No acute effect of reduced-exertion high intensity interval training (REHIT) on insulin sensitivity

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ABSTRACT

We have previously demonstrated that reduced-exertion high-intensity interval training (REHIT), requiring a maximum of two 20-s all out cycling sprints in a 10-min exercise session, improves insulin sensitivity in sedentary men over a 6-week training intervention. However, the acute effects of REHIT on insulin sensitivity have not previously been described. In this study fourteen men and women (mean±SD age: 23±5 y; BMI 22.7±4.7 $kg \cdot m^{-2}$; $\dot{V}O_2max$: 37.4±8.6 $mL \cdot kg^{-1} \cdot min^{-1}$) underwent oral glucose tolerance testing 14-16 hours after an acute bout of reduced-exertion high-intensity interval training (2 x 20-s all-out sprints; REHIT), moderate-vigorous aerobic exercise (45 minutes at ~75% VO_2max; AER), and a resting control condition (REST). Neither REHIT nor AER were associated with significant changes in glucose AUC (REHIT 609±98 vs. AER 651±85 vs. REST 641±126 $mmol \cdot l^{-1} \cdot 120$ min), insulin AUC (REHIT 30.9±15.4 vs. AER 31.4±13.0 vs. REST 35.0±18.5 $nmol \cdot l^{-1} \cdot 120$ min) or insulin sensitivity estimated by the Cederholm index (REHIT 86±20 vs. AER 79±13 vs. REST 82±24 $mg \cdot l^{2} \cdot mmol^{-1} \cdot mU^{-1} \cdot min^{-1}$). These data suggest that improvements in insulin sensitivity following a chronic REHIT intervention are the result of training adaptations rather than acute effects of the last exercise session.

INTRODUCTION

The finding that lack of time is a major barrier to performing regular exercise has led to a rise in studies investigating high-intensity interval training (HIT) as a time-efficient method for improving aerobic fitness and metabolic health [16]. However, it is noteworthy that due to the required recovery intervals the time-commitment of most HIT protocols is generally similar to current guidelines for aerobic exercise. We [26] and others [18] have recently demonstrated that a modified HIT protocol requiring two or three 20-s Wingate sprints in a 10-min cycling session (reduced-exertion HIT; REHIT) can improve aerobic capacity in sedentary men and women, and insulin sensitivity in men. These benefits were observed despite the low total time-commitment (30 min per week) and manageable ratings of perceived exertion, suggesting that REHIT may be a suitable alternative or adjunct to current exercise recommendations [26]. However, more studies are required to further characterise the acute and chronic effects of REHIT on human health and metabolism, both in isolation and in combination with more traditional exercise modes.

Insulin sensitivity is an important biomarker in the development of type 2 diabetes and metabolic syndrome and is a primary target for preventative intervention [8,33]. The effects of exercise on insulin sensitivity are thought to be largely explained by improved glucose uptake in skeletal muscles [9,10]. From this perspective, exercise has been shown to exert three distinct regulatory roles on skeletal muscle glucose uptake. Firstly, skeletal muscle contractions themselves recruit glucose transporter 4 (GLUT4) molecules to the cell membrane and increase glucose uptake in an intensity dependent manner, through signalling pathways that are independent of and additive to insulin [14,29,34,38,41]. This effect is transient, subsiding completely ~2-3 hours after the cessation of the muscle contractions [24]. However, it appears to be replaced by an acute enhancement of insulin-stimulated recruitment of GLUT4 and hence postprandial glucose disposal in the exercised muscle, which can be detected for 24-48 hours post-exercise, and which appears to track with the replenishment of

skeletal muscle glycogen stores [2,5,19]. Lastly, the cumulative effect of many repeated bouts of acute exercise (i.e., exercise training) can bring about a favourable change in skeletal muscle phenotype and body composition which correlates with a more prolonged increase in insulin sensitivity that can be detected for several days after the final training bout [9].

