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Continuous moderate-intensity exercise with or without intermittent high-intensity work: effects on acute and late glycaemia in athletes with Type 1 diabetes mellitus

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Abstract

Aims Individuals with Type 1 diabetes mellitus are susceptible to hypoglycaemia during and after continuous moderate-intensity exercise, but hyperglycaemia during intermittent high-intensity exercise. The combination of both forms of exercise may have a moderating effect on glycaemia in recovery. The aims of this study were to compare the physiological responses and associated glycaemic changes to continuous moderate-intensity exercise vs. continuous moderate-intensity exercise + intermittent high-intensity exercise in athletes with Type 1 diabetes.

Methods Interstitial glucose levels were measured in a blinded fashion in 11 trained athletes with Type 1 diabetes during two sedentary days and during 2 days in which 45 min of afternoon continuous moderate-intensity exercise occurred either with or without intermittent high-intensity exercise. The total amount of work performed and the duration of exercise was identical between sessions.

Results During exercise, heart rate, respiratory exchange ratio, oxygen utilization, ventilation and blood lactate levels were higher during continuous moderate-intensity + intermittent high-intensity exercise vs. continuous moderate-intensity exercise (all $P < 0.05$). Despite these marked cardiorespiratory differences between trials, there was no difference in the reduction of interstitial glucose or plasma glucose levels between the exercise trials. Nocturnal glucose levels were higher in continuous moderate-intensity + intermittent high-intensity exercise and in sedentary vs. continuous moderate-intensity exercise ($P < 0.05$). Compared with continuous moderate-intensity exercise alone, continuous moderate-intensity + intermittent high-intensity exercise was associated with less post-exercise hypoglycaemia (5.2 vs. 1.5% of the time spent with glucose < 4.0 mmol/l) and more post-exercise hyperglycaemia (33.8 vs. 20.4% of time > 11.0 mmol/l).

Conclusions Although the decreases in glucose level during continuous moderate-intensity exercise and continuous moderate-intensity + intermittent high-intensity exercise are similar, the latter form of exercise protects against nocturnal hypoglycaemia in athletes with Type 1 diabetes.

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Keywords continuous glucose monitoring system, exercise, hypoglycaemia, intermittent, Type 1 diabetes

Abbreviations HR_{max}, maximum heart rate; V_E, minute ventilation; VO_2peak, peak aerobic capacity; WRpeak, peak work rate

Introduction

Continuous moderate-intensity aerobic exercise frequently causes hypoglycaemia in persons with Type 1 diabetes [1–4]. The decline in blood glucose concentration is primarily attributable to the inability of circulating insulin levels to be lowered at the onset of continuous exercise, thereby causing impaired glucose production and high rates of glucose disposal

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[5]. Biochemical hypoglycaemia (i.e. blood glucose < 4 mmol/l, with or without symptoms) can also occur immediately following exercise and again 7–11 h later in recovery [6–8], likely as a result of a biphasic change in insulin sensitivity post-exercise [9]. If exercise is performed in the late afternoon, hypoglycaemia typically occurs during night-time sleep with a glucose nadir, as assessed by continuous glucose monitoring technology or intravenous catheterization, somewhere between 00.00 and 04.00 h [6–8]. In contrast to continuous moderate-intensity exercise, high-intensity exercise (e.g. sprinting at > 80% of maximal aerobic capacity for a short duration) often causes an increase in blood glucose concentrations in individuals with Type 1 diabetes [10]. Without the concomitant increase in insulin secretion to counteract the hyperglycaemic effects of brief but intense exercise, individuals with Type 1 diabetes may have elevations in glycaemia well into recovery unless corrective insulin doses are given [11].

Many recreational team or field sports, such as soccer, basketball or football, and some training regimens (i.e. Fartlek or interval training) are comprised of a combination of steady-state continuous moderate-intensity exercise intermixed with short bursts of higher intensity effort. Typically, these types of activities have lengthy periods of continuous moderate-intensity exercise activity [i.e. between 55–75% of maximum heart rate (HR_{max})] interspersed with intermittent bouts of high-intensity exertion (i.e. > 90% HR_{max}). Recently, Guelfi, Bussau and colleagues [12–17] have reported that a brief 'sprint' or a series of intermittent high-intensity exercise bouts, typically in the form of sprints, attenuates the usual drop in blood glucose concentration normally associated with continuous moderate-intensity aerobic exercise. Although intermittent high-intensity exercise may protect against acute exercise-induced hypoglycaemia, the effects of intermittent high-intensity exercise on glucose levels in recovery is not well described. On the one hand, as intermittent high-intensity exercise uses muscle glycogen as a predominant fuel source (because of the higher intensity of exercise), recovery blood glucose levels may decline even more with this form of exercise because of an increased need for muscle glycogen restoration. On the other hand, the increase in glucose counter-regulatory hormones associated with intermittent high-intensity exercise, such as catecholamines and cortisol, or elevations in other metabolites (such as free fatty acids) may lower glucose clearance and may be associated with higher blood glucose concentrations in recovery. In one study, intermittent high-intensity exercise has been shown to increase glycaemia in early recovery and help prevent post-exercise hypoglycaemia in patients with Type 1 diabetes [17]. In contrast, in one other study, late recovery from continuous moderate-intensity + intermittent high-intensity exercise was associated with increased risk for nocturnal hypoglycaemia when compared with continuous moderate-intensity exercise alone in non-trained patients with Type 1 diabetes [18]. As such, more research is needed using continuous glucose monitoring technology to compare the effects of continuous moderate-intensity exercise and intermittent high-intensity exercise on glucose levels in early and late recovery.

