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Effects of interval aerobic training combined with strength exercise on body composition, glycaemic and lipid profile and aerobic capacity of obese rats

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ABSTRACT

The purpose of this study was to investigate the effects of interval aerobic training combined with strength exercise in the same training session on body composition, and glycaemic and lipid profile in obese rats. Sixteen lean Zucker rats and sixteen obese Zucker rats were randomly divided into exercise and sedentary subgroups (4 groups, $n = 8$). Exercise consisted of interval aerobic training combined with strength exercise in the same training session. The animals trained 60 min/day, 5 days/week for 8 weeks. Body composition, lipid and glycaemic profiles and inflammatory markers were assessed.

Results showed that fat mass was reduced in both lean and obese rats following the exercise training (effect size (95% confidence interval (CI)) = 1.8 (0.5–3.0)). Plasma low-density lipoprotein–cholesterol and fasting glucose were lower in the exercise compared to the sedentary groups ($d = 2.0$ (0.7–3.2) and 1.8 (0.5–3.0), respectively). Plasma insulin was reduced in exercise compared to sedentary groups ($d = 2.1$ (0.8–3.4)). Some exercise × phenotype interactions showed that the highest decreases in insulin, homeostatic model assessment-insulin resistance, fasting and postprandial glucose were observed in the obese + exercise group (all, $P < 0.01$). The findings of this study suggest that interval aerobic training combined with strength exercise would improve body composition, and lipid and glycaemic profiles, especially in obese rats.

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KEYWORDS
Insulin sensitivity; metabolic syndrome; cholesterol; body composition

Introduction

Metabolic syndrome is a constellation of interrelated metabolic risk factors that may promote the development of cardiovascular disease (Funahashi & Matsuzawa, 2007; Grundy et al., 2005; "Third Report of the National Cholesterol Education Program (NCEP)," 2002).

The effects of exercise on metabolic syndrome have been studied for decades (Becker-Zimmermann et al., 1982; Lash, Sherman, Betts, & Hamlin, 1989). Haram et al. (2009) have reported that high-intensity exercise is more beneficial than moderate-intensity exercise at reducing cardiovascular disease risk in rats with metabolic syndrome. Moreover, recent studies have demonstrated that high-intensity aerobic–anaerobic interval training promotes improvements on obesity and lipid profile (Donnelly et al., 2009; Hamlin, Draper, Blackwell, Shearman, & Kimber, 2012; Kemi et al., 2005; Pratley et al., 2000). Strength training also demonstrates important metabolic effects by reducing fat and plasma lipids reduction (Houston et al., 2009; Williams et al., 2007; Wolfe, 2006). Consequently, the American College of Sports Medicine recommends the combination of strength training with "classical" aerobic exercise for a greater weight loss (Donnelly et al., 2009). Results of recent studies (Earnest et al., 2014; Sigal et al., 2014) comparing aerobic, strength training and combined aerobic-strength training encouraged us to further explore the metabolic effects of this combined type of exercise.

As far as we know, very few studies have focused on the metabolic effects of a combined aerobic interval and strength training protocols within the same session in obese individuals. Nevertheless, some studies have compared both types of exercise in humans with metabolic syndrome (Stensvold, Slordahl, & Wisloff, 2012). A similar study also compared both training protocols and their combination in the same session and they did not find changes in body weight, fasting glucose or high-density lipoprotein levels within or between the groups (Stensvold et al., 2010).

In this context, the genetically obese Zucker rat is an adequate animal model for the study of metabolic syndrome as it presents obesity, dyslipidaemia, insulin resistance and hypertriglyceridaemia (Mittwede, Xiang, Lu, Clemmer, & Hester, 2013; Stepp, Pollock, & Frisbee, 2004). Therefore, the present study aimed: (1) to investigate the effects of a training programme based on interval aerobic training combined with strength exercise on body composition, physical performance, glycaemic and lipid profile and some inflammatory markers in obese Zucker rats; and (2) to study the interactions taking place between the rat's phenotype and an interval aerobic training combined with strength exercise protocol.

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Methods

Animals and experimental design

Thirty-two male Zucker rats were separated into two subgroups ($n = 16$ each) based on their phenotype: lean or obese. Since the Zucker rat strain includes a control variety that does not present leptin resistance and consequently the obesity-derived disturbances, these rats were used as the "lean phenotype" control group. Each phenotype was further randomised and divided into two subgroups (exercise or sedentary) based on whether the animals undertook the training protocol or not. The above-described selection resulted in the following experimental groups: lean + exercise, lean + sedentary, obese + exercise and obese + sedentary (all, $n = 8$).

