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Brain response to images of food varying in energy density is associated with body composition in 7- to 10-year-old children: Results of an exploratory study

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HIGHLIGHTS

- Activity in brain reward regions is associated with children's body composition
- Lean mass positively correlated with substantia nigra response to high energy foods
- Findings support fat-free mass as an appetitive driver in children

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ABSTRACT

Energy balance is regulated by a multifaceted system of physiological signals that influence energy intake and expenditure. Therefore, variability in the brain's response to food may be partially explained by differences in levels of metabolically active tissues throughout the body, including fat-free mass (FFM) and fat mass (FM). The purpose of this study was to test the hypothesis that children's body composition would be related to their brain response to food images varying in energy density (ED), a measure of energy content per weight of food. Functional magnetic resonance imaging (fMRI) was used to measure brain response to High (>1.5 kcal/g) and Low (<1.5 kcal/g) ED food images, and Control images, in 36 children ages 7–10 years. Body composition was measured using bioelectrical impedance analysis. Multi-subject random effects general linear model (GLM) and two-factor repeated measures analysis of variance (ANOVA) were used to test for main effects of ED (High ED vs. Low ED) in a priori defined brain regions of interest previously implicated in energy homeostasis and reward processing. Pearson's correlations were then calculated between activation in these regions for various contrasts (High ED–Low ED, High ED–Control, Low ED–Control) and child body composition (FFM index, FM index, % body fat). Relative to Low ED foods, High ED foods elicited greater BOLD activation in the left thalamus. In the right substantia nigra, BOLD activation for the contrast of High ED–Low ED foods was positively associated with child FFM. There were no significant results for the High ED–Control or Low ED–Control contrasts. Our findings support literature on FFM as an appetitive driver, such that greater amounts of lean mass were associated with greater activation for High ED foods in an area of the brain associated with dopamine signaling and reward (substantia nigra). These results confirm our hypothesis that brain response to foods varying in energy content is related to measures of child body composition.

1. Introduction

Energy balance is regulated by a complex system of peripheral and central physiological signals. These signals arise from compartments of adipose and lean tissue, as well as the gastrointestinal tract and accessory organs, to influence energy intake and expenditure [1,2]. The effects

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of the energy balance system on central appetite regulation pathways have not been fully examined in pre-adolescent children. In addition, it is not known whether the effects of fat mass (FM) and fat-free mass (FFM) on energy balance are mediated by processes in appetite-regulating centers of the brain. Variability in the brain's response to food could partially be explained by differences in levels of metabolically active tissues (FM and FFM) throughout the body. However, this has not previously been tested using neuroimaging in children or adults, and the physiological factors underlying differences in the brain's response to food are not known. This exploratory study aims to address some of these gaps by examining the relationship between body composition and children's brain responses to images of food that vary by energy density (ED).

Emerging evidence, predominantly in adults, suggests that FFM is the best predictor of meal size and energy intake due to its influence on resting metabolic rate and total energy expenditure [1–5]. In controlled laboratory studies with adults, it has been shown that the effects of FFM on objectively-measured intake are mediated almost entirely by resting metabolic rate [6]. Therefore, the research thus far suggests that the effect of FFM on energy intake is primarily homeostatic. However, the direct effects of these homeostatic signals on areas of interest in the brain, including the hypothalamus (e.g., energy homeostasis, hunger) and the thalamus (e.g., sensory processing), have not been fully explored. In addition, there are several areas of the brain that communicate with the hypothalamus (e.g., limbic system) which have a variety of functions (e.g., reward, motivation, emotion processing, learning, memory). Due to the connections between these regions, it is possible that FFM may also be related to activation in areas of the brain involved with reward processing.

Previous studies have also found effects of overall body weight on brain activation in response to high ED and low ED food stimuli, noting increased activation for food stimuli in the striatum (caudate and putamen), anterior cingulate gyrus, amygdala, and insula in persons with obesity compared to healthy-weight controls [7–13]. It is assumed that this association is driven by higher levels of body fat, since adipose tissue is known to send appetite-regulating signals to the brain [3,14]. However, it is unknown whether food cue-related activation in these brain regions is related to levels of adipose tissue or FFM independently of one another. Examining the independent contribution of FM and FFM to the activation in reward networks will help clarify this relationship.

