HIT improves aerobic capacity without a detrimental decline in blood glucose in people with type 1 diabetes

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FULL TITLE:

HIGH INTENSITY INTERVAL TRAINING IMPROVES CARDIO-METABOLIC HEALTH IN PEOPLE WITH TYPE 1 DIABETES AND WITHOUT EXERCISE-ASSOCIATED DECLINE IN BLOOD GLUCOSE

SHORT TITLE:

6 weeks of HIT in type 1 diabetes

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ABSTRACT

OBJECTIVE – To compare the effects of six weeks of high intensity interval training (HIT) to moderate intensity continuous training (MICT) on markers of cardio-metabolic health, and glucose variability in people with type 1 diabetes.

RESEARCH DESIGN AND METHODS – Fourteen previously sedentary people with type 1 diabetes (*n*=7 per group) completed six weeks of HIT or MICT three times per week and the effect on glucose variability using continuous glucose monitors (CGMS) and markers of cardio-metabolic health (aerobic capacity, blood lipid profile and arterial stiffness) were measured. Capillary blood glucose values were also recorded pre and post exercise to assess change in blood glucose concentration during exercise in the fed state.

RESULTS – Six weeks of HIT or MICT improved $\dot{V}O_{2peak}$ by 14% and 15%, respectively (P<0.001), and aortic pulse wave velocity by 12% (P<0.001), with no difference between groups. CGMS data revealed no differences in incidence or percentage of time spent in hypoglycaemia following training in either group (P>0.05). The mean change in blood glucose concentration in response to HIT was -0.2 ± 0.5 mmol/L, whereas blood glucose decreased by -5.5 ± 0.4 mmol/L in response to MICT in the fed state.

CONCLUSIONS - Six weeks of HIT improved cardio-metabolic health markers to a similar degree as MICT. However, the finding that blood glucose remains stable during HIT in the fed state but consistently falls with MICT suggests that HIT may be a more practical option for patients with type 1 diabetes.

ABREVIATIONS

HIT – High intensity interval training

MICT – Moderate intensity continuous training

CON – Control day of no exercise

aPWV – Aortic pulse wave velocity

CGMS – Continuous glucose monitor system

CHO - Carbohydrate

SBP – Systolic blood pressure

DBP – Diastolic blood pressure

MAP – Mean arterial pressure

EXTOD – Exercising for type 1 diabetes

INTRODUCTION

Regular exercise is recommended for people with type 1 diabetes to maintain overall health and reduce the risk of macrovascular and microvascular complications, which are a major cause of mortality and morbidity (1-3). The current guidelines for people with type 1 diabetes are to undertake at least 150 minutes of moderate to vigorous aerobic exercise per week, spread over at least three days per week, with no more than two consecutive days without activity (4). Benefits of exercise for those with type 1 diabetes include improved aerobic capacity ($\dot{V}O_{2max}$), insulin sensitivity, body composition, endothelial function and blood lipid profile (1; 5-7). Despite the benefits, few people with type 1 diabetes achieve exercise targets and many programmes designed to increase physical activity have failed (8; 9). In addition to the barriers to exercise cited by the general population, such as a perceived lack of time, work commitments and cost (10-12), people with type 1 diabetes face additional barriers including fear of hypoglycaemia, loss of glycaemic control and inadequate knowledge around exercise management (10; 12).

To overcome a perceived lack of time, high intensity interval training (HIT) is purported as a time-efficient alternative to moderate-intensity exercise to improve numerous cardio-metabolic risk factors including $\dot{V}O_{2max}$, insulin sensitivity and glycaemic control in people without type 1 diabetes (13; 14). However these benefits have not been explored in people with type 1 diabetes. Recent results from our laboratory (Scott et al. companion paper) show that HIT can be undertaken in the fasted state safely and without hypoglycaemia. However this has not been explored in the fed state.

