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REGULATION OF ENERGY EXPENDITURE IN AGING HUMANS

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INTRODUCTION

Energy balance is the net result of energy input minus energy output. The extremes of fatness and leanness, which are the result of fluctuations in energy balance, are important health concerns in aging humans. Although it is generally recognized that energy balance can be achieved by adjustments in

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both energy intake and energy output, food intake is generally regarded as the more important factor in this process. Energy intake declines with age (39). Despite this decline, the "average" older person is 20% above the ideal body weight for a given height in the United States (86). This finding suggests that excess adiposity occurs in older individuals as a result of the failure to decrease food intake sufficiently to compensate for the decrease in energy expenditure that often accompanies advancing age. The "mismatching" of energy intake to energy expenditure in older individuals suggests an age-related breakdown in the regulation of body weight homeostasis. Physical activity is frequently prescribed for older individuals as a means of increasing total energy expenditure, improving cardiovascular fitness, and increasing their functional independence. Recently, physical activity has been found to influence resting energy metabolism in younger individuals (47, 49). In this review, we examine the influence of physical activity as a modulator of resting energy metabolism in aging humans. Because limited space precludes an exhaustive review of both animal and human work, only human studies are discussed.

We examine the influence of age on two components of resting energy expenditure: (*a*) the resting metabolic rate (RMR) and (*b*) the thermic effect of food (TEF). Second, we examine the interaction of physical activity on RMR and TEF in older and younger individuals. Third, the influence of age and physical activity on sympathetic nervous system activity (SNSA), a hormonal system implicated in the control of energy balance, will be discussed briefly.

THE COMPONENTS OF 24-HOUR ENERGY EXPENDITURE

For theoretic and analytic purposes, energy expenditure can be divided into several components (Figure 1). RMR is the most significant contributor to 24-h energy expenditure and makes up ~60–75% of total daily energy expenditure in sedentary humans. The energy cost associated with RMR is that commonly viewed as the irreducible energy expended to maintain the body's organ systems. Several factors influence RMR, including age, body composition, nutritional state, and thyroid function. It is generally agreed that when individuals of different body size, sex, or age are compared, the most meaningful data are obtained when RMR is normalized for fat-free weight (FFW) (28, 41). RMR has been reported to show a strong genetic influence (7, 21) and a familial resemblance (6). Changes in RMR in response to exercise training (56) have also been shown to be genotype dependent.

The TEF is the increment in energy expenditure after a meal. The increase in energy expenditure after food ingestion is due to the energy cost of digestion, transformation, and storage. It makes up approximately 10% of

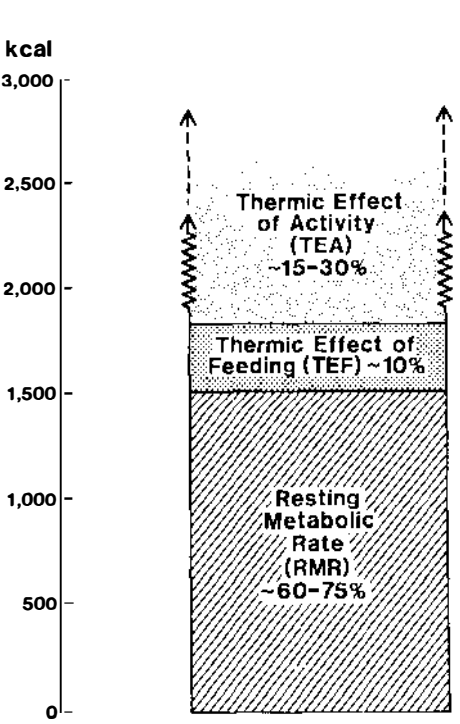

Figure 1 The three major components of daily energy expenditure. From Poehlman (47).

24-h energy expenditure and is thought to be quantitatively important in the long-term regulation of body weight (12). The TEF is proportional in magnitude and duration to the size of the ingested meal (26, 42) but varies with meal composition (83). Individual variations in TEF in response to overfeeding and exercise training are reported to be genetically influenced (55, 56).

The most variable component of 24-h energy expenditure is the thermic effect of activity (TEA). This component includes the additional energy expended above RMR and TEF as a result of physical activity and muscular activity, including shivering and fidgeting as well as purposeful physical exercise. In sedentary humans, TEA may make up approximately 15% of total daily energy expenditure, whereas in individuals who regularly engage in exercise, it may contribute 30% or more of daily energy expenditure. Thus, purposeful physical activity represents the most significant stimulus to alter total 24-h energy expenditure in humans. These three components, however, represent only partially distinct entities of total 24-h energy expenditure because they often overlap during the course of a normal day.

RESTING METABOLIC RATE, BODY COMPOSITION, AND AGING

Numerous studies have demonstrated that RMR declines with age. Whether this decline is an immutable consequence of aging or is influenced primarily by changes in body composition remains unclear, however. Shock et al (69) related changes in RMR to alterations in the water content of the body in 193 apparently healthy individuals between the ages of 20 and 95 years. They determined RMR by the Tissot open-circuit method and estimated the total body water by the dilution technique. They found a reduction in total body water and intracellular water in the absence of change in extracellular water. This finding was interpreted as a loss of functioning cells with increasing age. Absolute RMR diminished significantly with age (0.4% per year). On the other hand, when RMR was adjusted for total body water or intracellular water, no significant regression of RMR on age was noted. The authors concluded that the oxygen uptake of functioning cells in older individuals is not significantly different from that in younger subjects.

