Influence of Aerobic Capacity, Body Composition, and Thyroid Hormones on the Age-Related Decline in Resting Metabolic Rate

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It has been suggested that changes in fat-free weight may not fully explain the decline of resting metabolic rate (RMR) that occurs with aging. We therefore examined the hypothesis that a reduction in maximal aerobic capacity ($\dot{V}O_2$max) may partially explain the lower RMR in older men, after accounting for differences in fat-free weight and fat weight. We also considered differences in energy intake and plasma thyroid hormones as possible modulators of the age-related decline in RMR in men. Three-hundred healthy men (aged 17 to 78 years) were characterized for: (1) RMR (kcal/min) from indirect calorimetry; (2) body composition from underwater weighing; (3) maximal aerobic capacity from a test of $\dot{V}O_2$max; (4) plasma thyroid hormones (total triiodothyronine [T_3], free T_3, total thyroxine [T_4], and free T_4); and (5) estimated energy intake (kcal/d) from a 3-day food diary. A curvilinear decline of RMR with age was found ($P < .01$), in which no relationship was found in men less than 40 years of age ($r = .10$, slope = 0.002 kcal/min/yr), whereas in men older than 40 years, RMR was negatively related to age ($r = -.52$, slope = -0.008 kcal/min/yr). After statistical control for differences in fat-free weight and fat weight, a negative relationship between age and RMR persisted (partial $r = -.30$, $P < .01$). It was only after control for fat-free weight, fat weight, and $\dot{V}O_2$max (partial $r = -.10$, $P > .05$) that no association between age and RMR was noted. When subgroups of younger and older individuals were paired for age and fat-free weight, but different $\dot{V}O_2$max values, a higher RMR was noted in the trained younger (8%) and trained older men (11%) compared with untrained younger and older men, respectively. Thyroid hormones and daily energy intake were negatively related to age on a univariate basis, but no independent association was noted after control for fat-free weight. We conclude that, in addition to the loss of fat-free weight, the decline in $\dot{V}O_2$max is an additional factor associated with the decline of RMR in aging men. Age-related changes in energy intake, fat weight, and thyroid hormones appear to be less important in explaining the reduction of RMR in aging men. Maintenance of fat-free weight and $\dot{V}O_2$max by regular physical activity may attenuate the age-related RMR in healthy men.

RESTING METABOLIC RATE (RMR) comprises approximately 60% to 75% of daily energy expenditure, and thus represents a major component in the regulation of energy balance and body composition in humans.[1] Earlier studies[2,3] and more recent cross-sectional and longitudinal investigations have identified a decline in RMR with advancing age[4-7] that has been primarily attributed to alterations in body composition, specifically the decline in fat-free weight. However, it has recently been demonstrated that the loss of fat-free weight does not fully explain the lower RMR in older individuals,[8-10] suggesting that other physiological and/or lifestyle factors may contribute to the reduction of RMR.

Maximal aerobic capacity ($\dot{V}O_2$max) declines with age[11] and has been reported to explain some of the individual differences in RMR in younger and older men, even after differences in body composition were taken into account.[7] Although the metabolic link between $\dot{V}O_2$max and RMR is unclear, recent findings suggest that changes in $\dot{V}O_2$max in response to long-term exercise stimulates sympathetic nervous system activity and food intake, which are both related to alterations in RMR.[12] Taken together, these observations suggest the hypothesis that age-related alterations in $\dot{V}O_2$max or $\dot{V}O_2$max-related factors contribute to the lower RMR in aging males.

Because energy intake also declines with advancing age,[13,14] and RMR is sensitive to alterations in energy intake, primarily by influencing energy balance,[15-18] we also considered the possibility that a decline in energy intake may contribute to the lower RMR in healthy older men. Finally, we considered the influence of age-related changes in circulating concentrations of thyroid hormones to the decline in RMR. Although thyroid hormones are generally considered important regulators of metabolic rate,[19] their association with RMR in euthyroid individuals has yielded inconsistent results.[20,21] Furthermore, it has been unclear whether healthy individuals exhibit age-related changes in plasma concentrations of thyroid hormones.[22,23]

Therefore, the purpose of the present study was to examine data from a large cohort of healthy men to determine whether differences in $\dot{V}O_2$max, energy intake, and thyroid hormones could explain age-associated changes in RMR after differences in fat-free weight were taken into account.

