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Brain function predictors and outcome of weight loss and weight loss maintenance ☆

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ABSTRACT

Obesity rates are associated with public health consequences and rising health care costs. Weight loss interventions, while effective, do not work for everyone, and weight regain is a significant problem. Eating behavior is influenced by a convergence of processes in the brain, including homeostatic factors and motivational processing that are important contributors to overeating. Initial neuroimaging studies have identified brain regions that respond differently to visual food cues in obese and healthy weight individuals that are positively correlated with reports of hunger in obese participants. While these findings provide mechanisms of overeating, many important questions remain. It is not known whether brain activation patterns change after weight loss, or if they change differentially based on amount of weight lost. Also, little is understood regarding biological processes that contribute to long-term weight maintenance. This study will use neuroimaging in participants while viewing food and non-food images. Functional Magnetic Resonance Imaging will take place before and after completion of a twelve-week weight loss intervention. Obese participants will be followed though a 6-month maintenance period. The study will address three aims: 1. Characterize brain activation underlying food motivation and impulsive behaviors in obese individuals. 2. Identify brain activation changes and predictors of weight loss. 3. Identify brain activation predictors of weight loss maintenance. Findings from this study will have implications for understanding mechanisms of obesity, weight loss, and weight maintenance. Results will be significant to public health and could lead to a better understanding of how differences in brain activation relate to obesity.

Abbreviations: ACC, Anterior cingulate cortex; BMI, Body Mass Index; EBL, Energy Balance Laboratory; EBI, Eating Behavior Inventory; fMRI, Functional magnetic resonance imaging; MFC, Medial prefrontal cortex; NDS-R, Nutrition Data Systems for Research; OFC, Orbitofrontal cortex; PA, Physical activity; PET, Positron emission tomography; PCMs, Portion controlled meals; PWS, Prader–Willi Syndrome; rCBF, Regional Cerebral Blood Flow; ROI, Region of Interest; SCT, Social Cognitive Theory; wk, week.

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1. Introduction

Overweight (body mass index [BMI] of 25 to 29.9 kg/m^2) and obese (BMI of 30 kg/m^2 or greater) individuals represent approximately 69.2% of adults in the United States [1]. Both overweight and obesity are characterized by the accumulation of excessive levels of body fat and contribute to heart disease, hypertension, diabetes, and some cancers, as well as psychosocial and economic difficulties [2–5]. The cost of treatment for weight reduction is now estimated to exceed 147 billion dollars annually [6]. Reduction in obesity prevalence remains a major aim of Healthy People 2020 [7].

Obesity is a complex medical and behavioral problem that can be impacted by energy balance interventions that reduce energy intake and increase energy expenditure. However, the factors underlying obesity are still poorly understood. On the energy intake side, eating behavior is influenced by a convergence of processes in the brain, including homeostatic factors and motivational processing. Motivational processes are an especially important contributor to overeating in humans [8]. Food is a highly salient reinforcer [9] and its presentation is associated with increased activity in limbic and paralimbic networks in the brain. Abnormal activity in these networks may lead to increased eating behavior. As such, overeating and obesity may be conceptualized as reflecting failures in impulse control that are associated with unique patterns of brain activation to food stimuli. Therefore, the increasing concern surrounding the dramatic rise of obesity has this has led to research aimed at understanding the neural mechanisms of appetitive function in humans [10–13].

Positron emission tomography (PET) and Functional Magnetic Resonance Imaging (fMRI) studies examining neural responses to food stimuli in healthy weight and obese adults have consistently demonstrated that the paralimbic cortical and prefrontal areas support motivation and cognitive control processes [14–16]. These activation studies have utilized two approaches to stimulating response in appetite control regions: 1) Participants are scanned while anticipating and then tasting liquid food after a prolonged fast [17]; or 2) Participants are scanned while viewing pictures of food, after a fasting period and soon after feeding [18–21]. Both approaches have produced similar findings, pointing to changes in activation in brain regions known to play a role in taste, reward, motivation, and regulation and control of behavior [14].

The most consistent findings include activations within healthy weight individuals in studies that compare food images relative to non-food images. Studies with healthy weight individuals implicate brain structures in the paralimbic cortex, including the orbitofrontal cortex (OFC), medial prefrontal cortex (MFC), anterior cingulate cortex (ACC), amygdala, hippocampal formation, and insula [14,16,22–29]. The nucleus accumbens has also been found to be predictive of subsequent food consumption and subsequent weight gain [30,31].

In obese individuals, as compared to healthy weight individuals, findings suggest that activation in the anterior insula, amygdala, striatum, and OFC occurs in response to the sight of food [14,16,32–41]. Increased connectivity between the OFC and accumbens has also been observed [42]. Functional connectivity studies have also suggested that the striatal network, including the occipital lobe and inferior parietal cortex, is engaged when obese individuals observe food stimuli as compared to non-food stimuli. Obese individuals have also displayed decreased functional connectivity between the OFC and the inferior occipital gyrus [43] and decreased activity in the amygdala, lateral and medial PFC, and anterior cingulate has been observed during passive viewing as compared to increased activation during the taste imagination [44]. Increased recruitment of the insula has also been observed when obese individuals passively view food as compared to reappraising food's reward value, which is associated with greater activity in the lateral PFC [39]. Taken together, findings from imaging studies examining brain response to food cues show that obesity is characterized by hyper-responsiveness in regions of the brain typically associated with reward, emotion, and taste processing.

Weight loss has been associated with differential patterns of brain activation in obese individuals [14,16]. Rosenbaum and colleagues [19] examined the reward system activation in response to visual food cues in individuals that reported successfully losing and maintaining at least 10% of their initial body weight and found that individuals who maintained weight loss showed decreased activation in the ACC, amygdala, precentral gyrus, fusiform gyrus, and hypothalamus. To date, there are very few longitudinal studies that have compared pre- and post-weight loss changes in brain activation. Bruce and colleagues [45] found that, among individuals who lost weight following bariatric surgery, surgery, there was decreased activation in regions of the brain previously implicated in food motivation and reward (e.g., the parahippocampus, medial prefrontal cortex, insula, and inferior frontal gyrus) when viewing food vs non-food pictures following weight loss surgery. Increased activation to food vs nonfood pictures after weight loss was observed in the anterior prefrontal cortex, a region of the brain that has been implicated in cognitive control and inhibition. Murdaugh et al. [46] conducted a small study including 25 obese individuals and found greater pre-weight loss treatment activation to high-calorie food vs. control pictures in brain regions implicated in reward-system processes including the nucleus accumbens, anterior cingulate, and insula. Murdaugh et al also observed similar correlations with weight loss in brain regions implicated by other studies in vision and attention, such as superior occipital cortex, inferior and superior parietal lobule, and prefrontal cortex. Less successful weight maintenance at follow-up was predicted by greater post-treatment activation in insula, ventral tegmental area, putamen, and fusiform gyrus. Thus, successful weight loss has been associated with diminished activation in areas of the brain that process reward, motivation, and taste, as well as with increased activation in areas of the brain known to facilitate cognitive and behavioral control.

Although a variety of literature exists examining the relationship between food and the brain, there still are several limitations. First of all, no well controlled longitudinal trials have been conducted to evaluate the influence weight loss changes the brain and its activation relative to food cues in overweight and obese adults. In addition, trials have not been conducted to determine if baseline brain activation can be used to predict weight loss post diet. Finally, very little research is available regarding weight maintenance and if brain activation can be used to predict those that will be able to maintain their weight loss as compared to those who do not. The study proposed herein is designed to address these limitations within the present research.