The primary purpose of this study was to compare the physiologic and glycaemic responses to two different types of exercise (continuous moderate-intensity exercise vs. intermittent high-intensity exercise) performed in the late afternoon in athletes with Type 1 diabetes. A secondary purpose was to contrast the glycaemic excursions associated with these two different types of exercise with sedentary days. Our study reveals that glucose reductions during late-day preprandial exercise are similar between continuous moderate-intensity exercise and intermittent high-intensity exercise days, but that the latter form of activity is associated with higher glucose levels at bedtime and thus protection against nocturnal hypoglycaemia. Our study also reveals that both forms of exercise are associated with glucose instability when compared with continuous glucose monitoring measurements made during sedentary days. These findings are important when attempting to establish clinical strategies to limit exercise-associated dysglycaemia in physically active persons with Type 1 diabetes.

Methods

Participants

Eleven persons with Type 1 diabetes (six female and five male) participated in the study. Women were studied in the midfollicular phase of the menstrual cycle. These subjects ranged in age (35.1 ± 3.5 years; mean ± SEM; range 18–51 years), height (174.0 ± 3.6 cm), weight (73.1 ± 3.6 kg) and body fat (22.7 ± 2.2%), but were all physically active for at least 30 min per day, 3 days per week, and were in good aerobic fitness (VO_2peak; 42.4 ± 1.6 ml kg^{-1} min^{-1}). Participants had been diagnosed with diabetes for an average of 15.6 ± 5.6 years (0.5–30 years), but all were free from disease complications, as assessed by their own clinical teams, and were in fair to good metabolic control [glycated haemoglobin (HbA_{1c}) 7.8 ± 0.4% (62 ± 19 mmol/mol); range 5.5–9.9% (37–85 mmol/mol)]. Six subjects were using pump therapy while the remaining five used multiple daily injections of insulin. Average reported daily insulin use was 34 ± 5 units (range 12–66 units). All subjects had regular sleep–wake cycles and none worked varying day/night shifts. None of the participants had experienced any episodes of severe hypoglycaemia in the previous year (requiring medical assistance). Subjects received instruction about all experimental procedures and signed written informed consent, complying with the ethics policy of York University.

Design

The patients were evaluated on three occasions (baseline data collection and two prolonged continuous glucose monitoring investigations). On one occasion, anthropometric measurements were conducted and peak aerobic capacity (VO_2peak) was determined from a progressive cycling test to exhaustion on an

electromagnetically braked cycle ergometer (ErgoSelect 100P/100K; Ergoline, Windhagen, Germany) with continuous gas analysis (Vmax 29, SensorMedics, CareFusion, San Diego, CA, USA). VO_2peak was considered to have been achieved if two of the following criteria occurred: (i) a levelling of oxygen consumption in spite of an increase in work rate; (ii) heart rate achieved age predicted maximum (220 – age in years); (iii) volitional exhaustion in spite of verbal encouragement and (iv) a respiratory exchange ratio of ≥ 1.10. Peak work rate (WRpeak) during the incremental test was calculated from the last completed work stage plus the fraction of time spent in the final non-completed work stage multiplied by the work rate increment as shown below:

$$W_1 + (W_2 \times t/60)$$

where W_1 is the work rate at last completed stage, W_2 is the work rate increment at final uncompleted stage and t is the time in seconds at final uncompleted stage.

On another occasion, at least 72 h following maximal exercise testing, each subject was fitted with a continuous glucose monitoring system (CGMS®Gold™; Minimed Medtronic, Northridge, CA, USA) for the first of two exercise trials. This continuous glucose monitoring system model was chosen as it does not provide the subject with real-time glucose levels that could influence their actions to control blood glucose and render an inaccurate portrayal of their 'typical' glycaemic patterns [19,20]. We [7] and others [21] have previously reported that interstitial glucose concentration, as measured by this technology, generally reflects the trends in whole blood glucose changes associated with a time delay of approximately 10–20 min. This sensor was used to capture temporal changes in glycaemia on a sedentary day and a subsequent exercise day (i.e. continuous moderate-intensity exercise or intermittent high-intensity exercise). A new sensor was inserted 1–4 weeks later for the capture of another sedentary day and the subsequent exercise day (continuous moderate-intensity exercise or intermittent high-intensity exercise). The type of exercise was randomized for each subject and counterbalanced by one of the investigators (KEI). After completion of each trial, continuous glucose monitoring system data were uploaded using Solutions™ Software (Medtronic). For each subject, averages of the two representative sedentary days were determined and used to compare against the two different exercise days. A timeline of the experimental protocol is shown in Fig. 1. Continuous glucose monitoring systems require repeated calibrations with capillary glucose values throughout the day, ideally when glucose levels are relatively stable before exercise or before meals [22]. As such, we asked subjects to calibrate blood glucose values from their own validated blood glucose meter at standardized times on each of the two trials (as shown in Fig. 1).

