

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

Adams SH, Stanhope KL, Grant RW, Cummings BP, Havel PJ. *Endocrinology* 2008;149(6):3002-8.

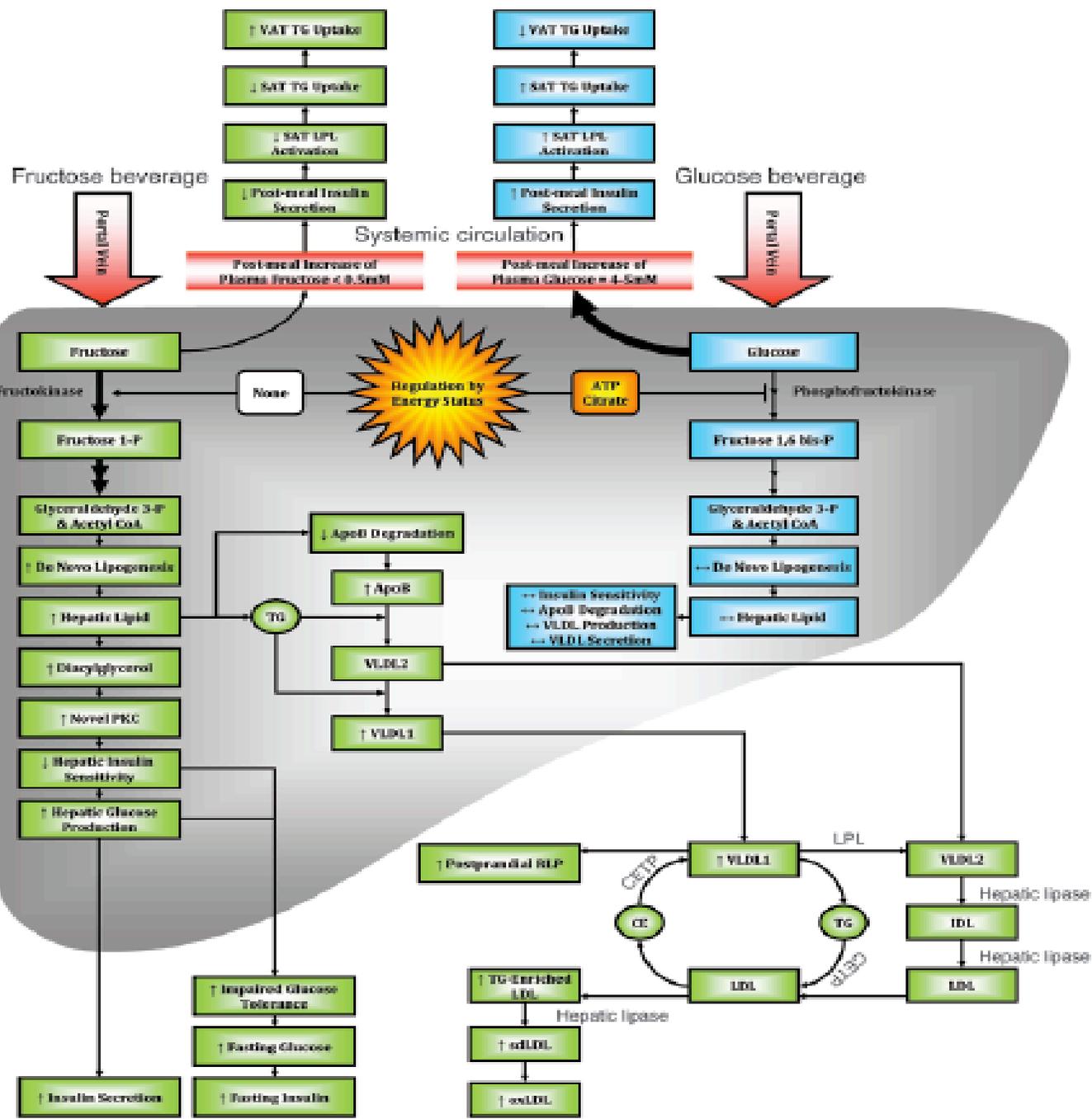
# Background

- 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



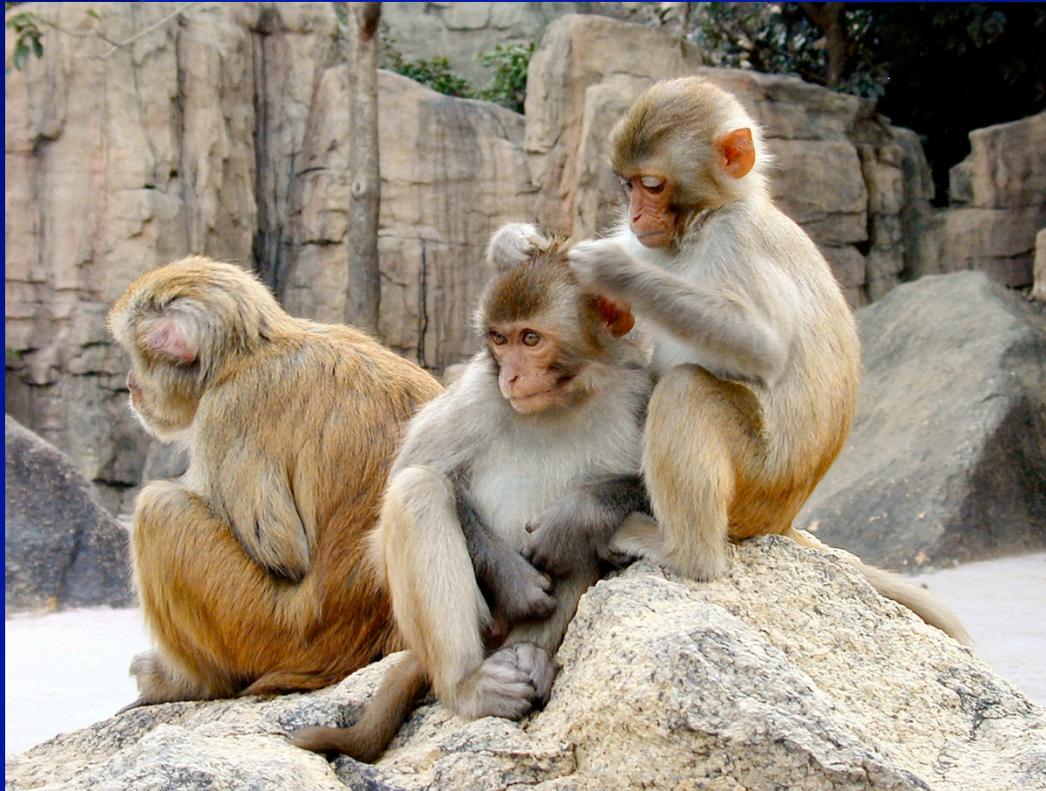
