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A Cellular Level Approach to Predicting Resting Energy Expenditure: Evaluation of Applicability in Adolescents

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Abstract

We previously derived a cellular level approach for a whole-body resting energy expenditure (REE) prediction model by using organ and tissue mass measured by magnetic resonance imaging (MRI) combined with their individual cellularity and assumed stable-specific resting metabolic rates. Although this approach predicts REE well in both young and elderly adults, there were no studies in adolescents that specifically evaluated REE in relation to organ–tissue mass. It is unclear whether the approach can be applied to rapidly growing adolescents. The aim of the present study was to evaluate the applicability of the previous developed REE prediction model in adolescents, and to compare its applicability in young and elderly adults. Specifically, we tested the hypothesis that measured REE can be predicted from a combination of individual organ and tissue mass and their related cellularity. This was a 2-year longitudinal investigation. Twenty healthy male subjects with a mean age of 14.7 years had REE, organ and tissue mass, body cell mass, and fat-free mass (FFM) measured by indirect calorimetry, whole-body MRI, whole-body ⁴⁰K counting and dual-energy X-ray absorptiometry, respectively. The predicted REE (REE_p; mean ± SD, 1,487 ± 238 kcal/day) was correlated with the measured REE (REE_m, 1,606 ± 237 kcal/day, $r = 0.76$, $P < 0.001$). The mean difference (118 ± 165 kcal/day) between REE_m and REE_p was significant ($P = 0.0047$), accounting for 7.3% of REE_m for the entire group. The present study, the first of its type in adolescents, does not support the applicability of the organ–tissue-based REE prediction model during rapid adolescent growth. A modified general REE prediction model is thus suggested which may account for the higher REE/FFM ratio observed in adolescents.

Resting energy expenditure (REE) is the largest fraction (65–75%) of total energy expenditure, and is defined as the whole-body energy expenditure under standard conditions (FAO/WHO/UNU, 2004). Over the past 100 years, major efforts have been made to predict REE from body components (Wang et al., 2001). These efforts provide new insights into the mechanism of energy metabolism, and greatly contribute to our understanding of the inherent relationships between REE and body composition.

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ZMW was responsible for all aspects of the study including study design, subject recruitment, data collection, model development, and manuscript writing. ZY was responsible for statistical analysis. SG was responsible for medical examination. DG provided existing database of adult subjects and assistance with manuscript writing; and SH and RNP provided consultation and assistance with manuscript writing.

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Based on a comprehensive concept that all organs and tissues are metabolically active, our group for the first time developed a REE prediction model at the organ–tissue level of body composition (Gallagher et al., 1998). As whole-body REE is equal to the sum of the resting energy consume of all tissues and organs in the human body, REE can be predicted as the sum the products of individual organ/tissue mass and their corresponding specific resting metabolic rates,

$$\text{REEp} = 200T_{\text{liver}} + 240T_{\text{brain}} + 440T_{\text{heart}} + 440T_{\text{kidneys}} + 13T_{\text{SM}} + 4.5T_{\text{AT}} + 12T_{\text{residuals}}, \quad (1)$$

where REEp is the predicted REE (in kcal/day); T is the mass of individual organs and tissues (in kg) and can be measured by magnetic resonance imaging (MRI); and the coefficients are the specific resting metabolic rate (in kcal/ kg per day) of individual organs and tissues in Reference Man (Elia, 1992). Residuals in this model include skeleton, blood, skin, connective tissue, gastrointestinal tract, lung, spleen, and other components present in small amount. Residuals mass is calculated as body mass minus the sum of liver, brain, heart, kidneys, skeletal muscle (SM), and adipose tissue (AT) mass. Four organs (i.e., liver, brain, heart, and kidneys) have high specific metabolic rate. In contrast, the specific metabolic rate of SM is only 1/35 that of the heart and kidneys; and AT has the lowest specific metabolic rate among these organs/tissues (Table 1).

Compared with REE measured by indirect calorimetry, Eq. (1) has been well validated in young healthy adults (Gallagher et al., 1998). However, further investigation found that this model significantly over-REEp by 11% in a group of elderly adults (Gallagher et al., 2000), but under-REEp by 24% in a children group (Hsu et al., 2003). These observations revealed that there are intrinsic defects in Eq. (1) when applied to children and elderly adults.