The improvements in insulin sensitivity in men following REHIT have been noted at 3 days following the final exercise session and were ascribed to chronic training adaptations [18,26]. However, this contention remains unsubstantiated since no study has examined the effects of a single bout of REHIT on insulin sensitivity. Understanding the role of both single and accumulated bouts of exercise on parameters of metabolic health is important from the perspective of exercise prescription. Therefore, the aim of this study was to determine the impact of a single bout of REHIT on insulin sensitivity measured the following day in comparison to a bout of moderate-vigorous aerobic exercise and a no-exercise control condition. Based on the findings of Brestoff et al [3], our primary hypothesis was that there would be no acute effect of REHIT on insulin sensitivity, whilst our secondary hypothesis speculated there would be an increase in insulin sensitivity following an acute bout of moderate-vigorous intensity aerobic exercise.

MATERIALS AND METHODS

Participants

Fourteen healthy young men (n=8) and women (n=6) gave their written informed consent to take part in this study (mean±SD age: 23±5 y; BMI 22.7±4.7 $kg \cdot m^{-2}$; $\dot{V}O_2max$: 37.4±8.6 $mL \cdot kg^{-1} \cdot min^{-1}$). All participants were sedentary or recreationally active according to the International Physical Activity Questionnaire. The study was approved by the Heriot-Watt University School of Life Sciences Ethics Committee and conducted in accordance with the *Declaration of Helsinki* and ethical standards for sport and exercise science research [20].

Baseline Testing and Familiarisation

Prior to the main trials participants visited the laboratory on four occasions. During the initial visit maximal oxygen uptake capacity ($\dot{V}O_2max$) was determined during an incremental cycling test to volitional exhaustion on an electrically-braked cycle ergometer (25 $W \cdot min^{-1}$ ramp; Lode Excalibur Sport, the Netherlands) with analysis of $\dot{V}O_2$ using an online metabolic cart (SensorMedics, Bilthoven, the Netherlands). $\dot{V}O_2max$ was taken as the highest value of a 15-breath rolling average. Participants performed two familiarisation sessions for the REHIT trial and one for the aerobic exercise trial (AER). The REHIT familiarisation sessions were used to familiarise participants with the procedures and the effort required during Wingate-type sprints. The AER session was used to check the intensity predicted to elicit 75% $\dot{V}O_2max$. Participants cycled for 15-min at the prescribed intensity and $\dot{V}O_2$ was measured continuously throughout (SensorMedics, Bilthoven, the Netherlands). If necessary, adjustments were made to the intensity used during the main trials.

Experimental Procedures

Participants completed three main experimental trials (REHIT, AER and REST) in a randomised cross-over design, with each trial taking place over a 2-day period. During each

trial participants underwent an oral glucose tolerance test (OGTT) on the morning after performing either: 1) a single bout of REHIT, 2) a single bout of moderate-vigorous intensity aerobic exercise (AER), or 3) a no-exercise control condition (REST). Each trial was separated by at least 1 week and prior to each trial participants were asked to refrain from performing strenuous/prolonged physical activities and consuming alcohol/caffeine for 2 days and 1 day respectively.

On the evening prior to each OGTT, participants attended the laboratory between 4:30 pm and 7:00 pm to perform the exercise session. Participants were given a standardised evening meal (energy: 3234±494 kJ; carbohydrate: 107±17 g; fat: 21±7 g; protein: 35±10 g) 30 min after completion of the exercise bout. For each participant the time of attendance was consistent between conditions. Participants fasted overnight and returned to the laboratory the following morning between 7:00 am and 9:30 am. An OGTT was performed after 15 min of seated rest.

Exercise Protocols

All exercise protocols were performed on an electrically-braked cycle ergometer (Lode Excalibur Sport, the Netherlands). The aerobic exercise protocol involved 45 min of cycling at an intensity predicted to elicit ~75% of $\dot{V}O_2$max as previously used by Brestoff et al. [3]. Cadence was self-selected and the exercise was completed in three intervals of 15 min with 2 min of resting recovery in between. $\dot{V}O_2$ was determined during the final 5 min of the first bout (SensorMedics, Bilthoven, the Netherlands) and heart rate was measured throughout (Polar Electro, Vansbro, Sweden). The REHIT condition involved 10 min of unloaded pedalling and two 20-s Wingate sprints at 3:00 min and 6:40 min as previously described [26]. Just before each sprint, participants increased their pedal cadence to their maximal speed, a braking torque was applied to the ergometer (0.70 and 0.60 $Nm \cdot kg^{-1}$ for men and women, respectively), and participants sprinted maximally against the braking torque for 20 s.

