Muscle loss with aging

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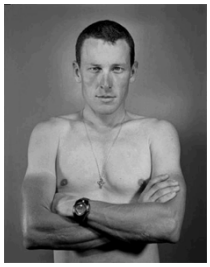
Muscle reconditioning

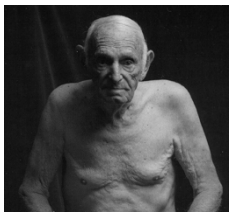


Lance Armstrong

Jay Cutler

Lifestyle changes

Muscle deconditioning



- immobilisation
- sarcopenia
- cancer cachexia
- COPD
- type 2 diabetes
- cardiovascular disease

Models of accelerated aging

Table 2
Body Composition and Muscle Strength

	Normoglycemic ($n = 32$)	Type 2 Diabetes ($n = 60$)	*P* Value
Body composition			
Body mass (kg)	83.8 ± 1.7	83.9 ± 1.3	.097
Lean mass (kg)	61.8 ± 1.1	62.0 ± 0.8	.051
Leg lean mass (kg)	19.7 ± 0.3	19.1 ± 0.3*	.013
Fat mass (kg)	19.2 ± 0.9	19.2 ± 0.6	.949
Fat %	22.7 ± 0.8	22.6 ± 0.5	.534
ASM (kg)	26.7 ± 0.5	25.9 ± 0.4*	.005
Strength			
Leg press (kg)	204 ± 2	202 ± 2	.201
Leg extension (kg)	91 ± 2	84 ± 2*	.024

ASM, appendicular skeletal muscle mass.
Data represent mean ± SEM. Data were analyzed using ANCOVA.
*Significantly different from normoglycemic group.

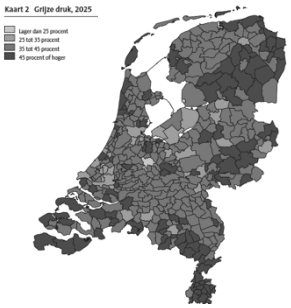
Leenders *et al., JAMDA, 2013.*

Population demographics

In Europe, the number of people aged 65 years and over are projected to rise by almost 80% over the next 50 years, from 85 million in 2008 to up to 152 million by 2060.

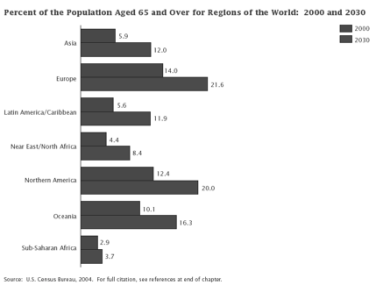
By the year 2060, people with an age of 65 and over will comprise more than 30% of the total EU population.

Demographics



CBS Demografie van de vergrijzing *juni 2011*

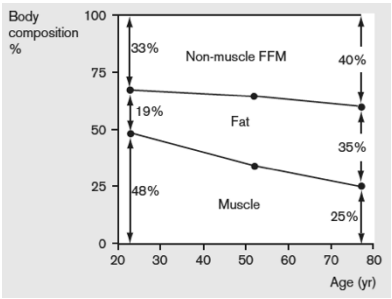
Population demographics



Functional capacity in the elderly

Leenders *et al*, *Med. Sci. Sports Exerc*., *2013*.

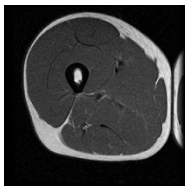
Muscle mass maintenance



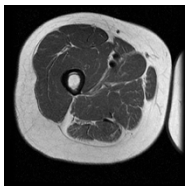
Short and Nair, 2000

Loss of muscle mass with aging

Height and weight matched



Young Male, age 25

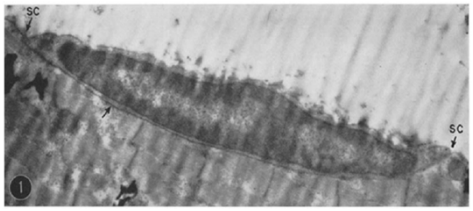


Older Male, age 63

Sarcopenia

- type II muscle fiber atrophy
- muscle fiber type grouping
- muscle fiber necrosis

