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

Layne Norton, B.S.
Division of Nutritional Sciences
University of Illinois

Overview

Background

Determining optimal protein intake

Optimal Frequency

Refractory Phenomenon

Future Research

Background

High protein diets are popular amongst athletes and body builders

Purported to have various beneficial effects

- Increase muscle mass
- Decrease body fat
- 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)

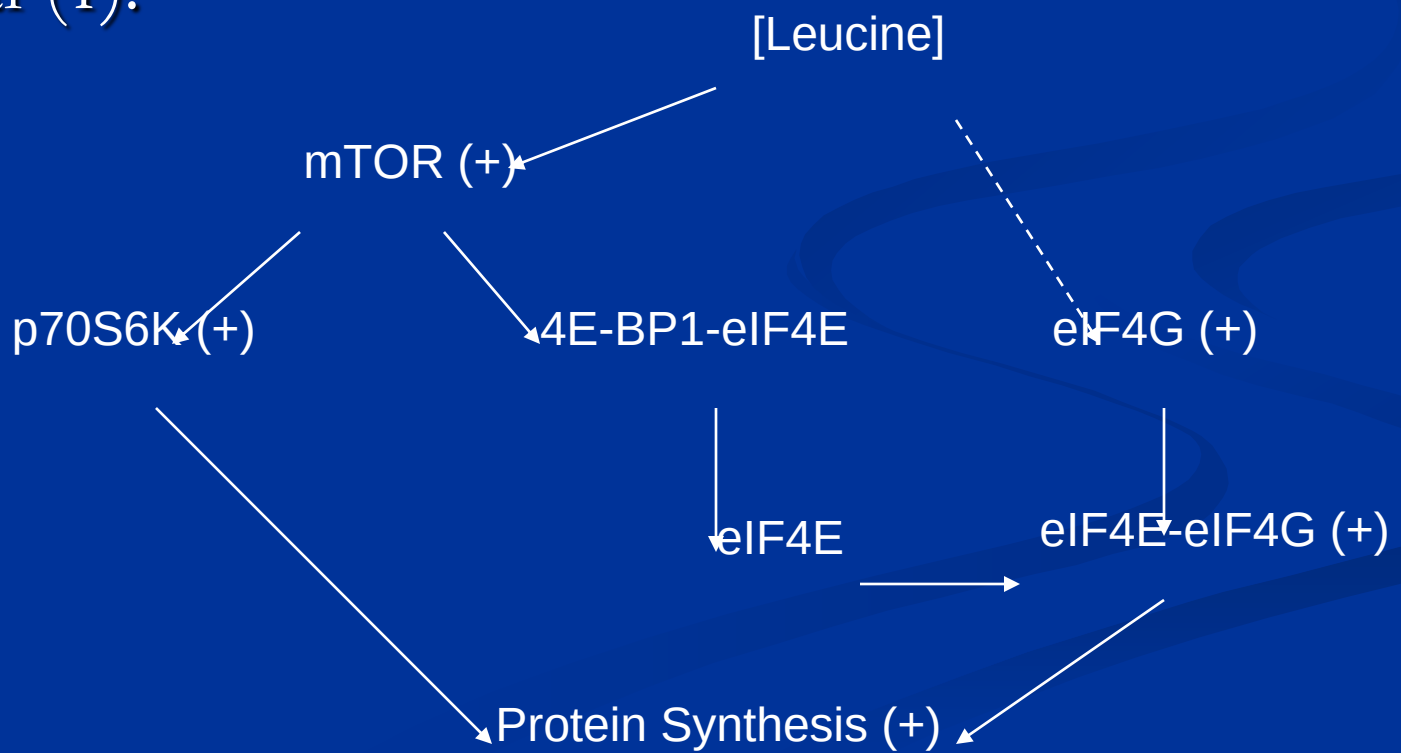
Determine optimal frequency of meal intake

These variables will dictate total protein intake

- Specific meal recommendations are likely more beneficial than daily recommendations

