Concurrent physical activity increases fat oxidation during the shift to a high-fat diet[1–3]

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ABSTRACT

Background: It takes several days to adapt to a high-fat diet. In an earlier study, we observed a large degree of interindividual variation in the capacity to adapt to a high-fat diet. We hypothesized that concurrent physical activity would accelerate fat oxidation during an isoenergetic high-fat diet.

Objective: The objective of this study was to determine the effect of increased physical activity on the ability of young healthy men to increase fat oxidation during the shift to a high-fat diet.

Design: Six young healthy men participated in a randomized, single-blind crossover study. The volunteers consumed a diet contributing 37% of energy as fat, 14% as protein, and 49% as carbohydrate for 4 d. Energy expenditure and macronutrient balance were then measured in a respiration chamber as the energy content of the isoenergetic diet was changed to 50% fat, 14% protein, and 36% carbohydrate. Treadmill walking, as the physical activity, was used to increase total daily energy expenditure to 1.8 times the resting metabolic rate during 1 of 2 stays in the metabolic chamber. Total daily energy expenditure was maintained at 1.4 times the resting metabolic rate for the other stay.

Results: Energy balance was not significantly different between the 2 conditions. The 24-h respiratory quotient decreased more rapidly and to a greater extent under conditions of increased energy expenditure. Further, there was a decrease in the interindividual variability in the response of the respiratory quotient to a high-fat diet with increased energy expenditure (physical activity). Cumulative carbohydrate and protein balances were greater under conditions of increased physical activity. Conversely, cumulative fat balance was greater under sedentary conditions.

Conclusion: Concurrent physical activity increases fat oxidation during the shift to a high-fat diet. *Am J Clin Nutr* 2000;72: 131–8.

KEY WORDS Dietary fat, fat oxidation, physical activity, macronutrient oxidation, young healthy men

INTRODUCTION

Epidemiologic studies have implicated increased amounts of dietary fat as a causative factor in the obesity epidemic that is sweeping the Western world (1). High-fat foods are energy dense and generally considered palatable (2, 3), which encourages overconsumption (4). As the proportion of fat in the diet increases, so does the incidence of obesity (1). Switching from a high- to a low-fat diet typically results in a decrease in body weight and probably prevents weight gain.

It takes several days to adapt to a high-fat diet by increasing fat oxidation (5). In an earlier study, we observed that the capacity of individuals to increase fat oxidation in response to an increase in dietary fat was highly variable; some individuals adapted quickly and others did not increase fat oxidation at all. The interindividual variability in the capacity to oxidize fat was directly related to maximal oxygen consumption ($\dot{V}O_2max$) during treadmill exercise and inversely related to insulin sensitivity as measured by the fasting insulin concentration (5). These data suggest that the capacity to increase fat oxidation in response to a high-fat diet might be modulated by environmental factors.

Exercise acutely increases fat oxidation. Exercise before consumption of a high-fat diet increases fat oxidation, presumably by decreasing carbohydrate stores (6). Exercise increases mitochondrial adenosine triphosphate–generating capacity in as few as 5 d (7), and an increase in the enzymes necessary for triacylglycerol hydrolysis and transport are seen as soon as 7 d after the onset of training (8). Acute episodes of physical activity increase the activity of pyruvate dehydrogenase (PDH), a key enzyme that regulates the flux of carbohydrate into the tricarboxylic acid (TCA) cycle (9). On the basis of these data, we hypothesized that concurrent physical activity would accelerate fat oxidation in individuals eating an isoenergetic high-fat diet compared with a sedentary state. To test this hypothesis, we examined the effect of increased physical activity on the ability of young healthy men to increase fat oxidation, measured in a respiration chamber, during the shift from a diet contributing 37% of energy as fat to a diet contributing 50% of energy as fat.

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SUBJECTS AND METHODS

Study volunteers

Six volunteers were recruited through print advertising and completed a comprehensive laboratory and physical examination before signing a written, informed-consent document. The study protocol, consent form, and advertising were approved by the Pennington Biomedical Research Center Institutional Review Board.

Protocol

The aim of this study was to evaluate the effects of increasing physical activity on macronutrient oxidation. Six volunteers participated in a single-blind crossover trial. Each volunteer completed 2 chamber stays separated by ≥7 d. Before the 5-d stay in the respiration chamber, the volunteers consumed a standard weight-maintenance diet contributing 37% of energy as fat for 4 d. On the first day the volunteers spent in the metabolic chamber, the diet also contributed 37% of energy as fat; this was raised to 50% for the next 4 d.

