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

Background

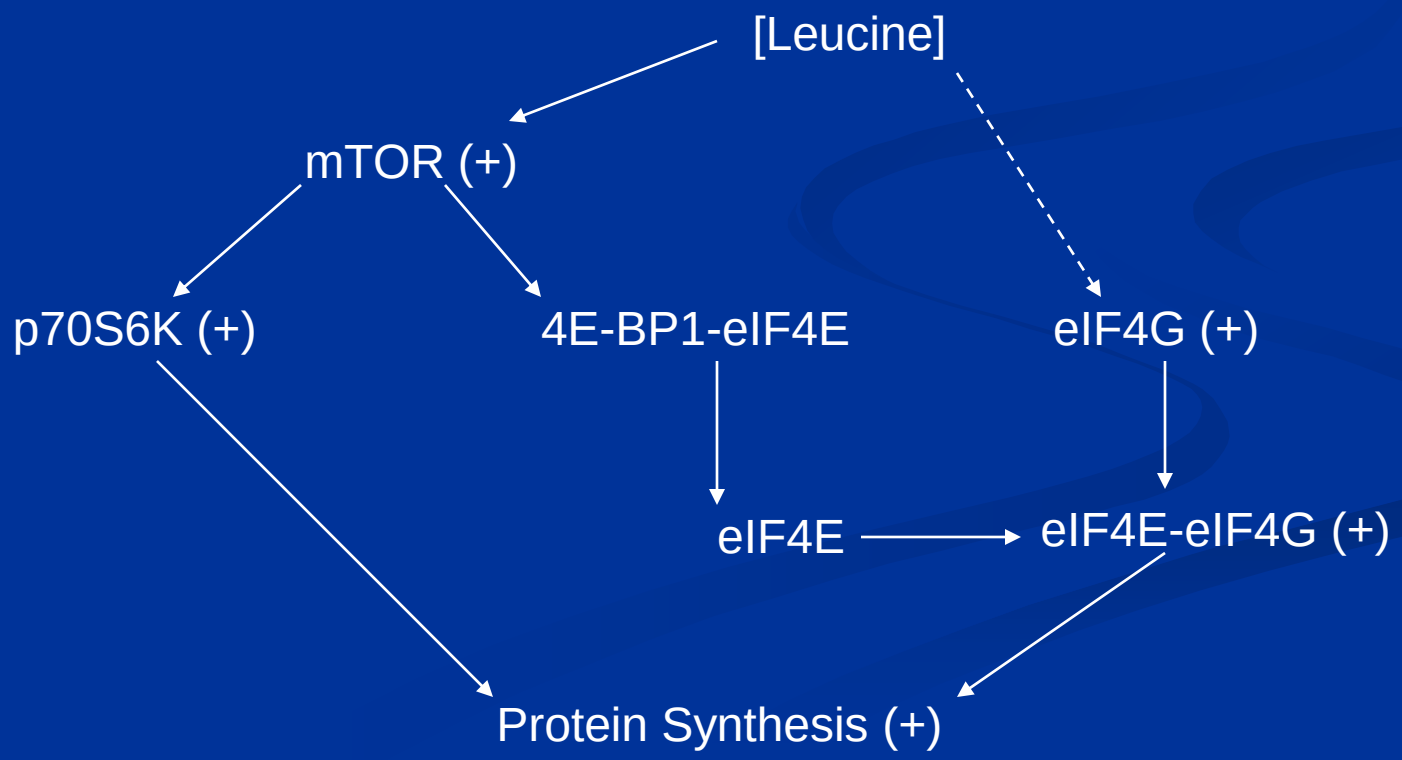
- Current RDA is 0.8g/kg for protein intake.
- Current recommendations are based on minimum needs to achieve short-term nitrogen balance
  - Often do not control for protein distribution, protein source, and are often not applicable to meal feeding.
- Empirical evidence suggests many trainers and coaches 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

