Resting energy expenditure-fat-free mass relationship: new insights provided by body composition modeling

ZIMIAN WANG, STANLEY HESHKA, DYMPNA GALLAGHER, CAROL N. BOOZER,
DONALD P. KOTLER, AND STEVEN B. HEYMSFIELD
*Obesity Research Center, St. Luke's-Roosevelt Hospital, College of Physicians and Surgeons,
Columbia University, New York, New York 10025*

Wang, ZiMian, Stanley Heshka, Dympna Gallagher, Carol N. Boozer, Donald P. Kotler, and Steven B. Heymsfield. Resting energy expenditure-fat-free mass relationship: new insights provided by body composition modeling. *Am J Physiol Endocrinol Metab* 279: E539–E545, 2000.—The relationship between resting energy expenditure (REE) and metabolically active fat-free mass (FFM) is a cornerstone in the study of physiological aspects of body weight regulation and human energy requirements. Important questions, however, remain unanswered regarding the observed linear REE-FFM association in adult humans. This led us to develop a series of REE-body composition models that provide insights into the widely used simple linear REE-FFM prediction model derived experimentally in adult humans. The new models suggest that the REE-FFM relationship in mammals as a whole is curvilinear, that a segment of this function within a FFM range characteristic of adult humans can be fit with a linear equation almost identical to that observed from a composite review of earlier human studies, and that mammals as a whole exhibit a decrease in the proportion of FFM as high metabolic rate organs with greater FFM. The present study thus provides a new approach for examining REE-FFM relationships, advances in a quantitative manner previously observed albeit incompletely formulated REE-body composition associations, and identifies areas in need of additional research.

energy metabolism; body composition

ALL LIVING ORGANISMS expend energy for the maintenance of cellular homeostasis. Energy produced by metabolic processes in humans consists of three main portions, resting energy expenditure (REE), the thermic effect of food, and physical activity-induced energy expenditure (6, 19). REE, measured at rest after an overnight fast, is usually the largest portion (~60–75%) of total energy expenditure.

A major investigative focus of energy metabolism research over the past four decades is the development of REE prediction formulas based on fat-free mass (FFM). Most investigators have reported that, for healthy adult humans, the relationship between REE and FFM is fit by a linear function

$$\text{REE} = a + b \times \text{FFM} \qquad (1)$$

where a and b are the regression line intercept and the slope, respectively. Fifteen descriptive REE-FFM linear regression equations are presented in Table 1 (4–6, 13, 14, 17, 18, 24–31). FFM has been measured by the use of diverse body composition methods such as anthropometry, underwater weighing, total body potassium, ^3H_2O and ^2H_2O dilution techniques, and, more recently, dual-energy X-ray absorptiometry. Despite the dissimilar methodologies used to estimate FFM, all of these descriptive regression equations report a positive intercept varying from 186 to 662 kcal/day and similar slopes varying from 19.7 to 24.5 kcal · kg $FFM^{-1} \cdot day^{-1}$ (Table 1).

Although investigators have expressed an increasing interest in REE-FFM relationships, several fundamental questions remain unanswered. For example, when REE in adult humans is plotted against FFM, a linear relationship with a non-zero intercept is observed within the FFM range of ~40–80 kg. This provides the implausible inference that a component of REE (~400 kcal/day) remains when there exists no (i.e., zero) FFM by extrapolation. The non-zero positive intercept of this relation also implies that subjects with a small FFM have a relatively high resting metabolic rate compared with those with a large FFM. If FFM is a homogeneous heat-producing metabolically active compartment, how can these observations be reconciled?

The aim of this paper is to present a new modeling approach aimed at elucidating the biological and related mathematical relationships between REE and FFM. The chosen strategy involved creating REE-FFM models at the whole body level and the tissue/organ body composition level, respectively. Several fundamental unanswered questions regarding REE-FFM relationships were then examined in the context of the developed models. The present study extends the work of Brody (2), Grande (12), Holliday and colleagues (15, 16), Elia (6), Calder III (3), and Weinsier et al. (37) on REE-body composition relationships.

Address for reprint requests and other correspondence: Z. Wang, Weight Control Unit, 1090 Amsterdam Ave., 14th Floor, New York, NY 10025 (E-mail: ZW28@Columbia.edu).

