Proteins and physical activity: specificities in different age groups

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Muscle protein kinetics during post-exercise recovery

![Bar graph showing muscle protein kinetics]

- **Protein Synthesis**
  - Rest: [Value] ± [Error]
  - Recovery: [Value] ± [Error]
  - Significance: P<0.05

- **Protein Breakdown**
  - Rest: [Value] ± [Error]
  - Recovery: [Value] ± [Error]
  - Significance: P<0.05

**Protein Balance**
- Rest: [Value] ± [Error]
- Recovery: [Value] ± [Error]
  - Significance: P<0.05

Biolo & Wolfe AJPENDO 1995
Prolonged Bed Rest Decreases Skeletal Muscle and Whole Body Protein Synthesis

A. Ferrando  AJPENNO 1996

Before bed rest

During bed rest

Protein Degradation

Protein Synthesis
Dual energy X-ray absorptiometry (DXA)

CHANGES IN BODY COMPOSITION
DURING TWO-MONTH EXPERIMENTAL BED REST IN WOMEN (n=8)

Lean body mass          Fat mass (energy balance)

kg

-15  0  15  30  45  60

BED REST (days)

ESA/NASA/CNES WISE-study
EFFECTS OF EXERCISE AND BED REST ON POSTPRANDIAL ANABOLIC EFFICIENCY
The rates of post-prandial amino acid deposition into body protein is greatly accelerated after resistance exercise.
RESISTANCE TRAINING TO COUNTERACT THE CATABOLISM OF A LOW-PROTEIN DIET IN PATIENTS WITH CHRONIC RENAL INSUFFICIENCY

Castaneda et al., Ann Intern Med 2001

26 OLDER PATIENTS (ABOUT 65 YR) WITH MODERATE RENAL INSUFFICIENCY WHO HAD ACHIEVED STABILIZATION ON A LOW-PROTEIN DIET (0.6 G/KG/DAY) WERE RANDOMLY ASSIGNED TO RESISTANCE EXERCISE TRAINING OR NO INTERVENTION FOR 12 WEEKS.

![Graph showing absolute change in total body potassium and percent change in lower body strength](chart.png)

- **Absolute change in total body potassium (kg)**
  - Low-protein diet alone
  - Low-protein diet plus resistance training
  - P=0.01

- **Percent change in lower body strength (knee extension)**
  - P<0.001
The rates of post-prandial amino acid deposition into body protein is impaired in bed rest conditions.
EFFECTS OF AMINO ACID INFUSION ON SKELETAL MUSCLE PROTEIN BALANCE IN SEVERELY BURNED PATIENTS

* P<0.05 vs. postabsorptive state  
#, P<0.05 vs. healthy volunteers
Aging is associated with diminished accretion of muscle proteins after the ingestion of a small bolus of essential amino acids\(^1\)-\(^3\)

Christos S Katsanos, Hisamine Kobayashi, Melinda Sheffield-Moore, Asle Aarsland, and Robert R Wolfe


**FIGURE 5.** Mean (±SEM) leg phenylalanine net balance 3.5 h after the ingestion of essential amino acids calculated by measuring the area under the phenylalanine net balance response curve (in the calculations, basal net balance was taken as zero) in the elderly (\(n = 11\)) and the young (\(n = 8\)). Data were analyzed with a \(t\) test. *Significantly different from the young, \(P = 0.010\).*
Protein-containing nutrient supplementation following strength training enhances the effect on muscle mass, strength, and bone formation in postmenopausal women.


Adjusting for covariates (age at inclusion, BMI at inclusion, and BMD of the femoral neck at inclusion) a significant (P < 0.05) difference was seen in the response to training between the two groups.
Dietary omega-3 fatty acid supplementation increases the rate of muscle protein synthesis in older adults: a randomized controlled trial\textsuperscript{1–3}

Gordon I Smith, Philip Atherton, Dominic N Reeds, B Selma Mohammed, Debbie Rankin, Michael J Rennie, and Bettina Mittendorfer


