PHILOSOPHICAL CONTEXT

- Environmental exposure prompts movement on the Biological Spectrum.
- Optimal environmental “dose” depends upon internal capacity.
- Muscle health depends upon regular exposure to tension.

SARCOPENIA

- Sarco = flesh/muscle; Penia = poor
- Characterized by progressive and generalized loss of skeletal muscle mass and strength.
  - 0.8% skeletal muscle loss per year from the fifth decade of life (50+)
- Sarcopenia is strictly correlated with physical disability, poor quality of life, and death.
- Results in:
  1. Chronic Metabolic Disease
     i. Fatty Organ Disease
  2. Reduced Functional Capability
     - Fast Twitch muscle fibers are preferentially targeted (lost)
       - Loss of Strength
       - Loss of Speed
       - Loss of Control
     - Increased likelihood of falls
       ↓ probability of recovery
       ↑ dependence on others
       ↓ quality of life
       ↑ comorbidities
       ↓ average life expectancy

UNDERSTANDING SKELETAL MUSCLE

- Preserving muscle means promoting regular protein synthesis

MAMMALIAN TARGET OF RAPAMYCIN (MTOR)

- Protein complex that senses cellular conditions (nutrients, redox state, growth factors, energy charge, and mechanical tension) and controls protein synthesis
- Responsive to:
  - Nutrients (amino acids)
  - Mechanical Tension (eccentric muscle actions)
  - Growth Factors (e.g., IGF-1)
- Coincidence Detector: Activates when both tension and nutrients are present.

SATELLITE CELLS

- Stem cell on the periphery of skeletal muscle cells
- Mechanical strain results in their activation:
  - Chemical signaling – growth and repair
  - Proliferation – division (more satellite cells)
  - Fusion and Differentiation (add nuclei to existing muscle fibers)
- **Myonuclear Domain**
  - A given myonucleus in the muscle fiber syncytium can only transcriptionally govern a finite jurisdiction.
  - More nuclei = ↑ protein synthesis = HYPERTROPHY
- Satellite cell-mediated myonuclear accretion is **required** for overload-induced hypertrophy.
- **DOMS** is likely needed to induce myonuclear accretion.

**TENSION (ADAPTIVE CHALLENGE)**

**MECHANOTRANSDUCTION**

There is a “continuous physical link between the extracellular matrix, cytoskeleton, sarcomere, and nuclear matrix as a means to rapidly regulate gene expression following a mechanical stimulus.”

There are several Mechanotransducing Pathways:

- GPCR (G-Coupled Protein Receptors)
- DAG (Dystrophin-Associated Glycoprotein Complexes)
- α7β1 (Alpha7β1 Integrin)
- SAC (Stretch Activated Channels)
- MAPK (Mitogen Activated Protein Kinases)

Mechanical Stimulus → mTORC1 → Protein Synthesis

**ECCENTRIC MUSCLE ACTIONS**

- **DEFINITION:** Muscle force is less than the resistance resulting in the *muscle lengthening*.
- Fewer muscle fibers recruited
  - Recruits more FT fibers
  - Recruits less ST fibers
  - ↑ mechanical force by the working fibers (FT).
- Recruitment of rapidly contracting fibers having a short relaxation time is most appropriate for better control of fast movements.
- **Eccentric Actions** Result in:
  - Increased protein synthesis
  - Increased mTORC1 signaling
  - Increased satellite cell activation
  - Increased muscle membrane integrity
  - Increased DOMS

**DOMS (DELAYED ONSET MUSCLE SORENESS)**

- Unaccustomed exercise, predominantly *eccentric muscle actions*, results in mechanical muscle damage
- Factors leading to skeletal muscle damage:
  - Longer *duration* (number or repetitions)
  - Higher *intensity* (greater percentage of maximal *eccentric loading*)
  - Higher exercise intensity seems to have more influence than duration of exercise.
- Disrupted Calcium Homeostasis
  - Calcium activated proteases; Lysosomal proteases
  - ROS production
  - Cytokine release
• Neutrophil and Macrophage activation → inflammation
• Cytokines from immune cells play a key role in satellite cell activation/recruitment
• Lactic Acid is NOT a significant contributor to DOMS

FASTING AND SATELLITE CELLS
• Fasting causes muscle SCs to enter a deep quiescent state.
• Deep Quiescent State (DQS)
  • Smaller cell size
  • Less mitochondrial content
  • Less oxygen consumption
  • Less RNA content
• Delayed ROI (return on investment)
  • Lasts for 72 hours after feeding (delayed muscle regeneration)
  • Enhanced resilience to nutrient, cytotoxic, and proliferative stress
• Deep Quiescent State Results from:
  • Fasting;
  • Ketogenic Diet or;
  • Feeding BHB (Beta Hydroxybutyrate)

NUTRITION

PROTEIN

Window of Opportunity: 48 hours after exercise = ↑ sensitivity to leucine

AMOUNT
The amount is the ideal to maximize protein synthesis for hypertrophy, not an amount to prevent disease.

Adults
• Young: 0.24 g/kg body mass
• Old: 0.40 g/kg of body mass
• Young: 0.25 g/kg lean body mass
• Old: 0.60 g/kg of lean body mass

| 220lbs = 100kg |
| 100kg (.75 lean) = 75kg lean body mass |
| 0.25(75) = 20 grams of protein (per meal) |
| 0.6(75) = 42 grams of protein (per meal) |

QUALITY
Certain Amino Acids are critical for stimulating mTORC1:
• Leucine
• Methionine
• Arginine
• Glutamate/Glutamine

Maximal mTORC1 Activation (meal)
• >2.2g leucine younger adults
• >2.5g leucine for older individuals

Upper Limit for leucine is over 500 mg/kg/d (38 g/d for a 75 kg person)

AVAILABILITY
PDCAAS – protein digestibility-corrected amino acid score
DIAAS – digestible indispensable amino acid score
EAA-9 – essential amino acid 9 score
ANTINUTRIENTS
• Natural or synthetic compounds that interfere with the absorption of nutrients.
  • Drugs, Chemicals, Dietary Fiber, Proteins, Overconsumption of nutrients

EXCESSIVE PROTEIN
Consumption of 2g/kg (bodyweight)/day is safe for healthy adults.
Tolerable upper limit of 3.5 g/kg(bodyweight)/day for well-adapted persons.

UNBALANCED DISTRIBUTION
Most adults >60% of daily protein consumed during a single evening meal and ≤ 15 g at breakfast.
Overnight fast = Breakfast starts with negative net protein balance.

ADDITIONAL ONLINE CONTINUING EDUCATION
- INTERMITTENT FASTING
- GUT MICROBIOTA
- GLUTEN AND CELIAC DISEASE

REFERENCES
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