Here we investigated the hypothesis that six weeks of HIT would improve markers of cardio-metabolic health, including $\dot{V}O_{2peak}$, glycaemic control and vascular

health, in people with type 1 diabetes. A moderate intensity continuous training (MICT) group was used as a control. During this 6-week training period blood glucose concentrations were monitored before and after all exercise sessions to explore the acute effects of HIT and MICT on blood glucose concentration.

RESEARCH DESIGN AND METHODS

Fourteen previously sedentary people with type 1 diabetes (10 men/4 women; see Table 1 for subject characteristics) on a basal-bolus insulin regimen completed six weeks of supervised HIT (n = 7) or MICT (n = 7) three times per week. Participants were pair-matched based on sex, age and $\dot{V}O_{2peak}$ to the two training groups. Exclusion criteria were duration of type 1 diabetes <6 months, insulin pump therapy, significant history of hyper or hypoglycaemia, obesity (BMI >32 $kg \cdot m^{-2}$), pregnancy or planning pregnancy, uncontrolled hypertension (>180/100 mmHg), angina, autonomic neuropathy, taking any medication that affects heart rate, major surgery planned within 6 weeks of the study, severe nonproliferative and unstable proliferative retinopathy. Testing took place in the laboratory of the School of Sport and Exercise Sciences at Liverpool John Moores University. The study was approved by the Black Country NHS Research Ethics Committee (West Midlands, UK) and all participants gave written informed consent to a protocol conforming to the *Declaration of Helsinki*.

Pre-training assessments

Participants first performed an incremental exercise test to exhaustion on an electromagnetically braked cycle ergometer (Excalibur Sport V2.0, Lode, Groningen,

The Netherlands) to determine maximal aerobic power output (W_{max}) and $\dot{V}O_{2peak}$ using an online gas collection system (MOXUS modular oxygen uptake system, AEI technologies, Pittsburgh, PA). The test consisted of 3-minute stages starting at 60 W, and the workload was increased by 35 W at each stage until subjects could not maintain a cadence of >50 rpm, at which point the test was terminated. $\dot{V}O_{2peak}$ was taken as the highest value achieved over a 15 second recording period. Participants also completed a food diary over a minimum of three days in order to calculate habitual caloric and macronutrient intake.

Three to 7 days after the incremental exercise test, participants attended the laboratory after an overnight fast (>10 h) for a second pre-training assessment session. Following 15 minutes rest, supine brachial artery blood pressure measurements were made in triplicate using an automated sphygmomanometer (GE DINAMAP Pro 300 V2). Aortic pulse wave velocity (aPWV) measurements were made using a semi-automated device and software (SphygmoCor, AtCor Medical, Sydney, Australia), as previously described Cocks et al. (15). A fasting blood sample was used to determine fasting plasma cholesterol and triglyceride concentrations, using a semi-automatic spectrophotometer (Randox RX Series, the RX Daytona™).

A Dexcom G4 Platinum (Dexcom, San Diego, CA, USA) CGMS was inserted subcutaneously on the abdomen. A habitual free-living 24-hour glucose profile was at least 24 hours after the CGMS was inserted. Participants were trained to use the CGMS and instructed to calibrate the device a minimum of four times daily using capillary blood tests. Participants were provided with a standardised diet of three meals (breakfast, lunch and dinner) during the CGMS period (50% CHO; 30% fat; 20% protein) in accordance with their habitual calorie intake. No additional snacks were

permitted and participants only consumed the food provided by the research team during this period, unless they needed to prevent hypoglycaemia. Participants were instructed to consume these meals at pre-determined time points throughout the day and no additional snacks were permitted other than to prevent hypoglycaemia. A food diary was completed to confirm that they had consumed the prescribed food at the correct times. Participants were instructed to avoid alcohol and caffeine, as well as exercise throughout the CGMS period.

