Calorie Control Council Response to Bocarsly et al

High-fructose corn syrup causes characteristics of obesity in rats: Increased body weight, body fat and triglyceride levels

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Background

The authors are from the Princeton University Department of Psychology, the Princeton Neuroscience Institute and the Rockefeller University Laboratory of Behavioral Neurobiology.

Author Justification

One study reported that nearly 7% of daily caloric consumption in the U.S. is from HFCS and linked it to the rise in obesity since its introduction (1), while another estimated that >10% of calories come from fructose (2). Because of its prevalence in the American diet, it is crucial to understand the behavioral and physiological effects of dietary HFCS.

There are differences in how HFCS and sucrose are metabolized and used in the body:

- Meals high in fructose reduce circulating insulin and leptin in women (3), so HFCS would presumably not produce the degree of insulin or leptin-induced satiety that would ensue with a meal of sucrose, potentially fueling overeating;
- Pure fructose leads to increased plasma free fatty acids, leptin, adiponectin, abdominal adipose tissue and impaired insulin sensitivity (4);
- Pure fructose leads to increased leptin resistance and exacerbated weight gain in rats subsequently maintained on a high-fat diet (5);
- Very few studies have actually tested HFCS and the literature is deficient in long-term studies (6).

Hypothesis

A standard diet supplemented with HFCS will cause obesity in male and female outbred rats.

Experimental Setup

Both short- and long-term effects of HFCS were measured on body weight, body fat and circulating triglycerides.

<u>Experiment 1 – short term</u>

Male rats were maintained for 8 weeks on 1 of 4 diets:

- 12 h/d 10% sucrose solution + *ad libitum* rodent chow;
- 12 h/d of 8% HFCS solution + *ad libitum* rodent chow;
- 24 h/d HFCS + *ad libitum* rodent chow; or
- *ad libitum* chow alone (control group).

<u>Experiment 2 – long term</u>

Male rats were maintained for 6 months on 1 of 3 diets:

- 12 h/d of 8% HFCS solution + *ad libitum* rodent chow;
- 24 h/d HFCS + *ad libitum* rodent chow; or
- *ad libitum* chow alone (control group).

Female rats were maintained for 7 months on 1 of 4 diets:

- 12 h/d 10% sucrose solution + 12 h/d rodent chow;
- 12 h/d of 8% HFCS solution + 12 h/d rodent chow;
- 24 h/d HFCS + *ad libitum* rodent chow; or
- *ad libitum* chow alone (control group).

Author Conclusions and *Specific Critiques*

1. Male rats with 12 h/d HFCS + *ad libitum* chow gained more weight in 8 weeks than animals with equal access to sucrose + *ad libitum* chow.

Whether intentional or not, the authors make it difficult to check their interpretation of the data by not graphing or tabulating the results of Experiment 1, and by not reporting weight gains or calorie intakes for 24 h/d HFCS + ad libitum chow and chow only rats. What is clear is that the data are inconsistent: no explanation is offered for why 24 h/d HFCS rats didn't gain more weight than 12 h/d HFCS rats.

The authors set out to prove differences between HFCS and sucrose. How, then, did HFCS and sucrose rat weight gains compare with chow fed rats? The authors withheld data that may have provided the answer.

2. Male rats with ad libitum HFCS and chow for 6 months have increased body weight, abdominal fat and TG levels compared to controls.

In their interpretation of Fig. 1, the authors pick and choose which data to display. In this case, chow only rats serve as the control against which rats fed incremental amounts of HFCS (12 and 24 h/d) and unlimited chow show incremental increases in body weight. This is to be expected, since the HFCS rats presumably consumed incrementally more calories, though the authors made it impossible to confirm when they withheld the data.

The authors exaggerated the effect of HFCS on fat pads and TG (triglyceride) levels. For male rats, the data in Fig. 2 demonstrate no differences between 12 and 24 h/d HFCS + chow vs. chow only controls for gonadal and intestinal fat pads. It was again inexplicably surprising that 24 h/d HFCS + chow and chow only control rats were statistically indistinguishable and that only the 12 h/d HFCS rats were significantly different. The authors again offered no explanation.

