

The Age-Related Decline in Resting Energy Expenditure in Humans Is Due to the Loss of Fat-Free Mass and to Alterations in Its Metabolically Active Components¹

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ABSTRACT There is conflicting evidence as to whether the age-related decline in resting energy expenditure (REE) can be attributed to *i)* absolute changes in fat-free mass (FFM), *ii)* alterations in the composition of FFM or *iii)* decreasing organ metabolic rates. This study directly addressed the first and second hypotheses by quantification of metabolically active components of FFM assuming constant tissue respiration rates to calculate REE (REEc). REE was measured (REEm) in 26 young (13 females, 13 males, age 22–31 y) and 26 elderly subjects (15 females, 11 males, age 60–82 y) by indirect calorimetry and detailed body composition analysis was obtained using bioelectrical impedance analysis (BIA), dual energy X-ray absorptiometry (DXA), and MRI. Specific organ metabolic rates were taken from the literature. REEm adjusted for differences in FFM was lower in older subjects than in younger control subjects (5.43 ± 0.61 MJ/d compared with 6.37 ± 0.48 MJ/d; $P < 0.001$). Skeletal muscle mass plus liver mass accounted for 86% and 48% of the variance in REE in young and elderly subjects, respectively. The difference between REEm and REEc was 0.03 ± 0.40 MJ/d and -0.36 ± 0.70 MJ/d in young and elderly subjects, respectively. In the elderly 58% of the difference in variance was attributed to heart mass. REEm – REEc was -1.40 ± 0.44 MJ/d in subjects with hypertensive cardiac hypertrophy, i.e., heart mass > 500 g, suggesting a decrease in heart metabolic rate with increasing heart mass. Excluding five elderly subjects with cardiac hypertrophy resulted in agreement between REEm and REEc in the elderly (-0.10 ± 0.48 MJ/d). We concluded that the age-related decline in REE is attributed to a reduction in FFM as well as in proportional changes in its metabolically active components. There is no evidence for a decreasing organ metabolic rate in healthy aging. *J. Nutr.* 133: 2356–2362, 2003.

KEY WORDS: • aging • dual energy X-ray absorptiometry • magnetic resonance imaging • organ mass • resting energy expenditure

Resting energy expenditure (REE)³ per kg body mass varies during the life span. It declines during childhood growth and also with advanced age (1). The age-related decline in energy requirements is thought to affect positive energy balance and favors an increase in fat mass. This reflects a loss in the metabolically active components of the body (e.g., a loss in muscle mass). Both factors are considered as risk factors for age-associated morbidity. Therefore understanding the age-related decline in REE is a fundamental prerequisite in providing a basis for interventions aimed at its attenuation.

It is still a matter of debate whether the age-related decline in REE is merely a function of alterations in body composition

[i.e., reductions and/or changes in the composition of fat-free mass (FFM)] or results from lower organ metabolic rates during aging. FFM is the main determinant of REE accounting for ~65–90% of its interindividual variance (2–5). Metabolically, FFM is a heterogeneous compartment, consisting of internal organs and skeletal muscle mass. The sum of visceral organs and the brain comprises ~5% of body weight but accounts for 70–80% of REE because of a high metabolic rate (6). In contrast, muscle mass comprises ~35% of body weight but accounts for 20% of REE (6). The heterogeneous composition of FFM explains why REE per kg FFM is not constant; REE per kg FFM decreases with increasing body weight because of a disproportional increase of muscle mass (7). It may be hypothesized that the age-related decrease in FFM plus changes in the relative composition of FFM may both add to the age-related decline in REE.

The present knowledge of the metabolically active components of FFM and the impact of the composition of FFM on REE is limited to a few recent studies (8–11). In these studies REE was calculated from detailed body composition analysis by a combined approach weighting the masses of the different

¹ This work was supported by a grant from the Deutsche Forschungsgemeinschaft (DFG Mü 714/8–1) and by Precon, Bickenbach, Germany.

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³ Abbreviations: AT, adipose tissue; BCM, body cell mass; BIA, bioelectrical impedance analysis; BMC, bone mineral content; DXA, dual energy X-ray absorptiometry; ECM, extracellular mass; FFM, fat-free mass; FM, fat mass; MM, skeletal muscle mass; LBM, lean body mass; MAP, mean arterial pressure; OM, organ mass; REE, resting energy expenditure; TBW, total body weight.

tissue compartments [by MRI or computer tomography, and dual energy X-ray absorptiometry, (DXA)] with their specific metabolic rates (3). REE calculated from organ tissue masses (REEc) was then compared to measured REE by indirect calorimetry (REEm) showing a mean prediction error of 83 kJ/d and 96 kJ/d, respectively (9,11). The use of metabolically active components of FFM instead of total FFM reduces the variance in REE prediction. However, the improved prediction model is based on experimentally derived organ metabolic rates that are not specified for age (3). Therefore using this model in elderly subjects assumes constant tissue respiration rates per kg organ mass with aging. If this is correct, no difference in the mean REE prediction error in young and old adults would be expected. This finding could also be interpreted as indirect evidence that the age-related decline in REE is due to changes in body composition rather than to organ metabolic rates. The present investigation was designed to test the hypothesis that the decline in REE with advancing age is mainly attributed to a reduction in quantity and composition of metabolically active components of FFM.

