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Effects of exercise training in the elderly: impact of progressive-resistance training on skeletal muscle and whole-body protein metabolism

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The changes in cardiovascular and muscular performance associated with advancing age closely parallel the age-related changes observed in the musculoskeletal and cardiorespiratory systems. In sedentary individuals, maximal O_2 uptake declines at a rate of 1% per year after the third decade of life (Astrand, 1960) and isometric and dynamic muscle strength begin to decrease after the fifth decade (Larsson, 1983). These declines in exercise capacity throughout an individual's life span can affect functional capacity and impinge on the ability to perform activities of daily living. The decreased cardiorespiratory function and reduced muscle mass and strength observed with advancing age resemble the change in these variables which occur with bedrest or reduced activity (Saltin & Rowell, 1980; Bortz, 1982). Together with these declines in physiological and metabolic function are alterations in voluntary food intake and energy requirements. Energy intake as well as total daily energy expenditure decline with advancing age (McGandy *et al.* 1966). The relative importance of the ageing process itself, nutritional inadequacies, and the documented age-related declines in voluntary physical activity on the decline in fat-free mass (FFM) and exercise tolerance have yet to be fully understood.

Nutritional status, functional capacity and body composition are all interrelated. Alterations in whole-body composition particularly the FFM or lean body mass component have a significant impact on both nutrient requirements (particularly energy and protein) and the functional exercise capacity of an individual. Declines or deficits in functional capacity can be caused by inadequate nutrient intake as well as a reduction in the FFM. These relationships are of particular importance in the elderly whose functional capacity may already be compromised.

The present review describes the age-related changes in body composition with particular reference to the loss of skeletal muscle mass or 'sarcopenia'. The effects of this reduced skeletal muscle mass on functional status and the impact of exercise interventions on skeletal muscle structure and function in the elderly are also discussed. Finally, the effects of ageing on whole-body and skeletal muscle protein turnover are discussed with specific reference to the effects of exercise on protein metabolism in the elderly.

'SARCOPENIA' AND THE AGE-RELATED LOSS OF SKELETAL MUSCLE

The most visible and, perhaps, the most profound changes which occur with advancing age are the alterations in whole-body composition. There is a progressive decline in the FFM and a corresponding increase in fat mass during adulthood. Estimates from several studies have indicated that beyond the third decade of life fat mass increases and continues to increase well into the eighth decade (Parizkova, 1974; Cohn *et al.* 1980). Arm circumference and skinfold thickness measurements from 700 male participants in the Baltimore Longitudinal Aging Study aged 20–92 years revealed a slow progressive loss of lean tissue until age 65 years, followed by a more rapid decline (Borkan & Norris, 1977).

By far the most important changes in body composition which occur with advancing age that affect function are the reductions in active skeletal muscle mass. FFM or body cell mass, as measured by the total body K:N ratio, reveals that non-muscle lean tissue is preserved at the expense of the loss of skeletal muscle mass (Cohn *et al.* 1980). Tzankoff & Norris (1978) confirmed that skeletal muscle mass measured by 24 h urinary creatinine excretion declines on average 6% per decade and that this decline in muscle mass is largely responsible for the age-related decrease in resting metabolic rate. Flegg & Lakatta (1988) have demonstrated also that the decline in muscle mass observed with age as measured by 24 h urinary creatinine excretion can explain approximately 50% of the age-related decline in maximal O_2 uptake. These findings indicate that the alterations in body composition and, in particular, the declines in skeletal muscle mass have profound effects on basal metabolism and functional exercise capacity. In addition, loss of lean body mass or FFM appears to affect disease outcome in patients with chronic illness (DeWyss *et al.* 1980). In light of the clinical and functional significance of this age-related decline in skeletal muscle mass, a new term 'sarcopenia' (from Greek: sarcos, flesh, and penia, poverty; i.e. a loss of flesh) has been adopted to characterize this age-associated syndrome (Evans & Campbell, 1993).

By far the most significant functional component of the FFM or skeletal muscle mass to decrease with age is the loss in the total body N or protein. The loss of body protein mass with advancing age may be a result of several factors, including a decreased rate of protein synthesis, increased protein degradation, a decreased intake of protein and/or energy, and/or a reduction in voluntary contractile activity.