3. Female rats with 7 months of HFCS access gain significantly more body weight, have more abdominal fat and elevated TG levels compared with chow- and sucrose-fed controls

The authors' weight gain and TG analyses would better have concluded there was no *significant difference between 12 h/d HFCS, 12 h/d sucrose and chow fed controls over the whole 7 month course of the experiment. It was only in the final month of the study that 24 h/d HFCS rats developed significant differences from the others. But once again, we're given no calorie intake data to prove these observations are not simply a result of energy excess.*

General Critiques

- Laboratory animals - especially rodents - are generally considered poor models for human metabolism. FDA, in its evidence-based approach to evaluating research, counts animal studies as considerably less reliable than human studies.
- In their justification for the present study, the authors state "there are differences in how these sugars [sucrose and HFCS] are metabolized and utilized in the body," but all differences cited (see **Author Justification** section, above) are common to both sugars once they reach the bloodstream, because of their similarity in composition.
- In citing studies using high fructose concentrations as justification for the present work with HFCS, the authors ignore 1) obvious differences in composition between fructose and HFCS, and 2) the physiologic irrelevance of these extreme diets to human fructose experience.
- The authors' stated objective to compare HFCS and sucrose effects on obesity was unsuccessful, at least in male rats, since the sucrose variable was either incompletely reported (Experiment 1) or missing entirely from the experimental design (Experiment 2). This made it impossible to prove a unique effect for HFCS.
- The authors claimed to provide evidence that excessive consumption of HFCS may contribute to the incidence of obesity, but failed to put into perspective the outrageous amount consumed by rats in their experimental design. Translating reported rat intakes to human proportions, the energy gained from HFCS alone would be equal to 3000 kcal/day. This is the equivalent of drinking 20 12-oz cans of soda - clearly an unlikely volume for even the thirstiest teen. The amount of sweetener intake alone would be sufficient to cause obesity in many adults. It is irresponsible to claim that one sweetener is more likely to cause obesity than the other at such exaggerated intake levels.
- Put another way, this amount of sweetener by itself - either HFCS or sucrose - contains more calories than most Americans should consume in a day from *all* dietary sources.
- Authors: **When rats are drinking high-fructose corn syrup at levels well below those in soda pop, they're becoming obese -- every single one, across the board.** This statement misleads the reader by purposely confusing the finite volume (12 oz) in a soda can containing 10-11% HFCS with the unrestricted volume of 8% HFCS test solution offered rats in the present study. This clearly leads to a highly biased and indefensible interpretation of the data.

The authors have taken considerable criticism for this paper from unexpected sources.

New York University nutrition activist Marion Nestle expressed skepticism about the study, writing: *"How they came to these conclusions is beyond me. So does HFCS make rats fat? Sure if you feed them too many calories altogether. Sucrose will do that, too (7)."*

And Karen Teff, a physiologist at the Monell Chemical Senses Center in Philadelphia and frequent collaborator of Peter Havel, said: *"This study is poorly designed and poorly controlled and does not prove or even suggest that HFCS is more likely to lead to obesity than sucrose* (8)*."*

References

1. Bray GA, Nielsen SJ, Popkin BM. Consumption of high-fructose corn syrup in beverages may play a role in the epidemic of obesity. Am J Clin Nutr 2004;79:537-43.
2. Vos MB, Kimmons JE, Gillespie C, Welsh J, Blanck HM. Dietary fructose consumption among US children and adults: the Third National Health and Nutrition Examination Survey. Medscape J Med 2008;10:160.
3. Teff KL, Elliott SS, Tschop M, et al. Dietary fructose reduces circulating insulin and leptin, attenuates postprandial suppression of ghrelin, and increases triglycerides in women. J Clin Endocrinol Metab 2004;89:2963-72.
4. Alzamendi A, Giovambattista A, Raschia A, et al. Fructose-rich diet-induced abdominal adipose tissue endocrine dysfunction in normal male rats. Endocrine 2009.
5. Shapiro A, Mu W, Roncal C, Cheng K-Y, Johnson RJ, Scarpace PJ. Fructose-induced leptin resistance exacerbates weight gain in response to subsequent high-fat feeding. Am J Physiol Regul Integr Comp Physiol 2008;295:R1370-1375.
6. Bray GA. Soft drink consumption and obesity: it is all about fructose. Curr Opin Lipidol 2010;21:51-7.
7. Nestle M. HFCS makes rats fat? Blog: Food Politics, 24 Mar 2010.
8. Micco N. Why the new study on high-fructose corn syrup and weight gain is flawed. Blog: Eat Well, Be Well, 26 Mar 2010.