Exercise Training

Training started ~72h after completion of the pre-experimental procedures. Participants trained three times per week for six weeks under researcher supervision on a Lode Corival cycle ergometer (Corival Lode BV, Groningen, The Netherlands). Following a 3 minute low-intensity warm-up, the HIT group performed repeated 1 minute bouts of high intensity cycling at a workload equivalent to 100% $\dot{V}O_{2peak}$ interspersed with 1 minute of recovery at 50 W, whereas the MICT group performed continuous moderate intensity cycling at a workload equivalent to 65% $\dot{V}O_{2peak}$. The number of intervals in the HIT group increased from 6 in weeks 1 and 2, to 8 in weeks 3 and 4 to 10 in weeks 5 and 6. The duration of the sessions in the MICT group were 30 minutes in weeks 1 and 2, 40 minutes in weeks 3 and 4 and 50 minutes in weeks 5 and 6.

Acute change in blood glucose with exercise

Before starting and after completing each training session during the 6 week training period, participant's blood glucose concentrations were required to be between 7-14

mmol/L, in accordance with the Exercising for Type 1 Diabetes (EXTOD) guidelines (16). If blood glucose concentrations fell outside of this range corrective measures were taken; glucose was ingested if blood glucose <7 mmol/L, and a light walk or insulin was advised if glucose >14 mmol/L, as well as checking blood ketones (17). During the MICT sessions participants were advised to check their blood glucose concentrations part-way through the exercise and to consume carbohydrate as necessary to prevent hypoglycaemia. Capillary blood glucose concentrations were recorded before and after exercise and whether the exercise session was undertaken in the fasted (>10 hours) or fed state (last meal consumed <4h previous). As such, over the course of the six weeks of training we gathered pre and post exercise blood glucose concentrations from a total of 108 MICT training sessions and 87 HIT sessions in the fed state. The proportion of total sessions that blood glucose was recorded was 86%.

Post-training assessments

Approximately 72h after the final training session, participants attended the laboratory on two occasions (separated by 72h) to complete a series of post-training assessments. These assessments were identical in all respects to those undertaken prior to training (pre-training assessments).

Statistical analyses

The primary outcome variable was $\dot{V}O_{2peak}$. Previous research in our group (18; 19) has suggested a SD of 2.7-3.2 to detect a change in $\dot{V}O_{2peak}$ of 3.5 ml·kg·min^{-1}, which is a clinically significant increase in $\dot{V}O_{2peak}$ (20). A power calculation suggested that

7-9 participants were required in each group to detect a within-group difference with a paired *t* test with 80% power at a significance level of 0.05. Continuous glucose monitor data were downloaded from the device using Dexcom Studio™ software (12.0.4.6) and analysed in accordance with the International Consensus on Use of Continuous Glucose Monitoring (21). Glycaemic thresholds were defined as follows: target range (3.9-10 mmol/L), level 1 hypoglycaemia (≤3.9 mmol/L), level 2 hypoglycaemia (≤2.9 mmol/L) and hyperglycaemia (≥10 mmol/L). The 24-hour period was defined as 08:00-08:00h and the nocturnal period was defined as 24:00-06:00h. All variables were analysed using a two-way mixed ANOVA, with the between factor 'group' (HIT vs. MICT) and repeated factor 'training status' (pre-training vs. post training), followed by Bonferroni *post-hoc* corrections. A two way mixed ANOVA, with the between factor 'group' and the repeated factor 'time point' (pre-training vs. post training) was used to assess whether there was an acute change in blood glucose concentration following HIT and MICT in the fed state over the 6 weeks of training. The CGMS did not work on one participant in the MICT group. Aortic PWV readings were obtained from five participants in the HIT group and six in the MICT group. All analyses were performed using IBM SPSS Statistics for Windows, Version 22.0. Armonk, NY: IBM Corp. Data are presented as mean ± SEM and significance was set at $P \leq 0.05$.