SUBJECTS AND METHODS

Subjects

Three-hundred white men (aged 17 to 78 years) participated in this study. Their physical characteristics are presented in Table 1.

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Table 1. Physical Characteristics in Healthy Males

Variable	Mean	Range
Age (yr)	40.3 ± 1.1	17-78
Height (m)	1.77 ± 0.04	1.62-2.00
Weight (kg)	78.1 ± 0.7	55.9-132.2
Percent body fat (%)	15.8 ± 0.4	5.3-39.4
Fat-free weight (kg)	65.4 ± 0.5	48.4-98.3
$\dot{V}O_2$max (L/min)	3.6 ± 0.05	1.3-6.1
$\dot{V}O_2$max (mL/kg/min)	47.0 ± 0.7	15.7-80.2
Leisure time physical activity (kcal/d)	429 ± 14	50-1,517
Daily intake (kcal/d)	2,766 ± 39	1,123-4,647

NOTE. Values are means ± SE.

A subsample of these volunteers has previously been examined.[7] All subjects were characterized by the following: no clinical symptoms or signs of heart disease; resting blood pressure less than 140/90 mm Hg; normal resting electrocardiogram (ECG); normal ECG response to an exercise stress test; absence of any medication that could affect cardiovascular function or metabolic rate; and no family medical history of diabetes. Extremely obese individuals were excluded due to the possibility of it being a genetically mediated metabolic trait that could skew other metabolic parameters. Subjects were weight stable (±2 kg) by medical history within the past year. The nature, purpose, and possible risks of the study were carefully explained to each subject before he gave consent to participate. The experimental protocol was approved by the Committee on Human Research for the Medical Sciences of the University of Vermont.

Timing of Measurements

Volunteers were admitted to the Clinical Research Center the afternoon before their metabolic testing at 4:00 PM. Subjects were fed a weight-maintaining meal and were thereafter given practice with the ventilated hood to alleviate any concern or apprehension over testing conditions. The Leisure Time Physical Activity questionnaire[24] was administered, and instructions for measuring dietary intake were provided. After an overnight fast during which volunteers slept in the Clinical Research Center, the following tests were performed the next morning: RMR, followed by a 10-mL blood draw, underwater weighing, and a test of $\dot{V}O_2$max.

RMR

RMR was established for each subject by indirect calorimetry for 45 minutes. RMR was determined at least 48 hours after the last exercise session, since this delay has been shown to eliminate the residual effects of exercise on energy expenditure.[25] Briefly, a clear plastic, ventilated hood was placed over the subject's head for the calorimetric tests. Room air was drawn through the hood, and the flow rate was measured by a pneumotachograph (Vertek, Burlington, VT). A constant fraction of expired air was withdrawn, dried, and delivered to a zirconium cell oxygen analyzer (Ametek, Pittsburgh, PA), and an infrared carbon dioxide analyzer (Ametek, Pittsburgh, PA). Energy expenditure (kcal/min) was calculated from the equation of Weir.[26] The intraclass correlation and coefficient of variation (CV) for duplicate measures of RMR in our laboratory (n = 17) are $r = .90$ and 4.3%, respectively.[7]

$\dot{V}O_2$max

$\dot{V}O_2$max was assessed by a progressive and continuous test to exhaustion on the treadmill as previously described.[7] All subjects reached their age-predicted maximal heart rate and a maximal respiratory exchange ratio greater than 1.0 during the exercise test. The intraclass correlation and CV for duplicate measures of $\dot{V}O_2$max in our laboratory[7] are 0.94 and 3.8%, respectively.

