Affect Modulates Appetite-Related Brain Activity to Images of Food

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ABSTRACT

Objective: We examined whether affect ratings predicted regional cerebral responses to high and low-calorie foods.

Method: Thirteen normal-weight adult women viewed photographs of high and low-calorie foods while undergoing functional magnetic resonance imaging (fMRI). Regression analysis was used to predict regional activation from positive and negative affect scores.

Results: Positive and negative affect had different effects on several important appetite-related regions depending on the calorie content of the food images. When viewing high-calorie foods, positive affect was associated with increased activity in satiety-related regions of the lateral orbitofrontal cortex, but when viewing low-calorie foods, positive affect was associated with increased activity in hunger-related regions including the medial orbitofrontal and insular cortex. The opposite pattern of activity was observed for negative affect.

Conclusion: These findings suggest a neurobiologic substrate that may be involved in the commonly reported increase in cravings for calorie-dense foods during heightened negative emotions.

Keywords: functional magnetic resonance imaging; neuroimaging; food; eating; orbitofrontal cortex; anterior cingulate gyrus; insula; positive affect; negative affect; Positive and Negative Affect Schedule

Introduction

The regulation of food choices and eating behavior in humans is complex and poorly understood.1 Although the appetitive behavior of laboratory animals is well documented and appears to be regulated predominantly by hypothalamic, thalamic, and limbic activity,2 the food seeking and eating behavior of humans appear to be greatly influenced by a variety of cognitive processes mediated by higher-order regions of the cerebral cortex.3,4 Two cortical regions in particular, the insula and orbitofrontal cortices, appear to be critically involved in processing food-related stimuli and influencing the appetitive behavior of humans.5

Neuroimaging research suggests that a primary function of the insula is to monitor interoceptive cues and the ongoing status of internal bodily states.6–9 Some data suggest that the insula may function as the primary gustatory cortex within humans, as it responds directly to changes in specific taste stimuli.10–12 The insula is activated directly when subjects taste a salty or sweet stimulus13,14 and shows increased activity in response to the smell of food.15 Neuroimaging studies have also shown that the insular cortex is sensitive to appetitive status,16 with heightened activation of the insula during hunger17,18 and decreased activation after subjects have eaten to satiation.16,18–20

A second region of the brain, the orbitofrontal cortex, is critical to appetitive behavior in humans and shows changes in activity that correlate with hunger and satiety. This complex brain region receives afferent projections from a variety of feeding-related areas including the lateral hypothalamus and multimodal sensory regions.21 These interoceptive and exteroceptive sources of information converge within the orbitofrontal cortex and are evaluated for their reward potential.22–25 The orbitofrontal cortex appears to be particularly important for evaluating reinforcement contingencies and learning to modify behavioral strategies when the contingencies for obtaining a reward have changed.24 Recent functional neuroimaging studies suggest that the lateral and medial aspects of the orbitofrontal cortex may be functionally dif-
differentiated in their contributions to eating behavior in humans. Specifically, the experience of hunger and motivation to eat is associated with increased activity within the medial and caudal regions of the orbitofrontal cortex. However, once hunger is satisfied and the individual is no longer motivated to eat, there is an increase in activity within the lateral regions of the orbitofrontal cortex, which is accompanied by a decline in activity within the medial and posterior regions. These data suggest that the lateral regions of the orbitofrontal cortex may serve an inhibitory function that leads the satiated individual to stop eating.

In humans, the decision to consume food is modulated by multiple factors. Although internal cues such as nutritional status and immediate energy needs contribute to the brain changes that lead to eating behavior, other factors such as fluctuations in emotions or mood states, can influence the human appetite as well. Food cravings correlate with emotion-related eating. For instance, craving intensity is positively correlated with a variety of negative mood states in self-described carbohydrate cravers. At the extreme, affective disturbances such as those seen in depressive disorders are often accompanied by changes in appetite and carbohydrate cravings, and such changes are even included in the diagnostic criteria of major depression. It still remains unclear, however, whether mood-dependent changes in appetite are directly associated with changes in regional activation within hunger/satiety-related brain regions or whether these changes occur exclusive from these mechanisms.

