

Why are nutritionally stunted children at increased risk of obesity? Studies of metabolic rate and fat oxidation in shantytown children from São Paulo, Brazil¹⁻³

Daniel J Hoffman, Ana L Sawaya, Ieda Verreschi, Katherine L Tucker, and Susan B Roberts

ABSTRACT

Background: Previous research suggested that nutritionally stunted children may have increased risk of obesity, but little is known about potential underlying mechanisms.

Objective: We sought to test the hypothesis that stunted children have a low metabolic rate and impaired fat oxidation relative to nonstunted children.

Design: The subjects were 58 prepubertal boys and girls aged 8–11 y from the shantytowns of São Paulo, Brazil. Twenty-eight were stunted (height-for-age *z* score < -1.5) and 30 had similar weight-for-height but normal height (height-for-age *z* score > -1.5). Parents of children in the 2 groups had equivalent height and body mass index values. Fasting and postprandial energy expenditure, respiratory quotient (RQ), and substrate oxidation were measured with indirect calorimetry in a 3-d resident study in which all food was provided and body composition was measured with dual-energy X-ray absorptiometry.

Results: Stunted children had normal resting energy expenditure relative to body composition compared with control children (4559 ± 90 and 4755 ± 86 kJ/d, respectively; *P* = 0.14) and had normal postprandial thermogenesis (2.4 ± 0.3% and 2.0 ± 0.3% of meal load, respectively; *P* = 0.42). However, fasting RQ was significantly higher in the stunted group (0.92 ± 0.009 compared with 0.89 ± 0.007; *P* = 0.04) and consequently, fasting fat oxidation was significantly lower (25 ± 2% compared with 34 ± 2% of energy expenditure; *P* < 0.01).

Conclusions: Childhood nutritional stunting is associated with impaired fat oxidation, a factor that predicted obesity in other at-risk populations. This finding may help explain recent increases in body fatness and the prevalence of obesity among stunted adults and adolescents in developing countries. *Am J Clin Nutr* 2000;72:702–7.

KEY WORDS Fat oxidation, obesity, stunting, energy expenditure, children, metabolic rate, respiratory quotient, malnutrition, undernutrition, Brazil

INTRODUCTION

The prevalence of obesity is increasing worldwide, even in developing countries that have traditionally experienced high rates of undernutrition (1, 2). Countries in economic transition from undeveloped to developed, such as China, Brazil, and

South Africa, are particularly affected and have an increasing prevalence of obesity across all economic levels and age groups (3). Traditional explanations for these observations include reduced physical activity and consumption of high-fat diets. However, there is still no consensus about the importance of these factors, even for individuals in developed countries (4–9).

Research has suggested that undernutrition in early life may play a role in promoting adult obesity. In particular, studies on 3 continents showed that nutritional stunting, which is usually caused by chronic undernutrition (10), is positively associated with adult fatness (11–14). In addition, we previously observed an association between excess weight gain and dietary fat content in stunted Brazilian children but not in nonstunted control children (14). This is suggestive of an increase in the efficiency of dietary fat utilization that could lead to increased body fat content over time. Consistent with these observations, permanent effects of early diet on long-term energy regulation have been observed in both rodents and nonhuman primates (15–21). However, researchers still need to identify the underlying mechanisms by which early nutritional stunting may lead to an increased risk of obesity, both to provide a rational basis for understanding the observed effects and to rule out the possibility that unrecognized confounding factors influenced the results obtained.

The general concept that early-life stimuli may have permanent effects on metabolism and development was first shown conclusively by Hubel and Wiesel (22), who observed a critical period in the early development of cats during which deprivation of visual stimuli resulted in permanent loss of sight. The concept of critical periods is consistent with the literature on childhood nutrition, which shows a generalized programming effect of early diet on metabolism, growth, and cognition (23–25). The mechanisms

¹From the Federal University of São Paulo, Escola Paulista de Medicina, São Paulo, Brazil, and the Jean Mayer US Department of Agriculture Human Nutrition Research Center on Aging at Tufts University, Boston.

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³Address reprint requests to AL Sawaya, Federal University of São Paulo, Rua Botucatu, 862, Vila Clementino, 04023-900, São Paulo, SP, Brazil. Address correspondence to SB Roberts, Energy Metabolism Laboratory, Jean Mayer USDA Human Nutrition Research Center on Aging, Tufts University, 711 Washington Street, Boston, MA 02111.

