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

<u>Subjects</u>

15 Healthy normal weight adult women

16 Healthy normal weight adolescent females.

<u>Clinical Scales and Measurements</u>

Structured Clinical Interview for DSM-IV (SCID)

Positive and Negative Affect Schedule (PANAS)

Body Mass Index (BMI)

((Weight (lbs) / Height (in) x Height in) x 703)

Challenge Paradigm

Subjects were scanned between 1500 - 1900 hr.

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

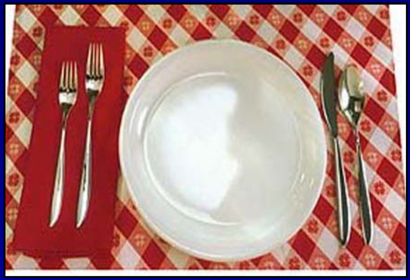
Subjects were asked to view visual stimuli and told to remember them.

Conditions:

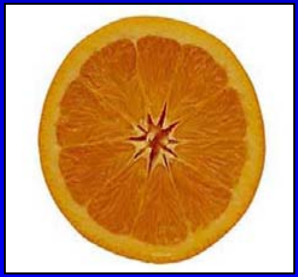
1. High Fat Food Items
2. Low Fat Food Items
3. Food-related Utensils
4. Non-food Items

