Higher Insulin-sensitizing Response after Sprint Interval Compared to Continuous Exercise

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- glucose metabolism
- glycogen oxidation
- fatty acids
- energy expenditure

Abstract

This study investigated which exercise mode (continuous or sprint interval) is more effective for improving insulin sensitivity. Ten young, healthy men underwent a non-exercise trial (CON) and 3 exercise trials in a cross-over, randomized design that included 1 sprint interval exercise trial (SIE; 4 all-out 30-s sprints) and 2 continuous exercise trials at 46% VO_2peak (CE_{LOW}) and 77% VO_2peak (CE_{HIGH}). Insulin sensitivity was assessed using intravenous glucose tolerance test (IVGTT) 30 min, 24 h and 48 h post-exercise. Energy expenditure was measured during exercise. Glycogen in vastus lateralis was measured once in a resting condition (CON) and immediately post-exercise in all trials. Plasma lipids were measured before each IVGTT. Only after CE_{HIGH} did muscle glycogen concentration fall below CON ($P<0.01$). All exercise treatments improved insulin sensitivity compared with CON, and this effect persisted for 48-h. However, 30-min post-exercise, insulin sensitivity was higher in SIE than in CE_{LOW} and CE_{HIGH} (11.5±4.6, 8.6±5.4, and 8.1±2.9 respectively; $P<0.05$). Insulin sensitivity did not correlate with energy expenditure, glycogen content, or plasma fatty acids concentration ($P>0.05$). After a single exercise bout, SIE acutely improves insulin sensitivity above continuous exercise. The higher post-exercise hyperinsulinemia and the inhibition of lipolysis could be behind the marked insulin sensitivity improvement after SIE.

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Introduction

Active lifestyle and programmed exercise is recommended to regain glycemic control in populations with prediabetes or type 2 diabetes (T2D; [11]) A single session of moderate-intensity continuous exercise (60 min at 65% VO_{2max}) improves insulin sensitivity in healthy individuals for the following 2 days [19]. Additionally, a short bout of continuous but intense exercise (10 min at 85% VO_{2max}) increases insulin sensitivity in healthy people [8] and T2D patients [5]. Furthermore, high-intensity interval exercise used to deplete muscle glycogen improves insulin sensitivity in healthy [3] and T2D patients [12]. Thus, although it is well established that a single session of exercise improves insulin sensitivity, it is unclear which exercise mode (i.e., interval or continuous at low or high-intensity) is more efficacious for improving insulin sensitivity.

Sprint interval exercise (SIE) is an exercise training modality based on sessions of 4–8 supramaximal efforts of 30-s "all-out" sprints against a resistance set at 0.075 kg/kg body mass (i.e., Wingate Test). SIE has gained popularity since there is data to support that training based on SIE elicits similar metabolic benefits (e.g., gains in muscle oxidative capacity) to those achieved using continuous endurance training [14] while being more time-efficient. For instance, after 1 week of training using SIE (4–6 Wingate tests per session), Burgomaster et al. found a 20% increase in muscle GLUT4 content, a strong determinant of insulin sensitivity [9]. SIE-based training over 2 weeks (6 sessions, 4–7 Wingate tests per session), improves insulin sensitivity by 23–27% in sedentary and recreationally active participants [1,22], with a 6% increase in cardiorespiratory fitness [1]. However, a single session of sprint interval exercise using 4–5 modified Wingate test (i.e., resistance below 0.075 kg/kg body mass) does not seem to improve insulin sensitivity when assessed by an oral glucose tolerance test 24 h after exercise [6,29]. Likewise, the effects on insulin sensitivity of a single bout of SIE (4 bouts of regular Wingate tests) are not present when

measured by the gold standard hyperinsulinemic euglycemic clamp method 72 h following exercise in active individuals [22]. Thus, it is unclear to what extent a single session of SIE affects insulin sensitivity and the persistence of the effects (i.e., hours, days).

