# The Effects Of Fructose On Health

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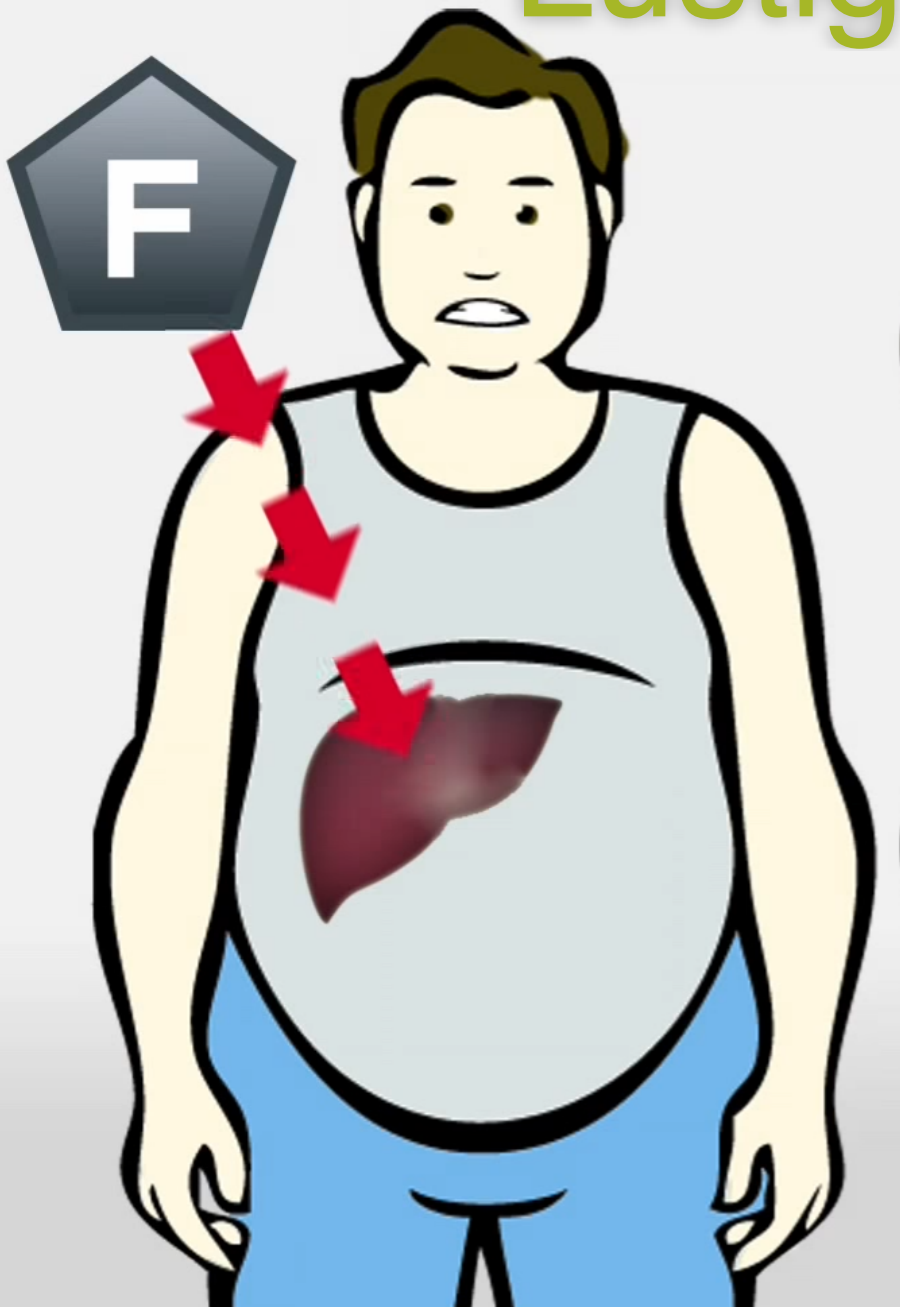
# Background On The Sugar Debate

