Interaction of Branched Chain Amino Acids and Adipose Lipid Metabolism

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Introduction

- Branched chain amino acids (BCAAs) have the ability to regulate not just protein metabolism, but lipid metabolism as well.
- Studies have found significant links between BCAAs, mitochondrial metabolism and dysfunction, and lipid metabolism, specifically in metabolic diseases *(1).*
- The mechanism by which BCAAs modulate lipid metabolism in the adipose tissue is poorly understood.
- Presence of high BCAA levels in blood predict the development of diabetes (*2*).
- BCAA catabolism is sensitive to insulin, but impaired during insulin resistance. *(3)*
- BCAAs may compound the effects of insulin resistance by further stimulating lipolysis.

Hypothesis: Supplementation of branched chain amino acids will increase lipolysis from white adipose tissues, further worsening the effects of insulin resistance.

Study Design

~30-36 weeks on diet, fasted overnight before tissue collection

Low Fat (LF) (10% Fat)

Low Fat + BCAA (LB) (10% Fat, 150% BCAAs)

High Fat (HF) (60% Fat)

High fat + BCAA (HB) (55% Fat, 150% BCAAs)

Perigonadal white adipose tissue (WAT) collected for *in-vitro* lipolysis assay

Plasma for free-fatty acid analysis

Lipolysis Assay

~20 mg tissue incubated in media with 2 treatments for 2 hrs

Basal Media

Isoproterenol (ISP): β –adrenoreceptor agonist, stimulates lipolysis

Results

Fig. 1: BCAA supplementation had no effect on body weight, but did alter adipose weight. WAT was significantly reduced in the LB group, but nearly doubled when comparing the HF and HB groups.

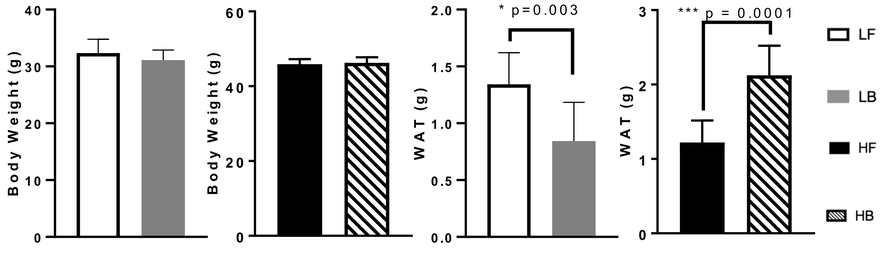


Fig. 2: Plasma non-esterified fatty acids (NEFA) were higher in the LB group, indicating higher rates of adipose lipolysis.

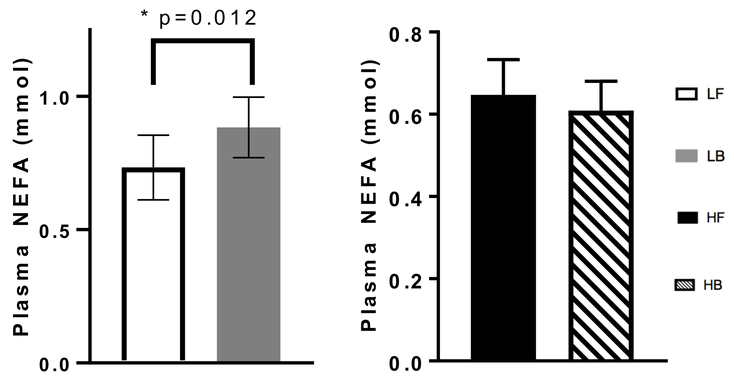


Fig. 3: A strong correlation was found between the adiposity (WAT/BW) and the rate of WAT lipolysis when stimulated with isoproterenol.