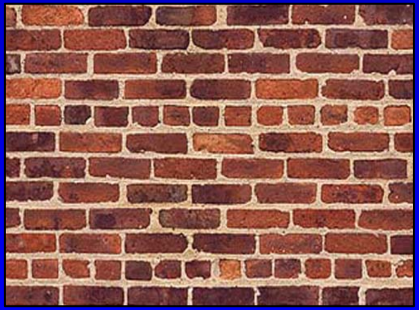




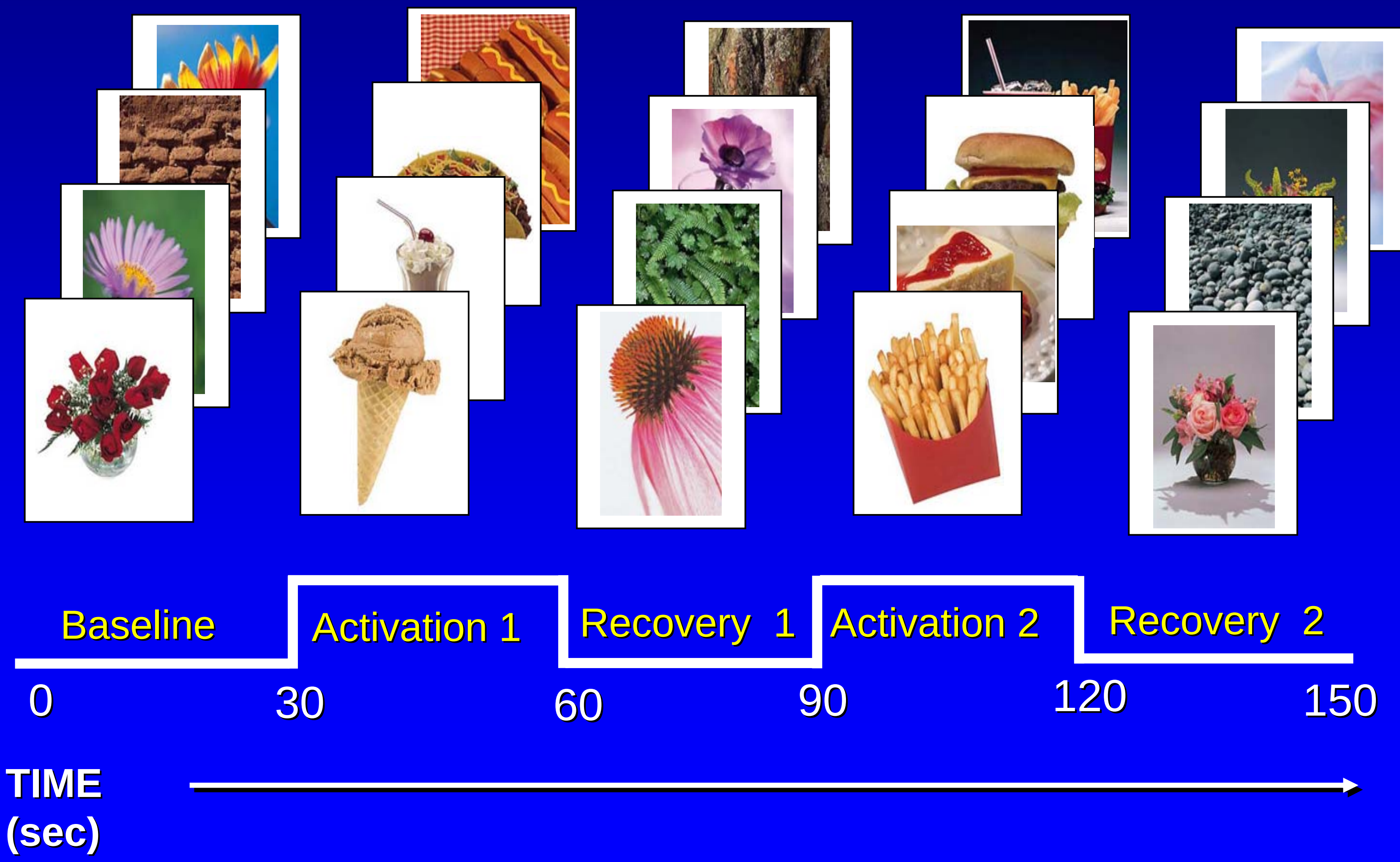




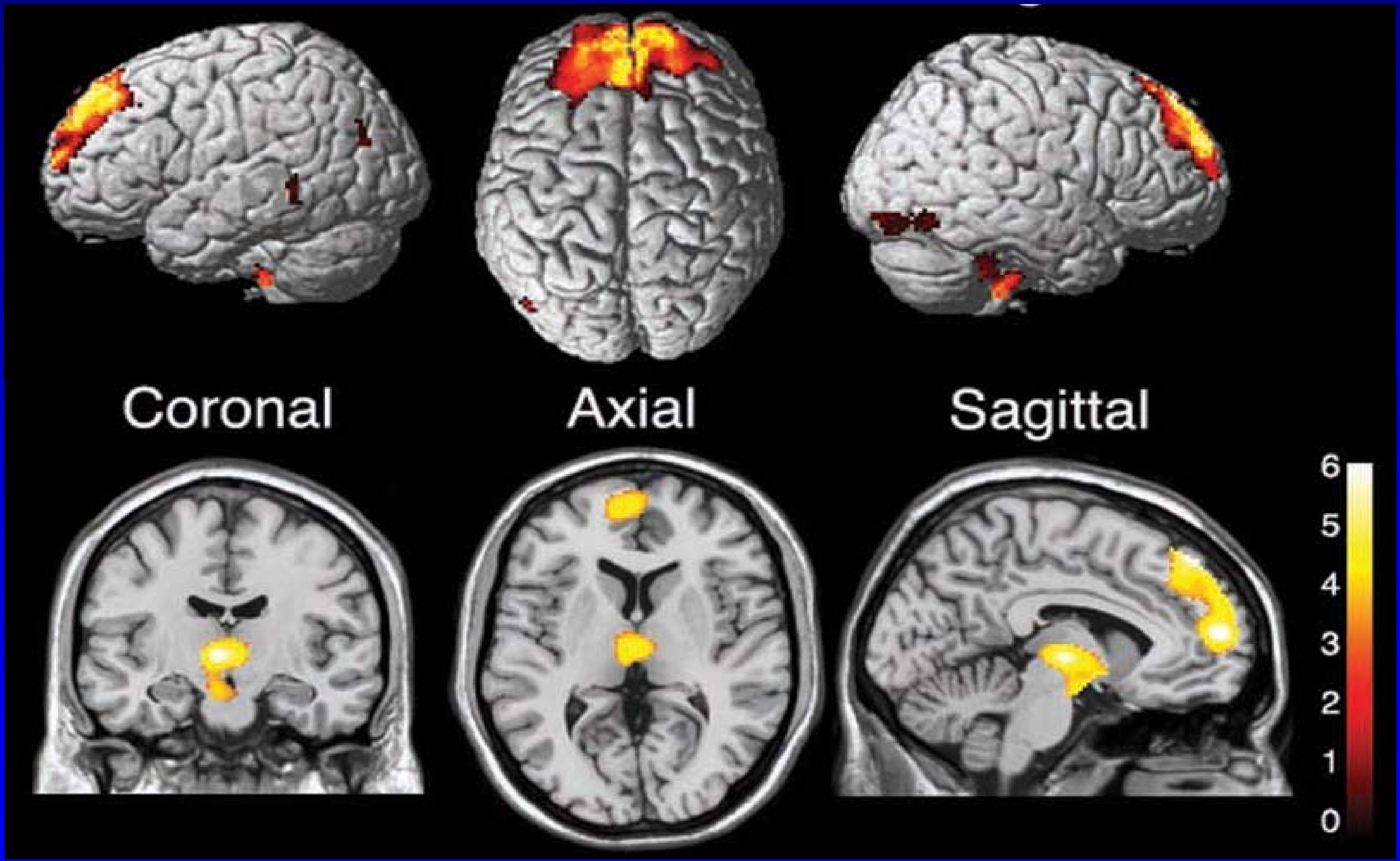



fMRI Paradigm



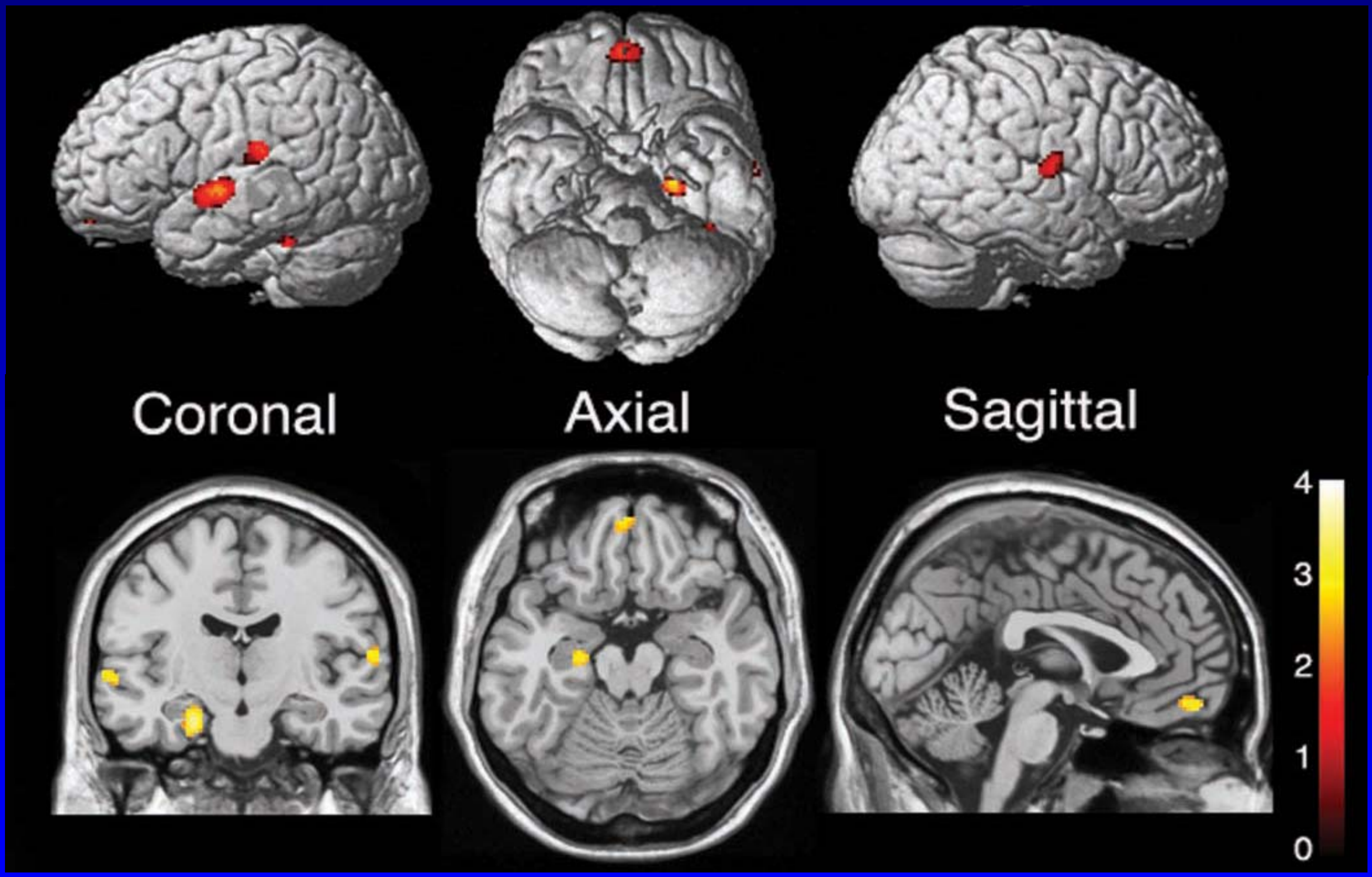
Activation in Adults: High Calorie Foods



