Training-induced alterations in fat and carbohydrate metabolism during exercise in elderly subjects

Shahid Sial, Andrew R. Coggan, Robert C. Hickner, and Samuel Klein

Department of Internal Medicine, Washington University School of Medicine, St. Louis, Missouri 63110, and Department of Anesthesiology, The University of Texas Medical Branch, Galveston, Texas 77555

Training-induced alterations in fat and carbohydrate metabolism during exercise in elderly subjects. Am. J. Physiol. 274 (Endocrinol. Metab. 37): E785–E790, 1998.—Compared with young adults, fat oxidation is lower in elderly persons during endurance exercise performed at either the same absolute or relative intensity. We evaluated the effect of 16 wk of endurance training on fat and glucose metabolism during 60 min of moderate intensity exercise [50% of pretraining peak oxygen consumption (Vo2peak)] in six elderly men and women (74 ± 2 yr). Training caused a 21% increase in mean Vo2peak. The average rate of fat oxidation during exercise was greater after (221 ± 28 µmol/min) than before (166 ± 17 µmol/min) training (P = 0.002), and the average rate of carbohydrate oxidation during exercise was lower after (3,180 ± 461 µmol/min) than before (3,937 ± 483 µmol/min) training (P = 0.003). Training did not cause a significant change in glyceroal rate of appearance (Rg), free fatty acid (FFA) Rfa, and FFA rate of disappearance during exercise. However, glucose Rfa during exercise was lower after (1,027 ± 95 µmol/min) than before (1,157 ± 69 µmol/min) training (P = 0.01). These results demonstrate that a 16-wk period of endurance training increases fat oxidation without a significant change in lipolysis (glycerol Rg) or FFA availability (FFA Rfa) during exercise in elderly subjects. Therefore, the training-induced increase in fat oxidation during exercise is likely related to alterations in skeletal muscle fatty acid metabolism.

Endogenous fat is an important fuel for working muscles during endurance exercise. We have recently found that fat oxidation is lower in elderly (66–79 yr old) compared with young adult (20–30 yr old) persons during endurance exercise performed at either the same absolute or relative intensity (34). This phenomenon is presumably related to changes in skeletal muscle itself, because whole body lipolysis and plasma free fatty acid (FFA) availability were not rate limiting. In fact, during exercise performed at the same absolute intensity, fatty acid uptake from plasma was higher but fat oxidation was lower in the elderly compared with the young adults. Impairment of fat oxidation during physical activity could have important clinical implications by decreasing exercise capacity and making it more difficult to decrease body fat mass. Exercise training could have beneficial metabolic effects during exercise in elderly persons. Endurance training has been shown to increase fat oxidation during exercise in young adults (23, 30) and increase resting rates of fat oxidation in elderly persons (31). However, the effect of training on lipid metabolism during exercise has not been studied in elderly persons.

The present study was undertaken to evaluate the effect of endurance training on fat and carbohydrate metabolism during moderate intensity exercise in elderly subjects. We hypothesized that a program of physical training would normalize substrate oxidation by either correcting or compensating for the alterations in skeletal muscle metabolism. Stable isotope tracers and indirect calorimetry were used to assess substrate metabolism at rest and during 60 min of cycle ergometer exercise in elderly subjects before and after 16 wk of cycle ergometer exercise training.

METHODS

Subjects. Six elderly subjects (74 ± 2 yr, 3 men and 3 women; Table 1) participated in this study, which was approved by the Institutional Review Board and the General Clinical Research Center (GCRC) Scientific Advisory Board of The University of Texas Medical Branch. All subjects performed normal daily activities, such as shopping, driving, and walking short distances, but none participated in regular aerobic exercise, such as walking, jogging, or cycling. All subjects were within 10% of ideal body weight according to the 1983 Metropolitan height-weight tables and were considered to be in good health after a comprehensive medical evaluation including history, physical examination, routine screening blood tests, and an oral glucose tolerance test. Subjects with a history of cigarette smoking, cardiovascular disease, diabetes, hypertension, or hyperlipidemia or those taking any medications were excluded. Subjects also completed an exercise stress test, and those with evidence of cardiovascular disease were excluded.

