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“NEURAL MECHANISMS OF FOOD AND MONETARY REWARDS AND THEIR RELATION TO OVEREATING IN CHILDREN”

A Dissertation in
Nutritional Sciences
by
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Abstract

Currently, 17% of American children are considered obese. Yet, the reasons as to why some children are more susceptible to overeating are poorly understood. Deficits in decision-making abilities, such as how the brain responds to rewards in regions implicated in reward processing and inhibitory control, have been linked to obesity in children. This suggests that fundamental differences in decision-making abilities may be a risk factor for overeating, and potentially, a target for prevention. However, it is currently unknown if deficits in key decision-making regions relate to objectively measured food intake. This dissertation adds to the literature by investigating how brain determinants of decision making for food and money relate to food intake and weight status in a cohort of children 7-11-years-old. Neural correlates of decision-making were assessed by having children undergo a functional magnetic resonance imaging (fMRI) scan while completing a modified card-guessing task that assessed anticipating and winning food and monetary rewards. Behavioral correlates of decision-making were assessed with a Go/Nogo (reactive inhibitory control) task with and without food and monetary reward incentives. Objectively measured food intake was assessed using three different laboratory test meals aimed at measuring different aspects of eating behavior. Results from all three papers identified potential decision-making mechanisms that were associated with obesity risk development. For the first time, we showed that how the brain responds to rewards might play a crucial role in identifying behaviors that can lead to future weight gain. Brain response to food vs. money rewards in regions associated with emotion, reward processing, and inhibitory control predicted food-
approach behaviors and laboratory measures of overeating independently of how much a child weighed. In addition, weight status negatively correlated with reactive inhibitory control performance during a reward incentivized Go/Nogo task. Reactive inhibitory control was not related to food intake under controlled settings, however, since weight status was related to reactive inhibitory control this might provide insight into how these decision-making processes relate to overeating outside of the laboratory. Altogether, findings from this dissertation identified some of the neural mechanisms contributing to maladaptive eating behavior. This dissertation provides the groundwork for understanding how cognitive mechanisms contribute to eating behavior in children, providing insight into why some children are more susceptible to overeating than others. Understanding how reward processing and inhibitory control relates to food intake in children may be the key to increased success of intervention and prevention programs.
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List of Abbreviations

BMI: Body mass index
BOLD: Blood-oxygen-level-dependent
CEBQ: Children’s Eating Behavior Questionnaire
dlPFC: Dorsolateral prefrontal cortex
FA: Food anticipation
fMRI: Functional magnetic resonance imaging
FW: Food win
IFG: Inferior frontal gyrus
MA: Money anticipation
mPFC: Medial prefrontal cortex
MW: Money win
NA: Neutral anticipation
NW: Neutral anticipation

ROI: Region of interest
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Chapter 1

Introduction

Childhood obesity is a significant concern in the United States (1) and globally (2). Despite the widespread existence of prevention and intervention strategies, approximately 17% of children in the United States are considered obese (3). Obesity in children is associated with the early onset of obesity-induced medical consequences, such as diabetes, cardiovascular disease, and cancer (4–6) as well as psychosocial implications, including depression and weight-based stigma (7, 8). In addition, childhood is a period marked by rapid growth and development (9), which makes this population more vulnerable to excess weight gain. Studies find that anywhere between 24-90% of children with obesity become adults with obesity (10, 11). This suggests that adult obesity rates will only continue to increase. To reverse the current trends, it is imperative to investigate and understand the mechanisms that contribute to excess food intake in children. Currently, success rates of current intervention and prevention efforts are low (12–14), therefore, understanding the mechanisms by which some children are more vulnerable to overeating than others may enable development of successful prevention and intervention strategies.

The primary contributor to obesity is the overconsumption of highly palatable, high-energy-dense foods (15–18). Yet, there are various reasons why children have difficulty with
resisting the temptation to overeat. The current food environment is rich in the availability of highly palatable foods (18, 19), which may make it harder for children to resist the temptation of overconsuming them. Even though all children are exposed to similar environments filled with tempting foods, not every child becomes obese, which highlights the need to study individual differences. In particular, understanding the vast nuances of decision-making in regards to food choice behavior could shed crucial insight into risk factors for obesity development. One key component of food intake is rooted in basic decision-making and given the current prevalence of childhood obesity it may be that differences in decision-making may explain why some children are more susceptible to overeating than others.

Decision-making is a broad term for a collection of cognitive processes, which contribute to behavioral outcomes. Reward processing and inhibitory control mechanisms are two processes that contribute to decision-making. Reward circuitry plays a critical role in food intake and weight regulation (20), whereas inhibitory control is involved in stopping processes or behaviors (21), such as overeating. In adults, poor decision-making abilities have been associated with obesity and eating disorders such as binge eating (22–24), while in children, deficits in decision-making also correlate with obesity (25, 26). Thus, it is thought that deficits in decision-making relate to overconsumption and subsequent weight gain, but this has yet to be tested in children.

Recent advances in brain imaging technology have allowed for the investigation of the neural correlates of reward processing and inhibitory control and their relationship to weight status. Functional magnetic resonance imaging (fMRI) studies have shown that obesity in adults and children relates to the brain response to palatable food cues in regions
implicated in reward processing and inhibitory control (27–32). Additionally, adults with obesity showed altered neural processing for multiple reward types (33) suggesting that reward processing in general, is altered in individuals with obesity. Collectively, these foundational studies have provided insight into how individuals with obesity respond to rewards but they give limited insight into how this relates to actual eating behavior. Therefore, it is unclear if overeating relates to the brain response to reward. Understanding the neural mechanisms underlying eating behaviors may have impacts on obesity intervention and prevention programs.

The purpose of this dissertation is to bridge the gap in the literature by assessing how reward and inhibitory control processing relates to food intake and weight status in children 7-11-years-old. This dissertation has three main objectives. The first objective is to investigate how the brain responds to multiple reward types and if this relates to weight status in children. The second objective is to assess if the brain response to rewards is related to food intake. The third objective is to assess if inhibitory control response differs in the presence of a reward and if inhibitory control abilities relate to overeating. This introductory chapter will provide a brief overview of relevant topics to better understand the concepts presented in the present dissertation. First, a brief overview of fMRI will be provided. fMRI is a state-of-the-art method for imaging human brain function. Next, the importance of investigating decision-making processes and the relation to food intake in children will be discussed. This will be done by detailing the normal developmental changes associated with reward processing and inhibitory control circuitry and how these processes may be further compromised in children with obesity. The literature focused on the association between reward and inhibitory control circuitry and increased weight status will be reviewed. Following this, the current neurotheoretical models of overeating will be discussed. Finally,
this chapter will provide a brief outline of the objectives and hypotheses contained in this dissertation.

1.1 fMRI as a tool to investigate neural correlates of behavior

Historically, science has used animal and human lesion studies to learn about the complexities of brain function. For example, the famous case study of H.M., in which the hippocampus of a 27-year-old man was removed to provide relief from chronic seizures, provided insight into memory formation. Removal of the hippocampus caused H.M. to develop anterograde amnesia while his working and procedural memory remained intact (34). The example of H.M. demonstrates the importance of lesion studies for providing information about how specific brain regions are necessary for particular functions. However, today, it is unnecessary to rely solely on invasive studies to understand brain function in humans. Advancements in neuroimaging technology, such as fMRI, have revolutionized science. fMRI is a non-invasive in-vivo imaging tool with high spatiotemporal resolution that can provide insight into neurobiological mechanisms that contribute to behavior (35).

In order to understand fMRI, a basic description of MRI is needed. MRI is a tool used to create 3D images of anatomical structures. This is done by detecting the magnetic properties associated with hydrogen (H) and water molecules (H₂O) in various tissues (36). These hydrogen atoms are then aligned according to a strong magnetic field emitted by the MRI scanner. A radio frequency magnetic pulse is then applied, causing the hydrogen nuclei
to absorb energy and create a magnetic resonance signal. The radio frequency coils of the scanner then detect the magnetic resonance signal. MRI is used to classify anatomical structures by applying different pulse sequences (i.e., the combination of changing gradients and oscillating electromagnetic fields) (37) to measure differences in magnetic properties across biological tissues.

fMRI relies on the same principles as MRI but the BOLD signal is based on contrast in magnetic susceptibility due to differences in hemoglobin within anatomical regions over time. Thus, fMRI provides insight into how brain functions across the anatomical regions change. It is important to note that structural and functional images are required to interpret brain function. Pairing fMRI with experimental manipulations allows researchers the ability to observe how changes (i.e., increases or decreases) in blood-oxygen-level-dependent (BOLD) signal differ throughout the brain in response to stimuli and/or cognitive demands. fMRI is related to neuronal firing (38). This is based on theories regarding the hemodynamic response: the process of replenishing recently fired neurons with oxygen. fMRI measures the exchange of oxyhemoglobin and deoxyhemoglobin by detecting differences in their magnetic properties (39). Although fMRI can only measure indirect activation, changes in BOLD response are thought to reflect neuronal firing (38) by measuring the metabolic requirements of active neurons (37). Therefore, BOLD responses are thought to symbolize neural activation in specific regions of the brain.

fMRI has several limitations that need to be discussed. The poor temporal resolution does not give precise timing associated with processing speed of neuronal firing. One technique to increase the temporal resolution of fMRI is to increase image acquisition time, but this can decrease the quality of the image produced, and subsequently, compromise
spatial resolution. Therefore, the speed-accuracy tradeoff is a major limitation of fMRI (37, 40). Another limitation is that the fMRI signal cannot distinguish between neuronal activity associated with excitation (i.e., glutamatergic neurotransmission) versus inhibitory neural firing (i.e., GABAergic neurotransmission) (37). For example, increased BOLD response in inhibitory control regions may be the result of neurons firing to increase excitation, leading to decreased cognitive control. In contrast, increased BOLD response in inhibitory control regions may be related to neurons firing to increase excitation, which may suggest increased cognitive control. Although this limitation makes it difficult to interpret the directionality of findings, pairing fMRI with behavioral tasks aids in the interpretation of brain-behavior relationships. Moreover, it is difficult to quantify the fMRI signal; the response magnitude between regions or between tasks even within the same region cannot be compared (40). There are also challenges in regards to the accuracy of spatial mapping as fMRI is extremely sensitive to motion (41). The slightest movement can cause issues in the alignment of tissues and anatomical structures. To decrease the chance of motion-related errors, participants can be trained in mock scanner environments prior to fMRI data collection. Although fMRI has known limitations, it is currently the best non-invasive tool to provide insight into human brain function (40).

1.2 Neurodevelopmental effects

Over the past 20 years, fMRI has provided an understanding of how developmental changes correspond to behavior. Childhood is a period marked by changes in brain maturation, particularly in regions associated with reward processing and inhibitory control
(42). However, changes in these processes happen at different times: reward circuitry develops earlier and more quickly than inhibitory control (43, 44). This creates a mismatch in the maturation between these two processes. In adolescents, maturational asynchrony is associated with increased risk-taking and reward-seeking behavior (45–47), perhaps due to the compelling nature of the hedonic values of reward coupled with an immature cognitive control system. For example, normal developmental changes in the ventral striatum and in the prefrontal cortex could be contributing to heightened sensitivity to reward and subsequent decreased cognitive control (45, 48). This may be more problematic in children with obesity who have increased sensitivity for rewards. However, little is known about how developmental changes in these decision-making regions affect food choice behavior in children.

Increased maturation of developmental processes occurs with the onset of puberty (49). This may increase the disparity between reward processing and inhibitory control maturation. Due to the fact that children with obesity often undergo puberty onset earlier than healthy weight children (50, 51) increased reward-seeking behavior may occur earlier in development. Therefore, in children with obesity, normative developmental changes may exacerbate maladaptive eating behaviors, which could have detrimental impacts on weight gain trajectory. Given that eating behaviors are formed early in life (52, 53) and are sustained throughout the lifetime (54, 55), it is important to understand how the child’s brain responds to rewards and how these responses relate to weight status and food intake. Understanding cognitive developmental differences in children with and without obesity may be critical for successful obesity prevention and intervention.
1.3 Homeostatic and hedonic regulation of food intake

Food intake is controlled via homeostatic and hedonic pathways (56–59). Homeostatic mechanisms are tightly controlled and are best described by a negative/positive feedback loop that unconsciously controls hunger and meal termination (56, 59). For example, when circulating insulin and leptin levels become low, anabolic mechanisms become stimulated and increase food intake while catabolic processes associated with the termination of eating is inhibited (60). Once metabolic requirements are met, anabolic processes release a series of hormones expressed within the gut and brain to stimulate catabolic processes to terminate food intake. This tightly controlled homeostatic process is controlled by the hypothalamus and has little room for variation (61, 62).

Homeostatic processes work hand-in-hand with hedonic pathways (58, 63), which is associated with the pleasantness of food: homeostatic processes send information to regions of the brain involved in reward processing (i.e., hedonic processing). Further, areas involved in reward processing, such as the nucleus accumbens, ventral tegmental area, orbitofrontal cortex, and the insular and cingular cortexes, communicate with the hippocampus (a region associated with memory), and other areas involved in decision-making and executive control (e.g., the dorsolateral prefrontal cortex [dLPFC]) (56). Combined, these aforementioned brain regions communicate with each other to process stimuli and make decisions about whether or not to continue to consume a food (64). Once a decision is made, signals are transmitted back to the supplementary motor cortex, which drives motor behavior (i.e., the processes needed to procure and consume food).
In an optimal environment, homeostatic and hedonic pathways work together to increase food intake in response to metabolic requirements and stop when energy needs are met. However, hedonic mechanisms can override homeostatic processes and contribute to excess food intake (58, 65). For example, anticipatory responses to food such as smell, sight, or thought can also stimulate mechanisms driving ingestive behavior (66). Thus, hedonic mechanisms may play a role in obesity development. The high prevalence of obesity in adults and children (3) suggests that although there are other factors that contribute to obesity, increased sensitivity to hedonic properties of food may explain why some individuals are more susceptible to overeating than others.

1.4 Food is rewarding: Reward and obesity

With the use of fMRI, studies have evaluated if the BOLD response to hedonic properties of food is altered in individuals with and without obesity. The theory exists that altered response to hedonic properties of food could be a contributing factor to overeating. Most studies have focused on assessing how the brain responds to the sight of food by using tasks in which pictures of food are presented during fMRI. Two types of tasks (passive and active) are utilized in fMRI to evaluate how the brain responds to the hedonic properties of food. Passive viewing tasks do not involve other experimental manipulations as participants just view pictures of food. On the contrary, active tasks involve participation, in which responses are made or measured. For example, active tasks have mostly involved assessing differences in brain response to anticipating and receiving drops of milkshake during the
scanning session (32, 67–69). In these tasks, differences in brain response to the anticipation and receipt of a palatable food (e.g., milkshake) can be compared.

