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ORIGINAL ARTICLE

The effect on glycaemic control of low-volume high-intensity interval training versus endurance training in individuals with type 2 diabetes

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Aim: To evaluate whether high-intensity interval training (HIIT) with a lower time commitment can be as effective as endurance training (END) on glycaemic control, physical fitness and body composition in individuals with type 2 diabetes.

Materials and Methods: A total of 29 individuals with type 2 diabetes were allocated to control (CON; no training), END or HIIT groups. Training groups received 3 training sessions per week consisting of either 40 minutes of cycling at 50% of peak workload (END) or 10 1-minute intervals at 95% of peak workload interspersed with 1 minute of active recovery (HIIT). Glycaemic control (HbA1c, oral glucose tolerance test, 3-hour mixed meal tolerance test with double tracer technique and continuous glucose monitoring [CGM]), lipolysis, VO_2peak and body composition were evaluated before and after 11 weeks of intervention.

Results: Exercise training increased VO_2peak more in the HIIT group (20% $\pm$ 20%) compared with the END group (8% $\pm$ 9%) despite lower total energy expenditure and time usage during the training sessions. HIIT decreased whole body and android fat mass compared with the CON group. In addition, visceral fat mass, HbA1c, fasting glucose, postprandial glucose, glycaemic variability and HOMA-IR decreased after HIIT. The reduced postprandial glucose in the HIIT group was driven primarily by a lower rate of exogenous glucose appearance. In the CON group, postprandial lipolysis was augmented over the 11-week control period.

Conclusions: Despite a ~45% lower training volume, HIIT resulted in similar or even better improvements in physical fitness, body composition and glycemic control compared to END. HIIT therefore appears to be an important time-efficient treatment for individuals with type 2 diabetes.

KEYWORDS

exercise intervention, glucose metabolism

1 | INTRODUCTION

The prevalence of type 2 diabetes (T2D) is increasing worldwide.[1] Regular exercise is an effective therapeutic strategy for prevention and treatment of T2D.[2,3] Therefore, exercise training is prescribed as one of the first-line treatments for T2D.[4–6] Traditionally, moderate-intensity training has been recommended for individuals with T2D, but high-intensity training may be more effective for improving glycaemic control.[5,7–9] In energy expenditure-matched studies comparing interval training (walking/running) with endurance training, interval training has been shown to be superior in improving body composition and muscle metabolism in patients with lifestyle diseases,[10] obesity[11] and T2D,[12] as well as superior in improvements in VO_2peak in patients with coronary heart disease.[13] It remains unknown whether high-intensity interval training (HIIT) with a lower training-derived energy expenditure and time commitment can be as effective as moderate-intensity endurance training in improving glycaemic control. Addressing this question is particularly important

given that "lack of time" is one of the most cited barriers to participation in regular physical activity.[14,15]

The aim of the present study was to evaluate the effect of 11 weeks of low-volume HIIT compared to traditional moderate-intensity endurance training (END) on glycaemic control, with HbA1c as the primary outcome, and on physical fitness and body composition as secondary outcomes in individuals with T2D. We hypothesized that, despite the lower training-derived energy expenditure, low-volume HIIT would be as effective as END in improving glycaemic control, physical fitness and body composition.

2 | MATERIALS AND METHODS

2.1 | Participants

After initial screening of 193 individuals with T2D, we enrolled 29 in the study. A standardized medical examination including blood chemistry analysis, a resting 12-lead electrocardiogram and an oral glucose tolerance test (OGTT) were performed before inclusion.

Participants were excluded if they were treated with exogenous insulin; were smokers; had unstable weight (change >5 kg/6 months); had illness that contraindicated physical training; or demonstrated evidence of renal, liver or cardiovascular disease. All participants were under adequate treatment at baseline and none changed medication during the study. The study (ClinicalTrials.gov ID no: NCT02001766) was approved by the Ethics Committee of the Capital Region of Denmark (H-2-2011-070) and signed informed consent was obtained from all participants before enrolment.

An incremental cycling test using a bicycle ergometer (839E; Monark, Varberg, Sweden) was performed to determine VO_2peak (Cosmed Quark b_2, Rome, Italy), peak workload (W_{peak}) and peak heart rate (HR_{peak}). The test consisted of a 5-minute warm-up, followed by 1-minute periods of increasing workload until 2 of the following criteria were met: plateauing of VO_2 with incremental workloads, respiratory exchange ratio >1.1, cycling cadence <60 rpm or volitional exhaustion. The VO_2peak test was repeated after 4 and 8 weeks of training to ensure that the relative workload was maintained throughout the training period.

2.2 | Experimental design

A parallel 3-group, prospective design was applied. After baseline tests, participants were given opaque sealed envelopes randomly allocating them to 3 groups: control (CON) (initially n = 8), END (initially n = 10) and HIIT (initially n = 11). Two participants dropped out of the study for personal reasons unrelated to the experiment (one from the CON group and one from the HIIT group) and one participant from the HIIT group was excluded because of unstable diabetes treatment. Participants in the CON group were offered re-randomization to 1 of the training groups after the intervention period; 6 accepted re-allocation. The final study population after dropout and including reallocation consisted of 26 participants (CON, n = 7; END, n = 12; HIIT, n = 13) (Figure S1).