# Background

- 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

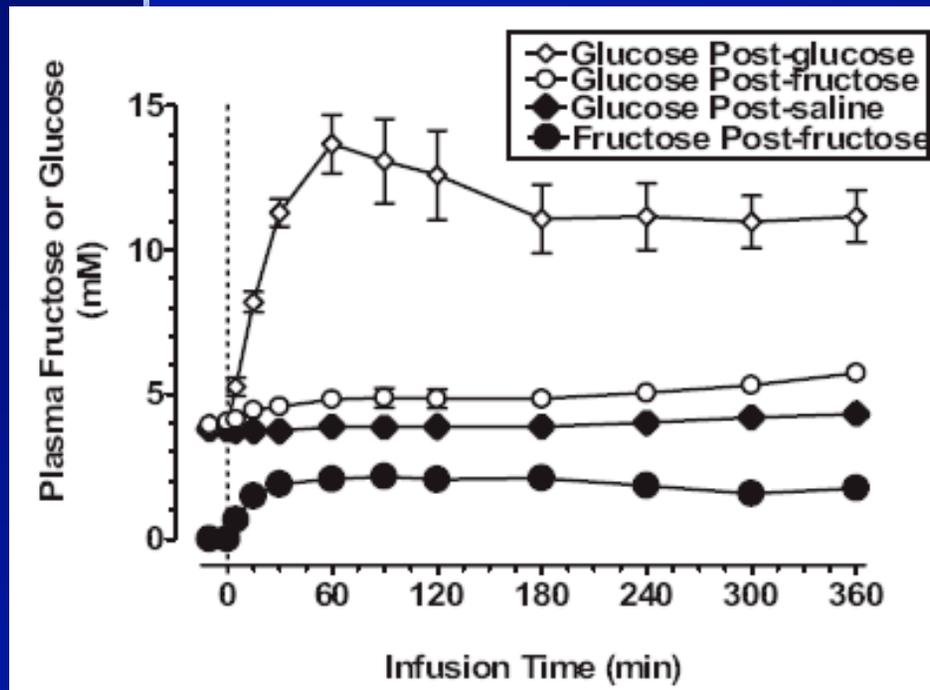
# Methods

- 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

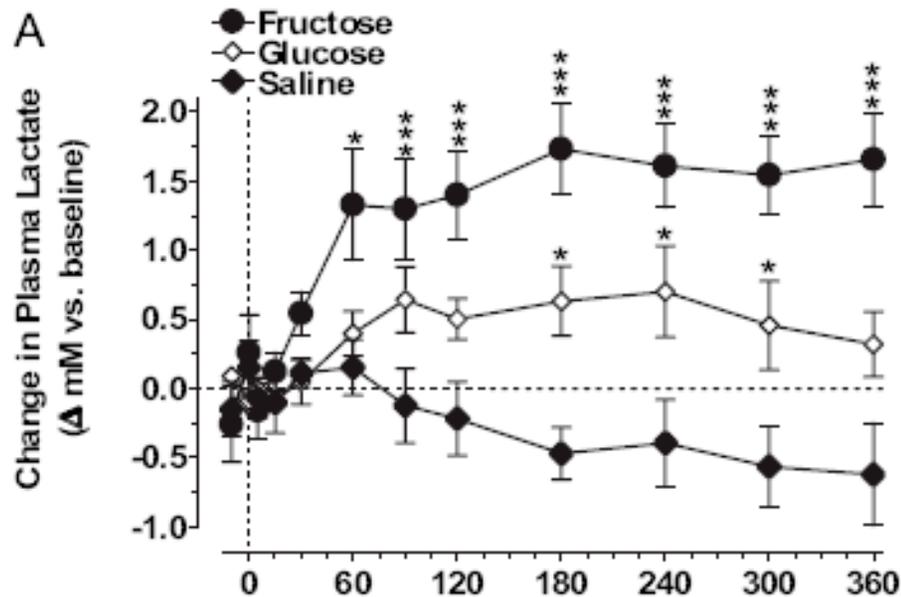
- Blood samples used to measure glucose, lactate, triglycerides, insulin, leptin, and fructose
