Meal-induced thermogenesis in lean and obese prepubertal children[1-4]

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ABSTRACT The resting metabolic rate (RMR) and the thermic effect of a meal (TEM) were measured in a group of 16 prepubertal (8.8 ± 0.3 y) obese children (43.6 ± 9.2 kg) and compared with a group of 10 age-matched (8.6 ± 0.4 y), normal-weight children (31.0 ± 6.0 kg). The RMR was higher in the obese than in the control children (4971 ± 485 vs 4519 ± 326 kJ/d, $P < 0.05$); after the RMR was adjusted for the effect of fat-free mass (FFM) the values were not significantly different (4887 ± 389 vs 4686 ± 389 kJ/d). The thermic response to a liquid mixed meal, expressed as a percentage of the energy content of the meal, was significantly lower in obese than in control children (4.4 ± 1.2% vs 5.9 ± 1.7%, $P < 0.05$). The blunted TEM shown by the obese children could favor weight gain and suggests that the defect in thermogenesis reported in certain obese adults may have already originated early in life. *Am J Clin Nutr* 1993;57:481-5.

KEY WORDS Resting metabolic rate, meal-induced thermogenesis, obesity, children

Introduction

A prolonged positive imbalance between energy intake and energy expenditure produces an increase in the size of adipose tissue, progressively leading to obesity. Numerous studies on adults have emphasized the importance of a defect in energy metabolism in the etiology of obesity. In particular, impaired thermogenesis was frequently thought to play a role in some cases of human obesity (1-6).

Little data have been published on the thermic effect of a meal (TEM) in the prepubertal period. Therefore, the present study was undertaken to examine the meal-induced rise in energy expenditure in obese school children compared with a matched group with normal body weight.

Subjects and methods

Subjects

The investigations were carried out in 26 prepubertal healthy children: 16 obese children with > 20% excess weight-for-height calculated on the basis of Tanner's tables (7) and 10 nonobese children with body weights ranging from 90% to 110% of the weight predicted from height.

Physical characteristics of the two groups of children are shown in **Table 1.** Their age, height, and fat-free mass (FFM) were not significantly different, whereas body weight, percent body fat, and body mass index (BMI; in kg/m^2) were significantly greater in the obese children than in the children with normal body weight.

Subjects with diabetes mellitus or other metabolic or endocrine disorders were excluded from the study. Physical examination and routine laboratory tests documented the absence of any health problems. None of the subjects reported significant changes in body weight during the month preceding the study. None of the children were taking any drug or medication. Exclusively prepubertal children were included in the study group (8).

Informed consent was obtained from the parents of all children. The protocol was approved by the Ethical Committee of the University of Verona and was in accordance with the Helsinki Declaration of 1975 as revised in 1983.

A dietary-history interview was done with mothers (9) to obtain information on the food intakes of each child. The databank developed by the Italian National Institute of Nutrition was used to calculate the energy and nutrient intakes (10).

Anthropometrical measurements were carried out by one investigator only and included weight, height, and skinfold thickness. Skinfold thicknesses were measured at four sites—biceps, triceps, suprailiac, and subscapular—to the nearest millimeter in triplicate with a Harpenden skinfold caliper (CMS Weighing Equipment Ltd, London).

Lohman's (11) formulas were used to estimate the body fat mass (FM), expressed as a percentage of body weight.

Fasting basal venous blood samples were taken for plasma glucose concentrations, immunoreactive insulin (IRI), and free fatty acid (FFA) concentrations. Plasma glucose was measured

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[2] Part of the results of this study were presented at the Third European Congress on Obesity, Nice, France, May 30-June 1, 1991, as an oral presentation and was published in the proceedings.

