Effects of ageing and human whole body and muscle protein turnover

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Prevalence of sarcopenia is up to 60% of those individuals over 80 years of age and is associated with increased disability. The causes behind the age-related loss of muscle are difficult to discern. Measurements of protein synthesis/breakdown and net protein balance are important, and further methodological development is warranted. Whole body protein turnover is changed only little – if at all – with ageing, when corrected for fat free mass of the individuals. Discrepancies in reports are often related to inconsistent recordings of energy intake especially protein and variation in subject, gender and physical activity level. Ageing is associated with reduced sensitivity toward amino acids, increased first pass uptake in a splanchic region and a reduced postprandial stimulation of protein synthesis. Physical activity and amino acids are additive in effect also in elderly individuals, and timing of training and protein intake is crucial, in that early intake of amino acids is advantageous with regards to stimulation of protein synthesis.

Beginning in mid life, ageing is associated with a time dependent loss of muscle sarcopenia. This loss appears mainly to be consequences of old age, although chronic illness, poor diet and inactivity all accelerate its progression. Sarcopenia is a major cause of disability, frailty and loss of independence in the elderly due mainly to the associated loss of muscle strength and to a lesser extent stamina. Strategies to prevent or reduce sarcopenia are receiving increased attention due to pressures on health care of the growing numbers of elderly members of society in developed countries.

Unfortunately, the links between causes and effects are not easy to discern. Wasting is associated with a loss of tissue protein and this must mean an imbalance between the rates of tissue protein synthesis and tissue protein breakdown. The purpose of this review is to examine the current evidence for such changes in whole body protein and muscle protein turnover.

Extent of muscle wasting

Factors suggested to be responsible for the age related changes in skeletal muscle associated with sarcopenia include a decline in muscle protein synthesis (Welle, Thornton, Jozefowicz, Stat, 1993; Proctor, Balagopal, Nair, 1998), inadequate nutrition (Campbell & Evans, 1996), inactivity (Evans, 1995) and hormonal changes (Urban et al., 1995; Butterfield, Thompson, Rennie, Marcus, Hintz, Hoffman, 1997).

It is in fact likely that sarcopenia is caused by a combination of many factors (Volpi, Sheffield-Moore, Rasmussen, Wolfe, 2001).

Loss of muscle mass is mainly caused by a loss of type II fibres and a reduction of fibre size, beginning at ~25 years and accelerating thereafter. By 50 years approximately 10% of the muscle area is lost, and the average reduction in muscle area in vastus lateralis between 20 and 80 years is 40% (Lexell, 1995). The fibre size reduction is due to a selective atrophy of type II (fast-twitch) muscle fibres, whereas type I (slow-twitch) fibres are less affected. Individuals who take part in moderate dynamic exercise retain cardiovascular fitness but the rate of loss of muscle mass is approximately the same as in sedentary individuals (Rutherford & Jones, 1992). Those who keep fit by resistance exercise (e.g., weight lifting, etc.) have a higher muscle mass than their peers mainly because their peak bone mass is higher but they also appear to suffer continued loss of muscle mass as they age (Rutherford, 1997).

Prevalence

In an experiment involving 833 elderly men and women in New Mexico (Baumgartner et al., 1998) sarcopenia was defined as possession of an appendicular skeletal muscle mass (kg)/height² (m²) being up to two standard deviations below reference values for young healthy
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men and women (measured by dual energy X-ray absorptiometry). Thus defined, a prevalence of sarcopenia of 13–24% was found in those younger than 70 years and 43–60% in those older than 80 years. Sarcopenia was associated with a three four-fold increase in disability in both men and women independent of age, morbidity, obesity, income, and behaviour.

