Food Intake and Neural Food Responses in Lean, Overweight and Obese Adolescents

Abstract

Background: Obesity (BMI ≥30kg/ m^2) is prevalent worldwide, especially in the United States, and leads to many health risks. Neuroimaging techniques such as functional magnetic resonance imaging (fMRI) have become increasingly common technique in obesity research, allowing networks of neural activation in response to stimuli such as food to be investigated. Greater brain activity in areas related to reward, emotion/memory and sensory/motor processing, along with decreased activity in areas related to homeostatic satiety and cognitive control/attention, have been found to cause eating behavior phenotype leading to obesity.

Methods: In the present study, subjects (lean, overweight, and obese adolescents between the age of 14 and 18) drank 2 bottles of Boost as early in the day as possible, and fasted for the remainder of the day leading up to an fMRI scan. Brain activation was measured in response to presentations of high energy-dense, low energy-dense food cues, and non-food (control) office supply cues. After the scan, subjects were directed to an ad libitum buffet-meal comprised of high energy-dense and low energy-dense foods and beverages.

Results: Results showed that there was a strong positive correlation ($R=0.62$, $p<.001$) between BMI z-score and total food intake (in calories). Additionally, when observing the high energy dense foods, obese adolescents compared to lean adolescents showed greater activation in the hippocampus ($p<.05$). Lean adolescents showed greater activation than obese adolescents when observing high energy dense foods compared to control objects in the cerebellum ($p<.05$). Lean adolescents also showed greater activation than obese adolescents when observing high energy dense foods compared to control objects in the orbitofrontal cortex (OFC) ($p<.05$).

Conclusions: This study shows that obese adolescents want to eat more high energy dense foods because of their emotional attachment to these types of food, as well as the reward they feel from it when observing these types of food. This study supports the cerebellum's role in response to food. Additionally, lean adolescents appear to be more conscious about what they eat.

Introduction

Prevalence and Risks of Overweight/Obesity in Adulthood:

According to the World Health Organization (WHO), worldwide obesity (BMI ≥30kg/ m^2) rates have more than doubled since 1980 (WHO, 2012), with National Health and Nutrition Examination Survey (NHANES) data showing that the prevalence of obesity in the United States is 35.5% among adult men and 35.8% among adult women (Flegal et al., 2012). Obesity disproportionately affects ethnic minorities and low income groups (Ogden et al., 2006). The number of states in the U.S. with obesity prevalence of ≥30% increased from none in 2000 to nine in 2009, with none of the states meeting the *Healthy People 2010* target of 15% prevalence of obesity (Sherry et al., 2010).

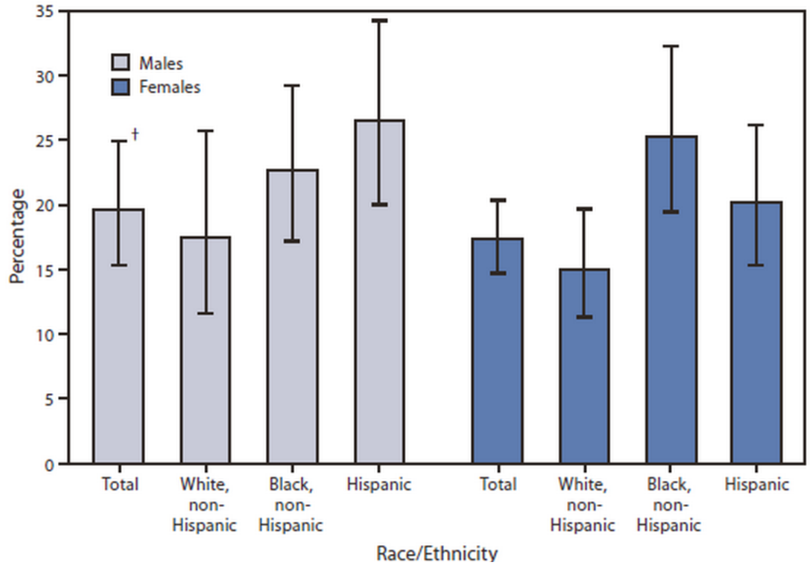
In addition to high rates of obesity, more than 1.4 billion adults (age ≥20) are now overweight (BMI ≥25kg/ m^2) worldwide, and together, overweight and obesity represent the fifth leading risk for global deaths (WHO, 2012). Taken together, overweight and obesity contribute to approximately 10% of all deaths each year in the U.S. (Danaei et al., 2009), with related conditions including heart disease, diabetes, some cancers, hypertension, dyslipidemia, stroke, and sleep apnea (CDC, 2012). For the first time in nearly two centuries, longevity in the United States may decline due to the damaging effects of this epidemic (Olshansky et al., 2005).

Prevalence and Risks of Child and Adolescent Overweight/Obesity:

Obesity not only affects the health of at least 400 million adults, but also 20 million children (≥ 5 y) worldwide (WHO, 2012). Notably, the definitions of obesity/overweight are different for children/adolescents (aged 2-19) compared to adults being based on BMI percentiles: a child or teen is considered overweight if his/her BMI falls in the 85th to less than the 95th percentile for BMI, and obese if his/her BMI is equal to or greater than the 95th percentile (CDC, 2012). According to NHANES data, 17% of children and adolescents in the U.S. are currently obese (Ogden et al., 2012) and the rate of obesity among U.S. children has tripled between 1998 and 2008 (Ogden et al., 2006). Specifically, in adolescents aged 12-19, 19.6% of males and 17.1% of females were designated obese (Ogden et al., 2012 [Figure 1]).