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TABLE 1
Physical characteristics and body composition of children*

	Obese (n = 8 M, 8 F)	Control (n = 4 M, 6 F)
Age (y)	8.8 ± 0.3	8.6 ± 0.4
Height (cm)	134.9 ± 7.9	134.3 ± 2.9
Weight (kg)	43.6 ± 9.2†	32.0 ± 6.0
BMI‡	24.3 ± 4.2†	18.3 ± 1.7
Weight-for-height (%)	135.1 ± 15.4†	103.6 ± 4.5
Body fat (% of wt)	29.7 ± 5.3†	20.6 ± 6.0
Body fat (kg)	13.2 ± 4.4†	6.8 ± 2.6
Fat-free mass (kg)	30.3 ± 5.5	25.6 ± 4.7

* $\bar{x}$ ± SD.
† Significantly different from control subjects, $P < 0.001$.
‡ In kg/m^2.

enzymatically (12), whereas plasma IRI was assayed by radioimmunoassay (13). Plasma FFAs were extracted by using the method of Dole and Meinertz (14) and determined according to Heindel et al (15).

Experimental protocol

During the days preceding the indirect calorimetry test, children were at home and had free access to food. The day immediately before the test they did not perform any intense physical activity. On the day of the test children arrived by car at the Institute of Pediatrics at 0730, in a fasting condition; their last meal was eaten at 2000 the day before. The child lay down on a hospital bed in a temperature- (24 °C) and humidity-controlled environment upon arrival at the institute. After 30 min of absolute rest, considered an adaptation period during which the procedure to be used was explained to each child, continuous respiratory-exchange measurements were initiated after an additional adaptation period of 15 min under a transparent ventilated hood. During the calorimetric measurement the child rested quietly watching television. Special attention was given to prevent possible extra movements of the child because this contributes to increased energy expenditure.

Indirect calorimetry

Respiratory gas exchange was measured continuously for 45 min in the basal resting state and then for 3 h after the ingestion of a mixed meal in liquid form (Ensure; Zwolle, The Netherlands) made up of 53% carbohydrates, 30% lipids, and 17% protein energy. The meal was designed to correspond to 30% of the resting energy expenditure (extrapolated to 24 h) as measured in the premeal baseline. The test meal was ingested within 5 min.

The respiratory-exchange measurements were determined with an open-circuit computerized indirect calorimeter (Deltatrak; Datex Inc, Kempele, Finland) with use of a transparent ventilated hood system. The system was calibrated before each test with a reference gas mixture (95% O_2 and 5% CO_2).

The precision of the indirect calorimeter was assessed by burning a given volume of alcohol and measuring oxygen consumption ($\dot{V}O_2$) and carbon dioxide production ($\dot{V}CO_2$) and energy expenditure for 30 min on six different occasions. The coefficient of variation of repeated RMR determinations averaged 3.1%.

$\dot{V}O_2$ and $\dot{V}CO_2$ were printed out at 1-min intervals and the mean of the 45-min measurement period was calculated for premeal RMR whereas the mean of the 15-min measurement periods was calculated for expressing the thermogenic response. RMR and TEM were calculated according to Lusk's classical formula (16). At the end of the indirect calorimetry test, medical anamnesis, and dietary-history interview, a physical examination was performed and anthropometrical data were obtained for each child.

Calculation of TEM

To obtain the 1-h mean energy expenditure after ingestion of the meal, the $\dot{V}O_2$ and $\dot{V}CO_2$ for the 15-min interval were averaged over the total 3-h thermogenic response. TEM was calculated by subtracting the premeal RMR value (kJ/min) from the respective average postprandial energy expenditure (kJ/min) and this was multiplied by the duration of the postprandial period (180 min). The TEM was expressed both as a percentage increase over the premeal RMR and as a percentage of the metabolizable energy value of the test meal.

Statistical analysis

All the results given are expressed as mean ± SD. The relationship between two variables as assessed by using Pearson product-moment linear-correlation coefficients.

Statistical differences were assessed by using the unpaired t test to compare the obese with the control group. The RMRs of both groups were compared, after adjustment for the effect of FFM, by means of analysis of covariance (ANCOVA), with FFM as the covariate.

To evaluate differences of postprandial energy expenditure between obese and control children, analysis of variance was carried out with the split-plot design, considering each subject as a whole plot allocated to one of the two categories (obese or nonobese children) of the main treatment. Six subtreatments (subplots or split plots) corresponding to the six 15-min intervals of measurement were considered for each child. Time was the subplot treatment. The effects of the main subplot treatment were considered fixed. A significance level of 0.05 was used.