The few neuroimaging studies conducted in children have mostly used passive viewing tasks to examine brain response to food rewards (70, 71) and the brain’s relationship to weight status (72, 73, 28). Studies have shown that the BOLD response to food cues differ based on the stimuli presented. In a sample of mostly healthy weight children, greater response in the caudate, a region of the brain associated with reward processing, was observed in response to high versus low-energy-dense foods (71). However, large versus small portions of food, regardless of energy density, correlated with increased response in the inferior frontal gyrus (IFG), a region implicated in inhibitory control (70, 71). In another study, compared to healthy weight children, children with obesity showed an increased response to highly palatable food pictures in the orbitofrontal cortex (OFC) (a region involved in motivation) (72) but a decreased response to food logos in the middle/inferior prefrontal cortex (inhibitory control) (73). Obesity in children is also associated with greater resting-state functional connectivity between the middle frontal gyrus and reward processing regions, (e.g., ventromedial prefrontal cortex, lateral OFC) (28). In sum, these data suggest a link between altered brain activity and obesity. However, at present, it is unclear how these altered brain regions relate to objectively measured overeating.

The pivotal studies offer insight into how the child’s brain responds to viewing pictures of food rewards differs between children of various weight statuses. However, reward processing can be separated into two distinct processes: anticipation and receipt, which are consequences of learned, subjective responses to rewarding outcomes. Therefore, passive viewing tasks are limited in their ability to provide insight into the different
components of reward processing. The majority of studies evaluating anticipation and receipt have been conducted in adolescents and adults, and furthermore, findings between individuals with and without obesity are mixed (32, 68, 74–76). In children, only two studies have evaluated the BOLD response to food receipt and the relationship to obesity (30, 31). These studies showed that greater BOLD response in the insula (30) and hippocampus (31) was related to receipt of sucrose compared to a tasteless solution and this correlated with increased weight status. In the same cohort, eating in the absence of hunger, a measure in which children eat after being fed to satiety (77, 78), correlated with greater activation in the hippocampus in response to receiving a food reward and this also correlated with obesity in children. This suggests that functional responses to reward receipt may be predictive of overeating. However, these studies did not assess brain response to the anticipation of food rewards and the relation to childhood obesity; findings in adults suggest that hyperactivation to the anticipation of food rewards in reward processing regions may play a role in overeating (67). Therefore, future research is needed to understand how children with obesity respond to anticipation and receipt of rewards and the relationship between these responses and overeating. Moreover, studies that have been conducted in adults and adolescents at risk for developing obesity propose that how the brain responds to food is similar to how the brain responds to other rewarding stimuli, such as money (33, 68, 79, 80). These studies suggest that obesity is associated with a general impairment in reward processing that is not domain specific. However, no studies have examined if children with obesity exhibit altered reward processing to multiple reward types and how this relates to overeating and weight status.
1.5 The ability to stop: Inhibitory control and obesity

Food intake is also regulated by inhibitory control mechanisms. Inhibitory control is defined as the cognitive and motor ability involved in stopping or withholding inappropriate responses in order to achieve appropriate tasks or goals (21, 81–83). Therefore, successful inhibitory control is needed for weight maintenance as it can override hedonic responses to food and stop intake. fMRI and behavioral studies have shown correlations between poor performance on inhibitory control tasks and increased weight status. This suggests that adults and children with obesity have impaired inhibitory control (27, 84–86). Therefore, researchers have posited that overeating is a result of deficits in inhibitory control systems. In other words, overeating is thought to occur when the desire for an immediate reward of a highly palatable food overrides the ability to stop intake (87). This theory is supported by a finding showing altered connections between brain regions implicated in inhibitory control and reward processing (under no experimental manipulations [i.e., at rest]) in children with obesity (28). This finding suggests that altered connections between these regions may contribute to overeating. Combined, these early studies provide preliminary evidence for a relationship between behavioral and neural correlates of inhibitory control and childhood obesity. However, no studies to date have assessed if inhibitory control in response to a reward relates to overeating. Understanding how the neural correlates of reward and inhibitory control processing relate to actual food intake might be the key to increasing success rates of intervention programs.
1.5.1 Components of inhibitory control

Inhibitory control is composed of two distinct mechanisms: proactive and reactive control. Proactive inhibitory control is defined as the ability to prepare to inhibit a response (e.g., the ability to plan to diet). It is a slow and controlled process, allowing cognitive control to be selective and flexible to prepare for interference or obstacles (88, 89). In comparison, reactive inhibitory control is mobilized only as needed in a just-in-time manner, such as when an interference with a goal is detected (e.g., the response to the unexpected presentation of cookies at work) (88). Reactive control is a fast, automatic, impulsive, process that responds to urges with little cognitive regard (90). Thus, whereas proactive control is focused on anticipating and preventing interference, reactive control reacts to interference when it occurs (88). Although proactive control is equally important, the remainder of the discussion will focus on reactive inhibitory control.

1.5.2 Assessment of reactive inhibitory control

In the laboratory, reactive inhibitory control is measured objectively with motor-based paradigms. It is important to note that response suppression cannot be measured with self-report questionnaires; questionnaires are subject to faults of memory, honesty, and insight (91). Reactive inhibitory control is measured with behavioral paradigms such as the Go/Nogo. The Go/Nogo investigates the ability to suppress inappropriate responses to unexpected stimuli. Briefly, the Go/Nogo requires responding to “go” stimuli but withholding responses to infrequent (and different) “nogo” stimuli. Repeated responses to “go” stimuli sets up a prepotent response tendency (i.e., respond to the urge), which makes it
difficult to stop responses to “nogo” stimuli (92). The strength of the prepotent response can be manipulated by changing the ratio of “go” to “nogo” trials. Tasks with a greater percentage of “go” trials create a stronger urge to respond (93). Thus, this primes a prepotent response and makes withholding a response even more difficult. Task performance is assessed by examining accuracy (the ability to withhold responses) and secondarily by reaction times (how fast responses to “go” stimuli were executed) (81). Individuals can then be classified into groups with respect to their performance. Poor inhibitory control is defined by slower reaction times to “go” stimuli and higher error rates whereas better performance is characterized by faster reaction times and low error rates.

1.5.3 Neural mechanisms of inhibitory control

Numerous studies have focused on investigating the neural circuitry involved in reactive inhibitory control. Response inhibition (i.e., withholding a response) involves pre-supplementary motor circuits (94). Response inhibition is also supported by the ventrolateral prefrontal cortex, including the superior, middle, and inferior frontal gyrus, and precentral gyrus, anterior cingulate, insula precuneus, and inferior parietal lobule (94–97). However, lesion studies suggest that successful inhibitory control is associated with the IFG, middle and medial frontal gyrus, and the presupplementary motor area (preSMA) (98–100). fMRI studies have indicated that successful reactive inhibition is associated specifically with activation in the right IFG (98, 99) and to a lesser extent the middle and medial frontal gyrus (99). Since the preSMA is connected structurally and functionally to the IFG activation in this region is thought to reflect the speed at which stopping occurs (100, 101). The dlPFC is another region associated with inhibitory control (102). However, transcranial magnetic
stimulation, a technique that temporarily disrupts neural activity by creating a virtual lesion, has suggested that the dIPFC may not be associated with response inhibition. Instead, dIPFC is thought to be associated with top-down control, which is a slow, cognitively taxing control mechanism (103, 104). Therefore, dIPFC activity may be reflective of inhibiting behavior based on information and values and not in regards to stopping motor impulses (100, 103, 104).

1.6 Neurotheoretical models of overeating

Dysfunctional reward processing has been observed in adults and adolescents with obesity (32, 68, 76, 105). Thus, findings from fMRI studies investigating how the brain responds to rewards have led to the development of theoretical models of overeating. Some theorize that overeating is due to a hyper- or hyposensitivity to reward (106). However, others pose that deficits in inhibitory control contribute to overeating (27, 84, 86, 107, 108). Therefore, the mechanisms contributing to overeating remain controversial. Independent of theory driving these models, no study in humans has investigated how these models relate to objective measures of overeating. Next, the research utilized to inform these models will be discussed.
1.6.1 The Reward Surfeit Model of Overeating

The reward surfeit model proposes that a hypersensitivity to reward drives excess food intake, possibly due to the rewarding properties of food (106, 109). This theory posits that increased reward response to food drives overeating and subsequent obesity. It is strengthened by numerous fMRI studies showing that the brain response to food cues positively relates to body mass index (BMI) in both adults (32, 110, 111) and children (72, 112). In addition, studies in adults have shown that heightened brain response to other rewards, such as money, also relates to increased BMI (24, 33, 68, 113, 114), suggesting that an impaired reward system exists in individuals with obesity. Support for this model also comes from studies that have examined polymorphisms in the dopamine D2 receptor during positron emission tomography (PET). Specifically, increased receptor density of the A2 allele was positively correlated with BOLD response in the dorsal striatum and weight status (74). Therefore suggesting overeating is due to an increased reward response in the striatum.

1.6.2 The Reward Deficit Model of Overeating

In contrast to the reward surfeit model, the reward deficit model of overeating suggests that a hyposensitivity to reward drives excess food intake (106). In this model, it is proposed that individuals who show a decreased response to reward overeat in order to compensate for a reward deficiency. This model is in part based on observances in individuals who partake in other maladaptive behaviors, such as substance use, as similarities in dopamine availability have been observed among individuals with obesity and illicit drug use (115, 116). However, unlike drugs, food is necessary for survival; thus, the cause of
overeating is multifactorial. Some fMRI studies have shown that adults with obesity exhibit a decreased response in regions implicated in reward processing to receipt of milkshake when compared to healthy weight counterparts (117–119). Thus, this suggests that adults with obesity have a hyposensitivity to reward. Hyposensitivity to reward has been speculated to be diet-induced, as an attenuated response to reward are observed in habituation studies (120, 121); similar theories have been made in those who are substance abusers (122). However, other studies have suggested that hyposensitivity to reward is caused by the lack of dopamine receptor density. Lower dopamine D2 receptor density (A1 allele of the TaqIA polymorphism) has been observed in adults with obesity (123, 124), which has also been correlated with a decreased BOLD response (118). Therefore, it is also possible that the relationship between hyposensitivity to reward and obesity is explained by a decrease in dopamine availability.

1.6.2 The Reflective-Impulsive Dual Processes Model of Overeating

Together, findings from studies showing that obesity is associated with deficits in inhibitory control (84, 108, 125–136) and reward sensitivity (24, 30–32, 69, 72, 113, 137, 138) have formed the theory behind the Reflective-Impulsive Dual-Processes Model. The Reflective-Impulsive Dual-Processes Model (87, 139) describes the conflict of temptation as the power of giving into a more pleasurable (i.e. rewarding) outcome and self-control (e.g., the ability to stop) to choose the more reasonable choice. The reflective system is a slow acting control system geared towards achieving long-term goals. It is elicited as a consequence of a decision process. On the contrary, the impulsive system is a fast acting, automatic system driven by affective and motivational responses to stimuli (140). Both
processes operate in parallel, yet asymmetry exists. Constant imbalances between reward processing and inhibitory control may lead to obesity development via repeated excess consumption of highly palatable, high-energy dense, low-nutrient dense foods (141) a known contributing factor to obesity (18, 142, 143). Thus, overeating may occur when the need for an immediate reward (24, 144–146) is stronger than the ability to stop consumption (126, 128, 147).

1.6.4 So, Which Model Explains Overeating?

Although models of overeating exist, whether these aforementioned theories coincide with actual behavior has not been tested. The models have been based on endpoints (e.g., BMI) but give little insight into the etiology of the mechanisms that may drive behavior. Furthermore, little research has been conducted to examine the validity of these models in children. Due to known developmental influences, it is imperative to understand how the BOLD response to reward relates to actual eating behavior in a population that is undergoing rapid developmental changes in regions implicated in reward and inhibitory control processing (148–150). Since these regions are changing based on the course of normative development, alterations in reward sensitivity due to overeating and/or weight gain may pose severe detrimental attributes that may not be reversible.
1.7 Overall aim of the dissertation:

The current dissertation attempts to bridge the gap in research by investigating how reward processing and inhibitory control relates to actual food intake in children with and without overweight/obesity. This will be done by presenting three papers that examine different aspects of decision-making, child weight status, and objectively measured food intake. The first paper will examine the relationship between the BOLD response to rewards and weight status. The second paper will aim to understand the relationship between BOLD response to rewards and objectively assessed overeating. The third paper will investigate the relationship between inhibitory control, food intake, and child weight status. Each paper is designed to be a standalone paper including its own introduction and discussion. A general discussion that draws conclusions and future directions from all three manuscripts follows the third paper. A brief overview of the aims and hypotheses for each paper are listed below.

Paper 1: Food or money? Children’s brains respond differently to rewards regardless of weight status.

Paper 1, Aim 1: To evaluate how the brain responds to multiple reward types using one experimental task in an attempt to determine whether brain response to rewards is related to obesity. To do this children underwent fMRI while playing a card-guessing task that was previously used in adult smokers to dissociate the effects of various reward types (e.g., cigarettes, money) on brain activity. The fMRI paradigm
used with children included three rewards: food (i.e., a piece of candy instead of puffs of a cigarette), money, and neutral (i.e., no reward).

**Paper 1, Hypothesis 1:** Anticipation of food vs. neutral and money vs. neutral would positively correlate with BOLD response in regions previously implicated in reward anticipation in adolescents, such as the striatum, frontal operculum, and supplementary motor cortex.

**Paper 1, Hypothesis 1.2:** Receipt of (winning) food vs. neutral and winning money vs. neutral would correlate with increased BOLD response in regions previously implicated in reward outcome in adolescents, such as the striatum, insular cortex, putamen, paracingulate gyrus, and postcingulate gyrus.

**Paper 1, Hypothesis 1.3:** For both anticipation and winning, food vs. money would correlate with increased BOLD response in the aforementioned regions. We made the latter prediction based on the assumption that food would be more biologically salient and would, therefore, elicit greater BOLD responses than money for children at this age.

**Paper 1, Aim 2:** To examine if differences in BOLD response to anticipating and winning food and money rewards differ based on child weight status.

**Paper 1, Hypothesis 2:** In comparison to those with a healthy weight, children with obesity would have elevated BOLD responses to anticipating and winning food rewards relative to money and neutral trials.

Paper 2, Aim 1: To test the hypersensitivity model of overeating by assessing how objectively measured food intake relates to the BOLD response to anticipating and winning food and monetary rewards. Unrestricted food intake was assessed at three separate meals: 1) a standard lab meal; 2) a highly palatable buffet meal designed to elicit overconsumption; 3) a validated measure of children’s intake of palatable snacks when not hungry.

Paper 2, Hypothesis 1: BOLD response to the anticipation of food relative to money in reward processing regions would positively correlate with intake at the palatable buffet meal and EAH, independent of weight status.

Paper 2, Aim 2: Based on previous work in our laboratory showing that BOLD responses in inhibitory control regions to food brand cues positively associated with how much children ate in branded compared to unbranded meals (151), we assessed how brain response in inhibitory control regions for anticipating and winning food compared to money related to food intake.