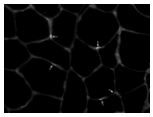
Satellite cells



Mauro *et al.*, 1961

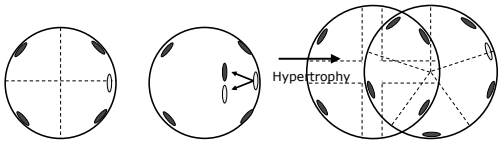
Satellite cells (SC)

- SC: skeletal muscle satellite cells
  - Between sarcolemma and basal lamina
  - Normally "quiescent"
  - Stimulation: activation, proliferation, differentiation

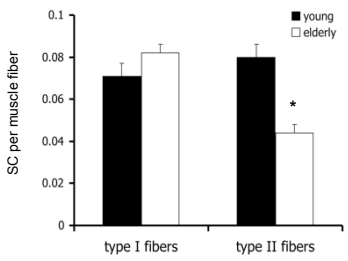


- Function
  - Provide new myonuclei
  - Essential for myofiber maintenance, growth and repair

Myonuclear domain theory

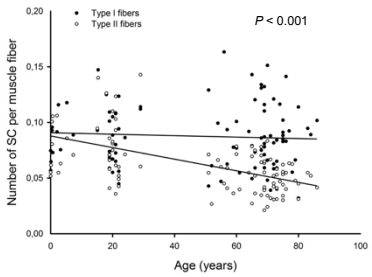


Fiber type specific SC content



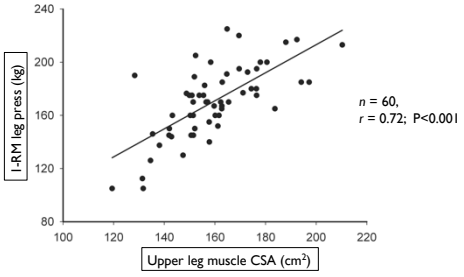
Verdijk *et al.*, *Am. J. Physiol*, 2007

Fiber type specific SC content



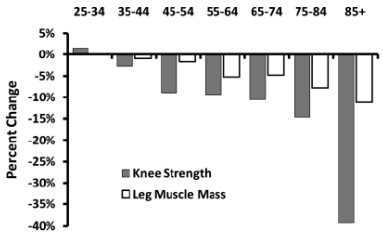
Verdijk *et al.*, *unpublished*

Muscle mass versus muscle strength



Verdijk *et al., unpublished*

Muscle loss versus strength loss



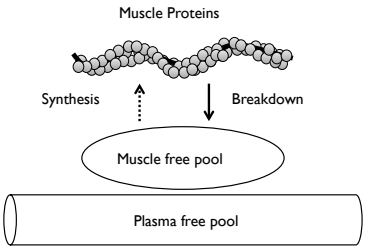
Ferrucci *et al., J. Gerontology*, 2012

Age related decline in muscle strength

- functional capacity
- metabolic disease
- quality of life

What regulates muscle maintenance?

Muscle protein synthesis



Burd *et al., Exerc Sport Sci Rev*, 2013

Fractional muscle protein synthesis

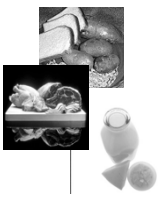
1-2 % per day

(0.04 – 0.14 %·h^{-1})

