Calorie Control Council Response to Parks *et al*

"Dietary sugars stimulate fatty acid synthesis in adults"

Parks EJ, Skokan LE, Timlin MT, Dingfelder CS.
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Background
This study comes out of the Center for Human Nutrition, University of Texas Southwestern Medical Center, Dallas (author Parks); Department of Biomedical Engineering, University of Texas at Arlington (Skokan); and Department of Food Science and Nutrition, University of Minnesota, St. Paul (Timlin & Dingfelder).

Hypothesis
The authors hypothesized that a fructose-induced rise in lipogenesis (fat production) in the morning would further increase triglyceride (TG) concentrations after the next meal.

Justifications

- Fructose has been used in controlled over-feeding studies to elevate daylong serum triglyceride concentrations in healthy and diabetic subjects;
- Elevated TG could lead to an accumulation of lipoprotein remnants, which could be atherogenic;
- The natural pattern of blood TG is diurnal (occurring during the day), rising throughout the day and peaking around midnight.

Experimental Design
Human subjects consumed a carbohydrate bolus (single large dose) of sugars (85 g each) in a random and blinded order, followed by a standardized lunch 4 h later. Carbohydrate boluses consisted of glucose (100G:0F), a mixture of 50G:50F glucose:fructose or a mixture of 25G:75F glucose:fructose.

Author Conclusions

- Lipogenesis (lipid synthesis) was stimulated for all treatments, but it was nearly double after the 50G:50F and 25G:75F treatments compared to the 100G:0F treatment.
- An early stimulation of lipogenesis after fructose, administered in a mixture of sugars, augments subsequent postprandial (after a meal) lipemia (excess lipids in the blood).
- Acute intake of fructose stimulates lipogenesis and may create a metabolic milieu that enhances esterification of fatty acids flowing to the liver to elevate postprandial TG synthesis.

Critique

- Administration of test carbohydrates by bolus in the absence of other dietary nutrients is not representative of the way humans take in sugars. Humans typically eat complex meals consisting of protein, fat and carbohydrate *together*.

Bolus administration would be expected to give exaggerated results.

- To their credit the authors do compare various glucose:fructose blends, however some of the data (Table 2) are inconsistent: It is puzzling that there is so little difference in morning fractional and absolute lipogenesis, and in post lunch triglycerides between 50G:50F and 25G:75F variables. There also is little distinction between these variables for total glucose, total insulin and fatty acids. This is at odds with historical data, which show distinct, titratable differences in metabolic parameters vs. fructose dose.
- Though the experiment is presented as being more representative of real life - ie, the bolus is presented as mixed sugars - it is actually quite high in fructose. When fructose calories from the morning bolus are summed with those from lunch (Table 1), the 50G:50F variable received 22% of calories as fructose, while the 25G:75F variable received 29% of calories as fructose - two and three times the typical dietary exposure in just two meals. Thus, a health risk for the general public should NOT be generated from these data.
- The authors acknowledged that the 100G:0F bolus stimulated a lower rise in lipogenesis in the current study (8%) than in their previous study (23%). The peak in lipogenesis after both fructose treatments (50:50 and 25:75) was 17% — twice the glucose treatment in the current study, but substantially lower than the previous one. The magnitude of the lipogenesis seems somewhat dependent on whether the sugars delivery solution also contains fat and protein (observation made in comparing present with higher TG levels in past experiment). Fat and protein were absent in the present study, resulting in fewer calories fed. It is not above researchers to manipulate protein and fat to produce favorable results.
  It matters a great deal whether the current or previous glucose control value is correct: viewed against the current value, fructose appears to have an effect; viewed against the previous value, fructose has no unique effect on lipogenesis. This seems a serious inconsistency and the results must be discounted until one or the other glucose value is validated.
- Human metabolism can be rather simplistically viewed as a factory with many assembly lines producing many possible products. It seems reasonable that if one assembly line is primed more with raw materials than another, it will be able to make product faster. It also seems reasonable that if the assembly lines are shut down for a period of time (between the bolus and lunch), the one best primed at the next startup (lunch) will begin making product the fastest. This is, in essence, what Parks has done. With an exaggerated bolus of fructose, she has primed the fructose-to-lipid pathway - a more focused and direct route to lipids than the glucose-to-lipid pathway, which has more controls and more optional pathways.
- Finally, the small sample size — only six subjects — is another significant limitation. Because of the admitted "metabolic flexibility" of human metabolism (last line, p.1044), individual variations in lipogenesis rates with different sugars blends could appreciably skew experimental results in so small a sample size.