The *GLIM* package (Royal Statistical Society, London) was used for the analysis.

Results

The mean daily energy intake of the obese group was significantly higher than that of the control group (9970 ± 2309 vs 8058 ± 1971 kJ/d, $P < 0.05$).

Calculated per unit body weight, the energy intake was lower in obese than in control children (220 ± 31 vs 259 ± 69 kJ · kg body wt^{-1} · d^{-1}, $P < 0.05$); however, calculated on the basis of FFM, it was found to be similar in the two groups (329 ± 29 vs 312 ± 56 kJ · kg FFM^{-1} · d^{-1}).

Compared with the control group, the obese group derived a similar percentage of energy from protein, fat, and carbohydrate (14%, 36%, and 50% vs 13%, 35%, and 52%, respectively). The ratio of polyunsaturated to saturated fatty acids was similar in both groups (0.25 ± 0.11 in obese vs 0.24 ± 0.14 in the normal-weight children).

The obese children had normal fasting blood glucose (4.66 ± 0.51 mmol/L) and FFA (643 ± 121 μmol/L) when compared

TABLE 2
Resting metabolic rate (RMR) measured before the meal, postprandial energy expenditure, thermic effect of the meal (TEM), and respiratory quotient (RQ) in obese and control children*

	Obese (n = 16)	Control (n = 10)
RMR (kJ/min)	3.45 ± 0.33†	3.14 ± 0.23
RMR (kJ/d)	4971 ± 485†	4519 ± 326
Test meal energy (kJ)	1489 ± 142†	1356 ± 96
Postprandial energy expenditure (kJ/min)	3.82 ± 0.38	3.58 ± 0.31
Postprandial energy expenditure (kJ · kg FFM^{-1} · min^{-1})‡	0.128 ± 0.012	0.137 ± 0.017
TEM (kJ/min)	0.37 ± 0.09	0.44 ± 0.11
TEM (kJ/3 h)	67 ± 17	79 ± 21
TEM (% meal energy)	4.4 ± 1.2†	5.9 ± 1.7
TEM (% RMR)	10.6 ± 3.0†	14.0 ± 4.3
Preprandial RQ	0.85 ± 0.03	0.86 ± 0.03
Postprandial RQ	0.90 ± 0.02	0.90 ± 0.03

* $\bar{x}$ ± SD.
† Significantly different from control, $P < 0.05$.
‡ FFM, fat-free mass.

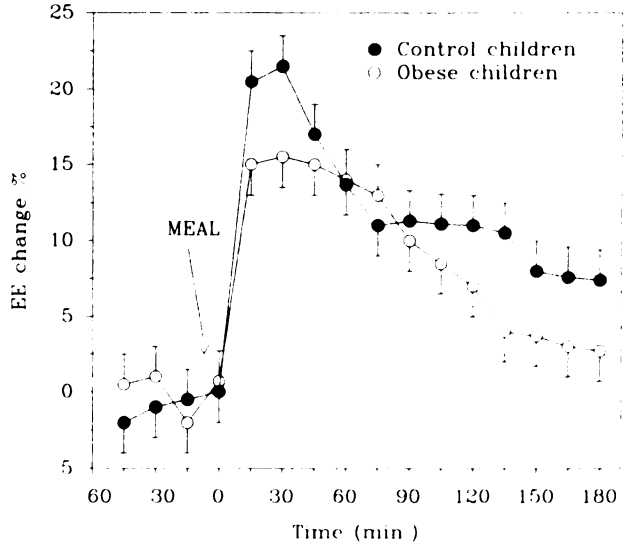

FIG 1. Time course of postprandial energy expenditure (EE) expressed as a percentage of premeal baseline for 16 obese and 10 control children. $\bar{x}$ ± SE.

with control children (4.61 ± 0.64 mmol/L and 681 ± 237 μmol/L, respectively). Nevertheless, plasma IRI concentrations were significantly higher in obese than in control children (111 ± 12 vs 80.0 ± 3.0 pmol/L, respectively, $P < 0.05$).

