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Short-term effects of weight loss with or without low-intensity exercise training on fat metabolism in obese men¹⁻³

Dorien PC van Aggel-Leijssen, Wim HM Saris, Gabby B Hul, and Marleen A van Baak

ABSTRACT

Background: Energy restriction is known to induce a decline in fat oxidation during the postdiet period. Reduced fat oxidation may contribute to weight regain.

Objective: The present study investigated the effect of the addition of low-intensity exercise training to energy restriction on postdiet fat oxidation and on the contribution of the sympathetic nervous system to fat oxidation.

Design: Forty obese men were divided randomly into 2 groups: diet (D) and diet plus exercise (DE). Both groups followed an energy restriction program for 10 wk. Subjects in the DE group also participated in a low-intensity exercise training program [40% maximal oxygen uptake ($\dot{V}O_{2max}$)] for 12 wk. Before the intervention and after 12 wk, with subjects at stable body weights, we measured body composition, $\dot{V}O_{2max}$, and substrate oxidation at rest, during exercise at 50% $\dot{V}O_{2max}$, and during recovery. Measurements were made with and without administration of the β -adrenergic antagonist propranolol.

Results: Both interventions led to significant decreases in body weight, fat mass, and fat-free mass ($P < 0.001$); these decreases did not differ significantly between the D and DE groups. Neither intervention significantly affected $\dot{V}O_{2max}$. The effect of the intervention on the respiratory exchange ratio differed significantly between the D and DE groups [two-way analysis of variance (ANOVA), $P < 0.05$]. The effect on the β -adrenergic-mediated respiratory exchange ratio tended to be different between the 2 groups (two-way ANOVA, $P = 0.09$).

Conclusion: Addition of low-intensity exercise training to energy restriction counteracts the decline in fat oxidation during the postdiet period. *Am J Clin Nutr* 2001;73:523-31.

KEY WORDS Propranolol, sympathetic nervous system, respiratory exchange ratio, β -adrenergic antagonist, exercise training, obesity, overweight, obese men, weight loss, weight reduction, fat oxidation, energy restriction, low-energy diet, low-calorie diet

INTRODUCTION

Obesity is a risk factor for the development of cardiovascular diseases (1) and type 2 diabetes (2). The prevalence of obesity is increasing in both the United States (3) and Europe (4) and obesity has been identified as a serious health problem. A common treatment for obesity is energy restriction. Although this treat-

ment is usually effective in achieving short-term weight loss, there is a high rate of weight regain over the long term (5-8).

The poor long-term outcome of energy restriction may be a result of metabolic adaptations to weight loss in obese persons. Body weight reduction was shown to decrease fat oxidation (9) and resting metabolic rate (10-13) after body weight had stabilized. A negative relation between weight gain and either resting metabolic rate or fat oxidation in obese subjects was suggested by some studies (14, 15) but not by others (16, 17).

We found previously that low-intensity exercise training in obese men increases fat oxidation (18). Therefore, low-intensity exercise training might be able to prevent the decline in fat oxidation that occurs after weight loss. Previous studies reported that addition of exercise training to energy restriction prevents the post-weight-loss decline in fat oxidation in obese women at rest (9), but not during exercise at a workload of 30 W (19). Although Nicklas et al (9) used low-intensity exercise training, they did not report on fat oxidation during exercise. Selecting an exercise training program of low intensity could improve compliance and reduce the risk of musculoskeletal injuries in obese subjects (20). Therefore, the first aim of the present study was to investigate whether low-intensity exercise training can prevent the post-weight-loss decline in fat metabolism during rest and exercise in obese subjects after stabilization of body weight.

Our second aim was to study the effects of weight loss and exercise training on the role of the sympathetic nervous system in the regulation of fat oxidation. To our knowledge, no data are available on the effect of exercise training in combination with diet-induced weight loss on β -adrenergic-mediated fat metabolism. The results of studies on the effect of β -adrenergic stimulation on relative fat oxidation after weight loss are inconsistent (21, 22). Exercise training was found to increase β -adrenergic-mediated fat metabolism

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TABLE 1Subject characteristics before and after the intervention in the diet (D) group ($n = 17$) and the diet plus exercise (DE) group ($n = 20$)¹

	D group		DE group	
	Before	After	Before	After
Age (y) ²	38.6 ± 6.5	—	39.3 ± 7.7	—
Body weight (kg) ²	103.5 ± 11.0	88.8 ± 9.5	101.9 ± 11.2	86.7 ± 9.3
BMI (kg/m ²) ²	32.0 ± 2.1	27.5 ± 1.8	32.6 ± 2.5	27.8 ± 2.5
Body fat (%) ²	34.6 ± 4.9	25.9 ± 6.1	33.5 ± 4.2	25.0 ± 5.0
FFM (kg) ²	67.6 ± 9.3	65.6 ± 8.2	67.7 ± 8.1	65.0 ± 7.8
Fat mass (kg) ²	35.8 ± 6.1	23.2 ± 6.6	34.2 ± 6.1	21.7 ± 5.2
$\dot{V}O_2$ max (mL/min)	2994 ± 373	2903 ± 412	2949 ± 508	2906 ± 445
$\dot{V}O_2$ max/FFM (mL·min ⁻¹ ·kg ⁻¹)	44.7 ± 5.8	44.5 ± 6.2	43.4 ± 4.5	44.6 ± 4.0

¹ $\bar{x} \pm$ SD. FFM, fat-free mass; $\dot{V}O_2$ max, maximal oxygen uptake. There were no significant time \times group interactions (two-way ANOVA).²Significant time effect, $P < 0.001$ (two-way ANOVA).

in adipose tissue from obese subjects in vitro (23) and in situ (24), but no in vivo data are available. Therefore, the present study also investigated the effect of weight loss with or without exercise training on the contribution of the β -adrenergic nervous system to fat oxidation.

