

Longitudinal changes in fatness in white children: no effect of childhood energy expenditure¹⁻³

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See corresponding editorial on page 190.

ABSTRACT Reduced energy expenditure may predispose children to the development of obesity, but there are limited longitudinal studies to support this theory. We studied 75 white, preadolescent children over 4 y by taking annual measures of body composition and resting energy expenditure (by indirect calorimetry) and two annual measures of total energy expenditure and physical-activity-related energy expenditure (by doubly labeled water). Body composition of parents was assessed at the onset of the study with use of underwater weighing. The major outcome variable was the individual rate of change in fat mass (FM) adjusted for fat-free mass (FFM). The influence of sex, energy expenditure components, initial FM, and parental FM on the rate of change in FM was analyzed by hierarchical linear modeling and analysis of variance. The rate of change in absolute FM was 0.89 ± 1.08 kg/y (range: -0.44 to 5.6 kg/y). The rate of change in FM adjusted for FFM was 0.08 ± 0.64 kg/y (range: -1.45 to 2.22 kg/y) and was similar among children of two nonobese parents and children with one nonobese or one obese parent, but was significantly higher in children with two obese parents (0.61 ± 0.87 kg/y). The major determinants of change in FM adjusted for FFM were sex (greater fat gain in girls), initial fatness, and parental fatness. None of the components of energy expenditure were inversely related to change in FM. The main predictors of change in FM relative to FFM during preadolescent growth are sex, initial fatness, and parental fatness, but not reduced energy expenditure. *Am J Clin Nutr* 1998;67:309-16.

KEY WORDS Obesity, children, body composition, growth, preadolescents, energy expenditure, fat mass, fat-free mass

INTRODUCTION

It has been hypothesized that a relatively low level of energy expenditure is a predisposing factor in obesity (1, 2). Two longitudinal studies, one in infants of underweight compared with overweight mothers (1) and the other in Pima Indian adults (2), provide support for this theory. However, cross-sectional studies in adults (3-5), adolescents (6), and children (7, 8), as well as a meta-analysis (9), suggest that absolute total energy expenditure (TEE) and resting energy expenditure (REE) are similar in obese and lean individuals after these measurements are normalized for differences in body composition.

In a previous cross-sectional analysis we showed that energy expenditure components in children [TEE, REE, and physical-

activity-related energy expenditure (AEE)] were similar among children from lean and obese parents (8). Because of the inherent limitations of cross-sectional studies, longitudinal studies in growing children have examined whether low energy expenditure predisposes to accelerated weight gain and increased fat mass (1, 10). The purpose of the present study was to extend our previous cross-sectional analysis and examine systematic interindividual differences in the longitudinal development of body fat during preadolescent growth, and, specifically, to examine whether childhood energy expenditure influences the rate of change in body fat.

Because growth of the individual components of body composition is likely to be a nondiscrete, continuous process represented by the parameters of each subject's individual growth trajectory, we used a multiple-measure, longitudinal design and hierarchical linear modeling to examine our hypotheses. Thus, we examined whether childhood energy expenditure components (REE, AEE, and TEE) or parental body composition were related to the rate of change in body fat over 4 y in growing prepubertal children of obese and nonobese parents.

SUBJECTS AND METHODS

Subjects

Our sample included 75 white children (35 girls and 40 boys) aged 5.2 ± 0.9 y (range: 4-7.2 y) at their initial test visit, and their mothers (34 ± 5 y) and fathers (37 ± 5 y). The sample consisted of 21 sib pairs and 33 unrelated children. The children were recruited from Burlington, VT, and the surrounding area (predominantly Chittenden County) through newspaper adver-

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² Supported by the US Department of Agriculture (95-37200-1643), the National Institute of Child Health and Human Development (R29 HD 32668, RO1 HD/HL 33064), and a National Research Service Award to TRN (F32-HD-08025).

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Received April 23, 1997.

Accepted for publication August 13, 1997.

tisements and word of mouth. There were no major inclusion or exclusion criteria other than the absence of major illness since birth. We chose to study preadolescent children because this period of growth is relatively stable and is not confounded by differences in hormone concentrations or dramatic shifts in body composition. In addition, this period of growth is a susceptible period for obesity development (11).