Nutrition and insulin

Standardized meals and snacks were provided to the subjects for all days under investigation (two sedentary days and two exercise days). The composition of these meals and snacks was based on current recommendations for athletes with Type 1 diabetes to achieve a neutral energy balance with ∼60% of calories from carbohydrates, ∼20% from protein and ∼20% from fat [23]. The food was consumed at standardized times and was identical in composition for each subject. However, because of variations in activity levels and thus caloric needs, the total consumed calories between subjects varied. Subjects were asked to take their usual insulin dose for the carbohydrates provided at the lunch before the planed exercise session as the physical activity was to be performed in the postabsorptive state (5 h after a meal) when rapid-acting insulin analogues have little to no action [24–27]. In addition, each subject consumed a low glycaemic index beverage (30 g carbohydrate, Glucerna®Shake; Abbott Nutrition, Columbus, OH, USA) as a bedtime snack on both the sedentary night and on the nights following exercise (the exercise night) to guard against nocturnal hypoglycaemia. The timing and amount of food consumed in addition to all insulin dosages were recorded in a journal by the participant.

Prolonged exercise trials

Following the VO_2peak test, subjects attended the exercise physiology laboratory on two more occasions spaced 1–4 weeks apart in a randomized and counterbalanced order. They then completed 45 min of continuous cycling exercise (continuous moderate-intensity exercise trial) or continuous exercise mixed with intermittent high-intensity exercise bouts (intermittent high-intensity exercise trial). Exercise commenced at 17.00 h on both occasions to replicate a common time to exercise in the post-absorptive state, such as after work or school (Fig. 1). The continuous moderate-intensity exercise trial consisted of constant cycling on an electrically braked ergometer (60–90 revolutions per min) at 55% of the subjects' WRpeak, as determined from the previously conducted VO_2peak aerobic test. The intermittent high-intensity exercise trial included cycling at 50% of the subjects' WRpeak with the addition of nine, 15-s bouts of 100% of WRpeak, spaced 5 min apart. In both trials, the cycling cadence, including during the intense bouts of activity, was held between 60 and 90 revolutions per min. It is important to note that these work rates were chosen in an attempt to equalize the total work performed, as well as the duration of the entire exercise activity, between trials. These two different exercise tasks were selected because athletes tend to perform either continuous steady-state exercise (jogging, cycling) or intermittent exercise that demands near maximal power output (some team sports, interval training). As the total work carried out was identical between tasks, we assumed that any difference in post-exercise glycaemia was attributable to the difference in the exercise type (continuous moderate-intensity exercise vs. continuous moderate-intensity + intermittent high-intensity exercise) rather than total energy expenditure or exercise time.

Expired gas was analysed continuously during exercise to determine caloric expenditure and substrate oxidation, assuming

