Increased fat oxidation in prepubertal obese children: A metabolic defense against further weight gain?

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The purpose of this study was to measure postabsorptive fat oxidation at rest and to assess the association between fat mass and fat oxidation rate in prepubertal children, who were assigned to two groups: 35 obese children (weight, 44.5 ± 9.7 kg; fat mass; 31.7 ± 5.4%) and 37 nonobese children (weight, 30.8 ± 6.8 kg; fat mass, 17.5 ± 6.7%). Postabsorptive fat oxidation expressed in absolute value was significantly higher in obese than in nonobese children (31.4 ± 9.7 mg/min vs 21.9 ± 10.2 mg/min; $p < 0.001$) but not when adjusted for fat-free mass by analysis of covariance with fat-free mass as the covariate (28.2 ± 10.6 mg/min vs 24.9 ± 10.5 mg/min). In obese children and in the total group, fat mass and fat oxidation were significantly correlated ($r = 0.65$; $p < 0.001$). The slope of the relationship indicated that for each 10 kg additional fat mass, resting fat oxidation increased by 18 gm/day. We conclude that obese prepubertal children have a higher postabsorptive rate of fat oxidation than nonobese children. This metabolic process may favor the achievement of a new equilibrium in fat balance, opposing further adipose tissue gain. (J PEDIATR 1995;126:15-20)

Fat balance, calculated from the ratio between dietary fat and fat oxidation, may play a critical role in the regulation of body weight.[1] Fat intake does not promote fat oxidation[2]; the latter, which includes the proportion of energy expenditure that is not included by protein and carbohydrate oxidation, does not affect fat intake per se.[3] Therefore if the lipid content of the diet is higher than the overall fuel mix oxidized, a positive fat balance will produce fat storage. The maintenance of this process leads to a progressive increase in body fat mass. It has been hypothesized that increased fat stores, induced by a high proportion of fat in the diet, might promote fat oxidation,[1] favoring lipid balance readjustment and the maintenance of a new weight equilibrium at a higher level.

This study was undertaken to determine the relationship between fat mass and postabsorptive fat and carbohydrate oxidation rates in obese and nonobese prepubertal children studied in the same experimental conditions.

ANCOVA	Analysis of covariance
BMI	Body mass index
FFM	Fat-free mass
FM	Fat mass
PMR	Postabsorptive metabolic rate
RQ	Respiratory quotient
$\dot{V}CO_2$	Carbon dioxide output
$\dot{V}O_2$	Oxygen uptake

METHODS

Subjects. We studied 80 prepubertal white children aged 7 to 10 years who formed two groups: 40 obese children and 40 nonobese children. Some of the children participated in previous studies exploring the validity of energy intake re-

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ported by obese and nonobese children[4] or of energy expenditure during walking and running.[5] Obesity was defined as body mass index >97th percentile of the reference values for age and sex. Control children were selected based on BMI ≤97th percentile of the reference values for age and sex.[6] Physical examination and routine laboratory tests excluded health problems other than obesity. Pubertal stage was assessed according to Tanner.[7] None of the subjects reported significant changes in body weight during the month preceding the study. No child was taking any drugs. Informed consent was obtained from the parents of all subjects. The protocol was approved by the ethics committee of the University Hospital of Verona.

Physical characteristics. Anthropometric measurements (weight, height, and skin-fold thicknesses) were performed by the same investigator. Height was measured to the nearest 0.5 cm on a standardized, wall-mounted height board. Weight was determined to the nearest 0.1 kg by standard physician's beam scale with the child dressed only in light underwear and without shoes. Body mass index was calculated as weight (in kilograms) divided by height squared (in square meters). Skin-fold thicknesses were measured in triplicate to the nearest millimeter at the triceps and subscapular sites by means of an Harpenden skin-fold caliper (CMS Weighing Equipment Ltd., London, United Kingdom). The Lohman formulas were used to calculate the percentage of body fat from the sum of the two skin folds.[8] Fat mass was obtained by multiplying the percentage of body fat by body weight. Fat-free mass was obtained by subtracting body fat from body weight.

