Sprint Training Increases Muscle Oxidative Metabolism During High-Intensity Exercise in Patients With Type 1 Diabetes

ALISON R. HARMER, PHD[1,2]
DONALD J. CHISHOLM, MD[3]
MICHAEL J. MCKENNA, PHD[4]
SANDRA K. HUNTER, PHD[2]
PATRICIA A. RUELL, PHD[2]
JUSTINE M. NAYLOR, PHD[1]
LYNDAL J. MAXWELL, PHD[1]
JEFF R. FLACK, MD[5]

OBJECTIVE — To investigate sprint-training effects on muscle metabolism during exercise in subjects with (type 1 diabetic group) and without (control group) type 1 diabetes.

RESEARCH DESIGN AND METHODS — Eight subjects with type 1 diabetes and seven control subjects, matched for age, BMI, and maximum oxygen uptake ($\dot{V}O_{2peak}$), undertook 7 weeks of sprint training. Pretraining, subjects cycled to exhaustion at 130% $\dot{V}O_{2peak}$. Posttraining subjects performed an identical test. Vastus lateralis biopsies at rest and immediately after exercise were assayed for metabolites, high-energy phosphates, and enzymes. Arterialized venous blood drawn at rest and after exercise was analyzed for lactate and [H^+]. Respiratory measures were obtained on separate days during identical tests and during submaximal tests before and after training.

RESULTS — Pretraining, maximal resting activities of hexokinase, citrate synthase, and pyruvate dehydrogenase did not differ between groups. Muscle lactate accumulation with exercise was higher in type 1 diabetic than nondiabetic subjects and corresponded to indexes of glycemia (A1C, fasting plasma glucose); however, glycogenolytic and glycolytic rates were similar. Posttraining, at rest, hexokinase activity increased in type 1 diabetic subjects; in both groups, citrate synthase activity increased and pyruvate dehydrogenase activity decreased; during submaximal exercise, fat oxidation was higher; and during intense exercise, peak ventilation and carbon dioxide output, plasma lactate and [H^+], muscle lactate, glycogenolytic and glycolytic rates, and ATP degradation were lower in both groups.

CONCLUSIONS — High-intensity exercise training was well tolerated, reduced metabolic destabilization (of lactate, H^+, glycogenolysis/glycolysis, and ATP) during intense exercise, and enhanced muscle oxidative metabolism in young adults with type 1 diabetes. The latter may have clinically important health benefits.

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Repeated bouts of brief, high-intensity exercise are characterized not only by marked metabolic and ionic destabilization in exercising muscle but also by progressively increasing aerobic ATP generation, such that by just the third 30-s bout, 63% of ATP is generated oxidatively (1). It is therefore not entirely surprising that high-intensity (sprint) exercise training results in oxidative adaptations in muscle. These adaptations include reduced glycogenolysis and lower accumulation of muscle lactate and hydrogen ions during high-intensity matched-work exercise (2); increased activity of oxidative enzymes such as citrate synthase (3–5), cytochrome c oxidase (6), and β-hydroxyacyl-CoA dehydrogenase (β-HAD) (4); reduced ATP degradation during intense exercise (2,5,7); and increased peak oxygen consumption ($\dot{V}O_{2peak}$) (2–5,8).

The only study (9) to examine muscle metabolism during exercise in patients with type 1 diabetes (compared with control subjects) reported lower muscle oxidative capacity and higher glycolytic flux and acidosis. No studies have directly investigated the longitudinal effects of exercise training on muscle metabolism in these patients. Thus, while young adults with type 1 diabetes undertake exercise and sports of various intensities, including high-intensity exercise and training, clinicians have little evidence upon which to provide advice. Based on adaptations in healthy subjects, we hypothesized that high-intensity exercise training in young adults with type 1 diabetes would increase muscle oxidative capacity, attenuate glycogenolytic rate, and reduce myocellular metabolic destabilization during high-intensity exercise.