Oral Glucose Tolerance Test

A fasting blood sample was obtained from a forearm vein by venepuncture using the vacutainer system, after which 75 g of anhydrous glucose (Fisher Scientific, Loughborough, UK) in 100 mL of water was orally ingested and further blood samples collected at 60 and 120 min after glucose ingestion. Blood samples were collected into cooled plastic tubes containing EDTA and stored on ice during the OGTT. Samples were centrifuged for 10 min at 2000 *g* and 4°C to separate the plasma, which was stored at -20°C until analysis. Plasma glucose concentration was determined in duplicate with a CV of <1% (YSI Stat 2300, Yellow Spring Instruments, Yellow Spring, OH). Plasma insulin concentrations were measured in duplicate using a commercially available ELISA with a CV of 4% (Invitrogen, UK). Area under the curve (AUC) for plasma glucose and insulin responses was calculated using the trapezoid rule, whilst insulin sensitivity was determined using the Cederholm Index [6].

Statistics

. Statistical analysis was performed using SPSS statistical software. To simplify analysis and interpretation of an otherwise complex data set, the OGTT responses for each condition were converted into simple summary statistics (i.e., within subject fasting, total AUC and insulin sensitivity scores). As two-way repeated measures ANOVAs revealed no gender × group interactions for any OGTT-derived variables, all data was pooled and comparisons were made using 1-factor repeated measures ANOVA with *post hoc* Ryan Holm Bonferroni corrected t-tests if appropriate. Significance was accepted at $P<0.05$. Exercise characterisation data are presented as mean ± SD, whilst the effects of the exercise bouts on OGTT-derived variables is presented in text as the mean change from the REST condition with 95% confidence intervals. Data in figures are presented as mean ± SD unless otherwise stated.

RESULTS

Exercise Characteristics

During the AER exercise session participants cycled at 76±4% of $\dot{V}O_2$max and this elicited 86±7%, 90±6% and 91±6% of maximal heart rate (HRmax) during bouts 1, 2 and 3 respectively. Peak, mean and minimum power output for REHIT were 12.2±2.1, 6.6±1.5 and 4.4±1.4 $W \cdot kg^{-1}$ for the first sprint, and 11.9±2.0, 5.9±1.5 and 3.9±1.3 $W \cdot kg^{-1}$ for the second sprint. Heart rate peaked at 93±4% and 94±3% of HRmax for the first and second sprints respectively. The total amount of work performed in the AER and REHIT bouts was 312.8±118.3 and 16.7±5.4 kj, respectively.

Glucose and Insulin Responses to the OGTTs

The insulin and glucose responses to the OGTTs are presented in Figure 1. There was no effect of either exercise condition on fasting glucose concentration (mean change [95% CI's]: REHIT: -.066 [-.192, .059] $mmol \cdot l^{-1}$; AER: -.090 [-.273, .093] $mmol \cdot l^{-1}$) or fasting insulin concentrations (REHIT: -.006 [-.021, .008] $nmol \cdot l^{-1}$; AER: -.017 [-.038, .005] $nmol \cdot l^{-1}$) when compared with REST. Similarly, neither REHIT or AER were associated with any changes in glucose AUC (REHIT: -32.3 [-77.8, 13.1] $mmol \cdot l^{-1} \cdot 120min$; AER: +9.38 [-45.9, 64.7] $mmol \cdot l^{-1} \cdot 120min$), insulin AUC (REHIT: -4.19 [-10.7, 2.28] $nmol \cdot l^{-1} \cdot 120min$; AER: -3.73 [-8.97, 1.52] $nmol \cdot l^{-1} \cdot 120min$) or insulin sensitivity (REHIT: +4.91 [-.941, 10.8] $mg.l^2.mmol^{-1}.mU^{-1}.min^{-1}$; AER: -2.64 [-12.1, 6.86] $mg.l^2.mmol^{-1}.mU^{-1}.min^{-1}$) when compared with REST.

DISCUSSION

The aim of this study was to examine the effect of a single bout of REHIT on insulin sensitivity measured the following day in comparison to a single bout of moderate-vigorous aerobic exercise and a no-exercise control condition. In agreement with our primary hypothesis, these data demonstrate that a single bout of REHIT does not improve insulin sensitivity, and this strengthens our previous contention that the increase in insulin sensitivity detected 3 days following a 6-week REHIT intervention in sedentary men can be ascribed to chronic training adaptations [18,26]. In contrast, our secondary hypothesis was not supported, with no increase in insulin sensitivity observed following a single bout of moderate-vigorous intensity aerobic exercise.

