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Neural mechanisms underlying food motivation in children and adolescents

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Dramatic increases in childhood obesity necessitate a more complete understanding of neural mechanisms of hunger and satiation in pediatric populations. In this study, normal weight children and adolescents underwent functional magnetic resonance imaging (fMRI) scanning before and after eating a meal. Participants showed increased activation to visual food stimuli in the amygdala, medial frontal/orbitofrontal cortex, and insula in the pre-meal condition; no regions of interest responded in the post-meal condition. These results closely parallel previous findings in adults. In addition, we found evidence for habituation to food stimuli in the amygdala within the pre-meal session. These findings provide evidence that normal patterns of neural activity related to food motivation begin in childhood. Results have implications for obese children and adults, who may have abnormal hunger and satiation mechanisms.

Keywords: Amygdala; Obesity; fMRI; Food motivation; Pediatric

Introduction

Nearly 20% of the US adult population is clinically obese (body mass index [BMI] $\geq$30 kg/m^2; Mokdad et al., 2000), a condition associated with increased morbidity, mortality, and health care costs (Allison et al., 1999; Colditz, 1999). The roots of adult obesity are likely established in childhood and adolescence, and increases in obesity prevalence have been documented that are comparable to those found in adults (Strauss and Pollack, 2001). Recent estimates of childhood overweight (BMI greater than 95 percentile for age and sex) in the United States range from 12 to 22% of the population (Strauss and Pollack, 2001).

Although several factors contribute to weight gain, consistent eating in excess of daily energy requirements plays a primary etiological role across the lifespan (Nielsen et al., 2002). Neural mechanisms are central to the regulation of these motivationally mediated behaviors (Tataranni and DelParigi, 2003); thus, the increasing concern surrounding the dramatic rise of obesity (Mokdad et al., 1999; 2000) has led to research aimed at understanding the neural substrates of appetitive function in humans (Tataranni and DelParigi, 2003; Wang et al., 2004). The role of the hypothalamus in food motivation is well established in literature on non-human primates (Rolls et al., 1976) as well as humans (Rolls, 1981; Stellar, 1954). More recently, however, limbic–frontal connectivity has become increasingly implicated in normal food motivation (Zald et al., 1998), as well as abnormal food intake and obesity (Tataranni and DelParigi, 2003). Previous human and animal studies suggest coordinated involvement of these areas in processing of emotional stimuli and representation of reward (Baxter and Murray, 2002; Gottfried et al., 2003; Kringelbach and Rolls, 2004; Rolls, 2004; Whalen, 1998). Specifying these networks has become an aim of brain activation studies using PET and fMRI.

Previous functional neuroimaging studies of food motivation have utilized a broad array of paradigms, including passive viewing of food images, conditioned responses to olfactory and gustatory stimuli, and inclusion of pre- and post-meal scans for comparison of motivational state within subjects. Across these studies, the most consistent findings include activation of orbitofrontal cortex (OFC), medial frontal cortex (MFC), amygdala, hippocampal formation, and insula (Gordon et al., 2000; Hinton et al., 2004; Killgore et al., 2003; LaBar et al., 2001; Morris and Dolan, 2001; O'Doherty et al., 2002; Small et al., 2001; Tataranni et al., 1999). For example, LaBar et al. (2001) scanned

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normal weight adults while they passively viewed images of food both before and after eating. They found differential responses to food stimuli in the amygdala, hippocampal formation, and fusiform gyrus during hunger, which resolved after eating.

Thus, there is consistent evidence from studies of food motivation in healthy weight individuals that limbic–frontal neural networks underlie normal processes of food motivation and regulation of food intake. It has been hypothesized that these neural systems also play an important role in controlling hyperphagia in obese individuals (e.g., Tataranni and DelParigi, 2003). Though still in its infancy, neuroimaging research on obese and overweight adults has shown differential patterns of neural activity in obese compared to lean individuals, including abnormal functioning in the hypothalamus (Matsuda et al., 1999), insula (DelParigi et al., 2003; Gautier et al., 2000), hippocampus (DelParigi et al., 2003; Gautier et al., 2000), and OFC (Gautier et al., 2000). These findings offer evidence for discrepancies in neural circuits involved in food motivation between obese and lean adults.

