The Emerging Science of Rehabilitative Nutrition: *Protein's Role as the Protagonist*

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Disclosures

- **Research Support**
  - Beef Checkoff
  - National Dairy Council
  - American Egg Board
  - USDA, NIH, American Heart Association
- **Speaker's Bureau and Advisory Boards**
  - National Dairy Council
  - National Cattleman's Beef Association
  - Whey Protein Advisory Panel

Presentation Outline

- Introduction
- Protein as a protagonist
  - Essential macronutrient
  - Requirement vs recommended/optimal Intakes
  - Significance of protein quality
  - Concept of protein turnover
- Supporting roles
  - Essential amino acid availability
  - Energy status
- Translation to the emerging science of rehabilitative nutrition in context of disuse atrophy
  - ACL reconstruction
  - Total joint arthroplasty
- Summary and future directions

Introduction

Scientific contributions to diet and exercise initiatives

A foods first approach to….

- Studies considering relationships in children
- Protein intake, energy status, and exercise
  - Observations with endurance exercise training
  - Significance of habitual protein intake
  - Muscle protein utilization during acute energy deficit

Emerging areas of exploration…..

- Protein quality/essential amino acid density
- **Rehabilitative nutrition**

Protein is Fundamental to Life

Protein is made up of amino acids and provides structural components for various proteins required for numerous physiological functions and optimal health

Protein's Roles in Health

- Build, maintain, and repair muscle
- Deliver oxygen to tissues
- Boost immunity
- Support brain development and function
- Assist/coordinate nutrient metabolism
- Build stronger bones
- Aids in satiety/fullness
- Energy source

Protein Recommendations: Minimum vs Optimal Intakes

- RDA: 0.8 g/kg BW/d for adults
  - *"…estimate of the minimum daily average dietary intake level that meets the nutrient requirements of nearly all (97 to 98%) healthy individuals"*
- Acceptable Macronutrient Distribution Range (AMDR): 10-35% total calories
  - *"a range of intakes for a particular energy source that is associated with reduced risk of chronic diseases while providing adequate intakes of essential nutrients"*
- Research supports some may benefit from protein intakes greater than the RDA
  - Athletes / highly active adults
  - Older adults


The Recommended Dietary Allowance of Protein
A Misunderstood Concept

Robert R. Wolfe, PhD
Sharon L. Miller, PhD

At periodic intervals the Food and Nutrition Board of the Institute of Medicine produces a report entitled the *Dietary Reference Intakes* (DRI). The recent DRI report for macronutrients (energy, carbohydrate, fiber, fat, fatty acids, cholesterol, protein, and amino acids) was published in 2005.[1] For each macronutrient, a series of values is published, along with a detailed review of all data used to derive

on circulating glucose as an energy substitute. It was determined that there is no particular requirement for total fat intake, and therefore there is no RDA. Minimal values for required intake of linoleic acid (between 12-17 g, depending on age and sex) and n-3 polyunsaturated fats (between 1.1-1.6 g) were provided.[1] In addition, the requirement for protein for adults older than 18 years was determined to be 0.8 g of protein per kilogram body weight per day (g/kg/d).[1]

The RDA for protein was based on the results of all available studies that estimated the minimum protein intake necessary to avoid a progressive loss of lean body mass as re-

Effective translation of current dietary guidance: understanding and communicating the concepts of minimal and optimal levels of dietary protein[1–5]

Nancy R Rodriguez and Sharon L Miller

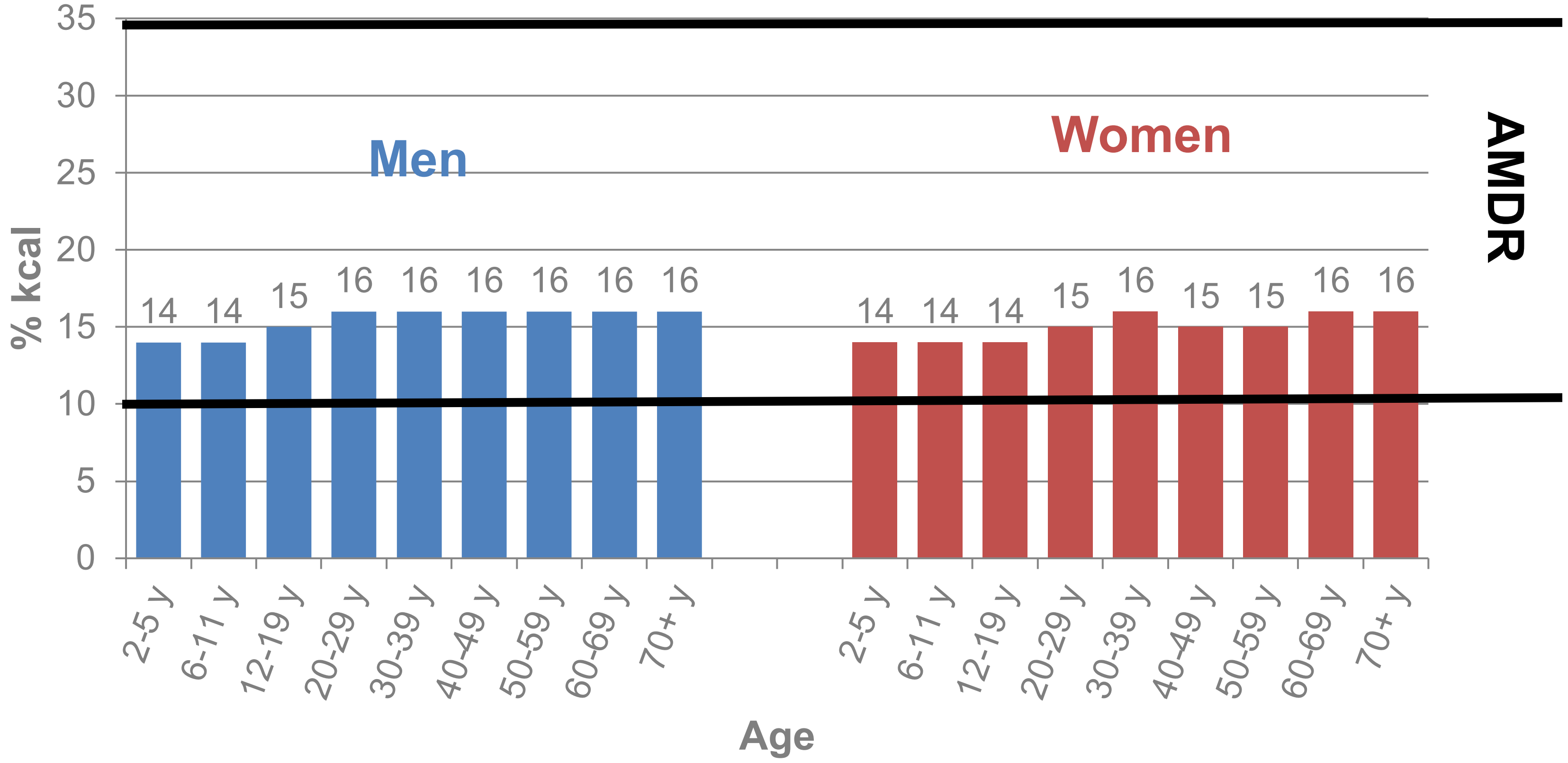
ABSTRACT

Dietitians and health care providers have critical roles in the translation of the dietary guidance to practice. The protein content of diets for adults can be based on the Recommended Dietary Allowance (RDA) of 0.80 g/kg per day. Alternatively, the most recent Dietary Reference Intakes (DRIs) for macronutrients reflect expanded guidance for assessing protein needs and consider the relative relation of absolute amounts of protein, carbohydrate, and fat to total energy intake in the context of chronic disease prevention. The Acceptable Macronutrient Distribution Range (AMDR) reflects the interrelation between the macronutrients and affords dietitians and clinicians additional flexibility in diet planning. Accounting for the caloric value of RDAs for carbohydrate and fat, "flexible calories" emerge as an opportunity to create varied eating plans that provide for protein intakes in excess of the RDA but within the AMDR. Protein Summit

clude Adequate Intake (AI) and Tolerable Upper Intake Level (UL). Acceptable Macronutrient Distribution Ranges (AMDRs), which aim to minimize chronic disease risk while maintaining adequate macronutrient intakes against the back drop of adequate energy intake and physical activity, were also introduced (2). This article considers DRIs in the context of translating the science specific to current and recommended protein intakes for improved health outcomes, including weight management, preservation of lean body mass, and maintenance of functional abilities with age, in populations targeted by Protein Summit 2.0. Considerations for the role that protein quality has in diet design, specifically acknowledging that providing essential amino acids (EAAs) is central to the protein requirement, are presented along with suggested approaches for accomplishing better health and well-being by focusing on dietary protein.

Rodriguez NR & Miller SL, *Am J Clin Nutr* 2015; Wolfe RR & Miller SL, *JAMA* 2008

Protein Consumption Across the Lifespan



NHANES 2011-2011 (similar to NHANES 2001-2014, Berryman CE, et al. *Am J Clin Nutr* 2018; 108:405-413)

Considering Protein Quantity

Recommended Protein Intakes

Athletes AND Routinely Active Adults: 1.2 – 2.0 g/kg[1]

Healthy Older Adults: 1.0 – 1.2 g/kg[2,3]

Older Adults with Acute or Chronic Disease: 1.2 – 1.5 g/kg[2]

Older Adults with Severe Illness/Marked Malnutrition: Up to 2 g/kg[2]

Middle-Aged Men and Women – 1.0-1.5 g/kg[3]

[1] *J Acad Nutr Diet*. 2016: 116:501-528.
[2] Bauer J et al., *JAMDA* 2013; Deutz NEP et al., Clinical Nutrition, 2014
[3] English, K.L. and D. Paddon-Jones, *Curr Opin Clin Nutr Metab Care*, 2010. **13**(1): p. 34-9.