2.3 | Exercise intervention

Participants in the training groups entered an 11-week bicycle intervention consisting of either 40 minutes/session (END) or 20 minutes/session (HIIT), 3 d/wk. Each training session was initiated with a brief 5-minute standardized warm-up (40% of W_{peak}), after which the END group performed 40 minutes of cycling at 50% of W_{peak} and the HIIT group performed 20 minutes of cycling consisting of periods of 1 minute at 95% W_{peak} and 1 minute of active recovery (20% W_{peak}). Heart rate was measured continuously during each training session (Team^2 system, Polar, Kempele, Finland). Including the warm-up, the total duration of the exercise protocol was 75 minutes per week in the HIIT group and 135 minutes per week in the END group. Training-derived energy expenditure was estimated based on the American College of Sports Medicine's equation.[16]

2.4 | Investigations

Testing took place on 2 days (A and B), separated by one day, before and immediately after the intervention (Figure 1). On testing days, participants refrained from taking anti-diabetic medication and arrived in a fasting state (≥10 hours). They refrained from alcohol and caffeine intake for at least 24 hours prior to the testing days and from exercise for 24 hours or 48 hours before test days A and B, respectively.

On day A, whole body weight and resting blood pressure were measured and body composition was assessed by dual-energy X-ray absorptiometry (Lunar Prodigy Advance; GE Healthcare, Madison, Wisconsin). An 18Ga catheter was placed in an antecubital vein, and baseline blood samples were collected for determination of plasma glucose, lipids, HbA1c, C-peptide and serum insulin. A 2-hour, 75-g OGTT was then performed with blood collection at T = 10, 20, 30, 60, 90 and 120 minutes. Finally, participants underwent the incremental cycling test.

On day B, a catheter was placed in an antecubital vein for tracer infusion (Cambridge Isotope Laboratories, Andover, Massachusetts) and a venous catheter was placed in the bilateral hand (n = 15) or femoral vein (n = 17) for blood sampling. Blood samples were drawn at T = −120 minutes, followed by a primed (17.6 μmol/kg and 2 μmol/kg), continuous (0.6 μmol/kg/min and 0.1 μmol/kg/min) infusion of [6,6-$^2H_2$]glucose and a [1,1,2,3,3-D_5]glycerol tracer was initiated and continued until the end of the study. Participants remained in a supine position for a 2-hour tracer loading period and blood samples were drawn at T = −30 and 0 minutes. At T = 0 minutes, 60 minutes of 1-legged knee-extensor exercise (exercise) (6 W)[17] was completed and blood samples were drawn at T = 30 and 55 minutes. Immediately (<5 minutes) after exercise (T = 60 minutes), a 3-hour mixed meal tolerance test (meal) was initiated by ingestion of a 300-mL solution containing 72 g of glucose, 21.2 g of rapeseed oil and 25.5 g of whey protein spiked with 3 g of [U-$^{13}C_6$]glucose tracer. Blood samples were collected at T = 70, 80, 90, 100, 110 and 120 minutes, and every 30 minutes following, for determination of plasma glucose and tracer enrichment. Plasma insulin and C-peptide were measured by ELISA (Mercodia AB, Uppsala, Sweden).

