Fuel oxidation during exercise in middle-aged men: role of training and glucose disposal

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ABSTRACT

MANETTA, J., J. F. BRUN, A. PEREZ-MARTIN, A. CALLIS, C. PREFAUT, and J MERCIER. Fuel oxidation during exercise in middle-aged men: role of training and glucose disposal. *Med. Sci. Sports Exerc*., Vol. 33, No. 3, pp. 423–429, 2002. **Purpose:** The purpose of this study was to test the hypothesis that carbohydrate (CHO) utilization in middle-aged trained men is increased during hard-intensity exercise and decreased during moderate-intensity exercise in comparison with age-matched sedentary men. We also investigated whether a relationship between CHO utilization and glucose disposal exists. **Methods:** Seven trained cyclists (Tr) and seven age-matched sedentary men (Sed) underwent an intravenous glucose tolerance test after an overnight fast (minimal model method) to determine their glucose disposal; they also performed two 1-h trials on a cycle ergometer below and above their individual ventilatory threshold (VT). Substrate oxidation was evaluated by indirect calorimetry. Hormonal responses were investigated during exercise. **Results:** Insulin sensitivity (SI) and glucose effectiveness (Sg) were significantly higher in the Tr group than in the Sed group ($P < 0.001$, $P < 0.03$). CHO oxidation was significantly higher in the Tr group than in the Sed group when exercise was performed above VT, whereas CHO oxidation was higher in the Sed group when exercise was performed below VT ($P < 0.05$). Epinephrine (Epi) response during hard-intensity exercise was higher in the Tr group than in the Sed group ($P < 0.01$). SI was negatively correlated to CHO oxidation in the Tr group ($r = -0.743$, $P < 0.05$). **Conclusion:** Endurance training results in increased CHO utilization during hard-intensity exercise and reduced CHO oxidation during moderate-intensity exercise in middle-aged men. During hard-intensity exercise, the increased CHO utilization in middle-aged trained men is associated with a greater response in Epi and is inversely related with SI. **Key Words:** INDIRECT CALORIMETRY, AGING, MINIMAL MODEL, ENERGY BALANCE, SUBSTRATE, EPINEPHRINE

The two main sources of energy for muscular metabolism are carbohydrate (CHO) and fat. Whereas fat is the predominant fuel at moderate intensity, CHO becomes the main energy source at hard intensity (4,29). Therefore, a point of "crossover" between lipids and CHO has been described (4). This point corresponds to the power at which CHO becomes the predominant fuel (4). Endurance training results in a higher capacity to oxidize lipids during mild to moderate exercise (5). Thus, after training, this "crossover point" is shifted toward a higher intensity because of muscular biochemical and endocrine adaptations. In addition, it is noteworthy that in humans exercise training also increases the ability to utilize CHO (22), an important effect that explains the beneficial consequences of regular exercise in type 2 diabetic patients (11). Training thus appears to increase the ability to oxidize both lipids and CHO. Among the factors involved in this process, catecholamines, particularly epinephrine, have been shown to play a key role (4). Since high epinephrine concentrations during exercise increase CHO oxidation (13), epinephrine may explain in part the increase in CHO oxidation that occurs above the transitional zone where the crossover point is located.

CHO disposal is disturbed in aged subjects, as evidenced by lower insulin sensitivity (SI) and an increased frequency of glucose intolerance (11). This process is particularly relevant to the middle-aged population, since the insulin resistance of aging that is initiated as early as the third decade of life may be prevented with exercise training (11). Furthermore, decrements in GLUT-4 protein concentration, which is involved in insulin resistance (16), may also be corrected by exercise training (15).

Although the combined effects of training and exercise intensity on substrate oxidation have been investigated in young subjects (9,18), the fuel oxidation balance at hard-intensity versus moderate-intensity exercise in middle-aged

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TABLE 1. Characteristics and ergometric parameters of sedentary and endurance-trained subjects.

	Sedentary ($N = 7$)	Trained ($N = 7$)
Age, yr	52.33 ± 1.6	52.25 ± 1.7
Height, cm	173.33 ± 1.9	173 ± 1.5
Weight, kg	75.41 ± 2.4	73.24 ± 2.2
BMI, $kg \cdot m^{-2}$	25.08 ± 0.6	24.47 ± 0.5
Body fat, %	22.08 ± 1.5	21.09 ± 0.9
$\dot{V}O_{2max}$, $mL \cdot min^{-1} \cdot kg^{-1}$	33.37 ± 1.1	50.41 ± 2.3*
W_{max}, W	204 ± 9.3	305.63 ± 17.7*
$VT/\dot{V}O_{2max}$, %	54.66 ± 2.1	54.81 ± 2.4
W/VT, W	98.7 ± 8.1	152.8 ± 7.9*