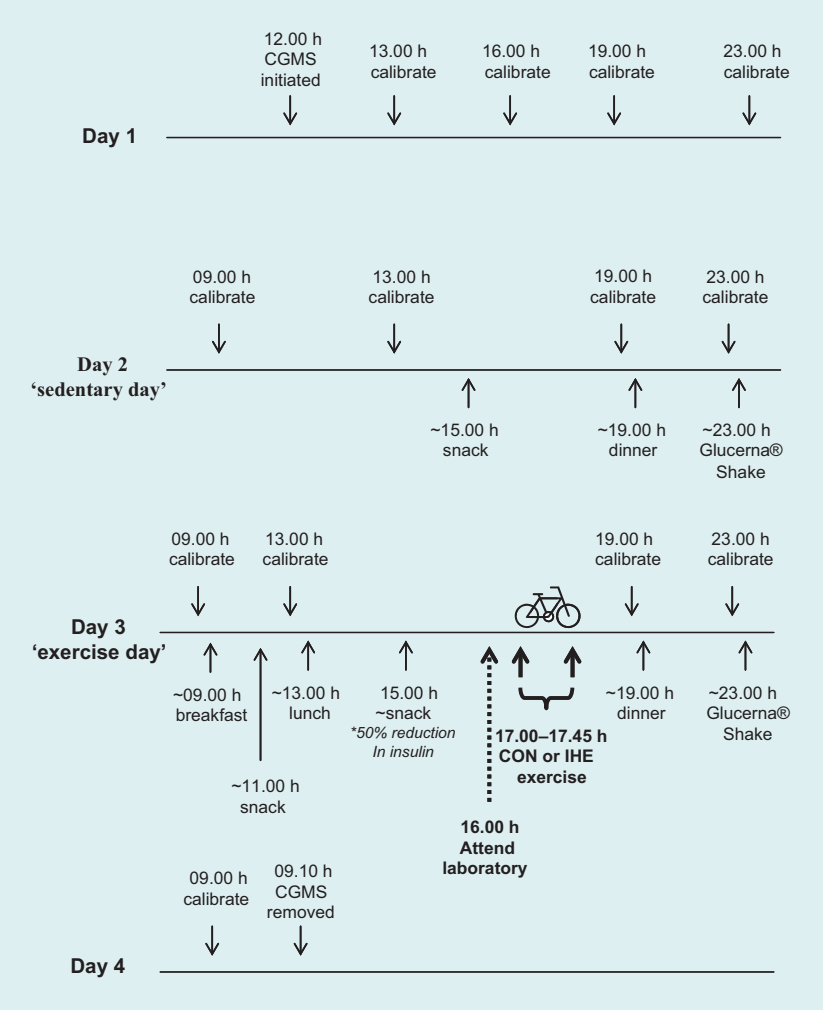

FIGURE 1 Time line for the study. Participants attended the exercise laboratory on day 1 for continuous glucose monitoring system (CGMS) initialization. Finger-stick capillary blood glucose calibrations were performed using the participants own blood glucose meters at standardized times, as shown. As manufacturers caution the accuracy of CGMS readings obtained during the first several hours after initiation [30], only day 2 (sedentary day) and day 3 (exercise day) data were used for analysis. On day 3, participants performed either continuous moderate-intensity exercise (CON) or continuous moderate-intensity + intermittent high-intensity exercise (CON+IHE), in a randomized and counterbalanced order. On day 4, CGMSs were removed and the data were uploaded. On another occasion, spaced at least 1 week later, the entire protocol was repeated with the exercise type changed (on day 3). As such, two sedentary days and two exercise days (continuous moderate-intensity exercise, continuous moderate-intensity + intermittent high-intensity exercise) were captured. *All CGMS calibrations are carried out prior to meals or insulin injections.

negligible protein oxidation occurred [28,29]. Capillary glucose samples were taken using a lancing device and a portable blood glucose monitor (OneTouch®UltraSmart®, LifeScan Inc., Milpitas, CA, USA). Whole blood was also collected pre- and post-exercise via finger capillary lancing into heparinized disposable micropipettes (Fisher Scientific, Nepean, ON, Canada), stored at −80 °C and subsequently analysed for epinephrine and norepinephrine concentrations (BA-1500 CATE; Rocky Mountain Diagnostics, Colorado Springs, CO, USA). Plasma was also isolated via centrifugation for 90 s at 6000 g and assayed within 5 min for plasma glucose and lactate levels using a YSI 2300 STAT Plus Glucose and L-Lactate Analyzer (YSI Inc., Yellow Springs, OH, USA). A saliva sample was collected and stored at −80 °C for the subsequent analysis of salivary 'free' cortisol (Salivary Cortisol Enzyme Immunoassay Kit; Salimetrics LLC, State College, PA, USA).

Statistical analysis

For measurements made repeatedly on subjects (e.g. hormones, glucose, cardiorespiratory measures during exercise), a two-way (trial by time) repeated-measures ANOVA was conducted. If a significant interaction was found, a Bonferroni post-hoc test was conducted. Values are presented as mean ± SEM. GraphPad Prism® Software version 4.0 (GraphPad Software Inc., San Diego, CA, USA) and Statistica® Software (StatSoft Inc., Tulsa, OK, USA) were used for all analyses and graphical representations.

Results

Nutrition and insulin intake

As planned, meal intake and insulin dosages remained virtually identical among the two sedentary and the two exercise days. However, as subjects could freely treat (or prevent ensuing) hypoglycaemia with extra carbohydrates and/or modify insulin dosages in anticipation of the exercise bouts and in recovery, some slight differences in total carbohydrate intake and insulin administration occurred. Although total carbohydrate intake, including meals, snacks and carbohydrates used to treat hypoglycaemia, was higher in continuous moderate-intensity exercise (171 ± 22 g) than in continuous moderate-intensity + intermittent high-intensity exercise (149 ± 20 g) and sedentary (118 ± 17 g) days ($P < 0.05$), no significant differences occurred in total insulin intake (either basal or bolus). Calculated carbohydrate-to-bolus insulin ratios, which represent the amount of carbohydrates in grams that should be effectively metabolized for every unit of bolus insulin, were not significantly different between continuous moderate-intensity exercise (14 ± 3 units) and continuous moderate-intensity + intermittent high-intensity exercise (12 ± 3 units) trials. However, there was significantly higher carbohydrate:insulin ratio on the continuous moderate-intensity exercise day compared with the sedentary days (10 ± 2 units) ($P < 0.01$), indicating that the subjects were more insulin sensitive following continuous moderate-intensity exercise than during a sedentary day.

Response to exercise

Cardiovascular, substrate utilization and rating of perceived exertion during exercise

Compared with continuous moderate-intensity exercise, continuous moderate-intensity + intermittent high-intensity exercise caused large fluctuations in heart rate, respiratory exchange ratio, VO_2 and V_E (Fig. 2). As such, a significant trial by time interaction existed for all these physiologic variables (all $P < 0.001$). Despite this, the total amount of work performed did not differ significantly between trials (continuous moderate-intensity exercise 33 333 ± 2670 watts vs. continuous moderate-intensity + intermittent high-intensity exercise 32 913 ± 2530 watts; $P = 0.11$), nor did the estimated total calories utilized (continuous moderate-intensity exercise 488.3 ± 33.2 kcal vs. continuous moderate-intensity + intermittent high-intensity exercise 506.4 ± 32.5 kcal; $P = 0.12$). For data collapsed across exercise time, average heart rate between the continuous moderate-intensity exercise trial [150 ± 3 b min^{-1} (81 ± 2% age-predicted HR_{max})] and the continuous moderate-intensity + intermittent high-intensity exercise trial [149 ± 3 b min^{-1} (80 ± 1% age-predicted HR_{max})] also did not differ. There was no difference between average oxygen consumption [continuous moderate-intensity exercise 28.8 ± 1.3 ml kg^{-1} min^{-1} (or 67.8 ± 1.5% of VO_2peak) and continuous moderate-intensity + intermittent high-intensity exercise 29.1 ± 1.1 ml kg^{-1} min^{-1} (or 68.9 ± 2.0% VO_2peak); $P = 0.47$)] or V_E [(continuous moderate-intensity exercise = 56.5 ± 3.4 l/min vs. continuous moderate-intensity + intermittent high-intensity exercise = 58.4 ± 4.1 l/min; $P = 0.29$)] between trials.