SUBJECTS AND METHODS

Subjects

Forty obese men participated in this study; they were recruited with an advertisement in a local newspaper. All subjects were in good health as assessed by a medical history and physical examination. The subjects did not spend >2 h/wk in sports activities and did not have physically demanding jobs. All subjects had stable body weights (<3 kg change) over the past 3 mo and did not take any medications known to influence the variables measured. Subjects were divided randomly into 2 groups, the diet (D) group and the diet plus exercise (DE) group, after matching in pairs with respect to age, body mass index (BMI), percentage body fat, weight, and maximal oxygen uptake ($\dot{V}O_2$ max). The study protocol was approved by the Ethics Committee of Maastricht University. Written, informed consent was obtained from all subjects.

Three subjects in the D group did not complete the weight-loss intervention; the reasons were illness (enteritis) for 1 subject and lack of motivation for 2 subjects. Characteristics of the remaining study population are shown in **Table 1**.

Experimental design

All subjects in the D and DE groups participated in an energy restriction program for 10 wk. Twenty subjects (DE group) also participated in a low-intensity exercise training program for 12 wk, starting at the beginning of the energy restriction period and continuing for 2 wk after it ended. Before the start of the intervention program and after 12 wk, we measured body composition, maximal aerobic capacity, basal metabolic rate, and energy and substrate metabolism at rest and during exercise with and without administration of a nonselective β -adrenergic antagonist.

Diet

During the first 6 wk of energy restriction, subjects received a very-low-energy diet (Modifast; Novartis Nutrition, Breda, Netherlands). This protein-enriched formula diet provided 2.1 MJ, 50 g carbohydrate, 52 g protein, and 7 g fat daily; the micronutrient contents met the Dutch recommended daily

allowance (25). This type of diet is commonly used in weight-reduction studies that result in weight losses of ≈ 1.5 –2.0 kg/wk (26, 27). From week 7 until week 10, subjects increased their energy intake gradually; they received less of the formula diet and were instructed to supplement this with foods of their choice. In weeks 7 and 8, subjects received 1.4 MJ/d of the formula diet and supplemented this with up to ≈ 3.5 MJ energy from foods of their choice. In weeks 9 and 10, they received 0.7 MJ/d of the formula diet and supplemented this with up to ≈ 4.9 MJ energy from foods. From week 7 until week 10, subjects were asked to keep a food diary. In weeks 11 and 12, subjects were instructed to return to energy balance to stabilize their body weights. They completed a 3-d food diary during 2 weekdays and 1 weekend day at the end of week 11. This diary was used only for discussion with the subject; dietary advice was provided to change eating habits if necessary. During the entire 12 wk, subjects came to the laboratory once a week for body weight measurements and dietary advice.

Exercise training

Subjects in the D group were instructed to maintain their habitual activity patterns without making changes during the study. Subjects in the DE group participated in an exercise training program for 12 wk. They trained 4 times/wk for 1 h each time. Three of these sessions were at the laboratory under the supervision of a professional trainer and the other session was at home. The exercise training program consisted of cycling on an ergometer (Bodyguard Cardiocycle; Bodyguard, Sandnes, Norway or Excalibur; Lode, Groningen, Netherlands), walking, and aqua-jogging (jogging and doing exercises in 1-m-deep water). All of the exercises were performed at a low intensity (40% $\dot{V}O_2$ max). The heart rate corresponding to 40% $\dot{V}O_2$ max was determined during an incremental cycle ergometer test (*see* section on maximal aerobic capacity, below). Training intensity was checked by monitoring heart rate during the laboratory training sessions (Polar Electro, Oy, Finland). Subjects were instructed to engage in low-intensity endurance exercise once a week at home. The subjects' attendance at the training sessions was recorded and the trainer asked subjects regularly about the exercises performed at home.

Measurements

Body composition

Body weight was measured on a digital balance accurate to 0.1 kg (model D-7470; Sauter, Ebingen, Germany). Height was measured to the nearest 0.1 cm with a wall-mounted stadiometer

(model 220; Seca, Hamburg, Germany). BMI was calculated from weight and height (kg/m^2). Body density was measured by hydrostatic weighing with a correction for residual lung volume, which was estimated by helium dilution with a spirometer (Volu-graph 2000; Mijnhardt, Bunnik, Netherlands) at the moment of underwater weighing. Body composition was calculated according to the formula of Siri (28).

Maximal aerobic capacity

$\dot{V}\text{O}_2\text{max}$ during cycling exercise was determined for each subject by an incremental exercise test on an electromagnetically braked cycle ergometer (Excalibur; Lode). After a warm-up period of 5 min at 80 W, workload was increased every 4 min by 40 W until the subject was exhausted. During the experiment, ventilatory and gas exchange responses were measured continuously with indirect calorimetry (Oxycon β ; Mijnhardt). Heart rate was recorded continuously by electrocardiography. The highest oxygen uptake achieved over 30 s was used as the $\dot{V}\text{O}_2\text{max}$.

