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Development and cross-validation of prediction equations for estimating resting energy expenditure in severely obese Caucasian children and adolescents

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The objectives of the present study were to develop and cross-validate new equations for predicting resting energy expenditure (REE) in severely obese children and adolescents, and to determine the accuracy of new equations using the Bland–Altman method. The subjects of the study were 574 obese Caucasian children and adolescents (mean BMI *z*-score 3·3). REE was determined by indirect calorimetry and body composition by bioelectrical impedance analysis. Equations were derived by stepwise multiple regression analysis using a calibration cohort of 287 subjects and the equations were cross-validated in the remaining 287 subjects. Two new specific equations based on anthropometric parameters were generated as follows: (1) REE = (Sex × 892·68) − (Age × 115·93) + (Weight × 54·96) + (Stature × 1816·23) + 1484·50 (R^2 0·66; SE 1028·97 kJ); (2) REE = (Sex × 909·12) − (Age × 107·48) + (fat-free mass × 68·39) + (fat mass × 55·19) + 3631·23 (R^2 0·66; SE 1034·28 kJ). In the cross-validation group, mean predicted REE values were not significantly different from the mean measured REE for all children and adolescents, as well as for boys and for girls (difference $<2\,\%$) and the limits of agreement (± 2 SD) were $+2·06$ and $-1·77$ MJ/d (NS). The new prediction equations allow an accurate estimation of REE in groups of severely obese children and adolescents. These equations might be useful for health care professionals and researchers when estimating REE in severely obese children and adolescents.

Prediction equation: Energy expenditure: Children: Adolescents: Body composition: Obesity

The increasing prevalence of obesity in childhood during the last decades (Lobstein & Frelut, 2003) is considered to result mainly from a mismatch between energy intake and energy expenditure (Bouchard & Blair, 1999; Flatt, 2001). In spite of their reduced physical activity and a relatively lower thermic effect of food (Maffeis *et al.* 1993; Salas-Salvado *et al.* 1993), obese children and adolescents exhibit a higher daily energy expenditure than non-obese subjects (Ekelund *et al.* 2002; Lazzer *et al.* 2003). This apparent paradox is due to both a higher resting energy expenditure (REE) than that of non-obese subjects (Dietz *et al.* 1994; Molnar & Schutz, 1997) and similar or higher physical activity energy expenditure because of the higher energy cost of weight-bearing activities (Ekelund *et al.* 2002; Lazzer *et al.* 2003). REE corresponds to energy expended for homeostatic processes mainly in organs. It accounts for 60–70 % of daily energy expenditure in sedentary individuals (Lazzer *et al.* 2004). The higher REE of obese subjects is mostly related to their higher fat-free mass (FFM) and fat mass (FM) (Dietz *et al.* 1994; Molnar & Schutz, 1997).

The ability to predict REE accurately in obese subjects is of utmost importance for adequate dietary therapy because it provides the basis to attain a desired level of energy deficit. The gold method for the measurement of REE is indirect calorimetry; however, its complex nature, the lack of skilled staff, and the high cost of equipment limit its regular use at clinical level, both for diagnostic and prognostic purposes. Since the beginning of the 20th century, several authors have tried to address the problem by developing equations for predicting REE in children and adolescents on the basis of anthropometric and body composition parameters (Harris & Benedict, 1919; Schofield, 1985; World Health Organization, 1985; Tverskaya *et al.* 1998; Derumeaux-Burel *et al.* 2004). FFM and FM explain inter-individual variance in REE better than does body weight in obese subjects (Ravussin *et al.* 1986; DeLany *et al.* 2002), but body composition is rarely considered in the equation to estimate REE.

Previous studies that tested the accuracy of REE equations in children and adolescents (Dietz *et al.* 1991) concluded that the World Health Organization (1985) or the Schofield (1985)

Abbreviations: BIA, bioelectrical impedance analysis; FFM, fat-free mass; FM, fat mass; MREE, measured resting energy expenditure; PREE, predicted resting energy expenditure; REE, resting energy expenditure.