RESEARCH DESIGN AND METHODS

— Eight subjects (five men and three women) with type 1 diabetes (type 1 diabetic group) ([means ± SD] duration of diabetes 7.1 ± 4.0 years; A1C 8.6 ± 0.8%) and seven subjects (four men and three women) without diabetes (control group) (A1C 5.3 ± 0.3%) were recruited concurrently over 3 years. Control subjects closely matched those with diabetes for age (type 1 diabetic group aged 25 ± 4 years; control group aged 25 ± 4 years), BMI (type 1 diabetic group 25.4 ± 3.2 kg/m^2; control group 23.8 ± 5.0 kg/m^2), and $\dot{V}O_{2peak}$ (type 1 diabetic group 3.30 ± 0.97 l/min; control group 3.17 ± 0.79 l/min), as detailed in a separate report on this study (10). Potential type 1 diabetic subjects were excluded for proteinuria, microalbuminuria, proliferative retinopathy (>10 microaneurysms in the last year), and autonomic or peripheral neuropathies. Control subjects had no family history of metabolic disorders. No subject smoked or took regular

From the [1]Discipline of Physiotherapy, University of Sydney, Lidcombe, New South Wales, Australia; the [2]Discipline of Exercise and Sports Science, University of Sydney, Lidcombe, New South Wales, Australia; the [3]Garvan Institute of Medical Research, Darlinghurst, New South Wales, Australia; the [4]School of Human Movement, Recreation, and Performance, Centre for Aging, Rehabilitation, Exercise, and Sport, Victoria University, Melbourne, Victoria, Australia; and the [5]Diabetes Centre, Bankstown-Lidcombe Hospital, Bankstown, New South Wales, Australia.
Corresponding author: Alison Harmer, a.harmer@usyd.edu.au.
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medication (except insulin). Participants were sedentary (i.e., no regular exercise; type 1 diabetic group, $n = 1$; control group, $n = 2$) or were recreationally active. Each subject provided voluntary written consent. This study was approved by the institutional human research ethics committees.

Testing was conducted after overnight fasting. Subjects in the type 1 diabetic group reduced their evening insulin dose by 1–2 units to prevent hypoglycemia on the morning of the tests and delayed their morning insulin dose until after testing. All subjects replicated their pretraining dietary intake (photocopied record) for the 2 days before posttesting. Subjects abstained from alcohol consumption and vigorous exercise for 2 days before each test. Subjects in the type 1 diabetic group recorded daily insulin dose for 2 weeks before and throughout training. Seven subjects used a combined protocol of short-acting and basal insulin, and one subject used 15/85 neutral/isophane mixed insulin.

Exercise testing

Incremental test. As previously described for these subjects (10), a submaximal, then incremental (10 W/30 s), cycle test to fatigue was conducted before (2 days after a familiarization trial) and after training on an electronically braked ergometer (Ergoline 800s; Mijnhardt, the Netherlands). Steady-state $\dot{V}O_2$, $\dot{V}CO_2$, and respiratory exchange ratio were determined during the final minute of 4-min workrates of 60, 90, 120, and 150 W. Three female subjects (TID group, $n = 2$; control group, $n = 1$) could not complete 150 W before training; thus, an intermediate load of 110 W was substituted for the purpose of generating an individual regression equation of $\dot{V}O_2$ versus power. Peak $\dot{V}O_2$ ($\dot{V}O_{2peak}$) was determined, and the power output required to elicit 130% $\dot{V}O_{2peak}$ was calculated.

Constant load sprint tests. Pretraining, following an identical test on a separate day (used to collect respiratory data), a sprint test to exhaustion was conducted on the cycle ergometer. After a 3-min warm-up at 20 W, subjects pedaled at a power output equivalent to 130% $\dot{V}O_{2peak}$ until exhaustion. Muscle and blood were sampled. Posttraining, a test was conducted at the same power output and for the same duration (i.e., identical work, with blood and muscle sampling times matched to pretraining). On a separate day, respiratory data were collected (time matched with the pretraining respiratory test). Expired volume was determined using a pneumotachometer (Hans Rudolph), and expired gas fractions were determined by O_2 and CO_2 analyzers (Ametek; Thermox Instruments, Pittsburgh, PA), which were calibrated immediately before and after each test.