Values are means ± SE.
BMI, body mass index; $\dot{V}O_{2max}$, maximal O_2 uptake; W_{max}, maximum workload; VT, ventilatory threshold.
Significant difference between trained and sedentary subjects, * $P < 0.001$.

men is unknown. In addition, the relationships of these mechanisms with the changes in glucose disposal (insulin sensitivity, non–insulin-dependent glucose uptake) induced by training (22,23) are quite unclear. This study was thus undertaken to investigate in middle-aged subjects (a) to what extent and at which intensity level (moderate- or hard-intensity or both) training modifies the balance of substrate oxidation and (b) whether these effects are related to the glucose disposal alterations induced by training. We investigated substrate utilization, as well as glucose disposal, in sedentary and trained middle-aged subjects. Substrate oxidation rates were determined by indirect calorimetry during exercise (26,30) and basal glucose disposal parameters were measured by the frequently sampled intravenous glucose tolerance test (FSIVGTT) using Bergman's minimal model method (3).

METHODS

Subjects

Seven middle aged endurance-trained cyclists (Tr) and seven middle-aged sedentary men (Sed) participated in this study. None had a family history of diabetes or hypertension. Smokers or those currently using medication for the control of blood arterial pressure or lipid or carbohydrate metabolism were excluded. No subject exhibited electrocardiogram abnormalities at rest or during the maximal cycle ergometer test. The physical characteristics of subjects are shown in Table 1. Body composition was assessed with a four-terminal impedance plethysmograph (Dietosystem Human IM-Scan, Milan, Italy). The training program for the cyclists was in fact the same as their usual cycling club program, which amounted to almost 10 h of cycling per week (300 ± 15 km) for the past 10 ± 1.5 (SE) yr.

After receiving a complete and accurate verbal description of the procedure, risks, and benefits associated with the study, the subjects provided written consent. The experimental protocol was approved by the Committee on Research for the Medical Sciences.

Protocol

The subjects came to the laboratory on four separate days for 1) the glucose tolerance test (day 1), 2) an incremental maximal exercise test for the determination of the maximal oxygen uptake ($\dot{V}O_{2max}$) and ventilatory threshold (VT) (day 2), and 3) two 60-min steady-state exercise tests, one below (−15%) and the other above (+15%) their individual VT. The tests were performed in random order (days 3 and 4).

The tests were separated by at least 4 d and never more than 7 d. All subjects were requested to refrain from exercise performance and consumption of cola drinks and coffee for the 3 d before the glucose tolerance and exercise tests. Before study enrollment, a brief interview was conducted to ascertain that all subjects had approximately the same dietary habits.

FSIVGTT. This test was performed according to Brun's method (7). Subjects were asked to fast for 12 h before the test, which began at 9:00 a.m. A cannula was inserted in the cephalic vein at the level of the cubital fossa for blood sampling at various times, and glucose injection was administered via the contralateral cephalic vein. Glucose (0.5 $g \cdot kg^{-1}$, solution at 30%) was slowly injected over 3 min. Insulin (0.02 units$\cdot kg^{-1}$ body weight, i.e., 1–2 units) was injected intravenously immediately at 19 min. Blood samples were drawn twice before the glucose bolus and at 1, 3, 4, 8, 10, 15, 19, 20, 22, 30, 41, 70, 90, and 180 min following the end of glucose injection. The least-square slope of the log of the absolute glucose concentration between 4 and 19 min after the glucose bolus was used as an index of glucose tolerance (Kg). This Kg value describes glucose assimilation by tissue and depends on three factors: insulin release, insulin sensitivity, and glucose effectiveness independent of insulin.

Measurement of insulin sensitivity and glucose effectiveness. Minimal model analysis of FSIVGTT was performed according to the method of Bergman et al. (3) with TISPAG software from the Department of Physiology of the University of Montpellier I, France, using a nonlinear least square estimation (7). This program gave the values of SI and glucose effectiveness (Sg). Sg is the fractional disappearance rate of glucose, independent of any insulin response. SI is an index of the influence of plasma insulin to change glucose's own effect on glucose concentration. Sg was divided into its two components: the contribution of hyperglycemia *per se* to tissue glucose utilization and the effect of basal insulin on glucose uptake. The basal insulin component of Sg is termed the basal insulin effect (BIE) and can be calculated as the product of basal insulin (BI) and SI. Thus the contribution of non–insulin-dependent glucose uptake (glucose effectiveness at zero insulin (GEZI)) to glucose uptake is the difference between total Sg and the BIE: $BIE = BI \times SI$ and $GEZI = Sg - BIE$.