**Whole body protein turnover**

There are some discrepancies in reports of the effects of ageing on whole body protein turnover. Most workers now agree that age related changes in whole body protein turnover are small, if they occur at all (Fukagawa, Minaker, Rowe, Matthews, Bier, Young, 1988; Fukagawa, Minaker, Young, Matthews, Bier, Rowe, 1989; Welle et al., 1993; Yarasheski, Zachwieja, Bier, 1993; Welle, Thornton, Statt, McHenry, 1994; Benedek, Berclaz, Jéquier, Schutz, 1995; Millward, Fereday, Gibson, Pacy, 1997; Hasten, Pak-Loduca, Obert, Yarasheski, 2000; Volpi et al., 2001). When data, which shows a lower rate of whole body protein synthesis, are normalised for fat-free mass (FFM) (Winterer, Steffee, Perera, Uauy, Scrimshaw, Young, 1976; Golden & Waterlow, 1977; Uauy et al., 1978; Lehmann, Johnston, James, 1989; Morais, Gougeon, Pencharz, Jones, Ross, Marliss, 1997) the age effect mainly disappears. However, even after correcting for fat-free mass Balagopal, Rooyackers, Adey, Ades, Nair (1997) still detected an age-related decline of 20% in whole body protein turnover in elderly subjects. The explanation for this may be the 5-days “weight-maintaining” diet given to elderly subjects before measurements were made; the protein requirements for elderly people have been suggested to be greater than those of younger individuals (Pannemans, Wagenmakers, Westerterp, Schaafsma, Halliday, 1998); by limiting elderly subjects to a controlled diet the result may have been to further reduce whole body protein synthesis. Against this must be placed the findings of some authors reporting no effect of age on whole body protein synthesis even when controlled diets were used (Welle et al., 1993; Yarasheski et al., 1993; Welle et al., 1994; Hasten et al., 2000), although they were only for 3 days. Unfortunately, not all the groups reported how many grams of protein/kg/day were given, so possible explanations on the basis of protein requirements cannot be suggested. Neither Volpi et al. (2001) nor Benedek et al. (1995) used any dietary manipulations.

When postprandial protein utilization (PPU) was investigated in young and old subjects there was no significant overall age effect (Millward et al., 1997). This group also reported that the metabolic demand in elderly subjects was markedly reduced (per kilogram body weight or per kilogram fat-free mass) compared with the younger control subjects. With a lower metabolic demand in the elderly and with no change in the efficiency of protein utilisation, the apparent protein requirement calculated from these values was also lower in the elderly, conflicting with findings by Pannemans et al. (1998).

Lean body mass diminishes with age, especially the skeletal muscle component that accounts for only ~30–50% of whole body protein turnover in lean young adults. Whole-body protein turnover includes the protein synthesis of many different tissues and is not specific to muscle protein synthesis. This may explain why substantial changes in skeletal muscle protein synthesis (up to 20%) are not necessarily reflected by whole body measurements. Thus, it makes sense to measure muscle protein synthesis rates directly when the effect of ageing on skeletal muscle is to be investigated.

**Muscle protein turnover in the basal state**

Increases and decreases in muscle protein mass are mainly due to alterations in protein synthesis (as a facilitated process) and alterations of muscle protein breakdown usually adapt to the changes in synthesis (Smith & Rennie, 1996). Thus a number of authors have suggested that the metabolic alteration responsible for sarcopenia is a reduction in basal muscle protein synthesis rate in elderly people (Welle et al., 1993; Yarasheski et al., 1993; Welle, Thornton, Statt, 1995; Rooyackers, Adey, Ades, Nair, 1996; Balagopal et al., 1997; Hasten et al., 2000). However, others disagree with these findings, having found that basal muscle protein synthesis does not change with age (Volpi et al., 1999, 2001). One of the problems in the study by Rooyackers et al. is the marked discrepancy in fitness between the young and middle aged and elderly subjects, who were much less fit and may have been relatively inactive. The relationship between habitual physical activity and muscle turnover is likely to be complex but it would seem wise before ascribing effects of age to make sure that activity and fitness were controlled.

