Relationship Between Basal Metabolic Rate, Gender, Age, and Body Composition in 8,780 White Obese Subjects

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The objective of the present study was to explore the relationship between basal metabolic rate (BMR), gender, age, anthropometric characteristics, and body composition in severely obese white subjects. In total, 1,412 obese white children and adolescents (BMI > 97° percentile for gender and age) and 7,368 obese adults (BMI > 30 kg/m^2) from 7 to 74 years were enrolled in this study. BMR was measured using an indirect calorimeter equipped with a canopy and fat-free mass (FFM) were obtained using tetrapolar bioelectrical impedance analysis (BIA). Using analysis of covariance, we tested the effect of gender on the relationship between BMR, age, anthropometry, and body composition. In children and adolescents, the predictor × gender interaction was significant in all cases except for FFM × gender. In adults, all predictor × gender interactions were significant. A prediction equation based on body weight (BW), age, and gender had virtually the same accuracy of the one based on FFM, age, and gender to predict BMR in both children and adults (R^2_{adj} = 0.59 and 0.60, respectively). In conclusion, gender was a significant determinant of BMR in children and adolescents but not in adults. Our results support the hypothesis that the age-related decline in BMR is due to a reduction in FFM. Finally, anthropometric predictors of BMR are as accurate as body composition estimated by BIA.

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INTRODUCTION

The increasing prevalence of obesity during the last decades (1) is ascribed mainly to a mismatch between energy intake and energy expenditure (EE) (2,3). The factors that influence this balance are numerous and complex, involving genes, environment, and their interaction. However, the rationale of weight management strategies is to identify and modify the amount of energy introduced and expended in order to regain normal body weight (BW) (1). EE is a major determinant of energy balance and body composition. According to an usually accepted scheme in human nutrition, daily EE (DEE) can be partitioned between basal metabolic rate (BMR) extrapolated to 24 h, which corresponds to the energy needed to sustain the body functions at rest and which accounts for ~65% of DEE in sedentary subjects (4); EE associated with physical activity (often referred to as the thermic effect of activity), which accounts for ~25% of DEE (5); and the thermic effect of food, which includes EE due to digestion, absorption, and metabolism of nutrients and which accounts for ~10% of DEE (5). Because of its large contribution to DEE, especially in obese subjects, BMR has frequently been the main focus of attention in the studies on the development and treatment of obesity.

BMR can be considered as the sum of the EEs of tissues and organs in a fasting and resting state and in thermoneutral conditions. It depends on the mass and metabolic rate of tissues and organs (6). For instance, EE is ~10, 15, 20, 35, and 35 times higher in the digestive tract, liver, brain, heart, and kidney than in resting muscle, whereas it is only ~1/3 of resting muscle in white adipose tissues (7). Thus, although organs only account for ~7% of BW, they contribute ~60% of BMR. In comparison, skeletal and adipose tissues account for 35–40% of BW but only 18–22% and 3–4% of BMR, respectively (8). Generally, BMR depends on body composition as expressed by fat-free mass (FFM) and fat mass (FM) and on gender, age, physical activity, and nutritional status. The main determinant of BMR is FFM (6), whereas FM is significant only in obese subjects (9). Gender is also a significant determinant of BMR, with men having a greater BMR than females after adjustment for body composition (9,10). In addition, BMR markedly decreases with advancing age in sedentary populations (11) at a rate

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of ~1–2% per decade after the age of 20 (ref. 12). Such a decline in EE probably contributes to an impaired ability to regulate energy balance with age. Several studies have addressed the issue of whether EE decreases with age and whether females have lower EE than males, but the literature is equivocal on this topic concerning obese subjects. The aim of the present study was therefore to explore the relationship between BMR, gender, age, anthropometric characteristics, and body composition in a very large sample of severely obese white subjects.

METHODS AND PROCEDURES

Subjects

In total, 1,412 obese white children and adolescents (age range: 7–18 years) and 7,368 obese adults (age range: 18–74 years) were consecutively enrolled into the study between January 2003 and December 2007 at the Division of Auxology and between January 1999 and December 2007 at the 3rd Division of Metabolic Diseases of the Italian Institute for Auxology (Italy). The inclusion criteria were: (i) age between 7 and 74 years and (ii) BMI above the 97th percentile for gender and age using Italian reference values for children and adolescents (13) and BMI ≥ 30 kg/m^2 for adults. Subjects who had overt metabolic and/or endocrine diseases (e.g., diabetes, hypothyroidism, hypertension, amenorrhea), and those taking any drug known to influence energy metabolism were excluded from the study. The experimental protocol was approved by the Ethics Committee of the Italian Institute for Auxology. The purpose and the objectives were carefully explained to the subjects and written informed consent was obtained from them or their legal guardians.

The measurements were performed during a stable BW period before the beginning of a weight-reduction program at the Italian Institute of Auxology. The fasting subjects were taken to the laboratory and BMR, BW, height, and body composition were assessed.