Additional Recommendations[2]

- 25-30 g of protein per meal
- 2.5-2.8g of leucine per meal

Protein Quality

***Complete** proteins provide ALL*
*all 9 essential amino acids**

***High quality** proteins* are complete proteins which provide sufficient amounts of *all 9 essential amino acids* AND* support growth and maintenance of body tissues

**Must be provided by the diet; cannot be made by the body*

Review of Protein Turnover

Body Protein/ Muscle

Food Protein Sources

Whole Body/Muscle Protein Balance

Protein Balance =

Protein Synthesis (PS) – Protein Breakdown (PB)

+ **Positive Net Balance** +

⬆

PS > PB = lean body mass gain

PB > PS = lean body mass loss

⬇

- **Negative Net Balance** -

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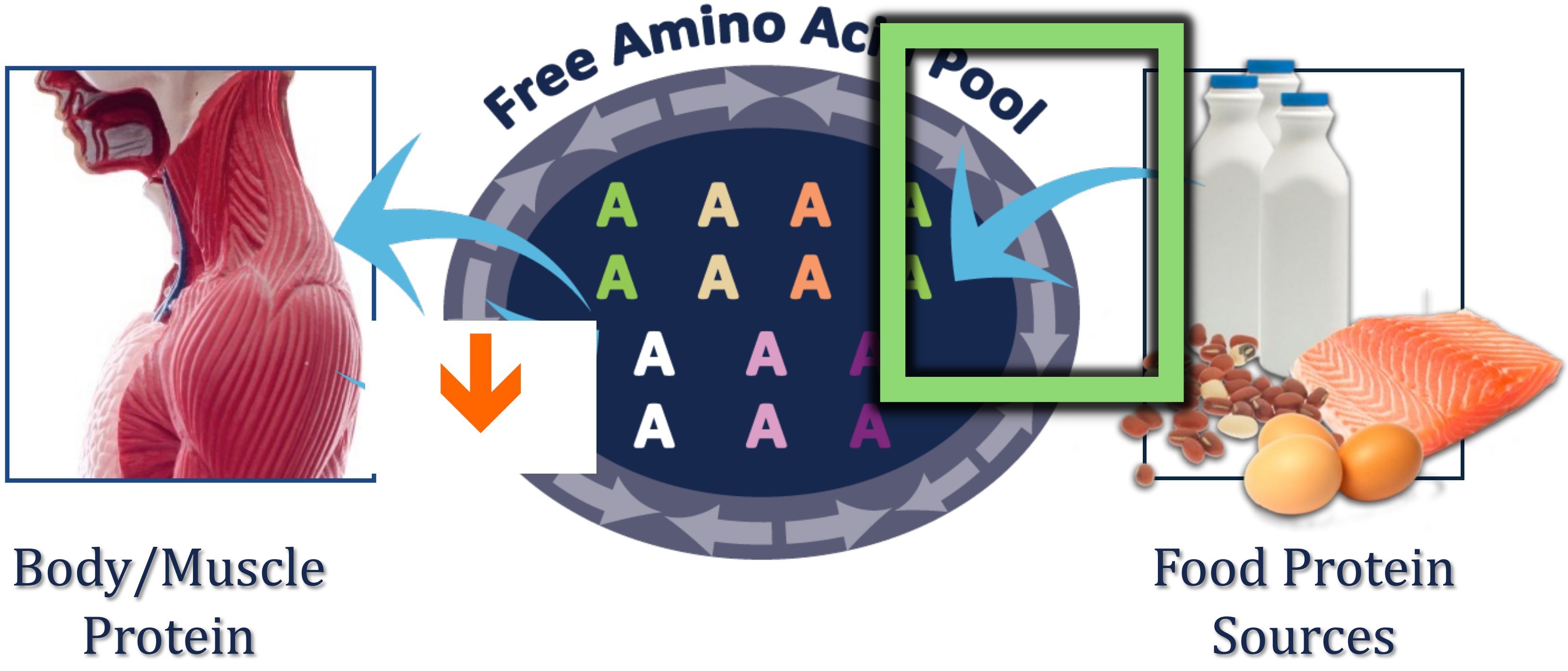
Review of Protein Turnover: Effects of Exercise

Routine exercise increases protein turnover

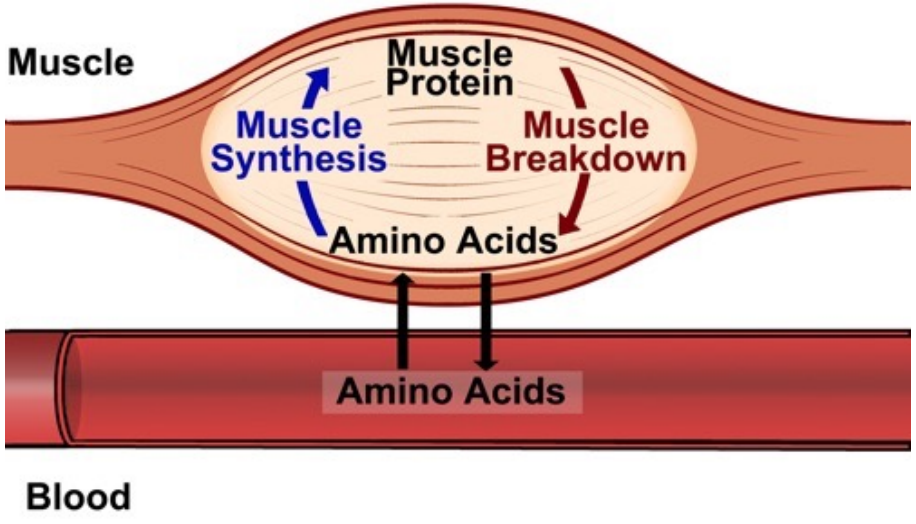
Review of Protein Turnover:
Effects of Nutrition



Consuming protein reduces protein breakdown

Skeletal Muscle Protein Turnover*

***Skeletal muscle protein turnover regulates muscle mass**



Hypertrophy occurs when

Muscle Synthesis > Muscle Breakdown

Only Essential Amino Acids Needed to Achieve a Positive NET Balance

MAA =
6g mixed amino acids

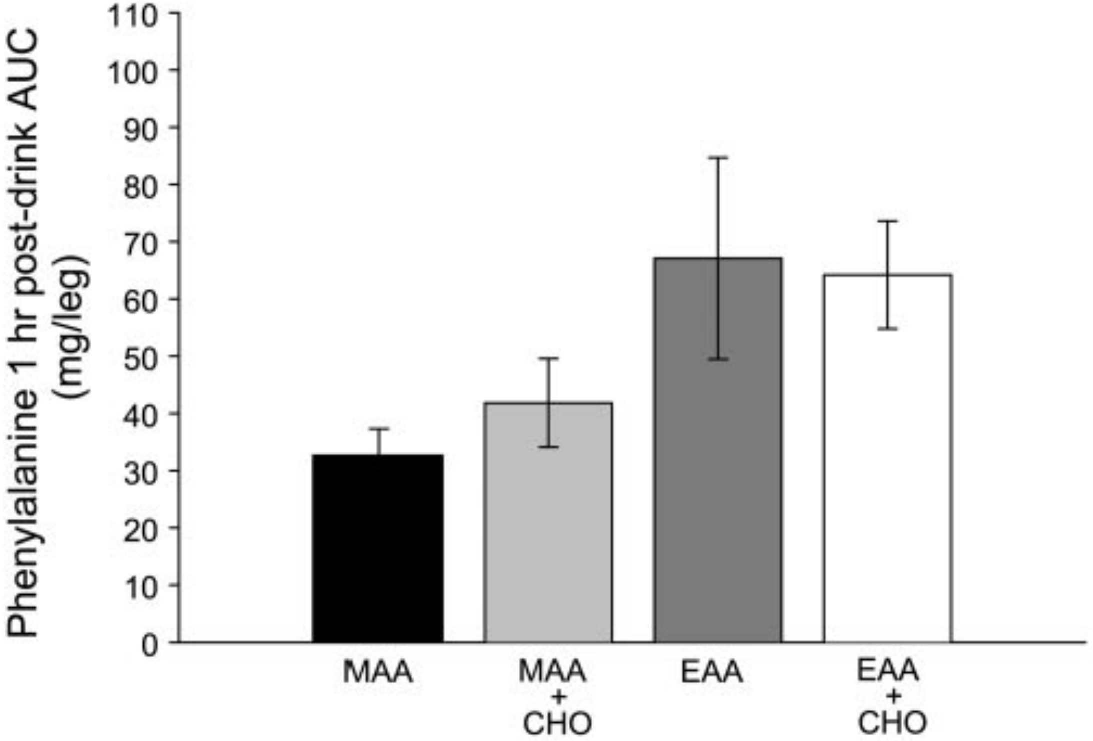
EAA =
6g essential amino acids

MAA + CHO =
6g mixed amino acids

+ 35g carbohydrate

EAA+CHO =
6g essential amino acids

+ 35g carbohydrate



Borsheim E et al., Am J Physiol Endocrinol Metab. 2002

Concept of Anabolic Resistance in Older Adults

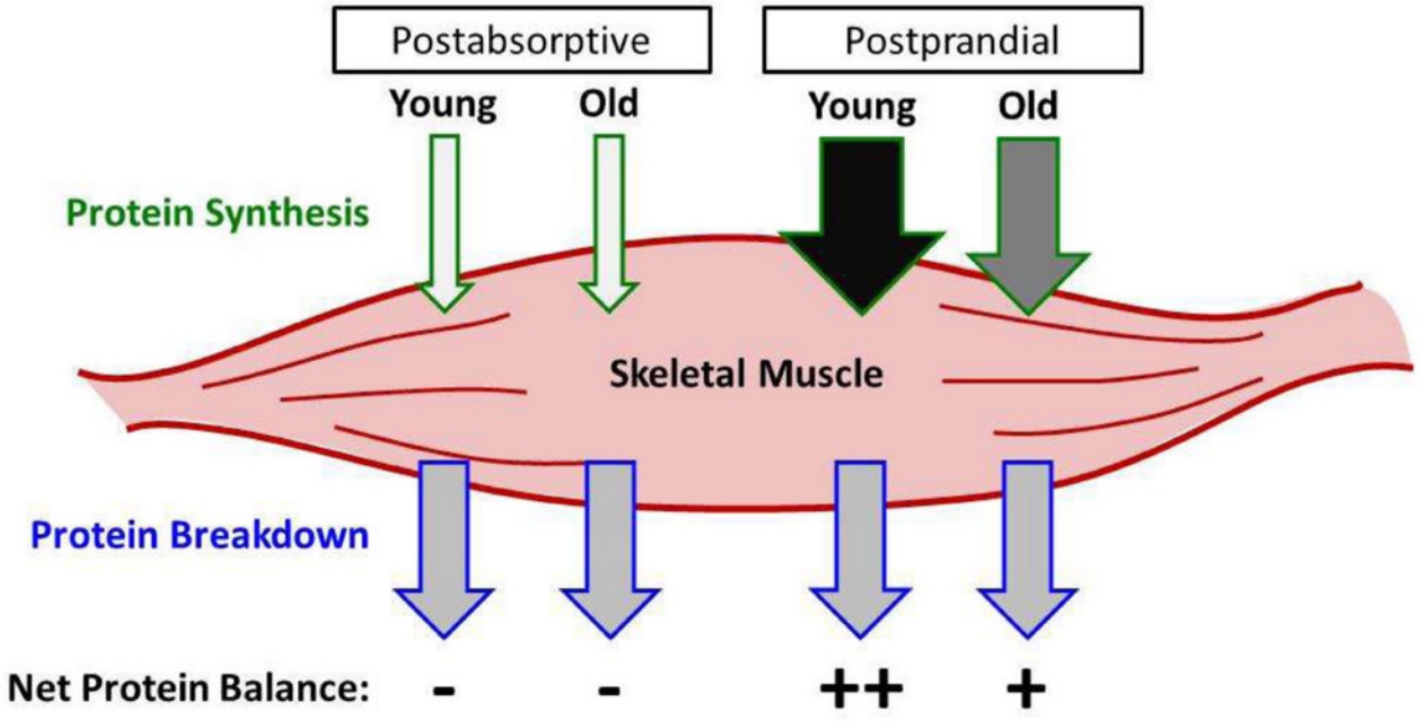


Figure 1. Skeletal Muscle Protein Turnover
Balance between protein synthesis and breakdown in skeletal muscle switches from negative (−) net balance in the fasted (postabsorptive) state to positive (+) following AA intake (postprandial), primarily due to an upregulation of protein synthesis. The anabolic sensitivity to AA availability is blunted with age, which can result in a diminished acute synthetic response following meal ingestion in Old (+) when compared to Young (++) muscle.