The animals, aged four weeks old, with an initial body weight of 165 ± 10 g were housed in group cages of 30*55*20 cm dimensions (4 rats per cage). The cages were located in a well-ventilated thermostatically controlled room (21 ± 2°C) with a relative humidity ranging 40–60% and a reverse 12 h light–12 h dark cycle (08:00–20:00 h). Throughout the experimental period (8 weeks), all rats had free access to distilled type 2 water (water with a lower resistivity than >15 MΩ cm) and consumed the diet *ad libitum*. Experimental diets were formulated to meet the nutrient requirements of rats (National, Research, & Council, 1995) based on the AIN-93M formulation described by Reeves, Nielsen, and Fahey (1993). Body weight was measured weekly at the same time, and the amount of food consumed was registered daily (Ohaus® Adventurer™ *Pro*. New Jersey, USA). At the end of the experimental period, the animals were anaesthetised with ketamine–xylazine (85 mg/kg body weight of ketamine and 10 mg/kg body weight of xylazine) and euthanised by cannulation of the abdominal aorta. Blood was collected (with heparin as anticoagulant) and centrifuged (1458 × g/15 min/4°C) to separate the plasma, which was subsequently removed and frozen in liquid nitrogen (N_2) and stored at −80°C.

All experiments were performed according to Directional Guides Related to Animal Housing and Care (Council, 2010), and all procedures were approved by the Animal Experimentation Ethics Committee of the University of Granada.

Exercise protocol

The experimental groups trained 5 days/week following a combined protocol based on interval aerobic training combined with strength exercise in the same training session. The animals ran on a motorised treadmill especially designed for rats (Panlab, Harvard apparatus, LE 8710R) and all sessions were performed during the dark cycle of the animals (active period). An electrical stimulus at the end of the treadmill forced the animals to keep running during the whole training session. Nonetheless, the maximum discharge was set at 0.8 mV, following the manufacturer's instructions.

The training protocol was designed based on recent studies that have demonstrated that high-intensity interval aerobic–anaerobic training promotes positive results on obesity and induces plasma and hepatic lipid reductions (Donnelly et al., 2009; Hamlin et al., 2012; Kemi et al., 2005; Pratley et al., 2000). Additionally, in the same training session, an aerobic strength training protocol was implemented since this kind of exercise has been postulated as a good tool for the improvement of insulin sensitivity and lipid profile (Donnelly et al., 2009).

A week before the beginning of the experimental period, the animals were adapted to the training procedures through a low-intensity running protocol, carried out daily during 20 min in the treadmill at 18 m/min. To establish the velocity for each maximal oxygen consumption, a maximal incremental test was performed at the start of the experimental period and was repeated every 2 weeks (Hamlin et al., 2012). This protocol, implemented via computer software (SeDaCom V2, Panlab, Harvard apparatus), provides an appropriate ratio of oxygen consumption and carbon dioxide production. Using the same software, maximal oxygen consumption, running time, maximal speed and total distance achieved were measured. The test ends when the animal is visibly exhausted and sited on the shock bar for >5 s. Blood lactate concentrations from the animals' tail were measured at the end of the incremental test (Lactate Pro, Arkray, The Netherlands).

The animals of sedentary groups were touched and transported from their cages to the treadmills and back every day in order to undergo similar experimental stressful conditions as the ones of the exercise groups. The sedentary control animals also ran on the treadmill for 5 min once a week.

The interval aerobic training combined with strength exercise protocol was designed and adapted from Haram et al. (2009) and Kemi et al. (2005) (Table 1). All sessions consisted of 60 min of effective work. The sessions started with a 10-min warm-up at 40% maximal oxygen consumption, followed by the strength training consisting on eight 2-min running bouts separated by 1 min of rest where the animals ran with an inclination which was progressively increased every two weeks from 10° up to 25° at a constant slow speed (20–25 cm/s, equivalent to ~30–40% maximal oxygen consumption). The strength exercise was followed by 30 min of aerobic interval

Table 1. Details of the aerobic interval exercise and resistance training protocol performed by the training groups.

		Week 1	Week 2	Week 3	Week 4	Week 5	Week 6	Week 7	Week 8
Warm-up 10 min		40% VO2max	40% VO2max	40% VO2max	40% VO2max	40% VO2max	40% VO2max	40% VO2max	40% VO2max
Resistance training. eight 2-min bouts, 1 min rest	Inclination	10%	10%	15%	15%	20%	20%	25%	25%
	Speed	20 cm/s	25 cm/s	20 cm/s	25 cm/s	20 cm/s	25 cm/s	20 cm/s	25 cm/s
Aerobic interval training 30 min		4 min at 50% VO_2max alternated with 3 min at 65%	4 min at 55% VO_2max alternated with 3 min at 65%	4 min at 55% VO_2max alternated with 3 min at 70%	4 min at 60% VO_2max alternated with 3 min at 70%	4 min at 60% VO_2max alternated with 3 min at 75%	4 min at 65% VO_2max alternated with 3 min at 75%	4 min at 65% VO_2max alternated with 3 min at 80%	4 min at 65% VO_2max alternated with 3 min at 85%

exercise, alternating 4 min bouts at 50–65%. Maximal oxygen consumption with 3 min bouts at submaximal intensity at 65–85% maximal oxygen consumption.