Table 1. *Fifteen descriptive equations for predicting REE from FFM in adult humans*

Author	Descriptive Equation	Reference
Owen et al.	REE = 19.7 × FFM + 334	28
Mifflin et al.	REE = 19.7 × FFM + 413	25
Luke & Schoeller	REE = 20.0 × FFM + 585	22
Jensen et al.	REE = 20.0 × FFM + 662	17
Ravussin et al.	REE = 20.82 × FFM + 471	30
Ravussin et al.	REE = 20.93 × FFM + 478.7	31
Elia	REE = 21.11 × FFM + 450	6
McNeil et al.	REE = 21.5 × FFM + 329	24
Heymsfield et al.	REE = 21.6 × FFM + 302	14
Cunningham	REE = 21.6 × FFM + 501.6	5
Ravussin & Bogardus	REE = 21.8 × FFM + 392	29
Owen et al.	REE = 22.3 × FFM + 290	27
Heshka et al.	REE = 22.94 × FFM + 356.7	13
Owen	REE = 23.6 × FFM + 186	26
Kashiwazaki et al.	REE = 24.5 × FFM + 304	18
Mean ± SD	REE = (21.5 ± 1.4) × FFM + (407 ± 128)	

FFM, fat-free mass (kg); REE, whole body resting energy expenditure (kcal/day).

RESTING ENERGY EXPENDITURE AND BODY COMPOSITION

The presently available REE-body composition models are based on two fundamental concepts: *1*) that only metabolically active components contribute to REE; and *2*) that there are quantitative and measurable associations between REE and metabolically active components. All metabolically active components can be organized according to the five-level model, which indicates that the ~40 body components are distributed into five distinct but connected levels: atomic, molecular, cellular, tissue/organ, and whole body (36). The available literature allows us to derive the quantitative associations between REE and metabolically active components at four levels: molecular, cellular, tissue/organ, and whole body (Wang ZM, Gallagher D, Heshka S, Zhang K, Boozer C, Testolin C, and Heymsfield SH, unpublished observations).

At the molecular level, the human body can be divided into fat and FFM, with FFM considered the only metabolically active component. Although experimental studies reveal a linear relationship between REE and FFM in healthy adult humans (Table 1), the previously mentioned questions regarding these models remain unanswered. In the present investigation, therefore, we examine the REE-FFM relationship in adult humans at the whole body and tissue/organ levels.

The cellular level is the first body composition level at which discrete sites of energy production can be identified. The cellular level is thus central when examining REE-body composition relationships. At the cellular level, the human body is composed of various categories of cells, extracellular fluid, and extracellular solids. Cells are the only metabolically active compartment at this level, and various cell types differ in their resting metabolic rates. Although the cellular level is important in the study of energy metabolism, very little REE-body composition research has been directed at this level, perhaps because of the difficulty in quantifying specific cell categories. Improved in vivo methods of quantifying cell mass (e.g., nuclear magnetic resonance) and energy exchange (e.g., positron emission tomography) of individual cell categories are needed in future REE studies. At present, therefore, we are not able to explore REE-FFM relationships at the important cellular level.

At the tissue/organ level, all tissues and organs are metabolically active components, and various tissues and organs differ in their resting metabolic rates. Whole body REE is thus determined by two factors, the individual mass of tissues/organs and their corresponding resting metabolic rates. The quantitative relationships between tissues/organs and FFM allow us to examine and model the REE-FFM relationship.

At the whole body level, the only metabolically active component is body mass (BM), and REE is a function of body mass (2, 3). The quantitative relationship between BM and FFM allows us to explore and model the REE-FFM function.

WHOLE BODY LEVEL REE MODEL

BM, which can be measured easily and with high accuracy, was the first physical characteristic applied in the development of descriptive REE equations. Kleiber (20) was one of the first investigators to report the relationship between REE and BM in mammals. He surveyed REE estimates for mature mammals, ranging from rats to steers, with an ~2,800-fold difference in body size. By expressing REE as a function of BM, Kleiber found a nonlinear relationship between REE (in kcal/day) and BM (in kg). The best fit for his data was

$$REE = 73.3 \times BM^{0.74} \qquad (2)$$

Several years later, Brody (2) included some additional species, ranging from mice to elephants, and published the well known mouse-to-elephant curve. The power of Brody's equation, 0.734, was nearly identical with that of *Eq. 2*

$$REE = 70.5 \times BM^{0.734} \qquad (3)$$

In 1961, Kleiber (21) suggested a new descriptive REE-BM equation

$$REE = 70.0 \times BM^{0.75} \qquad (4)$$

Equations 2–4 are very similar, and Kleiber pointed out that the numerical difference in the exponent between 0.75 and 0.734 and in the coefficient between 70 and 73.3 is not statistically significant. These REE-BM models were aimed at providing broad insights and did not consider gender, age, and other secondary factors in their development. In the following years, there was considerable discussion devoted to explaining why mammalian REE scales to ~$BM^{0.75}$ (3, 23, 32, 38).