Physical characteristics and body composition

BW was measured to the nearest 0.1 kg with a manual weighing scale (Seca 709, Hamburg, Germany). Height was measured to the nearest 0.5 cm using a standardized wall-mounted height board (Wunder, Milan, Italy). BMI was calculated as BW (kg)/height^2 (m) (14). The standard deviation score of BMI was calculated applying the LMS method (15) to Italian reference values for children and adolescents (13).

Body composition was measured using bioelectrical impedance analysis (BIA) with a tetrapolar impedance meter (Human-IM Scan; DS-Medigroup, Milan, Italy). Measurements were performed according to the method of Lukaski (16) and the National Institutes of Health guidelines (17). FFM was estimated using the prediction equations developed by Lazzer *et al.* (18) for children and adolescents, and those of Gray *et al.* (19) for adults. FM was obtained by subtracting FFM from BW and %FM as (FM/BW) × 100. The within-day coefficient of variation for three repeated assessments of FFM in 10 obese subjects (with repositioning of electrodes) was 2.4%.

BMR

BMR was measured in the morning (between 8 and 10 AM) after an overnight fast and in thermoneutral conditions (in a 22–25 °C room) using an open-circuit, indirect computerized calorimeter equipped with a canopy (Vmax 29; Sensor Medics, Yorba Linda, CA). The medical charts of fertile females were reviewed for regularity of menses and the date of last menstrual period. BMR was always determined during the follicular phase of the menstrual cycle. The gas analyzers were calibrated before each test using a reference gas mixture (15.0% O_2 and 5.0% CO_2). Subjects were measured at rest in a supine position for a period of at least 45 min, including a 10-min acclimation period (20). Data from the initial 10 min of measurement, reflecting adjustment to the procedural environment and subjects adaptation, were not considered for BMR calculation. After achieving a steady state, O_2 consumption and CO_2 production standardized for temperature, barometric pressure, and humidity were recorded at 1-min intervals for a minimum of 30 min and averaged over the whole measurement period. EE was calculated from O_2 uptake and CO_2 output using the equation of Weir (21).

Statistical analysis

Values of continuous variables are given as mean and standard deviation and those of categorical variables as the number or percentage of subjects with the characteristic of interest. Between-gender comparisons were performed using Student's unpaired *t*-test. The univariable relationships between BMR and continuous predictors (age, BW, height, FFM, and FM) were first studied using scatterplots and nonparametric regression plots. A first-degree linear model was as accurate as more complex models to describe all the BMR-predictor relationships and was thus chosen as the reference model for all univariable analyses. In order to test the effect of gender on the BMR-predictor relationships, we used analysis of covariance (22). Four prespecified models were used to test the accuracy of anthropometry and body composition in multivariable prediction of BMR. Model 1 was based on BW, age, and gender; Model 2 added height to the predictors of Model 1; Model 3 was based on age, gender, and FFM; Model 4 added FM to the predictors of Model 3. Standard diagnostic plots were used to test univariable and multivariable model fit (23). Regression residuals were normally distributed for all univariable and multivariable models. The adjusted coefficient of determination (R^2_{adj}) and the root mean squared error of the estimate (RMSE) were used as measures of model fit. The 95% confidence intervals (95% CI) of the regression coefficients, R^2_{adj} and RMSE were calculated using bootstrap on 1,000 random samples of 1,412 children and adolescents and 7,368 adults (24). Statistical analysis was performed using STATA 10.0 (STATA, College Station, TX).

RESULTS

The physical characteristics of the 1,412 obese children and adolescents and 7,368 obese adults are shown in **Table 1**. In both groups, 58% of the children and adolescents and 73% of the adults were females. In both groups, mean age and percent FM were significantly higher in females than males, whereas BW, height, FFM, and BMR were significantly lower in females.

Figure 1 shows the regression of BMR vs. age, BW, height, FFM, and FM in children and adolescents and in adults stratified by gender. On visual inspection of the graphs, males have higher values of BMR for the same value of the predictor. **Table 2** shows the analysis of covariance models formally testing the effect of gender on the regression lines mentioned earlier. In children and adolescents (**Table 2**), the predictor × gender interaction was significant in all cases except for FFM × gender. However, when BW, FFM, or FM were used as predictors, the effect of gender as main effect was not statistically significant. Judging from R^2_{adj} and RMSE, the univariable predictions based on BW were as accurate as those based on FFM (R^2_{adj}: 0.59 vs. 0.59 and RMSE (kJ): 1,073 vs. 1,079, respectively).

In adults (**Table 2**), all predictor × gender interactions terms and main effects were significant. As for children and adolescents, the predictions based on BW were as accurate as those based on FFM (R^2_{adj}: 0.59 vs. 0.59 and RMSE (kJ): 1,065 vs. 1,059, respectively).