Children were stratified according to parental obesity status into four groups: both parents nonobese, obese mother and nonobese father, obese father and nonobese mother, and both parents obese. For recruitment purposes, parents were classified as obese based on a body mass index above or below the 85th percentile for their age and sex (12). We previously reported no difference in energy expenditure components in a cross-sectional comparison of children of lean parents with children of obese parents (8). All studies were performed during the school year, but not during the severe winter months (December to February). The nature, purpose, and possible risks of the study were carefully explained to both parents before consent was obtained. All measurements were performed at the General Clinical Research Center at the University of Vermont between 1991 and 1996. The experimental protocol was approved by the Committee on Human Research for the Medical Sciences of the University of Vermont.

General outline of protocol

Children returned for testing annually; follow-up visits were scheduled to occur on the same date as the original visit within ± 4 wk. All subjects had either three or four annual measures of height, weight, anthropometric indexes, body composition, and REE and a physical activity assessment by questionnaire. TEE was measured with the doubly labeled water method at the first and second study visits. The following variables were measured in both parents at the time of the initial visit: height, weight, anthropometric indexes, REE, body composition by underwater weight, and physical activity by questionnaire.

The protocol was as follows: on the evening before testing, children came to the laboratory for collection of baseline urine samples, oral dosing with doubly labeled water, and familiarization with the investigators and testing equipment (for years 1 and 2 only). On the following morning the children returned to the laboratory for other test procedures. The children returned to the laboratory 2 wk after the initial testing for repeated measurement of REE and body composition, and in years 1 and 2, for the collection of two additional urine samples for doubly labeled water analysis.

Measurement of energy expenditure components

REE was measured under postprandial conditions (2–3 h after the children consumed their usual breakfasts at home) in duplicate (14 d apart) by indirect calorimetry with a metabolic monitor (Deltatrac, Yorba Linda, CA) as described previously (8). In our experience, postprandial measurements of REE provide the environment for reproducible measures of energy expenditure in children; we reported previously that the CV for 169 repeat measures with use of this protocol is $5.4 \pm 4.1\%$ for metabolic rate and $2.9 \pm 2.2\%$ for respiratory quotient (13). We also established previously that REE is 11% higher when the postprandial protocol is used compared with typical postabsorptive conditions (13). The postprandial protocol thus includes the average energy cost for meal-induced thermogenesis, which occurs 2 h after a meal in children (14).

TEE was measured over 14 d under free-living conditions with the doubly labeled water technique, using a protocol with a theoretical error of $<5\%$, as described previously (8). Samples were analyzed in triplicate for H_2^{18}O and $^2\text{H}_2\text{O}$ by isotope-ratio mass spectrometry at the University of Vermont (samples from year 1) and the University of Alabama at Birmingham (samples from year 2) as described previously (15). The instruments in both laboratories have been cross-validated against one another (15). When all samples for deuterium and ^{18}O were reanalyzed in seven subjects, TEE values were in close agreement ($\pm 4.3\%$), as described previously (15). The carbon dioxide production rate was calculated by using Equation R2 of Speakman et al (16), energy expenditure was calculated by using equation 12 of de Weir (17), and the mean value for the food quotient of the children's diet (0.90) was determined from a food-frequency questionnaire. AEE was estimated from the difference between TEE and postprandial REE. No correction for the thermic effect of feeding was necessary because REE was measured under postprandial conditions.

Qualitative information on physical activity patterns in children was estimated by using the structured activity questionnaire of Kriska et al (18). Mothers were interviewed in the presence of the child. The questionnaire is designed to assess hours per day spent sleeping, viewing television, and performing various recreational physical activities.

Assessment of anthropometric indexes and body composition

Height was measured with a stadiometer with subjects not wearing shoes. Weight was measured on an electronic scale with subjects wearing light clothing. Skinfold thicknesses (axilla, chest, subscapular, suprailiac, abdomen, triceps, calf, and thigh) were measured with use of the procedures of Lohman et al (19). Whole-body resistance was measured in duplicate (14 d apart) in children with a bioelectrical impedance analyzer (model 101A; RJL, Mt Clemens, MI) and was used to calculate fat-free mass as described previously (20). The body-composition data from the bioimpedance analysis were used specifically for adjusting energy expenditure data in children.