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equations were the most accurate. However, because current Western populations show a greater degree of severe childhood obesity than those where the available equations for obese children and adolescents have been developed, there is a need for new equations for this population.

The objectives of the present study were: (1) to develop and cross-validate new equations for predicting REE in severely obese Caucasian children and adolescents; (2) to validate the new equations with a second independent population of obese adolescents; and (3) to determine the accuracy of new equations using the Bland–Altman method (Bland & Altman, 1986).

Subjects and methods

Subjects

The participants in the study were 574 obese Caucasian children and adolescents (242 boys and 332 girls) aged 7–18 years. The subjects were recruited from the Division of Auxology, Italian Institute for Auxology, IRCCS, Piancavallo (VB), Italy. The inclusion criteria were: age between 7 and 18 years, BMI above the 97th percentile for gender and chronological age (Luciano *et al.* 1997). Subjects who had previously participated in weight management programmes, had overt metabolic and/or endocrine diseases (e.g. diabetes, hypothyroidism, hypertension, amenorrhoea), and those taking medications regularly or using any drugs known to influence energy metabolism were excluded. In particular, at recruitment, 18 % of subjects were excluded for their high blood pressure (NHBP, 2004) and 2 % for their higher glycaemia (American Diabetes Association, 2000).

The experimental protocol was approved by the Ethics Committee of the Italian Institute for Auxology, Milan (Italy). Before the study began, the purpose and objectives were carefully explained to each subject and his or her parents. Written informed consent was obtained from all adolescents and their parents.

Measurements were performed during the stable body weight period before the beginning of the weight-reduction programme. The fasting subjects were taken to the laboratory and the REE, body weight, stature and body composition by bioelectrical impedance analysis (BIA) were determined.

Physical characteristics and body composition

Body weight was measured to the nearest 0·1 kg with a manual weighing scale (Seca 709; Seca, Hamburg, Germany). Stature was measured to the nearest 0·5 cm on a standardised wall-mounted height board. The standard deviation score for BMI *z*-score was determined by the following formula:

$$z = [(Q/M)^L - 1]/(L \times S)$$

where Q is the observed BMI; BMI variations (Rolland-Cachera *et al.* 1991; Luciano *et al.* 1997) were used to obtain L (power variation with age), S (coefficient of variation) and M (the 50th centile). Pubertal stage was evaluated according to the methods of Tanner (1961) (genitalia and pubic hair).

Body composition was measured using BIA with a tetrapolar impedancemeter (Human-IM Scan; DS-Medigroup, Milan, Italy). Measurements were performed according to the method of Lukaski (1987) after 20 min rest in a supine position with relaxed arms and legs without any contact with other body parts. FFM and FM were estimated using the prediction equations developed by Lazzer *et al.* (2005) from BIA, with a group of 143 obese adolescents (BMI *z*-score: 3·2; %FM: 34·5) aged 12–17 years and validated by dual-energy X-ray absorptiometry:

Boys :

$$FM = 0{\cdot}775 \times \text{Weight} - 0{\cdot}720 \times (\text{Stature}^2/\text{Resistance}) - 0{\cdot}221 \times \text{Reactance} + 17{\cdot}84$$

$$R^2\ 0{\cdot}96\ (\text{SE}\ 1{\cdot}66)\ \text{kg}$$

Girls :

$$FM = 0{\cdot}705 \times \text{Weight} - 0{\cdot}522 \times (\text{Stature}^2/\text{Resistance}) - 0{\cdot}133 \times \text{Reactance} + 8{\cdot}83$$

$$R^2\ 0{\cdot}93\ (\text{SE}\ 1{\cdot}80)\ \text{kg}$$

where FM and weight are in kg, stature in cm, resistance and reactance in ohm.