Both, the training protocol and training sessions were designed and supervised by graduates in sport sciences in collaboration with specialists in working with animals.

Body composition analysis

Determination of body composition was assessed by means of a whole body composition analyser based on magnetic resonance imaging (EchoMRI™; EchoMedical Systems, Houston TX). This analyser estimated fat tissue (g), lean tissue (g), free water (ml) and total body water (ml) in live animals.

Biochemical analyses

Plasma total cholesterol, low-density lipoprotein–cholesterol, high-density lipoprotein–cholesterol, phospholipids, triglycerides and glucose were measured using an autoanalyser (Hitachi-Roche p800, F. Hoffmann-La Roche Ltd., Switzerland). The cytokines tumour necrosis factor alpha and interleukin-1 and interleukin-10 were measured with the rat kit (Milliplex. MAP kit; Millipore) and calibrated with Luminex 100/200 calibration kit. Adiponectin was measured with the Sandwich Rat Adiponectin ELISA kit. Plasma leptin and insulin concentrations were measured using the panel Rat Bone for rats (Milliplex. MAP kit; Millipore) and Luminex 200TM. The homeostatic model assessment for insulin strength was calculated using the formula [fasting insulin (μIU/ml) × fasting glucose (mg/dl)]/405.

On week 8, a 12 h urine sample from each animal was collected. Prior to recollection, rats were allocated in individual metabolic cages designed for the separate collection of faeces and urine. Urine volumes were recorded and urine glucose was measured using an autoanalyser (Hitachi-Roche p800, F. Hoffmann-La Roche Ltd., Switzerland).

Forty-eight hours prior to the end of the experimental period, an oral glucose tolerance test was performed following the protocol described by Prieto, Cancelas, Villanueva-Peñacarrillo, Valverde, and Malaisse (2004). Blood glucose concentration from the animals' tail was recorded at periods 0, 15, 30, 90 and 120 min (Breeze®2, Bayer) in order to calculate the area under the curve.

Statistical analysis

Results are presented as mean and standard deviation. The effects of the rat phenotype and interval aerobic training combined with strength exercise (sedentary vs. exercise) on body composition, aerobic capacity markers, lipid and glycaemic profile and cytokines were analysed by two-way factorial analysis of variance (ANOVA), with rat's phenotype and exercise as fixed factors. Two-way interaction terms were introduced into the models to test interactions between phenotype × exercise. A significant *P* value indicates that there are differences at least between two of the groups. *Cohen's d* and its exact 95% confidence interval (CI) were used in all the comparisons to estimate the standardised effect size. The "phenotype effect size" has been calculated combining both groups of the same phenotype compared to the other two groups (i.e. lean + sedentary and lean + exercise vs. obese + sedentary and obese + exercise). The "exercise effect size" has been calculated combining both groups of exercise compared to the two sedentary groups (i.e. lean + sedentary and obese + sedentary vs. lean + exercise and obese + exercise). Values of Cohen's $d \sim 0.2$, ~0.5 and ~0.8 were considered to represent small, medium and large effects, respectively.

Additionally, Bonferroni's adjustment was made on oral glucose tolerance test results to identify between which groups the differences were significant (e.g. obese + sedentary vs. lean + exercise group). All analyses were performed using the Statistical Package for Social Sciences (IBM-SPSS for Windows, version 22.0, Amonk, NY), and the level of significance was set at 0.05.

Results

Food intake, body weight and body composition

The effects of the rat's phenotype and exercise on final body weight, food intake and body composition are shown in Table 2. Body weight ($P < 0.01$) was lower in the exercise compared to the sedentary groups of the same phenotype. Exercise groups showed reduced fat mass compared to the sedentary groups for both phenotypes ($P < 0.001$). Lean body mass was increased in both exercise compared to the sedentary groups ($P < 0.05$). Obese + sedentary rats showed the highest fat mass whereas exercise interacted at reducing it ($P < 0.004$). An exercise × phenotype interaction was also found on food intake that increased by 17% when exercise was introduced to the lean phenotype while only increased by 8% when it was introduced to the obese phenotype ($P < 0.001$).

