Highly Palatable Foods: The Brain Reward Pathways and Connections to Overeating

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Agenda

- Excessive food consumption and the brain’s pleasure pathways
- Obesity and reduced food reward
- Connection between the pleasure pathways, habits, and addiction
- Drives for highly palatable foods
- Brain reward circuitry and stress related food intake
- Treating obesity by changing the brain
Global Obesity Epidemic

World Health Organization Estimates

2005
1.6 million overweight & 400 million obese
20 million children under 5 y/o overweight

2015
2.3 million overweight
700 million obese adults

Health Risks
Cardiovascular disease
Diabetes
Osteoarthritis
Some cancers

Causes
Too many calories
Not enough exercise
The Brain is Reward Driven
Brain Pleasure Centers

- Reward circuit
  - Ventral tegmental area (VTA)
  - Nucleus accumbens
  - Septum
  - Amygdala
  - Prefrontal cortex
Brain Pleasure Centers

Higher dopamine levels = higher gratification

Pleasure perception

“Incentive value” and “pleasure seeking”

Gratifying behavior

Memory
Obesity & Reduced Food Reward
Brain Pleasure Centers

What do the colors mean?

**RED**
High dopamine
Normal pleasure & interest

**YELLOW**
Medium dopamine
Difficult feeling joy or pleasure

**GREEN**
Low dopamine
Lack of pleasure

- Lower dopamine D2 receptors in obese than control subjects
- Lower D2 make the obese individual less sensitive to reward stimuli
- Obese similar to drug addicted

Wang et al., Lancet 2001
Wang et al., Lancet 2004

Brookhaven Science Associates
U.S. Department of Energy
BRAIN REWARD CENTER

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Genetic Variations

- A genetic variation may be the cause in some obese
- Association between the Taq 1 A allele and lower levels of dopamine D2 receptors

Felsted JA, et al., *The J Neurosci,* 2010
Connection Between Pleasure Pathways, Habits, and Addiction
The Brain is Plastic

- The brain is plastic, meaning it can change
- Experience-dependent plasticity
- Learning occurs in the brain through the process of strengthening or weakening synapses
- The brain will be modified by the repeated act of overeating
Memories, Learning & Conditioning

• The brain creates memories about eating behaviors

• Glutamate, an excitatory neurotransmitter, plays a role in synaptic plasticity
  – Involved in cognitive functions such as learning and memory
  – Important in storing information about eating experiences, such as pleasure felt when eating.

• Cues in the environment can “trigger” memories of the pleasurable experience.

• Pleasurable memories can lead to cravings and relapse
Addiction

• Pleasure circuits are “hijacked”

• There is a cascade of pleasure neurotransmitters
  – serotonin, dopamine, enkephalin, and GABA

• With repeated abuse the amount of neurotransmitter released in response to normal stimuli is reduced

• More substance is needed to get the same sense of pleasure
Drives for Highly Palatable Foods
**Why Don’t We Binge on Broccoli?**

Low calorie foods lead to little activation in the brain reward centers

High calorie foods with high reward lead to significant activation in the brain reward centers

Killgore et al., 2003
# Neurotransmitters Involved in Food Intake Regulation

<table>
<thead>
<tr>
<th>Stimulate Feeding (usually decrease energy expenditure)</th>
<th>Inhibit Feeding (usually increase energy expenditure)</th>
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<tbody>
<tr>
<td>• Anandamide</td>
<td>• Cholecystokinin (CCK)</td>
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<tr>
<td>• β-endorphin</td>
<td>• Corticotropin-releasing factor (CRF)</td>
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<tr>
<td>• Dynorphin</td>
<td>• Dopamine</td>
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<td>• GABA</td>
<td>• Insulin</td>
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<td>• Ghrelin</td>
<td>• Leptin</td>
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<td>• Growth hormone releasing hormone</td>
<td>• Neurotensin</td>
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<tr>
<td>• Neuropeptide Y</td>
<td>• Thyrotropin-releasing hormone</td>
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<tr>
<td>• Norepinephrine</td>
<td>• Melanocyte-stimulating hormone</td>
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Are We Addicted to Sugar?