Physical activity

Habitual physical activity was estimated before the intervention and after 12 wk by using the Baecke questionnaire (29). This questionnaire is subdivided into physical activity at work, sports during leisure time, and physical activity excluding sports during leisure time.

Energy and substrate metabolism

The effect of weight loss with or without exercise training on energy and substrate metabolism at rest and during exercise was determined when subjects were weight stable before and after the intervention. Experiments were performed 36–65 h after the last exercise session in a room with an ambient temperature of 23–25°C. After an overnight fast, subjects came to the laboratory by car or public transportation to minimize physical activity. A catheter was inserted in an arm vein for blood sampling. Subjects remained in a semisupine position for 30 min and subsequently cycled on an ergometer (Excalibur; Lode) for 45 min at 50% of their preintervention $\dot{V}\text{O}_2\text{max}$. After cycling, subjects recovered in a semisupine position for 15 min.

During the experiment, carbon dioxide production, oxygen consumption, and the respiratory exchange ratio (RER; carbon dioxide production/oxygen consumption) were determined with an open-circuit ventilated hood system (Oxycon β ; Mijnhardt). Energy expenditure was calculated according to the formula of Weir (30). During exercise, subjects used a mouthpiece. For the subjects' convenience, measurements were conducted only from $t = 10$ –15, 25–30, and 40–45 min. The accuracy of the system for measurements of carbon dioxide production and oxygen consumption was tested regularly by combustion of a known amount of ethanol and was found to be $\geq 95\%$. During the experiment, heart rate was recorded continuously by electrocardiography. Blood was sampled after 30 min of rest ($t = 0$); after 5, 15, 30, and 45 min of cycling; and after 15 min of recovery. The blood sample was divided into chilled 10-mL tubes containing EDTA or 300 μL glutathione (45 $\mu\text{g}/\text{L}$ saline) plus heparin. Blood was then immediately centrifuged at $800 \times g$ for 10 min at 4°C. Plasma was stored at -80°C until analyzed. The blood containing EDTA was used for analyses of plasma glucose, free fatty acid (FFA), insulin, glycerol, and lactate concentrations. Blood containing heparin and glutathione was used for analyses of plasma epinephrine and norepinephrine concentrations.

β -Adrenergic receptor-mediated energy and substrate metabolism

The same experiment described above was conducted on another day with infusion of the nonselective β -antagonist propranolol (Zeneca BV, Ridderkerk, Netherlands). An extra catheter was inserted in a vein of the contralateral arm for propranolol infusion. Propranolol was infused with a Harvard syringe pump in a dosage of $0.71 \mu\text{g} \cdot \text{kg fat-free mass}^{-1} \cdot \text{min}^{-1}$ after a priming dose of $229.4 \mu\text{g}/\text{kg fat-free mass}$; the latter was administered over a period of ≥ 10 min. During the experiment, we measured blood pressure every 10 min and heart rate continuously by electrocardiography. The infusion was stopped when the heart rate had reached 45 beats/min. The tests with and without propranolol infusion were performed in random order.

Biochemical analyses

Plasma concentrations of FFAs (NEFA C kit; Wako Chemicals, Neuss, Germany), glucose (GLUC HK kit; Hoffmann-La Roche, Basel, Switzerland), glycerol (glycerol kit; Boehringer Mannheim, Mannheim, Germany), and lactate (31) were measured on a COBAS FARA centrifugal spectrophotometer (Roche Diagnostica, Basel, Switzerland). Standard samples with known concentrations were included in each run for quality control. Plasma insulin concentrations were measured with a double-antibody radioimmunoassay (Insulin RIA 100; Pharmacia, Uppsala, Sweden). For the test without propranolol infusion, plasma epinephrine and norepinephrine concentrations were analyzed by HPLC with electrochemical detection (32).

Statistical analyses

The data are expressed as means \pm SDs. Data were analyzed with STATVIEW (SAS Institute Inc, Cary, NC). Because fat-free mass decreased significantly during the intervention in both groups, data on energy expenditure were corrected for individual changes in fat-free mass, according to the method described by Ravussin et al (33). Differences between the groups in baseline subject characteristics were evaluated with unpaired t tests. Subject characteristics and substrate oxidation, energy expenditure, and plasma variables measured before and after the intervention in the 3 conditions (rest, exercise, and recovery) within the D and DE groups were compared by two-way repeated-measures analysis of variance (ANOVA) (time \times condition). Post hoc testing was done by using a paired t test in the rest, exercise (mean of $t = 15, 30,$ and 45), and recovery periods. P values of the post hoc comparisons were corrected according to Bonferroni inequalities.

Group differences in baseline measurements of substrate oxidation, energy expenditure, and plasma variables during rest, exercise, and recovery were tested with a two-way repeated-measures ANOVA (group \times condition). To compare the effects of the D and DE interventions on the measured parameters, we compared the before- and after-intervention results in the rest, exercise (mean of $t = 15, 30,$ and 45), and recovery periods. A two-way repeated-measures ANOVA (group \times condition) was used to test for differences between the D and DE groups. Post hoc testing was done by using an unpaired t test over the rest, exercise (mean of $t = 15, 30,$ and 45), and recovery periods. P values for the post hoc comparisons were corrected according to Bonferroni inequalities. Areas under the curve (AUCs) of the graph showing RER over time were calculated and differences between groups were measured by using a two-way ANOVA

