No evidence of mass dependency of specific organ metabolic rate in healthy humans¹–³

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ABSTRACT
Background: In humans, resting energy expenditure (REE) can be calculated from organ and tissue masses using constant specific organ metabolic rates. However, interspecies data suggest allometric relations between body mass and organ metabolic rate with higher specific metabolic rates in mammals with a smaller body mass.

Objective: The objective was to compare the accuracy of REE prediction with the use of either constant or body mass–dependent specific organ metabolic rates.

Design: Healthy subjects (79 women, 75 men) within the normal range of fat mass (FM) expected for a healthy body mass index and aged 18–78 y were stratified into tertiles of body mass. Fifty subjects were grouped as tertile 1 (<66.3 kg), 52 as tertile 2 (≥66.3 to ≤77.2 kg), and 52 as tertile 3 (>77.2 kg). Magnetic resonance imaging was used to assess the volume of 4 internal organs (brain, heart, liver, and kidneys). REE was measured by indirect calorimetry (REEm) and compared with REE calculated from previously published constant (REEc1) and body mass–dependent organ metabolic rates (REEc2).

Results: REEm increased significantly with weight tertile (tertile 1: 5536 ± 529 kJ/d; tertile 2: 6389 ± 672 kJ/d; tertile 3: 7467 ± 745 kJ/d; P < 0.01). The deviation REEm–REEc1 did not differ between weight tertiles (tertile 1: 66 ± 382 kJ/d; tertile 2: 167 ± 507 kJ/d; tertile 3: 86 ± 480 kJ/d; NS) and showed no relation with body mass (r = −0.05, NS). By contrast, REEm–REEc2 increased with increasing weight tertile (tertile 1: −45 ± 369 kJ/d; tertile 2: 150 ± 503 kJ/d; tertile 3: 193 ± 482 kJ/d; P < 0.05) and correlated significantly with body mass (r = 0.16, P < 0.05).

Conclusion: Our data do not support a lower specific organ metabolic rate in humans with a larger body mass than in those with a smaller body mass. Am J Clin Nutr 2008;88:1004–9.

SUBJECTS AND METHODS
Subjects
The original study population consisted of 217 healthy white volunteers (109 women and 106 men) aged 18–78 y with a BMI

INTRODUCTION
In 1932, Max Kleiber formulated an exponential equation expressing resting energy expenditure (REE) as a function of body mass across mammals: REE = 293 × body mass⁰⁷⁷⁵ (1). Today, Kleiber’s law remains one of the most important laws in bioenergetics but is still considerably discussed (2, 3). The allometric relation between body mass and metabolic rate described by Kleiber has been confirmed in several interspecies studies at the organ-tissue level by the finding of lower specific tissue and organ metabolic rates in larger mammals than in smaller mammals (4–7).

However, in contrast with interspecies comparisons, there are few data on intraspecies (ontogenetic) scaling of organ metabolic rate. Decreasing metabolic rate in cells of various tissues with increasing body mass has been documented in rats (8), mice (9), some fish (10–12), and invertebrates (13, 14). In contrast, other authors found no relation between tissue respiration and body size in juvenile and adult albino rats (15).

Because data on the specific metabolic rate of large and small organs are lacking for humans, constant organ and tissue metabolic rates are commonly assumed for the calculation of REE (16, 17). In healthy normal-weight, underweight, and overweight subjects, REE can be accurately estimated from the sum of tissue and organ weights multiplied by corresponding constant specific metabolic rates (18–23). However, the assumption of a body mass dependency in organ metabolic rates may even improve the REE prediction from detailed body-composition analysis. Following this idea, Wang et al (2) used interspecies data as well as results from humans differing in body mass to develop prediction equations for specific organ metabolic rates based on body mass. However, to our knowledge the body mass dependency of organ metabolic rates in humans of different body size has not been investigated.