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TABLE 1
Characteristics of the study children and parents¹

	Control group	Stunted group
Children		
Age (mo)	120 ± 17	122 ± 15
Height (cm)	136 ± 10	126 ± 9 ²
Weight (kg)	32 ± 6	26 ± 5 ²
Height-for-age <i>z</i> score	-0.56 ± 0.80	-2.16 ± 0.70 ²
Weight-for-height <i>z</i> score	0.46 ± 0.76	-0.08 ± 1.10
Percentage body fat (%)	20 ± 7	17 ± 5
Fathers		
Height (cm)	165 ± 8	160 ± 12
BMI (kg/m ²)	26 ± 3	25 ± 3
Mothers		
Height (cm)	153 ± 7	151 ± 9
BMI (kg/m ²)	25 ± 4	26 ± 5

¹ $\bar{x} \pm$ SD. For control group, *n* = 30 children, 16 fathers, and 20 mothers. For stunted group, *n* = 28 children, 10 fathers, and 18 mothers.

²Significantly different from control group, *P* < 0.001 (Student's unpaired *t* test).

by which early nutrition exerts long-term programming effects in humans are not known, but proposed mechanisms include functional alterations in growth processes, gene expression, cell number, and clonal selection within organs and tissues (24, 26, 27).

The purpose of this study was to test the hypothesis that nutritional stunting is associated with impaired fat oxidation, a factor previously shown to strongly predict body fat gain in other populations at risk of obesity, including Pima Indians (28), weight-reduced obese women (29–31), and middle-aged men (32). We also examined the possibility that stunted children might have low resting metabolic rate, a factor that predicted subsequent body fat gain in some (33–35), but not all (36, 37), prospective studies of high-risk populations.

SUBJECTS AND METHODS

Subjects

Children were identified as potential subjects during population surveys of 3 shantytowns in the city of São Paulo, Brazil. More than 300 children aged 7–11 y were weighed and measured and were found to be potentially eligible to participate on the basis of anthropometric criteria. All subjects had to have a normal weight-for-height *z* score (WHZ of -2.0 to 1.5) according to the National Center for Health Statistics (NCHS) standards (38). Children recruited for the stunted group (*n* = 28) had to have a height-for-age *z* score (HAZ) < -1.5, and children recruited for the control group (*n* = 30) had to have an HAZ > -1.5. Note that well-nourished Brazilian children grow adequately relative to NCHS standards in terms of both weight and height (39) and that low HAZ is widely believed to be a result of chronic, moderate undernutrition (10). In addition, the 2 groups were matched for age and WHZ. The characteristics of the study children and their parents are shown in **Table 1**. Although it was not possible to match stunted and control children for parental height and weight, these values were measured in all families in which the biological parents lived with the children; there were no significant differences between the groups (Table 1).

Subjects who appeared to be eligible for the study on the basis of weight and height and who were willing to participate were

given a screening examination. This included a medical history, physical examination, evaluation of Tanner stage (40), blood collection for glucose and iron concentrations, and fecal and urine screening for acute infections. Children were excluded from the study if they were taking any medication, if their Tanner stage for ≥ 1 criterion was >1, or if we identified any past medical problems that might influence current health status or metabolic condition (such as hyperthyroidism or chronic anemia). Any child who had an acute health problem, such as an acute intestinal or urinary infection, was treated according to the usual procedures of the São Paulo Hospital and began the study only after successful completion of treatment.

Ethical approval for the study was obtained from the Federal University of São Paulo Hospital and the Human Investigation Review Committee at the New England Medical Center, Tufts University. Written informed consent was obtained from both the subjects and their parents before the study began.

Study protocol

The children were admitted to the metabolic research unit of the Center for Nutritional Recovery and Education at the Federal University of São Paulo at 0700 on study day 1 and were returned to their homes at 2100 on day 3. They were admitted in groups of 4; 2 stunted children and 2 control children were admitted together when possible. Continuous daytime supervision was provided by investigator DJH and 2 assistants and nighttime supervision was provided by a nurse. Throughout the 3 d, subjects consumed only food and drinks prepared by the research center and refrained from vigorous physical activities.

Resting energy expenditure (REE) was measured in the fasted state 12 h after the evening meal on all 3 mornings (one 30-min measurement and two 15-min measurements) under thermoneutral conditions by indirect calorimetry with a DeltaTrac metabolic monitor (SensorMedics, Yorba Linda, CA). Subjects were instructed to relax and avoid hyperventilation, fidgeting, and sleeping during the measurements and were allowed to watch taped movies if they so desired. The calorimeter was calibrated with a standard gas mixture (96% O₂ and 4% CO₂) before each measurement and alcohol burn tests were conducted every 2 wk to ensure the accuracy of the calorimeter. Values for REE were determined by using the mean volumes of oxygen consumed ($\dot{V}O_2$) and carbon dioxide produced ($\dot{V}CO_2$) for each measurement (41).