There are many oddities observed in the extent of basal changes and in the rates of protein synthesis in multiple muscle fractions (Table 1). For example Hasten et al. (2000) found the synthetic rate of myosin heavy chain (MHC) to be 40% lower in elderly subjects, but when they measured mixed muscle protein and actin synthetic rates there were no significant differences. Also, Balagopal et al. (1997) reported lower rates of MHC and mixed muscle protein synthesis in elderly but their sarcoplasmic synthetic rates were similar in the young and the elderly.

When studying Table 1 it is obvious that there are many possible reasons why authors might have found conflicting data. For example, there are only two groups to have conducted their experiments on male
<table>
<thead>
<tr>
<th>Author</th>
<th>Muscle fraction</th>
<th>Tracer used</th>
<th>Precursor</th>
<th>Analysis</th>
<th>Conditions</th>
<th>Male, Female young; old</th>
<th>Young</th>
<th>Old</th>
<th>Conclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Volpi et al. (2001)</td>
<td>Mixed</td>
<td>300 min L-[ring²H₅] Phe</td>
<td>Ic Phe</td>
<td>GCMS</td>
<td>Regular diet usual routine</td>
<td>All male</td>
<td>0.06 ± 0.02</td>
<td>26 28 ± 2</td>
<td>0.06 ± 0.02</td>
</tr>
<tr>
<td>Volpi et al. (1999)</td>
<td>Mixed</td>
<td>480 min L-[ring²H₅] Phe</td>
<td>Ic Phe</td>
<td>GCMS</td>
<td>Regular diet usual routine</td>
<td>3.4; 2.6</td>
<td>0.04 ± 0.01</td>
<td>22% 7 30 ± 2</td>
<td>0.05 ± 0.03</td>
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<tr>
<td>Hasten et al. (2000)</td>
<td>Actin</td>
<td>840 min L-[¹³C] leucine</td>
<td>Ic Phe</td>
<td>GC-C-IRMS</td>
<td>3 days meet free controlled protein</td>
<td>4.3; 3.4</td>
<td>0.06 ± 0.04</td>
<td>58% 7 27 ± 1</td>
<td>0.09 ± 0.04</td>
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<tr>
<td>Hasten et al. (2000)</td>
<td>Mixed</td>
<td>840 min L-[¹³C] leucine</td>
<td>Ic Phe</td>
<td>GC-C-IRMS</td>
<td>3 days meet free controlled protein</td>
<td>4.3; 3.4</td>
<td>0.06 ± 0.02</td>
<td>28% 7 27 ± 1</td>
<td>0.06 ± 0.02</td>
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<td>Balagopal et al. (1997)</td>
<td>Sarcomplasmic</td>
<td>600 min L-[¹³C] leucine</td>
<td>Plasma KIC</td>
<td>GC-IRMS</td>
<td>5 days weight maintaining diet</td>
<td>4.4; 4.4</td>
<td>0.04 ± 0.02</td>
<td>40% 8 23 ± 1</td>
<td>0.04 ± 0.02 5*</td>
</tr>
<tr>
<td>Yarasheski et al. (1993)</td>
<td>Mixed</td>
<td>840 min L-[¹³C] leucine</td>
<td>Plasma KIC</td>
<td>GC-C-IRMS</td>
<td>3 day meet free controlled protein</td>
<td>4.2; 2.4</td>
<td>0.05 ± 0.01</td>
<td>20% 6 24 ± 1</td>
<td>0.03 ± 0.01</td>