SUBJECTS AND METHODS

The study groups consisted of 26 elderly subjects (15 females and 11 males) age 60 to 82 y (mean age 67.7 ± 6.6 y) and 26 younger control subjects (13 females and 13 males) age 22 to 31 y (mean age 25.4 ± 2.4 y). Young subjects were recruited from students and staff at the University of Kiel. Elderly volunteers were recruited by notice board postings in local supermarkets. All participants were healthy and weight stable. None had a history of recent illness or endocrinopathy. All participants underwent basal physical examination (heart rate, blood pressure, blood glucose and lipid profile). Mean arterial pressure (MAP) was calculated as $RR_{diastolic} + ((RR_{systolic} - RR_{diastolic})/3)$. Each subject had a normal physical examination. The prevalence of elderly participants having an elevated blood pressure defined as $>140/90$ mm Hg (mean values for the hypertensive subjects 161 ± 12 mm Hg systolic blood pressure, 90 ± 6 mm Hg diastolic blood pressure) was 38.5%. One elderly subject was taking medication for hypertension. In the elderly group, the prevalence of hypertriglyceridemia (>2.29 mmol/L) and hypercholesterolemia (>5.2 mmol/L) was 11.5% and 38.5%, respectively. One subject was taking drugs that controlled plasma lipoprotein concentrations. All subjects were weight stable two weeks before investigation. The study protocol was approved by the ethical committee of the Christian-Albrechts-Universität zu Kiel. Each subject provided informed written consent before participation.

Study protocol. All volunteers completed a 7-d dietary record before coming to the metabolic unit of the Institut für Humanernährung. REE was then measured by indirect calorimetry (REEm). A description of the procedure, its accuracy, precision and stability is reported elsewhere (11,12). Briefly, measurements were performed between 0700 and 0900 h in a metabolic ward at constant humidity (55%) and room temperature (22°C). The day before testing the subjects had eaten their last evening meal between 1800 and 1900 h. Continuous gas exchange measurements were obtained for 1 h. Data obtained during the first 15 min were omitted. Calibration of the gas analyzers was performed immediately before each measurement.

Body composition analysis. Height was measured to the nearest 0.5 cm with a stadiometer. Weight was assessed by use of an electronic scale coupled to the BOD POD[®]-Body Composition System (Life Measurement Instruments, Concord, CA). Body composition measurements by the use of bioelectrical impedance analysis (BIA) were performed after gas exchange measurements. Dual energy X-ray absorptiometry (DXA) and MRI were performed within 3 d thereafter. Bone mineral content (BMC) and whole body and regional bone-free lean body mass (LBM) were measured by DXA using a Hologic whole body dual-energy X-ray absorptiometer (Hologic QDR 4500A, software version V8.26a:3; Hologic, Waltham, MA). Skeletal muscle mass was calculated from the sum of appending LBM_{DXA} (e.g., LBM_{arms} + legs), using the formula of Kim et al. (13). Skeletal

bone_{DXA} was calculated as $\text{DXA-derived BMC} \times 1.85$ (14). Fat-free mass (FFM_{DXA}) resembles $\text{LBM}_{\text{DXA}} + \text{BMC}_{\text{DXA}}$ and was calculated as body weight minus FM_{DXA} . Adipose tissue (AT_{DXA}) was calculated from FM_{DXA} assuming a fat content of 80%. BIA was performed as described previously (15). A body impedance analyzer (BIA 2000-S, Data Input, Frankfurt, Germany) and the manufacturer's software was used for data analyses to calculate total body water (TBW), body cell mass (BCM) and extracellular mass (ECM). The volume of internal organs (brain, heart, liver, kidneys, spleen) was measured by transversal MRI images. The scans were obtained by use of a 1.5-Tesla Magnetom Vision scanner (Siemens, Erlangen, Germany) (6,11). Volume data were transformed into organ weights using the following densities: 1.036 g/cm^3 for brain, 1.06 g/cm^3 for heart and liver, 1.05 g/cm^3 for kidneys, and 1.054 g/cm^3 for spleen (16). Residual mass was calculated as body mass minus the sum of $\text{brain}_{\text{MRI}}$, $\text{heart}_{\text{MRI}}$, $\text{liver}_{\text{MRI}}$, $\text{kidneys}_{\text{MRI}}$, $\text{skeletal muscle}_{\text{DXA}}$, $\text{skeletal bone}_{\text{DXA}}$ and AT_{DXA} .