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

Killgore et al., 2003

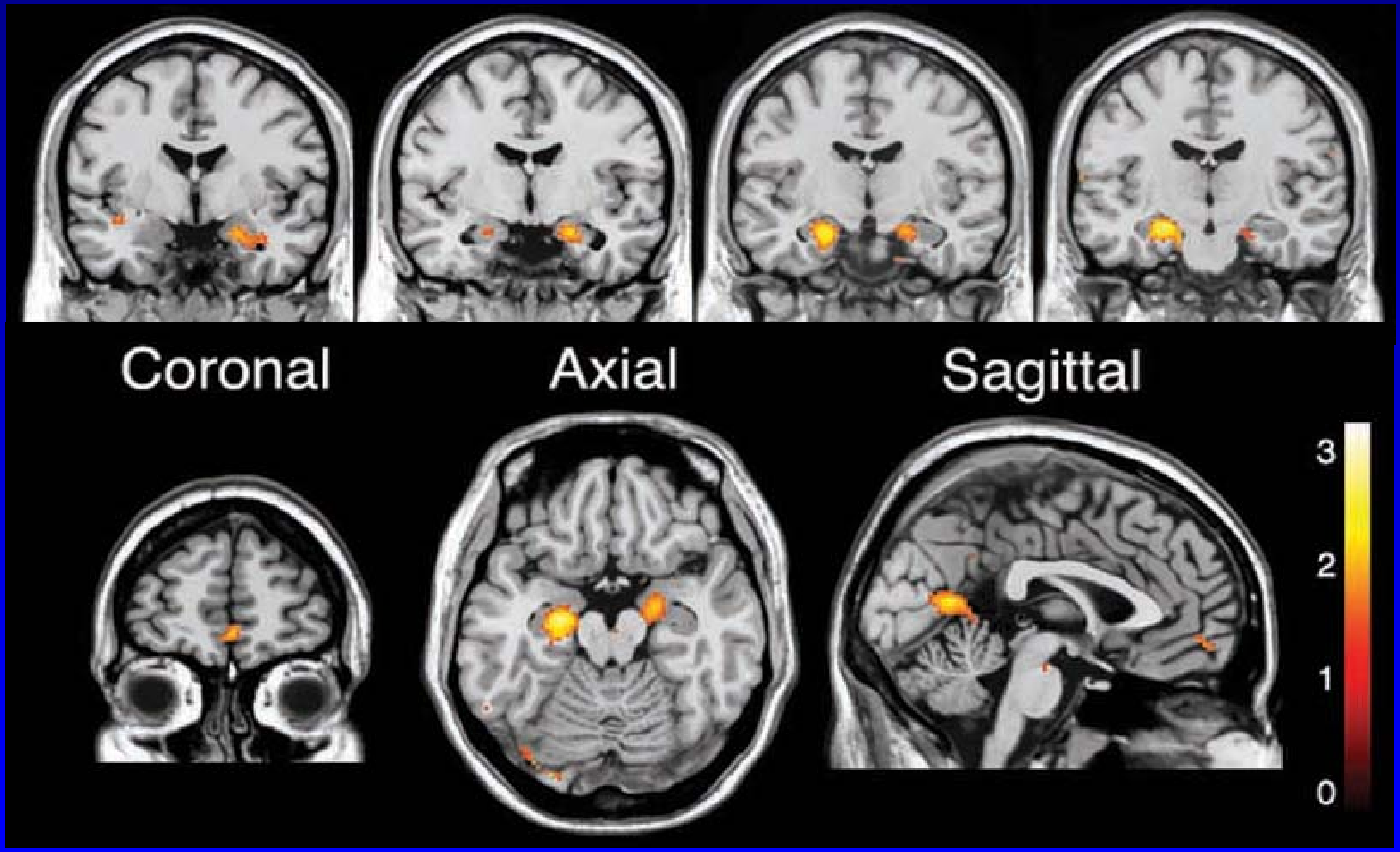
Activation in Adults: Low Calorie Foods



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

Killgore et al., 2003

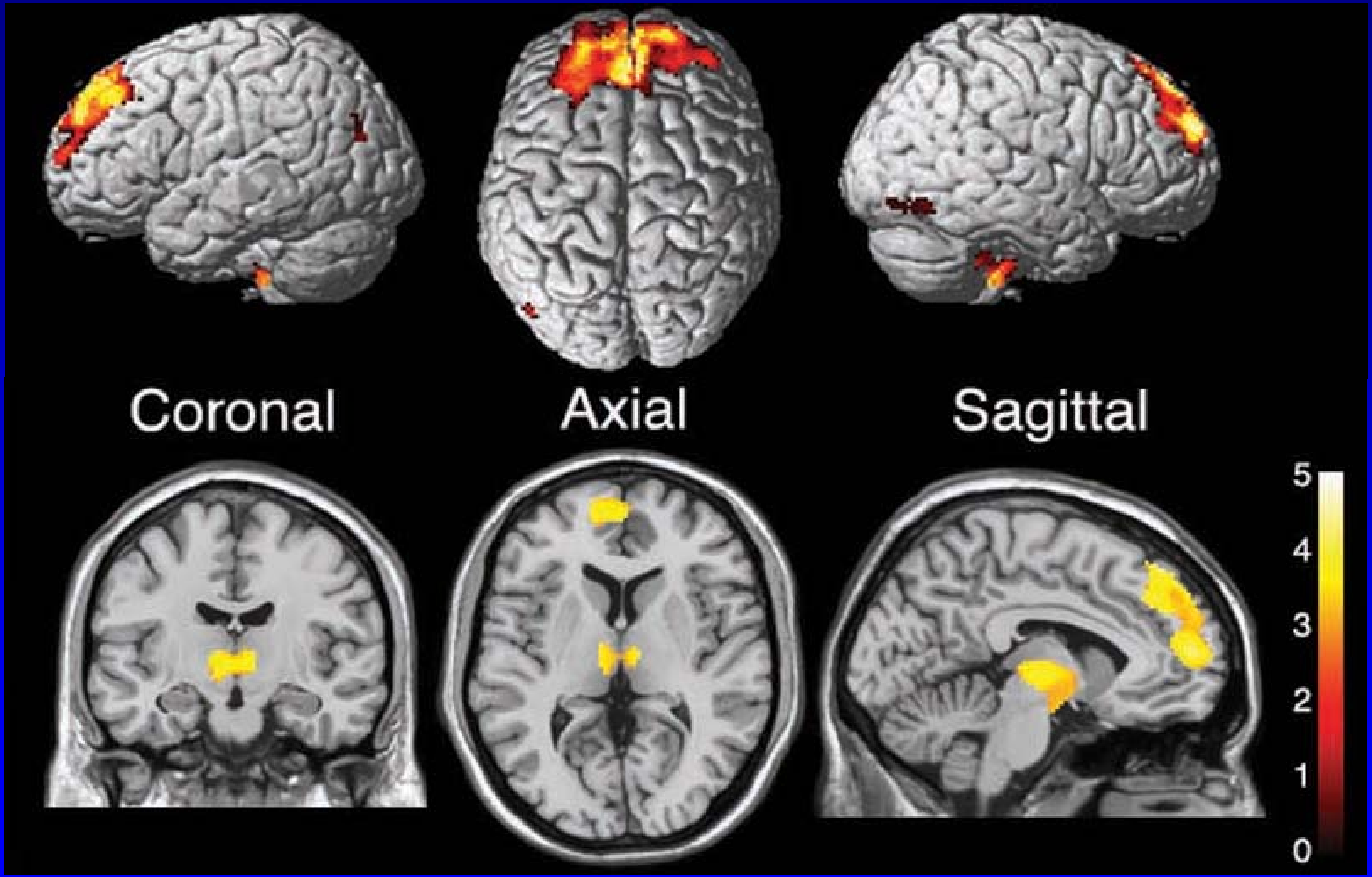
Activation in Adults:
High and Low Calorie Conjunction