The four models of increasing complexity for the prediction of BMR are shown in **Table 3**. Model 1 is the simplest one

Table 1 Physical characteristics of subjects

	Children and adolescents (n = 1,412)			Adults (n = 7,368)		
	Females (n = 823)	Males (n = 589)	P value[a]	Females (n = 5,368)	Males (n = 2,000)	P value[a]
Age (years)	14.5 (2.1)	14.0 (2.3)	0.006	47.8 (13.9)	46.3 (13.8)	<0.001
Body weight (kg)	94.1 (19.4)	102.4 (26.8)	<0.001	105.8 (17.5)	123.9 (22.6)	<0.001
Height (m)	1.60 (0.10)	1.70 (0.10)	<0.001	1.60 (0.10)	1.70 (0.10)	<0.001
BMI (kg/m^2)	36.6 (6.0)	36.7 (6.6)	0.740	41.9 (6.5)	41.6 (6.8)	0.098
z-BMI (SDS)	3.0 (0.5)	3.0 (0.7)	0.056	—	—	—
FFM (kg)	44.4 (8.8)	51.3 (13.5)	<0.001	53.4 (9.0)	78.2 (14.4)	<0.001
FM (kg)	49.7 (10.7)	51.1 (13.6)	0.042	52.4 (8.6)	45.8 (8.5)	<0.001
FM (%)	52.7 (1.5)	49.8 (1.9)	<0.001	49.5 (1.0)	36.9 (1.4)	<0.001
BMR (kJ)	7,652 (1,246)	9,101 (1,826)	<0.001	7,418 (1,255)	9,409 (1,723)	<0.001

Values are given as means and s.d.
BMR, basal metabolic rate; FFM, fat-free mass; FM, fat mass; SDS, standard deviation score; z-BMI, z-score of BMI.
[a]Unpaired t-test for males vs. females.

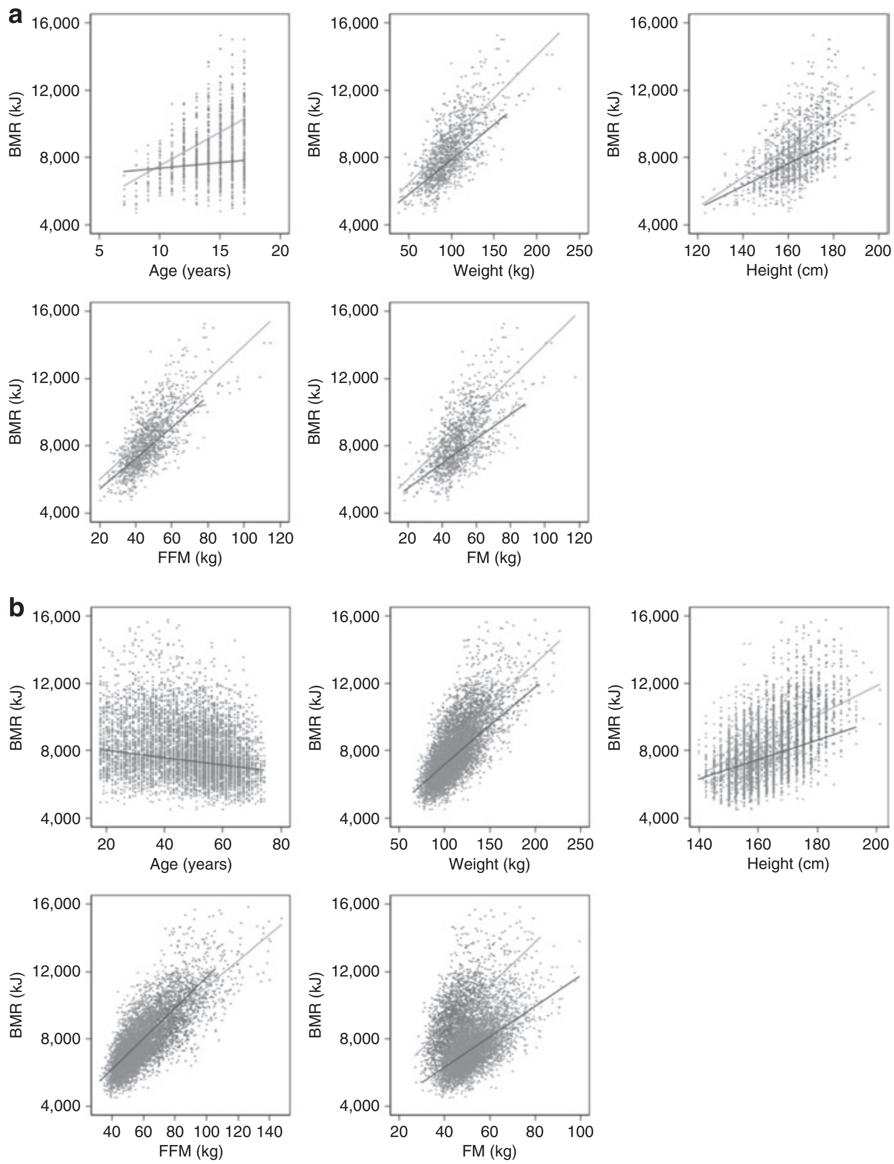

Figure 1 Basal metabolic rate (BMR, kJ/die) plotted as a function of age (years), body weight (kg), height (m), fat-free mass (FFM, kg) and fat mass (FM, kg) for (**a**) children and adolescents (n = 1,412) and (**b**) adults (n = 7,368) (gray line = males; black line = females).