Calculation of REE. Calculation of REE (REEc) was based on the sum of 8 body compartments ($\text{brain}_{\text{MRI}}$, $\text{heart}_{\text{MRI}}$, $\text{liver}_{\text{MRI}}$, $\text{kidneys}_{\text{MRI}}$, $\text{skeletal muscle}_{\text{DXA}}$, $\text{skeletal bone}_{\text{DXA}}$, AT_{DXA} and residual mass) times the corresponding tissue-respiration rate, on the basis of specific tissue-metabolic rates reported by Elia [(12) eq. 1]. For skeletal bone_{DXA} a specific metabolic rate of $9.63 \text{ kJ}/(\text{kg}\cdot\text{d})$ was assumed (17).

$$\begin{aligned} \text{REEc (kJ/d)} = & (1008 \times \text{brain mass}_{\text{MRI}}) + (840 \times \text{liver mass}_{\text{MRI}}) \\ & + (1848 \times \text{heart mass}_{\text{MRI}}) + (1848 \times \text{kidney mass}_{\text{MRI}}) \\ & + (55 \times \text{skeletal muscle mass}_{\text{DXA}}) + (9.63 \times \text{skeletal bone}_{\text{DXA}}) \\ & + (19 \times \text{adipose tissue}_{\text{DXA}}) + (30 \times \text{residual mass}) \quad (1) \end{aligned}$$

Data analyses. All data are given as mean \pm SD. Statistical analyses were performed using SPSS[®] for Windows 8.0 (SPSS, Chicago, IL). Differences between sex and age groups were analyzed by 2-way ANOVA with Bonferroni post hoc test. Wilcoxon signed ranks test was calculated for related samples (comparison of REEm and REEc in the same group). Pearson's correlation coefficients were calculated for relationships between variables. A multivariate regression analysis was performed using REE as dependent variable. All tests were two-tailed and a *P* value of 0.05 was accepted as the limit of significant difference. REE was adjusted for FFM according to Ravussin and Bogardus (5) by using the following equation:

$$\text{REE}_{\text{adj.}} = \text{REEm} + ((\text{FFM}_{\text{group mean}} - \text{FFM}_{\text{measured}}) \times \text{slope}) \quad (2)$$

The slope is derived from the regression equation between REEm and FFM_{DXA} .

RESULTS

The physical characteristics and resting energy expenditure of the two study groups were assessed (Table 1). Additionally in the elderly, five subjects (four males and one female) with a heart mass > 500 g were analyzed separately. When compared to young subjects the elderly subjects had higher BMI, MAP, ECM_{BIA} and fat mass but lower FFM_{DXA} , skeletal muscle mass_{DXA}, BMC_{DXA} (both for males only) body height and organ masses_{MRI} (brain, liver, kidneys, spleen). Differences in organ masses_{MRI} between age groups remained after adjusting organ mass for FFM_{DXA} (data not shown). There was a close association between FFM_{DXA} and skeletal muscle mass_{DXA} (Fig. 1). This association was similar in both age groups. Measured as well as calculated REE were lower in the elderly group when compared to young men (-20.9% for REEm and -15.5% for REEc, respectively). In the women only the REEm differed between age groups (-11.9%). REEm adjusted for differences in FFM was also significantly lower in older subjects than in the younger control group ($5.43 \pm 0.61 \text{ MJ/d}$ compared with $6.37 \pm 0.48 \text{ MJ/d}$; $P < 0.001$). Com-