The expected error of predicting body fat from triceps and subscapular measurements in the age-specific group of 8- to 9-year-old children is ≅5% of body fat predicted by densitometry. The prediction error is slightly higher than the prediction error of percentage body fat from more skin folds, and is comparable with that reported in adults.[9, 10] Although the use of skin-fold thickness to assess FM is not completely satisfactory, particularly in obese subjects, other more valid techniques such as underwater weighing may lead to practical problems when applied to prepubertal children because of fear of the water or incomplete immersion. In addition, because the density of FFM changes during childhood,[8] further uncertainty is involved unless body density and total body water are measured simultaneously.

Experimental design. Before the postabsorptive metabolic rate measurement, children consumed an unrestricted diet. The day before the test they did not perform any intense physical exercise. The children arrived by car at the Department of Pediatrics at 7:30 AM in fasting condition; the last meal had been eaten at 8 PM the day before. After 30 minutes of rest on a hospital bed in a comfortable, temperature-controlled environment, continuous respiratory exchange was initiated by indirect calorimetry. During the 30-minute measurement period, children rested quietly watching cartoons. Throughout the PMR measurement, a technician observed the child to verify that he or she was motionless and relaxed during the respiratory exchange measurement. Special attention was given to prevent extra body movements or hyperventilation because the former increase PMR and the latter increases the respiratory quotient. Data from eight children (five obese and three nonobese) were not included in the statistical analysis because hyperventilation induced RQs greater than 1.0.

In a subsample of 23 obese and 11 nonobese children, a blood sample was taken from an antecubital vein immediately after the PMR measurements, to measure plasma immunoreactive insulin, glucose, and free fatty acids concentrations. Blood could not be drawn from the other children because either the children or parent refused. Plasma glucose[9] and free fatty acids[10] were measured enzymatically, whereas the plasma immunoreactive insulin level was assayed by radioimmunoassay.[11]

Postabsorptive metabolic rate. Postabsorptive metabolic rate was measured by respiratory gas exchange for 30 minutes as previously described.[12] An open-circuit computerized indirect calorimeter (Deltatrac, Datex Division, Instrumentarium OY, Helsinki, Finland) connected to a transparent hood system was used. The instrument was calibrated before each test with a gas mixture (95.2% oxygen and 4.8% carbon dioxide). Records of oxygen consumption and carbon dioxide production were printed out at 1-minute intervals. The mean of the last 20 minutes was used to evaluate PMR. The energy expenditure was derived from oxygen uptake and carbon dioxide output according to the formula by Lusk.[13]

Macronutrient oxidation rate. The macronutrient oxidation rate was calculated from $\dot{V}O_2$, $\dot{V}CO_2$, and RQ by means of the following formulas[14]:

$$F_{ox}\ (gm/min) = 1.67\ \dot{V}O_2\ (L/min) - 1.67\ \dot{V}CO_2\ (L/min) - 0.307\ P_{ox}$$

$$G_{ox}\ (gm/min) = 4.55\ \dot{V}CO_2\ (L/min) - 3.21\ \dot{V}O_2\ (L/min) - 0.459\ P_{ox}$$

where F_{ox} = fat oxidation; G_{ox} = glucose oxidation, and P_{ox} = protein oxidation. The protein oxidation was estimated as follows:

$$P_{ox}\ (gm/min) = \frac{PMR\ (kJ/min) \cdot 0.15}{16.74\ kJ}$$

We assumed that protein oxidation covered 15% of PMR in both obese and nonobese children. This assumption does not affect the relative partition between carbohydrate and fat oxidation determined by indirect calorimetry; 16.74 kJ is the energy produced by the oxidation of 1 gm of protein.