RESULTS

By design, there were no differences in age ($P=0.877$), $\dot{V}O_{2peak}$ ($P=0.371$) or duration of type 1 diabetes ($P=0.291$) between the training groups at baseline. BMI was, however, significantly higher in the HIT group compared to the MICT group

(*P*=0.038). Pre and post training variables are presented in Table 1. Training increased $\dot{V}O_{2peak}$ (HIT 14%, MICT 15%; *P*<0.001) and W_{max} (HIT 13%, MICT 14%; *P*<0.001), with no difference between groups (Fig. 1). Six weeks of training also improved aPWV (*P*=0.001) and there was no difference between groups. Systolic, diastolic and mean arterial blood pressure did not improve following training (*P*=0.219; *P*=0.476; *P*=0.268, respectively). There was also no change in plasma cholesterol or triglyceride concentrations with training (*P*=0.881; *P*=0.652).

Glycaemic control

Glucose data from the CGMS obtained over a 24-hour period pre and post training are presented in Table 2. There was no difference in the time spent in level 1 hypoglycaemia (≤3.9 mmol/L) over the 24-hour period (P=0.727) or nocturnal period (P=289) with training. Similarly, there was no difference in time spent in level 2 hypoglycaemia (≤2.9 mmol/L) with training over the 24-hour period (*P*=0.442) or nocturnal period (*P*=0.397). There were also no differences in the time spent in target range over the 24-hour (*P*=0.412) or nocturnal periods (*P*>0.382). Furthermore, there was no difference in the time spent in hyperglycaemia over the 24-hour (*P*=0.540) or nocturnal period (*P*=0.118). However, there was an interaction effect for the time spent in target range (*P*=0.034) and time in hyperglycaemia over the nocturnal period (*P*=0.039). Post hoc analysis revealed that the HIT group spent significantly less time in target glycaemia during the nocturnal period (*P*=0.038) which was due to a greater time spent in hyperglycaemia over the nocturnal period (*P*=0.016). The incidence of level 1 hypoglycaemia over the 24-hour period (*P*=0.675) and nocturnal period (*P*=0.363) was no different with training. There were no

differences in the incidence of level 2 hypoglycaemia over the 24-hour (*P*=0.174) or nocturnal (*P*=0.549) with training.

Acute change in blood glucose during training

When quantifying the change in blood glucose concentration during exercise training sessions undertaken in the fed state over the six week intervention, the mean change in blood glucose concentration in response to HIT was -0.2 ± 0.5 mmol/L whereas blood glucose decreased by -5.5 ± 0.4 mmol/L in response to MICT (Fig. 2).

CONCLUSIONS

This study demonstrates for the first time that six weeks of HIT improves $\dot{V}O_{2peak}$ and aPWV in people with type 1 diabetes to a similar magnitude as MICT. Secondly, we observed that blood glucose concentration remained stable during HIT when participants exercised in the fed state throughout the training programme, but there was a consistently large drop in blood glucose during MICT, with patients at risk of hypoglycaemia. The CGMS data revealed no difference between HIT and MICT other than during the nocturnal period where there was an increase in the time spent in hyperglycaemia. The fact that HIT is as effective as MICT but does not cause a fall in glucose during exercise means that it may be a more practical exercise for patients with type 1 diabetes.

Aerobic capacity improved to a similar extent following six weeks of HIT and MICT, despite the weekly time commitment being 47-60% less for HIT than for MICT. The 14% increase in $\dot{V}O_{2peak}$ observed in our investigation following HIT (a mean

increase of 4.9 ml·kg·min^{-1}) is high in comparison to other studies using similar protocols that tend to report changes of 7-10% in populations without type 1 diabetes (22) and the only other study to examine the effect of sprint interval training in type 1 diabetics (repeated 30-second maximal cycling bouts interspersed with 3-4 minutes of rest 3 times a week for 7 weeks) reported a 7% increase in $\dot{V}O_{2peak}$ (23). This has clinical importance given that $\dot{V}O_{2max}$ is reported to be the strongest prognostic marker of cardiovascular mortality (20) and improvements in $\dot{V}O_{2max}$ with exercise training are associated with a reduction in all-cause mortality risk (24). In fact, Myers (20) found that there is a 8-17% reduction in all-cause mortality for each 1-MET (~3.5 ml·kg·min^{-1}) increase in $\dot{V}O_{2max}$. Although these correlations have not been specifically confirmed in people with type 1 diabetes, it is likely that the HIT programme used here induces clinically meaningful benefits to this population, which is especially important as they are at increased risk of cardiovascular disease compared to a non-diabetic population (1; 2).