Based on a consideration that the cellular fraction of organs/tissues should relate to resting energy consumption, we proposed a cellular level prediction model for REE (Wang et al., 2005),

$$\text{REEp} = (\text{BCM/FFM})_{\text{R}} \times (200T_{\text{liver}} + 240T_{\text{brain}} + 440T_{\text{heart}} + 440T_{\text{kidneys}} + 13T_{\text{SM}} + 4.5T_{\text{AT}} + 12T_{\text{residuals}}), \quad (2)$$

where $(\text{BCM/FFM})_{\text{R}}$ is the relative cellularity, i.e., the fraction of fat-free mass (FFM) as body cell mass (BCM/FFM) relative to the BCM/FFM of the Reference Man (0.58). This approach was validated in both young and elderly adults aged from 23 to 88 years (Wang et al., 2005). However, the applicability of this model in a pediatric age group is unknown.

The aim of the present investigation was to evaluate the applicability of the cellular level form of the REE prediction model [i.e., Eq. (2)] in adolescents, and to compare its applicability in young and elderly adults. Specifically, we tested the hypothesis that the REEm can be predicted from a combination of organ and tissue mass with their relative cellularity. As adolescence is a time of rapid growth with new tissue synthesis, the present study provides a chance to evaluate the applicability of our model cross the human lifespan.

SUBJECTS AND METHODS

Protocol

This was a 2-year longitudinal investigation that measured subjects twice. Visit I was for the baseline of subject's body composition; and Visit II was for the measures of REE and organs/

tissues, and for the changes of body composition. Existing databases of young and elderly adults (Gallagher et al., 1998, 2000) were applied to compare REE predictions in adolescents.

Visit I—Subjects fasted for ~12 hours and reported to the Center for testing in the early morning. Each subject participated in a medical examination and body composition analysis including dual-energy X-ray absorptiometry (DXA), whole-body ^{40}K counting, and anthropometry. All tests were performed within 3 hours.

Visit II—The mean interval between the Visits I and II are 356 ± 22 days. Subjects reported to the center on the evening of day 1, fasted for 12 hours after the evening meal, and had an overnight stay in the Center for early morning REE measurement on day 2. Additional evaluations included MRI, echocardiogram, DXA, whole-body ^{40}K counting, anthropometry, medical examination, and blood studies. All tests were performed within 6 hours.

The study was approved by the Institutional Review Board at St. Luke's-Roosevelt Hospital Center.

Subjects

Subject recruitment—Thirteen- to 14-year-old healthy male adolescents were recruited through flyers posted in the local community. The rationale for including only males at age 13–14 years is to avoid the potential influence of gender and age on REE prediction, noting that the maximum FFM gain occurs at about this age in male adolescents (Forbes, 1987).

Medical evaluation—A medical examination was conducted on each subject. All subjects were free of any medical conditions that could affect energy metabolism, including Blounts disease, precocious puberty, major prematurity, birth weight significantly small or large for gestational age, and type II diabetes. The Tanner stage for the subjects was changed from II ($n = 2$), III ($n = 4$) and IV ($n = 14$) at the Visit I to III ($n = 1$), IV ($n = 13$), and V ($n = 6$) at the Visit II.

Fasting blood specimens were obtained for free T3, insulin, and glucose. Standard-panel blood testing was conducted on each subject; and specimens were stored at -40°C in a secured freezer. Assays were performed in uniform batches in the Hormone and Metabolite Laboratory of New York Obesity Research Center. The group mean ($\pm\text{SD}$) of serum concentrations of free T3 was 3.00 ± 0.76 pg/ml with a range from 1.30 to 3.94 pg/ml; insulin was 14.2 ± 5.5 $\mu\text{U/ml}$ with a range from 5.0 to 27.3 $\mu\text{U/ml}$; and glucose was 88.7 ± 6.8 mg/dl with a range from 75 to 99 mg/dl.

Resting energy expenditure measurement

Subjects reported to the Center in the evening and slept there overnight. No food or calorie containing beverages (water only) were consumed after 7 PM until the REE and all body composition tests were completed in the morning. REE was measured with subjects resting comfortably on a bed with a plastic transparent ventilated hood placed over their heads for 30 min. A TrueOne 2400 Metabolic Measurement System (ParvoMedics, Sandy, Utah) was applied to analyze the rates of oxygen consumption and carbon dioxide production. Gas exchange results were evaluated during the stable measurement phase and were converted to REEm by the formula of Weir (1949). A single technician performed all REE measurements on the participants.

The REE evaluations were strictly controlled to ensure their validity. Because eating, physical activity, mental activity and cold room temperature can increase REE and sleep lowers energy expenditure, all gas exchange data were collected under standard conditions, i.e., early morning

after wake up, a resting state 8 hours after physical activity, environmental temperature of around 25°C, and a post-absorptive state 10–12 hours after feeding.

