

Functional and Metabolic Consequences of Sarcopenia¹

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ABSTRACT The capacity of older men and women to adapt to regularly performed exercise has been demonstrated by many laboratories. Aerobic exercise results in improvements in functional capacity and reduced risk of developing type II diabetes in the elderly. High intensity resistance training (above 60% of the 1 repetition maximum) causes large increases in strength in the elderly, and resistance training significant increases muscle size. Resistance training also significantly increases energy requirements and insulin action of the elderly. We recently demonstrated that resistance training has a positive effect on multiple risk factors for osteoporotic fractures in previously sedentary post-menopausal women. Because the sedentary lifestyle of individuals in a long-term care facility may exacerbate losses of muscle function, we applied this same training program to frail, institutionalized elderly men and women. In a population of 100 nursing home residents, a randomly assigned high intensity strength training program resulted in significant gains in strength and functional status. In addition, spontaneous activity, measured by activity monitors, increased significantly in those participating in the exercise program; there was no change in the sedentary control group. Before the strength training intervention, the relationship of whole-body potassium and leg strength was relatively weak ($r^2 = 0.29$, $P < 0.001$), indicating that in very old persons muscle mass is an important but not the only determiner of functional status. Thus exercise may minimize or reverse the syndrome of physical frailty prevalent among very old individuals. Because of their low functional status and high incidence of chronic disease, there is no segment of the population that can benefit more from exercise training than the elderly. *J. Nutr.* 127: 998S–1003S, 1997.

KEY WORDS: • sarcopenia • muscle mass • aging • muscle strength • exercise

Loss of muscle mass with age in humans has been demonstrated both indirectly and directly. The excretion of urinary creatinine, reflecting muscle creatine content and total muscle mass, decreases by nearly 50% between the ages of 20 and 90 y (Tzankoff and Norris 1978). Computed tomography of individual muscles shows that after age 30 y, there is a decrease in cross-sectional areas of the thigh along with decreased muscle density associated with increased intramuscular fat. These changes are most pronounced in women (Imamura et al. 1983). Muscle atrophy may result from a gradual and selective loss of muscle fibers. The number of muscle fibers in the midsection of the vastus lateralis of autopsy specimens is lower by about 110,000 in elderly men (age 70–73 y) than in young men (age 19–37 y), a 23% difference (Lexell et al. 1983). The decline is more marked in type II muscle fibers, which fall from an average 60% in sedentary young men to less than 30% after the age of 80 y (Larsson 1983); this decline is significantly related to age-related decreases in strength ($r = 0.54$, $P < 0.001$).

A reduction in muscle strength is a major component of normal aging. Data from the Framingham (Jette and Branch 1981) study indicate that 40% of the female population aged

55–64 y, almost 45% of women aged 65–74 y, and 65% of women aged 75–84 y were unable to lift 4.5 kg. In addition, a similarly high percentage of women in this population reported that they were unable to perform some aspects of normal household work. Larsson et al. (1979) studied 114 men between the ages of 11 and 70 y and found that isometric and dynamic strength of the quadriceps increased up to the age of 30 y and decreased after the age of 50 y. The reductions in strength between the ages of 50 and 70 y ranged from 24 to 36%. They concluded that much of the reduction in strength was due to a selective atrophy of type II muscle fibers, which were 36% smaller in diameter compared with those of 40-y-old subjects. It seems that muscle strength losses are most dramatic after the age of 70 y. Knee extensor strength of a group of healthy 80-y-old men and women studied in the Copenhagen City Heart Study (Danneskoild-Samsøe et al. 1984) was 30% lower than in a previous population study (Aniansson et al. 1981) of 70-y-old men and women. Thus cross-sectional as well as longitudinal data indicate that muscle strength declines by approximately 15% per decade in the sixth and seventh decade and about 30% thereafter (Danneskoild-Samsøe et al. 1984, Harries and Bassey 1990, Larsson 1978, Murray et al. 1985, Sohlstrom et al. 1993, Spraul et al. 1993). Although there is some indication that muscle function is reduced with advancing age, the overwhelming majority of the loss in strength results from an age-related decrease in muscle mass. We (Frontera et al. 1991) examined more than 200 men and women between the ages of 45 and 78 y. Isokinetic and isometric strength of the upper and lower body dif-

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TABLE 1

Strength corrected for body composition in older women¹

Age, y	Strength, Nm	Nm/FFM	Nm/muscle mass
45–54	108 ± 22	2.7 ± 0.4	6.1 ± 0.9
55–64	98 ± 20	2.6 ± 0.4	5.9 ± 1.2
65–78	89 ± 15*	2.5 ± 0.4	5.8 ± 1.1

¹ From Frontera et al. (1991). * Significantly different from the value for the age 45–54 y group ($P < 0.05$). FFM = fat-free body mass (kg).

ferred significantly different between men and women and decreased with advancing age. However, when corrected for fat-free mass (estimated from hydrostatic weighing) and total body muscle mass (estimated from 24-h urinary creatinine), age-related differences disappear (Table 1).