Paper 2, Hypothesis 2: Greater brain responses in inhibitory control regions to anticipating food relative to money would positively correlate with intake. No a priori hypotheses were made regarding the relationship between winning rewards in regions implicated in reward processing and inhibitory control and laboratory intake.

Paper 3, Aim 1: To assess the relationship between reactive inhibitory control. To do this children completed a child-friendly Go/Nogo task to determine if reactive inhibitory control related to child weight status and food intake.

Paper 3, Hypothesis 1: Deficits in inhibitory control performance as assessed by error rates and various decision-making components (as assessed by a drift-diffusion model) would positively correlate with weight status and objective measures of overeating.

Paper 3, Aim 2: To test the Reflective-Impulsive Dual-Processes Model, which suggests that overeating may occur due to the inability to stop a behavior in response to highly rewarding stimuli. We measured reactive inhibitory control via the Go/Nogo task that had reward incentives to see if performance related to child body weight and food intake.

Paper 3, Hypothesis 2: Inhibitory control deficits would be exacerbated in the presence of reward incentives such as food or money, and this would correlate with increased weight status and objective measures of overeating.
1.8 References


151. Masterson TD, Bermudez M, Stein W, Beidler E, English L, Keller KL. Brain response to food brands is positively associated with laboratory intake at a branded meal in children. *FASEB J* 2017;31:962.6-962.6.
Chapter 2

Food or money? Children’s brains respond differently to rewards regardless of weight status.

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2.1 Abstract

Brain responses to both food and monetary rewards have been linked to weight gain and obesity in adults, suggesting general hypersensitivity to reward contributes to overeating. However, the relationship between brain reward response and body weight in children is unclear. We tested this by performing functional magnetic resonance imaging (fMRI) while children (7-11-years-old; healthy weight [n=31], overweight/obese [n=30]) played a modified card-guessing task to assess blood-oxygen-level-dependent (BOLD) response to anticipating and receiving food and money rewards. fMRI data were analyzed using a region of interest (ROI) and exploratory whole-brain approach. ROI results demonstrated increased BOLD response in the striatum to anticipating food vs. neutral (control) and winning money vs. neutral. Whole-brain data showed that winning money vs. food was associated with increased activation in the striatum and regions associated with cognitive control and emotion. Notably, for both approaches, these effects were independent of child weight status. Additionally, children’s reported food responsiveness and emotional overeating were negatively correlated with the BOLD response in the left cingulate gyrus for winning food vs. money. Overall, findings from this study provide insight into reward sensitivity in children, which may have implications for understanding overeating and the development of obesity.
2.2 Introduction

Excess energy intake is a contributing factor to the increasing prevalence of childhood obesity in the United States (1) and globally (2). The early onset of metabolic consequences associated with obesity (3) highlights the critical need to clarify the mechanisms that contribute to overeating. Although the causes of overeating are multifactorial, one likely contributor is how the brain responds to rewarding properties associated with food. Reward circuitry drives motivated behaviors such as appetite (4), while inhibitory control is important to limit overeating (5); alterations in these processes are thought to contribute to overeating and the development of obesity (6, 7). The current study will help to identify individual differences in how the brain responds to rewards, which will provide insight into why some children are more vulnerable to weight gain than others (8).

Functional magnetic resonance imaging (fMRI) studies have shown positive correlations between viewing palatable food stimuli and blood-oxygen-level-dependent (BOLD) response in regions implicated in reward and inhibitory control (9–11). Alterations in these responses have been positively linked to weight gain (12, 13) and obesity in adults (14–16) and children (17, 18). Thus, it has been hypothesized that how the brain responds to palatable food cues may be predictive of excess food consumption (7, 19–23). Moreover, children with obesity show positive correlations between exposure to palatable food images and BOLD response in the dorsolateral prefrontal cortex, a region implicated in inhibitory control (17). Additionally, children with obesity have greater functional connectivity at rest between brain regions involved in reward processing (i.e., ventromedial prefrontal cortex,
orbitofrontal cortex) and inhibitory control (i.e., middle frontal gyrus) (7). This suggests that interactions between these regions may be associated with overeating.

Additional studies have explored the relationship between general reward processing and obesity. These studies revealed that brain response to non-food rewards, such as money, also correlated with weight status and risk for obesity (24–28). As a result, it has been hypothesized that a general alteration in brain response to rewards may increase the risk for developing obesity. Yet, the conclusions that can be made from these studies are limited. Only a few studies have evaluated BOLD response to multiple reward types (e.g., food, money) in the same population (27–29). However, these studies utilized different paradigms for each reward contingency, limiting conclusions that can be drawn. For example, food reward paradigms largely consist of viewing pictures of palatable foods (e.g., hamburgers, French fries) (30) or receiving small amounts of food in the scanner (31, 32). On the other hand, games in which participants win and lose money are used to assess the brain’s response to monetary rewards (27, 28). Different reward paradigms may delineate different neural circuitry that is specific to the task, and not how the brain responds to both food and monetary rewards. Food and money both have rewarding properties, however, primary and secondary rewards may activate different neurobiological regions (33, 34).

To date, only one study in adults modified a monetary incentive delay task to include both food and monetary rewards (29). However, no studies have tested how sensitivity to multiple rewards (e.g., food, money) relates to weight status in children. Childhood is a period marked by developmental changes in brain maturation, particularly in reward processing regions (35, 36). These normative changes in development may further complicate how the brain responds to reward in a pediatric population. In addition, studies
suggesting that general sensitivity to rewards is related to obesity in adolescents and adults have shown mixed results (27–29, 37, 38), possibly due to the multiple paradigms used to evaluate this phenomenon. Given the variability in results between adolescents and adults, examining how the brain responds to anticipating and winning food in childhood would provide insight into how this phenomenon relates to weight status in an age group that is not only susceptible to vast changes in reward sensitivity but is vulnerable to rapid weight gain due to development (8).

The current study is part of a larger investigation that examined how differences in behavioral and neurobiological correlates of decision-making relate to objective measures of overeating in 7-11-year-old children with and without obesity. The objectives of this paper are two-fold. First, we evaluated how the brain responds to the anticipation and winning (i.e., receipt) of food and money rewards using a single fMRI paradigm modified to include multiple reward types. Second, we evaluated whether brain responses to reward were related to weight status and appetitive traits in children 7-11-years-old. We hypothesized that 1) anticipation of food (F_A) compared to neutral (N_A) and money (M_A) compared to N_A would positively correlate with the BOLD response in regions previously implicated in reward anticipation in adolescents, such as the striatum, frontal operculum, and supplementary motor cortex (39); 2) winning food (F_W) compared to neutral (N_W) and winning money (M_W) compared to N_W would correlate with increased BOLD response in regions previously implicated in reward outcome in adolescents, such as the striatum, insular cortex, putamen, paracingulate gyrus, and postcingulate gyrus (39); 3) for both anticipation and winning, food compared to money would be correlated with increased BOLD response in the aforementioned regions. We made the latter prediction based on the assumption that food would be more biologically salient and would, therefore, elicit greater BOLD responses
than money for children this age. We also hypothesized that in comparison to those with a healthy weight, children with obesity would have elevated BOLD responses to anticipating and winning food rewards relative to money and neutral trials.

2.3 Materials and methods

2.3.1 Study design

We recruited 71 children ages 7-11-years-old to participate in a cross-sectional study examining how behavioral and neurological correlates of decision-making relate to objective measures of overeating and child weight status. This paper focuses on a subset of the data examining the relationship between child brain response to anticipation of food and money rewards and weight status. The larger study consisted of behavioral and neurological testing over four visits, each one week apart, that occurred at either lunch time (11:00-1:00 PM) or dinner time (4:00-6:30 PM) based on family availability. Participants were fasted for at least three hours prior to each visit; fullness was assessed before and after meals and the fMRI scan with a validated visual analog scale for children (40). Parental consent for child participation and child assent were obtained on the first visit. During visits 1-3, children completed behavioral tasks and were fed either a meal or a snack. On the fourth visit, children underwent an fMRI scan. The current study includes data collected from the fMRI scan, in which children performed a modified card-guessing task (41) that assessed brain response to anticipation and winning of food and monetary rewards. This study was
approved by The Pennsylvania State University Institutional Review Board. Parents provided written informed consent for their child’s participation and children provided verbal assent.

2.3.2 Participants

There were no prior studies assessing brain response to multiple rewards and body weight status in children. Therefore, we determined sample size by consulting the food cue literature in children (7, 9, 10, 42) to estimate expected effect sizes in brain regions of interest (ROI). Based on these expected effects, we aimed to recruit 80 children matched by weight status (i.e., healthy weight, overweight/obese) and sex. This sample size was determined by assuming 25% loss due to attrition and loss of data due to motion effects in the MRI. Weight status was self-reported by parents on the phone and confirmed in the laboratory from measured height and weight.

Children were recruited using flyers and postings on popular websites. Interested families were screened over the phone to determine eligibility. Exclusion criteria were assessed by parent report over the phone and included food allergies and dietary restrictions, left-handedness, common MRI contraindications such as metal implants or dental work containing metal, impaired or uncorrected vision, major psychiatric diagnoses and neurological illnesses, learning disabilities, use of prescription medications, and children that were underweight (BMI percentile < 5%). Children with familial psychiatric problems were also excluded; therefore, children who were adopted were excluded due to potentially unknown familial medical history.
One hundred and ninety-five families were screened over the phone. Fifty-six children were excluded for the following reasons: BMI percentile < 5 (n = 2), medical/psychological disorders contraindicative of fMRI (e.g., attention deficit hyperactivity disorder (n = 8), colorblindness (n = 3); learning disability (n = 3); left-handedness (n = 3), medication usage (n = 1), under/over age limit (n = 6), food allergies or would not eat the study foods (n = 8), non-biological child (n = 2), metal implants (n = 9), and failure to complete eligibility screening (n = 10). Sixty-nine additional children were screened but not enrolled for the following reasons: lost contact (n = 8), not interested (n = 8), and waitlisted (n = 53).

Seventy-one children were successfully enrolled. Eight children were not included in the analyses for the following reasons: refusing to complete the fMRI (n = 1), excessive movement (i.e., unsuccessful MRI scan) (n = 2), technical error (n = 1), lost to follow-up (n = 4), drop out (n = 1), and failure to provide correct eligibility criteria (n = 1). This resulted in the final sample of 61 children (33 females, 28 males; 3% Asian, 5% Black, and 92% White) (see Table 2.1 for participant characteristics). Participants in the final sample included 31 healthy weight children with a BMI-for-age % < 85th (mean age = 8.7 ± 1.4 years; 13 males) and 30 children classified as overweight or obese with a BMI-for-age % ≥ 85th (mean age = 9.4 ± 1.2 years; 15 males; 17 obese) (43). Chi-squared tests revealed no differences between groups and age (p = 0.2), sex (p = 0.6), or parent education level of the accompanying child (p = 0.3). Weight groups differed by total family income (p = 0.04) with parents of healthy weight children reporting higher total family income (i.e., more parents reported earning more than $51,000-75,000) than parents of children with overweight/obesity. However, the mean reported income for both weight groups was between $51,000-75,000.
Table 2.1 Descriptive statistics for participants (n = 61; 54% female). SD = standard deviation; kg = kilograms; m^2 = meters squared. *Body fat percentage was missing for one participant.
2.3.3 Anthropometric measurements and body composition

On the first visit, a trained researcher measured children’s height and weight to the nearest 0.1 cm and 0.1 kg. Children were weighed and measured twice in light clothing and stocking feet using a standard scale (Detecto model 437, Webb City, MO) and stadiometer (Seca model 202, Chino, CA). Averaged height and weight were converted to child BMI (kg/m\(^2\)), BMI \(z\)-score, and BMI percentile. The Center’s for Disease Control and Prevention cut-offs for child age- and sex-specific BMI percentile were used to define healthy weight (< 85th %ile) overweight/obese (≥ 85%ile) (43).

2.3.4 Pubertal assessment

Children and parents completed the 5-item Peterson Pubertal Development Scale on their first visit to the laboratory (44). This questionnaire assesses sex-specific questions pertaining to pubertal status. Each item on the questionnaire was scored based on a range from one (has not begun) to four (seems complete) with respect to pubertal development. An overall pubertal development score was computed by summing of three questions (e.g., body hair growth, vocal changes, menstruation), with higher scores depicting advanced reported pubertal stage. To obtain values for additional analyses, parent and child reported scores were averaged. Similar methods have been reported elsewhere (45). This 5-item questionnaire was completed without the researcher present. In addition, sex-specific Tanner stage drawings, which corresponded to the child’s level of development, were completed by both the child and parent (46). Again, Tanner stages selected by parents and children were
averaged. Pubertal status and Tanner scores were entered as separate covariates of interest in our model.

2.3.5 Behavioral measures

Parents completed the Child Eating Behavior Questionnaire (CEBQ), a validated assessment of trait-based measures of child appetite (47, 48). This measure was included to help us interpret the BOLD response to food and money. This 35-item questionnaire has eight sub-scales, which assessed the child’s satiety responsiveness, enjoyment of food, food fussiness, desire to drink, food responsiveness, emotional under and overeating, and slowness in eating. Responses were coded on a 5-point Likert scale from never to always. Previous studies have found positive relationships between child weight status and food approach subscales, including enjoyment of food, food responsiveness, and emotional eating (49, 50).

2.3.6 Mock training

Mock (i.e., simulation) training has been shown to improve the success rate and quality of the data collected (51). The mock scanner simulates the appearance, bore size, and sounds of the actual 3T magnet. For the present study, children underwent mock training on three separate days. The first mock session was designed to introduce the child to the scanner. During this time, the children were allowed to explore the area and ask any questions. On the second mock visit, children were trained to remain still, respond to
questions without head motion, and to use a button press for responses. During this 10-minute mock training session, children were shown non-food related pictures (e.g., stuffed animals, trees, Legos) on the screen. On the day of the actual fMRI acquisition, participants completed another short training session, which lasted about 5 minutes. During this time, participants were familiarized with the task and underwent a short practice session to ensure that they understood directions. In addition, participants were informed of the amount available for correct guesses on each trial (i.e., $0.50, or six pieces of Skittles or M&M’S). Participants were led to believe that the total reward amounts earned were based on how they performed during the task; these methods correspond to other studies in the literature that have used a card-guessing task (37, 41). No previous studies have used this task to evaluate the anticipation and receipt of food rewards. Therefore, Skittles or M&M’S were chosen as the food reward because it was a discrete unit food, which could be distributed in even increments similar to monetary rewards. In addition, the shape was also similar to the monetary reward. The child selected their preferred candy (either Skittles or M&M’S) before the fMRI in attempt to ensure the food was salient.