These whole body level observations can be applied to examination of the experimentally observed linear REE-FFM relationship in adult humans (*Eq. 1* and Table 1). Previous studies indicate that adipose tissue (AT, in kg) is an exponential function of BM across
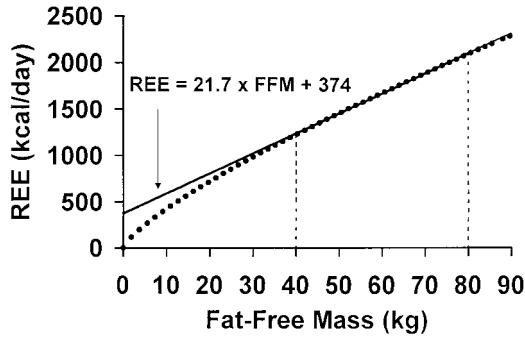
Fig. 1. Whole body modeling approach. Whole body resting energy expenditure (REE, in kcal/day) on the ordinate is indicated vs. fat-free mass (FFM, in kg) on the abscissa. REE and FFM were calculated from *Eqs 4* and *5*, respectively. The REE-FFM relationship (●) is curvilinear. When FFM varies within the interval from 40 to 80 kg, the REE-FFM relation (—) can be fit by a linear equation, REE = 21.7 × FFM + 374, as developed by linear regression analysis.

mature mammals, AT = $0.075 \times BM^{1.19}$ (3). Assuming that 80% of AT is fat (34), FFM can be calculated as

$$\begin{aligned} FFM &= BM - 0.8 \times AT \\ &= BM - 0.06 \times BM^{1.19} \end{aligned} \quad (5)$$

BM can thus be used to calculate for REE and FFM using *Eqs. 4* and *5*, respectively. The derived function, presented graphically in Fig. 1, shows that the REE-FFM relationship is nonlinear across the FFM range in mammals. For the FFM range observed in normal adult humans (40 to 80 kg), however, the relationship between REE (in kcal/day) and FFM (in kg) can be fit by a linear function ($r = 0.99$, $P < 0.001$)

$$REE = 21.7 \times FFM + 374 \quad (6)$$

Equation 6 and the experimentally derived composite REE-FFM equation have very similar slopes (21.7 vs. 21.5 ± 1.4 kcal $\cdot$ kg FFM$^{-1} \cdot$ day^{-1}) and intercepts (374 vs. 407 ± 128 kcal/day) (Table 2). The curvilinear interspecies REE-FFM model for mammals as a whole

Table 3. *Various tissues and organs: resting metabolic rate and relationship to body mass*

Component	Mass $= p \times BM^q$, kg	Resting Metabolic Rate, kcal$\cdot$ kg$^{-1}\cdot$ day^{-1}
Liver	$0.0491 \times BM^{0.70}$	200
Kidney	$0.0089 \times BM^{0.71}$	440
Brain	$0.1025 \times BM^{0.71}$	240
Heart	$0.006 \times BM^{0.98}$	440
Skeletal muscle	$0.468 \times BM^{0.99}$	13
Adipose tissue	$0.075 \times BM^{1.19}$	4.5
Lung	$0.0092 \times BM^{0.92}$	
Thyroid	$0.0001 \times BM^{0.92}$	
Adrenal	$0.0003 \times BM^{0.80}$	
Spleen	$0.003 \times BM^{1.02}$	
Gut	$0.075 \times BM^{0.94}$	
Skin	$0.106 \times BM^{0.94}$	
Blood	$0.069 \times BM^{1.02}$	
Skeleton	$0.061 \times BM^{1.09}$	

Information based on Calder III (3) and Elia (6).

is thus consistent with the linear REE-FFM model for adult humans.

TISSUE/ORGAN LEVEL REE MODEL

Although the whole body level REE model may guide us in examining the relationships between REE and FFM, the model per se does not provide insight into the underlying sources of energy expenditure. Therefore, the next step in this expanded analysis involves a REE model at the tissue/organ body composition level. The fundamental REE model at the tissue/organ level can be expressed as

$$REE = \sum_{i=1}^{n} (k_i \times T_i) \quad (7)$$

where T_i is the mass of individual tissue or organ, k_i is the corresponding resting metabolic rate of the tissue or organ, and n is component number.

