

The Effects of leucine and fat metabolism

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Abstract

Consistently protein diets rich in leucine have been demonstrated to stimulate greater fat loss, maintenance of lean tissue mass, higher satiety, lower post absorptive insulin levels, and lowered plasma triglyceride levels relative to standard recommended daily allowance diets which recommend low protein intakes. The purpose of this paper is to review this evidence, and provide explanations as to why this occurs.

Introduction

According to standard recommendations as of 2000, individuals should be able to meet their daily protein needs with as little as 50-100 grams of protein or a mean of 75 grams. The AHA restates the common Mantra: "There is at present no scientific evidence to support the concepts that high protein diets result in sustained weight loss, significant changes in metabolism, or improved health." Fat intake is recommended to be approximately 60 grams per day (Layman, 2003). The remainder of calories are encouraged to come in the form of carbohydrates. When taken together Layman (2003) suggests that standard recommendations allot for a 3.5 to 1 ratio of carbohydrates to protein.

However, an analysis of the literature demonstrates that this type of ratio impairs glycemic control (Layman, 2003a, b), causes sustained hyperinsulemia after food absorption (Layman, 2003b), reduces blood glucose levels post absorptively (Layman, 2003b), reduces fat oxidation due to increased inhibition of carnitine transferase (Sidossis et al, 1998; Sidossis et al., 1999), if consumed in a higher GI form stimulates greater hunger, and can lead to greater increases in blood triglyceride levels (Sidossis et al., 1998).

In contrast when protein intake is such that the ratio of carbohydrates to protein is lowered to 1.5, evidence suggests greater fat loss, maintenance of lean tissue mass, higher satiety, lower post absorptive insulin levels, and lowered plasma triglyceride levels (each concept will be discussed below).

Evidence suggests that leucine plays a critical role in each of the above results (Layman, 2003a). The purpose of this paper is to analyze recent data on higher protein, and the effects of leucine on fat metabolism, maintenance of lean tissue mass, and glycemic control.

Studies comparing the effects of a 1.5 to 3.5 ratio of carbohydrates to fats on body composition

To date some of the more notable research has been conducted by Layman and associates. As an illustration Layman and colleagues (2003a, Layman et al., & Layman et al., 2003b) conducted two excellent studies in adult women. The first study consisted of a 10 week intervention, followed by a second 16 week intervention. Both studies compared a diet consisting of a 1.5 to 3.5 ratio of carbohydrates to protein. Study one examined the effects without exercise, while study two examined the effects with exercise.

In study one participants in the high protein group lost 12.5 pounds of fat compared to 10.4 pounds of fat in the low protein group, while lean body mass loss was -1.9 in the high protein group compared to -2.7 pounds of lean mass lost in the high carbohydrate condition.

Results were even more dramatic in study two. Fat loss was nearly double in the high protein condition relative to the high carbohydrate condition (19.4 vs 12.3 pounds), while lean tissue loss was more than double in the high carbohydrate group (-0.9 vs. 2.7). It is interesting to note however that during the first 10 weeks the high protein diet had gained lean tissue mass. However they only consumed 1.5 grams of protein per kg of bodyweight daily with low meal frequency. Perhaps with higher protein intakes no lean tissue loss would have occurred.

These results suggest that a decreased ratio of carbohydrates to protein enhances fat lost and lean tissue mass spared during a dieting intervention meant to induce a 500 calorie deficit per day.

Studies comparing the effects of a 1.5 to 3.5 ratio of carbohydrates to fats on glycemic control

In the above 10 week study, Layman et al. (2003a) also examined resting glucose levels after an overnight fast, and 2 hours after a meal, along with the plasma insulin response to a 400 calorie test meal.

Results indicated that the adult women on a higher protein diet had more stable blood glucose levels following the overnight fast, as well as after the test meal. What was really intriguing however was that the plasma glucose levels following an overnight fast became progressively lower in the CHO group compared to the protein group, which maintained plasma glucose levels the entire study, indicating a progressive decline in glycemic control.