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

Killgore et al., 2003

Activation in Adults: High – Low Calorie Foods



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

Killgore et al., 2003

Adult Study of Food

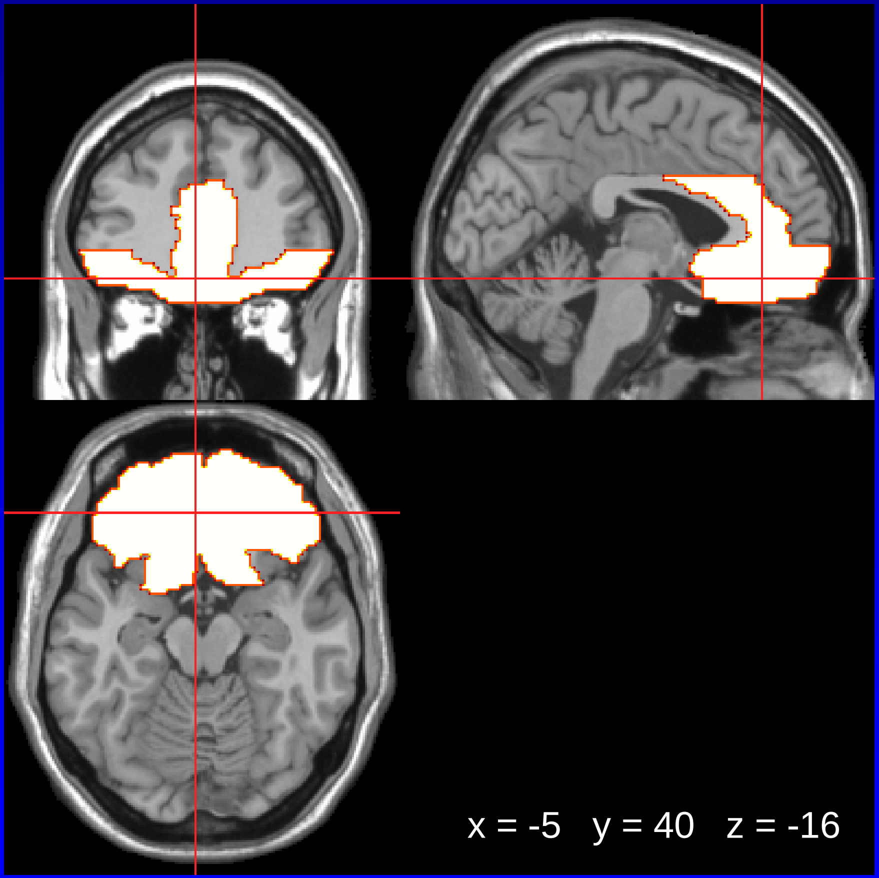
- Our results demonstrated significant activation within the limbic system, particularly the hippocampus and parahippocampal gyri, in response to images of food, regardless of the calorie content.

