

Changes in Resting Metabolic Rate and Substrate Oxidation After 16 Months of Exercise Training in Overweight Adults

Jeffrey A. Potteiger, Erik P. Kirk, Dennis J. Jacobsen,
and Joseph E. Donnelly

Purpose: To determine whether 16 months of moderate-intensity exercise training changes resting metabolic rate (RMR) and substrate oxidation in overweight young adults. **Methods:** Participants were randomly assigned to nonexercise control (CON, 18 women, 15 men) or exercise (EX, 25 women, 16 men) groups. EX performed supervised and verified exercise 3–5 d/wk, 20–45 min/session, at 60–75% of heart-rate reserve. Body mass and composition, maximal oxygen consumption ($\text{VO}_{2\text{max}}$), RMR, and resting substrate oxidation were assessed at baseline and after 9 and 16 months of training. **Results:** EX men had significant decreases from baseline to 9 months in body mass (94.6 ± 12.4 to 89.2 ± 9.5 kg) and percent fat (28.3 ± 4.6 to 24.5 ± 3.9). CON women had significant increases in body mass (80.2 ± 8.1 to 83.2 ± 9.2 kg) from baseline to 16 months. $\text{VO}_{2\text{max}}$ increased significantly from baseline to 9 months in the EX men (3.67 ± 0.62 to 4.34 ± 0.58 L/min) and EX women (2.53 ± 0.32 to 3.03 ± 0.42 L/min). RMR increased from baseline to 9 months in EX women ($1,583 \pm 221$ to $1,692 \pm 230$ kcal/d) and EX men ($1,995 \pm 184$ to $2,025 \pm 209$ kcal/d). There were no significant differences within genders for either EX or CON in fat or carbohydrate oxidation. Fat oxidation was significantly higher for women than for men at 9 months in both CON and EX groups. **Conclusions:** Regular moderate-intensity exercise in healthy, previously sedentary overweight and obese adults increases RMR but does not alter resting substrate oxidation. Women tend to have higher RMR and greater fat oxidation, when expressed per kilogram fat-free mass, than men.

Keywords: weight loss, cardiorespiratory fitness, fat oxidation, carbohydrate oxidation, training, energy expenditure

The number of overweight and obese individuals is at the highest level since the initiation of data collection in the NHANES studies (Flegal, Carroll, Ogden, & Johnson, 2003). Preventing weight gain and facilitating weight loss are critical

Potteiger is with the Dept. of Kinesiology and Health, Miami University, Oxford, OH 45056-3491. Kirk is with the Dept. of Internal Medicine–Applied Physiology, Washington University, St. Louis MO 63110. Jacobsen and Donnelly are with the Institute for Life Span Studies, University of Kansas, Lawrence, KA.

for reducing the risk of various types of diseases including heart disease, hypertension, diabetes mellitus, and some types of cancer (Flegal, Williamson, Pamuk, & Rosenberg, 2004). Regular exercise is a key component of clinical weight-management programs because of its ability to increase energy expenditure and promote fat utilization.

Because resting metabolic rate (RMR) represents the largest percentage of an individual's daily energy expenditure (60–75% of total energy expenditure; Ravussin & Bogardus, 1989) many researchers have been interested in the role of regular aerobic exercise in altering RMR. The results of previous studies examining the effects of aerobic exercise training on RMR are equivocal. The results of cross-sectional studies indicate that aerobically trained individuals have higher RMR than untrained persons (Ballor & Poehlman, 1992; Poehlman et al., 1992; Toth & Poehlman, 1995; Tremblay et al., 1986). Longitudinal studies have shown increases in RMR (Ballor & Poehlman; Broeder, Berke, Gardner, Goran, & Poehlman, 1992; Burrhus, Svanevik, & Wilmore, 1992; Poehlman et al., 1992; Toth & Poehlman; Tremblay et al.; Whatley et al., 1994), whereas the results of other studies indicate that RMR is unchanged (Keytel, Lambert, Johnson, Noakes, & Lambert, 2001; Meredith, Frontera, Fisher, Hughes, & Herland, 1989; Sjodin et al., 1996; Volpe, Huang, Larpadisorn, & Lesser, 2001; Wilmore et al., 1998) or is decreased slightly (Byrne & Wilmore, 2001; Santa-Clara, Szymanski, Ordille, & Fernhall, 2006) after aerobic exercise training ranging from moderate to moderately high intensity and approximately 30–60 min in duration. The lack of a consistent response likely results in part from participant variability in age, body weight and composition, length of training, intensity and duration of training, and the influence of dietary manipulations designed to induce weight loss.