STRENGTH AND FUNCTIONAL CAPACITY

Bassey et al. (1988) measured muscle strength and the amount and speed of customary walking in a large sample of men and women older than 65 y. They found an age-related decline in muscle strength and a significant negative correlation between strength and chosen normal walking speed for both sexes ($r = 0.041$, $P < 0.001$ for men; $r = 0.36$, $P < 0.01$ for women). Bassey and co-workers (1989) measured flexibility and found that the mean value for the elderly was 30 degrees less than those accepted for younger men and women. Nearly one-half of the distribution fell below the accepted threshold level of 120 degrees for adequate function. Fiatarone and colleagues (1990) observed a closer relationship between quadriceps strength and habitual gait speed ($r = -0.745$, $P < 0.01$) in a group of frail institutionalized men and women above the age of 86 y. In these subjects, fat-free mass ($r = 0.732$) and regional muscle mass estimated by computerized tomography ($r = 0.752$) were correlated with muscle strength. In the same population, we (Bassey et al. 1992) recently demonstrated that leg power is closely associated with functional performance. In older, frail women, leg power was highly correlated with walking speed ($r = 0.93$, $P < 0.001$), accounting for up to 86% of the variance in walking speed (Table 2). Leg power, which represents a more dynamic measurement of muscle function, may be a useful predictor of functional capacity in very old persons. These data suggest that with the advancing age and very low activity levels seen in institutionalized patients, muscle strength is a critical component of walking ability.

TABLE 2

Correlation coefficients between leg extensor power and functional performance¹

	Men	Women	All, n
Chair rising speed, s	0.45	0.83***	0.65*** (24)
Stair-climbing speed, m/s	0.76**	0.85***	0.81*** (22)
Walking speed, km/h	0.58*	0.93***	0.80*** (25)
Stair-climbing power, W	0.91***	0.86***	0.88*** (23)

¹ Leg extensor power (W/kg, both legs together) is the independent variable. The subjects were 26 nursing home residents (men averaged 88 ± 1.6 y, women averaged 86 ± 1.5 y). Statistical significance: * $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$. From Bassey et al. 1992.

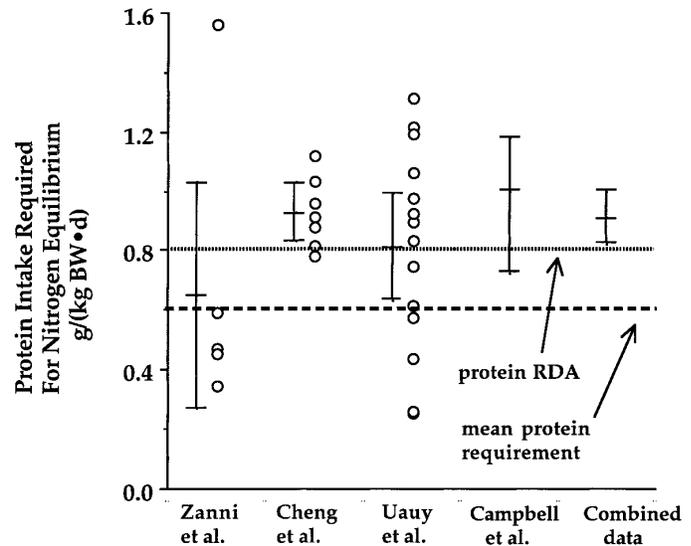


FIGURE 1 Recalculated data from three previous studies examining the dietary protein requirements of the elderly along with data of Campbell et al. (1994). The mean requirement for these four studies is greater than the current RDA of $0.8 \text{ g protein} \cdot \text{kg}^{-1} \cdot \text{d}^{-1}$. These three studies provide evidence for a higher dietary protein requirement for healthy elderly than previous estimates. Redrawn from Campbell et al. (1994). BW = body weight.