Recently, Gallagher et al. (11) used multiscan magnetic resonance imaging (MRI) to measure the mass of

Table 2. *Derivation of whole body and tissue organ level REE-FFM models*

	Mammals BM, 0.03 kg (mice)–6650 kg (elephant)	Humans FFM, 40–80 kg
Experimental approach		REE = $(21.6 \pm 1.4) \times$ FFM + (391 ± 118)
Whole body level modeling approach	REE = $70.0 \times BM^{0.75}$	
	↓ as FFM = BM $- 0.06 \times BM^{1.19}$	
	REE-FFM function (Fig. 1) ——————→	REE = $21.7 \times$ FFM + 374
Tissue/organ level modeling approach	$REE = \sum_{i=1}^{n} (k_i \times T_i)$	
	↓ as T = p $\times$ BM^q	
	REE-FFM function (Fig. 2)	
	$REE = \sum_{i=1}^{n} (k_i \times p \times BM^q)$ ——————→	REE = $24.6 \times$ FFM + 175

BM, body mass, in kg; k, resting metabolic rate; p, constant; q, scaling exponent; T, individual tissues/organs.

seven tissue/organ level components, including liver, kidney, brain, heart, skeletal muscle, AT, and miscellaneous tissues. The authors then predicted REE based on these individual tissue/organ masses and their corresponding resting metabolic rates (k values), as provided by Elia (Table 3). They found a strong correlation between the REE predicted by *Eq. 7* and REE measured by indirect calorimetry ($r = 0.94$, $P = 0.0001$), with no significant difference between the predicted REE (1,666 $\pm$ 348 kcal/day) and the measured REE (1,685 $\pm$ 347 kcal/day) of 13 healthy young adult subjects. This study strongly supports the concept that whole body REE can be predicted at the tissue/organ level with *Eq. 7*. We now discuss the two REE determinants, tissue/organ resting metabolic rate (k) and corresponding mass (T).

Tissue/organ resting metabolic rate. Expanding upon previous reviews, Elia (6) highlighted the existence of large between tissue and organ differences in resting metabolic rate in adult humans (Table 3).

Although skeletal muscle and adipose tissue are the largest components, their resting metabolic rates are low. In contrast, organs, including liver, kidneys, heart, and brain, which account for only ~5–6% of body mass, have much higher resting metabolic rates. Other body components, including skeleton, skin, and lungs, have low resting metabolic rates, and an average k value (12 kcal$\cdot$kg$^{-1}\cdot$day^{-1}) was applied for these components. The k values of the individual tissues and organs were assumed to be relatively stable among healthy adult humans, although some factors, such as training and disease, might affect the metabolic function of various tissues and organs.

Tissue/organ mass-BM relationships. In developing our expanded REE model, we considered 14 major tissues and organs, including liver, kidneys, brain, heart, skeletal muscle, AT, lungs, thyroid, adrenals, spleen, gut, skin, blood, and skeleton. For a 70-kg human, the sum of these 14 tissues and organs is 69.2 kg, or 98.9% of BM (34). Among mature mammals ranging in BM from mice to elephants, each tissue and organ mass can be expressed as an exponential function of BM (2, 3, 6)

$$\text{T} = p \times \text{BM}^q \qquad (8)$$

where T is the individual tissue/organ mass, p is a constant, and q is a scaling exponent. Previous studies provide us with the allometric functions that relate these tissues and organs to BM (Table 3). Allometric scaling is based on the concept that organisms are not isometric; rather, specific proportions change in a regular manner. Nonisometric scaling in biology is often referred to as "allometric," from the Greek "allos" meaning "different" (32).

Tissue/Organ Level Model

Combining *Eqs. 7* and *8*, we develop a REE-BM model at the tissue/organ body composition level

$$\text{REE} = \sum_{i=1}^{n} (k_i \times p \times \text{BM}^q) \qquad (9)$$

Using k, p, and q values of individual tissues and organs (Table 3), whole body REE in *Eq. 9* can be expressed as

$$
\begin{aligned}
\text{REE} = {} & k_1 \times \text{liver} + k_2 \times \text{kidney} + k_3 \times \text{brain} + k_4 \times \text{heart} + k_5 \times \text{SM} + k_6 \times \text{AT} + K_7 \\
& \times (\text{lung} + \text{thyroid} + \text{adrenal} + \text{spleen} + \text{gut} + \text{skin} + \text{blood} + \text{skeleton}) \\
= {} & 200 \times (0.0491 \times \text{BM}^{0.70}) + 440 \times (0.0089 \times \text{BM}^{0.71}) + 240 \times (0.1025 \times \text{BM}^{0.71}) \\
& + 440 \times (0.006 \times \text{BM}^{0.98}) + 13 \times (0.468 \times \text{BM}^{0.99}) + 4.5 \times (0.075 \times \text{BM}^{1.19}) \\
& + 12 \times (0.0092 \times \text{BM}^{0.92} + 0.0001 \times \text{BM}^{0.92} + 0.0003 \times \text{BM}^{0.80} + 0.003 \times \text{BM}^{1.02} \\
& + 0.075 \times \text{BM}^{0.94} + 0.106 \times \text{BM}^{0.94} + 0.069 \times \text{BM}^{1.02} + 0.061 \times \text{BM}^{1.09})
\end{aligned}
\qquad (10)
$$

where REE is in kilocalories per day, and BM is in kilograms. *Equation 10* is an expansion of Kleiber's allometric model, in which total BM in *Eq. 4* is replaced by each tissue/organ level component.