The influence of aerobic exercise training on substrate utilization and particularly fat oxidation in overweight and obese individuals is also unclear. It has been shown that exercise training increases fat oxidation in lean individuals during exercise and rest (Blaak & Saris, 2002; Poehlman, Gardner, Arciero, Goran, & Calles-Escandon, 1994; Romijn, Klein, Coyle, Sidossis, & Wolfe, 1993; van Baak, 1999). The capacity to mobilize and oxidize fat has been shown to be impaired, however, in overweight and obese and postobese people (body-mass index 30–40; van Baak). Several studies have examined the role of aerobic exercise training on resting substrate oxidation. These studies show mixed results, with exercise preventing the decrease in fat oxidation observed with weight loss (Nicklas, Rogus, & Goldberg, 1997; van Aggel-Leijssen, Saris, Hul, & van Baak, 2001) or having no effect on fat oxidation (Bumann, Astrup, & Christensen, 1992; Kanaley, Cryer, & Jensen, 1993; Toth & Poehlman, 1995; van Aggel-Leijssen, Saris, Hul, & van Baak, 2002). Similar to the response seen in the effects of exercise on RMR, the levels of body composition and weight loss are potential confounders when examining the influence of exercise on substrate utilization.

Although exercise is a key component of health-promotion programs, the data are unclear about the effect of regular long-term exercise on RMR, and little is known about the role of exercise training on fat and carbohydrate oxidation in previously sedentary individuals (van Baak, 2001). Furthermore, most of the prospective investigations employing an aerobic-exercise training model cited previously had small sample sizes and were of relatively short duration (8–20 weeks), with none

of the studies approaching the duration of the current investigation (68 weeks). With these considerations in mind, the purpose of the current investigation was to determine whether 16 months of supervised, verified moderate-intensity exercise training changes RMR and resting substrate oxidation in overweight and obese young adults who were consuming an ad libitum diet.

Methods

Participants

The participants in this experiment were part of the Midwest Exercise Trial, a large multiyear trial examining the effects of 16 months of exercise on body weight and body composition (Donnelly, Hill, et al., 2003). Initially, 131 overweight or moderately obese individuals were enrolled and randomized to either an exercise intervention or control condition for 16 months. Seventy-four participants completed the control (CON; women $n = 18$, men $n = 15$) or exercise (EX; women $n = 25$, men $n = 16$) conditions and all laboratory testing described in this article. All participants completed a health-history questionnaire and provided written informed consent in accordance with university guidelines for human experimentation. The participants were 17–35 years old, with body-mass indexes of 25.0–34.9 kg/m². Before beginning the study, the participants were sedentary and did not exceed 500 calories of physical activity per week as measured by a physical activity recall questionnaire (Blair et al., 1993). Exclusionary criteria included a history of chronic disease (e.g., diabetes, heart disease, etc.), elevated blood pressure (>140/90), elevated lipids (cholesterol >6.72 mmol/L, triglycerides >5.65 mmol/L), or elevated fasting glucose (>7.8 mmol/L). Participants were excluded if they were smokers, took medications that would affect physical performance or metabolism, or lacked the ability to perform the laboratory tests or participate in moderate-intensity exercise.

Research Design

Participants reported for testing at baseline and after 9 months and 16 months of exercise training. During testing the participants were measured for body mass, body composition, waist and hip circumferences, maximal oxygen consumption ($\text{VO}_{2\text{max}}$), and RMR. After baseline testing, the participants were randomized at approximately a 2:1 ratio (~65% to the exercise group and ~35% to the control group) under the supervision of a project investigator (D.J.J.). This assignment ratio was in anticipation of greater attrition in the exercise group than in the control group.

Maximal Oxygen Consumption

Participants performed a maximal graded exercise test (GXT) on a treadmill, with $\text{VO}_{2\text{max}}$ considered as the highest observed value during the GXT. Heart rate was recorded at 1-min intervals with an electrocardiograph, and blood pressures were recorded during the last 30 s of each 3-min stage. Expired air was measured for oxygen and carbon dioxide at 1-min intervals using a SensorMedics 2900 metabolic measurement cart. The system was calibrated before each test according to

the specifications of the manufacturer (SensorMedics Corp., Yorba Linda, CA). A test was considered maximal if any three of the four following criteria were achieved: a plateau in oxygen consumption with an increase in exercise intensity, a respiratory-exchange ratio (RER) ≥ 1.10 , a maximal heart rate within ± 10 beats per minute of age-predicted maximum, and the participant's reaching exhaustion (Duncan, Howley, & Johnson, 1997).

Assessment of Resting Metabolic Rate

The participants reported to the laboratory at 6:00 a.m. for measurement of RMR, having refrained from food or any liquids except water for 12 hr and from any exercise for 48 hr before testing. This time period has been shown to eliminate any residual effects from the most recent exercise session (Bahr, Inghes, Vaage, Sejersted, & Newsholme, 1987; Poehlman et al., 1989). After entering the laboratory the participants rested supine for 20 min. RMR was determined using a ventilated canopy-hood system and a SensorMedics 2900 metabolic cart calibrated according to the manufacturer's specifications. Each RMR test involved at least 30 min of measurement. The test was continued until at least three 5-min blocks of steady state were obtained. Steady state was defined as all minute values for ventilation (L/min) within 10%, nonprotein RER within 5%, and oxygen consumption within 10%. These 5-min blocks were then averaged, and RMR was determined using Weir's equation (1949). A test was repeated if the calculated RMR was more than 300 kcal different than predicted by the Harris-Benedict equation (Hunt & Groff, 1990).