The aim of the study was to analyze the accuracy of REE prediction from detailed body-composition analysis using either constant or body mass–dependent specific organ metabolic rates. In 154 healthy subjects within the normal range of FM expected for a healthy body mass index (BMI; in kg/m²), REE was predicted from organ masses assessed by magnetic resonance imaging (MRI) and was compared with REE measured by indirect calorimetry.
range of 16.8 to 43.1 kg/m². Participants were recruited from students and staff at the University of Kiel and by notice board postings in local supermarkets and pharmacies. All subjects were nonsmokers and took no medication known to influence energy metabolism or body composition. Because REE increases with insulin resistance, type 2 diabetes, and metabolic risk factors associated with obesity (24–27), 63 subjects were excluded from the study because of a high percentage body fat mass according to cutoffs defined by Gallagher et al (28) and/or on the basis of a high HOMA of the study population. The final study population of 154 participants (79 women and 75 men) was stratified into tertiles according to their body mass (kg), independent of sex. Fifty subjects were grouped as tertile 1 (<66.3 kg), 52 as tertile 2 (66.3–77.2 kg), and 52 as tertile 3 (>77.2 kg). The study protocol was approved by the local ethical committee of the Christian-Albrechts-Universität zu Kiel. Each subject provided informed written consent before participation.

Study protocol

All participants arrived at the metabolic unit of the Institute of Human Nutrition and Food Science in the morning at 0730 after an overnight fast of >8 h. Subjects were instructed to avoid heavy exercise before arrival. Venous blood samples for the analyses of plasma lipids, glucose, insulin, and thyroid hormone concentrations were collected and frozen at −40 °C until analyzed. The HOMA index was calculated as an indicator of insulin resistance from fasting plasma glucose and insulin concentrations as glucose (mmol/L) × insulin mU/mL/22.5 (29).

Body-composition analysis

Anthropometric measurements

Body height was measured to the nearest 0.5 cm with subjects in underwear and without shoes (Seca stadiometer; Vogel & Halke, Hamburg, Germany). Weight was assessed with an electronic scale (TANITA, Tokyo, Japan).

Dual-energy X-ray absorptiometry

Whole body measurements by DXA were performed with the use of a Hologic absorptiometer (QDR 4500A; Hologic Inc, Waltham, MA). Scans were carried out by a licensed radiological technician. The manufacturer’s software (version V8.26a:3) was used for the analyses of percentage fat mass (FM).

Magnetic resonance imaging

The volumes of 4 internal organs (brain, heart, liver, and kidneys) were measured by transversal MRI images. Scans were obtained with a 1.5T scanner (Magnetom Vision Siemens, Erlangen, Germany). Brain and abdominal organs were examined with a T1-weighted sequence (FLASH) (TR: 177.8 ms for abdominal organs; TR: 170.0 ms for brain; TE: 4.1 ms/echo). ECG-triggered, T2-weighted, turbo spin-echo ultrashot scans (HASTE) (TR: 800.0 ms; TE: 43 ms/echo) were used to examine the heart. The slice thickness ranged from 6 mm for brain to 7 mm for the heart to 8 mm for the internal organs without interslice gaps. Cross-sectional organ areas were determined manually using segmentation software (SliceOmatic, version 4.3; TomoVision Inc, Montreal, Canada). Volume data were transformed into organ masses by using the following densities: 1.036 g/cm³ for brain, 1.06 g/cm³ for heart and liver, and 1.05 g/cm³ for kidneys (30).

Resting energy expenditure

REE was measured by indirect calorimetry (REEint) with a ventilated-hood system (Vmax Spectra 29n; SensorMedics BV, Viaysys Healthcare, Bilthoven, Netherlands; software Vmax, version 12-1A) for 30 min. During calibration of flow and gas analyzers immediately before each measurement, the subjects were resting for 5 min to habituate to the measurement conditions. Flow calibration was performed with a 3-L calibration syringe, and gas analyzers were calibrated by using 2 standard gas concentrations (16% O₂, 4% CO₂, 26% O₂; room air 20.94% O₂, 0.05% CO₂). REE measurements were conducted in a metabolic ward at a constant humidity (55%) and room temperature (22 °C). During the measurements, the subjects were awake and lay quietly and motionless (31). Continuous gas exchange measurements were obtained for a minimum of 30 min. The first 15 min of each measurement were discarded. The CV for repeated measures of REE in 11 subjects was 5.0% (31).

