**Fructose, but not Glucose, impairs insulin signaling in the three major insulin-sensitive tissues.**  
  
**AMENDENT 1:** Although the weights were not significantly different after 8 weeks, it seems that they are creeping up in the glucose & fructose groups, so I would venture to guess that if the study had lasted another 8 weeks or beyond, the increased caloric consumption would have led to significant weight differences between Glucose, Fructose vs Control.   
  
**Introduction**This study investigates the impact fructose (not High Fructose Corn Syrup) and glucose have on three different bodily tissues (muscle, white adipose tissue, and the liver).   
  
**Methods**  
  
- Used 30 female only rats  
- Three different conditions:  
 - Control: Normal food consumption, water fluid consumption  
 - Fructose: Normal food consumption + 10% fructose in fluid consumption  
 - Glucose: Normal Food consumption + 10% glucose in fluid consumption  
- Measured consumption, anthropometric measures, as well as removed white adipose tissue (white fat), muscle, and liver for molecular measures of insulin, glucose, and inflammatory markers.   
- Rats consumed their diet for 2 months.   
  
**Results**  
  
*Table 3*  
They are showing the quantified consumption, body weight, and various physiological markers of health in all three conditions.   
- Fructose and Glucose conditions consumed less solid food vs Control.   
- F & G conditions consumed more liquid calories vs Control.   
- F & G conditions consumed more overall kcalories vs Control.   
- Final bodyweight and fat mass were the same for all three conditions.   
- Fasting insulin was elevated for Fructose (although it certainly looks like Glucose is also elevated – not statistically significant, apparently).   
- Fasting glucose was the same for all conditions.   
- Triglycerides are elevated in F & G.   
  
Take away: Implies insulin resistance for fructose and elevated triglycerides for fructose and glucose, independent of bodyweight (see amendment 1) and fat mass.   
  
**AMENDENT 1:** Although the weights were not significantly different after 8 weeks, it seems that they are creeping up in the glucose & fructose groups, so I would venture to guess that if the study had lasted another 8 weeks or beyond, the increased caloric consumption would have led to significant weight differences between Glucose, Fructose vs Control.   
  
  
*Figure 1*  
They are showing molecular measures in liver for lipogenesis (fat synthesis), but only comparing Fructose vs Control (no Glucose condition, yet).   
  
1A. Amounts of different types of lipid/fat.  
- More monounsaturated fats and less polyunsaturated fats with Fructose vs Control.   
  
1C. Amount of SCD1 (Stearoyl CoA Desaturase: converts saturated fat to unsaturated fat).  
- Higher amount of the enzyme in Fructose vs Control.   
  
1D. Amount of ChREBP (Carbohydrate Response Element Binding Protein: Controls lipogenesis/ fat synthesis)  
- Increased with Fructose vs Control.  
  
Take away: Shift in fat type with fructose – also, increased fat synthesis with fructose.   
  
*Figure 2*  
Quantified intracellular liver molecules that are implicated in glucose intake into the cell via insulin.   
  
2A. IRS2 (Insulin Receptor Substrate: regulates, pushes forward the insulin signaling in the cell)  
- IRS2 is dampened with Fructose vs Control.   
  
2B. Same as 2A, but with a different isoform/version of IRS (IRS-1)  
- IRS-1 is the same between conditions.   
  
Take away: Fructose decreases insulin signaling/sensitivity through the reduced levels of IRS-2, which is not compensated for by IRS-1.   
  
*Figure 3*  
Microscopy images looking at the health of the liver tissue between Fructose and Control.   
  
3A & B. Looking for cell necrosis and/or fibrosis.   
- No difference between Fructose vs Control.   
  
Take away: Morphology shows no difference in health between Fructose and Control livers.   
  
*Table 2*  
They are showing the quanitifcation of various mRNA transcripts of genes associated with oxidative stress and inflammation.   
- Nrf2 (Nuclear factor erythroid related factor 2: regulates antioxidants, reducing oxidative stress) is lower with Fructose vs Control, in liver.   
- Mt 1&2 (Metallothioneins: reduces oxidative stress, high or too low expression lead to cell death) is lower in Fructose vs Control  
- ALT (alanine aminotransferase: a marker for liver damage) protein (not mRNA) content is lower with Fructose vs Control.  
  
Take away: Fructose leads to decreases in anti-inflammatory mRNA, yet also decreases in liver damage marker, but as mRNA is unreliable to make conclusions, it is unlikely fructose has a negative impact on liver here.   
  
*Figure 4*  
Glucose challenge administered – given glucose (after fasting animals) and see what happens to glucose & insulin.   
  
4 A&B. Measure of glucose in all three conditions.   
- Fasting glucose levels are similar between all conditions.   
- Elevated blood glucose levels with Fructose only vs Glucose & Control.   
- Fructose condition takes longer to normalize back to fasting levels.   
  