Forbes & Reina (22) longitudinally assessed changes in FFW in four men older than 25 years by using total body potassium (TBK) counting. The trend for changes in FFW was clearly downward and tended to be more rapid in later years. The authors estimated that by age 65–70 years, the average male has 12 kg less FFW than at age 25 years. The average rate of loss of FFW was estimated to be 0.24 kg per year. Novak (44) examined body composition of 215 men and 305 adult women aged 18–85 years from determinations of TBK. Body fat in the men increased with age from 17.8 to 36.2%, whereas the FFW decreased from 82.2% to 63.8%. In women, body fat increased with age from 33.0 to 44.8% and FFW declined from 67.0 to 55.2%. In a recent study, Flynn et al (20) calculated TBK from longitudinal measurements over 18 years in 564 male and 61 female healthy subjects. Males showed a decrease in TBK from the age of 41 years; the most rapid loss occurred between the ages of 41 and 60 years. The rate of change of TBK, however, was different in females. Whereas TBK was preserved in females during their child-bearing years, a rapid loss was observed after 60 years of age; the rate of change was greater than that in males. Therefore, there appears to be a sexual dimorphism in the rate of change in body composition over time. These results should be interpreted with caution, however, owing to the disparity in sample size between males and females.

Keys et al (30) reported RMR and body composition findings as assessed by underwater weighing of 63 healthy young men who were restudied after 19 years and of middle-aged men who were studied repeatedly over a period of 24 years. RMR was measured with a closed-circuit Sanborn metabolism machine for two successive 15-min periods. The authors reported a decline in

absolute RMR at a rate of 3.2% per decade, equivalent to 9% per decade when adjusted per kilogram of body weight and 6% per decade when adjusted per square meter of body surface. These volunteers had obviously gained a great deal of body fat and lost some muscle mass, which probably contributed to their rapid decline in RMR, regardless of how the RMR data were expressed. In the same study, an older group of 115 men with a mean age of 50 years were examined on five occasions covering a time span of 17 years. Interestingly, in this older group of men, body weight and composition were remarkably stable over this period. From the first to the last measurement of RMR over the 17-year span, the RMR declined by only 2.1% (1.2% per decade). Over the period of 15 years (from year 4 to year 19), the corresponding change was only 0.36% per decade. These findings imply that maintenance of "proper levels" of body fat and FFW may attenuate the age-related decline in RMR.

Robinson et al (61) examined RMR in a group of college students at age 18–22 years and again (in the same group) at age 49–53 years. The most significant changes with age were the large gains in body weight (~8 kg) in this population. RMR was reported to decline and most probably reflected the loss of FFW and increase in body fat with age.

Webb & Hiestand (81) performed continuous recordings of oxygen consumption during sleep in 20 men between the ages of 19 and 63 years. Their data showed a linear inverse relation between age and oxygen consumption ($r = -0.46$), even though the older men slept less and awoke more often than the younger volunteers. No relation was found between the stage of sleep and level of oxygen consumption. Both the decreased energy expenditure during sleep and the decreased RMR in older men support a conclusion that lowering of RMR contributes to a gradual increase in body fat reserves and reduced caloric requirement in middle age and later years.

Tzankoff & Norris (78) concluded that a decrement in muscle mass may be wholly responsible for the age-related decrease in RMR. In the Baltimore Longitudinal Study between 1959 and 1975, they measured RMR by an open-circuit method in 959 participants who had fasted overnight. No differences in mean basal $\dot{V}_{O_2}$ were found in volunteers up to the age of 45 years. For each increasing age decade thereafter, significant decreases in the average RMR values were found. Twenty-four-hour creatinine excretion, which was assumed to be proportional to the loss of muscle mass, was also lower in progressively older age groups. Whereas the whole-body RMR was lower for each age group after the age of 45 years, RMR was similar among age groups after the skeletal muscle contribution to basal V_{O_2} was subtracted out. The authors concluded that an age-related decrease in the mass of creatinine-producing tissues, principally skeletal muscle, can account for all of the decrease in RMR with age. In a follow-up study, they (79) extended

their previous findings by measuring longitudinal changes in RMR over the whole adult range. The overall change in RMR was -0.82 ml of O_2 min^{-1} $year^{-1}$. These data are consistent with the rate of change in RMR derived previously from their cross-sectional data (78).

Several other recent cross-sectional studies have reported a lower RMR in older individuals than in younger individuals. Calloway & Zanni (9) reported that RMR was 13% lower in six healthy older men (63–77 years old) than in younger men but was similar when it was adjusted per unit of body potassium. The TBK content in this study was 12% lower in older men than in younger men. The lower absolute RMR in older individuals than in younger individuals and the similarity of RMR among individuals of different ages when adjusted for an index of FFW has been confirmed in other studies (4, 23, 42, 51, 65). Interestingly, in the study of Morgan & York (42), younger and older subjects had similar levels of FFW. Despite this similarity, the RMR was still lower in older men. Therefore, one could conclude from this study that factors other than a reduction in the quantity of FFW contributed to the lower RMR in older men. The authors speculated that age-related differences in the concentrations of thyroid hormones or sensitivity to circulating plasma levels of thyroid hormones may have contributed to this finding.