Exercise frequency recommendations for training programs geared to improve glycemic control should emanate from scientific evidence on the duration of the insulin sensitizing effect of a single bout of exercise. With this knowledge, exercise sessions could be scheduled when the insulin-sensitizing effects of the last bout of exercise begin to fade. To our knowledge, the time-course effects on insulin sensitivity of a single bout of SIE have not been systematically measured. Furthermore, few studies address which exercise mode (continuous or sprint interval) has larger or more prolonged effect on insulin sensitivity [6]. Provision of these data could help to improve exercise recommendation for populations at risk of developing insulin resistance (i.e., overweight and sedentary adults).

The primary aim of this study was to determine which exercise mode (continuous vs. sprint interval) is more effective at improving post-exercise insulin sensitivity. A secondary aim was to investigate which exercise mode has the most persistent positive effects on insulin sensitivity. We addressed these objectives using a single bout of exercise and following its effects up to 48 h. We correlated insulin sensitivity against indexes of fat and carbohydrate metabolism to search for possible mechanisms explaining the insulin sensitivity response.

Methods

10 young (24.1 ± 1.9 years; mean ± SD) healthy non-obese (BMI 25 ± 1.0 $kg \cdot m^{-2}$) and physically active but untrained (VO_{2max} 47.9 ± 2.2 $mL \cdot kg^{-1} \cdot min^{-1}$) males were recruited from the university student and employee population. None of the subjects were currently engaged in a formal exercise program. However, 4 subjects participated in local indoor soccer competition once a week (~20 games per year). After being provided with detailed information on the benefits and risks involved, all participants gave their written informed consent to participate in the study, which was approved by the local hospital's ethics committee and conformed to the latest revision of the Declaration of Helsinki and according to the current standards in sports and exercise science research [15].

Before the trials, participants underwent a cycling graded exercise test (GXT) starting at 100 W and increasing 25 $W \cdot min^{-1}$ until volitional exhaustion. Integrated standard 12-lead ECG (Quark T12, Cosmed, Italy) was monitored at each stage to ensure that all participants had a normal cardiovascular response to exercise. During the GXT, indirect calorimetry data were obtained (Quark B^2, Cosmed, Italy) and maximal oxygen consumption identified.

All participants underwent 4 experimental trials in a random counter-balanced order with at least 6 days in between. Trials started in the morning after an overnight 10-h fast that followed a standardized dinner (i.e., 2941 kJ, 50% from carbohydrate). Participants filled a 3-day dietary log, and dietary counseling was given to help them reach an appropriate carbohydrate intake (7 $g \cdot kg^{-1}$ body weight). In addition, they were asked to refrain from vigorous exercise 48 h prior to each trial and to ingest 500 mL of bottled water upon awakening to promote euhydration.

Insulin sensitivity was measured using a 50-min long intravenous glucose tolerance test (IVGTT) as proposed by Tura et al. (i.e., C_{SI} index [27]) following the recommendations of the ICARUS group [2]. C_{SI} has been validated in healthy and insulin-resistant population [27], and its reproducibility and responsiveness to a bout of exercise has been recently described [20]. IVGTT was performed using a glucose load of 0.5 $g \cdot kg^{-1}$ body mass with a maximal dose of 35 g of glucose for participants surpassing 70 kg of body weight. We used a 30% glucose solution (Glucosada 30%, Grifols, Spain) manually infused at an even rate over 3 min using two 60-mL syringes (BD Plastipak, Spain). Next, 5-mL blood samples were obtained every 10 min (i.e., 10, 20, 30, 40 and 50 min), and the catheter was flushed with 3 mL 0.9% saline after every sample to ensure patency. Insulin sensitivity assessments using this IVGTT procedure show a high day-to-day intraclass reproducibility (0.955 [20]) and a marked increase after 60 min of moderate-intense exercise (50 ± 3%; [20]).

IVGTT were performed in 4 experimental conditions; i) once without prior exercise (CON), ii) 30 min after 60 min of continuous pedaling at 45% VO_2peak (CE_{LOW}), iii) 30 min after 35 ± 2 min of continuous pedaling at 80% VO_2peak (CE_{HIGH}), or iv) 30 min after 4 bouts of 30 s all-out Wingate sprints (braking resistance of 0.075 kg per kg of body mass) interspersed with 4.5 min of active unloaded recovery (SIE). While the CE_{LOW} trial lasted 60 min, CE_{HIGH} was time-adjusted to match the energy expended during CE_{LOW} in each individual (~35 min). IVGTTs were reassessed 24 and 48 h after exercise to evaluate the persistence of the exercise actions on insulin sensitivity. Participants refrained from exercise, and their diet was carefully replicated during the 48 h following the experimental exercises trials.