Obese children and adults share certain risk factors; for example, like obese adults, obese children are more likely to have high blood pressure (Freedman et al., 2007), type 2 diabetes (Whitlock et al., 2005), and sleep apnea (Han et al., 2010). In addition, obese children and adolescents have a greater risk of impaired psychological well-being, such as discrimination and poor self-esteem, which can continue into adulthood (Dietz, 1998; De Niet et al., 2011). Obese children are also more likely to become obese adults (Serdula et al., 1993; Guo et al., 2002; Biro et al., 2010), with overweight adolescents having a 70% chance of becoming overweight or obese adults (U.S. Department of Health and Human Services, 2012). Indeed, adolescence is a particularly important period to study since it is period of growth and maturation accompanied by radical behavioral (such as diet, physical activity, and sedentary behavior) and psychological changes (such as increased risk for depression and body esteem issues) (Alberga et al., 2012), as well as a variation in BMI resulting from pubertal status (Medscape Reference, 2012).

Figure 1



(CDC, 2012)

Figure 1 shows the prevalence of obesity among person aged 12–19 Years, by ethnicity and gender. 26.5% of Hispanic males, 22.6% of non-Hispanic black males, and 17.5% of non-Hispanic white males were obese. Prevalence of obesity was 24.8% among non-Hispanic black females 14.7% among non-Hispanic white females and 19.8% among Hispanic females.

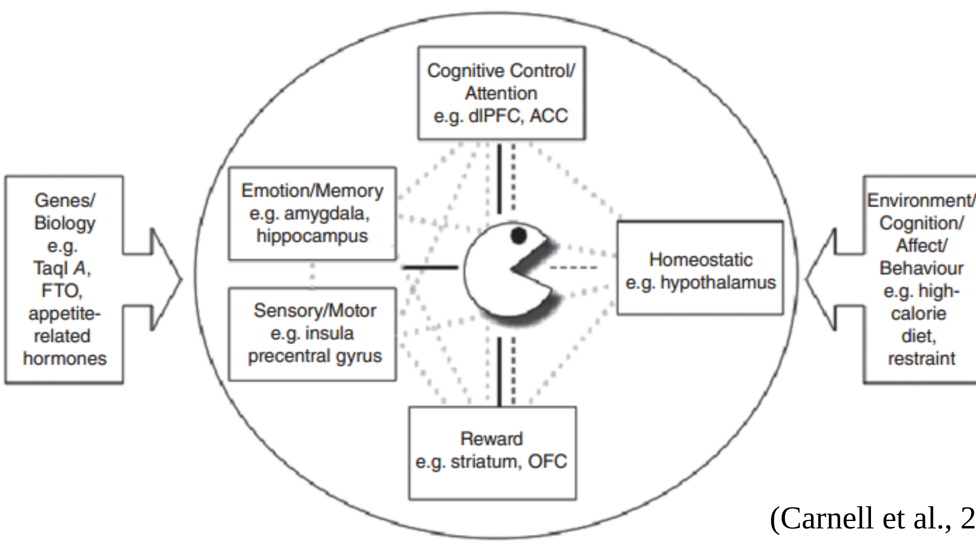
Eating Behavior Differences Between Obese vs. Normal Weight Individuals:

In general, obesity can be attributed to eating habits resulting in excessive energy intake (Schwartz et al., 2000). In one study of females, obese individuals consumed significantly more than normal weight individuals when there was accessible food when they were doing both boring and interesting tasks (Abramson et al., 1977). Evidence also suggests that obese individuals consume a higher energy-dense diet than normal-weight individuals, highlighting the importance of fruit and vegetable consumption (Ledikwe et al., 2006). Similar patterns are also seen in childhood, with several studies demonstrating that obese children also show higher food responsivity and lower satiety responsivity compared to normal-weight children (Carnell et al., 2008; Webber et al., 2009; Viana et al., 2008) as well as increased intake of palatable foods even following a satisfying meal (Hill et al., 2008).

Neuroimaging and Obesity:

Informed efforts to prevent or treat childhood obesity could significantly impact the nation's health (Southern, 2004), but in order to develop the best interventions, more knowledge regarding the biobehavioral basis of obesity is needed. See Figure 2 for a summary of the different influences on obesity. Recently, neuroimaging techniques such as positron emission tomography (PET), functional magnetic resonance imaging (fMRI), and magnetic resonance imaging (MRI) have become increasingly common technique in obesity research, because they allow networks of neural activation in response to stimuli such as food to be investigated.

Figure 2



(Carnell et al., 2012)

In Figure 2, the bold lines represent exaggerated appetitive-related signals, broken lines represent impaired appetite-related signals, and grey dotted lines represent functional interactions between brain areas. This model explains that in relation to food, increased activity in brain areas related to reward, emotion/memory and sensory/motor processing, along with decreased activity in areas related to homeostatic satiety and cognitive control/attention, cause eating behavior phenotype leading to obesity.

One neuroimaging method of particular interest, functional Magnetic Resonance Imaging (fMRI), measures brain activity by detecting associated changes in blood flow (Huettel et al., 2009). Through this technique, researches have been able to explore differences in individuals' neuronal activity in response to exposure to food and non-food items (St-Onge et al., 2005; van der Laan et al., 2011). For example, the insula has been found to be involved in cognitive aspects of food related behaviors (St-Onge et al., 2005), while brain regions associated with motivation, the reward value of food, cognitive processing, decision-making and self-control have all been shown to demonstrate activation in response to visual food stimuli (Schloegl et al., 2011).

A number of studies have also used fMRI to reveal differences in neural responses to food intake in obese compared with lean individuals. Following oral glucose intake in obese and lean individuals, obese subjects have shown an attenuated and delayed inhibitory signal in the hypothalamus suggesting that this functional abnormality of the hypothalamus may lead to increased energy intake (Matsuda et al., 1999). Also, while viewing pictures of high-caloric foods, obese women selectively activated the dorsal striatum (dopaminergic reward area) and as BMI increased, BOLD (Blood Oxygen Level-Dependent) activation was greater in regions associated with taste processing (anterior insula, orbitofrontal cortex [OFC]), motivation (OFC), and emotion and memory (posterior cingulate) (Rothemund et al., 2007). Obese women have also shown greater BOLD activation while viewing pictures of high calorie foods in medial and lateral orbitofrontal cortex, amygdala, nucleus accumbens/ventral striatum, medial prefrontal cortex, insula, anterior cingulate cortex, ventral pallidum, caudate, putamen, and hippocampus, many of which areas are hypothesized to mediate motivational effects of food cues (Stoeckel et al., 2008). Other studies have shown that before a meal, obese (compared to lean) adults showed increased activation in the anterior cingulate and medial prefrontal cortex in response to high and low calorie food images (versus nonfood) images (Martin et al., 2010), and that obese (versus lean) subjects had greater responses to food (versus non-food) images after eating in frontal, temporal, and limbic regions, along with corticolimbic regions (lateral OFC, caudate, anterior cingulate) (Dimitropoulos et al., 2012). This indicates a heightened response in brain regions implicated in reward and addiction even after eating.