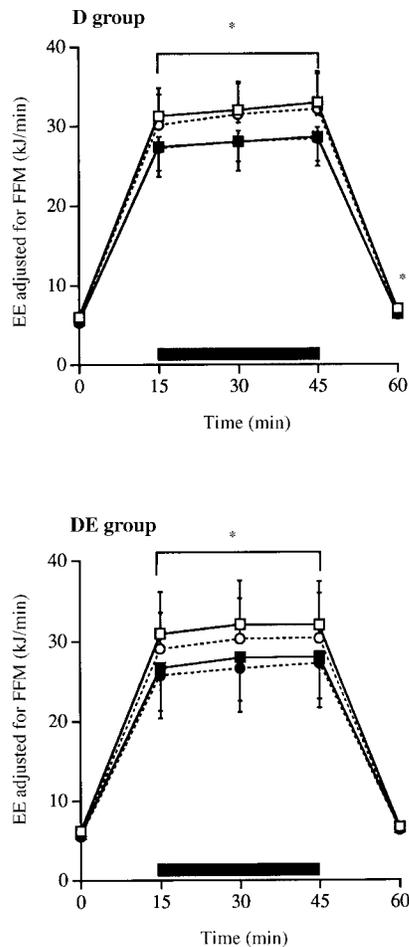


FIGURE 1. Energy expenditure (EE) adjusted for changes in fat-free mass (FFM) in the diet (D) and diet plus exercise (DE) groups before and after the intervention, at rest ($t = 0$), during exercise ($t = 15, 30$, and 45 ; black bar shows entire exercise session), and during recovery ($t = 60$) with and without propranolol administration. □: before intervention, without propranolol; ■: after intervention, without propranolol; ○: before intervention, with propranolol; ●: after intervention, with propranolol. Results of the two-way ANOVAs were as follows: D group without propranolol, time effect and time \times condition, $P < 0.001$; DE group without propranolol, time effect, $P < 0.05$ and time \times condition, $P < 0.01$; D group with propranolol, time effect and time \times condition, $P < 0.01$; DE group with propranolol, time effect and time \times condition, $P < 0.05$. *Significant difference between before and after the intervention in each group, both with and without propranolol, $P < 0.05$.

(time \times group). A paired t test was used to test for differences within groups. $P < 0.05$ was considered statistically significant.

RESULTS

Subject characteristics

None of the subject characteristics differed significantly between the 2 groups before the intervention (Table 1). In both groups, the intervention induced significant decreases in body weight (14.8 ± 5.3 and 15.2 ± 6.3 kg in the D and DE groups, respectively), BMI, percentage body fat, fat mass, and fat-free mass (two-way ANOVA: time effect, $P < 0.001$ for all). For all

of these variables, the effect did not differ significantly between the D and DE groups (two-way ANOVA: group effect, NS; time \times group, NS).

Heart rate and respiratory quotient at maximal workload did not differ significantly before and after the intervention within each group. The intervention also did not significantly affect $\dot{V}O_{2\max}$ or $\dot{V}O_{2\max}/\text{fat-free mass}$ in either group. In the DE group, the score for sports activity during leisure time, including participation in the exercise training program of the present study, increased significantly from before to after the intervention (from 2.3 ± 0.7 to 2.9 ± 0.7 ; $P < 0.05$); the scores ranged from 1 to 4 with 1 = inactive and 4 = very active (29). In the D group, sports activity during leisure time did not change significantly, but physical activity excluding sports during leisure time increased significantly (from 2.4 ± 0.5 to 2.6 ± 0.4 ; $P = 0.05$). Subjects in the DE group increased their sports activity during leisure time to a significantly greater extent than did subjects in the D group ($P < 0.05$), whereas changes in physical activity excluding sports during work and leisure time did not differ significantly between the groups.

To assess weight balance, we calculated percentage change in body weight during the last week of the study; the subjects' body weight changed by a mean of $0.17 \pm 0.96\%$ (0.14 ± 0.89 kg), which was not significant. These changes did not differ significantly between groups. Subjects in the DE group attended $75 \pm 20\%$ of the training sessions at the laboratory between the last preintervention test and the first postintervention test. Subjects who could not attend a training session at the laboratory because of work responsibilities were required to exercise (walking or cycling) at home for 1 h. They received a heart rate monitor and were asked to check their training intensity at home. The causes of absence from training sessions were illness, holidays, and work responsibilities. Because the subjects' attendance was $< 100\%$, our results underestimate the potential effect of the exercise training. If the subjects performed the same percentage of the required exercise sessions at home (ie, 75% of once a week) as they did in the laboratory (75% of 3 times/wk), this suggests that they exercised 3 instead of 4 times/wk on average. The mean calculated energy expenditure per training session was 1.4 ± 0.2 MJ.

Effects of weight loss with or without low-intensity exercise training on substrate metabolism

Before the intervention, energy expenditure during rest and exercise was not significantly different between the groups. Energy expenditure adjusted for changes in fat-free mass was significantly lower after the intervention in both the D group and the DE group (two-way ANOVA: time effect, $P < 0.05$; time \times condition, $P < 0.01$; **Figure 1**). Changes in adjusted energy expenditure were not significantly different between the groups.

RER before the intervention was not significantly different between the groups. RER increased significantly as a result of the intervention in the D group (two-way ANOVA: time effect, $P < 0.05$) but not in the DE group (**Figure 2**). The effect of the intervention on RER differed significantly between the D and DE groups (two-way ANOVA, $P < 0.05$). In the D group, the AUC of the RER over time was significantly higher after the intervention than before the intervention (two-way ANOVA, $P < 0.05$) and the interaction effect for time \times group was nearly significant ($P = 0.07$) (**Figure 3**). In the DE group, the AUC of the RER over time did not change significantly from before to after the intervention.