Outpatient studies. Peak oxygen consumption (Vo2peak) and body composition were determined during two outpatient visits 3–5 days before each isotope infusion protocol, which was performed before and after 16 wk of training. Exercise testing was started with a “warm-up” by having the subjects cycle on a cycle ergometer for 5–10 min. The workload during exercise after this warm-up was increased by 10 W every 2 min in women and by 15 W every 2 min in men until volitional exhaustion. Oxygen consumption (V02) and carbon dioxide production (VCO2) were monitored continuously by open-circuit spirometry using a 2900 metabolic Cart (Sensormedics, Yorba Linda, CA). At least two of the following three criteria were met to establish that Vo2peak was attained: 1) respiratory exchange ratio (RER) > 1.15, 2) a leveling off of Vo2 and heart rate despite increases in the workload, and 3) attainment of age-predicted maximal heart rate. Fat mass and fat-free mass were determined by dual energy X-ray absorptiometry using Enhanced Whole-Body Software Ver. 5.64 (Hologic QDR 1,000/W, Waltham, MA).

Inpatient studies. Subjects were admitted to the GCRC in the afternoon 1 day before the isotope infusion study. A standard meal and a snack were consumed at 1800 and at
One and EGTA. These samples were centrifuged immediately at
further processing. Samples for insulin were collected in tubes
separated by centrifugation at 4°C and frozen at
glass tubes containing lithium heparin. Plasma was immediately
tations and isotopic enrichments was collected in chilled 10-ml
samples were drawn for insulin and catecholamine concentra-
to measure basal glucose and lipid kinetics and at 10, 15,
and after training
Subject characteristics before
primed (1.2 µmol/kg), constant (0.08 µmol·kg
sion of [1- 13C]palmitate (98% APE, Isotec) bound to human
albumin were initiated and continued for 135 min. The exact
isotope infusion rate was determined for each study by
measuring glucose, palmitate, and glycerol concentrations in the
infusates. After 120 min of isotope infusion at rest (–120
to 0 min), the subjects exercised on a Monarch 829E cycle
ergometer at 50% V˙O2peak for 60 min. At the onset of exercise,
the isotope infusion rates were increased by 60% to minimize
changes in substrate isotopic enrichment. Blood samples were
drawn before the start of the isotope infusion to deter-
mine background substrate enrichment at –20, –10, and 0
min to measure basal glucose and lipid kinetics and at 10, 15,
20, 25, 30, 35, 40, 45, 50, 55, and 60 min in order to
determine glucose and lipid kinetics during exercise. Blood
samples were drawn for insulin and catecholamine concen-
trations at the end of the basal (0 min) and exercise (60 min)
periods. Blood obtained for the analysis of substrate concen-
trations and isotopic enrichments was collected in chilled 10-mL
glass tubes containing lithium heparin. Plasma was immediately
separated by centrifugation at 4°C and frozen at –20°C until
further processing. Samples for insulin were collected in tubes
containing EDTA and aprotinin. Samples for plasma catechol-
amine were collected in ice-cold tubes containing reduced glutathi-
one and EGTA. These samples were centrifuged immediately at
4°C and stored at –70°C until analysis. V02 and VCO2 were
determined at the end of basal period and every 10 min during
during the last 20 min of the resting (preexercise) period,
whereas Steele’s equation for non-steady-state conditions
(37) was used to calculate R4 during the last 20 min of the resting (preexercise) period,
whereas Steele’s equation for non-steady-state conditions
(37) was used to calculate R4 during the last 20 min of the resting (preexercise) period.
Fatty acid Ra was calculated by dividing palmitate Ra by the percent
contribution of palmitate to total FFA concentration.
The effective volume of distribution was assumed to be 270 mL/kg for
glycerol, 50 mL/kg for palmitate, and 100 mL/kg for glucose.
Triglyceride and carbohydrate oxidation rates were calculated
from measurement of VCO2, VO2, and estimated urinary nitrogen excretion (8). It was assumed that nitrogen excretion
was 8 µg·kg–1·min–1, based on the results of an earlier exercise study (2), and that palmitoyl oleyl triglyceride
(860 g/mol) was a typical triglyceride.

Statistical analysis. All data are expressed as means ± SE. Comparisons between pretrained and postraining data
were analyzed for statistical significance by using two-way
(trial × time) ANOVA for repeated measures, using Sigma-
Stat 2.0 (Jandel Scientific, San Rafael, CA). Where appropri-
ate, significant differences identified by ANOVA were isolated
using Tukey’s highly significant difference tests. An α value of
0.05 was used for all significance testing.