Dillion, EL. Nutritionally essential amino acids and metabolic signaling in aging. 2013, *Amino Acids*, 45(3): 431-441

In the recent publication “Medical Nutrition Matters” of the Medical Nutrition DPG, there is an article on “Dietitians in Physical Medicine and Rehab (Witten, W. Dietitians in physical medicine and rehab. *Med Nutr Practice Group*. 35(1):14, 2015) this article highlights the opportunities for registered dietitians in an entirely unexplored area of practice.

Dietitians in Physical Medicine and Rehabilitation (DPM&R)

The Dietitians in Physical Medicine and Rehabilitation (DPM&R) sub-unit is a resource for dietetic professionals providing MNT for people with loss of function due to illness, injury or surgery. The goals of rehabilitation are to reach and maintain the highest possible level of function and quality of life and prevent secondary complications. Nutrition has a strong role in achieving these goals. Services are provided in a variety of settings including acute hospitals, sub-acute rehabilitation facilities, skilled-care nursing homes, home health, clinics and private practice. There is great potential for research in nutrition for the variety of conditions treated in rehabilitation.

Conditions treated include: Dysphagia, Spinal Cord Injury, Traumatic Brain Injury, Stroke, Multiple Sclerosis, Amyotrophic Lateral Sclerosis, Sport Injuries, Amputation, Osteoporosis, Cardiovascular and Pulmonary Rehabilitation, Orthopedics - Joint Reconstruction, Wound Care and Parkinson's.

DMNT Dietitians in Physical Medicine and Rehabilitation (DPM&R) Discussion Board

Post New Message

Feb 1, 2024

Discussions

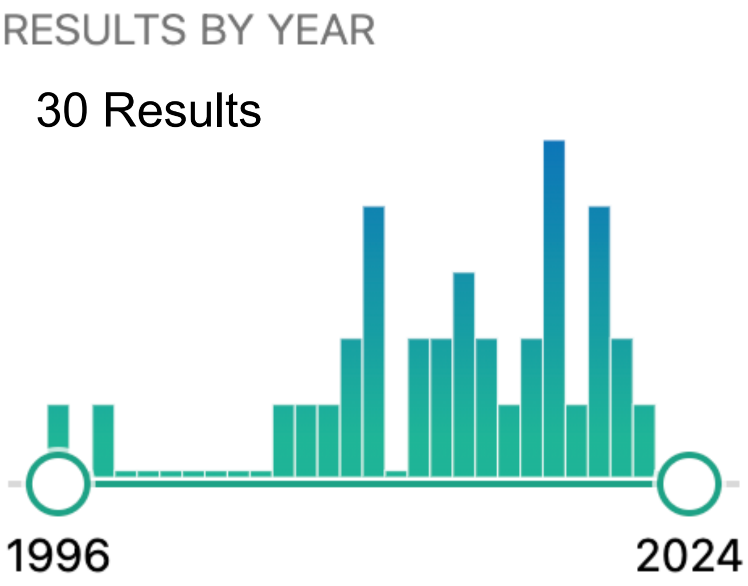
started 10 hours ago, Stephanie Ansley (0 replies)

Presentation Ideas for Physical Therapist Collaboration

1. Greeting All, I am a new member of the (DPM... Stephanie Ansley

Search Terms: Rehabilitative Nutrition and Muscle Disuse Atrophy

Filters applied: Clinical Trial, Randomized Controlled Trial, Review. Clear all



Introduction

Nutrients Involved with Healing/Recovery of Muscle Health

PROTEIN
Calories (Energy Status)
Vitamin C
Zinc
Phosphorus
Magnesium
Vitamin D

Skeletal Muscle Disuse Atrophy and the Rehabilitative Role of Protein in Recovery from Musculoskeletal Injury

Emily E Howard,[1,2,3] Stefan M Pasiakos,[2] Maya A Fussell,[1] and Nancy R Rodriguez[1]
[1] Department of Nutritional Sciences, University of Connecticut, Storrs, CT, USA; [2] Military Nutrition Division, U.S. Army Research Institute of Environmental Medicine, Natick, MA, USA; and [3] Oak Ridge Institute for Science and Education, Oak Ridge, TN, USA Adv Nutr. 2020 11(4):989-1001.

Am J Physiol Cell Physiol 322: C1068–C1084, 2022.
First published April 27, 2022; doi:10.1152/ajpcell.00425.2021

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CELL PHYSIOLOGY

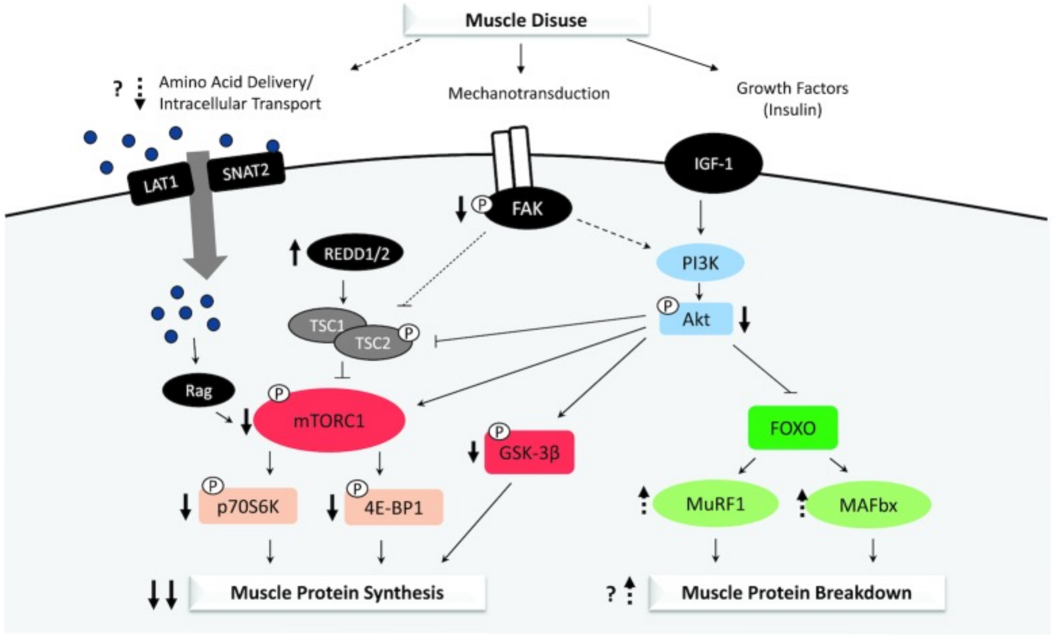
REVIEW

Muscle Wasting: Cellular and Molecular Mechanisms

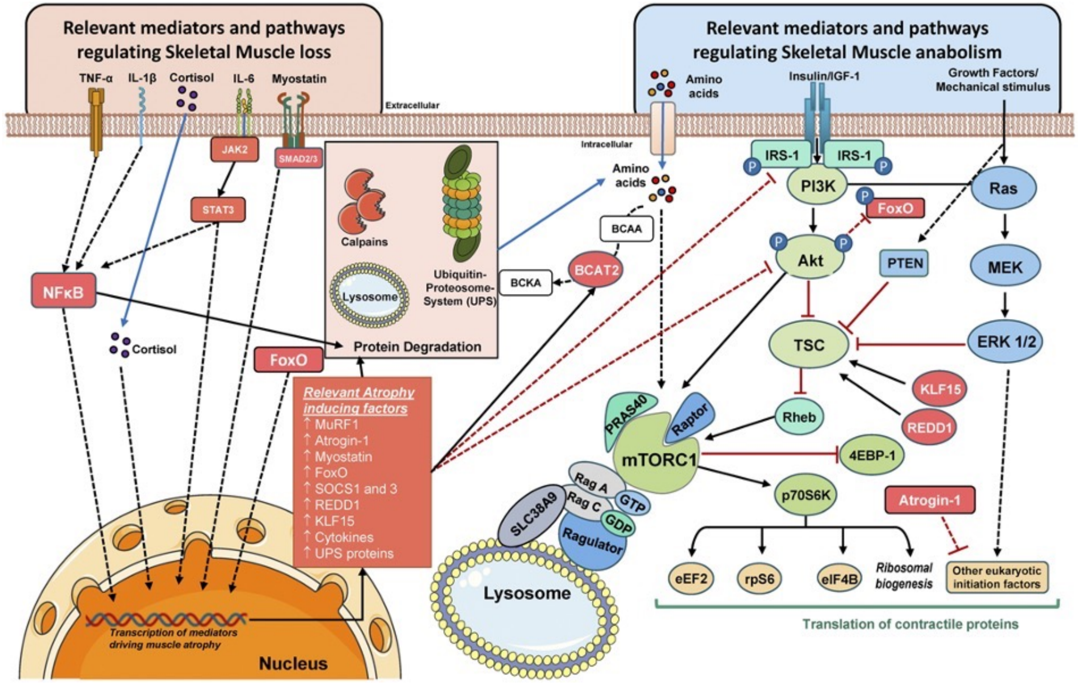
Disuse-induced skeletal muscle atrophy in disease and nondisease states in humans: mechanisms, prevention, and recovery strategies

Everson A. Nunes,[1,2] Tanner Stokes,[1] James McKendry,[1] Brad S. Currier,[1] and Stuart M. Phillips[1]
[1] *Exercise Metabolism Research Group, Department of Kinesiology, McMaster University, Hamilton, Ontario, Canada and*
[2] *Laboratory of Investigation of Chronic Diseases, Department of Physiological Sciences, Federal University of Santa Catarina, Florianópolis, Brazil*

Mechanisms and mediators that regulate skeletal muscle protein turnover in context of disuse atrophy