Incremental maximal exercise test. The subject's $\dot{V}O_{2max}$ was measured during 8–12 min of exercise performed on an electronically braked cycle ergometer (550 ERG, Bosch, Berlin, Germany). During exercise, gas exchanges were measured breath-by-breath using a mass spectrometer (Marquette MGA 1100, Marquette Electronics, Milwaukee, WI). The calibration of the mass spectrometer was checked before each test with standard calibration gases. A 3-L syringe was used to calibrate the volume

turbine using flow rates similar to subject ventilation. Heart rate was monitored throughout the exercise test. Exercise testing started with a 3-min warm-up at 40 W. The workload was increased by steps of 20 W for the sedentary group and 30 W for the trained group every minute until maximal exercise was reached, which was evaluated in terms of maximal heart rate, respiratory exchange ratio (RER) values (> 1.15), and O_2 consumption ($\dot{V}O_2$) stability. The results of this test were used to determine the VT according to the method of Beaver et al. (2).

Steady-state exercise tests. Subjects arrived at the laboratory at 8:00 a.m. after a 12-h overnight fast. A Teflon catheter was inserted in the cephalic vein at the level of the cubital fossa for blood sampling at various times. At 8:30 a.m., a resting blood sample was drawn for subsequent analysis and subjects then exercised either below (−15%) or above (+15%) their VT for 60 min on an electronically braked cycle ergometer (550 ERG). During the 60 min of exercise, the subjects were instructed to maintain a pedaling rate of 75 rpm. Ventilation ($\dot{V}E$), RER, $\dot{V}O_2$, and carbon dioxide production ($\dot{V}CO_2$) were measured continuously, as described above. During this period, the $\dot{V}O_2$ and $\dot{V}CO_2$ varied by less than 0.1 $L \cdot min^{-1}$ and $\dot{V}E$ varied by less than 0.5 $L \cdot min^{-1}$.

Indirect calorimetry and substrate oxidation measurements. The percentages of carbohydrate and lipid oxidation were calculated by using the following equations (26): % lipid = ((1 − RER)/0.29) × 100, and % carbohydrate = ((RER − 0.71)/0.29) × 100. The RER value was the average of every 5-min period throughout the entire 60 min of exercise.

The rates of substrate oxidation of carbohydrate and fat were calculated from gas exchange measurements according to the table of nonprotein respiratory quotient (30): carbohydrate = $4.585 \times \dot{V}CO_2 - 3.226 \times \dot{V}O_2$, and lipid = $1.695 \times \dot{V}O_2 - 1.701 \times \dot{V}CO_2$, with mass expressed in grams per minute and gas volume in liters per minute. $\dot{V}O2$ and $\dot{V}CO_2$ values were the averages of every 5-min period throughout the entire 60 min of exercise.

Sample collection and analysis. Blood samples were drawn at rest (t0); at 5, 15, 30, 45, and 60 min of exercise; and after 10 min of recovery. Blood samples were immediately placed in a tube containing lithium heparin (glucose, insulin, catecholamines) or EDTA (glycerol, lactate). The plasma was immediately separated by centrifugation at 4°C and was stored at −80°C until analysis. Plasma glucose (Sigma Diagnostics, Lyon, France), glycerol (Sigma Diagnostics), and lactate (Boehringer Mannheim, Meylan, France) concentrations were determined by specific enzymatic methods adapted to the spectrophotometer (Beckman DU 640, Fullerton, CA). Plasma insulin (Insik-5, Sorin Biomedica, Saluggia, Italy) was measured by radioimmunoassay. Plasma catecholamine concentration was determined using reverse-phase high-performance liquid chromatography procedures (Waters, 460 Electrochemical Detector, Saint Quentin en Yvelines, France). Hematocrit (Hct) was determined at rest and during exercise to ensure that measurements of metabolite and hormone concentrations were not influenced by changes in plasma volume. Water was given *ad libitum* during exercise tests.

TABLE 2. Minimal model analyses of FSIVGTT parameters in sedentary and endurance-trained subjects.

	Sedentary ($N = 7$)	Trained ($N = 7$)
Basal glucose ($mmol \cdot L^{-1}$)	5.03 ± 0.1	4.53 ± 0.1*
Basal insulin ($\mu U \cdot mL^{-1}$)	10.5 ± 1.3	6.87 ± 0.7*
Kg ($\%\cdot min^{-1}$)	1.97 ± 0.2	2.65 ± 0.4
Sg ($\%\cdot min^{-1}$)	2.77 ± 0.2	4.35 ± 0.7*
SI ($\times 10^{-4}$ ($\mu U \cdot mL^{-1} \cdot min^{-1}$))	2.99 ± 0.6	13.84 ± 2.4§
BIE ($\%\cdot min^{-1}$)	0.293 ± 0.04	1.72 ± 0.6§
GEZI ($\%\cdot min^{-1}$)	2.48 ± 0.2	2.63 ± 0.4
Insulin peak ($\mu U \cdot mL^{-1}$)	68.83 ± 11.3	41.75 ± 5.5*

Values are means ± SE.
Kg, glucose tolerance; Sg, glucose effectiveness; SI, insulin sensitivity; BIE, basal insulin effect; GEZI, glucose effectiveness at zero insulin.
Significant difference between trained and sedentary subjects. * $P < 0.03$; § $P < 0.001$.