Main anabolic stimuli

Nutrition is an anabolic stimulus

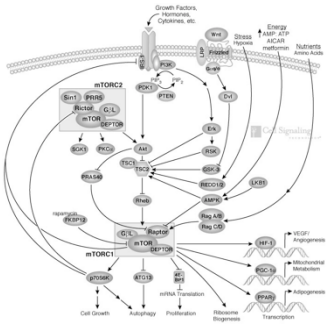
Food intake a an anabolic signal



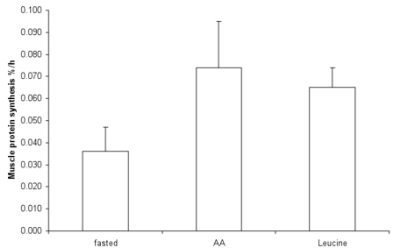
- Mosoni *et al.*, 1995
- Arnal *et al.*, 1999 and 2002
- Volpi *et al.*, 1999 and 2000
- Dardevet *et al.*, 2000 and 2002
- Rieu *et al.*, 2003
- Prod' homme *et al.*, 2005
- Katsanos *et al.*, 2005
- Cuthbertson *et al.*, 2005
- Koopman *et al.*, 2006

Amino acids

Amino acids stimulate protein synthesis

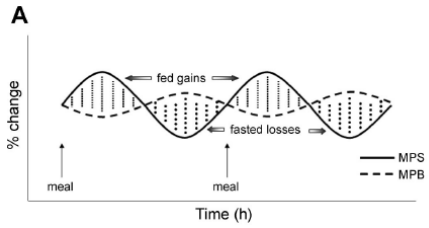


Leucine as a main anabolic signal



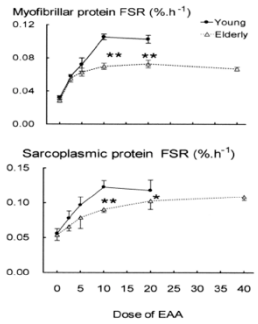
Bennet *et al.*, 1989
Smith *et al.*, 1992 and 1998

Muscle protein balance



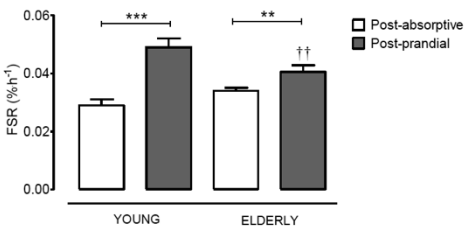
Burd *et al., J Appl Physiol*, 2008

Anabolic resistance



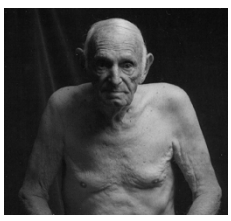
Cuthbertson *et al., FASEB J.*, 2005

Anabolic resistance



Wall *et al., unpublished observations*

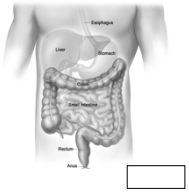
Anabolic resistance



- immobilisation
- sarcopenia
- cancer cachexia
- COPD
- type 2 diabetes
- cardiovascular disease

Anabolic resistance

- protein digestion
- amino acid absorption
- plasma amino acid availability
- hormonal response
- postprandial perfusion
- muscle protein signaling proteins
- myofibrillar protein synthesis



