Dietary isoleucine restriction increases catabolic flux of valine and leucine in lubber grasshoppers

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Dietary isoleucine restriction has metabolic benefits.

- Dietary modification is a promising agent in the prevention of age-related disease.
- Modifications of protein quality can have benefits.
- Restriction of isoleucine specifically:
  - Improves metabolic health by increasing hepatic insulin sensitivity and ketogenesis to a greater degree than valine and leucine restriction in mice (Yu et al. 2021).
  - Increased nicotine tolerance in flies (Fulton et al. 2022).
  - Increased lifespan in mice (Green et al. 2023) and flies (Weaver et al. 2023).
- Diets low in one EAA may increase organismal catabolism of other EAAs (Elango et al. 2008).
- Catabolism of leucine contributes to ketosis which is known to extend lifespan (Veech et al. 2017)
  - Decreased catabolism of branched-chain amino acids (BCAAs: leucine, valine, and isoleucine) contributes to diabetes (Zhou et al. 2019) and cancers (Peng et al. 2020).

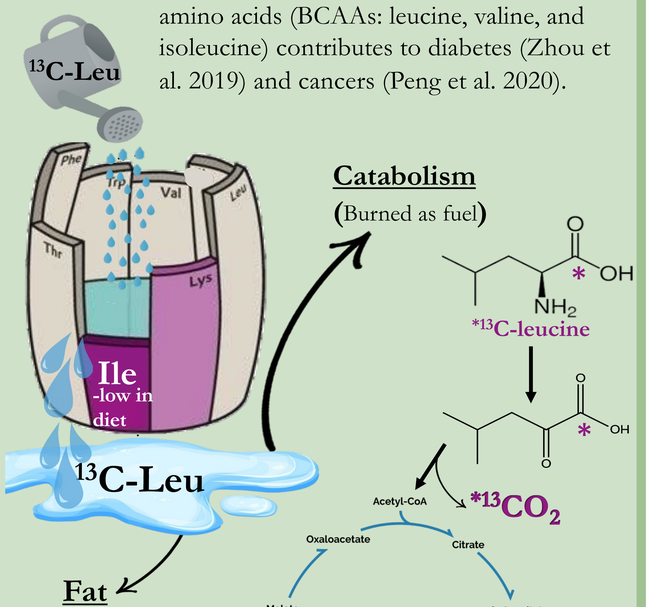

Figure 1: Mechanism of excess leu burned as fuel upon a low ile diet .

- **Hypothesis: Increased catabolism of leucine contributes to the benefits of dietary isoleucine restriction.**