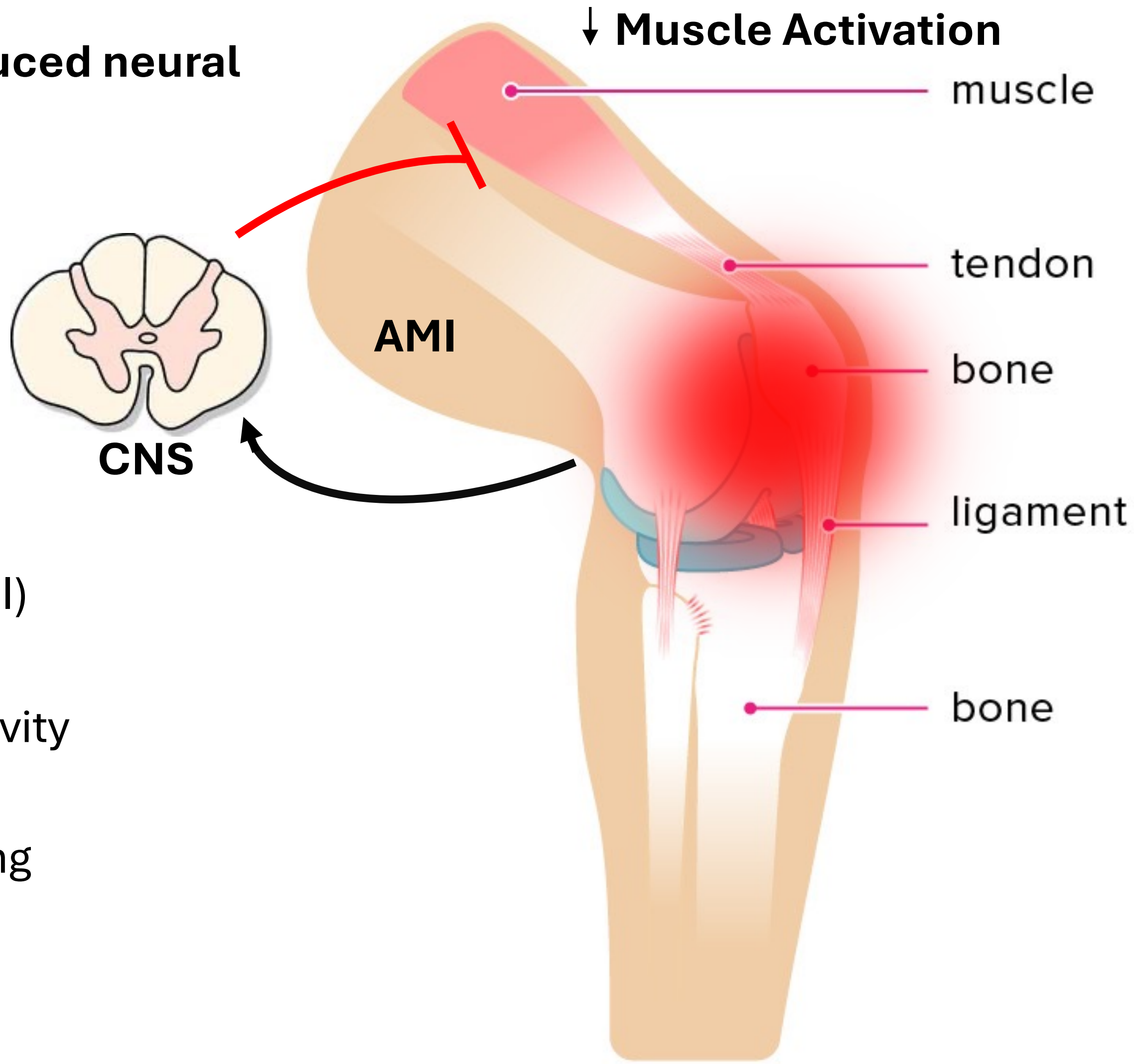
Howard et al., 2020



Nunes et al., 2022 **DOI: (10.1152/ajpcell.00425.2021)**

Muscle disuse following injury

→ **Period of unloading and reduced neural activation of muscle**



1. Arthrogenic Muscle Inhibition (AMI)

2. Decrease in habitual physical activity

3. Limb immobilization and unloading

Physiological response to Musculoskeletal Injury

Pain
Inflammation
Swelling

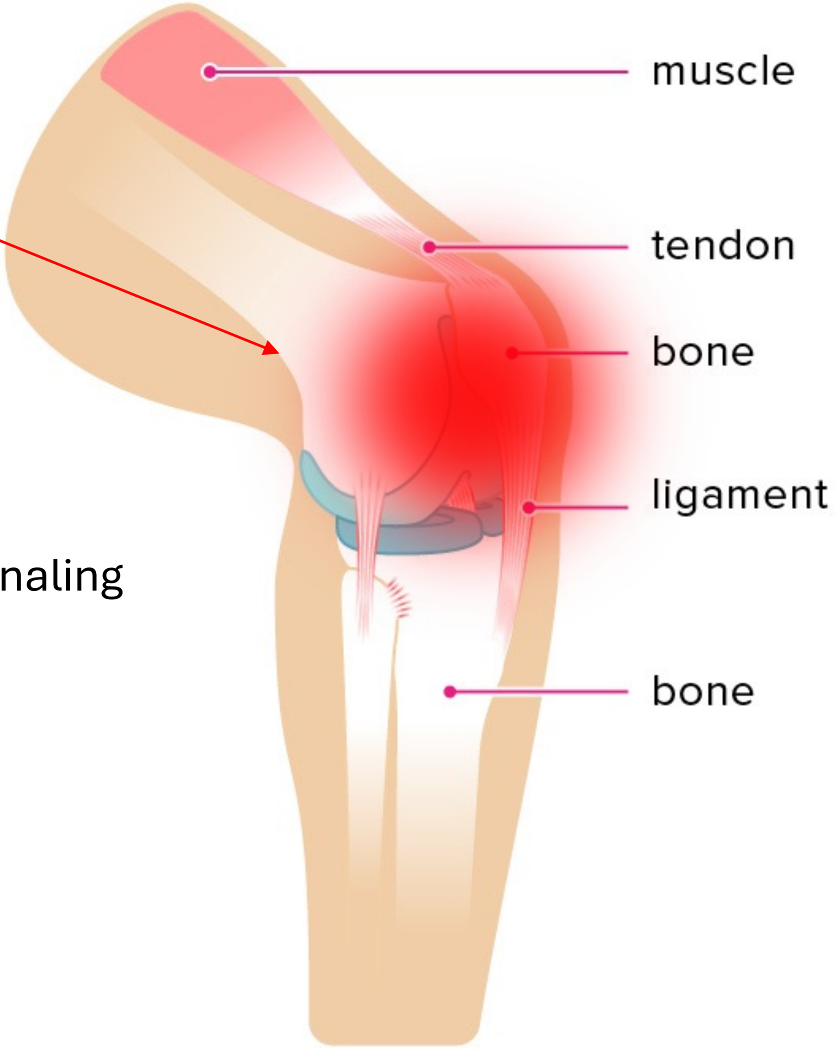
↓

⬇ **Function**

- ↓ Range of motion
- ↓ Neuromuscular signaling
- ↓ Strength

↓

⬆ **Muscle Disuse**

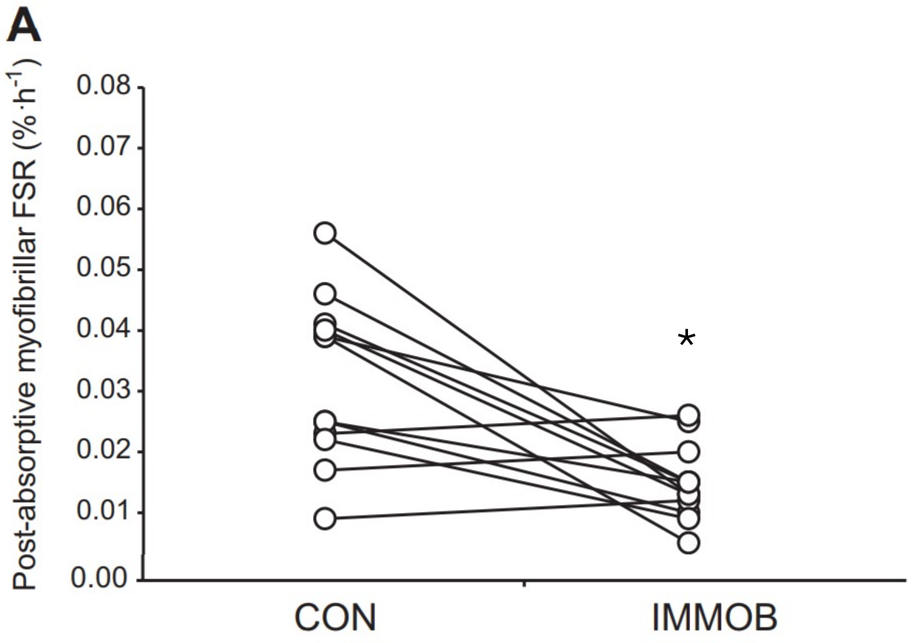


Altered skeletal muscle protein turnover underlies changes in muscle mass

→ 5 days one-legged knee immobilization with a full leg cast (n = 12, 22 ± 1 yr)

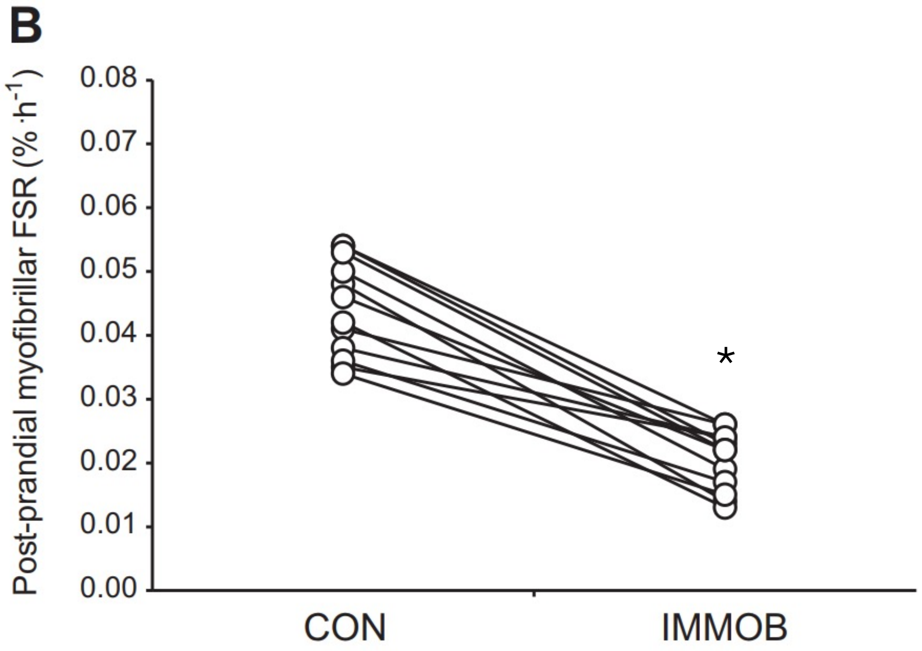
Post-absorptive

41 ± 13 % lower in IMMOB v. CON



Post-prandial (25 g whey protein)