Body composition measurements

Body mass was measured to the nearest 0.1 kg with a digital scale (Weight Tronix, New York) and height to the nearest 0.5 cm with a wall-mounted stadiometer (Holtain, Crosswell, UK).

Magnetic resonance imaging—Organ and tissue volumes were measured using whole-body multi-slice MRI. Subjects were positioned on the 1.5 T MRI scanner (GE 6X Horizon; Milwaukee, WI) platform with arms extended above their head. The SM and AT protocol involved the acquisition of axial images, 1.0-cm thick, at 4.0 cm intervals along the whole body (Ross, 1996). About 35 slices were acquired from feet to extended hands for this group of subjects.

Brain images were obtained using a body coil with a fast-spin-echo T2-weighted sequence with 5-mm contiguous axial images, and a $40 \times 40 \text{ cm}^2$ ($256 \times 256/1$ number of excitation) field of view. Liver and kidney images were produced by an axial spin-echo T1-weighted sequence with 5-mm slice thickness, no inter-slice gap, and a $40 \times 40 \text{ cm}^2$ ($256 \times 192/2$ number of excitations) field of view.

Organ and tissue masses—Tomovision SliceOmatic 4.2 image analysis software (Montreal, Canada) was applied for analyzing the images on a PC workstation (Gateway, Madison, WI). All MRI scans were analyzed by a single well-trained observer using strict quality control measures. The measurement precisions for individual organs and tissues are presented in Table 1. In our laboratory, the technical error for repeat measurements on the same scan by the same observer for MRI-derived whole-body SM and AT is $0.7 \pm 0.1\%$ and $1.1 \pm 1.2\%$, respectively (Gallagher et al., 1998).

Organ and tissue cross-sectional areas on each axial image were integrated to provide whole body volume estimates (in liters) as,

$$\text{Organ/tissue volume} = 0.001 \times \sum [A \times (B_1 + B_2) / 2]. \quad (3)$$

In Eq. (3), A is the distance (in cm) between adjacent scans, and B_1 and B_2 are the organ/tissue cross-sectional areas (in cm^2) in adjacent scans. A sample of eight MRI scans of the liver in healthy 26- to 70-year-old adults was analyzed by two observers to estimate inter-observer reading error. The standard deviation of the volume differences was 0.14 l (mean volume 1.58 l). In a sample of 20 subjects the standard error due to reading variability was 0.03 kg.

Organ/tissue mass (in kg) was calculated from estimated volumes (in liters) and assumed constant densities (in kg/l),

$$\text{Organ/tissue mass} = \text{Organ/tissue volume} \times \text{Density}. \quad (4)$$

As Table 1 shows, the accepted–assumed density is 0.92 for AT, 1.03 for brain and heart, 1.04 for SM, and 1.05 for liver and kidneys (Snyder et al., 1975). The mass of residual tissues was defined as the difference between body mass and the sum of six organs and tissues (i.e., liver, brain, heart, kidneys, SM, and AT).

Echocardiography—Left ventricular mass (LVM) was measured with a two-dimensionally guided M-mode echocardiogram (VIVID 7; GE Healthcare) interfaced with a strip chart

recorder, two-dimensional video recorder, and 1.7 MHz probe. Subjects were studied in the left lateral decubitus position. Left ventricular dimensions were recorded from the parasternal long axis view at or below the tips of the mitral valve leaflets. The hard copy strip chart recording was used for all measurements. End-diastolic and end-systolic dimensions were measured at the peak of the R wave and the peak of the posterior wall motion, respectively, according to the American Society of Echocardiography convention (Jahn et al., 1978). Wall thickness was measured using the Penn convention; and LVM was calculated according to the formula of Devereux and Reichek (1977). A minimum of five cardiac cycles was used for all measurements. All echocardiographic tracings were read by a single observer. The technical error for repeated echo measurements of the same scan by the same observer for LVM was $\pm 1.1\%$. LVM was multiplied by a factor of 1.5 to obtain a value for total heart mass (Jones, 1953).