Substrate Oxidation

Oxygen-consumption and nonprotein RER values obtained during the RMR were used to determine substrate oxidation. The following equations were used for carbohydrate and fat oxidation (Jequire, Acheson, & Schultz, 1987): CHO oxidation (g/min) = $VO_2 \times (RER - 0.707) / 0.293 \times 0.746$, and fat oxidation (g/min) = $VO_2 \times (1.0 - RER) / 0.293 \times 2.019$, where VO_2 is measured in liters per minute, 1.0 is RER for total carbohydrate oxidation, 0.293 is the difference between 1.0 and 0.707, the value of 0.707 is the RER for total fat oxidation, 0.746 is the number of liters of oxygen consumed per gram of glucose oxidized, and 2.019 is the number of liters of oxygen consumed per gram of triacylglycerol oxidized. Substrate oxidation was normalized to fat-free body mass.

Energy Intake

Dietary intake was ad libitum and was measured for energy and macronutrient composition at baseline, 9 months, and 16 months by weigh-and-measure techniques and by multiple-pass 24-hr recall procedures that used food models and standardized, neutral probing questions (Gibson, 1990). Results from the weigh-and-measure approach and from diet recalls were entered into a computerized nutrition database for analysis (ESHA, Research, Version 7.1, Salem, OR). The nutrition data are presented elsewhere (Donnelly, Kirk, et al., 2003) and not included in this article.

Intervention Program

Each participant's initial exercise prescription was calculated from the GXT at baseline. Exercise duration progressed from 20 min at baseline to 45 min at 6 months, and exercise intensity progressed from 60% of the heart-rate reserve at baseline to 75% at 6 months. This exercise duration and intensity were maintained for the remainder of the study. This level of exercise corresponded to 55–70% of $\text{VO}_{2\text{max}}$. The targeted minimum energy expenditure of exercise was ~400 calories per session (~2,000 kcal/week). This goal was gradually achieved during the first 6 months of training, and then participants performed moderate-intensity exercise for 45 min per day, 5 days per week for the duration of the study. This level of energy expenditure is in agreement with the recommendations of the American College of Sports Medicine (2001) for exercise programs designed for weight reduction, as well as the recent position statement regarding appropriate strategies for weight loss and prevention of weight regain for adults.

Exercise consisted primarily of walking on motor-driven treadmills; however, alternative activities such as stationary biking and walking on stationary elliptical trainers were allowed for 20% of the total exercise sessions (1 out of 5 days). All exercise was performed under direct supervision of research personnel. Exercise intensity was verified during each exercise session by use of a Polar heart-rate monitor (Accurex Plus). To document the level of energy expenditure achieved during the exercise sessions, energy expenditure was measured during at least two exercise sessions by indirect calorimetry at ~4-month intervals. In addition to measuring the energy expenditure of exercise, a maximal GXT was completed at baseline and 4, 9, and 12 months to allow for adjustments of the exercise prescription as changes in $\text{VO}_{2\text{max}}$ occurred.

Participants in the control group participated in the same testing as the exercise group, with the exception of the additional GXTs performed at 4 and 12 months. The participants were instructed to maintain their usual physical activity and dietary intake patterns throughout the study.

Statistical Analysis

Descriptive statistics were calculated at each assessment period for all dependent measures. A three-factor (Group \times Gender \times Time) analysis of variance (ANOVA) with repeated measures on time was used to examine interactions and main effects using body-weight change as a covariate. When appropriate, Tukey's means separation was used as a post hoc test. Significance was set at $p < .05$. All analyses were performed using SAS (Version 8.2, Cary, NC).

Results

Exercise Adherence

There were no baseline differences for age, body weight, body-mass index, body composition, or $\text{VO}_{2\text{max}}$ between participants who completed the study and those who terminated participation. Reasons for termination generally included lack of

time, unwillingness to take meals in the university cafeteria, and conflict with work. In addition, participants were released from the study if adherence fell below 85% of the scheduled exercise sessions. Participants who completed the study included 1 Native American, 5 Asians, 6 African Americans, 1 Hispanic, and 61 Whites. Adherence to the exercise protocol was $90.3\% \pm 2\%$ and $89.6\% \pm 2\%$ of the total sessions completed for men and women, respectively.

