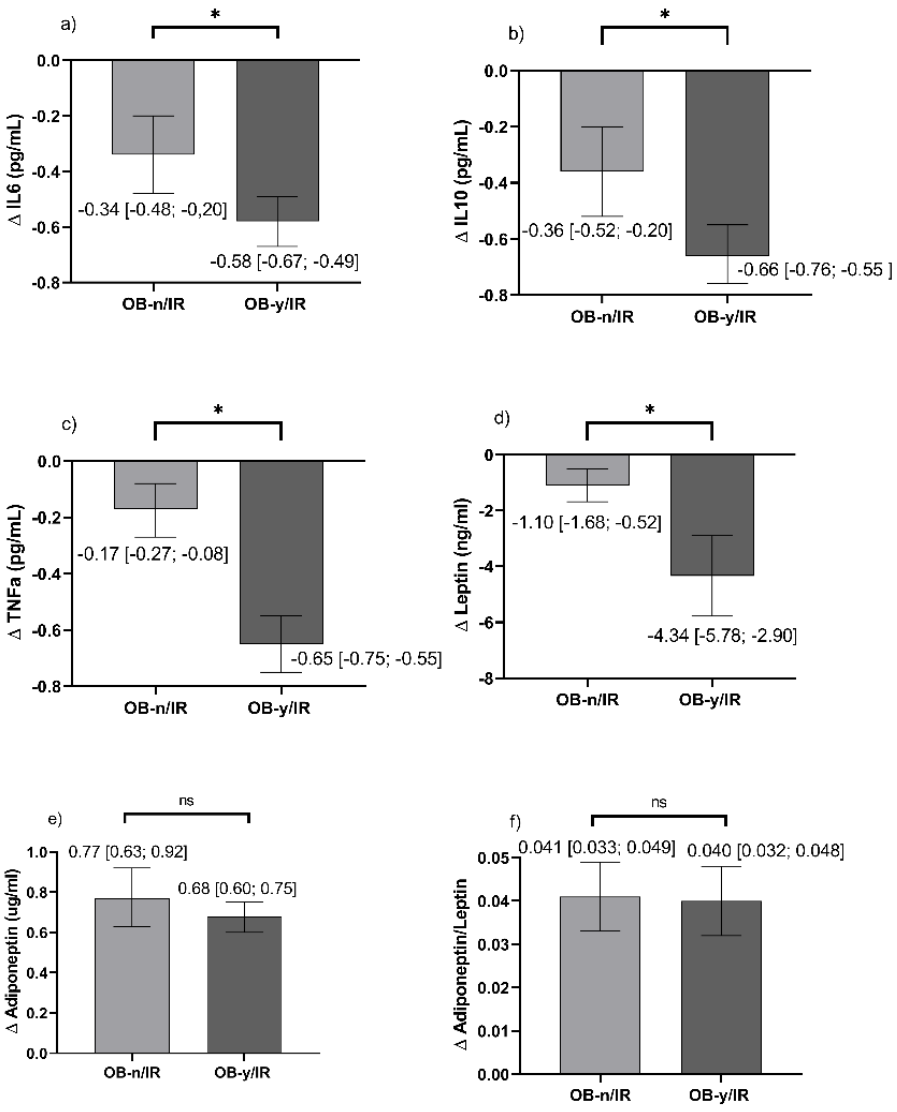

Figure 2. Difference of inflammatory markers between y/IR and n/IR groups. (a): exchange rate IL6 (interleukins); (b) exchange rate IL10 (interleukins); (c) exchange rate TNF-α (Tumour Necrosis Factor alfa); (d) exchange rate leptin; (e) exchange rate adiponeptin; (f) exchange rate adiponeptin/leptin

* Significant differences between groups ($p < 0.05$); ns: no significant differences ($p > 0.05$).