RESULTS

Although six subjects participated in this study, plasma hormone concentrations and substrate kinetics are not available for one subject because of technical
problems in handling the plasma samples. Therefore, the body composition and indirect calorimetry data represent values from six subjects, while plasma hormone and substrate kinetic data represent values from five subjects.

Body composition and \( V\dot{O}_2\text{peak} \). Training did not cause a change in total body weight (Table 1). However, there was a small increase in fat-free mass \( (P < 0.05) \), and fat mass tended to be lower \( (P = 0.07) \) in the trained state. Mean \( V\dot{O}_2\text{peak} \) increased by 21% as a result of training \( (P < 0.01; \text{Table 1}) \).

Indirect calorimetry. Resting \( V\dot{O}_2 \) was the same before \( (0.214 \pm 0.024 \text{ l/min}) \) and after \( (0.198 \pm 0.014 \text{ l/min}) \) training as was resting \( V\dot{CO}_2 \) \( (0.167 \pm 0.019 \text{ and } 0.167 \pm 0.016 \text{ l/min, respectively}) \). Resting RER was numerically but not statistically significantly greater after \( (0.824 \pm 0.033) \) than before \( (0.789 \pm 0.011) \) training because one subject had a high and possibly erroneous resting value after training. Resting energy expenditure was also the same before and after training \( (84 \pm 4 \text{ and } 78 \pm 4 \text{ kJ} \cdot \text{min}^{-1} \cdot \text{kg}^{-1} \text{ fat-free mass, respectively}) \).

\( V\dot{O}_2 \) increased at the onset of exercise and remained relatively constant throughout the exercise period. The absolute intensity of the exercise bout performed during the isotope infusion study was the same before and after training; average \( V\dot{O}_2 \) values during 60 min of cycle ergometer exercise before and after training were \( 0.852 \pm 0.090 \text{ and } 0.847 \pm 0.093 \text{ l/min, respectively} \). The RER increased during exercise \( (P < 0.001) \) during studies performed both before and after training. However, average RER during the exercise bout was lower after \( (0.858 \pm 0.013) \) than before \( (0.892 \pm 0.006) \) training \( (P = 0.006) \).

Substrate oxidation. Fat oxidation increased from \( 79 \pm 11 \text{ \mu mol/min} \) at rest to an average of \( 166 \pm 17 \text{ \mu mol/min} \) during exercise before training \( (P < 0.001) \) and from \( 59 \pm 12 \text{ \mu mol/min} \) at rest to an average of \( 221 \pm 28 \text{ \mu mol/min} \) during exercise after training \( (P < 0.001; \text{P} = 0.002 \text{ for values obtained during exercise before training compared with values after training; Fig. 1}) \). Carbohydrate oxidation increased from \( 315 \pm 81 \text{ \mu mol/min} \) at rest to an average of \( 3,937 \pm 483 \text{ \mu mol/min} \) during exercise before training \( (P < 0.001) \) and from \( 587 \pm 190 \text{ \mu mol/min} \) at rest to an average of \( 3,180 \pm 461 \text{ \mu mol/min} \) during exercise after training \( (P < 0.001; \text{P} = 0.003 \text{ for values obtained during exercise before training compared with values after training; Fig. 1}) \).

Plasma hormone concentrations. Before training, plasma epinephrine and norepinephrine concentrations increased two- to threefold during exercise (from \( 0.30 \pm 0.06 \text{ and } 1.45 \pm 0.16 \text{ nmol/l, respectively, at rest to } 0.94 \pm 0.018 \text{ and } 4.44 \pm 0.51 \text{ nmol/l, respectively, during exercise; } P < 0.001 \). After training, basal plasma epinephrine and norepinephrine concentrations \( (0.25 \pm 0.04 \text{ and } 1.75 \pm 0.36 \text{ nmol/l, respectively}) \) were similar to values obtained before training. Plasma epinephrine and norepinephrine concentrations also increased two- to threefold during exercise \( (P < 0.001) \) after training to values \( (0.56 \pm 0.11 \text{ and } 6.07 \pm 1.81 \text{ nmol/l, respectively}) \) that were not significantly different from those observed before training. Mean basal plasma insulin concentrations were the same before \( (57.4 \pm 7.2 \text{ pmol/l}) \) and after \( (57.4 \pm 21.5 \text{ pmol/l}) \) training. During exercise, plasma insulin concentrations did not change significantly from baseline values either before \( (43.1 \pm 7.2 \text{ pmol/l}) \) or after \( (57.4 \pm 14.4 \text{ pmol/l}) \) training.