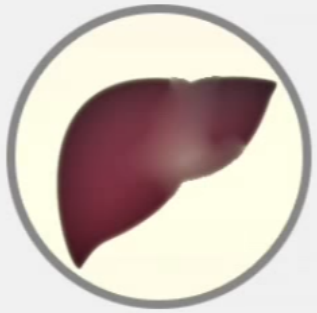
| Ancel Keys | John Yudkin |
| --- | --- |
| 1970s – American Scientist Ancel Keys put forth ecological data from his seven countries study that posited saturated fat was the main driver of heart disease | 1972 – British scientist, John Yudkin, who published the book 'Pure, White and Deadly' the pointed the finger at sugar being responsible for increased rates of heart disease and diabetes |
| Dr. Keys could provide a more robust dataset for his hypothesis at the time, it gained traction and was accepted into many national dietary guidelines | Used lower quality data with little to no statistical analysis.<br>Relied heavily upon non-randomized, uncontrolled trials using doses of ~260g of sugar (1,040 kcal/day) in short term settings (3 weeks) |

# Present Day: The Debate Continues

| Dr. John Sievenpiper, PhD | Dr. Robert Lustig, MD |
| --- | --- |
| Argues that the human data on fructose consumption does not support the “unifying hypothesis of metabolic syndrome” | Dr. Lustig has published journal articles arguing that sugar is a “toxic” substance that threatens public health and has drawn parallels between the metabolism of fructose and ethanol, calling it “alcohol, without the buzz” |
| Has put forth a series of systematic reviews and meta-analyses investigating the claims made by Dr. Lustig | Has proposed fructose as a main mechanism in his “unifying hypothesis of metabolic syndrome”, wherein he claims that fructose |