TABLE 1

Physical characteristics and energy expenditure of the study population

	Elderly subjects, (n)					
	Young subjects, (n)		Normal cardiac mass		Cardiac hypertrophy	
	Female (13)	Male (13)	Female (14)	Male (7)	Female (1)	Male (4)
Age, y	24.8 ± 2.4	26.2 ± 2.1	69.1 ± 5.3 ^c	64.9 ± 2.7 ^c	66	71.5 ± 5.6
Weight, kg	62.8 ± 9.1	77.3 ± 9.8	69.5 ± 8.6	73.2 ± 15.2 ^d	77.2	89.9 ± 9.7
Height, m	1.70 ± 0.06	1.85 ± 0.07	1.62 ± 0.06 ^a	1.70 ± 0.08 ^{cf}	1.67	1.80 ± 0.07
BMI, kg/m ²	21.8 ± 2.2	22.5 ± 1.8	26.4 ± 2.7 ^c	25.0 ± 3.0 ^b	27.7	28.1 ± 4.3
MAP, mmHg	79 ± 6	86 ± 7	98 ± 9 ^e	101 ± 13 ^b	113.3	109 ± 15
TBW _{BIA} , kg	32.8 ± 3.0	46.2 ± 4.8 ^d	32.7 ± 3.0	40.0 ± 7.7 ^f	36.5	48.1 ± 4.2
BCM _{BIA} , kg	23.8 ± 3.3	35.2 ± 4.2 ^f	21.8 ± 2.5	30.2 ± 5.9 ^f	25.4	32.1 ± 4.7
ECM _{BIA} , kg	14.1 ± 1.3	19.9 ± 2.1 ^d	22.9 ± 2.4 ^c	24.5 ± 6.7 ^{ae}	24.5	24.5 ± 6.7
FFM _{DXA} , kg	43.6 ± 4.7	64.4 ± 7.5 ^e	41.9 ± 4.9	55.1 ± 10.6 ^{af}	49.8	67.6 ± 7.6
MM _{DXA} , kg	20.7 ± 2.7	33.6 ± 3.3 ^f	18.1 ± 2.4	25.9 ± 4.7 ^{cf}	21.1	32.2 ± 3.2
BMC _{DXA} , kg	2.4 ± 0.3	3.2 ± 0.6 ^e	2.0 ± 0.3	2.5 ± 0.3 ^{bf}	2.2	3.2 ± 0.4
OM _{MRI} , kg	3.8 ± 0.3	4.3 ± 0.5	2.9 ± 0.2 ^c	3.2 ± 0.4 ^{ce}	3.1	3.8 ± 0.2
Brain _{MRI} , kg	1.5 ± 0.1	1.6 ± 0.2	1.1 ± 0.1 ^c	1.3 ± 0.1 ^c	1.1	1.2 ± 0.1
Heart _{MRI} , kg	0.3 ± 0.0	0.4 ± 0.0 ^d	0.3 ± 0.1	0.4 ± 0.0 ^e	0.5	0.6 ± 0.1
Liver _{MRI} , kg	1.5 ± 0.2	1.7 ± 0.3	1.1 ± 0.2 ^c	1.1 ± 0.3 ^c	1.1	1.4 ± 0.1
Spleen _{MRI} , kg	0.2 ± 0.0	0.3 ± 0.1 ^d	0.1 ± 0.0 ^b	0.2 ± 0.0 ^c	0.1	0.2 ± 0.1
Kidneys _{MRI} , kg	0.3 ± 0.0	0.4 ± 0.1 ^d	0.2 ± 0.0 ^b	0.3 ± 0.1 ^{be}	0.2	0.3 ± 0.1
Residual, kg	10.3 ± 1.8	18.0 ± 3.5 ^f	10.4 ± 2.3	17.0 ± 4.4 ^f	14.7	20.4 ± 3.4
FM _{DXA} , kg	19.2 ± 5.7	12.9 ± 4.3 ^d	27.6 ± 5.6 ^b	18.1 ± 5.0 ^{ad}	27.4	22.3 ± 4.2
EI, MJ/d	7.66 ± 1.4	11.05 ± 3.3 ^d	7.29 ± 0.9	8.51 ± 1.0 ^{are}	8.31	11.89 ± 1.2
REEm, MJ/d	5.74 ± 0.7	7.24 ± 0.8 ^e	5.09 ± 0.5	5.73 ± 0.8 ^{ce}	4.87	5.58 ± 0.7
REEadj., MJ/d	6.28 ± 0.4	6.46 ± 0.5	5.75 ± 0.4 ^a	5.37 ± 0.5 ^c	5.01	4.54 ± 0.3
REE _c , MJ/d	5.78 ± 0.5	7.18 ± 0.8 ^d	5.09 ± 0.4 ^a	6.07 ± 0.8 ^{be}	5.75	7.11 ± 0.6
REE _m -REE _c , MJ/d	-0.04 ± 0.3	0.10 ± 0.5	-0.01 ± 0.5	-0.33 ± 0.4	-0.89	-1.53 ± 0.3
EI/REEm	1.36 ± 0.3	1.56 ± 0.4	1.42 ± 0.2	1.54 ± 0.3	1.71	2.19 ± 0.4

¹ Values are means ± SD. ^a $P < 0.05$, ^b $P < 0.01$, ^c $P < 0.001$; young vs. elderly subjects of the same sex with normal cardiac mass; ^d $P < 0.05$, ^e $P < 0.01$, ^f $P < 0.001$; females vs. males of the same age group with normal cardiac mass by ANOVA and Bonferroni post hoc test. Abbreviations: MAP, mean arterial pressure; BIA, bioelectrical impedance analysis; TBW, total body water; BCM, body cell mass; ECM, extracellular mass; FFM, fat-free mass; FM, fat mass; DXA, Dual-energy X-ray absorptiometry; MM, skeletal muscle mass; BMC, bone mineral content; OM, organ mass; Residual, residual mass (body weight - MM - OM - adipose tissue - (BMC × 1.85)); EI, energy intake; REEm, measured resting energy expenditure; REEc, calculated REE according to organ/tissue metabolic rates (eq. 1); REEadj., REE adjusted for FFM_{DXA} (eq. 2).

pared with women men had a higher FFM_{DXA}, skeletal muscle mass_{DXA}, BMC_{DXA} and a lower FM_{DXA}. Heart, kidney, spleen and residual masses were also higher in men. In contrast, a higher REEm in men occurred only in the group of young subjects (Table 1). When compared to women REEc was higher in young as well as elderly men. Sex and age differences in REEm-c were similar. In contrast, subjects with cardiac hypertrophy had REEm-c substantially greater (-1.40 ± 0.44 MJ/d) than in subjects with normal heart mass. REEm and

masses of the other organs were similar in these groups. Skeletal muscle mass and the ratio of energy intake to REEm were high in subjects with increased cardiac mass suggesting a high level of physical activity.