Table 2 Effect of gender on the relationship between BMR, anthropometry, and body composition

	Age	Body weight	Height	BMI	FFM	FM
Children and adolescents						
Male	−3,147*** (−4,105, −2,190)	133 (−366, 633)	−2,557* (−4,740, −374)	−1,051** (−1,810, −292)	419 (−92, 929)	−8 (−499, 483)
Age (years)	66** (21, 111)	—	—	—	—	—
Male × age	331*** (265, 398)	—	—	—	—	—
Body weight (kg)	—	41*** (37, 45)	—	—	—	—
Male × weight	—	10*** (5, 14)	—	—	—	—
Height (cm)	—	—	66*** (56, 77)	—	—	—
Male × height	—	—	22** (8, 35)	—	—	—
BMI (kg/m²)	—	—	—	107*** (94, 121)	—	—
Male × BMI	—	—	—	68*** (47, 88)	—	—
FFM (kg)	—	—	—	—	92*** (83, 100)	—
Male × FFM	—	—	—	—	8 (−3, 18)	—
FM (kg)	—	—	—	—	—	73*** (66, 80)
Male × FM	—	—	—	—	—	27*** (17, 36)
Intercept	6,693*** (6,032, 7,353)	3,771*** (3,408, 4,135)	−2,963*** (−4,612, −1,314)	3,723*** (3,210, 4,236)	3,574*** (3,196, 3,953)	4,001*** (3,649, 4,354)
N	1,412	1,412	1,412	1,412	1,412	1,412
R^2_{adj}	0.31	0.59	0.41	0.47	0.59	0.58
RMSE (kJ)	1,393	1,073	1,282	1,223	1,079	1,083
P model	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001
Adults						
Male	2,605*** (2,361, 2,849)	744*** (431, 1,058)	−4,065*** (−5,568, −2,562)	799*** (407, 1,191)	796*** (488, 1,104)	940*** (624, 1,257)
Age (years)	−21*** (−24, −19)	—	—	—	—	—
Male × age	−14*** (−19, −9)	—	—	—	—	—
Body weight (kg)	—	46*** (45, 48)	—	—	—	—
Male × weight	—	3* (1, 6)	—	—	—	—
Height (cm)	—	—	58*** (53, 63)	—	—	—
Male × height	—	—	31*** (22, 39)	—	—	—
BMI (kg/m²)	—	—	—	98*** (93, 103)	—	—
Male × BMI	—	—	—	29*** (20, 39)	—	—
FFM (kg)	—	—	—	—	91*** (88, 94)	—
Male × FFM	—	—	—	—	−14*** (−18, −9)	—
FM (kg)	—	—	—	—	—	91*** (88, 95)
Male × FM	—	—	—	—	—	36*** (30, 43)
Intercept	8,436*** (8,307, 8,565)	2,522*** (2,348, 2,697)	−1,745*** (−2,534, −957)	3,324*** (3,113, 3,536)	2,541*** (2,371, 2,711)	2,642*** (2,463, 2,820)
N	7,368	7,368	7,368	7,368	7,368	7,368
R^2_{adj}	0.33	0.59	0.38	0.47	0.59	0.57
RMSE (kJ)	1,351	1,065	1,306	1,209	1,059	1,088
P model	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001

95% confidence intervals in brackets.
BMR, basal metabolic rate; FFM, fat-free mass; FM, fat mass; R^2_{adj}, adjusted coefficient of determination; RMSE, root mean squared error.
$^*P < 0.05$, $^{**}P < 0.01$, $^{***}P < 0.001$.

and is based on BW, age, and gender; Model 2 adds height to the predictors of Model 1; Model 3 is based on age, gender, and FFM and Model 4 adds FM to the predictors of Model 3. Because there was no meaningful improvement in model fit obtained by adding the predictor × gender interactions (data not shown), we kept the models simpler by removing these interactions also, when statistically significant.

All models had virtually the same accuracy for predicting BMR in children and adolescents as in adults (R^2_{adj} from 0.59 to 0.60). In detail, height added nothing practically relevant

Table 3 Comparison of different models for the prediction of basal metabolic rate