To clarify the neurobiologic mechanisms by which affect may influence appetite, we presented healthy, normal-weight participants with color photographs of foods differing in fat content/calorie density (i.e., high-calorie or low-calorie foods) while they underwent blood oxygen level dependent (BOLD) functional magnetic resonance imaging (fMRI). Although preliminary data from these subjects have been reported previously, we now present novel analyses that correlate brain activity with never before presented mood ratings from these same participants. Given the reported relation between affective state and appetite, we hypothesized that cerebral activity within hunger/satiety-related regions such as the lateral and medial orbitofrontal and insular cortices would covary with ratings of positive affect (PA) and negative affect (NA), and that the pattern of covariance would differ as a function of the fat/calorie content of the food images.

**Method**

This research was reviewed and approved by the local institutional review board of McLean Hospital.

**Participants**

Thirteen (N = 13) healthy right-handed women were presented with a series of food-related images while undergoing BOLD contrast fMRI. We have previously published preliminary data contrasting brain responses of these same participants to the food stimuli used in this study. However, in the current article, we present new data and findings that clarify how these brain responses covary with the affective status of the participants. Participants were 21–28 years of age (M = 23.5, SD = 2.1) and were within normal limits for body mass index (BMI; M = 22.1, SD = 2.4 kg/m²) according to the guidelines outlined by the Department of Health and Human Services Consensus Conference on Obesity (April 1992). All participants were recruited from the staff of McLean Hospital (Belmont, MA), and were free of any history of eating disorders, psychiatric diagnoses, or neurologic illnesses. All participants reported having normal or corrected-normal vision (i.e., with contact lenses). The volunteers were prohibited from consuming any food for ≥ 90 min before the fMRI session, although most had abstained for much longer (M = 3.9 hr, SD = 1.5; range = 1.6–6.8 hr). All scans were conducted between the times of 1500 and 1900 hr.

**Imaging Methods**

Echoplanar images were acquired on a 1.5-Tesla GE LX magnetic resonance imaging scanner (General Electric Medical Systems, Waukesha, WI) equipped with a birdcage quadrature RF head coil (scan repeat time [TR] = 3 s, echo time [TE] = 40 ms, flip angle = 90°). Functional images were collected over 20 contiguous coronal slices with a 20-cm field of view and a 64 × 64 acquisition matrix (in-plane resolution = 3.125 × 7.000 × 3.125 mm). Each scanning run lasted for 150 s during which time 50 images were collected. At the start of each scan, three dummy images were collected and discarded from analysis. For anatomic localization, matched T1-weighted high-resolution images were collected for every subject. To minimize head motion, each participant’s head was secured with foam padding and a forehead stabilization strap.

**Stimulation Paradigms**

Stimuli were presented in three separate scanning runs, which included (a) low-fat/calorie-lean foods (e.g., fresh vegetables and fruits, salads, sushi), (b) high-fat/calorie-dense foods (e.g., ice cream, cheeseburgers, cake, hot dogs, french fries, cookies), and (c) nonedible food-related utensils (e.g., spoons, forks, dishes). The order of the three conditions was counterbalanced across subjects. These stimulation paradigms have been described in greater detail elsewhere. Although three conditions were presented to the subjects, in the current article, we only...
report correlation data from the two food conditions. Each stimulus paradigm lasted 150 s, and consisted of 5 alternating 30-s periods (i.e., control, stimulus, control, stimulus, control). The control stimuli consisted of photographs of nonfood objects that were similar in texture, color, and visual complexity to the food images (e.g., flowers, bricks, rocks, shrubs, trees). Ten photographs were presented during each 30-s period (2,500-ms stimulus presentation followed by a 500-ms interstimulus interval). Stimuli were presented via a Macintosh computer running the PsychoScope program. Images were back-projected onto a translucent screen located at the foot of the scanning bed and were visible via a mirror mounted on the head coil.