In addition to research in adults, a small number of neuroimaging studies have focused on adolescents. This population is important to research not only because that developmental stage can give important insight into obesity, but also because age-related changes in the frontal and parietal neural networks involved in spatial working memory change (Shweinsburg et al., 2005), and changes in functional integration relating to emotion (Burnett et al., 2009), could affect the brain's responses to food cues. One study showed there was increased neural response to food stimuli in the amygdala, OFC, medial prefrontal cortex (medial PFC), and frontal operculum (Holsen et al., 2005; (Wallner-Liebmann et al., 2010). Another fMRI study using anticipated (conditioned cue) tastes of chocolate milkshake showed that obese adolescents had greater BOLD activation in the anterior and middle insula and somatosensory brain areas (Rosenbaum et al., 2008), suggested as emotional, executive, and sensory areas related to food.

Research Focus:

One aim of the present study is to observe differences in total food intake between low-weight, mid-weight, overweight, and obese adolescents. It is hypothesized that the greater the adolescent's weight group (and BMI percentile), the greater his or her food intake, particularly of high energy-dense foods, will be. Another aim is to compare fMRI brain activation differences between lean and overweight/obese adolescents. It is hypothesized that overweight/obese adolescents will show greater brain activation than lean adolescents, when presented with high energy-dense food words compared to low energy-dense food words, and food words compared to nonfood words, in brain regions associated with appetitive reward (such as the striatum and orbitofrontal cortex), taste processing (such as the insula), and emotion, memory, and motivation (such as the hippocampus). It is also hypothesized that lean adolescents will have greater brain activation compared to obese adolescents when presented with high energy-dense food words compared to low energy-dense and nonfood words in brain regions associated with satiety and restraint (such as the anterior cingulate cortex). Exploring food intake and brain activation differences between lean and obese adolescents will enable a better understanding of the biobehavioral basis of overweight and obesity.

Methods

Subjects:

The subjects were adolescents between the age of 14 and 18. Subjects had to be post pubertal, speak English fluently, and be right handed. In addition, they could not have a current physical or psychiatric illness, be on prescription medications (which may influence appetite or weight), be participating in a structured weight loss program or dieting, have claustrophobia (given the nature of the MRI apparatus), be pregnant (or have breast fed within the last 6 months), have dietary restrictions (such as vegetarianism), have non-removable metal in their body (which is not permitted in an MRI), be a current smoker or smoker within the past 6 months, drink more than 2 alcoholic drinks per day, have substance use or dependence, be over 300 pounds (unable to have the MRI done), exercise for more than 6 hours per week (vigorous exercise can influence appetite), have a Liking score of <50 (on a scale of 1-100) for fMRI food words and buffet meal foods and beverages, or have unfamiliarity with >20% of fMRI food words or buffet meal foods and beverages. For sample characteristics see Table 1a, 1b, 1c, and 1d. Due to time restraints, there was a reduced number for the reporting of the fMRI results. Also, Socio-economic differences, such as mothers' income and education, were compared between weight groups to ensure that the results are not partly due to socioeconomic differences. Chi square analysis showed there were no significant differences between income and education between weight groups.

Table 1a: Sample Characteristics of Total Participants (n=35)

	Different Weight Groups				
	Less than 50th percentile (n=11)	50th to less than 85th percentile (n=14)	85th to less than 95th percentile (n=4)	95th and greater than 95th percentile (n=6)	Total (n=35)
Age	16.1 ± 2.0	15.4 ± 1.3	16.0 ± 2.3	15.5 ± 1.4	15.7 ± 1.6
BMI	19.2 ± 1.2 [a,b,c]	22.3 ± 1.3 [a,d,e]	26.2 ± 1.9 [b,d,f]	37.0 ± 5.7 [c,e,f]	24.3 ± 6.7
BMI percentile	30.8 ± 10.8[a,b,c]	69.6 ± 10.9 [a,d,e]	90.3 ± 1.7[b,d]	98.2 ± 1.6[c,e]	64.7 ± 27.1
BMI z-score	-0.5 ± 0.3 [a,b,c]	0.5 ± .33 [a,d,e]	1.3 ± 0.1 [b,d,f]	2.3 ± 0.3 [c,e,f]	0.6 ± 1.0
Male	6 (55%)	6 (43%)	3 (75%)	3 (50%)	18 (51%)
Female	5 (45%)	8 (57%)	1 (25%)	3 (50%)	17 (49%)

a,b,c,d,e,f = Similar letters indicate significant differences (p < .05) between weight groups in each row.