Body Composition

Body fat was estimated from body density by underwater weighing using the Keys and Brozek equation,[27] with simultaneous measurement of residual lung volume by helium dilution. Fat-free weight was estimated as total body weight minus fat weight, and is defined for purposes of the present study as total body weight minus the total fat content of the body (in contrast to the term of lean body mass, which contains some essential lipids). The intraclass correlation of body fat in 28 men in our laboratory is 0.98, and the CV is 4.9%.[7]

Estimated Energy Intake

Daily energy and macronutrient intake was estimated from a 3-day food diary (2 weekdays, 1 weekend day).[28] Special attention was given to the importance of subjects maintaining their usual food habits and describing the quantity of food ingested with the aid of a dietary scale and measuring cups and spoons. We have previously shown that 3 days of self-recorded "free-living" energy intake approximates spontaneous energy intake covertly monitored in our clinical research environment.[29]

Thyroid Hormone Determinations

Plasma thyroxine (T_4), free T_4, and triiodothyronine (T_3) concentrations were measured using clinical assay kits (Baxter, Cambridge, MA), and plasma free T_3 was measured using an analog assay (Diagnostic Products, Los Angeles, CA). Thyroid hormone determinations were not available for all subjects due to delays and methodological problems associated with the assay procedure.

Statistics

Means, SDs, and ranges for each study variable were calculated. Pearson correlations were calculated to estimate the relation between pairs of variables. Linear and nonlinear regression analysis were used to test the relation between RMR and age and between RMR and fat-free weight. Partial correlation analysis was used to examine the relation between RMR and age, with fat-free weight, fat weight, $\dot{V}O_2$max, energy intake, and thyroid hormones serving as covariates. RMR was also compared in subgroups of subjects who were matched for age and fat-free weight but with different levels of $\dot{V}O_2$max, using unpaired t tests. All data are expressed as means ± SE, unless otherwise indicated.

RESULTS

The physical characteristics of the volunteers are displayed in Table 1. These healthy male individuals represent a broad range of age, $\dot{V}O_2$max, physical activity level, body composition, and estimated energy intake.

Figure 1 shows the significant ($P < .01$) curvilinear decline in RMR with age in our population. Further analysis shows that no relationship between age and RMR was noted in men under 40 years of age, and the slope was not statistically significant from zero ($r = .10$, slope = 0.002 kcal/min/yr). In contrast, a negative relationship between RMR and age was noted in men older than 40 years ($r = -.52$, $P < .01$), and the slope was negative (−0.008 kcal/min/yr).

Figure 2 shows the negative linear relationship between age and fat-free weight ($r = -.29$, $P < .01$). The relationship between age and fat-free weight showed a tendency to

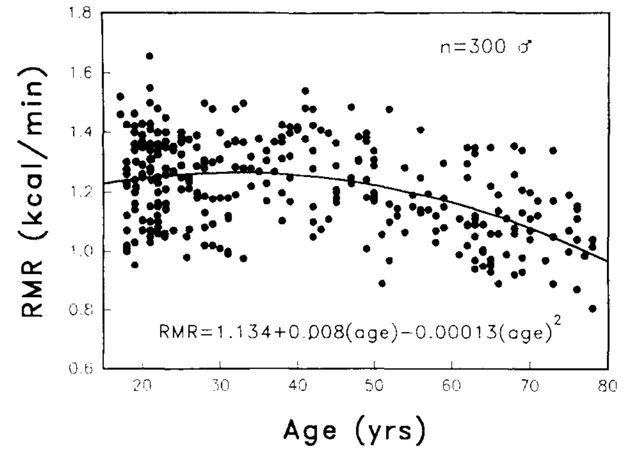

Fig 1. Curvilinear decline in RMR (kcal/min) with age in 300 healthy men.

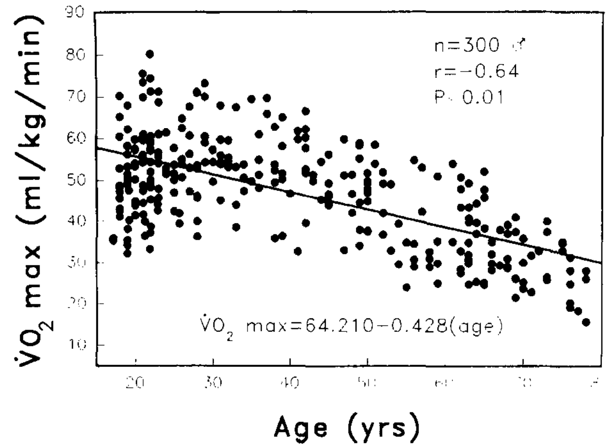

Fig 3. Negative relation between $\dot{V}O_2$max (mL/kg/min) and age in 300 healthy men. $\dot{V}O_2$max was measured from a treadmill test to exhaustion.