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<td>Welle et al. (1993)</td>
<td>Myofibrillar</td>
<td>480 min L-[¹³C] leucine</td>
<td>Plasma KIC</td>
<td>IRMS</td>
<td>3 days controlled diet + activity meat free</td>
<td>All male</td>
<td>0.05 ± 0.01</td>
<td>19% 8 21–31</td>
<td>0.04 ± 0.09</td>
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<td>Welle et al. (1995)</td>
<td>Myofibrillar</td>
<td>480 min L-[¹³C] leucine</td>
<td>Plasma KIC</td>
<td>IRMS</td>
<td>3 days controlled diet + activity meat free</td>
<td>5.4; 5.4</td>
<td>0.06 ± 0.01</td>
<td>20% 9 22–31</td>
<td>0.04 ± 0.02</td>
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<td>Hasten et al. (2000)</td>
<td>Myosin heavy chain</td>
<td>840 min L-[¹³C] leucine</td>
<td>Ic Phe</td>
<td>GC-C-IRMS</td>
<td>3 days meet free controlled protein</td>
<td>4.3; 3.4</td>
<td>0.05 ± 0.01</td>
<td>23% 7 27 ± 1</td>
<td>0.03 ± 0.01</td>
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<tr>
<td>Balagopal et al. (1997)</td>
<td>Myosin heavy chain</td>
<td>600 min L-[¹³C] leucine</td>
<td>Plasma KIC</td>
<td>GC-IRMS</td>
<td>5 days weight maintaining diet</td>
<td>4.4; 4.4</td>
<td>0.04 ± 0.00</td>
<td>7% 8 23 ± 1</td>
<td>0.03 ± 0.01 23*</td>
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<tr>
<td>Balagopal et al. (1997)</td>
<td>Mixed</td>
<td>600 min L-[¹³C] leucine</td>
<td>Plasma KIC</td>
<td>GC-IRMS</td>
<td>5 days weight maintaining diet</td>
<td>4.4; 4.4</td>
<td>0.05 ± 0.01</td>
<td>17% 8 23 ± 1</td>
<td>0.03 ± 0.01 23*</td>
</tr>
<tr>
<td>Rooyackers et al. (1996)</td>
<td>Mixed</td>
<td>240 min L-[¹³C] leucine</td>
<td>Plasma KIC</td>
<td>GC-IRMS</td>
<td>5 days weight maintaining diet</td>
<td>6.6; 7.7</td>
<td>0.04 ± 0.01</td>
<td>16% 12 24 ± 1</td>
<td>0.04 ± 0.01 23*</td>
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<tr>
<td>Rooyackers et al. (1996)</td>
<td>Mitochondrial</td>
<td>240 min L-[¹³C] leucine</td>
<td>Plasma KIC</td>
<td>GC-IRMS</td>
<td>5 days weight maintaining diet</td>
<td>6.6; 7.7</td>
<td>0.08 ± 0.01</td>
<td>17% 12 24 ± 1</td>
<td>0.05 ± 0.02 33*</td>
</tr>
</tbody>
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Phe, phenylalanine; Ic, intracellular; GCMS, gas chromatography mass spectrometry; GC-IRMS, gas chromatography-isotope ratio mass spectrometry; GC-C-IRMS, gas chromatography-combustion-isotope ratio mass spectrometry; KIC, ketosiscaproic acid. *Data from middle aged subjects.
subjects exclusively (Welle et al., 1993; Volpi et al., 2001). All others investigated mixed numbers (which differ between age groups) of men and women except Balagopal et al. (1997) who studied four men and four women in each age group.