Statistical Analysis

A Student's *t*-test was used to compare the physical characteristics and glucose disposal between the two groups. The significance of differences between the Tr and Sed groups during moderate and hard exercise intensity were determined using a two-way analysis of variance (ANOVA). To assess the patterns of response in the groups, plasma substrates and/or hormone concentrations were compared with ANOVA with repeated measures. To evaluate the relationship between glucose disposal and substrate utilization, Pearson correlation analysis was performed. Significance was defined as $P < 0.05$. Data are presented separately as mean ± SE.

RESULTS

Physical characteristics, ergometric parameters, and $\dot{V}O_2$ measurement. The Sed and Tr groups did not differ with respect to age, height, weight, body fat, or body mass index (BMI). However, $\dot{V}O_{2max}$, maximal power (W_{max}), and power at VT (W/VT) were higher in the Tr group compared with the Sed group: respectively, 51.06%, 49.8%, and 54.81% ($P < 0.001$). When exercise level during both sessions (below VT and above VT) was expressed as percentages of $\dot{V}O_{2max}$, these percentages were quite similar for Tr and Sed groups: 49.6 ± 3.2% versus 51.2 ± 3.1% below VT and 71.8 ± 1.4% versus 73.6 ± 2.4% above VT, respectively.

Parameters of glucose disposal. The parameters of glucose disposal are shown in Table 2. The fasting values of plasma glucose and plasma insulin were lower in Tr than in Sed subjects (4.53 ± 0.13 $mmol \cdot L^{-1}$ vs 5.03 ± 0.15 $mmol \cdot L^{-1}$, $P < 0.02$ and 6.87 ± 0.74 $\mu U \cdot mL^{-1}$ vs 10.5 ± 1.36 $\mu U \cdot mL^{-1}$, $P < 0.03$). Compared with Sed subjects, Tr subjects had higher SI (+461%, $P < 0.001$), higher BIE (+56%, $P < 0.001$), higher Sg (+57%, $P < 0.03$), and lower peak insulin (−54%, $P < 0.03$).

Substrate oxidation during steady-state exercise. During steady-state exercise performed below VT, the percentage of CHO oxidation was higher in Sed than in

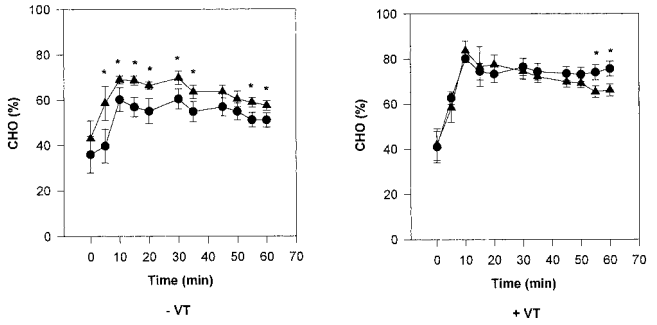

FIGURE 1—Calculated percentage of CHO during 60 min of cycle ergometer exercise performed below (−VT) and above (+VT) the ventilatory threshold in middle-aged endurance-trained cyclists ($N = 7$; *circles*) and in middle-aged sedentary men ($N = 7$; *triangles*). Values are means ± SE; * $P < 0.05$ in Tr vs Sed subjects.

Tr subjects ($P < 0.05$) (Fig. 1). Total fat expenditure was higher in Tr than in Sed subjects (214.24 ± 30.4 kcal vs 128.4 ± 14.46 kcal, $P < 0.05$) (Fig. 2).

During steady-state exercise performed above VT, the percentage of CHO oxidation was higher in Tr than in Sed subjects near the end of exercise ($P < 0.05$) (Fig. 1). Total CHO expenditure was higher in Tr than in Sed subjects (630 ± 31.8 kcal vs 459.8 ± 32.6 kcal, $P < 0.05$) (Fig. 2). The RER values at rest and during exercise are presented in Table 3.

In both groups of subjects, a higher percentage of CHO combustion was maintained during exercises performed above VT than during exercises performed below VT ($P < 0.05$). Figure 3 shows that the CHO oxidation rate was higher above VT than below VT in both Tr and Sed groups ($P < 0.05$). However, the CHO oxidation rate was markedly higher in the Tr group than in the Sed group during exercise above VT ($P < 0.05$), and the lipid oxidation rate was markedly higher in the Tr group than in the Sed group during exercise below VT ($P < 0.05$).