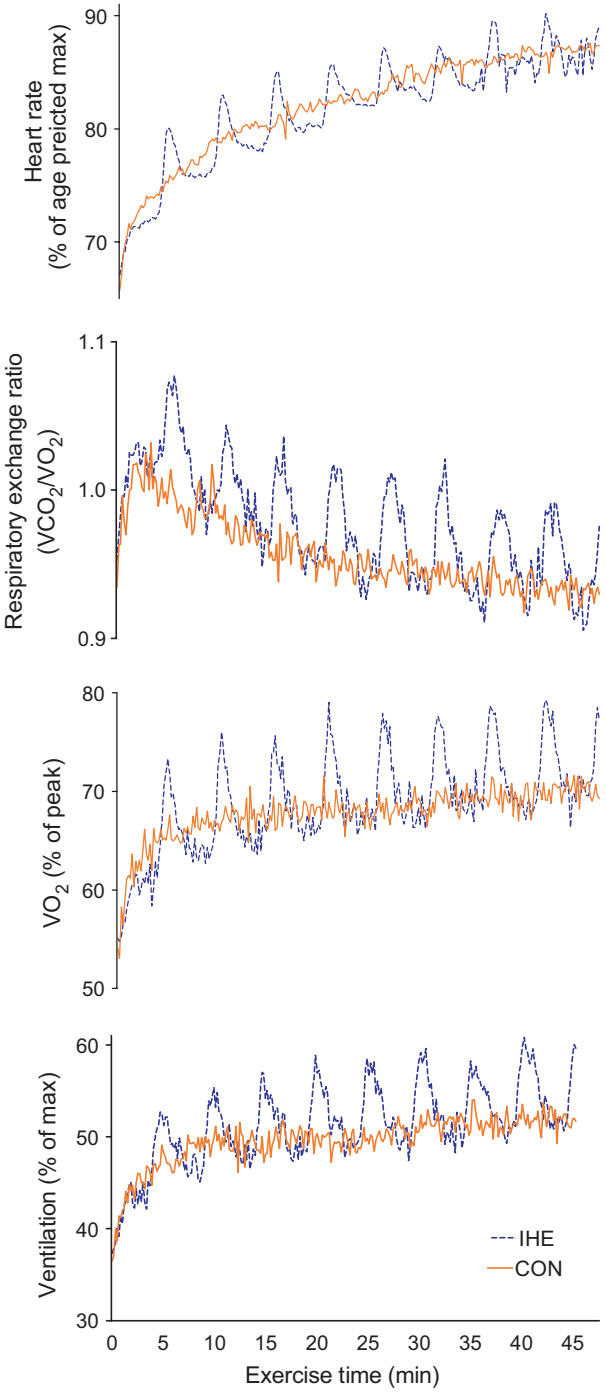

FIGURE 2 Cardiovascular and metabolic data from 45 minutes of either continuous moderate-intensity exercise (CON; solid line) or continuous moderate-intensity + intermittent high-intensity exercise (CON+IHE; dashed line) exercise: (a) heart rate, (b) respiratory exchange ratio, (c) VO_2 and (d) V_E. Significant trial by time interactions with all cardiorespiratory variables (all $P < 0.05$).

Acute glycaemic responses to exercise

Interstitial glucose declined similarly in continuous moderate-intensity exercise and continuous moderate-intensity + intermittent high-intensity exercise trials and remained relatively stable in the sedentary trials ($P < 0.05$; group by trial interaction, Fig. 3).The absolute fall in whole blood glucose (continuous moderate-intensity exercise = −5.1 ± 0.7 mmol/l vs. continuous moderate-intensity + intermittent high-intensity exercise = −5.0 ± 0.5 mmol/l; $P = 0.8$) and the relative fall in whole blood glucose (continuous moderate-intensity exercise = 51.6 ± 4.7% vs. continuous moderate-intensity + intermittent high-intensity exercise = 50.6 ± 4.2%; $P = 0.9$) (from time 0 to 45 min), as measured by a validated blood glucose meter, were similar between continuous moderate-intensity exercise and continuous moderate-intensity + intermittent high-intensity exercise. During continuous moderate-intensity + intermittent high-intensity exercise, three of the 11 subjects (27%) developed biochemical hypoglycaemia (< 4.0 mM), based on the blood glucose meter readings, while seven of the 11 subjects (64%) became hypoglycaemic during continuous moderate-intensity exercise ($P = 0.2$; Fisher exact probability test). There was no significant difference in the mean drop in plasma glucose levels from 0 to 45 min of exercise, as measured by the YSI analyser, between the continuous moderate-intensity exercise (−5.1 ± 0.6 mmol/l) and continuous moderate-intensity + intermittent high-intensity exercise (−4.4 ± 0.05 mmol/l) trials.