DECLINE IN MUSCLE STRENGTH AS A FUNCTION OF AGE

A decline in dynamic, isokinetic and static muscle strength has been noted with advancing age (Aniansson *et al.* 1980). However, despite the declines in skeletal muscle mass which begin in the third decade, maximum dynamic and isometric strength and maximum knee extension velocity are maintained until the fifth decade of life and then decline precipitously thereafter (Larsson *et al.* 1979). Larsson *et al.* (1979) have reported that there is a selective loss of type II (fast twitch) muscle fibres associated with this decline in strength. Dissections of whole thigh muscle in cross sections from cadavers, also, have demonstrated an 18% decline in total muscle area and a 25% decrease in the total number of muscle fibres in older cadavers, with a specific decrease in the number of type II muscle fibres (Lexell *et al.* 1983). However, other studies have reported a reduction in mean fibre areas of both type I and type II fibre with no reduction in type II muscle fibre populations (Grimby *et al.* 1982; Essen-Gustavsson & Borges, 1986).

Several studies in the elderly have suggested that muscle strength is closely associated with functional activities of daily living. The declines in muscle strength with age are related to impairment in function even in ambulatory free-living older individuals. Using a survey questionnaire, Jette & Branch (1981) evaluated the exercise habits of 2654 men and women aged 55–84 years. They reported that 40% of the females aged 55–64 years, nearly 45% of the females aged 65–74 years, and 65% of females aged 75–84 years responded that they were unable to lift 4·5 kg. The trends reported in this study were similar for men, although of a lower absolute level. In a sample of men and women aged 65 years and older, Bassey *et al.* (1988) reported a significant inverse relationship between isometric muscle strength of the *plantar flexors* of the foot and age (men: r −0·29, $P<0·05$; women: r −0·37, $P<0·01$) and lower isometric strength in older women than in men. Customary walking speed, also, was related to isometric muscle strength (men: r 0·42, $P<0·001$; women: r 0·36, $P<0·01$). These findings suggest, particularly in women, that physical disability is prevalent in a large segment of the population over the age of 55 years and this prevalence increases as the population examined becomes older. The over-75 year age-category encompassed the greatest number of men and women with impairment.

Frontera *et al.* (1990) have examined isokinetic knee and elbow joint strength in 200 men and women aged 45–78 years. They noted that, at an angular velocity of 60°/s, the oldest subjects had significantly lower absolute strength in all muscle groups tested. In addition, when muscle strength was expressed per kg of muscle mass, gender and age-related differences were reduced or disappeared completely, suggesting that the reductions in isokinetic strength with age are to a large extent a result of decreased muscle mass. The age-related decline in skeletal muscle mass, also, has been shown to partially explain the age-related declines in isometric handgrip strength (Kallman *et al.* 1990). In fact, in institutionalized elderly individuals dynamic knee extension strength correlates well with body cell mass as measured by total body ^{40}K counting (Fiatarone *et al.* 1994).

The loss of muscle mass and strength may not be an inevitable part of the ageing process but may, in fact, be more related to changes in habitual activity patterns which accompany advancing age. Klitgaard *et al.* (1990) have reported that in older men (69 years), who had been strength-training approximately 12–17 years before being studied, maximal isometric torque and muscle mass, as measured by computed tomography (CT) scan of the upper arm and mid-thigh, were significantly greater than those in age-matched swimmers or runners and similar to young controls. The subjects examined in this study exercised an average of three times per week at approximately 70–90% of their one repetition maximum (1RM). It is interesting, also, to note that only the older strength-trained men (neither the runners nor the swimmers) had muscle cross-sectional areas and strength similar to those of the young control subjects.

