Is there evidence for an age-related reduction in metabolic rate?

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1Unit of Nutrition and Preventive Medicine, Department of Epidemiology and Preventive Medicine, Monash University, Monash Medical Centre, Clayton, Victoria 3168; 2Department of Nutrition, Dietetics, and Food Science, Curtin University of Technology, Perth, Western Australia 6845; and 3School of Nutrition and Public Health, Deakin University, Malvern, Victoria 3144, Australia

Piers, Leonard S., Mario J. Soares, Leanne M. McCormack, and Kerin O’Dea. Is there evidence for an age-related reduction in metabolic rate? J. Appl. Physiol. 85(6): 2196–2204, 1998.—To determine whether the age-related reduction in basal metabolic rate (BMR) is explained by a quantitative and/or qualitative change in the components of lean tissue, we conducted a cross-sectional study in groups of young (n = 38, 18–35 yr) and older (n = 24, 50–77 yr) healthy individuals. BMR was measured by indirect calorimetry. Body composition was obtained by using dual-energy X-ray absorptiometry (DEXA), which permitted four compartments to be quantified [bone mineral mass, fat mass (FM), appendicular lean tissue mass (ALTM), and nonappendicular lean tissue mass (NALTM)]. Absolute BMR and ALTM were lower, whereas FM was significantly higher in the older, compared with young, subjects. BMR, adjusted for differences in FM, ALTM, and NALTM, was significantly lower in the older subjects by 644 kJ/day. In separate regression analyses of BMR on body compartments, older subjects had significantly lower regression coefficients for ALTM and NALTM, compared with young subjects. Hence, the age-related decline in BMR is partly explained by a reduction in the quantity, as well as the metabolic activity, of DEXA-derived lean tissue components.

Basal metabolic rate; body composition; dual-energy X-ray absorptiometry; physical activity level; elderly humans

A reduction in the basal metabolic rate (BMR) with advancing age has been observed in a number of studies. Some researchers have attributed the decrease in BMR associated with aging to a change in body composition, i.e., an increase in body fat mass (FM) and a decrease in fat-free mass (FFM) (9, 16). Shock et al. (36) related changes in resting metabolic rate (RMR) to alterations of the water content of the body. They demonstrated a reduction in total body water (TBW) and intracellular water but no change in the extracellular water content in older individuals. This was interpreted to be a loss of functioning cells with increasing age. However, when the RMR was adjusted for the differences in TBW or intracellular water, there was no significant difference between young and older subjects. Calloway and Zanni (3) observed a 13% reduction in RMR in six healthy older men (63–77 yr) compared with younger men; however, RMR adjusted for total body K+ was similar between the two groups. Still, in other studies, in which changes in body composition were taken into account, older individuals had a significantly lower BMR compared with young subjects (11, 18, 24, 43). This would indicate that a quantitative reduction in FFM alone cannot explain the lower BMR observed in older subjects. The work of Tzankoff and Norris (42) showed that after 45 yr of age there was a progressive reduction of the RMR, which was related to a concomitant reduction in skeletal muscle mass (measured by 24-h urinary creatinine excretion). They concluded that an age-related decrease in skeletal muscle mass accounted for all the reduction in RMR seen with increasing age. Recent data confirm the significant contribution of skeletal muscle to variance in BMR (52).

FFM is not a single homogenous mass but is composed of tissues and organs that differ in mass and rate of metabolic activity (5). For example, in relative terms, bone mineral is energetically inert and skeletal muscle has a low metabolic rate in the resting state, whereas organ and visceral tissues have a relatively high metabolic rate in the resting state (5, 8). A reduction in skeletal muscle with no change in organ tissue mass would result in a higher proportion of organ tissue within FFM. For the same amount of FFM, one could then expect older subjects to have a higher BMR, in comparison to young subjects. Elia (5) has suggested that such changes in the composition of FFM may contribute to the abnormally high energy expenditure that has been observed in certain disease states. However, the observation of a higher BMR adjusted for FFM, in older individuals, has never been made. Instead, most studies have demonstrated either a similar or lower BMR after adjusting for differences in FFM between older and young subjects (11, 18, 24, 43). If one accepted the above alteration in the composition of FFM per se, then the only way the BMR of older individuals could be similar or lower than in younger subjects would be for the metabolic activity of the components of fat-free tissue to be reduced. Theoretically, similar arguments have been proposed to explain the lower BMR and whole body protein turnover of chronically energy-deficient individuals in whom skeletal muscle mass, but not nonskeletal muscle mass, was significantly reduced (39, 40). Therefore, we hypothesized that the BMR of healthy older individuals would be lower than that of young subjects, even after adjusting for differences in the mass of components of fat-free tissue.

