Metabolic and Endocrine Profiles in Response to Systemic Infusion of Fructose and Glucose in Rhesus Macaques

Background

- 19% increase in caloric sweetener consumption from 1970-2005 in the U.S.

- Fructose, in the form of high fructose corn syrup (42-55% fructose) has been proposed to cause weight gain, dysregulation of lipid metabolism, and insulin resistance/glucose intolerance.
Background

- Fructose
  - Elevates postprandial triglyceride levels in humans via activation of fructokinase without regulation by phosphofructokinase
  - Reduces postprandial blood insulin
  - Reduces postprandial leptin
Leptin is a protein produced by adipocytes that controls food-seeking behavior.

- Leptin deficiency & leptin resistance have been associated with weight gain.
- Defects in leptin signaling → hyperphagia → obesity.
Hypothesis

- Fructose, unlike glucose, is a poor stimulus for leptin production even when its systemic availability is increased through IV infusion of the sugar.
  - Plasma leptin responses to IV saline, fructose, or glucose administration will be measured in adult male rhesus monkeys.
Methods

- 9 adult (11-14 yo) male rhesus monkeys used for the study
  - Excluded if signs of disease – screened with physical exam, CBC, biochemistry panel
Methods

- Animals were fasted overnight then treated with
  - Saline infusion
  - Glucose infusion
  - Fructose infusion
- 7 days between each infusion
- Blood samples collected at time -10, 0, 5, 15, 30, 60, 90, 120, 180, 240, 300, and 360 minutes. Catheter removed and final blood sample taken 2 hours later
Methods

- Blood samples used to measure glucose, lactate, triglycerides, insulin, leptin, and fructose
- Repeated-measures ANOVA used to test for differences in these values between the 3 infusions
Results

- Fructose undetectable in fasted state
- Fructose plateaued at 30-60 min during fructose infusion
- Glucose peaked at 30-60 min during glucose infusion
Results

- Lactate – large and sustained release during fructose infusion compared to glucose and saline
Results

- Triglycerides significantly decreased after glucose, no significant difference between saline and fructose
Results

- Insulin – marked and sustained release during glucose
Results

- Leptin – progressive increase after glucose after 240 min, no difference between saline and fructose.
Discussion

- Why does fructose not stimulate leptin?
  - Lower amount exposed to adipocytes compared to glucose – limited gut absorption, more liver uptake, converted to other metabolites like lactate
  - Decreased uptake and metabolism of fructose by adipocytes – may be due to limited insulin response
  - Fructose does not stimulate insulin, which is known to increase leptin expression
Discussion

- In rats, fructose uptake and metabolism increases in a concentration-dependent manner
  - Leptin secretion increases with exposure to 5 mmol fructose

- No leptin response seen in this study at 2 mmol fructose concentration
  - Humans have fructose levels of ~0.3-0.5 mmol after substantial fructose intake
Discussion

- Triglyceride decrease during glucose infusion
  - Increased insulin → activates lipoprotein lipase, suppresses lipolysis, increases free fatty acid reesterification
Limitations

- Low fructose concentrations after fructose infusion – most likely due to liver uptake and conversion to other metabolites
- Plasma fructose assay – used commercial glucose/fructose analytical kit with fructose standards diluted in plasma from fasted human subjects with no detectable fructose
Limitations

- No data tables provided
- For parameters with wide variability (i.e. insulin) it may have been helpful to present the data set from each animal, particularly in the glucose infusion group
Conclusion

- IV infusion of fructose to increase plasma fructose concentration to 2 mmol was sufficient to result in tissue uptake and metabolism to lactate, but not enough to increase leptin production.