Fat mass and fat-free mass were also estimated from anthropometry by using an equation developed in children with dual-energy X-ray absorptiometry (DXA) as a criterion method (21). Body composition derived by anthropometry was used for the analysis of longitudinal changes in fat mass and fat-free mass. In a subset of children who also had three or more measures of body composition by DXA, the rate of change in absolute fat mass by DXA (1.41 ± 1.30 kg/y) was highly correlated and not significantly different from the rate of change in absolute fat mass derived by anthropometry (1.36 ± 0.60 kg/y; $r = 0.85$).

Procedures in parents

Height, weight, anthropometric indexes, and postprandial REE were measured in parents as described above for children. In addition, body composition was determined by underwater weight as described previously (22) with the Siri (23) equation. The test-retest reliability of fat mass with our underwater weighing system has an intraclass correlation coefficient of >0.98 and a CV $<5\%$ (24). Leisure-time physical activity was assessed with the Minnesota leisure-time activity questionnaire (25) as described previously (26).



Data adjustment

To examine the rate of change in body fat independent of that expected as a result of growth, we examined the rate of change in fat mass adjusted for fat-free mass. Adjusted fat mass was calculated for each “wave” of data collection on the basis of the residual fat mass derived from a regression with fat-free mass. For each individual, the residual fat mass at each time point was plotted as a function of age (ie, time) to obtain an individual slope, or rate of change in residual fat mass. Thus, our major dependent variable was the rate of change in fat mass adjusted for fat-free mass, which represents the change in fat mass relative to that expected for the observed change in fat-free mass. We also examined the data by using absolute fat mass at each year as the major dependent variable and the results were essentially the same. Also, to examine the effects of energy expenditure components relative to body size, all values were adjusted for fat-free mass (as measured by bioelectrical resistance in children and underwater weight in adults) through use of a regression-based approach.

Statistical analysis

We used two different approaches to examine whether various independent parameters influenced change in adjusted body fat. The first approach involved two-level, hierarchical linear modeling (HLM) as described by Bryk and Raudenbush (27). At level 1, the annual measures of body composition were used to estimate linear growth models for each child. The growth curves for each child were defined by a unique intercept and slope parameter that described the within-child, time-dependent relation for change in adjusted fat mass. Variation in the individual growth curves was examined by first fitting random coefficients, or unconditional models, to the data. Estimates of the level 1 growth curves for residualized fat were computed. The level 1 growth curve data were then weighted differentially by using a generalized least-squares approach that assigned higher weights to children whose growth curve estimates were more reliable at predicting outcome measures.

At level 2, HLM was used to explain between-child variability in the parameters (ie, slope and intercept) defining the individual growth curves. The conventional starting point for most HLM analysis is estimating an unconditional model for the level 1 growth curve parameters. Unconditional models do not include level 2 predictors and are essentially baseline models with which theoretical models can be compared. The equation for each level 1 growth parameter is specified in terms of an intercept that reflects the population means for the initial status and rate-of-change parameters and a residual term that represents the between-person variance, or the random contribution of each

child to the parameter estimates. The HLM unconditional model provides tests of the statistical significance for the pooled level 1 intercepts averaged across persons. In our analysis, the statistical significance of the unconditional model indicated whether the average relation between time and residual fat was different from zero, and tested whether there was sufficient variance around the growth parameters to warrant additional modeling (28). The variance in the unconditional growth parameters was then examined by specifying a series of models that were “conditional” with respect to hypothesized level 2 (children’s level) variables. HLM analysis was performed by using HLM FOR WINDOWS, version 4.01 (Assessment Systems Corporation, St Paul).

In addition, analysis of variance (ANOVA) and multiple regression techniques were used to examine the influence of factors such as sex, childhood energy expenditure, and parental body composition on the rate of change in fat mass adjusted for fat-free mass as derived by the level 1 HLM as described above. Data were analyzed by using SAS software version 6.10 (SAS Institute Inc, Cary, NC), with significance set at $P < 0.05$ for all tests.

Because our sample included 21 sibling pairs, the data were analyzed twice for each statistical approach. All children were included in the first analysis. The data were then reanalyzed after random deletion of one child from each sibling pair. The main results and major findings were essentially the same with use of both of these approaches; thus, to maximize the power of the analyses,¹ we present data based on analysis of all children in the sample.