Prediction of energy requirements before entry into the metabolic chamber

Resting metabolic rate (RMR; in kJ/d) and respiratory quotient (RQ) were measured by using a ventilated-hood system (model 2900Z metabolic cart; Sensormedics, Yorba Linda, CA) after the volunteers had fasted overnight and lay in a semirecumbent position. The RMR was combined with a 3-d measurement of free-living energy expenditure (EE) by using a triaxial activity monitor (Tritrac; Hemokinetics, Madison, WI) and measured EE on the treadmill to estimate energy requirements and treadmill time within the metabolic chamber with use of the following equations:

$$\text{Expected sedentary EE in metabolic chamber} = \text{free-living EE} \times 0.85 \quad (1)$$

This equation assumes a 15% lower EE from physical activity in the metabolic chamber than under free-living conditions (H Roy and J Lovejoy, unpublished observations, 1998). The obtained estimate of total daily EE (TDEE) was used to calculate treadmill time needed to achieve a daily EE of 1.4 or 1.8 times the RMR as follows:

$$\text{Treadmill time (min)} = [\text{desired TDEE (kJ/24 h)} - \text{expected sedentary EE in metabolic chamber (kJ/24 h)}] / \text{EE at 4.8 km/h and 3\% incline (kJ/min)} \quad (2)$$

The energy cost of physical activity was calculated by measuring $\dot{V}O_2$ with use of a metabolic cart (Vmax series 29; Sensormedics) while the volunteers walked on a treadmill under conditions similar to those used for exercise in the metabolic chamber. Briefly, the volunteers were allowed to warm up by walking on the treadmill at 4.8 km/h (3 miles/h) and a 0% incline for 2 min. The treadmill speed was then set at 4.8 km/h and the incline raised to 3% and EE was measured continuously for the next 10 min. This EE was then used to calculate exercise time in the chamber as described above. $\dot{V}O_2$max was measured during exercise treadmill testing to exhaustion at the same visit by using the same equipment.

General chamber protocol and maintenance of energy balance

The volunteers entered the chamber each morning before breakfast at 0900 after an overnight stay. Three meals were provided at scheduled intervals. Two or 3 bouts of exercise on the treadmill were prescribed (midmorning, midafternoon, and before a bedtime snack) at 4.8 km/h and a 3% incline to keep TDEE at the targeted level as described above. The lights were turned out at 2230. The volunteers were awakened at 0700, and at 0730 they left the chamber for 90 min. Between 0730 and 0900, the volunteers were allowed to bathe; however, physical activity was limited to time spent on the treadmill. The EE while the volunteers were outside the chamber was extrapolated from the EE readings obtained from 0900 to 1030. At the end of each day, EE was compared with energy intake to estimate energy balance. For the purposes of this interim calculation, metabolizable energy intake was estimated as 90% of the total daily energy intake. On the basis of the interim energy balance result, 3 options were available. If the energy balance was <418 kJ (100 kcal), the intake and exercise times were not changed. If the energy balance was positive, energy intake was decreased or the treadmill time increased, or both, to move the volunteer toward energy balance. If the energy balance was negative, energy intake was increased or the treadmill time decreased to move the volunteer toward energy balance. Only rarely was an adjustment of >1250 kJ (300 kcal)/d necessary.

Body composition

Body composition was measured by using dual-energy X-ray absorptiometry (Hologic QDR 2000; Hologic, Waltham, MA). Visceral adipose tissue was measured with a high-speed CT scanner (General Electric, Milwaukee) and analyzed by using ANALYZE (version 7.5; CNSoftware, London). Body weight was measured each day before the volunteers entered the metabolic chamber and on completion of the 5-d stay in the metabolic chamber.

Design of the metabolic diets

The diets were designed to provide either 37% or 50% energy as fat. In the design of the diets, composites were analyzed by the food chemistry laboratory and adjusted accordingly. Protein content was fixed at 15% of energy. Carbohydrate content was 48% and 35% of energy for the standard and high-fat diets, respectively. The ratio of polyunsaturated to saturated fats was similar for both diets (0.7) .

Calculation of energy and macronutrient balances

EE and substrate oxidations were calculated from $\dot{V}O_2$, carbon dioxide production ($\dot{V}CO_2$), and urinary nitrogen by using the equations of Acheson et al (10). The calculated macronutrient oxidations (in g) were converted to kcal by using the Atwater factors (4.442, 4.183, and 9.461 kcal/g for protein, carbohydrate, and fat, respectively) and multiplied by 4.189 to convert kilocalories to kilojoules. For balances presented in Results, fecal energy was measured by collection of fecal samples marked with carmine red and charcoal and bomb calorimetry in a portion from a 4-d composite. Urine was collected for each 24-h period and nitrogen was measured in each sample to calculate protein oxidation. For each volunteer and for each day in the chamber, duplicate meals were prepared and sent to the food chemistry laboratory for analysis. The values for macronutrient oxidation were then subtracted from

TABLE 1
Characteristics of the study population[1]

Characteristic	Value
Age (y)	24 ± 4.8 (19–27)
Height (m)	1.75 ± 0.005 (1.68–1.83)
Weight (kg)	71.5 ± 5.9 (61.2–81.4)
BMI (kg/m^2)	23.6 ± 5.8 (19.8–27.7)
Percentage body fat (%)	15.3 ± 5.9 (8.3–25.7)
VAT (cm^2)	43.3 ± 14.4 (27.9–64.2)
SAT (cm^2)	110.9 ± 67.6 (23.7–223.8)
Fasting insulin (pmol/L)	45.2 ± 31.6 (10.8–104)
Fasting triacylglycerol (mmol/L)	0.585 ± 0.19 (0.36–0.92)
$\dot{V}O_2$max (mL·kg body wt^{-1}·min^{-1})	50.4 ± 5.9 (39.9–55.2)
Postabsorptive respiratory quotient	0.84 ± 0.06 (0.76–0.92)
Free-living EE (kJ/d)	10431 ± 1545 (8602–13104)
EE:RMR[2]	1.48 ± 0.22 (1.2–1.8)