- Repeated-measures ANOVA used to test for differences in these values between the 3 infusions

# Results



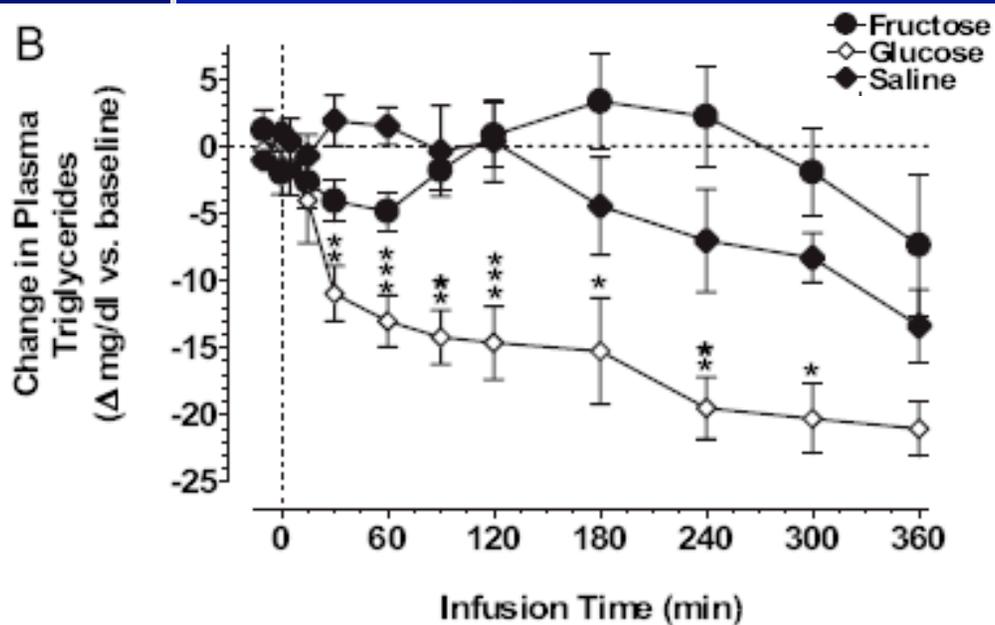
- Fructose undetectable in fasted state
- Fructose plateaued at 30-60 min during fructose infusion
- Glucose peaked at 30-60 min during glucose infusion