RESULTS

General descriptive characteristics

The physical characteristics of the children and their parents at entry to the study are shown in **Table 1**, and the body composition of children at each assessment year is summarized in **Table 2**. Fat mass in year 1 was strongly correlated ($P < 0.001$) with fat mass in year 2 ($r = 0.92$), year 3 ($r = 0.93$), and year 4 ($r = 0.87$). The rate of change in absolute fat mass was highly variable with an average of 0.89 ± 1.08 kg/y (range: -0.44 to 5.6 kg/y). The average rate of change in fat mass adjusted for fat-free mass was 0.08 ± 0.64 kg/y and was highly variable between subjects (range: -1.45 to 2.22 kg/y; **Figure 1**). In two-way ANOVA, the rate of change in fat mass adjusted for fat-free mass was significantly influenced by parental obesity group ($P = 0.0009$), with a marginal effect of sex ($P = 0.07$) and no significant interaction ($P = 0.75$), as summarized in **Table 3**. In post hoc analysis with the sexes combined, the influence of parental obesity was explained by a significantly higher rate of change in fat mass adjusted for fat-

TABLE 1

Physical characteristics of children and their parents at the initiation of the study¹

	Children (n = 75)	Mothers (n = 54)	Fathers (n = 54)
Weight (kg)	20.2 ± 3.8 (14.7–34.0)	77.8 ± 22.5 (45.2–38.6)	90.9 ± 18.9 (58.9–137.6)
Fat mass (kg)	3.4 ± 1.7 (1.1–9.9)	28.5 ± 15.4 (7.3–69.6)	24.4 ± 12.4 (5.4–57.5)
Fat-free mass (kg)	16.8 ± 2.7 (11.9–24.1)	49.2 ± 10.4 (27.2–89.8)	66.5 ± 9.4 (44.0–84.9)
Percentage body fat (%)	16.4 ± 5.3 (6.9–39.2)	34.6 ± 10.5 (13.2–64.2)	25.6 ± 8.5 (7.6–43.8)

¹ $\bar{x} \pm SD$; range in parentheses.

TABLE 2
Mean physical characteristics in children at each year of measurement¹

	Year 1 (n = 75)	Year 2 (n = 75)	Year 3 (n = 71)	Year 4 (n = 53)
Age (y)	5.2 ± 0.9	6.2 ± 0.9	7.2 ± 0.9	8.3 ± 0.8
Weight (kg)	20.2 ± 3.8	23.2 ± 5.0	26.6 ± 6.4	29.9 ± 7.5
Height (m)	1.11 ± 0.07	1.18 ± 0.07	1.24 ± 0.07	1.31 ± 0.07
Fat mass (kg)	3.4 ± 1.6	4.3 ± 2.3	5.5 ± 3.2	6.4 ± 3.5
Fat-free mass (kg)	16.8 ± 2.7	18.9 ± 3.2	21.1 ± 3.8	23.5 ± 4.5
Percentage body fat (%)	16.4 ± 5.3	17.8 ± 5.8	19.4 ± 6.7	20.4 ± 6.0

¹ $\bar{x} \pm SD$.

free mass in children with two obese parents (0.61 ± 0.87 kg fat mass/y) than in the other groups (Table 3). A subset of the longitudinal data showing absolute change in fat mass for subjects in the upper and lower 10th percentiles for rate of change in fat mass adjusted for fat-free mass is provided in **Figure 2**.

Description of HLM findings

The intercept parameter (ie, initial fat level) was significantly related to the child's sex ($\beta_{01} = -1.88$ kg/y, $P < 0.001$; higher value in girls) and maternal residual fat level ($\beta_{02} = 0.036$ kg · y⁻¹ · kg⁻¹, $P < 0.01$). These variables explained 71% of the intercept parameter variance. None of the measures of energy expenditure or physical activity in children (on an absolute basis or after adjustment for fat-free mass) were significant in the level 2 model for the intercept parameter. The rate of change in residual fat (ie, the individual slopes for the rate of change in fat mass adjusted for fat-free mass) was also significantly associated with sex ($\beta_{11} = -0.403$ kg/y, $P < 0.001$; higher in girls) and paternal residual fat level ($\beta_{12} = 0.013$ kg · y⁻¹ · kg⁻¹, $P < 0.01$). There was a trend for a positive coefficient associated with TEE adjusted for REE ($P = 0.052$), suggesting that higher levels of AEE are associated with a more rapid rate of residual fat accumulation. Together, these variables accounted for $\approx 67\%$ of the variance in the slope for change in residual fat. None of the other measures of energy expenditure or physical activity in children (on an absolute basis or after adjustment for fat-free mass) were significant in the level 2 model for the change in residual fat.