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In regard to the HRV variables, y/IR presented greater changes in SDNN (-13.72), PNN50 (-10.53) and HF (-7.35), with LF/HF showing a greater decrease (0.77); the change differences were significant in PNN50 (p=0.001), HF (p=0.001) and LF/HF (p=0.001). On the other hand, the values of RMSSD (p=0.052) and LF (p=0.402) did not present significant changes, although they showed greater changes in OB-y/IR (Figure 3).

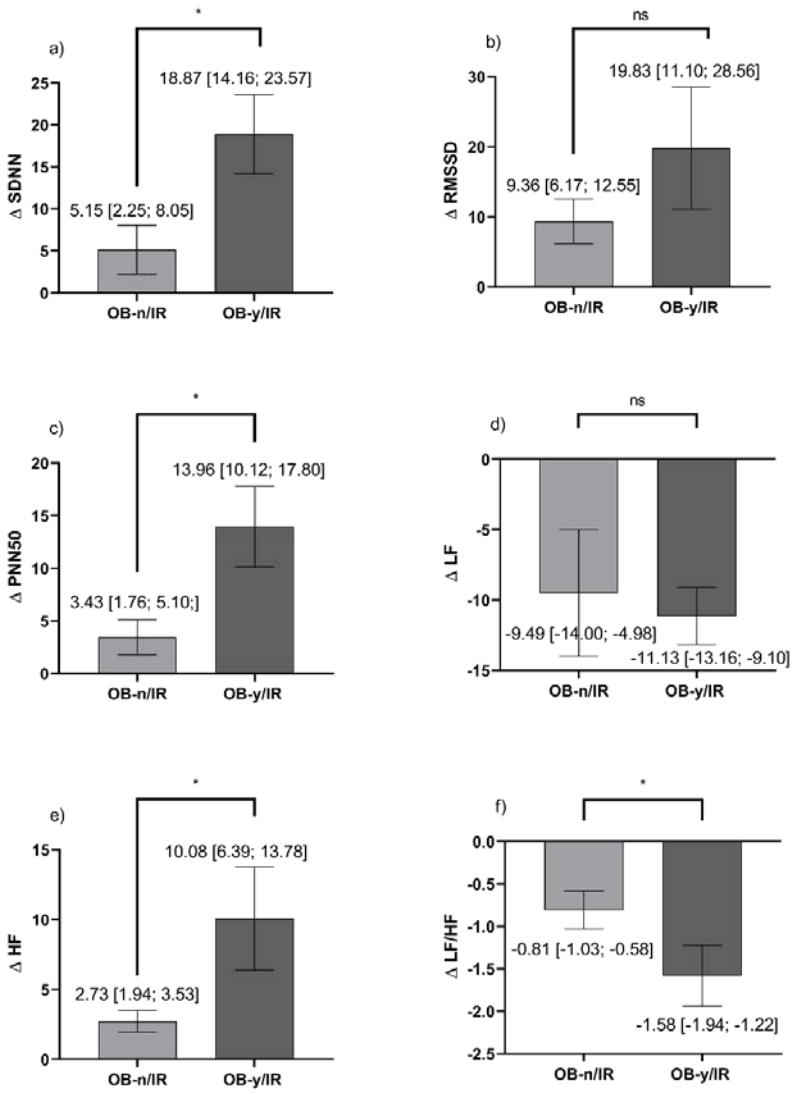

Figure 3. Difference of HRV parameters in frequency and time domain between y/IR and n/IR groups. (a) exchange rate SDNN (standard deviation of NN intervals); (b) exchange rate RMSSD (root mean square of successive RR interval differences); (c) exchange rate PNN50 (percentage of successive RR intervals that differ by more than 50 ms); (d) exchange rate LF (low frequency); (e) exchange rate HF (high frequency); (f) exchange rate LF/HF (ratio of LF-to-HF power).

* Significant differences between groups ($p < 0.05$); ns: no significant differences ($p > 0.05$).

4. Discussion

This study was focused on analyzing the effect of a vagal exercise protocol on the inflammatory and autonomic response in people with obesity.