Controlling activity and diet of participants preceding the study could decrease basal rates of muscle protein synthesis especially in elderly subjects. It has been suggested that the recommendation for protein dietary intake in elderly subject (greater than 55 years) is higher than that of younger subjects (less than 55 years) (Pannemans et al., 1998). Therefore, standard recommendations for diet may not adequately fulfill dietary needs of elderly subjects.

The coefficient of variance (SD as percentage of mean) was very high in most studies and in some cases greater than 50% (Balagopal et al., 1997; Volpi, Mittendorfer, Wolf, Wolfe, 1999; Hasten et al., 2000). With such rates of variability (Table 1) the power of the techniques used to detect physiologically meaningful differences must be in question for small groups.

Muscle protein synthesis alone cannot provide enough information about overall protein turnover because protein mass is the resultant of processes of both synthesis and breakdown. If the elderly subjects who were reported to show the greatest decreases in muscle protein synthesis, e.g., up to 39% (Yarasheski et al., 1993; Balagopal et al., 1997) did not also show a decrease in muscle protein breakdown, muscle should be lost to a greater extent than is observed in real life.

Unfortunately only Volpi and colleagues (Volpi et al., 1999, 2001) measured protein breakdown directly (as leg protein breakdown); they found a small but significant increase in whole leg proteolysis in older men using the AV tracer exchange method. Other investigators used whole body 3-methylhistidine excretion (Welle et al., 1993, 1994; Yarasheski et al., 1993; Hasten et al., 2000). This method is not as sensitive or specific, and does not allow the estimation of muscle net protein balance (Rennie & Millward, 1983).

On reviewing the data available on basal muscle protein synthesis we have concluded that to be able to understand the mechanisms behind sarcopenia, measurements of protein breakdown and net protein balance are essential, and methodological improvements are required to increase the sensitivity and precision of analysis.

Responsiveness of muscle to feeding


The availability of plasma amino acids takes between 30 min and 1 h to have any measurable effect on muscle protein synthesis (Bohé, Low, Wolfe, Rennie, 2001). However, synthesis is then inhibited despite continued amino acid availability and falls to a value similar to that at basal. The reduction suggests that amino acids supplied in excess of the requirements of protein synthesis are used elsewhere for fuel or stored as fat. This result indicates the importance of the time samples is taken during studies off the effects of possible regulators of protein metabolism (Bohé et al., 2001). If measurements are made too early or too late during the infusion the stimulation window will be missed.

Increasing amino acid availability stimulates the net incorporation of amino acids into muscle proteins in elderly individuals demonstrating that increasing amino acids alone can stimulate muscle protein anabolism in elderly individuals with a reduced muscle mass (Volpi, Ferrando, Yeckel, Tipton, Wolfe, 1998). However, it has also been shown that muscle anabolism is blunted in the elderly during the intake of amino acid glucose mixture due to an impaired response of muscle protein synthesis (Volpi, Mittendorfer, Blake, Rasmussen, Wolfe, 2000). This result is confusing and hard to explain: when amino acids and glucose are given together the fractional synthetic rate of muscle protein in young subjects is greater than when amino acids are given alone. However, in the elderly subjects this is not the case: a lower rate of muscle protein synthesis is observed when amino acids are given with glucose than with amino acids alone. This seems strange, especially when this group previously reported that amino acids alone could stimulate muscle protein synthesis in elderly people. The authors themselves found these results surprising especially as the elderly subjects had normal glucose tolerance and insulin concentrations. An explanation is that amino acids could be diverted to other tissues such as fat, liver or the gut when hyperaminoacidemia and hyperinsulinemia are combined in the elderly. An alternative explanation is that an age-related alteration in the responsiveness to insulin of one or more of the factors or enzymes involved in signalling pathways stimulated by both insulin and amino acids (e.g., those leading to the phosphorylation of the eukaryotic initiation factor 4E-binding protein-1) could lead to the inhibition of the positive effects of amino acids on muscle protein synthesis (Volpi et al., 2000).

First-pass splanchnic extraction of amino acids is greater in the elderly than in younger individuals (Volpi et al., 1999). This could lead to a reduction in the delivery of amino acids for protein synthesis in muscles.

In contrast to results reported by Volpi et al. (1998, 2000) stimulation of in vitro muscle protein synthesis by
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leucine was found to be impaired in old rats. This suggests that the decrease in muscle mass with age could be due to a decrease in sensitivity to amino acids (Dardevet, Sornet, Balage, Grizard, 2000). However postprandial muscle protein synthesis in rats was reportedly restored by a leucine rich diet in vitro (Dardevet, Sornet, Bayle, Prugnaud, Pouyet, Grizard, 2002). Could sarcopenia be explained by a postprandial defect? This could arise due to a decrease in the delivery of dietary amino acids to the muscle due to increased first pass uptake in the gut, a diminished sensitivity to regulatory amino acids together with a reduced postprandial stimulation of protein synthesis.