Muscle sampling and analyses

Percutaneous muscle biopsies with suction were performed at rest and immediately after exercise (on the cycle ergometer). Muscle samples (type 1 diabetic group, $n = 7$; control group, $n = 6$) were immediately immersed in liquid nitrogen then divided and stored at −80°C. For enzymes, frozen wet muscle (~30 mg) was homogenized in a medium comprising 50 mmol/l Tris-HCl, 20 mmol/l EGTA, 25 mmol/l NaF, and 1 mmol/l benzamidine, pH 7.4. Activities of hexokinase (11), the activated form of pyruvate dehydrogenase (PDHa), and citrate synthase (12) were determined spectrophotometrically (Cary3; Varian, Mulgrave, Victoria, Australia) at 30°C in the assay media for each enzyme and expressed relative to the respective pre- or posttraining peak total creatine (TCr) content as millimoles per minute per kilogram of dry mass. For metabolites, muscle was weighed, freeze dried, reweighed, dissected free of connective tissue and blood, powdered, and extracted. Extracts were analyzed for ATP, PCr, creatine, glucose, glycogen, glycolytic intermediates, and lactate on a luminescence spectrometer (Aminco Bowman Series 2; SLM Instruments, Urbana, IL) as previously described (2). Metabolites (except glycogen, glucose, pyruvate, and lactate) in pre- and posttraining samples were expressed relative to the peak TCr obtained before and after training, respectively, as millimoles per kilogram of dry mass. The rate of glycogenolysis in muscle was calculated as $[(\Delta G1\text{-}P + \Delta G6\text{-}P + \Delta F6\text{-}P) + 0.5\,(\Delta Lac + \Delta Pyr)]$/time in s; and the rate of glycolysis as $0.5\,(\Delta Lac + \Delta Pyr)$/time in seconds and expressed as millimoles per kilogram of dry mass per second, where G1-P is glucose 1-phosphate, G6-P is glucose 6-phosphate, F6-P is fructose 6-phosphate, Lac is lactate, and Pyr is pyruvate.

Blood sampling and analyses

Arterialized blood was sampled from a dorsal hand vein at rest in the final seconds of exercise and during an hour of recovery. As previously described for this study, A1C (13), catecholamines, blood gases, hemoglobin, hematocrit, plasma sodium, potassium, and glucose, glucagon, and insulin levels were determined (10). pH was determined in duplicate immediately by blood gas analysis (Corning 865; Chiron Diagnostics) and plasma $[H^+]$ calculated. The remaining blood was centrifuged, and 250 μl of plasma was mixed with 500 μl 0.6 mol/l perchloric acid, centrifuged, the supernatant removed, and stored at −20°C until analysis. Plasma lactate concentration was determined in triplicate as previously described (2).

Exercise training

Subjects undertook 7 weeks of supervised, progressive high-intensity cycling training, thrice weekly, as previously described (2,8,10,13). Each training session comprised 4–10 30-s "all out" sprints on an ergometer (Monark 668; Varberg, Sweden), with each sprint separated by a 3- to 4-min passive rest. The number of sprint bouts per session was increased from four in week 1 to six in week 2, eight in week 3, and 10 in weeks 4–7; the rest interval was reduced from 4 to 3 min in weeks 5–7 of training.

Statistics

Data were analyzed using *t* tests for baseline variables and insulin dosage data and repeated-measures ANOVA for muscle, blood, and respiratory measures (within-subject factors: training status ± sample time; between-subject factor: group; SPSS 10.0 for Windows). The Wilks' λ multivariate adjustment was used for blood data. Significant *F* ratios for blood data were further examined using a post hoc contrast technique. Data are expressed as means ± SE.

RESULTS

Performance

Power output in the constant-load tests did not differ between groups (type 1 diabetic group, 340 ± 41 W; control group, 350 ± 39 W; $P = 0.86$). Pretraining, in both groups, time to fatigue did not differ between the respiratory (65 ± 4 s) and blood and muscle (70 ± 5 s; $P = 0.14$) tests.

Daily insulin dosage

The daily insulin dose in the type 1 diabetic group (52.4 ± 3.8 units/day) was not altered by training (51.2 ± 4.6 units/day; $P = 0.66$).