Whole body REE and FFM can be calculated from BM with *Eqs. 10* and *5*, respectively. One is thus able to model REE as a function of FFM (Fig. 2), again showing that the relationship between REE and FFM is curvilinear across the FFM range of mammals. Accordingly, REE increases with FFM but at a rate less than BM$^{1.0}$.

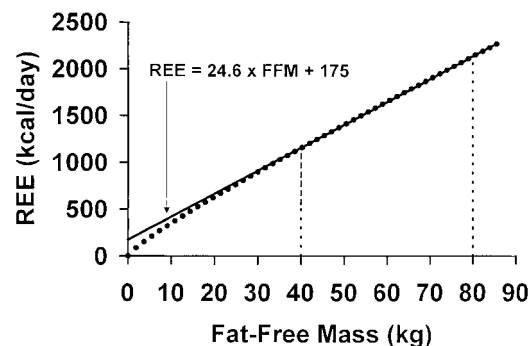The REE-FFM relationship for humans can be evaluated on the tissue/organ level. When FFM = 0, as

Fig. 2. Tissue/organ level modeling approach. Whole body REE (in kcal/day) predicted from *Eq. 10* on the ordinate vs. FFM (in kg) on the abscissa. The REE-FFM relationship (●) is curvilinear. When FFM varies within the interval from 40 to 80 kg, the REE-FFM relationship (—) can be fit by a linear equation, REE = 24.6 × FFM + 175, as developed by linear regression analysis.

shown in Fig. 2, predicted REE = 0. Although the relationship between REE and FFM is nonlinear for the entire range of available mammalian data, the REE-FFM function within the FFM interval from 40 to 80 kg for adult humans is characterized by the linear regression equation ($r = 0.99$, $P < 0.001$)

$$REE = 24.6 \times FFM + 175 \qquad (11)$$

Equation 11 and the experimentally derived composite REE-FFM equation (Table 2) have similar slopes (24.6 vs. 21.5 ± 1.4 kcal $\cdot$ kg FFM^{-1} $\cdot$ day^{-1}) and positive intercepts (i.e., 175 vs. 407 ± 128 kcal/day).

CURVILINEAR REE-FFM FUNCTION ACROSS MAMMALS

An important inference can be derived from the whole body and tissue/organ level interspecies REE-FFM mammalian models. As shown in Figs. 1 and 2, small mammals like the rat and guinea pig may have linear REE-FFM regression line slopes larger than that observed in humans and other large mammals. Support for interspecies FFM-related differences in the mammalian REE-FFM relationship (larger FFM associated with smaller REE vs. FFM slope) comes from our own laboratory, in which humans and rats had measurements of both REE and FFM. The slope of REE vs. FFM in adult humans was 22.9 kcal/kg in the study of Heshka et al. (13). In contrast, the REE vs. FFM slope in adult Sprague-Dawley rats was 139.5 kcal/kg [REE (kcal/day) = $139.5 \times$ FFM (kg) $-$ 25.3; $r^2 = 0.62$, $P < 0.01$; unpublished data].

Several relevant questions thus arise. Why is the REE-FFM relationship a curvilinear function across mammalian species? Why would small and large mammals differ in the relationship between REE and the mass of metabolically active tissue expressed as the FFM component? We explored these interrelations with the tissue/organ level REE-FFM model, extending the qualitative observations of earlier investigators. Specifically, we examined the influence of body size on k values and on the proportion of FFM as individual tissues and organs.

Mammalian tissue/organ resting metabolic rate. Individual tissues and organs can be divided into two groups, one with high resting metabolic rates (e.g., brain, heart, liver, and kidney) and the other with low metabolic rates (e.g., skeletal muscle, skeleton, and adipose tissue; Table 3). Although Elia (6) provided the resting metabolic rates of individual tissues and organs for adult humans, it is questionable whether these k values can also be applied to estimate REE in other mammals. Early studies favored the hypothesis that the resting metabolic rates of homologous tissues and organs (e.g., liver) are relatively constant, irrespective of body size (35). However, subsequent well controlled studies showed that the resting metabolic rates of homologous tissues and organs were lower with greater body size (33).