Sympathetic nervous activation affects relevant aspects of the physiopathology of obesity and its metabolic effects. However, the mechanisms involved in this relationship remain unclear, since most of them present a bidirectional effect. For example, IR may be caused by the sympathetic activation, although, in turn, the associated hyperinsulinemia may activate the sympathetic branch of the ANS [5].

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The data obtained in this study show that people with obesity and IR present greater sympathetic activity at rest, accompanied by a greater presence of inflammatory markers (Table 2). This could be explained by an imbalance in inflammatory signaling [31], triggering a state of low-grade chronic inflammation; consequently, immune cells infiltrate, altering the structure and function of the adipose tissue [32]. In this sense, the effects of abdominal obesity should not be focused only on the change in body composition, but also on the potential impact on the physiopathology of the metabolic syndrome [3]. Thus, with the presence of morphofunctional changes, different types of obesity profiles are recognised, as was observed in our study, which identified a group of participants with obesity and no metabolic response (n/IR) and a group of participants with obesity who were metabolically active (y/RI) (Table 2).

Weight loss and physical exercise are key treatments in the control of obesity and metabolic syndrome. In this line, the reduction of visceral fat is linked to weight loss. One of the methods to favor weight loss is physical exercise in its high-intensity modality, which, in turn, is associated with a decrease in sympathetic nervous activity. In this sense, the scientific evidence highlights the benefits of HIIT in people with obesity in relation to weight composition [33], the reduction of inflammatory markers [34] and the decrease of the sympathetic response [35]. Furthermore, HIIT has been recognised as an effective tool for the treatment of obesity, not only for its improvements in health parameters (Sawyer et al. 2016) but also for its adherence, as it is a time-effective modality [36].

In line with the results of Khalafi and Symonds [34], out findings show a decrease in the inflammatory markers (IL-6, IL-10, TNF-α) and leptin after the exercise protocol, along with an increase in the levels of adiponectin, with greater changes for y/IR, (Figure 2). Although the physiological mechanisms are not fully understood, some studies have shown the anti-inflammatory effect of HIIT. For instance, in the meta-analysis of Khalafi et al. (2020), 29 scientific studies (84 participants) demonstrated that, after a physical exercise protocol, there was a decrease in inflammatory markers and leptin, and an increase in adiponectin. However, IL-6 did not show a decrease in its parameters [34]. Similar results have also been obtained by Santos et al. (2016) [37], who evaluated the effect of a 16-week exercise protocol on inflammatory markers (IL- 6, IL-10, TNF-α and adiponectin) and insulin in 32 people with obesity and overweight. Of the two groups of participants, one performed a treadmill-training protocol 3 times per week of HIIT 1×4 min at 90% HRmax, whereas the other group performed continuous strain at 70% HRmax. At the end of the training, the values of IL-6 and adiponectin decreased only in the HIIT group (P=0.035) [37]. In this line, it has been reported that a concurrent 8-week training (three times per week) significantly increased the levels of the adiponectin/leptin index in both men (+ 63.5%) and women with obesity (+ 59.2%) [38].

In addition to the abovementioned, HIIT could generate modifications in the autonomic response, through changes in vagal activity. This could be explained by the effect of the transitions of high and low intensity, which would be associated with an increase of the central blood volume, resulting in a greater ejection volume. This greater ejection volume, after being detected by the arterial and/or carotid baroreceptors, would send a signal to the central nervous system, which would trigger a sympathetic retreat and a vagal activation during the recovery phase [21,22]. Thus, this study obtained a decrease in the sympathetic response (LF) and an increase of all variables related to the parasympathetic response (temporal variables SDNN, RMSSD, PNN50 and frequency variables HF and LF/HF) (Table 2). Similar results have been reported in the study of Silva et al. (2019) [39], in which 10 individuals completed three protocols: 1) a 30:30 HIIT (29 repetitions of 30 seconds each at 100% VO2max), 2) a 4:3 HIIT (3 repetitions of 4 minutes each at 90% VO2max), and 3) a continuous moderate-intensity protocol (21 minutes at 70% VO2max). Of the 3 protocols, HIIT 4:3 showed significant improvements in the linear variables related to the vagal response (greater sympathetic modulation of HF and lower parasympathetic modulation of LF) [39]. In the same line, Duarte et al. (2013) [20,40] con-