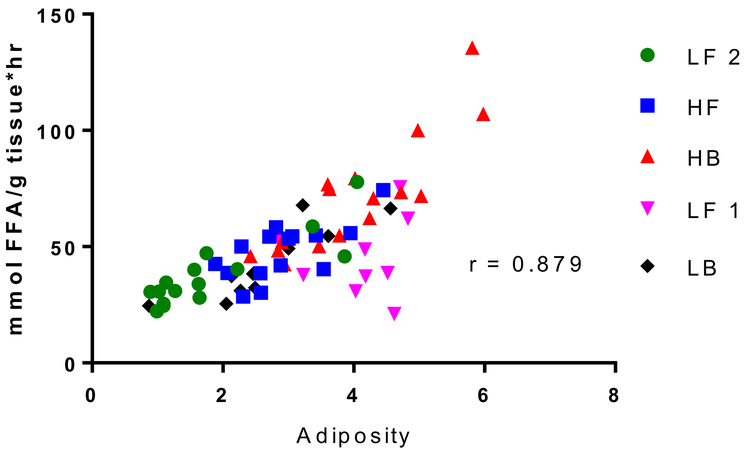


Fig. 4: BCAA supplementation, under low fat conditions, increases basal lipolysis. This agrees with the plasma NEFA results (Fig. 2)

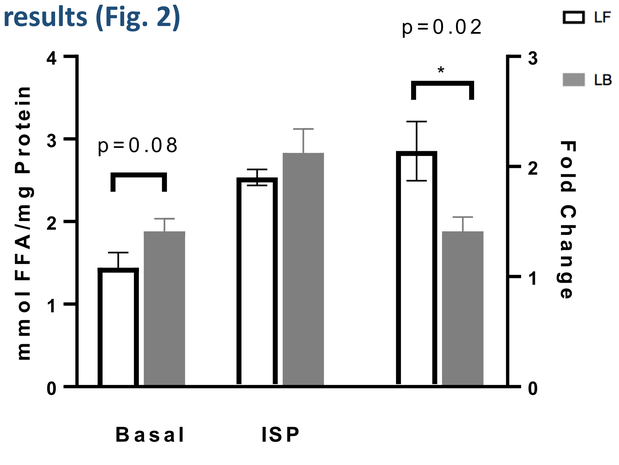
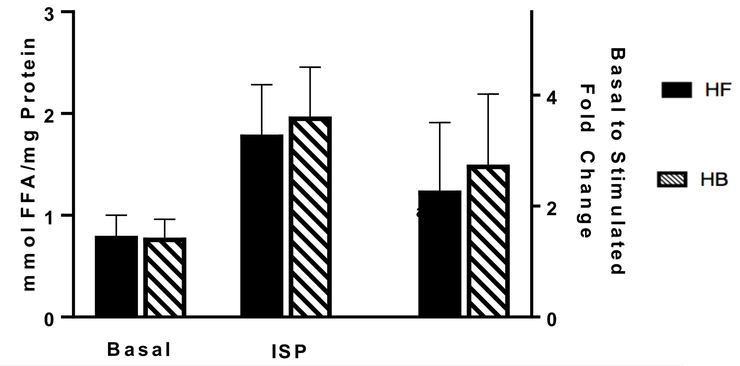


Fig. 5: No change in lipolysis was observed between the HF groups.



Summary

- Under normal physiological conditions, BCAA supplementation reduces adipose weight, increases lipolysis (per mg protein), and increases plasma NEFA.
- Under the high fat condition, BCAAs raise adipose weight and but do not change the rate of lipolysis.
- There is a strong correlation between the amount of adipose tissue and the rate of lipolysis
- BCAA's are interacting with adipose tissue, but whether it is a beneficial interaction is still unknown. Discovery of a mechanism may shed light on this.
- The lack of difference between the HF groups may have been due to the prolonged maintenance on diet

Conclusion

The results of this study demonstrate that there is a link between BCAAs and lipolysis. This link is dependent on the system, and seems to change in the presence of insulin resistance.

Future Directions

Studying the expression of proteins and genes directly involved in lipolysis could elucidate a mechanism for this cross-talk between BCAAs and lipid metabolism.

- Proteins like hormone sensitive lipase (HSL), protein kinase A (PKA), and AMPK (AMP-activated kinase) are regulating proteins in lipolysis.

References

1) Sunny, N.E., et al. (2015). Cross-talk between branched-chain amino acids and hepatic mitochondria is compromised in nonalcoholic fatty liver disease. *Am J Physiol Endocrinol Metab, 309*(4), E311-E319.
2) Wang, T.J. et al. (2011). Metabolite profiles and the risk of developing diabetes. *Nature medicine. Vol 17*(4), 448-453.
3) Wang, J., et al. (2019). BCAA Catabolic Defect Alters Glucose Metabolism in Lean Mice. Frontiers in Physiol.

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