[1] $\bar{x}$ ± SD; n = 6; range in parentheses. VAT, visceral adipose tissue measured at the L4-L5 vertebral interspace; SAT, subcutaneous adipose tissue measured at the L4-L5 vertebral interspace; EE, energy expenditure; RMR, resting metabolic rate.

[2] Calculated by dividing the free-living EE (measured with a triaxial activity monitor) (kJ/d) by the RMR. This value provides an index of free-living activity corrected for body size (RMR).

the energy, fat, carbohydrate, and protein intakes to calculate energy and macronutrient balances for each day.

Analytic methods

Urinary nitrogen was measured by using pyrochemiluminescence on an Antek 735 nitrogen analyzer (Antek Instruments, Houston). Urinary creatinine was measured by using the Jaffe rate reaction on a Beckman Synchron CX7 (Beckman Instruments, Brea, CA). Fecal samples were collected, weighed, and homogenized with an equal volume of water. After homogenization, ≈50 g fecal homogenate was freeze-dried and stored in an airtight container. The samples were weighed before and after freeze-drying. On the day of analysis, the dried fecal material was compressed into a pellet of ≈0.5–1 g and analyzed for total energy content with an oxygen bomb calorimeter (model 1241; Parr Instrument Company, Moline, IL).

Food composites were collected, weighed, homogenized, and frozen at −20°C until analyzed. Composites were analyzed for moisture, protein, fat, and ash. Moisture was analyzed by using a Labwave 9000 microwave oven (CEM, Matthews, NC). Protein was analyzed by using a combustion method on a nitrogen analyzer (Series II 2410; Perkin Elmer, Norwalk, CT). Ash was measured by using an MAS 7000 microwave muffle furnace (CEM). Carbohydrate was calculated by difference [100% − (ash + protein + fat + moisture)]. Energy content was determined by using standard formulas (9 kcal/g fat, 4 kcal/g protein, and 4 kcal/g carbohydrate). Calories were converted to kilojoules by using 4.189 kJ/kcal as the conversion factor.

Statistical methods

Data were analyzed by using SAS (version 6.12; SAS Institute Inc, Cary, NC) and graphed by using STATVIEW for WINDOWS (version 5.0; SAS Institute). The response variables were analyzed by using PROC MIXED with day and treatment as the repeated variables. Bonferroni adjustment was used to correct for multiple comparisons. Baseline values were included as covariates for all of the models. Significance was set a priori at $P < 0.05$. All values are presented as means ± SEs unless otherwise noted.

RESULTS

The study population included young men with similar anthropometric characteristics (**Table 1**). These healthy, but sedentary, young men were able to complete the protocol successfully with minimal musculoskeletal complaints related to the treadmill exercise. The average time on the treadmill under the high-activity condition was 146.6 ± 12 min, compared with 33.3 ± 9.8 min under the low-activity condition. Treadmill walking was associated with an average of 34.8 ± 2.1% of $\dot{V}O_2$max. $\dot{V}O_2$max was measured before and after the completion of the study and did not change significantly (data not shown).

Analyzed compositions of the diets are shown in **Table 2**. Overall, dietary fat intakes were not significantly different from the target values of 37% or 50% of energy. EEs for the 2 chamber conditions over the 5-d chamber stays are shown in **Table 3** and **Figure 1**. Energy intake was closely matched to EE (Table 3). Energy balance differed significantly between the 2 groups only for the first day of the high-fat diet (Table 3). Cumulative energy balance over the 4-d high-fat diet was not significantly different between the 2 groups (Figure 1).

The increase in dietary fat resulted in an expected fall in nonprotein RQ (npRQ) at both high and low EEs (**Figure 2**). There was a significantly greater and more rapid fall in npRQ when EE was increased (1.8 times the RMR) than under sedentary conditions (1.4 times the RMR). The individual values for each chamber day are presented in **Figure 3**. Under conditions of low physical activity, the interindividual variability in change in npRQ was large. Some volunteers did not appear to increase fat oxidation substantially under sedentary conditions, as exemplified by one volunteer with no change in npRQ. The interindividual variability was diminished under conditions of increased physical

TABLE 2
Compositions of the study diets[1]