53 ± 4 % lower in IMMOB v. CON

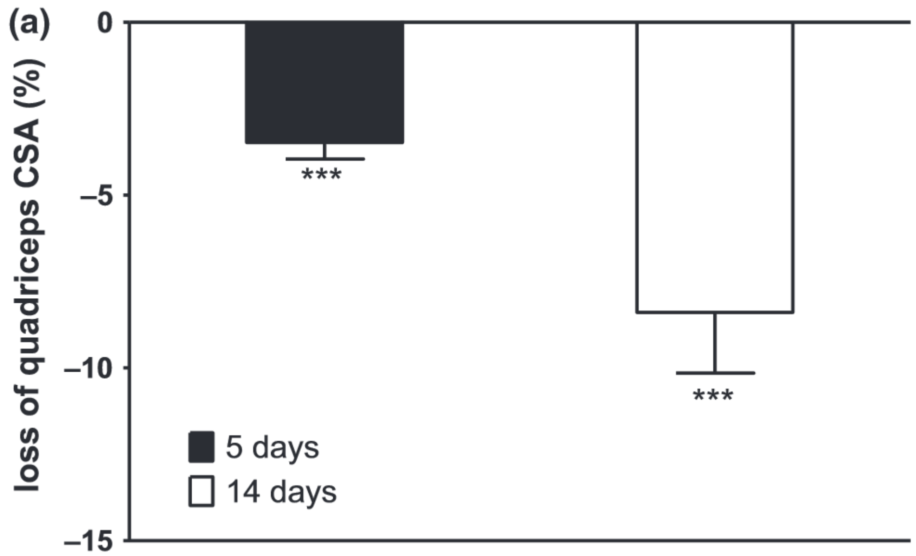


Wall et al., Am J Physiol Endocrinol Metab. 2015

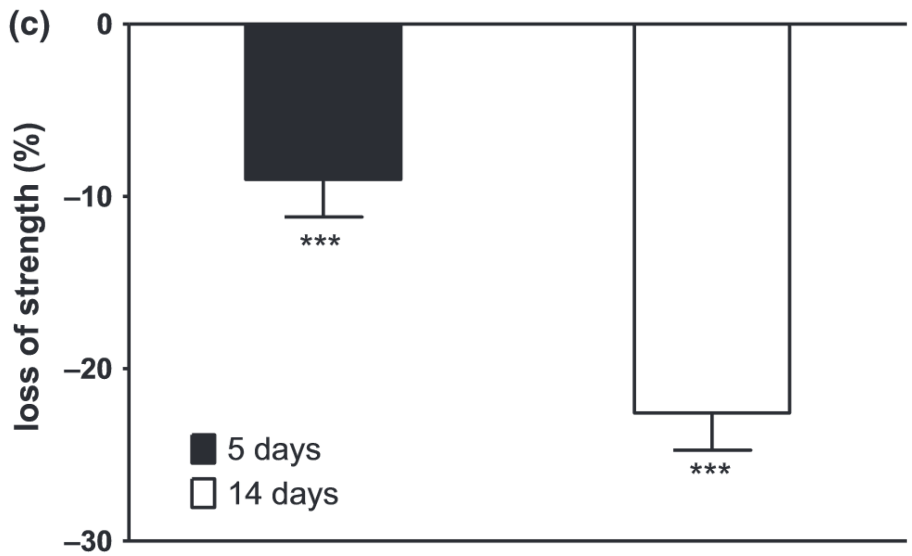
Effect of experimental disuse on muscle mass and strength

→ 5 or 14 days of one-legged knee immobilization with a full leg cast (n = 24, 23 ± 1 yr)

Quadriceps CSA



Quadriceps Strength



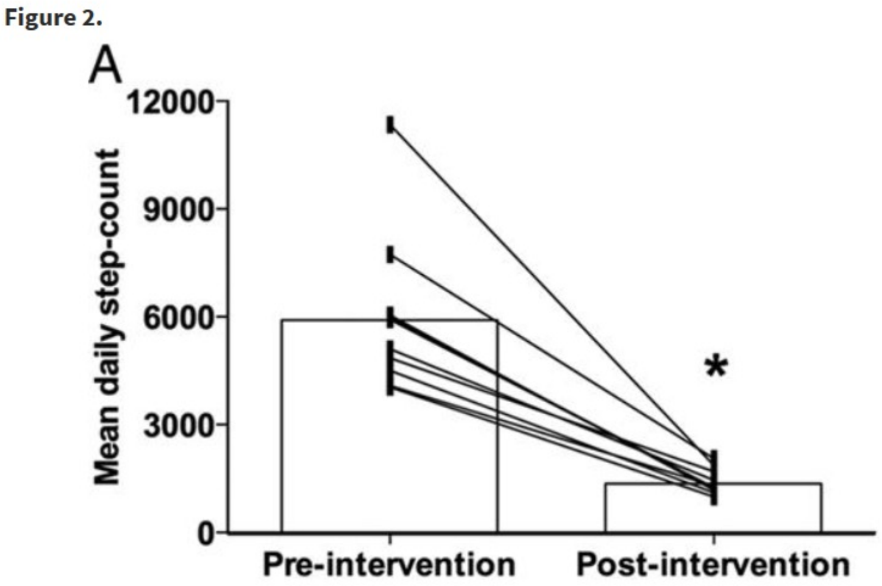
*** $p < 0.001$ compared with pre-immobilization

Wall et al., Acta Physiol (Oxf). 2014

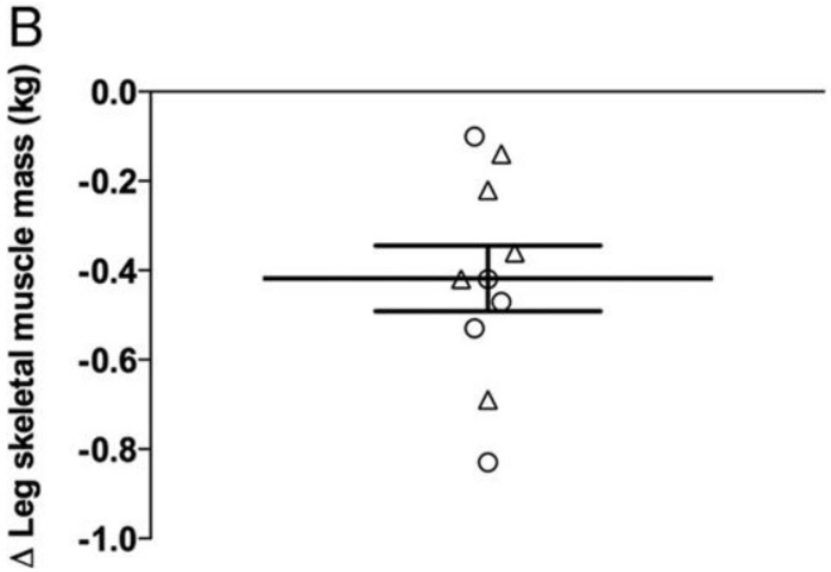
Effect of experimental disuse on muscle mass and strength

→ 14 days of reduced daily step count (n =10, 72 ± 1 yr)

Mean daily step-count



Leg skeletal muscle mass



Breen et al., J Clin Endocrinol Metab. 2013

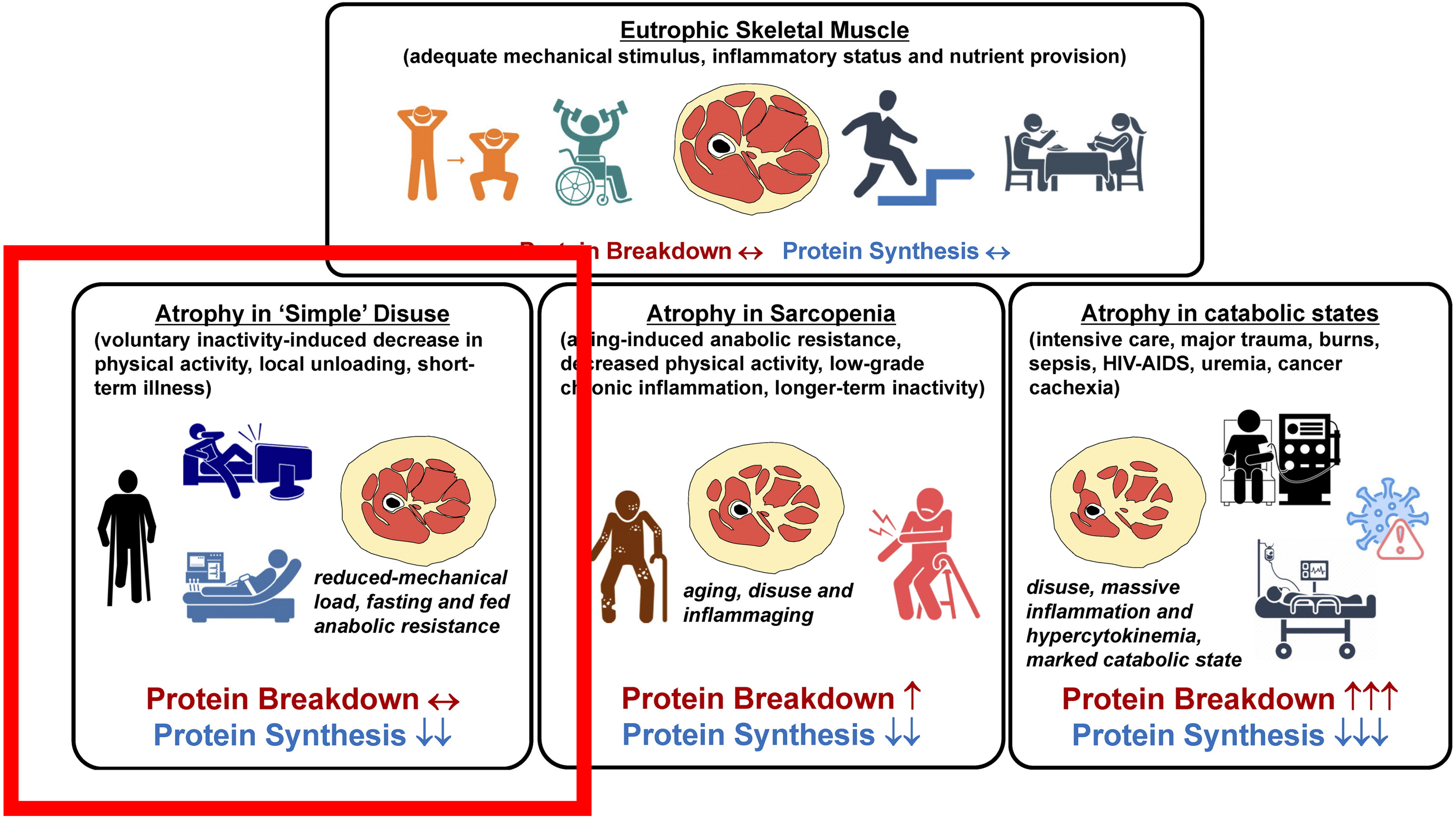
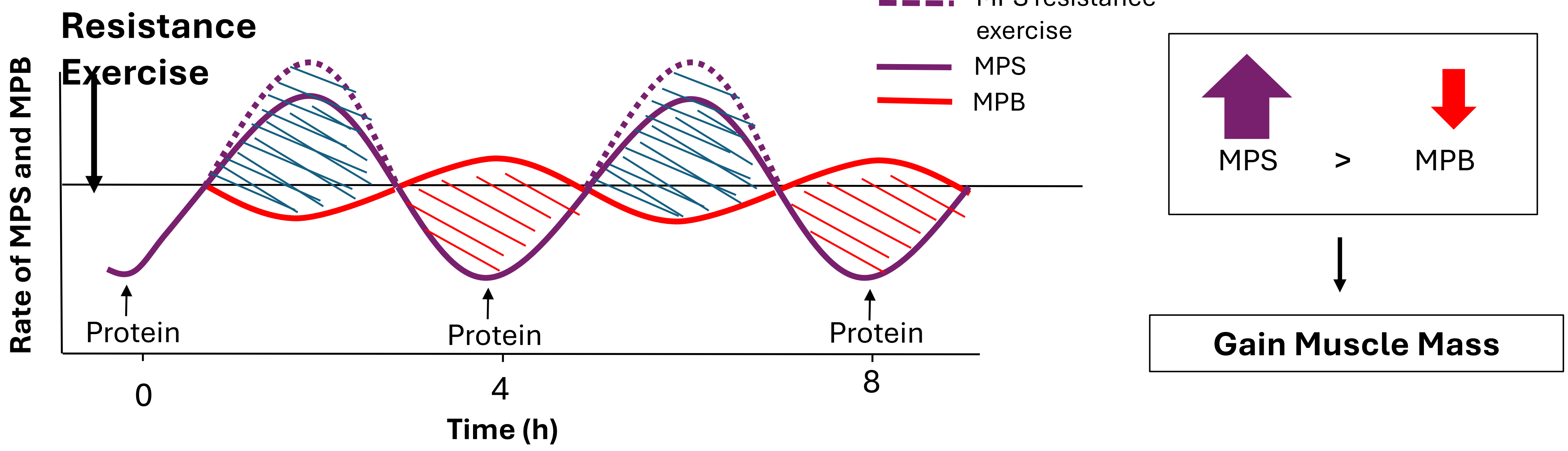