Metabolic and hormonal response to exercise

Baseline plasma lactate levels were similar between the exercise trials, but levels increased more after the continuous moderate-intensity + intermittent high-intensity exercise trial (delta: 4.7 ± 0.1 mmol/l) than after the continuous moderate-intensity exercise trial (delta: 2.8 ± 0.3 mmol/l; $P < 0.01$). There was a significant increase in salivary cortisol concentration in both exercise trials (continuous moderate-intensity exercise = 0.07 ± 0.02 μl/dl; continuous moderate-intensity + intermittent high-intensity exercise 0.07 ± 0.03 μl/dl; $P < 0.1$), but no difference occurred between trials. Finally, there was a significant increase in plasma epinephrine (continuous moderate-intensity exercise = 571.8 ± 148.9 pmol/l; continuous moderate-intensity + intermittent high-intensity exercise = 551.7 ± 81.2 pmol/l) and norepinephrine (continuous moderate-intensity exercise = 2.90 ± 0.85 nmol/l; continuous moderate-intensity + intermittent high-intensity exercise = 3.50 ± 0.60 nmol/l) levels in both trials ($P < 0.01$), although no differences in response occurred between trials.

Post-exercise

Continuous glucose monitoring

The overall interstitial glycaemic profile during the late recovery period is shown in Fig. 4. Compared with the continuous moderate-intensity exercise and continuous moderate-intensity + intermittent high-intensity exercise days, the sedentary day had lower glucose levels at bedtime (between 21.00 and 22.00 h) but remained relatively stable during sleep, drifting downward only slightly. In contrast, glucose levels during the continuous moderate-intensity exercise and continuous moderate-intensity + intermittent high-intensity exercise trials were higher at bedtime than on the sedentary day, but dropped sooner in continuous moderate-intensity exercise when compared with continuous moderate-intensity + intermittent high-intensity exercise. Values in continuous moderate-intensity + intermittent high-intensity exercise were higher than in continuous moderate-intensity exercise, until approximately

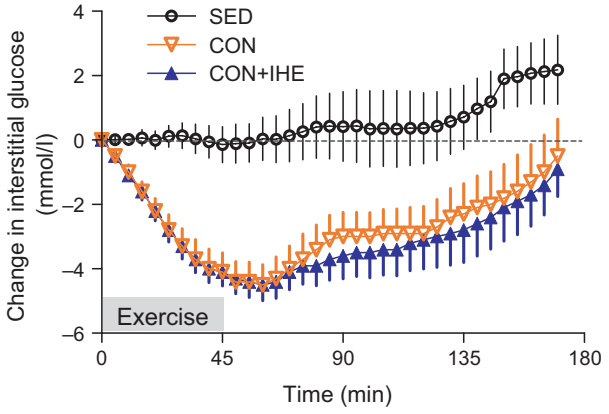

FIGURE 3 Changes in interstitial glucose levels as estimated by continuous glucose monitoring system during late day continuous moderate-intensity exercise (CON) and continuous moderate-intensity + intermittent high-intensity exercise (CON+IHE). Data are means ± SEM. Significant trial by time interactions exist ($P < 0.05$). Exercise was performed in the post-absorptive state (17.00 h). SED, sedentary.

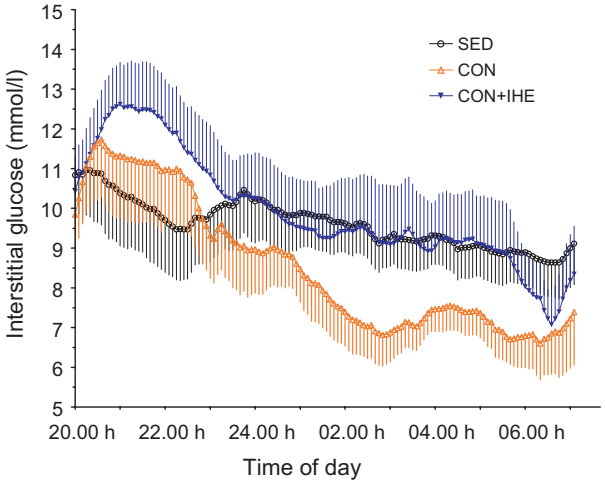

FIGURE 4 Nocturnal interstitial glucose levels as estimated by continuous glucose monitoring system following two sedentary days (data collapsed across days; sedentary), 45 min of late day continuous moderate-intensity exercise (CON) and 45 min of late day continuous moderate-intensity + intermittent high-intensity exercise (CON+IHE). Data are means ± SEM. Significant trial by time interactions exist ($P < 0.05$).