- 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



<u>Orbitofrontal Cortex</u>

medial orbitofrontal cortex: inferior, middle, superior

gyrus rectus

olfactory cortex

anterior cingulate gyrus

insular cortex

Killgore & Yurgelun-Todd, 2005

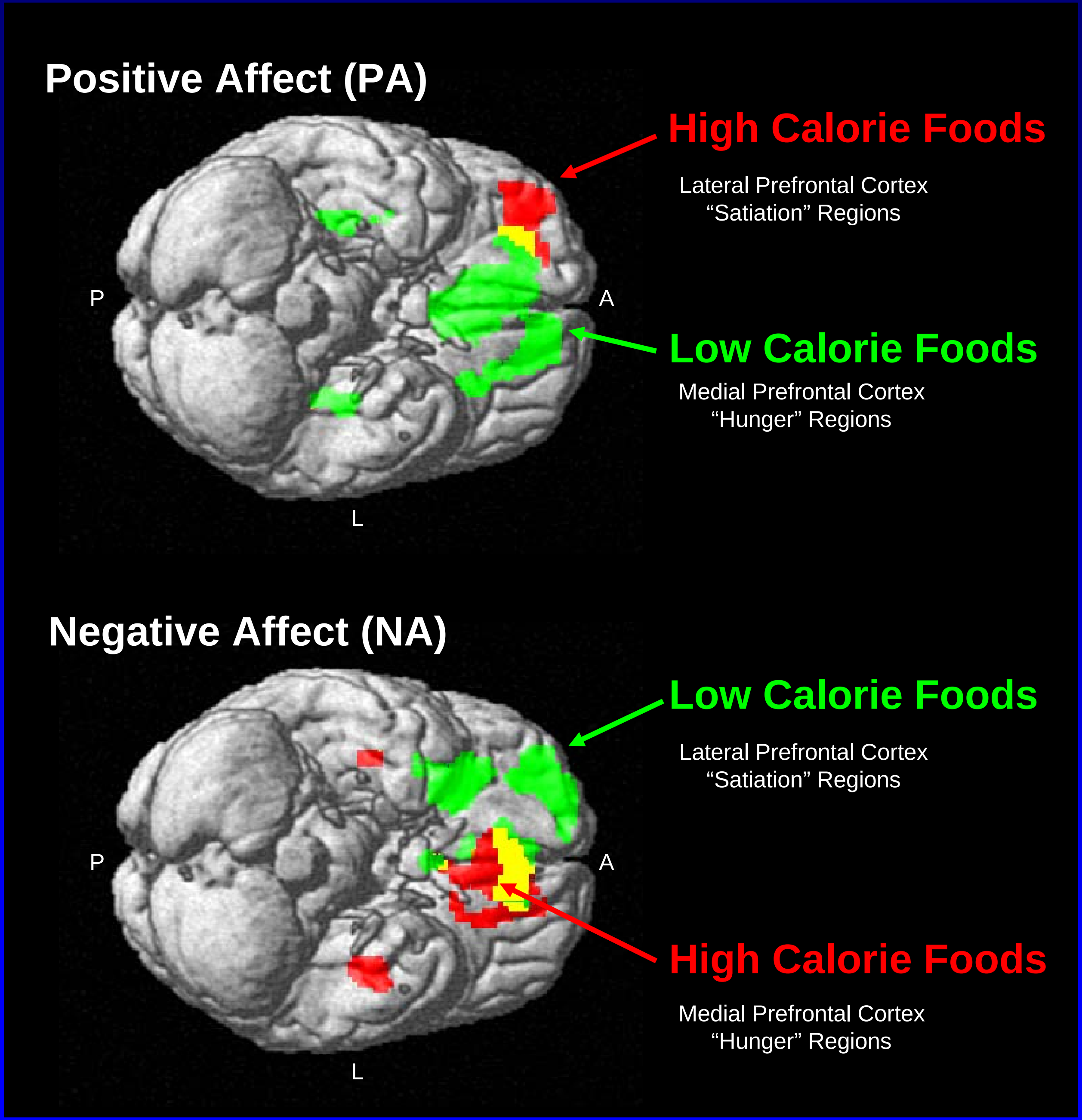
Food Study: Effects of Mood

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.