Upon the participant's arrival to the laboratory, nude body weight (Hawk, Mettler Toledo, USA) and urine specific gravity (U_{SG}) (Uricon-NE, Atago, Japan) were measured to assess hydration status. An intravenous catheter was then inserted into an antecubital vein for blood sampling and glucose infusion. After 15 min of rest in supine position a baseline blood sample was obtained to measure blood lipids. Thereafter in the CON trial a muscle biopsy was obtained followed by the IVGTT. In the rest of the trials, participants exercised according to their randomized pre-assigned trial after the baseline blood sample was collected. After exercise, a biopsy from the vastus lateralis was obtained approximately 25 min after the end of exercise. A post-exercise basal blood sample was then drawn and the IVGTT performed. The IVGTT was repeated the next morning (i.e., 24 h) after a standardized dinner and an overnight fast, and then again the following morning (i.e., 48 h).

Exercise for the CE trials was performed on an electronically braked cycle-ergometer (Ergoselect 200, Ergoline, Germany) and for the SIE trial on a mechanically braked cycle-ergometer (Monark 894E, Sweden). After a 5-min warm-up at 100 W the workload was increased to the load for that exercise trial. In SIE oxygen consumption (VO_2) and carbon dioxide production (VCO_2) were continuously measured (Quark B^2, Cosmed, Italy) during the 1st and 3rd sprints. During the CE trials VO_2 and VCO_2 were recorded for 2 min every 5 min until the end of exercise. We calculated the workload for both CE trials (intended 45% and 80% VO_2peak) using the individual linear relationship between workload and VO_2 from the GXT.

Of the 10 participants, 6 volunteered for muscle biopsy sampling (4 extractions in each participant). Muscle biopsy samples were taken from the vastus lateralis according to procedures described

Table 1 Exercise measurements. Oxygen consumption, peak workload, exercise time and substrate oxidation (including glycogen concentrations) during a bout of continuous (CE_{LOW}, and CE_{HIGH}) or sprint interval exercise (SIE). Values are means ± SD. * Different from CE_{LOW} ($P<0.05$). † Different from CE_{HIGH} ($P<0.05$). ‡ Lower than glycogen concentrations in the non-exercise CON trial (545 ± 51 mmol · kg dry wt^{-1}).

	CE_{LOW}	CE_{HIGH}	SIE (only sprints)
mean VO_2 ($L \cdot min^{-1}$)	1.9 ± 0.2	3.2 ± 0.3*	3.5 ± 0.2*†
$\%VO_{2peak}$	46 ± 3	77 ± 5*	86 ± 10*†
mean workload (W)	108 ± 16	195 ± 27*	583 ± 78*†
fat oxidation rate (g/min)	0.3 ± 0.1	0.2 ± 0.1*	0.2 ± 0.2*
carbohydrate oxidation rate (g/min)	1.7 ± 0.3	3.9 ± 0.6*	4.5 ± 0.7*†
post-exercise glycogen concentration (mmol · kg dry wt^{-1})	382 ± 30	260 ± 46‡	434 ± 70
energy expenditure (kJ)	2397 ± 298	2349 ± 297	621 ± 31*†