Body Mass, Body Composition, and Maximal Oxygen Consumption

No statistically significant differences for either men or women were found at baseline between EX and CON for body weight, body-mass index, percent body fat, fat mass, or fat-free mass (Table 1). The body-weight and body-composition changes have been reported and discussed previously (Donnelly, Hill, et al., 2003). Table 2 shows the changes over the 16 months of the investigation. Briefly, for men, exercise resulted in significant decreases in body mass, body-fat percentage, and fat mass at 9 months, with no further reduction at 16 months. The EX men had significantly lower body mass, body-fat percentage, and fat mass at 16 months than the CON men. The EX men had significant decreases in both waist and hip circumference at 9 months with no further change, whereas the CON men had no significant changes. $\text{VO}_{2\text{max}}$ was significantly higher after 9 months for EX, and the 16-month value was significantly different for EX men compared with CON men.

EX women remained weight stable (0.6 ± 3.8 kg) over the 16-month study period while the CON women gained a significant amount of weight (2.9 ± 5.5 kg). A nonsignificant decrease in fat mass of 0.3 ± 2.7 kg was observed for the EX women, and a significant increase of 2.1 ± 4.8 kg of fat mass was observed for CON women. At 16 months, the EX women had significantly lower body weight and fat mass than CON. EX and CON women had small, nonsignificant increases

Table 1 Baseline Characteristics of the Participants

	Women		Men	
	Control (n = 18)	Exercise (n = 25)	Control (n = 15)	Exercise (n = 16)
Age (years)	21 ± 4	24 ± 5	24 ± 4	22 ± 4
Height (cm)	165.2 ± 6.6*	163.5 ± 6.7*	180.2 ± 6.6	177.7 ± 9.5
Weight (kg)	80.2 ± 8.1*	76.9 ± 11.3*	94.7 ± 11.4	94.6 ± 12.4
Body-mass index (kg/m ²)	29.3 ± 2.3	28.7 ± 3.2	29.0 ± 3.0	29.7 ± 2.9
Body fat (%)	36.7 ± 4.0*	35.3 ± 4.6*	26.8 ± 4.6	28.3 ± 4.6
Fat weight (kg)	29.4 ± 5.1*	27.4 ± 7.1*	25.5 ± 6.8	26.8 ± 6.8
Fat-free weight (kg)	50.5 ± 4.6*	49.5 ± 5.8*	68.6 ± 6.4	67.1 ± 8.3
$\text{VO}_{2\text{peak}}$ (mL · kg ⁻¹ · min ⁻¹)	32.4 ± 3.1*	32.8 ± 4.2*	39.5 ± 5.7	39.2 ± 5.2

Note. Values are $M \pm SD$. There were no significant differences within genders or between groups.

*Significant difference between genders within the exercise and control groups.

Table 2 Body Mass and Composition, Maximal Oxygen Consumption, and Resting Metabolic Rate for Women and Men Over 16 Months of Exercise or Control Conditions

	Women		Men	
	Control (n = 18)	Exercise (n = 25)	Control (n = 15)	Exercise (n = 16)
Body mass (kg)*				
baseline	79.9 ± 8.1 ^a	77.0 ± 11.4	94.1 ± 11.4	94.0 ± 12.6 ^a
9 months	81.8 ± 8.4 ^b	77.1 ± 12.5	92.9 ± 11.0	88.7 ± 9.7 ^b
16 months	82.8 ± 9.2 ^{b†}	77.6 ± 12.8	93.6 ± 11.6 [†]	88.8 ± 9.5 ^b
Body fat (%)*				
baseline	36.7 ± 4.0	35.3 ± 4.6	26.8 ± 4.6	28.3 ± 4.6 ^a
9 months	37.9 ± 4.4	35.4 ± 4.8	26.4 ± 5.5	24.5 ± 3.9 ^b
16 months	37.8 ± 4.5 [†]	34.5 ± 4.5	25.9 ± 6.2 [†]	24.6 ± 5.1 ^b
Fat mass (kg)*				
baseline	29.4 ± 5.1 ^a	27.4 ± 7.1	25.5 ± 6.9	26.8 ± 6.8 ^a
9 months	31.2 ± 5.9 ^b	27.7 ± 7.8	24.9 ± 7.4	21.8 ± 4.5 ^b
16 months	31.6 ± 6.4 ^b	27.2 ± 7.9	24.8 ± 8.1 [†]	21.9 ± 5.5 ^b
Fat-free mass (kg)*				
baseline	50.5 ± 4.6	49.6 ± 5.8	68.6 ± 6.4	67.1 ± 8.3
9 months	50.6 ± 4.6	49.4 ± 5.7	68.0 ± 5.8	66.9 ± 7.6
16 months	51.2 ± 4.5	50.4 ± 5.8	68.9 ± 5.9	66.9 ± 7.8
Waist circumference (cm)				
baseline	108.3 ± 6.2 ^a	109.0 ± 8.2	107.5 ± 6.7	110.8 ± 6.8 ^a
9 months	110.8 ± 6.6 ^{b*}	107.7 ± 7.8	106.3 ± 5.6	106.5 ± 5.8 ^b
16 months	111.0 ± 6.8 ^{b*}	108.1 ± 8.5	106.9 ± 5.3	106.6 ± 5.8 ^b
Hip circumference (cm)				
baseline	85.7 ± 5.3 ^{a*}	81.6 ± 7.2 [*]	94.0 ± 6.6	94.4 ± 7.3 ^b
9 months	87.2 ± 5.3 ^{b*}	80.7 ± 8.0 [*]	92.8 ± 7.6	89.7 ± 5.5 ^b
16 months	87.8 ± 6.6 ^{b*}	81.7 ± 8.4 [*]	93.5 ± 7.2	89.6 ± 6.6 ^a
VO ₂ (L/min)*				
baseline	2.52 ± 0.32	2.53 ± 0.32 ^a	3.67 ± 0.50	3.67 ± 0.62 ^a
9 months	2.67 ± 0.33	2.99 ± 0.42 ^b	4.00 ± 0.69	4.36 ± 0.55 ^b
16 months	2.71 ± 0.24 [†]	3.03 ± 0.42 ^b	4.03 ± 0.55 [†]	4.34 ± 0.58 ^b
Resting metabolic rate (kcal/day)*				
baseline	1,594 ± 189	1,583 ± 221 ^a	2,015 ± 205	1,995 ± 184 ^a
9 months	1,682 ± 307	1,692 ± 230 ^b	2,087 ± 201	2,025 ± 209 ^a
16 months	1,707 ± 232	1,715 ± 238 ^b	2,089 ± 221	2,124 ± 270 ^b