Plasma substrate concentrations. No significant differences in plasma substrate concentrations were observed after training compared with values obtained before training. Plasma FFA concentrations decreased during early exercise but increased as exercise continued so that mean values at the end of the exercise bout were similar to the mean resting values both before and after training \( (0.472 \pm 0.050 \text{ and } 0.463 \pm 0.039 \text{ nmol/ml before and at the end of exercise, respectively, before training; } 0.397 \pm 0.026 \text{ and } 0.364 \pm 0.020 \text{ nmol/ml before and at the end of exercise, respectively, after training}) \). Plasma glycerol concentration increased progressively during exercise, and values obtained at the end of exercise were greater \( (P < 0.001) \) than resting values both before and after training \( (0.076 \pm 0.006 \text{ and } 0.137 \pm 0.010 \text{ nmol/ml before and at the end of exercise before training; } 0.054 \pm 0.011 \text{ and } 0.116 \pm 0.019 \text{ nmol/ml before and at the end of exercise after training}) \). Plasma glucose concentrations did not change during exercise performed either before or after
training (5.56 ± 0.25 and 5.54 ± 0.23 µmol/ml before and at the end of exercise before training; 5.45 ± 0.20 and 5.50 ± 0.17 µmol/ml before and at the end of exercise after training).

Substrate kinetics. Fatty acid Ra increased from 379 ± 21 µmol/min at rest to an average of 497 ± 49 µmol/min during exercise before training (P < 0.01) and from 406 ± 42 µmol/min at rest to an average of 559 ± 79 µmol/min during exercise after training (P < 0.01) (Fig. 2). Fatty acid Rd increased from 379 ± 21 µmol/min at rest to an average of 491 ± 47 µmol/min during exercise before training (P < 0.001) and from 406 ± 42 µmol/min at rest to an average of 554 ± 78 µmol/min during exercise after training (P < 0.001). Neither fatty acid Ra nor Rd during exercise was significantly different after training compared with values obtained before training.

Glycerol Ra increased from 161 ± 16 µmol/min at rest to an average of 232 ± 23 µmol/min during exercise before training (P < 0.01) and from 201 ± 22 µmol/min at rest to an average of 288 ± 33 µmol/min during exercise after training (P < 0.01) (Fig. 2). Glycerol Rd increased from 21 ± 22 µmol/min at rest to an average of 57 ± 57 µmol/min during exercise before training (P < 0.001) and from 201 ± 33 µmol/min at rest to an average of 1,015 ± 69 µmol/min during exercise after training (P < 0.001). Glycerol kinetics during exercise was not significantly different after training compared with values obtained before training.

Glucose Ra increased from 877 ± 33 µmol/min at rest to an average of 1,157 ± 69 µmol/min during exercise before training (P < 0.001) and from 846 ± 79 µmol/min at rest to an average of 1,027 ± 95 µmol/min during exercise after training (P < 0.001; Fig. 2). Glucose Rd increased from 1,168 ± 57 µmol/min at rest to an average of 1,887 ± 57 µmol/min during exercise before training (P < 0.001) and from 846 ± 79 µmol/min at rest to an average of 1,015 ± 69 µmol/min during exercise after training (P < 0.001). Glucose kinetics during exercise after training was significantly different from values obtained during exercise before training (P = 0.01).

**DISCUSSION**

Endogenous fat stores provide an important source of fuel for endurance exercise. We have recently found that elderly persons oxidize less fat than young adults during endurance exercise performed at either the same absolute or relative intensity (34). The decrease in fat oxidation was presumably related to alterations in skeletal muscle metabolism because FFA release from adipose tissue was higher in elderly than young adults during exercise performed at the same absolute intensity. The results of the present study demonstrate that endurance training can correct, or compensate for, the reduced rate of fat oxidation during exercise in elderly persons. Sixteen weeks of supervised exercise training increased the rate of fat oxidation during exercise to values previously observed in young adults exercising at the same absolute intensity (34).