EXERCISE AND WHOLE-BODY PROTEIN METABOLISM

Regular physical activity has differential effects on whole-body protein turnover and daily protein requirements. Using measurements of N balance, several studies have now suggested that regular endurance training increases the daily requirement for dietary protein. Gontzea *et al.* (1974) reported that in untrained men beginning an endurance training programme while consuming 1 g protein/kg per d that there was an initial

increase in urinary N excretion. This increased excretion returned to pre-training levels within approximately 2 weeks. Meredith *et al.* (1992) have reported, also, that endurance-trained young and middle-aged men achieve zero N balance at a protein intake of 0·95 g/kg per d. More recently, Tarnopolsky *et al.* (1992) have reported that elite endurance athletes achieved zero N balance at 1·37 g protein/kg per d suggesting a protein requirement in these endurance athletes which is twice the established requirement for sedentary individuals. These findings all suggest an increased requirement for dietary protein in exercise-trained individuals.

Studies using isotope tracers of individual amino acids have also confirmed the increase in protein requirements observed in N balance studies. The rate of oxidation of the indispensable amino acid leucine has been shown to increase several-fold during prolonged submaximal exercise (Rennie *et al.* 1981; Wolfe *et al.* 1982), while oxidation of the indispensable amino acid lysine increases by about 40% (Wolfe *et al.* 1984). The exaggerated increase in the oxidation of leucine and potentially the other branched-chain amino acids may be due to the selective activation of the branched-chain keto acid dehydrogenase (*EC* 1.2.4.4) enzyme during exercise (Kasperek *et al.* 1985). Lamont *et al.* (1990) have reported, also, that whole-body leucine flux, as assessed by primed constant infusion of L-[1-^{13}C]leucine, was 30% higher in endurance-trained men and women compared with sedentary controls. In addition, Carraro *et al.* (1990) have observed a significant increase in the fractional rate of skeletal muscle protein synthesis following 4 h of low-intensity exercise. They have proposed that following exercise there is a redistribution of whole-body protein synthesis from liver to skeletal muscle which agrees with previous studies showing that exercise resulted in no change in whole-body protein synthesis or urea flux (Wolfe *et al.* 1982, 1984).

High-intensity strength training has been shown to increase skeletal muscle mass despite resulting in increased myofibrillar proteolysis, suggesting a disproportionate increase in myofibrillar protein synthesis (Frontera *et al.* 1988). Recent animal studies have confirmed the increase in muscle fractional protein synthetic rate following both prolonged concentric and eccentric muscle contractions (Wong & Booth, 1990*a*,*b*). These studies also demonstrated that relatively minor increases in selected contractile protein mRNA occur immediately following electrically-stimulated muscle contractions. This suggests that following contractile activity, translational and post-translational events may regulate changes in muscle protein synthesis. These same studies also reported that eccentric muscle contractions induced a more prolonged increase in muscle protein synthesis than concentric muscle contractions and that with chronic bouts of electrical stimulation only the eccentrically-contracting muscle groups demonstrated hypertrophy. In addition using the same protocol, a 40% increase in immunoreactivity to insulin-like growth factor I has been observed in transverse sections of rat muscle 4 d after 192 electrically-stimulated eccentric contractions (Yan *et al.* 1993).

Studies in humans have also examined the effects of high-intensity strength-training exercise on changes in protein turnover. Evidence from N balance studies suggests that the protein requirements for individuals performing strength-training may be increased (Lemon *et al.* 1992; Tarnopolsky *et al.* 1992). Chesley *et al.* (1992) have demonstrated significant increases in fractional synthesis rates of mixed muscle protein in response to a bout of strength-training exercise (four sets of six to twelve repetitions of the elbow flexors at 80% of the 1RM). A similar effect has been reported by Yarasheski *et al.* (1993) following 2 weeks of a progressive-resistance training programme. In healthy

older men in response to 12 weeks of progressive-resistance training, Frontera *et al.* (1988) reported a 12% increase in mid-thigh muscle cross-sectional area together with a 40% increase in urinary 3-methylhistidine excretion, illustrating the increased muscle protein degradation which occurs in conjunction with the resultant muscle hypertrophy. These studies suggest that skeletal muscle protein turnover is increased in response to progressive-resistance exercise.