Table I. Physical characteristics of obese and nonobese children

	Obese (n = 35)	Nonobese (n = 37)	p
Gender (M/F)	18/17	19/18	
Age (yr)	8.7 ± 1.5	8.8 ± 1.0	NS
Weight (kg)	44.5 ± 9.7	30.8 ± 6.8	<0.001
Height (cm)	134 ± 9	133 ± 7	NS
BMI (kg/m^2)	24.5 ± 2.9	17.0 ± 2.1	<0.001
FM (%)	31.7 ± 5.4	17.5 ± 6.7	<0.001
FM (kg)	14.5 ± 5.2	5.7 ± 3.8	<0.001
FFM (kg)	30.0 ± 5.7	24.1 ± 3.9	<0.001
Skin-fold thickness			
Triceps (mm)	22.6 ± 6.4	11.8 ± 4.2	<0.001
Suscapular (mm)	25.3 ± 9.2	8.4 ± 4.8	<0.001

Data reported as mean ± SD.
NS, Not significant.

Statistical analysis. The results are expressed as mean ± SD. An unpaired *t* test was used to compare obese and nonobese children. The degree of association between two variables was quantified by using the Pearson product-moment linear correlation coefficient. Analysis of covariance, with FFM as the covariate, was used to calculate PMR and macronutrient oxidation rates adjusted for FFM (i.e., the metabolic active tissue). To assess the relationship between fat oxidation as the dependent variable and body weight, FFM, and FM as the independent variables, a stepwise regression procedure was used. The Statistical Analysis Systems/STAT statistical package, version 6.0 (SAS Institute Inc., Cary, N.C.) was used to analyze the data.

RESULTS

Age and height were comparable in the two groups; weight, BMI, percentage of FM, FM, and FFM were significantly higher in the obese group (Table I). The measurement of skin-fold thickness confirmed the diagnosis of obesity estimated by means of the BMI. In each of the obese children the triceps skin fold was greater than the reference value (85th percentile for age and sex, assessed on the tables devised by Tanner and Whitehouse[15]), frequently used as a cutoff point to define obesity in children.[16] In addition triceps and subscapular thicknesses were both significantly correlated to BMI ($r = 0.92$ and $r = 0.91$; $p < 0.001$, respectively).

Postabsorptive metabolic rate was significantly higher in obese than in nonobese children (Table II). Postabsorptive metabolic rate adjusted for FFM by means of ANCOVA, with FFM as the covariate, was comparable in the two groups. The postabsorptive RQ was slightly lower in obese than in nonobese children (Table II).

The postabsorptive fat oxidation rate was significantly higher in obese than in nonobese children. When expressed as a percentage of PMR (32.3 ± 7.5% vs 25.5 ± 12.1%) or of PMR adjusted for FFM (32.7 ± 9.6% vs 25.9 ± 12.5%), it was significantly ($p < 0.01$) higher in obese than in nonobese children. In obese children, FFM explained 48.6% of the variance of fat oxidation ($r = 0.697$), versus 14.6% ($r = 0.382$) in nonobese children. In the whole group, a significant positive correlation was found between postabsorptive fat oxidation rate and FM expressed both in absolute values and as a percentage of body weight (Table III). The degree of correlation was higher in the obese group and not significant in the nonobese group. The narrow range of body fat in the nonobese group may explain these results. When the postabsorptive fat oxidation was adjusted for FFM by

Table II. Postabsorptive metabolic rate, respiratory quotient, fat and glucose postabsorptive oxidation rates in obese and nonobese children

	Obese (n = 35)	Nonobese (n = 37)	p
PMR (kJ/day)	5218 ± 718	4559 ± 499	<0.001
PMR adjusted for FFM (kJ/day)	4953 ± 421	4810 ± 421	NS
RQ	0.862 ± 0.024	0.882 ± 0.039	<0.01
F_{ox} (mg/min)	31.4 ± 9.7	21.9 ± 10.2	<0.001
F_{ox} adjusted for FFM (mg/min)	28.2 ± 10.6	24.9 ± 10.5	NS
G_{ox} (mg/min)	110.9 ± 19.1	110.4 ± 25.8	NS
G_{ox} adjusted for FFM (mg/min)	109.1 ± 26.5	112.0 ± 26.5	NS

Data are reported as mean ± SD.
F_{ox}, Fat oxidation; G_{ox}, glucose oxidation; *NS*, not significant; see text for other abbreviations.