Although neural mechanisms of hunger and satiation have been examined in neuroimaging studies of both normal and obese adults, to our knowledge, no studies have been published in children and adolescents. This is of note since neuroimaging findings in children and adolescents are not always consistent with those in adults (Davidson et al., 2003). In particular, the amygdala and OFC show continued development into adulthood (Durston et al., 2001; Happaney et al., 2004) and may respond differently to appetitive stimuli based on age. Thus, investigation of the neural mechanisms underlying hunger and satiation in children is necessary for a complete understanding of normal and abnormal human appetitive function across the lifespan. The current study explores changes in neural response to food stimuli before and after eating in healthy weight children and adolescents, with the goal of identifying the normal neural circuitry of these processes for future research on overweight children and adolescents. Based on findings in previous studies on adults, we hypothesized greater activation in response to food stimuli in the OFC, MFC, insula, amygdala, and hippocampal formation during a pre-meal state compared to a post-meal state.

Materials and methods

Subjects

Written informed consent was obtained for the 5 female and 4 male children and adolescents who participated in this study. Participants ranged in age from 10 to 17 [mean (±SD) = 13.4 (±2.8)]. Participants were within the healthy weight-for-height ratio (BMI) for age and sex as determined by growth curve charts from the Center's for Disease Control [mean (±SD) = 18.5 (±2.4)]. All individuals were free from psychiatric diagnoses and neurological illnesses (based on parental interview) and had normal vision. Eight individuals were right-handed. This study was approved by the Human Subjects Committee (IRB) at the University of Kansas Medical Center.

fMRI acquisition

Scanning was performed on a 3T head-only Siemens Allegra scanner (Siemens, Erlangen, Germany) fitted with a quadrature head coil. Participants' heads were immobilized with head cushions. T1-weighted anatomic images were acquired with a 3D SPGR sequence (TR/TE = 23/4 ms, flip angle = 8°, FOV = 256 mm, matrix = 256 × 192, slice thickness = 1 mm). Single shot gradient echo fMRI scans were acquired in 43 contiguous coronal slices (repetition time/echo time [TR/TE] = 3000/40 ms, flip angle = 90°, field of view [FOV] = 192 mm, matrix = 64 × 64, slice thickness = 3 mm (0.5 mm skip), in-plane resolution = 3 × 3 mm, 130 data points). One anatomical and two functional sequences were run in each scanning session (i.e., pre-meal and post-meal).

Experimental paradigm

The experimental paradigm was based closely on LaBar et al. (2001). Participants viewed pictures of food, animals, and Gaussian-blurred low-level baseline control images during two scanning sessions: one after fasting for 4 h (pre-meal) and one immediately after eating a small uniform meal (post-meal) that was standardized for total number of calories [Kcal = 500], as well as macro- and micronutrient content. Previous studies examining the effect of satiation on brain activity have included a longer fasting period, typically 8 h, and utilized meals designed to fully sate participants (LaBar et al., 2001; Morris and Dolan, 2001). The current study implemented a 4 h fast and a meal standardized to provide approximately 500 Kcal. Our goal was to design a paradigm that accurately reflected the normal hunger and eating cycles. The order of sessions (pre-meal, post-meal) was counterbalanced across subjects so that approximately half the group (n = 5) started with the pre-meal session and half (n = 4) started with the post-meal session.

Activation paradigm

Stimuli of two categories (food and blurred baseline control images) were obtained from LaBar et al. (2001). Due to the age of the participants in this study, the comparison stimuli group of animals (rather than tools, as used by LaBar et al.) was chosen to keep participants attentive to the task and to control for general familiarity. All images for the animal category were obtained from professional stock CD-ROMs and matched to food and blurred control images on brightness, resolution, and size. In addition, by applying a Gaussian kernel to a subset of the animal images (so that the objects were not identifiable), approximately 150 new blurred baseline control images were obtained. To the greatest degree possible, animals that were reminiscent of food (i.e., fish) were removed from the stimuli pool to prevent the possible confusion between animal/food categorizations. Blurred objects were included as a low-level baseline comparison. All images were presented one time only to each subject.

Each functional scan involved three repetitions of each block of each stimulus condition type (i.e., food, animal), alternated between blocks of blurred images. Visual stimuli were projected through 3D limited view goggles (Resonance Technology, Inc., Northridge, California) connected to the stimuli-generating computer program (NeuroSTIM, Neuroscan, El Paso, TX). Stimulus presentation time was 2.5 s, with an interstimulus interval (ISI) of 0.5 s. Within each of the two functional scans, there was a total of 13 blocks of stimuli presentation; within each block, 10 images were presented. The order of category presentation was counterbalanced across subjects.