06.00 h ($P < 0.05$) when values then decreased sharply. Maximum continuous glucose monitoring system values during the night were 12.6 ± 1.0 mmol/l (sedentary), 12.4 ± 1.3 mmol/l (continuous moderate-intensity exercise) and 14.9 ± 1.3 mmol/l (continuous moderate-intensity + intermittent high-intensity exercise) trials ($P < 0.05$). Minimum continuous glucose monitoring system values during the night were 6.3 ± 0.5 mmol/l (sedentary), 5.0 ± 0.7 mmol/l (continuous moderate-intensity exercise) and 4.9 ± 0.6 mmol/l (continuous moderate-intensity + intermittent high-intensity exercise) ($P < 0.05$). During the two sedentary nights, only four hypoglycaemic events occurred (averaging two of 11 subjects per night), whereas, in the evenings following exercise, the hypoglycaemic occurrence was higher following continuous moderate-intensity exercise (five out of 11 subjects, nadir < 4.0 mmol/l) than with continuous moderate-intensity + intermittent high-intensity exercise (three of 11 subjects < 4.0 mmol/l). Standard deviation scores, as an index of glycaemic variability, for the interstitial glucose levels were also higher in continuous moderate-intensity exercise (2.6 ± 0.51 mmol/l) and in continuous moderate-intensity + intermittent high-intensity exercise (2.8 ± 0.44 mmol/l) when compared with sedentary days (2.0 ± 0.31 mmol/l) ($P < 0.05$).

Whole blood capillary glucose concentrations, as measured by the blood glucose meter at standardized times throughout the day (see Methods), were strongly correlated to interstitial glucose levels as measured by the continuous glucose monitoring system ($r^2 = 0.94$, $n = 274$ matched pairs).

Discussion

The main findings of this study are that 45 min of post-absorptive continuous cycling exercise, either with or without intermittent high-intensity exercise by athletes with Type 1 diabetes, causes similar reductions in glucose levels during the activity, but that the addition of intermittent high-intensity exercise is associated with less risk for late-onset post-exercise hypoglycaemia. This finding is in agreement with earlier work by Guelfi *et al.*, [17], but is in contrast with the recent observation by Maran *et al.* [18] who found that, compared with continuous moderate-intensity exercise, continuous moderate-intensity + intermittent high-intensity exercise was associated with increased risk for nocturnal hypoglycaemia in non-trained patients with Type 1 diabetes. The reasons for the discrepancy in findings are unclear but may be related to the training status of the individuals, differences in bedtime blood glucose levels observed following continuous moderate-intensity exercise compared with continuous moderate-intensity + intermittent high-intensity exercise and/or the nature of intermittent high-intensity exercise performed (see below). This study also reveals that both forms of exercise (continuous moderate-intensity exercise or continuous moderate-intensity + intermittent high-intensity exercise) cause considerably more glycaemic variation both during and after the exercise compared with sedentary behaviour, despite strategies in place that should limit dysglycaemia (exercise in the preprandial state with less 'on board' insulin and with supplementary bedtime carbohydrate intake).

Prolonged steady-state aerobic exercise has long been known to cause a decrease in blood glucose levels in individuals with Type 1 diabetes, particularly if the exercise is performed soon after an insulin administration [31]. More recently, it has been established that the high risk for hypoglycaemia associated with prolonged exercise may exist in two phases, as increased insulin sensitivity occurs immediately following the exercise and again 7–11 h later in recovery [9]. However, short-term high-intensity exercise (>80% VO_2max) has been shown to cause a rise in blood glucose levels because of the release of catecholamines that increases glucose production beyond what is taken up by the contracting muscles [10]. The effect of 'intermittent' exercise, as is typically performed in a variety of exercise training regimens and sporting activities, on circulating glucose levels in early and late recovery is less clear. Work by Bussau, Guelfi and colleagues [12–14,16,17] suggests that intermittent bouts of 'sprinting' exercise may attenuate the drop in glucose associated with more moderate-intensity prolonged activities and may offer some additional protection against hypoglycaemia, at least in early recovery. Surprisingly, there is a paucity of data on the glycaemic responses in prolonged recovery following exercise of this type. In only one study has a comparison between continuous moderate-intensity exercise and continuous moderate-intensity + intermittent high-intensity exercise been investigated, with the authors reporting that continuous moderate-intensity + intermittent high-intensity exercise increases the risk for nocturnal hypoglycaemia [18]. In that study, it was concluded that the addition of intermittent high-intensity exercise increases the risk for post-exercise late-onset hypoglycaemia in non-trained patients with Type 1 diabetes and thus would be considered an undesirable form of exercise for persons with Type 1 diabetes. In contrast to this, we found that continuous moderate-intensity + intermittent high-intensity exercise is associated with higher post-exercise glucose levels than continuous moderate-intensity exercise alone and that values remain similar to a sedentary day throughout most of the early evening and night. The reasons for the discrepancy in findings are unknown but may be related to when slightly different forms of intermittent high-intensity exercise were performed (see below) and to the fact that the subjects in our study were active athletes with Type 1 diabetes (with higher VO_2peak levels than the subjects in the Maran study) and were familiar with both forms of activity in their training regimen. It is important to note that continuous moderate-intensity + intermittent high-intensity exercise in our study was associated with a later drop in glycaemia, occurring at ~06.00 h, perhaps indicating a more delayed increase in insulin sensitivity post-exercise (i.e. 12 h after the end of exercise). Nonetheless, the overall incidence of hypoglycaemia was less following continuous moderate-intensity + intermittent high-intensity exercise compared with continuous moderate-intensity exercise, even though there was higher carbohydrate intake in the continuous moderate-intensity exercise day. This finding is in

agreement with previous work showing that continuous moderate-intensity + intermittent high-intensity exercise does not increase the risk of post-exercise hypoglycaemia [17] and may in fact confer some long-term protection against hypoglycaemia in active individuals with Type 1 diabetes.