It is well known that endurance training increases fat oxidation during exercise at a given absolute exercise intensity in sedentary young adults. The present study demonstrates that a training-induced shift in substrate oxidation also occurs in elderly subjects. Because endurance training did not cause a significant increase in lipolytic rate (glycerol Ra) or FFA availability (FFA Rd), the increase in fat oxidation was presumably caused by adaptive changes within skeletal muscle itself, most likely related to the training-induced increase in skeletal muscle mitochondrial content. Although muscle mitochondrial respiratory enzyme activities are 25–40% lower in sedentary elderly persons than in sedentary young adults (26, 32), endurance exercise training can increase muscle respiratory capacity in both elderly and young subjects (4, 5, 32). The increase in mitochondrial mass favors the oxidation of fat over carbohydrate (6, 12, 26, 27). Increased muscle respiratory capacity decreases skeletal muscle glycolytic flux (12), which in turn facilitates the oxidation of fatty acids. Although the cellular mechanism(s) responsible for this relationship is not known, it is clear that alterations in skeletal muscle carbohydrate metabolism affect the oxidation of fat. It has recently been shown that decreasing glycolytic flux during exercise by manipulating exercise intensity (35) or dietary intake (7) increases plasma long-chain, but not medium-chain, fatty acid oxidation. These findings suggest that decreased glycolytic flux may enhance long-chain fatty acid transport into skeletal muscle mitochondria. Alternatively, a decrease in glycolytic flux and acetyl-CoA production from pyruvate may simply allow more fatty acid-derived acetyl-CoA to enter the tricarboxylic acid cycle. In either case, it is likely that a training-induced increase in muscle respiratory capacity in our subjects contributed to the observed increase in fat oxidation.

The source of the additional fatty acids oxidized during exercise after training cannot be directly determined from our study. It is unlikely that plasma triglycerides contributed to the increase in fat oxidation because plasma triglycerides are not normally an important fuel during exercise (28), and training does not increase triglyceride uptake during exercise (17). Although training did not have a significant effect on FFA Rd, it is possible that a greater percentage of FFAs...
Training on FFA $R_a$ with a $\beta$ value of 0.9 and an $\alpha$ value of 0.05; 19 subjects would be needed to demonstrate a difference in glycerol $R_a$.

The adaptive changes in carbohydrate metabolism in our subjects were similar to those reported in younger persons. Glucose $R_a$ and glucose oxidation during 60 min of cycle ergometer exercise decreased significantly after training. Coggan et al. (3) and Phillips et al. (30) found similar changes in young adults after 84 and 31 days of endurance training, respectively.

Our posttraining studies were performed 72 h after the last bout of exercise to eliminate the influence of acute exercise. It is possible that fat oxidation rates at rest and during exercise might have been different had we studied our subjects closer to the last exercise session, particularly if glycogen stores were not fully repleted. For example, although we did not observe a training effect on the rate of fat oxidation during resting conditions, Poehlman et al. (31) found that fat oxidation at rest was greater after than before training when elderly subjects were studied ~36 h after exercise.

The results from our study demonstrate that endurance training can improve aerobic fitness and cause moderate alterations in body composition in elderly persons. Sixteen weeks of cycle ergometer exercise training increased $V\dot{O}_2$ peak by 21%, which is similar to the relative effect of training reported in younger subjects (5, 21, 23, 36). In addition, we found that total body fat mass tended ($P = 0.07$) to be lower and fat-free mass was higher after training compared with values obtained before training. Other longitudinal training studies have reported either no change in body composition after 12 wk of endurance training (26) or a small increase in fat-free mass and a decrease in body fat mass after as much as 12 mo of endurance training in elderly persons (10, 22, 33). The small decrease in body fat mass may seem surprising in view of the rigorous training program completed by our subjects. However, alterations in body fat mass reflect alterations in total energy balance. Cycling exercise was performed for only 45 min 3–5 days per week, so most of the day was spent in nonexercise activities. Furthermore, Goran and Poehlman (9) found that endurance training in elderly subjects did not increase total daily energy expenditure, presumably because of a compensatory decrease in physical activity the rest of the day.

In summary, a 16-wk period of endurance training increases fat oxidation and decreases carbohydrate oxidation during exercise in elderly subjects to values similar to those observed in untrained young adults. Training did not cause a significant change in lipolysis (glycerol $R_a$) or FFA availability (FFA $R_a$) during exercise. Therefore, the training-induced increase in fat oxidation during exercise is likely related to changes within skeletal muscle, possibly an increase in the fractional oxidation of plasma fatty acids taken up by muscle and/or an increase in the use of nonadipose tissue, presumably intramuscular triglycerides.
REFERENCES