**FIGURE 1.** Mean (±SEM) mixed skeletal muscle protein fractional synthesis rate (FSR), calculated by using the average plasma free phenylalanine enrichment as the precursor pool enrichment, during basal, postabsorptive conditions and during the hyperaminoacidemic-hyperinsulinemic clamp before and after 8 wk of supplementation with either corn oil (\(n = 7\)) or omega-3 fatty acids (\(n = 8\)). There was no difference in the muscle protein FSR between the omega-3 fatty acid and corn oil groups before the intervention [ANOVA showed a significant effect of clamp (\(P < 0.001\)), no significant effect of group (\(P = 0.47\)), and no interaction (\(P = 0.60\))]. \(^a\)In the corn oil group, ANOVA showed a significant main effect of clamp (\(P < 0.01\)). In the omega-3 fatty acid group, ANOVA showed a significant effect of clamp (\(P < 0.01\)) and an interaction (\(P < 0.001\)), which was followed by Tukey’s post hoc analysis. \(^b\)Significantly different from the corresponding basal value, \(P < 0.01\). \(^c\)Significantly different from the corresponding value before omega-3 fatty acid supplementation, \(P < 0.01\). Furthermore, the before-after intervention change in the anabolic response (increase in the muscle protein FSR from basal values) was significantly greater in the omega-3 fatty acid group than in the corn oil group (\(P = 0.01\), Student’s \(t\) test for independent samples).
FIGURE 2. Mean (±SEM) concentrations (arbitrary units) of mTOR<sup>Ser2448</sup> and p70s6k<sup>Thr389</sup> during basal, postabsorptive conditions and during the hyperaminoacidemic-hyperinsulinemic clamp before and after 8 wk of supplementation with either corn oil (n = 7) or omega-3 fatty acids (n = 8). aANOVA showed a significant main effect of clamp (P < 0.01). bANOVA showed a significant main effect of time (P < 0.05). cThere was a trend for a greater clamp-induced increase in mTOR<sup>Ser2448</sup> after omega-3 fatty acid supplementation than before supplementation (interaction: P = 0.08). dANOVA showed a significant interaction (P < 0.05), which was followed by Tukey's post hoc analysis. eSignificantly different from corresponding basal value, P < 0.05. fSignificantly different from corresponding value before omega-3 fatty acid supplementation, P < 0.05. Furthermore, the before-after intervention changes in the insulin/amino acid–mediated increase in p70s6k and mTOR phosphorylation above basal values were greater in the omega-3 fatty acid group than in the corn oil group (P < 0.05 and P = 0.07, respectively; Mann-Whitney U test).
Long-term Bed-rest
WISE 2005 (Women International Space Simulation for Exploration) ESA/CNES/NASA/CSA
Toulouse France

**EXPERIMENTAL PERIOD (60 days)**

- **Ambulatory conditions**
  - "Bed Rest" - Eucaloric diet
    - 1 g protein / (kg · day)

**ADAPTATION (20 days)**

- **Ambulatory conditions**
  - "Bed Rest" - Eucaloric diet
    - 1 g protein / (kg · day)

**REABILITATION (20 days)**

- **Ambulatory conditions**
  - "Bed Rest" - Eucaloric diet
    - 1.4 g protein / (kg · day)
    - 0.16 g BCAA / (kg · day)
      (leucine, valine, isoleucine)

**N = 8**

**DEXA**
Bed rest effect: $p = 0.01$; bed rest $\times$ diet interaction: $p = 0.01$ (repeated measures ANCOVA)
Cardiac atrophy in women following bed rest

Todd A. Dorfman,¹ ² Benjamin D. Levine,¹ ² Tommy Tillery,² Ronald M. Peshock,² Jeff L. Hastings,¹ ² Suzanne M. Schneider,³ Brandon R. Macias,⁵ Gianni Biolo,⁴ and Alan R. Hargens⁵ *

¹Institute for Exercise and Environmental Medicine, Presbyterian Hospital of Dallas, and ²Division of Cardiology, Department of Internal Medicine, University of Texas Southwestern Medical Center, Dallas, Texas; ³Division of Physical Performance and Development, University of New Mexico, Albuquerque, New Mexico; ⁴Department of Clinical, Technological and Morphological Sciences, and Division of Internal Medicine, University of Trieste, Trieste, Italy; and ⁵Department of Orthopaedic Surgery, University of California, San Diego, California