In this study, we found similar acute glycaemic responses to two differing forms of exercise that were identical in total work performed and exercise duration, but differed markedly in the composition of intensities and thus their cardiorespiratory and metabolic responses (Fig. 2). Based on blood lactate and respiratory exchange ratio levels, it was apparent that the continuous moderate-intensity + intermittent high-intensity exercise trial had a much higher energy contribution from anaerobic metabolism and muscle glycogen utilization. However, the intervals of the intermittent high-intensity exercise 'sprints' were brief (nine bouts at 15 s each for a total of 135 s) and the continuous cycling between these intermittent high-intensity exercise 'sprints' was in fact lower than in the continuous moderate-intensity exercise trial (50 vs. 55%, respectively). As a result of this 'likeness' in exercise composition and energy expenditure, the acute glucose responses between trials may not have differed because each exercise resulted in the same total work performed, caloric expenditure and average cardiovascular measures (heart rate, ventilation and oxygen consumption). In support of this notion, other studies confirm that, if two different types of exercise are of similar total energy expenditure, the glycaemic responses are quite reproducible for a given subject [32]. Indeed, when all variables are reproduced, including the timing, intensity and duration of exercise, the blood glucose responses are nearly identical on two different occasions, even although they may differ markedly among individuals [33]. These findings are important, as individualized strategies to limit dysglycaemia associated with exercise can be initiated once the total energy utilization has been quantified, as has been suggested in recent guidelines [24].

The stabilization of blood glucose during exercise in persons with Type 1 diabetes is primarily dictated by the neuroendocrine responses of epinephrine, norepinephrine, glucagon, growth hormone and cortisol, along with the levels of exogenously injected insulin. In this study, we observed similar increases in salivary cortisol, epinephrine and norepinehrine levels after both continuous moderate-intensity exercise and continuous moderate-intensity + intermittent high-intensity exercise. These findings were surprising, as we expected that the higher-intensity sprints during the continuous moderate-intensity + intermittent high-intensity exercise trial would have elicited a more pronounced catecholamine response in comparison with the continuous moderate-intensity exercise trial, as has been described previously [18,12–17]. The lack of difference between trials in this study may have been attributable to the heavier resistance-type exercise that was performed. In other words, the 15-sec intermittent high-intensity exercise bouts in this study included cycling against a greater resistance rather than a faster cycling cadence (revolutions per min), as has been carried out previously to increase catecholamine release [18,12–17]. It is likely that the increase in muscular resistance rather than an increase in speed may have resulted in a somewhat modest increase in sympathetic counter-regulatory response and thus a failure to observe differences in acute and early recovery glucose levels between trials.

In this study, we found a high incidence of nocturnal hypoglycaemia following continuous moderate-intensity exercise (45% of participants with glucose < 4.0 mmol/l) and a modest incidence of nocturnal hypoglycaemia following continuous moderate-intensity + intermittent high-intensity exercise (27% of participants with glucose < 4.0 mmol/l) when compared with sedentary behaviour (18% of participants < 4.0 mmol/l). It is important to note that incidence and severity of nocturnal hypoglycaemia following exercise in this study may have been somewhat attenuated, compared with other studies [34,7,8], in part because the subjects in our study ingested a low glycaemic index snack without bolus insulin at bedtime. It is clear, however, that the consumption of this snack was insufficient in preventing nocturnal hypoglycaemia in many of the participants, particularly during the continuous moderate-intensity exercise trial. As such, clinical recommendations to lower basal insulin levels at bedtime by ~20% may be needed to help prevent nocturnal hypoglycaemia, particularly following continuous moderate-intensity exercise, as has been demonstrated recently [34]. Based on our work, it is questionable if such reduction in insulin dose is required following continuous moderate-intensity + intermittent high-intensity exercise in athletes with Type 1 diabetes, given the observation that nocturnal glycaemia is similar to an evening following a sedentary day.

In summary, this study demonstrates that continuous moderate-intensity exercise, but not continuous moderate-intensity + intermittent high-intensity exercise, is associated with increased risk for nocturnal hypoglycaemia in athletes with Type 1 diabetes. This finding is in contrast with previously published literature showing that continuous moderate-intensity + intermittent high-intensity exercise increases risk of post-exercise late-onset hypoglycaemia in non-trained patients with Type 1 diabetes. Future studies should determine if endurance training or the exact nature of intermittent high-intensity exercise (heavier resistance vs. sprinting) influences risk for developing nocturnal hypoglycaemia in patients with Type 1 diabetes.

Competing interests

The authors acknowledge the lending of continuous glucose monitoring systems from Medtronic Ltd for the completion of this study. There were no external (non-academic) sources of funding. MCR has received speaker's fees from Medtronic Ltd, Canada. The authors have no other conflicts of interest to declare.

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