# Results



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

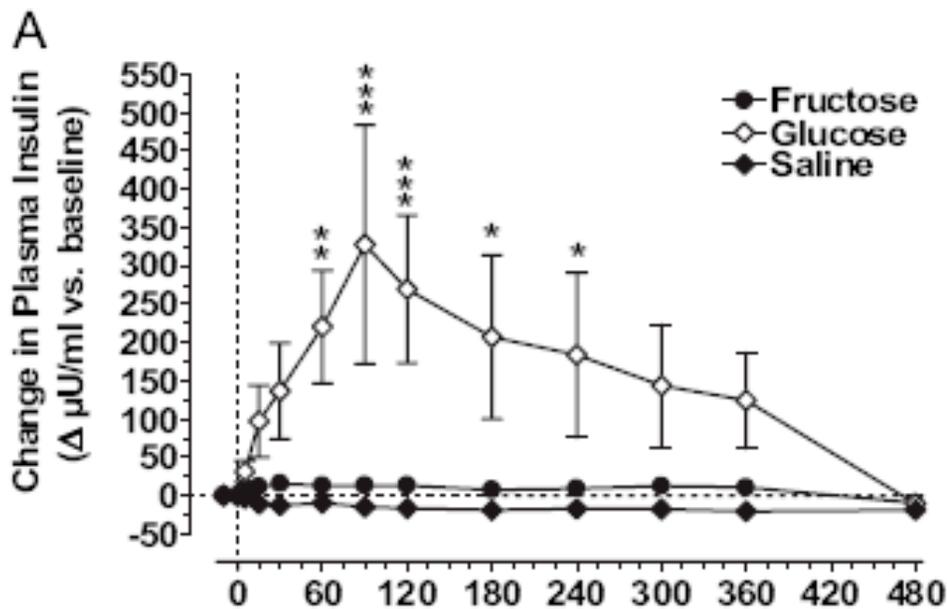
# Results



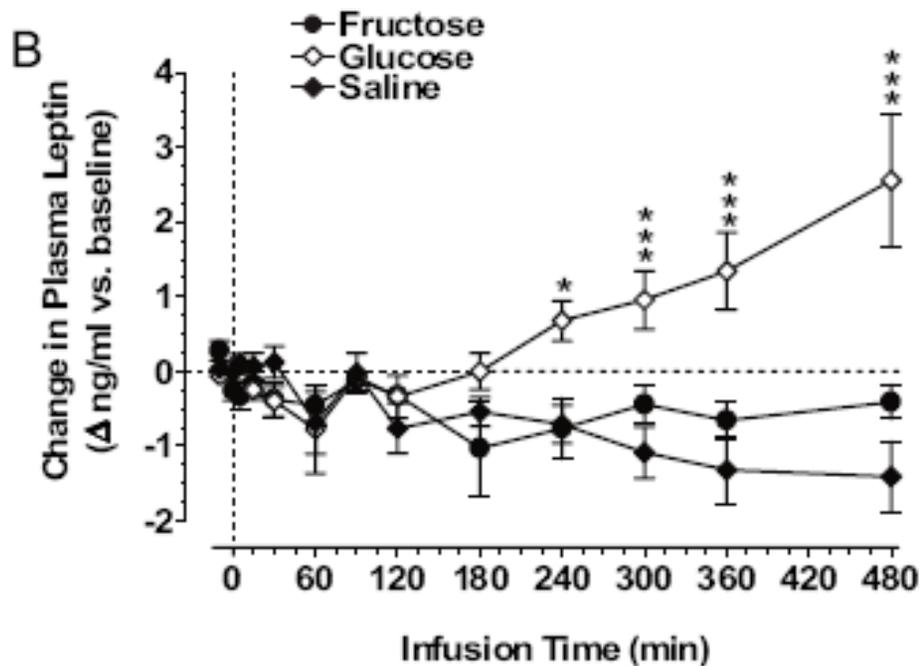
- Triglycerides – significantly decreased after glucose, no significant difference between saline and fructose