Table 1b: Sample Socio-economic Characteristics of Total Participants (n=35)

	Different Weight Groups				
	< 50th Percentile	50th to less than 85th percentile	85th to less than 95th percentile	95th &greater than 95th percentile	Total (n=35)

	(n=11)	(n=14)	(n=4)	(n=6)	
Income (# of moms who had an income of $40,000 or greater)	7 (64%)	6 (43%)	2 (50%)	0 (0%)	15 (43%)
Education (# of moms who were college graduates)	6 (55%)	8 (57%)	3 (75%)	1 (17%)	18 (51%)

Table 1c: Sample Characteristics of Participants for fMRI Results (n=22)

	Different Weight Groups		
	lean (n=15)	overweight/obese (n=7)	Total (n=22)
Age	15.3 ± 1.5	16.0 ± 1.7	15.5 ± 1.6
BMI	20.7 ± 2.1 [a]	33.6 ± 7.9 [a]	24.8 ± 7.6
BMI percentile	52.1 ± 23.0 [b]	94.7 ± 4.5 [b]	65.6 ± 27.8
BMI z-score	0.1 ± 0.7 [c]	1.9 ± 0.6 [c]	0.6 ± 1.1
Male	9 (60%)	5 (71%)	14 (64%)
Female	6 (40%)	2 (29%)	8 (36%)

a,b,c = Similar letters indicate significant differences ($p < .05$) between weight groups in each row.

Table 1d: Sample Socio-economic Characteristic of Participants for fMRI Results (n=22)

	Different Weight Groups		
	lean (n=15)	overweight/obese (n=7)	Total (n=22)
Income (# of moms with an income of $40,000 or more)	7 (47%)	1 (14%)	8 (36%)
Education (# of moms who were college graduates)	8 (53%)	3 (43%)	11 (50%)

Experimental Procedure:

The subject drank 2 bottles of Boost as early in the day as possible, and fasted for the remainder of the day leading up to the scan. The adolescent signed HIPAA (to protect patients' medical records and other health information provided) and consent forms (with mothers signing consent for the adolescents aged 14-17y) and completed questionnaires to more fully determine eligibility based on the criteria mentioned above. Adolescents also had their height, weight, waist and body fat measured. Adolescents completed questionnaires assessing their mood, activities of the day, and compliance with energy drink consumption. Females also took a pregnancy test. The adolescent was trained on the fMRI word stimuli task on an office computer. The adolescent was able to practice an 8-minute trial of the fMRI paradigm to ensure an understanding of the task and an ability to complete the task. After the training, the adolescent was prepped for the scan. A metal detector was used to ensure the adolescent could safely enter the fMRI room. The adolescent was positioned in the scanner, and the projector and a mouse for the word stimuli task was prepared.

The scan took about an hour, with brain activation being recorded in response to presentations of high energy-dense, low energy-dense food cues, and non-food (control) office supply cues (see Figure 3 for the cue presentation paradigm). Subjects participated in three "runs", with each run randomly comprised of nine high energy-dense foods, nine low energy-dense foods, and nine control cues, with all stimuli similar in word length and number of syllabi. The subject was asked to focus on a stimulus word for six seconds. For foods, subjects were asked to think about how the given food looked, felt, smelt, and tasted, and how it would feel to

Figure 3

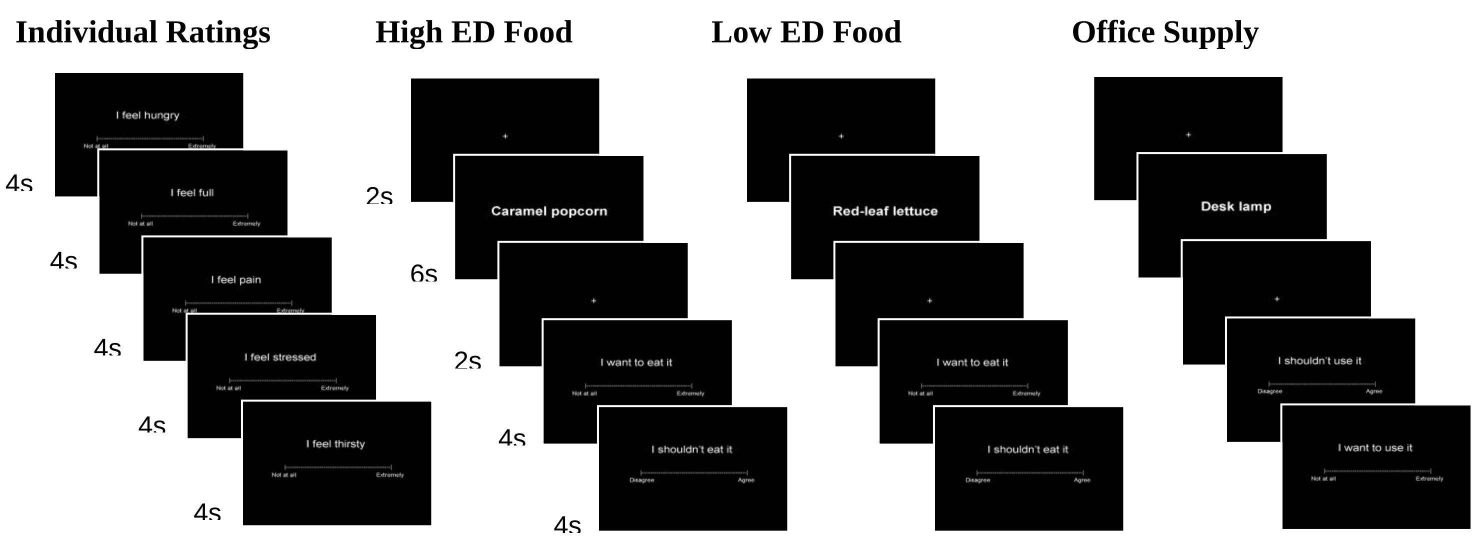
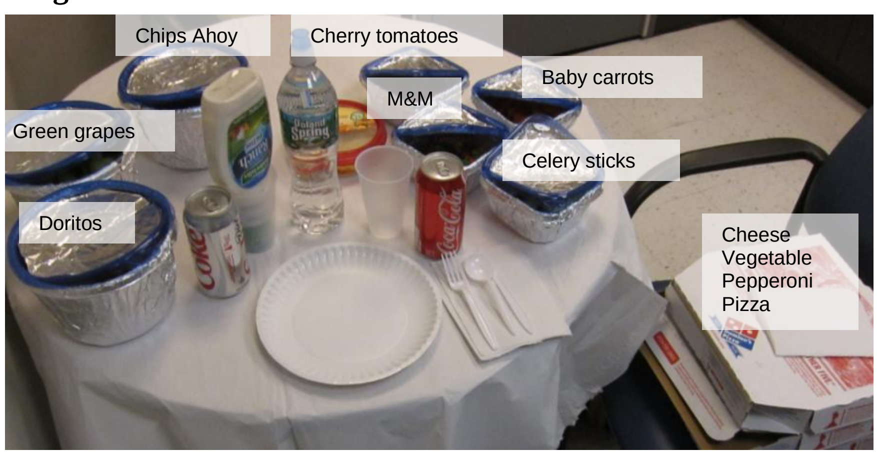