Note. Values are $M \pm SD$. Means with the same superscript are not different within group, $p > .05$.

*Between-gender difference within group for all periods. †Between-group difference within gender.

in fat-free mass of 0.8 ± 1.8 kg and 0.7 ± 1.7 kg, respectively. The EX women had no significant changes in waist or hip circumference over 16 months, whereas the CON women had a significant increase in both waist and hip circumference. EX women significantly increased their $\text{VO}_{2\text{max}}$ by 9 months, and the 16-month value was significantly higher than that of the CON women at 16 months.

Resting Metabolic Rate

RMR increased significantly by 174 ± 243 kcal/day for EX men and 129 ± 154 kcal/day for EX women from baseline to 16 months (Table 2). There were no significant changes in RMR for the CON men or CON women over the 16 months. RMR expressed per kilogram of fat-free mass per day increased by 1.98 ± 2.6 for EX men and 1.33 ± 3.6 for EX women (Figure 1). There were no significant changes in RMR expressed per kilogram of fat-free mass per day for the CON men or CON women over the 16 months.

Substrate Oxidation

There were no significant group differences over the 16 months for either fat or carbohydrate oxidation when expressed as g/min or g/period in EX or CON men or EX or CON women (Table 3). There was a nonsignificant ($p = .08$) increase of ~60% from baseline to 16 months in carbohydrate oxidation expressed as g/min and g/period in the EX women. At baseline there were significant differences between the EX men and women for carbohydrate oxidation expressed as g/min and g/period. There were significant differences between EX men and women

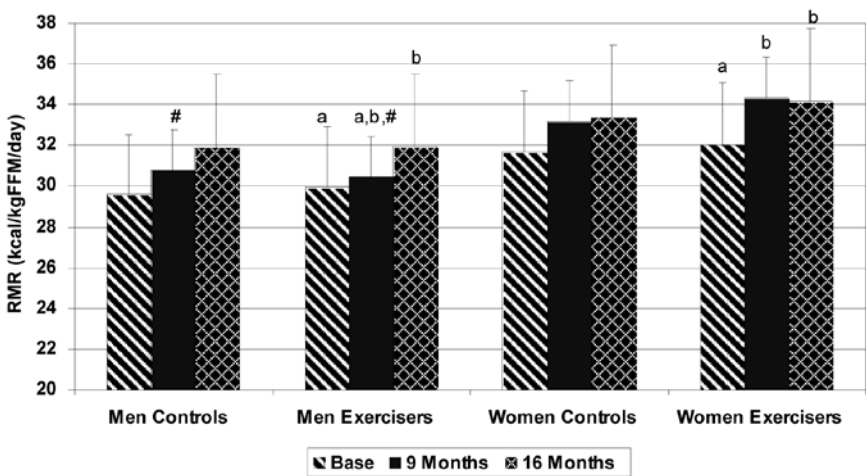


Figure 1 — Resting metabolic rate expressed as kilocalories used per kilogram of fat-free mass per day across 16 months for men and women. Values are $M \pm SD$. Means with the same superscript are not different within group, $p > .05$. #Between-gender difference within group. No between-group differences within gender.