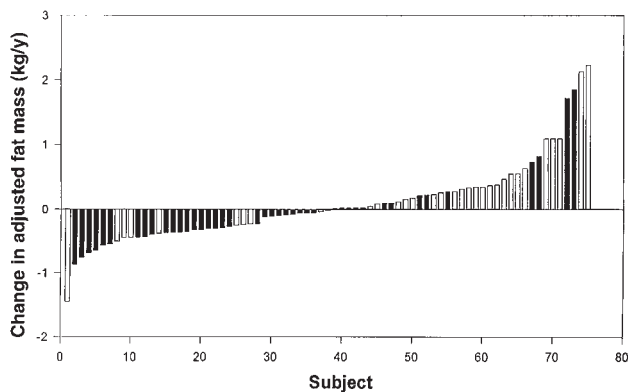


FIGURE 1. Individual ranking of the rate of change in adjusted fat mass. Each bar represents the individual slope derived from repeat measures and the individual growth trajectories. □, girls; ■, boys.

ANOVA and multiple regression analysis

The rate of change in adjusted fat mass was significantly and positively related to fatness in mothers ($r = 0.29$, $P = 0.013$) and in fathers ($r = 0.40$, $P < 0.001$) and was not inversely related to energy expenditure; in fact, change in fatness was significantly and positively related to TEE ($r = 0.28$, $P = 0.025$) and TEE adjusted for REE ($r = 0.33$, $P = 0.008$) and was not significantly related to REE ($r = 0.14$, $P = 0.24$). In multiple regression, the strongest predictors of change in adjusted fat mass were fatness in fathers (partial $R^2 = 0.19$) and fatness in mothers (partial $R^2 = 0.06$; combined model $R^2 = 0.24$). After parental fatness was adjusted for, energy expenditure in children was not significantly related to change in adjusted fat mass in children. In the absence of initial childhood fatness and parental fatness data, the significant predictors of change in adjusted fat mass were TEE adjusted for REE (positive and weak effect, $r^2 = 0.10$) and sex (higher in girls). The lack of relation between change in fat mass adjusted for change in fat-free mass and energy expenditure components is shown in **Figure 3**.

In an additional analysis we compared energy expenditure values in children in the upper and lower 10th percentiles for change in adjusted fat mass. On the basis of two measurements performed 1 y apart, average energy expenditure components were not significantly different in these two extreme subgroups (**Table 4**). We also compared change in fat mass adjusted for fat-free mass in subgroups of children who had consistently high or low values for energy expenditure components. Children were defined as high or low if their residual values of energy expenditure relative to fat-free mass were consistently greater (high energy expenditure) or lower (low energy expenditure) than zero in the first 2 y of data collection. The rate of change in fat mass adjusted for fat-free mass was not significantly different between children who had consistently high and those who had consistently low energy expenditure components (Table 4).

DISCUSSION

We provided evidence against the theory that reduced levels of energy expenditure are involved in excess body fat accumulation during preadolescent growth. Our major finding was that the main predictors of change in fat mass adjusted for fat-free mass during preadolescent growth are initial fatness, parental fatness, and sex.

The hypothesis that altered energy expenditure might be involved in the obesity in children is based on the results of two studies (1, 10). Griffiths and Payne (10) found that TEE and REE were lower in children with one or more obese parents than in



TABLE 3

Change in fat mass adjusted for change in fat-free mass as a function of parental obesity and sex¹

Subgroup	Change in girls	Change in boys
	<i>kg/y</i>	
Children with two nonobese parents	0.02 ± 0.34 [11]	-0.32 ± 0.27 [9]
Children with obese mother and nonobese father	-0.12 ± 0.69 [6]	-0.10 ± 0.36 [12]
Children with obese father and nonobese mother	0.21 ± 0.56 [6]	-0.18 ± 0.31 [12]
Children with two obese parents	0.72 ± 0.78 [12]	0.42 ± 1.05 [7]

¹ $\bar{x} \pm SD$; *n* in brackets. In two-way ANOVA there was a significant group effect of parental obesity ($P < 0.001$), a trend toward a sex effect ($P = 0.07$), and no significant interaction ($P = 0.75$); with the interaction effect removed, the sex effect was $P = 0.06$. In post hoc analysis with sexes combined, all groups were similar except for children with two obese parents.