Recently, Couture and Hulbert (4) determined the resting metabolic rates of liver and kidney cortex from mouse, rat, rabbit, sheep, and cattle, representing a
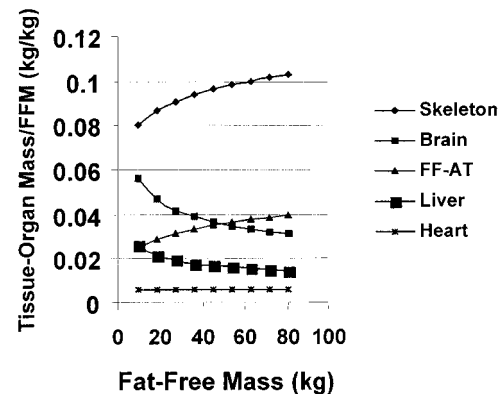

Fig. 3. Ratio of tissue and organ mass to FFM (in kg/kg) on the ordinate vs. FFM (in kg) on the abscissa. Tissue/organ mass and FFM were calculated with *Eqs. 8* and *5*, respectively. FF-AT, fat-free adipose tissue.

$\sim$12,000-fold difference in BM. There was a highly significant "hypoallometric" ($P < 0.01$) relationship (scaling factor <0) between the oxygen consumption rate of slices from both organs and BM. Mouse liver and kidney slices respired per unit mass 5.9 and 3.4 times faster than the corresponding slices from cattle. The higher respiration rate of slices from smaller animals could not be explained by interspecies differences in tissue extracellular space or tissue protein content. The observations of Couture and Hulbert strongly support the concept that mammals with a small BM, such as the mouse and rat, have higher k values than humans. In contrast, high BM mammals like the cow and elephant have lower k values than humans.

Between-mammal tissue/organ mass-BM relationship. The proportion of BM as individual tissue/organ is not constant across mammalian species. With increasing BM, most organs are hypoallometric ($q < 1$) as they occupy a decreasing fraction of BM. Skeletal muscle is almost directly proportional ($q = 1$) to BM. In contrast, AT and skeleton are "hyperallometric" ($q > 1$)
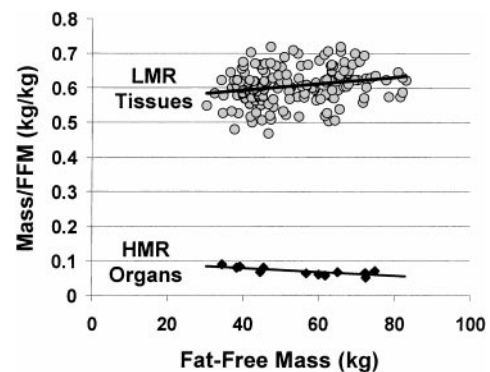

Fig. 4. Ratio of low metabolic rate tissues (LMR) and high metabolic rate organs (HMR) to FFM on the ordinate vs. FFM on the abscissa in 174 healthy adult humans. LMR is the sum of FF-AT, skeletal muscle, and bone mineral; and HMR is the sum of brain, heart, liver, and kidneys. LMR/FFM = $0.56 + 0.001 \times$ FFM, $r = 0.24$, $P = 0.004$; HMR/FFM = $0.102 - 0.0006 \times$ FFM, $r = 0.81$, $P < 0.001$; $n = 13$/subgroup.

across mammalian species because they occupy increasing fractions of BM (Table 3).

We explored this question by calculating for representative body weights the mass of five respective tissues and organs (heart, liver, brain, skeleton, and fat-free portion of AT) with *Eq. 8* and the data in Table 3. The corresponding FFM was then calculated with *Eq. 5*. The fraction of FFM as each of the five tissues and organs is plotted in Fig. 3 as a function of FFM. The figure indicates that, with greater FFM, skeleton and the fat-free portion of adipose tissue increase, and brain, liver, and heart decrease or remain unchanged in mammals as a fraction of FFM.

We also explored this question in humans, because there have been relatively few published evaluations comprehensive in vivo tissue/organ mass. Data from the Columbia Body Composition Program Project Grant allow an initial analysis of these associations in healthy young men and premenopausal women (age <45 yr). There were 174 subjects with measured FFM, AT mass, skeletal muscle mass, and bone-mineral mass. A subset of these subjects ($n = 13$) also had brain, heart, liver, and kidney mass measured, as previously reported (11). The tissue/organ mass-to-FFM ratios plotted as a function of FFM are presented in Fig. 4 as two pooled groups, one with high resting metabolic rates (i.e., sum of brain, heart, liver, and kidneys) and the other with low resting metabolic rates (i.e., sum of fat-free AT, skeletal muscle, and bone mineral). The observed trends are qualitatively similar to those developed earlier for mammals as a whole, with a relative decrease in high metabolic rate organs and a corresponding increase in low metabolic rate tissues with greater FFM.

Hence, although specific details remaining to be elucidated may vary, a similar and highly consistent pattern emerges in mammals as a whole: small mammals have larger proportions of FFM as organs with higher resting metabolic rates compared with large mammals having higher proportions of tissues with lower resting metabolic rates.