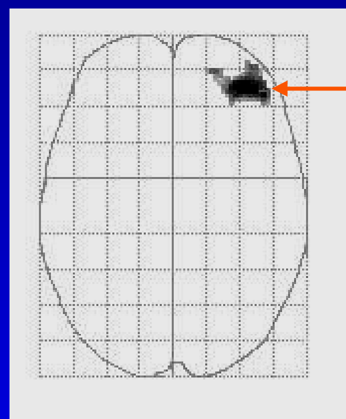
Killgore & Yurgelun-Todd, 2006

Effects of Mood

	Positive Affect	Negative Affect
High Calorie/Fat		
Low Calorie/Fat		

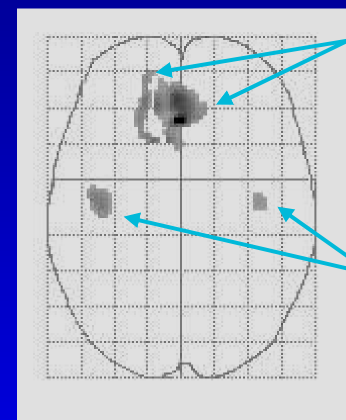
High Calorie/Fat

Positive Affect



Lateral Orbitofrontal Cortex

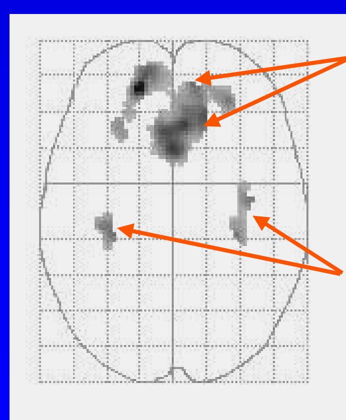
Negative Affect



Medial Orbitofrontal Cortex/ Anterior Cingulate

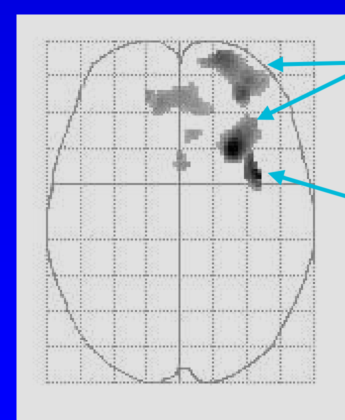
Posterior Insula

Low Calorie/Fat



Medial Orbitofrontal Cortex

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

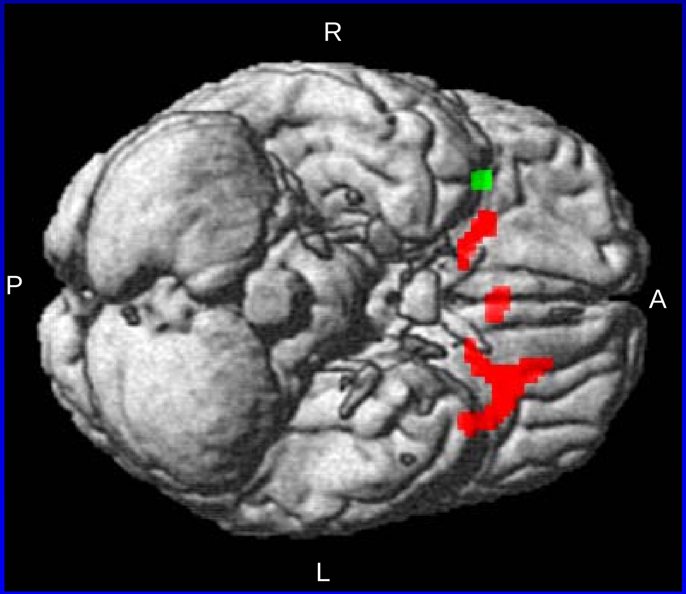
Effects of Body Mass

- 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

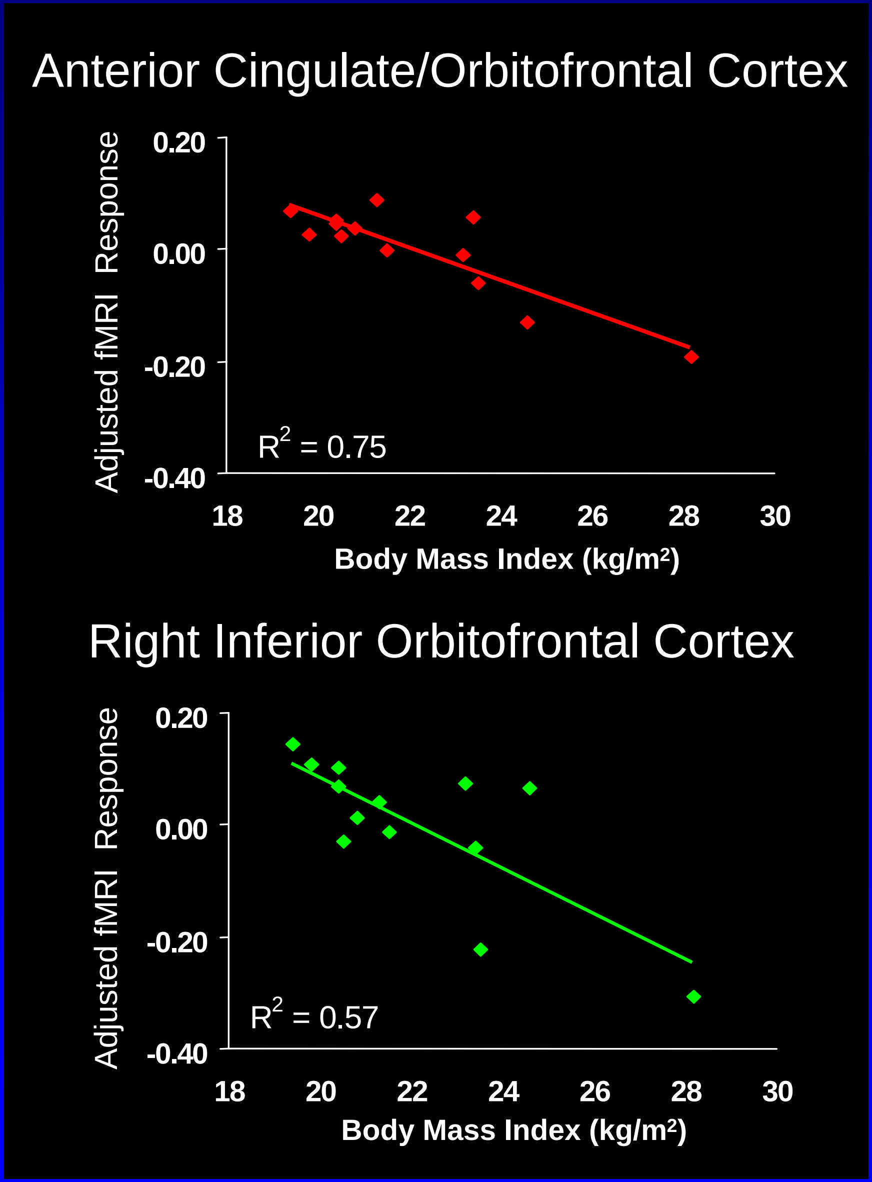
- There was a negative correlation between body mass index (BMI) and activation in the orbitofrontal ROI for both high-fat and low-fat conditions.
- It was reversed during the food-absent utensil control condition provides further support for the specificity of the findings to visual images of food.

Body Mass Index (BMI)



High Calorie/Fat

Low Calorie/Fat



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.

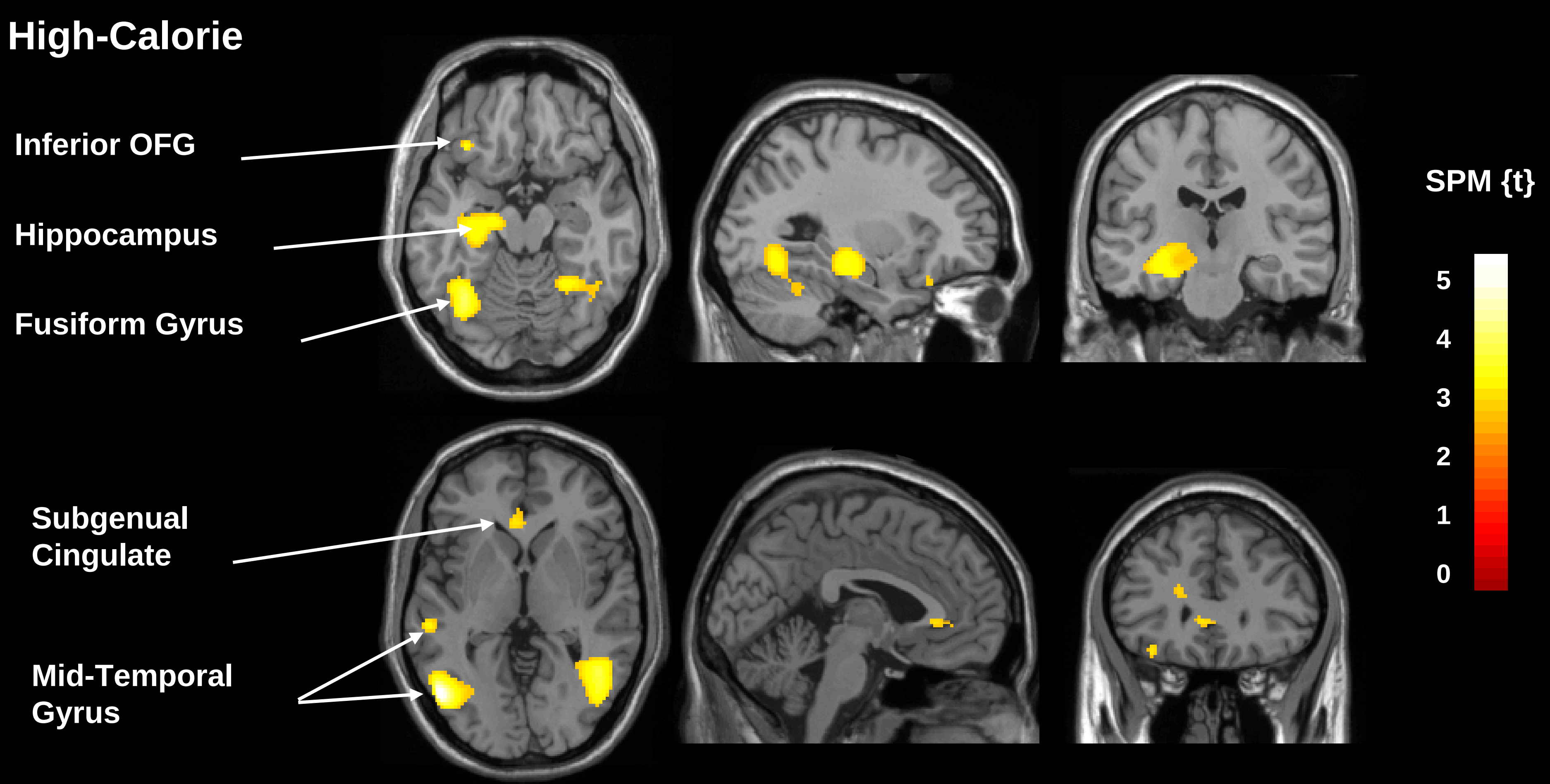
- This suggests a relationship between weight status and responsiveness of the orbitofrontal cortex to rewarding food images.