Calculation of REE

Calculation of REE (REEint) is based on the sum of 4 internal organs (brainMRI, heartMRI, liverMRI, and kidneysMRI) multiplied by their corresponding tissue-respiration rate. The residual mass (RM) was calculated as the difference between body mass and these organ masses. The metabolic activity of RM was assumed to be 40 kJ · kg⁻¹ · d⁻¹ (REEin—energy expenditure of brainMRI + heartMRI + liverMRI + kidneysMRI/RM). To compare the accuracy of body mass–dependent and mass-independent REE estimations, a constant metabolic rate model (REEc1) and a body mass–dependent metabolic rate model (REEc2) were calculated according to the method of Wang et al (2). These authors developed exponential equations for a specific organ metabolic rate based on body mass (2). When inserting the mean weight of the study population (73 kg) into these equations, constant specific metabolic rates for brain, heart, liver, and kidneys were derived, and REEc1 was calculated as follows:

\[
\text{REEc1(kJ/d)} = (1868 \times 73^{-0.14}) \times \text{brainMRI,kg} + (2861 \times 73^{-0.27}) \times \text{liverMRI,kg} + (3725 \times 73^{-0.12}) \times \text{heartMRI,kg} + (2887 \times 73^{-0.08}) \times \text{kidneysMRI,kg} + 40 \times \text{RM,kg}
\] (1)

REEc2 was also calculated by using body mass-dependent exponential equations for estimation of specific organ metabolic rates (2):

\[
\text{REEc2(kJ/d)} = (1868 \times M^{-0.14}) \times \text{brainMRI,kg} + (2861 \times M^{-0.27}) \times \text{liverMRI,kg} + (3725 \times M^{-0.12}) \times \text{heartMRI,kg} + (2887 \times M^{-0.08}) \times \text{kidneysMRI,kg} + 40 \times \text{RM,kg}
\] (2)

where M is body mass.
When compared with women, men had significantly higher masses (REEc1 and REEc2) stratified by sex are given in measured and calculated REE (REEm–REEc1 and REEm–REEc2) in women.

brain masses the exponents were nearly twice as high in men than the exponents for body mass were higher in men, e.g., for liver and were euthyroid.

higher %FM and HOMA index (thyroid hormone concentrations. Men had a higher BMI, organ mass, residual mass (body weight – OM); M, body mass; DXA, dual-energy X-ray absorptiometry; TSH, thyrotropin; T3, triiodothyronine; T4, thyroxine. Coefficients of determination for regression equations lay between $R^2$ values of 0.56 and 0.19 (all $P < 0.05$).

### RESULTS

Anthropometric and body-composition characteristics of the study population are given in Table 1. There were significant differences between men and women for all variables except for thyroid hormone concentrations. Men had a higher BMI, organ mass, and residual mass than women, whereas women had a higher %FM and HOMA index ($P < 0.05$). No significant between-group differences were observed for thyroid hormones (thyrotrpin, triiodothyronine, and thyroxine), and all subjects were euthyroid.

Equations predicting organ mass from body mass (Table 1) differed between men and women. When compared with women, the exponents for body mass were higher in men, e.g., for liver and brain masses the exponents were nearly twice as high in men than in women.

Measured REE (REEm) and REE calculated from organ masses (REEc1 and REEc2) stratified by sex are given in Table 2. When compared with men, measured and calculated REE were also significantly different between sex ($P < 0.01$, with higher inaccuracies in REE prediction for men. Constant as well as body mass–dependent REE predictions overestimated REE in women, whereas an underestimation was observed in men.

Both measured and calculated REE increased significantly with body weight ($P < 0.01$) (Table 3). The deviation REEm–REEc2 increased with body mass and a significant difference in REEm–REEc2 between weight tertile 1 and tertile 3 (45 compared with 193 kJ/d; $P < 0.05$) was found. By contrast, the deviation REEm–REEc2 did not differ between weight tertile 1 and tertile 3 (66 compared with 86 kJ/d; $P = 0.974$). The mean difference between both REE calculations REEc1–REEc2 differed between weight tertile 1 and tertile 3 ($-111$ compared with 106 kJ/d; $P < 0.01$). Assuming a power of 0.8, the minimum detectable difference between REEc1–REEc2 for a total of 154 subjects was $31.9$ kJ/d ($P < 0.05$; SD $REE_{c1} - REE_{c2} = 99$ kJ/d).