Table 1—*Respiratory data during the pre- and posttraining respiratory tests conducted at 130% pretraining $\dot{V}O_{2peak}$*

Variable	Pretraining	Posttraining
$\dot{V}E_{peak}$ (l/min)*		
Type 1 diabetic group	96.1 ± 10.3	79.5 ± 7.0
Control group	104.6 ± 10.4	94.3 ± 8.1
$\dot{V}O_{2peak}$ (l/min)*		
Type 1 diabetic group	3.44 ± 0.33	3.14 ± 0.27
Control group	3.12 ± 0.28	3.03 ± 0.35
Mean $\dot{V}O_2$ (l/min)		
Type 1 diabetic group	2.49 ± 0.21	2.33 ± 0.18
Control group	2.32 ± 0.23	2.35 ± 0.23
$\dot{V}CO_{2peak}$ (l/min)†		
Type 1 diabetic group	3.52 ± 0.42	3.01 ± 0.30
Control group	3.47 ± 0.42	3.20 ± 0.38
$\dot{V}E/\dot{V}CO_2$		
Type 1 diabetic group	28.0 ± 1.1	26.9 ± 1.3
Control group	30.7 ± 1.6	30.4 ± 1.8

Data are means ± SE. Type 1 diabetic group, $n = 8$; control group, $n = 7$. $\dot{V}E_{peak}$, peak expired ventilation, BTPS; $\dot{V}O_{2peak}$, peak oxygen uptake, STPD; $\dot{V}CO_{2peak}$, peak carbon dioxide output, STPD; $VE/\dot{V}CO_2$, peak ventilatory equivalent for carbon dioxide. *$P < 0.05$; †$P < 0.01$ pretraining vs. posttraining.

Submaximal fuel oxidation

During submaximal exercise posttraining, the respiratory exchange ratio was lower ($P < 0.05$), with no group differences ($P = 0.95$) (60 W: pretraining, type 1 diabetic group 0.88 ± 0.02 and control group 0.90 ± 0.03; posttraining, type 1 diabetic group 0.86 ± 0.02 and control group 0.86 ± 0.03; 90 W: pretraining, type 1 diabetic group 0.97 ± 0.02 and control group 0.94 ± 0.03; posttraining, type 1 diabetic group 0.92 ± 0.02 and control group 0.91 ± 0.02; and 120 W: pretraining, type 1 diabetic group 1.01 ± 0.04 and control group 0.98 ± 0.03; posttraining, type 1 diabetic group 0.98 ± 0.03 and control group 0.94 ± 0.03).

Ventilation and plasma acidosis

Peak $\dot{V}O_2$ did not differ between the constant-load (3.29 ± 0.21 l/min) and incremental tests (3.24 ± 0.22 l/min; $P = 0.56$). Pretraining in the constant-load test, the groups did not differ on any respiratory variable (Table 1). Posttraining, during identical exercise, estimated to elicit 125 ± 0.03% of pretraining $\dot{V}O_{2peak}$ ($P = 0.06$), peak expired ventilation and carbon dioxide output were reduced, with no group differences. Plasma lactate and $[H^+]$ were less elevated posttraining, with no group differences (Fig. 1*A* and *B*).

Muscle metabolism

Peak TCr did not differ with training (117.6 ± 3.5 vs. 119.5 ± 3.4 mmol/kg dm, pre- vs. posttraining, respectively; $P = 0.35$) or between groups ($P = 0.63$). Muscle free glucose content rose with exercise (Table 2), was unaffected by training, and was higher in the type 1 diabetic group. Glycogen content was reduced 37 ± 3% by exercise pretraining (Table 2), with no group differences. Posttraining, glycogen degradation tended to be less ($P = 0.07$). Glycolytic intermediate (glucose 1-phosphate, glucose 6-phosphate, and fructose 6-phosphate) content increased with exercise (Table 2), with no difference after training or between groups. Muscle pyruvate content increased approximately sixfold with intense exercise and was nearly halved after training (Table 2), with a tendency for a greater effect in the type 1 diabetic group ($P = 0.06$). Muscle lactate during exercise was higher in the type 1 diabetic group pretraining (Table 2), and lactate accumulation was strongly correlated with indexes of glycemia (A1C and fasting plasma glucose; both $r^2 = 0.45$, $P = 0.01$). Posttraining, lactate during exercise was reduced, more so in the type 1 diabetic group, and there was no relationship between lactate accumulation and A1C ($r^2 = 0.02$, $P = 0.96$) or fasting plasma glucose ($r^2 = 0.16$, $P = 0.60$). Estimated rates of glycogenolysis and glycolysis during exercise pretraining did not differ between groups and were ~20% lower posttraining (Fig. 1*C*). Muscle ATP content was reduced with exercise before training ($P < 0.001$; type 1 diabetic group, rest 22.8 ± 1.0 mmol/kg dm, exercise 16.1 ± 0.6 mmol/kg dm; control group, rest 22.9 ± 0.8 mmol/kg dm, exercise 17.5 ± 0.5 mmol/kg dm). Posttraining, ATP degradation during exercise was attenuated ($P < 0.01$; type 1 diabetic group, rest 21.3 ± 0.5 mmol/kg dm, exercise 19.5 ± 1.0 mmol/kg dm; control group, rest 20.6 ± 0.7 mmol/kg dm, exercise 17.5 ± 1.0 mmol/kg dm) more so in the type 1 diabetic group ($P < 0.05$).

