Cardiometabolic response to a single high-intensity interval exercise session versus breaking up sedentary time with fragmented high-intensity interval exercise

Abstract

This study compared the effects of interrupting prolonged sedentary time with high-intensity physical activity (SED-ACT), a volume and duration-matched high-intensity interval exercise session followed by prolonged sedentary time (HIIE), and prolonged uninterrupted sedentary time (SED) on postprandial glucose, insulin and triglyceride concentrations. Twelve sedentary and inactive, but otherwise healthy, adults completed three, 6.5 h conditions in an incomplete counterbalanced order. During SED, participants sat continuously. For HIIE, participants completed 10 x 60 s cycling bouts at 90% maximum oxygen update ($\dot{V}O_{2max}$) with 1 min active recovery between bouts. In SED-ACT, 60 s cycling bouts at 90% $\dot{V}O_{2max}$ were completed every 30 min (10 times in total) with 30 s of active recovery immediately before and after. Standardised meals were consumed at 0 h and 3 h and capillary blood samples were collected fasted and every 30 min. Compared with SED, postprandial glucose incremental area under the curve (iAUC) was significantly lower in SED-ACT by 1.91 mmol/L·6.5 h (p=0.022) and triglyceride iAUC was significantly lower in HIIE by 1.02 mmol/L·6.5 h (p=0.030). Interrupting sedentary time with high-intensity physical activity can lower postprandial glucose concentrations, whereas a HIIE session can lower postprandial triglyceride concentrations.

Keywords: sedentary behaviour, physical activity, postprandial metabolism, glucose, lipids, HIT

Introduction

Elevated postprandial glucose and lipid concentrations are significant risk factors for cardiometabolic diseases [28], such as cardiovascular disease (CVD) and Type 2 diabetes (T2D), which are leading causes of morbidity and death [8, 13]. Increased cardiometabolic disease incidence is associated with high levels of sedentary behaviour, often independent of physical activity (PA) levels [36]. Interrupting sedentary time with 2-5 min of light or moderate-intensity PA every 20-30 min can acutely suppress postprandial glucose, insulin and triglyceride levels [3-5, 27, 30, 33]. However, the effects of breaking up sedentary time with high-intensity PA on postprandial metabolism has received much less attention. It is possible that high-intensity PA may result in more pronounced effects than light or moderate-intensity PA due to increased energy expenditure and carbohydrate oxidation rates [21]. The available evidence has shown that hourly bouts of 2 min 32 s high-intensity treadmill PA lowered postprandial triglyceride concentrations, but not glucose, compared to uninterrupted sitting [24], while 6 min high-intensity cycling every 40 min increased triglyceride concentrations [15]. Breaking up sitting with 2 min bouts of high-intensity walking every hour, however, suppressed continuously monitored glucose levels for 18.7 h [7]. The potential benefits of interrupting sedentary time with high-intensity PA thus requires further research.

High-intensity interval exercise (HIIE) has been defined as “involving repeated short-to-long bouts of rather high-intensity exercise interspersed with recovery periods” [9]. Short bouts are considered to be ≤45 s in duration and long bouts ≥1-2 min and it has been recommended that individuals spend at least several minutes of a HIIE session at ≥90% maximum oxygen uptake ($\dot{V}O_{2max}$) for optimal physiological adaptations and that active recovery periods last between 1-3 min for such sessions [9]. A 20-min HIIE session of 10 x 60 s cycling at 90% maximum heart rate suppressed 24 h continuous glucose concentrations in people with T2D [17]. When the postprandial assessment occurred the morning after a HIIE session, postprandial triglyceride concentrations were suppressed by sprint interval exercise (SIE) [11, 34] and by 10 x 60 s cycling at 85% peak oxygen uptake [23]. However, it is unknown whether performing this type of PA spread across the day is beneficial.

The aim of this study was to compare the postprandial cardiometabolic effects of interrupting prolonged sedentary time with high-intensity PA, a volume and duration-matched HIIE session followed by prolonged sedentary time, and prolonged uninterrupted sedentary time.