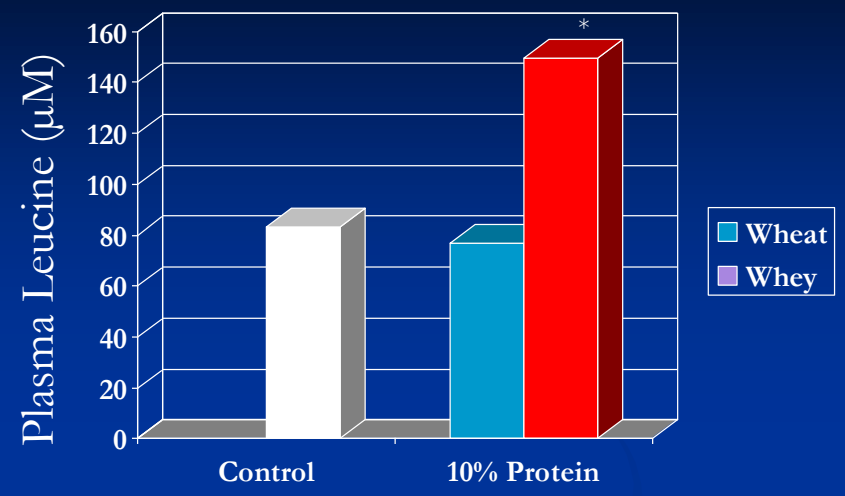
- Determine optimal protein intake at individual meals to maximize protein synthesis (MPS)
- Determine optimal frequency of meal intake
- These variables will dictate total protein intake
  - Specific meal recommendations are likely more beneficial than daily recommendations
    - MPS is regulated from meal to meal, not day to day.

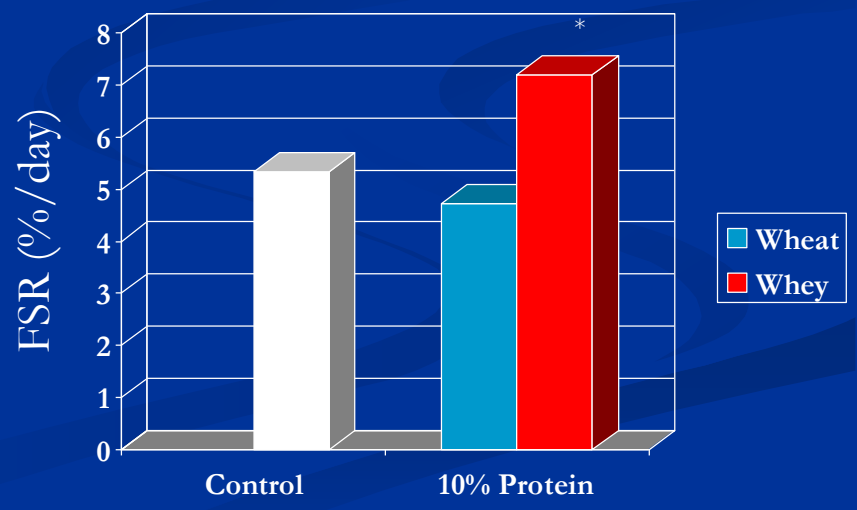
Leucine in regulation of protein synthesis

- 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).