	Model 1	Model 2	Model 3	Model 4
Children and adolescents				
Body weight (kg)	50*** (46, 53)	44*** (40, 48)	—	—
Age (years)	−57*** (−85, −28)	−95*** (−126, −64)	−28* (−55, −0)	−50** (−81, −19)
Male	1,007*** (884, 1,131)	889*** (759, 1,018)	749*** (621, 877)	938*** (767, 1,109)
Height (cm)	—	24*** (16, 32)	—	—
FFM (kg)	—	—	99*** (92, 106)	63*** (39, 86)
FM (kg)	—	—	—	37** (14, 60)
Intercept	3,804*** (3,439, 4,169)	1,044* (92, 1,997)	3,640*** (3,268, 4,012)	3,759*** (3,385, 4,134)
N	1,412	1,412	1,412	1,412
RMSE (kJ)	1,074*** (1,029, 1,118)	1,062*** (1,016, 1,107)	1,078*** (1,033, 1,123)	1,073*** (1,029, 1,118)
R^2_{adj}	0.59*** (0.56, 0.62)	0.60*** (0.56, 0.63)	0.59*** (055, 0.62)	0.59*** (0.56, 0.62)
P model	<0.001	<0.001	<0.001	<0.001
Adults				
Body weight (kg)	46*** (44, 47)	44*** (42, 45)	—	—
Age (years)	−14*** (−16, −12)	−13*** (−14, −11)	−10*** (−11, −8)	−14*** (−16, −11)
Male	1,140*** (1,075, 1,206)	997*** (919, 1,074)	−44 (−130, 43)	1,003*** (725, 1,282)
Height (cm)	—	13*** (10, 17)	—	—
FFM (kg)	—	—	82*** (79, 84)	50*** (41, 59)
FM (kg)	—	—	—	41*** (30, 51)
Intercept	3,252*** (3,076, 3,427)	1,270*** (679, 1,861)	3,517*** (3,340, 3,694)	3,270*** (3,097, 3,443)
N	7,368	7,368	7,368	7,368
R^2_{adj}	0.60*** (0.58, 0.61)	0.60*** (0.59, 0.62)	0.59*** (0.58, 0.61)	0.60*** (0.58, 0.61)
RMSE (kJ)	1,048*** (1,026, 1,070)	1,045*** (1,023, 1,067)	1,054*** (1,032, 1,076)	1,048*** (1,026, 1,070)
P model	<0.001	<0.001	<0.001	<0.001

Bootstrapped 95% confidence intervals in brackets.
FFM, fat-free mass; FM, fat mass; R^2_{adj}, adjusted coefficient of determination; RMSE, root mean squared error.
$^*P < 0.05$, $^{**}P < 0.01$, $^{***}P < 0.001$.

to the simpler model based on BW and age and gender and FM added nothing practically relevant to the model based on age, gender, and FFM (**Table 3**). Thus, a simple model based on BW, age, and gender is as accurate as more complex models based on body composition. Therefore, the new equations for the prediction of BMR in children and adolescents (Eqs. 1 and 2) and adults (Eqs. 3 and 4) are the following:

$$BMR = 50 \times BW - 57 \times Age + 1{,}007 \times gender + 3{,}804 \qquad (1)$$

(R^2_{adj}: 0.59; RMSE: 1,074 kJ; accurate prediction: 59%)

$$BMR = 99 \times FFM - 28 \times Age + 749 \times gender + 3{,}640 \qquad (2)$$

(R^2_{adj}: 0.59; RMSE: 1,078 kJ; accurate prediction: 59%)

$$BMR = 46 \times BW - 14 \times Age + 1{,}140 \times gender + 3{,}252 \qquad (3)$$

(R^2_{adj}: 0.60; RMSE: 1,048 kJ; accurate prediction: 56%)

$$BMR = 82 \times FFM - 10 \times Age - 44 \times gender + 3{,}517 \qquad (4)$$

(R^2_{adj}: 0.59; RMSE: 1,054 kJ; accurate prediction: 56%),

where gender = 1 for males and 0 for females, BMR is expressed in kJ, age in years, BW and FFM in kg (R^2_{adj} = adjusted coefficient of determination; RMSE: root mean squared error; accurate prediction: percentage of all subjects whose BMR predicted was within 90–110% of measured BMR. These equations are given in **Appendix 1** with BMR expressed as kcal).

DISCUSSION

We evaluated the relationship between BMR, gender, age, anthropometry, and body composition in the largest sample of obese white children, adolescents, and adults studied so far.

In children and adolescents, gender was a significant predictor of BMR. As shown in **Table 3**, gender entered all prediction models, contributing from 749 to 1,007 kJ more in males than in females. In agreement with previous studies performed in obese children and adolescents (10,25), the higher BMR of our male subjects can be explained mostly by their higher FFM as compared to females. FFM, the metabolically active component of the body, explained ~60% of the variability of BMR in our children and adolescents, which suggests that other factors influence BMR. In particular, after adjustment for FFM, gender remained a significant multivariable predictor of BMR in children and adolescents (regression coefficient = 749, 95% CI: 621–887 kJ), which may be explained by higher proportions of

Table 4 Comparison between BMR and predicted BMR by WHO (35), Mifflin *et al*. (36) and new equations