In the present study there was a 12% reduction in aPWV following both training modes, which is greater than has previously been reported in other training studies in populations without type 1 diabetes (25; 26). To the authors' knowledge, this is the first study to investigate changes in arterial stiffness following HIT and MICT in people with type 1 diabetes. The reduction in aPWV is of clinical relevance as increased arterial stiffness is associated with negative cardiovascular outcomes (27).

Neither training mode improved glycaemic control according to the CGMS data, measured as time spent in target range (euglycaemia) or hypoglycaemia or the incidences of hypoglycaemia. Previous studies using HbA1c and daily insulin dosage as a marker of glycaemic control have also failed to show overall improvements in

glycaemic control with exercise training (23; 28; 29), although studies reporting positive effects of training on glycaemic control do exist (30). There was a reduction in the time spent in euglycaemia in the HIT group which was due to an increase in the time spent in hyperglycaemia. Although increasing the proportion of time spent in hyperglycaemia during the nocturnal period is not desirable, it at least reduces the risk of developing hypoglycaemia. It could be speculated that participants in the HIT group consumed additional carbohydrates before bed to prevent hypoglycaemia and as a result spent more time in hyperglycaemia. However, the study was performed under strict dietary control and participants in the HIT group did not report consuming additional snacks. The small sample size and the fact that just one 24 hour period was recorded is more likely to account for these differences. Although the use of CGMS in our investigation allowed a detailed analysis of glycaemic control, we acknowledge that longer duration exercise training programmes with larger sample sizes are needed to assess the effects of exercise training on long-term glycaemic control. Furthermore, the current guidelines suggest that a minimum of 14 consecutive days should be recorded when analysing CGMS data (21). Unfortunately, these guidelines were published after our data collection was completed so will have to form the recommendations for our future work.

Before the training sessions, we recorded blood glucose concentration for safety reasons to prevent participants from exercising when glucose concentrations were too high or low based on the EXTOD guidelines (16), and after the sessions so that they did not leave the laboratory while they were at increased risk of hypoglycaemia. This meant that we collected pre and post exercise blood glucose readings from up to 18 training sessions for each participant over the course of six weeks HIT or MICT. We found that blood glucose concentration remained stable

during HIT when participants exercised in the fed state throughout the training programme, but there was a consistently large drop in blood glucose during MICT in the fed state, with patients at risk of hypoglycaemia. This was a consistent observation across all participants undertaking MICT (Fig. 2b). The changes in blood glucose concentration during the exercise we have reported here are striking and are the first of their kind in the literature over so many training sessions. Furthermore, they are supported by Garcia-Garcia et al. (31) who conducted a systematic review and meta-analysis in which they aggregated results from 10 studies to estimate rate of change of glucose concentration during and after different types of exercise in people with type 1 diabetes. Their results showed a rapid decline in glycaemia during continuous exercise (-4.43 mmol/L h^{-1} on average) while the results were more variable during intermittent high intensity exercise depending on the protocol.