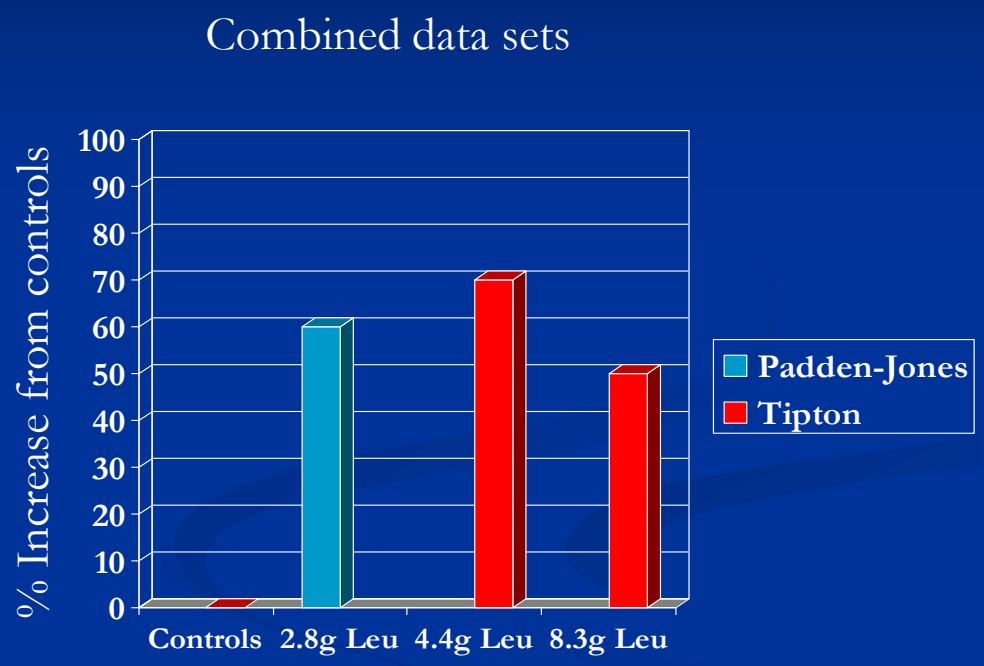
- Possible that activating and maximizing MPS is dependant upon achieving a specific post-prandial concentration of leu in the plasma.
- A certain amount of dietary leu is required to increase plasma leu levels and activate mTOR signaling and MPS.
- What level of dietary leu at a meal is required to 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

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

Recap

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

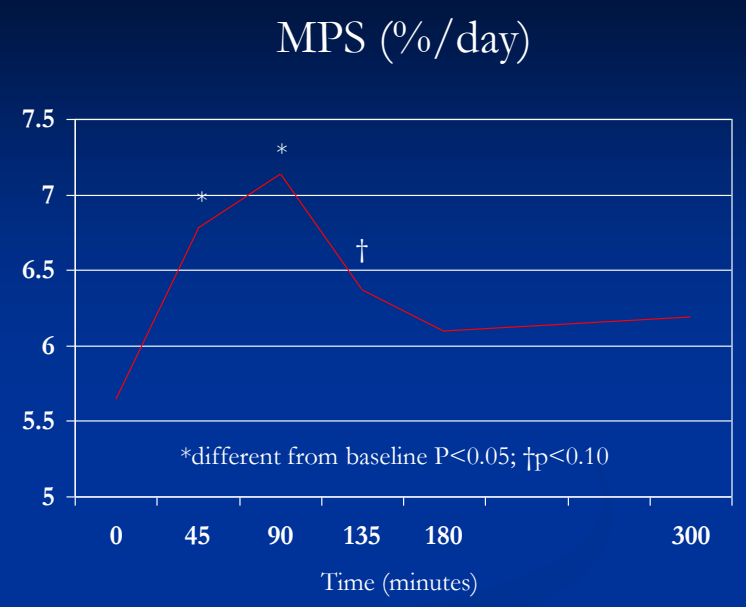
- Key Questions:
  - How long does the MPS response last?
  - When can this response be stimulated again?