2.3.7 fMRI experimental paradigm

Functional images were collected as children played a modified card-guessing task shown to dissociate the effects of various reward types (e.g., money, puffs of a cigarette) in adult smokers (41) (see Figure 2.1). The task was a slow event-related design comprised of four runs, each with 18 trials of three different reward types (i.e., six food trials, six money trials, six neutral [i.e., no reward = control] trials) and two outcomes (i.e., win, no win for each reward type [e.g. food win, money win]) and was presented using E-Prime (version 2.0
Professional; Psychology Software Tools (PST), Pittsburgh, PA); each run lasted 6 minutes and 38 seconds. Using a button press, participants earned rewards by guessing (duration 4 seconds) if a computer-generated number was higher or lower than five. After 6 seconds, a picture of the reward (i.e., money, candy, or book [neutral]) that could be won for that trial was presented. No rewards were won during neutral (i.e., book) trials regardless of the outcome; this trial type served as a control. Next, the actual number appeared (0.5 seconds) followed by feedback (win or no win; duration 1 second). A 9-second intertrial interval was presented between guess periods. Trials were fixed using a pseudorandom order. Across the four runs, there were 24 trials of each reward anticipation condition, and 12 trials of each reward outcome condition (e.g. food win, food no win). There was a 50% win rate for each reward condition. The total scan time was approximately 38 minutes.

Regardless of the accuracy of participants’ guesses, across four runs they won $5 and 66g of either Skittles or M&M’S (equivalent to one regular-sized package of candy, 2.17 ounces). The won rewards were delivered immediately after the scanning session. The child was allowed to consume the food reward after the study visit completed, which was typically about 30 minutes after the fMRI scan. The duration of the entire visit lasted an hour and a half, approximately.
Figure 2.1 A visual representation of the modified card-guessing task used in the scanner, which was presented via E-Prime 2.0 Professional.
2.3.8 Image acquisition

BOLD functional images were acquired using a Siemens MAGNETOM Prism Fit whole-body MRI scanner (Siemens Medical Solutions, Erlangen, Germany) with a 20-channel head coil and a 64-channel neck coil at the Social Life and Engineering Imaging Center (SLEIC) at the Pennsylvania State University. Four functional runs were collected using a T2*-weighted gradient single-BOLD echo planar imaging (EPI) sequence to acquire 38 interleaved slices, TR = 2000ms, TE = 24 ms, flip angle = 90°, matrix 64 x 64, FOV = 220 mm, slice thickness = 3 mm, AC-PC transverse, oblique plane determined by the mid-sagittal section, and 3.0 x 3.0 x 3.0 mm voxel size. Each run consisted of 196 volumes.

Structural images were collected using a T1-weighted magnetization-prepared rapid acquisition gradient echo (MPRAGE) sequence resulting in 192 slices in the sagittal plane, TR/TE = 1700/2.28 ms, flip angle = 8°, FOV = 256 mm, slice thickness = 1 mm, sagittal plane, and 1.0 x 1.0 x 1.0 mm voxel size.

2.3.9 fMRI preprocessing

Functional images were preprocessed and analyzed using a combination of FMRIB Software Library’s (FSL) and Analysis of Functional NeuroImages (AFNI) (52–55). The first three volumes of functional scans were removed to control for stabilization of the magnetic gradient. Functional images were corrected for slice timing effects. Next, rotational and translational head motion estimates were calculated and images were corrected by aligning each volume in the time series to the volume that had the least movement (i.e., minimum outlier). Volumes with motion exceeding 1mm in any direction were excluded. In addition, any run in which 25% of the TRs were censored was removed from the data analyses. This
resulted in 3% of runs being discarded for motion effects. For each participant, an average of 3.81 successful runs was completed (range 2-4; 98% success rate for completion of all four runs). Motion correction was conducted using six-parameter rigid-body in three dimensions. Functional images were spatially normalized in a nonlinear fashion into Montreal Neurologic Institute (MNI) space. Images were smoothed with a Gaussian filter set at 6 mm full-width at half maximum and baseline signal was detrended using a 3rd order polynomial. Finally, the signal intensity for each run was scaled to a mean of 100. The anatomical image was skull stripped using FSL’s brain extraction tool (BET) and then transformed in a nonlinear fashion to MNI space. We chose to align to the MNI template as for children over age 6 years, as there are subtle differences in anatomical variation between children and adults (56), therefore aligning to an adult template would pose minimal differences in our data. To visualize alignment and confirm that there were minimal differences, we also aligned the data to AFNI’s Haskins Pediatric template (n = 75, children 7-12-years-old). However, we chose to use the data that was aligned to the MNI template in order to make cross-study comparisons as the coordinates used for our ROI analyses were defined using an adult template (39). For reward outcome, trials within which no response was made were excluded from the analyses (n = 241, 5.6 % of all trials for all participants).

2.3.10 fMRI data analyses

Preprocessed data were analyzed using deconvolution methods as outlined in Ward (2002) (57). Similar to previous studies using this task (41), task events were modeled to include three levels of reward anticipation (F, M, or N), six possible outcomes (win or no win for each reward type). Thus, for each participant, our model consisted of the following
regressors of interest: 1) F_A; 2) M_A; 3) N_A; 4) F_W; 5) M_W; 6) N_W; 7) food no win (F_{NW}); 8) money no win (F_{NW}); 9) neutral no win (N_{NW}); 10) guess period. Six motion parameters and the first derivations of motion were added as nuisance regressors. We estimated the hemodynamic response function for F_A M_A, and N_A in our model by convolving stimulus onset times with a block function with (duration 6 seconds). The hemodynamic response function for reward outcome (win or no win) was modeled with a gamma function (duration 1 second). The output of our model included several goodness-of-fit statistics including partial F-statistics for each regression and t-scores comparing each of the 10 estimated beta weights (from our regressors of interest) with zero. For the reward outcome trials, the analyses focused on win trials; no win comparisons are reported in the supplemental material.

2.3.11 Regions of interest analyses

There are no meta-analyses assessing reward anticipation and receipt in children. Therefore, we selected a set of a priori defined ROIs known to be involved in adolescent reward anticipation (five regions) and reward outcome (eight regions), as defined in the meta-analysis by Silverman et al., (2015) (39) (see Table 2.2). ROIs were defined by drawing a 6 mm radius sphere in AFNI around the MNI coordinates reported for each region. Mean voxel-wise parameter estimates (beta coefficients) were extracted from each ROI on an individual subject level and entered into IBM SPSS Statistics for Macintosh V.22.0.0.2 (Armonk, NY: IBM Corp.) for group-level analyses. Repeated measure ANOVAs were run to assess differences between conditions. Post-hoc tests were conducted with the LSD approach. A Greenhouse-Geisser correction was used to correct for cases in which
Mauchly’s Test of Sphericity was violated ($p < 0.05$). A separate mixed model was conducted to control for covariates of interest including age, sex, fullness ratings (the difference between pre- and post-scan fullness), pubertal status, time of day in which the visits occurred, and parent-reported income were included in the model but removed if not significant. Since Stice et al. (2011) (28) observed group differences between adolescents at low- and high-risk for developing obesity, as assessed by parental BMI, we calculated the child’s risk of developing obesity (determined by the average BMI class between accompanying parent’s BMI [measured] and the second parent’s BMI [reported by the accompanying parent]) and included it as a covariate of interest.


<table>
<thead>
<tr>
<th>Brain Region</th>
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<th>x</th>
<th>y</th>
<th>z</th>
</tr>
</thead>
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<td>10</td>
<td>12</td>
<td>-2</td>
</tr>
<tr>
<td>Frontal Operculum Cortex</td>
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<td>43</td>
<td>13</td>
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<td>8</td>
<td>-6</td>
</tr>
<tr>
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<td>- 2</td>
<td>2</td>
<td>54</td>
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<tr>
<td>Insular Cortex</td>
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<td>18</td>
<td>-8</td>
</tr>
<tr>
<td>R</td>
<td>40</td>
<td>14</td>
<td>-6</td>
<td></td>
</tr>
<tr>
<td>Nucleus Accumbens</td>
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<td>10</td>
<td>14</td>
<td>-6</td>
</tr>
<tr>
<td>Putamen</td>
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<td>-22</td>
<td>10</td>
<td>4</td>
</tr>
<tr>
<td>Paracingulate Gyrus</td>
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<td>36</td>
<td>28</td>
</tr>
<tr>
<td>Posterior Cingulate Gyrus</td>
<td>L</td>
<td>0</td>
<td>-34</td>
<td>32</td>
</tr>
</tbody>
</table>

**Table 2.2** Regions of interest coordinates taken from a meta-analysis by Silverman et al., (2015) (39) that examined monetary reward anticipation and outcome in adolescents. MNI coordinates. R = right; L = left.
Group differences (i.e., differences between children with and without overweight/obesity) were assessed in SPSS using a mixed model with the BOLD response as the dependent variable and reward type and weight group as our independent variables; subject ID was entered as a random factor. A separate mixed model was conducted with the covariates of interest including age, sex, fullness ratings, pubertal status, time of day, parent-reported income and obesity risk score. All covariates were entered into the model and removed if not significant. Correction for family-wise error (FWE) was conducted using the Bonferroni-Holm approach (58) with a corrected significance level of $q = 0.05$; corrections were applied to each hypothesis separately (anticipation vs. outcome).

2.3.12 Exploratory whole-brain approach

Given that this task was novel in children, we also took a more exploratory, data-driven analytic approach. For this approach, we first created separate maps of the main effect of reward anticipation and the main effect of reward outcome. For each map, we identified significantly activated clusters for further analysis. These activated regions collapsed across subjects and reward conditions, delineated the reward-related neurocircuitry for our study population. This allowed us to avoid circular inference by determining voxels that were activated in the paradigm as a whole but was not specific to contrasts of interest (59, 60). This also enabled us to characterize areas that were functionally involved in our task but were outside the range of our a priori selected ROIs. To generate the main effect of reward map in AFNI, beta values from regressors of interest from the subject-level deconvolution analysis were entered into a voxel-wise multivariate model (3dMVM) with weight status (healthy weight vs. overweight/obese) as the between-subjects factor, reward
type as the within-subjects factor, and subjects as a random factor. For reward anticipation, the within subject factors were as follows: $F_A, M_A,$ and $N_A$. For reward outcome, the within subject factors were as follows: $F_W, M_W, N_W, F_{NW}, M_{NW},$ and $N_{NW}$. Group maps for the main effect of weight and interactions between weight and reward were also generated for both anticipation and outcome. Each group map was then corrected for multiple comparisons by entering the estimated average smoothness of 0.37201, 5.6184, and 13.638 mm into 3dClustSim with the \texttt{–acf} option as outlined in Cox (2017) (61). This program ran 10,000 Monte Carlo simulations to estimate a minimum cluster size threshold based on the estimated smoothness of noise and a voxel-wise $p$-threshold ($p < 0.001$, uncorrected). Results from the Monte-Carlo simulation revealed that 68 continuous voxels at a per voxel threshold of $p < 0.001$ were needed to achieve a corrected map of $p < 0.05$. Effect sizes were calculated using Cohen’s $d$: $d = 0.10$, $d = 0.5$, $d = 0.8$, which represent effect sizes of small, medium and large, respectively. Parameter estimates were extracted from each individual subject and entered into IBM SPSS Statistics for Macintosh V.22.0.0.2 (Armonk, NY: IBM Corp.) for further analyses.

Differences in regards to BOLD response to each reward type (food, money, neutral) and condition (win, no win) were analyzed using repeated measures ANOVA in SPSS. Post-hoc tests were conducted with the LSD approach. The Greenhouse-Geisser correction was used to correct for cases in which Mauchly’s Test of Sphericity was violated ($p < 0.05$). A separate mixed model was conducted to control for covariates of interest, such as age, sex, fullness ratings, pubertal status, time of day in which the visits occurred, parent-reported income and obesity risk score, but removed if not significant.
2.3.13 CEBQ analyses

For both the ROI and the whole-brain approaches, we calculated contrast values in regions that showed significant differences by reward type and correlated these responses to child appetitive traits. Contrast values were calculated for each individual participant by subtracting BOLD response from one reward condition from another (e.g., $F_A - M_A; F_W - M_W$). Pearson’s correlations were then calculated to determine the relationship between the CEBQ subscales and BOLD response for each contrast. An independent $t$-test was conducted to determine if there were differences between weight status and subscales on the CEBQ. To control for weight effects, partial correlations controlled for child weight status (using BMI $z$-score), were calculated between subscales on the CEBQ and mean difference scores between BOLD responses for each contrast. Correction for family-wise error (FWE) was conducted using the Bonferroni-Holm approach with a corrected significance level of $q = 0.05$ (58); corrections were applied to each hypothesis separately.

2.4 Results

2.4.1. CEBQ results

Results of an independent $t$-test indicated that in comparison to healthy weight children, parents of children who were classified as overweight or obese said that their child had lower satiety responsiveness ($p = 0.02$), and higher enjoyment of food ($p = 0.04$), food responsiveness ($p = 0.001$), and emotional overeating ($p < 0.001$). There were no
differences between weight groups and parental report of children’s desire to drink ($p = 0.8$), food fussiness ($p = 0.8$), emotional undereating ($p = 0.07$), or slowness in eating ($p = 0.2$) subscales.

2.4.2 ROI approach anticipation

Anticipation of reward collapsed across trials was associated with increased BOLD response in the striatum. Within the striatum, the right caudate ($F(2,120) = 6.4, p < 0.002, d = 0.8$) and the left nucleus accumbens ($F(2,120) = 8.6, p < 0.001, d = 0.7$) survived LSD correction. Post-hoc tests conducted using the LSD approach showed that the brain responded more to $F_A$ vs. $N_A$ in both the right caudate ($m_{diff} = 0.06, p < 0.001$) and left nucleus accumbens ($m_{diff} = 0.08, p < 0.001$). Post-hoc tests also revealed a difference for $M_A$ vs. $N_A$ in the nucleus accumbens ($m_{diff} = 0.05, p = 0.04$). Results of a mixed model showed that controlling for age, sex, fullness, puberty and time of day tested, parent-reported income or obesity risk score did not influence the primary outcomes. No main effects of reward anticipation were observed in the frontal operculum, insular cortex, or supplementary motor cortex.

2.4.3 ROI approach weight effects and anticipation

There were no main effects or interactions with child weight status and reward anticipation.
2.4.4 ROI approach outcome

Outcome (win, no win) collapsed across reward (food, money, neutral) trials was associated with the BOLD response in two sites in the left caudate (L1: $F(4.3, 258.0) = 8.9, p < 0.001, d = 0.8$; L2: $F(4.2, 250.5) = 3.5, p = 0.004, d = 0.6$) and right nucleus accumbens ($F(4.3, 258.7) = 5.8, p < 0.001, d = 0.6$). Post hoc tests using the LSD approach revealed that BOLD response in the left caudate (L1) was increased for $M_W$ vs. $N_W$ trials ($m_{\text{diff}} = 0.08, p = 0.02$), but no differences were observed for $F_W$ compared to $M_W$ or $N_W$ trials. BOLD response in the left caudate (L2) was decreased for $F_W$ vs. $M_W$ trials ($m_{\text{diff}} = -0.08, p = 0.03$) but no differences were observed for $F_W$ vs. $N_W$ or $M_W$ vs. $N_W$ trials. Post hoc tests for the nucleus accumbens revealed that effects were driven by no win conditions (see Supplemental Material Table S2.7.1). Results of a mixed model showed that controlling for age, sex, fullness, puberty, time of day tested, parent-reported income and obesity risk score did not influence the primary outcomes.