Aerobic capacity

The effects of the rat's phenotype and exercise on aerobic capacity markers are shown in Table 3. Post-maximal incremental test, blood lactate was lower in the lean compared to the obese groups ($P < 0.001$). Maximal oxygen consumption was higher in the exercise compared to the sedentary groups ($P < 0.001$). The total running time, maximal speed and the distance covered in the incremental test by the exercise groups were higher than the sedentary groups for both phenotypes (all, $P < 0.001$). An exercise × phenotype interaction was found in post-maximal incremental test blood lactate concentrations. The obese + sedentary group obtained the highest lactate concentrations and exercise decreased it by 34% in the obese phenotype while increased it by 6% in the lean phenotype (interaction $P < 0.01$). Significant interactions were also found in maximal oxygen consumption that was increased by 63% when the exercise group was introduced to the obese phenotype, while only increased by 13% in the lean phenotype (interaction $P < 0.001$). Obese + sedentary rats obtained the lowest values for total running time, maximal speed and distance covered in the maximal treadmill tests and exercise interacted by increasing these levels (all interactions, $P < 0.001$).

Table 2. Effects of the training protocol on final body weight, food intake and body composition for lean and obese rats.

	Lean + sedentary	Lean + exercise	%*	Obese + sedentary	Obese + exercise	%*	*P* phenotype	*P* Exercise	*P* exercise × phenotype	Effect size phenotype†[a]	Effect size exercise†[b]
Final body weight (g)	318.5 (16.1)	282.3 (12.2)	−11.4	462.2 (33.0)	438.3 (28.3)	−5.2	<0.001	0.003	0.518	−6.3 (−8.8, −3.7)	1.3 (0.2, 2.5)
Food intake (g/day)	20.5 (0.2)	23.9 (0.1)	16.6	25.4 (0.2)	27.5 (0.2)	8.3	<0.001	<0.001	<0.001	−24.0 (−33.1, −15.0)	−15.6 (−21.4, −9.7)
Fat mass (g)	20.0 (5.2)	15.0 (3.3)	−25.0	218.3 (13.3)	184.7 (21.6)	−15.4	<0.001	<0.001	0.004	−14.5 (−20.0, −9.0)	1.8 (0.5, 3.0)
Lean mass (g)	241.0 (36.4)	244.5 (27.6)	1.5	186.5 (29.1)	204.2 (19.1)	9.5	<0.001	0.025	0.144	1.7 (0.5, 2.9)	−0.4 (−1.4, 0.7)
Total body water (ml)	114.2 (8.1)	110.4 (8.1)	−3.3	164.4 (12.4)	174.7 (9.1)	6.3	<0.001	0.375	0.063	−0.6 (−8.5, −3.5)	−0.3 (−1.4, 0.7)

Notes: Values expressed as mean (standard deviation). †Effects size statistics are expressed as Cohen's *d* (95% exact CI). *Percentage of difference between the sedentary and exercise groups was computed as ((exercise − sedentary)/sedentary) × 100. [a]Effect size corresponds to lean + sedentary and lean + exercise versus obese + sedentary and obese + exercise. [b]Effect size corresponds to lean + sedentary and obese + sedentary versus lean + exercise and obese + exercise.

Table 3. Effects of the training protocol on aerobic capacity markers for lean and obese rats.

	Lean + sedentary	Lean + exercise	%*	Obese + sedentary	Obese + exercise	%*	*P* phenotype	*P* exercise × phenotype	*P* exercise	Effect size†[a] phenotype	Effect size†[b] exercise
Exercise lactate (mmol/L)	5.5 (1.8)	5.8 (3.7)	5.5	12.5 (3.7)	8.3 (4.0)	−33.6	<0.001	0.002	0.278	−1.4 (−2.6, −0.2)	0.6 (−0.5, 1.7)
VO_2max (ml/min/kg$^{0.75}$)	14.2 (2.5)	16.1 (5.9)	13.4	14.7 (5.9)	24.0 (4.9)	63.3	<0.001	<0.001	<0.001	−0.9 (−2.0, 0.2)	−1.2 (−2.3, 0.0)
Running time (min)	15.6 (1.2)	20.3 (4.2)	30.1	12.2 (1.2)	16.6 (1.4)	36.1	<0.001	0.455	<0.001	1.7 (0.5, 2.9)	−2.1 (−3.4, −0.8)
Maximal speed (cm/s)	58.4 (5.6)	78.3 (17.1)	34.1	44.2 (4.7)	63.3 (7.1)	43.2	<0.001	0.435	<0.001	1.6 (0.4, 2.8)	−2.1 (−3.4, −0.8)
Distance (cm)	19836 (3932)	40604 (18533)	104.7	11456 (2182)	23741 (5379)	107.2	<0.001	0.428	<0.001	1.5 (0.3, 2.7)	−1.9 (−3.2, −0.6)