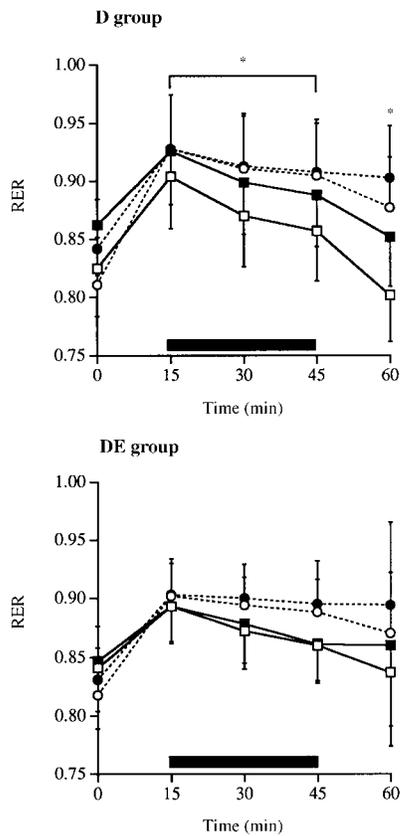


FIGURE 2. Respiratory exchange ratio (RER; carbon dioxide production/oxygen consumption) in the diet (D) and diet plus exercise (DE) groups before and after the intervention, at rest ($t = 0$), during exercise ($t = 15, 30$, and 45 ; black bar shows entire exercise session), and during recovery ($t = 60$) with and without propranolol administration. \square : before intervention, without propranolol; \blacksquare : after intervention, without propranolol; \circ : before intervention, with propranolol; \bullet : after intervention, with propranolol. RER increased significantly as a result of the intervention in the D group (two-way ANOVA: time effect, $P < 0.05$) but not in the DE group. *Significant difference between before the intervention with propranolol and before the intervention without propranolol during exercise (mean of values for 15, 30, and 45 min) and during recovery (60 min).

Heart rates at rest, during exercise, and during recovery were 69 ± 9 , 129 ± 18 , and 85 ± 12 beats/min, respectively, in the D group and 72 ± 10 , 117 ± 17 , and 81 ± 10 beats/min, respectively, in the DE group before the intervention (no significant difference between groups). After the intervention, heart rates were not significantly different in the D group but were significantly lower in the DE group at rest (-10 ± 8 beats/min; $P < 0.001$) and during recovery (-11 ± 11 beats/min; $P < 0.01$), but not during exercise (-8 ± 16 beats/min; NS).

For concentrations of plasma metabolites, none of the changes from before to after the intervention differed between the groups, but there were some changes in metabolites within the groups (Figure 4). Plasma FFA and glycerol concentrations decreased significantly as a result of the intervention in both groups. Plasma lactate concentrations tended to be lower after the intervention than before the intervention, but only decreased significantly in the DE group during exercise ($P < 0.01$) and in the D group during recovery ($P < 0.05$). Plasma glucose con-

centrations did not change significantly in either group at any time (data not shown). From before to after the intervention, plasma insulin concentrations declined significantly in both groups at rest and during recovery ($P < 0.05$; Table 2). Plasma epinephrine and norepinephrine concentrations decreased significantly in both groups (two-way ANOVA: time effect, $P < 0.05$ and $P < 0.0001$ for epinephrine and norepinephrine, respectively); these changes were not significantly different between the D and DE groups.

Effects of weight loss with or without low-intensity exercise training on β -adrenergic receptor-mediated substrate metabolism

Energy expenditure in the test with propranolol administration was not significantly different from that in the test without propranolol in both groups before and after the intervention (Figure 1). RER at rest, during exercise, and during recovery increased with propranolol administration in the D group ($P < 0.01$; Figure 2). The propranolol-mediated change in RER (expressed as the AUC of the RER) before the intervention was significantly higher in the D group than in the DE group ($P < 0.05$; Figure 3). The propranolol-mediated change in RER tended to be different between the D and DE groups (two-way ANOVA: time \times group, $P = 0.09$; Figure 3). Propranolol administration decreased the heart rate significantly (two-way ANOVA, $P < 0.05$) during rest, exercise, and recovery in both groups (D group: -10 ± 5 , -26 ± 12 , and -15 ± 11 beats/min, respectively; DE group: -10 ± 7 , -18 ± 16 , and -17 ± 19 beats/min, respectively). The propranolol-induced changes in heart rate were not significantly different before and after the intervention.

Propranolol administration lowered plasma FFA concentrations in the D group both before and after the intervention (two-way ANOVA: time effect, $P < 0.05$; time \times condition, $P < 0.0001$ before intervention and $P = 0.09$ after intervention). Propranolol-induced changes in FFA concentrations did not differ significantly before and after the intervention. Propranolol administration lowered glycerol concentrations in the D group before the intervention (two-way ANOVA: time effect, $P < 0.05$; time \times condition, $P < 0.0001$) and in the DE group after the intervention (two-way ANOVA: time effect, $P < 0.05$; time \times condition, NS; Figure 4). Plasma glycerol concentrations were significantly lower with propranolol administration after the intervention than before the intervention in both groups (two-way ANOVA: time effect, $P < 0.01$). The propranolol-induced change in plasma glycerol concentration was significantly reduced after the intervention compared with before the intervention in the D group (two-way ANOVA, $P < 0.05$). Propranolol infusion did not significantly affect plasma glucose concentrations (data not shown) or plasma lactate concentrations.