	High-fat, low-activity	High-fat, high-activity
Fat (%)		
Baseline	36.9 ± 0.4	37.9 ± 0.4
Day 1	47.6 ± 0.8	45.8 ± 1.3
Day 2	48.9 ± 0.3	46.8 ± 1.1
Day 3	49.6 ± 0.8	47.8 ± 0.9
Day 4	49.2 ± 1.6	50.6 ± 1.4
Carbohydrate (%)		
Baseline	49.7 ± 0.6	48.6 ± 0.3
Day 1	39.8 ± 0.7	39.4 ± 1.2
Day 2	36.7 ± 0.3	38.9 ± 1.3
Day 3	36.6 ± 1.0	37.0 ± 0.7
Day 4	36.6 ± 1.8	34.9 ± 0.7
Protein (%)		
Baseline	13.7 ± 0.4	13.5 ± 0.3
Day 1	13.6 ± 0.3	14.8 ± 0.6
Day 2	14.4 ± 0.3	14.3 ± 0.6
Day 3	13.7 ± 0.5	15.1 ± 1.2
Day 4	14.2 ± 0.4	14.6 ± 1.3
P:S	0.7	0.7

[1] $\bar{x}$ ± SE; n = 6. P:S, ratio of polyunsaturated to saturated fatty acids, estimated from database values. All other values are measured from duplicate meals analyzed by the Food Chemistry Laboratory (*see* Methods).

TABLE 3
Energy intake, energy expenditure, fecal energy, and energy balance under conditions of low and high activity[1]

	Energy intake	Ratio of energy intake to resting metabolic rate	Energy expenditure	Fecal energy[2]	Energy balance
	kJ/d		*kJ/d*	*kJ/d*	*kJ/d*
Low activity					
Baseline	11257 ± 450	1.33 ± 0.03	9334 ± 265	714.5 ± 62	1209 ± 356
Day 1	11239 ± 353	1.37 ± 0.04	9692 ± 463	714.5 ± 62	832 ± 487
Day 2	11327 ± 483	1.39 ± 0.02	9828 ± 453	714.5 ± 62	784 ± 181
Day 3	11484 ± 479	1.42 ± 0.03	10001 ± 365	714.5 ± 62	768 ± 192
Day 4	11600 ± 515	1.38 ± 0.02	9774 ± 413	714.5 ± 62[3]	1110 ± 254
High activity					
Baseline	11324 ± 516	1.35 ± 0.03	9545 ± 380	886.5 ± 73	892 ± 422
Day 1	13369 ± 490	1.78 ± 0.03	12521 ± 528	886.5 ± 73	−38 ± 511[4]
Day 2	14026 ± 535	1.78 ± 0.03	12528 ± 576	886.5 ± 73	611 ± 360
Day 3	14215 ± 674	1.76 ± 0.03	12434 ± 542	886.5 ± 73	895 ± 218
Day 4	14119 ± 781	1.75 ± 0.03	12350 ± 520	886.5 ± 73[3]	883 ± 253

[1] $\bar{x}$ ± SE; n = 6.
[2] Measured in samples pooled from baseline and days 1–3.
[3] Fecal energy for day 4 is assumed to be equal to the total 4-d fecal collection.
[4] Significantly different from baseline and from low activity, $P < 0.05$.

activity. It is notable that the individual with the least change in RQ under sedentary conditions had a substantial fall in npRQ when eating a high-fat diet under conditions of increased EE.

Daily macronutrient balances are shown in **Figure 4** and **Table 4**. Compared with baseline and day 1, the isoenergetic high-fat diet resulted in a more positive fat balance under the low- but not the high-activity condition. The increased fat balance under the low-activity condition did not change over time ($P > 0.05$ for post hoc comparison of days 1, 2, 3, and 4). Cumulative fat balance over the 4 d was greater under the low-activity condition than under the high-activity condition (Figure 4).

Carbohydrate balance was negative for the first day with the isoenergetic high-fat diet under both the high- and low-activity conditions (Table 4). Under the low-activity condition, carbohydrate balance remained negative or neutral for the remainder of the high-fat diet. However, under the high-activity condition, carbohydrate balance increased back to levels seen at baseline. As a result, cumulative carbohydrate balance over the 4 d was higher under the high-activity condition than under the low-activity condition (Figure 4A).

Nitrogen balance increased as a result of the isoenergetic high-fat diet under both the low- and the high-activity conditions ($P < 0.05$ for time effect; Table 4). The increment above baseline was not significantly greater for the high-activity condition ($P > 0.05$ for treatment effect). The positive nitrogen balance was the result of a decrease in protein oxidation under the low-activity condition. Under the high-activity condition, protein intake increased as total energy intake increased. Protein oxidation increased significantly but was insufficient to offset the higher protein intake.

Cumulative fat balance over the 4 d was highly negatively correlated with the cumulative carbohydrate balance (**Figure 5**). The correlation coefficient was significant for both conditions together and for the low-activity condition alone ($P < 0.05$).