Table 3 Fat and Carbohydrate Oxidation Over 16 Months for Women and Men Controls and Exercisers

	Women		Men	
	Control (<i>n</i> = 18)	Exercise (<i>n</i> = 25)	Control (<i>n</i> = 15)	Exercise (<i>n</i> = 16)
Fat oxidation (g/min)				
baseline	0.089 ± 0.027	0.090 ± 0.024	0.102 ± 0.029	0.103 ± 0.026
9 months	0.097 ± 0.026	0.095 ± 0.026	0.110 ± 0.022	0.107 ± 0.031
16 months	0.094 ± 0.032	0.085 ± 0.031*	0.114 ± 0.036	0.109 ± 0.043
Fat oxidation (g/period)				
baseline	1.330 ± 0.404	1.353 ± 0.355	1.537 ± 0.440	1.540 ± 0.386
9 months	1.457 ± 0.397	1.424 ± 0.391	1.653 ± 0.332	1.600 ± 0.467
16 months	1.403 ± 0.474	1.273 ± 0.469*	1.707 ± 0.537	1.640 ± 0.649
Carbohydrate oxidation (g/min)				
baseline	0.069 ± 0.053*	0.063 ± 0.064*	0.112 ± 0.062	0.107 ± 0.075
9 months	0.064 ± 0.069	0.071 ± 0.046	0.105 ± 0.048	0.103 ± 0.056
16 months	0.077 ± 0.058	0.100 ± 0.072	0.115 ± 0.073	0.114 ± 0.075
Carbohydrate oxidation (g/period)				
baseline	1.031 ± 0.790*	0.941 ± 0.961*	1.676 ± 0.930	1.612 ± 1.118
9 months	0.955 ± 1.033	1.065 ± 0.696	1.582 ± 0.716	1.544 ± 0.834
16 months	1.158 ± 0.877	1.507 ± 1.083	1.731 ± 1.092	1.716 ± 1.129

Note. Values are $M \pm SD$. Period is designated as 15 min of steady state measured during the resting-metabolic-rate test.

*Between-genders difference within group, $p < .05$. No significant difference across time within group, $p > .05$. No significant difference between groups within gender, $p > 0.05$.

for fat oxidation expressed as g/min and g/period at 16 months. For CON, there were significant differences between men and women for carbohydrate oxidation expressed as g/min and g/period.

There were no significant differences within genders over the 16 months for either fat oxidation (Figure 2) or carbohydrate oxidation (Figure 3) expressed as $\text{g} \cdot \text{min}^{-1} \cdot \text{kg FFM}^{-1}$ in EX or CON men or women. The EX women, however, had a nonsignificant increase in carbohydrate oxidation of 57% from baseline to 16 months. There was a significant difference for fat oxidation expressed as $\text{g} \cdot \text{min}^{-1} \cdot \text{kg FFM}^{-1}$ at 9 months between men (0.00159 ± 0.00038) and women (0.00191 ± 0.00042) in the EX group, as well as between men (0.00162 ± 0.00026) and women (0.00192 ± 0.00048) in the CON group. There were no other significant differences between genders for either the EX or the CON group.

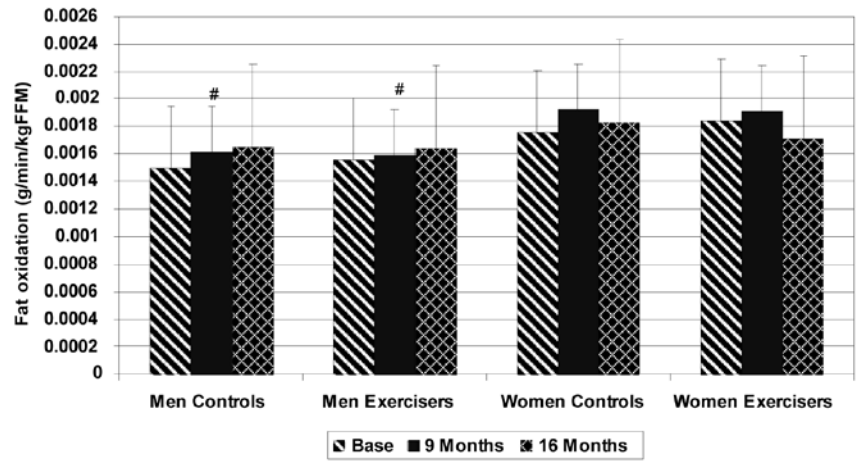


Figure 2 — Grams of fat oxidized per minute per kilogram of fat-free mass over 16 months for men and women. Values are $M \pm SD$. No significant difference within group or gender across time. #Between-genders difference within group. No between-groups differences within gender.

