

Calorie Control Council Response to Shapiro *et al*

“Fructose-induced leptin resistance exacerbates weight gain in response to subsequent high fat feeding”

Shapiro A, Mu W, Roncal CA, Cheng K-Y, Johnson RJ, Scarpace PJ.
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Background

This study comes from several departments at the University of Florida in Gainesville, including the Department of Nephrology, home to Richard J. Johnson. Johnson is a high-profile fructose antagonist who has just published a new diet book called, *The Sugar Fix – The high-fructose fallout that is making you fat and sick*. He acknowledges this in the following disclaimer: “Dr. Johnson is listed as an inventor on several patent applications related to fructose and obesity and has a lay book on fructose that was published by Rodale, Inc in 2008.” Where are the conflict of interest police when you need them?

Hypotheses

- Chronic high-fructose feeding induces leptin resistance; and
- Leptin resistance leads to an increased susceptibility to weight gain.

Justifications

- Obesity has been increasing rapidly among children and adolescents, suggesting that environmental factors are involved.
- There is increasing evidence that certain food items, such as fructose, may have a pathogenic role.
- Epidemiological studies indicate a correlation between the introduction and spread of fructose-enriched products, sugar consumption and the increased rate of obesity.
- Rodents administered a high fructose diet develop most of the features of metabolic syndrome, changes not observed in animals fed equivalent amounts of glucose.
- Chronic fructose ingestion is associated with an increase in plasma leptin levels in rats and humans; some studies report this increase precedes the obesity. Elevated plasma leptin is sometimes a sign of leptin resistance and could potentially be a major mechanism for inducing obesity.

Experimental Design

- Rats were fed a fructose-free control or 60% fructose diet (est. 66% of calories) for six months and then tested for insulin resistance.
- Half the rats in each group were then switched to high fat diet for two weeks, while the remaining half continued on their respective diets.

Author conclusions

- Chronic fructose consumption caused leptin resistance; serum leptin levels, weight and adiposity were the same as in control rats that were leptin responsive.

- Subsequent exposure of the fructose-mediated leptin-resistant rats to a high fat diet (60% calories from fat, 7% from sucrose) lead to exacerbated weight gain compared with leptin-responsive animals that were pre-treated with the fructose-free diet (50.2 ± 2 g vs. 30.4 ± 5.8 g).
- Chronic fructose consumption induces leptin resistance prior to body weight, adiposity, serum leptin, insulin or glucose increases, accelerating high fat induced obesity.

Critique

- While the weight gain and leptin resistance of the fructose+fat rats compared to controls appears significant, it must be remembered that the rats were exposed to the some of the highest levels of fructose (est. 60% of calories) we have ever seen. This is equivalent to six times typical human fructose intake.
- Likely to their dismay, the authors succeeded in blurring what, to this point, was a pretty clear distinction between metabolic effects of fructose vs. glucose.
 - Control and high fructose fed rats demonstrated no differences in food intake or body weight gain over the course of six months.
 - After six months of high fructose consumption there was only mild evidence of metabolic syndrome.
 - Rats on the 60% fructose diet had elevated serum triglycerides but displayed no changes in weight, adiposity, blood glucose, fasting insulin, or serum uric acid levels.

These results will become part of the record arguing for few significant metabolic differences between sugars, though they'll be discounted because of the rat model used and because the data are so different from those already in the record.

- The following concluding statement attempts to stake out a venerable position for the authors for having exposed a silent enemy with no distinguishing characteristics or visible signs (my emphasis added):

*A key finding in this study is that a **silent** leptin resistance has occurred with almost **no physiological or biochemical differences** detected between the fructose and control fed groups. Thus, high fructose diet predisposes to obesity, and deleterious effects of chronic fructose consumption develop **long before any visible signs** of elevated leptin or the metabolic syndrome.*

Viewed from a different perspective, this statement acknowledges that the study found no measurable differences between glucose control rats and those fed grossly exaggerated amounts of fructose, unless they were subsequently fed grossly exaggerated amounts of fat. Thus, the study has no relevance to the human experience.