Research methods



Measuring muscle FSR

$$\mathrm{FSR} = \frac{\Delta E_p}{E_{\mathrm{precursor}} \cdot t} \cdot 100$$


Intrinsically labeled protein

Glowing cow project

van Loon *et al., J Dairy Sci*, 2009

Intrinsically labelled dairy protein

[1-^{13}C] Phenylalanine enrichment 30-40 MPE

van Loon *et al, J Dairy Sci*, 2010

Pennings *et al, J Dairy Sci*, 2011

Post-prandial protein synthesis

 - source of protein

 - amount of protein

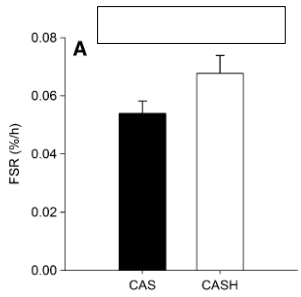
 - macronutrients

 - timing

 - food compounds

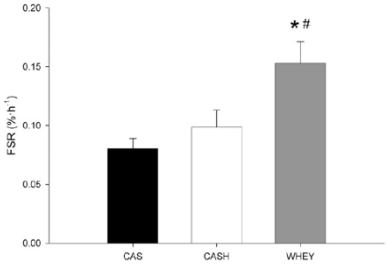
Source of dietary protein

Intact protein versus protein hydrolysate



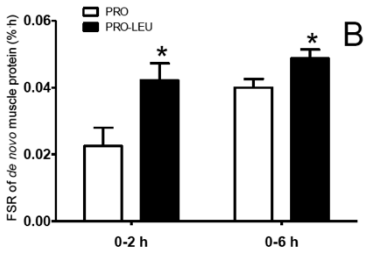
Koopman *et al., Am J Clin Nutr*, 2009

Whey versus casein



Pennings *et al., Am J Clin Nutr*, 2011

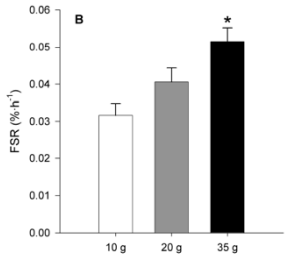
Leucine co-ingestion



Wall *et al., Clin Nutr, 2012*

Amount of dietary protein

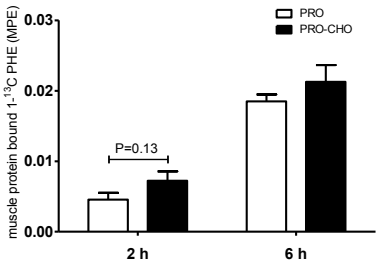
Dose response effect



Pennings *et al., Am J Physiol*, 2012

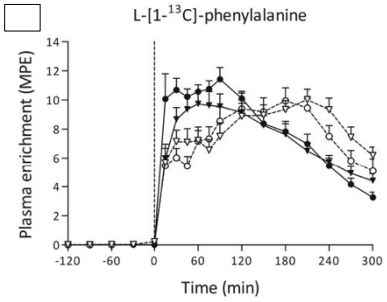
Carbohydrate co-ingestion

Carbohydrate co-ingestion



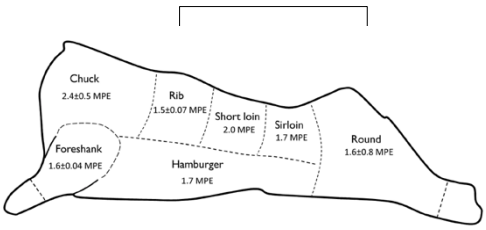
Hamer *et al., Nutr Metab*, 2013

Carbohydrate co-ingestion



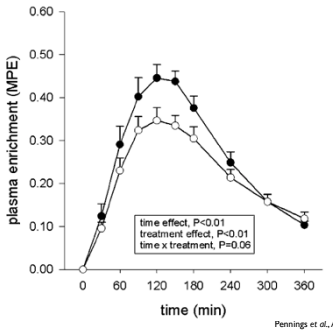
Gorissen *et al., J Clin Nutr Metab*, 2014

Intrinsically labeled meat



Burd *et al., Plos One*, 2013

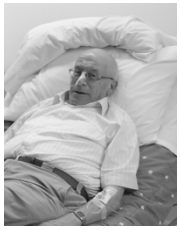
Beefsteak versus minced beef

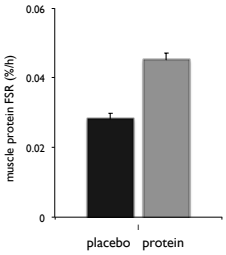


Pennings *et al., Am J Clin Nutr*, 2013

Timing of protein ingestion

Muscle protein synthesis during sleep





Groen *et al., Am J Physiol,* 2012

Muscle contraction is an anabolic stimulus

Muscle contraction

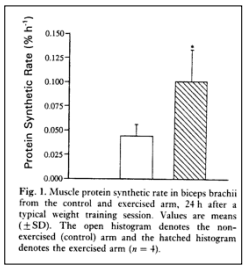
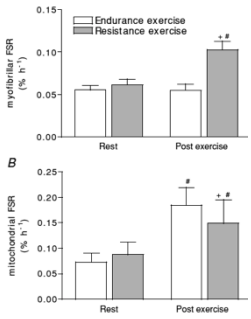


Fig. 1. Muscle protein synthetic rate in biceps brachii from the control and exercised arm, 24 h after a typical weight training session. Values are means (±SD). The open histogram denotes the non-exercised (control) arm and the hatched histogram denotes the exercised arm ($n = 4$).