Collectively, these findings suggest that there is no important difference in the metabolic activity of body cell mass, per se, between younger and older individuals. That is, the loss of tissue or of tissue function with age is proportional between skeletal muscle, viscera, and other lean tissues. Unfortunately, the calculation of FFW based on either body density or total body water is subject to error due to age-related changes in mineralization of the skeleton and water content, with shifts in the proportions of adipose and lean wet tissues. More accurate methods for determining body composition in the older population are needed to substantiate age-related changes in body composition and its relation to RMR.

RESTING METABOLIC RATE, PHYSICAL ACTIVITY, AND AGING

The fact that RMR has proven to be closely correlated with body size (25, 60) has led to the view the basal energy requirements are constant for a given body size, body composition, age, and sex. However, RMR has been found to vary between individuals independently of these determinants. Another factor that may influence individual variation in RMR is the level of physical activity. Both cross-sectional and exercise intervention study designs have been used to examine the effects of physical activity on RMR. Most of these studies, however, have been performed with younger individuals.

In an early field study by Wilson (84), young men were subjected to 3

weeks of vigorous physical conditioning and demonstrated a large increase in RMR adjusted for body surface area. RMR was measured 24 h after the last session, so the higher RMR is not likely to be due to the residual effects of the last exercise bout. Interestingly, body fat as estimated from skinfold measures was reported to increase. This finding may suggest that individuals overcompensated in food intake in response to the exercise regimen, which may have contributed to the higher RMR after training.

Tremblay et al (74) noted a higher unadjusted RMR in 20 physically trained men (1.17 ± 0.03 kcal min^{-1}) relative to 39 untrained men (1.05 ± 0.02 kcal min^{-1}). This trend persisted but did not reach statistical significance when RMR was adjusted per kilogram of FFW. In the same study, Tremblay et al (74) also submitted eight moderately obese women to an 11-week program of physical training and found an 8% increase in RMR (per kilogram of FFW). The studies of Lawson et al (32) and Lennon et al (35) also showed a higher RMR after exercise training in females. The fact that Lennon et al found the higher RMR in the exercise group performing at a greater intensity suggests that a threshold of exercise in a physical conditioning program may be necessary to increase RMR. Taken together, the results of these studies suggest that exercise training may increase RMR. That is, in addition to the direct caloric cost of exercise, long-term physical activity may enhance energy expenditure at rest in younger individuals. This additional energy loss associated with exercise is potentially important for the prevention and treatment of obesity. These findings, however, are in contrast to those of Bingham et al (3). In this study, RMR in groups of six volunteers showed no difference after 9 weeks of vigorous exercise training. The volunteers, however, were reported to be in a negative energy balance at the end of the study, which makes the interpretation of the results more complex. Possibly a state of energy balance must be maintained in an exercise program if a higher RMR is to be found. This balance would be achieved by matching a high rate of energy expenditure, generated by exercise, with a high level of energy intake. Future studies may want to consider refeeding the energy lost by exercise training to maintain energy balance so that the effects of exercise training on RMR may be examined separately from a state of energy deficit.

In cross-section designs, RMR in younger active and inactive subjects has been examined. We studied (52) RMR in highly active men and inactive men 24 h after the last exercise session. We found a higher RMR in highly trained men than in untrained men (1.18 ± 0.04 versus 1.05 ± 0.03 kcal kg of FFW^{-1} 60 min^{-1}; $p < 0.05$). This observation persisted when subjects were matched for body fat content. This result suggests a role for high levels of physical activity independent of adiposity as a determinant of RMR. In another study (54), we examined a wide range of maximal aerobic fitness levels in healthy males and found a linear relation between $\dot{V}_{O_2(max)}$ and RMR

($r = 0.77$; $p < 0.01$). Furthermore, when volunteers were classified into fitness levels, the highest RMR (per kilogram of FFW) was found in the highly trained men, whereas the RMRs in moderately trained and untrained men were indistinguishable. These results are concordant with those of Tremblay et al (73), who noted a higher RMR in a group of highly trained men relative to individuals who were participating in less vigorous levels of physical activity. Collectively, these findings raise the possibility that the energy requirement of the "active metabolic tissue" is increased with high levels of physical training. Furthermore, at least in young men, high levels of physical training may be needed to achieve a high RMR per kilogram of FFW relative to less trained individuals. Not all cross-sectional studies, however, have found differences in RMR per kilogram of FFW when comparing trained and untrained individuals (26, 33, 34, 48, 72). Factors that may contribute to discrepant findings among studies may include (*a*) insufficient sample sizes and statistical power to detect differences in RMR between groups that vary in aerobic fitness (26); (*b*) the timing of indirect calorimetry measurements relative to the last exercise bout (75); (*c*) technical or methodologic errors in determining energy expenditure; and (*d*) between-subject variability due to preceding dietary practices and the state of energy balance (47).