Correlation coefficients between REEm and parameters of body composition were summarized (Table 2). In the group of young subjects REEm was closely related to all parameters of body composition except FM_{DXA} (data not shown). In subgroups of males and females correlations for brain, heart and

FIGURE 1 Associations between skeletal muscle mass (MM_{DXA}), OM_{MRI} or heart mass_{MRI} and FFM_{DXA} in 26 young and 26 elderly subjects. FFM, fat-free mass; OM, organ mass.

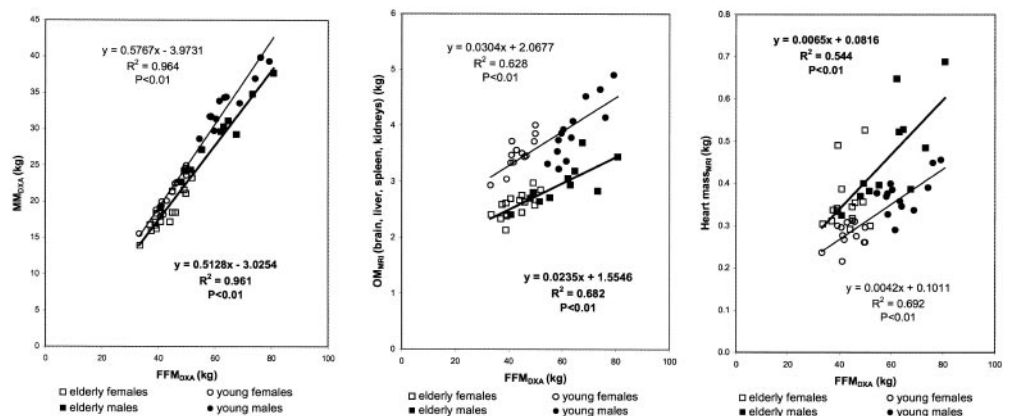


TABLE 2

Pearson correlation coefficients between measured REE (REEm, according to eq. 1) and parameters of body composition in subjects with normal cardiac mass¹

	REEm			
	Young subjects, (n)		Elderly subjects, (n)	
	Female (13)	Male (13)	Female (14)	Male (7)
BMI, kg/m ²	0.72 ^b	0.69 ^b	0.07	0.86 ^a
TBW _{BIA} , kg	0.81 ^b	0.80 ^b	0.55 ^a	0.67
BCM _{BIA} , kg	0.89 ^b	0.71 ^b	0.42	0.65
ECM _{BIA} , kg	0.81 ^b	0.80 ^b	0.50	0.55
FFM _{DXA} , kg	0.91 ^b	0.78 ^b	0.53	0.77
MM _{DXA} , kg	0.94 ^b	0.68 ^a	0.66 ^a	0.65
brain _{MRI} , kg	0.26	0.49	0.42	0.03
heart _{MRI} , kg	0.13	0.46	-0.24	0.26
liver _{MRI} , kg	0.77 ^b	0.82 ^b	0.35	0.93 ^b
spleen _{MRI} , kg	0.53	0.43	0.20	-0.18
kidney _{MRI} , kg	0.54	0.74 ^b	0.27	0.88 ^a
Residual, kg	0.02	0.84 ^b	0.40	0.84 ^a
FM _{DXA} , kg	0.66 ^a	0.35	0.02	0.68

¹ a $P < 0.05$, b $P < 0.01$. Abbreviations: BIA, bioelectrical impedance analysis; TBW, total body water; FFM, fat-free mass; FM, fat mass; DXA, dual-energy X-ray absorptiometry; MM, skeletal muscle mass; BMC, bone mineral content; Residual, residual mass [body weight - MM - OM - adipose tissue - (BMC × 1.85)]; REE, resting energy expenditure; REEc, calculated REE according to organ/tissue metabolic rates (eq. 1).

spleen mass and kidney or residual mass (both for females only) were no longer significant. In females FM_{DXA} also correlated with REEm. In the group of elderly subjects associations between REEm and parameters of body composition were less pronounced and no significant correlations were found between REEm and FM_{DXA}, heart and spleen mass, respectively (data not shown). In subgroups of males and females the only remaining significant correlations with REEm were found for TBW_{BIA} and skeletal muscle mass_{DXA} in females and for BMI, liver, kidney and residual mass in males. Plotting REEm against FFM_{DXA} showed a lower coefficient of determination as well as a lower slope of the regression line in the elderly group when compared with young subjects (Fig. 2). In young subjects FFM_{DXA} accounted for 82% of the variance in REEm. In contrast in the elderly group FFM_{DXA} accounted for 43% of variance in REEm. In a stepwise multiple regression analysis skeletal muscle mass_{DXA} and liver mass_{MRI} accounted for 86% of the variance in REEm in young subjects (eq. 3) but only 48% in elderly subjects (eq. 4).