Leucine in regulation of protein synthesis

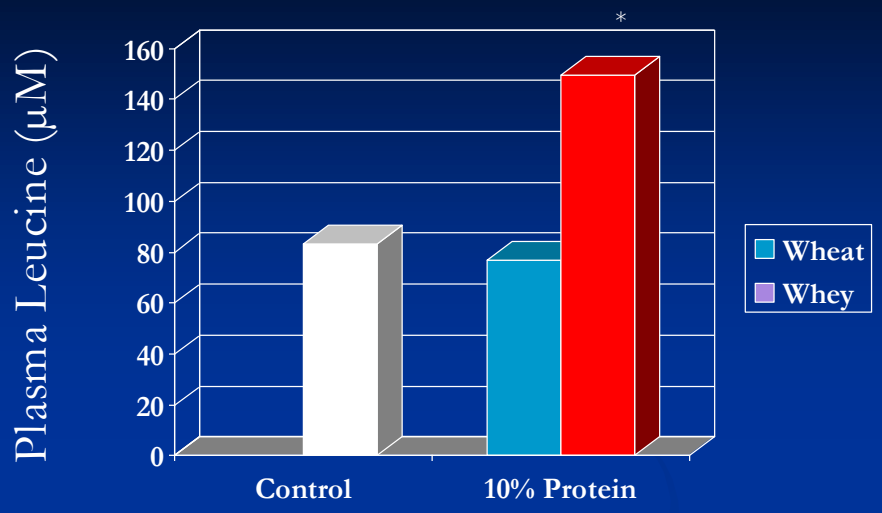
Leucine (leu) has been shown to stimulate protein synthesis and translation initiation to the same extent as a complete meal and is likely the major amino acid responsible for the anabolic effects of a meal (1).

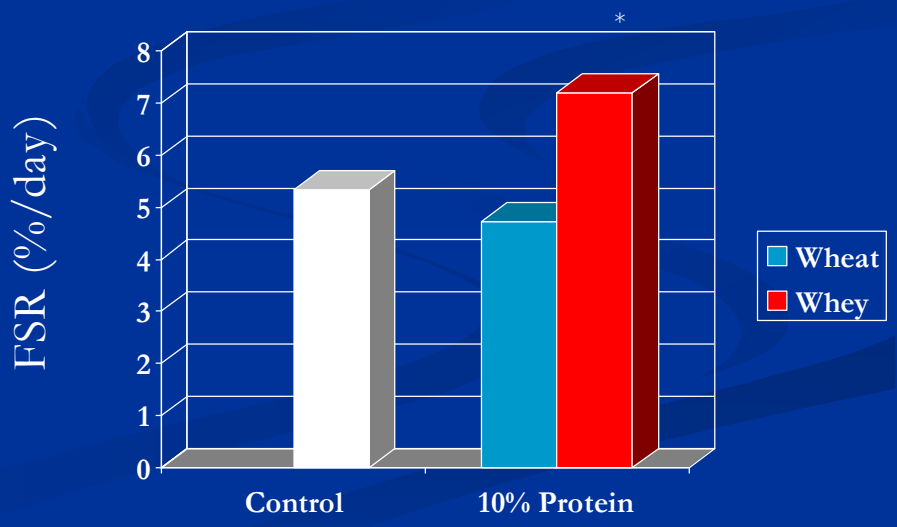


Possible that activating and maximizing MPS is dependant upon achieving a specific post-prandial concentration of leu in the plasma.

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?