If this is the case postprandial delivery of amino acids needs to be increased in elderly subjects. Protein-pulse feeding (where 80% of the daily protein intake is given in one meal) improved protein retention in elderly women, whereas protein-spread feeding (same daily protein intake spread over four meals) did not (Arnal et al., 1999). The differential effects of the protein pattern of feeding are apparently age-dependant as there was no significant difference observed between the effects of feeding with spread and pulse patterns in young subjects (Arnal et al., 2000). This specific age-related effect suggests that alterations in the regulation of protein turnover are occurring during ageing.

Effects of exercise

It is agreed that resistance exercise (e.g., weight lifting) stimulates muscle protein synthesis in both the young and the elderly. There was a 30% increase after a single bout of exercise in young exercised subjects are compared to unexercised controls (Chesley, MacDougall, Tarnopolsky, Atkinson, Smith, 1992). The basal fractional rate of protein synthesis in both young and old subjects increased 36% and 60%, respectively, after 2 weeks of resistance exercise (Yarasheski et al., 1993). However, there is conflicting data as to whether or not exercise training can actually increase baseline rates. Yarasheski et al. (1993), Yarasheski, Pak-Loduca, Hasten, Obert, Brown, Sinacore (1999), Hasten et al. (2000) and Balagopal, Schimke, Ades, Adey, Nair (2001) all report that baseline rates of MHC and mixed muscles proteins did increase with exercise whereas Welle et al. (1995) found that there was no significant increase in myofibrillar protein synthesis. It is still unclear as to what the nature of the effect is.

In untrained subjects a single exercise session (eight sets of single-leg knee flexion, at 10 repetitions per set) increased mean muscle protein synthesis 112% after 3 h, 65% after 24 h, and 34% after 48 h (Phillips, Tipton, Ferrando, Wolfe, 1999). However, in the trained subjects (engaged in a regular program of resistance training for ≥ 5 years) the values for protein synthesis are much less: 50% 4 h after a single bout of resistance exercise, 109% after 24 h, and only 14% after 36 h. The magnitude of the effect on muscle protein synthesis probably depends on the relative intensity of the exercise and the amount of training the subject is accustomed to, but because repeated strenuous resistance exercise is anabolic there is no reason to suspect a higher basal rate of synthesis.

Individuals recovering from exercise in the post-absorptive state have negative net leg protein balance. However, if they are fed oral amino acids net protein balance becomes positive (Tipton, Ferrando, Phillips, Doyle, Wolfe, 1999). In agreement with this, Biolo, Tipton, Klein, Wolfe (1997) reported an enhanced rate of leg protein synthesis and a lack of rise of leg protein breakdown when subjects were infused with mixed amino acids after exercise compared with hyperaminoacidemia at rest or the effects of exercise alone (Biolo et al., 1997). This suggests that amino acids and exercise are additive in effect.

There were no strength training induced increases in strength in 20–30-year-old men and women (34%) compared to 65–75-year-old men and women (28%) (Lemmer et al., 2000). However, after 31 weeks of abstinence from exercise there was a greater loss of strength in the older than in the young subjects. In agreement with this Ivey et al. (2000) found that aging in human subjects has no effect on the response of muscle to strength training, although their results showed that there was also no difference in detraining after 31 weeks. These findings suggest that disuse atrophy does not entirely explain the decreases in muscular strength with advancing age and shows that elderly muscle responds to the same extent as young muscle to an intense training stimulus.

Physical inactivity likely contributes to sarcopenia; even individuals who are physically active throughout life demonstrate decreases in functional ability, and appear to demonstrate losses in muscle mass (Roth, Ferrell, Hurley, 2000). This is especially important in the context of the papers from the Nair and Yarasheski groups.