The thermic effect of feeding (TEF) was measured over a 3-h period on either day 2 or day 3 after the measurement of REE. For the TEF measurement, subjects consumed a standard breakfast (bread with margarine and chocolate milk) that supplied 42 kJ (10 kcal) per kg body wt. All the children received the same proportions of the different foods. The children were instructed to consume their meal within 5 min and the measurement began 15 min later. Energy expenditure was measured for 15 min of every one-half hour during the measurement period. Urine was collected during a 24-h period that included the TEF measurements. Urine was analyzed for nitrogen excretion by using a modification of the Kjeldahl technique that involved microwave digestion of the samples (Kjelfast; CEM, Matthews, NC). The TEF was calculated as the energy expenditure increment over fasting at baseline and was expressed as a percentage of ingested energy. Fat oxidation was calculated from $\dot{V}O_2$ and $\dot{V}CO_2$ during the fasting and postprandial measurement periods and from urinary nitrogen excretion, with the assumption that nitrogen excretion was steady over the 24-h collection period

TABLE 2
Energy expenditure of control and stunted children¹

	Control (n = 30)	Stunted (n = 28)
REE, unadjusted (kJ/d)	4933 ± 118	4369 ± 91 ²
REE/kg body wt (kJ/d)	159 ± 5	173 ± 5 ³
REE, adjusted for LBM (kJ/d)	4755 ± 86	4559 ± 90
REE, adjusted for body wt (kJ/d)	4742 ± 91	4573 ± 95
Total TEF (% of meal load)	2.0 ± 0.3	2.4 ± 0.3

¹ $\bar{x} \pm \text{SEM}$. REE, resting energy expenditure; LBM, lean body mass; TEF, thermic effect of feeding.

^{2,3}Significantly different from control group (multiple linear regression): ² $P < 0.001$, ³ $P < 0.05$.

(42, 43). Substrate oxidation was calculated by subtracting the volumes of oxygen and carbon dioxide attributed to protein metabolism from the measured volumes and then determining the nonprotein respiratory quotient (RQ). The nonprotein RQ was then used in the equations described by Livesey and Elia (43) to determine the percentage of energy expenditure attributable to fat and carbohydrate oxidation.

Diets

A standardized breakfast that supplied 42 kJ (10 kcal) per kg body wt was given to the children each morning at 0900. For lunch (1230), snack (1530), and dinner (1900), the children ate foods ad libitum from standardized menus prepared in the metabolic kitchen; their intake was measured at all meals. The children were not allowed any food after 2000, when fasting began for the metabolic testing.

Body composition

Height and weight were measured as described elsewhere (11). Body fat and lean body mass were measured with dual-energy X-ray absorptiometry by using a Lunar X-ray densitometer (Lunar Corp, Madison, WI) with an adult quick-scan program shown to be accurate for this age and weight group (44).

Statistical analysis

Values are expressed as means ± SDs or SEMs as noted. Statistical analyses were performed by using the procedures of SPSS 7.0 for WINDOWS and SYSTAT 7.0 for WINDOWS (SPSS Inc, Chicago). Differences between groups for single measurement variables were tested by using Student's unpaired *t* test. Analysis of covariance was used to assess postprandial RQ differences, with group as the between-subjects factor, time as the repeated measure, and fasting RQ as a covariate. Differences between groups in REE were determined by using a multiple linear regression model in which REE was regressed against 1) group and lean body mass, and 2) group and weight. Results were considered statistically significant when $P < 0.05$.

RESULTS

The control and stunted groups were not significantly different in age and WHZ but, as intended, the control group had greater height, HAZ, and body weight than did the stunted group (Table 1). The 2 groups did not differ significantly in percentage body fat or lean body mass. In the subset of parents whose anthropometric measurements could be obtained ($n = 64$), there

were no significant differences in either height or body mass index (BMI; in kg/m²) between the groups (Table 1).

REE and TEF data are shown in Table 2. Compared with control children, stunted children had lower unadjusted REE and higher REE/kg body wt. However, after adjustment for lean body mass by multiple linear regression (45), REE did not differ significantly between the groups. TEF was also not significantly different between the groups. TEF data are summarized in Table 2 and the time course of TEF over the 3-h measurement is shown in Figure 1. The possibly unusual pattern of TEF (specifically, the relatively low value at 60 min after the meal) could not be explained on the basis of any specific study procedures.