Body cell mass—There are no direct in vivo methods for estimating the cell-mass of the whole-body. A useful surrogate concept, BCM, was introduced and defined as the working, energy-metabolizing portion of the human body in relation to its supporting structure (Moore et al., 1963). BCM includes the protoplasm in fat cells but does not include the stored fat, which occupies 85–90% of fat cells by volume. As ~97% of body potassium is intracellular, the BCM can be calculated from total body potassium (TBK) measured by whole-body ^{40}K counting. Moore et al. (1963) developed a BCM estimation equation: $\text{BCM (in kg)} = 0.00833 \times \text{TBK (in mmol)}$. Cohn et al. (1985) and our group (Wang et al., 2004) experimentally estimated BCM independently of TBK. A modified BCM model was derived and applied in this study as $\text{BCM (in kg)} = 0.0092 \times \text{TBK (in mmol)}$.

The St. Luke's 4π whole-body counter was used to detect the naturally occurring 1.46 MeV γ -ray of ^{40}K decay. The raw counts collected over 9 min were adjusted for body size on the basis of an experimental ^{42}K calibration equation (Pierson et al., 1984). TBK was calculated as $^{40}\text{K}/0.000118$ (Forbes, 1987). The current technical error for repeated subject ^{40}K counting is $\pm 2.3\%$ (CV) in our laboratory (Wang et al., 2004).

Dual-energy X-ray absorptiometry—Body composition was measured with a whole-body DXA scanner (DXA Prodigy; GE, Madison, WI; pediatric version software). The system software provides the measurements of whole-body and regional fat, lean-soft tissue, and bone mineral mass. DXA measurements are associated with relatively low radiation dose, about 1% of that from a chest X-ray. Subjects were scanned in different modes according to the systems' automatic interpretation based on sagittal diameter at the iliac crest: thin mode (<13 cm), standard mode (13–25 cm), and thick mode (>25 cm). The between-measurement technical error for FFM in the same adult subject is $\pm 1.2\%$ and the CV for repeated bone mineral measurement is $\pm 1.5\%$ (Ma et al., 1996).

Relative cellularity—At the cellular level, the human body consists of fat, BCM, extracellular fluid and solids (Wang et al., 1992). Of the four components, only the BCM consumes oxygen and produces heat. In the present study, the subject's cellularity is defined as the fraction of the FFM as metabolically active BCM, and is calculated as the ratio of BCM to FFM. The cellularity of the Reference Man is 0.58 (Snyder et al., 1975). Therefore, the relative cellularity of the subject is calculated as the ratio of BCM/FFM to 0.58 for men.

Statistical analysis

Descriptive subject data are expressed as mean $\pm$ SDs. A Student's *t*-test was applied to compare the REEm with REEp, and to compare the mass of body components in adolescents with that in adults. Simple linear regression analysis was used to explore the correlation between REEm and REEp. Bland-Altman analysis was applied between (REEm – REEp) and

the mean of REEm and REEp. Data were analyzed by using Microsoft Excel version 5.0 (Microsoft, Redmond, WA), and statistical significance was set at $P < 0.05$, two-tailed.

RESULTS

Physical characteristics and body composition

Twenty healthy male adolescents, including four African Americans, three Asians, seven Caucasians and six Hispanics, finished the body composition measurements. The physical characteristics of the adolescents as well as the young and elderly adults are shown in Table 2.

Visit II vs. Visit I—The group of adolescents was heavier and taller at Visit II, compared with the Visit I ($P < 0.001$). There were no significant changes in body mass index (BMI) during the 1-year period. With respect to body composition, all adolescent subjects had significantly greater FFM, TBK, BCM and bone mineral at Visit II than at Visit I (all $P < 0.001$ for between-visit difference). The fraction of FFM as the metabolic-active BCM (i.e., BCM/FFM) was estimated (Table 2). There was no significant change in the BCM/FFM ratio from Visit I to Visit II (0.572 ± 0.032 vs. 0.580 ± 0.024 , $P = \text{N.S.}$).

Adolescents vs. adults—While there was no difference in height ($P = 0.92$), the adolescent group at Visit II was lighter (body mass, $P = 0.0025$) and leaner (BMI and %fat, both $P < 0.001$), compared with the young adults. With respect to body composition, there were no differences in BCM ($P = 0.68$) and FFM ($P = 0.33$) between the adolescents and young adults (Table 2). While the adolescent group at Visit II was higher in BCM/FFM than the young adults (0.580 ± 0.028 vs. 0.538 ± 0.039 , $P < 0.001$), the relative cellularity in the adolescents was equal to that in the Reference Man (1.000 ± 0.049 vs. 1, $P = 0.980$).