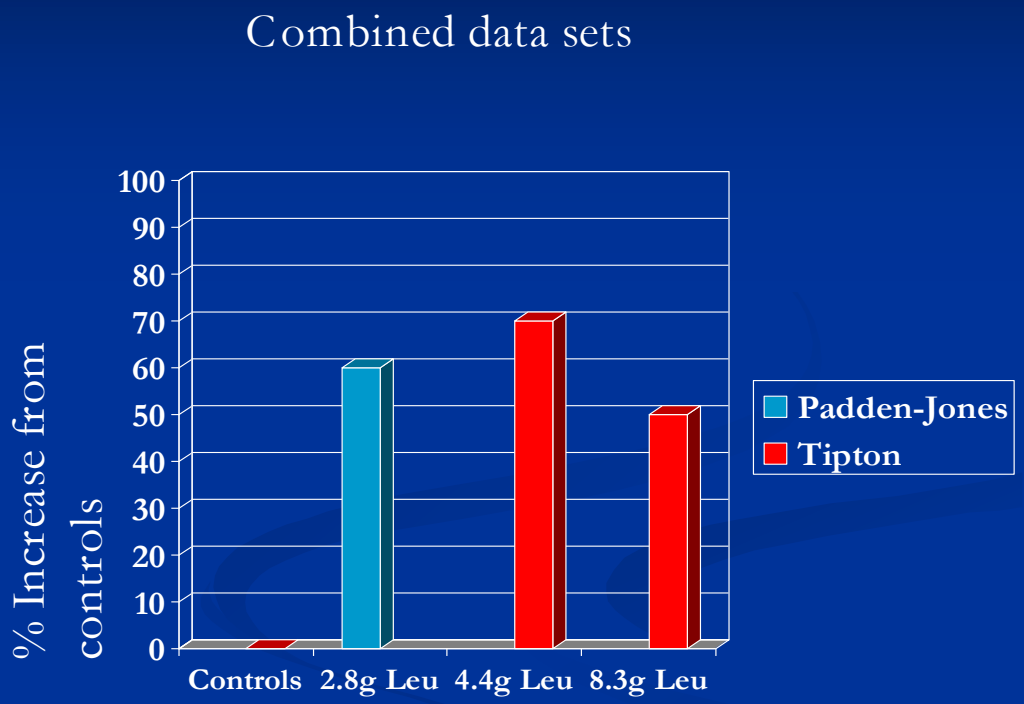


*unpublished data

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).

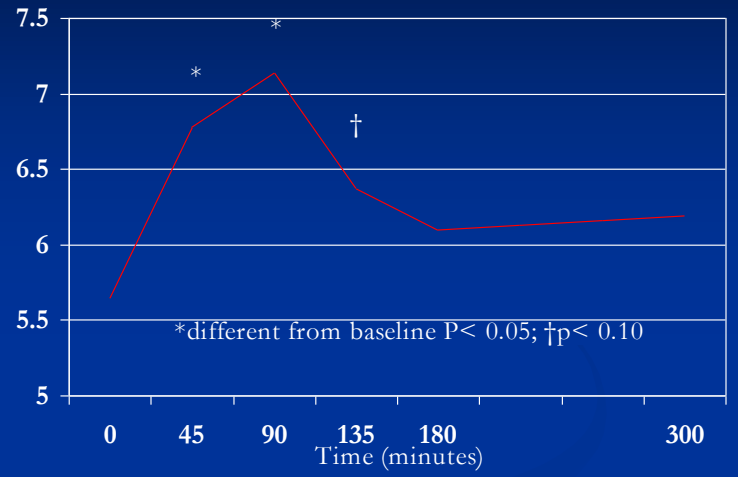
Bohe et al. infused EAA for 6 hours but this only produced an MPS response lasting 2 hours though plasma amino acids remained elevated for the entire duration of the experiment.

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).