Materials & Methods

Study design

This three-condition randomised crossover trial took place at the University of Bedfordshire Sport and Exercise Science Laboratories. The study was approved by the University of Bedfordshire Institute for Sport and Physical Activity Research Ethics Committee (approval number 2016ISPAR006) and meets the ethical standards in sport and exercise science research [19]. Participants were recruited between March and July 2016 and data collection was completed by October 2016. Following informed consent and preliminary measures, participants completed three experimental conditions with a washout of ≥6 days to eliminate potential carryover effects. To minimise carryover effects, condition order was pre-determined using an incomplete counterbalanced Latin square method in which participants were allocated to complete the conditions in one of six orders. Participants were blinded to the first two conditions until arriving at the laboratory to complete these conditions. Due to effects of the menstrual cycle on glucose metabolism [35], females were tested in the follicular phase (days 1-10), which was identified via written or verbal communication with the participant. Females who were using birth control that prevented menstruation were not restricted with regards to the days that they could complete the conditions.

Participants

Sedentary (≥7 h/day of self-reported sitting) and inactive (<150 min/week of moderate-intensity PA or ≤75 min/week of vigorous PA) adults aged 18-55 years were invited to take part. Exclusion criteria were a known blood borne disease, pregnancy, diabetes, using glucose-lowering and/or lipid-lowering medication, PA contraindications, major illness/injury, or allergies to the test meals.

Preliminary measures

Body mass and body fat % were measured with the Tanita BC-418 MA Segmental Body Composition Analyzer (Tanita Corp., Tokyo, Japan). Waist circumference was measured

using an adjustable tape measure (HaB Direct, Southam, UK). Participants competed a graded cycling exercise test on a Lode bike (Excalibur sport; Lode, Groningen, Netherlands) starting at 100 W for males and 50 W for females and increasing by 25 W every 3 min until volitional exhaustion. Participants were asked to cycle at 70 rpm throughout the test. Pulmonary gas exchange was measured using the Cortex Metalyzer 3B (GmbH, Germany). $\dot{V}O_{2max}$ was recorded as the highest $\dot{V}O_2$ value in $mL \cdot kg^{-1} \cdot min^{-1}$ averaged over a 10-s period and was accepted as valid if a plateau in VO_2 ($\leq 2.1\ mL \cdot kg^{-1} \cdot min^{-1}$) occurred despite increasing workload. A plateau in VO_2 was observed in all participants. The power output (W) that elicited 90% $\dot{V}O_{2max}$ was predicted from the relationship between power output (W) and submaximal $\dot{V}O_2$ values calculated during the final minute of each stage.

Experimental protocol

Participants attended the laboratory having not exercised for 48 h previously, fasted overnight for ≥10 h and minimised their PA in the morning by travelling by car and parking as near to the laboratory as possible. Participants were provided with a food diary and digital scales alongside verbal and written instructions on how to record all food and liquids consumed the 24 h preceding the first condition and were asked to replicate this intake the day prior to each subsequent condition [3]. Upon arrival, participants rested for 30 min before a fasting blood sample was taken. A standardised breakfast was then consumed and the 6.5 h experimental period commenced after the last mouthful. As shown in Figure 1, the experimental conditions were:

1) *Prolonged sedentary time (SED)*: uninterrupted sedentary time for 6.5 h.

2) *High-intensity interval exercise followed by prolonged sedentary time (HIIE)*: a 20 min HIIE session was completed 45 min after breakfast consisting of a warm up for 1 min at 60 W before completing 10 x 60 s cycling bouts at predicted 90% $\dot{V}O_{2max}$ with 1 min of active

recovery at 60 W between bouts. The HIIE session was followed by uninterrupted sedentary time for the remainder of the condition.

3) *Sedentary time interrupted with high-intensity physical activity (SED-ACT)*: sedentary time was interrupted with high-intensity cycling at predicted 90% $\dot{V}O_{2max}$ for 60 s (with 30 s cycling at 60 W immediately before and after) at 45, 75, 105, 135, 165, 195, 225, 255, 285 and 315 min. The PA was volume and duration-matched to the HIIE condition.

Participants were permitted to work on a laptop, read books, watch DVDs or talk when not performing PA. Participants were transported in a wheelchair to the toilets and the laboratory kitchen to consume meals so they remained sedentary.

Meal and water consumption

The standardised breakfast consisted of cornflakes, whole milk and croissant; the energy content comprised 57% carbohydrate, 29% fat and 14% protein. The standardised lunch provided at 3 h consisted of white bread, chicken, butter, chocolate and crisps; the energy content comprised 47% carbohydrate, 39% fat and 14% protein. Each meal provided 30% of estimated individual daily energy requirements for each participant, calculated using the Mifflin equation with a PA factor of 1.4 [25]. The glycaemic indexes of the breakfast and lunch meals were 71 and 66, respectively [5]. The mean carbohydrate, fat and protein content was 90 ± 14 g, 22 ± 3 g and 19 ± 3 g for breakfast and 80 ± 13 g, 25 ± 4 g and 22 ± 4 g for lunch. There was a 15 min time limit for meal consumption and the time taken to consume each meal in the first condition was replicated in the subsequent conditions. Water was provided *ad libitum* during the first main condition and the volume replicated in subsequent conditions.