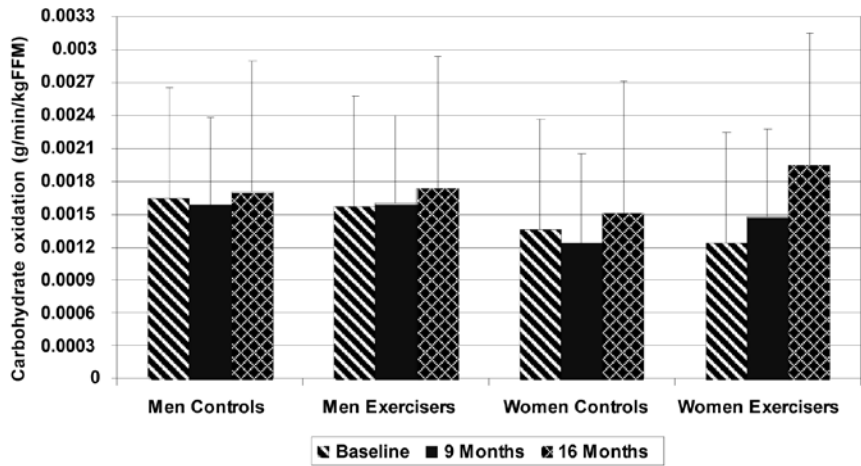


Figure 3 — Grams of carbohydrate oxidized per minute per kilogram of fat-free mass over 16 months for men and women. Values are $M \pm SD$. No significant difference within group or gender across time. No between-groups differences within gender.

Discussion

The effect of aerobic exercise training on RMR has received considerable attention in part because of the potential increase in daily energy expenditure that could be derived from an elevation in RMR. Increased daily energy expenditure has sig-

nificant implications for weight management, particularly in individuals interested in preventing weight gain or promoting weight loss. A significant finding of the current investigation is that 9 months of moderate-intensity aerobic exercise training increased RMR in both men and women, and this increase was maintained throughout the 16-month study. Of particular importance is that the increase in RMR occurred with (EX men) and without (EX women) weight loss.

Previous investigations of exercise training and RMR have produced mixed results. RMR has been shown to increase with exercise training (Ballor & Poehlman, 1992; Berke et al., 1992; Broeder et al., 1992; Poehlman et al., 1992; Toth & Poehlman, 1995; Tremblay et al., 1986; Whatley et al., 1994), remain unchanged (Keytel et al., 2001; Meredith et al., 1989; Sjodin et al., 1996; Volpe et al., 2001; Wilmore et al., 1998), or decrease slightly (Byrne & Wilmore, 2001; Santa-Clara et al., 2006). A key issue affecting any change in RMR is the change in fat-free mass. There are, however, other factors that could cause an increase in RMR after exercise training with and without weight loss. These factors include increases in the concentrations of metabolic hormones (e.g., cortisol, catecholamines, growth hormone, thyroid hormone), increased activity of various enzymatic reactions and shuttle systems, increased substrate flux, repair of exercise-induced trauma to tissues, and increased protein synthesis (Ballor & Poehlman, 1992; Dolezal & Potteiger, 1998). We believe that several of these factors might have contributed to the increase in RMR observed in the EX men despite the concurrent weight loss. It is also interesting to note that many of the body-weight and -composition measures (Table 2) for the EX men showed significant improvement after 9 months of exercise and then no further change, while the RMR continued to increase through the 16 months of moderate-intensity exercise training. This is clearly an area that warrants further investigation.

The increase in RMR in EX women is consistent with previous research demonstrating increased RMR after aerobic exercise training (Ballor & Poehlman, 1992; Berke et al., 1992; Broeder et al., 1992; Poehlman et al., 1992; Toth & Poehlman, 1995; Tremblay et al., 1986; Whatley et al., 1994). It is interesting to note that the EX women did not lose weight despite the increase in RMR. Because our nutrition-intake data (Donnelly, Kirk, et al., 2003) show no change in self-selected energy intake, we believe that the EX women might have reduced their level of overall physical activity in response to the 5-days-per-week, 45-min-per-session exercise program. This is also an area that warrants further investigation.

Although aerobic exercise training has been shown to increase fat oxidation during exercise, its influence on resting substrate metabolism is less clear. Studies have shown aerobic exercise training to increase fat oxidation (Calles-Escandon, Goran, O'Connell, Nair, & Danforth, 1996; Morio et al., 1999; Poehlman et al., 1994), prevent the decrease in fat oxidation observed with weight loss (Nicklas et al., 1997; van Aggel-Leijssen et al., 2001), or have no effect on fat oxidation (Buemann et al., 1992; Kanaley et al., 1993; Toth & Poehlman, 1995; van Aggel-Leijssen et al., 2002). A number of confounding factors have played a role in the ability to determine whether aerobic exercise training influences resting substrate oxidation. These factors include but are not limited to age, training status, duration of the training program, the level of overweight or obesity, and the amount of weight loss. Readers are referred to an excellent review of these factors by Blaak and Saris (2002).

Overweight individuals do not spare carbohydrates in favor of fat oxidation despite long-term exercise training. With chronic aerobic exercise training, it is believed that fuel utilization at rest will shift to a greater percentage of fat oxidation than carbohydrate oxidation (Goodpaster, Katsiaras, & Kelley, 2003; van Baak, 1999). The mechanisms responsible for this adaptive response to training, however, are not fully understood (Romijn et al., 1993). Randle et al. (1998, 1965) proposed the glucose–fatty-acid cycle to explain the reciprocal relationship between carbohydrate and fat metabolism. The suggested mechanisms were based on the premise that an increase in fatty-acid availability would result in increased fat metabolism and inhibition of carbohydrate metabolism. There might, however, be a limiting factor to the mobilization or oxidation of plasma fatty acids and intramuscular triglycerides in overweight and obese individuals (Kanaley et al., 1993; Kim, Hickner, Cortright, Dohm, & Houmard, 2000) that is not present in lean individuals (Kelly, Goodpaster, Wing, & Simoneau, 2000).