# Lustig's "Unifying Hypothesis"



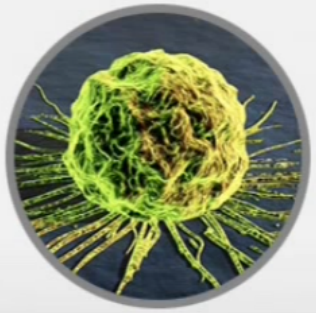
LIVER FAT

INSULIN RESISTANCE

WEIGHT GAIN

HIGH BLOOD PRESSURE

HEART DISEASE

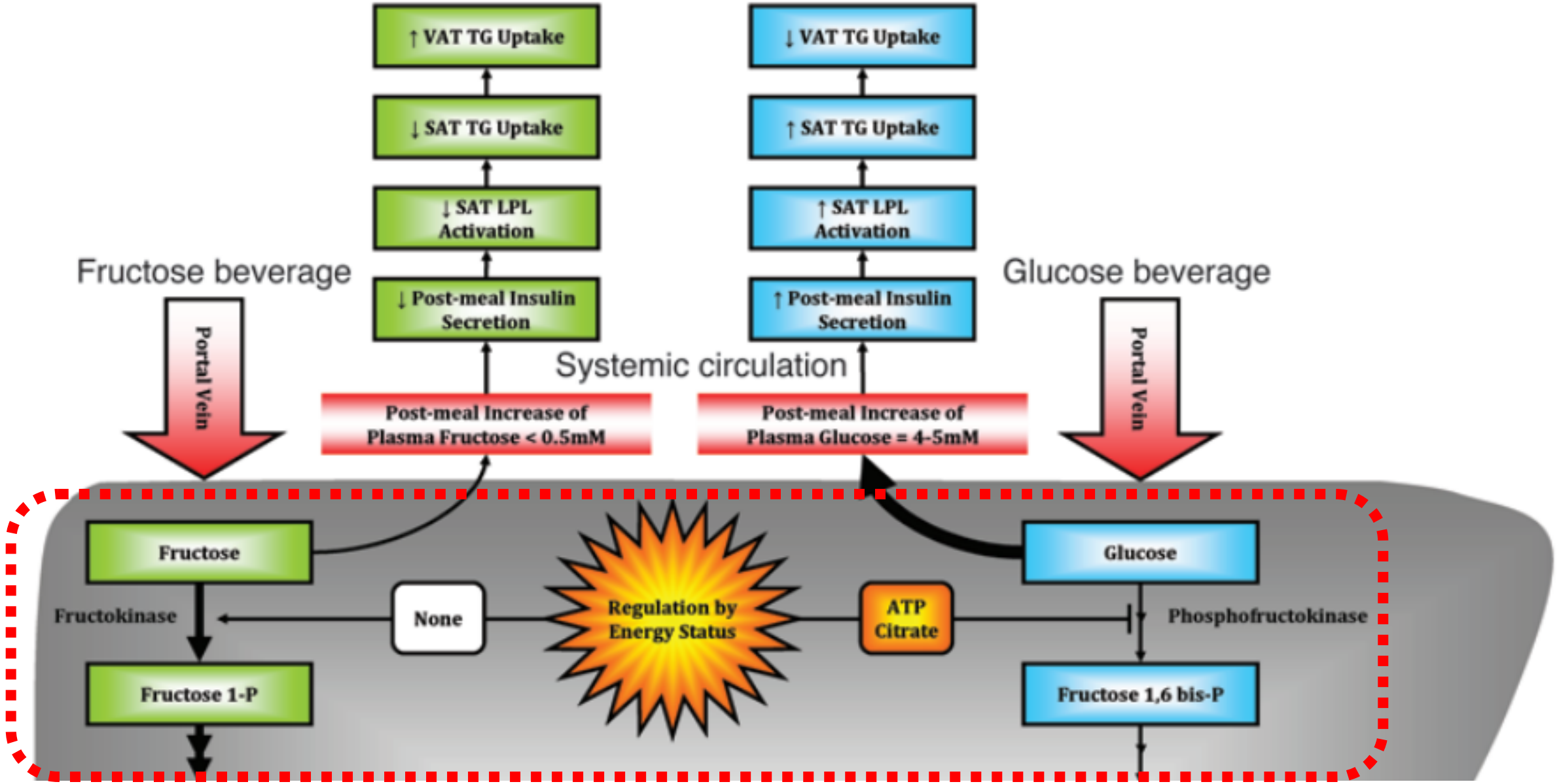


CANCER

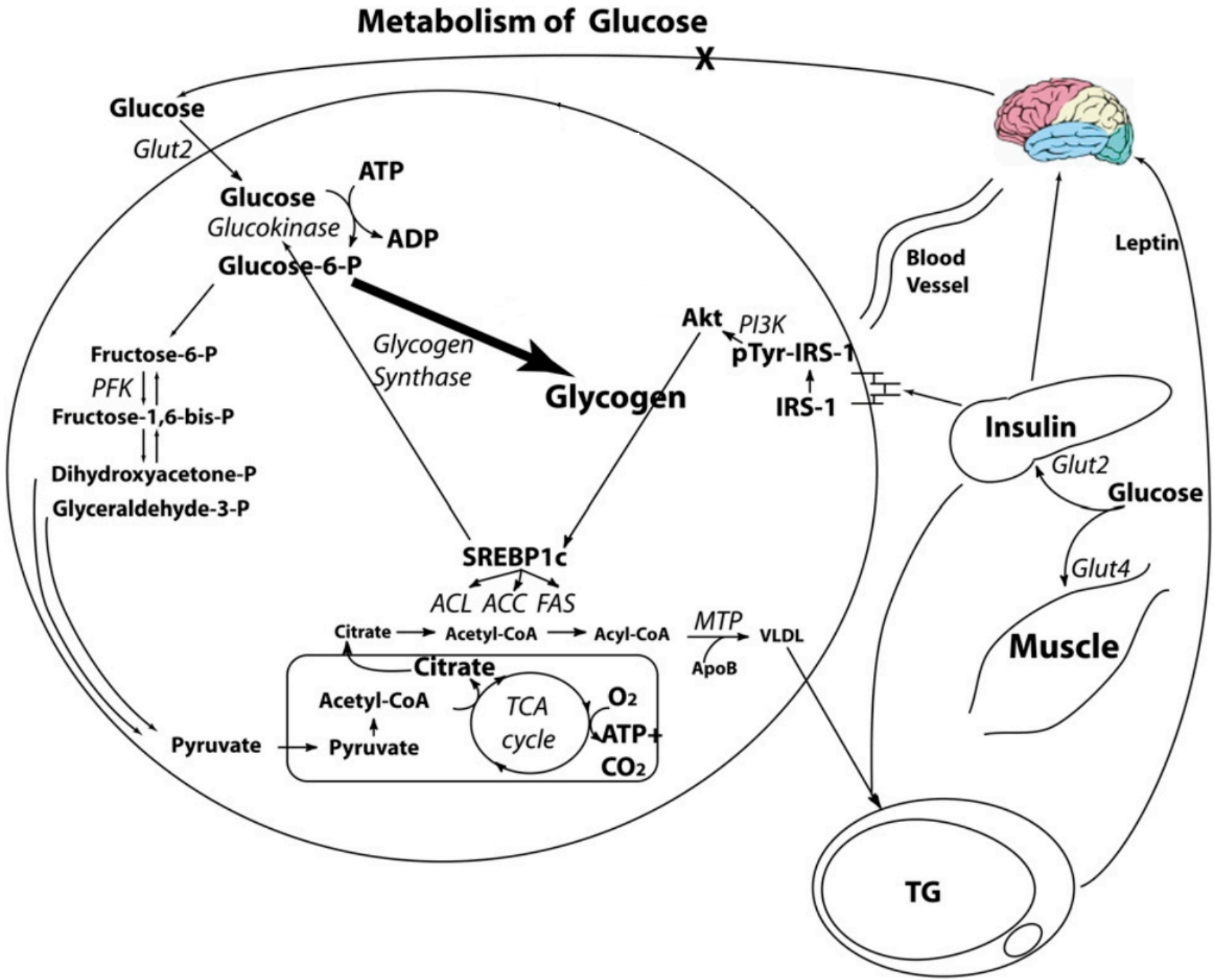
DEMENTIA

DIABETES

Lustig, R. (2013). The Complete Skinny on Obesity:

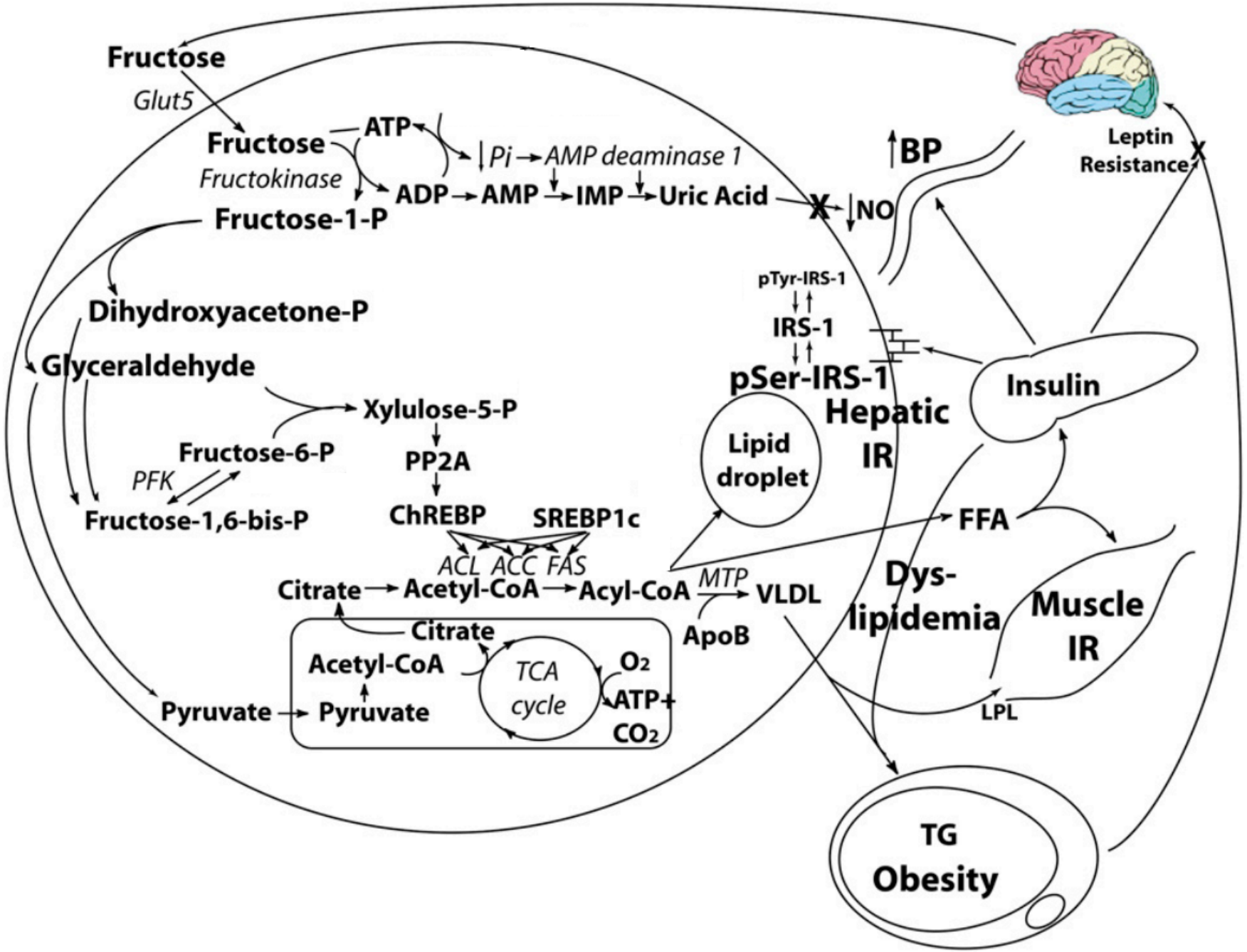



Pediatrics. 2012 Mar;129(3):557-70. doi: 10.1542/peds.2011-2912.




Bremer, A. A., M. Mietus-Snyder and R. H. Lustig (2012). "Toward a unifying hypothesis of metabolic syndrome." Pediatrics 129(3): 557-570.

# Metabolism of Fructose




Bremer, A. A., M. Mietus-Snyder and R. H. Lustig (2012). "Toward a unifying hypothesis of metabolic syndrome." Pediatrics 129(3): 557-570.

# Research

- Isocaloric Trials - included eucaloric and hypercaloric trials
  - both arms were calorie matched.
- Hypercaloric Trials - compared control diet alone to a control diet with an added fructose supplement.
  - Meant to simulate a more natural pattern of fructose consumption, which is often added on top of a usual diet
  - Had the limitation that total calories were a confounding factor as caloric intake was not matched between arms.

# Research: Meta-Analyses

- Blood pressure (Ha et al., 2012; Jayalath et al., 2015; Jayalath et al., 2014)
- Glycemic control (Cozma et al., 2012)
- Lipids (Chiavaroli et al., 2015; David Wang et al., 2014)
- Body weight (Sievenpiper et al., 2012; Te Morenga, Mallard, & Mann, 2012)
- Uricemia (gout) (Wang et al., 2012)
- Non-alcoholic fatty liver disease (NAFLD) (Chiu et al., 2014; Chung et al., 2014)

# Research

- The common theme seen among all these analyses was that negative health effects of fructose were not observed until fructose was administered in caloric excess, indicating that it may be the excess calories and nothing inherent to fructose that may be the issue.

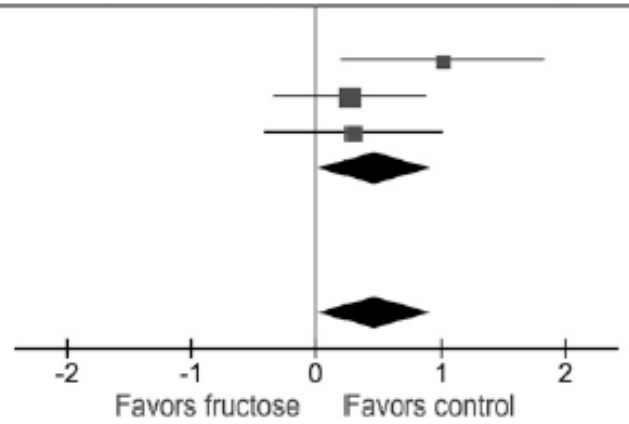
# Except one…

- A recent systematic review and meta-analysis saw interesting finding regarding fructose consumption and hepatic insulin sensitivity in nondiabetics (Ter Horst, Schene, Holman, Romijn, & Serlie, 2016).
- The study examined the effects of fructose on:
  - fasting plasma insulin concentration
  - HOMA-IR
  - insulin-stimulated glucose disposal during euglycemic hyerinsulinemic clamp
  - hepatic insulin sensitivity
- All but the hepatic insulin sensitivity findings fell into the normal pattern:
  - No difference in energy-matched comparisons and poorer outcomes in hypercaloric trials.
  - Hepatic insulin sensitivity saw worse outcomes for both energy-matched and hypercaloric dietary comparisons, a novel finding.