Layman (2004) also examined the effects of high vs. low protein conditions on the postprandial to post absorptive transition (PP-PA transition). The PP-PA transition is a characteristic of feeding which occurs approximately two hours after feeding. After a meal, glucose levels rise, as well as plasma insulin levels. Near two hours time glucose levels return to basal and the individual enters into a post absorptive state. However, insulin levels still remain elevated, which means that the liver must provide endogenous glucose output to match the higher insulin levels. More sustained and stable glucose levels, and lower insulin levels suggest greater glycemic control during the transition. Figure 1 displays the typical glucose and insulin response during postprandial, and transition periods, to a standard 400 calorie meal consisting of approximately 50 carbohydrates..

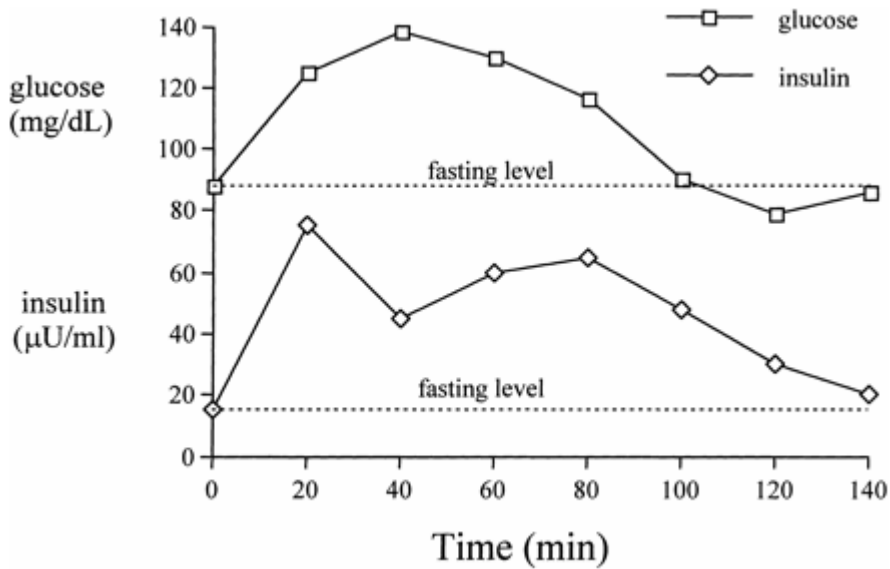


Figure 1. Standard glucose and insulin response to a 400 calorie meal. Adapted from Layman (2003)

Layman et al. (2004) had overweight subjects with abnormally high insulin responses at 2 h after a test meal either consume the higher protein or higher carbohydrate diet previously described. Results are displayed in figure 2 which graphically demonstrates the abnormally high insulin response at 2 hours following a 400 calorie test meal. It was found that the protein group had reached a normative range by week four and continued to improve to week 10 (12 µU/mL). While the CHO diet improved, most likely due to weight loss they still had abnormally high transition levels of insulin (38 µU/mL).

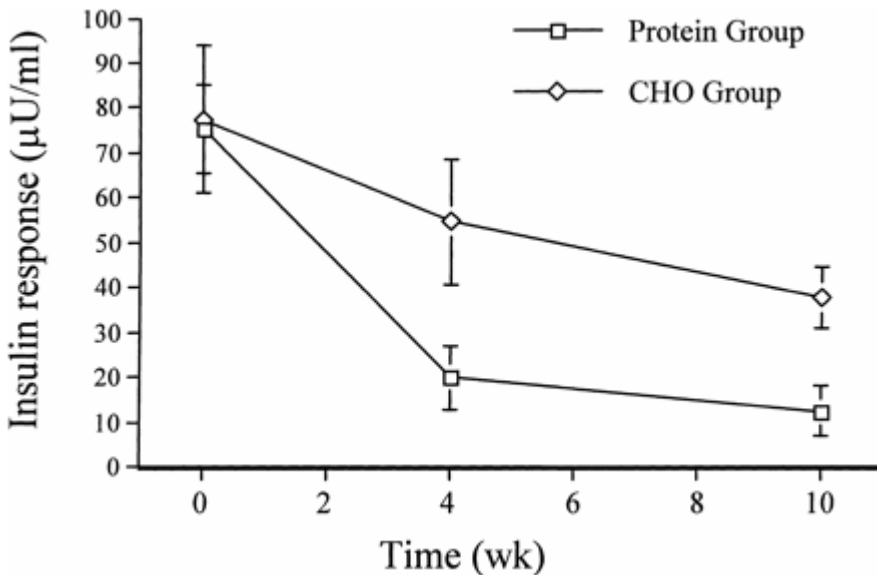


Figure 2. Comparison of insulin levels 2 hours after a test meal in Protein and CHO conditions. Adapted from Layman et al. (2004)