Chesley *et al., 1992*

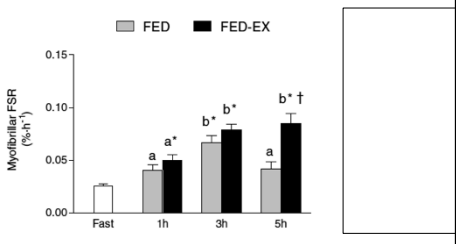
Post-exercise muscle protein synthesis



Wilkinson *et al., J Physiol,* 2008

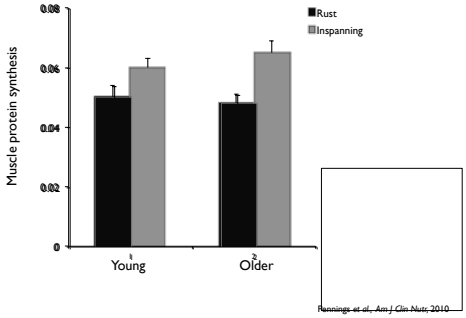
Interaction between exercise and food intake

Exercise and nutrition



Moore *et al., J. Physiol.*, 2009.

Post-prandial muscle protein synthesis



Rennings *et al., Am J Clin Nutr*, 2010

Post-exercise muscle protein synthesis

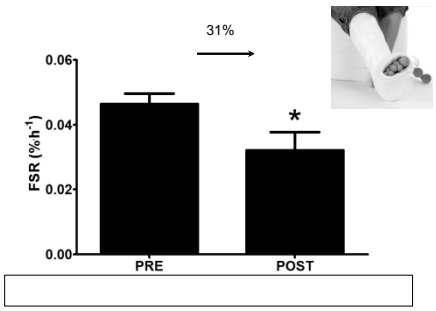

- amount of dietary protein


- type of protein


- carbohydrate co-ingestion

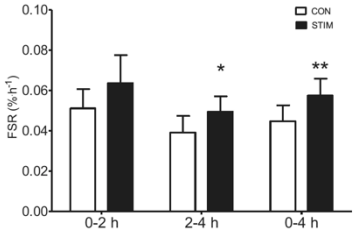

- nutritional compounds

Anabolic resistance to protein intake



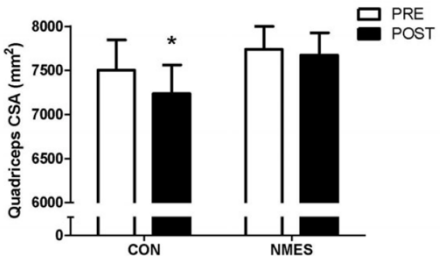
Wall *et al. J Clin Endocrinol Metab*, 2013