Author	BMR[a] (kcal/day)	Difference[a] (kcal/day)	Difference (%)	Accurate[b] prediction	*P* value[c]
Measured REE (boys <18 years)	2,181 ± 437				
WHO (boys <18 years)	2,416 ± 458	234 ± 315	11	**36**	<0.001
Mifflin (boys <18 years)	2,007 ± 322	−174 ± 288	−8	**46**	<0.001
New (boys <18 years)	2,191 ± 305	10 ± 290	0	**57**	0.377
Measured REE (girls <18 years)	1,825 ± 297				
WHO (girls <18 years)	1,685 ± 174	−140 ± 227	−8	**50**	<0.001
Mifflin (girls <18 years)	1,708 ± 228	−117 ± 227	−6	**50**	<0.001
New (girls <18 years)	1,834 ± 223	9 ± 226	0	**60**	0.237
Measured REE (male >18 years)	2,244 ± 413				
WHO (male >18 years)	2,299 ± 362	55 ± 345	2	**45**	<0.001
Mifflin (male >18 years)	2,087 ± 278	−157 ± 308	−7	**47**	<0.001
New (male >18 years)	2,269 ± 262	25 ± 310	1	**54**	0.342
Measured REE (female >18 years)	1,771 ± 301				
WHO (female >18 years)	1,764 ± 210	−6 ± 240	0	**53**	0.021
Mifflin (female >18 years)	1,650 ± 221	−120 ± 228	−7	**49**	<0.001
New (female >18 years)	1,795 ± 204	25 ± 225	1	**58**	0.132

BMR, basal metabolic rate; REE, resting energy expenditure; WHO, World Health Organization.
[a]Mean ± s.d. [b]Percentage of subjects whose predicted BMR is within 90–110% of measured BMR. [c]Paired *t*-test for predicted vs. measured BMR.

skeletal glycolytic fibers (26), higher Na^+–K^+ ATPase activity (27), and different hormonal status (28).

However, male gender (regression coefficient = −44, 95% CI −130 to 43) did not enter the multivariable prediction model for adults based on FFM. This is an agreement with previous studies showing that the confounding effect of gender is eliminated when FFM is taken into account (29).

In all prediction models (**Table 3**), there was an inverse relationship between age and BMR. As expected, the increase of BMR for each year of age was higher in children and adolescents than in adults (**Table 2**). These results confirm previous observations that there is a reduction in BMR adjusted for differences in body composition in older subjects compared with younger ones (30,31). Our results therefore support the hypothesis that the age-related decline in BMR is mainly attributed to a reduction in FFM quantity. Gallagher *et al*. (8,32) first addressed the age-related decline in BMR in normal weight subjects by applying a BMR-prediction model based on seven organ/tissue components. Subsequently, Wang *et al*. (6,31) confirmed that the decline in both the mass and the cellular fraction of organs and tissues may account for the lower BMR observed in elderly adults. Whereas body composition cannot fully explain the interindividual variability of BMR, FFM explained ~60% of the variability of BMR in both children and adolescents and in adults in the present study. It is possible that there are other factors that may contribute to predicting BMR in severely obese subjects. Ponderal history, genetic factors, such as physical activity level (33) and differences in organ mass and metabolic rate (31,32), and hormonal status (34) may also influence BMR. Whether the addition of these variables can improve the accuracy of predicting BMR in the severely obese deserves further study. However, at present, we cannot offer any plausible metabolic mechanism explaining this observation, and further research is needed.

In the present study, the main predictors of BMR for children and adolescents (**Table 3**) and adults (**Table 3**) were investigated. The prediction equation based on anthropometric (BW, height, gender, and age) and body composition measurements (FFM, FM, gender, and age) had the same R^2_{adj} and similar RMSE. Thus, an estimation of BMR in obese subjects can be obtained with the same accuracy using anthropometric or body composition measurements. Clearly, the equations based on anthropometric measurements are easier to use in clinical practice because they are based on routine measurements. The equations based on body composition (FFM and FM as assessed by BIA) are also generally more population-specific than those based on anthropometric measurements (10,25), and require specific equipment and more time to assess body composition. In addition, the new equations are characterized by good accuracy and better agreement between predicted and measured BMR than that provided by WHO (35) and Mifflin *et al*. (36) as well as independently from age and gender (**Table 4**). As BMR makes up more than 60% of EE in obese subjects, a better understanding of the main factors influencing it and its prediction is necessary to develop a dietary treatment able to induce a desired level of energy deficit for obese subjects.

In the present study, body composition was measured using BIA on the basis of the water content in the body (16). All measurements of body composition in our study were performed under strictly controlled conditions in accordance with the National Institutes of Health guidelines (17). BIA is a common, simple, rapid, and noninvasive method to estimate total body water and FFM in healthy subjects as well as in obese subjects (37). BIA has been cross validated in children and adolescents against measurements of total body water by deuterium dilution (38) and total body potassium (39). Similar validation studies are available for adults (40). The accuracy of BIA is highly dependent on the equations used to calculate FFM. The BIA prediction equations developed by our group against dual-energy X-ray absorptiometry (18) allowed an estimate of body composition in obese youths similar to those studied here. Moreover, the fatness-specific prediction equations employed for adults have been cross-validated in adults (19) within a wide range of BMI (up to 53.3 kg/m^2). Das *et al*. (40) reported that the BIA estimate of percent body fat obtained with fatness-specific equations in extremely obese women was within 1.1–1.5% of the value obtained using body density and doubly labeled water as gold standards.