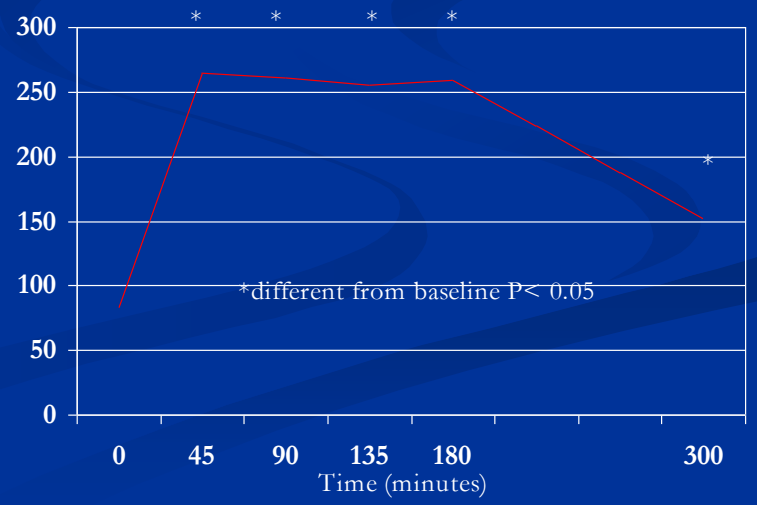
MPS time course was complete at 3 hours but plasma amino acids were still elevated.

MPS decreasing though plasma leu remains elevated.

MPS (%/day)



Plasma Leucine (μM)



The Refractory Phenomenon

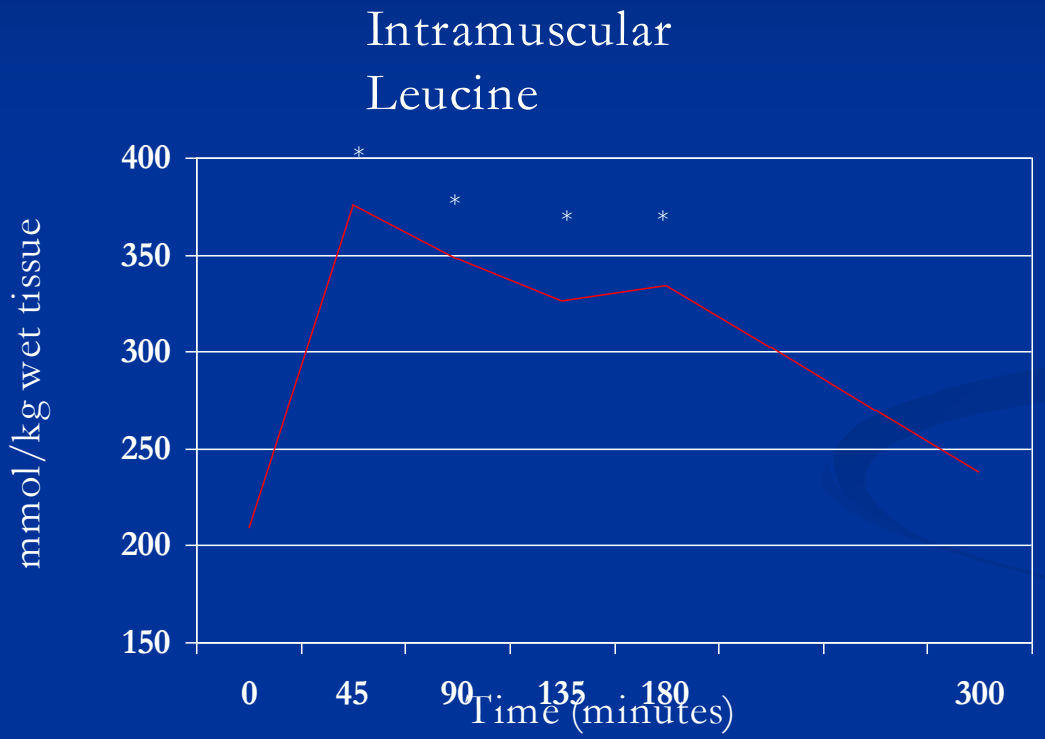
MPS becomes ‘refractory’ to constant elevations in leu.

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?