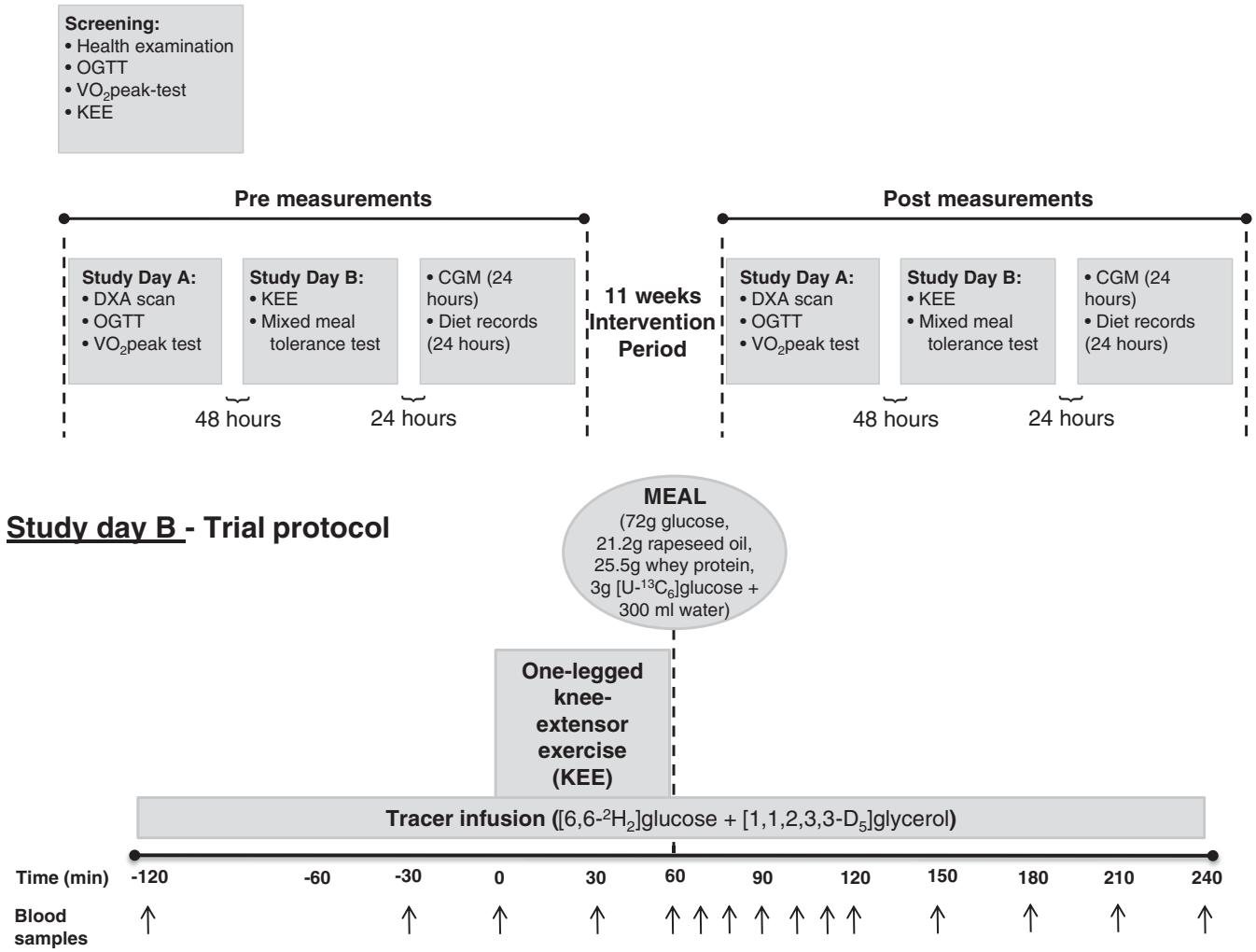

FIGURE 1 Experimental protocol. CGM, continuous glucose monitoring; KEE, one-legged knee-extensor exercise; MEAL, mixed meal tolerance test; OGTT, oral glucose tolerance test

After the experiment, a continuous glucose monitoring (CGM) system (Guardian Real-Time; Medtronic, Santa Rosa, California) was inserted (Sof-Sensor; Medtronic) in the abdominal subcutaneous tissue for 4 days. The CGM system was calibrated 3 times per day using a point-of-care glucose monitor (Contour Link; Bayer, Zürich, Switzerland). Data from 2 full days (days 2 and 3) were used for analyses.[18] Participants were instructed to maintain normal diet habits during the entire experimental period and to record food intake during the collection of CGM data. Post intervention, fasting blood sampling and OGTT were performed 24–120 hours after the last exercise session, a meal test was performed ~48 hours and CGM measurements commenced ~72 hours after the final VO_2peak test.

2.5 | Calculations

Glucose and glycerol tracer analyses were performed using liquid chromatography mass spectrometry by a hexobenzoyl derivatization method.[19] Glucose and glycerol kinetics were determined using non-steady-state assumptions as previously described.[20] Total rate of glucose and glycerol appearance (R_{aTotal}) and disappearance (R_d) were determined from plasma [6,6-$^2H_2$]glucose and [1,1,2,3,3-D_5]glycerol enrichment. Rate of exogenous glucose appearance (R_{aMeal}) was determined from plasma [U-$^{13}C_6$]glucose enrichment. Rate of endogenous glucose appearance (R_{aEND}) was calculated as the difference between total R_a and R_{aMeal}. Postprandial suppression of R_{aEND} was determined as the incremental response during the first 30 minutes, calculated as delta of T = 0 and T = 30 (Δ0-30 minutes). Glucose clearance during exercise (T = 0-55 minutes) and during the meal (T = 60-240 minutes) was calculated as R_d divided by plasma glucose concentration. Basal steady state concentrations and enrichment were determined before exercise as a mean of T = −30 and 0 minutes.

Glucose, insulin, C-peptide and glycerol responses were calculated using the standard trapezoidal method as area under the curve (AUC) change from baseline during OGTT (apart from glycerol) and the meal test.[21]

The initial first phase insulin and C-peptide responses during OGTT and the meal test were determined as the incremental response during the first 10 minutes, calculated as delta of T = 0 and T = 10 (Δ0-10 minutes).[22] Insulin resistance was assessed applying HOMA-IR,[23] the Matsuda index[24] and the hepatic insulin resistance index, multiplying insulin concentrations by endogenous glucose production (R_{aEND}).[25]

2.6 | Statistical analyses

Glucose variability was calculated as the percent coefficient of variation (%CV). A 1- or 2-way repeated measures ANOVA (group × time) was used to detect differences within groups. Likewise, a 1-way (for Δ values) or 2-way ANOVA was used to compare intervention-induced differences between groups. For all ANOVAs, Bonferroni post hoc tests were used to examine the difference between means in the event of a significant finding. Training variables were compared using the unpaired, 2-tailed Student *t*-test. Statistical significance was accepted when *P* was less than .05. All data are presented as mean ± SD. For technical reasons and/or because of catheter displacement all tracer samples could not be obtained either pre- or post-intervention in 7 participants (CON, *n* = 2; END, *n* = 1; HIIT, *n* = 4).

3 | RESULTS

3.1 | Participant characteristics

Participant characteristics and intervention-induced changes in variables of interest are presented in Table 1. Energy intake did not change in any of the groups (Table 2). However, energy intake was lower in the CON group compared to the END group after the intervention (*P* < .05).

