Optimal protein intake and meal frequency to support maximal protein synthesis and muscle mass.

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Overview

- Background
- Determining optimal protein intake
- Optimal Frequency
- Refractory Phenomenon
- Future Research
**Background**

- High protein diets are popular amongst athletes and bodybuilders
  - Purported to have various beneficial effects
    - Increase muscle mass
    - Decrease bodyfat
    - Improve exercise performance and recovery
Current RDA is 0.8g/kg for protein intake.

Current recommendations are based on minimum needs to achieve short-term nitrogen balance.

- Often do not control for protein distribution, protein source, and are often not applicable to meal feeding.

Empirical evidence suggests many trainers and coaches frequently recommend amounts that are 2-4g/kg or even greater.

How do we define optimal protein intakes to maximize muscle mass?
Determining Optimal Intake

- Determine optimal protein intake at individual meals to maximize protein synthesis (MPS)

- Determine optimal frequency of meal intake

- These variables will dictate total protein intake
  - Specific meal recommendations are likely more beneficial than daily recommendations
    - MPS is regulated from meal to meal, not day to day.
Leucine in regulation of protein synthesis

- Leucine (leu) has been shown to stimulate protein synthesis and translation initiation to the same extent as a complete meal and is likely the major amino acid responsible for the anabolic effects of a meal (1).

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[Leucine]

mTOR (+) -> p70S6K (+) -> 4E-BP1-eIF4E

4E-BP1-eIF4E -> eIF4E

eIF4E -> eIF4G (+) -> eIF4E-eIF4G (+)

Protein Synthesis (+)
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Possible that activating and maximizing MPS is dependant upon achieving a specific post-prandial concentration of leu in the plasma.

A certain amount of dietary leu is required to increase plasma leu levels and activate mTOR signaling and MPS.

What level of dietary leu at a meal is required to maximize this response?

*unpublished data
Padden-Jones et al. showed that administration of an essential amino acid (EAA) solution containing 2.8g leu increased MPS by ~60% in adult humans (2).

Tipton et al. demonstrated that amino acid solutions containing 4.4g and 8.3g leu stimulate MPS similarly (50-70% increase) in adults (3).

It is likely ~3-4g leucine (~0.045-0.06 g/kg) will maximize MPS at a meal in adults.
## Leucine content of various protein sources

<table>
<thead>
<tr>
<th>Protein Source</th>
<th>Leu % of total protein</th>
<th>Amount of protein from source to reach 3-4g Leucine</th>
<th>Amount of food source required</th>
</tr>
</thead>
<tbody>
<tr>
<td>Whey Protein Isolate</td>
<td>12.0%</td>
<td>25-33g</td>
<td>27-36g</td>
</tr>
<tr>
<td>Milk Protein Isolate</td>
<td>9.8%</td>
<td>31-41g</td>
<td>34-46g</td>
</tr>
<tr>
<td>Casein</td>
<td>9.3%</td>
<td>32-43g</td>
<td>variable depending upon casein powder type</td>
</tr>
<tr>
<td>Egg</td>
<td>8.6%</td>
<td>35-47g</td>
<td>280-376g or approx 4.5-6.5 large whole eggs</td>
</tr>
<tr>
<td>Fish</td>
<td>8.1%</td>
<td>38-50g</td>
<td>158-208g</td>
</tr>
<tr>
<td>Beef</td>
<td>8.0%</td>
<td>38-51g</td>
<td>126-170g</td>
</tr>
<tr>
<td>Pork</td>
<td>8.0%</td>
<td>38-51g</td>
<td>133-179g</td>
</tr>
<tr>
<td>Chicken</td>
<td>7.5%</td>
<td>41-54g</td>
<td>132-174g</td>
</tr>
<tr>
<td>Wheat</td>
<td>6.8%</td>
<td>44-59g</td>
<td>440-590g or 15-20 slices of bread</td>
</tr>
</tbody>
</table>
Recap

- MPS is maximized by an oral administration of 3-4g (0.045g-0.06g/kg) leu in adults and elderly.