PROTEIN NEEDS AND AGING

Previous estimates of dietary protein needs of the elderly (using nitrogen balance) have ranged from 0.59 to $0.8 \text{ g} \cdot \text{kg}^{-1} \cdot \text{d}^{-1}$ (Gersovitz et al. 1982, Uauy et al. 1978, Zanni et al. 1979). However, the low value was reported by Zanni et al. (1979), who preceded their 10-d dietary protein feeding with a 17-d protein-free diet, which was likely to improve nitrogen retention during the 10-d balance period. Recently, we (Campbell et al. 1994) reassessed the nitrogen balance studies mentioned above using the currently accepted World Health Organization nitrogen-balance formula (WHO/FAO/UNU 1985). These newly recalculated data were combined with nitrogen balance data collected on 12 healthy older men and women (age range 56–80 y, eight men and four women) consuming the current Recommended Daily Allowance (RDA) for protein or double this amount (0.8 or $1.6 \text{ g} \cdot \text{kg}^{-1} \cdot \text{d}^{-1}$, respectively) in our laboratory. Our subjects consumed the diet for 11 consecutive days, and nitrogen balance ($\text{mg N} \cdot \text{kg}^{-1} \cdot \text{d}^{-1}$) was measured during d 6 to 11. The estimated mean protein requirements from the three retrospectively assessed studies and the current study can be combined by weighted averaging to produce an overall protein requirement estimate of $0.91 \pm 0.043 \text{ g} \cdot \text{kg}^{-1} \cdot \text{d}^{-1}$. The combined estimate excluding the data from our 12 subjects is $0.894 \pm 0.048 \text{ g protein} \cdot \text{kg}^{-1} \cdot \text{d}^{-1}$. Figure 1 shows the mean values for achieving nitrogen equilibrium for the three retrospectively assessed studies as well as our more current data.

The current RDA in the United States of $0.8 \text{ g} \cdot \text{kg}^{-1} \cdot \text{d}^{-1}$ is based on data collected, for the most part, on young subjects. The RDA includes an upward adjustment based on the CV of the average requirement established in these studies ($0.6 \text{ g} \cdot \text{kg}^{-1} \cdot \text{d}^{-1}$). On the basis of the CV previously established for nitrogen balance studies, an adequate dietary protein level for 97.5% of the elderly population would be provided by an intake of 25% (twice the SD) above the mean protein requirement. Our data suggest that the safe protein intake for elderly adults is $1.25 \text{ g} \cdot \text{kg}^{-1} \cdot \text{d}^{-1}$. On the basis of the current

and recalculated short-term nitrogen balance results, a safe recommended protein intake for older men and women should be set at 1.0 to 1.25 g high quality protein \cdot kg⁻¹ \cdot d⁻¹. Hartz (1992) reported that approximately 50% of 946 healthy free-living men and women above the age of 60 y living in the Boston, Massachusetts, area consumed less than this amount of protein, and 25% of the elderly men and women in this survey consumed <0.86 and <0.81 g protein \cdot kg⁻¹ \cdot d⁻¹, respectively. A large percentage of homebound elderly people consuming their habitual dietary protein intake (0.67 g mixed protein \cdot kg⁻¹ \cdot d⁻¹) have been shown (Bunker et al. 1987) to be in negative nitrogen balance. Inadequate dietary protein intake may be an important cause of sarcopenia. The compensatory response to a long-term decrease in dietary protein intake is a loss in lean body mass.

ENERGY METABOLISM

Daily energy expenditure in weight-stable adults declines progressively throughout adult life (McGandy et al. 1966). In sedentary individuals, the main determinant of energy expenditure is fat-free mass (Ravussin et al. 1986), which declines by about 15% between the third and eighth decade of life, contributing to a lower basal metabolic rate in the elderly (Cohn et al. 1980). Tzankoff and Norris (1978) saw that 24-h creatinine excretion (an index of muscle mass) was closely related to basal metabolic rate at all ages. Nutrition surveys of those over the age of 65 y show a very low energy intake for men [5878 MJ/d, 96kJ/(kg \cdot d⁻¹)] (Hartz 1992). These data indicate that preservation of muscle mass and prevention of sarcopenia can help prevent the decrease in metabolic rate. Although body weight increases with advancing age, an age-associated increase in relative body fat content has been demonstrated by a number of investigators. This increase in body fatness results from a number of factors, but chief among these causes are a declining metabolic rate and activity level coupled with an energy intake that does not match this declining need for energy. Meredith et al. (1989a and 1989b) demonstrated that endurance-trained men between 20 and 60 y old consumed a diet very high in energy but that body fat levels were negatively correlated with the total number of hours spent exercising per week. Age was not found to be a covariate in this study. More recently, Roberts and co-workers (1992) examined the relationship between total energy use (using the doubly labeled water technique) and body composition in a group of sedentary young and old men and found that energy spent in daily activity accounted for 73% of the variability in body fat content.