3.2 | Exercise

Training compliance did not differ between the END and the HIIT groups (Table 2). Estimated energy expenditure during training sessions was 36% higher in the END group, when compared to the HIIT group (*P* < .05). VO_2peak and W_{peak} increased in both the END and the HIIT groups (*P* < .05) and the increase in VO_2peak was higher (20% ± 20%) in the HIIT group compared to the END group (8% ± 9%: *P* < .05).

3.3 | Body composition

HIIT lowered whole body mass (*P* < .05) (Figure 2A), the overall amount of android fat (*P* < .05) (Figure 2B) and the amount of visceral fat mass (*P* < .05) (Figure 2D). No changes in whole body mass, android fat or visceral fat mass were found in the CON or END groups. However, the END group showed a reduction in gynoid fat mass (*P* < .05) (Figure 2C) and a tendency to reduction in whole body mass (*P* = .08) and visceral fat mass (*P* = .06).

3.4 | Glycaemic control

No changes in any OGTT variables were observed among the 3 groups (Table 1), but fasting glucose, HbA1c levels and glycaemic variability were reduced in the HIIT group (*P* < .05), whereas the END group showed a significant decrease in mean CGM glucose concentration and in time in hyperglycemic range (*P* < .05).

3.5 | Glucose and glycerol kinetics during exercise and meal tests

3.5.1 | Plasma glucose

Basal plasma glucose values did not differ within or between groups after the intervention (Figure S2A). In the HIIT group there was a time × trial interaction (*P* < .05) and post hoc analyses showed that in the HIIT group, plasma glucose during exercise (T = 30-55; *P* < .05) and during the meal test (T = 150-240; *P* < .05) was lower after the training period. Plasma glucose during exercise was also lowered in the CON group at 1 time point only (T = 55; *P* < .05). In addition, maximum plasma glucose values during meals were lower in the HIIT group (*P* < .05), while it was unaltered in both the CON and END groups. Plasma glucose AUC decreased only in the HIIT group (*P* < .05).

No group differences in R_{aTotal}, R_d, R_{aEND} or R_{aMeal} were found. During exercise, R_{aTotal} and R_d were lower in the END group after the intervention (T = 55; both *P* < .05) (Figure S2B,C), whereas R_{aEND} was lower in all groups (CON, T = 55; END, T = 55; HIIT, T = 30, all *P* < .05) (Figure S2D) during exercise. In the HIIT group, AUC R_{aTotal} decreased (*P* < .05) and R_d during the meal was lower after the intervention (T = 180–240; *P* < .05) in the HIIT group, while R_{aTotal} and R_d during the meal were unaltered in both the CON and END groups. R_{aEND} was lower during the meal, at T = 70 to 120 (*P* < .05) in the CON group, at T = 120 (*P* < .05) in the END group and at T = 80 to 90 in the HIIT group (both *P* < .05). In addition, R_{aEND} AUC during the meal decreased in the END group (*P* < .05) after the intervention, and tended to decrease in the CON group (*P* = .052). Postprandial suppression of R_{aEND} tended to be larger in the HIIT group after the intervention (*P* = .06), and the change was greater when compared to the END group (*P* < .05). R_{aMeal} AUC decreased in the HIIT group (*P* < .05) (Figure S2E) after the intervention, while it was unaltered in both the CON and END groups.

3.5.2 | Rate of glucose clearance

In the END and HIIT groups there was a time x trial interaction (*P* < .05) and glucose clearance during exercise was lower in the END group (T = 55) and during the meal in the HIIT group (T = 80) after the intervention, while no difference was found in the CON group.

3.5.3 | Plasma glycerol

Plasma glycerol values did not differ within or between groups after the intervention (Figure S3), but tended to be higher in the CON group at baseline (*P* = .07) and during exercise after the intervention (T = 30; *P* = .06).

No differences among groups in R_{aTotal}, R_d, absolute R_{aEND} or R_{aEND} at baseline or during exercise were found, but AUC R_{aTotal} and AUC R_d were higher in the CON group, as compared to the END group (both *P* < .05) and AUC R_{aTotal} tended to be higher than in the HIIT group (*P* = .051) (Figure S4), while AUC R_d was higher (*P* < .05). Also, AUC absolute R_{aEND} and AUC R_{aEND} were higher in the CON group (*P* < .05), and this change was different as compared to the END and HIIT groups (all *P* < .05). In the END and HIIT groups, $R_{aTotal, Rd}$, absolute R_{aEND} and R_{aEND} during exercise were lower after the intervention (END, T = 30-55; all *P* < .05; HIIT, T = 30; *P* < .05).