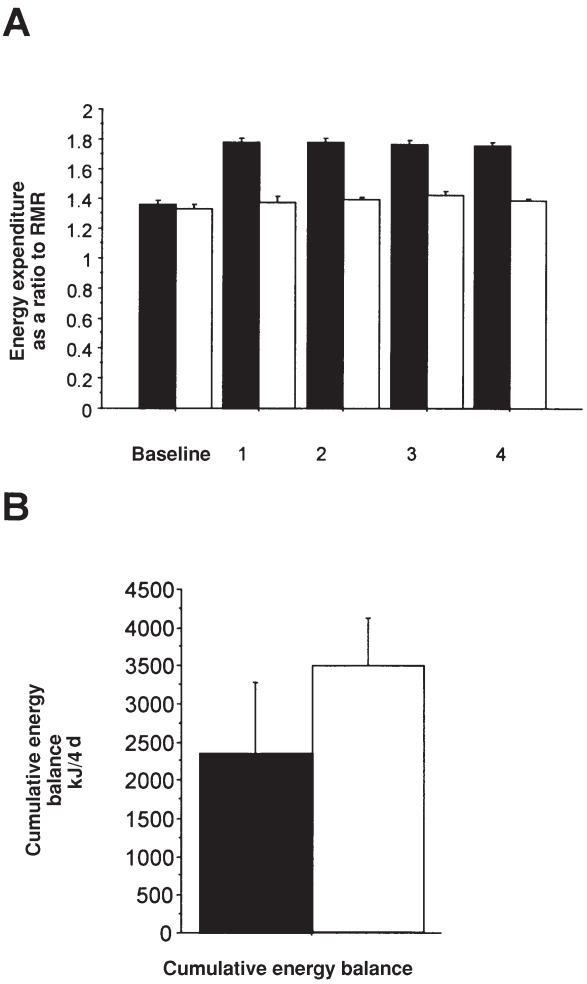

FIGURE 1. Energy expenditure as ratio to resting metabolic rate (RMR) (A) and cumulative energy balance (B) under the low-activity (□) and high-activity (■) conditions. Error bars represent SEMs. n = 6.

DISCUSSION

Adaptation to a high-fat diet is not instantaneous. Several days are required to increase fat oxidation to match fat intake

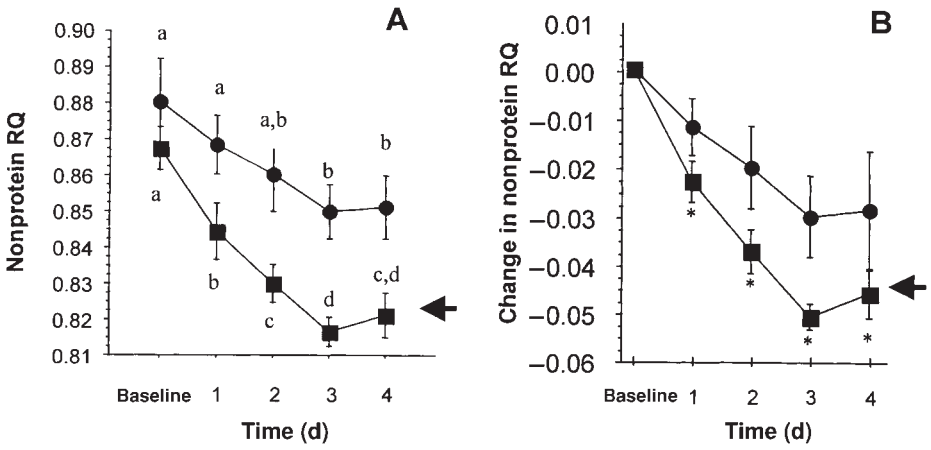

FIGURE 2. Mean nonprotein respiratory quotient (RQ) (A) and change from baseline for the high- (■) and low-activity (●) high-fat diet periods. The high-fat diet began on day 1. For the baseline day, dietary fat was set at 37% of energy. Means that are significantly different are noted by different letters. Error bars represent SEMs. $n = 6$. *Significantly different from baseline, $P < 0.05$. The arrows represent the expected change in RQ with the high-fat diet if fat oxidation and fat intake were equal.

when dietary fat increases (5, 6). We proposed the hypothesis that the rate at which an individual adapts to a high-fat diet is accelerated by increasing physical activity during the shift to an isoenergetic high-fat diet. To test this hypothesis, we studied 6 young healthy men in a respiration chamber while they switched from a standard diet to an isoenergetic high-fat diet under sedentary conditions and under conditions of increased physical activity. Under sedentary conditions (1.4 times the RMR), there was a large degree of variability between individuals in the ability to adapt to a high-fat diet by increasing fat oxidation. In the present study, we found that increasing the level of physical activity to 1.8 times the RMR accelerated the adaptation to a high-fat diet. Also, physical activity decreased the interindividual variability in RQ response, decreasing the amount of fat energy stored overall.

There are several mechanisms by which physical activity could accelerate fat oxidation during a high-fat diet. Exercise is known to increase the metabolic machinery that is necessary to oxidize fat, such as lipoprotein lipase, CPT-I, and mitochondrial number (8). Importantly, in our earlier study we found that the maximal aerobic capacity during treadmill exercise measured before diet intervention explained 70% of the variability in fat oxidation in response to a high-fat diet (5). This suggested that oxidative capacity was somehow linked to the response to a high-fat diet.