Notes: Values expressed as mean (standard deviation). †Effects size statistics are expressed as Cohen's *d* (95% exact CI). VO_2max, maximal oxygen consumption. *Percentage of difference between the sedentary and training groups was computed as ((exercise − sedentary)/sedentary) × 100. [a]Effect size corresponds to lean + sedentary and lean + exercise versus obese + sedentary and obese + exercise. [b]Effect size corresponds to lean + sedentary and obese + sedentary versus lean + exercise and obese + exercise.

Plasma lipid profile

The effects of the rat's phenotype and exercise on plasma triglycerides, low-density lipoprotein–cholesterol, high-density lipoprotein–cholesterol and phospholipids are shown in Table 4. Plasma triglycerides, low-density lipoprotein–cholesterol, high-density lipoprotein–cholesterol and phospholipids were lower in the lean compared to the obese groups (all, $P < 0.001$). Plasma low-density lipoprotein–cholesterol and total cholesterol were lower in the exercise compared to the sedentary groups for both phenotypes (all, $P < 0.001$). A significant decrease of plasma phospholipids was found in the exercise compared to the sedentary groups ($P < 0.01$). The obese + sedentary group obtained the highest values for low-density lipoprotein–cholesterol, whereas exercise interacted reducing these values ($P < 0.01$). Exercise increased high-density lipoprotein–cholesterol levels in the lean group and decreased these levels in the obese group (interaction $P < 0.05$).

Glycaemic profile

The effects of the rat's phenotype and exercise on glycaemic profile are shown in Table 4. Figure 1 additionally shows fasting and postprandial glucose after the oral glucose tolerance test. Fasting glucose and insulin were higher in the obese compared to the lean phenotype (both, $P < 0.001$), and in the sedentary compared to the exercise groups (both, $P < 0.001$). Urine glucose was also higher in the obese compared to the lean phenotype ($P < 0.01$). The obese and sedentary groups obtained an increased homeostatic model assessment index than their respective lean and exercise groups (both, $P < 0.001$).

Regarding the oral glucose tolerance test, postprandial blood glucose at 15, 30, 60 and 90 min was lower in the exercise compared to the sedentary groups for both phenotypes (all, $P < 0.01$). Some exercise × phenotype interactions were found for plasma insulin, homeostatic model assessment index (both, $P < 0.001$), fasting glucose and the area under the curve after the oral glucose tolerance test (both, $P < 0.01$), showing a higher effect of interval aerobic training combined with strength exercise on improving glycaemic profile markers in the obese than in the lean group. Finally, obese + sedentary rats obtained the highest fasting and postprandial glucose after 120 min but exercise reduced these levels (both interactions, $P < 0.01$).

Inflammatory markers

Tumour necrosis factor alpha was increased in both exercise compared to sedentary groups ($P < 0.01$). In addition, obese rats showed lower levels of adiponectin than lean rats ($P < 0.001$). Exercise reduced levels of interleukin-1 and interleukin-10 in the lean group but increased these levels when exercise was introduced in the obese group (both interactions, $P < 0.05$).

Table 4. Effects of the training protocol on lipid profile, glycaemic profile and inflammatory markers for lean and obese rats.