Blood collection and biochemistry

Approximately 600 µl of whole blood was collected via finger prick into two microvettes (Microvette CB300 EDTA, Sarstedt Ltd, Leicester, UK) fasted and at 75, 105, 150, 210, 240,

270, 330 and 390 min. Prior to the sample being taken, the hand was submerged in warm water for up to 5 min to encourage blood flow to the area. Blood glucose concentration was measured immediately using the YSI 2300 STAT plus glucose and lactate analyzer (YSI Inc., Yellow Springs, OH, USA). The remaining sample was spun at 2000 x g for 5 min using the Heraeus Pico 17 microcentrifuge (Thermo Scientific, Loughborough, UK). The plasma was extracted and stored at -80ºC for later batch analysis of triglycerides via spectrophotometry using the lipase hydrolysis method (GOP-PAP; Randox, Crumlin, Ireland) and insulin using an enzyme linked immunosorbent assay kit (Mercodia, Uppsala Sweden).

Outcome variables

The primary outcome was net incremental area under the curve (iAUC) for postprandial glucose. Secondary outcomes were iAUC for insulin and triglycerides and total AUC (tAUC) for glucose, insulin and triglycerides. The trapezoidal rule was used to calculate tAUC; the area under the baseline value was subtracted to calculate net iAUC.

Sample size calculations

Sample size was calculated using GPower [16]. Based on previous work [30], it was estimated that nine participants would be required for this three-condition crossover design study to detect a minimum effect size of d=0.54 between conditions for glucose iAUC with 90% power and an α of 0.05.

Statistical analyses

Statistical analysis was conducted using SPSS version 22.0 (SPSS INC., Armonk, N.Y., USA). Normality of the data were checked using quantile-quantile plots and was deemed plausible for all variables. Linear mixed models were used to compare the dependent variables between conditions. Fixed factors for each model were condition and fasting outcome variables values (as covariates) and participants were random factors. Post-hoc analyses between the three individual conditions were completed using Sidak adjustment when a significant main effect

was present. Cohen's d effect sizes of 0.2 (small), 0.5 (medium) and 0.8 (large) were calculated to described the magnitude of differences between conditions [12]. Data are presented as mean (95% CI) unless stated otherwise. Significance was accepted as $p<0.05$.

Results

Fourteen participants consented to take part in this study with two withdrawals prior to preliminary measures. Twelve participants (seven female) completed the study and provided 100% of data. Participant characteristics are shown in Table 1. The mean power output estimated to elicit 90% $\dot{V}O_{2max}$ was 179±31 W and 121±25 W for males and females, respectively.

Fasting glucose, insulin and triglyceride concentrations did not differ significantly between conditions (Table 2). Cardiometabolic responses over time for each condition can be seen in Supplementary File 1. As shown in Table 2, a significant main effect of condition was present for glucose iAUC with glucose concentrations being significantly lower in SED-ACT than SED with a large effect size for this difference ($p=0.022$; $d=0.96$). There was no significant difference between HIIE and SED ($p=0.557$; $d=0.40$) or between SED-ACT and HIIE ($p=0.262$; $d=0.54$), although there was a medium effect size for these differences. There was a significant main effect of condition for triglyceride iAUC with concentrations being significantly lower in HIIE than SED with a large effect size for this difference ($p=0.030$; $d=0.77$). No significant difference was seen between SED-ACT and SED ($p=0.645$; $d=0.25$; small effect size) or between SED-ACT and HIIE ($p=0.257$; $d=0.48$; medium effect size). The main effect of condition for insulin iAUC was not significant ($p=0.758$) with trivial effect sizes for differences between the conditions (all $d\leq0.17$). The significant differences observed for glucose tAUC, triglyceride tAUC and insulin tAUC were the same as those for iAUC.