### Table 1

**Characteristics of the study population**

<table>
<thead>
<tr>
<th>Age (y)</th>
<th>All (n = 154)</th>
<th>Men (n = 75)</th>
<th>Women (n = 79)</th>
</tr>
</thead>
<tbody>
<tr>
<td>43.0 ± 15.8</td>
<td>46.7 ± 15.7</td>
<td>41.2 ± 15.5</td>
<td></td>
</tr>
<tr>
<td>Body mass (kg)</td>
<td>72.3 ± 12.0</td>
<td>79.3 ± 10.4</td>
<td>65.6 ± 9.4</td>
</tr>
<tr>
<td>Height (m)</td>
<td>1.7 ± 0.1</td>
<td>1.8 ± 0.1</td>
<td>1.7 ± 0.1</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>24.2 ± 3.0</td>
<td>25.1 ± 2.9</td>
<td>23.3 ± 2.9</td>
</tr>
<tr>
<td>FMBODY (%)</td>
<td>24.5 ± 8.4</td>
<td>18.6 ± 5.1</td>
<td>30.1 ± 6.9</td>
</tr>
<tr>
<td>HOMA</td>
<td>2.4 ± 0.9</td>
<td>2.2 ± 0.9</td>
<td>2.5 ± 1</td>
</tr>
<tr>
<td>TSH (mU/L)</td>
<td>2.3 ± 1.3</td>
<td>2.2 ± 1.1</td>
<td>2.5 ± 1.4</td>
</tr>
<tr>
<td>T4 (pg/mL)</td>
<td>4.3 ± 0.7</td>
<td>4.3 ± 0.6</td>
<td>4.2 ± 0.8</td>
</tr>
<tr>
<td>T3 (pg/mL)</td>
<td>15.0 ± 2.1</td>
<td>15.6 ± 2.1</td>
<td>14.4 ± 2.0</td>
</tr>
<tr>
<td>MRI</td>
<td></td>
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</tr>
<tr>
<td>OMMRI (kg)</td>
<td>3.036 ± 0.384</td>
<td>3.288 ± 0.325</td>
<td>2.781 ± 0.245</td>
</tr>
<tr>
<td>BrainMRI (kg)</td>
<td>1.265 ± 0.113</td>
<td>1.337 ± 0.090</td>
<td>1.193 ± 0.083</td>
</tr>
<tr>
<td>HeartMRI (kg)</td>
<td>0.321 ± 0.082</td>
<td>0.367 ± 0.083</td>
<td>0.275 ± 0.048</td>
</tr>
<tr>
<td>LiverMRI (kg)</td>
<td>1.176 ± 0.218</td>
<td>1.282 ± 0.214</td>
<td>1.072 ± 0.166</td>
</tr>
<tr>
<td>KidneyMRI (kg)</td>
<td>0.270 ± 0.043</td>
<td>0.303 ± 0.057</td>
<td>0.238 ± 0.037</td>
</tr>
<tr>
<td>RM (kg)</td>
<td>69.4 ± 11.5</td>
<td>75.7 ± 9.8</td>
<td>63.0 ± 9.3</td>
</tr>
<tr>
<td>OM as a function of M</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BrainMRI (kg)</td>
<td>0.4475 × M$^{0.245}$</td>
<td>0.9032 × M$^{0.089}$</td>
<td>0.9751 × M$^{0.048}$</td>
</tr>
<tr>
<td>HeartMRI (kg)</td>
<td>0.0053 × M$^{0.954}$</td>
<td>0.0725 × M$^{0.805}$</td>
<td>0.0273 × M$^{0.549}$</td>
</tr>
<tr>
<td>LiverMRI (kg)</td>
<td>0.0493 × M$^{-0.766}$</td>
<td>0.0221 × M$^{0.927}$</td>
<td>0.1412 × M$^{0.482}$</td>
</tr>
<tr>
<td>KidneyMRI (kg)</td>
<td>0.0061 × M$^{0.882}$</td>
<td>0.0056 × M$^{0.913}$</td>
<td>0.0255 × M$^{1.532}$</td>
</tr>
</tbody>
</table>

1 All values are $\bar{x} ±$ SD. FM, fat mass; HOMA, homeostasis model assessment; MRI, magnetic resonance imaging; OM, organ mass; RM, residual mass (body weight – OM); M, body mass; DXA, dual-energy X-ray absorptiometry; TSH, thyrotropin; T3, triiodothyronine; T4, thyroxine. Coefficients of determination for regression equations lay between $R^2$ values of 0.56 and 0.19 (all $P < 0.05$).

