Body composition changes with aging: The cause or the result of alterations in metabolic rate and macronutrient oxidation?

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Abstract
It has been well documented that as individuals age, body composition changes, even in the absence of changes in body weight. Studies have shown that fat mass increases and muscle mass decreases with age. However, it is unclear why such changes occur. Resting metabolic rate (RMR) and substrate oxidation rates have been examined with aging. It has been proposed that reductions in RMR and fat oxidation may lead to changes in body composition. Alternatively, changes in body composition with aging may lead to reductions in RMR. The purpose of this review is to provide an overview of the literature surrounding the impact of aging on RMR and substrate oxidation. Although long-term longitudinal studies are lacking, most cross-sectional studies or short-term longitudinal studies show a reduction in RMR with aging that cannot be explained by changes in body composition including loss in fat-free mass, where the latter includes atrophy or decreases in the mass of high metabolic rate organs. There is indirect evidence suggesting that the metabolic rate of individual organs is lower in older compared with younger individuals. With aging, we conclude that reductions in the mass of individual organs/tissues and in tissue-specific organ metabolic rate contribute to a reduction in RMR that in turn promotes changes in body composition favoring increased fat mass and reduced fat-free mass.

Keywords
Aging; Metabolic rate; Substrate oxidation; Body composition

Introduction
The aging process brings about many changes in body composition, often without concomitant changes in body weight and body mass index (BMI) [1]. In general, as individuals age, percent body fat increases and lean mass and bone mineral density decrease. Furthermore, the increase in fat mass (FM) is distributed more specifically in the abdominal region, an area associated with cardiovascular disease and diabetes. A recent cross-sectional study from the Florey Adelaide Male Aging Study actually determined that the increase in percent FM was mostly due to reduced lean mass, whereas the increase in abdominal percent FM was due to more FM deposited in the abdominal region [2].

It is generally agreed that changes in body composition are due to alterations in energy balance, with a positive energy balance leading to weight gain and a negative balance resulting in weight loss. However, body composition changes associated with aging often occur in the absence of weight fluctuations. The purpose of this review is to examine the impact of aging on resting metabolic rate (RMR) and macronutrient oxidation rates as potential causes for the observed
body composition changes of aging. Alternatively, it can be argued that changes in RMR with aging may be due in part to changes in body composition. These seemingly divergent views are also explored.

**Impact of aging on RMR**

Krems et al. [3] recently compared the RMR of young (20–35 y) and older (≥60 y) men and women. Measured RMR was lower in older individuals compared with younger individuals, even after adjusting for fat-free mass (FFM), FM, and smoking history. They also calculated RMR based on estimated organ masses. For young men, measured and calculated RMRs were not significantly different, whereas for young women and older men and women, measured RMR was lower than calculated RMR. The differences between calculated and measured RMR were greater for the older group than the younger group. The investigators concluded that the decline in RMR with advancing age could not be totally explained by changes in body composition.

Similar results were obtained by Frisard et al. [4] when comparing young (20–34 y), older (60–74 y), and very old (≥80 y) individuals. RMR was lower in older and very old individuals than in young individuals after adjusting for FFM, FM, and gender. Another study examined RMR across the life cycle of women [5]. In this study, RMR, adjusted for FFM, was significantly higher in young (20–30 y) and middle-aged (40–50 y) women compared with older women (≥60 y). However, another study in women examining metabolic rate in very old age failed to find a reduced RMR in the very old [6]. In fact, when middle-aged (<65 y), older (66–94 y), and very old (≥95 y) women were compared, middle-aged and very old women had a similar RMR, which was higher than that of older women. Respiratory quotient (RQ) also varied with age, with middle-aged women having the lowest RQ, followed by the very old; older women had the highest RQ. However, in this study, the uncharacteristic longevity of the very old women may be due to some genetic advantage or lifestyle characteristic that may be protective against reductions in metabolic rate with age. Alternatively, these women may live to a very old age because they did not have a decline in their RMR.

These recent cross-sectional studies have shown a reduction in RMR with increasing age independent of differences in body composition between younger and older individuals. Very few longitudinal studies have measured RMR with aging. A longitudinal study on the nutrition and health status of an aging German population was initiated to study energy expenditure during the course of aging in men and women >60 y of age [7]. Over the 8-y follow-up period, subjects lost height, increased BMI and FM, and decreased FFM and waist-to-hip ratio with no change in weight. After adjusting for body composition, men had a 5% reduction in RMR per decade and women, a 3% reduction per decade. Physical activity energy expenditure also decreased, resulting in a decrease in total energy expenditure of 7.5% per decade for men and 6% per decade for women. The researchers concluded that the decline in RMR was not entirely due to changes in body composition. Similar results were found over a 5-y follow-up in a small sample of 73-y-old women (n =9) and men (n = 2) [8]: RMR at age 78 y was significantly lower than at age 73 y, even after controlling for FFM. In the Baltimore Longitudinal Study of Aging, adults enrolled from 1958 to 1982 were followed until 2000 [9]. RMR decreased in both genders, independently of changes in BMI. In men, for whom more than two measurements were performed, the rate of decline in RMR was faster at age 70–80 y than at age 40–50 y.