Figure 3 shows the fMRI paradigm. The subject had four seconds to answer each of the "Individual Rating" questions. For the high/low calorie food and object words, the word was shown for six seconds, there was two seconds allotted for resting, and finally the subject had four seconds to answer the want/restraint questions following each food/object word.

eat it at that moment. For the office supplies, subjects were asked to imagine how the object looked and felt, and how it would feel to use it at that moment. Following each stimulus, there was a two second fixation period. For foods, subjects were then given four seconds to respond to the statement, “I want to eat it” on a horizontal line on which subjects could click anywhere between the left endpoint “Not at all” to the right end point “Extremely.” Subjects were then given four seconds to respond to the prompt “I shouldn’t eat it?” with the same available responses. For object words, subjects were given four seconds to respond to the prompt, “I want to use it” and then four seconds to respond to the prompt, “I shouldn’t use it” with the same available answers. Both before and after the scan, subjects were asked to rate their hunger, fullness, stress, pain, thirst, and desire to eat.

After the scan, subjects were directed to an ad libitum buffet-meal comprised of the following high energy-dense and low energy-dense foods and beverages: Doritos, green grapes, Chips Ahoy, cherry tomatoes, baby carrots, celery sticks, M&Ms, Coke, Diet Coke, hummus, water, ranch dressing, and Domino’s hand-tossed cheese, pepperoni, and vegetable pizzas. The subject was not allowed to bring a bag into the room to make sure that no unconsumed food was removed from the kitchen. The buffet meal was pre-weighed and arranged in the same way for each subject (see Figure 4). Upon entering the kitchen, the subject was asked to “treat the meal like their dinner” and “not to eat for 5 hours following the buffet meal” to encourage ad libitum eating. The subject was advised that he/she would have 30 minutes to eat as much of the meal as he/she would like, but could finish early if preferred. Entry to the room was restricted to ensure the subject ate in private and was not disturbed during the meal. After the meal, the subject was brought out of the kitchen to complete remaining questionnaires and paperwork, and the remaining food from the meal was weighed to determine how much of each type of food was eaten.

Figure 4



Food intake analysis:

Univariate ANOVAs (SPSS software) were used to compare total food, healthy food, and high energy-dense food intake in calories between weight groups. Post-hoc analysis was used to compare intake between each weight group and to test for significance ($p < .05$). Post-hoc analysis was also done between weight groups to test for significant food intake differences between weight groups. Chi square tests were used to compare income and education of the adolescents' mothers. Correlations were used to test associations between total food intake (in calories) and the adolescent's BMI z-score, which is also known as the BMI standard deviation (s.d.) score and represents a measure of relative weight adjusted for child age and sex.

fMRI analysis:

Imaging was performed with a 3.0 Tesla GE LX Scanner (55 cm diameter bore and) hydraulic scanner table (300 lb capacity) with an 8-channel head coil. First, three-plane localization was used to verify head position and then a structural scan was taken. A 3D spoiled gradient recal (SPGR) image was acquired for coregistration with the axial functional images and with the standard image coordinate system. Then the functional scans were taken while the subjects were doing the tasks. Functional T_2*-weighted echo planar image (EPI) parameters were: 2,800 msec repetition time (TR), 25 msec echo time (TE), 90º flip angle, 64 x 64 acquisition matrix, 24 cm x 2m cm field of view (FOV) and 3 mm slice thickness. In each run, axial scans of the whole brain were acquired, each scan consisting of 43 contiguous slices per volume and 185 volumes per run .

BOLD imaging data was then analyzed using SPM8. Prior to statistical analyses, realigned T2-weighted volumes were slice-time corrected, spatially transformed to a standardized brain (Montreal Neurologic Institute) and smoothed with a 8-mm full-width half-maximum Gaussian kernel. First level regressors were created by convolving the onset of each trial type with the canonical hemodynamic response function [HRF] with duration of 4 sec. High-ED > low-ED, high ED > NF and low-ED > NF were then contrasted. Contrasts were then passed on to 2nd level analyses which employed RM ANOVAs to analyze contrast by group where we compared lean vs. obese/overweight subjects.

Results/Discussion

Food Intake Results/Discussion:

Figure 5

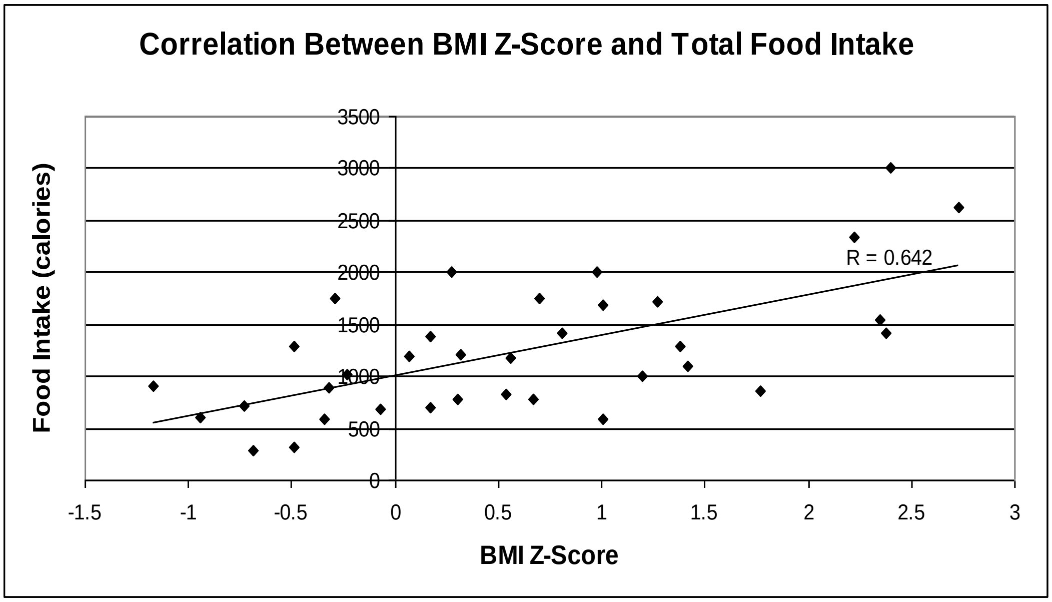
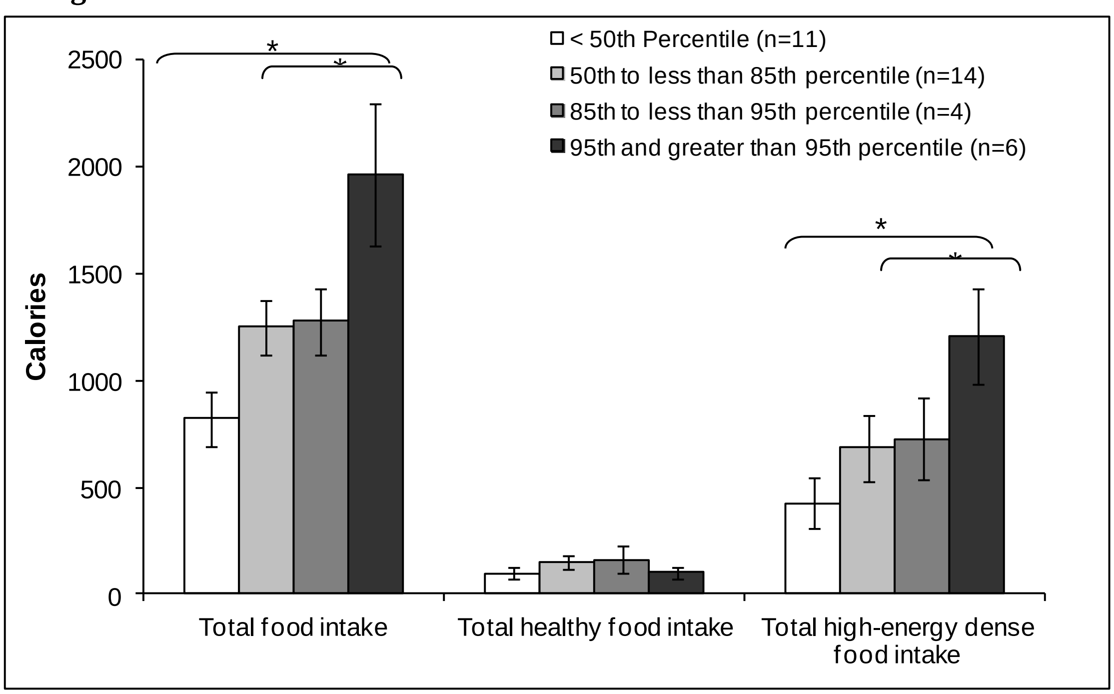


Figure 5 shows the correlation between BMI z-score and total food intake. This graph shows that there is a strong positive correlation (R=0.62, p<.001) between BMI z-score and total food intake (in calories).

Figure 6



* = significant (p<.05) differences between weight groups

Figure 6 illustrates total food intake, total healthy food intake, and total energy-dense food intake in calories between adolescents in different weight groups: less than 50th percentile (low-weight), the 50th to less than 85th percentile (mid-weight), the 85th to less than 95th percentile (overweight), and the 95th and greater than 95th percentile (obese). Figure 6 shows that there were significant group differences in total food intake (p=.002) and total high-energy dense food intake (p=.039), but not in total healthy food intake (p=.573). Also, through post-hoc analysis, significant differences between weight groups were found. For example, there were significant differences in total food intake between low-weight and obese adolescents (p<.001), mid-weight and obese adolescents (p=.009), and slightly significant differences between overweight and obese adolescents (p=.05). There were also significant differences in total high-energy dense food intake between low-weight and obese adolescents (p=.004) and between mid-weight and obese adolescents (p=.041). However, there were no significant differences observed for total healthy food intake (p > .05).

As hypothesized, total food intake was overall higher in adolescents with a higher BMI z-score, as well as in the obese groups compared to other groups, especially the high energy dense foods. However, while obese adolescents had the most total food intake and total high energy dense food intake, they did not have a great amount of healthy food intake. These findings suggest that obese individuals have a higher intake because of their increased amount of high ED food. This could help in preventative methods for obesity by trying to substitute high energy dense foods with healthy foods in daily diets.

fMRI Results:

Figure 7a illustrates regions where there was greater brain activation (p<.05, K=50) in obese adolescents versus lean adolescents in response to high energy dense foods compared to low energy dense foods (Comparison Condition 1).