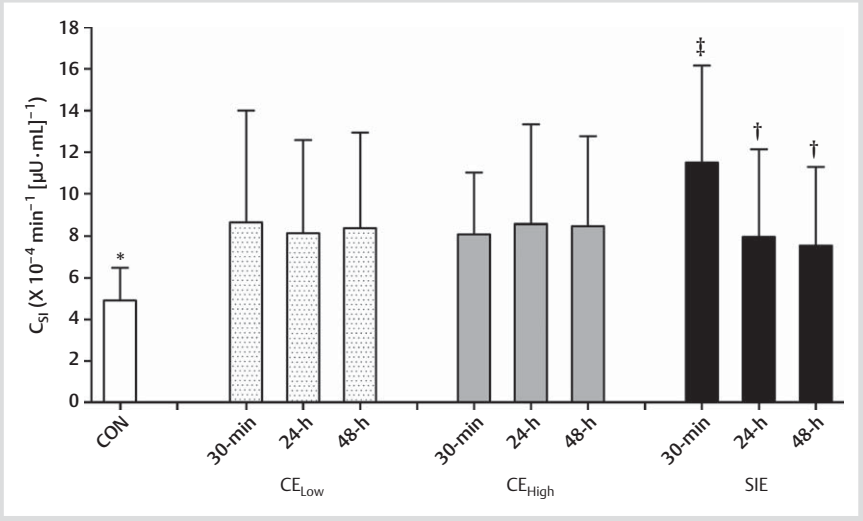

Fig. 1 Insulin sensitivity index (C_{SI}) in the basal state (CON), and 30 min, 24 h and 48 h after each exercise trial (CE_{LOW}, CE_{HIGH}, SIE). Values are means ± SD. * Lower than the rest of the trials. † Different from 30 min in the same exercise mode. ‡ Different from the other exercise trials at the same time point.

by Tarnopolsky et al. [26]. To limit participants' burden in terms of number of biopsies only one baseline muscle sample was obtained from each participant used as control (CON) for all trials. Since we imposed a strict control of carbohydrate in diet and physical activity before trials and because trials were separated (i.e., 10 days) to allow full recovery, we assumed that participants started with similar glycogen levels in all trials.

C_{SI} was calculated using IVGTT data as proposed by Tura et al. [27]. VO_2 and VCO_2 were used to calculate energy expenditure (EE) and substrate oxidation as proposed by Brouwer [7], and Jeukendrup and Wallis [16], respectively. During the 30 s all-out sprints of SIE, energy expenditure was calculated from indirect calorimetry with the assumption that aerobic energy expenditure represents 34% of total energy expended during the first sprint and 49% for the following [4].

Enzymatic assays were used to measure glucose (Enzymatic Glucose Reagent, Thermoscientific, USA), triglycerides (BioSystems, Spain) and free fatty acids (WAKO Chemicals, Germany) using a multichannel spectrometer plate reader (Versamax, Molecular Devices, USA). Insulin concentration was analyzed by chemiluminescence (Architect System Insulin, Abbott Diagnostics Division, Germany). Muscle glycogen was determined from the measurement of glucose after acid hydrolysis [21]. Shapiro-Wilk test revealed that data were normally distributed. Two-way (times × exercise mode) repeated measures ANOVA was used to identify differences in insulin sensitivity between the experimental trials. One-way repeated measures ANOVA was used to analyze glycogen content, energy expenditure and baseline pre-trial parameters. Following a significant F test (Geisser-Greenhouse correction for the assumption of sphericity), differences between means were identified using Tukey's HSD post hoc procedure. Associations between selected variables were determined using Pearson correlations using all the available time points in each trial. Statistical significance was set at $P<0.05$. Results are reported as means ± SD. All of the tests were performed with SPSS for windows (Version 18, SPSS Inc., USA).

Results

Body weight and U_{SG} values were not different before any of the experimental trials (83.5 ± 0.4 kg and 1.019 ± 0.004 with $P=0.625$ and $P=0.561$, respectively) evidencing a similar pre-test hydration status. In addition, baseline fasting plasma glucose and insulin were not different among trials (4.8 ± 0.3 mmol · L^{-1} and 6.5 ± 1.5 μU · mL^{-1} with $P=0.334$ and $P=0.244$, respectively) suggesting compliance with the prescribed diet and exercise refraining before each trial.

Mean workload (W), average oxygen consumption during exercise, substrate oxidation, glycogen concentrations and energy expenditure are shown in **Table 1**. Exercise time during CE_{HIGH} (35 ± 2 min at 77 ± 5% VO_{2peak}) was calculated to match the energy expenditure of the CE_{LOW} trial (60 min at 46 ± 3% VO_{2peak}). However, SIE trial consisted of 4 bouts of 30-s "all-out" Wingate test sprints followed by 4.5 min of active recovery for a total of 20 min of exercise [10]. Vastus lateralis glycogen content in CON was 545 ± 51 mmol · kg dry wt^{-1}. Post-exercise glycogen content was lower than CON only after CE_{HIGH} ($P<0.001$; **Table 1**). There were no differences in glycogen concentration among post-exercise biopsies.

