Healthy aging: the role of nutrition and lifestyle

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Mechanisms of Sarcopenia in the Elderly: Possible Countermeasures using Nutrition and Exercise

• The nature of the problem

• Problems with basal muscle protein metabolism?

• Problems with responses of turnover to food?

• Problems with responses of protein turnover to insulin?

• Problems with responses to exercise?

• How can we optimize muscle maintenance?
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Loss of muscle mass revealed as loss of muscle strength
Hypothesis:

The aging-related fall in muscle mass is due to two different sets of processes

1. Time related and mostly immutable, random, only partly genetic etc (loss of fibres etc)

2. A decrease in environmentally and behaviourally changeable stimuli i.e. nutrition, activity, etc

NB! Only the second is amenable to intervention
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Feeding and exercise are obviously important for growth, development and maintenance of the musculoskeletal mass, but the mechanisms involved are not well understood.
Mechanisms of Sarcopenia in the Elderly: Possible Countermeasures using Nutrition and Exercise

- The nature of the problem

- Maintenance of muscle mass by regulation of protein turnover - the drivers of anabolism

- *Problems with basal muscle protein metabolism?*

- Problems with responses of turnover to food?

- Problems with responses of protein turnover to insulin?

- Problems with responses to exercise? Effects of inactivity?

- Sex differences complicate the picture

- How can we optimize muscle maintenance?
Muscle Protein Turnover in Healthy Young and Healthy Old Men (~ 10% muscle wasting)

Protein Synthesis (%h)

Protein Breakdown (nmol Phe/100ml leg)

Volpi et al. JAMA 2001
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Euglycaemic insulin clamp conditions in old and young - identical

Plasma insulin (m IU.l\(^{-1}\)) or glucose (mM)

![Graph showing plasma insulin and glucose levels over time for young and elderly individuals.](image)
Accumulation of blood AA in elderly caused by failure to utilize protein?
Myofibrillar protein FSR above basal (%·h⁻¹)

Sarcoplasmic protein FSR above basal (%·h⁻¹)

Plasma leucine area under curve (µ mol·l⁻¹·min⁻¹)
Clues as to underlying mechanisms of sarcopenia in the elderly

Protein Concentration (absolute units)
- Young
- Elderly

Phosphoproteins (all arbitrary units)
- 0 g EAA
- 10 g EAA

- Phospho-mTOR
- Phospho-p70S6 kinase

Young     Elderly
Deficiency in anabolic signalling in elderly men at high insulin

** Significantly diff from response in young
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Is there anabolic resistance to blunting of muscle proteolysis by insulin?

Euglycaemic, isoaminoacidaemic clamps at 5 and 15 µU.ml⁻¹
Effect of insulin on leg protein balance (i.e. S-B) is less in elderly.
Evidence of insulin resistance of protein metabolism in elderly

- 5 µIU/ml Insulin
- 15 µIU/ml Insulin

Leg Leu Ra (nmol AA.100ml leg$^{-1}$.min)

Leg Phe RA (nmol AA.100ml leg$^{-1}$.min)

* P < 0.05 vs. 5 µU/ml Insulin

Young Elderly Young Elderly
Leu Flux Phe Flux
Thus “anabolic resistance” extends to blunting of insulin effects on muscle protein breakdown.
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Anabolic resistance of muscle to exercise in older men

Dose response of myofibrillar synthesis 1-2 h post exercise

FSR (% h⁻¹)

- Young
- Older

Exercise intensity (% 1RM)
Anabolic resistance of ageing extends to muscle signalling in exercise

Signalling responses to exercise at 60, 75 and 90% 1RM

- Phosphorylation of p70S6k (AU)
- Phosphorylation of 4EBP1 (AU)

* Young
* Older

- Basal
- 10 min post ex
- 1h post ex
- 2h post ex
- 4h post ex
Does immobilization have the opposite effect to exercise?
Effect of immobilisation on human quadriceps size and protein synthesis