Data on fasting and postprandial RQ and substrate oxidation are shown in Table 3. The fasting RQ and nonprotein fasting RQ were significantly higher in the stunted group than in the control group. These differences remained even when children who had an RQ >1.00 ($n = 5$) were excluded from the analyses or when the previous day's energy intake and food quotient (calculated ratio of $\dot{V}\text{CO}_2$ to $\dot{V}\text{O}_2$ during complete combustion of consumed foods) were examined as confounding variables in multiple regression models. The control group also oxidized a significantly lower percentage of their fuel mix as carbohydrate and a significantly greater percentage as fat than did the stunted group.

Concerning postprandial fat oxidation, mean postprandial RQ was not significantly different between the 2 groups when averaged over the 3-h experimental period (Table 3), and consequently, mean postprandial rates of fat and carbohydrate oxidation were also not significantly different. However, as shown in Figure 2, RQ tended to remain elevated in the stunted group compared with the control group. Consequently, during the postprandial phase, the control group had a significantly lower RQ at 30 min (assessed statistically as described in the Statistical Analysis section; Figure 2). Also note that postprandial changes in RQ from baseline did not differ significantly between the 2 groups. We interpret these observations to indicate that fasting RQ was significantly higher in the stunted group, but the change in RQ with feeding did not differ between groups.

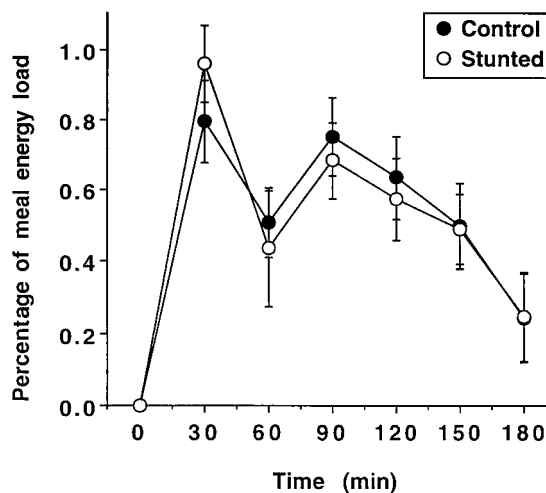


FIGURE 1. The thermic effect of feeding during a 3-h period in stunted and control children. Values are mean (\pm SEM) energy expenditure in excess of fasting baseline during each 30-min period. There were no significant differences between the groups at any time.

TABLE 3Fasting and postprandial respiratory quotient (RQ) and substrate oxidation in control and stunted children¹

	Control (n = 30)	Stunted (n = 28)
Fasting		
RQ	0.89 ± 0.007	0.92 ± 0.009 ²
Nonprotein RQ	0.90 ± 0.009	0.94 ± 0.009 ²
Carbohydrate oxidation (% of energy expenditure)	66 ± 2	75 ± 2 ³
Fat oxidation (% of energy expenditure)	34 ± 2	25 ± 2 ³
Postprandial		
RQ	0.93 ± 0.007	0.94 ± 0.007
Cumulative carbohydrate oxidation (% of energy expenditure)	80 ± 3	84 ± 3
Cumulative fat oxidation (% of energy expenditure)	20 ± 2	16 ± 3

¹ $\bar{x} \pm \text{SEM}$.^{2,3}Significantly different from control group (Student's unpaired *t* test): ²*P* < 0.05, ³*P* < 0.01.

DISCUSSION

Impaired fat oxidation was shown previously to be a risk factor for excess weight gain in several populations known to be susceptible to obesity, including Pima Indians, previously obese women who had completed a weight-reduction program, and middle-aged men (28–32). In the present study, we found that nutritionally stunted children had measurably impaired fat oxidation compared with nonstunted control children living in the same environment. Specifically, stunted children had significantly higher RQs and lower fat oxidation in the fasting state and 30 min after a meal (subsequent postprandial measurements remained higher but not significantly so). This finding of reduced fat oxidation in the fasting and early postprandial states may help to explain previous observations (11–13) of increased prevalence of overweight among stunted adolescents and adults in developing countries, because fat that is not oxidized must be stored. Our findings also add to the literature suggesting that diet early in life has a significant effect on later metabolism and health (24, 26, 27).