Most previous studies on BMR had employed a two-compartment model of body composition (11, 18, 24, 42, 43). We, however, were interested in partitioning the body into components with distinctly different metabolic rates. Hence, we used a model incorporating four tissue compartments: fat, bone mineral, appendicular lean tissue mass (ALTM), and nonappendicular lean tissue mass (NALTM). With the exception of a small amount of skin, connective tissue, etc., the fat-free soft
tissue of the appendages is almost entirely skeletal muscle (14). Wang et al. (44) have shown that ALTM accounts for almost 80% of the total skeletal muscle mass in young males. Based on these observations, we validated dual-energy X-ray absorptiometry (DEXA)-derived total skeletal muscle mass to that estimated from 72-h urinary creatinine excretion while the subjects were on a meat-free diet, by using p-aminobenzoic acid to check for completeness of urine collection (38). The mean difference of $-0.26 \pm 0.88$ (SE) kg was not significant and unrelated to the mean of the two measurements (1, 38). Whereas this proximate relationship between ALTM and total skeletal muscle mass holds true for young men, there remains the possibility that it may differ in women or older age groups (38, 44). Hence, NALTM would include, in addition to organs/viscera, a small, perhaps variable, portion of skeletal muscle. We have made no attempt to separate out this skeletal muscle component from NALTM. Instead, we have worked on the assumption that ALTM and NALTM are largely representative of total skeletal muscle mass and organ/visceral tissue mass, respectively, in the groups studied. The data of Svendsen et al. (41) support such an assumption, since DEXA-derived trunk LTM (analogous to NALTM in this study) was a better predictor of resting energy expenditure than was peripheral LTM (analogous to ALTM).

METHODS

Experimental Design

The study was cross-sectional in nature. BMR was measured by indirect calorimetry, and body composition was measured by DEXA in all subjects. DEXA measurements of body composition were validated against deuterium oxide ($^2$H$_2$O) dilution in a subset of these subjects. All variables were compared between a young and an older group of healthy Australians of European descent.

Subjects

Subjects from two age groups were recruited by advertisement in the local media and by personal approach. All were resident in Melbourne, Australia. The subjects in the first group were aged between 18 and 35 yr, whereas in the second group participants were over 50 yr of age. Inclusion criteria were as follows: 1) absence of clinical signs or symptoms of chronic disease; 2) weight stability (± 2 kg for preceding 12 mo); 3) not on any medication that could affect metabolic rate or body composition; 4) body mass index in the range of 20–30 kg/m$^2$; and 5) resting diastolic blood pressure < 90 mmHg. All subjects gave written informed consent to participate in the study. Deakin University Ethics Committee approved the experimental protocol, and all measurements were made at the clinical rooms of the Toorak campus of Deakin University.

Anthropometry

Standing height was measured with a stadiometer fixed to the wall and recorded to the nearest 0.1 cm. Body weight, recorded to the nearest 100 g on a beam balance, was measured immediately after voiding, with subjects wearing light indoor clothing and no shoes. Mid arm, waist, and hip circumferences were measured as described by Callaway et al. (2). Body Composition by DEXA

System preparation. Quality assurance tests, as described by the manufacturer (Lunar, Madison, WI), were performed each morning to check the operation of the DEXA system before the subjects were scanned. No scans were performed until a valid quality assurance test was run.

Subject preparation. Subjects were questioned about recent fractures, metal implants, and treatments that could affect bone density. Subjects had not ingested, or had been injected with, any radionuclide or radiopaque agents in the previous 3–5 days. All young female subjects were offered a spot pregnancy test to ensure that they were not pregnant. The subjects were requested to remove any material that could attenuate the X-ray beam. Such materials included jewelry, watches, and clothing with zippers, snap buckles, and buttons. They were asked to wear a cotton examination gown and remove their shoes for the duration of the scan. They were then asked to lie supine on the scan table as required by the manufacturer. Subjects were asked not to move after they had been correctly positioned on the table. Ankles and knees were strapped firmly together. This served the dual purpose of greater comfort and immobilization of the legs during the scan.

Scan details. A typical scan lasted 10 min, and the subject received 0.02 mrem of radiation. The maximum scan time was determined by the total area to be scanned (depending on the scan length and width values). Typical scan times were, however, shorter, as the auto width and auto length functions were employed, which adjusted the scan width and length on locating the subject’s bone mass. All subjects were scanned by using the fast 150-μA mode, with a voltage of 76 kV being applied to the X-ray tube.

Analysis of total body DEXA scans. Lunar software (Version 1.3) was used to calculate total and regional body composition. The regions of interest were indicated on screen by analysis markers. The analysis program identified four major anatomical regions: head, arms, legs, and trunk (which included ribs, pelvis, thoracic spine, and lumbar spine). The extended research mode of the analysis program was used to determine bone mineral mass (BMM), LTM, and FM, in grams, for each anatomical region and the body as a whole. ALTM was obtained from the sum of the LTM in the four limbs; NALTM was obtained by subtracting ALTM from LTM. DEXA FFM (FFMDEXA) was obtained by subtracting FM from body weight.

DEXA scans were performed on five subjects on five separate occasions over a period of 2 wk to assess intrindividual variability. The coefficient of variation (CV) of FM was 2.2%, that of LTM was 1.7%, and of BMM was 1.0% values that are comparable to those from the literature (21). The CVs of estimates of ALTM and NALTM were 2.5 and 2.7%, respectively, values that are comparable to those from the literature (10, 11, 23).