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ducted an 8-week study applying a protocol 3 times per week to 44 participants who performed a vagal training in a cycle ergometer (5 repetitions of 5 seconds each at maximum speed without load, with 55 seconds of rest between repetitions). The mentioned study obtained improvements in the vagal tone after the applied protocol [20]. At the beginning of the exercise, an immediate decrease of the vagal tone was observed, with an increase in cardiac output and HR during the first the seconds; then, when the high intensity was over, there was an overload of volume/pressure in the carotid bodies and baroreflex activation. With a training period of multiple repetitions, the reeducation of the reflex arc returns to the vagal activation induced by exercise. Immediately after the exercise protocol, the HR kinetics show a biphasic behaviour [20,40], characterised by a rapid decrease due to an increase in vagal activity, followed by a second, longer phase of HR decrease due to a slow sympathetic-adrenal retreat [40].

Similarly, HIIT could also explain the decrease in visceral fat. It has been reported that HIIT is more effective in weight loss than continuous aerobic exercise [41,42], which plays an important role in the regulation of body composition and the local consumption of fat. HIIT promotes the secretion of catecholamines, adrenaline [43], noradrenaline [44] and growth hormone, favouring the use of fat [45] to attain an effective weight loss.

Furthermore, the inflammatory, autonomic and WC values were greater in y/IR (Table 1). This could be due to the fact that the increase of central obesity increases fat mass through hypertrophy, resulting in a structural and functional remodeling, thus promoting a mild chronic inflammatory process, mainly at the expense of a change in the state of macrophages toward a pro-inflammatory state [46,47]. As a result of this, the infiltration of macrophages is responsible for the secretion of pro-inflammatory cytokines. The secretion of TNF-α plays an important role in the development of IR [48,49], affecting the insulin sensitivity of adipocytes through alterations in the signaling pathways and due to a functional and structural decrease in insulin receptor substrate (IRS) proteins, which results in a state of hyperinsulinemia due to the lack of hypoglycemic capacity [50].

It has been hypothesised that peripheral signals transmitted by insulin reach they hypothalamus and are associated with the activation of the proopiomelanocortin (POMC) pathway, which, in turn, activates melanocortin receptors (MC4) [3]. The activation of melanocortin receptor MC4 modulates the peripheral sympathetic activation, presumably through direct and indirect signaling processes. However, the current evidence suggests that the activation of the autonomic load from the reticular formation in the brain stem depends on a metabolic pathway associated with IRS-2 and PI3K [50, 51]. Thus, it is considered that the increase of TNF-α in blood causes a failure in the intracellular signaling of the sympathetic and parasympathetic efferent neurons of the brain stem, increasing the heart and kidney sympathetic discharge [52]. However, on the other hand, the increase in adipose tissue generates a great concentration of leptin, which contributes to sympathetic activation and the development of IR in people with obesity [53]. High levels of leptin are strongly related to the activation of the renal sympathetic system, which is caused by changes that take place in neural signaling [3]. Therefore, with the increase of inflammatory markers and leptin, there is a change in the sympathetic response [5].

Two limitations of this study are the small sample size and the short duration of the intervention. A longer training programme would produce more consistent information about the stability of these responses to this type of training.

5. Conclusions

The results of this study indicate that, after 8 weeks of cardiovagal training, there was a decrease in the inflammatory markers and a better vagal response in people with obesity. Similarly, the group of obese people with insulin resistance showed a greater response to the vagal training protocol than the group of obese people without insulin resistance.

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