Organs and tissues masses

The high metabolic rate organ mass (i.e., liver, brain, heart, and kidneys) and the mass of two tissues (i.e., SM and AT) and residuals are presented in Table 3. There were no differences in liver ($P = 0.12$), brain ($P = 0.17$), and heart ($P = 0.95$) mass between the adolescent males and young adults, although the kidney mass was less in the adolescents than in the young adults (0.30 ± 0.06 vs. 0.35 ± 0.08 kg, $P = 0.0036$). Similarly, there were no significant differences in the fractions of the FFM as liver ($P = 0.18$), brain ($P = 0.65$), and heart ($P = 0.48$) between the adolescents and young adults, although the fraction of FFM as kidneys was smaller in the adolescents than in the young adults ($0.59 \pm 0.11\%$ vs. $0.68 \pm 0.12\%$, $P = 0.0098$).

Combining the weight of four high metabolic rate organs, there were no differences in the sum of the four organs (3.41 ± 0.40 vs. 3.64 ± 0.51 kg, $P = 0.067$) and the fraction of FFM as the four organs ($6.85 \pm 0.49\%$ vs. $7.11 \pm 0.84\%$, $P = 0.136$) between the adolescents and young adults (Table 3).

Measured and predicted REE

The REEm of the male adolescents were $1,606 \pm 237$ kcal/day with a range from 994 to 2,166 kcal/day. According to Eq. (2), the REEp was calculated from organ/tissue mass and relative cellularity as $1,487 \pm 238$ kcal/day with a range from 1,116 to 2,237 kcal/day (Table 4). The REEp was correlated with REEm in the adolescent group ($r = 0.76$, $P < 0.001$).

The difference between REEm and REEp was significant ($\text{REEm} - \text{REEp} = 118 \pm 165$ kcal/day, $P = 0.0047$), accounting for 7.3% of REEm in the entire adolescent group. In contrast, ($\text{REEm} - \text{REEp}$) was not significant in both young adults (-21 ± 123 kcal/day, $P = 0.31$) and the elderly adults (-21 ± 90 kcal/day, $P = 0.41$).

Bland-Altman analysis indicated no significant bias in (REEm – REEp) related to the mean REE values for all of the three groups ($r = -0.0045$ for the adolescents; $r = -0.014$ for the young adults; and $r = -0.078$ for the elderly adults, all $P > 0.05$) (Figs. 1, 2, and 3).

REEm/FFM ratio

The ratio of REEm to FFM was calculated for the three groups. This ratio was highest in the 14.7-year-old adolescents (32.2 ± 4.0 kcal/kg per day), followed by the young adults (29.9 ± 3.3 kcal/kg per day, $P = 0.034$), and lowest in the elderly adults (27.6 ± 2.7 kcal/kg per day; young vs. elderly adults $P = 0.015$).

DISCUSSION

Over the past 100 years, major efforts have been made to predict REE in humans to understand the inherent relationships between energy metabolism and body components (Wang et al., 2001). Our research group has developed REE prediction models at the organ–tissue and cellular levels, respectively (Gallagher et al., 1998; Wang et al., 2005). In the present investigation, a new effort was made to evaluate the applicability of the proposed REE prediction model [i.e., Eq. (2)] in adolescents.

Applicability of REE prediction model in adults and adolescents

In adults—For healthy young adults (exempting obese adults and pregnant and lactating women) body composition and REE can be considered to be in a steady-state, defined as a dynamic homeostasis over a specified time period, when body weight and the mass of various body components is maintained relatively constant (Wang et al., 1992). Our previous and present studies revealed that the cellular level REE approach [i.e., Eq. (2)] can reasonably predict REE in both young and elderly adults, revealing that adult humans in a nongrowth state are not expending energy to form new lean tissues.

In adolescents—By contrast, growing children and adolescents are not at steady-state body composition and are gaining FFM, including new cells and new intracellular solids. Growing children and adolescents thus expend extra energy for the formation of new FFM (Heird, 1999). However, an important question remains unanswered: what is the magnitude of energy expenditure for growth in children and adolescents? This is a gap in our knowledge of pediatric energy metabolism.

REE is the energy spent summed over a 24-hour period by an individual under standard conditions. The cellular level approach of the REE model [i.e., Eq. (2)] was developed based on studies in adults for predicting the maintenance energy expenditure, so that it worked well in young and elderly adults (Wang et al., 2005). In growing children and adolescents REE can be partitioned into two components, maintenance energy expenditure and growth energy expenditure (GEE) for constructing new FFM, including new cells and noncell components (Fidanza, 1991; Heird, 1999).