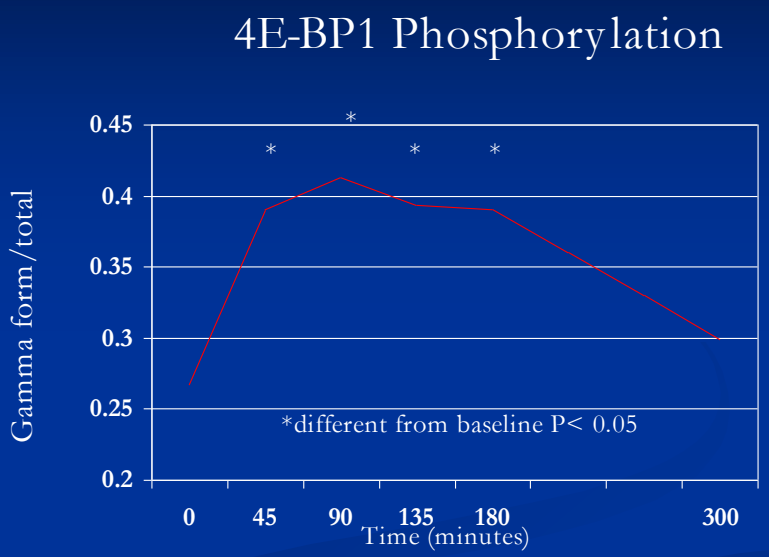
Reduced availability of intramuscular leu?

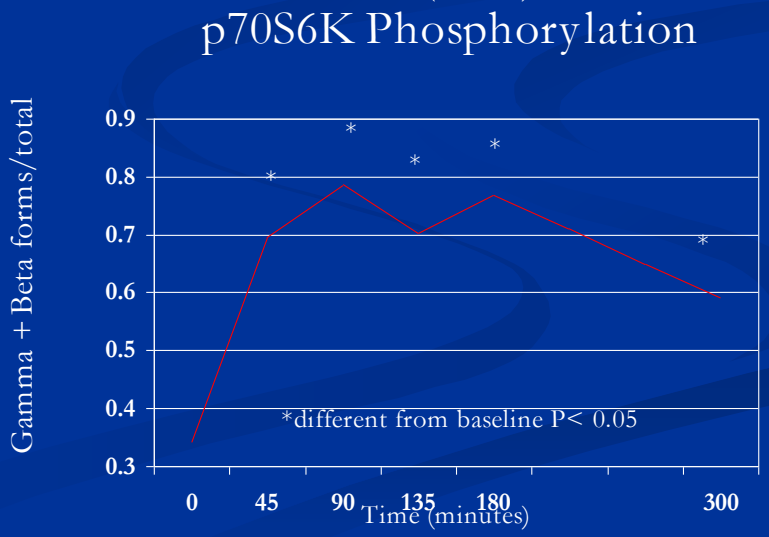


Does not explain refractory nature of MPS.

Possible Explanations?

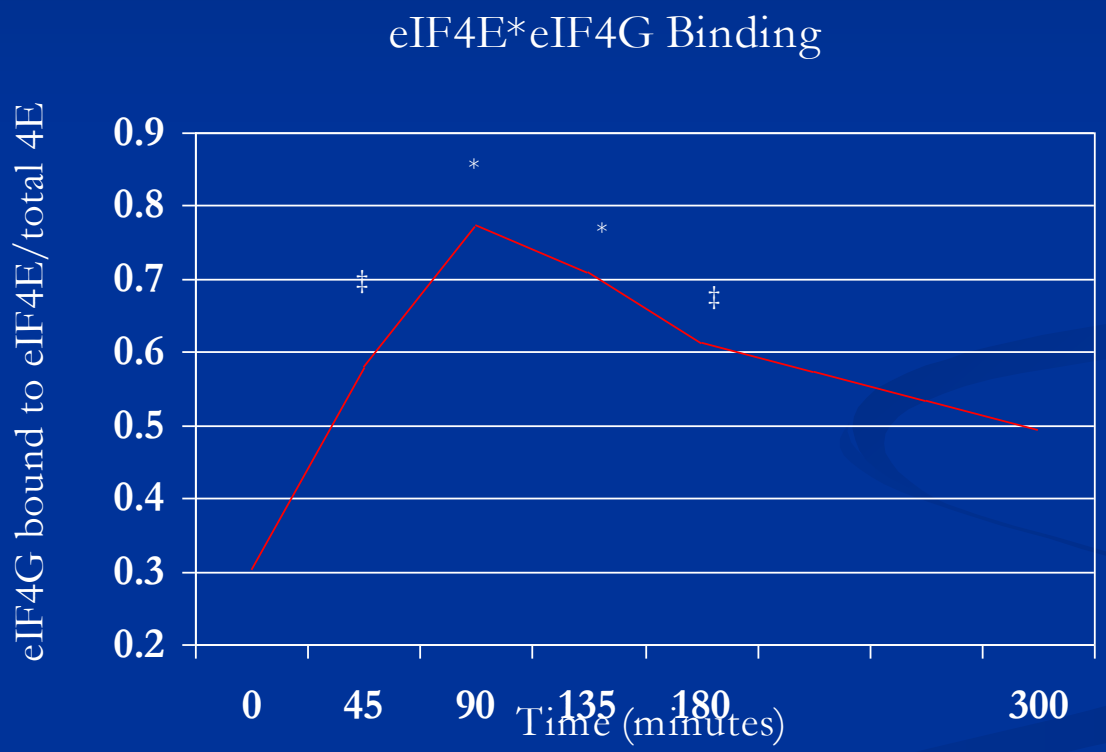
- Possible that translation factor activation is reduced?
- Phosphorylation of 4E-BP1 and p70S6K were closely associated with plasma leu concentrations.
- Translation factor activation remained elevated at 180 minutes but MPS had returned to baseline.
- Does not explain refractory phenomenon.