Several aspects of the study design were critical to our interpretation of the results obtained. First, we used an inpatient protocol in which all food was provided to the children. This was important because dietary composition on the day preceding the measurement can influence fasting fat oxidation (46). In addition, none of the children were obese yet, which enabled us to measure factors contributing to an underlying susceptibility to weight gain rather than factors apparent only after weight gain has occurred. By selecting children for each group from the same environment and ensuring that the groups had values for parental height and BMI that were not significantly different, we also reduced the number of factors other than nutritional stunting that could explain our results. Note that we were unable to distinguish between different causes of nutritional stunting in this population. Therefore, we cannot exclude the possibility that different underlying causes (for example, chronic deficiency of multiple nutrients including energy as opposed to chronic deficiency of a specific nutrient such as zinc) might have different effects. Further studies will be needed to address the question of whether different underlying causes of nutritional stunting may influence fat oxidation to different extents.

Although the mechanisms by which chronic undernutrition leading to stunting causes an alteration in fat oxidation are not known, there are several potential explanations. At the level of fat oxidation versus storage, fat that is not oxidized must be stored. Thus, impaired fat oxidation will tend to cause increased fat deposition over time. In theory, impaired fat oxidation will accelerate fat deposition particularly quickly when a high-fat diet is consumed, because the excess fat intake will be deposited. With regard to this possibility, we previously obtained preliminary data suggesting that stunted children gain weight over time at an accelerated rate when they consume a high-fat diet (14).

It can be speculated that in nutritionally stunted children, long-term adaptations to undernutrition that affect enzyme and hormone function may underlie impaired fat oxidation. For example, long-term undernutrition is accompanied by reduced concentrations of insulin-like growth factor I (IGF-I) (14, 47). Because IGF-I increases the activity of hormone-sensitive lipase to lipolytic hormones (48, 49), any reduction in IGF-I may also result in decreased fat oxidation (50). In addition, studies in rodents have suggested long-term effects of litter size (a classic tool for studying the effects of early nutrition) on enzymes involved in carbohydrate and fat oxidation 20 wk after weaning (17). For example, 20-wk-old rats undernourished at birth had elevated concentrations of gluconeogenic enzymes, which might promote increased carbohydrate oxidation relative to fat oxidation (17).

Although we studied children living in Brazil, it is important to note that children in other countries are susceptible to undernutrition and stunting also; ≈250 million children worldwide are thought to suffer from malnutrition (51) and 5–10% of children in the United States have been classified as stunted (52). In developing populations, nutritional stunting is primarily related to undernutrition, but in developed populations it is more commonly associated with a range of common childhood problems, including severe burns (53), excess fruit juice consumption (54), fear of obesity (55), and low social class (56). Most previous reports on stunting did not provide information on body fatness, but stunting in children with previous burn injuries was associated with a disproportionate gain in weight relative to height 3 y

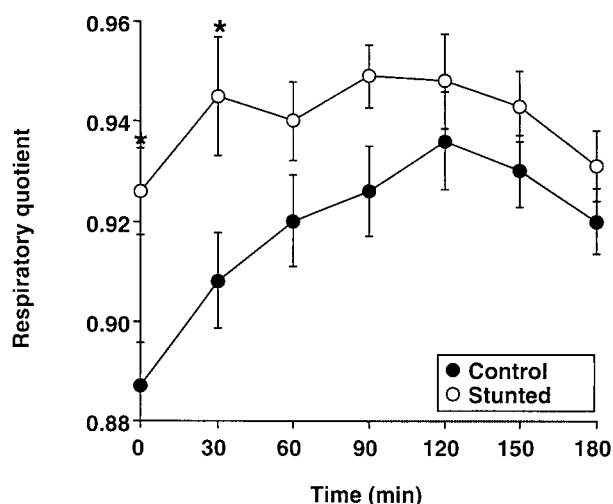



FIGURE 2. Mean (±SEM) fasting (0 min) and postprandial respiratory quotient in stunted and control children. *Significantly different from the stunted group, *P* < 0.05. The average respiratory quotient did not differ significantly between the 2 groups.

after the burn accident (53). Also, short adults of low social class had a significantly greater BMI than did taller individuals of higher social class in England (56) but not in France (57).

In summary, this study showed that nutritionally stunted children have impaired fat oxidation compared with nonstunted control children from the same environment. This finding suggests that stunted shantytown children are at increased risk of obesity and may gain weight over time when food supplies become sufficient to allow *ad libitum* consumption. Our results may therefore help to explain the previous finding of an increased prevalence of obesity among stunted children and short adults in developing countries. 

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