Using ^{13}C to track catabolism of each BCAA

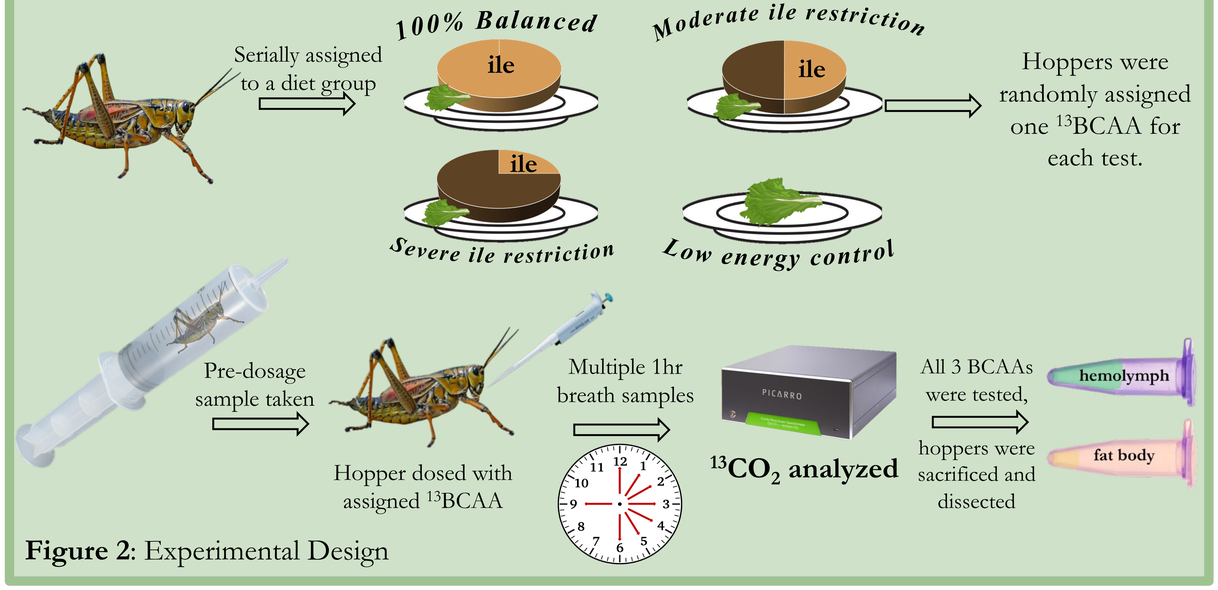

Figure 2: Experimental Design

Storage protein analysis

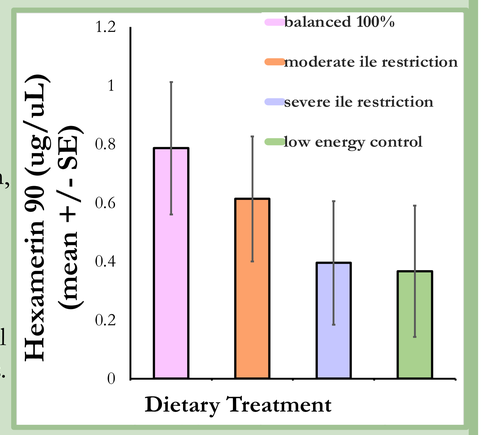

Figure 5: Storage protein, hexamerin 90, amount per dietary group (ug/uL) analyzed via gel electrophoresis. No statistical significance.

Future studies

- Biomolecular damage accumulation will be assessed through fat body carbonyl quantification (oxidized proteins.)

Leucine and valine catabolism increased upon severe restriction of dietary isoleucine.

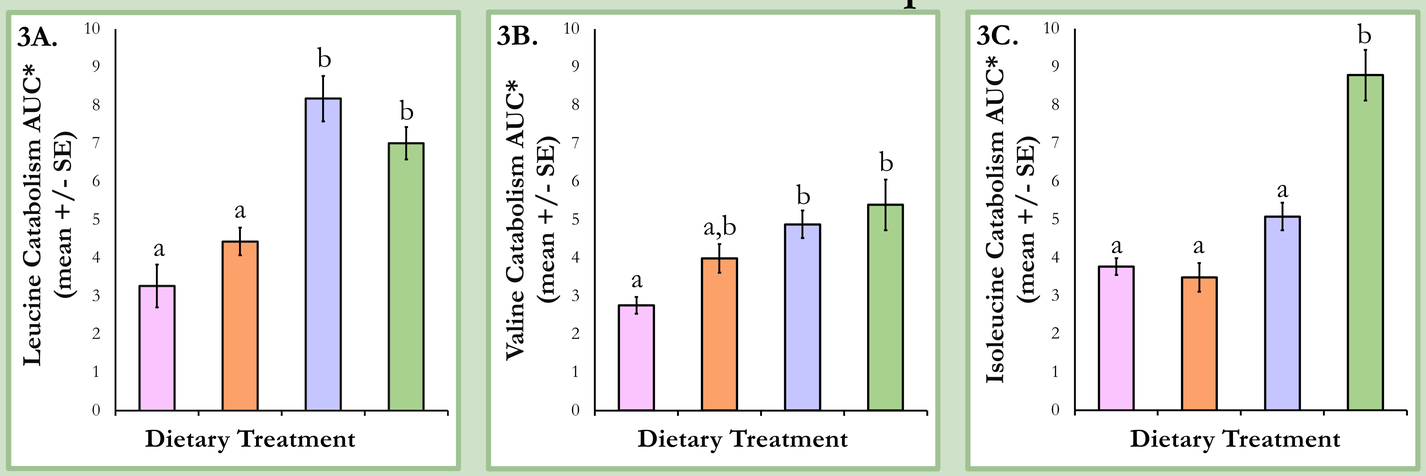

Figure 3: Instantaneous catabolism for leucine (3A), valine (3B), and isoleucine (3C). Three one-way ANOVAs. P<0.05. *AUC represents area under the curve analysis for cumulative BCAA catabolism over 24 hours post dose (3D).

Fat body and ovarian mass decreased upon dietary isoleucine restriction.

Chronic isoleucine restriction prevents reproduction, but short-term isoleucine restriction has health benefits in flies (Fulton et al. 2022).

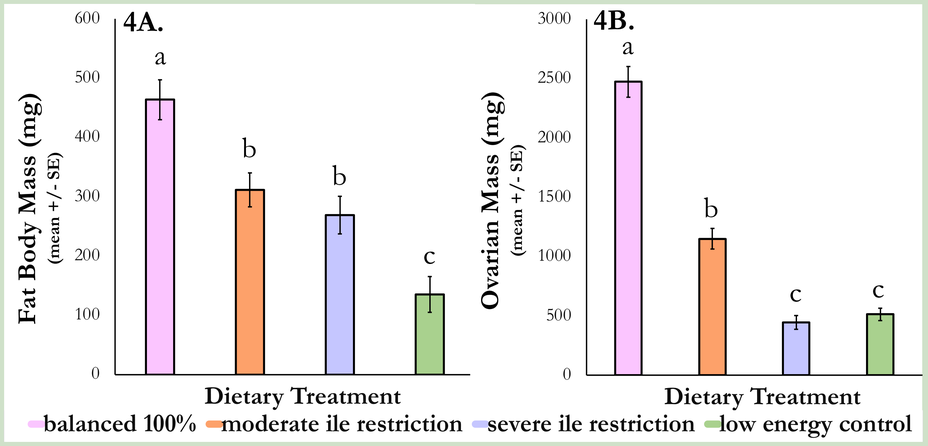

Figure 4: 4A. Average fat body mass. 4B. Average ovarian mass. MANOVA P<0.05.

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References