Table III. Correlation coefficients between body weight, fat-free mass, body fat, and fat and carbohydrate postabsorptive oxidation rates in obese, nonobese, and obese and nonobese children combined

	Obese (n = 35)	Nonobese (n = 37)	Total (n = 72)
Body weight (kg) vs:			
F_{ox} (mg/min)	0.746*	0.300†	0.635*
G_{ox} (mg/min)	0.135	0.164	0.127
Fat-free mass (kg) vs:			
F_{ox} (mg/min)	0.697*	0.382	0.627*
G_{ox} (mg/min)	0.143	0.151	0.108
Fat mass (kg) vs:			
F_{ox} (mg/min)	0.651*	0.103	0.555*
G_{ox} (mg/min)	0.103	0.140	0.008
Fat mass (%) vs:			
F_{ox} (mg/min)	0.326†	−0.007	0.414*
G_{ox} (mg/min)	0.006	0.122	0.052

F_{ox}, Fat oxidation; G_{ox}, glucose oxidation; see text for abbreviations.
*$p < 0.001$.
†$p < 0.05$.

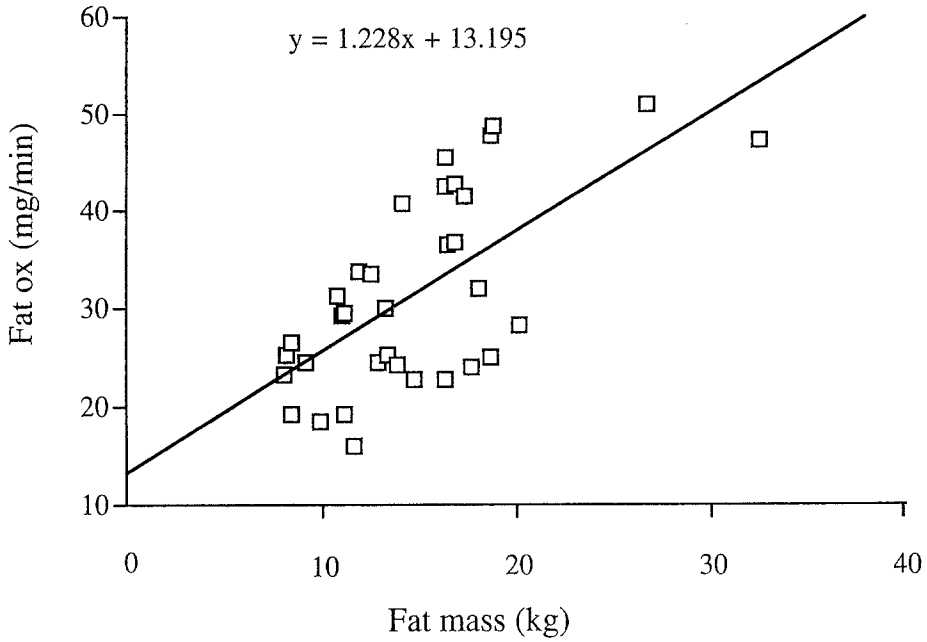

Fig. 1. Regression line between absolute fat mass (in kilograms) and postabsorptive fat oxidation *(fat ox)* rate in 35 obese children. The regression equation is as follows: Postabsorptive fat oxidation rate (mg/min) = 1.228 · Fat mass (kg) + 13.195 ($r = 0.651$; $p < 0.001$).

