Modulators of Orbitofrontal Activation in Response to Food Stimuli

Insights on Obesity and Drug Addiction from Brain Imaging

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Introduction

- It has been hypothesized that addictive drugs activate the same brain reward pathways involved in the control of normal appetitive behavior.

- Food is inherently rewarding.

- Rewarding properties of food are determined by:
  - body’s nutritional needs
  - physical properties of food (appearance)
  - inherited traits
  - Other factors ?
Objective

- To clarify the neurobiological mechanisms by which body weight, mood and age may influence appetitive response.

- We presented healthy, normal-weight adolescent and adult females with color photographs of foods differing in fat-content/calorie-density (i.e., high-reward or low-reward) while they underwent blood oxygen level dependent (BOLD) functional magnetic resonance imaging (fMRI).
Overview

I. Adult fMRI Study of Food
   – Orbitofrontal activation and Affect
   – Orbitofrontal activation and BMI

II. Adult vs. Adolescent fMRI Study of Food
   – Orbitofrontal activation and Age
Food Study: Adults
Study Design

Subjects
15 Healthy normal weight adult women
16 Healthy normal weight adolescent females.

Clinical Scales and Measurements
Structured Clinical Interview for DSM-IV (SCID)
Positive and Negative Affect Schedule (PANAS)
Body Mass Index (BMI)
\[
\text{BMI} = \left( \frac{\text{Weight (lbs)}}{\text{Height (in)}} \times \text{Height in} \right) \times 703
\]
Challenge Paradigm

Subjects were scanned between 1500 - 1900 hr.

Total calorie consumption on scan day was determined for each subject.

Subjects were asked to view visual stimuli and told to remember them.

Conditions:

1. High Fat Food Items
2. Low Fat Food Items
3. Food-related Utensils
4. Non-food Items
fMRI Paradigm

TIME (sec)

Baseline 30 60 90 120 150

Activation 1 Recovery 1 Activation 2 Recovery 2

0 30 60 90 120 150
Activation in Adults: High Calorie Foods

Activation for high calorie food compared to control condition includes dorsolateral and medial PFC, thalamus and hypothalamus.

Killgore et al., 2003
Activation for low calorie food compared to control condition includes superior temporal gyrus, parahippocampal gyrus and orbitofrontal gyrus.

Killgore et al., 2003
Activation in Adults: High and Low Calorie Conjunction

Activation in common for both high and low calorie food perception includes amygdala, anterior hippocampus and medial PFC.

Killgore et al., 2003
Activation differentiating high calorie and low calorie food includes DLPFC and medial PFC, basolateral thalamus, hypothalamus, and cerebellum.

Killgore et al., 2003
Our results demonstrated significant activation within the limbic system, particularly the hippocampus and parahippocampal gyri, in response to images of food, regardless of the calorie content.

Prefrontal regions were activated when viewing high-fat calorie-rich foods (high reward).
Orbitofrontal Cortex

- The orbitofrontal cortex is critical to appetitive behavior in humans and shows changes in activity that correlate with hunger and satiety.

- It receives afferent projections from a variety of feeding-related areas, including the lateral hypothalamus and multimodal sensory regions.

- These interoceptive and exteroceptive sources of information converge within the orbitofrontal cortex and are evaluated for their reward potential.
ROI Analysis: Orbitofrontal Cortex

Orbitofrontal Cortex
medial orbitofrontal cortex: inferior, middle, superior
gyrus rectus
olfactory cortex
anterior cingulate gyrus
insula cortex

Killgore & Yurgelun-Todd, 2005
Food Study: Effects of Mood
Effects of Mood

- Fluctuations in affect are often associated with changes in food-cravings, but the neural basis for these phenomena is not well-established.

- We examined the relationship between affective state and orbitofrontal brain response to images of food in healthy normal-weight adult women.
Effects of Mood

- When viewing high-calorie foods (high-reward), higher ratings of negative affect were associated with greater activity within medial orbitofrontal cortex.