Estimation of TBW

TBW was measured by $^2$H$_2$O dilution in a subset of subjects. A 10-ml fasting blood sample was taken from the subject immediately before and 2 h after the oral administration of 10 g of $^2$H$_2$O (99.8%, Australian Nuclear Science and Technology Organisation, Lucas Heights, NSW, Australia). Blood samples were centrifuged at 4°C for 10 min, and plasma was separated and frozen at −20°C until nuclear magnetic resonance (NMR) analysis was performed. $^2$H$_2$O concentrations were determined as described by Khaled et al. (17).
NMR analysis. Plasma samples were thawed and vortexed. An external standard of 1% deuterated trifluoroacetic acid in benzene (Sigma Chemical, St. Louis, MO) was sealed in a 5-mm NMR tube and placed coaxially into a 10-mm NMR tube containing ~3 ml of plasma. 2H2O spectra for each plasma sample were obtained by using a Jeol NMX270 NMR spectrometer (Jeol, Tokyo, Japan). An operating frequency of 41.47 MHz was used with a recycle time of 1.238 s. Two thousand and forty eight sample points were determined across a 900-Hz observation range. The digital resolution was 0.88 Hz. The instrument was shimmed on 2H2O and then run unlocked, without spinning. Each sample was scanned 128 times to obtain a good signal-to-noise ratio. Results from the NMR analysis were then transferred to an IBM-compatible computer. The spectra were analyzed by using the NUTS software package (Acorn NMR, CA), and peaks for the external standard and plasma sample were obtained following Fourier transformation and phasing. The peak areas of the external standard (which was arbitrarily assigned a peak area of 1) and of the plasma sample were integrated by using the NUTS software package. The peak area ratio (PAR) of the plasma sample to the external standard was then obtained. PAR was also obtained by using standard solutions of known 2H2O enrichment (ranging from 0.01 to 0.05 g/100 ml deionized distilled water), together with a distilled water blank. The relationship of the PAR to 2H2O enrichment of the standard solutions was then obtained by regression analysis. The 2H2O enrichment of the plasma samples, collected before and 2 h after the dose of 2H2O, was then estimated by using this regression equation. The change in 2H2O enrichment was determined by subtracting the predose enrichment from the 2-h postdose enrichment.

TBW was calculated as follows.

\[
\text{TBW (kg)} = \frac{\text{mass of } ^2\text{H}_2\text{O dose} \times \text{conc. of } ^2\text{H}_2\text{O dose} \times \text{change in } ^2\text{H}_2\text{O enrichment of plasma sample 2 h after dose}}{1,000} - 0.3^\dagger
\]

where conc is concentration, * indicates value estimated at 4%, and † is correction for mass of water (0.3 kg) administered with 2H2O dose.

FFM was estimated from TBW assuming a hydration of 73.2% (28). FM was calculated from the difference of body weight and FFM and was also expressed as a percentage of body weight.

In five subjects, plasma samples (both predose and 2 h postdose) were analyzed by NMR in triplicate. The PAR obtained from the NUTS software package on each of the three occasions was used to estimate the TBW in each subject. There were no significant differences between the three estimates of TBW in each of the five subjects on an analysis of variance for repeated measures (P = 0.33), with a within-sample CV of 1.96%.

BMR

The BMR was measured by indirect calorimetry using a Deltatrac II metabolic monitor (Datex, Finland), an open-circuit ventilated-canopy measurement system. The measurements were conducted under standardized conditions (29): subjects were lying 1) at complete physical rest, 2) in a thermally neutral environment, 3) 12-14 h after their last meal and a minimum of 8 h of sleep, 4) awake and emotionally undisturbed, and 5) without disease and fever.

The Deltatrac was calibrated by using a calibration gas mixture of oxygen (95%) and carbon dioxide (5%) (Quickcal, Datex, Finland) each morning before the BMR measurement. Airflow rates through the canopy (46.5 l/min) were checked by means of ethanol-burning tests, as described by the manufacturer (Datex, Finland), conducted once each month during the 3 mo of data collection. Performance of the Deltatrac monitor was also checked by monitoring the ratio of carbon dioxide produced to oxygen consumed during the ethanol burns. The mean (±SD) ratio for the last 15 min of the tests was 0.66 (±0.02), which was within the manufacturer’s recommended range of 0.64–0.69.

In a subgroup of subjects (n = 7), BMR and body weight were measured under similar conditions on three separate occasions, 2–4 wk apart. Intraindividual CV in BMR was 2.9%, whereas that for body weight was 0.9%, similar to other published values (4, 37).

Measurement Protocol

Subjects were transported to the laboratory early in the morning (7–9 AM) after a 12-h fast and a minimum of 8-h sleep while keeping physical activity to a minimum. Subjects were also requested to abstain from any strenuous exercise for 36 h before the BMR measurement. On arriving, subjects were asked to void and then asked to lie down for a mandatory 30-min rest period, during which time the Deltatrac was calibrated. During this period, a fasting blood sample was collected in a subset of subjects (n = 36). This was followed by the oral administration of 10 g of 2H2O. At the end of the mandatory rest period, the canopy of the Deltatrac was placed over the head of the subject. The subject was asked to remain awake and motionless, as much as possible, and the 35-min BMR measurement (as described earlier) commenced. We have shown earlier that this protocol yields a BMR not significantly different from a BMR measured immediately on waking, following an overnight stay in the laboratory (37).