TABLE 1 Participant characteristics and changes in VO_2peak, body composition, lipids, blood pressure and glycaemic control

	CON		END		HIIT	
	Pre	Post	Pre	Post	Pre	Post
***n* (male/female)**	7 (5/2)		12 (7/5)		13 (7/6)	
Age (y)	57 ± 7		58 ± 8		54 ± 6	
Time since diagnosis (y)	7 ± 5		6 ± 4		8 ± 4	
Medication						
Metformin	6		10		12	
DPP-4 inhibitor	0		0		3	
Sulfonylureas	1		2		3	
GLP-1 analogues	**1**		0		2	
No medication	0		1		0	
VO_2peak						
Absolute (L/min)*a	2.3 ± 0.5	2.3 ± 0.4	2.3 ± 0.6	2.5 ± 0.7*b	2.4 ± 0.5	2.8 ± 0.5*b,c,e
Relative (mL/kg/min)*a	27.2 ± 9.1	26.3 ± 6.8	27.8 ± 5.5	30.3 ± 7.5*b	28.4 ± 6.1	34.2 ± 6.3*b,c
Peak workload (watt)*a	158 ± 29	155 ± 33	164 ± 46	190 ± 58*b, d	178 ± 44	203 ± 49*b,c
Blood pressure						
Systolic (mm Hg)	139 ± 7	143 ± 9	134 ± 17	133 ± 22	140 ± 14	139 ± 16
Diastolic (mm Hg)	87 ± 7	85 ± 5	82 ± 7	79 ± 9	85 ± 5	84 ± 5
Resting heart rate	73 ± 14	69 ± 8	67 ± 12	61 ± 9*b	69 ± 12	62 ± 9*b
Body composition						
Body mass (kg)*a	87.7 ± 11.3	88.6 ± 11.2	82.1 ± 13.7	81.1 ± 13.8*d	84.2 ± 11.1	83.2 ± 11.2*b, c
BMI (kg/m^2)*a	28.0 ± 3.5	28.3 ± 3.2	27.4 ± 3.1	27.1 ± 3.2	28.1 ± 3.5	27.8 ± 3.5*b
Lean body mass (kg)	54.8 ± 7.2	55.5 ± 8.2	51.7 ± 10.9	51.4 ± 10.8	52.8 ± 9.2	52.6 ± 9.4
Fat mass (kg)	29.6 ± 7.9	30.0 ± 7.9	27.4 ± 6.1	26.5 ± 5.7	28.5 ± 7.3	28.0 ± 7.2
Android fat mass (kg)*a	3.4 ± 1.2	3.6 ± 1.1	2.9 ± 0.9	2.8 ± 0.8*d	3.2 ± 0.9	3.0 ± 0.9*b,c
Gynoid fat mass (kg)	3.8 ± 0.9	3.7 ± 1.0	4.0 ± 1.1	3.8 ± 1.0*b	3.6 ± 1.0	3.7 ± 0.9
Visceral fat (kg)*a	2.0 ± 0.6	2.1 ± 0.6	1.6 ± 0.8	1.4 ± 0.7	1.7 ± 0.8	1.5 ± 0.7*b
Lipids						
Total cholesterol (mmol/L)	4.0 ± 0.7	3.8 ± 0.6	4.7 ± 1.1	4.6 ± 0.9	4.7 ± 1.1	4.5 ± 1.0
HDL cholesterol (mmol/L)	1.1 ± 0.4	1.0 ± 0.3	1.4 ± 0.4	1.3 ± 0.4	1.3 ± 0.4	1.3 ± 0.3
LDL cholesterol (mmol/L)	2.1 ± 0.6	1.9 ± 0.7	2.8 ± 0.9	2.7 ± 0.9	2.7 ± 1.1	2.6 ± 0.9
Triglycerides (mmol/L)	2.2 ± 1.1	2.8 ± 2.1	1.2 ± 0.5	1.6 ± 0.9	2.3 ± 1.6	1.8 ± 0.7
Glycemic control (OGTT)						
HbA1c (%)	7.0 ± 1.15	6.9 ± 1.0	6.9 ± 0.9	6.9 ± 0.8	6.8 ± 0.8	6.7 ± 0.8*b
HbA1c (mmol/mol)	53.2 ± 12.6	51.8 ± 11.3	52.2 ± 10.1	51.4 ± 8.8	51.1 ± 9.1	49.5 ± 8.9*b
Fasting glucose (mmol/L)	8.9 ± 2.4	9.4 ± 2.1	8.0 ± 2.2	8.4 ± 2.6	8.7 ± 1.9	8.0 ± 1.5*b
Fasting insulin (pmol/l)	108 ± 75	105 ± 64	63 ± 25	77 ± 35	120 ± 131	104 ± 102
2-h glucose (mmol/L)	16.1 ± 3.2	15.5 ± 4.0	16.8 ± 6.1	16.5 ± 6.6	15.4 ± 3.2	14.4 ± 4.1
Maximum glucose (mmol/L)	18.1 ± 3.4	18.7 ± 2.5	18.6 ± 5.1	17.6 ± 5.9	17 ± 3.1	16.4 ± 3.6
AUC glucose (mmol/L×min)	1852 ± 337	1855 ± 267	1765 ± 446	1735 ± 543	1731 ± 330	1641 ± 352
iAUC glucose (mmol/L×min)	790 ± 102	729 ± 183	804 ± 324	733 ± 308	683 ± 216	686 ± 275
HOMA-IR	2.18 ± 1.32	2.18 ± 1.16	1.28 ± 0.56	1.58 ± 0.72	2.38 ± 2.24	1.79 ± 1.47*b
CGM						
Mean glucose (mmol/L)	9.3 ± 2.1	8.8 ± 1.7	8.2 ± 1.7	7.6 ± 1.3*b	8.4 ± 2.1	7.8 ± 1.6
Glycemic variability (%CV)	22 ± 7	20 ± 7	24 ± 10	21 ± 9	22 ± 7	17 ± 4*b