The instability in blood glucose that we observed during the MICT in the fed state is likely due to the effect of short-acting insulin in the circulation. During moderate intensity exercise in healthy individuals, blood glucose concentration remains stable because insulin secretion is suppressed at the onset of exercise and there is an increase in adrenaline and growth hormone, resulting in increased hepatic glucose production, lipolysis and reduced peripheral glucose uptake. However, because insulin is supplied exogenously in people with type 1 diabetes, they are unable to reduce circulating insulin which limits the effects of glucagon on hepatic glucose production, increases peripheral glucose uptake and delays lipolysis. The combination of insulin and exercise-mediated glucose disposal coupled with decreased hepatic glucose production increases the risk of hypoglycaemia. During HIT, insulin does not tend to decrease even in healthy individuals, presumably because the exercise bout is too short. Previous research has also shown there is a

rise in catecholamines and blood lactate during high intensity exercise which may increase gluconeogenesis and could also be a contributing factor for the attenuated decline in glucose during exercise where high intensity bouts are added to a MICT session (32-34). The implications from these findings are important for people with type 1 diabetes that want to exercise as they show that HIT can be performed in the fed state without significant reduction in blood glucose concentration.

Another important observation, although not quantitatively reported here, was the number of training sessions in which participants had to prevent or treat an episode of hypoglycaemia by consuming fast-acting carbohydrate. During the MICT sessions, participants were advised to stop exercising at least once to check their blood glucose concentration, correct accordingly with glucose if necessary, and then wait for their blood glucose to stabilise before recommencing the training. However, all participants were able to complete the HIT sessions without interruption. Many of the participants in the MICT condition found this frustrating and it would often mean that the already time consuming 50 minute cycling sessions were even longer while blood glucose was checked. The large drop in blood glucose concentration that we found during the MICT sessions highlights why the guidelines recommend that carbohydrate should be taken when doing more than 30 minutes of moderate intensity exercise (17).

The main strengths of this investigation were 1) the strict dietary standardisation under free-living conditions during the CGMS period pre and post training, and 2) the monitoring of acute changes in blood glucose concentrations during exercise throughout the intervention. However, we acknowledge that there are some limitations. The sample size of the study was small; however, the clear increases in $\dot{V}O_{2peak}$ suggest that we have the power to conclude that HIT is effective

at improving $\dot{V}O_{2peak}$ at least. Secondly, we did not record insulin dose before and after training. This would be useful to determine whether there is a change in insulin sensitivity as reduced insulin dosage is associated with decreased risk of cardiovascular complications in people with type 1 diabetes (35; 36).

In summary, this is the first study to demonstrate that six weeks of HIT leads to comparable improvements in $\dot{V}O_{2peak}$ and arterial stiffness to MICT. HIT though may be the preferred approach, as blood glucose remains stable during HIT but falls during MICT. We therefore recommend that HIT is a safe, effective, flexible and time efficient form of exercise for people with type 1 diabetes.

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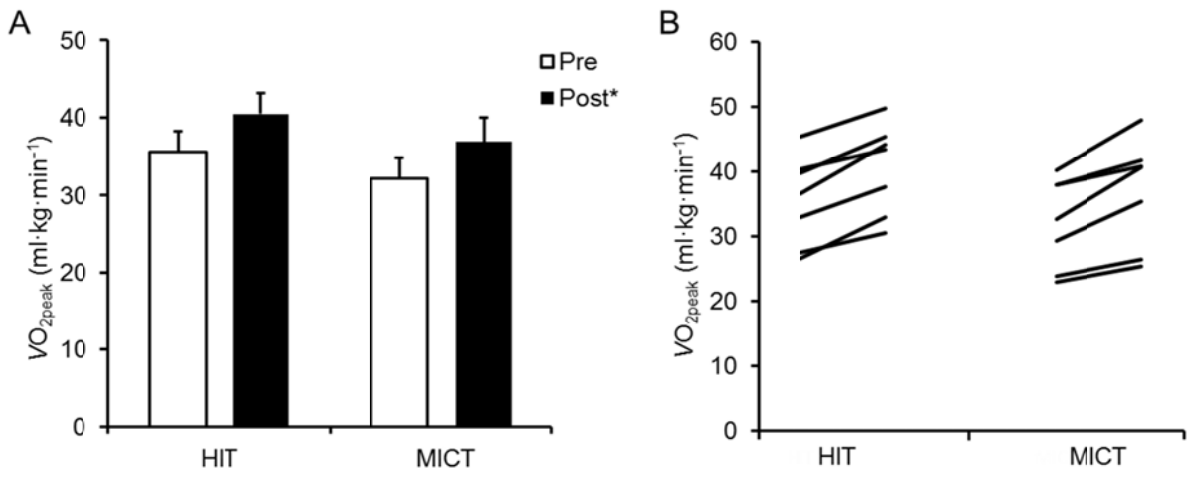

Figure 1 – Effect of six weeks of high intensity interval training HIT and moderate intensity continuous training on $\dot{V}O_{2peak}$.