have a curvilinear decline ($P = .07$). Additional analyses showed a nonsignificant increase in fat-free weight in men under 40 years ($r = .09$, slope = 0.12 kg/yr), whereas a negative relationship between age and fat-free weight was found in those men older than 40 years ($r = -.25, P < .01$; slope = −0.171 kg/yr). Figure 3 shows the negative relation between $\dot{V}O_2$max expressed per kilogram of body weight and age ($r = -.64, P < .01$).

Table 2 shows the Pearson product correlations of RMR and age with indicators of body composition, aerobic fitness, and estimated energy intake.

Fasting plasma thyroid hormone values and their relationship with RMR and age are shown in Table 3. All values were within the euthyroid range.

Table 4 shows the relation between RMR and age in the total group, using partial correlation analysis. The relationship between age and RMR was examined by using fat-free weight and fat weight as covariates, and thereafter, $\dot{V}O_2$max, energy intake, T_3, and free T_3 were added as additional covariates. After statistical control for both fat-free weight and fat weight, the partial correlation between RMR and age was still significant, indicating that differences in body composition reduced but did not eliminate the negative relationship between age and RMR. However, when $\dot{V}O_2$max was used as the third covariate (after control for fat-free weight and fat weight), the partial correlation between RMR and age became nonsignificant ($r = -.10$, $P > .05$). The consideration of $\dot{V}O_2$max in either absolute (L/min) or relative (mL/kg/min) terms yielded similar results. In contrast, when energy intake, T_3, or free T_3 were used as the third covariate (after adjustment for fat-free weight and fat weight), the partial correlations between RMR and age remained significant (see Table 4 note). In summary, it was only after the consideration of differences in fat-free weight and $\dot{V}O_2$max that the relation between age and RMR became nonsignificant.

Another statistical strategy is to compare RMR in subgroups of subjects matched for age and fat-free weight, but with different levels of $\dot{V}O_2$max. When trained younger subjects (n = 20, 24 ± 0.8 years) were matched with untrained younger subjects (n = 20, 25 ± 1.7 years) for fat-free weight (trained, 68.9 ± 1.5 kg *v* untrained, 68.8 ± 1.5 kg), but unmatched for $\dot{V}O_2$max (trained, 60.1 ± 0.9 mL/kg/min *v* untrained, 41.5 ± 1.1 mL/kg/min), an 8% higher RMR ($P < .01$) was noted in the trained younger subjects (1.29 ± 0.02 kcal/min) when compared with the untrained younger subjects (1.19 ± 0.02 kcal/min). When trained

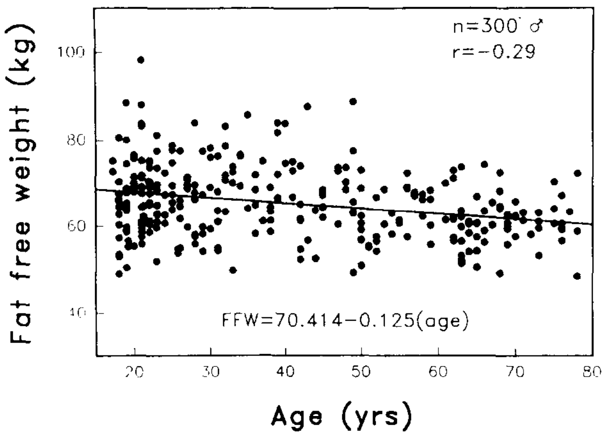

Fig 2. Negative relation between age and fat-free weight in 300 healthy men. Fat-free weight was estimated from underwater weighing.

Table 2. Pearson Correlation Coefficients Between RMR and Age With Indicators of Body Composition, Aerobic Fitness, and Energy Intake

	RMR (kcal/min)	Age (yr)
Body weight (kg)	0.51*	0.02
Fat-free weight (kg)	0.67*	−0.28*
Fat weight (kg)	0.02	0.34*
$\dot{V}O_2$max (L/min)	0.63*	−0.65*
$\dot{V}O_2$max (mL/kg/min)	0.31*	−0.64*
Leisure time physical activity (kcal/d)	0.20*	−0.32*
Energy intake (kcal/d)	0.34*	−0.49*

*$P < .01$.