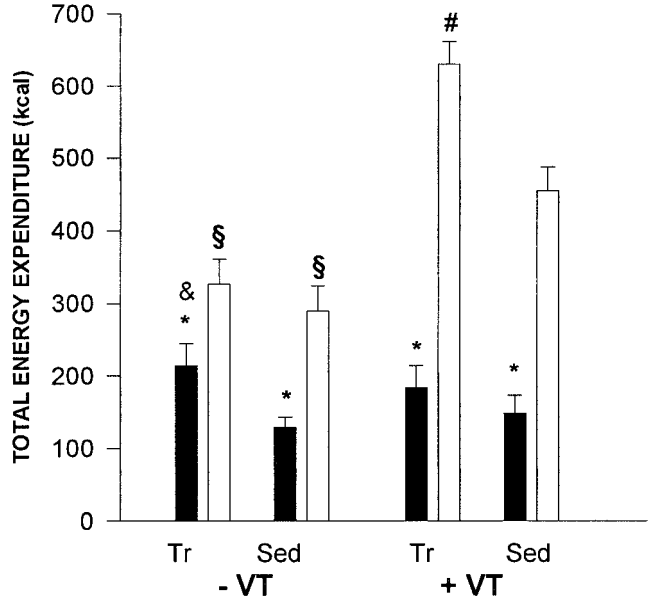

FIGURE 2—Total energy expenditure expressed in kcal during 60 min of cycle ergometer exercise performed below (−VT) and above (+VT) the ventilatory threshold in middle-aged endurance-trained cyclists (Tr; $N = 7$) and in middle-aged sedentary men (Sed; $N = 7$). Values are means ± SE; * $P < 0.05$ fat vs CHO. § −VT vs +VT. # $P < 0.05$ Tr vs Sed for carbohydrate oxidation. & $P < 0.05$ Tr vs Sed for fat oxidation. Solid bars, fat oxidation; open bars, carbohydrate oxidation.

Blood substrate and hormone concentrations at rest and during exercise. Hct values were not significantly different during exercise tests. Baseline plasma glucose concentration did not differ between Tr and Sed groups. However, glucose concentrations were higher at 45 and 60 min of exercise and during recovery in Tr subjects, although only when exercise was performed above VT ($P < 0.05$) (Fig. 4). Baseline plasma lactate concentrations did not differ between Tr and Sed groups. The lactate response to exercise was lower in both groups when exercise was performed below VT ($P < 0.05$) (Fig. 4); however, the lactate concentrations were lower in Tr than in Sed subjects at 30, 45, and 60 min of exercise below VT and at 15, 30, and 45 min of exercise above VT ($P < 0.05$) (Fig. 4). Baseline plasma glycerol concentrations were not different between Tr and Sed subjects, nor did they differ during exercise (Fig. 4). Baseline plasma insulin concentration was lower in Tr than in Sed subjects ($P < 0.05$), whereas insulin kinematic responses during exercise did not differ between them (Fig. 5). Baseline plasma epinephrine (Epi) and norepinephrine (Nor) concentrations were not different in Tr and Sed subjects (Fig. 5), but Epi concentration was markedly higher in Tr than in Sed subjects from 15 min to the end of exercise when performed above VT (Fig. 5). Epi and Nor concentrations were higher during exercise performed above VT than below VT in Tr but not in Sed subjects (Fig. 5).

CHO and glucose disposal relationships. Figure 6 shows that SI in Tr subjects was negatively correlated with the contribution of total energy expenditure of CHO (kcal) above VT ($r = -0.743$, $P < 0.05$). No correlation was noted on Sed subjects.

DISCUSSION

This study shows that during exercise performed at hard intensity (i.e., above VT), CHO utilization was higher in middle-aged Tr subjects than in middle-aged Sed subjects. Furthermore, during exercise performed below the VT, fat oxidation was higher in middle-aged Tr subjects than in age-matched Sed subjects. At the higher exercise intensity, CHO appeared to be the major fuel source utilized in both groups. Moreover, in the Tr subjects, a higher level of CHO oxidation was associated with a greater response in Epi and was inversely related with SI.

The measurement of fuel oxidation by indirect calorimetry during high-intensity exercise has been challenged (9,18,29). Nevertheless, it is well known that during high-intensity exercise, the accelerated lactic acid production increases plasma lactate concentrations and requires increased utilization of the bicarbonate buffering system to maintain a neutral pH. This mechanism results in elevated carbon dioxide production that may in turn induce an increase in the RER unrelated to substrate balance, which could have disturbed our calculation. In fact, it has been

TABLE 3. RER at rest and during steady-state exercise in sedentary and endurance-trained subjects.