Discussion

The main findings of this study were that interrupting sedentary time with 1 min high-intensity cycling (with 30 s of low-intensity cycling immediately before and after) every 30 min lowered postprandial glucose concentrations, while a HIIE session performed in the morning lowered postprandial triglyceride concentrations compared with prolonged sedentary time. This extends past work showing that interrupting sitting with 2-5 min of light or moderate PA every 20-30 min reduces postprandial glucose [3-5, 14, 20, 30]. However, no reduction in postprandial glucose was seen in response to high-intensity treadmill PA breaks lasting 2 min 32 s every 60 min [24] or moderate-intensity cycling breaks lasting 8 min every 60 min [2]. Thus, less frequent PA breaks may not be sufficient even if the intensity of the PA is high. Although a meta-analysis found that glucose responses to interrupting sedentary time were not influenced by PA break intensity [33], studies that incorporated high-intensity PA breaks were not included. Further research is thus required to compare the effects of interrupting sedentary time every 20-30 min with high-intensity PA versus lower intensity PA.

Interrupting sedentary time with high-intensity cycling did not appear to affect postprandial insulin concentrations in the present study as demonstrated by the lack of statistically significant differences and trivial effect sizes between conditions. However, as the study was not powered to statistically detect changes in postprandial insulin, we can only speculate as to whether the suppressions in glucose occurred via insulin-independent pathways, such as higher carbohydrate oxidation [30] (which increases with exercise intensity [21]), or increased GLUT-4 translocation [22]. Other studies have failed to observe a reduction in postprandial insulin [3, 5, 27] or change in the insulin-signalling pathway [6] in response to 2 min of light or moderate-intensity walking every 20 min over a single day, although these studies similarly were not powered to detect changes in these outcomes. Postprandial insulin reductions occurred in response to 2-5 min of light or moderate-intensity PA every 20-30 min and 20 min of light walking every hour in other studies that included larger sample sizes [10, 14, 20, 30, 32]. Future studies should thus be adequately powered to detect changes in

postprandial glucose and insulin to provide a greater understanding of the mechanistic regulation in response to interrupting sedentary time.

Our finding that postprandial triglyceride concentrations were not attenuated in response to interrupting sedentary time over a single day agrees with other single-day protocols in healthy adults [2, 30]. In contrast, reductions in triglyceride concentrations in response to interrupting sedentary time have been reported in those who are metabolically impaired, including postmenopausal women [27] and obese men [26], and in healthy adults in response to high-intensity treadmill PA breaks that were weight-bearing and involved upper and lower body muscle contractions [24]; potentially due to the higher energy expenditure of the PA breaks compared with our study. Importantly, lipoprotein lipase activity peaks 8-22 h following a continuous moderate-intensity PA bout [18], which is likely to be a fundamental reason why single-day protocols may not detect beneficial changes.

A HIIE session that was volume, intensity and duration-matched to the PA breaks reduced postprandial triglyceride concentrations, potentially because the timing of the exercise provided scope for a greater rise in lipoprotein lipase activity compared with the PA breaks condition where the same volume of PA was not reached until 4 h later. Indeed, cycling and whole-body HIIE sessions performed in the evening lowered postprandial triglyceride concentrations the following morning [23, 37]. There was a medium effect for postprandial glucose concentrations being lower in the PA breaks conditions than the HIIE condition in our study. This difference was not statistically significant despite our sample size calculations suggesting the sample size in this study would be sufficient to detect an effect size of $d \geq 0.54$. This suggests that there was greater variability in the present sample with respect to the difference between the SED-ACT and HIIE conditions than the between the conditions in the study on which the sample size calculations were based upon [30]. Thus, it is possible that interrupting sedentary time with high-intensity PA may benefit postprandial glucose more than a HIIE session, but this study may have lacked power to statistically detect this. The lack of a significant glucose suppression in response to HIIE is in contrast to participants with diabetes

[1] and when using SIE sessions in healthy adults [29]. Thus, higher-intensity all-out SIE may be required to benefit glycaemia in healthy adults.

This study is limited by its acute nature, which means that chronic interventions require investigation to convincingly recommend the type of short duration PA bouts used in the present study for the prevention of cardiometabolic disease. The sample were also generally healthy and the findings cannot be generalised to clinical populations with higher risk of CVD. Future studies should also consider using a verification phase during $\dot{V}O_{2max}$ tests to enhance validity of the $\dot{V}O_{2max}$ values and subsequent relative intensities used for the experimental trials [31]. Finally, we did not determine the physiological mechanisms underpinning the reported differences in cardiometabolic variables (e.g., lipoprotein lipase activity), which should thus be investigated in future research.

In conclusion, interrupting sedentary time with high-intensity PA attenuated postprandial glucose levels, whereas a volume and duration-matched HIIE session attenuated postprandial triglyceride levels. These findings may contribute to public health strategies for cardiometabolic disease risk reduction.