Neuromuscular electrical stimulation



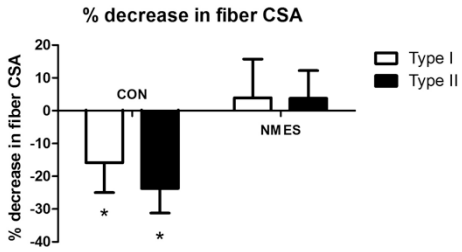
Wall *et al. Am J Physiol*, 2012

NMES to prevent disuse atrophy



Dirks *et al., Acta Physiol*, 2013

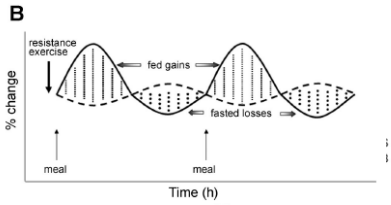
NMES during coma



Dirks *et al., unpublished*

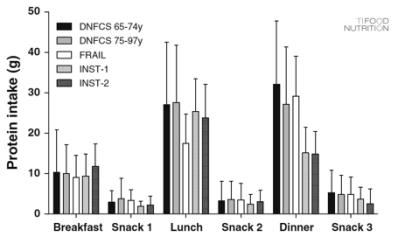
Clinical relevance

Prolonged nutritional intervention



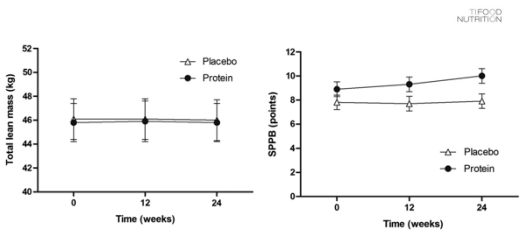
Burd *et al., J Appl Physiol*, 2008

Protein intake in the elderly populations



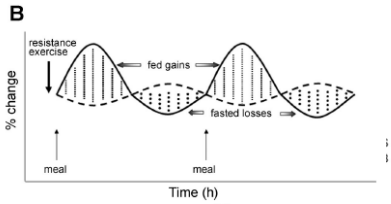
Tieland *et al., Eur J Nutr, 2011*

Protein supplementation in frail elderly



Tieland *et al., JAMDA, 2012-A*

Prolonged exercise training



Burd *et al., J Appl Physiol*, 2008



Exercise training in the elderly

Muscle mass and strength

Endurance capacity

Functional capacity

Frontera et al., 1988, 1990, 2003, Fiatarone et al., 1990, 1994, Charette et al., 1991, Lexell et al., 1995, Aniansson et al., 1986, Vincent et al., 2002, Bamman et al., 2003, Brose et al., 2003, Ferri et al., 2003, Roth et al., 2003, Short et al., 2003, 2004, Verdijk et al., 2009

Original Study

There Are No Nonresponders to Resistance-Type Exercise Training in Older Men and Women

Tyler A. Churchward-Venne PhD[a,b], Michael Tieland PhD[b,c], Lex B. Verdijk PhD[a,b], Marika Leenders MSc[a,b], Marlou L. Dirks MSc[a], Lisette C.P.G.M. de Groot PhD[b,c], Luc J.C. van Loon PhD[a,b,*]

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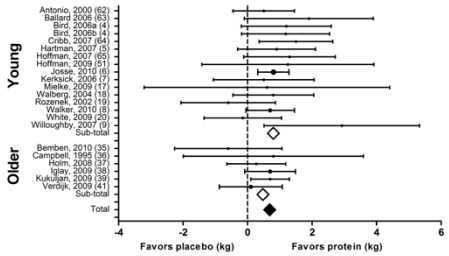
[b] *Top Institute Food and Nutrition, Wageningen, The Netherlands*
[c] *Division of Human Nutrition, Wageningen University, Wageningen, The Netherlands*

Churchward-Venne et al., JAMDA, 2015

Factors affecting long term adaptive response

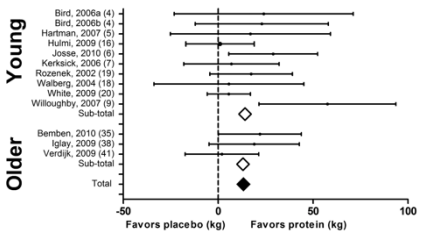
- training status
- exercise training
- adherence and compliance
- habitual physical activity
- habitual diet
- health
- age
- gender
- ……

Exercise training and protein supplementation



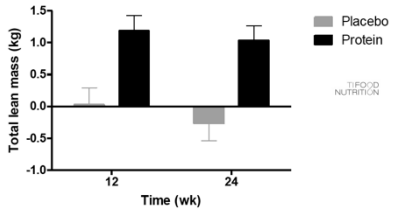
Cermak et al., Am J Clin Nutr, 2012.

Exercise training and protein supplementation



Cermak et al., Am J Clin Nutr, 2012.

Protein supplementation in frail elderly



Tieland *et al., JAMDA, 2012-8*