- When viewing high-calorie foods (high-reward), higher ratings of positive affect were associated with greater activity within lateral regions of the orbitofrontal cortex.
Positive Affect (PA)

High Calorie Foods
Lateral Prefrontal Cortex
“Satiation” Regions

Low Calorie Foods
Medial Prefrontal Cortex
“Hunger” Regions

Negative Affect (NA)

Low Calorie Foods
Lateral Prefrontal Cortex
“Satiation” Regions

High Calorie Foods
Medial Prefrontal Cortex
“Hunger” Regions

Killgore & Yurgelun-Todd, 2006
Effects of Mood

Positive Affect

High Calorie/Fat

Medial Orbitofrontal Cortex

Lateral Orbitofrontal Cortex

Posterior Insula

Low Calorie/Fat

Medial Orbitofrontal Cortex

Posterior Insula

Negative Affect

Medial Orbitofrontal Cortex/ Anterior Cingulate

Posterior Insula

Lateral Orbitofrontal Cortex

Anterior Insula

Killgore & Yurgelun-Todd, 2006
Effects of Mood

- There was an interaction between affective state and the calorie/fat-content of the food images on the pattern of brain activity in appetite-related regions, including the orbitofrontal cortex.

- These findings suggest orbitofrontal response may be associated with the commonly reported increase in cravings for calorie-dense foods during heightened negative emotions.
Food Study: Body Mass Index
Most studies examining the relationship between food-related cues and activity changes in the orbitofrontal cortex in humans have compared groups that fall outside the normal range for weight or body mass.

We examined the relationship between weight status and reward-related brain activity in normal weight women.
Effects of Body Mass

• There was a negative correlation between body mass index (BMI) and activation in the orbitofrontal ROI for both high-fat and low-fat conditions.

• It was reversed during the food-absent utensil control condition provides further support for the specificity of the findings to visual images of food.
Body Mass Index (BMI)

Adjusted fMRI Response

Anterior Cingulate/Orbitofrontal Cortex

R² = 0.75

Body Mass Index (kg/m²)

R² = 0.57

Body Mass Index (kg/m²)

Killgore & Yurgelun-Todd, 2005
Effects of Body Mass

• With greater body mass, activity was reduced in brain regions important for evaluating and modifying learned stimulus-reward associations.

• This suggests a relationship between weight status and responsiveness of the orbitofrontal cortex to rewarding food images.
Food Study: Adolescents
Objective

- To examine developmental brain changes in reward processing, we measured BOLD signal in healthy adults and adolescents viewing images of high- and low-calorie foods.
Activation in Adolescents: High Calorie Food

High-Calorie Food

Inferior OFG
Hippocampus
Fusiform Gyrus
Subgenual Cingulate
Mid-Temporal Gyrus

SPM \{t\}

Killgore & Yurgelun-Todd, 2005
Activation in Adolescents: Low Calorie Food

Low-Calorie

Inferior OFG

Fusiform Gyrus

Killgore & Yurgelun-Todd, 2005
Activation in Adolescents:
High and Low Calorie Conjunction

Conjunction

Inferior OFG
Hippocampus
Fusiform Gyrus

Killgore & Yurgelun-Todd, 2005
Adult versus Adolescent Differences in Activation: High Calorie Food

Killgore & Yurgelun-Todd, 2005
Effects of Age

Orbitofrontal Activation Increase with Age

Killgore & Yurgelun-Todd, 2005
Effects of Age

- Prefrontal activation seen in adults in response to high-calorie food was absent in adolescents.

- Age-related increases in orbitofrontal activation were seen for high-calorie but not low-calorie images.

- Regions important in reward evaluation and response inhibition show age-related increases in activation.
MR study samples are small and include selective samples of populations (female).

Cultural influences on diet preference.

Signal intensity changes are small, susceptibility effects can cause signal drop out and distortion.

Analyses were focused on selected brain regions.
These results indicate that mood state, body mass and development of the brain circuitry may moderate the reinforcing capacity of rewarding stimuli.

These findings have important implications for clarifying models underlying reward response and for the development of more effective therapies of eating disorders and drug addiction.