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**CONTROL**

Adjusted LV Mass - Control

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**HIGH-PROTEIN**

Adjusted LV Mass - Nutrition

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Fig. 2. A: adjusted left ventricular (LV) mass at baseline (pre) and after sedentary prolonged bed rest (post). B: adjusted LV mass at baseline and following protein supplementation during bed rest. *P < 0.05.
Rate of glucose disappearance during euglycemic hyperinsulinemic clamp

BEFORE BED REST

60 DAYS BED REST

Bed rest effect $p = 0.74$
Bed rest $\times$ diet $p = 0.01$
PROTEIN KINETICS IN RELATION TO ENERGY AVAILABILITY
INDIVIDUAL CHANGES IN FAT MASS

- **Study A** (spontaneous adaptation to decreased energy requirements)
- **Study B** (activity-matched eucaloric diet)

Changes in fat-free mass (bioimpedence)

Δ (kg)

Positive Energy Balance
Near-neutral Energy Balance

* p<0.05 significant different from zero;
§ p<0.05 versus lower energy balance
Positive energy balance is associated with accelerated muscle atrophy and increased erythrocyte glutathione turnover during 5 wk of bed rest\textsuperscript{1–3}

Changes in fat-free mass (bioimpedence)

Changes in vastus lateralis thickness (ultrasounds)

\[ \Delta (\text{kg}) \]

\[ \Delta (\text{cm}) \]

Positive Energy Balance

Near-neutral Energy Balance

*, \( p<0.05 \) significant different from zero;

§, \( p<0.05 \) versus lower energy balance

RELATIONSHIP BETWEEN CHANGES IN FAT AND LEAN MASS IN BED REST STUDIES (1-17 weeks) AT POSITIVE ENERGY BALANCE

(a) Lovejoy et al., Am J Physiol 1999; (b) Shackelford et al., J Appl Physiol 2004; (c) Scheld et al., Clin Chem 2001; (d) NNEB; (e) Krebs et al., Aviat Space Environ Med 1990; (f) Gretebeck et al., J Appl Physiol 1995; (g) Stein et al., Am J Physiol 1999; (h) Ferrando et al., Am J Physiol 1996; (i) PEB; (j) Barbe et al., J Appl Physiol 1999; (k) Blanc et al., Am J Physiol Regul Integr Comp Physiol 2000.

\[
\Delta \text{fat mass (percent/week)} \\
\Delta \text{lean or fat-free mass (percent/week)}
\]

\[
r = -0.87 \\
y = -0.33 \cdot x + 0.05 \\
P < 0.01
\]
CROSS-SECTIONAL STUDY
252 healthy subjects with normal body mass index, 35 to 65 years

BODY WEIGHT AND COMPOSITION

Clinica Medica – University of Trieste
Inter-relationships between adipose tissue and muscle
A mechanism leading to sarcopenic obesity
(Ageing, Critical illness, Chronic inflammatory diseases, Cancer)

DISEASES (CHRONIC INFLAMMATION) AGEING

- Muscle weakness
- ↓ Endurance capacity
- ↑ Fatigability
- Muscle wasting
- ↑ Inflammation
- ↑ Fatty infiltration
- ↓ Physical activity

WEIGHT GAIN

- ↓ Adiponectin
- ↑ Leptin
- ↑ TNF-alpha
- ↑ IL-6
- ↑ MCP-1

↓ Total/abdominal fat

Macrophage recruitment

↓ Energy expenditure

↑ Insulin resistance

Inflammation

Zamboni et al., Nutrition, Metabolism & Cardiovascular Diseases 2008
Changes in fat-free mass (bioimpedence)

Changes in vastus lateralis thickness (ultrasounds)

Δ (kg)

Δ (cm)

Positive Energy Balance
Near-neutral Energy Balance

PLASMA CRP

PLASMA MYELOPEROXIDASE

ERYTHROCYTE GLUTATHIONE SYNTHESIS RATE

*, p<0.05 significant different from zero; §, p<0.05 versus lower energy balance
Inactivity Amplifies the Catabolic Response of Skeletal Muscle to Cortisol

Ferrando et al., J Clin Endocrinol & Metab, 1999

12-h hydrocortisone infusion
(120 microg/kg/h)

<table>
<thead>
<tr>
<th>Ambulatory 5-days</th>
<th>Bed rest 14-days</th>
</tr>
</thead>
</table>

MUSCLE PROTEIN BALANCE

nmol phenylalanine/min/100 ml leg vol.