HIGH-INTENSITY STRENGTH-TRAINING INTERVENTIONS IN THE ELDERLY

Several studies have attempted to examine the effects of dynamic-resistance training (weight lifting) in older subjects with the goal of increasing muscle strength and mass and restoring function. Although studies on younger individuals have clearly demonstrated that resistance training below 40% of the 1RM results in no change in muscle strength (MacDougall, 1986), there has been a reluctance on the part of investigators and clinicians to allow older subjects to train at a high intensity (70–90% of the 1RM), which has repeatedly been shown to improve strength and muscle mass in young individuals (DeLorme, 1945; MacDougall, 1986). In several reports, subjects were trained at low to moderate intensities or the training was not progressive or limited in the number of sets performed (Aniansson & Gustafsson, 1981; Larsson, 1982; Hagberg *et al.* 1989). In general, these studies demonstrated little or no increase in muscle strength with 12 to 26 weeks of training.

Studies employing higher training intensities in older subjects have been more successful. Moritani & DeVries (1980) trained five healthy older men (mean age 70 years) for 8 weeks at 66% of the 1RM of their elbow flexors. They noted a 23% increase in isometric strength of the elbow flexors with no change in upper-arm girth. They concluded that changes in neural factors were responsible for the improvements in muscle strength seen in this study. More recently, Frontera *et al.* (1988) examined the effects of a high-intensity dynamic-resistance training programme in healthy older men (mean age 64 years; Frontera *et al.* 1988). Their subjects performed knee flexion and extension exercises 3 d/week at 80% of the 1RM (eight to ten repetitions) for 12 weeks. They found a 107% increase in knee extensor strength and a 226% increase in knee flexor strength. In addition, they observed an 11% increase in mid-thigh cross-sectional area as assessed by CT. Muscle biopsy analysis revealed a 33 and 27% increase in type I and II fibre area respectively. This was the first study to demonstrate that in healthy older men dynamic high-intensity strength-training can result in marked increases in muscle strength and muscle hypertrophy. In the same study, half the subjects were given a nutritional supplement during the training programme which provided an additional 2343 kJ/d (17% protein, 43% carbohydrate, 40% fat). There were no differences in strength gains between the supplemented subjects and those who did not receive the supplement. However, the subjects who received the supplement had greater increases in body weight, skinfold thicknesses at six sites, creatinine excretion and mid-thigh muscle cross-sectional area, suggesting that dietary intake may influence the magnitude of changes in body composition as a result of strength-training in the elderly (Meredith *et al.* 1992).

Subsequent studies have confirmed the positive impact of strength-training in healthy older subjects. Brown *et al.* (1990) examined a group of healthy older men who performed upper and lower body dynamic-resistance training for 12 weeks (70–90%

1RM, three times per week) and showed a 48% increase in muscle strength, a 17% increase in elbow flexor cross-sectional area by CT scan and a significant increase in type I and II muscle fibre area. Although the increases in type I fibre area were less than those reported by Frontera *et al.* (1990) the increases in type II fibre area and total muscle cross-sectional area were similar. Recently, Charette *et al.* (1991) confirmed that dynamic-resistance training (upper and lower body) of a similar intensity in healthy elderly women (mean age 69 years) results in significant increases in muscle strength (28–115%) and a 20% increase in type II muscle fibre area. In contrast to Frontera *et al.* (1990) they reported no change in type I fibre area following training. The apparent discrepancies regarding the magnitude of the change in type I fibre area may be related to the differences in the intensity and duration of the warm-up and cool-down period or to the initial pre-training activity patterns of the various subject populations. The subjects in the study of Frontera *et al.* (1990) were extremely sedentary before the start of the study, shown by the fact that the resistance training resulted in a significant increase in leg maximal O_2 uptake and a 38% increase in citrate synthase (*EC* 4.1.3.7) activity of the *vastus lateralis* muscle. This increased oxidative capacity is consistent with the type I muscle fibre hypertrophy observed. No measures of whole-body or cellular oxidative metabolism were reported by Brown *et al.* (1990) or by Charette *et al.* (1991). More recently, Pyka *et al.* (1994) have reported that strength-training intervention for 1 year in older men and women resulted in a 58 and 67% increase in type I and type II muscle fibre cross-sectional area reflecting greater increase in muscle fibre size with strength-training in the elderly over the course of 1 year than had previously been reported in several short-term studies lasting only a few months.