2.4.5 ROI approach weight effects and outcome

There were no main effects or interactions with child weight status and reward outcome.

2.4.6 ROI approach correlations with behavioral measures

No correlations were observed between child appetitive traits assessed by the CEBQ and BOLD response in the ROIs tested to either reward anticipation or outcome.
2.4.5 Whole-brain approach anticipation

Anticipation of reward collapsed across trials was associated with increased BOLD response in the bilateral lingual gyrus (left: $F(2,120) = 66.7, p < 0.001, d = 1.7$; right: $F(2,120) = 12.7, p < 0.001, d = 0.9$). Post hoc tests using the LSD approach showed that the BOLD response was decreased in the right lingual gyrus for $F_A$ vs. $M_A$ ($m_{\text{diff}} = 0.05, p = 0.02$), but increased for $F_A$ vs. $N_A$ ($m_{\text{diff}} = 0.06, p = 0.009$) and $M_A$ vs. $N_A$ ($m_{\text{diff}} = 0.11, p < 0.001$). BOLD response was also increased in the left lingual gyrus for $F_A$ vs. $N_A$ ($m_{\text{diff}} = 0.18, p < 0.001$) and $M_A$ vs. $N_A$ ($m_{\text{diff}} = 0.32, p < 0.001$), but $F_A$ vs. $M_A$ ($m_{\text{diff}} = -0.14, p < 0.001$) was associated with reduced BOLD response in this region. Mixed models showed that controlling for age, sex, fullness, puberty, time of day tested, parent education or obesity risk score did not influence the primary outcomes.

2.4.6 Whole-brain approach weight effects and anticipation

No main effects or interactions were observed for weight status and reward anticipation.

2.4.7 Whole-brain approach outcome

Outcome collapsed across trials was associated with increased activation in the right lentiform nucleus ($F(4.2, 254.4) = 12.2, p < 0.001, d = 0.9$), left superior temporal gyrus ($F(5,300) = 10.4, p < 0.001, d = 0.8$), left inferior frontal gyrus ($F(4.2, 251.1) = 10.0, p < 0.001, d = 0.8$), left posterior cingulate ($F(4.1, 244.0) = 7.5, p < 0.001, d = 0.7$), bilateral
lingual gyrus (left: $F(5, 300) = 4.6, p < 0.001, d = 1.4$; right: $F(2, 120) = 2.6, p = 0.023, d = 0.4$), and right middle frontal gyrus (right 1: $F(4.2, 259.1) = 7.7, p < 0.001, d = 0.7$; right 2: $F(5, 300) = 7.7, p < 0.001, d = 0.7$) (see Table 2.3). Post-hoc comparisons for these main effects are detailed below (see Figure 2.2). Results of the win to no win outcomes are reported in the Supplemental Material (see Supplemental Material Table S.2.7.2) Mixed models that controlled for age, sex, fullness, puberty, time of day tested, parent education or obesity risk score did not influence the primary outcomes.
<table>
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<tr>
<th>Anatomical Location</th>
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<th>$z$</th>
<th>$F$</th>
<th>$p$</th>
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<th>$F_{W-N_W}$</th>
<th>$F_{W-F_{NW}}$</th>
<th>$M_{W-N_W}$</th>
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<td>0.05</td>
<td>0.18**</td>
<td>0.10*</td>
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<td>0.08*</td>
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<td>-0.04</td>
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<td>10.4</td>
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<td>-0.01</td>
<td>0.07*</td>
<td>0.08*</td>
<td>0.16**</td>
<td>0.09*</td>
<td>0.8</td>
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Table 2.3: Regions from the whole-brain analysis with significant main effects for reward outcome. Results from the repeated measures ANOVA, with reward type as the within subjects factor. Anatomical locations were defined by the Talaraich Demon Atlas in AFNI. $k$ = cluster size (voxels); $H$ = hemisphere; $L$ = left; $R$ = right; $F$ = statistical $F$-value. * = $p < 0.05$; ** = $p < 0.001$. $F_{W-M_W}$ = food win compared to money win; $F_{W-N_W}$ = food win compared to neutral win; $F_{W-F_{NW}}$ = food win compared to food no win; $M_{W-N_W}$ = money win compared to neutral win; $M_{W-M_{NW}}$ = money win compared to money no win; $N_{W-N_{NW}}$ = neutral win compared to neutral no win; $d$ = Cohen's $d$ (i.e., effect size).
Figure 2.2 (A) Regions showing a main effect during reward outcome. The group-level analysis was conducted using 3dMVM with reward type (e.g. food win, money win) as fixed factors and subject ID as a random factor. Results were thresholded at a voxel-wise $p$-value of $p < 0.001$. Parameter estimates of the BOLD response for each reward outcome in the (B) lentiform nucleus. (C) cingulate gyrus. (D) right inferior frontal gyrus (IFG). (E) middle frontal gyrus (MFG). FW = food win; MW = money win; NW = neutral win; IFG = inferior frontal gyrus; R1 = right 1. * $p < 0.05$; ** $p < 0.001$. 
Post hoc tests using the LSD approach revealed the following:

*Winning food compared to money*

BOLD response was decreased for $F_W$ vs. $M_W$ in the right lentiform nucleus ($m_{\text{diff}} = -0.07, p = 0.005$), left superior temporal gyrus ($m_{\text{diff}} = -0.09, p = 0.002$), left IFG ($m_{\text{diff}} = -0.09, p = 0.007$), right lingual gyrus ($m_{\text{diff}} = -0.06, p = 0.05$), left posterior cingulate ($m_{\text{diff}} = -0.07, p = 0.04$) and the right (R1) middle frontal gyrus ($m_{\text{diff}} = 0.16, p < 0.001$).

*Winning food compared to neutral*

BOLD response was decreased for $F_W$ vs. $N_W$ in the bilateral lingual gyrus (left: $m_{\text{diff}} = -0.09, p = 0.006$; right: $m_{\text{diff}} = -0.07, p = 0.009$).

*Winning money compared to neutral*

BOLD response was increased for $M_W$ vs. $N_W$ in the right lentiform nucleus ($m_{\text{diff}} = 0.09, p < 0.001$), left superior temporal gyrus ($m_{\text{diff}} = 0.08, p = 0.009$), and right middle frontal gyrus (R1: $m_{\text{diff}} = 0.12, p = 0.001$; R2: $m_{\text{diff}} = 0.10, p = 0.006$).

2.4.8 Whole-brain approach weight effects and outcome

There were no main effects of weight status or interactions between weight status and reward outcome.
2.4.9 Whole-Brain Approach Correlations with Behavioral Measures

**Anticipation**

BOLD response in the bilateral lingual gyrus was not correlated with any measures of the CEBQ for any of the contrasts tested.

**Outcome**

Pearson’s correlations showed that BOLD response for $F_w$ vs. $M_w$ in the left cingulate gyrus was negatively correlated with food responsiveness ($r = 0.47, p < 0.001$) and negatively correlated with emotional overeating ($r = -0.39, p = 0.002$) (see Figure 2.3). These results remained significant after controlling for child weight status (food responsiveness: $r = -0.45, p < 0.001$; emotional overeating: $r = -0.35, p = 0.006$). No other correlations survived corrections for multiple comparisons. However, results are reported below for exploratory purposes.
Figure 2.3 Pearson’s correlations between BOLD response in the cingulate gyrus for winning food compared to winning money and scores on the (A) food responsiveness ($r = -0.47$, $p < 0.001$), (B) emotional overeating ($r = -0.39$, $p = 0.002$) subscales of the CEBQ. Child weight status did not affect results. FW - MW = food win – money win.
Food Responsiveness

Food responsiveness was negatively correlated with the BOLD response for $F_W$ vs. $M_W$ in the right lentiform nucleus ($r = -0.27, p = 0.04$), left superior temporal gyrus ($r = -0.38, p = 0.003$) and right lingual gyrus ($r = -0.28, p = 0.029$). BOLD response for $M_W$ vs. $N_W$ was positively correlated with food responsiveness in the right lentiform nucleus ($r = 0.33, p = 0.01$) and left superior temporal gyrus ($r = 0.31, p = 0.01$).

Emotional Overeating

Emotional overeating was negatively correlated with the BOLD response for $F_W$ vs. $M_W$ in the right lentiform nucleus ($r = -0.34, p = 0.007$) and left superior temporal gyrus ($r = -0.33, p = 0.009$). Emotional overeating was positively correlated with the BOLD response for $M_W$ vs. $N_W$ in the right lentiform nucleus ($r = 0.29, p = 0.02$), and left superior temporal gyrus ($r = 0.35, p = 0.005$).

Enjoyment of food

Enjoyment of food was negatively correlated with the BOLD response for $F_W$ vs. $M_W$ in the left posterior cingulate ($r = -0.29, p = 0.03$).
2.5 Discussion

The results of the current study provide insight into neurobiological regions associated with reward processing in a pediatric population. This is of critical importance given that alteration in general reward processing has been postulated to be one of the drivers of overeating (7, 19–28), which subsequently leads to the development of obesity. We used a modified card-guessing paradigm to evaluate the brain’s response to common incentives (e.g., food, money). This provided the opportunity to compare children’s response to food and money incentives in the same paradigm.

Results attained using an ROI approach showed that in the striatum, a region implicated in reward processing, the brain responded more to both anticipating food over neutral and winning money compared to neutral trials. Whole-brain activation in the striatum for reward anticipation did not survive threshold correction. However, winning food compared to money was associated with decreased activation in the striatum and regions associated with cognitive control. Importantly, in both approaches, effects were independent of weight status, which contradicts other studies that have found positive associations between obesity and BOLD response to palatable food cues in regions implicated in reward processing (18, 42). In sum, we found that the brain elicits different neural responses based on each reward contingency. Further, our results do not support the theory that general impairment in processing for food and monetary rewards are associated with obesity (27, 28, 62) in 7-11-year-old children.
To date, no studies have evaluated BOLD response to multiple reward types in children. Therefore, we took two approaches to analyzing the data. By testing coordinates previously associated with reward anticipation and receipt in adolescence (i.e., ROI approach), we were able to compare findings to other studies in adolescents that have evaluated the BOLD response to anticipating and receiving monetary rewards (39). There is a lack of replication studies in fMRI (63); therefore, this approach allowed us to determine how consistent the current findings were with the literature. Although this approach allowed for direct comparisons across studies, the regions tested may not have represented sufficient coverage of the brain to fully characterize the differences in brain responses present in the current sample, especially since we were also looking at food rewards; neural processing pathways may differ for each reward contingency (27, 33). Therefore, we also took a second, data-driven analytical whole-brain approach that allowed for broad and more extensive coverage of the whole brain.

In line with other analyses in adolescents (39) and adults (41), we found that BOLD response to reward engaged the striatum. The striatum is associated with decision-making (64) and due to its projections with other reward-related regions is thought to help integrate signals that influence goal-directed behavior (65, 66). In addition, the striatum is thought to be involved in hedonic valuation of monetary rewards (67) and prediction error (34, 68–70), and is also implicated in motivational processing of incentives more generally (71). Results from the ROI approach indicated that BOLD response near the border of the dorsal/ventral striatum was increased for anticipating food vs. neutral and winning money vs. neutral rewards. The whole-brain analysis revealed that striatal activity was also observed, but only for reward outcome (i.e., winning money compared to neutral and winning money compared to food). One explanation for differences between the results from each approach could be
that although there may be observed differences in striatal activity for reward anticipation at a specific voxel location, differences may not be substantial to survive threshold correction using current, stricter guidelines (61). Based on our whole-brain analysis, one interpretation of our results is that greater striatal activation to receiving monetary but not food rewards may be related to hedonic valuation and motivation associated with money.

The whole-brain approach also showed that BOLD responses in the middle and inferior frontal gyrus, regions associated with inhibitory control (72), were associated with winning money relative to a food incentive. In children, palatable food cues (4) and large portions (9) have been shown to activate the middle and inferior frontal gyrus, respectively, highlighting the role of these regions in response to food cue reactivity. Since obese children exhibit a greater BOLD response to food cues in the middle frontal gyrus compared to lean counterparts (18), it has been suggested that increased activation in these regions may be associated with increased demands for cognitive control. Contrary to previous results, we observed less activation in these regions when children won food relative to money and this was independent of weight status. Taken together with findings from the literature, it may be that brain responses implicated in cognitive control are increased when anticipating food cues, but these same responses are not observed for winning (i.e., receipt) food relative to money.

Based on previous findings (17, 18) we hypothesized that compared to healthy weight children, obese children would show an increased BOLD response to rewards, but our results did not support this prediction. One possibility is that the relationships observed in previous studies between weight status and reward processing may only exist in older populations. In adolescents and adults, weight status and risk of developing obesity has been
related to the BOLD response to both anticipating and receiving food and monetary rewards (14, 28, 29, 37, 38, 73). However, in children of similar age to the current study sample, weight status was positively correlated with the BOLD response during passive viewing of food images (7, 18) and receipt (i.e., consumption) of a palatable sucrose solution (74). Passive versus active viewing tasks may activate different neural pathways, thus offering a possible explanation for the differences in findings across studies. Additionally, no studies have evaluated the BOLD response to monetary rewards and the relation to childhood obesity. It is possible that in children these brain regions may be undergoing maturation (75, 76), therefore, it may be too early in development to reflect differences between weight groups in response to these different neural processes. This highlights the need to develop longitudinal studies to examine the relationships between reward processing and weight status throughout development.

In addition, we did not exclude children who may have been at risk of developing obesity based on parental weight status. This could partially explain why we did not observe large differences in brain response between weight groups. Out of thirty-one healthy weight participants, 14 children had one parent who was overweight or obese and for 13 children, both of their parents were either overweight or obese. To account for this potential confound, we included an obesity risk score as a covariate in our models. Although it did not significantly influence the main outcomes in the current study, future studies should aim to recruit equal numbers of children at low- and high-risk of obesity development (based on family history) to determine possible relationships between reward processing and the development of obesity.
To help interpret our findings, we included exploratory analyses to determine the relationship between reward processing and validated trait-based measures of child appetitive behaviors (48, 77). Results showed that children who had decreased BOLD responses to winning food compared to money in the left posterior cingulate, a region associated with emotion (78), had higher reports of emotional overeating and food responsiveness. In other words, parents of children who had decreased brain responses to winning food rewards reported that their children were more inclined to eat when emotional and have higher attention to food. Although food responsiveness and emotional overeating were positively associated with weight status, child appetitive traits were independently associated with brain response to food rewards in the posterior cingulate. In line with our findings, Bohon et al., (2017) also found negative correlations between the BOLD response for food receipt and both of these appetitive traits, but only in children who were classified as overweight (79). Here, we found that independent of weight status, how the brain responds to food cues predicts food-approach behaviors, which may be a risk factor for the development of obesity. Food-approach tendencies, such as food responsiveness and emotional overeating, are stable traits that have both been linked to the development of obesity in children (49, 50, 80–82). Because the relationship between brain response to food cues and appetitive traits may be observed prior to the development of obesity, these behavioral phenotypes may provide targets for prevention in future studies.