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



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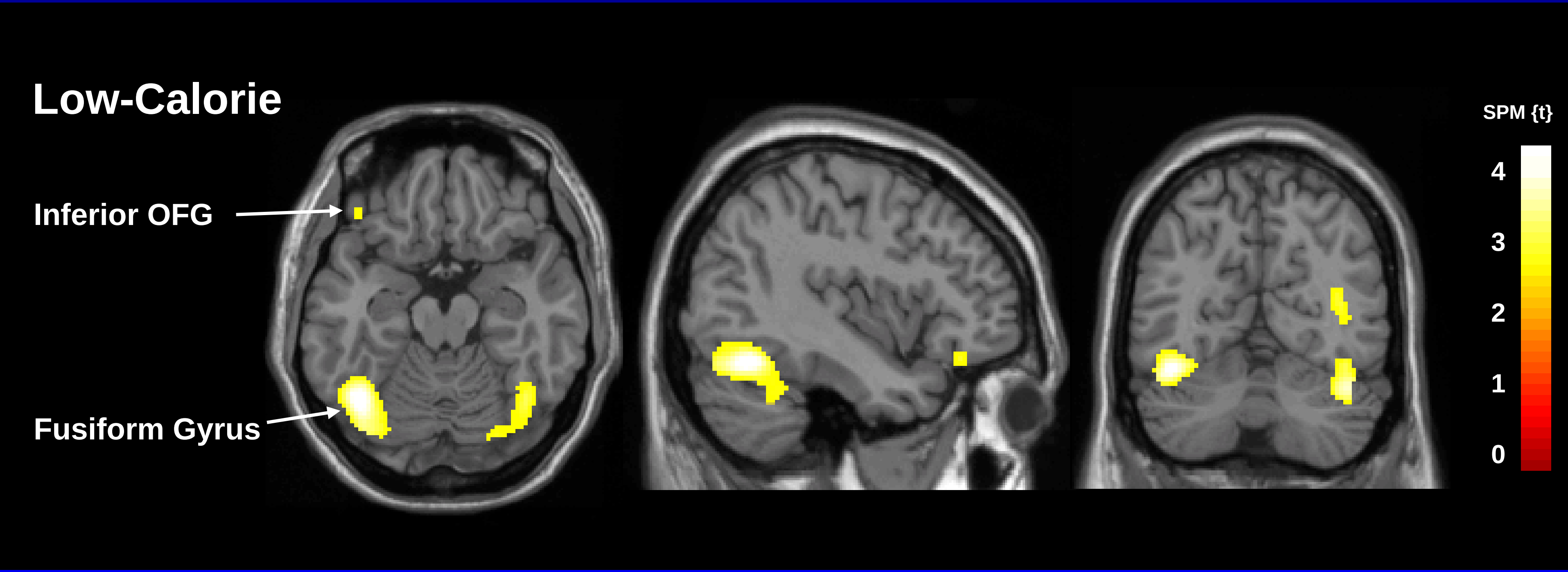
Activation in Adolescents: Low Calorie Food



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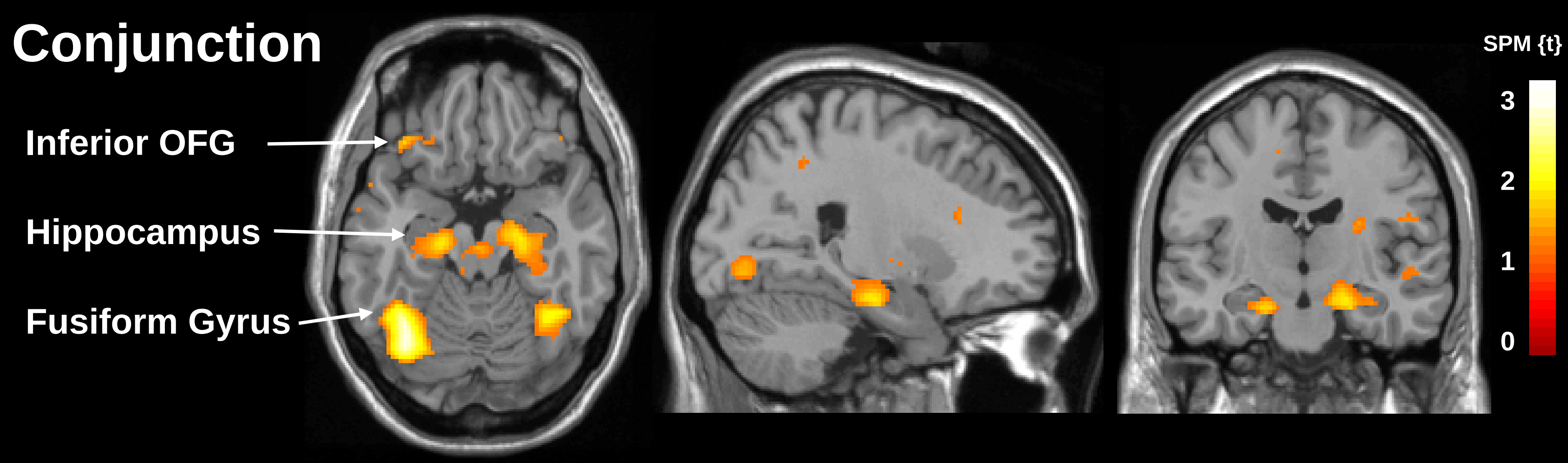
Activation in Adolescents: High and Low Calorie Conjunction