Resting energy expenditure

REE was determined after an overnight fast by means of an open-circuit, indirect computerised calorimetry (Vmax 29; Sensor Medics, Yorba Linda, CA, USA) with a rigid, transparent, ventilated canopy. Before each test the gas analysers were calibrated using a reference gas mixture (15·00 % O_2 and 5·00 % CO_2). After achieving steady state in the lying position, REE of subjects was measured for 30 min. O_2 consumption and CO_2 production, standardised 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. Results from the first 5–10 min (corresponding to adjustment to the procedural environment) and from any minutes associated with a RQ exceeding 0·95 were excluded from the analysis. Energy expenditure was derived from the measured O_2 uptake and CO_2 output according to the formula of de Weir (1949).

Development and validation of resting energy expenditure predictive equations

The data set of 574 measured REE (MREE) values (Group 1) was randomly split into two equal groups: a calibration group (cohort 1) for the development of predictive equations and a cross-validation group (cohort 2) for the validation of the predictive equations. In addition, the new predictive equations were validated against the data from an independent group (Group 2) of obese adolescents (Table 1). The latter was composed of fifty-three subjects (nineteen boys and thirty-four girls), aged 12–18 years, recruited from the Paediatrics Department of the Clermont-Ferrand Hospital (France), who participated in a previously published study (Lazzer *et al.* 2004).

Table 1. Physical characteristics of subjects

	Group 1†						Group 2‡					
	All (*n* 574)		Boys (*n* 242)		Girls (*n* 332)		All (*n* 53)		Boys (*n* 19)		Girls (*n* 34)	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Age (years)	14·53	2·16	14·09	2·19	14·84***	2·08	14·18	1·43	13·70	1·42	14·44	1·39
Pubertal stage§	3·85	1·21	3·17	1·23	4·35***	0·92	3·51	1·50	2·63	1·50	4·00***	1·28
Weight (kg)	93·05	21·88	98·18	25·78	89·31***	17·65	84·21	17·04	86·14	19·23	83·13	15·89
Stature (m)	1·62	0·10	1·64	0·11	1·60***	0·09	1·63	0·09	1·63	0·11	1·63	0·09
BMI (kg/m^2)	35·28	6·14	36·05	6·64	34·71**	5·69	31·41	4·47	32·08	4·48	31·04	4·49
BMI *z*-score	3·29	0·79	3·43	0·75	3·20***	0·81	3·48	0·82	3·95	0·71	3·22***	0·77
FFM (kg)	48·10	10·25	50·67	12·36	46·23***	7·90	54·54	10·13	57·06	12·86	53·12	8·12
FM (kg)	44·95	14·98	47·51	17·14	43·08***	12·90	29·72	8·29	29·15	7·63	30·03	8·74
FM (%)	47·62	7·32	47·68	7·67	47·57	7·08	34·88	4·52	33·74	4·20	35·52	4·62
SBP (mmHg)	117·78	6·49	119·18	6·72	116·92***	6·21	113·65	3·32	112·56	3·86	114·26	3·12
DBP (mmHg)	74·07	6·84	73·78	7·36	74·25	6·52	71·69	2·32	70·38	2·21	72·42	2·35
RQ	0·85	0·06	0·85	0·06	0·84	0·06	0·84	0·01	0·84	0·01	0·84	0·01
REE (MJ/d)	8·15	1·69	9·01	1·89	7·53***	1·20	7·67	1·40	8·54	1·45	7·18***	1·12
REE (MJ/d)‖	8·16	1·52	8·73	1·73	7·74***	1·16	7·67	1·36	8·33	1·40	7·30***	1·19

DBP, diastolic blood pressure; FFM, fat-free mass; FM, fat mass; REE, resting energy expenditure; SBP, systolic blood pressure.
Mean values were significantly different from those of the boys (ANOVA): ** $P<0·01$; *** $P<0·001$.
† Group 1 subjects were recruited from the Division of Auxology, Italian Institute for Auxology, IRCCS, Piancavallo (VB), Italy.
‡ Group 2 subjects were recruited from the Paediatrics Department of the Clermont-Ferrand Hospital, France.
§ Pubertal stage according to Tanner (1961).
‖ REE adjusted for FFM and FM.