This study has several strengths. This was the first study to evaluate food and money rewards in the same experimental paradigm in children, which allowed us to make critical comparisons about how children’s brains respond to these two incentives. We showed that this novel task could be implemented in children with high scan success rates. The card-guessing task successfully produced activation in regions known to be associated with reward
anticipation and outcome (39, 41). There is a critical need for neuroimaging studies in children to better understand the developmental trajectory of food cue processing and its relationship to weight status. As such, this study provides an essential first step to understanding the basic neural processes associated with food decision-making in a pediatric population. In addition, another strength of this study is that by using a two-step analytic approach, we were able to compare the results to previous findings in the literature while also evaluating study-specific findings. Results from our data-driven approach provided a deeper insight into the regions associated with winning food and money rewards in this sample of 7-11-year-old children.

There were also limitations to the present study. The card-guessing task was modified to include a food reward and was previously utilized in adult smokers; thus, the experimental paradigm has not been validated for the current population (i.e., children). We did not collect measures of how much the rewards were valued. Therefore, we do not have behavioral measures of which reward was more salient. However, other studies have found that BOLD response to rewards correlates with the willingness to work for food and money (28), suggesting that differences in BOLD response may reflect reward saliency. Future studies should incorporate behavioral measures to provide clearer interpretations of BOLD responses in this age group. Furthermore, our study sample was racially homogenous, and the generalizability of these findings is not known. Finally, children were in a fasted state, this might have influenced brain responses. However, since we observed hyposensitivity to receiving food rewards, this may not be likely. Future studies should evaluate how the BOLD response for anticipating food and monetary rewards correlates is affected in a fed state.
2.6 Conclusion

In conclusion, the current study demonstrates for the first time that children’s brains respond differently to food and money rewards, and these responses occur independently of weight status. Winning money compared to food elicited greater brain responses in regions implicated in reward, motivation, and cognitive control. However, children who had higher parentally reported food-approach behaviors such as emotional overeating and food responsiveness exhibited reduced brain responses to winning food over money in the posterior cingulate, a region implicated in emotion. Therefore, reduced sensitivity to winning food relative to money may predict food-approach behaviors, which could be a risk factor for developing obesity. The present findings contribute critical insight about the relationship between reward processing, appetitive traits, and weight status in a pediatric sample.
2.7 Supplemental Material

2.7.1 ROI approach: Outcome win vs. no win (see Table S2.7.1).

Main effects of reward outcome were reported in the original paper. Results of the post hoc tests using the LSD approach revealed the following win to no win results:

*Winning Food Compared to Not Winning Food*

BOLD response was increased for F<sub>W</sub> vs. F<sub>NW</sub> in the left (L1) caudate (m<sub>diff</sub> = 0.12, p < 0.05) and nucleus accumbens (m<sub>diff</sub> = 0.08, p < 0.05).

*Winning Money Compared to Not Winning Money*

BOLD response was increased for M<sub>W</sub> vs. M<sub>NW</sub> in the left (L1) caudate (m<sub>diff</sub> = 0.08, p < 0.05).

*Winning Neutral Compared to Not Winning Neutral*

BOLD response was increased N<sub>W</sub> vs. N<sub>NW</sub> in both sites in the left caudate (L1: m<sub>diff</sub> = 0.07, p < 0.05; L2: m<sub>diff</sub> = 0.06, p < 0.05) and right nucleus accumbens (m<sub>diff</sub> = 0.07, p < 0.05).
<table>
<thead>
<tr>
<th>Region</th>
<th>H</th>
<th>F</th>
<th>p</th>
<th>F&lt;sub&gt;W&lt;/sub&gt; − M&lt;sub&gt;W&lt;/sub&gt;</th>
<th>F&lt;sub&gt;W&lt;/sub&gt; − N&lt;sub&gt;W&lt;/sub&gt;</th>
<th>F&lt;sub&gt;W&lt;/sub&gt; − F&lt;sub&gt;NW&lt;/sub&gt;</th>
<th>M&lt;sub&gt;W&lt;/sub&gt; − N&lt;sub&gt;W&lt;/sub&gt;</th>
<th>M&lt;sub&gt;W&lt;/sub&gt; − M&lt;sub&gt;NW&lt;/sub&gt;</th>
<th>N&lt;sub&gt;W&lt;/sub&gt; − N&lt;sub&gt;NW&lt;/sub&gt;</th>
<th>d</th>
</tr>
</thead>
<tbody>
<tr>
<td>Caudate</td>
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<td>0.08&lt;sup&gt;*&lt;/sup&gt;</td>
<td>0.16&lt;sup&gt;**&lt;/sup&gt;</td>
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<tr>
<td></td>
<td>L2&lt;sup&gt;+&lt;/sup&gt;</td>
<td>3.5</td>
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<td>-0.08&lt;sup&gt;*&lt;/sup&gt;</td>
<td>-0.05</td>
<td>0.03</td>
<td>0.04</td>
<td>0.10&lt;sup&gt;*&lt;/sup&gt;</td>
<td>0.06&lt;sup&gt;*&lt;/sup&gt;</td>
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<td>0.01</td>
<td>-0.04</td>
<td>0.09&lt;sup&gt;*&lt;/sup&gt;</td>
<td>0.06</td>
<td>0.04</td>
<td>0.4</td>
</tr>
<tr>
<td>Nucleus Accumbens</td>
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<td>5.8</td>
<td>0.000</td>
<td>-0.05</td>
<td>-0.01</td>
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<td>0.05</td>
<td>0.11&lt;sup&gt;*&lt;/sup&gt;</td>
<td>0.07&lt;sup&gt;*&lt;/sup&gt;</td>
<td>0.6</td>
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<tr>
<td>Putamen</td>
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<td>-0.04</td>
<td>0.01</td>
<td>0.06</td>
<td>0.05</td>
<td>0.08&lt;sup&gt;*&lt;/sup&gt;</td>
<td>0.03</td>
<td>0.5</td>
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<td>0.03</td>
<td>0.04</td>
<td>0.11&lt;sup&gt;*&lt;/sup&gt;</td>
<td>0.08</td>
<td>0.4</td>
</tr>
</tbody>
</table>

Table S2.1: ROIs (defined by coordinates from the literature (39)) with significant main effects for reward outcome. Results from the repeated measures ANOVA with reward type as the within subjects factor. H = hemisphere; L = left; R = right; F = statistical F-value.

* = p < 0.05; ** = p < 0.001. F<sub>W</sub>−M<sub>W</sub> = food win compared to money win; F<sub>W</sub>−N<sub>W</sub> = food win compared to neutral win; F<sub>W</sub>−F<sub>NW</sub> = food win compared to food no win; M<sub>W</sub>−N<sub>W</sub> = money win compared to neutral win; M<sub>W</sub>−M<sub>NW</sub> = money win compared to money no win; N<sub>W</sub>−N<sub>NW</sub> = neutral win compared to neutral no win; d = Cohen's d (i.e., effect size). * = survived correction for multiple comparisons correction using the Bonferroni-Hochberg approach.
S7.2 Whole-brain approach: Outcome win vs. no win (see Table S2.7.2).

Main effects of reward outcome were reported in the original paper. Results of the post hoc tests using the LSD approach revealed the following win to no win results:

**Winning Food Compared to Not Winning Food**

BOLD response was increased for $F_W$ vs. $F_{NW}$ in the right lentiform nucleus ($m_{\text{diff}} = 0.08, p < 0.05$), left superior temporal gyrus ($m_{\text{diff}} = 0.07, p < 0.05$), left inferior frontal gyrus ($m_{\text{diff}} = 0.07, p < 0.05$), and right (R2) middle frontal gyrus ($m_{\text{diff}} = 0.09, p < 0.05$). BOLD response was decreased for $F_W$ vs. $F_{NW}$ in the right lingual gyrus ($m_{\text{diff}} = 0.08, p < 0.05$).

**Winning Money Compared to Not Winning Money**

BOLD response was increased for $M_W$ vs. $M_{NW}$ in the right lentiform nucleus ($m_{\text{diff}} = 0.15, p < 0.001$), left superior temporal gyrus ($m_{\text{diff}} = 0.16, p < 0.001$), left lingual gyrus ($m_{\text{diff}} = 0.07, p < 0.05$), left inferior frontal gyrus ($m_{\text{diff}} = 0.18, p < 0.001$), left posterior cingulate gyrus ($m_{\text{diff}} = 0.16, p < 0.001$) and both sites in the right middle frontal gyrus (R1: $m_{\text{diff}} = 0.14, p < 0.001$; R2: $m_{\text{diff}} = 0.17, p < 0.001$).

**Winning Neutral Compared to Not Winning Neutral**

BOLD response was increased $N_W$ vs. $N_{NW}$ in the right lentiform nucleus ($m_{\text{diff}} = 0.07, p < 0.05$), left superior temporal gyrus ($m_{\text{diff}} = 0.09, p < 0.05$), left inferior frontal gyrus ($m_{\text{diff}} = 0.10, p < 0.05$), left posterior cingulate gyrus ($m_{\text{diff}} = 0.1, p < 0.05$), and right middle frontal gyrus (R1: $m_{\text{diff}} = 0.08, p < 0.05$).
<table>
<thead>
<tr>
<th>Anatomical Location</th>
<th>Hemisphere</th>
<th>$k$</th>
<th>$x$</th>
<th>$y$</th>
<th>$z$</th>
<th>$F$</th>
<th>$p$</th>
<th>$F_{W - M_W}$</th>
<th>$F_{W - N_W}$</th>
<th>$M_W - N_W$</th>
<th>$M_W - M_{NW}$</th>
<th>$N_W - N_{NW}$</th>
<th>$d$</th>
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<td>Cingulate Gyrus</td>
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<td>33</td>
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<td>0.16*</td>
<td>0.10*</td>
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<tr>
<td>Inferior Frontal</td>
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<td>279</td>
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<td>-48</td>
<td>0</td>
<td>10.0</td>
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<td>0.07*</td>
<td>0.18**</td>
<td>0.10*</td>
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<td>Lentiform Nucleus</td>
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<td>3</td>
<td>-9</td>
<td>12.2</td>
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<td>-0.07*</td>
<td>0.02</td>
<td>0.08*</td>
<td>0.09**</td>
<td>0.07*</td>
<td>0.9</td>
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<td>Lingual Gyrus</td>
<td>L</td>
<td>316</td>
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<td>-93</td>
<td>-12</td>
<td>4.6</td>
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<td>-0.06</td>
<td>-0.09*</td>
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<td>0.01</td>
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<tr>
<td></td>
<td>R</td>
<td>260</td>
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<td>0.023</td>
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<td>-0.07*</td>
<td>0.01</td>
<td>0.06</td>
<td>0.02</td>
<td>0.4</td>
</tr>
<tr>
<td>Middle Frontal Gyrus</td>
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<td>131</td>
<td>45</td>
<td>54</td>
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<td>7.7</td>
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<td>-0.16**</td>
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<td>0.04</td>
<td>0.12**</td>
<td>0.08*</td>
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<tr>
<td>Superior Temporal Gyrus</td>
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<td>48</td>
<td>18</td>
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<td>0.04</td>
<td>0.09*</td>
<td>0.10*</td>
<td>0.17**</td>
<td>0.4</td>
</tr>
</tbody>
</table>

Table S.2.7.2 Regions from the whole-brain analysis with significant main effects for reward outcome. Results from the repeated measures ANOVA, with reward type as the within subjects factor. Anatomical locations were defined by the Talairach Demon Atlas in AFNI. $k$ = cluster size (voxels); $H$ = hemisphere; $L$ = left; $R$ = right; $F$ = statistical $F$-value. $* = p < 0.05; ** = p < 0.001$. $F_{W - M_W}$ = food win compared to money win; $F_{W - N_W}$ = food win compared to neutral win; $F_{W - N_{NW}}$ = food win compared to food no win; $M_W - N_W$ = money win compared to neutral win; $M_W - M_{NW}$ = money win compared to money no win; $N_W - N_{NW}$ = neutral win compared to neutral no win; $d$ = Cohen's $d$ (i.e., effect size).
2.7 References


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Chapter 3

Is brain response to food rewards related to overeating? A test of the reward surfeit model of overeating in children.

Formatted for Submission to the Journal of Neuroscience

3.1 Abstract

The reward surfeit model of overeating suggests that heightened brain response to rewards contributes to overeating and subsequent weight gain. However, previous studies have not tested whether brain response to reward is associated with food intake, particularly during childhood, a period of dynamic development in reward and inhibitory control neurocircuitry. We conducted functional magnetic resonance imaging (fMRI) with 7-11-year-old children (n = 59; healthy weight, n = 31; overweight, n = 28; 54% female) while they played a modified card-guessing paradigm to examine blood-oxygen-level-dependent (BOLD) response to anticipating and receiving rewards (food, money, neutral). Food intake was assessed at three separate meals that measured different facets of eating behavior: 1) typical consumption (baseline), 2) overindulgence (palatable buffet), and 3) eating in the absence of hunger (EAH). *A priori* regions of interest included regions implicated in reward processing and inhibitory control. Multiple stepwise regressions were conducted to examine the relationship between intake and BOLD response to rewards. Results showed that a greater BOLD response in the medial prefrontal cortex for anticipating food compared to money positively correlated with how much children ate at the baseline and palatable buffet meal. BOLD response in the dorsolateral prefrontal cortex for winning food compared to money was positively correlated with intake at the palatable buffet meal and EAH. All aforementioned relationships were independent of child weight status. Findings support the reward surfeit model by showing that increased brain response to food compared to money rewards positively correlate with laboratory measures of food intake in children.
3.2 Significance Statement

Previous studies have not tested how the brain response to rewards relates to objective measures of overeating. Thus, little is known about the mechanisms driving excess consumption. Therefore, we tested how the brain responds to food compared to money rewards and related this measure to objectively assessed food intake in children varying in weight status. Results showed that greater response in brain regions implicated in both reward and inhibitory control to food compared to money predicted laboratory food consumption. Findings from this study suggest that heightened brain responses to food over monetary incentives may be a risk factor for excess food consumption in 7-11-year-old children.
3.3 Introduction

Studies using functional magnetic resonance imaging (fMRI) suggest that hypersensitivity to pictures of food, particularly in brain regions implicated in reward processing, contributes to overeating as measured by the outcome of body mass index (BMI) (1–3). However, the neural processing of food cues is complex and subject to individual differences. BMI has positively correlated with BOLD response in reward regions to anticipating (4, 5) and receiving (6–9) food. As a result, a reward surfeit model has been proposed. This model suggests that overeating is due to a hypersensitivity to rewards, which then drives intake. (10). However, BMI has also negatively correlated with the receipt of food rewards in similar brain regions implicated in reward and motivational processing (4, 11, 12). Thus, this model suggests that hyposensitivity to reward receipt may be associated with excess food intake. These contradictory findings suggest that greater brain response to reward anticipation may increase motivation to seek food, while reduced brain response to food receipt may sustain the cycle of overeating (13). In addition to competing theories, little is known about how the BOLD response to reward actually relates to objectively measured food intake. Understanding the neurobiological factors associated with overeating during this period is an essential step toward clarifying why some children are more susceptible to obesity than others.