The premeal and postmeal energy expenditures are shown in **Table 2.** RMR was found to be higher in obese than in normal-weight children when expressed as an absolute value.

Expressed per unit body weight, RMR was significantly ($P < 0.05$) lower in obese than in control children (113 ± 18 vs 138 ± 25 kJ · kg body wt^{-1} · d^{-1}), whereas when calculated per kg FFM it was similar to that of control children (167 ± 17 vs 171 ± 26 kJ · kg FFM^{-1} · d^{-1}). This was confirmed by ANCOVA (with FFM as covariate), which indicated a similar RMR in obese and control children (4887 ± 389 vs 4686 ± 389 kJ/d). In addition, FFM was significantly correlated with RMR, accounting for ≈70% (r^2) of its variance in both obese and control children.

Figure 1 shows the net increase in energy expenditure after meal ingestion, expressed as a percentage above the basal RMR value. During the first 30–45 min, energy expenditure increased rapidly and then progressively decreased during the following hours both in obese and in control children. However, the overall increase in energy expenditure (surface area under the curve) in obese children was the same as in control children (Table 2), despite the fact that the test-meal energy was greater ($P < 0.05$).

Calculated as a percentage above the premeal RMR or as a percentage of the metabolizable energy, TEM was found to be significantly ($P < 0.05$) lower in obese (10.6 ± 3.0% and 4.4 ± 1.2%, respectively) than in control children (14.0 ± 4.3% and 5.9 ± 1.7%, respectively).

As expected, the time effect was significant ($P < 0.05$). However, the interaction between the main treatment (obese vs non-obese children) and time was also significant ($P < 0.05$). These results indicate that the difference between mean values of postprandial energy expenditure is not constant between obese and control children.

Both average premeal and postmeal respiratory-quotient values (Table 2) were not different in either obese or in control children, although the rise in postprandial respiratory quotient was delayed in the obese group (**Fig 2**).

Discussion

The results indicate that in prepubertal children, obesity seems to be accompanied by a reduction of TEM in the early phase of the postprandial period. This supports results obtained in several studies on adults that demonstrated a diminished thermogenic response to a mixed meal in some obese individuals (1–6), thereby contributing to body-weight gain and perhaps difficult

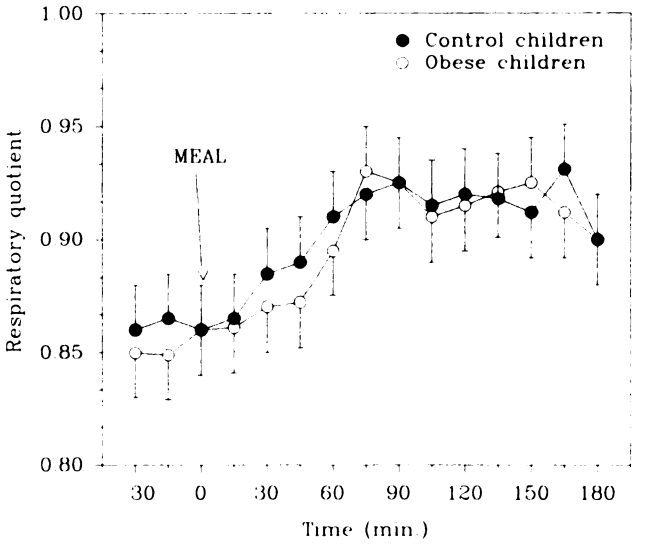

FIG 2. Time course of respiratory quotient during the postprandial response for 16 obese and 10 control children. $\bar{x}$ ± SE.

weight loss. This suggests that the thermogenic defect encountered in adulthood may have already originated early in life.

Only speculations about the underlying mechanism explaining the reduced TEM in children suffering from obesity can be made from the present results. One factor that may play a role is the apparent peripheral insulin resistance accompanying obesity, as indirectly evidenced in the present study by elevated fasting insulin concentrations in conjunction with normal blood glucose (5, 17). Activation of the sympathetic nervous system by ingestion of nutrients might represent an important factor in determining the magnitude of TEM (18–21). In the present study however, no information is available on this so-called "facultative" component of thermogenesis.