Statistical analysis

Statistical analyses were performed using Statistica for Windows (Kernel version 5.5 A; StatSoft, Maisons-Alfort, France) with significance set at $P<0·05$. All results are expressed as means and standard deviations.

In the calibration group (cohort 1), statistical analyses were performed by simple linear regression on variables related to MREE. Multivariate analyses were conducted using multiple linear regressions integrating all the significant factors in the simple linear regressions. This multivariate analysis enabled us to obtain new equations by using a stepwise selection. At each step, R^2, standard error and likelihood ratio were studied. Variables were selected if they met the 5 % level of significance. These factors were introduced in a final model to predict REE.

The new prediction equations, established in the calibration group (cohort 1), were tested in the cross-validation group (cohort 2) using the Bland–Altman method to ascertain the degrees of systematic and magnitude of bias when predicted resting energy expenditure (PREE) was compared with MREE. To validate the new equations in the cross-validation group, the slope and the intercept of simple linear regression between PREE and MREE were compared with 1 and 0, respectively.

In addition, the new predictive equations were validated against the data of the independent group of fifty-three obese adolescents (Table 1) using the Bland–Altman method to study the differences between MREE and PREE.

Results

Subject characteristics

The physical characteristics of subjects are shown in Table 1. All subjects were severely obese since BMI for gender and chronological age was above the 99th percentile.

In Group 1, with 574 subjects, BMI ranged from 25·4 to 62·0 kg/m^2 and BMI *z*-score ranged from 2·01 to 5·65, age and pubertal stage were significantly lower in boys than in girls ($P<0·001$), whereas body weight, stature, BMI and BMI *z*-score were significantly higher in boys than in girls (+10, +3, +4 and +7 %, respectively, $P<0·001$). Boys had higher body weight, FFM and FM, on average, than girls (+8·87, +4·44 and +4·43 kg, respectively, $P<0·001$; Table 1).

In the independent group (Group 2) of fifty-three subjects BMI ranged from 23·0 to 44·0 kg/m^2 and BMI *z*-score from 2·23 to 5·40. Pubertal stage was significantly lower in boys than in girls ($P<0·001$) and BMI *z*-score was significantly higher in boys than in girls ($P<0·001$).

MREE was on average 19 % higher in boys than in girls in both groups of subjects ($P<0·001$). After adjustment for FFM and FM in each group, the difference in REE between sexes decreased but REE remained significantly higher in boys than in girls (+13 %, $P<0·001$; Table 1).

Development of new equations to predict resting energy expenditure

The data set corresponding to the calibration group (cohort 1) was used to develop new prediction equations. The major determinants of REE were body weight and FFM. They explained 56 % and 44 % of the variance in simple linear regressions, respectively. Interestingly, of the remaining variables, FM exhibited the strongest relationship to REE (R^2 0·41), followed by BMI (R^2 0·36), stature (R^2 0·32), sex (R^2 0·19), BMI *z*-score (R^2 0·14) and age (R^2 0·05).

In a multivariate analysis, the variables included in the equations provided a significant independent contribution to the model ($P<0·05$). When age, weight and stature were entered in the model, R^2 was 0·66 in boys and 0·48 in girls. In addition, when sex, age, weight and stature were entered in the model R^2 was 0·66.