![Graph showing the effect of immobilisation on muscle CSA and myofibrillar FSR](image)

- **Muscle CSA cm²**
- **Myofibrillar FSR % h⁻¹**

Days of immobilization:
- 0 days
- 10 days
- 20 days

Myofibrillar FSR %.
- 0.00
- 0.01
- 0.02
- 0.03
- 0.04
- 0.05
- 0.06

Muscle CSA cm²
- 30
- 40
- 50
- 60

Myofibrillar Synth Rate
- 0.00
- 0.01
- 0.02
- 0.03
- 0.04
- 0.05
- 0.06
Anabolic resistance after 14 d disuse

FSR (%/h)

Basal 1h 2h 4h

AA 43 mg/kg/h

Non-Immobilized

Immobilized

AUC (% protein synthesized)

Non-Immobilized

Immobilized

**
Acute response of MPS to exercise disappears in older women and is not restored by resistance training.

**Young**

**Old**
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How can we optimize muscle maintenance?
What to eat and when to eat it to maintain muscle mass and function?
Protein requirements in elderly, incidence of inadequate intake and need for more protein in physically active older people?

1. WHO/FAO/UNU suggest no extra requirement - but only 1 N balance study of elderly included (WHO Tech Rep Ser 2007;935.)


3. Many authors claim increased requirements for active elderly subjects - even tho sarcopenia is lessened at moderate N intakes and extra protein has no further effect (Campbell et al J Physiol 2002;542, 2:631–42; Campbell. Nutr Rev 2007;65:416–2).

Recent N balance data may settle part of this argument…….
Mean protein requirement Y vs. O = 0.61 ± 0.14 vs. 0.58 ± 0.12 g/kg/d

Adequate protein for both groups 0.85 ± 0.21 g/kg/d

(Campbell, et al AJCN in press (2008))

At these rates using NHANES data only 6-8 % older people deficient

(?an overestimate given under-reporting; similar for UK NDNS 2001)
Protein and energy requirements: changes with age

Protein requirements (g/kg)

Energy requirements (kcal/kg)

Protein

Energy pal = 1.5

P:E ratio of requirements (kcal %)

P: E ratio

Protein and energy requirements: changes with age
Ageing decreases capacity and sensitivity of muscle maintenance in elderly men.
What about exercise as a means of preserving muscle mass?
Only “resistance” exercise – weightlifting preserves muscle mass.

Jack LaLanne, age 94
Vegetarian, former bulimic, began weight-lifting at 15
Benefits of Resistance Training: the Evidence Base

- Improved muscle size and strength, bone density, aerobic capacity
- Improved gait and balance, mobility
- Improved functional independence
- Improved depression, morale, insomnia, quality of life
- Cardiac, pulmonary, renal, orthoped rehabilitation, arthritis
- Treatment of type 2 diabetes mellitus
- Treatment of wasting conditions, HIV cancer
- Improved insulin resistance, visceral obesity, hypertension, systemic inflammation
- Prevention of type 2 diabetes (with diet)
- Prevention of metabolic syndrome, cardiovascular disease*
Effect of PRT and Multinutrient Supplementation on Muscle Fiber Area in Frail Nursing Home Residents

Type I Fiber Area

Type II Fiber Area

PRT
Supplementation
PRT + Supplementation
Control

Fiatarone, AJP
Boston FICSIT Study 1999

p=0.033
Effect of food with or without previous exercise on muscle protein synthesis in the elderly

Welle and Thornton 1998 AJP
Increases in muscle fibre area and muscle cross sectional area after resistance training with feeding at once or delayed by 2 h

Esmark et al 2001
Effect of fish oil supplementation (4 g/day) on muscle protein synthesis in elderly men and women (66-75 y)
Recommendations to maintain muscle with ageing

Eat to fulfil energy requirements

1. Maintain P:E ratio at upper level

2. Do resistance exercise (in addition to any endurance exercise)

3. Eat soon after exercise

4. (Include sufficient n-3 PUFA in diet?)
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