Assessment of Affect

Immediately after completion of the functional imaging session, participants exited the scanner and completed the Positive and Negative Affect Schedule (PANAS), a 20-item self-report measure of current affective state. The scale provides 2 scores, PA and NA, which each ranges from 10 to 50. The scale is based on the theoretical two-dimensional model of affective experience. PA can be described as a dimension of pleasant enthusiasm and active positive engagement whereas NA can be described as a dimension of subjective distress and unpleasant emotional activation. These scales are well validated and have been shown to correlate highly with several measures of mood, anxiety, and depression.

Image Processing and Analysis

Functional imaging data were processed and analyzed in SPM99. Time series images were corrected for head motion and convolved into three-dimensional space. Images were spatially smoothed using a nonisotropic gaussian kernel (full width half maximum [FWHM] = 10 mm) and were resliced to $2 \times 2 \times 2$ mm within stereotaxic space using sinc interpolation. Analyses proceeded through two levels. First, individual contrast maps were constructed to compare activation between the stimulation and control conditions in SPM99. Second, individual SPM contrast maps were entered into a multiple regression model with PA and NA scores from the PANAS entered as separate covariates of interest. High-fat/calorie-dense and low-fat/calorie-lean conditions were analyzed separately. For the current study, our hypothesis was constrained to a few specific cortical and limbic regions believed to be involved in the motivation to eat. Therefore, we restricted our analysis to the following brain regions: orbitofrontal cortex (i.e., inferior, middle, superior, and medial orbitofrontal cortex, gyrus rectus, and olfactory cortex), anterior cingulate gyrus, and insular cortex. To constrain our analyses, we created a region of interest (ROI) mask using the WFU Pickatlas utility. This ROI mask was used to exclude other regions and adjust statistical thresholds using the small volume correction implemented in SPM99. Given that the hypothesized regions have been directly related to appetite and feeding behavior in previous research, we set our statistical height threshold at $p < .050$, corrected for multiple comparisons using the small volume correction implemented within SPM99. Only active clusters with a minimum extent threshold of 10 contiguous voxels were considered as significant. For visualization, the resulting SPM [t] maps were superimposed on an average template brain normalized to fit the standardized coordinate space of the Montreal Neurological Institute (MNI; Quebec, Canada).

Results

High-Calorie Foods

Data for PA and NA were entered together into a random-effects multiple regression analysis on the contrast images for each food image condition. Significant areas of activation related to each affect rating (PA or NA) are reported, while statistically controlling for the effects of the other affect rating. Accordingly, with ratings of NA statistically controlled, presentation of photographs of high-calorie foods (e.g., cheesesburgers, french fries, chocolate cake) yielded a significant relation between ratings of PA and greater BOLD activity within the right lateral orbitofrontal cortex (Figure 1). As evident in Table 1, the local maximum of this cluster of activity was within the right inferior orbitofrontal gyrus. In contrast, higher ratings of NA were associated with greater BOLD activity within medial regions of the orbitofrontal cortex, subcollosal anterior cingulate gyrus, and posterior insula (Figure 1).

Low-Calorie Foods

The pattern of regional activation observed for low-calorie/low-fat foods was nearly opposite from that observed for high-calorie foods. Specifically, when participants viewed images of low-calorie foods (e.g., salads, fruits), greater PA was associated with increased activity primarily within the medial regions of the orbitofrontal cortex, including the superior and middle orbitofrontal gyri, and the bilateral posterior insula (Figure 1). In contrast, when participants viewed low-calorie foods, greater NA was associated with increased activity within the right lateral and caudal orbitofrontal cortex (Figure 1). As evident in Table 1, NA was also associated with increased activity in the medial orbitofrontal cortex and right anterior insula.

Conclusion

The responsiveness of reward and feeding-related regions of the brain was significantly related to cur-
rent ratings of PA and NA. Moreover, the relation between these affective ratings and brain activity demonstrated virtually opposite patterns for the two levels of calorie density of the food images. When viewing high-calorie foods, higher ratings of PA were associated with greater activity within the lateral regions of the orbitofrontal cortex, whereas higher ratings of NA were associated with greater activity within the medial orbitofrontal and insular cortex. Conversely, participants showed essentially the reverse pattern of relations when viewing low-calorie/low-fat foods. For low-calorie foods, higher ratings of PA were associated with more activity within the medial orbitofrontal and insular cortex, whereas greater NA was associated with greater activity within the lateral orbitofrontal cortex.