- Key Questions:
  - How long does the MPS response last?
  - When can this response be stimulated again?
Optimal Frequency

- The duration of MPS in response to a purified leu or EAA solution has been previously characterized and lasts approximately 2 hours in rats and humans (4,5).

- Bohe et al. infused EAA for 6 hours but this only produced an MPS response lasting 2 hours though plasma amino acids remained elevated for the entire duration of the experiment.
Our lab has characterized the time course of MPS in rats fed a complete meal containing 20, 50, and 30% of energy from protein, carbohydrates, and lipids respectively (6).

MPS time course was complete at 3 hours but plasma amino acids were still elevated.

MPS decreasing though plasma leu remains elevated.
The Refractory Phenomenon

- MPS becomes ‘refractory’ to constant elevations in leu.
- Perhaps leu availability stimulates MPS but sustained elevations in plasma leu are insufficient to maintain elevated MPS.
- Why are constant elevations in plasma leu unable to produce sustained increases in MPS?
Possible explanations?

- Reduced availability of intramuscular leu?

Does not explain refractory nature of MPS.
Possible Explanations?

- Possible that translation factor activation is reduced?
- Phosphorylation of 4E-BP1 and p70S6K were closely associated with plasma leu concentrations.
- Translation factor activation remained elevated at 180 minutes but MPS had returned to baseline.
- Does not explain refractory phenomenon.
Possible Explanations?

- Reduced eIF4E*eIF4G binding?

Unlikely to be responsible for MPS becoming refractory
Possible Explanations?

- Reductions in other plasma EAA?

  - At 180 minutes most EAA were still elevated above baseline levels.

  - Bohe et al. maintained elevated EAA during an infusion for 6 hours but could not overcome the refractory phenomenon.
Possible Explanations?

- Insulin?
- Similar time course as MPS.
- Similar time course to MPS in other studies (4,5).
- Cause or coincidence?
  - Insulin exerts stimulatory effects on MPS through mTOR pathway.
Possible Explanations?

- At the moment the cause of the refractory phenomenon to constant elevations in amino acids is unknown but may involve insulin.
- Likely downstream of the mTOR pathway.
- Possible that changes in leu concentrations are more important than absolute leu concentrations?
Possible explanations?

- Paddon-Jones et al. demonstrated MPS could be improved by taking an EAA supplement containing 2.8g leu in between meals consumed every 5 hours compared to an unsupplemented group consuming the same meals (7).

- Possible that a free amino acid supplement is able to increase plasma leu concentrations greater than a meal alone and improve MPS.
Optimal Meal Frequency?

- Unlikely that another meal will stimulate MPS while it is refractory.
- Possible that plasma leu levels may need to fall before MPS can be stimulated again.
- Unlikely that consuming small amounts of protein over many meals will produce sustained elevations in MPS.
- It is likely better to consume larger doses of protein to maximize the MPS response and spread these doses apart by at least 4-6 hours.
- Consuming an EAA/leu supplement in between meals may help optimize MPS.
Example: 200 lb male athlete/bodybuilder
5 meals per day (one meal every 4-6 hours)
Goal: 4g/leu per meal (0.045g leu/kg BW/meal)

Meal protein sources:
- 2 meals: whey (33g protein at each meal)
- 2 meals: chicken (54g protein at each meal)
- 1 meal: beef (51g protein)

Total protein intake: 225g/day

3-4g leu supplement consumed between meals may optimize MPS response.
Other Considerations

- Age
- Digestion rates of protein sources
- Total calorie intake
- Training intensity and duration
- Protein degradation
- Countless variables will make pinpointing specific numbers very difficult.
Future research

- Determine when MPS can be stimulated again after a complete meal.
- Further examine the role of insulin in maintaining MPS after a meal.
- Determine if an oral dose of BCAAs producing supraphysiological concentrations of plasma leu can overcome the refractory response of MPS.
- Elucidate differences in MPS responses to meals containing different isonitrogenous protein sources with varying leu contents.
References


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Questions?