After the BMR measurement, subjects were asked to void again, remove all jewelry and metal, and change into hospital gowns to have their body weight, height, and body composition measured. The DEXA scan was then carried out as described previously. A final 10-ml blood sample was collected 2 h after the administration of the 2H2O.

Physical Activity and Total Energy Expenditure

All subjects were asked to maintain a 3-day (nonconsecutive) physical activity diary of days most representative of their habitual activity pattern, including 1 weekend day. The diary consisted of ninety six 15-min blocks for each of the 3 days. Subjects were asked to write down the nature of the activity predominantly performed during each 15-min block. These activities were then coded from one to nine, depending on the type and intensity of activity. Each block was then appropriately coded, and the total number of 15-min blocks at each of the 9 levels of activity was determined. Energy expenditure at each level of activity was obtained by multiplying the BMR (kJ/15 min) by an activity factor obtained from the literature (7), appropriate for the type of activity being performed, and by the number of 15-min blocks for which the activity was performed during the day. The sum of the energy expenditure associated with the nine levels of activity over 5 days gave total energy expenditure (TEE, kJ/day). Physical activity levels (PAL) were calculated by dividing the mean...
Table 1. Anthropometric characteristics

<table>
<thead>
<tr>
<th>Age, yr</th>
<th>Young Subjects (n = 38)</th>
<th>Older Subjects (n = 24)</th>
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<tbody>
<tr>
<td></td>
<td>23 ± 3</td>
<td>62 ± 8*</td>
</tr>
<tr>
<td>Height, cm</td>
<td>169.7 ± 7.7</td>
<td>170.4 ± 7.5</td>
</tr>
<tr>
<td>Weight, kg</td>
<td>65.9 ± 10.9</td>
<td>72.6 ± 10.8*</td>
</tr>
<tr>
<td>Body mass index, kg/m²</td>
<td>22.7 ± 3.2</td>
<td>24.9 ± 3.4*</td>
</tr>
<tr>
<td>Waist circumference, cm</td>
<td>73.5 ± 8.3</td>
<td>85.1 ± 13.5*</td>
</tr>
<tr>
<td>Hip circumference, cm</td>
<td>95.5 ± 6.2</td>
<td>100.0 ± 6.7*</td>
</tr>
<tr>
<td>Waist-to-hip ratio</td>
<td>0.77 ± 0.06</td>
<td>0.85 ± 0.10*</td>
</tr>
</tbody>
</table>

Values are means ± SD. *Significantly different (P = 0.01) by a 2-way ANOVA from young subjects; there was no significant age × gender group interaction for any of the variables studied.

TEE (kJ/day) over 3 days by the BMR (kJ/day) measured in each subject.

Thyroid Hormones

In a subset of the young (n = 16) and older (n = 20) subjects, a 10-ml fasting blood sample was taken from the antecubital vein. The blood sample was centrifuged at 4,000 rpm for 10 min, and the plasma was separated and stored at −20°C. Plasma concentrations of thyroxine (T₄) and 3,3',5-triiodo-L-thyronine (T₃) were measured by radioimmunoassay using a coated-tube radioimmunoassay kit (Spectria, Orion Diagnostica, Finland) and a LKB Wallac multigamma 1261 gamma counter (Wallac Oy, Turku, Finland). Intra-assay variation was <4%, whereas interassay variation was <6% for both assays.

Statistics

Data were analyzed by using the SPSS for Windows (Version 6.1, SPSS) statistical software package. All data are presented as means ± SD unless otherwise stated. Anthropometric, body composition, energy expenditure, physical activity, and hormonal data were compared between age and gender groups, by using a two-way ANOVA. Estimates of FFM obtained by DEXA and from TBW were compared by the method suggested by Bland and Altman (1). This method requires the absolute difference between the two measurements in question (FFM estimated from TBW and DEXA, in this case), when made in the same individual, to be small and statistically unrelated to the mean of the two measurements.

BMR (dependent variable) was analyzed for differences, between the two age (0 = young, 1 = older subjects) and gender groups (0 = women, 1 = men) studied, by stepwise regression analysis with 1) body weight; 2) FFM and FM (2 compartments); 3) LTM, FM, and BMM (3 compartments); and 4) FM, BMM, NA_LTM, and A_LTM (4 compartments), as independent variables. BMR was also similarly analyzed in each age group separately, and the regression coefficients (slopes) for each corresponding compartment, and constant (intercept) of each body-composition model, were compared between the two age groups studied by testing for equality of slopes and intercepts as described by Kleinbaum et al. (19).

RESULTS

Of the 113 subjects recruited, 62 met all inclusion criteria. These consisted of 38 young subjects (15 men, 23 women) and 24 older subjects (12 men, 12 women). Of the 38 young subjects, 23 were students (1 man and 22 women), whereas one of the older women was also a student. The young women studied were not on oral contraceptive agents of any kind; however, four of the older women were on hormone-replacement therapy. None of the subjects studied performed any regular weight training or muscle-building exercises.