Leucine's Role in Greater Fat Loss, Lean Tissue Maintenance, and Glycemic Control

Higher protein diets appear to enhance fat loss through a number of mechanisms. Wilson G. (2004) provided power evidence that protein has a higher satiation effect than glucose. The mechanism is most likely linked to the glucostatic theory explained in that paper, which suggests that satiety is closely linked to blood glucose levels. Because higher protein diets sustain plasma glucose levels to a greater extent in the post absorptive period, individuals are less likely to have a need to search out and consume extra food.

A second factor concerns efficiency of energy use with proteins. For example 1 gram of protein converts to approximately 0.6-0.7 grams of glucose.

Further, muscle tissue is extremely metabolically active. Because leucine is able to positively enhance lean mass, it is able to maintain an overall higher metabolic rate for the duration of a dietary intervention.

Leucine is also the major signaling molecule for protein synthesis which is itself an extremely costly process.

Finally higher protein diets, and in particular leucine are able to enhance glycemic control. The mechanisms of protein synthesis and leucine were discussed in article one, and cover maintenance of lean muscle tissue as well, while Satiation was discussed previously by Wilson G. (2004).

Therefore the remainder of the article will primarily discuss the role of leucine in improving glycemic control

Leucine's Effects on Glycemic Control

Glucose homeostasis is controlled by two primary regulators, including insulin mediated and hepatic mediated glucose homeostasis (note that a number of hormones interact in this process, but insulin and hepatic regulation are of primary concern in this article, for reviews of fast acting hormones and their effects on glucose homeostasis see Wilson & Wilson, 2005).

During post absorptive periods the liver is the primary regulator of glucose homeostasis and produces endogenous glucose output proportional to tissue needs. During this time gluconeogenesis provides the majority of endogenous glucose output (Alborg et al., 1982). The major amino acids used to produce glucose are alanine and glutamine. One of the major contributors for these amino acids are the BCAAs. In particular BCAAs donate their amino group to pyruvate, converting it to alanine. Alanine then circulates to the liver where it provides substrate for endogenous glucose production.

Therefore a high proportion of BCAAs in the diet during caloric deficit conditions, when energy is low is able to provide exogenous substrate which spares muscle tissue, which itself is comprised of over 80 % BCAAs. The greater substrate is able to also assist in maintenance of stable blood glucose levels.

During postprandial states, particularly when consuming a high carbohydrate meal there is a rapid rise in glucose which stimulates insulin secretion. Insulin hinders gluconeogenesis and gluconeogenic enzymes (Wilson & Wilson, 2005).

However, during the transition period when glucose levels return to basal and insulin remains elevated, the liver must balance the higher levels of insulin with endogenous glucose output. Because insulin inhibits endogenous glucose output, levels of blood glucose remain low for time periods proportional to the magnitude of the insulin response.

It has been well established that proteins consumed orally have a much lower insulin response than carbohydrates. However when amino acids are administered by infusion they have the capacity to greatly increase the insulin response (Krebs, 2002). The difference between oral and infused administration appears to be related to absorption patterns (Layman et al., 2004). Amino acids are slowly absorbed in the gut, and therefore they are able to be slowly metabolized in the body. In contrast infusion requires rapid handling of the amino acids. Similarly, consumption of CHO causes rapid rises in substrate relative to amino acids, and absorption is handled within two hours of consumption, requiring a rapid handling of the CHO, unlike orally administered protein. This rapid handling of the CHO therefore requires great increases in insulin to maintain glucose levels within normative physiological ranges.