Surprisingly, the influence of physical activity on the regulation of resting energy expenditure in older individuals has received little consideration. Shock (67) first raised the possibility that physical activity influences RMR in older individuals. He noted that the decrement in RMR with age was much lower in a group of physically active individuals living in a community in New York (36) than in two institutionalized populations living in St. Louis (31) and Baltimore (70). This difference led Shock (67) to inquire, "Are the differences in RMR due to sampling, or are individuals who are participating in active community life, metabolically different from those who live a more sheltered and less active life in an institution?" In other words, does physical activity alter the rate of aging of RMR? The rate of aging of several other biological systems has been considered previously (68).

Several studies have examined the relation between the level of physical activity and RMR. Dill et al (14) examined changes in RMR and body composition in 16 champion runners during and 20 or more years after competition. Unfortunately, measurements of body fat and FFW were not made in the original studies and so were estimated on the basis of observations of cross-country runners with similar exercise training habits. The authors assumed a mean body composition of 8% body fat and 92% FFW in their first series of measurements. Follow-up measurements 27 years later showed modest group changes in estimated FFW, with only two of the volunteers exhibiting a considerable loss in FFW. The average decline in FFW was estimated to be 1% per decade in these active men. RMR, expressed per body

surface, exhibited a decline from 38.5 kcal m^{-2} in the fifth decade to 35.5 kcal m^{-2} in the eighth decade.

Recently, we (51) examined the influence of age and level of physical activity on RMR in healthy, nonobese men. RMR in 42 inactive and active younger (18–36 years of age) and 26 older inactive and active (59–76 years of age) men was examined with a ventilated-hood system. All metabolic measurements were performed at least 36 h after the last exercise bout. We found that RMR in active younger and older men was 6% higher, when normalized per kilogram of FFW, than in inactive younger and older men (Figure 2). This finding persisted when analysis of covariance was performed with FFW as the single covariate and RMR as the dependent variable. The higher RMR in active individuals, if extrapolated for a 24-h basis, would account for an additional increase of approximately 90 kcal per day. Therefore, in addition to the energy cost associated with the direct cost of exercise, the higher RMR in active individuals may also contribute to their lower body fat reserves. In this study, no effect of age on RMR was noted when normalized per kilogram of FFW. This result is in keeping with the suggestion that the decrease in skeletal muscle mass is the principal reason for the age-related decrement in RMR (78). By using a stepwise linear regression model, $\dot{V}_{O_2\,(max)}$ was found to be a significant predictor of RMR, independent of FFW. Collectively, these results suggest that the level of physical activity

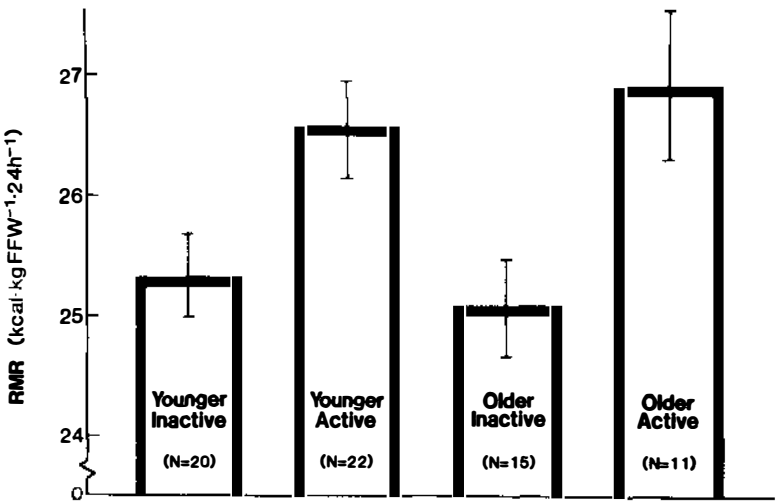

Figure 2 The effects of age and level of physical activity on the ratio of RMR to FFW. Active younger and older men had a higher RMR (~6%) than inactive younger and older men did. From Poehlman et al (51). Results were similar using analysis of covariance with RMR as dependent variable and FFW as covariate.

is associated with a higher RMR in both younger and older men and that differences in the physical activity level may contribute to individual variation in RMR.

Lundholm et al (38) also examined resting energy metabolism in older men and reported a higher RMR in active older men than in inactive older men when differences in FFW and body fat were taken into account. In an exercise intervention study, Meredith et al (40) did not find any changes in RMR in older individuals who exercised for 12 weeks at 70% of their peak oxygen consumption. $\dot{V}_{O_2\,(max)}$ increased by approximately 6% in the older men, but this increase was not accompanied by any alterations in RMR. Prolonged periods of exercise training may be necessary before alterations in RMR are observed in older men. Future research is needed to consider the duration and intensity of exercise necessary to enhance RMR in older individuals.