A shows the mean responses and B shows individual responses in $\dot{V}O_{2peak}$ with training. *Indicates a significant difference from baseline (P<0.05).

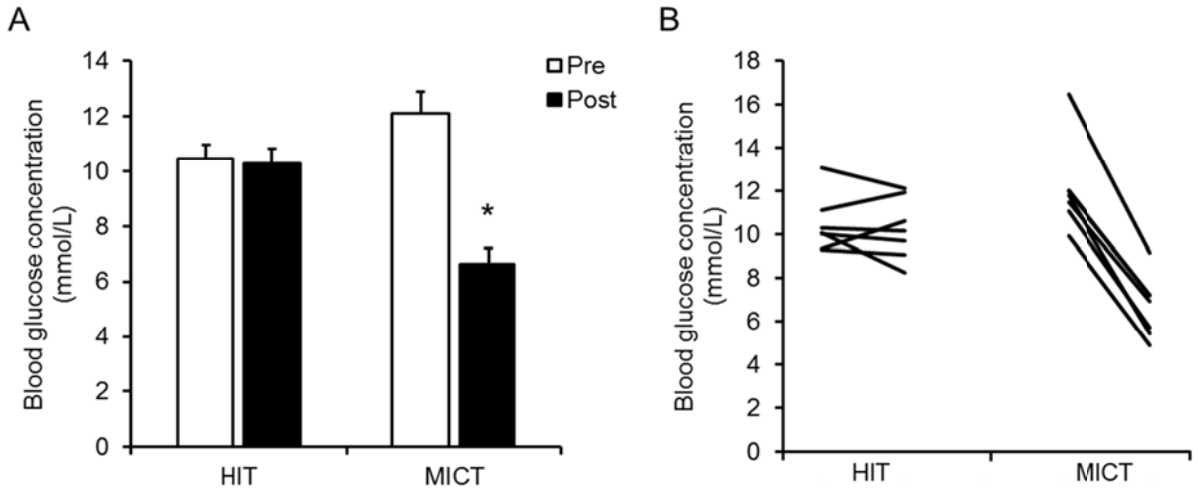

Figure 2 - Change in blood glucose following exercise in the fed state

Finger prick blood glucose concentrations were recorded before and after exercise and whether the exercise session was undertaken in the fasted (>10 hours) or fed state, as well as information about the timing of the last insulin dose. As such, over the course of the six weeks of training we gathered pre and post exercise blood glucose concentrations from a total of 108 MICT training sessions and 87 HIT sessions in the fed state (86% of total possible sessions). A shows mean change in blood glucose concentration and B shows individual changes during HIT and MICT. *denotes a significant change from baseline (P<0.05).

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Table 1 - General characteristics