In addition to its role in energy metabolism, skeletal muscle and its age-related decline may contribute to such age-associated changes as reduction in bone density (Bevier et al. 1989, Sinaki et al. 1986, Snow-Harter et al. 1990), insulin sensitivity (Kolterman et al. 1980) and aerobic capacity (Flegg and Lakatta 1988). For these reasons, strategies for preservation of muscle mass with advancing age and for increasing muscle mass and strength in the previously sedentary elderly may be an important way to increase functional independence and decrease the prevalence of many age-associated chronic diseases.

AEROBIC EXERCISE

Maximal aerobic capacity has been demonstrated to decrease at the rate of approximately 1%/y. This decline is due to a number of factors, including decreased maximal cardiac output due to lower maximal heart rate and contractility, de-

creased muscle mass (Flegg and Lakatta 1988) and the decreased oxidative capacity of skeletal muscle (Meredith et al. 1989a). As tasks of everyday living represent a larger and larger percentage of maximum aerobic capacity, it is not difficult to see why many elderly persons (particularly women because of a lower fitness level at all ages) choose not to perform them. The capacity of elderly men and women to respond to increased levels of physical activity with improvements in strength and/or aerobic capacity depends, in large measure, on the frequency, intensity and duration of the exercise program. With aerobic exercise training, intensity is generally reported as a percentage of VO_{2max} or of maximal heart rate. Aerobic training involves high repetition muscle contractions and leads to minimal strength gains. Intensity of resistance training is generally reported as a percentage of the one repetition maximum (1 RM), the maximum amount of force that a muscle group can generate with one single contraction.

A number of studies have shown a great capacity of elderly persons to respond to aerobic exercise. A study (Seals et al. 1984b) examining the effects of 6 mo of low intensity and 6 mo of high intensity exercise demonstrated that healthy 60- to 70-y-old subjects increase their average VO_{2max} by 30% with a range of 2–40%. There was no change in maximal cardiac output as a result of the year-long intervention; however, a decrease in blood lactate levels during a standard exercise task was observed. The authors concluded that the increase in maximal aerobic capacity occurred as a result of peripheral rather than central adaptations. Our laboratory (Meredith et al. 1989a) compared the peripheral effects of vigorous endurance exercise (stationary cycling: 45 min/d, 3 d/wk at 70% of maximal heart rate reserve) in young (24-y-old) and older (65-y-old) men and women. The muscle oxidative capacity (from vastus lateralis muscle biopsies) of the older subjects increased by an average of 128%, whereas that of the younger subjects showed only a 27% increase. The absolute increase in VO_{2max} was not different between the two groups; however, the relative improvement in the older subjects was 20% versus 12% in the younger subjects. Kohrt and co-workers (1991) examined the adaptations of 53 men and 57 women between the ages of 60 and 71 y to 9–12 mo of regular aerobic exercise (walk/run: 4 d/wk, 45 min/d, 80% maximal heart rate). They observed an average 24% increase in VO_{2max} with a large range (0–58%). In a subset of 23 men and women in this study, Coggan et al. (1992) observed large increases in muscle mitochondrial enzyme activity and capillary density, indicating a substantial capacity of skeletal muscle to respond to regular aerobic exercise.

It is well established that aging is associated with decreased glucose tolerance and a greatly increased incidence of noninsulin-dependent diabetes mellitus (NIDDM). It is generally accepted that decreasing glucose tolerance of aging is associated with the previously mentioned age-associated changes in body composition and activity levels (Kolterman et al. 1980). Improved fitness as a result of aerobic exercise has also been demonstrated to improve glucose tolerance in previously sedentary subjects (Holloszy et al. 1986, Seals et al. 1984a), and exercise has been shown to prevent the onset of NIDDM. Recently, our laboratory examined the effects of 12 wk of high or low intensity aerobic exercise (cycle ergometry: 4 d/wk, 45 min/d at 55 or 75% of maximal heart rate) with no weight loss on aspects of muscle and whole-body carbohydrate metabolism. Men and women with impaired glucose tolerance were selected for participation after an oral glucose tolerance test. No differences in results were seen between low and high intensity exercise. Significant improvements in oral glucose tolerance and insulin-stimulated glucose disposal rate were ac-