DISCUSSION

The most important finding of the present study is that low-intensity exercise training can prevent the weight-loss-induced decline in fat oxidation in the postdiet period in obese men. The sympathetic nervous system might be involved in these metabolic changes, because the responsiveness of lipolysis and fat oxidation to sympathetic stimulation tended to be reduced by weight loss and these changes were prevented by low-intensity exercise training.

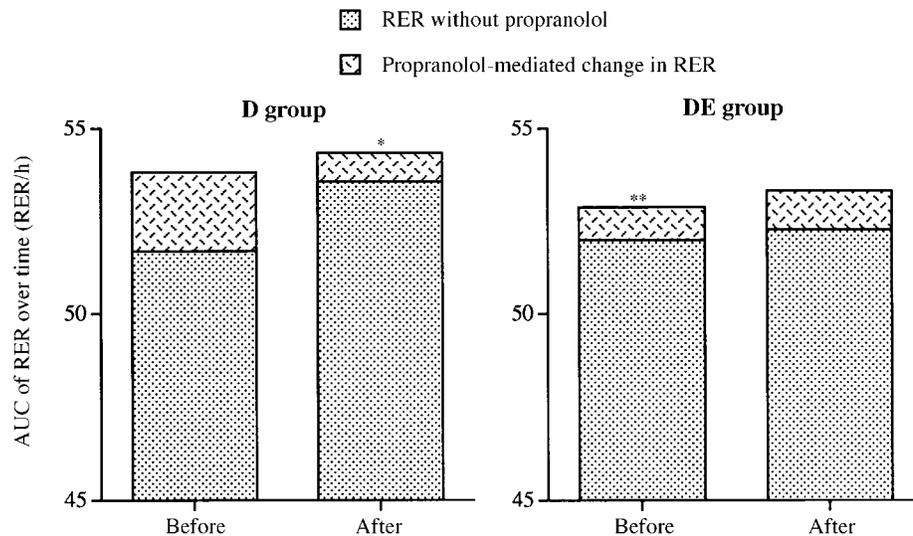


FIGURE 3. Area under the curve (AUC) of the respiratory exchange ratio (RER; carbon dioxide production/oxygen consumption) over time in the diet (D) and diet plus exercise (DE) groups before and after the intervention without propranolol administration and the propranolol-mediated change in RER. The SDs were as follows: for RER without propranolol before and after the intervention: D group, 2.2 and 2.9, respectively, and DE group, 1.7 and 2.1, respectively; for propranolol-mediated change in RER before and after the intervention: D group, 1.8 and 2.2, respectively, and DE group, 1.5 and 1.7, respectively. The results of the two-way ANOVAs were as follows: for RER without propranolol, time effect, $P < 0.05$, and time \times group interaction, $P = 0.07$; for RER with propranolol, time effect, NS, and time \times group interaction, $P = 0.09$. *RER without propranolol administration significantly different from before intervention, $P < 0.05$. **Propranolol-mediated change in RER significantly different from D group, $P < 0.05$.

The present study showed that a decrease in fat oxidation in the postdiet period ($P < 0.05$) is a metabolic adaptation to loss of body fat mass. Other researchers reported an association between reduced fat mass and reduced fat oxidation (10, 12). Furthermore, the significantly reduced plasma FFA and glycerol concentrations ($P < 0.05$) in the present study suggest that adipose tissue lipolysis may have decreased. Reduced lipolysis after body weight loss is consistent with data from previous studies (9, 34–36); in one study, this decreased lipolysis was reported to be caused by a reduction of hormone-sensitive lipase activity after weight loss (36).

Addition of exercise training to a weight-loss diet caused no short-term additional effects on changes in body mass and composition, which agrees with the outcome of a meta-analysis of weight-loss studies conducted over the past 25 y (37). Nevertheless, addition of exercise training to the weight-loss diet program was successful in preventing the undesirable decline in fat oxidation during the postdiet period. Weight loss resulted in a decline in fat oxidation at rest, during exercise, and during recovery in weight-stable individuals (two-way ANOVA, $P < 0.05$) that was counteracted when weight loss was combined with low-intensity exercise training. This finding is consistent with the results of a previous study showing that low-intensity exercise training without body weight loss improves fat oxidation in obese subjects (18). In a different study with obese, weight stable women, a decrease in resting fat oxidation resulting from weight loss was prevented by exercise training (9). These women participated in a walking program that was probably of comparable intensity to the training program used in our study; no data on fat oxidation during exercise and recovery from exercise were available.

The present study produced data on the involvement of the sympathetic nervous system in metabolic adaptations to weight loss. However, the propranolol-mediated increase in RER before

the intervention was significantly higher in the D group than in the DE group ($P < 0.05$). Because the subjects were divided randomly into the 2 groups, we cannot explain this unintended difference. Although we must interpret the results with caution, the changes resulting from the interventions could still be relevant. The propranolol-mediated change in RER tended to be different between the D and the DE groups (two-way ANOVA: time \times group, $P = 0.09$). In the D group, blockade of β -receptors tended to increase RER to a smaller extent after weight loss than before weight loss (two-way ANOVA, $P = 0.09$). In addition, β -adrenergic blockade induced a smaller decline in plasma glycerol concentration after the intervention than before the intervention ($P < 0.05$). In contrast, in the DE group, the changes in RER and glycerol concentrations during β -adrenergic blockade did not differ significantly before and after the intervention. Furthermore, plasma catecholamine concentrations before the intervention and changes resulting from the intervention did not differ significantly between the D and DE groups.