2 Significantly different from women, $P < 0.05$ (t test).

### Table 2

**Measured and calculated resting energy expenditure (REE) stratified by sex**

<table>
<thead>
<tr>
<th></th>
<th>All (n = 153)</th>
<th>Men (n = 75)</th>
<th>Women (n = 78)</th>
</tr>
</thead>
<tbody>
<tr>
<td>REEm (kJ/d)</td>
<td>6476 ± 1026</td>
<td>7229 ± 808</td>
<td>5752 ± 607</td>
</tr>
<tr>
<td>REEc1 (kJ/d)</td>
<td>6401 ± 896</td>
<td>6986 ± 755</td>
<td>5808 ± 584</td>
</tr>
<tr>
<td>REEc2 (kJ/d)</td>
<td>6405 ± 804</td>
<td>6935 ± 675</td>
<td>5869 ± 518</td>
</tr>
<tr>
<td>REEm–REEc1 (kJ/d)</td>
<td>107 ± 460</td>
<td>277 ± 464</td>
<td>-15 ± 426</td>
</tr>
<tr>
<td>REEm–REEc2 (kJ/d)</td>
<td>130 ± 465</td>
<td>277 ± 455</td>
<td>-76 ± 406</td>
</tr>
</tbody>
</table>

1 All values are $\bar{x} ±$ SD. REEm, measured REE; REEc1, calculated REE using constant specific metabolic rates; REEc2, calculated REE using body mass–dependent metabolic rates.

2 Significantly different from women, $P < 0.01$ (t test).
TABLE 3
Measured and calculated resting energy expenditure (REE) stratified by weight tertiles

<table>
<thead>
<tr>
<th>Tertile 1 (n = 50)</th>
<th>Tertile 2 (n = 52)</th>
<th>Tertile 3 (n = 52)</th>
</tr>
</thead>
<tbody>
<tr>
<td>REEm (kJ/d)</td>
<td>5536 ± 529</td>
<td>6389 ± 672</td>
</tr>
<tr>
<td>REE&lt;sub&gt;c1&lt;/sub&gt; (kJ/d)</td>
<td>5501 ± 389</td>
<td>6246 ± 416</td>
</tr>
<tr>
<td>REE&lt;sub&gt;c2&lt;/sub&gt; (kJ/d)</td>
<td>5612 ± 360</td>
<td>6264 ± 403</td>
</tr>
<tr>
<td>REEm–REE&lt;sub&gt;c1&lt;/sub&gt; (kJ/d)</td>
<td>66 ± 382&lt;sup&gt;ab&lt;/sup&gt;</td>
<td>167 ± 507&lt;sup&gt;bc&lt;/sup&gt;</td>
</tr>
<tr>
<td>REEm–REE&lt;sub&gt;c2&lt;/sub&gt; (kJ/d)</td>
<td>−45 ± 369&lt;sup&gt;a&lt;/sup&gt;</td>
<td>150 ± 503&lt;sup&gt;bc&lt;/sup&gt;</td>
</tr>
<tr>
<td>REE&lt;sub&gt;c1&lt;/sub&gt;–REE&lt;sub&gt;c2&lt;/sub&gt; (kJ/d)</td>
<td>−111 ± 48&lt;sup&gt;b&lt;/sup&gt;</td>
<td>−17 ± 26&lt;sup&gt;bc&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

<sup>1</sup> All values are ± SD. Tertile 1, <66.3 kg body weight; tertile 2, ≥66.3 to <77.2 kg body weight; tertile 3, ≥77.2 kg body weight; REEm, measured REE; REE<sub>c1</sub>, calculated REE using constant specific metabolic rates; REE<sub>c2</sub>, calculated REE using body mass–dependent metabolic rates. Means with different superscript letters are significantly different, P < 0.05 (ANOVA, Tukey’s post hoc test).