When age and the body-composition variables (FFM and FM) were entered in the model, R^2 was 0·65 in boys and 0·47 in girls. In addition, when sex, age, FFM and FM were entered in the model, R^2 was 0·66 (Table 2). The new equations based on anthropometric parameters (equation 1) or body composition (equation 2) are as follows:

$$\text{REE} = (\text{Sex} \times 892{\cdot}68) - (\text{Age} \times 115{\cdot}93) + (\text{Weight} \times 54{\cdot}96) + (\text{Stature} \times 1816{\cdot}23) + 1484{\cdot}50; \quad (1)$$

$$R^2\ 0{\cdot}66\ (\text{SE}\ 1028{\cdot}97)\ \text{kJ}$$

$$\text{REE} = (\text{Sex} \times 909{\cdot}12) - (\text{Age} \times 107{\cdot}48) + (\text{FFM} \times 68{\cdot}39) + (\text{FM} \times 55{\cdot}19) + 3631{\cdot}23; \quad (2)$$

$$R^2\ 0{\cdot}66\ (\text{SE}\ 1034{\cdot}28)\ \text{kJ}$$

where sex = 1 for males and 0 for females, REE is expressed in kJ, age in years, weight in kg, stature in m, FFM and FM in kg.

Cross-validation of the new prediction equations

Internal cross-validation. The data set of cohort 2 was used to validate the new equations. Mean PREE estimated with new equations 1 and 2 were not significantly different from the mean MREE (8·22 (SD 1·39) *v.* 8·07 (SD 1·63) MJ/d, NS) for all adolescents, as well as for boys (9·10 (SD 1·42) *v.* 8·88 (SD 1·87) MJ/d, NS) and girls (7·58 (SD 0·94) *v.* 7·48 (SD 1·11) MJ/d, NS).

The correlation coefficients between PREE and MREE were R 0·80 ($P<0{\cdot}001$) for the whole sample, R 0·81 ($P<0{\cdot}001$) for boys and R 0·65 ($P<0{\cdot}001$) for girls. When the Bland–Altman method and Student's t tests were used to compare PREE and MREE, the mean difference between PREE and MREE was 0·14 (SD 0·98) MJ/d and the limits of agreement (±2 SD) were +2·06 and −1·77 MJ/d (NS) (Fig. 1). When a simple linear regression was applied between PREE and MREE, the slope was significantly different from 1 ($P<0{\cdot}01$) and the intercept was not significantly different from 0.

External cross-validation. The new prediction equations were also validated against the independent group of fifty-three obese adolescents. The mean PREE estimated using equations 1 and 2 were not significantly different from MREE (7·75 (SD 1·15) and 7·78 (SD 1·16) *v.* 7·67 (SD 1·40) MJ/d, NS). The Bland–Altman method and Student's t tests did not show any significant differences between PREE and MREE for both equations. The mean differences between PREE and MREE were 0·08 (SD 0·67) MJ/d (NS) and 0·11 (SD 0·66) MJ/d (NS) for all adolescents, −0·06 (SD 0·70) MJ/d (NS) and 0·01 (SD 0·71) MJ/d (NS) for boys, 0·16 (SD 0·65) MJ/d (NS) and 0·17 (SD 0·64) MJ/d (NS) for girls, with equations 1 and 2, respectively.

Discussion

In the present study two new specific equations for predicting REE in obese children and adolescents were developed. These

Table 2. Stepwise multiple linear regression analysis of resting energy expenditure (kJ/d) in the calibration group of 287 subjects

	Regression coefficient																
	Sex		Age		Weight		Stature		FFM		FM		Intercept				
	Coefficient	SE	Coefficient	SE	Coefficient	SE	Coefficient	SE	Coefficient	SE	Coefficient	SE	Coefficient	SE	SE	R^2	P
Boys			−193·98	73·97	62·23	6·73	2921·27	1466·22					952·65	1832·07	1125·79	0·66	0·001
Girls			−105·68	39·64	48·45	4·91	995·97	1043·89					3225·81	1432·01	935·04	0·48	0·001
All subjects	892·68	134·23	−115·93	36·17	54·96	3·96	1816·23	864·78					1484·50	1124·60	1028·97	0·66	0·001
Boys			−175·30	75·54					83·30	13·48	62·52	7·64	4404·35	669·20	1137·38	0·65	0·001
Girls			−99·30	39·75					53·25	10·94	49·75	6·15	4443·94	592·20	937·51	0·47	0·001
All subjects	909·12	135·99	−107·48	36·56					68·39	8·15	55·19	4·79	3631·23	436·32	1034·28	0·66	0·001

FFM, fat-free mass; FM, fat mass.