Table 3. Fasting Plasma Thyroid Hormone Values and Pearson Correlation Coefficients With RMR and Age

Variable	Mean ± SE	RMR (kcal/min)	Age (yr)
Total T_3 (ng/dL) (n = 199)	113 ± 1.7	0.15*	−0.16*
Free T_3 (pg/mL) (n = 141)	2.2 ± 0.05	0.21†	−0.30†
Total T_4 (μg/dL) (n = 175)	7.1 ± 0.10	0.04	0.07
Free T_4 (ng/dL) (n = 141)	1.5 ± 0.02	−0.26†	0.08

*$P < .05$.
†$P < .01$.

older subjects (n = 15, 65 ± 0.8 years) were matched with untrained older subjects (n = 15, 69 ± 1.4 years) for fat-free weight (trained, 60.1 ± 1.3 kg *v* untrained, 60.3 ± 1.3 kg), but unmatched for $\dot{V}O_2$max (trained, 46.1 ± 1.1 mL/kg/min *v* 27.8 ± 1.6 mL/kg/min), an 11% higher RMR ($P < .01$) was noted in the trained older subjects (1.19 ± 0.03 kcal/min) when compared with the untrained older subjects (1.06 ± 0.02 kcal/min).

DISCUSSION

The purpose of the present study was to examine data from a large cohort of healthy men to determine whether differences in $\dot{V}O_2$max, estimated energy intake, and/or thyroid hormones may explain the lower RMR in older men after differences in fat-free weight are taken into account. The major findings are: (1) differences in fat-free weight cannot fully explain the decline in RMR in men; (2) a decline in aerobic fitness (ie, $\dot{V}O_2$max) is an independent factor contributing to the decline in RMR; and (3) variation in concentrations of thyroid hormones, daily energy intake, and age, per se, appear to be less important than fat-free weight and $\dot{V}O_2$max in explaining the reduction of RMR in healthy aging men.

Age, RMR, and Fat-Free Weight

In agreement with others,[4-6] we noted an age-related decline of RMR in the present study. Upon closer inspection of our data, the decline of RMR with age was characterized by a curvilinear relationship (Fig 1). In other words, no relationship between RMR and age was discernible in men up to 40 years of age, whereas in men older than 40 years, a linear decline of RMR with age was found. In practical terms, our data predict a 25% decline in RMR from 40 years (1.28 kcal/min) to 80 years (0.96 kcal/min) of age.

Table 4. Partial Correlation Coefficients Between RMR and Age After Control for Body Composition, $\dot{V}O_2$max, Energy Intake, and Thyroid Hormones

Dependent Variable = RMR (kcal/min)	
Covariates	Partial Correlation With Age
(1) None	−0.40*
(2) Fat-free weight	−0.29*
(3) Fat-free weight, fat weight	−0.30*
(4) Fat-free weight, fat weight, $\dot{V}O_2$max	−0.10

NOTE. Partial correlation coefficients for the following variables with age after control for fat-free weight and fat weight: energy intake (r = −.26, $P < .01$); T_3 (r = −.27, $P < .01$); and free T_3 (r = −.43, $P < .01$).
*$P < .01$.

Although there is general agreement regarding the decline of RMR with age, it is unclear whether differences in fat-free weight can fully explain the decrement. Although Tzankoff and Norris[5] did not measure fat-free weight, they concluded that decrements in skeletal muscle mass (as estimated from 24-hour creatine excretion) were principally responsible for the decrease in whole-body oxygen consumption with age. Keys et al[4] found that the lower RMR in older men studied until age 50 was caused by changes in body composition as estimated from body densitometry. We have found discrepant results in our own laboratory, in which differences in fat-free weight between younger and older men could[7] or could not[10] fully account for the lower RMR in older men. This may be related to the examination of younger and older men with varying levels of physical activity and differences in bone mineral density and its subsequent influence on underwater weighing measurements (which assumes a constant bone mineral mass). Other investigators[8,9,30] have found that differences in fat-free weight, measured by a variety of different methods (densitometry, total body water, skinfolds, etc.), could not fully explain the lower RMR in older individuals.