A cause-and-effect relation between physical activity and a high RMR cannot be established from the aforementioned studies. A significant genetic effect on RMR has been reported (6, 7, 21). Furthermore, changes in RMR (56) as well as alterations in $\dot{V}_{O_2\,(max)}$ (57) in response to short-term exercise training have exhibited a genetic effect. Therefore, it is unclear whether the influence of physical activity preceded the higher RMR or the elevated RMR was present in individuals who self-selected to participate in physical activity. Nonetheless, a compelling argument can be made in favor of a relation between long-term participation in physical activity and a higher RMR in light of evidence of both cross-sectional (52, 54, 73) and longitudinal (32, 35, 74) designs in which exercise was introduced to a sedentary population.

The effects of a higher RMR for older individuals would influence both energy intake and energy expenditure. An increase in energy expenditure by exercise and a higher RMR would significantly increase total 24 h energy expenditure. This increase would help stabilize body composition and permit greater food intake without a concomitant increase in body fat mass. This assumes that an increase in energy expenditure by physical activity would be matched by an increase in food intake in older individuals. At present, the adaptive changes in food intake to fluctuations in physical activity in older individuals are unclear and represent an interesting area of research.

THERMIC EFFECT OF A MEAL, PHYSICAL ACTIVITY, AND AGING

There is less extensive research on the effects of age on TEF. In fact we are unaware of any longitudinal studies that have examined the effects of aging on TEF. The paucity of longitudinal data is probably related to the difficulty in recruiting volunteers to participate in long-duration TEF experiments (i.e. 1–6 h) and the fact that the contribution of TEF to total 24-h

energy expenditure is quantitatively less significant than that of RMR and TEA. Several cross-sectional studies have been performed to examine the effects of age on TEF.

Tuttle et al (77) compared TEF in response to a protein meal challenge in eight younger men (20–30 years old) and six older men (72–84 years old) for 4.5 h. The meal challenge consisted of 150 g of ground beef and 30 g of egg white. The older subjects showed a slower initial thermic response to the meal challenge in the first 2 h of the postprandial period. However, the percent increase in the total postprandial oxygen consumption over basal levels was similar in the younger (9.7%) and older (11.9%) men. Thus, this study does not support an age-related difference in TEF. The authors indicated that the measurement of TEF was repeated in the same volunteers, but unfortunately the test–retest data were not reported. Given the scarcity of data on the reproducibility of TEF in humans, this information would have made a significant contribution to our understanding of the biological variability of TEF.

The effects of age on TEF were not examined again until the 1980s. Golay et al (24) measured glucose-induced thermogenesis in 17 younger (23 ± 1, mean ± SEM) and 13 older (53 ± 3) individuals for 3 h following ingestion of a 100-g oral glucose load. When the glucose-induced thermogenesis was related to the energy content (~400 kcal) of the load given, the value was 8.6% in the younger group and 5.8% in the older control group ($p < 0.05$). Glucose-induced thermogenesis was also negatively correlated ($r = -0.26$; $p < 0.05$) with age. The authors speculated that the insulin resistance associated with aging may contribute to the depressed TEF in the older volunteers. In a follow-up study, Golay et al (23) confirmed their previous findings. The energy expenditure associated with glucose ingestion was approximately 25% lower in older individuals (38–68 years of age) than in younger volunteers (19–39 years of age). The lower energy expenditure in the older group was also accompanied by a significant decrease in the postprandial glucose oxidation rate, despite a similar time course of glycemia. The lower TEF in older individuals may represent an additional factor that contributes to the decreased energy requirement with age and propensity to gain body fat.

Morgan & York (42) examined the TEF for 3 h in younger (24 ± 0.7 years of age) and older (71 ± 1.4 years of age) men in response to two "mixed" meals with different energy contents (480 and 950 kcal). TEF in both younger and older men was positively related to the meal size. The major finding was that the total thermic response expressed in absolute terms and as a percent increase over RMR was significantly greater for the younger group than for the older group. It is interesting that the diminished TEF in older individuals was found even though both test meals represented a relatively larger portion of their daily intake than in the younger group. The authors speculated that the

reduced thermogenic capacity in older individuals may represent a long-term adaptation to a lower energy intake in an effort to preserve energy. However, it is unclear whether the low energy intake and changes in body composition preceded the low TEF or whether alterations in TEF are primary to the decrease in energy intake with age.

Bloesch et al (4) attributed the decrease in TEF in older individuals primarily to an alteration in body composition (i.e. a decrease in FFW). Twelve elderly (61 ± 3 years of age) and 12 younger (25 ± 1 years of age) volunteers were administered a 75 g glucose load, and postprandial energy expenditure was measured for 3 h. The elderly group had a 15% lower TEF than the younger individuals. However, no differences were noted in TEF between younger and older individuals when postprandial data were normalized per kilogram of FFW. It is unclear why the authors normalized TEF data per unit of body potassium, since the level of FFW has not been shown, to our knowledge, to be a significant determinant of TEF. In our work, we did not observe any significant association between FFW and TEF in younger (55) or in older (53) individuals. In the work of Bloesch et al (4), fasting levels of plasma glucose, insulin, or free fatty acids were not different between younger and older individuals. In contrast, in response to the glucose challenge, the elderly showed a slight glucose intolerance and a higher insulin response. No differences in postprandial levels of free fatty acids were noted. The authors speculated that because similar amounts of glucose were stored in younger and older individuals, the cost of "obligatory thermogenesis" was the same in both groups. This raises the possibility that the association between aging and a lower TEF is influenced by a decrease in "facultative thermogenesis," possibly by a reduction in the responsiveness of SNSA to a meal or glucose challenge.