(*Continues*)

TABLE 1 (Continued)

	CON		END		HIIT	
	Pre	Post	Pre	Post	Pre	Post
CGM glucose time in range						
<3 mmol/L (% time)	0 ± 0	0 ± 0	1 ± 4	0 ± 0	0 ± 0	0 ± 0
<3 to 3.9 mmol/L (% time)	0 ± 0	0 ± 0	2 ± 3	1 ± 2	0 ± 1	1 ± 3
3.9 to 10 mmol/L (% time)	66 ± 34	77 ± 26	73 ± 23	86 ± 17[*b]	80 ± 27	85 ± 18
>10 mmol/L (% time)	34 ± 34	23 ± 26	24 ± 22	13 ± 17[*b]	20 ± 27	14 ± 20
>13.9 mmol/L (% time)	5 ± 9	4 ± 6	2 ± 5	1 ± 2	7 ± 16	0 ± 0

Abbreviations: AUC, area under the curve; CGM, continuous glucose monitor; iAUC, incremental area under the curve. Statistical differences were analysed by a 1- (Δ values) or 2-way ANOVA (between groups) and a 1-way repeated measures ANOVA within groups. Data are presented as mean ± SD. * indicates $P < 0.05$, [a] time × group interaction, [b]within group pre vs post, [c]Δ CON vs HIIT, [d]Δ CON vs END, [e]Δ END vs HIIT.

3.6 | Insulin and C-peptide

Fasting (OGTT) (Table 1), basal (Meal) (Figure S5) plasma insulin and C-peptide levels and insulin during exercise did not differ within or between groups after the intervention. Within groups, C-peptide was lower during exercise in the END group (T = 30-55; both $P < .05$) and during meals in the HIIT group (T = 210-240, $P < .05$) after the intervention, whereas C-peptide AUC increased in the CON group. In addition, maximum C-peptide values during the meal were lower in the HIIT group and higher in the CON group after the intervention (both $P < .05$). Furthermore, HIIT lowered HOMA-IR ($P < .05$) (Table 1). First phase insulin and C-peptide responses during OGTT and the meal did not differ in any group. In addition, no change in the Matsuda index or in the hepatic insulin resistance index was found.

4 | DISCUSSION

The main finding of the study was that 11 weeks of low-volume high-intensity interval training (HIIT) in individuals with T2D induced

TABLE 2 Energy intake and training data

	CON		END		HIIT	
	Pre	Post	Pre	Post	Pre	Post
Energy intake[*a]						
Energy intake (kcal/d)	2264 ± 915	1974 ± 741	1914 ± 511	2061 ± 694[*b]	1932 ± 681	2020 ± 724
Carbohydrate (%)	55.3 ± 17.0	44.9 ± 12.1	48.0 ± 8.7	49.5 ± 9.7	51.4 ± 7.9	52.8 ± 5.0
Protein (%)	16.5 ± 3.5	17.1 ± 4.0	16.9 ± 2.5	16.9 ± 1.5	19.2 ± 5.4	16.5 ± 3.5
Fat (%)	28.2 ± 14.0	34.8 ± 11.5	35.1 ± 9.5	33.6 ± 9.8	29.4 ± 6.1	29.3 ± 4.2
Training amount						
Training sessions			30.9 ± 2.6		29.4 ± 6.3	
Training duration per session (min)			44.9 ± 1.1		25.2 ± 0.6[*c]	
Training sessions per week			2.8 ± 0.3		2.7 ± 0.6	
Overall compliance (%)			94 ± 9		91 ± 18	
Training heart rate						
Interval			-		149 ± 9	
Recovery period			-		145 ± 10	
Mean			125 ± 10		140 ± 10[*c]	
Peak			137 ± 13		168 ± 7[*c]	
Training intensity (% peak heart rate)						
Interval			-		87.4 ± 3.2	
Recovery period			-		85.0 ± 3.6	
Mean			74.9 ± 3.6		82.0 ± 3.6[*c]	
Energy expenditure during training session						
Per session (kcal)			312 ± 83		200 ± 38[*c]	

Training intensity (% peak heart rate) refers to fraction of average training heart rate as compared with the peak heart rate measured during VO_2peak tests. Data are presented as mean ± SD. * indicates $P < 0.05$, [a]time × group interaction (2-way ANOVA), [b]Δ CON vs END (1-way ANOVA), [c]END vs HIIT (unpaired, 2-tailed Student *t*-test).