	Lean + sedentary	Lean + exercise	%*	Obese + sedentary	Obese + exercise	%*	*P* phenotype	*P* exercise	*P* exercise × phenotype	Effect size †[a] phenotype	Effect size †[b] exercise
Lipid profile											
Triglycerides (mmol/L)	0.83 (0.59)	0.45 (0.12)	−46.1	5.97 (1.17)	6.27 (1.44)	5.0	<0.001	0.906	0.335	−5.7 (−8.1, −3.3)	0.1 (−1.0, 1.1)
LDL cholesterol (mmol/L)	0.16 (0.03)	0.11 (0.02)	−31.7	1.11 (0.28)	0.51 (0.29)	−53.5	<0.001	<0.001	0.001	−3.3 (−5.0, −1.7)	2.0 (0.7, 3.2)
HDL cholesterol (mmol/L)	0.50 (0.09)	0.63 (0.11)	26.0	1.78 (0.21)	1.66 (0.17)	−7.8	<0.001	0.914	0.019	−7.8 (−10.8, −4.7)	0.0 (−1.0, 1.1)
Total cholesterol (mmol/L)	2.03 (0.19)	1.63 (0.20)	−20	5.80 (0.66)	4.86 (0.26)	−16.2	<0.001	<0.001	0.062	−10.0 (−13.8, −6.1)	2.0 (0.7, 3.3)
Phospholipids (mmol/L)	1.75 (0.29)	1.29 (0.12)	−26.4	5.05 (0.47)	4.65 (0.43)	−8.0	<0.001	0.002	0.818	−9.5 (−13.2, −5.8)	1.3 (0.1, 2.5)
Glycaemic profile											
Blood fasting glucose (mmol/L)	4.9 (0.30)	4.7 (0.36)	−3.9	7.1 (0.62)	5.7 (0.53)	−19.8	<0.001	<0.001	0.001	−3.3 (−4.9, −1.7)	1.8 (0.5, 3.0)
Area under the curve (A.U.)	3836 (1080)	1709 (378)	−55.4	6190 (1812)	2252 (751)	−63.6	0.002	<0.001	0.038	−1.4 (−2.6, −0.2)	2.8 (1.3, 4.2)
Urine volume (ml/12 h)	3.0 (0.8)	3.8 (1.2)	26.7	7.1 (3.2)	5.9 (1.8)	−16.9	<0.001	0.682	0.097	−1.6 (−2.8, −0.4)	0.1 (−0.9, 1.2)
Urine glucose (mmol/L/12 h)	3.0 (2.04)	2.2 (0.65)	−25.6	4.0 (1.75)	3.7 (1.88)	−7.4	0.006	0.200	0.569	−0.8 (−1.9, 0.3)	0.3 (−0.7, 1.4)
Urine glucose ((mmol/L)/ml/12 h)	0.94 (0.81)	0.69 (0.47)	−26	0.67 (0.65)	0.85 (0.44)	21.4	0.800	0.776	0.214	0.1 (−1.0, 1.1)	0.1 (−1.0, 1.1)
Insulin (pmol/L)	8.90 (2.96)	8.73 (1.57)	−1.9	38.72 (6.85)	21.82 (4.42)	−43.8	<0.001	<0.001	<0.001	−5.0 (−7.2, −2.9)	2.1 (0.8, 3.4)
HOMA	0.3 (0.1)	0.2 (0.1)	−33.3	6.1 (1.9)	1.6 (0.6)	−73.8	<0.001	<0.001	<0.001	−4.1 (−5.9, −2.2)	3.1 (1.5, 4.6)
Leptin (µg/L)	8.31 (10.49)	3.88 (4.78)	−53.4	574.24 (133.68)	51.94 (28.29)	21.5	0.121	0.169	0.166	−5.3 (−7.6, −3.1)	5.0 (2.9, 7.2)
Inflammatory markers											
IL-1 (pg/ml)	150.2 (162.6)	45.7 (67.3)	−69.6	60.7 (40.8)	98.9 (54.2)	62.9	0.861	0.333	0.049	0.2 (−0.8, 1.3)	0.4 (−0.7, 1.5)
IL-10 (pg/ml)	134.6 (96.5)	99.2 (111.5)	−26.3	84.7 (42.2)	206.5 (93.3)	143.8	0.920	0.119	0.023	−0.3 (−1.4, 0.7)	−0.5 (−1.6, 0.6)
TNF alpha (pg/ml)	0.8 (0.5)	1.3 (1.1)	62.5	0.2 (0.2)	0.4 (0.3)	100.0	0.006	0.288	0.788	1.3 (0.1, 2.4)	−0.6 (−1.7, 0.4)
Adiponectin (µg/ml)	0.21 (0.05)	0.20 (0.02)	−3.6	0.14 (0.03)	0.17 (0.04)	43.2	<0.001	0.311	0.084	1.5 (0.3, 2.6)	−0.3 (−1.4, 0.7)

Notes: Values expressed as mean (standard deviation). †Effects size statistics are expressed as Cohen's *d* (95% exact CI). [a]Effect size corresponds to lean + sedentary and lean + exercise versus obese + sedentary and obese + exercise. [b]Effect size corresponds to lean + sedentary versus lean + exercise and obese + exercise. LDL: low-density lipoprotein; HDL: high-density lipoprotein; A.U.: Arbitrary Units; HOMA: homeostasis model assessment; IL: interleukin; TNF: tumour necrosis factor. *Percentage of difference between the sedentary and training groups was computed as ((exercise − sedentary)/sedentary) × 100.