Figure 7a

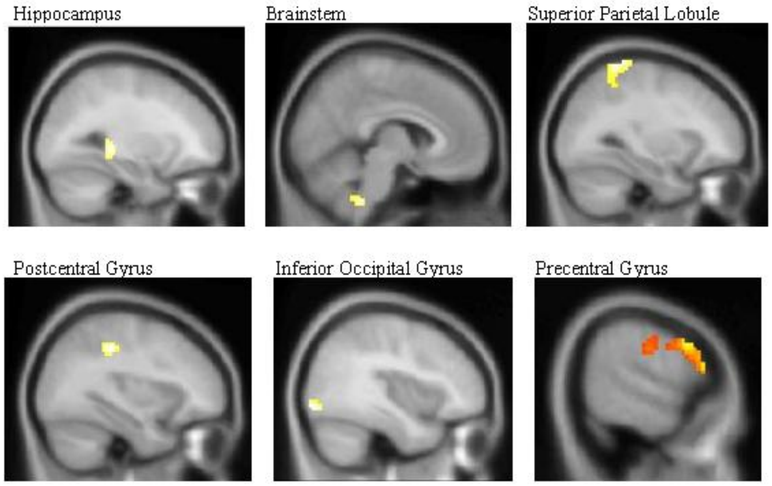


Table 2a summarizes these preliminary results.

Table 2a

		MNI coordinates		
Region	**Side**	**x**	**y**	**z**
Hippocampus	L	-27	-34	-2
Brainstem	R	6	-43	-47
Superior Parietal Lobule	L	-30	-46	70
Postcentral Gyrus	L	-33	-34	40
Inferior Occipital Gyrus	R	39	-85	-11
Precentral Gyrus	R	60	14	34

x,y,z=Montreal Neurological Institute coordinates

Figure 7b illustrates regions where there was greater brain activation ($p<.05$, $K=50$) in lean adolescents versus obese adolescents in response to the same condition.

Figure 7b

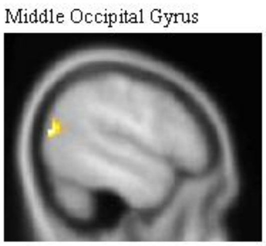


Table 2b

		MNI coordinates		
Region	**Side**	**x**	**y**	**z**
Middle Occipital Gyrus	L	-51	-76	16

x,y,z=Montreal Neurological Institute coordinates

Table 2b summarizes these preliminary results.

Figure 7c illustrates regions where there was greater brain activation ($p<.05$, $K=50$) in lean adolescents versus obese adolescents in response to high energy dense foods compared to control objects (Comparison Condition 2).

Figure 7c

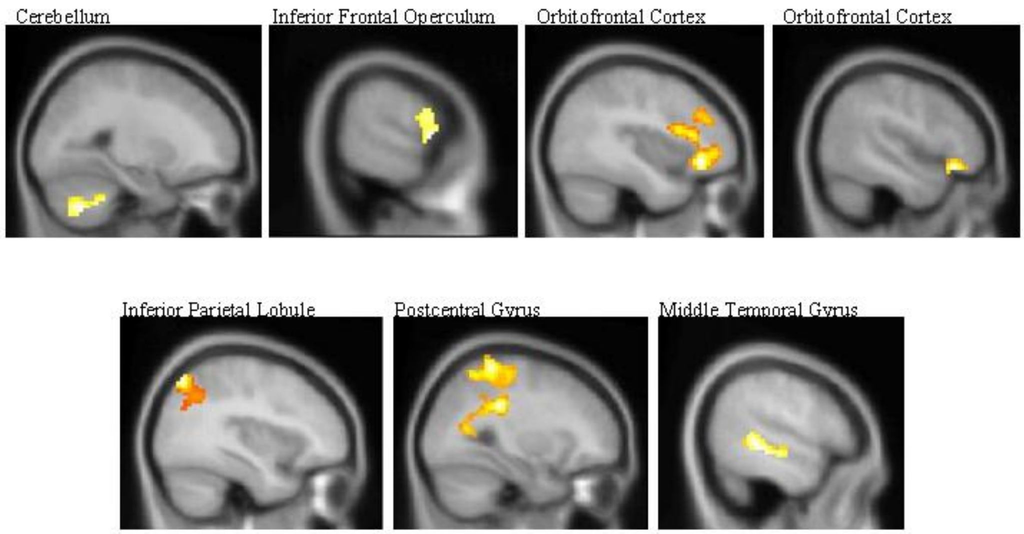


Table 2c summarizes these preliminary results.

Table 2c

		MNI coordinates		
Region	**Side**	**x**	**y**	**z**
Cerebellum	L	-24	-64	-44
Inferior Frontal Operculum	R	63	11	7
Orbitofrontal Cortex	L	-39	32	-8
Orbitofrontal Cortex	R	48	26	-14
Inferior Parietal Lobule	L	-36	-73	49
Postcentral Gyrus	R	30	-40	64
Middle Temporal Gyrus	L	-54	-40	-2

x,y,z=Montreal Neurological Institute coordinates

Figure 7d illustrates regions where there was greater brain activation ($p<.05$, $K=50$) in lean adolescents versus obese adolescents in response to high and low energy dense foods compared to control objects (Comparison Condition 3). There were not many significant differences in activation for conditions 2 and 3. This shows that comparing control objects to high energy dense foods, as well as both high and low energy dense foods, have similar results.

Figure 7d

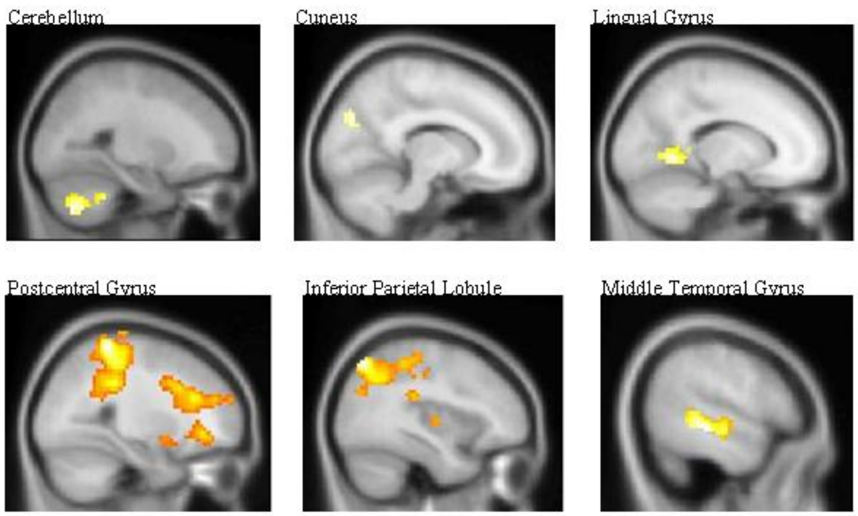


Table 2d summarizes these preliminary results.