For assessing the maximum difference in REE calculation between small and large organs, the minimum and maximum body weights of our study population (44 and 104 kg) were inserted into the body mass–dependent metabolic rate model according to Wang et al (2). The derived organ metabolic rates (44 compared with 104 kg) were then applied to a person with a 44-kg body weight. The resulting differences in REE were 55 kJ/d for heart (567 compared with 512 kJ), 172 kJ for liver (825 compared with 653 kJ), 136 kJ for brain (1193 compared with 1048 kJ), and 27 kJ for kidneys (415 compared with 388 kJ). The total difference between both REE calculations was 1390 kJ (4667 compared with 3277 kJ).

The regression line between measured and calculated REE according to either a constant or a body mass–dependent prediction model is shown in Figure 1A and B. We found strong relations between REE<sub>m</sub> and REE calculated from constant (Figure 1A) or body mass–dependent specific metabolic rates (Figure 1B) (REE<sub>c1</sub>: r = 0.89; REE<sub>c2</sub>: r = 0.89; P < 0.01). The slopes of the regression lines were not significantly different between men and women for both prediction models (REE<sub>m</sub> versus REE<sub>c1</sub>: y = 0.7767x + 1383.1 for men and y = 0.7651x + 1347.2 for women, Figure 1A; REE<sub>m</sub> versus REE<sub>c2</sub>: y = 0.6936x + 1932 for men and y = 0.645x + 2130.6 for women, Figure 1B). Pearson correlation coefficients showed a significant positive association between REE<sub>m</sub>–REE<sub>c1</sub> and body mass (r = 0.16, P < 0.05), whereas no significant correlation with body mass was observed in the case of the constant model (REE<sub>c1</sub>) (r = −0.05, P = 0.550). Body mass plotted against REE<sub>m</sub>–REE<sub>c1</sub> and REE<sub>m</sub>–REE<sub>c2</sub> showed a significant relation between REE<sub>m</sub>–REE<sub>c2</sub> and body mass (Figure 1B) but no relation between REE<sub>m</sub>–REE<sub>c1</sub> and body mass (Figure 1A).

There were no associations between organ masses and REE<sub>m</sub>–REE<sub>c1</sub> or REE<sub>m</sub>–REE<sub>c2</sub> except for a positive correlation of brain mass versus both deviations (REE<sub>m</sub>–REE<sub>c1</sub>: r = 0.26; REE<sub>m</sub>–REE<sub>c2</sub>: r = 0.35, P < 0.01).

DISCUSSION
The present study provides no evidence for a body mass dependency of specific organ metabolic rate in healthy subjects within the normal range of FM and ranging in body weight from 44 to 104 kg within species. The calculation of REE from organ mass using body mass–dependent specific organ metabolic rates according to Wang et al (2) resulted in higher deviations between measured and calculated REE (REE<sub>m</sub>–REE<sub>c2</sub>) with increasing body mass when compared with constant REE-prediction models. There was a significant relation between body mass and REE<sub>m</sub>–REE<sub>c2</sub>.

FIGURE 1. Resting energy expenditure (REE) measured by indirect calorimetry (REE<sub>m</sub>) plotted against calculated REE using constant specific metabolic rates (REE<sub>c1</sub>) and mass-dependent metabolic rates (REE<sub>c2</sub>) in women (n = 79: ●) and men (n = 75: ○), including body mass (kg) plotted against deviations of measured and calculated REE. A: REE<sub>m</sub>–REE<sub>c1</sub> vs body mass (r = −0.05, NS); B: REE<sub>m</sub>–REE<sub>c2</sub> vs body mass (r = 0.16, P < 0.05).
An allometric relation between body mass and basal metabolic rate has been confirmed at the organ tissue level in several interspecies studies. Analysis of liver and kidney cortex slices from mouse, rat, rabbit, sheep, and cattle resulted in an 11-fold difference in body mass–specific basal metabolic rates between small and larger mammals (7). Porter and Brand (4, 5) explained the differences in metabolic rate between mammals of different body size (ranging from mice to horse) by a body mass–dependent decrease in proton leak and ATP turnover in liver mitochondria with increasing body mass. Higher respiration rates in isolated liver cells were found in smaller birds (eg, finches) when compared with birds of greater body mass (eg, emus) (6).