children with two nonobese parents. However, the study had a small sample size and estimated TEE with heart rate monitoring, a technique that may be unreliable in children (29). In a later study reporting 12-y prospective data, energy expenditure did not predict weight gain (30). Roberts et al (1) found that TEE was lower in infants born to overweight compared with underweight mothers, and that the infants with lower energy expenditure gained more weight in the initial 3 mo of life. It is important to consider that the "control" infants were born to severely undernourished mothers, and an alternative explanation of these findings could be that energy expenditure is higher in babies born to undernourished mothers. Furthermore, only six infants with overweight mothers gained excess weight, two of whom had energy expenditure levels below the expected physiologic range. Additionally, the findings of Roberts et al (1) were refuted in a much larger study ($n = 124$ infants) by other investigators from the same institute (31) in which there were no significant correlations between TEE or sleeping metabolic rate in infants and maternal or paternal body mass index.

The longitudinal findings from this study are consistent with those from many cross-sectional studies suggesting that energy expenditure is not abnormal in obese children (7, 32). Energy expenditure components do not appear to be unusually low in other groups of children at high risk of developing obesity, including Mohawk Indian children (33) and Pima Indian chil-

dren (34). However, in black children there is some evidence of a relatively low REE (35) and lower oxygen consumption during exercise (36). Thus, reduced energy expenditure does not necessarily explain the greater prevalence of obesity in subgroups of the pediatric population at greater risk of obesity, and further longitudinal studies in these groups are warranted.

The HLM analysis revealed that $\approx 70\%$ of the variance in initial fat amount and rate of change in fat were explained by sex and parental fat. Other factors could be involved in the regulation of relative fatness during this period of growth. For example, although our study does not support a role for AEE, this does not rule out a role for other aspects of physical activity, eg, exercise intensity, activity time, metabolic efficiency, overall energy cost, and type of physical activity (recreational, occupational, obligatory, or spontaneous movement). In a previous cross-sectional analysis we showed that fat mass was inversely related to reported activity time in h/wk, but not to AEE in kcal/d (15). These earlier data suggest that obesity in children may be more related to time devoted to recreational activity than to the combined daily energy expenditure related to physical activity. It is also important to consider the possibility that differences in energy expenditure may be involved in the pathogenesis of obesity during other stages of growth (eg, early infant growth or adolescence) or in other subgroups of the population at increased risk of obesity (eg, African Americans), as previously shown in Pima Indian adults (2).

Other important factors to consider are dietary factors, although we (37) and others (38) previously showed cross-sectionally that dietary factors explain only a small portion of the variance in body fat in children. However, other behavioral or environmental factors related to diet may be important. For example, control of maternal feeding has been shown to be related to obesity in children (39). Also, there is some evidence that prenatal factors may be important. An interesting animal study by Lim et al (40) found that when rats were raised on similar diets of medium fat content (22.5%), offspring of rats who were fed a high-fat diet (40%) gained more fat than did offspring of rats fed a low-fat (5%) diet. The fact that initial childhood and parental fatness were identified as major factors points to the known genetic involvement in the pathogenesis of obesity (41). In addition, as discussed above, gene-by-environment interactions are likely to contribute to the variability in change in fatness over time.

Our results also show that the development of obesity during prepubertal growth is a slow and gradual process. For example, when children of two obese parents were compared with children of two nonobese parents, the difference in the rate of change in

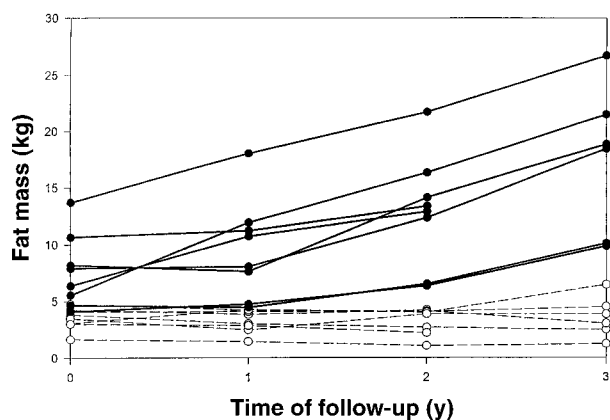


FIGURE 2. Absolute fat mass plotted against time for children showing extreme changes in body fat over time. Solid circles and lines represent individual children in the upper 10th percentile for change in fat mass adjusted for fat-free mass. Open circles and dotted lines represent individual children in the lower 10th percentile for change in fat mass adjusted for fat-free mass.