Figure 1. Muscle protein breakdown and synthesis in distinct atrophy scenarios (Nunes et al., 2022 **DOI: (10.1152/ajpcell.00425.2021)** ..

Resistance exercise sensitizes muscle to protein intake

Early Rehabilitation

- Body weight or light load resistance exercise to fatigue
- Neuromuscular electrical stimulation (NMES)



Phillips et al., J Appl Physiol (1985). 2009 Sep;107(3):645-54

Anabolic potential of dietary protein following light-load exercise

- 10 healthy males
- Light-load resistance exercise at 16% of 1-RM
- Oral protein boluses every hour for 10 hour period

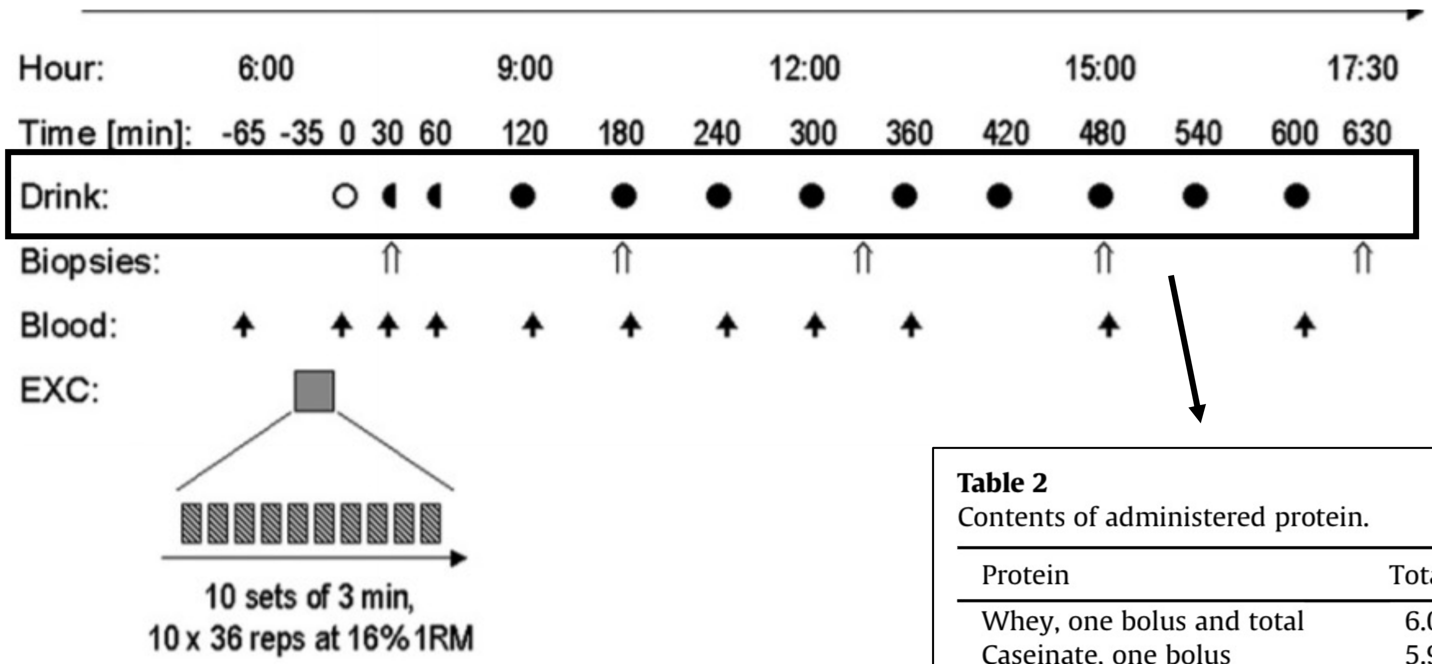
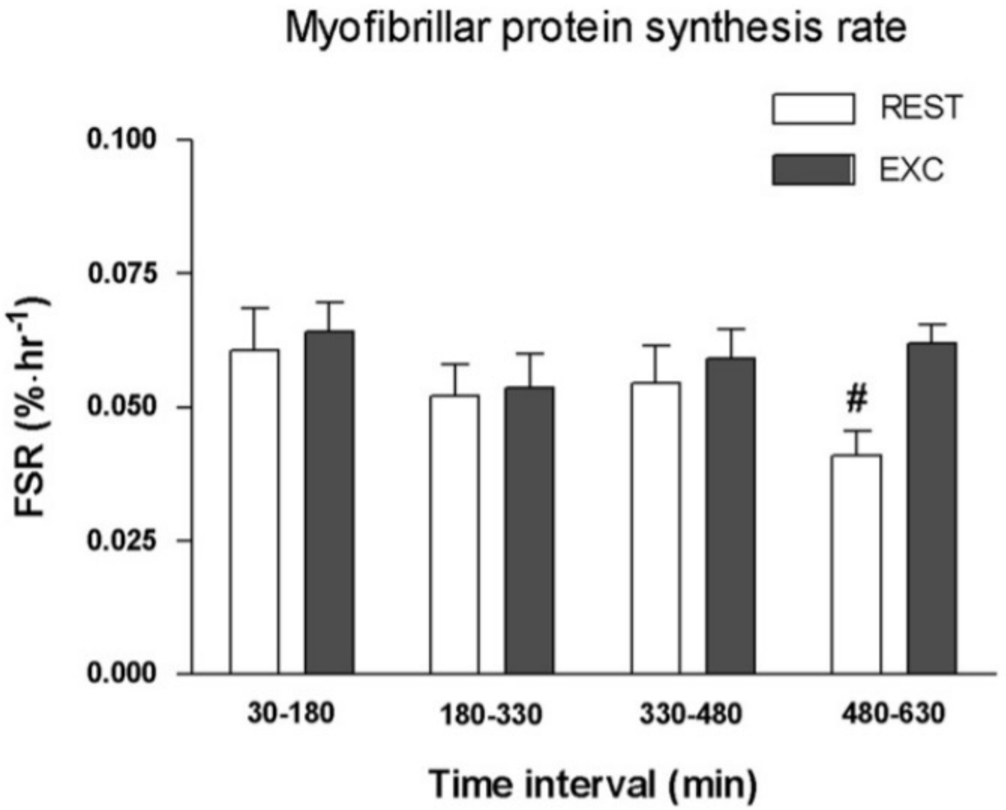


Table 2
Contents of administered protein.

Protein	Total (g)	Leucine (g)	EAA (g)
Whey, one bolus and total	6.0 ± 0.2	0.9 ± 0.03	3.5 ± 0.1
Caseinate, one bolus	5.9 ± 0.2	0.6 ± 0.02	2.9 ± 0.1
Caseinate, total	59.0 ± 1.9	6.2 ± 0.2	28.5 ± 0.9
Protein, total	64.9 ± 2.1	7.1 ± 0.2	32.0 ± 1.0

Bechshoeft et al., Clinical Nutrition. 2013

Anabolic potential of dietary protein following light-load exercise



lower than EXC and decline from 30-150 min time point ($p < .05$)

Non-exhaustive light-load contractions prior to protein intake prolonged the elevation in muscle protein synthesis rates in response to hyperaminoacidemia

Bechshoeft et al., Clinical Nutrition. 2013

Anabolic potential of dietary protein following NMES

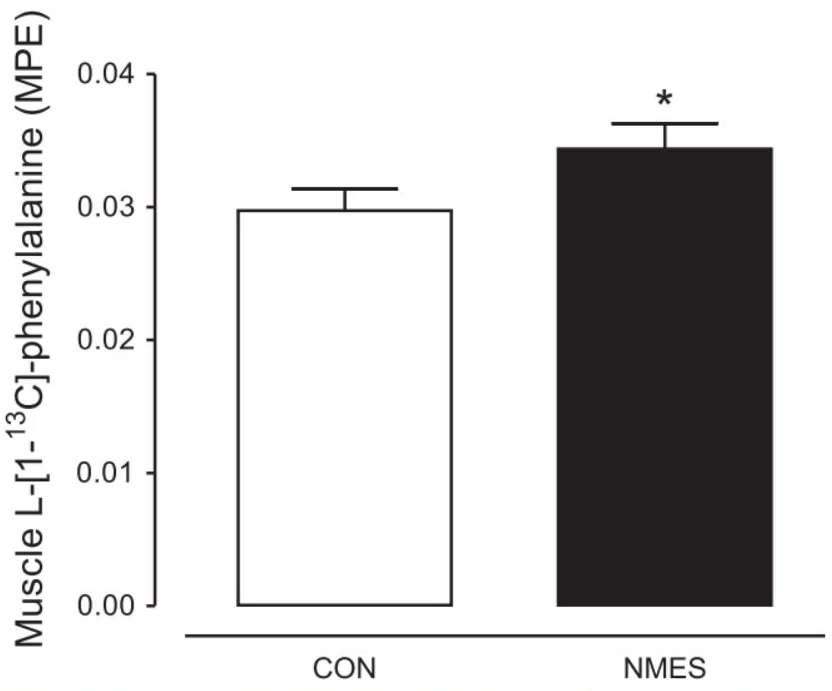


Fig. 5. Muscle tissue L-[1-^{13}C]-phenylalanine enrichments. Values are expressed as means ± SE. Data were analyzed with a paired Student's *t*-test. *Significantly different from the control leg ($P < 0.01$).