Figure captions

Figure 1: Schematic of experimental protocol. HIIE, high-intensity interval exercise.

Supplementary File 1: Glucose, insulin and triglyceride responses during the uninterrupted sedentary time (SED), high-intensity interval exercise followed by prolonged sedentary time (HIIE), and sedentary time interrupted with high-intensity physical activity (SED-ACT) conditions.

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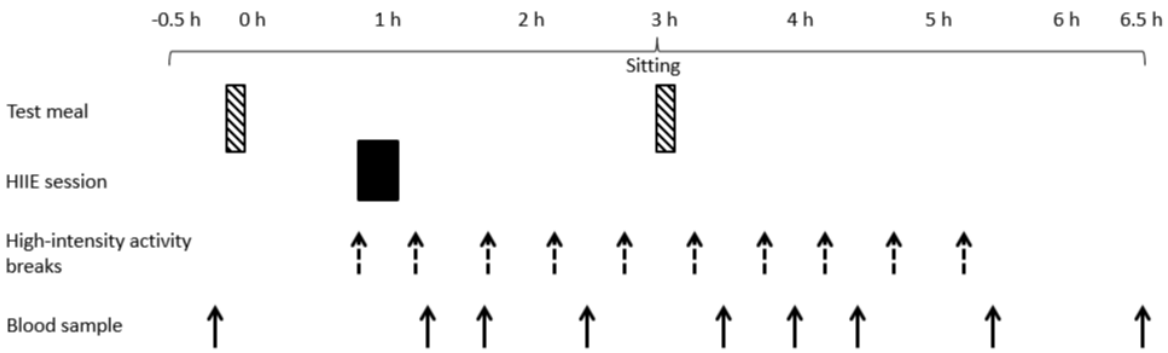
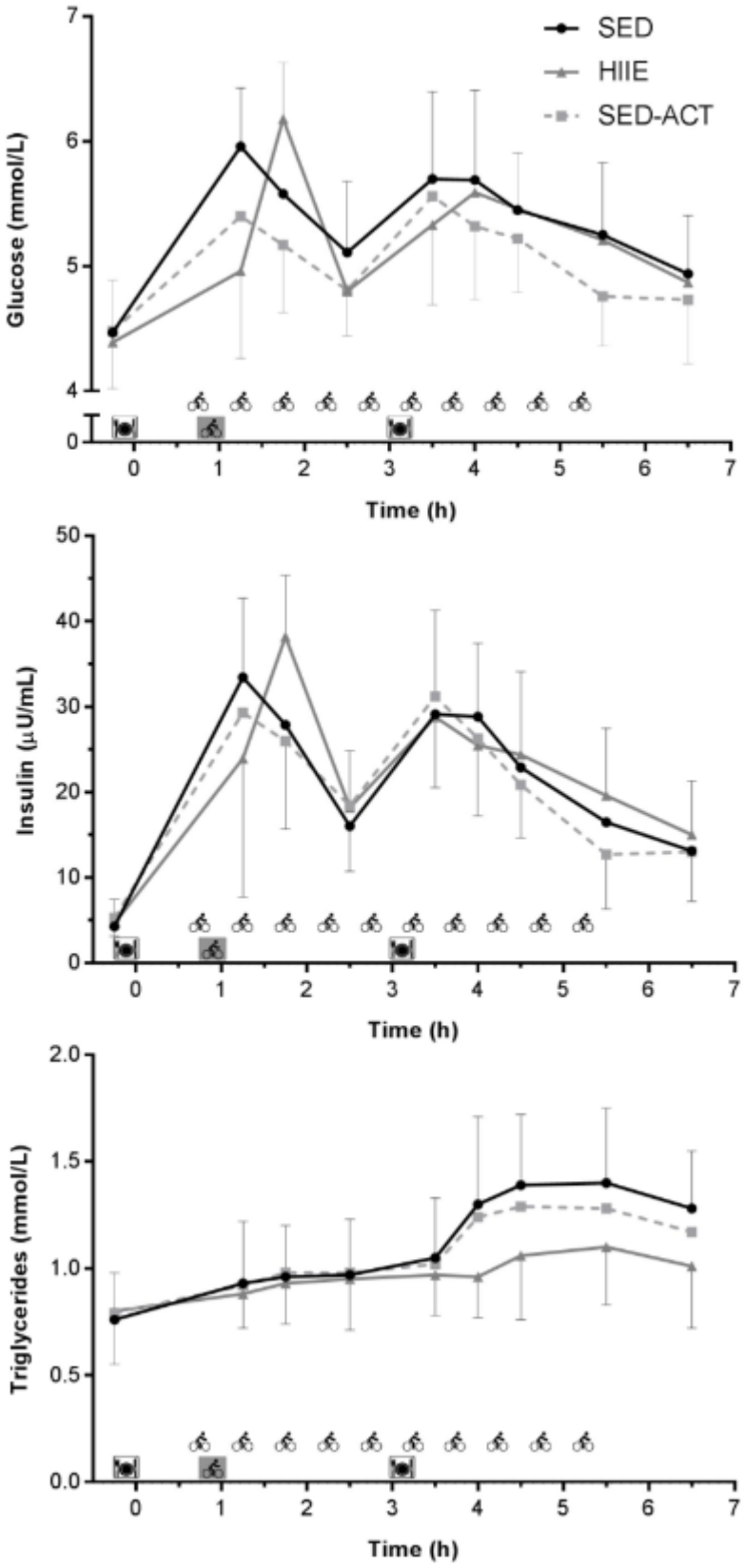