A clear example of the response of a high protein vs. high carbohydrate meal was again examined by Layman and colleagues (2003a). They administered subjects a 400 calorie meal consisting of either the 1.5 or 3.5 ratio of carbs to protein. Results indicated that the high protein condition increased leucine along with other BCAAs by 80 %, this was paralleled by a rise in plasma alanine levels, which is reflective of useable substrate for the liver for the maintenance of plasma glucose levels. In contrast the high carbohydrate condition had an overall 6 % decrease in plasma BCAA, alanine, and glutamine levels, which not only would hinder plasma glucose levels in the post absorptive period, but also would negatively effect protein balance. As indicated in article 1, lowered BCAAs decreases protein synthesis.

When examining the transition period which occurred at 2 hours it was found that plasma glucose levels in the high carbohydrate group was 30 % below fasting, and 30 % below the high protein group! This was reflective of double the insulin levels seen at fasting in the high carbohydrate group, and corresponded to a 40 % value above the protein condition.

Leucine not only provides substrate, but has metabolic roles in each of these processes. First leucine hinders the oxidation of pyruvate by inhibiting its rate limiting enzyme pyruvate dehydrogenase (Chang et al., 1978), and partitions it towards the glucose alanine cycle. Further, increased leucine concentrations activate the rate limiting enzyme for BCAA oxidation (energy use) known as branched-chain ketoacid dehydrogenase.

References

Sidossis LS, Mittendorfer B, Walser E, Chinkes D, Wolfe RR. Hyperglycemia-induced inhibition of splanchnic fatty acid oxidation increases hepatic triacylglycerol secretion. *Am J Physiol.* 1998 Nov; 275(5 Pt 1): E798-805.

Sidossis LS, Mittendorfer B, Chinkes D, Walser E, Wolfe RR. Effect of hyperglycemia-hyperinsulinemia on whole body and regional fatty acid metabolism. *Am J Physiol.* 1999 Mar; 276(3 Pt 1):E427-34.

Warren JM, Henry CJ, Simonite V. Low glycemic index breakfasts and reduced food intake in preadolescent children. *Pediatrics.* 2003 Nov; 112(5):e414.

Layman DK. Free Full Text The role of leucine in weight loss diets and glucose homeostasis. *J Nutr.* 2003 Jan; 133(1):261S-267S. Review.

Layman DK, Shiue H, Sather C, Erickson DJ, Baum J. Increased dietary protein modifies glucose and insulin homeostasis in adult women during weight loss. *J Nutr.* 2003a Feb; 133(2):405-10.

Layman, D. K., Shiue, H., Sather, C., Erickson, D. J. & Baum, J. (2003)b Increased dietary protein modifies glucose and insulin homeostasis in adult women during weight loss. *J. Nutr.* 133:405-410

Layman DK, Baum JI. Dietary protein impact on glycemic control during weight loss. *J Nutr.* 2004 Apr; 134(4):968S-73S.

Chang TW, Goldberg AL. **Leucine inhibits oxidation of glucose and pyruvate in skeletal muscle during fasting.** *J Biol Chem.* 1978; 253: 3696–701

Wilson, G. (2004) An Investigation of the Satiety Mechanism: A Research Initiative. *The Journal of HYPERplasia Research.*
<http://www.abcbodybuilding.com/investigation.php>

Wilson J., and Wilson, G. (2005) Fast Acting Hormones and their Role in Fuel use during Exercise *The Journal of HYPERplasia Research.* 5
<http://www.abcbodybuilding.com/Nutrientpartitioningpart1.php>

Ahlborg G, Felig P. Lactate and glucose exchange across the forearm, legs, and splanchnic bed during and after prolonged leg exercise. *J Clin Invest.* 1982 Jan; 69(1):45-54.

Krebs, M., Krssak, M., Bernroider, E., Anderwald, C., Brehm, A., Meyerspeer, M., Nowotny, P., Roth, E., Waldhausl, W. & Roden, M. (2002) Mechanism of amino acid-induced skeletal muscle insulin resistance in humans. *Diabetes* 51:599-605

Chang, T. W. & Goldberg, A. L. (1978) Leucine inhibits oxidation of glucose and pyruvate in skeletal muscle during fasting. *J. Biol. Chem.* 253:3696-3701