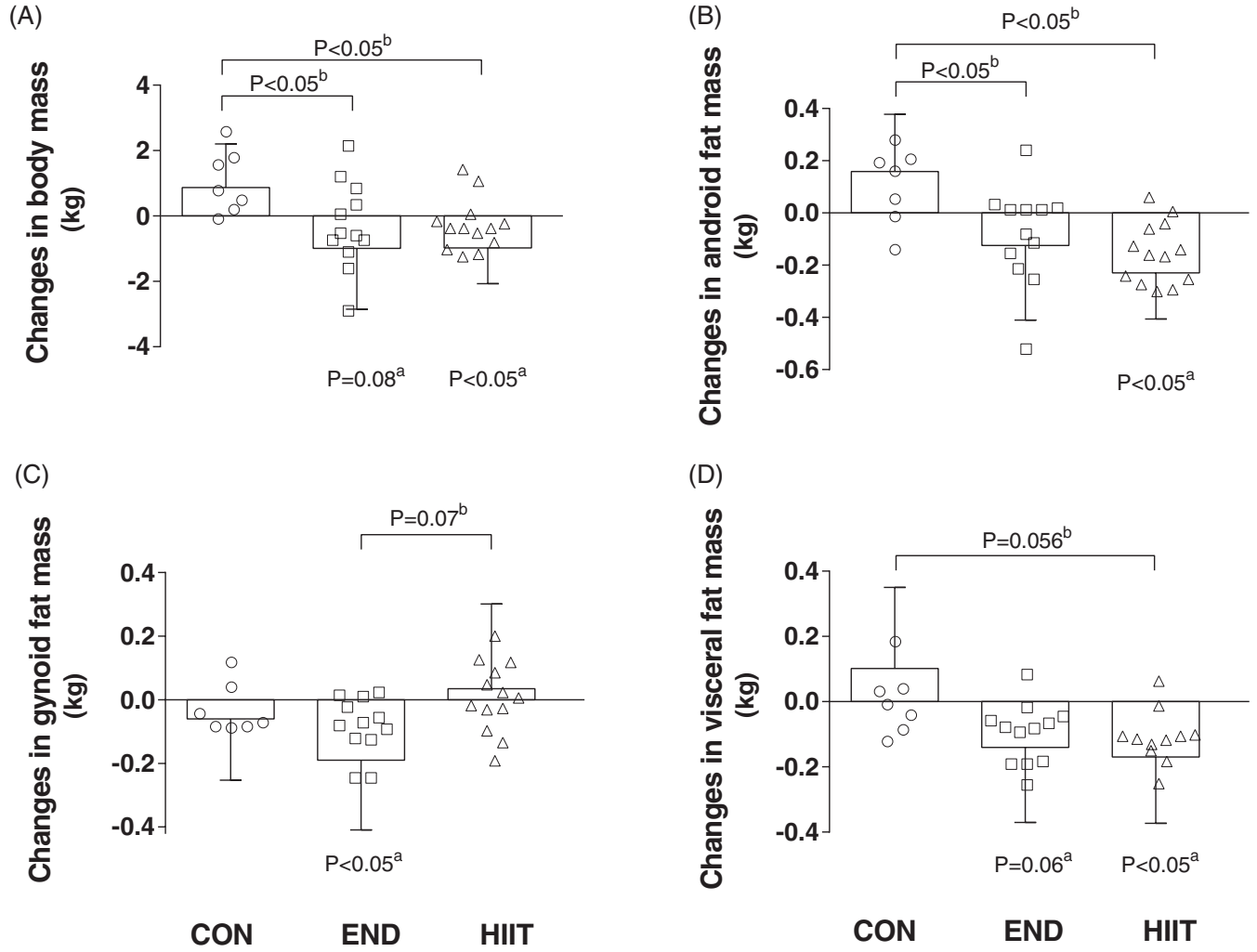

FIGURE 2 Participants with type 2 diabetes were allocated to a CON group (white circles), an END group (white squares) or an HIIT group (white triangles). Body mass (A), android fat mass (dual-energy X-ray absorptiometry) (B), Gynoid fat mass (dual-energy X-ray absorptiometry) (C) and visceral fat mass (dual-energy X-ray absorptiometry) (D) were measured at baseline and after 11 weeks. Data are presented as mean Δ values (post- and pre-intervention values) ± SD as well as individual values. [a]pre- to post-changes within groups (1-way repeated measures ANOVA) [b]differences between groups (1-way ANOVA)

similar or greater improvements in glycaemic control, body composition and physical fitness to moderate-intensity endurance training (END). Postprandial plasma glucose during the mixed meal test was lower in the HIIT group after the training period, despite a decrease in C-peptide concentration.

To investigate whether HIIT can be recommended as a time-efficient alternative to traditional endurance training for patients with T2D, we designed our protocol so that the training volume was ~45% lower in the HIIT group. Despite this difference in training volume, the HIIT and END groups displayed comparable effects on the peak workload and VO_2peak increased more in the HIIT group than in the END group (20% vs 8%). There were no injuries, hypoglycaemic events or drop-out related to HIIT, and overall compliance in the HIIT group (91%) was similar to that in the END group (94%). Collectively, these observations suggest that HIIT is a safe exercise modality, with greater effects on aerobic fitness compared with END.

We observed a reduction in HbA1c and fasting glucose in the HIIT group, indicating that endogenous glucose production was affected in the group performing HIIT. The lower endogenous glucose appearance induced by HIIT was predominantly of hepatic origin. Lower endogenous glucose production after exercise training in T2D patients has been demonstrated previously by Kirwan et al.,[26] who found that 7 days of vigorous exercise training enhanced the suppression of hepatic glucose production as a result of improved hepatic insulin sensitivity. This finding is in agreement with the improvement in HOMA-IR in the HIIT group in the present study. Although we found no change in either the Matsuda index, the hepatic insulin resistance index or in the insulin response to OGTT or the meal test, postprandial C-peptide was lower during the meal after HIIT, indicating that hepatic insulin sensitivity indeed was affected by HIIT. C-peptide is a better indicator of insulin secretion than insulin itself[27] and, in healthy individuals, glucose-stimulated insulin secretion is normally lowered after a training period, as the result of improved insulin sensitivity.[28,29] In contrast to the HIIT group, we observed an increased postprandial C-peptide response in the CON group, indicating that the amount of insulin needed to maintain a normal glucose level was increased, that is, an impaired insulin sensitivity.