This interanimal anatomic difference, combined with a difference in specific tissue/organ metabolic rates (k values), is consistent with the curvilinear REE-FFM relationship observed in mammals and with the finding that small mammals have larger REE-to-FFM ratios compared with their larger mammalian counterparts.

SUMMARY AND CONCLUSIONS

This study presents for the first time a series of models at the whole body and tissue/organ levels designed specifically to explore the observed relationships between REE and FFM. The segments of the curvilinear interspecies mammalian functions between 40 and 80 kg FFM typical of adult humans fit well with linear models and were similar to the average REE prediction model formulated from 15 published experimental studies.

Our modeling efforts, based on available information, thus support the hypothesis that the linear REE-FFM relationship long observed in adult humans is qualitatively consistent with the curvilinear REE-BM relationship observed in mammals as a whole. Our analysis, supported by preliminary human experimental data, also suggests that mammals exhibit a decrease in the proportion of FFM as high metabolic rate organs with greater FFM. FFM may thus not be a "metabolically homogeneous" compartment across mammals generally, and humans specifically, varying widely in BM.

Our literature review identified a limited number of studies, other than those for small rodents and humans, in which REE, FFM, and various organs and tissues were quantified in the same animals. That information would be useful for extending the modeling efforts presented in this report.

The derived whole body level and tissue/organ level REE-FFM models are general and unsuitable for individual REE prediction. Future studies are needed to extend these observations and to analyze gender- and age-related, hormonal, ethnic, and other sources of variation in REE-FFM relationships (8–10, 26, 39). Major advances in our understanding of these relationships require linking additional body composition information across the human life span with an analysis of individual tissue/organ resting metabolic rates, an area in which there presently exists large gaps in our knowledge.

REFERENCES

1. **Arciero PJ, Goran MI, and Poehlman ET.** Resting metabolic rate is lower in women than in men. *J Appl Physiol* 75: 2514–2520, 1993.
2. **Brody S.** *Bioenergetics of Growth*. New York: Reinhold, 1945.
3. **Calder WA III.** *Size, Function, and Life History*. New York: Dover, 1996.
4. **Couture P and Hulbert AJ.** Relationship between body mass, tissue metabolic rate, and sodium pump activity in mammalian liver and kidney. *Am J Physiol Regulatory Integrative Comp Physiol* 268: R641–R650, 1995.
5. **Cunningham JJ.** A reanalysis of the factors influencing basal metabolic rate in normal adults. *Am J Clin Nutr* 33: 2372–2374, 1980.
6. **Elia M.** Organ and tissue contribution to metabolic rate. In: *Energy Metabolism: Tissue Determinants and Cellular Corollaries*, edited by JM Kinney and HN Tucker. New York: Raven, 1992, p. 61–80.
7. **Ferraro R, Lillioja S, Fontvielle AM, Rising R, Bogardus C, and Ravussin E.** Lower sedentary metabolic rate in women compared to men. *J Clin Invest* 90: 1–5, 1992.
8. **Foster GD, Warren TA, and Vogt RA.** Resting energy expenditure in obese African American and Caucasian women. *Obes Res* 5: 1–8, 1997.
9. **Fukagawa NK, Bandini LG, Dietz WH, and Young JB.** Effect of age on body water and resting metabolic rate. *J Gerontol Med Sci* 51: M71–M73, 1996.
10. **Fukagawa NK, Bandini LG, and Young JB.** Effect of age on body composition and resting metabolic rate. *Am J Physiol Endocrinol Metab* 259: E233–E238, 1990.
11. **Gallagher D, Belmonte D, Deurenberg P, Wang ZM, Krasnow N, Pi-Sunyer FX, and Heymsfield SB.** Organ-tissue mass measurement allows modeling of resting energy expendi-

ture and metabolically active tissue mass. *Am J Physiol Endocrinol Metab* 275: E249–E258, 1998.

12. **Grande F.** Energy expenditure of organs and tissues. In: *Assessment of Energy Metabolism in Health and Disease*, edited by JM Kinney. Columbus, OH: Ross Laboratories, 1989, p. 88–92.

13. **Heshka S, Yang M-U, Wang J, Burt P, and Pi-Sunyer FX.** Weight loss and change in metabolic rate. *Am J Clin Nutr* 52: 981–986, 1990.

14. **Heymsfield SB, Hoff RD, Gray TF, Galloway J, and Casper K.** Heart diseases. In: *Nutrition and Metabolism in Patient Care*, edited by JM Kinney, KN Jeejeebhoy, GL Hill, and OE Owen. Philadelphia: WB Saunders, 1988, p. 477–530.

15. **Holliday MA.** Metabolic rate and organ size during growth from infancy to maturity and during late gestation and early infancy. *Pediatrics* 47: 169–179, 1971.

