The key to weight loss maintenance: Exploring mechanisms of metabolic adaptation in a Göttingen Minipig model of obesity

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Metabolic adaptation

- Metabolic adaptation is the body's response to changes in diet, exercise, or hormonal levels, aimed at maintaining energy balance. This can result in the body becoming more efficient at using fewer calories to perform the same tasks, which can make weight loss more challenging over time.

Overall aim

- Establish new knowledge on how metabolic adaptation is regulated in obesity, with the aim to propose novel targets for pharmacologically induced reversal of the metabolic adaptation.

Hypotheses

- Obese Göttingen Minipigs displaying similar metabolic changes as humans when subject to a weight loss
- The metabolic adaptation is associated with:
  1) differential gene expression
  2) differential regulation of neuroendocrine pathways
  3) differential levels of circulating biomarkers
- The metabolic adaptation is larger for a dietary restriction as compared to pharmacological treatment with a GLP-1 analogue

Methods

- 24 Female DIO Göttingen Minipigs, 1.5-year-old

  Control
  Vehicle
  GLP-1
  Vehicle
  Semaglutide
  Diet restriction

  Intervention

  4 weeks
  12 weeks

  10 weeks
  Treatment period

  DEXA and EE

  Study outline

Results

Food intake

“Semaglutide decreased food intake by 44%”

Body weight

“Weight-matching was successful, but all groups gained weight”

Body composition

“Semaglutide improved body composition”

Energy expenditure

“Diet restriction decreased energy expenditure – and more so than semaglutide despite same BW change”

Preliminary Conclusion

- The data indicates that metabolic adaptation was observed in the minipigs, with a greater magnitude seen in the diet restricted group compared to the semaglutide treated group.

What’s next?

- Metabolic chambers

Purpose

- DEG’s associated with MA

Method

- Bulk RNA-sequencing, scRNA-seq and ISH

Tissue/ Blood

- Changes in blood parameters

- Lipolysis capacity test, WB, NE content and inflammation

Adipose tissue adaptation

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