		Time (min)					
		Rest	5	15	30	45	60
Sedentary subjects	–VT	0.82 ± 0.01*	0.87 ± 0.02*	0.90 ± 0.01*	0.89 ± 0.01	0.88 ± 0.01	0.87 ± 0.01*
	+VT	0.81 ± 0.01	0.89 ± 0.01	0.93 ± 0.01	0.91 ± 0.01	0.90 ± 0.01#	0.89 ± 0.01#
Trained subjects	–VT	0.791 ± 0.01	0.81 ± 0.02	0.87 ± 0.01	0.88 ± 0.01	0.87 ± 0.01	0.85 ± 0.01
	+VT	0.80 ± 0.02	0.88 ± 0.01	0.92 ± 0.02	0.92 ± 0.01	0.92 ± 0.01	0.92 ± 0.01

Values are means ± SE.
VT, ventilatory threshold.
Significant difference between sedentary and trained subjects during exercise performed below VT (–VT), * $P < 0.05$. Significant difference between sedentary and trained subjects during exercise performed above VT (+VT), # $P < 0.05$.

demonstrated (18) that this bicarbonate-derived CO_2 production exerts a quite moderate effect on $\dot{V}CO_2$ (it increases it by almost 1%). Furthermore, a good concordance between net substrate oxidation measured with stable isotope techniques and indirect calorimetry during submaximal exercise even at hard intensity (31) has been demonstrated. Thus, there is increasing evidence in the recent literature (8,17,33) supporting the accuracy of indirect calorimetry in the measurement of substrate oxidation during steady-state submaximal exercise sessions.

Whole-body glucose uptake is dependent on two mechanisms: insulin-mediated glucose uptake (IMGU) and non–insulin-mediated glucose uptake (NIMGU) (1). Although most studies have investigated IMGU, the measurement of NIMGU has been performed in very few studies because its determination during clamp experiments is rather sophisticated (7).

The minimal model technique, which consists of analysis of the FSIVGTT, is simpler than the clamp and allows accurate, reproducible measurement of the different components of glucose utilization (7). Recently, the accuracy of the minimal-model measurement of Sg has been a matter of discussion. Ni et al. (28) performed a modeling study that showed there was no overestimation of average Sg by the minimal model compared to the clamp. They thus concluded that minimal model–derived Sg could be considered a relevant biological parameter suitable for clinical and epidemiological investigations.

Although the relationship between exercise and insulin sensitivity has received widespread attention (14,15,19,22,23), the relationships between substrate oxidation and the glucose disposal parameters remain poorly investigated. As previously noted in trained individuals (22,23), SI and Sg in our study were higher in Tr than in Sed subjects. These results reflect a better glucose disposal in our cyclists, probably because of endurance training, which is responsible for an increased amount and recruitment of GLUT-4 glucose transporters (14,15). GEZI was not different between Tr and Sed subjects, a finding in contrast with other studies (22) that have shown a higher GEZI in young, trained men than in young, sedentary men. A possible explanation is the interaction of aging and training on these glucose uptake components. As shown in a recent study from our group (23), training in middle-aged men increases insulin-dependent glucose uptake rather than non–insulin-dependent glucose uptake (termed GEZI).

Data from the present study show that during moderate-intensity exercise (below VT), fat oxidation was higher in Tr than in Sed subjects. This finding can be explained by the previously reported enhancing effects of endurance training on fatty acid oxidation (27) and the mitochondrial capacity to oxidize fat (27). Moreover, it is also known that training decreases the RER (17). Thus, training increases lipid oxidation during moderate-intensity exercise (9).

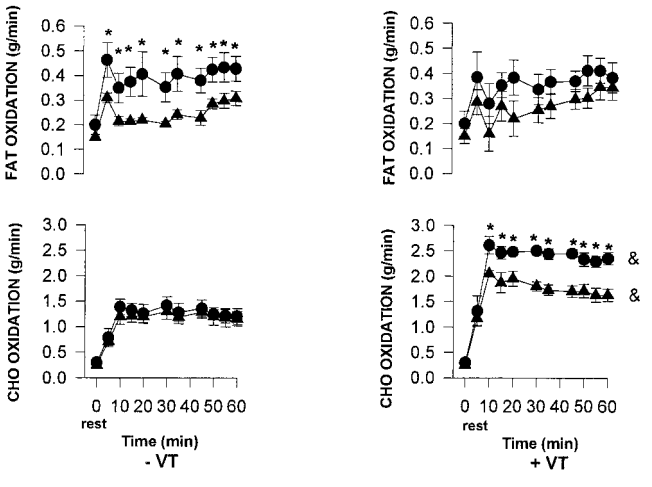

FIGURE 3—Fat and CHO oxidation rates at rest and during cycle ergometer exercise performed below (−VT) and above (+VT) the ventilatory threshold in middle-aged endurance-trained cyclists ($N = 7$; *circles*) and in middle-aged sedentary men ($N = 7$; *triangles*). Values are means ± SE; * $P < 0.05$ Tr vs Sed; & $P < 0.05$ −VT vs +VT.