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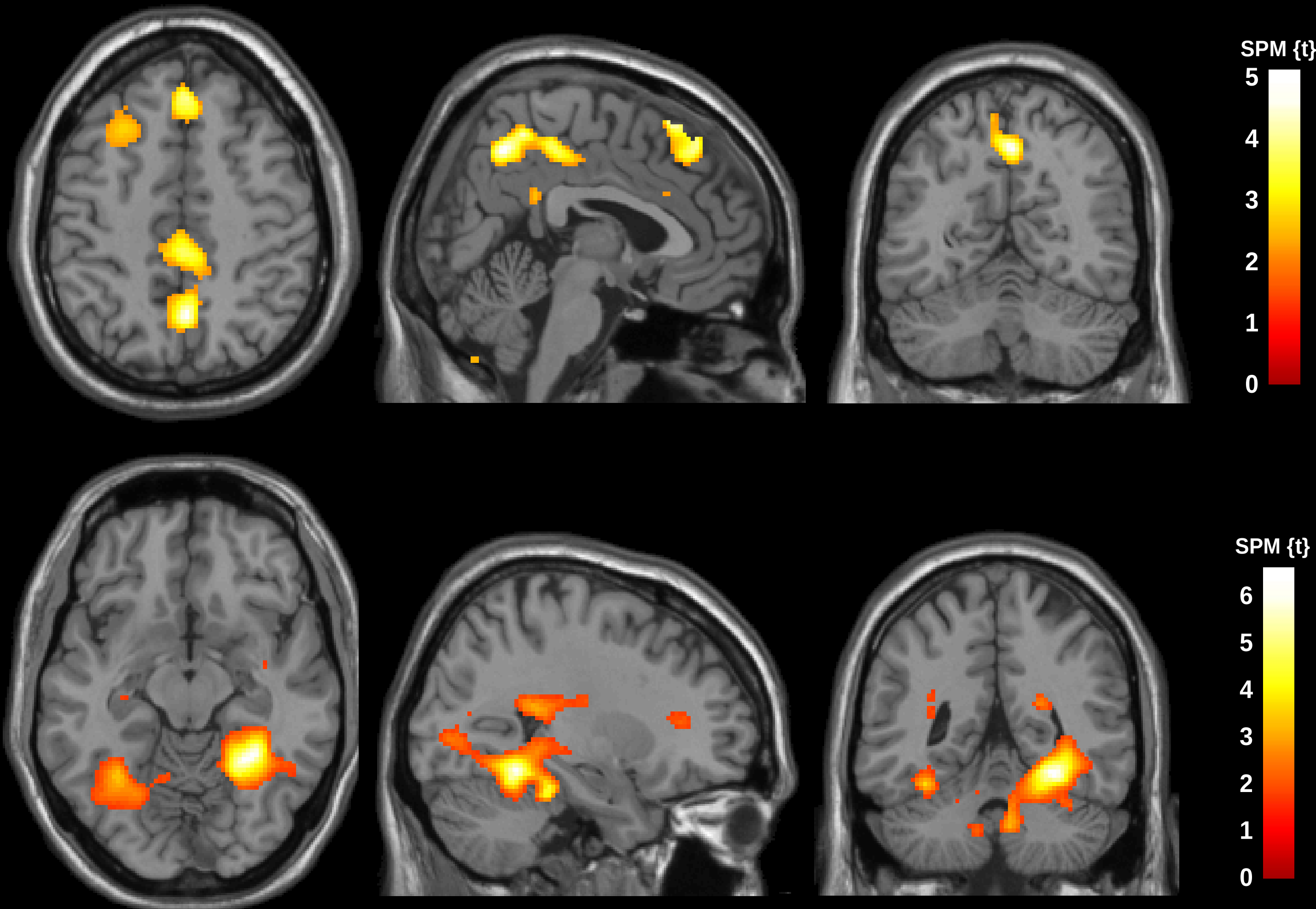
Adult versus Adolescent Differences in Activation: High Calorie Food

High-Calorie

Adults > Adolescents

Adolescents > Adults



Effects of Age

Orbitofrontal Activation Increase with Age

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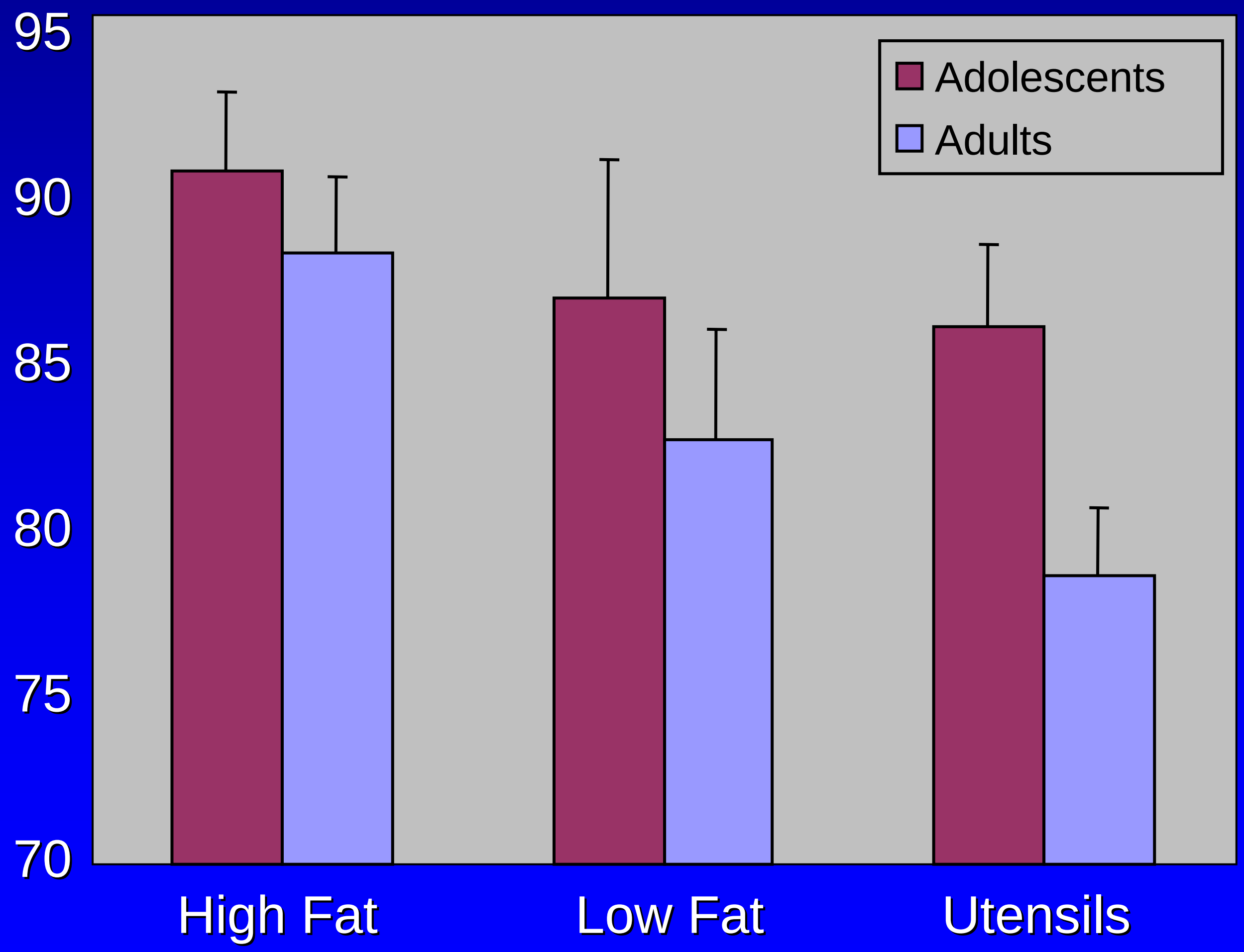
Recognition Memory Performance: Percent Correct



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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.

Limitations

- 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.

Implications

- 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.

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