In an attempt to resolve these discrepancies within our own laboratory and among other investigators, we have examined RMR in a large sample of healthy men across a wide age-span well characterized for body composition, $\dot{V}O_2$max, and thyroid hormone status. The present results are consistent with both cross-sectional[5,31] and longitudinal studies[4,32,33] that reported a decline in fat-free weight with advancing age. In the present study, the time-course of the decline in fat-free weight was similar to the decline of RMR. Specifically, little change in fat-free weight was found in individuals under 40 years of age, whereas in men older than 40 years, a negative relationship between age and fat-free weight was found ($r = -.25$, $P < .01$). However, two lines of evidence suggest that differences in fat-free weight could not fully account for the age-related decline in RMR. First, the partial correlation between RMR and age persisted (Table 4) after the effects of fat-free weight and fat weight were statistically removed (partial $r = -.30$, $P < .01$). Second, the slope of the decline in RMR was greater ($r = -.52$) than the decline in fat-free weight ($r = -0.25$). These data are therefore in agreement with other investigators,[8-10] who support the concept that changes in fat-free weight cannot fully explain the lower RMR in aging men. In contrast to some previous studies,[21,34] but not to all,[35,36] fat weight (or percent body fat) was not related to RMR after accounting for differences in fat-free weight.

RMR, $\dot{V}O_2$max, Thyroid Hormones, and Energy Intake

The present study represents an extension of previous works by providing new information regarding physiological factors other than body composition that may contribute to the age-related decline in RMR, independent of differences in fat-free weight. We have considered the influence of $\dot{V}O_2$max, daily energy intake, and plasma thyroid hormones as modulators of the age-related decline in RMR in men.

We have previously shown that differences in $\dot{V}O_2max$ accounted for a significant portion of the variation in RMR in younger and older men.[7] Furthermore, RMR has also been found to be higher in older active men relative to older inactive men after controlling for differences in body composition.[10,30] However, the limited sample sizes and the exclusion of middle-aged individuals in our previous reports have precluded firm conclusions regarding physiological factors accounting for differences in RMR across a larger age span.

To examine the association of other variables with the age-related decline in RMR, we used partial correlation analysis to control for differences in fat-free weight and fat weight. Thereafter, the relation between RMR and age was examined after statistically controlling for the influence of $\dot{V}O_2max$, thyroid hormones, and energy intake. The new finding is that when differences in $\dot{V}O_2max$ are taken into account (along with fat-free weight and fat weight), no significant association between RMR and age was found. This finding was significant whether absolute $\dot{V}O_2max$ (L/min) or $\dot{V}O_2max$ adjusted for body weight was entered into the analysis. On the other hand, a significant relation between RMR and age persisted when either total T_3, free T_3, or energy intake were considered as potential covariates. Collectively, our results suggest that the loss of fat-free weight can largely but not fully explain the decline in RMR with age. Furthermore, these findings suggest that the decline in $\dot{V}O_2max$ is an additional independent factor associated with a reduction RMR. Another statistical strategy that underscored the important relation between $\dot{V}O_2max$ and RMR was the subgroup analysis, in which a higher RMR was found in trained younger and trained older subjects when compared with untrained younger and older individuals after individuals were matched for age and fat-free weight, but unmatched for $\dot{V}O_2max$ (see Results).

Variations in antecedent dietary practices and plasma thyroid hormones appear to be secondary factors contributing to the decline in RMR. However, it should be noted that a cause-and-effect relation between the decline in RMR and the decline in $\dot{V}O_2max$ cannot be established in this study. One must also consider the possibility that variations in $\dot{V}O_2max$ could be secondary to age-related changes in fat-free weight. These issues can only be resolved in longitudinal designs.