The reduced rate of endogenous glucose appearance in the CON group may have occurred, in part, in the face of the observed increase in C-peptide response, which may have attenuated hepatic glucose production. However, paradoxically, this lower hepatic glucose production had no impact on postprandial plasma glucose. Moreover, the postprandial rate of glycerol appearance, a direct index of lipolysis, was increased in the CON group despite the higher C-peptide response. Thus, in the CON group, postprandial adipose tissue insulin sensitivity seemed to be reduced, whereas exercise training prevented this deteriorating effect in both the END and HIIT groups.

The reduced postprandial amount of total glucose appearing in the HIIT group after training was primarily driven by a reduced amount of exogenous glucose entering the circulation. Although our study did not allow us to control for differences in gastric emptying rates, in the glucose concentration gradient between the gut and the circulation or in hepatic glucose uptake, these finding support the idea that hepatic sensitivity was improved in the HIIT group. Moreover, the slow release of ingested glucose to the circulation probably explains the decreased C-peptide response in the HIIT group.

Surprisingly, we found a reduced postprandial glucose clearance after 80 minutes in the HIIT group. Together with the reduced disappearance of plasma glucose, this finding suggests that post-exercise peripheral insulin sensitivity may have been unaffected by HIIT. Alternatively, lower glycogen utilization during exercise may have reduced the postprandial skeletal muscle uptake of glucose during the recovery period.[30]

The meal test and CGM measurements were performed 48 to 72 hours after the last exercise bout. The reduced glycaemic variability in the HIIT group and the mean CGM glucose in the END group, therefore, reflect chronic,[31] rather than acute,[32,33] effects of exercise training. We did not observe a reduced mean CGM glucose level in the group undertaking HIIT, despite a lower plasma glucose level during the meal test after training and reduced glycaemic variability.[8,12] A large inter-individual variation, resulting from variations in disease progression,[34] may explain these divergent findings. Fluctuating plasma glucose levels may be more deleterious than a constant high steady glucose level,[35] and the reduced glycaemic variability in the HIIT group may, therefore, be of greater clinical importance than reducing the mean CGM level per se. When comparing OGTT with the meal test and CGM measurements, we did not observe any changes in maximum glucose level or 2-hour glucose during OGTT in the HIIT group. However, OGTT testing may not accurately reflect the impact of exercise on glycaemic control,[36] and OGTT responses may not reflect day-to-day glycaemic control,[37] given that it, unlike the meal test and CGM, does not represent a meal that participants encounter in real life.

Weight loss induced by exercise training is predominantly thought to be the result of increased energy expenditure during the actual exercise performed.[38] However, we found a significant reduction in whole body mass and the amount of android and visceral fat only in the HIIT group, despite the ~36% higher energy expenditure during training in the END group and a similar energy intake between training groups. This finding could be related to both an increased energy expenditure in the recovery phase of HIIT[39] and higher plasma catecholamine levels during HIIT, driving lipolysis post exercise.[40,41] The fact that the visceral fat mass was lowered in the HIIT group could be of clinical importance, as accumulation of visceral fat has been associated with increased risk of T2D and cardiovascular disease.[42]

In the present study, the END group trained 135 min/wk, which is less than the recommended 150 min/wk of moderate-to-vigorous exercise training, whereas the HIT group performed the minimum recommended time of vigorous intensity exercise (75 min/wk).[14] Exercise training for more than 150 min/wk has been linked to greater improvements in HbA1c (0.89%) compared to training less than 150 min/wk (0.36%),[6] and the overall stimulus may therefore have been suboptimal in the END group. Importantly, the change in HbA1c in the HIIT group was 2.1% despite the short duration of weekly training.

A limitation of the present study is the relatively small number of participants, which may have masked differences between HIIT and END. T2D is heterogeneous and between-group differences in baseline characteristics, albeit not significant, may potentially have prevented the finding of statistical differences during the intervention period. Moreover, it is important to recognize that precise determination of energy expenditure during non-steady state training is difficult.

In summary, we have demonstrated that low-volume HIIT can improve glycaemic control, aerobic fitness and body composition in individuals with T2D. HIIT results in similar or even greater adaptations when compared to moderate-intensity training, despite a lower training volume. Given that lack of time is the most cited barrier to regular exercise, low-volume HIIT appears to be clinically important as a time-efficient strategy to improve glycaemic control in individuals with T2D.

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Conflict of interest

No potential conflicts of interest relevant to this article were reported.

Author contributions

S. P. M., G. vH., B. K. P. and K. M. W. designed the study. G. W. M., U. W. I., S. P. M. and K. M. W. collected the data and performed the experiments. S. P. M., G. vH. and K. M. W. researched and analysed the data, and drafted the manuscript.

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SUPPORTING INFORMATION

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