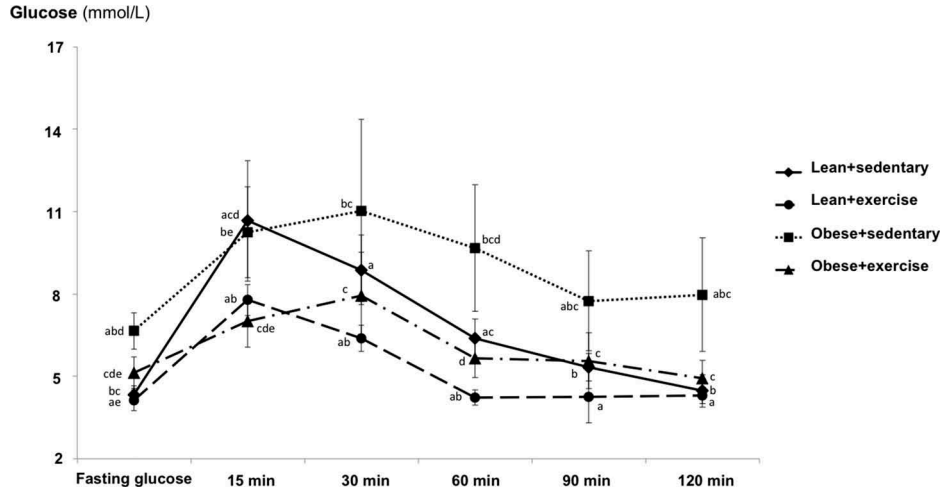

Figure 1. Fasting and postprandial glucose at 15, 30, 60, 90 and 120 min for lean and obese sedentary and trained rats.
[a,b,c,d]Common superscript indicates a pairwise significant difference ($P < 0.05$) between the groups. Pairwise comparisons were performed with Bonferroni's adjustment.

Discussion

The effects of interval aerobic training combined with strength exercise have not been previously studied in obese animals. The main findings of the current study show that sedentary rats, regardless of their phenotype, presented worse body composition, glycaemic and lipid profile than the animals that performed the interval aerobic training combined with strength exercise protocol. Moreover, even with a genetically adverse metabolic profile, exercise clearly resulted on restoring insulin sensitivity to normal ranges. Consequently, we suggest that interval aerobic training combined with strength exercise in the same work session might be a useful clinical tool in order to improve metabolic markers in obese individuals with metabolic syndrome.

Several studies have analysed the effects of exercise on body weight, fat mass, lipid profile or insulin sensitivity; however, most of them have solely used aerobic or strength training protocols. Some studies performed in rats have focused on the effects of aerobic training (Cameron, Alam, Wang, & Brown, 2012; Chan, Kendig, Boakes, & Rooney, 2013; Haram et al., 2009; Kim et al., 2013). In the study by Haram et al. (2009), 24 rats with a phenotype that closely resembles the metabolic syndrome were divided into three groups: continuous moderate exercise, aerobic interval training or sedentary group. The authors observed an increase in high-density lipoprotein–cholesterol by the aerobic interval training, whereas the other two groups remained unchanged. Contrary to our results, they found that both training protocols reduced triglycerides to an equal extent, whereas we have not observed decreases in triglycerides in our obese group. The absence of such differences could be explained by the severe hypertriglyceridaemia that characterises the obese Zucker rats (Mittwede et al., 2013; Stepp et al., 2004).

Kim et al. (2013) studied the effect of endurance training on glucose tolerance and body weight in Zucker rats. The animals ran on a treadmill for 60 min, 5 days/week. The obese training group decreased body weight and glucose tolerance. However, in contrast to our results, there was no body weight reduction in the lean Zucker rats, which could be due to the absence of strength training (Donnelly et al., 2009). Cameron et al. (2012) also investigated the effects of endurance exercise in a rat model of metabolic syndrome. According to our results, exercised rats showed decreased body weight and postprandial blood glucose. Exercise also improved plasma lipid profile, although contrary to our results Cameron et al. (2012) failed to find effects on fasting glucose. Finally, Chang, Chen, Chang, Liu, and Cheng (2006) performed a moderate exercise protocol consisting of 60 min running at 20 m/min, 7 days/week in 2 groups of obese and lean Zucker rats. Exercise reduced fasting glucose and insulin concentrations in the obese + exercise group, whereas in our study, fasting glucose was reduced in both lean and obese exercise groups. The lower effects observed in glycaemic metabolism in the above-mentioned studies might be explained by the fact that the intensity of the running exercise performed was low (an adult rat can run until a velocity equal to ~60 m/min).

A different protocol was used by Teixeira de Lemos et al. (2009) in which a group of lean and obese Zucker rats trained 3 days/week swimming for 60 min. A reduction of tumour necrosis factor alpha was observed in the obese + exercise rats. Similar results were obtained in our study but only in the lean + exercise group. Under our experimental design, interleukin-1 decreased 70% when the exercise was performed in the lean phenotype, although no reduction was observed in the obese phenotype. Finally, the protocol by Muhammad, Lokhandwala, and Banday (2011) performed at a low intensity in rats did not improve metabolic syndrome markers.