These more recent studies suggest that when the training stimulus is of an appropriate intensity (70–90% of the 1RM), the gains in muscle strength and size in older healthy individuals are comparable with the gains observed in young individuals. The range of strength gains (28–227%) reported in these various studies may be related to other factors, including the subject's initial strength, age and health status, the choice of muscle groups that were trained, the level of training supervision, and the rate of progression. It is clear that the gains in muscle strength are far greater than the observed increases in muscle size and this must be attributed to the profound neural adaptations which occur with high-intensity resistance training. Regardless of the mechanism, the capacity for senescent muscle to respond to overload persists and should be considered an effective strategy for restoring muscle function in the healthy elderly population.

MUSCLE FUNCTION IN THE FRAIL ELDERLY

It is well established that the frail elderly have by definition deficits in functional capacity that may make them dependent on others for daily care and that a multitude of factors contribute to these kinds of disability in the elderly. Some studies have shown that muscle weakness is associated with the risk of falling (Whipple *et al.* 1987; Nevitt *et al.* 1989) and may be related to functional dependence. There is now reasonable evidence that healthy older subjects respond favourably to strength-training interventions. However, there is a lack of information regarding the effects of these interventions on functional capacity or activities of daily living in the frail elderly or individuals over 80 years of age. Currently, high-intensity resistance training interventions in this high-risk population have been underutilized.

Two recent studies have demonstrated the profound effects of progressive-resistance training in frail institutionalized elderly individuals. Fiatarone *et al.* (1990) examined ten frail institutionalized elderly men and women (mean age 90 years) who performed knee extension exercise for 8 weeks (three times per week, three sets at 80% of their 1RM). These subjects all had a previous history of falls and suffered on average 4·5 chronic diseases and took on average 4·2 medications per d. Seven of the ten subjects studied used an assistive device for ambulation. At baseline, they observed a significant relationship between 6 m walk time and the combined leg 1RM of the knee extensors. Following 8 weeks of training a 174% increase in the 1RM of the knee extensors was observed along with a significant increase (9%) in the mid-thigh muscle cross-sectional area by CT. They also noted a 48% increase in tandem gait speed after training (Fiatarone *et al.* 1990). In a more recent study, using a randomized placebo-controlled intervention in 100 frail nursing home residents, Fiatarone *et al.* (1994) reported a 113% increase in muscle strength and a 2·7% increase in muscle cross-sectional area in response to a 10-week programme of progressive-resistance training of the lower extremity at 80% of the 1RM. Dietary supplementation with a protein–energy formula (1500 kJ/d; 60% carbohydrate, 23% fat, 17% soyabean protein) either alone or in combination with the exercise training had no effect on the gains in muscle strength or size. In addition to the measured gains in musculoskeletal strength, spontaneous physical activity in the strength-trained group increased 35%. These studies suggest that even in frail elderly subjects, the capacity for muscle strength increases and hypertrophy is still maintained. In addition, in individuals with marked impairments in functional capacity, strength-training interventions may restore some of the age-related loss in function.

While it appears that maintenance of muscle strength is an important outcome variable in the most elderly, the ability to generate muscular force over a given period of time (muscle power) may also play an important role in functional independence and fall prevention. For example, making balance corrections when a person stumbles or missteps may be intrinsically related to the ability of that person to generate a large amount of muscle power for brief moments at a time. Muscle power declines much more precipitously than the reported declines in dynamic and isometric strength (Bassey & Short, 1990). In a group of nursing home residents with a history of falling, Whipple *et al.* (1987) reported that lower-leg isokinetic power was significantly lower than that in a group of age-matched non-institutionalized controls, suggesting that muscle function is an important factor in gait and balance assessment. Using a specially designed leg power rig, Bassey *et al.* (1988) evaluated the leg extension power in twenty-six institutionalized frail elderly men and women (mean age 88 years). They reported a significant relationship between both single-leg and combined-leg extensor power and several functional tests of activities of daily living. The closest relationships were observed between leg extensor power and walking speed (R 0·80, $P<0·001$), chair-rising speed (R 0·65, $P<0·001$), and stair-climbing speed (R 0·81, $P<0·001$). An even stronger relationship to leg extensor power was found when stair-climbing power was calculated based on the vertical rise of their body weight during stair climbing (R 0·88, $P<0·001$). Fiatarone *et al.* (1994) have also noted in their nursing-home study a 28% increase in stair-climbing power in response to progressive-resistance training. The implications for changes in muscle power with age and increased falling risk have yet to be fully studied.