4 C&D. Measure of insulin in all three conditions.   
- Plasma fasting levels are elevated in Fructose vs Glucose and Control  
 Note: It looks to me that Glucose is elevated, as well, but statistics say otherwise…  
- Insulin remained higher in Fructose & Glucose vs Control.   
  
Take away: There is poor glucose tolerance with fructose only, and decreased insulin sensitivity – likely go hand in hand.   
  
*Figure 5*  
Quantified intracellular liver molecules that are implicated in glucose intake into the cell via insulin (same as Figure 2, but including Glucose this time) in liver.   
  
5A&B Quantified IRS2 & IRS1, respectively (like in Figure 2)  
- Fructose, again, shows decreased IRS-2, but no change in Glucose or Control.   
- No change in IRS-1 with any condition.   
  
5C Quantified amount of phospho-Akt (p-Akt is an activated molecule that regulates many processes, but in this context is mediated by the aforementioned IRS).  
- No differences between groups in the amount of p-Akt present.   
  
5D. Quantified p-FoxO (phospho FoxO is an inhibited form of FoxO, which would normally increase gluconeogenesis and antioxidant enzymes. Akt inhibits FoxO (typically) by phosphorylation.   
- p-FoxO is elevated in Fructose and Glucose vs Control.   
  
5E. Quantified PEPCK mRNA (Phosphoenolpyruvate carboxykinase: one of the crucial enzymes for gluconeogenesis)  
- PEPCK is the same in all three conditions.   
  
5F. Quantified G6Pc mRNA (Glucose 6 Phosphatase: last step of gluconeogenesis, releasing glucose into the blood stream).   
- Fructose reduces G6Pc mRNA vs Glucose and Control.   
  
Take away: Glucose signaling is not impaired with glucose, but may be confirmed impaired with fructose.   
  
*Figure 6*  
Quantification of growth regulating molecules in liver.   
  
6E. mTOR is considered the master cell growth stimulating molecule.   
- Fructose and Glucose conditions show elevated phospho-mTOR (presumably activated) vs Control.   
  
6F. TSC2 regulates mTOR by shutting it down, but when phosphorylated, it is inactivated.  
- Increased levels of phosphor-TSC2 in Fructose and Glucose vs Control.   
  
Take away: Fructose and glucose increase cell growth stimulus.   
  
*Figure 7*  
Quantification of insulin signaling molecules (p-Akt) in all three tissues (white adipose tissue, liver, and muscle) with or without the addition of insulin.   
  
7A. p-Akt amounts in liver.   
- Reduced p-Akt levels in Fructose vs Glucose and Control with the addition of insulin.   
  
7B. p-Akt amounts in White Adipose Tissue (White Fat).  
- Reduced p-Akt in Fructose vs Glucose and Control with insulin addition.   
  
7C. p-Akt amounts in muscle.  
- All conditions show elevated p-Akt with insulin addition.   
  
Take away: Fructose decreases p-Akt and, potentially, subsequent insulin signaling in liver and WAT, but not in muscle (the most insulin sensitive).   
  
*Figure 8*  
mRNA quantification of SCD1 (same as Figure 1), inflammatory markers (Mcp-1 and Tnf-a), and plasma/blood levels of Non Essential Fatty Acids.  
  
8C. Measures of SCD1 (Stearoyl CoA Desaturase: converts saturated fat to unsaturated fat) mRNA.  
- Glucose shows elevated SCD1 transcript expression (ironic, considering earlier it was shown that protein was elevated, for the same enzyme, in fructose).   
  
8D&E. Inflammatory markers mRNA transcript levels.   
- No differences between groups.   
  
8F. Amount of Non-Essential Fatty Acids in blood with or without the addition of insulin.   
- With the addition of insulin, reduced levels of NEFAs with all conditions compared to non-insulin stimulation.   
- NEFAs are elevated with Fructose vs Glucose & Control.   
  
Take away: Glucose may (but unlikely) increases saturated fat to unsaturated fat conversion (based on unreliable mRNA levels). Inflammatory markers are also not different based on unreliable inflammatory markers. Insulin addition leads to elevated blood fatty acid levels.   
  
Figure 9  
Protein levels of glucose signaling molecules (GLUT4 and AS160).   
  
9A. AS160 triggers the movement of GLUT4 to the membrane to allow the input of glucose into the cell.   
- Fructose and Glucose show elevated levels of AS160 vs Control.   
  
9C. GLUT4 is the glucose transporter that allows glucose from the blood stream into the cells.   
- GLUT4 protein levels are elevated with Glucose, but dampened with Fructose vs Control.   
  
Take away: Glucose shows normal insulin signaling allowing glucose into the cell, but fructose shows dampened/decreased insulin signaling.   
  
Additional Notes:   
- Rats consumed 60% of their energy intake/kcalories from fructose, which is considerably more than human consumption (high end is 25% of kcalories).   
  
- There is some evidence, as mentioned in the body of the paper, that the liver may protect itself by converting fructose and other intermediates to MUFA – if this persists, would you see insulin resistance?