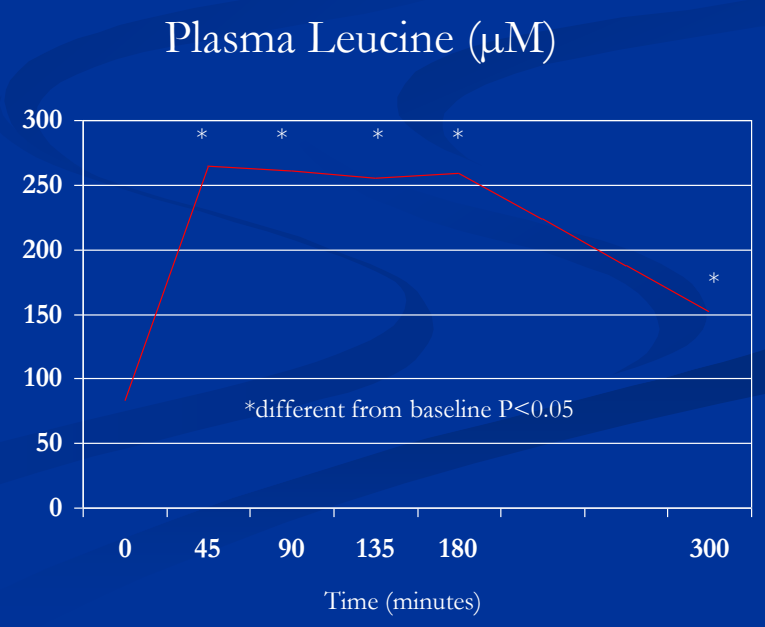
Optimal Frequency

- 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.



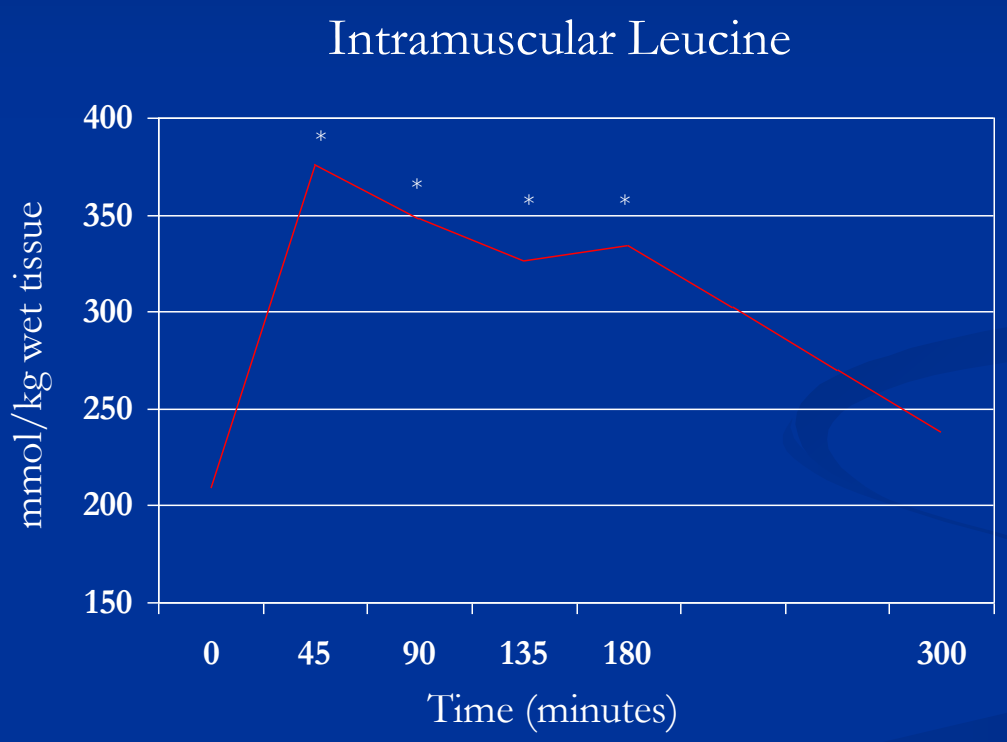


The Refractory Phenomenon

- 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?