These results might indicate that exercise training during weight loss maintains fat oxidation by maintaining the sensitivity of the β -adrenergic nervous system. This is in agreement with in vitro data from Nicklas et al (9) showing decreased cAMP- and epinephrine-stimulated lipolysis in the weight-loss group but not in the weight-loss plus exercise group. Moreover, decreased cAMP-stimulated lipolysis suggested a defect at the postreceptor mechanism. Tremblay et al (38) reported that β -adrenergic blockade decreased resting fat oxidation and metabolic rate in exercise-trained but not in untrained subjects, suggesting increased β -adrenergic sensitivity in trained subjects. Moreover, several in vitro studies found increased β -adrenergic-mediated lipolysis in the trained compared with the untrained state (23, 24, 39, 40). The results of studies investigating the effects of weight

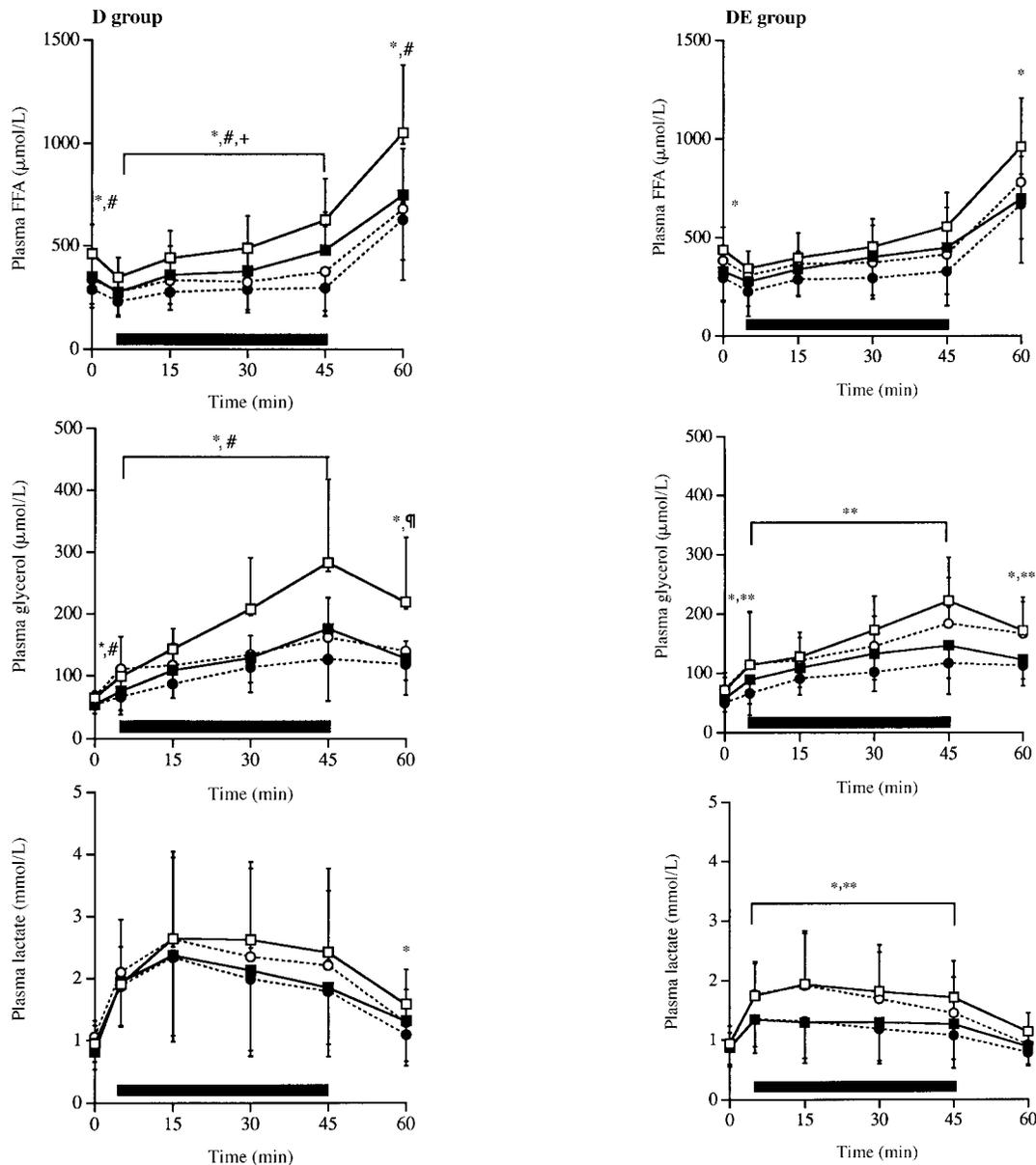


FIGURE 4. Plasma concentrations of free fatty acids (FFAs), glycerol, and lactate in the diet (D) and diet plus exercise (DE) groups before and after the intervention, at rest ($t = 0$), during exercise ($t = 5, 15, 30,$ and 45 ; black bar shows entire exercise session), and during recovery ($t = 60$) with and without propranolol administration. \square : before intervention, without propranolol; \blacksquare : after intervention, without propranolol; \circ : before intervention, with propranolol; \bullet : after intervention, with propranolol. The results of the two-way ANOVAs were as follows: Plasma FFA: D group without propranolol, time effect and time \times condition (conditions were rest, exercise, and recovery), $P < 0.01$; DE group without propranolol, time effect, $P < 0.01$, and time \times condition, $P < 0.0001$. Plasma glycerol: D group without propranolol, time effect, $P < 0.01$, and time \times condition, $P < 0.001$; DE group without propranolol, time effect, $P < 0.01$, and time \times condition, $P < 0.05$. Plasma glycerol: D group with propranolol, time effect, $P < 0.01$, and time \times condition, NS; DE group with propranolol, time effect, $P = 0.001$, and time \times condition, $P = 0.07$. Plasma lactate: D group without propranolol, time effect, $P = 0.09$, and time \times condition, $P = 0.01$; DE group without propranolol, time effect, $P < 0.01$, and time \times condition, $P < 0.001$. Plasma lactate: DE group with propranolol, time effect, $P < 0.05$, and time \times condition, $P < 0.01$. *After intervention without propranolol significantly different from before intervention without propranolol, $P < 0.05$. **After intervention with propranolol significantly different from before intervention with propranolol, $P < 0.05$. #Before intervention with propranolol significantly different from before intervention without propranolol, $P < 0.05$. +After intervention with propranolol significantly different from after intervention without propranolol, $P < 0.05$. \ddagger Propranolol-induced change (with propranolol – without propranolol) after intervention significantly different from before intervention, $P < 0.05$.

reduction in obese subjects on β -adrenergic sensitivity are not consistent. Although a study by Blaak et al (21) reported no significant effect of weight loss on β -adrenergic sensitivity of whole-body and skeletal muscle in obese subjects, the data