Most studies looking at the relation among aging, RMR, and body composition have concluded that RMR is reduced in older age compared with younger age beyond what can be explained by changes in body composition. However, these studies have only examined body composition using a two-compartment or three-compartment model where FM and FFM are
Impact of age on organ mass and implications for resting energy expenditure

Fat-free mass consists of chemical components, protein, water, and minerals, which by themselves do not expend energy. When organized into cellular-level components, the chemical constituents of FFM are distributed among body cell mass (BCM), extracellular fluid, and extracellular solids. Almost all resting thermogenesis occurs in the BCM component of FFM [10]. Using FFM or BCM as the denominator against which RMR is expressed makes the fundamental assumption that the constituents that make up BCM or FFM have a similar metabolic rate. This practice is inherently flawed because it pools together numerous organs and tissues that differ significantly in metabolic rate. The brain, liver, heart, and kidneys alone account for approximately 60% of RMR in adults, although their combined weight is less than 6% of total body weight or 7% of FFM [11–14]. The skeletal muscle component of FFM comprises 40–50% of total body weight (or 51% of FFM) and accounts for only 18–25% of REE [13]. We recently showed that age has a significant effect on the brain, kidneys, liver, spleen, and heart mass (all high metabolic rate organs), where all but the heart decrease in mass with advancing age [15]. The age effect was independent of race and sex.

Resting metabolic rate varies in relation to body size across mammalian species [16]. Within humans, RMR per kilogram of body weight or FFM is highest in newborns (~56 kcal · kg⁻¹ · d⁻¹) [17], declines sharply until 4 y, and continues to decline slowly thereafter to reach adult values (~25 kcal · kg⁻¹ · d⁻¹) [17]. Among adults, RMR is lower in the later adult years, to an extent beyond that explained by changes in body composition. That is, the loss of FFM cannot fully explain the decrease (5–25%) in RMR in healthy elderly. A series of studies have led to this conclusion.

Gallagher et al. [18] measured major organs (liver, brain, heart, and kidneys) and tissues (skeletal muscle and adipose tissue) in a cohort of young adult men and women. The investigators assumed stable organ tissue-specific RMRs and measured organ tissue volumes by magnetic resonance imaging to predict whole-body RMR. The calculated RMR for young subjects was nearly identical to values measured by indirect calorimetry [13]. In contrast, the calculated values in older subjects were higher (± standard deviation) than the measured values by 144 ± 64 kcal/d (P < 0.01) for men and 146 ± 78 kcal/d (P < 0.001) for women [18]. Other investigators [19,20] have shown similar findings.

The assumption that the specific RMRs of individual organs and tissues are stable across the adult age span is likely untrue. The observations of Gallagher et al. [18] show that the assumed organ tissue-specific metabolic rate values, which are based largely on young adults, may not be applicable in the elderly. Explanations for these findings include 1) the possibility that the elderly have a lower RMR per unit cell mass for individual organs and tissues (i.e., specific metabolic rate) than young subjects, and 2) the cellular fraction of organs and tissues may differ in young and older subjects. Accordingly, Wang et al. [21] proposed and evaluated a cellular-level RMR prediction model that provides support for the theory that the lower RMR observed in elderly subjects is due to the combination of two aging-related factors: declines in the mass and cellular fraction of organs and tissues.

Impact of aging on macronutrient oxidation

Results from studies examining the impact of age on substrate oxidation are varied and those studies have focused mostly on the impact of diet and physical activity on changes in

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macronutrient oxidation rates with aging. Solomon et al. [22] investigated the hypothesis that basal fat oxidation is reduced in obese elderly individuals as a function of age. Ten younger (35 y) and 10 older (60 y) sedentary individuals, matched for gender and BMI, were studied under basal conditions. Resting RQ, carbohydrate oxidation, and RMR did not differ between groups but older individuals had lower basal fat oxidation, adjusted for FFM, compared with younger subjects. A study by Levadoux et al. [23] also reported lower fat oxidation in older (>60 y) compared with younger (<35 y) subjects. However, in that study, younger subjects had a BMI ≤25 versus ≤30 kg/m$^2$ for older subjects and maximum oxygen consumption per unit time and FFM were higher in younger than older subjects.

Another study compared 24-h fat oxidation in sedentary older (65 y) and younger (25 y) men under sedentary and exercise conditions [24]. Energy intake was controlled for 3 d before and during each chamber stay and increased by 375 kcal during the exercise condition to account for the exercise and postexercise rise in energy expenditure. Twenty-four–hour energy expenditure was not different between older and younger men, but RQ was lower in older men under both conditions. After adjusting for FFM, 24-h fat oxidation was greater in older men during the exercise condition and tended to be higher during the sedentary condition compared with younger men.

Using a different study design, Davy et al. [25] also concluded that healthy, non-obese older men did not have impaired fat oxidation compared with younger men. Young (25 y) and older (63 y) men were tested in a whole-room calorimeter for four 24-h periods. The first session was performed to establish weight-maintenance energy requirements and the subsequent three sessions differed in macronutrient composition of the diet and were conducted in random order. Diets were mixed (protein/fat/carbohydrate 15%/30%/55% of energy), high in fat (60% of energy), or low in fat (15% of energy) and matched for protein content. Fat and carbohydrate oxidation rates did not differ between older and younger subjects across diet conditions, but protein oxidation was consistently higher in older compared with younger men. The investigators suggested that higher protein oxidation in older men may provide insight into the loss of muscle mass with aging. However, this study was done in a very small number of subjects ($n = 11$) and needs to be replicated in a larger sample.

**Conclusions**

Studies examining the role of aging on RMR and substrate oxidation indicate a reduction in RMR with age that is greater than what can be explained by simple body composition parameters such as FM and FFM. The lower RMR of older adults may be due in part to slowed organ metabolic rates and this may contribute to changes in FM and FFM that occur with aging. The impact of age on substrate oxidation has not been thoroughly studied, and findings are inconclusive on whether aging alters substrate oxidation. Longitudinal studies of adults under resting conditions should be done to further examine how RMR and substrate oxidation change as individuals age.

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