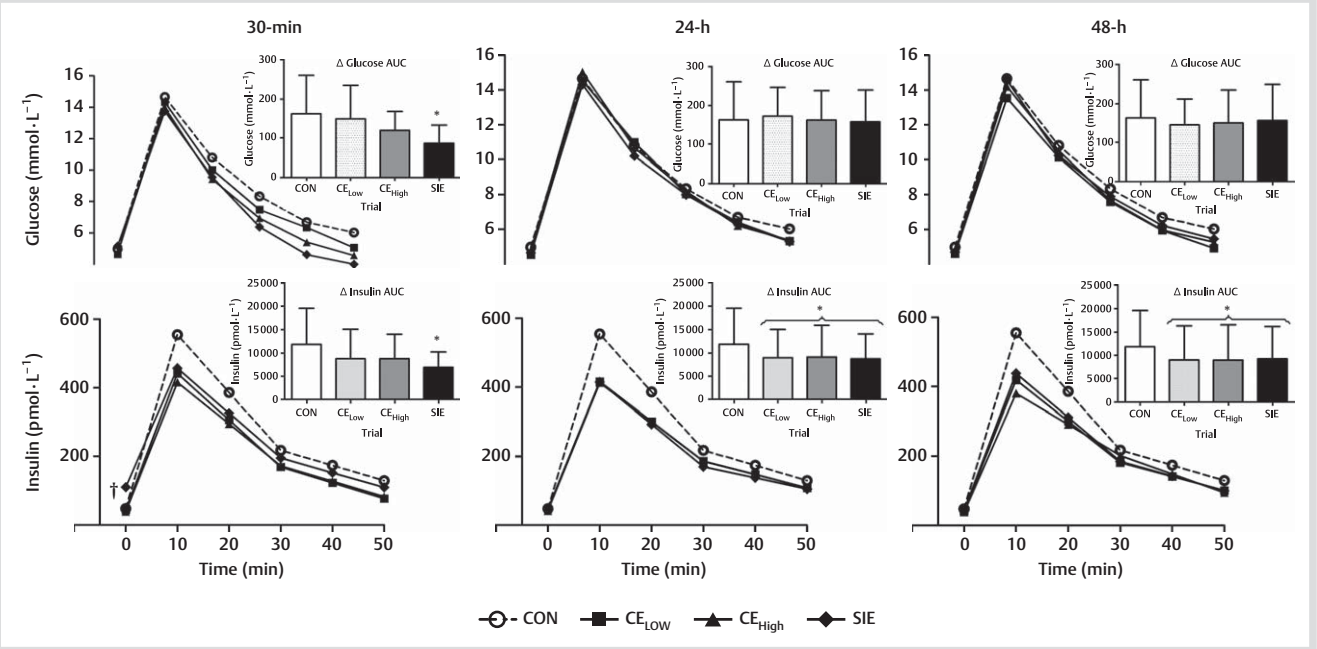

Fig. 2 Plasma glucose and insulin concentrations prior to (0 time point) and during the IVGTT, 30 min, 24 h and 48 h after exercise. Inserts represent the area under the curve of glucose and insulin (above baseline). Values are means ± SD. * Different from CON.

Table 2 Plasma metabolites. Blood lipids at rest (CON) and 30 min, 24 h and 48 h after a bout of continuous (CE_{LOW} and CE_{HIGH}) or sprint interval exercise (SIE). Values are mean ± SD. FFA, free fatty acid concentrations. * Different from CON ($P<0.05$).