# Results

- Insulin – marked and sustained release during glucose



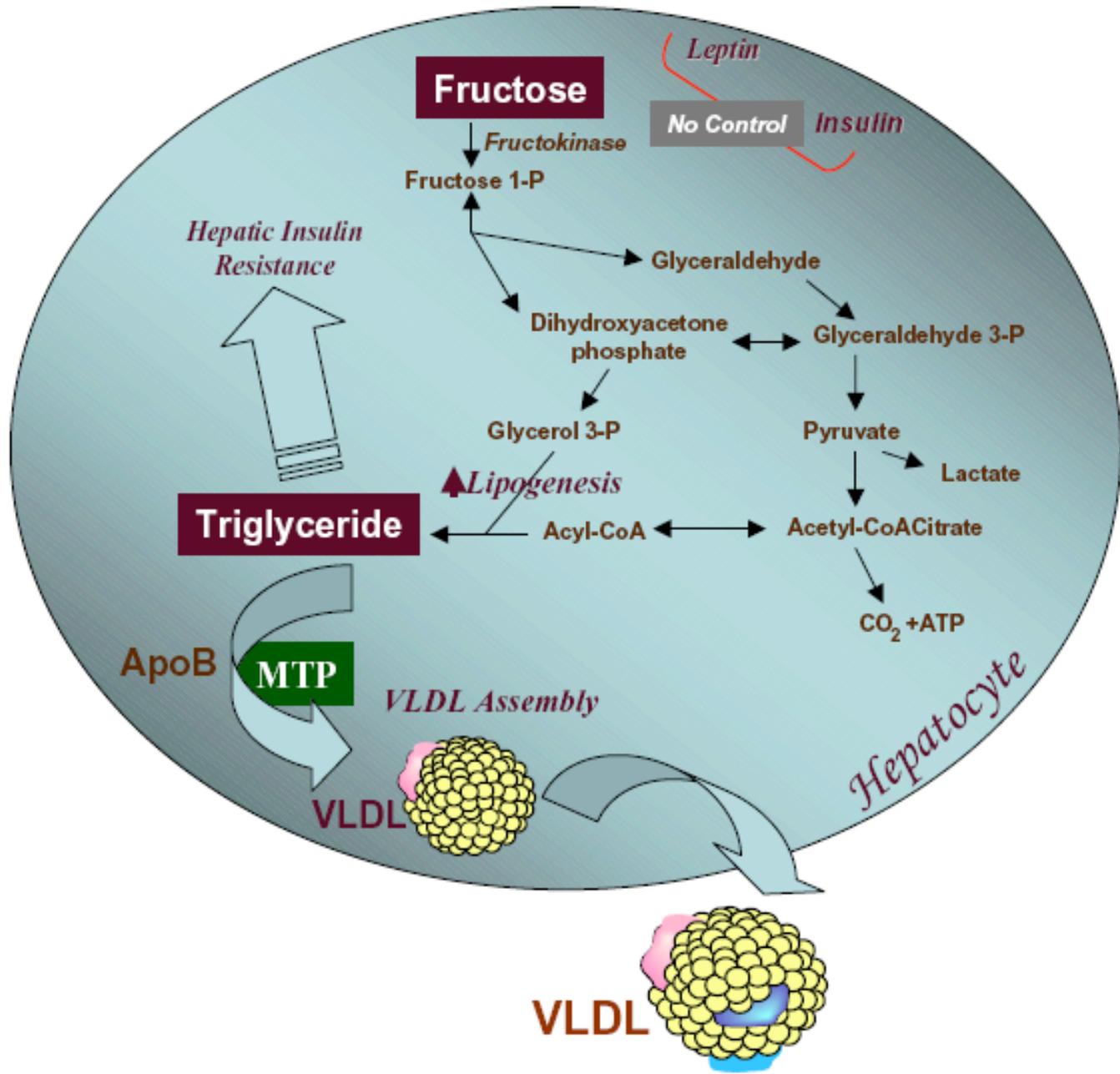
# Results



- 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  $\sim 0.3-0.5$  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