The observed significant differences between REEm and REEp motivated us to make the assumption that in adolescents the REEp calculated by Eq. (2) is used to maintain the minimum energy metabolism under standard conditions; and the difference between REEm and REEp should be the GEE for the gain of new FFM. In the male adolescent group the magnitude of GEE was 118 ± 165 kcal/day, accounting for 7.3% of REEm. We further divided the 20 boys into two subgroups by the average daily gain of FFM: the more rapidly growing subgroup (22.5 ± 4.0 g/day, $n = 10$), and the more slowly growing subgroup (11.0 ± 4.6 g/day, $n = 10$, $P < 0.001$). Accordingly, the difference between REEm and REEp in the more rapidly growing boys is much greater than that in the more slowly growing boys (214.1 ± 118.5 vs. 22.7 ± 152.9).

kcal/day, $P < 0.01$). This analysis is helpful in highlighting the extent to which growth factors are influencing REE in this sample.

A previous cross-sectional study found a difference between REEm and REEp in children (Hsu et al., 2003). These authors estimated REE in 15 children (8 males and 7 females) aged 6–12 years and REEp by using the original organ–tissue level REE prediction model [i.e., Eq. (1)]. The REEm was significantly greater than REEp ($1,223 \pm 184$ vs. 925 ± 147 kcal/day, $P < 0.001$) and the difference (298 ± 121 kcal/day) accounted for 24.4% of the REEm in the entire group. According to the authors, however, the REEm may be somewhat above true resting values of this group, because the subjects did not sleep in the laboratory but reported in the morning, and because some children tended to adhere less well to remaining in a nonfidgeting resting state during the REE measurement period (Hsu et al., 2003).

In the present study, the adolescent subjects slept at the Center overnight and the REE measurements were strictly controlled under standard conditions. In addition, we recruited only male adolescents of one age group to avoid the potential influence of gender and age on REE prediction. Even though the possibility of overestimating REEm has been carefully ruled out, the REEm was still significantly greater than the REEp by 7.3% in the 14.7-year-old adolescent group.

General REE prediction model at the cellular level

A modification is thus made to develop a general model for predicting REE across whole lifespan, from children to the elderly,

$$\begin{aligned} \text{REE} &= (\text{BCM/FFM})_R \times \sum (K_i \times T_i) + \text{GEE} \\ &= (\text{BCM/FFM})_R \times \sum (K_i \times T_i) + G_{\text{FFM}} \times \text{dFFM}, \end{aligned} \quad (5)$$

where $(\text{BCM/FFM})_R$ is the relative cellularity; K is the specific resting metabolic rate of the individual organs and tissues (in kcal/kg per day); T is the individual organ/tissue mass (in kg); i is the organ/tissue number ($i = 1, 2, \dots, n$); GEE is the growth energy expenditure (in kcal/day); dFFM is the average daily gain of FFM (in g/day); and G_{FFM} is the specific energy cost per unit gain of FFM (in kcal/g). We now calculate the dFFM and G_{FFM} values as follows.

Average daily gain of FFM—The present study measured subject's body composition twice. The mean interval between Visits I and II was 356 days with a range between 318 and 390 days. The average dFFM (in g/day) was calculated as

$$\text{dFFM} = (\text{FFM at Visit II} - \text{FFM at Visit I}) / (\text{Days between Visits I and II}). \quad (6)$$

Equation (6) assumes that the gain in FFM is linear from Visit I to Visit II. The dFFM was 16.7 ± 7.2 g/day with a range between 3.9 and 28.6 g/day in the adolescents of this group.

Energy costs for constructing FFM (G_{FFM})—The mean energy cost for constructing new FFM was calculated as $G_{\text{FFM}} = (\text{REEm} - \text{REEp})/\text{dFFM} = 118.4/16.7 = 7.1$ kcal/g for the entire adolescent group. Previous reports estimated the energy cost of body mass gain that on average turns out to be 4.0 and 5.0 kcal/g in infants (Reichman et al., 1981; Spady et al., 1976) and 4.7 kcal/g in adolescent girls for body mass gain (Forbes et al., 1984). These values are compatible with 7.1 kcal/g for FFM gain found in the male adolescents in the present study.

The REE/FFM ratio

The association between REE and FFM is a cornerstone in the study of physiological aspects of daily energy requirements and energy metabolism. Previous observations demonstrated that the REE/FFM ratio is not constant across the human lifespan with the largest value at birth, declining during growth (FAO/WHO/UNU, 2004). The present study confirms that the REEm/FFM ratio is significantly greater in adolescents than in adults: 32.2 kcal/kg per day for 14.7-year-old adolescents >29.9 kcal/kg per day for young adults >27.6 kcal/kg per day for elderly adults.