To our knowledge, only one study has examined the interaction of an acute exercise stimulus and meal ingestion on energy expenditure in older volunteers (63). This type of experiment represents "real-life" conditions because physiologic stimuli are frequently encountered in combination rather than in isolation. Some investigators have found a potentiating effect of exercise on TEF in younger individuals (8, 66), whereas others have found no additive effect of exercise and TEF when measured in close proximity (11, 82). Schutz et al (63) examined TEF at rest and during exercise in seven elderly men (68.6 ± 3.0 years of age) after ingesting meals containing different amounts of protein. As expected, the meal higher in protein content had a greater thermic effect than the meal lower in protein content, both at rest and during exercise. In this study, submaximal exercise failed to potentiate TEF, since the overall net increase in energy expenditure induced by meal consumption while exercising was not different from that at rest in older individuals. Thus, from these preliminary results, there appears to be no potentiating effect on energy expenditure when elderly individuals exercise soon after ingesting a meal.

The level of physical activity has recently been shown to influence TEF in younger individuals (13, 33, 34, 52, 54, 72, 73). Two recent studies have compared TEF in inactive older men with that in active older men to characterize TEF in older individuals who have maintained low levels of body fat and a physically active lifestyle for a long period. Lundholm et al (38) examined TEF in 10 physically well-trained elderly men and in 10 inactive elderly men. Each group consumed a 500-kcal liquid mixed meal, and TEF was measured for 180 min. Plasma concentrations of thyroid hormones and catecholamines were measured. The authors found a significantly higher TEF in trained older, men but no differences were noted in the postprandial respiratory quotient between the groups. No differences were noted in plasma norepinephrine before or after meal ingestion between the groups. These findings do not suggest that plasma catecholamines are unresponsive to a meal challenge in older individuals. The dissociation between circulating plasma catecholamines and TEF suggests that other energy-requiring factors may be implicated in the higher TEF in active older men.

We measured TEF in four groups of healthy men: sedentary younger, active younger, sedentary older, and active older men (53). The active younger and older men were comparable with respect to their level of physical activity. A mixed-composition liquid meal was administered that was tailored to the size of the FFW (i.e. 10 kcal per kg of FFW). Two important points should be noted: (*a*) no age-related decrement in TEF was found in these healthy, nonobese individuals; and (*b*) physically active men, regardless of age, had a higher TEF than their age-matched inactive controls did (Figure 3). These results suggests that physical activity, and not age per se, was the influencing factor on TEF in this study. Moreover, these findings persisted even after statistical control was exerted over differences in percent body fat by covariance analysis. A higher TEF in moderately active younger individuals has previously been reported (13, 26, 54). We have extended these previous findings to include active older men. The mechanism(s) for the higher TEF in active younger and older men remains to be determined. Again, a cause-and-effect relation between physical activity and TEF cannot be established from this study. Alterations in TEF in response to short-term exercise training have been shown to be genotype dependent (56). Therefore, it remains to be determined whether participation in physical activity caused the higher TEF or whether the higher TEF was already present in the physically active individuals. These studies suggest an association in older individuals between TEF and a physically active lifestyle, which is independent of adiposity. That is, in addition to the direct caloric cost of physical activity, an active lifestyle may increase postprandial energy expenditure. Long-term exercise intervention studies with subjects maintained in energy balance are needed to carefully characterize changes in RMR and TEF as a result of long-term participation in physical activity.

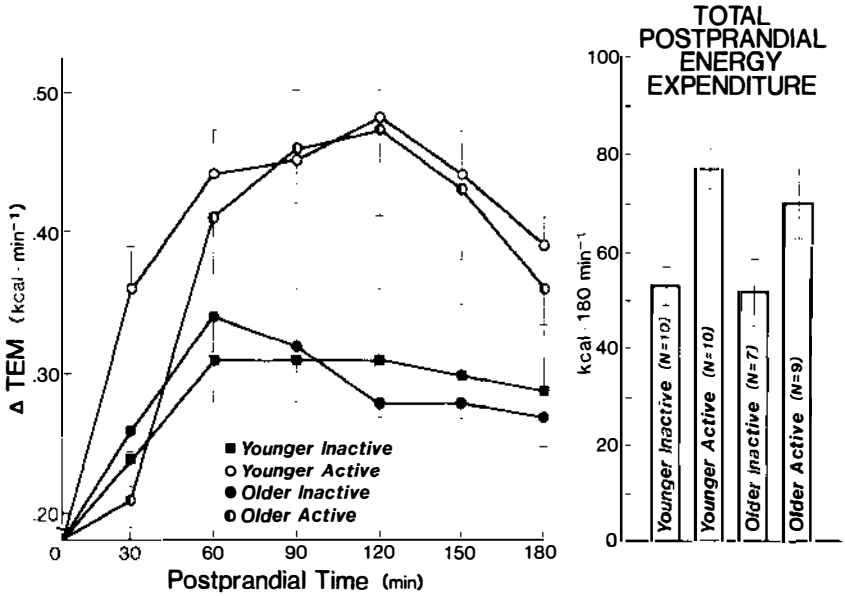

Figure 3 Increase in postprandial energy expenditure (TEF) for active and inactive younger and older men after ingestion of a liquid meal. The figure insert shows the total postprandial energy expenditure in the four groups. From Poehlman et al (53).