Muscle enzyme activity

Pretraining, resting activities of hexokinase, PDHa (Table 2), and citrate synthase (Fig. 1*D*) did not differ between groups nor did the hexokinase–to–citrate synthase ratio. Posttraining, hexokinase activity increased in the type 1 diabetic group only, whereas citrate synthase activity increased in both groups. Consequently, the hexokinase–to–citrate synthase ratio was increased in the type 1 diabetic group and reduced in the control group ($P < 0.01$; data not shown). For both hexokinase and citrate synthase, enzyme activity was reduced with exercise in the control group but unchanged in the type 1 diabetic group. Posttraining, PDHa activity at rest was reduced; however, there was no difference in PDHa immediately after exercise, and there were no group differences.

CONCLUSIONS — The key findings in this study were that high-intensity exercise training increased activity of citrate synthase and reduced activity of PDHa at rest; increased fat oxidation during submaximal exercise; and during intense exercise, reduced ventilation and carbon dioxide output, lowered plasma and muscle lactate accumulation, and lowered the glycogenolytic and glycolytic rates, and attenuated ATP degradation in young adults with type 1 diabetes. Together, these findings demonstrate that high-intensity training increased muscle oxidative capacity and reduced myocellular metabolic destabilization and glycolytic rate during intense exercise in type 1 diabetes.

Before training, muscle lactate accumulation was higher in the type 1 diabetes than the control group and was positively correlated with indexes of glycemia. The data may suggest lower muscle lactate transport and/or PDHa activity in the type 1 diabetic group. However, PDHa did not differ between groups. The only previous study to examine muscle PDHa in pa-