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?

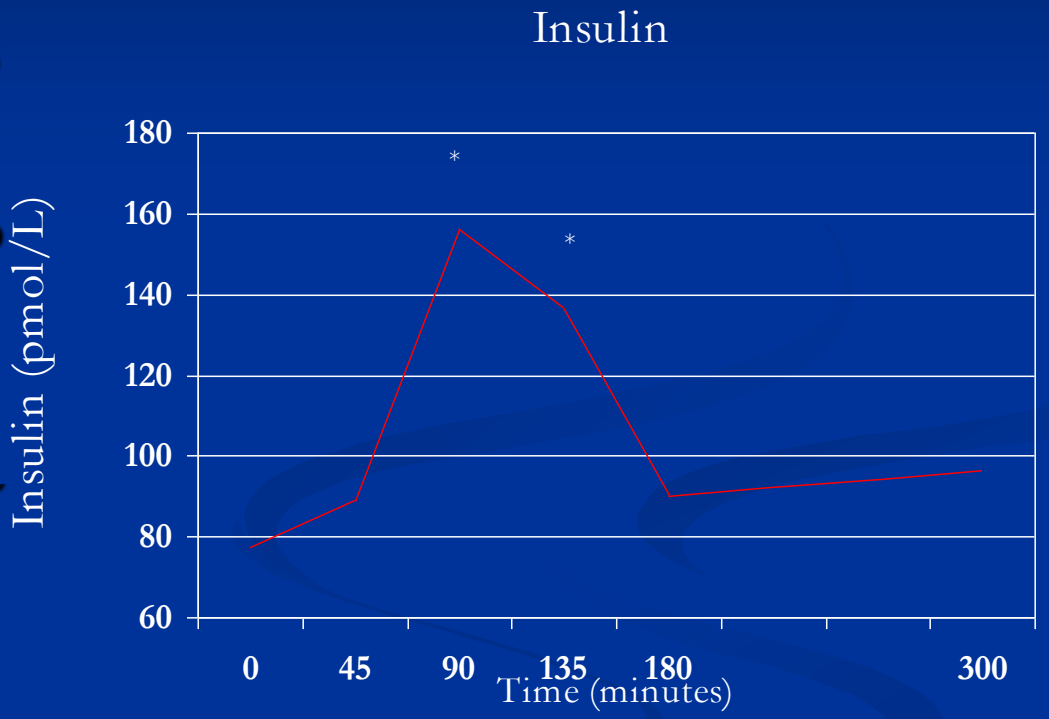
Insulin?

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?