Fructose metabolism and neural correlates of food reactivity in obese children

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Background

- Obesity rates in adolescents have doubled since 1970, with nearly 21% being diagnosed as clinically obese.¹
- Studies of children have found a relationship between excessive consumption of sugar-sweetened beverages (SSB) and obesity.²
- Consumption of fructose has increased 22% since 1970.
  - Adolescents are heavy consumers of SSB sweetened primarily with high fructose corn syrup (HFCS; 55/45).³,⁴
  - Adolescents ingest upwards of 100 grams per day in such beverages, 43% of their total daily caloric intake.⁴
Why Fructose?

- Fructose has similar metabolic and detrimental effects on the brain and gut as does ethanol.4
- Lipogenesis,5 gluconeogenesis,6 hepatic steatosis and inflammation,6,7 and stimulation of the neural reward circuit.8,9
- Children are particularly sensitive to sweet foods and demonstrate greater reward sensitivity for high sugar foods.10
- Obese children appear to have greater reward sensitivity to sugar than lean children.10

Neural Reward Circuit

a priori Hypothesis

The metabolic profile of fructose may play a key role in obese children’s development of addictive-like eating and thus, the development and perpetuation of obesity in a subset of at-risk children.

Purpose

To determine how the metabolic profile of fructose affects neural reward and cognitive control circuits in obese children and how that relates to phenotypic traits of addictive-like eating.
Study Design

- Cross-sectional
- 10-16 year olds
- Clinically obese
- Healthy otherwise
- 3 study visits to the CRC
- Assented & consented
- Fructose dose: 1 gm/kg of IBW, max 75 gm

Methods

Screening & Phenotypic Measures

Fructose Drink -> Serial blood, breath, and urine samples

Fructose Drink -> fRMI

Food Stroop

Go/No-go DD

SST

Measures of Addictive-Like Eating

- Yale Food Addiction Scale 11 – child version (YFASc)
- Food addiction symptom count and diagnostic threshold
- Food craving inventory 12 (FCI)
- Power of Food Scale – child version 13 (c-PFS)
- Appetitive responsiveness in food abundant environments

Yale Food Addiction Scale-child

- Loss of Control
- Inability to Cut Down
- Large Amount of Time Spent
- Tolerance
- Withdrawal
- Given up on Activities
- Clinically Significant Impairment or Distress

3+ symptoms plus Clinical Sig

=> Food addiction
Findings

- N=16
- 2 non-completers
- 3 scored as food addicted
- 4 scored with addictive-like eating (YFASc) but did not meet full criteria for FA
- 9 scored without addictive-like eating.
- 8 females/8 males
- 1 Black; 2 Native American; 13 White
- Ages 10-16
- Mean BMI 36.7
- Mean fructose dose 59.5 gm.
  - ~2 cans of soda
  - <½ Big Gulp
  - <½ Slurpee

Findings (n=14)

- Addictive-like eating correlated (YFASc) (p<.05) with greater appetitive responsiveness (c-PFS) and greater craving of carbohydrates and overall cravings independent of body mass index (BMI), age, and gender.
- BMI scores were significantly (p<.02) related to the frequency that the subjects “gave in” to their cravings and ate fats, carbohydrates, and sweets.
- No correlation was found between fructose levels, YFASc, BMIz score, gender, and age.
- No correlation was found between YFASc and ventral striatal response to oral fructose load.

Findings

Serum fructose, but not glucose, peak concentration (Cmax) was significantly and positively correlated with activation in the ventral striatum in response to the food cues (p<.001).
Findings

Fructose, but not glucose, time to peak (Tmax) was negatively correlated with the striatal response to food cues (p=.023).

Conclusions

- The VS response to fructose demonstrated a pattern of effects that is consistent with abuse potential of drugs leading to dependence (e.g. alcohol, cocaine).
- The lack of VS response to glucose suggests that different sugars affect neural reward mechanisms differently.
- Ingestion of fructose may have an important role in shaping the brain’s reward response to food stimuli.

Future Directions

- Replication using HFCS [55:45] that is more consistent with the general populations consumption of fructose.
- Examining the effect of refined sugars on the “gut–brain” axis to better understand neurobiological mechanism contributing to obesity in children.

Limitations

- Sample size
- Lack of lean controls
- No baseline fMRI
- State v. Trait???
Research Team

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References