Our finding that there was no acute impact of REHIT on insulin sensitivity is in line with recent acute studies demonstrating no change in OGTT-derived insulin sensitivity 14-16 hours following single bouts of HIT consisting of five sprints at ~125% $\dot{V}O_2$max [3] or four 30-s Wingate sprints [39]. Similarly, HIT did not appear to attenuate the systemic glucose or insulin response to a high-fat mixed meal challenge administered 14 hours post-exercise, although the overall lipemic response was reduced [12,13]. Conversely, Ortega et al. [31] reported a significant increase in insulin sensitivity measured using intravenous glucose tolerance testing (IVGTT) which lasted for at least 48 hours after four 30-s Wingate sprints, whilst Little et al. [25] reported a reduction in mean 24-h glucose concentrations and 24-h postprandial glucose AUC following ten 1-min sprints at >90% HR_{max} in a small cohort of overweight men. The reason for these discrepancies is unclear but may be related to the different methods of assessing insulin sensitivity and glycaemic control (IVGTT and continuous glucose monitoring vs. OGTT or oral mixed meals). Further studies are warranted examining the acute effects of HIT/REHIT, both in isolation and in combination with more traditional exercise modes, on insulin sensitivity using the gold standard hyperinsulinemic clamp in a range of populations. Nevertheless, the current data have important implications for the prescription of REHIT (in

isolation) as a preventative intervention in the general population. If reductions in postprandial systemic insulin and glucose concentrations are the primary targeted endpoint then single bouts will not be effective; rather REHIT needs to be repeated regularly over several weeks in order for adaptations to be accrued.

We could detect no increase in insulin sensitivity measured 14-16 hours following an acute bout of vigorous intensity aerobic exercise. This is in contrast to recent data from Brestoff et al. [3] who demonstrated a 25% reduction in insulin AUC during an OGTT using a comparable cohort of participants, exercise bout and post-exercise time point. However, the literature as a whole is somewhat inconsistent, with many studies in healthy lean individuals reporting no measurable changes at similar time-points following acute aerobic exercise of varying intensities and durations [1,2,11,21,35,37], whilst others show improvements for as long as 48 hours post-exercise exercise [27,32,36,40]. The lack of change in our study may be explained by a combination of two factors. Firstly, the timing and composition of post-exercise feeding appears to have a strong influence on the response. Several studies show that restriction of carbohydrate intake appears to prolong any increase in insulin sensitivity post-exercise both in rodents [5,19,23] and in humans [2,22,30]. This makes sense from an evolutionary perspective, as any metabolic acceleration following exercise is presumably an attempt to restore intramuscular substrate stores as quickly as possible so that further exercise may be performed [7]. Secondly, there is evidence that individuals with lower baseline levels of insulin sensitivity tend to exhibit a more prolonged increase in post-exercise insulin sensitivity which can be detected even after several meals have been consumed [4,11,15,28]. This is perhaps reflective of the decrement in insulin action resulting in delayed restoration of intramuscular substrate stores after exercise, thereby necessitating a more prolonged increase in insulin sensitivity. In any case, given that our cohort of participants already had a healthy level of insulin sensitivity, and we fed them a meal containing ~100 g of carbohydrate

30 min post-exercise, it is perhaps not all that surprising that we observed no change in insulin sensitivity following the aerobic exercise bout in the current study.

There are several limitations to the current analysis which provide opportunity for further study. Firstly, we could only include three time-points during the OGTT for our calculation of insulin sensitivity. Whilst this protocol was sensitive enough to detect the relatively large changes in insulin sensitivity observed following the REHIT training intervention [26], it must be acknowledged that we may have missed more subtle changes in the current analysis. It would therefore be useful to repeat the current study using the more sensitive gold standard euglycemic clamp methodology. Secondly, we only included a 14-16 hour post-exercise time point in this study and cannot therefore rule out that REHIT impacts on insulin sensitivity in the more immediate post-exercise period (i.e., in response to the first feeding). Lastly, in order to be able to make firm comparisons between the current acute study and the previous training intervention [26] we recruited a similar cohort of participants who, although sedentary, were young, lean and with a healthy level of insulin sensitivity. It is therefore necessary to investigate the acute impact of REHIT in populations with insulin resistance, particularly in light of the recent finding that other models of HIT substantially improve glycaemic control in middle aged men presenting with T2D [17].