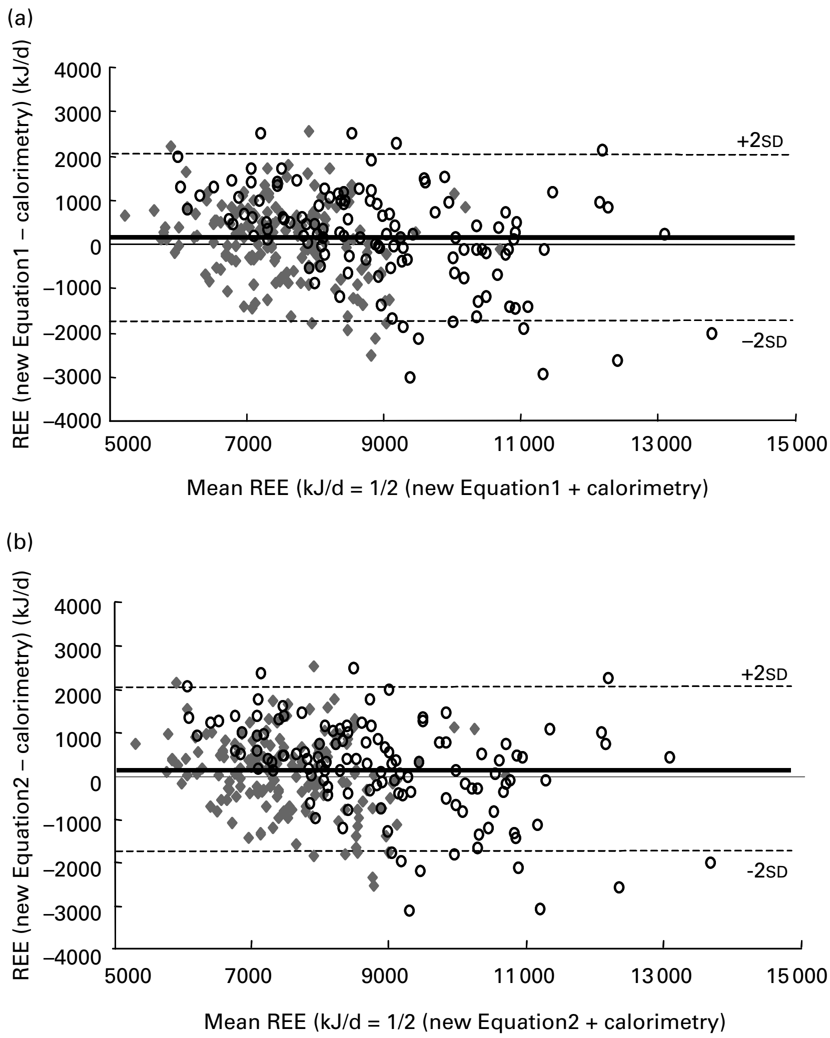

Fig. 1. The Bland–Altman representation of the difference between resting energy expenditure (REE) predicted by using the new equation 1 (a) and the new equation 2 (b) and measured REE by calorimetry in a validation cohort (compared with the Student's *t* test). For details of procedures, see p. 974. Predictor variables for new equation 1: sex, age, weight and stature. Predictor variables for new equation 2: sex, age, fat-free mass and fat mass. ○, Boys; ◆, girls; —, mean, – – –, limits of agreement (±2SD).