	Insulin ($pmol \cdot L^{-1}$)	Glucose ($mmol \cdot L^{-1}$)	Triglycerides ($mmol \cdot L^{-1}$)	FFA ($mmol \cdot L^{-1}$)
CON	46.4 ± 22.0	4.94 ± 0.37	1.18 ± 0.50	0.33 ± 0.11
CE_{LOW}				
30-min	44.2 ± 20.8	4.61 ± 0.28	0.94 ± 0.58	0.49 ± 0.13*
24-h	45.1 ± 16.6	4.58 ± 0.53	0.96 ± 0.58	0.35 ± 0.15
48-h	43.4 ± 14.0	4.68 ± 0.27	0.88 ± 0.43	0.35 ± 0.16
CE_{HIGH}				
30-min	43.6 ± 20.8	4.76 ± 0.25	0.94 ± 0.58	0.37 ± 0.17
24-h	41.9 ± 12.9	4.78 ± 0.41	0.78 ± 0.38	0.39 ± 0.13
48-h	41.4 ± 15.1	4.75 ± 0.39	0.75 ± 0.37	0.34 ± 0.11
SIE				
30-min	104.8 ± 86.3*	5.26 ± 0.98	0.92 ± 0.35	0.19 ± 0.06*
24-h	45.5 ± 12.7	4.71 ± 0.40	0.63 ± 0.35*	0.36 ± 0.08
48-h	44.3 ± 12.4	4.69 ± 0.24	0.81 ± 0.47	0.35 ± 0.06

Calculated insulin sensitivity index (C_{SI}) from the 50-min IVGTT data is shown in **Fig. 1**. C_{SI} in basal conditions (CON) averaged $4.94 \pm 1.62 \times 10^{-4} \cdot min^{-1} \cdot (\mu U \cdot mL)^{-1}$. 30 min post-exercise (30 min) C_{SI} improved 75 % in CE_{LOW}, 64 % in CE_{HIGH} and 142 % in SIE. However, at this time point C_{SI} was higher after SIE than after CE_{HIGH} and CE_{LOW} ($P<0.05$). C_{SI} remained similarly elevated above CON in all exercise trials 24 and 48 h after exercise (**Fig. 1**; $P<0.05$). Post-exercise, plasma glucose and insulin concentrations are shown in **Table 2**. Changes in glucose and insulin concentration during the IVGTTs and their respective areas under the curve are shown in **Fig. 2**.

After exercise and before starting the IVGTT, plasma insulin was higher after SIE than after both continuous trials (**Table 2**; $P=0.042$). However, plasma glucose after exercise was not different among trials (**Table 2**; $P=0.092$). During the IVGTT performed 30 min after exercise glucose and insulin areas under the curve above baseline were lower during SIE than CON ($P=0.047$ and $P=0.006$, respectively; **Fig. 2**). Plasma free fatty acids (FFA) increased 30 min after CE_{LOW} but were reduced 30 min after SIE (**Table 2**).

Correlation analysis from all available time points in each trial showed that neither energy expenditure nor glycogen concentrations correlated significantly with C_{SI} changes from CON ($r=-0.243$, $P=0.499$ and $r=-0.122$; $P=0.630$, respectively). Plasma FFA or TG concentrations were not correlated with C_{SI} ($r=-0.044$; $P=0.680$ and $r=-0.136$; $P=0.201$, respectively).

Discussion

The aim of this study was to identify the more efficacious exercise mode to improve insulin sensitivity in a group of untrained male participants. The ultimate goal is help in the improvement of exercise prescription for people at risk of developing insulin resistance (i.e., sedentary, overweight). We monitored the effects of a bout of continuous vs. sprint interval exercise on the insulin sensitivity response 30 min, 24 h and 48 h after exercise. We found that 30 min after a bout of low-volume, high-intensity sprint interval exercise (SIE) insulin sensitivity improved above the values of continuous intensity exercise (CE) of greater energy expenditure. Our data thus suggest that some other factor specific to sprint interval exercise (SIE) mode enhances insulin sensitivity beyond continuous exercise.

Acutely (i.e., 30 min after exercise), SIE improved insulin sensitivity above CE, but the improvement lasted as long as with the CE trials (48 h). However, Whyte et al., [29] and Bertroff et al., [6] reported no response when testing insulin sensitivity 24 h after a modified SIE (i.e., lower intensity). While we presently used the original design of SIE with 4 bouts of 30-s all-out sprints using a resistance of $0.075 kg \cdot kg$ body $mass^{-1}$ (i.e., a Wingate test) [14], Whyte et al., and Bertroff et al., used lower exercise intensity. In addition, these studies measured insulin sensitivity

using oral glucose tolerance test (OGTT). It is well known that OGTT shows a poor reproducibility, which limits the use of OGTT in studies with small sample size [20,28]. This may well be due to gastric emptying differences, which are removed by IVGTT, the latter being a more reproducible technique [20]. Those technical issues could partly explain the different results between our study and those previous studies cited.