One problem with the oxidative capacity view of the current data is that the time required to increase mitochondrial number

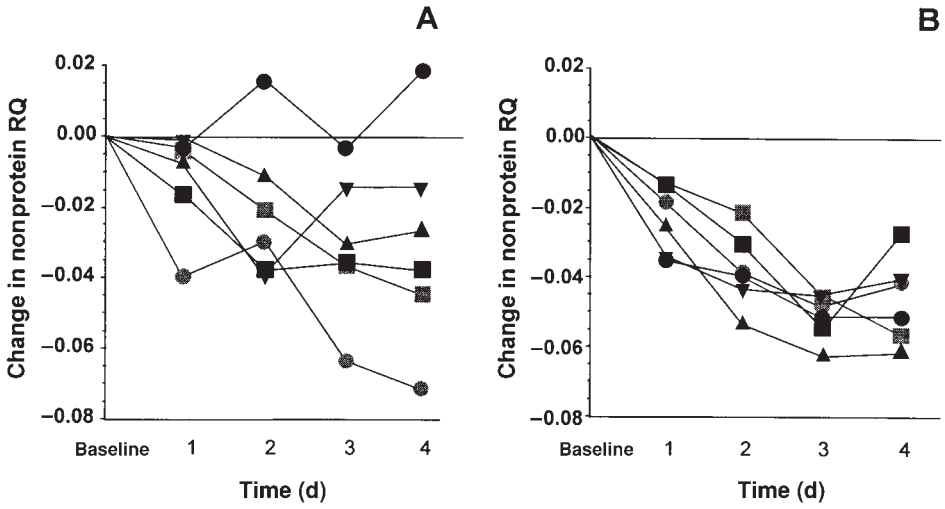

FIGURE 3. Individual values for the change in nonprotein RQ under the low-activity condition (1.4 times the resting metabolic rate; A) and the high-activity condition (1.8 times the resting metabolic rate; B). Each volunteer was given a unique symbol, which is the same in Figures 4A and 4B. $n = 6$. The arrows represent the expected change in RQ with the high-fat diet if fat oxidation and fat intake were equal.

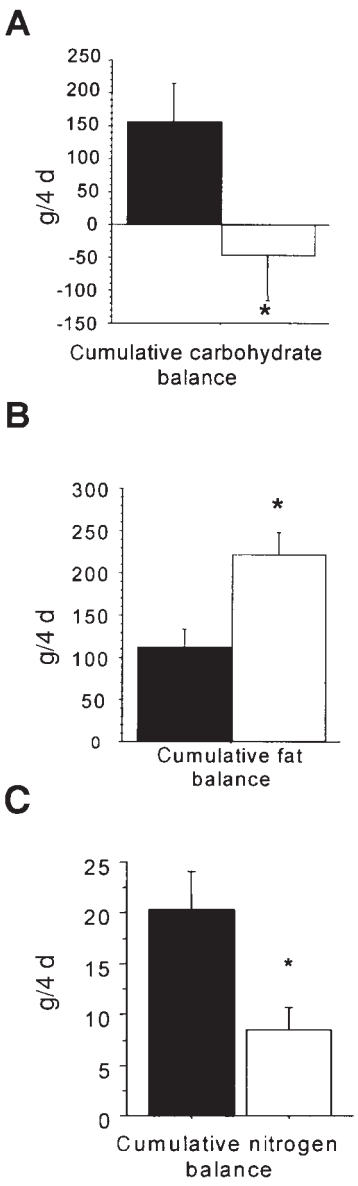

FIGURE 4. Cumulative 4-d carbohydrate balance (carbohydrate intake − carbohydrate oxidation), fat balance (fat intake − fat oxidation), and nitrogen balance (nitrogen intake − nitrogen oxidation) under the high- (■) and low-activity (□) conditions. *Significant difference in macronutrient balance over 4 d, $P < 0.05$. Note that the macronutrient balances were not corrected for fecal energy. Error bars represent SEMs. $n = 6$.

and CPT-I does not match the rapid changes in fat oxidation that we observed. We observed a significant difference in RQ within the first 24 h. It is unlikely that oxidative capacity of the skeletal muscle changes within 24 h. Rapid adjustments in substrate flux are necessary to prevent depletion of glycogen during exercise. PDH is a candidate enzyme for rapid regulation of carbohydrate flux into the TCA cycle. PDH and its upstream regulator, PDH kinase, regulate flux of carbohydrate into the TCA cycle. PDH appears to change rapidly in response to an acute bout of exercise (9) and high-fat diets (11). PDH kinase, by regulating PDH activity, may be an important signaling mechanism for the acute regulation of fat and carbohydrate oxidation.