Moreover, how the brain responds to secondary rewards, such as money, may also play a role in overeating. Monetary reward processing has been positively correlated with weight status in adolescents at risk for developing obesity (7) and adults (5, 14–16). These studies provide evidence that heightened brain response for multiple reward types may be a
risk factor for obesity. However, because most of this research was conducted in adults, there is a critical need to test these hypotheses in children, an age when cortical pathways implicated in reward processing are rapidly developing (17).

We previously observed that independent from BMI, children responded differently to anticipating and receiving food and money rewards (S. Adise et al., unpublished observations). BOLD response was increased in motivational and reward-related regions for anticipating food versus money, but decreased for winning (i.e., receipt) food versus money in similar brain regions. Currently, it is unknown how these differences relate to objectively measured food intake in children. Therefore, we tested the reward surfeit model of overeating by assessing the relationship between the BOLD response to the anticipation and receipt of food versus money rewards and laboratory assessed overeating. Food intake was measured with three meals: 1) an ad libitum baseline test-meal, 2) a highly palatable buffet designed to elicit overconsumption (18), and 3) a validated measure of children’s intake of palatable snacks when not hungry (i.e., eating in the absence of hunger [EAH]) (19). We hypothesized that BOLD response to the anticipation of food versus money in reward processing regions would positively correlate with intake at the palatable buffet and EAH, independent of weight status. In addition, our laboratory has found that BOLD responses in inhibitory control regions to food brand cues positively associated with how much children ate in branded compared to unbranded meals (20). Therefore, we hypothesized that greater brain responses in inhibitory control regions to anticipating food versus money would positively correlate with intake, but no a priori hypotheses were made regarding the relationship between reward receipt and laboratory intake.
3.4 Materials and methods

3.4.1 Experimental design

We conducted a cross-sectional study in children aged 7-11-years-old. The overall purpose of this study was to determine how differences in behavioral and neurological decision-making relate to objective measures of overeating and child weight status. This paper focuses on a subset of the data examining the relationship between brain responses to the anticipation and winning of food and money rewards and objective measures of food intake. The larger study included four laboratory sessions; each scheduled a week apart, at either lunch time (11:00AM-1:00 PM) or dinner time (4:00-6:30 PM), based on family availability. For all visits, participants were fasted for at least three hours, and satiety ratings were assessed before and after each test-meal and the fMRI using a validated visual analog scale for children (21). Over the first three visits, we measured children’s responses to behavioral decision-making tasks and assessed food intake at test-meals. The order of the first three visits was randomized. On the fourth visit, children underwent an fMRI scan. The current study focuses on the results of the fMRI scan and measures of food intake (visits 1-3). Findings from the other measurements are detailed elsewhere (Adise et al., 2017, unpublished observations). This study was approved by the Pennsylvania State University Institutional Review Board. Parental consent for child participation and child assent were obtained on the first visit to the laboratory.
3.4.2 Participants and sample size determination

Children were recruited via flyers and postings on popular websites. Interested families called the laboratory and were screened over the phone. The following were conditions or reasons for exclusion from the study which were assessed by parent-report: underweight (i.e., BMI-for-age < 5%), pre-existing food allergies and/or dietary restrictions, left-handedness, common MRI contraindications including metal implants or dental work containing metal, impaired or uncorrected vision, major psychiatric diagnoses and neurological illnesses, learning disabilities, and use of prescription medications known to affect MRI and food intake behavior. Children were also not eligible if there was a history of immediate familial psychiatric problems. Therefore, adopted children were not included due to potentially unknown familial medical history.

The goal of the study was to assess how brain response relates to weight status and food intake. Therefore, we aimed to recruit an even number of children who were healthy weight (i.e., BMI-for-age < 85th %) and overweight/obese (i.e., BMI-for-age ≥ 85th %)(22). Parents provided child height and weight over the phone, but these measures were confirmed in the laboratory. We aimed to recruit 80 children matched by weight status and sex, which would allow for 25% loss due to attrition and loss of data due to motion effects in the MRI. The justification for sample size determination is detailed elsewhere (Adise et al., 2017). In total, we screened 159 families. Fifty-six children were excluded for the following reasons: medical/psychological disorders contraindicative of fMRI (e.g., attention deficit hyperactivity disorder (n = 8), colorblindness (n = 3); learning disability (n = 3); left-handedness (n = 3), medication usage (n = 1), under/over age limit (n = 6), underweight (n = 2), food allergies or would not eat study foods (n = 8), non-biological child (n = 2), metal
implants (n = 9), and failure to complete eligibility screening (n = 10). Exclusion criteria were based on parental-report over the phone. An additional 69 children were screened but not enrolled for the following reasons: lost contact (n = 8), not interested (n = 8), or waitlisted (n = 53).

Out of the children screened, 71 were enrolled. Of those 71 children, 10 were excluded from the analyses for the following reasons: refusal to undergo fMRI (n = 1), excessive movement in the scanner (i.e., unsuccessful scan) (n = 2), technical error (n = 1), lost to follow-up (n = 4), participant dropout (n = 1), failure to provide accurate eligibility criteria (n = 1), and non-compliance with experimental procedures (n = 2). This resulted in the final sample of 59 children (32 females and 27 males; 2% Asian, 5% Black, and 93% White) (see Table 3.1 for participant characteristics). Participants in the final sample included 31 healthy weight children with a BMI-for-age % < 85th (mean ± SD age = 8.7 ± 1.4 years; 13 males) and 28 children classified as overweight or obese with a BMI-for-age % ≥ 85th (mean ± SD age = 9.4 ± 1.2 years; 14 males; 12 = overweight; 16 = obese).
<table>
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<th>Healthy Weight (n = 31)</th>
<th>Overweight/Obese (n = 28)</th>
</tr>
</thead>
<tbody>
<tr>
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<td>9.4 ± 1.2</td>
</tr>
<tr>
<td>Age (months)</td>
<td>111.0 ± 17.5</td>
<td>118.8 ± 14.7</td>
</tr>
<tr>
<td>BMI Percentile</td>
<td>53.4 ± 11.8</td>
<td>94.5 ± 4.0</td>
</tr>
<tr>
<td>BMI z-score (kg/m²)</td>
<td>0.1 ± 0.5</td>
<td>-1.25 – 0.96</td>
</tr>
<tr>
<td>Body Fat Percent*</td>
<td>17.1 ± 5.5</td>
<td>32.9 ± 6.8</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>31.5 ± 6.3</td>
<td>49.3 ± 10.0</td>
</tr>
<tr>
<td>Puberty Status</td>
<td>1.8 ± 0.7</td>
<td>1.8 ± 0.8</td>
</tr>
<tr>
<td>Tanner Stage</td>
<td>1.6 ± 0.8</td>
<td>1.9 ± 1.1</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>n</th>
<th>%</th>
<th>n</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>13</td>
<td>42</td>
<td>14</td>
</tr>
<tr>
<td>Female</td>
<td>18</td>
<td>58</td>
<td>14</td>
</tr>
<tr>
<td>Ethnicity</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Hispanic or Latino</td>
<td>3</td>
<td>10</td>
<td>0</td>
</tr>
<tr>
<td>Not Hispanic or Latino</td>
<td>28</td>
<td>90</td>
<td>28</td>
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<tr>
<td>Race</td>
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<td></td>
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<tr>
<td>Asian</td>
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<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Black</td>
<td>2</td>
<td>0.065</td>
<td>1</td>
</tr>
<tr>
<td>White</td>
<td>29</td>
<td>93.5</td>
<td>26</td>
</tr>
<tr>
<td>Total Combined Income</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Less than $20,000</td>
<td>0</td>
<td>0</td>
<td>3</td>
</tr>
<tr>
<td>$21,000-$35,000</td>
<td>2</td>
<td>6.5</td>
<td>1</td>
</tr>
<tr>
<td>$36,000-$50,000</td>
<td>4</td>
<td>12.9</td>
<td>4</td>
</tr>
<tr>
<td>$51,000-$75,000</td>
<td>6</td>
<td>19.4</td>
<td>10</td>
</tr>
<tr>
<td>$76,000-$100,000</td>
<td>10</td>
<td>32.3</td>
<td>1</td>
</tr>
<tr>
<td>$100,000+</td>
<td>9</td>
<td>29</td>
<td>9</td>
</tr>
<tr>
<td>Parent Education Level</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>High school</td>
<td>3</td>
<td>9.7</td>
<td>6</td>
</tr>
<tr>
<td>Associate’s Degree</td>
<td>3</td>
<td>9.7</td>
<td>4</td>
</tr>
<tr>
<td>Bachelor’s Degree</td>
<td>14</td>
<td>45.2</td>
<td>10</td>
</tr>
<tr>
<td>Master’s Degree</td>
<td>3</td>
<td>9.7</td>
<td>3</td>
</tr>
<tr>
<td>PhD/MD/JD</td>
<td>8</td>
<td>25.8</td>
<td>5</td>
</tr>
</tbody>
</table>

Table 3.1 Descriptive characteristics for the participants (n = 59; 54% female). SD = standard deviation; kg = kilograms; m² = meters squared. *Body fat percentage was missing for one participant.
3.4.3 Anthropometric measurements and body composition

Height and weight measurements were assessed on the first visit to the laboratory by a trained researcher. Children were measured to the nearest 0.1 cm and 0.1 kg in light clothing and stocking feet using a standard scale (Detecto model 437, Webb City, MO) and stadiometer (Seca model 202, Chino, CA). Children were weighed two times, and the average height and weight was converted to child BMI (kg/m$^2$). This information was used to determine BMI $z$-score and percentile, as well as classify children as healthy weight (< 85th %ile) or overweight/obese ($\geq$ 85%ile) (22).

3.4.4 Pubertal assessment

On the first visit, puberty was assessed via a 5-item pubertal development scale (23). We obtained child and parent-report separately, and averaged the two values to determine pubertal status. The questionnaire asked sex specific pubertal development questions; answers were coded from one (no) to four (seems complete). Although the assessment contained five items, total scores were obtained by summation of three questions (e.g., body hair growth, menstruation, breast development, facial hair), which is the standard procedure for scoring this questionnaire. In addition, we also asked children and parents to mark the sex-specific Tanner stage drawing that best corresponded to the child’s level of development (24). The parent and child’s scores on the Tanner staging drawings were averaged. Puberty and Tanner scores were entered as separate covariates of interest to determine if they influenced the final models.
3.4.5 Food intake measures

**Baseline meal**

We assessed children’s *ad libitum* intake at a baseline multi-item test-meal of common, age-appropriate foods including: macaroni and cheese, garlic bread, broccoli, tomatoes, grapes, and water (see Table 3.2 for food descriptions and quantities). Items for the meal were selected based on the Continuing Survey of Food Intakes of Individuals (25); these foods have previously been used in children by our laboratory and others (26–28). For the baseline meal, children were instructed that they had 30 minutes to eat until they were full. Children were not required to eat for the entire 30 minutes; however, a majority of the children ate for the entire duration. During the meal, a researcher sat with the child and read a nonfood related book to serve as a neutral distraction and to avoid the uncomfortable situation of the child eating alone in the laboratory. We have used similar methods in other studies with this age group (26, 29, 30).
## Baseline Test Meal

<table>
<thead>
<tr>
<th>Food Items</th>
<th>ED (kcal/g)</th>
<th>Weight (g)</th>
<th>Energy (kcal)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Macaroni &amp; cheese(^1)</td>
<td>1.05</td>
<td>400</td>
<td>420</td>
</tr>
<tr>
<td>Garlic Bread(^2)</td>
<td>3.44</td>
<td>100</td>
<td>344</td>
</tr>
<tr>
<td>Broccoli with butter and flavoring(^3)</td>
<td>0.31</td>
<td>180</td>
<td>56</td>
</tr>
<tr>
<td>Cherry Tomatoes(^4)</td>
<td>0.21</td>
<td>100</td>
<td>21</td>
</tr>
<tr>
<td>Red Seedless Grapes(^5)</td>
<td>0.77</td>
<td>200</td>
<td>154</td>
</tr>
<tr>
<td>Angel food cake(^6)</td>
<td>2.31</td>
<td>80</td>
<td>185</td>
</tr>
<tr>
<td>Water(^7)</td>
<td>0</td>
<td>1000</td>
<td>0</td>
</tr>
</tbody>
</table>

| Total food served                               | 1.35        | 1060       | 1180          |
| Total food & water served                       | 1.15        | 2060       | 1180          |

\(^1\)Macaroni and Cheese Dinner, Original, Kraft Foods Inc.  
\(^2\)Garlic Bread, Pepperidge Farm Inc.  
\(^3\)Large Broccoli Florets, Birds Eye; Unsalted Whipped Sweet Cream Butter, 45% less salt, Land O'Lakes Inc.; Molly McBee Butter Flavor Sprinkles, B&G Foods Inc.  
\(^4\)Wegman's Super Sweet Cherry Tomatoes.  
\(^5\)Wegman's Red Seedless Grapes.  
\(^6\)Angel Food Bundt Cake, Sara Lee Desserts, Hillshire Brands Co.  
\(^7\)Tap Water, University Park, PA.