accompanied by increased skeletal muscle glycogen levels and a 68% increase in muscle GLUT-4 levels. These data indicate that improvements in carbohydrate metabolism resulting from exercise occur primarily in skeletal muscle. Clearly, exercise can improve glucose metabolism in both subjects at high risk for NIDDM as well as those with the disease by increasing the opportunity for body fat loss as well as stimulating the adaptive response of skeletal muscle, the primary site of glucose disposal.

STRENGTH TRAINING

Strength conditioning is generally defined as training in which the resistance against which a muscle generates force is progressively increased over time. Muscle strength has been shown to increase in response to training between 60 and 100% of the 1 RM (MacDougall 1986). Strength conditioning increases muscle size, and this increase is largely the result of an increase in contractile protein content.

It is clear that when the intensity of the exercise is low, only modest increases in strength are achieved by elderly subjects (Aniansson and Gustafsson 1981, Larsson 1982). A number of studies have demonstrated that, given an adequate training stimulus, older men and women show similar or greater strength gains compared with young individuals as a result of resistance training.

Frontera et al. (1988 and 1990) showed that older men responded to a 12-wk progressive resistance training program (80% of the 1 RM, three sets of eight repetitions of the knee extensor and flexors, 3 d per week) by more than doubling extensor strength and more than tripling flexor strength. The increases in strength averaged approximately 5% per training session, similar to strength gains observed by younger men. Total muscle area estimated by computerized tomography increased by 11.4%. Biopsies of the vastus lateralis muscle revealed similar increases in type I fiber area (33.5%) and type II fiber area (27.6%). Daily excretion of urinary 3-methyl-L-histidine increased with training ($P < 0.05$) by an average of 40.8%, indicating that increased muscle size and strength resulting from progressive resistance training is associated with an increased rate of myofibrillar protein turnover. Half of the men who participated in this study were given a daily protein-energy supplement providing an extra 2343 ± 66.9 KJ/d (16.6% as protein, 43.3% as carbohydrate and 40.1% as fat) in addition to their normal ad libitum diet. The rest of the subjects received no supplement and consumed an ad libitum diet. By wk 12 of the study, dietary energy ($12,384 \pm 962.3$ KJ in supplemented subjects and 6778.1 ± 334.7 KJ in nonsupplemented subjects) and protein (118 ± 10 g in supplemented subjects and 72 ± 11 g in nonsupplemented subjects) intake were significantly different between the groups.

Composition of the mid thigh (as estimated by computerized tomography) showed that the supplemented group had greater gains in muscle than did the nonsupplemented men (Meredith et al. 1992). In addition, urinary creatinine excretion was greater at the end of the training in the supplemented group than in the nonsupplemented group, indicating a greater muscle mass in the supplemented group at the end of the 12 wk of training. The change in energy and protein intake (beginning vs. 12 wk) was correlated with the change in mid thigh muscle area ($r = 0.69$, $P = 0.019$; $r = 0.63$, $P = 0.039$, respectively). There was no difference in the strength gains between the two groups. These data suggest that a change in total food intake, or perhaps selected nutrients, in subjects beginning a strength training program can affect muscle hypertrophy. High intensity resistance training seems to have profoundly anabolic effects in the elderly. Data from our labora-

tory demonstrated a 10–15% decrease in nitrogen excretion at the initiation of training that persisted for 12 wk (Campbell et al. 1995). That is, progressive resistance training improved nitrogen balance; thus older subjects performing resistance training have a lower mean protein requirement than do sedentary subjects. These results are somewhat at variance with our previous research (Meredith et al. 1989b) demonstrating that regularly performed aerobic exercise causes an increase in the mean protein requirement of middle-aged and young endurance athletes. This difference probably results from increased oxidation of amino acids during aerobic exercise that may not be present during resistance training.