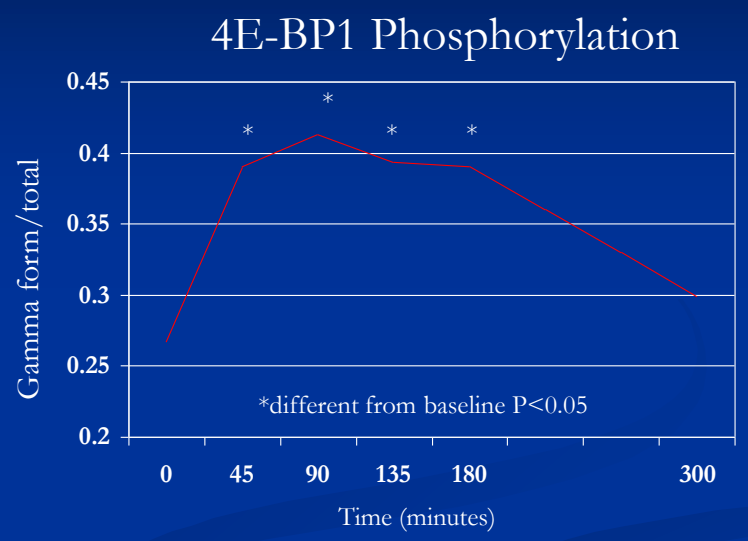
- Reduced availability of intramuscular leu?

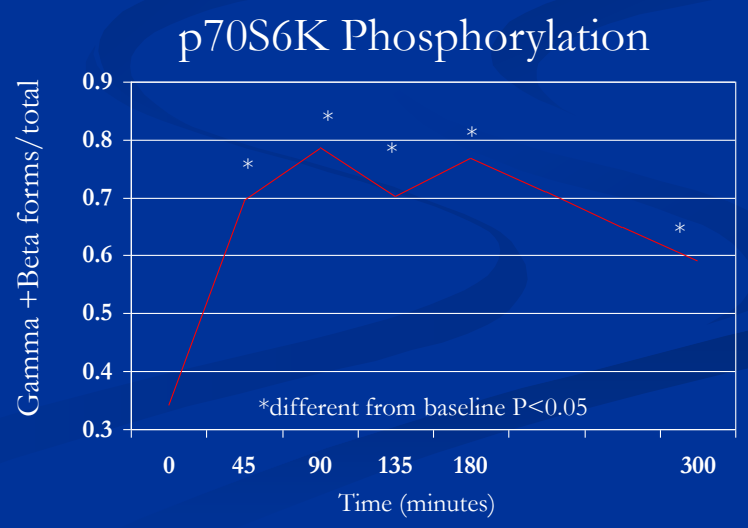


Does not explain refractory nature of MPS.

Possible Explanations?

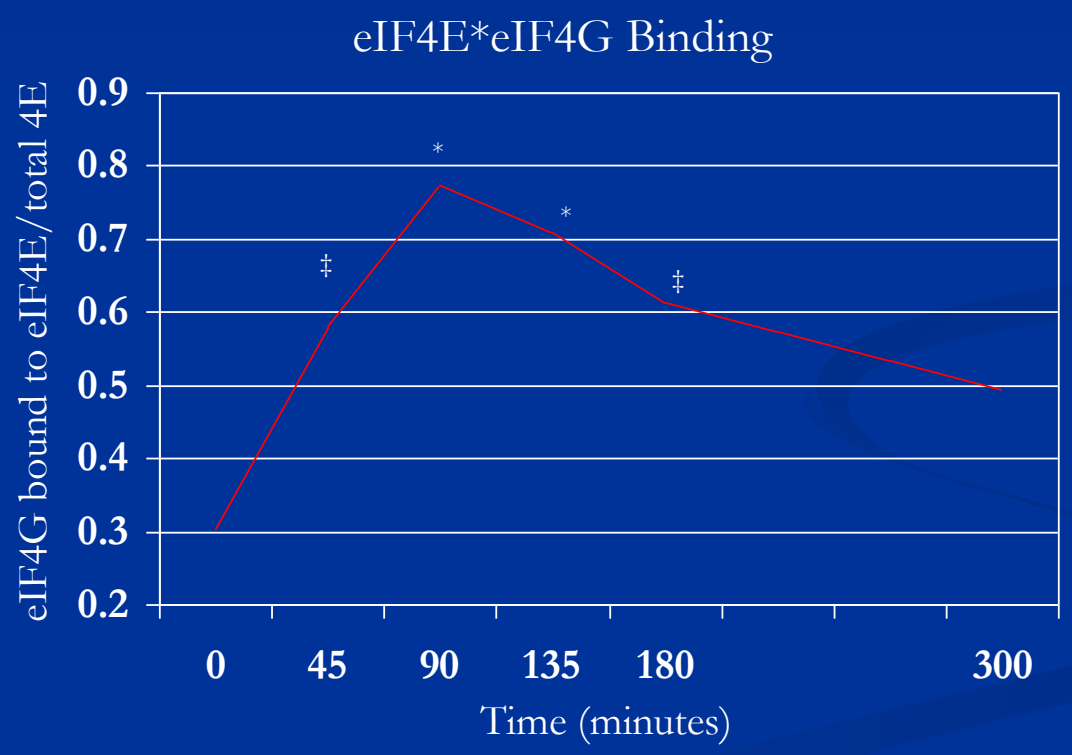
- Possible that translation factor activation is reduced?
- Phosphorylation of 4E-BP1 and p70S6K were closely associated with plasma leu concentrations.
- Translation factor activation remained elevated at 180 minutes but MPS had returned to baseline.
- Does not explain refractory phenomenon.