16. **Holliday MA, Potter D, Jarrah A, and Bearg S.** The relation of metabolic rate to body weight and organ size. *Pediatr Res* 1: 185–195, 1967.

17. **Jensen MD, Braun JS, Vetter RJ, and Marsh HM.** Measurements of body potassium with a whole body counter: relationship between lean body mass and resting energy expenditure. *Mayo Clin Proc* 63: 864–868, 1988.

18. **Kashiwazaki H, Suzuki T, and Inaoka T.** Postprandial resting metabolic rate and body composition in the moderately obese and normal-weight adult subjects at sitting posture. *J Nutr Sci Vitaminol (Tokyo)* 34: 399–411, 1988.

19. **Kinney JM and Tucker HN (Eds).** *Energy Metabolism: Tissue Determinants and Cellular Corollaries*. New York: Raven, 1992, p. 19–60.

20. **Kleiber M.** Body size and metabolism. *Hilgardia* 6: 315–353, 1932.

21. **Kleiber M.** *The Fire of Life: An Introduction to Animal Energetics*. New York: Wiley, 1961.

22. **Luke A and Schoeller DA.** Basal metabolic rate, fat-free mass, and body cell mass during energy restriction. *Metabolism* 41: 450–456, 1992.

23. **Mackenzie D.** New clues to why size equals destiny. *Science* 284: 1607–1609, 1999.

24. **McNeill G, Rivers G, Payne GPW, de Britto JJ, and Abel R.** Basal metabolic rate of Indian men: no evidence of metabolic adaptation to a low plane of nutrition. *Hum Nutr Clin Nutr* 41: 473–484, 1987.

25. **Mifflin MD, St Jeor ST, Hill LA, Scott BJ, Daugherty SA, and Koh YO.** A new predictive equation for resting energy expenditure in healthy individuals. *Am J Clin Nutr* 51: 241–247, 1990.

26. **Owen OE.** Resting metabolic requirements of men and women. *Mayo Clin Proc* 63: 503–510, 1988.

27. **Owen OE, Holup JL, D'Alessio A, Craig ES, Polansky M, Smalley KJ, Kavle EC, Bushman MC, Owen LR, Mozzoli MA, Kendrck ZV, and Boden GH.** A reappraisal of the caloric requirement of men. *Am J Clin Nutr* 46: 875–885, 1987.

28. **Owen OE, Karle E, Owen RS, Polansky M, Caprio S, Mozzoli MA, Kendrick ZV, Bushman MC, and Boden G.** A reappraisal of the caloric requirements of healthy women. *Am J Clin Nutr* 44: 1–19, 1986.

29. **Ravussin E and Bogardus C.** Relationship of genetics, age and physical fitness to daily energy expenditure. *Am J Clin Nutr* 49: 968–975, 1989.

30. **Ravussin E, Burnand B, Schutz Y, and Jequier E.** Twenty-four-hour energy expenditure and resting metabolic rate in obese, moderately obese and control subjects. *Am J Clin Nutr* 35: 566–73, 1982.

31. **Ravussin E, Lillioja S, Anderson TE, Christin L, and Bogardus C.** Determinants of 24-hour energy expenditure in man. *J Clin Invest* 78: 1568–1578, 1986.

32. **Schmidt-Nielsen K.** *Scaling: Why Is Animal Size So Important?* Cambridge, UK: Cambridge U. Press, 1984.

33. **Siesjo BK and Nilsson B.** A method for determining blood flow and oxygen consumption in the rat brain. *Acta Physiol Scand* 96: 72–82, 1976.

34. **Snyder WS, Cook MJ, Nasset ES, Karhausen LR, Howells GP, and Tipton IH.** *Report of the Task Group on Reference Man*. Oxford, UK: Pergamon, 1975.

35. **Terroine EF and Roche J.** La respiration des tissues. 1. Production calorique des homeothermes et intensité de la respiration in vitro des tissus homologues. *Arch Int Physiol Biochim Biophys* 24: 356–399, 1925.

36. **Wang ZM, Pierson RN Jr, and Heymsfield SB.** The five-level model: a new approach to organizing body composition research. *Am J Clin Nutr* 56: 19–28, 1992.

37. **Weinsier RL, Schutz Y, and 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* 55: 790–794, 1992.

38. **West GB, Brown JH, and Enquist BJ.** The fourth dimension of life: fractal geometry and allometric scaling of organisms. *Science* 284: 1677–1679, 1999.

39. **Weststrate JA, Dekker J, Stoel M, Begheijn L, Deurenberg P, and Hautvast GAJ.** Resting energy expenditure in women: impact of obesity and body fat distribution. *Metabolism* 39: 11–17, 1990.