$$\text{REEm (MJ/d)} = 1.364 \times \text{liver mass} + 0.103 \times \text{skeletal muscle mass} + 1.496 \quad (3)$$

$$\text{REEm (MJ/d)} = 1.271 \times \text{liver mass} + 0.04581 \times \text{skeletal muscle mass} + 2.781 \quad (4)$$

When REEc was plotted against REEm the lines did not regress through zero leaving a considerable y-intercept of 1.1 and 1.0 MJ for elderly and young subjects, respectively (Fig. 3). The difference in REEm-c was plotted against age (Fig. 4). REEm was not different from REEc in young or in elderly subjects. The mean difference between REEm and REEc was similar in the elderly group when compared to young subjects

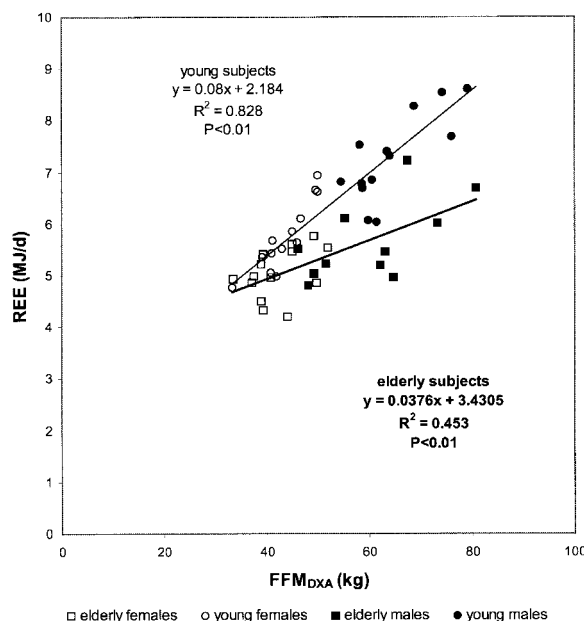


FIGURE 2 REEm plotted against FFM_{DXA} in 26 young and 26 elderly subjects. FFM, fat-free mass; REEm, resting energy expenditure measured.

(-0.36 ± 0.70 and 0.03 ± 0.40 MJ/d). A ±2 SD difference of the mean values in young subjects was considered the cut off criteria for identification of subjects with a high nonconformity of measured and calculated REE. By this means seven elderly subjects with REEm-c > 0.8 MJ/d were identified. Skeletal muscle mass_{DXA}, heart mass_{MRI}, ECM_{BIA} and MAP were higher in this subgroup when compared to the remaining

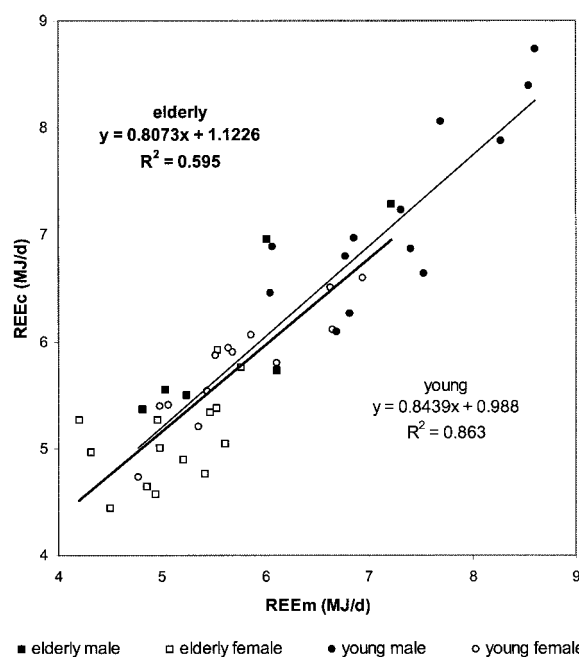


FIGURE 3 REEm plotted against REEc (according to eq. 1) in 26 young and 21 elderly subjects with normal cardiac mass. The dotted line is the line of identity. REEc, resting energy expenditure calculated; REEm, resting energy expenditure measured.