equations were derived from a random sub-sample of 287 accurate measurements of REE in severely obese children and adolescents (calibration cohort), aged 7–18 years, by ventilated hood indirect calorimetry. The first prediction equation, based on anthropometric parameters (body weight and stature), is easier to use by physicians during clinical settings because it does not need extra measurement. The second equation, based on body composition (FFM and FM as assessed by BIA), is more population-specific than equation 1 because in most studies FFM and FM were the main significant determinants of REE in obese subjects (Goran *et al.* 1994; DeLany *et al.* 2002; McDuffie *et al.* 2004). However, it requires specific equipment and more time to assess body composition. Nevertheless, in a similar random sub-sample of 287 subjects (validation cohort), both new equations predicted REE with a mean difference of 1·9 % from the MREE (NS) and did not produce any systematic bias. In addition, when an external validation was performed in an independent group of obese subjects, PREE estimated by both equations was also not significantly different from MREE. The Bland–Altman method used to validate the new equations allowed us to consider the new equations as a good tool for predicting REE in obese and in severely obese children and adolescents.

In the internal and external validation tests performed with obese children and adolescents, the two new equations showed the same small mean difference and similar standard deviation of differences between MREE and PREE even though FFM and FM have been shown to be the best predictors of REE in many studies.

Interestingly, FM showed a high correlation coefficient (R^2 0·41) with REE, which underlines the importance of using FM also to predict REE in severely obese subjects, in agreement with previous studies (Goran *et al.* 1994; DeLany *et al.* 2002; McDuffie *et al.* 2004). Surprisingly in equation 2 the regression coefficients were similar for FFM and FM even though FM is known to be less metabolically active than FFM (Elia, 1992). An explanation for FM being involved in REE is that fat tissue secretes a component, such as leptin, in proportion to FM, which in turn increases energy expenditure. In addition, body composition was measured by BIA. BIA is a common, simple, rapid, and non-invasive method to estimate total body water and FFM in healthy people. It is also widely used for estimating body composition in obese subjects (Houtkooper *et al.* 1996) and it has been cross-validated in children against measurements of total body water by ^{2}H dilution (Wabitsch *et al.* 1996) and total body K (Schaefer *et al.* 1994). Some factors limit BIA application to severely obese subjects such as body geometry, body water distribution and assumption of a constant hydration factor of FFM. Reduced accuracy of BIA measurement in this population could explain the surprisingly similar predictive R^2 of the two new equations, which used body composition (FM and FFM) or stature and weight as independent variables, in contrast to previous results in normal-weight or overweight subjects (Ravussin *et al.* 1986; DeLany *et al.* 2002). In addition, the relative accuracy of the BIA method is highly dependent on the equations used to calculate %FM. Therefore, the prediction equations elaborated by Lazzer *et al.* (2005) and validated by dual-energy X-ray absorptiometry permitted a satisfactory estimation of body composition in obese youths from measurements of stature, body weight, resistance and reactance by BIA and can reduce the methodological bias.

Sex was a significant determinant of REE and had a relevant importance in REE since after adjustment for FFM and FM, REE remained 13 % higher in boys than in girls, in agreement with previous studies (Weinsier *et al.* 1992; Goran *et al.* 1994). The higher REE in boys may be explained by higher proportions of skeletal glycolytic fibres (Simoneau & Bouchard, 1989), higher Na^+–K^+ ATPase activity (Simat *et al.* 1983) and differences in hormonal status (Ferraro *et al.* 1992). In addition, the difference between genders observed in the R^2 of the new equations is probably due to the power of body weight in determining REE and the difference in body geometry and body fat distribution between boys and girls, which might limit BIA precision in girls.

In conclusion, the new prediction equations elaborated and validated in the present study permit an accurate estimation of REE in groups of severely obese children and adolescents from measurements of either anthropometric characteristics alone or body composition by BIA. These equations would be useful for health care professionals and researchers when estimating REE in severely obese adolescents.

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