A Matter of Taste: the Brain and Obesity

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“Today’s kids may become the first generation in the history of man to have a life expectancy projected to be less than that of their parents.”

David Katz MD, Yale University
“It is a lot easier to lose weight than to keep weight off.”

“You don’t crave broccoli, and our generation has grown up craving a Big Mac.”
Portion Distortion

Which portion is the right one?

--

Portion Distortion

What you're served

What's one serving

Everyday excess

- 12 oz. cheeseburger, French fries, lettuce, 1/4 of large bag, 1,300 calories, 63 grams fat
- 24 oz. chocolate milk, 1/4 of large bag, 2,100 calories, 170 grams fat
- 24 oz. chocolate milk, 1/4 of large bag, 1,300 calories, 63 grams fat

DID YOU KNOW?

- A typical McDonald’s Big Mac weighs 12 ounces.
- A typical McDonald’s Big Mac contains 900 calories.
- A typical McDonald’s Big Mac contains 40 grams of fat.
- A typical McDonald’s Big Mac contains 20 grams of sugar.
- A typical McDonald’s Big Mac contains 9 grams of saturated fat.
- A typical McDonald’s Big Mac contains 28 grams of sodium.

Johns Hopkins Medicine
The Problem

*US News & World Report
Super-sized America

*US News & World Report
Guess how many calories?

- Grande Mocha Frappuccino with whipped cream: 420 Calories
- Toffee Crunch Bar: 430 Calories
- 1 slice of Iced Lemon Pound Cake: 500 calories
Thirty percent of teenagers and forty percent of adults eat fast food on a daily basis.

Fast food adds 187 kcal/day to caloric daily intake.

Over 50% of Americans consume 870 cans of soda (sugar drinks) a year.

America’s Meal: Fast Food

CHILDHOOD OBESITY
Because healthy food just plain sucks
Strategies to Treat Obesity

Traditional weight loss methods have limited effectiveness and sustainability.

In contrast, bariatric surgical procedures produce significant and durable weight reduction.
Long-Term Results: Medical Therapy

Patients regain all of their lost weight (or even more)
Long-Term Results: Surgical Therapy

Patients lose weight and keep it off

O’Brien, P.E. et al. Obesity Surgery, 16, 1032-1040
Current Bariatric Surgical Procedures

Vertical Sleeve Gastrectomy

- Restriction

Roux-en Y gastric bypass

- Restriction and malabsorption
How Does Bariatric Surgery Cause Weight Loss?

• Not everyone who undergoes bariatric surgery achieves sustained weight loss. Why?
• While restriction and malabsorption are the main effects, other mechanisms need to be explored.
• Bariatric surgical patients constitute a uniquely valuable resource to determine the underlying mechanisms that account for feeding behavior and weight loss.
Clinical Observations

- As a clinician, I have observed that many of my GBP patients develop an aversion to sweets and high-fat foods immediately following surgery.
- The aversion is not permanent and often returns to a pre-surgical pattern within 1 year.
- Food aversions are less pronounced in VSG patients than in GBP patients.
Background and Significance

Regulation of food has two control mechanisms:

**Homeostatic System**: hormonal regulators of hunger and satiety (leptin and grehlin), involves hindbrain and hypothalamus

**Hedonic system**: (pleasure) Reward centers of the brain mediated by dopamine and mu opioid receptors, involves midbrain, striatum and hypothalamus.

Food reward thought to have 2 components:
- **Food ‘liking’** – taste of food
- **Food ‘wanting’** – anticipation of food/food craving
Preliminary Data

- Five participants underwent PET scans pre-op and 6 weeks following gastric bypass surgery.
- Results: Sensitivity to dopamine appeared to increase following gastric bypass surgery.
- The increase in sensitivity appeared roughly proportional to the amount of weight loss.

Steele et al. Alterations of Central Dopamine Receptors Before and After Gastric Bypass Obes Surg. 2010 Mar;20(3):369-74
Changes in Dopamine Receptor Availability After Gastric Bypass

Avg. of ant. and post. putamen, caudate, ventral striatum

pre-op

6 wks post-op

Avg. of ant. and post. putamen, caudate, ventral striatum
“Neurobiological Alterations Induced by Bariatric Surgery: Taste Response and its Relationship to Weight Loss”

• Does bariatric surgery really alter a patient’s taste preferences and cravings?
• If so, is this one of the mechanisms of successful weight loss?
Hypothesis

Altered taste perception in bariatric patients leads to decreased liking and wanting of high caloric foods, which in turn leads to improved eating habits and consequent up-regulation of dopamine receptors.
Objectives

• How does taste preference change after a weight loss intervention? – Pre-intervention compared to 2 weeks, 3, 6, and 12 months post-intervention

• How does blood flow to reward centers (in response to tastants) in the brain change after a weight loss intervention? – Pre-intervention compared to 2 week and 3 month post-intervention – Blood flow assessed using blood-oxygen-level-dependent (BOLD) functional MRI (fMRI) signal activity

Taken together, these aims will assess the neurobiological alterations in taste preference induced by weight loss interventions
Taste Preference Assessment

- Pilot study with three weight loss interventions
  - 20 gastric bypass patients
  - 20 sleeve patients
  - 20 weight management patients
  - Current status: 21 of 60 patients recruited

- Twelve taste stimuli (tastants) of varying sweet and fat content are given to each participant in random order

- The patient chooses the tastant they prefer best, prior to weight loss intervention and then at 2 weeks, 3, 6 and 12 months following the weight loss intervention
Rating the Tastants

- 12 varying concentrations of milk and sugar (blinded)
- Participants asked to rate according to their preference on a 100 mm Visual Analog Scale

May 11, 2016
Visual Analog Scale for Rating

Q8. Please rate tastant 1C.

0  100

Q9. Please rate tastant 2A.

Q10. Please rate tastant 2B.
Assessing Blood Flow to Reward Centers

• How does fMRI of reward regions during sweet and fat consumption change from before to after a weight loss intervention?

• How does fMRI of reward regions during presentation of visual food stimuli change from before to after a weight loss intervention?
Functional MRI and Gustometer
Case Study

- 56 yr old woman, 220 lbs, BMI of 38
- Medical co-morbidities: type 2 diabetes, hypertension, reflux, and asthma
- Pre-op taste preference: heavy cream and 15% sucrose
- Post-op preference: skim milk and 5% sucrose
- Weight loss at 3 months: 40 lbs
  - all medical comorbidities resolved
The TASTE Paradigm
Now, get ready for Run #2.
Good luck…

Remember to push the button for **broccoli**, but not for **ice cream**.
Food Cue
Summary

• Bariatric surgery, while highly effective overall, works better in some patients than others.

• The mechanisms responsible for weight loss in bariatric surgery are incompletely understood, and probably involve changes in taste preference and food craving.

• We are assessing changes in taste preference and food craving, and the accompanying changes in brain fMRI activity in patients undergoing bariatric surgery and non-surgical weight loss.
Future Directions

• Combine PET and fMRI imaging modalities to better define and understand the neurobiologic alterations that occur following bariatric surgery.

• Tie together other mechanisms that may account for successful weight loss:
  – Genetic work (presently completing a retrospective genetic study in GBP patients)
  – Gut-brain hormonal axis

• Overall goal is to better predict which patients will succeed or fail with a given weight loss intervention, and to target therapy to the individual patient
David and Lincoln – Back in Their Day
David and Lincoln – In Present Time
The Real Answer to this Public Health Problem

“When meditating about a disease, I never think of finding a remedy for it but rather a means of preventing it.”

Louis Pasteur
The End of the Fast Food Era?