CHANGES IN BODY COMPOSITION AND ENERGY METABOLISM WITH STRENGTH-TRAINING

In addition to the studies on strength-training in the elderly cited previously, two recent studies have also reported that whole-body progressive-resistance training in older men and women induces a significant increase in resting energy expenditure. Pratley *et al.* (1994) reported an 8% increase in resting metabolic rate (RMR) following 16 weeks of whole-body strength-training in healthy men between the ages of 50 and 65 years. Even when expressed per kg FFM, the increase in RMR remained significant, suggesting an increase in the basal energy requirement of metabolically-active lean tissue. In addition, they observed a significant decrease in body fat mass as determined by hydrodensitometry. A similar effect of strength-training on RMR in elderly men and women was observed by Campbell *et al.* (1994) following 12 weeks of upper- and lower-body resistance training at 80% of the 1RM. Together with the increased RMR, mean daily energy requirements increased 15% over the course of the 12-week training programme along with a significant loss of fat mass (1·8 kg) and increase in FFM (1·4 kg). However, Campbell *et al.* (1994), by estimating changes in the protein plus mineral content of FFM, concluded that the increase in FFM after strength-training was largely due to the increase in total body water. The potential significance of this increase in total body water independent of changes in the remaining components of the FFM (protein plus mineral) remains to be determined.

Several other studies which have employed 'whole-body' strength-training interventions in the elderly have reported similar changes in body composition. Hagberg *et al.* (1989) reported an approximately 7% decrease in the sum of six skinfold sites in a group of nineteen older men and women (70–79 years) following 26 weeks of a relatively-low-intensity circuit weight-training programme. Strength gains in this study were of the order of 9–18%, which reflects the relatively low nature of the training stimulus. Craig *et al.* (1989), also, have reported a similar decrease in subcutaneous skinfold thicknesses in older men (62–64 years) in response to 12 weeks of progressive-resistance training. In addition, insulin responsiveness as assessed by an oral glucose-tolerance test improved by 30%. In contrast, Dupler & Cortes (1993), reported no changes in lean body mass calculated from skinfold thicknesses in response to 12 weeks of resistance training in twenty healthy older men and women at a training intensity of approximately 65% of the 1RM. However, since the direct skinfold measurements are not reported in the study of Dupler & Cortes (1993), it is difficult to speculate on the changes in body fat mass. Using hydrodensitometry, Koffler *et al.* (1992) reported a small but significant decrease in body fat mass in response to a 13-week whole-body strength-training programme.

Although the evidence for a significant increase in whole-body FFM in response to progressive-resistance training may be equivocal, based on the results of Campbell *et al.* (1994), the evidence for a significant decrease in body fat mass is more convincing. The cause of this reduced fat mass with progressive-resistance training in the elderly without dietary restriction remains unknown. However, the combination of the increased energy required to perform the exercise training sessions (Wilmore *et al.* 1978; Campbell *et al.* 1994), the elevations in RMR (Campbell *et al.* 1994; Pratley *et al.* 1994), and possible increases in skeletal muscle protein turnover (Yarasheski *et al.* 1993; Campbell *et al.* 1994) may combine to increase total daily energy requirements. It is possible that the use of progressive-resistance training interventions may become a useful strategy to promote loss of body fat mass while simultaneously preventing a decline or even increasing FFM.

SUMMARY AND CONCLUSIONS

The declines in functional capacity and muscle function with advancing age are well-documented. In addition, it appears that the age-related changes in body composition have profound effects on functional capacity and nutrient requirements. The overwhelming evidence presented in the present review suggests that the loss of muscle strength and function observed with advancing age is reversible even in the frail elderly. Along with the profound functional improvement in older individuals in response to progressive-resistance training, several studies have reported increases in resting energy expenditure and increased requirements for dietary protein. Exercise programmes designed to improve muscle strength should be recommended for older individuals as an effective countermeasure to the sarcopenia of old age.

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