The general REE prediction model [Eq. (5)] proposed in the present study is useful to explore the mechanism of the high REE/FFM ratio in adolescents. According to Eq. (5), there are four possible explanations for the well-known observation. First, the relative cellularity may be higher in the adolescents than in the adults. However, our results revealed no difference in the relative cellularity between 14.7-year-old male adolescents and the Reference Man (1.000 ± 0.049 vs. 1, $P = 0.980$). Second, adolescents may have higher fractions of FFM as highly metabolically active organs than do adults. However, our results demonstrated no difference in the fraction of FFM as the four organs between the 14-year-old adolescents and young adults ($6.85 \pm 0.49\%$ vs. $7.11 \pm 0.84\%$, $P = 0.136$), although the fraction of FFM as kidneys was marginally smaller in the adolescents than in the young adults. Therefore, the present study does not support the above two explanations.

The third possible explanation is that adolescent's REE contains a GEE component, compared with the adults. The REE/FFM ratio in adolescents is thus larger than that in young adults, due to the GEE component being equal to zero in adulthood. In the present study, the REE/FFM difference was 2.3 kcal/kg per day between the adolescents and the young adults (32.2 ± 4.0 vs. 29.9 ± 3.3 kcal/kg per day, $P = 0.0337$).

However, the existence of GEE does not rule out the fourth possible explanation that the mass-specific metabolic rates (i.e., K value) of individual organs/tissues are somewhat higher in 14.7-year-old adolescents than that in young adults. For example, previous study revealed that the metabolic rates of some brain regions were higher in children than in young adults (Chugani et al., 1987). By using 2-deoxy-2-[^{18}F]fluoro-D-glucose and positron emission tomography techniques, these authors found that the local cerebral metabolic rates for glucose in 3- to 4-year-old children were as high as about twice of the adult rates, maintained at high levels for the next 5–6 years, and then declined until adult rates were reached. Until now, however, no studies have been reported for the possible impact of age on the mass-specific metabolic rates of liver, heart, kidneys, and SM during growth.

In elderly adults, there are two explanations for the observed low REE/FFM ratio: a low relative cellularity and a low fraction of FFM as metabolically active organs (Wang et al., 2005).

CONCLUSIONS

The present study does not support the applicability of the REE prediction models defined by Eqs. (1) and (2) in adolescents. A general REE prediction model, Eq. (5), is suggested which may account for the high REE/FFM ratio observed during growth. Further study is needed to evaluate the applicability of the proposed general REE prediction model across the whole human lifespan.

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Fig. 1.

Differences between the measured resting energy expenditure (REEm) by indirect calorimetry and the predicted REE (REEp) by the cellular level approach [i.e., Eq. (2)] vs. the corresponding mean REE in 20 male adolescents. The difference between REEm and REEp was 118 ± 165 kcal/day for the entire adolescent group. $\text{REEm} - \text{REEp} = 122.9 - 0.0029 \times \text{REE mean}$; $r = -0.0045$, $P = \text{N.S.}$

Fig. 2.

Differences between the measured resting energy expenditure (REEm) by indirect calorimetry and the predicted REE (REEp) by the cellular level approach [i.e., Eq. (2)] vs. the corresponding mean REE in 38 young adults. The difference between REEm and REEp was -21 ± 123 kcal/day for the entire young adult group. $\text{REEm} - \text{REEp} = -11.9 - 0.0056 \times \text{REE mean}$; $r = -0.014$, $P = \text{N.S.}$

Fig. 3.

Differences between the measured resting energy expenditure (REEm) by indirect calorimetry and the predicted REE (REEp) by the cellular level approach [i.e., Eq. (2)] vs. the corresponding mean REE in 13 elderly adults. The difference between REEm and REEp was -21 ± 90 kcal/day for the entire elderly adult group. $\text{REEm} - \text{REEp} = 17.8 - 0.0296 \times \text{REE mean}$; $r = -0.078$, $P = \text{N.S.}$

TABLE 1

Specific resting metabolic rates and densities of various organs and tissues in Reference Man

	Specific metabolic rate (kcal/kg per day)	Density (kg/l)	Measurement precision of organ/tissue
Liver	200	1.05	±0.6% by MRI
Brain	240	1.03	±0.8% by MRI
Heart	440	1.03	±1.1% by echocardiogram
Kidneys	440	1.05	±1.2% by MRI
Skeletal muscle	13	1.04	±0.7% by MRI
Adipose tissue	4.5	0.92	±1.1% by MRI
Residuals	12	—	

Data of specific metabolic rates from Elia (1992); data of densities from Snyder et al. (1975); and measurement precisions of organs and tissues from Gallagher et al. (1998) and Illner et al. (2000).