However, intraspecies (ontogenetic) approaches investigating a body mass dependency of organ metabolic rate are very rare. Ontogenetic scaling of metabolic rates in fish has been documented by Oikawa and Itazawa (11). The combination of an increase in the relative size of low metabolically active tissues and a decrease in the metabolic activity of tissues with increasing body mass was found to explain the decline in metabolic rate per weight with increasing body mass in carp (11). In rats, allometric associations between body mass and cell metabolic rates of various tissues showed a decrease in metabolic rate with increasing body size (9, 32). Else (8) found large changes in liver oxygen consumption during development in rats. Weight-specific liver metabolism was significantly higher in young rats than in rats ≥20 d of age. These changes scaled with body mass (8). However, in growing or reproducing organisms (eg, juvenile animals), metabolic rate includes energy costs for growth and development (3, 33-35). Thus, a general limitation of ontogenetic approaches is the influence of energy costs for growth and development in immature mammals (3). These findings agree with those of a study in humans that compared REE modeling from constant specific organ metabolic rates in children and adults. Using this indirect approach, Hsu et al (23) provided evidence of a decline in measured REE per kilogram body weight during growth and development (23). Using the nitrous oxide method, Kennedy and Sokoloff (36) have shown that the specific metabolic rate of the brain is indeed significantly higher in children than in adults. Chugani et al (37) supported these findings by using positron emission tomography (PET). Local cerebral metabolic rates were maintained at high levels until the age of 6 y and then declined until adult rates were reached (37). Studies in adults using PET as well as data on arteriovenous (AV) differences (brain oxygen consumption per kilogram of organ weight) in adults confirmed our finding of a constant organ metabolic rate (38, 39). In addition, in vivo data suggest an increasing oxygen consumption with higher muscle mass with a constant specific energy expenditure in humans (40).

In 2001, Wang et al (2) reconstructed Kleiber’s law at the organ-tissue body-composition level based on available in vivo metabolic data in mature mammals. The authors used the metabolic rate of different species of mammals and 2 human subjects of different body mass to estimate exponential equations for body mass–dependent organ metabolic rates. We applied these equations, but, when compared with measured REE, we found no evidence of body mass dependency of specific organ metabolic rate in humans.

The present study showed significant between-sex differences in REEm, REEe, Body mass–dependent REEe was underestimated in men, likely because of a lower assumed specific organ metabolic rates for higher body weight. These findings accounting for differences in body weight were supported by comparing weight tertiles (Table 3). The deviation between REEm and body mass–dependent REEe (REEm–REEe) was significantly associated with weight showing a decreasing accuracy of body mass–dependent REE calculation with increasing body size. In contrast, no significant between-tetile differences were found for the accuracy of REE estimation with the use of constant organ metabolic rates. Accurate calculations of REE with the use of constant organ metabolic rates were shown in previous studies in normal-weight (20, 21) and underweight and overweight subjects (18, 19). Thus, the body mass–dependent model did not improve REE prediction. The accuracy of the body mass–dependent model decreased with increasing body mass, whereas the accuracy of the constant model was not affected by body weight. The present study provides no evidence for Wang et al’s (2) assumption of lower specific organ metabolic rates with increasing body size.

In vivo assessment of metabolic rate for the measurement of body size effects on specific organ metabolic rates in healthy humans is difficult to perform (17). For example, the specific liver metabolic rate has been analyzed by determining AV differences after starvation, under postprandial conditions, and in cirrhosis (41); however, data on organ metabolic rate in humans of different body sizes are still lacking. Therefore, further studies using in vivo techniques such as PET or 31P magnetic resonance spectroscopy for the measurement of mitochondrial ATP turnover within species with a wide range of body masses are needed.

In conclusion, the present study suggests that there is no body mass dependency of specific organ metabolic rate in a healthy population within the normal range of FM and with a body mass ranging from 44 to 104 kg body mass. Our data do not support a lower specific organ metabolic rate in humans with a larger body mass than in those with a smaller body mass.

The authors’ responsibilities were as follows—WL, AB-W, and BH: data collection; WL and AB-W: data analysis; WL, AB-W, and MJM: writing of the manuscript; AB-W and MJM: study design; and EK, C-CG, and MH: MRI protocol. None of the authors declared a conflict of interest.

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