Resistance training may be an important adjunct to weight loss interventions in the elderly. Campbell and co-workers (1995) examined the effects of high intensity resistance training on energy requirements of a group of 12 men and women aged 56–80 y. Energy intake was titrated for body weight maintenance in a group of older men and women living in a metabolic ward. These subjects were participating in both upper and lower body resistance training (3 d/wk, three sets of eight repetitions, 80% of 1 RM). At the end of 12 wk of training, these subjects required an average 15% increase in energy intake to maintain body weight. The increased energy expenditure included increased resting metabolic rate and the energy cost of resistance exercise. The results of this study are supported by the data of Pratley et al. (1994), who also demonstrated a significant increase in resting metabolic rate with resistance training. Resistance training is therefore an effective way to increase energy requirements, decrease body fat mass and maintain metabolically active tissue mass in healthy older people. In addition to its effect on energy metabolism, resistance training improves insulin action in older subjects (Miller et al. 1994).

Regularly performed aerobic exercise has positive effects on bone health in healthy, postmenopausal women (Gutin and Kasper 1992). Nelson and co-workers (1991) demonstrated that a 1-y program of vigorous walking preserved the bone density of the lumbar spine compared with results for a group of age-matched sedentary controls. However, no effect of exercise was seen at any other bone site or in total body calcium. Recently, we (Nelson et al. 1994) examined the effects of a high intensity resistance training program on bone health in a group of postmenopausal women. Forty women (aged 50–70 y) were randomized to a sedentary control or resistance training (80% of 1 RM, twice a week, 52 wk) group. The sedentary control group demonstrated typical age-associated declines in bone density and total body mineral content whereas the strength training had a protective effect on the femoral neck bone mineral density, lumbar spine bone mineral density, and total body mineral content. However, in addition to its effect on bone, the strength training also increase muscle mass and strength, dynamic balance and overall levels of physical activity. All of these outcomes may result in a reduction in the risk of osteoporotic fractures. In contrast, traditional pharmacological and nutritional approaches to the treatment or prevention of osteoporosis have the capacity to maintain or slow the loss of bone but not the ability to improve balance, strength, muscle mass or physical activity.

The very old and frail elderly experience skeletal muscle atrophy as a result of disuse, disease, undernutrition and the effects of aging per se. Muscle weakness that accompanies advanced age has been positively related to the risk of falling and fracture in these older individuals (Scheibel 1985). For this reason, we studied the effects of high intensity, progressive resistance training on quadriceps muscle strength in a group of institutionalized elderly men and women (age range 87–96

y). Initial strength levels were extremely low in these subjects, with a mean 1 RM of 8 kg for the quadriceps. The absolute amount of weight lifted by the subjects during the training increased from 8 to 21 kg. The average increase in strength after 8 wk of resistance training was $174 \pm 31\%$, and mean increase in muscle cross-sectional area via computerized tomography was $10 \pm 8\%$ (Fiatarone et al. 1990). The substantial increases in muscle size and strength were accompanied by clinically significant improvements in tandem gait speed and index of functional mobility. Repeat 1 RM testing in seven of the subjects after 4 wk of no training showed that quadriceps strength had declined 32%. Our preliminary data indicate that maintenance of the initial strength gains can be accomplished by as little as one exercise session per week at the appropriate training intensity (60–100% of 1 RM). Fiatarone and co-workers (1994) also demonstrated that increasing muscle strength in very old nursing-home residents improved balance, gait speed and spontaneous activity. In this study, the relationship between whole-body potassium levels (an index of active cell mass) and lower body strength was examined in 100 subjects between 72 and 98 y old. A significant correlation ($r^2 = 0.29$) was seen. This relatively weak relationship indicates that, although muscle mass is an important determiner of functional status in the very old, other factors such as overall levels of physical activity may be equally important. These studies demonstrate that frail elderly men and women, well into their tenth decade of life, retain the capacity to adapt to progressive resistance exercise training with significant and clinically relevant muscle hypertrophy and increases in muscle strength. Results from the resistance training studies performed in the young, middle-aged, elderly and the oldest old indicate that it is the intensity of the stimulus, not the underlying fitness or frailty of the individual, that determines the magnitude of the gains in strength and muscle size.

In summary, it is clear that the capacity to adapt to increased levels of physical activity is preserved even in the oldest old. Regularly performed exercise results in a remarkable number of positive changes in elderly men and women. Because sarcopenia and weakness may be almost universal characteristics of advancing age, strategies for preserving or increase muscle mass in the elderly should be implemented. With increasing muscle strength, increased levels of spontaneous activity have been seen in both healthy, free-living older subjects and in very old and frail men and women. Resistance training, in addition to its positive effects on insulin action, bone density, energy metabolism and functional status, may also be an important way to increase overall levels of physical activity in the elderly.

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