In conclusion, gender was a significant determinant of BMR in obese children and adolescents but not in obese adults. In children and adolescents, gender remained significant after adjustment for BW or FFM, with a BMR higher in males. In addition, the present study supports the hypothesis that the age-related decline in BMR is due to a reduction in FFM, which suggests that physical activity is essential for obese subjects both to maintain or increase BMR, as well as to increase DEE and contribute to weight loss. Finally, anthropometric measurements (BW, height, gender, and age) are as accurate as body composition estimated by BIA for the prediction of BMR. The equations developed in the present study may represent a useful tool for health care professionals, who do not have access to indirect calorimetry equipment, for the estimation of BMR in obese subjects.

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DISCLOSURE

The authors declared no conflict of interest.

REFERENCES

1. World Health Organization. Obesity: preventing and managing the global epidemic. Report of a WHO Consultation. Geneva, Switzerland, 2004.
2. Bouchard C, Blair SN. Introductory comments for the consensus on physical activity and obesity. *Med Sci Sports Exerc* 1999;31(11 Suppl):S498–S501.
3. Flatt JP. Macronutrient composition and food selection. *Obes Res* 2001;9(Suppl 4):S256–S262.
4. Foster GD, McGuckin BG. Estimating resting energy expenditure in obesity. *Obes Res* 2001;9(Suppl 5):S367–S372.
5. Goran MI. Energy metabolism and obesity. *Med Clin North Am* 2000;84:347–362.
6. Wang Z, Heshka S, Wang J *et al*. Metabolically active portion of fat-free mass: a cellular body composition level modeling analysis. *Am J Physiol Endocrinol Metab* 2007;292:E49–E53.
7. Elia M. Energy expenditure in whole body. In: Kinney MJ, Tucker HN (eds). *Energy Metabolism*. Raven Press: New York, 1992, pp 19–60.
8. Gallagher D, Belmonte D, Deurenberg P *et al*. Organ-tissue mass measurement allows modeling of REE and metabolically active tissue mass. *Am J Physiol* 1998;275:E249–E258.
9. Johnstone AM, Murison SD, Duncan JS, Rance KA, Speakman JR. Factors influencing variation in basal metabolic rate include fat-free mass, fat mass, age, and circulating thyroxine but not sex, circulating leptin, or triiodothyronine. *Am J Clin Nutr* 2005;82:941–948.
10. Goran MI, Kaskoun M, Johnson R. Determinants of resting energy expenditure in young children. *J Pediatr* 1994;125:362–367.
11. Fukagawa NK, Bandini LG, Young JB. Effect of age on body composition and resting metabolic rate. *Am J Physiol* 1990;259:E233–E238.
12. Keys A, Taylor HL, Grande F. Basal metabolism and age of adult man. *Metab Clin Exp* 1973;22:579–587.
13. Cacciari E, Milani S, Balsamo A *et al*. Italian cross-sectional growth charts for height, weight and BMI (6-20 y). *Eur J Clin Nutr* 2002;56:171–180.
14. Quetelet L, Adolphe J. A treatise on man and the development of his faculties. In: Chambers WaR (ed). *Comparative Statistics in the 19th Century*. Edinburgh, Scotland, 1842.
15. Cole TJ, Freeman JV, Preece MA. British 1990 growth reference centiles for weight, height, body mass index and head circumference fitted by maximum penalized likelihood. *Stat Med* 1998;17:407–429.
16. Lukaski HC, Bolonchuk WW, Hall CB, Siders WA. Validation of tetrapolar bioelectrical impedance method to assess human body composition. *J Appl Physiol* 1986;60:1327–1332.
17. NIHT. Bioelectrical impedance analysis in body composition measurement: National Institutes of Health Technology Assessment Conference Statement. *Am J Clin Nutr* 1996;64(3 Suppl):S524–S532.
18. Lazzer S, Bedogni G, Agosti F *et al*. Comparison of dual-energy X-ray absorptiometry, air displacement plethysmography and bioelectrical impedance analysis for the assessment of body composition in severely obese Caucasian children and adolescents. *Br J Nutr* 2008;100:918–924.
19. Gray DS, Bray GA, Gemayel N, Kaplan K. Effect of obesity on bioelectrical impedance. *Am J Clin Nutr* 1989;50:255–260.
20. Isbell TR, Klesges RC, Meyers AW, Klesges LM. Measurement reliability and reactivity using repeated measurements of resting energy expenditure with a face mask, mouthpiece, and ventilated canopy. *JPEN J Parenter Enteral Nutr* 1991;15:165–168.
21. Weir JB. New methods for calculating metabolic rate with special reference to protein metabolism. *J Physiol (Lond)* 1949;109:1–9.
22. Huitema BE. *The Analysis of Covariance and Alternatives*. Wiley: New York, 1980.
23. Chatterjee S, Hadi AS. *Regression Analysis by Example*. Wiley-Interscience: New York, 2006.
24. Efron B, Tibshirani R. *An Introduction to the Bootstrap*. Chapman & Hall: New York, 1993.
25. Weinsier RL, Schutz Y, Bracco D. Reexamination of the relationship of resting metabolic rate to fat-free mass and to the metabolically active components of fat-free mass in humans. *Am J Clin Nutr* 1992;55:790–794.
26. Simoneau JA, Bouchard C. Human variation in skeletal muscle fiber-type proportion and enzyme activities. *Am J Physiol* 1989;257:E567–E572.
27. Simat BM, Mayrand RR, From AH *et al*. Is the erythrocyte sodium pump altered in human obesity? *J Clin Endocrinol Metab* 1983;56:925–929.
28. Ferraro R, Lillioja S, Fontvieille AM *et al*. Lower sedentary metabolic rate in women compared with men. *J Clin Invest* 1992;90:780–784.
29. Cunningham JJ. Body composition as a determinant of energy expenditure: a synthetic review and a proposed general prediction equation. *Am J Clin Nutr* 1991;54:963–969.
30. Piers LS, Soares MJ, McCormack LM, O'Dea K. Is there evidence for an age-related reduction in metabolic rate? *J Appl Physiol* 1998;85:2196–2204.
31. Wang Z, Heshka S, Heymsfield SB, Shen W, Gallagher D. A cellular-level approach to predicting resting energy expenditure across the adult years. *Am J Clin Nutr* 2005;81:799–806.
32. Gallagher D, Allen A, Wang Z, Heymsfield SB, Krasnow N. Smaller organ tissue mass in the elderly fails to explain lower resting metabolic rate. *Ann N Y Acad Sci* 2000;904:449–455.
33. Lazzer S, Boirie Y, Bitar A *et al*. Assessment of energy expenditure associated with physical activities in free-living obese and nonobese adolescents. *Am J Clin Nutr* 2003;78:471–479.
34. Leibel RL, Rosenbaum M, Hirsch J. Changes in energy expenditure resulting from altered body weight. *N Engl J Med* 1995;332:621–628.
35. World Health Organization. Energy and protein requirements. Report of a Joint FAO/WHO/UNU Expert Consultation. WHO Technical Report Series, No. 724. Geneva, Switzerland, 1985.
36. Mifflin MD, St Jeor ST, Hill LA *et al*. A new predictive equation for resting energy expenditure in healthy individuals. *Am J Clin Nutr* 1990;51:241–247.
37. Houtkooper LB, Lohman TG, Going SB, Howell WH. Why bioelectrical impedance analysis should be used for estimating adiposity. *Am J Clin Nutr* 1996;64(3 Suppl):S436–S448.