ANCOVA, it was comparable in both the obese and nonobese children. In the obese group only, when a stepwise regression analysis was performed, addition of FM in the model increased by 8.1% ($r^2 = 0.567$), the proportion of the variance of postabsorptive fat oxidation already explained by FFM. As expected, postabsorptive fat oxidation was positively correlated to PMR in obese children ($r = 0.726$; $p < 0.001$), in nonobese children ($r = 0.454$; $p < 0.01$), and in the total group of children ($r = 0.663$; $p < 0.001$).

No significant difference in postabsorptive glucose oxidation rate was found in the two groups of children, and glucose oxidation was not correlated to FM (Table II). In the subgroup studied (n = 34), fasting insulin plasma levels were significantly higher in obese than in nonobese children (104 ± 32 pmol/L vs 73 ± 21 pmol/L, respectively; $p < 0.05$), whereas blood glucose (4.42 ± 0.22 mmol/L vs 4.35 ± 0.48 mmol/L; p not significant) and free fatty acid (591 ± 75 μmol/L vs 668 ± 227 μmol/L; p not significant) concentrations were comparable in the two groups of children. Plasma insulin concentration was significantly ($p < 0.05$) correlated to FM expressed both as an absolute value ($r = 0.551$) and as a percentage of body weight ($r = 0.546$). No significant association was found between insulin levels and postabsorptive fat oxidation rate ($r = 0.107$; p not significant) or postabsorptive glucose oxidation rate ($r = 0.367$; p not significant).

DISCUSSION

The results of this study show that moderately obese children had a greater fat oxidation rate than that in nonobese children. Obese children had a significant association between postabsorptive fat oxidation rate and FM. Postabsorptive fat oxidation rate adjusted for FFM by ANCOVA was comparable in the obese and in the nonobese groups. This relationship is expected because FFM is the only tissue in which fat oxidation occurs. However, after taking FFM into account, FM explained an additional 8.1% of the residual variance in postabsorptive fat oxidation. Therefore the expansion of FM seems directly involved in the mechanisms leading to an increased fat oxidation rate. Other factors, which were not evaluated in our study, might affect residual variance in fat oxidation (e.g., the degree of insulin resistance). Fasting insulin plasma levels, available for only a subgroup of children, were higher with increasing FM, confirming previous results.[17] In a previous study in children and adolescents, basal insulin levels were not associated with fat oxidation at rest.[18] Because in normal adults the sensitivity of lipid oxidation to hyperinsulinemia was about half the sensitivity of lipolysis to hyperinsulinemia,[19,20] it might be argued that only a sufficient degree of hyperinsulinemia may reduce lipid oxidation, by stimulating glucose oxidation. Therefore it might be assumed that in the study by

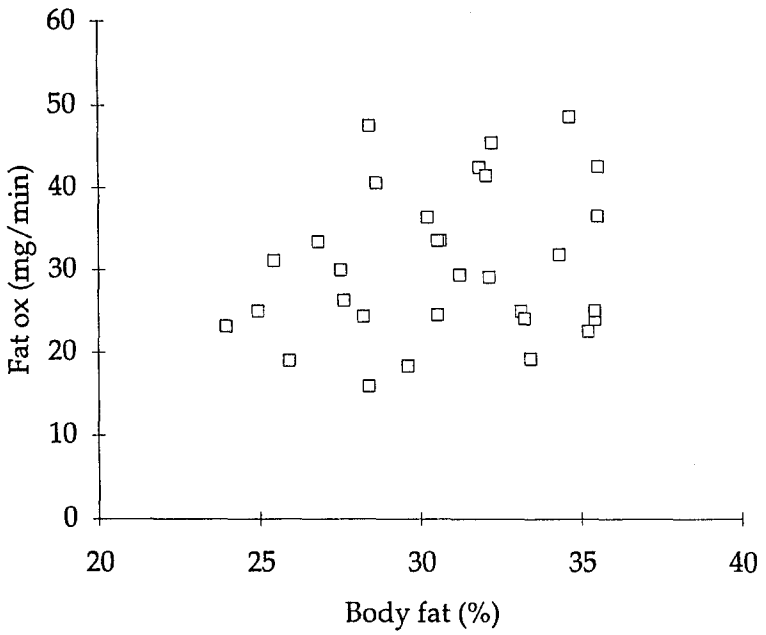

Fig. 2. Regression between relative fat mass (percentage) and postabsorptive fat oxidation *(Fat ox)* rate in 35 obese children. The regression equation is as follows: Postabsorptive fat oxidation rate (mg/min) = 0.599 · Fat mass (%) + 12.11 ($r = 0.336$; $p < 0.05$).