In addition to body composition, there is substantial research demonstrating that the rewarding aspects of food can also drive intake [15,16]. One food property that is known to increase palatability and drive intake is ED, defined as the energy content per unit weight (kcal/g) [17–19]. In general, people tend to have higher liking and preference for foods high in ED (e.g., cookies, pizza) relative to foods low in ED (e.g., fruits, vegetables) [18]. This increased liking for high ED foods is thought to be partially related to increases in activation in areas of the brain associated with reward processing [20]. Previous studies in children and adolescents have demonstrated that both reward and homeostatic regions of the brain are responsive to food-related cues [21–26]. The stimuli in these studies were generally divided into "high-calorie" or "fattening" versus "low-calorie" or "non-fattening" which correspond approximately to high ED and low ED foods, respectively. Regions of the brain that have previously been shown to respond to rewarding stimuli, like high ED foods, include the cingulate cortex, insula, caudate, putamen, substantia nigra, and amygdala, among others [27]. All of these regions have been implicated in processing of reward and emotions, but the relationship between body composition and brain activation in these regions has not been fully examined.

The purpose of this exploratory study was to determine the association between children's body composition, compartmentalized into FFM and FM, and brain activation in response to images of food that vary by ED. To our knowledge, this is one of the first studies to examine the integration of these systems in children. We hypothesized that variability in the brain's response to food images varying in ED would be partly explained by children's body composition, such that FFM would be positively associated with blood-oxygen level-dependent (BOLD) activation in homeostatic regions while FM would be positively associated with BOLD activation in reward centers. This hypothesis was based on prior research implicating FFM as a primary determinant of meal size and energy intake [4], while body weight (a proxy for FM) is related to increased brain activation in reward regions in response to food cues [7,8,11].

2. Methods

2.1. Study design

We conducted a cross-sectional study with a community-based sample of 36 children ages 7–10 years. The overall purpose of the study [28] was to investigate the neural mechanisms underlying the *portion size effect*, or the tendency to consume greater amounts of food when presented with larger portions [29]. This paper focuses on a secondary aim of the study to explore the relationship between body composition and the brain's response to food images varying in ED. The study consisted of 5 total visits. For visits 1–4, children reported to the laboratory once per week over four consecutive weeks to eat ad libitum from four randomized test-meals varying in ED and portion size (reported elsewhere). On visits 3 and 4, children completed mock (i.e., practice) fMRI training sessions to increase familiarity with the scanning environment. Children reported for a fifth visit to complete an fMRI scan while passively viewing images of food varying both in ED (high versus low) and portion size (large versus small), although only differences in response to ED will be reported in the present study. Following the scanning session, children completed a fitness test and rated liking and wanting for each of the images shown during the fMRI using visual analog scales. For the main purposes of this paper, only the anthropometric data collected on visit 1 and the fMRI scan collected on visit 5 were considered for analysis. This study was approved by the Institutional Review Board of The Pennsylvania State University.

2.2. Participants

Participants were recruited using flyers and postings on popular websites. Interested families were screened over the phone to ensure children were healthy, right-handed, without metal implants or dental work, without food allergies, and not taking prescription medications. On the first study visit, a parent signed informed consent for their child. Children provided written assent prior to their participation. Out of the 42 children initially enrolled in the study, 2 were lost to follow-up after completion of 2 test-meal visits. Of the children with complete behavioral data (i.e., meal intake, questionnaires; $n = 40$), 36 children completed a successful fMRI scan, defined as having at least one functional run and corresponding anatomical data. Sample characteristics for these 36 children are listed in Table 1.

2.3. Anthropometrics and body composition

Anthropometric measures (height and weight) were performed by a trained researcher to the nearest 0.1 cm and 0.1 kg. Children were weighed and measured twice using a standard scale (Detecto model 437, Webb City, MO) and stadiometer (Seca model 202, Chino, CA) in light clothing. Averaged height and weight were converted to BMI z-score (BMIz), and BMI percentile, calculated using the Centers for Disease Control and Prevention conversion program [30]. Cut-offs for child age- and sex-specific BMI percentiles were used to classify children as normal weight (<85%ile), overweight (85–95%ile), or obese (≥95%ile).