MRI, magnetic resonance imaging.

TABLE 2

Subject characteristics and body composition

	Adolescents visit I	Adolescents visit II	Young adults	Elderly adults
<i>N</i>	20	20	38 (12 M, 26 F)	13 (5 M, 8 F)
Age (years)	13.7 ± 0.6	14.7 ± 0.6	34.8 ± 8.3	76.2 ± 10.4
Body mass (kg)	55.7 ± 14.3	60.6 ± 13.4	73.3 ± 15.9	69.3 ± 12.4
Height (m)	1.640 ± 0.089	1.692 ± 0.084	1.689 ± 0.109	1.654 ± 0.090
BMI (kg/m ²)	20.5 ± 3.5	20.9 ± 3.2	25.7 ± 5.3	25.3 ± 3.9
Body fat (kg)	11.7 ± 9.4	10.7 ± 9.0	21.1 ± 12.0	21.6 ± 9.3
% Fat	19.8 ± 9.9	17.1 ± 8.9	27.7 ± 11.5	30.6 ± 10.2
Fat-free mass (kg)	44.0 ± 7.1	50.0 ± 6.2	52.2 ± 11.2	47.7 ± 8.8
Bone mineral (kg)	2.20 ± 0.40	2.54 ± 0.41	2.89 ± 0.56	2.68 ± 0.58
TBK (mmol)	2748 ± 504	3153 ± 448	3083 ± 832	2590 ± 589
BCM (kg)	25.2 ± 4.6	29.0 ± 4.1	28.4 ± 7.65	23.8 ± 5.4
BCM/FFM	0.572 ± 0.032	0.580 ± 0.028	0.538 ± 0.039	0.496 ± 0.035
Relative cellularity	0.986 ± 0.055	1.000 ± 0.049	0.950 ± 0.055	0.874 ± 0.055

The values represent mean ± standard deviation.

BCM, body cell mass; BMI, body mass index; FFM, fat-free mass; TBK, total body potassium.

TABLE 3

Subject organ/tissue masses and fractions of fat-free mass as organ/tissue

	Adolescents visit II	Young adults	Elderly adults
Liver (kg)	1.48 ± 0.26	1.60 ± 0.33	1.37 ± 0.27
Brain (kg)	1.40 ± 0.11	1.46 ± 0.18	1.39 ± 0.15
Heart (kg)	0.24 ± 0.06	0.23 ± 0.07	0.23 ± 0.05
Kidneys (kg)	0.30 ± 0.06	0.35 ± 0.08	0.30 ± 0.08
Four organs (kg)	3.41 ± 0.40	3.64 ± 0.51	3.30 ± 0.44
Skeletal muscle (kg)	23.1 ± 3.9	26.5 ± 6.8	22.2 ± 4.5
Adipose tissue (kg)	12.1 ± 7.4	19.1 ± 10.0	19.0 ± 7.2
Residuals (kg)	22.1 ± 3.1	24.1 ± 4.5	24.7 ± 4.7
Liver/FFM (%)	2.96 ± 0.35	3.11 ± 0.44	2.90 ± 0.39
Brain/FFM (%)	2.83 ± 0.25	2.88 ± 0.58	2.96 ± 0.39
Heart/FFM (%)	0.47 ± 0.08	0.45 ± 0.10	0.50 ± 0.10
Kidneys/FFM (%)	0.59 ± 0.11	0.68 ± 0.12	0.63 ± 0.12
Four organs/FFM (%)	6.85 ± 0.49	7.11 ± 0.84	6.99 ± 0.62

FFM, fat-free mass.

TABLE 4

Subjects measured and predicted resting energy expenditure

	Adolescents visit II	Young adults	Elderly adults
REEm (kcal/day)	1606 $\pm$ 237	1548 $\pm$ 296	1309 $\pm$ 236
REEp (kcal/day)	1487 $\pm$ 238	1568 $\pm$ 298	1330 $\pm$ 243
REEm – REEp (kcal/day)	118 $\pm$ 165	–21 $\pm$ 123	–21 $\pm$ 90
REEm/FFM (kcal/kg per day)	32.2 $\pm$ 4.0	29.9 $\pm$ 3.3	27.6 $\pm$ 2.7

FFM, fat-free mass; REEm, resting energy expenditure measured by indirect calorimetry; REEp, resting energy expenditure predicted by the cellular level approach of REE model [i.e., Eq. (2)].