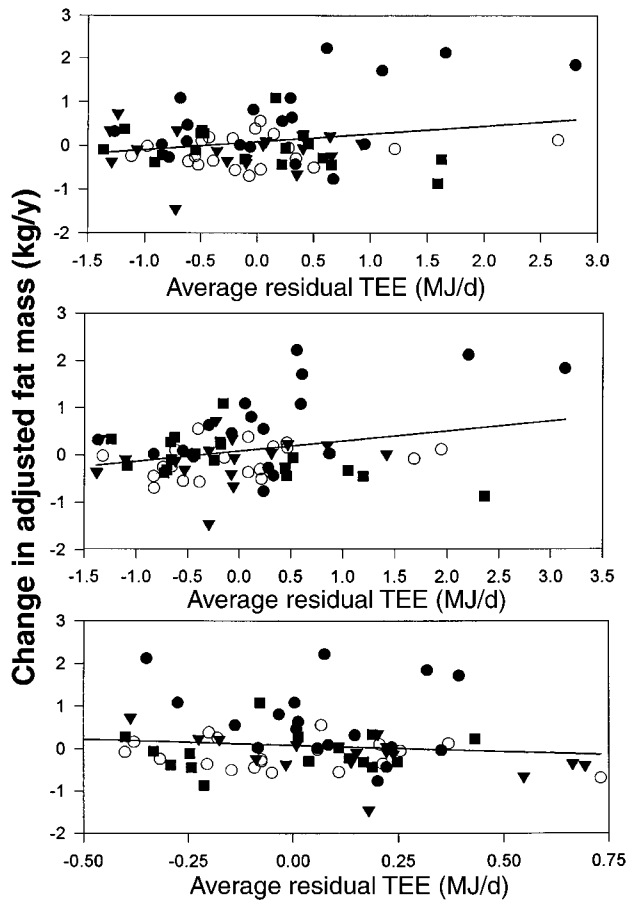


FIGURE 3. Relation between change in adjusted fat mass and energy expenditure components. ○, children from two nonobese parents; ■, children with obese fathers and nonobese mothers; ▼, children with obese mothers and nonobese fathers; ●, children with two obese parents. Change in fat mass adjusted for fat-free mass was derived from the individual growth trajectories. Energy expenditure components were measured in the first and second year of data collection and are expressed as the mean residual from the two measures performed 1 y apart. Top panel, total energy expenditure (TEE) adjusted for fat-free mass; middle panel, TEE adjusted for resting energy expenditure (REE); lower panel, REE adjusted for fat-free mass.

fat mass relative to fat-free mass was <1 kg fat/y, or <3 g excess fat gain/d. This is equivalent to a continual daily energy imbalance of 113 kJ (27 kcal; $\approx 2\%$ of total daily energy flux). From a methodologic standpoint, even the most sophisticated of current techniques would be unable to identify this energy imbalance as a defect in energy expenditure components (nor as an excess in energy intake relative to needs).

Although the results of this study suggest that inherent abnormalities in energy expenditure components are not involved in the pathogenesis of childhood obesity, our data confirm that sex, initial fatness, and parental fatness are important predictors of excess fat accumulation during preadolescent growth. Our study cannot identify the mechanism or mechanisms by which these factors cause increased accretion of fat mass in children, which must occur through an energy imbalance (ie, energy intake exceeds expenditure) or via preferential storage of energy as fat. There is evidence for the influence of genotype on the metabolic response to energy imbalance induced by overfeeding (42) or physical activity (43). Thus, it is conceivable that susceptible individuals (ie, children who are overweight to begin with or who have overweight parents) fail to compensate for periodic fluctuations in energy expenditure, most likely a reduced AEE (eg, periods of inactivity), or in energy intake, most likely increased intake of fat or energy or both (ie, periods of overfeeding). Our study may not have detected such periodic fluctuations because energy expenditure components were not measured daily throughout the year. Although the 14-d measure of energy expenditure with the doubly labeled water method is considered a long-term measure, this time period is actually short compared with the time scale over which changes in body fat were examined (4 y). Over time, a continual lack of compensation could evolve as an excess accretion of fat storage in susceptible compared with nonsusceptible individuals. This hypothesis could be tested by examining the metabolic response (eg, change in substrate utilization and adaptive changes in energy expenditure or intake) to overfeeding or inactivity in subjects who are either susceptible or not to obesity.