Le Stunff and Bougneres,[18] hyperinsulinemia did not reach a sufficient level to stimulate glucose oxidation and reduce fat oxidation in children and adolescents. An improvement in insulin sensitivity, leading to an increase in carbohydrate oxidation and a reduction of the fat oxidation rate, has been shown to increase the risk for further weight gain, as suggested by the results of a large study on insulin sensitivity and obesity in adult Pima Indians.[21] No association between postabsorptive fat oxidation rate and age, pubertal status, and duration of obesity was found in obese children.[18]

Increased postabsorptive fat oxidation in obese prepubertal children is important for two reasons: first, it shows that obese children must eat more fat than their lean counterparts to maintain fat balance. Second, the rise in fat oxidation in the obese children can be considered as a buffer mechanism to offset the excess fat intake, the possible initial defect in fat oxidation, or both, that must have occurred in their preobese state, by favoring a new lipid equilibrium. With the regression equation between FM (independent variable) and fat oxidation (dependent variable), it is possible to predict an increase of 18 gm/day in fat oxidation for each 10 kg increase in FM. This result is comparable to that previously reported for obese adult women.[22] The increased fat oxidation accompanying fat gain might explain why, after a dynamic phase of body weight gain, apparent FM stability might be reached, despite the fact that lipid continues to account for a relatively high proportion of energy intake.[23]

Although our results are not necessarily extensible to the postprandial state (a period when the contribution of fat oxidation to energy expenditure is lower than in the postabsorptive state), and the estimates of body composition by means of skin-fold thickness have a margin of error, the clinical implications of these results are evident: a modification in the proportion of the macronutrients in the diet by selectively reducing lipid intake is essential, and should be combined with the avoidance of a sedentary lifestyle (e.g., reduced TV viewing, using stairs instead of elevators) and with increased physical activity (programmed exercise and sports) so that the fat oxidation rate and thus fat loss will be enhanced. Reduced energy (fat) intake and increased activity are necessary to produce the negative energy (fat) balance, without which fat loss is impossible. Physical exercise of low intensity and of long duration (e.g., walking at various paces) appears to be realistic in practice and induces the utilization of fat as the major substrate for covering energy expenditure, and favors the maintenance of a negative fat balance.[1] In addition, the choice of a mixed diet with a low-lipid content favors the maintenance of a high rate of fat oxidation. This is particularly useful because the enhanced postabsorptive fat oxidation in obese individuals seems to be counteracted with fat loss. Data obtained in adults show that a weight loss of 12.7 kg, 77% of which was

fat, produced a reduction of the postabsorptive fat oxidation rate equal to that predicted by the regression equation calculated between fat oxidation and fat mass in a cross-sectional study.[22] Therefore in postobese individuals, the adjustment of the composition of the maintenance diet (food quotient) to the level of the fuel mix oxidized (RQ) should favor body weight stability and prevent the rapid relapse of obesity generally observed after the hypocaloric diet is discontinued. This concept is supported by the observation that a high 24-hour RQ was associated with a higher risk of body weight gain during a 2-year follow-up period in adult Pima Indians.[24]

We conclude that obesity in prepubertal children leads to an increased lipid oxidation rate at rest. This situation may favor the achievement of a new equilibrium in lipid balance, opposing further body fat gain. Modification of diet composition (i.e., a reduction in fat intake) concomitant with a stimulation of the level of physical activity (which increases fat oxidation) will favor fat loss by achieving a negative fat balance.

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