THERMOGENESIS, SYMPATHETIC NERVOUS SYSTEM ACTIVITY, AND AGING

Several studies have reported that aging is associated with an increase in SNSA. An earlier study found that plasma concentrations of norepinephrine, an index of overall sympathetic tone, was higher in older than in younger individuals (87). Although the results are still controversial, the heightened sympathetic tone has been reported to play a role in contributing to such medical complications as hypertension (16) and hyperlipidemia (62). More refined techniques for assessing SNSA have been developed (15). The infusion of tracer-labeled norepinephrine has been used to estimate plasma norepinephrine kinetics. This provides a more sensitive index of the resting sympathetic nervous system than do plasma concentrations alone, since it permits the in vivo estimation of two concurrent processes, appearance (or spillover) of norepinephrine into plasma after release from sympathetic nerve endings and subsequent removal of norepinephrine from the circulation. With this technique, the increase in sympathetic tone in older individuals has generally been attributed to an increase in plasma norepinephrine appearance (19, 27, 43, 58, 65), although Esler et al (18) have found that the increase in plasma norepinephrine concentration in older individuals was due to a reduc-

tion in norepinephrine clearance. The effects of age on norepinephrine kinetics have recently been reviewed (37).

It could be hypothesized that the age-related changes in the sympathetic nervous system are influenced by alterations in lifestyle that result in a decrease in physical activity and an increase in body fat (2, 10, 39) rather than a true aging effect per se. Since each bout of exercise activates the sympathetic outflow to many organs, adaptive changes in younger and older men might be predicted in the resting noradrenergic system as a result of long-term participation in physical activity.

Data on the effects of aerobic exercise on resting plasma norepinephrine concentrations in healthy younger individuals are discrepant. Some studies have found no effect of physical activity on resting norepinephrine concentrations in younger men (46, 71, 85), whereas others have found a reduction in plasma norepinephrine concentrations at rest after exercise training (5, 29, 45).

Several recent studies have considered the influence of exercise training on plasma norepinephrine kinetics. Jennings et al (29) found that exercise performed at 60–70% of $\dot{V}_{O_2\ (max)}$ (seven times a week) resulted in a 35% reduction in norepinephrine appearance in 8 of 10 subjects, whereas milder exercise did not affect the rate of norepinephrine appearance or clearance. The authors speculated that the decline in norepinephrine appearance probably contributed to the fall in blood pressure and total peripheral resistance index. These findings also suggest that a threshold of physical activity must be obtained before alterations in plasma norepinephrine appearance are observed.

Schwartz et al (64) prospectively examined the effects of diet and exercise on plasma norepinephrine kinetics in moderately obese young men who had been randomly assigned either to a 3-month diet program (1200 kcal/day) or to an aerobic exercise program [three or four times a week; 70–85% $\dot{V}_{O_2\ (max)}$]. They found no significant changes in blood pressure or pulse between the two groups. Weight loss was greater in the group assigned to the diet (13.6 kg) than in the group assigned to the exercise program (2.3 kg). The norepinephrine appearance rate declined by 17% after dietary weight loss, whereas no significant changes were noted after exercise training. The authors speculate that in moderately obese men, dietary weight loss is more effective than exercise training in reducing SNSA.

The influence of exercise training on resting sympathetic tone in older individuals has received little attention. However, we have recently examined the effects of age and level of physical activity on plasma norepinephrine kinetics in 67 younger and older healthy individuals well characterized for their level of aerobic fitness and body composition (50). All metabolic measurements were performed 36 h after the last exercise session. We found

no significant differences between younger active and younger inactive men for plasma norepinephrine appearance or clearance into circulation (Figure 4). On the other hand, we found a higher rate of norepinephrine appearance in active older men than in inactive older men. This suggests that physically active older men have higher resting sympathetic tone due to an elevated rate of norepinephrine appearance. No effects of age or physical activity on norepinephrine clearance were found (Figure 5). Furthermore, no significant associations were noted among percent body fat, supine blood pressure, and norepinephrine kinetics in younger and older men. Collectively, these results suggest that long-term participation in physical activity by older men is associated with a high level of norepinephrine appearance into circulation and that the degree of adiposity does not influence plasma norepinephrine kinetics in healthy younger and older men. Collectively, these results suggest that it is important to consider the habitual level of physical activity when evaluating SNSA in healthy older men.

We chose to normalize norepinephrine kinetics data per kilogram of FFW because the majority of norepinephrine clearance is reported to take place in the lungs, kidneys, and splanchnic region and probably also in skeletal muscle (17). Previous studies have normalized norepinephrine kinetics data by body surface area (19, 80). However, body surface area is never actually measured; it is only estimated from an equation in which height and weight are the variables. Furthermore, it does not consider that individuals with a similar body surface area may have significant differences in body composition.