	HIT		MICT	
	Pre	Post	Pre	Post
Age (years)	29 ± 3	-	29 ± 5	-

Sex	5M/2F	-	5M/2F	-
Duration of T1D (years)	13 ± 3	-	9 ± 2	-
Mass (kg)	90.0 ± 4.8	89.8 ± 4.8	76.7 ± 5.4	76.3 ± 5.3
BMI ($kg \cdot m^{-2}$)	29.2 ± 1.2	29.2 ± 1.2	25.3 ± 1.2	25.2 ± 1.2
$\dot{V}O_{2peak}$ ($ml \cdot kg \cdot min^{-1}$)	35.6 ± 2.6	40.5 ± 2.6*	32.1 ± 2.6	36.9 ± 3.2*
$\dot{V}O_{2peak}$ (L/min^{-1})	3.2 ± 0.3	3.7 ± 0.3*	2.5 ± 0.3	2.9 ± 0.4*
Wmax (W)	245 ± 16	277 ± 19*	202 ± 22	231 ± 24*
SBP (mmHg)	121 ± 3	119 ± 4	123 ± 4	122 ± 4
DBP (mmHg)	65 ± 3	63 ± 3	70 ± 5	68 ± 4
MAP (mmHg)	84 ± 3	82 ± 2	87 ± 4	86 ± 3
aPWV (m/s)	6.1 ± 0.5	5.4 ± 0.7*	6.1 ± 0.4	5.4 ± 0.4*
Cholesterol (mmol/L)	5.07 ± 0.29	5.12 ± 0.35	4.81 ± 0.41	4.93 ± 0.41
Triglycerides (mmol/L)	0.94 ± 0.09	1.03 ± 0.25	0.70 ± 0.04	0.65 ± 0.06

BMI = body mass index; SBP = systolic blood pressure; DBP = diastolic blood pressure; MAP = mean arterial pressure; aPWV = arterial pulse wave velocity. Data are presented as mean ± SEM. * denotes a significant change from pre-training to post-training ($P<0.05$).

Table 2 - Summary of continuous glucose monitor data

	HIT		MICT	
	Pre	Post	Pre	Post
24-hr period				

Mean glucose (mmol/L)	9.3±0.3	9.5±1.0	9.2±0.6	8.6±0.7
CV (%)	42.6±3.6	38.2±2.6	37.9±3.6	36.9±4.0
Time in level 1 hypoglycaemia (%)	6.1±2.6	5.4±3.1	3.4±1.5	2.8±1.9
Time in level 2 hypoglycaemia (%)	0.2±0.2	0.5±0.3	0.9±0.5	0.0±0.0
Time in range (%)	56.7±3.1	56.4±7.8	59.3±5.8	68.2±7.7
Time in hyperglycaemia (%)	37.0±2.0	37.7±8.9	36.3±6.5	28.9±8.5
Incidence of level 1 hypoglycaemia	1.8±0.6	1.2±0.5	0.9±0.5	1.4±0.6
Incidence of level 2 hypoglycaemia	0.2±0.2	0.2±0.2	0.4±0.2	0.1±0.1
Incidence of hyperglycaemia	3.0±0.5	2.8±0.5	3.2±0.5	2.5±0.5
Nocturnal period				
Mean glucose (mmol/L)	8.8±1.3	11.7±2.0	8.0±1.2	7.4±1.1
CV (%)	23.2±5.9	19.5±9.1	29.1±7.2	22.2±6.2
Time in level 1 hypoglycaemia (%)	9.3±9.0	3.0±2.0	7.6±5.0	4.9±4.9
Time in level 2 hypoglycaemia (%)	0.0±0.0	1.2±1.2	3.2±2.0	0.0±0.0
Time in range (%)	57.4±15.5	32.6±14.3*	60.0±15.4	71.3±16.5
Time in hyperglycaemia (%)	33.3±16.7	63.0±16.3*	28.5±15.9	23.6±15.8

Incidence of level 1 hypoglycaemia	0.5±0.2	0.3±0.2	0.3±0.2	0.1±0.1
Incidence of level 2 hypoglycaemia	0.0±0.0	0.2±0.2	0.3±0.2	0.0±0.0
Incidence of hyperglycaemia	0.5±0.2	0.8±0.2	0.5±0.2	0.3±0.2

The 24-hour period was defined as 08:00-08:00h and nocturnal period as 24:00-06:00h. Level 1 hypoglycaemia (≤3.9 mmol/L), level 2 (severe) hypoglycaemia (≤2.9 mmol/L), target range (3.9-10 mmol/L) and hyperglycaemia (≥10 mmol/L). There were no differences in any of the variables with training (P>0.05).