Combination of NMES and protein feeding may represent an effective strategy to attenuate any further losses of muscle mass during early rehabilitation

Application to rehabilitation setting

1. Protein-based interventions have been shown to preserve muscle mass and/or a degree of muscle function during disuse

2. Combining protein ingestion with light load resistance exercise or surrogates of muscle contraction in early rehab to attenuate further losses

EAA supplementation accelerates muscle strength recovery following hip arthroplasty

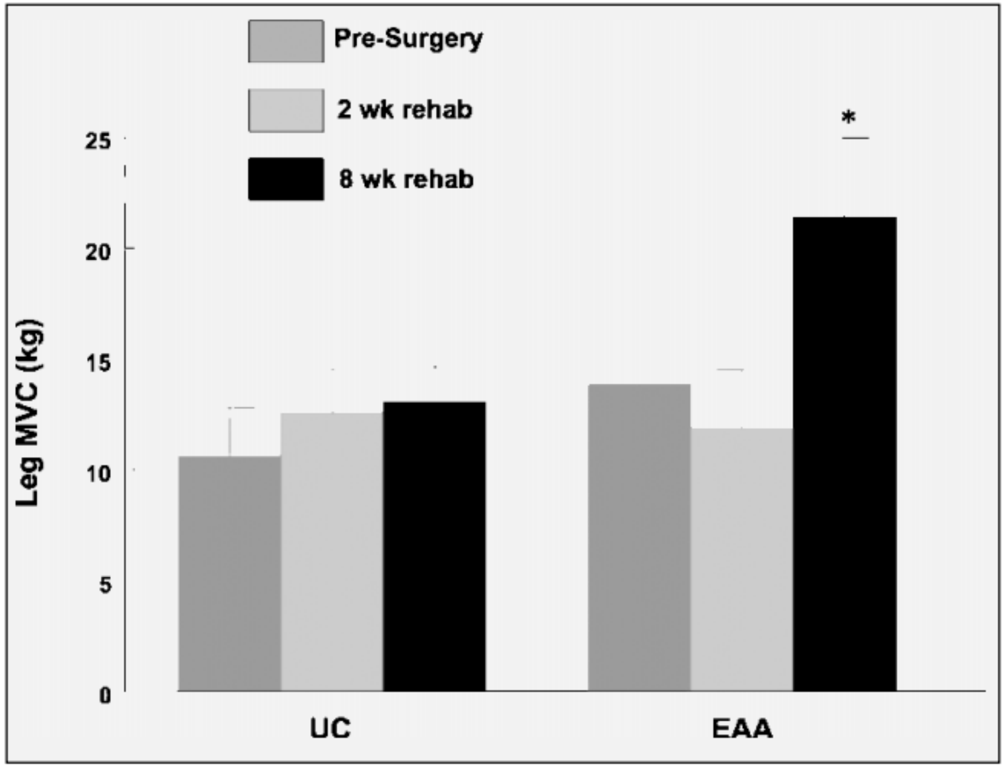
- Patients scheduled to receive elective hip arthroplasty (~55 y)
- EAA supplementation for 8 weeks post-operatively

Usual Care (UC)	**Essential Amino Acid (EAA)**
1.1 g /kg/d protein	1.7 g/kg/d protein **15 g EAA supplementation 3 times per day**

Ferrando et al., JARCP. 2013

EAA supplementation accelerates muscle strength recovery following hip arthroplasty

→ Unable to measure changes in lean mass in the affected limb to edema and/or the metal implant.



* Significant improvement with time (p < 0.02)

Improved rate of recovery with EAA supplementation

EAA supplementation mitigates muscle atrophy after total knee arthroplasty

- Patients scheduled to undergo total knee arthroplasty (~65 y)
- EAA supplementation for 1 week prior and 6 weeks postoperatively

Placebo	Essential Amino Acid (EAA)
20 g NEAA 2 x daily	20 g EAA 2 x daily

Dreyer et al., JBJS. 2018

EAA supplementation mitigates muscle atrophy after total knee arthroplasty

Muscle Volume

Placebo		Essential Amino Acid (EAA)	
Involved	Uninvolved	Involved	Uninvolved
-13.4 ± 1.9 %	-7.2 ± 1.4 %	-8.5 ± 2.5 % *	-1.5 ± 1.6 %*

* Significantly different than placebo ($p < 0.03$)

Dreyer et al., JBJS. 2018

nutrients

MDPI

Article

Effect of High-Protein Diets on Integrated Myofibrillar Protein Synthesis before Anterior Cruciate Ligament Reconstruction: A Randomized Controlled Pilot Study

Emily E. Howard [1,2,3], Lee M. Margolis [2], Maya A. Fussell [1], Clifford G. Rios [4], Eric M. Meisterling [5], Christopher J. Lena [4], Stefan M. Pasiakos [6] and Nancy R. Rodriguez [1,*]

Myofibrillar fractional synthetic rate for adequate (AP) and optimal (OP) protein intakes

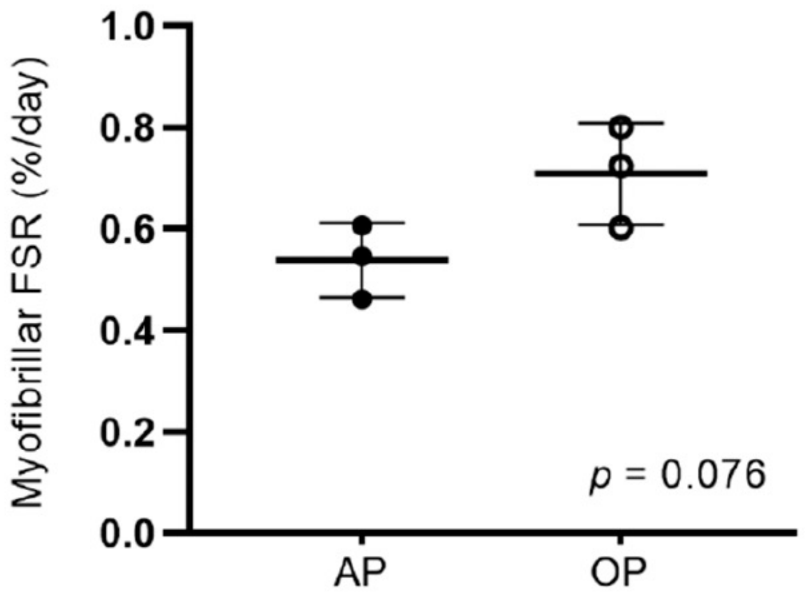


Figure 1. Myofibrillar FSR ($\%\cdot d^{-1}$) over a two week period before ACL reconstruction with AP ($1.2\ g\cdot kg^{-1}\cdot d^{-1}$) and OP ($1.9\ g\cdot kg^{-1}\cdot d^{-1}$). Differences between AP (n = 3) and OP (n = 3) were examined using unpaired t tests. Values are the mean ± SD. AP, adequate protein; FSR, fractional synthesis rate; OP, optimal protein.

Higher protein intake 2 wks prior to surgery resulted in higher myofibrillar FSR during ACL surgery

Howard et al., 2020

Relationship between myofibrillar FSR and MURF1 for adequate (AP) and optimal (OP) protein intakes

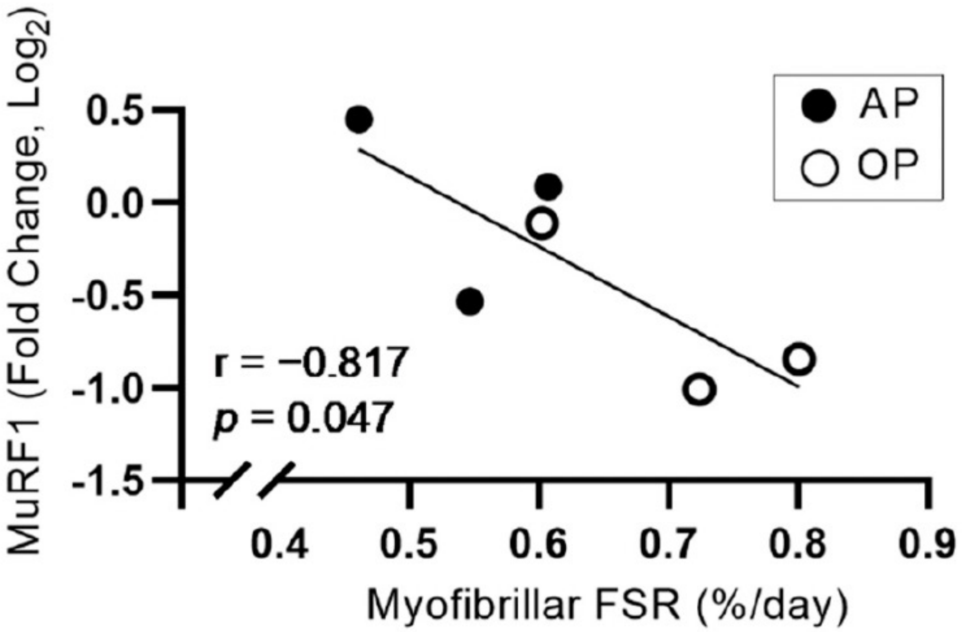


Figure 2. Relationship between myofibrillar FSR ($\%\cdot d^{-1}$) and MuRF1 gene expression in AP and OP. Associations were examined using Pearson's correlation. AP, adequate protein; FSR, fractional synthesis rate; OP, optimal protein.

Higher protein intake 2 wks prior to surgery resulted in lower muscle MURF1 suggesting reduced muscle protein breakdown during ACL surgery

Howard et al., 2020

Energy **S**tatus and **P**rotein Intake as **Pro**gnostic Indicators of Rehabilitative Outcomes (ESPI-PRO)

Specific Aims. Given that higher recommended dietary protein intakes attenuate muscle loss following injury and disuse and support recovery of muscle mass, strength and function following surgery, study aims were to:

- *Characterize energy status and protein intake in THA and TKA patients prior to surgery and throughout recovery*
- Explore whether energy status and protein intake at admission predicts rehabilitative outcome measures in THA and TKA patients

Clinical Significance

- *Contribute to* evidence-based rehabilitative nutrition practice guidelines for orthopedic patients.
- *Expand* scientific literature regarding role of perioperative nutrition on rehabilitative outcomes in patients undergoing elective total joint procedures.
- *Establish* research infrastructure as a foundation for federal and private extramural funding opportunities.