Possible Explanations?

- Reduced eIF4E*eIF4G binding?



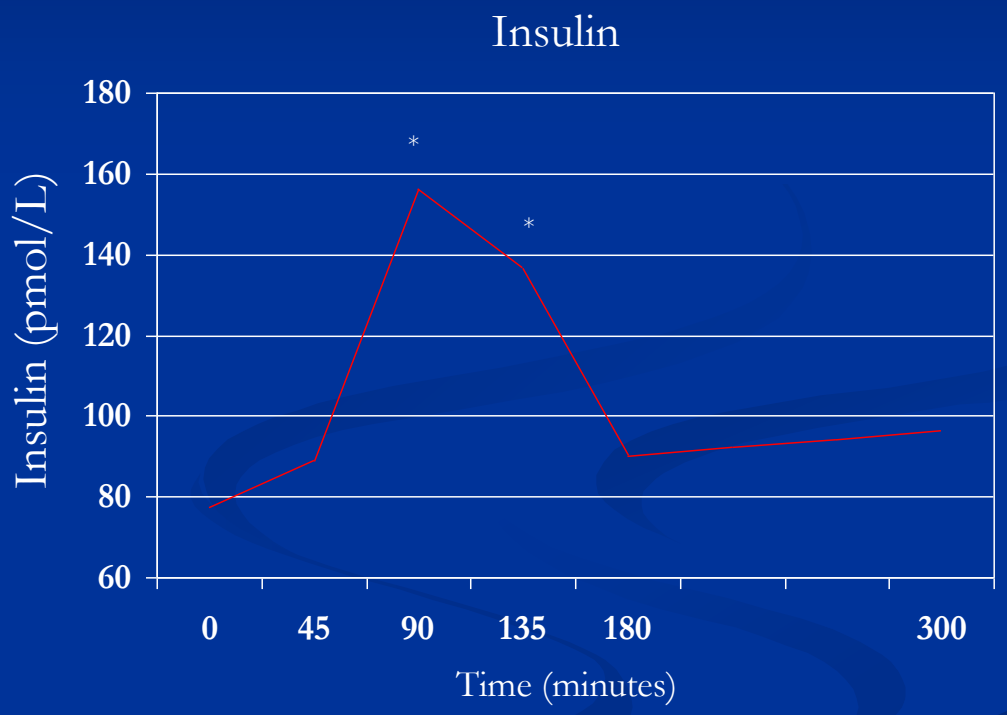
Unlikely to be responsible for MPS becoming refractory

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.

General recommendations?

- 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.

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Questions?