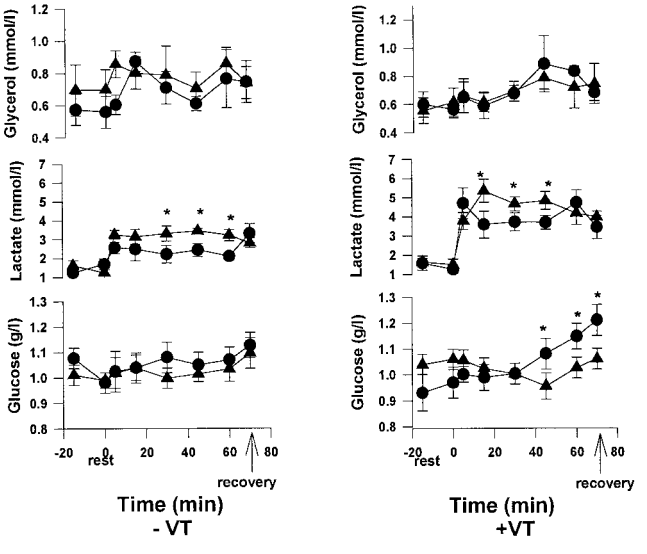

FIGURE 4—Plasma glycerol, lactate, and glucose concentrations at rest, during 60 min of cycle ergometer exercise below (−VT) and above (+VT) the ventilatory threshold in middle-aged endurance-trained cyclists ($N = 7$; *circles*) and in middle-aged sedentary men ($N = 7$; *triangles*). Values are means ± SE; * $P < 0.05$ Tr vs Sed.

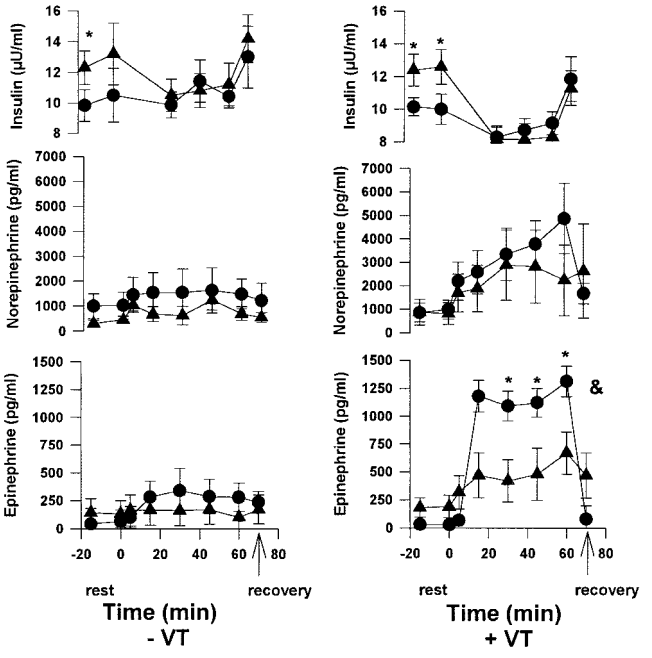

FIGURE 5—Plasma catecholamine and insulin concentrations at rest, during 60 min of cycle ergometer exercise performed below (−VT) and above (+VT) the ventilatory threshold and during recovery (10 min) in middle-aged endurance-trained cyclists (*N* = 7; *circles*) and in middle-aged sedentary men (*N* = 7; triangles). Values are means ± SE; * *P* < 0.05 Tr vs Sed; & *P* < 0.05 −VT vs +VT.