Research Settings

Hartford Hospital Bone & Joint Institute (BJI) and Orthopedic Associates of Hartford (OAH) Locations , 7 Total Joint Arthroplasty Surgeons

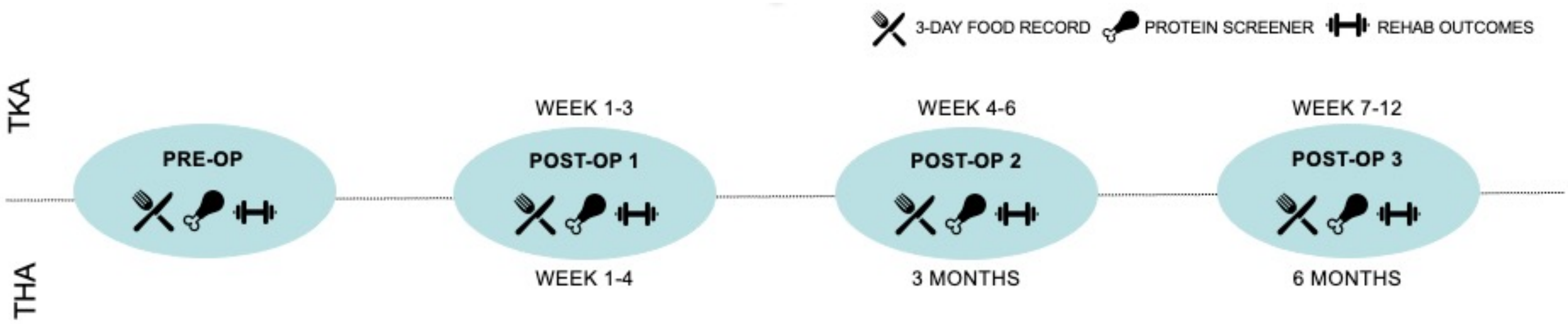
Recruitment/Enrollment

- Baseline Data Collection
  - PREPARE and In-Person Onsite at OAH Locations
  - Force Therapeutics Platform

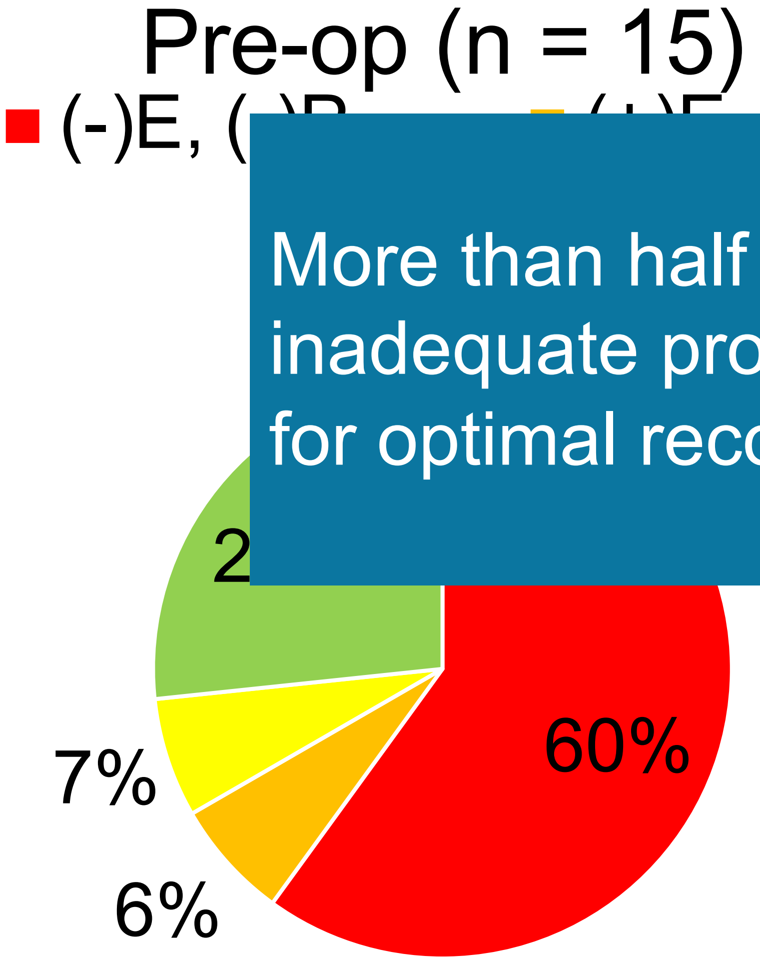
Physical Therapy Sites (5) – Rehab Outcome Data Collection

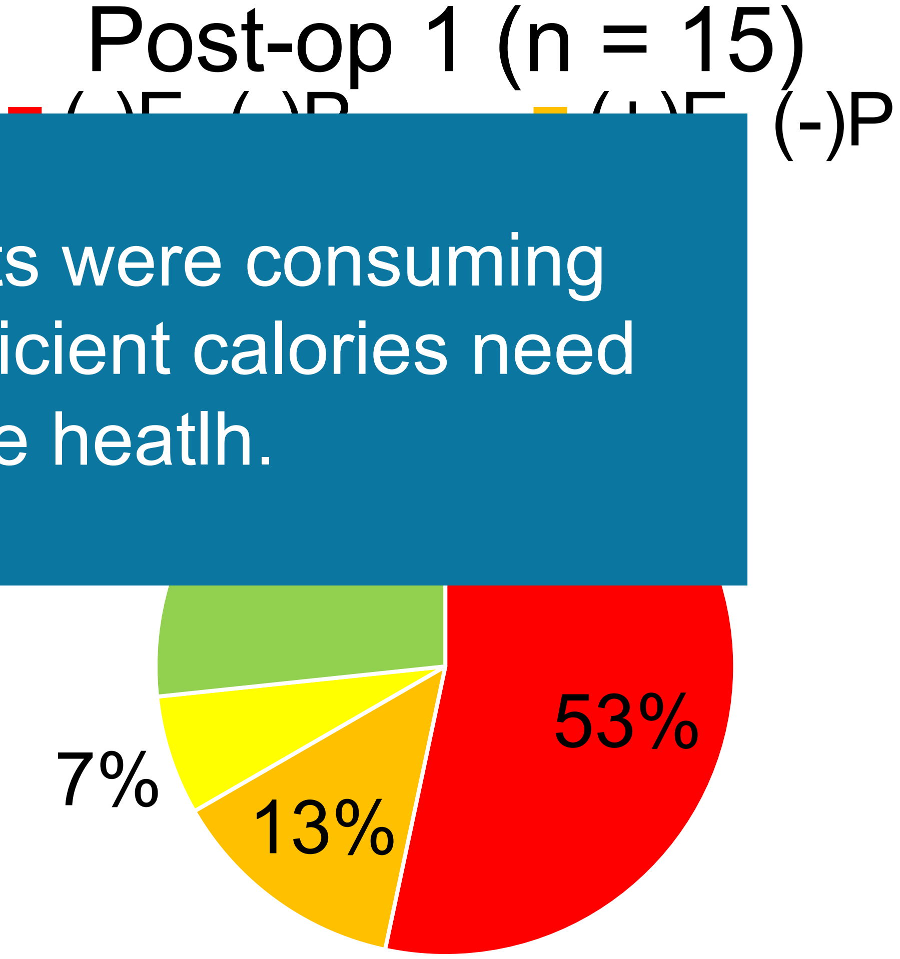
- Hartford Healthcare Rehab Network (BJI, Enfield)
- OAH (Farmington, Glastonbury, Rocky Hill)

ESPI-PRO Study Experimental Design



Energy Status and Protein Intake - THA

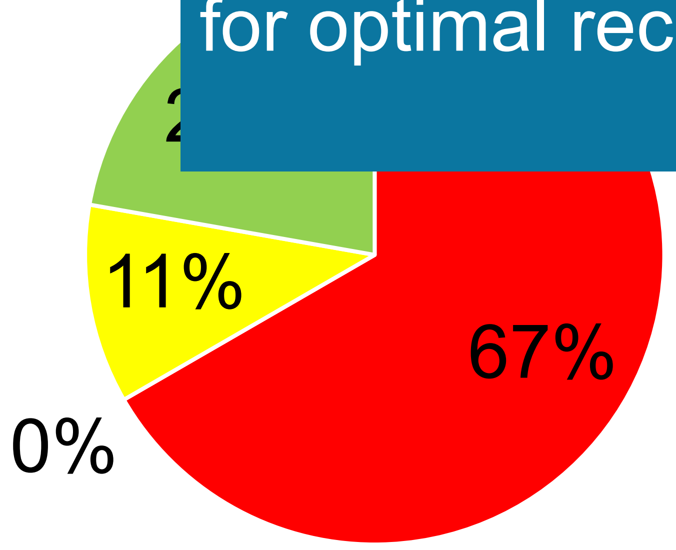




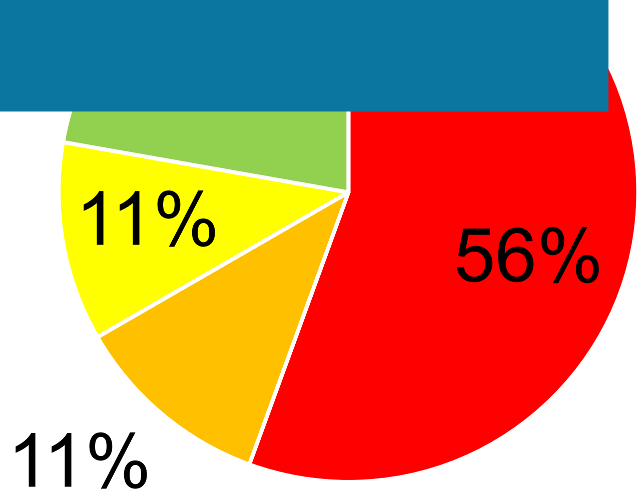
More than half of THA patients were consuming inadequate protein and insufficient calories need for optimal recovery of muscle heatlh.

Energy Status and Protein Intake - TKA

Pre-op (n = 9)



Post-op 1 (n = 9)



More than half of TKA patients were consuming inadequate protein and insufficient calories need for optimal recovery of muscle health.

Summary and Future Directions

- Protein post-injury is relevant given the underlying changes in skeletal muscle protein turnover underlying disuse atrophy and subsequent rehabilitation
- Protein protects muscle during disuse
- Synergistic effect of protein plus light load resistance exercise or neuromuscular electrical stimulation (NEMS)
- Practical application of this work post-musculoskeletal injury includes routine assessment of protein intake and energy status of patients and implementation of strategies to optimize these aspects of nutritional status in elective orthopedic patients

Thank you!!