38. Wabitsch M, Braun U, Heinze E *et al*. Body composition in 5-18-y-old obese children and adolescents before and after weight reduction as assessed by deuterium dilution and bioelectrical impedance analysis. *Am J Clin Nutr* 1996;64:1–6.
39. Schaefer F, Georgi M, Zieger A, Schärer K. Usefulness of bioelectric impedance and skinfold measurements in predicting fat-free mass derived from total body potassium in children. *Pediatr Res* 1994;35:617–624.
40. Das SK, Roberts SB, Kehayias JJ *et al*. Body composition assessment in extreme obesity and after massive weight loss induced by gastric bypass surgery. *Am J Physiol Endocrinol Metab* 2003;284:E1080–E1088.

APPENDIX 1

New equations for the prediction of BMR (kcal) in children and adolescents (Eqs. 5 and 6) and adults (Eqs. 7 and 8) are the following:

$$\mathrm{BMR} = 12 \times \mathrm{BW} - 14 \times \mathrm{Age} + 241 \times \mathrm{gender} + 909 \quad (5)$$

(R^2_{adj}: 0.59; RMSE: 257 kcal; accurate prediction: 59%)

$$\mathrm{BMR} = 24 \times \mathrm{FFM} - 7 \times \mathrm{Age} + 179 \times \mathrm{gender} + 870 \quad (6)$$

(R^2_{adj}: 0.59; RMSE: 258 kcal; accurate prediction: 59%)

$$\mathrm{BMR} = 11 \times \mathrm{BW} - 3 \times \mathrm{Age} + 272 \times \mathrm{gender} + 777 \quad (7)$$

(R^2_{adj}: 0.60; RMSE: 251 kcal; accurate prediction: 56%)

$$\mathrm{BMR} = 20 \times \mathrm{FFM} - 2 \times \mathrm{Age} - 11 \times \mathrm{gender} + 841 \quad (8)$$

(R^2_{adj}: 0.59; RMSE: 252 kcal; accurate prediction: 56%)

where gender = 1 for males and 0 for females, age in years, BW and FFM in kg ($R^2{}_{adj}$ = adjusted coefficient of determination; RMSE: root mean squared error; accurate prediction: percentage of all subjects whose BMR predicted was within 90–110% of measured BMR).