Anthropometry

The anthropometric characteristics of the volunteers are summarized in Table 1. The older subjects were significantly heavier than the young subjects (P = 0.007), and men were significantly heavier (P < 0.0005) and taller than women (P < 0.0005). The older subjects and men had a significantly higher BMI than did the young subjects (P = 0.012) and women (P = 0.047), respectively. Waist (P < 0.0005) and hip (P = 0.015) circumferences were significantly higher in the older age group. However, waist circumference (P < 0.0005), but not hip, was significantly larger in men. The waist-to-hip circumference ratio was significantly higher in older subjects (P < 0.0005) and men (P < 0.0005), compared with younger subjects and women, respectively. There were no significant age × gender group interactions for any these variables.

Body Composition

Body composition from DEXA was measured in all 62 subjects. In a subset of 35 subjects (15 young, 20 older), body composition was also estimated from TBW obtained by 2H₂O dilution. A comparison of FFM obtained by DEXA (FFM_DEXA, 52.9 ± 10.0 kg) and from TBW (FFM_TBW, 53.5 ± 9.8 kg), yielded no significant difference on a paired t-test (P = 0.31). Also, the bias (FFM_DEXA − FFM_TBW, 0.56 ± 3.2 kg) of the two methods was not significantly correlated (r = 0.12, P = 0.82) to the mean FFM (53.2 ± 9.8 kg) obtained by the two methods. On a paired t-test, the sum of DEXA-derived LTM and BMM compared with our estimate of FFM_DEXA (i.e., subtracting DEXA-derived FM from body weight) was not significantly different in either the young (mean difference ± SD, 0.09 ± 0.49 kg; P = 0.29) or older subjects (0.06 ± 1.48 kg; P = 0.85). An estimate of the “hydration” of FFM was obtained in these subjects (n = 35) by dividing TBW by FFM_DEXA (49), the 95% confidence interval (72.5, 75.4%) included the accepted normal of 73.2% (28). A comparison of hydration thus obtained between the young (75.2 ± 3.9%) and older (73.0 ± 4.5%) subjects and between men (73.5 ± 4.0%) and women (74.8 ± 5.0%), using a two-way ANOVA, showed no significant difference between either the age (P = 0.12) or gender (P = 0.14) groups; nor was there a significant age × gender group interaction (P = 0.21). These results suggest that the estimates of FFM (and, by extension, FM) by DEXA are comparable to those obtained by 2H₂O dilution in both the young and older subjects.

The older subjects had significantly higher FM in absolute terms (P < 0.0005) and also when expressed as a percentage of body weight (P < 0.0005). However, there were no significant differences in FFM_DEXA (P = 0.858) or LTM (P = 0.894) between the two age groups. Men had significantly more FM in absolute terms (P =
and physical-activity data

Table 2. Body composition and metabolic and physical-activity data

<table>
<thead>
<tr>
<th></th>
<th>Young Subjects (n = 38)</th>
<th>Older Subjects (n = 24)</th>
</tr>
</thead>
<tbody>
<tr>
<td>FFM, kg</td>
<td>49.5 ± 10.2</td>
<td>49.3 ± 9.7</td>
</tr>
<tr>
<td>FM, kg</td>
<td>16.4 ± 6.7</td>
<td>23.3 ± 7.1*</td>
</tr>
<tr>
<td>Fat (% body wt)</td>
<td>24.9 ± 9.0</td>
<td>32.2 ± 8.5*</td>
</tr>
<tr>
<td>BMM, kg</td>
<td>2.9 ± 0.5</td>
<td>2.9 ± 0.5</td>
</tr>
<tr>
<td>BMD, g/cm²</td>
<td>1.20 ± 0.10</td>
<td>1.18 ± 0.11</td>
</tr>
<tr>
<td>LTM, kg</td>
<td>46.1 ± 9.7</td>
<td>45.9 ± 9.3</td>
</tr>
<tr>
<td>ALTM, kg</td>
<td>20.9 ± 4.9</td>
<td>19.6 ± 4.4*</td>
</tr>
<tr>
<td>NAALTM, kg</td>
<td>25.2 ± 5.0</td>
<td>26.3 ± 5.3</td>
</tr>
<tr>
<td>ALTM/LTM, %</td>
<td>45 ± 2</td>
<td>43 ± 3</td>
</tr>
<tr>
<td>NALTM/LTM, %</td>
<td>55 ± 2</td>
<td>57 ± 3</td>
</tr>
<tr>
<td>BMR, kJ/day</td>
<td>6,184 ± 954</td>
<td>5,726 ± 761*</td>
</tr>
<tr>
<td>Fasting RQ</td>
<td>0.85 ± 0.05</td>
<td>0.83 ± 0.06</td>
</tr>
<tr>
<td>TEE, kJ/day</td>
<td>9,205 ± 1,570</td>
<td>9,467 ± 1,725</td>
</tr>
<tr>
<td>PAL</td>
<td>1.57 ± 0.14</td>
<td>1.64 ± 0.14</td>
</tr>
</tbody>
</table>

Values are means ± SD. For TEE and PAL, n = 21 for young subjects and n = 22 for older subjects. FFM, fat-free mass; FM, fat mass; BMM, bone mineral mass; BMD, bone mineral density; LTM, lean tissue mass; ALTM, appendicular LTM; NALTM, nonappendicular LTM; TEE, basal metabolic rate; RQ, respiratory quotient; TEE, total energy expenditure; PAL, physical activity level. Significantly different (*P < 0.01; †P < 0.05) by a 2-way ANOVA from young versus older subjects; there was no significant age × gender group interaction in any of the variables studied.