What is the practical importance of reduction in TEM in obese children? The extent to which the energy saved by a reduction of TEM may contribute to body-weight gain and possible difficulties in achieving weight loss is uncertain because the difference in postprandial thermogenesis (5.9% vs 4.4%) would constitute an energy saving of 150 kJ/d with the degree of energy intake observed in the present study. The importance of the reduction of TEM on the energy balance should be assessed together with the other components of total energy expenditure, ie, postabsorptive RMR and the energy expenditure from physical activity.

Finally, it should be pointed out that the duration of TEM measurement was limited to 3 h. This was certainly not enough to obtain a complete return to the premeal baseline energy expenditure (Fig 1). However, because the subjects studied were prepubertal children, it was difficult in practice to prolong the test for > 3 h.

In the present study, the RMR expressed as an absolute value was found to be higher in obese than in nonobese children (Table 2), confirming previous studies in children (22, 23). In contrast, when expressed per kg FFM, the difference in RMR between the two groups disappeared.

Although the use of skinfold thickness for assessing FFM could be challenged, particularly in obese subjects, it should be stressed that other techniques such as underwater weighing—known to be definitely more valid—may lead to practical problems when applied to prepubertal children, because of fear of the water, incomplete immersion, etc. In addition, because the density of FFM changes with age and maturation (reaching chemical maturity at 15–18 y), further uncertainty is involved unless body density and total body water are measured simultaneously.

The extent to which the rate of physical activity differs in obese vs nonobese children is unknown. However, the absolute difference between energy intake and postprandial RMR (expressed as a function of body weight, ie, $kJ \cdot kg\ body\ wt^{-1} \cdot d^{-1}$) can be assumed to represent a gross index of physical activity (neglecting the storage component in obese children) because the energy expenditure in weight-bearing activities is proportional to body weight. This index was found to be similar in obese ($102\ kJ \cdot kg\ body\ wt^{-1} \cdot d^{-1}$) and nonobese children ($94\ kJ \cdot kg\ body\ wt^{-1} \cdot d^{-1}$).

In the present investigation, the average energy intake of obese children was 24% higher than that of control children. Because of their increased FFM, the preprandial RMR of the obese children, however, was already 10% more elevated and the average postprandial RMR was 6.7% more elevated than that encountered in nonobese children. It can be calculated that less than one-quarter of the energy-intake difference observed between the obese and nonobese children could be explained by the excess absolute RMR observed in the former group. The remaining part could be accounted for by the activity-related energy expenditure as well as the increased energy storage that must accompany the dynamic phase of obesity. From the present data it is difficult to delineate the respective contribution of each of these two components of total energy expenditure.

Finally, it should be stressed that the ratio of the total energy intake to RMR was higher in obese children ($1.99 \times RMR$) than in control children ($1.77 \times RMR$). The higher ratio found in the obese children may be related to a greater absolute energy cost of body movement for a given physical activity as well as to hyperphagia. Experimental studies in which daily food intake and total energy expenditure are accurately measured for prolonged periods of time in prepubertal children living their normal life are badly needed to throw more light on this issue. The use of either the doubly labeled water (24) and/or the heart-rate methods (25) (the latter being particularly suited and convenient for studies in children) may provide more information on the total energy expenditure of obese children in free-living conditions.

In conclusion, the present study demonstrates that obesity in prepubertal children is accompanied by a blunted meal-induced thermogenesis. Whether or not the reduced TEM encountered in obese children will still remain low at puberty and in the postpubertal phase until adulthood remains the object of further prospective investigations. The quantitative importance of this energy saving may appear trivial because, despite this defect in thermogenesis, the RMR of obese children was still significantly greater than that of the control children. Further studies in which the TEM is measured in the same children before and after weight loss could establish to what extent the impaired TEM is a secondary phenomenon rather than a primary pathogenetic factor in childhood obesity.

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