The observed pattern of relations is particularly noteworthy when interpreted in light of recent neuroimaging studies, suggesting that there is a functional segregation of the medial and lateral orbitofrontal cortex with regard to the motivation to eat. A recent study by Small et al.\textsuperscript{18} used positron emission tomography (PET) to explore changes in brain activity as self-proclaimed chocolate lovers ate chocolate from a state of hunger until they past the point of satiation. Initial bites of chocolate, which were rated as highly pleasurable when the subjects were hungry, were associated with increased activity within the caudomedial orbitofrontal cortex and the insula. As their subjects ate chocolate past the point of satiation, however, motivation to eat and corresponding pleasantness ratings for chocolate declined and were accompanied by reduced activity within the medial orbitofrontal cortex and increased activity in the lateral orbitofrontal regions. A growing body of evidence suggests that activity in the medial orbitofrontal cortex is associated with experiences and cognition related to rewarding stimuli, whereas lateral orbitofrontal activity is related to punishing stimuli or inhibition of responses to stimuli that have been previously rewarded.\textsuperscript{45,46} Similarly, when individuals are hungry and food is highly rewarding, the medial and caudal regions of the orbitofrontal cortex are generally activated.\textsuperscript{16,17,26} However, once hunger is satiated, food is no longer rewarding and there is a decline
in activity within the medial and posterior regions and a corresponding increase in activity within the lateral regions of the orbitofrontal cortex.3,15,16,18,20 Together, these studies suggest a dissociation between activity within the medial and lateral orbitofrontal cortices, with the former associated with motivation to eat and the latter associated with motivation to terminate eating.

In the current study, we found that activity in these functionally dissociated regions of the orbitofrontal cortex was dependent on the affective state of the individual and the type of food being perceived. When viewing high-calorie/high-fat foods, NA was associated with greater activity in the medial orbitofrontal cortex, anterior cingulate, and insula—regions that have all been associated with increased motivation to eat and high perceived reward value from food.3,16,17,26 Higher PA during high-calorie viewing, in contrast, was associated with greater activity in the lateral orbitofrontal cortex, a region that has been associated with reduced motivation to eat and with aversion toward food.3,15,16,18,20 When the current findings are considered in this context, it suggests that one mechanism of the relation between mood and appetite may involve the relative changes in brain activity within the lateral and medial orbitofrontal cortices.

Our findings are consistent with other research showing that negative mood states and stress are associated with increased cravings for food,47,48 particularly foods that are high in carbohydrates.30,49–51 The prevailing explanation for the relation between negative mood and carbohydrate cravings suggests that people increase their carbohydrate consumption to “self-medicate” their negative moods.52 The putative mechanism for this effect is that high-carbohydrate foods increase the plasma concentration of the amino acid, tryptophan, a precursor to the brain neurotransmitter serotonin, which may potentially alleviate dysphoric mood.53,54 Consistent with this perspective, clinical mood disturbances such as major depressive episodes and seasonal affective disorder are also often associated with changes in appetite and food consumption.31–35 In fact, the region showing the strongest relation with NA during the high-calorie condition was the subgenual cingulate gyrus, a region that shows trait-like changes in activity in patients with heritable forms of mood disturbance, such as familial unipolar or bipolar depression.55,56 Given the sensitivity of this region to rewards25 and primary reinforcers,25 and its association with heritable mood disorders, the current findings suggest a potential, although speculative, link between the

Table 1. Regional local maxima demonstrating significant positive correlations with positive and negative affect for high and low-calorie food images