0.005 and also when expressed as a percentage of body weight (P < 0.0005), compared with women. However, they had significantly more FFMDEXA (P < 0.0005) and LTM (P < 0.0005) than did the women. There was no significant difference in BMM between the young and older subjects (P = 0.602), but men had significantly greater BMM than women (P < 0.0005). There were no significant age × gender group interactions for any of these variables (Table 2).

ALTM tended to be lower in the older subjects, compared with the younger subjects, but this difference was just short of statistical significance (P = 0.056). However, NALTM was not significantly different between the two groups (P = 0.122). The ratio of ALTM to LTM was significantly lower (P < 0.0005), whereas that of NALTM to LTM was significantly higher (P < 0.0005) in the older subjects compared with the young subjects (Table 2). ALTM (P < 0.0005) and NALTM values (P < 0.0005) were significantly lower in women compared with men, as was the ratio of ALTM to LTM (P = 0.019). However, the ratio of NALTM to LTM was significantly higher in the women compared with the men (P = 0.019). There were no significant age × gender group interactions for any of these variables.

Energy Expenditure and PAL

Absolute BMR was significantly lower in older subjects compared with the young subjects (P = 0.006) and in the women compared with the men (P < 0.0005). Fasting respiratory quotients, measured in all 62 subjects, were not significantly different between age (P = 0.186) or gender (P = 0.950) groups. There was no significant age × gender group interaction for either of these variables (Table 2).

On stepwise regression analysis, with BMR as the dependent variable and body weight, age, and gender groups as the independent variables, there were significant differences between the two age and gender groups in BMR (Table 3). When body composition variables replaced weight, the significant difference in BMR between the young and older subjects persisted. However, the gender differences were no longer apparent, and BMM was excluded from the equations (Table 3). Regardless of the model of body composition employed, there were significant differences in the adjusted BMR between the two age groups studied, the older group of subjects having a BMR ~600–650 kJ/day or 10% lower than the young group. ALTM accounted for 78.4% of the total variance in BMR when the four-compartment model of body composition was used, whereas NALTM, FM, and age group accounted for 4.0, 4.0, and 1.8%, respectively.

Age group-specific regression coefficients were obtained for each compartment of each body composition model. The older subjects had significantly lower (P < 0.05) coefficients for FFM, LTM, NALTM, and ALTM for all models of body composition employed (Table 3).

TEE and PAL estimates were obtained in 21 young and 22 older subjects studied. TEE (P = 0.435) and PAL (P = 0.133) were not significantly different between age groups. However TEE (P < 0.0005) and PAL (P = 0.006) were significantly higher in men compared with women. There were no significant age × gender group interactions for either of these variables. On pooling the data, for the 43 young and older subjects, PAL was significantly correlated with FFMDEXA (r = 0.49; P = 0.001), LTM (r = 0.47; P = 0.001), ALTM, (r = 0.39; P = 0.009), and NALTM (r = 0.50; P = 0.001); although it tended to

Table 3. Regression analyses of BMR on age and gender groups and on body weight and composition variables

<table>
<thead>
<tr>
<th>Body-Composition Model Employed</th>
<th>r²</th>
<th>SE, kJ/day</th>
<th>Age group</th>
<th>Gender</th>
<th>Body wt</th>
<th>FM</th>
<th>FFM</th>
<th>LTM</th>
<th>NALTM</th>
<th>ALTM</th>
<th>Constant, kJ/day</th>
</tr>
</thead>
<tbody>
<tr>
<td>One-compartment</td>
<td>0.90</td>
<td>401</td>
<td>-870 ± 110</td>
<td>657 ± 125</td>
<td>51 ± 6</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>2.541 ± 360</td>
</tr>
<tr>
<td>Two-compartment</td>
<td>0.89</td>
<td>310</td>
<td>-612 ± 91</td>
<td>x</td>
<td>-</td>
<td>25 ± 6</td>
<td>85 ± 4</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>1.569 ± 248</td>
</tr>
<tr>
<td>Three-compartment</td>
<td>0.88</td>
<td>318</td>
<td>-645 ± 93</td>
<td>x</td>
<td>-</td>
<td>29 ± 6</td>
<td>-</td>
<td>89 ± 4</td>
<td>-</td>
<td>-</td>
<td>1.595 ± 254</td>
</tr>
<tr>
<td>Four-compartment</td>
<td>0.88</td>
<td>321</td>
<td>-644 ± 105</td>
<td>x</td>
<td>-</td>
<td>29 ± 6</td>
<td>-</td>
<td>89 ± 20</td>
<td>90 ± 22</td>
<td>-</td>
<td>1.596 ± 261</td>
</tr>
</tbody>
</table>

Values for regression coefficients and constants are means ± SE for all subjects (n = 62). SE, SE of predicted BMR; x, gender excluded on stepwise regression; -, variable not considered as a predictor on stepwise regression. *All regression coefficients and constants significantly different from zero (P < 0.001).
be inversely correlated with FM, it was just short of statistical significance \((r = -0.30; P = 0.052)\) (Table 3). PAL, however, was not significantly correlated with BMR \((r = 0.27; P = 0.083)\).