<table>
<thead>
<tr>
<th></th>
<th>Ambulatory</th>
<th>Bed rest</th>
</tr>
</thead>
<tbody>
<tr>
<td>P</td>
<td>&lt;0.05</td>
<td></td>
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P<0.05
EXPERIMENTAL PROTOCOL

STBR study DLR – Cologne – Germany

14 days

Ambulatory-Eucaloric
(100% of total energy expenditure)

Bed Rest-Eucaloric
(100% of total energy expenditure)

Ambulatory-Hypocaloric
(80% of total energy expenditure)

Bed Rest-Hypocaloric
(80% of total energy expenditure)

9 NORMAL MALE VOLUNTEERS
Randomized Cross-Over

Whole body protein kinetics
Inflammatory markers

ENERGY INTAKE

- Eucaloric Ambulatory: 1.4 x REE
- Eucaloric Bed Rest: 1.2 x REE
- Hypocaloric Ambulatory: 80%
- Hypocaloric Bed Rest: 80%
CHANGES IN FAT MASS (DXA) DURING THE 14-DAY EXPERIMENTAL PERIODS (ENERGY BALANCE)

-1.4  -1  -0.6  -0.2  0.2
kg

Eucaloric
Ambulatory  Eucaloric
Bed Rest  Hypocaloric
Ambulatory  Hypocaloric
Bed Rest

a,b  a,b
CHANGES IN LEAN MASS (DXA) DURING THE 14-DAY EXPERIMENTAL PERIODS

<table>
<thead>
<tr>
<th>Conditions</th>
<th>Changes (kg)</th>
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<tbody>
<tr>
<td>Eucaloric</td>
<td>-1.4</td>
</tr>
<tr>
<td>Bed Rest</td>
<td>-1.0</td>
</tr>
<tr>
<td>Hypocaloric</td>
<td>-0.6</td>
</tr>
<tr>
<td>Ambulatory</td>
<td>-0.2</td>
</tr>
</tbody>
</table>

Am J Clin Nutr 2007
Calorie restriction accelerates the catabolism of lean body mass during 2 wk of bed rest\textsuperscript{1–3}

Gianni Biolo, Beniamino Ciocchi, Manuela Stulle, Alessandra Bosutti, Rocco Barazzoni, Michela Zanetti, Raffaella Antonione, Marion Lebenstedt, Petra Platen, Martina Heer, and Gianfranco Guarnieri

INACTIVITY ➔ AGING ➔ INFLAMMATION ➔ ANOREXIA ➔ SARCOPENIA

SARCOGENIC OBESITY ➔ ↑ FAT MASS ➔ SARCOGENIC OBESITY

MUSCLE LOSS AND DYSFUNCTION ➔ ↓ FAT MASS ➔ PRE-CACHEXIA ➔ CACHEXIA

↑ MORBIDITY, ↑ MORTALITY

Biolo & Muscaritoli
SARCOPENIA
SKELETAL MUSCLE LOSS AND DYSFUNCTION

- Mass depletion
- Contractile insufficiency
- Metabolic impairment
- Myokine dysregulation

- Altered energy expenditure
- Anabolic resistance
- Insulin resistance
- Glutamine depletion

↑ Morbidity
Dynapenia, fatigue, disability and falls, impaired ventilation, osteoporosis, bone fractures, dyslipidemia, metabolic syndrome, type 2 diabetes, increased cardiovascular risk, impaired immunity, infections, etc.

↑ Mortality
SUMMARY

1. Inactivity impairs amino acid-induced protein anabolism.


3. High protein-BCAA intake decreases inactivity-mediated loss of lean body and myocardial mass as well as prevents inactivity-mediated insulin resistance.

4. Overfeeding and underfeeding accelerate inactivity-mediated muscle atrophy.