Figure 1. Schematic of experimental protocol



Supplementary File 1. Changes in glucose, insulin and triglycerides during the prolonged sedentary time (SED), high-intensity interval exercise followed by prolonged sedentary time (HIIE), and sedentary time interrupted with high-intensity physical activity (SED-ACT)

388 conditions. Data are mean and 95% confidence interval. Some error bars have been omitted
389 for clarity.

390 **Table 1** Participant characteristics (mean±SD)

Characteristics	Males (n=5)	Females (n=7)
Age (years)	25.0±5.4	22.6±1.5
Height (cm)	176.4±6.8	165.9±6.3
Weight (kg)	77.8±11.9	58.8±10.9
Body mass index (kg/m^2)	25.0±3.9	21.3±3.9
Waist circumference (cm)	87.0±4.9	74.5±10.2
Body fat (%)	18.5±5.8	27.9±8.4
Maximum oxygen uptake ($mL \cdot kg^{-1} \cdot min^{-1}$)	41.0±4.9	32.9±7.4
Peak power attained (W)	219±24	146±23

391

Table 2 Cardiometabolic risk marker values for each condition

Variable	SED	HIIE	SED-ACT	p for main effect of condition
Fasting blood glucose (mmol/L)	4.47 (4.03, 4.92)	4.39 (3.95, 4.83)	4.48 (4.04, 4.92)	0.436
Fasting plasma insulin (μU/mL)	5.06 (2.63, 7.50)	5.38 (2.94, 7.82)	5.30 (2.86, 7.74)	0.332
Fasting triglycerides (mmol/L)	8.02 (4.91, 11.1)	7.19 (4.08, 10.3)	10.2 (7.13, 13.4)	0.814
Blood glucose iAUC (mmol/L·6.5 h)	5.54 (4.37, 6.71)	4.75 (3.58, 5.92)	3.63 (2.46, 4.80)*	0.024
Blood glucose total AUC (mmol/L·6.5 h)	32.22 (31.05, 33.39)	31.43 (30.26, 32.60)	30.31 (29.14, 31.48)*	0.024
Plasma insulin iAUC (μU/mL·6.5 h)	102.54 (71.92, 133.16)	103.44 (72.84, 134.05)	94.59 (64.01, 125.18)	0.740
Plasma insulin total AUC (μU/mL·6.5 h)	134.02 (103.40, 164.64)	134.92 (104.32, 165.52)	126.07 (95.49, 156.65)	0.740
Triglyceride iAUC (mmol/L·6.5 h)	2.01 (1.10, 2.93)	0.99 (0.70, 1.90)**	1.62 (0.70, 2.54)	0.032
Triglyceride total AUC (mmol/L·6.5 h)	6.72 (5.80, 7.63)	5.69 (4.77, 6.61)**	6.32 (5.41, 7.24)	0.032

Data are mean (95% CI). SED, prolonged uninterrupted sedentary time; HIIE, high-intensity interval exercise followed by prolonged sedentary time; SED-ACT, sedentary time interrupted with high-intensity physical activity; iAUC, incremental area under the curve.

[a]Estimated from pairwise comparisons of marginal means adjusted for age, gender, body fat% and fasting values for each biochemical measure.

*Significant difference between SED-ACT and SED.

**Significant difference between HIIE and SED.