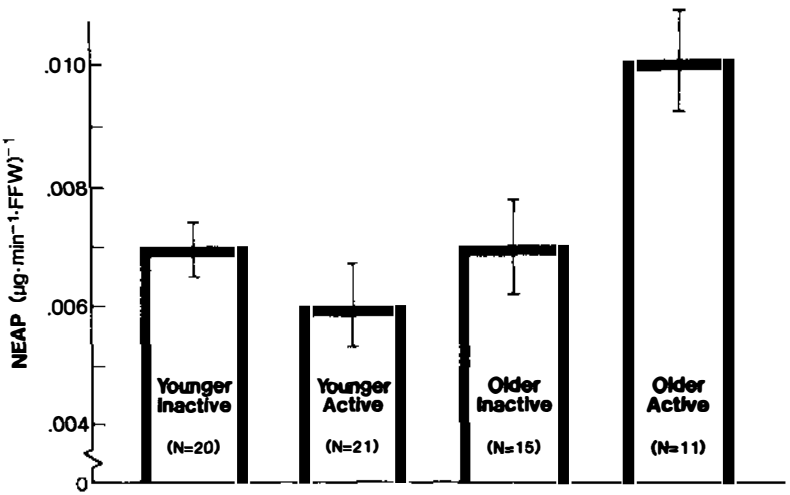

Figure 4 Resting levels of norepinephrine appearance normalized for FFW. Bars are ± SEM. A significant interaction was found ($F = 8.0$; $p < 0.01$). Posthoc testing revealed differences between older active men relative to younger active men. From Poehlman et al (50).

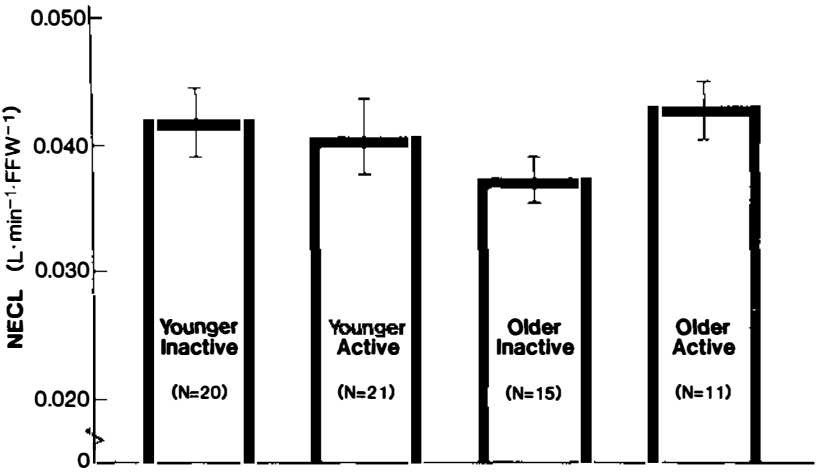

Figure 5 Resting levels of norepinephrine clearance normalized for FFW. Bars are means ± SEM. No effect of age or level of physical activity was noted. From Poehlman et al. (50).

Previous reports have indicated an association between TEF and SNSA (1, 59) as determined from plasma concentrations of norepinephrine and epinephrine. Because aging is associated with alterations in both SNSA and TEF, it is of interest to examine the relation between norepinephrine kinetics and thermogenesis. Schwartz et al (65) examined TEF and plasma norepinephrine kinetics in 11 younger and 9 older men matched for percentage of body fat before and after ingestion of a 800-kcal liquid meal. At baseline (i.e. before meal ingestion) the norepinephrine concentration and the rate of norepinephrine appearance were increased in the elderly group relative to the younger group. In contrast to our results (50), Schwartz et al (65) found that the percentage of body fat was an independent predictor of norepinephrine appearance at baseline. Discrepant results between the two studies may relate to the difference in adiposity of the volunteers involved. The volunteers in our study (50) were leaner than the individuals studied by Schwartz et al (65). Perhaps a higher degree of adiposity is associated with alterations in SNSA. After meal consumption, there was an increase in arterialized plasma norepinephrine appearance in the young group, whereas no significant increase was detected in the older group. TEF values in the elderly and younger individuals were not statistically different. The authors speculate that the lower TEF in elderly individuals was related to the smaller increment in plasma norepinephrine appearance, although no correlations were presented. The possibility of a blunted sympathetic nervous system in elderly individuals in response to a meal challenge deserves further consideration.

SUMMARY

A brief overview of the effects of aging on two components of energy expenditure, RMR and TEF, has been presented. Whereas the decline in RMR appears to be related primarily to the loss of muscle tissue, the reason for the lower TEF in older individuals is less clear. Evidence has been provided suggesting that physical activity influences RMR and TEF in younger and older individuals. The possibility is raised that regular physical activity will increase RMR and TEF in older individuals. The increase in resting energy expenditure (RMR and TEF), in addition to the direct energy cost of physical exercise, may help increase the total energy requirements in older individuals. The majority of studies support an increase in resting SNSA in older individuals. The level of physical activity and percentage of body fat may be two factors contributing to age-related alterations in resting sympathetic tone. Future studies should continue to examine the effects of physical activity and body composition on metabolic rate and SNSA in older individuals.

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