**Thyroid Hormones**

Mean \((\pm SD)\) plasma \(T_3\) [young \((n = 16)\) 1.91 \(\pm 0.26\); older subjects \((n = 20)\) 1.79 \(\pm 0.33\) nmol/l] and \(T_4\) [young \((n = 16)\) 83.3 \(\pm 11.7\); older subjects \((n = 20)\) 84.8 \(\pm 12.2\) nmol/l] concentrations were not significantly different between the two age groups \((T_3, P = 0.244; T_4, P = 0.706)\) or gender groups \((T_3, P = 0.06; T_4, P = 0.208)\), nor was there a significant age \(\times\) gender group interaction.

**DISCUSSION**

A low relative metabolic rate is one risk factor for weight gain (31–33). Hence, the demonstration of a relatively low BMR in older subjects is of importance, as it would contribute to the high prevalence of overweight and obesity in this age group. The relationship of BMR to FFM in older individuals is, however, confounded by a change in the composition of FFM per se. Hence, it is important to account for these changes when comparing the BMR of young and older subjects (46). This study attempted such a comparison, with the expectation that, in the older individuals, there would be a reduction in metabolic rate, even after accounting for changes in the mass of components of the fat-free tissue.

**DEXA-Derived Body Tissue Compartments**

The use of DEXA provided a four-compartment model of body composition that included FM, BMM, \(A_{\text{LTM}}\), and \(N_{\text{LTM}}\). Fuller et al. (12) concluded that DEXA enabled valid and reproducible estimation of fat, fat-free soft tissue, and bone and limb muscle mass. Additionally, evidence in the literature suggested that DEXA-derived FM is not affected by the hydration status of the individual (10, 13, 26). However, there are concerns that the partitioning by DEXA of soft tissue into FM and LTM may be inaccurate (15). We derived FFM\(_{\text{DEXA}}\) by subtracting DEXA-derived FM from body weight. In the present study, FFM (and FM) obtained independently from TBW and DEXA was not significantly different in the subset of 35 subjects in whom both these measurements were made. In addition, the hydration coefficient (ratio of TBW to FFM\(_{\text{DEXA}}\)) was not significantly different between the young and older subjects and was similar to the commonly accepted value of 0.732. Given the excellent precision and accuracy of DEXA-derived measurements of BMM (21, 23), and the validation of the DEXA-derived estimates of FFM and FM, we were confident of the accuracy of our estimates of LTM by DEXA. The partitioning of the limbs from the trunk was carried out by using standard methodology and the software package provided by Lunar. The precision of the technique in our laboratory had a CV of 2.5% for \(A_{\text{LTM}}\) and 2.7% for \(N_{\text{LTM}}\), values that are within the range of those obtained by other investigators in this field (10, 11, 23).

**BMR and the Composition of FFM**

\(A_{\text{LTM}}\) was the only compartment, both in absolute terms and as a percentage of total LTM, that was lower in the older subjects (Table 3). This resulted in a relatively greater proportion of \(N_{\text{LTM}}\) within LTM in older individuals. In such a situation for the same FFM, one could expect older individuals to have a higher BMR. Elia (5) has proposed this change in the proportion of metabolically active tissues (e.g., organs) to less active tissues (e.g., muscle) as being one of the several possible causes for the hypermetabolic state observed in some disease conditions. However, a higher BMR adjusted for FFM in older subjects has not been reported in the literature. Most recent studies support the finding of a “similar” (3, 16, 36) or a “lower” BMR in older subjects (11, 18, 24, 43), once data are adjusted for differences in FFM. We argue that the only way BMR adjusted for FFM can be similar or lower in older subjects is for the metabolic rate of the tissues that comprise FFM to also be reduced.