Effect of timing of exercise and feeding

The optimal timing of nutrient intake after exercise is important, as it should affect the extent of the muscle protein response. Whole body and leg protein synthesis were enhanced when an oral supplement was given immediately rather than 3 h after 60 min of moderate exercise on an exercise bicycle (Levenhagen, Gresham, Carlson, Maron, Borel, Flakoll, 2001). Esmaeck, Andersen, Olsen, Richter, Mizuno, Kjaer (2001) showed that when oral supplementation was given immediately after resistance exercise (30 min consisting of leg press, latissimus dorsi pulldown and knee extension. Three times a week for 12 weeks) in elderly men cross-sectional area and mean fibre area increased by 7 and 22%, respectively. Whereas, no significant changes
were found when a food supplement was given 2 h post exercise. However, there are conflicting data; in young men an amino acid-carbohydrate drink produced similar anabolic responses at 1 or 3 h after a bout of resistance exercise (leg press and leg extension ~45 min) (Rasmussen, Tipton, Miller, Wolf, Wolfe, 2000).

The lack of an effect when oral supplementation is given 2 h after resistance training in elderly subjects seems odd (Esmarck et al., 2001). Muscle fractional rate remains elevated for at least 48 h after a bout of heavy resistance exercise (Phillips, Tipton, Aarsland, Wolf, Wolfe, 1997), and the addition of oral supplementation within this time would be expected to enhance this effect (Biolo et al., 1997; Tipton et al., 1999). It could be that the length of time net muscle protein balance remains elevated after resistance exercise decreases during ageing. This would suggest that the timing of feeding after exercise is crucial in the elderly.

**Hormonal effects on muscle**

The secretion of several hormones including growth hormone, insulin-like growth factor (IGF)-1 and sex hormones decrease with age (Rudman, Kutner, Rogers, Lubin, Fleming, Baine, 1981; Nankin & Calkins, 1986; Rudman et al., 1990). Their decreasing availability may be a contributing factor to the changes in body composition observed with age.

Increased lean body mass, strength and function are reported when testosterone is administered in ageing men (Tenover, 1992; Urban et al., 1995; Ferrando et al., 2002). Testosterone also has been shown to increase skeletal muscle protein synthesis in young and elderly men (Urban et al., 1995; Ferrando, Tipton, Doyle, Phillips, Cortiella, Wolfe, 1998).

Administration of testosterone to elderly males also results in an increase in IGF-1 mRNA concentrations (Ferrando et al., 2002) and IGF-1 is known to accompany increases in muscle mass and strength (Sheffield-Moore, 2000). IGF-1 could be increasing muscle protein synthesis by stimulating the differentiation of satellite cells into mature myocytes, thereby increasing muscle cellularity and protein synthesis (Urban et al., 1995).

Women over 62 years have greater rates of protein synthesis when treated with recombinant human growth hormone (rhGH) or recombinant human insulin-like growth factor-I (rhIGF-I) (Butterfield et al., 1997). However, growth hormone does not enhance muscle growth after resistance exercise in either young or elderly men (Yarasheski, Campbell, Smith, Rennie, Holloszy, Bier, 1992; Yarasheski, Zachwieja, Campbell, Bier, 1995). It may be that the abuse of growth hormone by athletes is more to do with beneficial effects on collagen synthesis in epiperiosteum, which would strengthen hypertrophied muscles, and prevent injury, especially if the growth were the result of anabolic steroid abuse.

**Perspectives**

As sarcopenia affects an increasing amount of the population the importance of developing strategies for its prevention grow. The mechanisms behind this condition are complex and involve a variety of factors. In this review it is clear from the numerous conflicting data that further investigation into the causes of sarcopenia is necessary. To obtain efficient and practical methods of treatment for the general public, a better understanding of the interactions between factors such as exercise, feeding, timing of feeding, and hormonal secretion is necessary. It is also apparent that there is a need for the development of reliable and reproducible methods for investigating the adaptations and the variability in response of aging skeletal muscle to experimental stimuli.

**Key words:** sarcopenia; protein synthesis; protein breakdown; elderly; young; exercise; amino acids.

**References**


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