Although substrate oxidation during exercise has been widely investigated, to our knowledge there are currently no published reports on substrate oxidation in middle-aged subjects during prolonged exercise at hard intensity. In the present study, CHO oxidation was increased in Tr subjects in comparison with Sed subjects during hard-intensity exercise. This result is in line with the findings of another group that investigated this phenomenon in young men (29). Catecholamines are probably involved in this mechanism because, although the effects of catecholamines are less well documented during exercise than at rest, Epi is considered to be one of the most important factors that affect substrate utilization during exercise (4). In a recent study, Febbraio et al. (13) showed that intramuscular glycogen, glycolysis, and CHO oxidation are augmented by elevated Epi during submaximal exercise in trained men. Above VT, Epi concentrations are markedly increased (25) and thus can be expected to exert a higher effect, which may at least in part explain our results. As shown in Figure 5, Tr subjects achieved a higher power output than Sed subjects, and this higher power input induced a strong rise in Epi. Epinephrine was higher during exercise performed above VT than below VT in Tr but not in Sed subjects. Thus, the increased Epi concentrations in Tr subjects could be related to the external power output that the Tr subjects were able to maintain (20). Such a strong Epi secretory response to hard exercise is classical in trained individuals (20) and has been assumed to result in a greater CHO dependency (4). It is thus likely that this higher concentration in Tr subjects played a role, in association with other hormonal and metabolic factors that were not investigated here, in the shift toward a higher reliance on carbohydrates above VT. First, Epi is a regulator of lipid metabolism. Although its major reported effect is to stimulate lipolysis (24), the efficiency of this process has been shown to decrease with aging (21). Second, a down-regulation of β_2-adrenergic receptors occurs during intense exercise (4). In fact, very high catecholamine concentrations associated with intense exercise (13,29) may enhance anti-lipolytic α_2-adrenergic receptors (32). Epi may therefore become a potent inhibitor of lipolysis at high plasma concentration in middle-aged trained men. The effects of Epi on CHO metabolism can also explain our findings, since this hormone stimulates glycogenolysis and glycolysis (4,29).

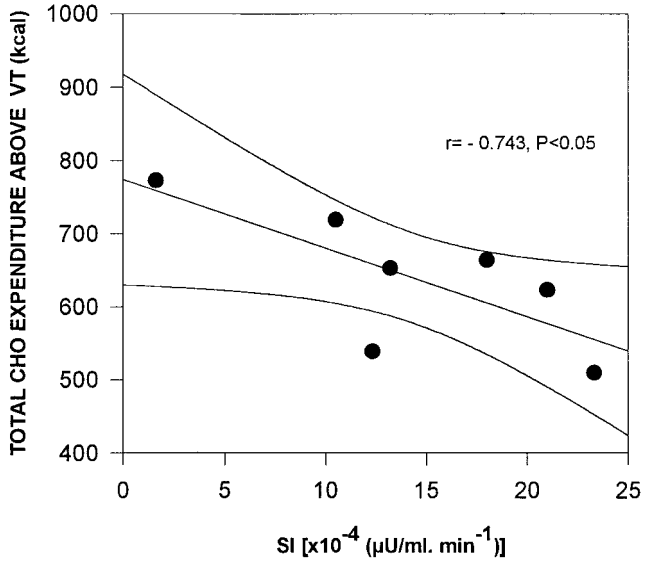

FIGURE 6—Relationships between insulin sensitivity (SI) and total carbohydrate expenditure (kcal) during 60 min of cycle ergometer exercise performed above the ventilatory threshold (VT) in middle-aged endurance-trained cyclists (*N* = 7). Pearson product correlation is represented with the confidence interval.

The second part of our study was an investigation of whether the pattern of substrate utilization is associated with an increase in insulin sensitivity and glucose disposal in trained individuals. As expected, Sg and SI were higher in Tr than in Sed subjects, which is consistent with other reports in the literature (22,23), but there was a negative relationship between SI and the total CHO utilization in Tr subjects during hard-intensity exercise. This finding seems paradoxical, though it may reflect a shift in fuel balance associated with high SI, with an improved ability to derive energy from fat (10) and thus a lower waste of CHO. There may also be a physiological limitation to the training-increase in CHO utilization in athletes, preventing hypoglycemia, which is consistent with a previous article from our laboratory (22).

In addition, Tr subjects showed a more pronounced CHO dependency and a higher blood glucose concentration at the end of the hard-intensity exercise than did Sed subjects, which is in accordance with the fact that at this intensity, lactate and muscle glycogen, but not blood glucose, were the major CHO for oxidation (5). Furthermore, lactate concentrations during exercise were higher in Sed than in Tr

subjects. This agrees with the finding that endurance training increases lactate oxidation rather than lactate production (12). More recently, Brooks et al. (6) demonstrated that lactate is the predominant monocarboxylate oxidized by the mitochondrial lactate shuttle.

In summary, our study shows the importance of exercise intensity and endurance training in middle-aged men to modulate the balance of substrate utilization in association with the rise in Epi response. The data from this investigation show that endurance training provided our middle-aged subjects with the ability to economize the CHO fuel source when exercise was moderate by a decrease in CHO combustion, and to increase CHO utilization at hard-intensity exercise in relationship with insulin sensitivity. CHO appeared to be the major substrate when exercise was performed at hard exercise intensity. This study further shows that glucose disposal parameters, particularly insulin sensitivity, certainly have an indirect effect on the balance of substrate utilization.

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