Strength training may be a perfect complement in the clinical struggle against the metabolic syndrome (Donatto et al., 2013; Donnelly et al., 2009), and some studies

performed in rats were based uniquely on strength exercise (Aparicio et al., 2011; Aparicio et al., 2013; Donatto et al., 2013). Our group previously analysed the effects of hypertrophy strength training on body weight and plasma lipid profile (Aparicio et al., 2013). In this study, the animals ran at 21 m/min, 5 days/week, with progressively increased weights in a bag tied with a cord to the tail. We found that body weight and plasma triglycerides were reduced and plasma high-density lipoprotein–cholesterol increased in the training group. We did not observe decreases in plasma total cholesterol like we did in the present study, which may be explained by the inclusion now of aerobic interval exercise. Donatto et al. (2013) performed a training protocol where Wistar rats climbed a vertical ladder, with weights secured to their tails. They found a reduction in glycaemia and low-density lipoprotein–cholesterol and an increase in high-density lipoprotein–cholesterol due to strength training as we but they did not find differences on triglycerides. Finally, they also demonstrated that strength training increased adiponectin levels and reduced interleukin-10 and tumour necrosis factor alpha (Donatto et al., 2013).

Other studies compared both types of training protocols in the same report (i.e. aerobic vs. strength exercise). Earnest et al. (2014) examined the effects of aerobic, strength or aerobic + strength training for 9 months in patients with metabolic syndrome and type 2 diabetes. They observed a decrease in the metabolic syndrome prevalence after both training programmes. They also found an association between these improvements and exercise efficiency, as measured by the maximal oxygen consumption. Under our experimental conditions, additional benefits were found on lipid and glycaemic profiles.

In addition to all the metabolic markers mentioned above, insulin resistance is thought to be essential in the development of metabolic syndrome (Reaven, 2004). In this sense, Hall et al. (2013) divided streptozotocin-induced type 1 diabetic rats into 5 groups; control, diabetic control, diabetic with strength training and diabetic with high- or low-intensity treadmill exercise. Strength-trained rats climbed a ladder with incremental loads, while high- or low-intensity-trained rats ran on a treadmill at 27 or 15 m/min, respectively. They found that all exercise groups had lower glucose area under the curve than diabetic animals. Trained rats required lower insulin doses, and the greatest reduction was evident in the high-intensity exercise group. This supports the idea that high-intensity exercise programmes show greater improvements in insulin sensitivity than other types of exercise (i.e. moderate or light intensities). Indeed, we have confirmed that the obese phenotype clearly presented insulin resistance (as indirectly measured through the oral glucose tolerance test and homeostatic model assessment-insulin resistance). Noteworthy, interval aerobic training combined with strength exercise interacted on reducing postprandial glucose 30, 60, 90 and 120 min after glucose intake.

Therefore, supported by our findings and the above-mentioned literature, we can hypothesise that the use of a combined training protocol, including aerobic and resistance training, is more beneficial than other programmes that only focus on the development of a unique type of training.

The present data suggest that a combined training protocol, including interval aerobic and strength exercise, may be an effective therapy for obese individuals with metabolic syndrome, more especially if they have obtained no results on improving their glycaemic and lipid profiles with other treatments. We believe that the experimental conditions of our sedentary groups of either lean or obese rats may reproduce the amount of movement that is currently done by most of sedentary population and can constitute a reliable experimental model that can be directly extrapolated to the sedentary lifestyle of many people.

Some limitations of the present study need to be mentioned: First, the current physiological results obtained in rodents must be confirmed in humans and cannot be directly extrapolated. Second, it is relevant to consider that the trainability of both phenotypes is not the same. Obese phenotype rats have greater difficulties for training and the velocity and total work volume were smaller, which may affect the potential improvements. Finally, we have not compared our training protocol with other exercise protocols (e.g. compared with only resistance training).

In response to the major objectives of the present study, we have observed that interval aerobic training combined with strength exercise performed in the same training session reduced body weight, fat mass, plasma triglycerides, phospholipids, total cholesterol, low-density lipoprotein–cholesterol, fasting and postprandial glucose, insulin and homeostatic model assessment-insulin resistance. Obese + sedentary rats presented an impaired lipid and glycaemic metabolism, but exercise ameliorated this adverse metabolic status. Therefore, these findings suggest that even in an obese phenotype, the practice of this type of exercise may enhance body composition and lipid profile and even restore glucose control to normal ranges. Other studies should confirm or contrast the present findings in humans.

Disclosure statement

No potential conflict of interest was reported by the authors.

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