# Ter Horst et al.

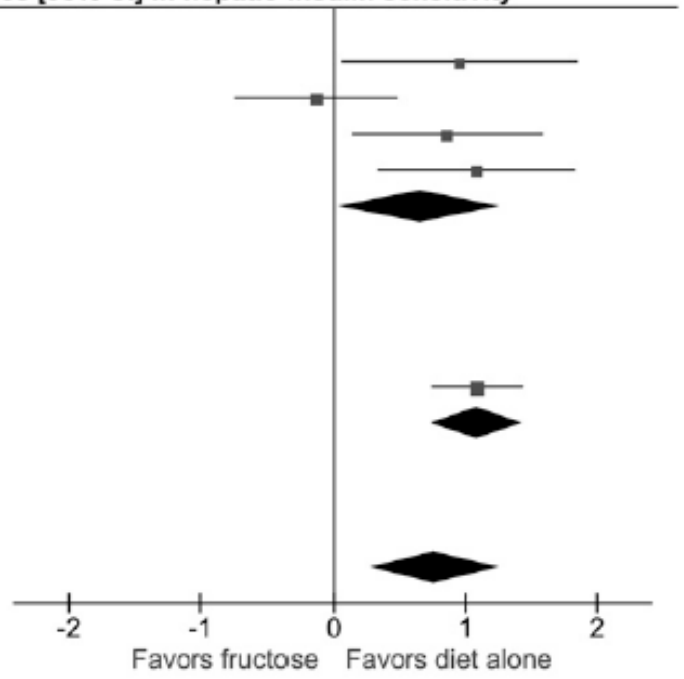
**A** **Energy-matched comparisons**

| Study | Weight | Standardized mean difference [95% CI] in hepatic insulin sensitivity |
|---|---|---|
| **Normal-weight participants** | | |
| Aeberli, 2013 **(48)** | 25.9% | 1.01 [0.21, 1.82] |
| Ngo Sock, 2010 **(56)** | 41.9% | 0.27 [-0.33, 0.87] |
| Schwarz, 2015 **(58)** | 32.2% | 0.30 [-0.41, 1.01] |
| **Subtotal (95% CI)** | **100.0%** | **0.47 [0.03, 0.91]** |
| Heterogeneity: $Tau^2 = 0.03$; $Chi^2 = 2.41$, df = 2 (P = 0.30); $I^2 = 17\%$ | | |
| Test for overall effect: Z = 2.10 (P = 0.04) | | |
| **Total (95% CI)** | **100.0%** | **0.47 [0.03, 0.91]** |
| Heterogeneity: $Tau^2 = 0.03$; $Chi^2 = 2.41$, df = 2 (P = 0.30); $I^2 = 17\%$ | | |
| Test for overall effect: Z = 2.10 (P = 0.04) | | |
| Test for subgroup differences: Not applicable | | |




**B** **Hypercaloric comparisons**

| Study | Weight | Standardized mean difference [95% CI] in hepatic insulin sensitivity |
|---|---|---|
| **Normal-weight participants** | | |
| Faeh, 2005 **(71)** | 15.3% | 0.95 [0.06, 1.85] |
| Lê, 2006 **(72)**[1] | 21.1% | -0.13 [-0.73, 0.47] |
| Lê, 2009 **(73)**[1] | 18.6% | 0.86 [0.14, 1.58] |
| Ngo Sock, 2010 **(56)** | 18.1% | 1.09 [0.34, 1.83] |
| **Subtotal (95% CI)** | **73.1%** | **0.65 [0.04, 1.26]** |
| Heterogeneity: $Tau^2 = 0.25$; $Chi^2 = 8.35$, df = 3 (P = 0.04); $I^2 = 64\%$ | | |
| Test for overall effect: Z = 2.10 (P = 0.04) | | |
| **Other metabolic features** | | |
| Lê, 2009 **(73)**[1] | 26.9% | 1.09 [0.75, 1.43] |
| **Subtotal (95% CI)** | **26.9%** | **1.09 [0.75, 1.43]** |
| Heterogeneity: Not applicable | | |
| Test for overall effect: Z = 6.24 (P < 0.00001) | | |
| **Total (95% CI)** | **100.0%** | **0.77 [0.28, 1.26]** |
| Heterogeneity: $Tau^2 = 0.20$; $Chi^2 = 12.45$, df = 4 (P = 0.01); $I^2 = 68\%$ | | |
| Test for overall effect: Z = 3.06 (P = 0.002) | | |
| Test for subgroup differences: $Chi^2 = 1.48$, df = 1 (P = 0.22), $I^2 = 32.6\%$ | | |



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