To summarise, the data of the present study demonstrate no effect of an acute bout of REHIT on insulin sensitivity. This suggests that the potential utility of REHIT for improving insulin sensitivity may be limited to a chronic training response.

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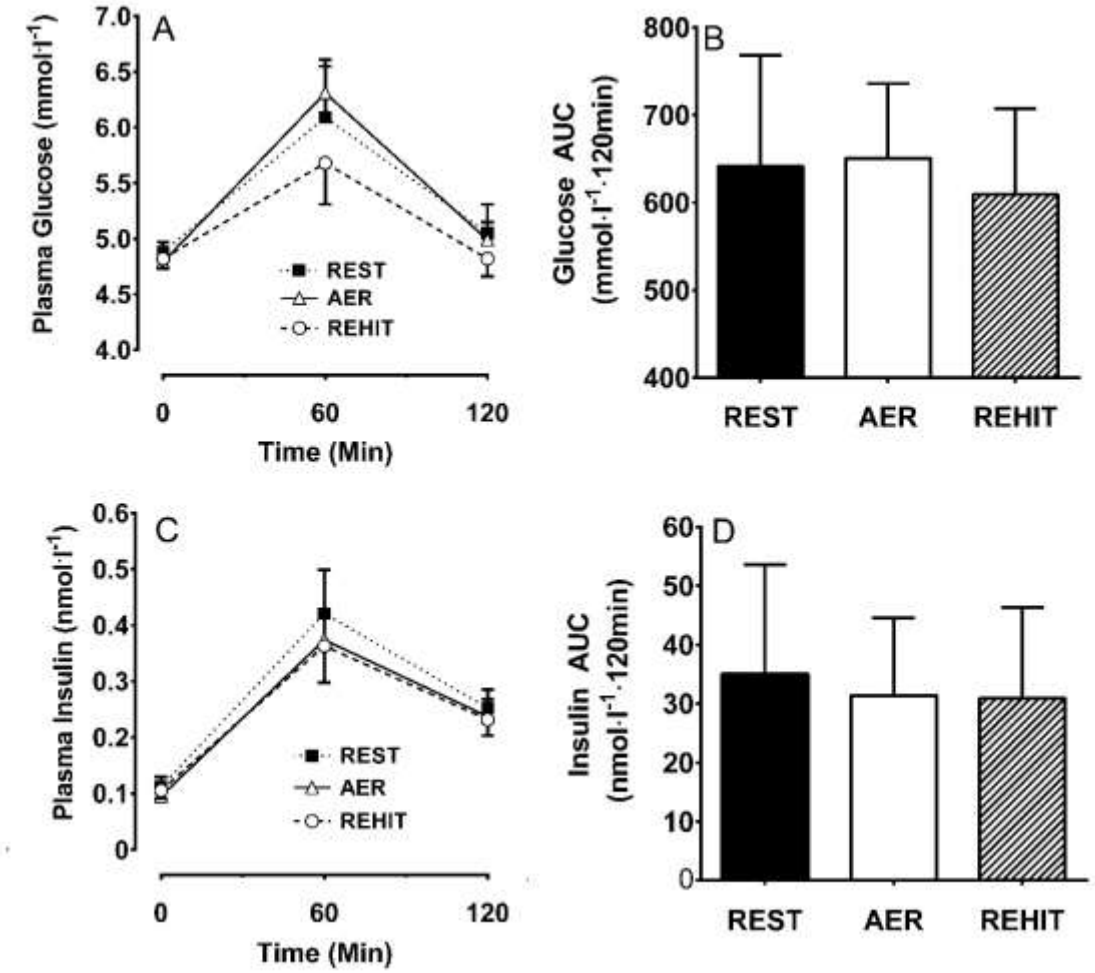

Figure 1 Plasma glucose (A+B) and insulin (C+D) responses to acute exercise. For clarity, the responses over time to the OGTT are presented as mean±SEM, whilst the AUC data is presented as mean±SD. REHIT: reduced-exertion HIT, AER: aerobic exercise, REST: no exercise control.