<table>
<thead>
<tr>
<th>Regions of Activation</th>
<th>Volume</th>
<th>Brodmann’s Area</th>
<th>x</th>
<th>y</th>
<th>z</th>
<th>z Score</th>
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<tr>
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<td></td>
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<tr>
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<tr>
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<td>47</td>
<td>42</td>
<td>44</td>
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<tr>
<td>R. superior orbital frontal gyrus</td>
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<td>11</td>
<td>−18</td>
<td>48</td>
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<tr>
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<tr>
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<td>—</td>
<td>6</td>
<td>26</td>
<td>16</td>
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Note: Atlas coordinates are listed in the standard space of the Montreal Neurological Institute (MNI; Quebec, Canada), such that x reflects the distance (mm) to the right or left of midline, y reflects the distance anterior or posterior to the anterior commissure, (AC-PC) and z reflects the distance superior or inferior to the horizontal plane through the AC-PC line. Only regions with z scores significant beyond p < .050 (small volume corrected) are reported. L = left hemisphere; R = right hemisphere.
subgenual cingulate and the appetite changes that are common in mood disorders.

It is noteworthy that we found that low-calorie/low-fat foods yielded essentially the inverse relation from that seen with high-calorie foods. When participants viewed low-calorie foods, NA was predominantly associated with greater activity in the right lateral orbitofrontal cortex, a region associated in other studies with reduced motivation to eat.\textsuperscript{15,16,18,20} whereas PA was associated with increased activity in the medial orbitofrontal and insular cortices, two regions that have been associated with the initiation of feeding and with the increased desire to eat.\textsuperscript{10,16,17,26} Although causal relations cannot be inferred from the correlational data obtained in the current study, these findings raise some speculative possibilities that there may be a neurobiologic mechanism underlying the relation between affective state and the propensity to select certain classes of foods. This mechanism potentially includes the insula and the lateral and medial aspects of the orbitofrontal cortex, which appear to respond differently to the calorie density of foods depending on the affective state of the individual. Specifically, based on our findings, we would predict that negative mood states would lead to patterns of brain activity that tend to be associated with unhealthy food choices, such as preferring high-calorie/high-fat foods and a tendency to shun low-calorie/low-fat foods. In contrast, the pattern of brain responses associated with PA states leads to a prediction that individuals in a good mood would be more likely to prefer healthier, low-calorie/low-fat foods and would tend to have fewer cravings for foods high in calorie or fat content. We did not collect simultaneous ratings of food cravings or preferences for each food item as it was presented, so it is impossible to evaluate the direct relation between the mood-dependent brain activation we observed and food cravings. Future research that specifically correlates individual food cravings with affect-dependent food activation may clarify the validity of these relations.

Several important limitations must be considered when interpreting these data. First, the primary region of interest in the current study, the orbitofrontal cortex, is often difficult to study with fMRI due to its proximity to air-filled sinuses. The air–water interface creates a field inhomogeneity that causes in-plane distortion of echoplanar images\textsuperscript{26} that could have affected the current data, and we advocate further research with alternative methodologies such as PET. Second, we only included female participants in the current study. Because some evidence suggests that males and females may differ in their carbohydrate cravings,\textsuperscript{30} follow-up studies will need to examine the possibility of gender differences in the currently observed patterns of activity. Finally, as mentioned earlier, we did not collect individual ratings of appetite, cravings, or behavioral approach to the individual food items as they were presented in the scanner. To definitively establish the relation between the lateral and medial orbitofrontal activity and food preferences, such ratings and behavioral indices will need to be included in further investigations. Given due consideration to these limitations, however, we believe that the current findings provide important insights into the relation between affective state and cerebral responses to food stimuli.

Affective state significantly influenced regional brain activity in response to images of food that differed in calorie density/fat content. These findings have important implications for understanding the relation between mood and food choices. PA appears to be associated with patterns of brain activity that may facilitate a greater likelihood to approach healthy low-calorie/low-fat foods while avoiding unhealthy, high-calorie/high-fat foods. NA, in contrast, was associated with a pattern of brain activity that suggests a potential attraction to foods that are less healthy by virtue of high-calorie and high-fat content and a potentially reduced appetite for low-calorie foods. This interaction between affect and food type suggests a possible neurobiologic substrate, which includes the insular and lateral and orbitofrontal cortices, through which affective state may influence appetitive function and food choices.

References

APPETITE-RELATED BRAIN ACTIVITY


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