In support of this hypothesis, we observed a highly negative correlation between carbohydrate and fat oxidation in our experiments with high and low amounts of physical activity, as would be expected under conditions of approximate energy balance. This is in contrast with the studies of Schutz et al (12), in which adding fat to the diet was not accompanied by an increase in fat oxidation and fat balance was not related to carbohydrate balance. This suggests that carbohydrate deficits may be an important signal to increase fat oxidation and that low-intensity aerobic exercise may decrease carbohydrate oxidation, leading to an increase in fat oxi-

TABLE 4
Macronutrient intake, oxidation, and balance in subjects consuming a high-fat diet under conditions of low and high activity[1]

	Intake	Oxidation	Balance
		kJ/d	
Low activity			
Carbohydrate			
Baseline	5560.2 ± 234.3	4871.0 ± 415.6	689.2 ± 401.3
Day 1	4367.7 ± 168.2[2]	4902.8 ± 422.2	−535.1 ± 386.1
Day 2	4158.3 ± 184.0[2]	4700.1 ± 392.8	−541.8 ± 363.8
Day 3	4194.6 ± 152.1[2]	4534.4 ± 359.8	−339.8 ± 216.2
Day 4	4208.5 ± 118.8[2]	4401.2 ± 390.6	−192.6 ± 413.7
Fat			
Baseline	4153.4 ± 186.8	2696.4 ± 281.2	1457.0 ± 368.5
Day 1	5347.3 ± 183.8[2]	3398.9 ± 171.1[2]	1948.3 ± 257.1[2]
Day 2	5535.8 ± 220.6[2]	3577.6 ± 296.1[2]	1958.2 ± 254.5[2]
Day 3	5711.7 ± 313.6[2]	3963.8 ± 160.6[2]	1747.9 ± 347.6[2]
Day 4	5749.4 ± 434.9[2]	3761.2 ± 185.8[2]	1988.2 ± 469.0
Protein			
Baseline	1544.3 ± 60.2	1790.7 ± 149.4	−246.3 ± 113.1
Day 1	1524.8 ± 52.8[2]	1398.8 ± 136.2	126.0 ± 130.9
Day 2	1633.7 ± 88.8[2]	1561.6 ± 146.2	72.2 ± 117.4
Day 3	1577.9 ± 87.8[2]	1509.3 ± 133.2	68.6 ± 57.3
Day 4	1642.1 ± 79.4[2]	1623.9 ± 70.0	18.2 ± 62.0
High Activity			
Carbohydrate			
Baseline	5501.6 ± 265.9	4791.7 ± 284.2	709.9 ± 224.4
Day 1	5253.0 ± 191.2	5539.3 ± 413.5	−286.3 ± 348.3
Day 2	5456.9 ± 250.3	4533.9 ± 631.0	923.0 ± 536.2
Day 3	5280.9 ± 330.5	4409.9 ± 258.0	871.0 ± 160.0
Day 4	4906.7 ± 221.0	4616.7 ± 417.7	290.0 ± 209.7
Fat			
Baseline	4297.9 ± 208.3	3388.7 ± 294.4	909.2 ± 349.6
Day 1	6145.3 ± 358.5	5393.5 ± 342.1	751.8 ± 365.4
Day 2	6578.8 ± 358.0	5904.9 ± 391.2	673.9 ± 306.2
Day 3	6817.6 ± 409.5	6295.6 ± 332.9	522.0 ± 250.8
Day 4	7188.3 ± 580.2	6053.6 ± 189.0	1134.7 ± 502.3
Protein			
Baseline	1524.8 ± 57.4	1372.6 ± 190.1	152.2 ± 225.2
Day 1	1971.6 ± 77.2	1585.7 ± 68.5	386.0 ± 67.8
Day 2	1991.2 ± 75.2	1652.0 ± 78.1	339.2 ± 59.4
Day 3	2116.8 ± 103.7	1722.3 ± 96.1	394.5 ± 186.0
Day 4	2024.7 ± 135.1	1674.1 ± 121.8	350.6 ± 167.0

[1] $\bar{x}$ ± SE; $n = 6$. The sum of the macronutrient balances do not equal the daily energy balances because fecal energy cannot be subtracted from each macronutrient intake. Combined with slightly positive energy balances, this results in macronutrient balances that are positive at baseline.

[2] Significantly different from high-fat, high-activity condition for that day, $P < 0.05$.

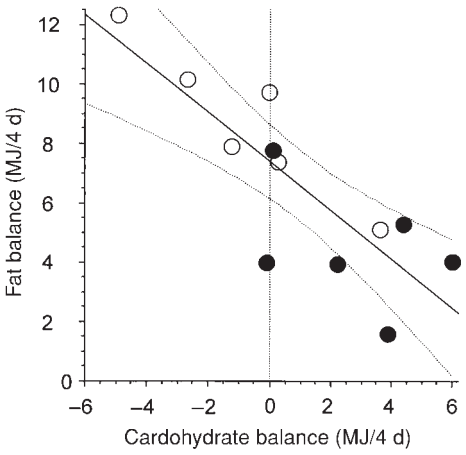

FIGURE 5. Relation between fat and carbohydrate balance during approximate energy balance under the high- (■) and low-activity (□) conditions. Significant relation for the low-activity condition and the combined high- and low-activity conditions, $P < 0.05$. The relation for the high-activity condition alone was not significant. Error bars represent SEMs. $n = 6$. Fat balance (MJ/d) = (7028 − 0.81) × carbohydrate balance (MJ/d); $r^2 = 0.686$.

dation. Carbohydrate is an essential fuel for the brain and other organs, but carbohydrate stores are tiny compared with fat stores. As such, carbohydrate deficits may increase food intake, leading to overconsumption of energy to replace the carbohydrate deficits (13). The overconsumption of energy in an attempt to replace carbohydrate deficits would then lead to obesity if the long-term signals to regulate body weight were inadequate.