- Behavioral and neurochemical changes in the brain resemble those seen in after taking drugs.

- Behavioral patterns after sugar-binging
  - Withdrawal, craving, and relapse

- Neurochemical changes after learning to binge on sugar
  - Binging on sugar triggered a surge of dopamine in the nucleus accumbens
  - Fewer dopamine receptors than before and more opioid receptors
    - Dopamine and opioid systems are involved in reward and motivation and are important in controlling wanting and liking something.

Are We Addicted to Sugar?

• The pleasure from the sweet taste of sugar-dense foods and beverages initially motivates over-consumption

• Sweet taste may be more rewarding and possibly more addictive than cocaine

• Choice between water sweetened with saccharin and intravenous cocaine - 94% of the animals preferred the saccharin

• Supra-normal stimulation of sweet receptors by sugar-rich diets could create a supra-normal reward signal in the brain

• Self-control mechanisms could be overridden and lead to addiction

Lenoir et al., *PloS one*. 2007
Does Eating High Fat Stimulate Eating?

- Animals fed a small HF meal early in the day ate more calories throughout the day compared to those fed a low fat meal

- TG levels increased 2-3 times in the HF group

- No changes in leptin or insulin levels

- Expression of orexigenic peptides were increased
  - galanin
  - orexin

Gaysinskaya et al., *Physiol Behav.* 2007
Does Eating High Fat Stimulate Eating?

- Maternal HF diet exposure lead to changes in rodent offspring following weaning
- In as little as two weeks of exposure to a HF diet, offspring increased
  - intake of calories
  - body weight
  - a stronger drive for fat intake
  - brain peptides that are stimulated by fat
- Brain systems involved in reward and palatability can each stimulate and be stimulated by the intake of diets rich in fat

Chang et al., *Neuroscience*. 2008
Brain Reward Circuitry & Stress Related Food Intake
UCSF Department of Psychiatry - Reward Based Stress Eating Model

- Relationship between stress, eating, and potential neuroendocrine mediators

- Cortisol and the reward circuitry affect motivation for calorically dense food intake

- Reward value of food may be influenced by cortisol via neuroendocrine & peptide mediators

Epel ES. *Physiol Behav*, 2007
Stress, Opioids & HPA Axis

- Stress stimulates hypothalamic-pituitary-adrenal (HPA) axis activity
  - Intake of comfort foods reduces HPA axis activity

- Stress can stimulate endogenous release of opioids

- Opioids (+) excessive intake of palatable food
  - Suppress brain mechanisms responsible for terminating eating

- Sensation of pain reduced by sucrose

- Withdrawal symptoms from opiates relieved by sweets
Treating Obesity by Changing the Brain
Strategies Aiming at Improving Dopamine Function

Comprehensive behaviorally based programs designed to “re-wire” the brains reward pathways can be an effective way to reduce food cravings and overeating.
Treating Obesity by Changing the Brain

• A variety of professionals along with a variety of formats might be incorporated

• Treatment should be individualized and incorporate a variety of cognitive and behavioral tools
  – decrease the reward value of the food or behavior
  – increase the reward of the new positive behaviors
  – reduce the power of triggers
  – strengthen new neural circuits by learning new habits
Treating Obesity by Changing the Brain

- Analysis of stimuli, situations, and cues that trigger out-of-control-eating is critical
  - Initially avoiding certain triggers or foods may be necessary

- Stress management tools should be incorporated daily to weaken neural circuits that promote stress
  - Exercise
  - Mindfulness meditation
To weaken the strong neural circuits that favor overeating, cognitive and behavioral tools must be practiced repeatedly.
Questions & Answers

Thank You!