showed a trend toward a reduction in β -adrenergic-mediated lipolytic activity in weight-reduced subjects. In contrast, Leibel et al (22) showed an increased lipolytic response to epinephrine infusion in weight-reduced obese subjects at stable body weight.

TABLE 2

Plasma insulin, epinephrine, and norepinephrine before and after the intervention in the diet (D) and diet-plus-exercise (DE) groups at rest, after 45 min of exercise, and after 15 min of recovery

	Rest	Exercise	Recovery	<i>P</i> (two-way ANOVA)	
				Time	Time × condition
Insulin (pmol/L)					
D group					
Before	92.4 ± 29.9 ¹	65.3 ± 16.7	134.0 ± 68.7	0.018	0.0005
After	70.1 ± 36.8 ²	56.2 ± 26.4	75.7 ± 43.1 ³		
DE group					
Before	99.3 ± 45.1	67.4 ± 31.2	108.3 ± 43.7	0.001	0.039
After	61.1 ± 27.1 ³	48.6 ± 20.1	71.5 ± 31.9 ²		
Epinephrine (ng/L)					
D group					
Before	43 ± 30	123 ± 63	49 ± 27	0.042	0.252
After	29 ± 21	89 ± 42	35 ± 17		
DE group					
Before	41 ± 19	142 ± 114	54 ± 31	0.024	0.043
After	29 ± 16 ³	88 ± 40	37 ± 17 ²		
Norepinephrine (ng/L)					
D group					
Before	511 ± 117	1500 ± 450	683 ± 188	< 0.0001	0.0002
After	344 ± 122 ⁴	940 ± 317 ⁴	416 ± 159 ⁴		
DE group					
Before	589 ± 164	1316 ± 311	684 ± 212	< 0.0001	< 0.0001
After	384 ± 186 ³	779 ± 270 ⁴	425 ± 169 ⁴		

¹ $\bar{x} \pm SD$.

²⁻⁴Significantly different from before (paired *t* test): ²*P* < 0.05, ³*P* < 0.01, ⁴*P* < 0.0001.

The present study showed that weight loss, whether combined with exercise training or not, did not induce significant changes in resting energy expenditure when energy expenditure was adjusted for changes in fat-free mass. This is in agreement with data from Ravussin et al (41) indicating that decreased resting energy expenditure after weight loss can be explained by decreased fat-free mass. However, other studies showed decreased resting energy expenditure adjusted for fat-free mass after body weight loss when body weight had stabilized (9) or probably stabilized (12, 42), but found no significant decrease in resting energy expenditure when exercise training was added to the weight-loss intervention (9, 43). However, as in our study, the change in resting metabolic rate did not differ significantly between the diet and diet plus exercise groups (9). The decreased energy expenditure (adjusted for fat-free mass) during exercise seems to result from increased mechanical efficiency, because the workloads before and after the intervention were similar.

Despite the difference in fat oxidation, there was no significant difference between the D and DE groups in weight change over the short term. Decreased fat oxidation after a weight-loss program increases the risk of a positive fat balance when an individual returns to a regular diet (44). A new fat balance will be achieved by increasing fat mass (10). Because addition of a low-intensity exercise training program to a weight-loss intervention maintains fat oxidation at a lower fat mass, fat balance can be achieved without increasing fat mass. However, the effects of continuing exercise training over the long term should be studied further.

In conclusion, addition of low-intensity exercise training to a weight-loss diet counteracts the decline in fat oxidation induced by body weight loss in the postdiet period. This effect might be mediated by maintenance of sympathetic nervous system sensitivity, which tends to be reduced after weight loss alone. 

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