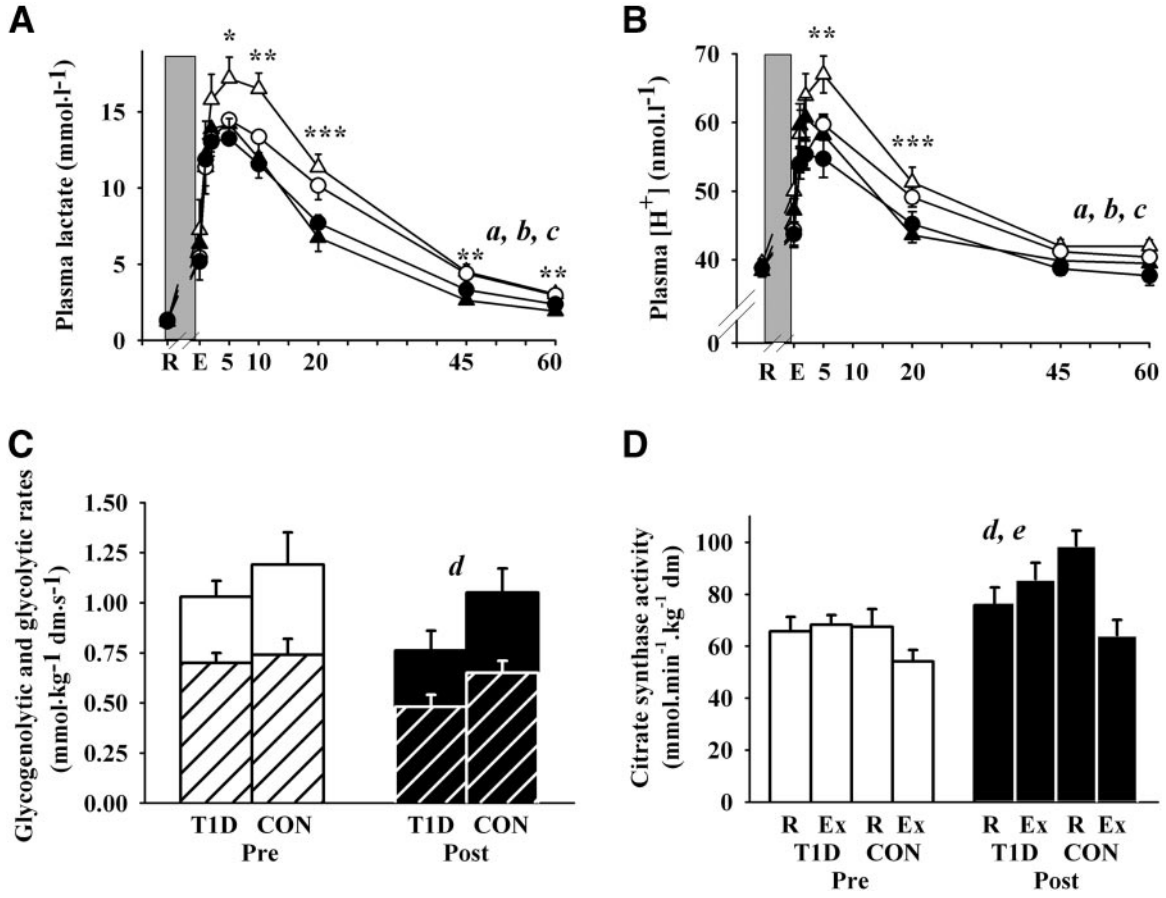

Figure 1— *All data are means ± SE.* A *and* B*: Plasma lactate and hydrogen ion concentrations at rest, in the final seconds of exercise (▨), and during 1 h of recovery in the group with type 1 diabetes (triangles) and the nondiabetic control group (circles), before (white symbols) and after (black symbols) training.* A*: Plasma lactate concentration:* a*, main effects of time,* $P < 0.001$*;* b*, training status,* $P < 0.05$*;* c*, training status-by-time interaction,* $P < 0.05$*, pre- > posttraining.* *$P < 0.05$*;* **$P < 0.01$*;* ***$P < 0.001$*. There were no significant interaction effects for group: training status-by-group,* $P = 0.27$*; time-by-group,* $P = 0.50$*; or training status-by-time-by-group,* $P = 0.75$*.* B*: Hydrogen ion concentration:* a*, main effects of time,* $P = 0.001$*;* b*, training status,* $P = 0.001$*;* c*, training status-by-time interaction,* $P < 0.05$*, pre- > posttraining.* **$P < 0.01$*;* ***$P < 0.001$*. There were no significant interaction effects for training status-by-group,* $P = 0.28$*; time-by-group,* $P = 0.44$*; or training status-by-time-by-group,* $P = 0.32$*. △, type 1 diabetes pretraining; ▲, type 1 diabetes posttraining; ○, control pretraining; ●, control posttraining.* C*: Estimated rates of glycogenolysis (total histogram) and glycolysis (hatched bar): both,* d*, main effect of training status,* $P < 0.01$*, pre- > posttraining.* D*: Citrate synthase activity (maximal in vitro). R, rest; Ex, end-exercise.* d*, main effect of training status,* $P < 0.01$*, post- > pretraining;* e*, time-by-group interaction,* $P < 0.05$*, type 1 diabetes unchanged, control reduced with exercise. T1D, type 1 diabetic group; CON, control group.*

tients with type 1 diabetes also reported no difference at rest compared with control subjects (14). Thus, although speculative, it is possible that our type 1 diabetic group had lower muscle lactate transport during intense exercise than the control group. While no study has examined muscle lactate transport in type 1 diabetes, the muscle lactate transporter content was reduced, and muscle lactate higher, in patients with type 2 diabetic compared with control subjects (15). The strong association between muscle lactate accumulation and glycemic indexes before training in the present study may reflect a degree of lactate-induced insulin resistance (16), or it is possible that mild insulin deficiency or hyperglycemia may affect lactate transport; however, this remains to be tested.