Table 2d

		MNI coordinates		
Region	**Side**	**x**	**y**	**z**
Cerebellum	L	-24	-70	-47
Cuneus	R	12	-79	31
Lingual Gyrus	L	-15	-58	-2
Postcentral Gyrus	R	-27	-43	67
Inferior Parietal Lobule	L	-36	-73	49
Middle Temporal Gyrus	L	-54	-31	-8

x,y,z=Montreal Neurological Institute coordinates

Figure 7e illustrates regions where there was greater brain activation (p<.05, K=50) in lean adolescents versus obese adolescents in response to low energy dense foods compared to control objects (Comparison Condition 4).

Figure 7e

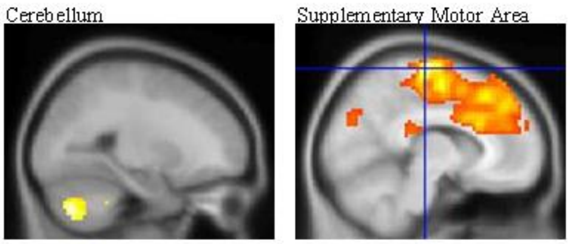


Table 2e summarizes these preliminary results.

Table 2e

		MNI coordinates		
Region	**Side**	**x**	**y**	**z**
Cerebellum	L	-24	-70	-44
Supplementary Motor Area	R	9	-22	70

x,y,z=Montreal Neurological Institute coordinates

fMRI Discussion

Results showed that obese adolescents showed greater activation in the hippocampus than lean adolescents when observing the high energy dense foods. This is significant because the hippocampus has been previously been seen to be related to emotion and memory (Carnell et al., 2012). The hippocampus has also been hypothesized to mediate motivational effects of food cues (Stoeckel et al., 2008). In addition, this region has been associated with reward and motivation (Plassman et al., 2008; Wallner-Liebmann et al., 2010). This is also concurrent with one study where obese compared to lean women showed greater activation in reward processing regions, like the hippocampus, in response to receipt and anticipated receipt of palatable food (Ng et al., 2011). Because obese adolescents showed increased activation in the hippocampus when observing the high ED foods, it can be hypothesized that obese adolescents may want to eat more high ED foods because of their emotional attachment to these types of food, as well as the reward they feel from it when observing these types of food.

Lean adolescents showed greater activation than obese adolescents when observing high energy dense foods compared to control objects in the cerebellum, a region associated with motor learning, emotion, attention, and motivation (Carnell et al., 2012; Killgore et al., 2003). Severe and early-onset obesity, as seen in conditions such as Prader-Willi syndrome (PWS), is associated with abnormalities of the frontal lobe, including the cerebellum. For example, a recent structural MRI study showed reduced cerebellar gray-matter volume in subjects with PWS as compared to normal controls (Ogura et al., 2011). Additionally, in another study examining brain activation differences in healthy-weight women, the cerebellum demonstrated the greatest activation observed in response to high calorie food images versus low calorie foods and non food words, and cerebellar responses to food may be modifiable via intervention (Killgore et al., 2003). Many studies have shown that successful weight reduction is accompanied by changes in brain activation in response to food cues (DelParigi et al., 2007; Le et al., 2006; Le et al., 2007). Furthermore, patients 1-month after undergoing Roux-en-Y gastric bypass (RYGB) showed reduced fMRI brain activation in the cerebellum in response to food cues, particularly high-energy density food images, which supports a role for the cerebellum in food responding (Ochner et al., 2011).

Lean adolescents also showed greater activation than obese adolescents when observing high energy dense foods compared to control objects in the orbitofrontal cortex (OFC), which has been associated with appetitive behavior through visual food presentations in primates and taste and smell in humans (De Araujo et al., 2003; O'Doherty et al., 2000). The OFC is known for its role in reward of food stimuli (Killgore et al., 2003). In addition, OFC activation is associated with the pleasantness ratings of the taste and smell of food (Kringelbach et al., 2003; Rolls and Grabenhorst, 2008). Obese adolescents were originally hypothesized to have increased activation in the OFC compared to the lean adolescents when viewing energy dense food words because of its role in reward. However, these results, in which the lean adolescents showed greater OFC activation are still significant because of the OFC has also been hypothesized to underlie termination of eating (Small et al., 2001). Also, in one study, the OFC was not only activated during exposure to a pleasant taste, but also during anticipation to receiving this taste (O'Doherty et al., 2002). This may show that the lean adolescents are more conscious about what they are going to eat. Interestingly, this still shows that lean adolescents feel that reward from the high energy dense foods like obese individuals.

There were some limitations of this research, which should be taken into consideration, especially for future research. One of the limitations is the small sample size, especially for the fMRI results. Because of time restraints regarding analysis, only 22 of the 35 subjects' fMRI results are reported in this study. Especially for weight group analyses, the obese group was particularly small which could have affected the results. Also, for the fMRI results specifically, lean was compared with both overweight and obese adolescents. There could have been a greater significance comparing lean and only obese adolescents. Another limitation is that food words were used as stimuli, rather than pictures. Words could be not as stimulating appetite as food images would have. However, the word provided a constant since there were no variations in palatability.

In conclusion, when observing high energy dense foods, obese adolescents compared to lean adolescents showed greater activation in regions such as the hippocampus, which is associated with emotion, memory, and reward, while lean adolescents showed greater activation in regions such as the cerebellum, associated with attention and the OFC, associated with reward. This research extended the results of existing behavioral and neuroimaging studies that indicate differences between lean and obese individuals to test a biobehavioral model of obesity susceptibility.

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