There might be a decrease in fatty-acid mobilization from adipocytes that might be caused by hormonal factors. It has been suggested that hormone-sensitive lipase (HSL) is the rate-limiting step in the mobilization of fatty acids from adipose tissue (Jeukendrup, Saris, & Wagenmakers, 1998). Studies have failed to demonstrate increased HSL and basal lipolytic rate in adipose tissue from obese individuals (Lewis, Carpentier, Adeli, & Giacca, 2002) or resistance to insulin's suppressive effect on HSL (Large & Arner, 1998). Several studies have actually demonstrated that the sensitivity or maximum insulin-induced inhibition of lipolysis was greater in obese individuals than in normal-weight controls before and after exercise (Arner, Bolinder, Engfeldt, Hellmer, & Ostman, 1984; Bolinder, Lithell, Skarfors, & Arner, 1986; Kelly et al., 2000; Lewis et al.). Confusion regarding whether HSL activity in individual adipocytes is actually resistant to the suppressive effect of insulin arises, because when normalized per total body fat, lipolysis appears in fact to be normal or reduced in obese individuals (Campbell, Carlson, & Nurjhan, 1994; Groop et al., 1992). It has also been demonstrated that exercise does not alter this effect without significant weight loss (Kelly & Goodpaster, 1999). In the current study the EX men lost ~6% of body weight while the exercising women did not lose any weight. Therefore, exercise by itself and without weight loss might not induce significant enzymatic or hormonal changes in the adipocytes or muscle that would allow for an increased oxidation of fat at rest.

It has also been demonstrated that muscle from obese individuals has a reduced capacity for uptake and oxidation of fatty acids derived from the plasma pool (Blaak et al., 2000) that could be attributed to defects of fatty-acid oxidation. Impaired muscle-fat oxidation could also be the result of excessive chronic exposure to fatty acids (Bavenholm, Pignon, Saha, Ruderman, & Efendic, 2000). Other potential determinants might be the patterns of expression of various fatty-acid-binding proteins (Bonen, Dyck, Ibrahim, & Abumrad, 1999) or a decrement in the activities of enzymes indicative of muscle mitochondrial content in obese human skeletal muscle (Kelley, Goodpaster, Wing, & Simoneau, 1999). Relatively little is known at present, however, concerning human skeletal muscle and the effect of obesity with or without engaging in long-term exercise. It could be assumed that 16 months of aerobic exercise should have provided the necessary stimulus to increase the capacity for uptake and oxidation of FA derived from the plasma pool regardless of the amount of weight loss. This type of response would be similar to that observed

in lean individuals (Blaak & Saris, 2002). The fact that we observed weight loss in EX men and no weight loss in EX women but no change in fat oxidation in either group was unexpected and warrants further investigation.

A limitation to the current investigation is that macronutrient content was not tightly controlled before measurement of RMR and substrate oxidation. Several studies have demonstrated that the macronutrient content of dietary intake can influence substrate oxidation by promoting a shift in fat and carbohydrate oxidation (Roy et al., 1998; Verboeket-Van De Venne, Westerterp, Hermans-Limpens, & de Graaf, 1996). High-fat diets increase resting fat oxidation, whereas high-carbohydrate diets increase resting carbohydrate oxidation. In the current investigation, no measures of dietary intake were made during the 24 hr preceding the measurement of RMR and substrate oxidation. It is possible that some participants consumed meals high in fat or carbohydrate, thereby affecting substrate oxidation. Our long-term data, however, support a consistent and stable dietary intake by the participants across the 16 months of the study (Donnelly, Kirk, et al., 2003). Consequently, we believe that the RMR and substrate-oxidation data were not influenced by pronounced and acute changes in dietary intake. A second limitation to the current study's design is that not all women were measured for RMR and substrate oxidation at similar stages of the menstrual cycle, and this could have influenced the results observed.

In conclusion, regular moderate-intensity exercise in healthy, previously sedentary, overweight adult men and women increases RMR but does not alter resting fat or carbohydrate oxidation. Women tend to have a higher RMR and greater fat oxidation, when expressed per kilogram fat-free mass, than men. The increase in RMR as a result of exercise has important implications for weight management. The dose of exercise used in the current investigation is consistent with recommendations for inducing weight loss and preventing weight gain (American College of Sports Medicine, 2001). Many Americans, however, do not meet these current guidelines. If long-term exercise has the added effect of altering resting metabolism, this can be an additional benefit derived from regular moderate-intensity exercise. Additional study is warranted to further elucidate the role of exercise and weight loss in altering resting substrate oxidation.

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