The similar glycolytic rate during exercise in both groups in the present study is consistent with findings in rats with and without streptozotocin-induced diabetes during intense isometric contraction (17). However, our data contrast with the higher glycolytic rate (and lower oxidative capacity) demonstrated with ^{31}P–magnetic resonance spectroscopy in the only other study to investigate muscle metabolism during exercise in patients with type 1 diabetes versus control subjects (9). The divergent findings in the two studies may be due to differing nutritional and insulin status and/or to within-study differences in aerobic fitness. In contrast to the present study, Crowther et al.'s (9) subjects had eaten and administered insulin before exercise and were not matched for $\dot{V}CO_{2peak}$ with control subjects. Further, the divergence may be partly explained by the differing nature of muscle contraction utilized (high-frequency dynamic versus isometric exercise, in which blood flow is effectively occluded).

After training, hexokinase activity increased, and while citrate synthase activity also increased, the hexokinase–to–citrate synthase ratio was increased in the type 1 diabetic group. Theoretically, this could favor glycolysis over oxidation during exercise after training; however, this was not evident and there was actually a 20% reduction in the glycolytic rate (in both groups), consistent with more ATP being generated oxidatively. An increased hexokinase–to–citrate synthase ratio is suggested to be an expression of insulin resistance in type 2 diabetes (18). In type

Table 2—*Muscle metabolites and enzyme activity*

	Type 1 diabetic group		Control group	
	Rest	Exercise	Rest	Exercise
Glycogen (glucosyl units)*				
Pretraining	491 ± 50	306 ± 37	526 ± 53	347 ± 60
Posttraining	499 ± 61	366 ± 63	537 ± 49	399 ± 39
Glucose 1-phosphate*				
Pretraining	0.1 ± 0.0	0.8 ± 0.2	0.1 ± 0.0	0.9 ± 0.2
Posttraining	0.1 ± 0.0	0.8 ± 0.2	0.1 ± 0.0	0.6 ± 0.1
Glucose*†				
Pretraining	3.8 ± 0.7	4.9 ± 0.6	1.8 ± 0.4	3.5 ± 0.6
Posttraining	2.9 ± 0.3	6.2 ± 1.1	1.3 ± 0.1	3.2 ± 0.3
Glucose 6-phosphate*				
Pretraining	1.5 ± 0.3	23.3 ± 1.8	1.4 ± 0.22	22.2 ± 2.7
Posttraining	1.5 ± 0.2	20.1 ± 2.2	1.2 ± 0.2	19.4 ± 1.8
Fructose 6-phosphate*				
Pretraining	0.2 ± 0.0	3.5 ± 0.2	0.2 ± 0.0	3.2 ± 0.4
Posttraining	0.2 ± 0.0	3.1 ± 0.3	0.2 ± 0.0	3.2 ± 0.4
Pyruvate*‡§				
Pretraining	0.2 ± 0.0	0.9 ± 0.2	0.1 ± 0.0	0.6 ± 0.0
Posttraining	0.1 ± 0.0	0.4 ± 0.1	0.2 ± 0.0	0.6 ± 0.1
Lactate*¶#**				
Pretraining	3.4 ± 0.3	114.8 ± 4.3	4.2 ± 0.7	88.6 ± 7.0
Posttraining	4.0 ± 0.6	80.0 ± 7.2	3.9 ± 0.5	78.3 ± 4.7
Hexokinase††‡‡				
Pretraining	8.9 ± 0.5	8.5 ± 0.4	9.0 ± 0.6	6.6 ± 0.6
Posttraining	12.9 ± 0.7	12.3 ± 0.4	9.5 ± 0.6	7.3 ± 0.6
Pyruvate dehydrogenase a*§§				
Pretraining	0.8 ± 0.1	1.9 ± 0.3	1.0 ± 0.2	2.1 ± 0.3
Posttraining	0.6 ± 0.1	1.7 ± 0.2	0.5 ± 0.1	1.7 ± 0.2

Data are means ± SE. Type 1 diabetic group, $n = 7$; Control group, $n = 6$. Units for muscle metabolites, mmol/kg dm; units for enzyme activity, mmol · min^{-1} · kg dm^{-1}. *$P < 0.001$, main effect of time, exercise > rest (except for glycogen, which is rest > exercise); †$P < 0.01$, Type 1 diabetic > Control group; ‡$P < 0.05$, main effect of training status; §$P < 0.05$, training status-by-time interaction; ‖$P < 0.01$, main effect of training status; ¶$P = 0.001$, training status-by-time interaction; #$P < 0.05$, time-by-group interaction; **$P < 0.05$, training status-by-time-by-group interaction; ††$P < 0.001$, time-by-group interaction: T1D group unchanged, CON group reduced with exercise; ‡‡$P < 0.01$, training status-by-group interaction: Type 1 diabetic > Control; §§$P < 0.05$, training status at rest, pre- > posttraining.