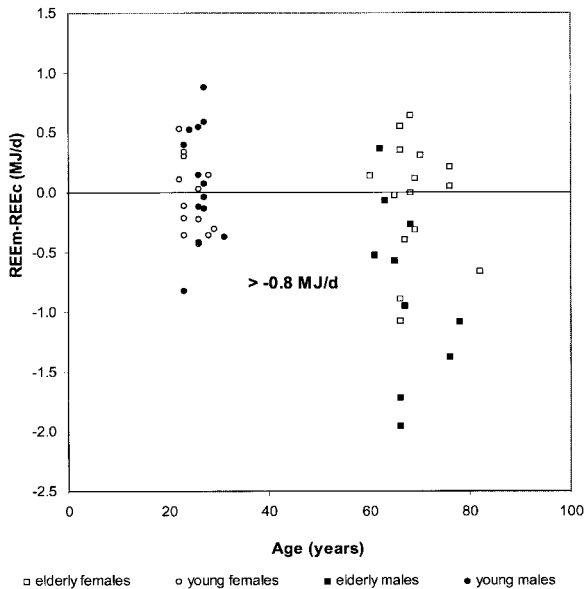


FIGURE 4 Deviation between REEm and REEc according to formula 1 vs. age in 26 young and 26 elderly subjects. REEc, resting energy expenditure calculated; REEm, resting energy expenditure measured.

19 elderly subjects (28.8 vs. 22.5 kg skeletal muscle mass_{DXA} ($P < 0.05$); 0.53 compared with 0.36 kg heart mass_{MRI} ($P < 0.01$), 31.0 compared with 22.9 kg ECM_{BIA} ($P < 0.05$)) and 109 compared with 98 mmHg MAP ($P < 0.05$). Exclusion of five subjects with heart mass_{MRI} > 500 g resulted in a reduced REE prediction error of -0.10 ± 0.48 MJ/d for the remaining 21 elderly subjects. There were positive correlations between MAP and age ($r = 0.69$, $P < 0.01$), ECM_{BIA} ($r = 0.67$, $P < 0.01$), and heart mass_{MRI} ($r = 0.58$, $P < 0.01$), in the whole group of young and elderly subjects.

In a linear stepwise multiple regression analysis using REEm-c as the dependent variable only heart mass_{MRI} entered the prediction model accounting for 58% of the variance in the deviation between REEm and REEc in elderly subjects. In **Figure 5** the respective regression line is shown (REEm-c vs. heart mass).

DISCUSSION

Progressive loss of FFM is a well-established attribute of aging (18). As a consequence, REE is lower in elderly subjects when compared to young control subjects (**Table 1**). Previous results suggest that the loss of FFM with aging cannot fully account for the age-related decrease in REE (13–23). It is estimated that FFM accounts for 75% of intraindividual variance in REE during aging (24). However, in these studies measurements of FFM are based on BIA (19,23), underwater weighing (20–22) and tritium dilution ($^3\text{H}_2\text{O}$) (13,22). These methods may have limitations in assessing the age-related decline in BCM at the expense of extracellular FFM (27). Alternatively the decline in BCM measured by total body potassium fully accounts for the age-related decrease in REE (27,28). These findings do not support the idea that elderly subjects have slower organ metabolic rates compared to young subjects.

In the present study REEm adjusted for FFM_{DXA} was significantly lower in elderly subjects when compared with young

control subjects (-8.4% and -16.9% in females and males, respectively; **Table 1**). This finding suggests a decrease in metabolic rate per FFM with age. However, this does not necessarily mean a decrease in metabolic rate per kg organ mass with age. The underlying cause might be age-related changes in FFM composition. FFM accounted for 82% and only 43% of the variance in REEm in young and elderly subjects, respectively. This finding may be explained by alterations in relative composition of FFM with age (e.g., the proportions of FFM constituents like internal organs and skeletal muscle mass; **Table 1**, **Fig. 1**). Extending the prediction model to distinct metabolically active components of FFM, skeletal muscle and liver mass improved REE prediction by 5% of interindividual variance in elderly subjects. Additionally, the REEc-modeling approach is applicable in the elderly, because REE prediction from specific body composition analysis resulted in an agreement with REEm in elderly subjects (**Table 1**, **Fig. 4**). Therefore our results dispute a decreasing organ metabolic rate in aging but support the hypothesis that the age-related decline in REE is mainly attributed to a reduction in quantity and composition of metabolically active components of FFM.

However, we found evidence that the overestimation of resting energy requirements in elderly subjects is associated with increasing heart mass (**Fig. 5**). Subjects with a high REEm-c value (>0.8 MJ/d) differed substantially in heart mass. Five of the seven subjects had a heart weight > 500 g, which is considered to indicate hypertensive hypertrophy (29,30). In these subjects REEm-c was -1.40 ± 0.44 MJ/d. In fact, in this study MAP correlated with heart weight. Therefore, chronic hypertensive overload leading to enhanced afterload and compensatory cardiac hypertrophy is a likely explanation for our findings in elderly subjects. Although some cellular hypertrophy is a normal result in the aging heart it is unlikely to compensate for progressive age-related cell loss to maintain normal cardiac mass (30). However, despite lower