We placed particular emphasis on delineating the rate of change in fat mass, which was our major outcome variable. Because the children were growing, an examination of absolute change in fat mass would be confounded by the changes expected to occur as a result of the growth process, whereas our purpose was to study the factors leading to an excess accumulation of body fat. Our major outcome variable was therefore expressed as change in fat mass adjusted for change in fat-free mass. In real terms, this variable

TABLE 4

Comparison of energy expenditure components and rate of gain in adjusted fat mass in extreme subgroups of children¹

	Comparison of energy expenditure between children in the upper and lower 10th percentiles for change in adjusted fat mass ²		Comparison of rate of change in adjusted fat mass between children with consistently high or low energy expenditure components			
	Lower 10th percentile for fat gain (n = 8)	Upper 10th percentile for fat gain (n = 8)	Mean residual energy expenditure		Change in adjusted fat mass	
			High	Low	High	Low
	<i>MJ/d</i>		<i>MJ/d</i>		<i>MJ/d</i>	
TEE	0.23 ± 0.74	0.74 ± 1.1	0.95 ± 0.83[15]	-0.71 ± 0.30[21]	0.34 ± 0.52	-0.01 ± 0.52
REE	0.22 ± 0.33	0.01 ± 0.26	0.30 ± 0.19[24]	-0.33 ± 0.16[22]	0.06 ± 0.78	0.19 ± 0.66
AEE	0.07 ± 1.1	0.89 ± 1.2	1.1 ± 0.93[15]	20.87 ± 0.38[13]	0.26 ± 0.88	0.10 ± 0.36

¹ TEE, total energy expenditure; REE, resting energy expenditure; AEE, physical-activity-related energy expenditure.


² Values are the average residual relative to fat-free mass.

represents the rate of change in fat mass (kg/y) over and above (or below) that expected for the given individual change in fat-free mass. This variable is highly correlated with the absolute change in fat mass ($r = 0.74$, $P < 0.001$), and thus, the major findings from this paper were similar when we examined the relation between energy expenditure and the absolute change in fat mass.

One of the unique aspects of this study was the multiple-measure longitudinal design. This approach allows examination of interindividual differences in growth and the correlates of growth. This is a major advantage over simple difference scores, which are used frequently in longitudinal research. Analysis of change over time with use of difference scores does not provide information on the properties of the change function or on the individual variability in the growth curve parameters. Our approach assumes that change in fatness is an ongoing dynamic process represented by continuous time-dependent curves at the level of the individual child.

A defining characteristic of the HLM approach is the hierarchical or nested arrangement of the data. In our analysis, for example, repeated individual observations of residualized fat represented the level 1 data units that were nested within each individual child, or level 2 unit. A principal advantage of the HLM approach as opposed to a repeated measures design lies in its ability to simultaneously examine the relations that occur both within and between hierarchically arranged data units. Because of its focus on both levels of data, the HLM approach can be used to identify systematic patterns of change and correlates of change that would be difficult to discern when examining mean change. Another major advantage of HLM as opposed to an ANOVA or multiple ANOVA design, especially with longitudinal data, is that it provides statistically efficient solutions for data that include missing or nonsynchronous observations (28).

We also paid particular attention to statistical techniques for data normalization in this study. An important issue is the use of regression (ie, using fat-free mass as a covariate in an analysis of covariance) compared with ratios (ie, dividing energy expenditure components by fat-free mass). In a previous study from our laboratory (8), we showed the spurious nature of inappropriate data normalization when examining the relation between energy expenditure and body composition. The use of ratios may explain why other investigators observed an inverse relation between energy expenditure and obesity (44–46).

In summary, this longitudinal study in growing children suggests that the rate of change in fat mass relative to fat-free mass is highly variable and is related to sex, initial fatness, and parental fatness, but is not inversely related to any of the components of daily energy expenditure. Thus, as Dietz et al (47) suggested, “the fatter of the fattest appear to be getting fatter fastest.” In addition, the results suggest that even in the most susceptible of children, the development of obesity is a slow and gradual process that is the end result of a daily energy imbalance of $\approx 2\%$ of daily energy flux. 

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