Schrauwen et al (14) showed that during a shift from a low- to a high-fat diet, 7 d were required for fat oxidation to match fat intake. Our study showed that the rate at which one adapts to a high-fat diet can vary. A concurrent increase in physical activity accelerates the rate of adaptation to an isoenergetic high-fat diet. Note that even when physical activity is increased by almost 30% above a sedentary state, there is still a delay in the fall of the RQ to match the food quotient. Schrauwen et al (6) showed that a single bout of glycogen-depleting exercise before the initiation of an isoenergetic high-fat diet increased fat oxidation. Taken together, these results suggest that physical activity, either before or during exposure to an isoenergetic high-fat diet, results in an increase in fat oxidation and a decrease in the positive fat balance that occurs under sedentary conditions.

Other neural or endocrine mechanisms to increase fat oxidation or decrease carbohydrate oxidation, such as increased sympathetic activity, could also act to increase fat oxidation. Aerobic exercise increases sympathetic nervous system activity, and it was recently shown that agonists of the β_3 adrenoreceptor may be able to increase fat oxidation, as evidenced by a lower 24-h RQ (15). Further work in the area of the interaction between sympathetic activity and fat oxidation seems warranted.

In our studies, carbohydrate balance was negative for only 1 d in the high-activity condition. Fat oxidation increased, as evidenced by a fall in the npRQ. A decrease in glycogen stores may be an important factor in causing increased fat oxidation, possibly by allowing insulin to decline to lower concentrations. Alternatively, other signals may act on the existing cellular machinery to increase fat oxidation. Cellular signals of energy status, such as adenosine monophosphate kinase (16) and long-chain fatty acid coenzyme A (17), have been described and might be important in regulation of substrate oxidation. To our knowledge, the regulation of these pathways during the shift to a high-fat diet has not been explored.

An increase in protein balance under the low- and high-activity conditions accompanied the shift in substrate from carbohydrate to fat. In addition, the magnitude of the effect was greater under the high-activity condition. The mechanism appears to be different for the low- and high-activity conditions. Under the low-activity condition, protein oxidation decreased. Under the high-activity condition, absolute protein intake increased as a result of the increase in energy intake. Protein oxidation increased but did not match the increase in protein intake over the 4 d. Few data are available on the effect of high-fat diets on nitrogen balance, and the significance of this finding is unclear.

The results of this study have 2 major implications. First, as the world adopts a Western diet that provides a higher proportion of energy as fat, the prevalence of obesity is increasing (1). Body fat mass and dietary fat intake are directly related (18). These data and many others support a role for high amounts of dietary fat and lower amounts of physical activity as promoting body fat gain.

Second, the large degree of interindividual variability in the oxidation of fat in response to a high-fat diet was observed by other investigators (A Astrup, personal communication, 1999) and may indicate phenotypes that predispose to weight gain in susceptible individuals. We observed previously that the interindividual variability in the increase in fat oxidation is closely correlated with the RQ measured after an overnight fast (5). The overnight fasted RQ has been shown to be a risk factor for weight gain (19–21). Understanding how to modify fat oxidation could affect our ability to prevent weight gain in susceptible individuals. Accelerating fat oxidation and blunting the positive fat balance that occurs when individuals switch to a high-fat diet may be an important mechanism by which physical activity prevents weight gain (22, 23). These studies lend support to the current recommendations that prevention, specifically increasing physical activity, is a key element to preventing obesity in populations that consume a high-fat diet (24).

In conclusion, we showed that individuals differ in their ability to increase fat oxidation in response to an isoenergetic high-fat diet under sedentary conditions. Some individuals could rapidly achieve fat balance, whereas others did not appear to be able to increase fat oxidation to match fat intake. These same individuals oxidized fat to a greater extent when they increased their physical activity by walking on a treadmill to increase their total daily EE to 1.8 times the RMR. Thus, despite the measurement of approximate energy balance under both conditions, the fat balance was less positive under the high- than under the low-activity condition. The large degree of interindividual variability present under low-activity conditions was substantially reduced.

The mechanism or mechanisms by which individuals adapt to acute changes in dietary fat are largely unknown. We showed previously that physical fitness, as measured by $\dot{V}O_2$max, and insulin sensitivity are related to the adaptation to high-fat diets under sedentary conditions (5). The current study showed that concurrent physical activity increases fat oxidation during the shift to a high-fat diet. A better understanding of the regulation

of fat oxidation during dietary fat excess has potential therapeutic importance. For example, individuals who have a low capacity to adapt fat oxidation to a high-fat diet may need more physical activity to prevent weight gain. These results support the role of physical activity as a protective measure against the positive fat balance that may occur when individuals are exposed to high intakes of dietary fat.

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