We felt it was important to consider the possible influence of thyroid hormones on the age-related decline in RMR. It is unclear whether there is an effect of aging, per se, on thyroid hormone concentrations that is independent of debilitating disease. Furthermore, it is unknown whether differences in thyroid hormone concentrations contribute to the age-related decline in RMR. Our findings show an inverse correlation between age and plasma concentrations of total T_3 and free T_3 (Table 3) that are in agreement with some[22] but not all investigators.[23] Thyroid hormones, particularly the metabolically active forms of T_3 and free T_3, have been reported to carry a major responsibility for regulating RMR.[19] However, it has been difficult to demonstrate a relation between circulating concentrations of these hormones and RMR in euthyroid individuals.[20,21] To our knowledge, our data are the first to show significant correlations between RMR and total T_3 and free T_3 in a large cross-section of euthyroid men.

The mechanism underlying the relation between $\dot{V}O_2max$ and RMR is beyond the current scope of this study. It is possible that $\dot{V}O_2max$ is a biological marker for several energy-consuming processes that may diminish as individuals age and become less physically active. We presently have evidence that $\dot{V}O_2max$ is a strong physiological predictor for total daily energy expenditure (as measured from doubly labeled water) in older men and women.[37] Recently, differences in protein turnover[21] and skeletal muscle metabolism[38] have been shown to account for a portion of the variance in RMR among individuals. Furthermore, Lamont et al[39] have shown that whole-body leucine turnover and RMR were higher in endurance-trained individuals. Based on the aforementioned evidence, it is reasonable to speculate that a decrement in muscle protein synthesis, due to a decline in physical activity, may contribute to the decrease in RMR in the elderly.

Several methodological considerations should be mentioned that reinforce the validity of our techniques for measuring RMR in this large sample size. These factors include the determination of metabolic rate 48 hours after vigorous exercise, as this time period has been shown to eliminate any residual effects of exercise on RMR.[25] Second, we measured RMR in volunteers who slept overnight in the Clinical Research Center and who were weight stable (by medical history) within the past year. This reduces variation in measurement due to different methods of transport to the laboratory or antecedent fluctuations in body weight. We now have evidence that outpatient assessment of RMR consistently overestimates resting energy requirements as compared with inpatient conditions.[40] Lastly, volunteers were habituated to the ventilated hood the night before actual measurement to reduce anxiety associated with novel experimental conditions.

The caveats associated with cross-sectional aging studies are well known. The most obvious issue is the natural selection bias that may tend to obscure or attenuate true aging processes because the selected older individuals may represent a group of "survivors." Another issue, which is probably related to the first, concerns the exclusion of individuals without "obvious disease." One could argue that an adequate description of aging must include an account of disease. Furthermore, our results cannot be extrapolated to the "oldest old" (> 80 years) segment of the population.

Lastly, there are limitations associated with the densitometry approach to estimating body composition in older individuals, due to the assumption in the technique that the density of fat-free weight is constant. It is possible that the use of underwater weight may have underestimated fat-free weight and overestimated body fat in our older male population.[41] On the other hand, the decrease in minerals (bone loss) during aging has recently been found to be similar to the decrease in protein and water (muscle) in the fat-free weight. As a consequence, the chemical composition of the fat-free weight was not significantly altered by aging in men.[42]

From our underwater weighing measures, an estimate of fat and fat-free weight was obtained. Fat-free weight is generally considered as total body weight minus all neutral fat, whereas lean body mass is generally considered as body weight minus ether-extractable fat, and hence includes the stroma of adipose tissues. Although fat-free weight is generally found to correlate highly with RMR, the determination of the body cell mass (by measurement of total exchangeable potassium) that comprises the oxygen-consuming cells (muscle, viscera, and brain) represents the most meaningful reference in terms of resting energy expenditure.[43] Thus, it is likely that the correlation of RMR with the size of the body cell mass would be higher than that of RMR with fat-free weight, due to the more representative nature of body cell mass as the metabolically active tissue.

Our results nevertheless have potential implications for the healthy aging individual regarding the regulation of energy balance. Specifically, clinical interventions designed to attenuate or reverse the decline in fat-free weight (ie, resistance training) and enhance cardiovascular capacity (aerobic activities) should be used in combination to increase overall energy needs, preserve fat-free weight, and offset the propensity to gain body fat.

In summary, we conclude that the decline in fat-free weight and $\dot{V}O_2max$ contributes to the lower RMR in older men. Age-related reductions in energy intake and plasma thyroid hormones appear to be less important in explaining the reduction of RMR in aging man.

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