1 diabetes, insulin resistance is also common and insulin action is inversely related to A1C (19). A1C was unchanged after training in the present study (pretraining 8.6%, posttraining 8.1%, $P = 0.09$) (13); however, we did not measure insulin sensitivity. Future studies investigating effects of high-intensity training on insulin sensitivity would be of interest.

During submaximal exercise after training, muscle fat oxidation was greater and carbohydrate oxidation less (as estimated by the respiratory exchange ratio). This typical "glycogen-sparing" effect of endurance training has recently been demonstrated after sprint training (4), and our study extends this finding to include those with diabetes. Interestingly, higher basal and insulin-stimulated fat oxidation in patients with type 1 diabetes compared with control subjects is associated with insulin resistance and manifests metabolic inflexibility (20). However, discussing a similar paradox, Kelley and Mandarino (21) suggest that muscle lipid handling should be interpreted relative to oxidative enzyme capacity. The type 1 diabetes and control groups adapted similarly to training, i.e., higher fat oxidation during submaximal exercise and also higher oxidative enzyme capacity. Additionally, there was no difference in glycogenolysis during intense exercise between the groups, which suggests that the type 1 diabetic group was as "metabolically flexible" (i.e., able to switch to greater carbohydrate oxidation) (21) as the control group.

During intense exercise after training, reduced metabolic destabilization was evident (i.e., less increase in ventilation, $\dot{V}O_2$, plasma lactate and $[H^+]$, muscle pyruvate and lactate, and less ATP degradation; the glycogenolytic and glycolytic rates were lower; and citrate synthase activity increased in both groups). These adaptations reflect an increase in leg muscle oxidative metabolism after training. This is supported by the increased $\dot{V}O_{2peak}$ during incremental exercise after training in these subjects (10). The results from the present study are consistent with our previous findings with sprint training in healthy men (2).

In the present study, PDHa was reduced at rest after exercise training. PDHa regulates pyruvate entry into the mitochondrion, thus being a key determinant of the amount of lactate accumulation and oxidative pyruvate metabolism. In rodents, PDHa is inhibited by pyruvate dehydrogenase kinase, which is increased by greater fat oxidation (22). Endurance-trained rats had lower muscle PDHa compared with sedentary controls, likely due to their higher activities of β-hydroxyacyl-CoA dehydrogenase (a β-oxidation enzyme) and pyruvate dehydrogenase kinase (23). This explanation for lower resting PDHa is plausible in the present study, as it has been shown that sprint training increases β-hydroxyacyl-CoA dehydrogenase (4). Since significant fat oxidation may occur during brief intense exercise (24), it is possible that a higher proportion of ATP was derived oxidatively from intramuscular fat after training. Also, although PDHa during exercise did not differ after training, the lower rate of glycogenolysis would likely permit a higher proportion of pyruvate to be oxidized, as we previously speculated (2), which is consistent with lower lactate accumulation and attenuated ATP degradation after training.

In summary, the major difference before training was higher muscle lactate accumulation during intense exercise in the type 1 diabetic group. Since glycolytic rates and PDHa activity were similar between the groups, this may have been due to lower muscle lactate transport. The key metabolic adaptations to high-intensity exercise training in both groups show that the glycolytic rate and metabolic destabilization were reduced and citrate synthase activity increased. These adaptations strongly suggest that muscle oxidative metabolism was increased during intense exercise after high-intensity training in young adults with type 1 diabetes. Importantly, high-intensity training was

well-tolerated and did not have any evident adverse effects in our patients, even though they were in moderate to poor metabolic control. Increased skeletal muscle oxidative capacity is a desirable health outcome, particularly for those with diabetes. The oxidative adaptations to high-intensity exercise training may confer clinically important health benefits in young patients with type 1 diabetes; however, this remains to be established.

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