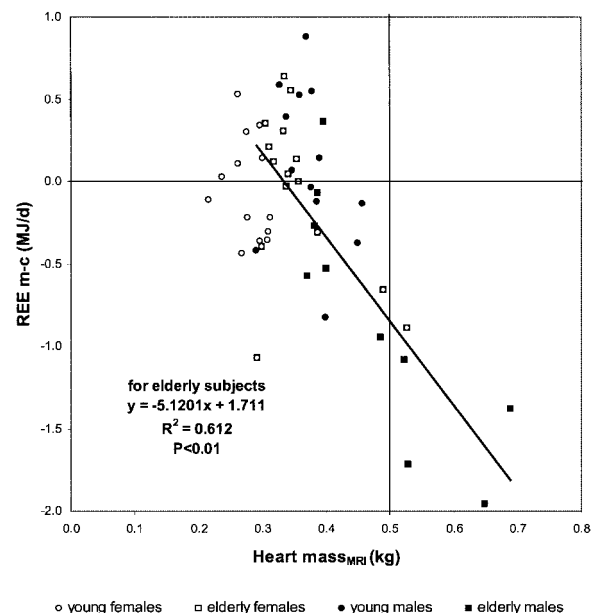


FIGURE 5 Deviation between REEm and REEc according to formula 1 vs. heart mass_{MRI} in 26 young and 26 elderly subjects. REEc, resting energy expenditure calculated; REEm, resting energy expenditure measured.

organ weights of the brain, liver, kidneys and spleen, heart mass was not reduced in the elderly subjects when compared to the young control subjects (Table 1). In addition, the effect of age on the FFM–organ mass (OM) association differed among organs. Elderly subjects had increased heart mass but reduced mass of the brain, liver, spleen and kidneys (Fig. 1). There is recent *ex vivo in vitro* evidence for a marked decrease in the metabolic rate of cardiomyocytes with advanced age (31). In an animal model for hypertension there are several alterations of cardiac bioenergetics, e.g., an impairment of cellular Ca^{2+} handling, phosphate transport and mitochondrial ATP synthesis/export (32). It is tempting to speculate that the age-related increase in heart mass is associated with concomitant decrease in cardiac metabolic rate. In elderly subjects heart mass accounted for 58% of the variance in the deviation of REEm-c. This might be due to the inclusion of five subjects with a pathological myocardial hypertrophy (Fig. 5) and would therefore indicate an additional effect of cardiac hypertrophy that exceeds the effect of normal aging. Altogether these results suggest that the metabolic rate of the aging myocardium declines with progressive cell loss and compensatory hypertrophy.

Gallagher et al. first addressed the age-related decline in REE by applying an REE-prediction model based on seven organ/tissue components to calculation of REE in 13 older men and women age >70 y (10). They reported a significantly lower REEm compared to REEc in these subjects. In contrast, in a previous study, the same group of authors found no significant deviation between REEm and REEc in young subjects (9). They therefore concluded that factors other than organ atrophy may contribute to the lower metabolic rate of older persons (i.e., lower organ metabolic rates). The difference between REEm and REEc in older subjects was slightly higher than the deviation we found for elderly individuals [−607 kJ (Gallagher et al.) and −364 kJ (this study)]. Methodological differences in the assessment of heart mass [ECG-triggered MRI (this study) compared with echocardiography (10)] possibly contribute to the differences in heart mass observed in this study. Unlike MRI, echocardiography measures only left ventricular mass, which accounts for only two thirds of cardiac weight. However, mean left ventricular mass reported by Gallagher et al. is low and therefore hypertensive heart hypertrophy is unlikely to have caused the difference between REEm and REEc in this study (10).

There are some limitations in our study protocol. Body weight and BMI of the elderly subjects were higher than those of young control subjects. This might have biased the comparison of body composition between the age groups and explains the fact that in females there was no decrease in FFM with age (Table 1). Additionally, the underlying assumption of the REE-tissue modeling is a constant tissue composition with age, e.g., there may be more interstitial tissue per 100 g of left ventricular muscle mass in hypertrophied than in normal myocardium (33). Because interstitial tissue consumes less oxygen than myocyte tissue, this might have contributed to a decrease of specific metabolic rate of the aging heart. The MRI protocol did not allow any qualitative analysis of the measured tissue volumes. Further studies are required that apply recently developed advanced MRI techniques.

In conclusion, a substantial difficulty encountered in all studies of the effects of aging on the decline in REE is the differentiation of the aging process itself from common age-associated diseases. When predicting energy requirements from organ masses, hypertension and compensatory myocardial hypertrophy results in a prediction error. However, when

excluding elderly subjects with pathologic cardiac hypertrophy, REE can be accurately calculated from a detailed body composition model assuming constant tissue respiration rates, resulting in a similar prediction error as in young adults. Thus we conclude that in healthy subjects the age-related decline in resting energy expenditure is not caused by a decreasing organ metabolic rate but is fully accounted for by a reduction in FFM and proportional changes in its metabolically active components.

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