In agreement with studies measuring the effects of exercise intensity on FFA turnover [24], we observed that FFA were elevated after prolonged low-intensity exercise (CE_{LOW}), but reduced after SIE. Imbalance between fatty acid uptake and oxidation in which uptake exceeds oxidation has been linked to insulin resistance [23], while exercise prevents the fatty acid-induced insulin resistance effect [25]. In accordance with the data from Schenk and Horowitz [25], the elevated FFA after CE_{LOW} exercise did not prevent insulin sensitivity increase after exercise. However, the reduction in circulating FFA after SIE (surrogate of reduced FFA turnover) could have been involved in the acute improvements of insulin actions observed after SIE.

During very intense exercise (>85% VO_{2max}) catecholamine-mediated hyperglycemia is developed as a consequence of adrenergic stimulation of glycogenolysis and inhibition of the pancreatic insulin secretion [18]. However, plasma insulin concentration increases rapidly during the post-exercise period when the release of adrenergic inhibition allows the pancreas to respond to the hyperglycemia [17]. The simultaneous increases of glucose and insulin concentrations after intense exercise creates a milieu that could enhance the glucose uptake by the skeletal muscle [18]. The hyperinsulinemia reported after SIE could have contributed to the marked increases in insulin sensitivity. Furthermore, SIE-induced hyperinsulinemia may have inhibited adipose tissue lipolysis, explaining the acute reduction in plasma FFA concentrations. A reduction in FFA delivery to the cell may have also enhanced insulin sensitivity [23].

We searched for an explanation for the greater acute insulin sensitivity improvement immediately after SIE. Peroxisome proliferator-activated receptor γ coactivator-1α (PGC-1α), AMP-activated protein kinase (AMPK) and calcium/calmodulin-dependent protein kinase II (CaMKII) have been compared after isocaloric bouts of high or low-intensity exercise. High-intensity exercise has been shown to elicit greater activation of these markers compared to low-intensity continuous exercise [13]. It is thus possible that the abrupt changes in the energy demand during the sprinting portion of SIE could be associated with an immediate increased expression of intracellular mediators linked to enhanced insulin sensitivity and glucose transport after SIE. Unfortunately, we do not have the data to support this possibility.

The limitations of this study must be noted. We performed the 30-min IVGTT in all the exercise trials just after a vastus lateralis biopsy. It is possible that the stress induced by the biopsy procedure could have triggered glucose counter-regulatory responses that partly blunted whole body insulin sensitivity. However, that effect would have been present in all trials and should not be responsible for the differences found among exercises. To limit the number of biopsies per participant, only one baseline muscle sample was obtained and glycogen concentration at the end of the exercise trials was compared to that of the non-exercise situation (i.e., CON). Our intra-participant day-to-day variability in resting muscle glycogen is 12% (CV). However, we expect this variability to be randomly distributed among trials and not affecting the glycogen data pattern. Finally, it is worth acknowledging that the hyperinsulinemia 30 min following SIE may represent a confounding factor in the assessment of C_{SI}. It is possible that the marked increases in C_{SI} 30 min after SIE could have been induced by the elevated post-exercise insulin concentration stimulating glucose disposal. Nevertheless, we think that the observed hyperinsulinemia is still a physiologically relevant outcome, which will likely influence post-exercise glucose disposal. Sprint interval exercise (SIE) using 4 bouts of high-intensity exercise (i.e., Wingate tests) is a powerful mode of exercise to acutely improve insulin sensitivity (142% improvement). However, in the following days after a bout of sprint interval exercise (up to 48 h) the insulin sensitivity improvement is similar to that obtained with continuous exercise. From an applied perspective, in a health-oriented training program the long term (48 h) improvements in insulin sensitivity are similar when using Wingate tests-based SIE or continuous exercise. However, on the same day of exercise the improvements with SIE are larger and, if tolerated, this exercise mode may be more efficacious for preventing and treating insulin resistance. These findings need to be confirmed in a population of obese, insulin-resistant individuals.

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Conflict of interest: The authors have no conflict of interest to declare.

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