<table>
<thead>
<tr>
<th>Body-Composition Model Employed</th>
<th>(r^2)</th>
<th>SE, kJ/dy</th>
<th>Young subjects ((n = 38))</th>
<th>Older subjects ((n = 24))</th>
</tr>
</thead>
<tbody>
<tr>
<td>Regression Coefficients*</td>
<td></td>
<td></td>
<td>FFM</td>
<td>FFM</td>
</tr>
<tr>
<td>Two-compartment</td>
<td>0.91</td>
<td>298</td>
<td>25 (\pm 7)</td>
<td>91 (\pm 5)</td>
</tr>
<tr>
<td>Three-compartment</td>
<td>0.90</td>
<td>303</td>
<td>31 (\pm 8)</td>
<td>–</td>
</tr>
<tr>
<td>Four-compartment</td>
<td>0.91</td>
<td>307</td>
<td>31 (\pm 8)</td>
<td>–</td>
</tr>
<tr>
<td>Two-compartment</td>
<td>0.85</td>
<td>309</td>
<td>26 (\pm 9)</td>
<td>74 (\pm 7)</td>
</tr>
<tr>
<td>Three-compartment</td>
<td>0.84</td>
<td>322</td>
<td>27 (\pm 10)</td>
<td>–</td>
</tr>
<tr>
<td>Four-compartment</td>
<td>0.84</td>
<td>329</td>
<td>27 (\pm 10)</td>
<td>–</td>
</tr>
</tbody>
</table>

Values for regression coefficients and constants are means \(\pm SE\). SE, SE of predicted BMR; –, variable not considered as a predictor on stepwise regression. *All regression coefficients and constants significantly different from zero \((P < 0.05)\). †Significantly different from young subjects on testing for equality of slopes \((P < 0.05)\).
instances, there were significant differences between the age groups studied (Table 3). These results support previous observations of a reduced BMR adjusted for differences in FFM in older, compared with young, subjects (11, 18, 24, 43). On using the four-compartment model for body composition, to adjust for variations in the composition of FFM per se, the BMR of older individuals was still lower by 644 kJ/day. This is indicative of a reduction in the metabolic rate of the tissues, a feature that may predispose to weight gain.

Significantly lower regression coefficients for the A_LTM and N_ALTM compartments of FFM were also observed in the older subjects, compared with the young subjects. If one accepts that these compartments are representative of the whole body skeletal muscle and organ/visceral tissue, respectively, then our results suggest that both these tissue compartments are metabolically less active in older individuals.

BMR and Physical Activity

There is evidence to suggest that physically active older men show very little change in their BMR or body composition (16). Self-reported PAL suggested that the majority of subjects studied were sedentary to moderately active, as defined by the Food and Agriculture Organization/World Health Organization/United Nations University report (8). There was a significant inverse correlation of PAL with FM and a direct correlation with all lean tissue components in this study. However, mean PAL of the young subjects (1.57 ± 0.14) was not significantly different from that of older subjects (1.64 ± 0.14). In addition, PAL was not a significant predictor of BMR on stepwise regression that included body-composition data. It is, therefore, unlikely that the PAL of these subjects influenced their BMR.

Possible Mechanisms Underlying the Reduction in BMR

A lower oxygen consumption and, hence, energy expenditure of some tissues and organs is also supported by the literature. Age-related changes in the oxygen consumption of the heart and hepatomesenteric bed have been documented. Aging is associated with a progressive loss of myocytes (27) and an increase in the rate of degenerative changes, such as lipid deposition, tubular dilation, and lipofuscin deposition (20, 27). In the liver, aging is associated with a decrease in liver volume (7) and a reduction in function, as indicated by a variety of hepatic function tests (7, 22, 35). These structural and functional changes can be expected to affect oxygen utilization and may explain, in part, the lower metabolic activity of the N_ALTM compartment in the older subjects.

There are several other possible mechanisms that may account for an age-related reduction in the metabolic rate. Poehlman et al. (30) examined the possibility that alterations in the Na^+-K^+ pump would contribute to the age-related decline in RMR. They estimated that a reduction in the Na^+-K^+ pump activity may account for a 3% reduction in the RMR of older individuals. Whole body protein turnover can account for between 15 and 20% of the BMR (34, 39, 45, 47), and a reduced turnover of protein has been demonstrated in older individuals (48). In addition, data suggest that the contribution of skeletal muscle to whole body protein turnover decreases with age, with a relatively larger contribution from the visceral organs in the elderly (25, 50, 51).

Morgan and York (24) speculated that factors like thyroid hormones, or the tissue sensitivity to them, may be implicated in the age-related decline in BMR. This study had young and older subjects with similar FFM but differing BMR. In the subset of older subjects in whom thyroid hormone concentrations were measured, plasma concentrations of T3 and T4 were normal and not significantly different from those observed in the young subjects. However, the possibility that the tissue responsiveness to these hormones was diminished cannot be ruled out. This may also be the case with the activity of the sympathetic nervous system. Although the available evidence suggests that aging increases the rate of sympathetic firing, at least in some organs, this is not necessarily translated into greater adrenergic responses (6). Factors such as adrenergic-receptor subsensitivity or uncoupling can blunt end-organ responsiveness (6). Because catecholamines stimulate cellular metabolism, it is conceivable that changes in sympathetic nervous system activity may in part explain the reduction in metabolic rate that occurs with aging.

In summary, the BMR of older individuals is significantly lower than that of young subjects, even after accounting for differences in the composition of FFM per se. We have demonstrated significantly lower regression coefficients for both N_ALTM and A_LTM of older subjects. These results are indicative of a reduction in the metabolic rate of LTM and its components, a feature that would contribute to a low relative BMR. It is likely that age-related gains in body weight are related, in part, to such changes.

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