**Table 3.2** Items served at the baseline test meal; amounts in weight (g) and energy (kcal) served are shown. ED = energy density; kcal = kilocalorie; g = grams.
Eating in the Absence of Hunger (EAH)

Twenty minutes after children ate the baseline meal to satiety we assessed EAH using a paradigm (31, 32). To assess EAH, children were exposed to a range of palatable snacks and treats (e.g., candies, cookies, cakes, chips) (see Table 3.3 for food descriptions and quantities). Children were instructed that they could play with the toys and/or eat any of the foods while the experimenter did work in the adjacent room. The experimenter left the room for 15 minutes. Amount consumed (in calories) was considered “eating in the absence of hunger”. Only children who reported that they were full prior to starting the EAH (determined as a rating of 75% or greater on the analog scale), were included in data analyses for this measure. This resulted in a sample of 46 children (78% of the total sample) for all EAH related analyses.
# Eating the Absence of Hunger Meal

<table>
<thead>
<tr>
<th>Food items</th>
<th>ED (kcal/g)</th>
<th>Weight (g) or serving size</th>
<th>Energy (kcal)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Popcorn¹</td>
<td>5.28</td>
<td>15</td>
<td>79</td>
</tr>
<tr>
<td>Potato Chips²</td>
<td>5.64</td>
<td>58</td>
<td>327</td>
</tr>
<tr>
<td>Pretzels³</td>
<td>5.89</td>
<td>39</td>
<td>230</td>
</tr>
<tr>
<td>Cheese crackers⁴</td>
<td>5.37</td>
<td>6 crackers (~44 g)</td>
<td>236</td>
</tr>
<tr>
<td>Mini-brownies⁵</td>
<td>4.36</td>
<td>4 mini-brownies (~51 g)</td>
<td>222</td>
</tr>
<tr>
<td>Chocolate Chip Cookies⁶</td>
<td>4.97</td>
<td>6 cookies (~66 g)</td>
<td>327</td>
</tr>
<tr>
<td>Fruit candies⁷</td>
<td>4.08</td>
<td>66</td>
<td>269</td>
</tr>
<tr>
<td>Chocolate candies⁸</td>
<td>4.86</td>
<td>66</td>
<td>321</td>
</tr>
<tr>
<td>Cheese-flavored corn chips⁹</td>
<td>5.14</td>
<td>58</td>
<td>298</td>
</tr>
<tr>
<td>Chocolate¹⁰</td>
<td>5.37</td>
<td>66</td>
<td>354</td>
</tr>
<tr>
<td>Total food served</td>
<td>4.89</td>
<td>529</td>
<td>2663</td>
</tr>
</tbody>
</table>

¹Butter flavored popcorn, Chester’s by Frito Lay’s
²Lay’s Potato Chips, by Frito Lay’s
³Rold Gold Tiny Twists Pretzels by Frito Lay’s
⁴Ritz Bits Cheese Crackers, Nabisco Foods
⁵Little Bites Fudge Brownies, Entenmann’s
⁶Chocolate Chip Cookies, Original, Chips A’Hoy, Mondelez International
⁷Skittles, Mars.
⁸M&M’S, Mars.
⁹Doritos by Frito Lay.
¹⁰Chocolate Kisses, The Hershey Company

**Table 3.3** Items served during eating in the absence of hunger; amounts in weight (g) and energy (kcal) served are shown. ED = energy density; kcal = kilocalorie; g = grams.
The buffet meal was designed to elicit overeating of highly palatable foods, and studies from our laboratory have previously found intake at this meal to be positively associated with child weight status and adiposity (18, 33). The meal consisted of three different types of foods: savory-fats (e.g., chicken nuggets, potato chips), sweet-fats (e.g., cupcake, cookies), and sweets (e.g., fruit candies and sugar-sweetened beverage) (see Table 3.4 for food descriptions and quantities). Children were instructed to eat as much or as little as they wanted. Additional servings were available, if requested. As with the baseline meal, a researcher sat with the child and read a nonfood related book during the meal.
### Palatable buffet meal

<table>
<thead>
<tr>
<th>Food Items</th>
<th>ED (kcal/g)</th>
<th>Weight (g) or serving size</th>
<th>Energy (kcal)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Savory Fats</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cheese bagel bites&lt;sup&gt;1&lt;/sup&gt;</td>
<td>2.28</td>
<td>8 pieces (~145 g)</td>
<td>331</td>
</tr>
<tr>
<td>Cheese pizza rolls&lt;sup&gt;2&lt;/sup&gt;</td>
<td>2.51</td>
<td>7 pieces (~85 g)</td>
<td>213</td>
</tr>
<tr>
<td>Chicken nuggets&lt;sup&gt;3&lt;/sup&gt;</td>
<td>2.99</td>
<td>7 nuggets (~105 g)</td>
<td>314</td>
</tr>
<tr>
<td>Mozzarella Sticks&lt;sup&gt;4&lt;/sup&gt;</td>
<td>3.03</td>
<td>4 sticks (~125 g)</td>
<td>379</td>
</tr>
<tr>
<td>Potato Chips&lt;sup&gt;5&lt;/sup&gt;</td>
<td>5.64</td>
<td>28 g</td>
<td>158</td>
</tr>
<tr>
<td><strong>Sweet-fats</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chocolate chip cookies&lt;sup&gt;6&lt;/sup&gt;</td>
<td>4.98</td>
<td>4 cookies (44 g)</td>
<td>219</td>
</tr>
<tr>
<td>Mini-brownies&lt;sup&gt;7&lt;/sup&gt;</td>
<td>4.36</td>
<td>4 brownies (60 g)</td>
<td>262</td>
</tr>
<tr>
<td>Chocolate cupcakes&lt;sup&gt;8&lt;/sup&gt;</td>
<td>4.71</td>
<td>1 cupcake (50 g)</td>
<td>236</td>
</tr>
<tr>
<td>Donut holes&lt;sup&gt;9&lt;/sup&gt;</td>
<td>5.07</td>
<td>4 donuts (58 g)</td>
<td>295</td>
</tr>
<tr>
<td>Whole-fat chocolate milk&lt;sup&gt;10&lt;/sup&gt;</td>
<td>0.83</td>
<td>1 cup (~245 g)</td>
<td>203</td>
</tr>
<tr>
<td><strong>Sweets</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Red licorice&lt;sup&gt;11&lt;/sup&gt;</td>
<td>3.39</td>
<td>50 g</td>
<td>170</td>
</tr>
<tr>
<td>Fruit leather&lt;sup&gt;12&lt;/sup&gt;</td>
<td>4.07</td>
<td>2 pieces (30 g)</td>
<td>122</td>
</tr>
<tr>
<td>Gummy candies&lt;sup&gt;13&lt;/sup&gt;</td>
<td>3.49</td>
<td>105 g</td>
<td>366</td>
</tr>
<tr>
<td>Fruit candies&lt;sup&gt;14&lt;/sup&gt;</td>
<td>4.04</td>
<td>86 g</td>
<td>347</td>
</tr>
<tr>
<td>Fruit punch&lt;sup&gt;15&lt;/sup&gt;</td>
<td>0.09</td>
<td>1 cup (~235 g)</td>
<td>21</td>
</tr>
<tr>
<td><strong>Total food served</strong></td>
<td>3.89</td>
<td></td>
<td>971</td>
</tr>
<tr>
<td><strong>Total food &amp; beverages served</strong></td>
<td>3.43</td>
<td></td>
<td>1451</td>
</tr>
</tbody>
</table>

<sup>1</sup>Cheese Bagel Bites, Three Cheese, H.J. Heinz Company  
<sup>2</sup>Cheese Pizza Rolls, Totino’s, General Mills  
<sup>3</sup>Chicken Nuggets, Tyson Foods Inc.  
<sup>4</sup>Mozzarella Sticks, Friday’s  
<sup>5</sup>Lay’s Potato Chips, by Frito Lay  
<sup>6</sup>Chocolate Chip Cookies, Original, Chips A’Hoy, Mondelez International.  
<sup>7</sup>Little Bites Fudge Brownies, Entenmann’s  
<sup>8</sup>Frosted Chocolate Cake with Creamy Filling, Hostess  
<sup>9</sup>Pop’ems Glazed Donut Holes, Entenmann’s.  
<sup>10</sup>Whole-fat Chocolate Milk, Schneider Farm.  
<sup>11</sup>Twizzler’s, Original, The Hershey Company.  
<sup>12</sup>Fruit Roll-up, Strawberry, Betty Crocker, General Mills.  
<sup>13</sup>Gummy bears, Haribo.  
<sup>14</sup>Skittles, Mars.  
<sup>15</sup>Kool-aid Bursts, Tropical Punch, Kraft Foods Inc.

**Table 3.4** Items served in the highly palatable buffet meal; amounts of weight and energy served are shown. ED = energy density; Kcal = kilocalorie; g = grams.
3.4.6 Food energy content calculations

For all of the above meals, foods were served on plates and prepared immediately before each visit. After the meal, leftovers were weighed to the nearest 0.1 g on a scale (Ohaus, Parsippany, NJ). Consumption of each food and/or beverage was computed as the difference between pre- to post-meal weights (grams) of each food. Intake was converted to kilocalories (kcal) using information from the nutritional facts panel and/or from standard nutrition databases (http://www.ars.usda.gov/ba/bhnrc/ndl).

3.4.7 Food liking

Before each meal, children tasted and rated samples (~5 gram) of each food and rated liking using a 5-point smiley face scale (34). To be consistent with other studies that have assessed EAH (19, 31, 35), children also ranked their preference for the foods used in the EAH procedure, on a 5-point Likert scale from most to least liked.

3.4.8 Mock training

Children underwent three mock training sessions before the fMRI. Details of the mock procedures are described elsewhere (Adise et al., 2017, unpublished observations). In brief, across the first two sessions, children were trained to remain still and respond to questions without moving their heads using a button press. During the third session, children were familiarized with and allowed to practice the task and were informed about the quantities for each of the rewards used in the fMRI paradigm ($0.50 or a few pieces of
Skittles or M&M’S). Preferred candy was selected before undergoing fMRI in attempt to ensure salience.

3.4.9 fMRI experimental paradigm

T2-weighted functional images were collected as children played a modified card-guessing task that has been previously shown to dissociate the effects of various reward types (i.e., money, puffs of a cigarette) in adult smokers (36). We modified the task to include food reward trials instead of the cigarette puff trials (see Figure 3.1). The task was a slow event-related design consisting of four runs utilizing three different reward types (i.e., food, money, neutral) and two conditions (i.e., win, no win), with 18 trials in each run; each run lasted 6 minutes and 38 seconds. The task was presented using E-Prime (version 2.0 Professional). Rewards were earned by guessing (duration 4 seconds) if a computer-generated number was higher or lower than the number five. After 6 seconds, a picture of the reward that could be earned for that trial was presented (i.e., money, candy, book [neutral]). Next, the actual number appeared (0.5 seconds) followed by feedback (win, no win; duration 1 second). A 9-second intertrial interval was presented between guess periods. The neutral reward was included to serve as a control and symbolized that no reward would be won during these trials. Trials were fixed using a pseudorandom order with 24 anticipation and 12 outcome trials of each reward type across all four runs (50% win rate for each reward condition). The total scan time was approximately 38 minutes.

Regardless of the accuracy of their guesses, across four runs participants won $5 and 66 g of either Skittles or M&M’S (equivalent to one regular size package of candy). Since no
previous studies had modified this task to include a food reward, we decided to use Skittles or M&M'S as these were discrete unit foods. In addition, these food rewards were similar in shape to the monetary reward and could be distributed in even increments. Prior to the scan, participants were allowed to pick their favorite candy to play for during the procedure (either Skittles or M&M'S). The earned rewards were delivered immediately after the scanning session but food rewards were not allowed to be consumed until after the visit was over.
Figure 3.1 A visual representation of the modified card-guessing task used in the scanner, which was presented via E-Prime 2.0 Professional.
3.4.10 Image acquisition

Scans were performed using a Siemens MAGNETOM Prism Fit whole body MRI scanner (Siemens Medical Solutions, Erlangen, Germany) with a 20-channel head coil and a 64-channel neck coil. Structural scans were collected using a T1-weighted magnetization-prepared rapid acquisition gradient echo (MPRAGE) sequence to acquire 192 slices, TR/TE = 1700/2.28 ms, flip angle = 8°, FOV = 256 mm, slice thickness = 1 mm, sagittal plane, and 1.0 x 1.0 x 1.0 mm voxel size. The MPRAGE sequence was approximately 4 minutes in duration. Four functional runs were collected using a T2*-weighted gradient single-shot blood-oxygen-level-dependent (BOLD) echo planar imaging (EPI) sequence to acquire 38 interleaved slices, TR = 2000 ms, TE = 24 ms, flip angle = 90°, matrix 64 x 64, FOV = 220 mm, slice thickness = 3 mm, AC-PC transverse, oblique plane determined by the mid-sagittal section, and 3.0 x 3.0 x 3.0 mm voxel size. Thirty-eight oblique sagittal slices were acquired in an interleaved and descending fashion. Each block consisted of 196 volumes.

3.4.11 fMRI preprocessing

Functional images were preprocessed and analyzed using a combination of FMRIB Software Library’s (FSL) and Analysis of Functional NeuroImages (AFNI) (37–40). FMRIB Software Library’s (FSL) brain extraction tool (BET) (38–40) was used to skull strip the anatomical image. This skull-stripped image was then transformed in a nonlinear fashion to standard space using the Montreal Neurologic Institute (MNI) template. There are subtle differences in anatomical variation between children and adults (41), therefore aligning to an adult template would pose minimal differences in our data.
Functional images were corrected for slice timing effects and aligned to the volume that had the least movement (i.e., minimum outlier) of the functional images. The first three volumes of functional scans were removed to control for T1 effects. Images were smoothed with a Gaussian filter set at 6 mm full-width at half maximum. AFNI’s motion detection software was implemented to identify and adjust for image artifacts related to intensity spiking and motion. Motion correction was conducted using six-parameter rigid-body in three dimensions. Motion exceeding 1 mm per TR in any direction was excluded. In addition, any runs in which 25% of the TRs were censored from the run were removed from the data analyses. This resulted in 3% of runs being discarded for motion effects across the entire sample, and an average of 3.81 successful runs (range 2-4) per child. For reward outcome, trials with missed guesses were excluded from the analyses (n = 241, 5.6 % of all trials across participants).

3.4.12 fMRI data analyses

For the first level analysis, we extracted statistical parametric maps using a general linear model, as implemented in the AFNI program 3dDeconvolve; deconvolution methods followed those outlined in Ward (2002) (42). Modeled task events included three levels of reward anticipation (food, money, or neutral), two possible outcomes (win or no win for each reward type), and a guessing period. Six motion parameters were added as nuisance regressors. Briefly, for each participant, our model consisted of the following regressors of interest: 1) food anticipation; 2) money anticipation; 3) neutral anticipation; 4) food win; 5) money win; 6) neutral win; 7) food no win; 8) money no win; 9) neutral no win. We estimated the hemodynamic response function for anticipation of food, money, and neutral
using a block function. Hemodynamic response functions for outcomes for each reward type (e.g., food no win) were estimated using a gamma function. Time courses for estimated hemodynamic response functions were based on stimulus presentation. For example, the picture of money was shown for six seconds; therefore, the specified duration of the response was 6 seconds (3 TRs). This method allowed us to model each of the components of this slow event-related task. AFNI’s 3dDeconvolution method then calculated several goodness-of-fit statistics including partial F-statistics for each regression and t-scores comparing each of the 10 estimated beta weights (from our regressors of interest) with zero. For the reward outcome, the analyses only focused on win trials between conditions.

3.4.13 Regions of interest

To test our primary hypotheses, we selected regions that have been previously associated with food-cue reactivity in reward and inhibitory control regions. We selected these regions prior to the experiment based on advice recommended for conducting a ‘brain-as-predictor’ approach outlined by Berkman and Falk (43). Spheres were drawn (6 mm) based on peak voxels on reverse inference functional co-activation masks generated from NeuroSynth (44) using the term names for each ROI (e.g., caudate) as a keyword (see Table 3.5 for coordinate locations and a list of ROIs); similar approaches have been used in the literature (45). The top two peak voxels were selected in order to have ROIs in both the left and right hemispheres. However, in the dorsolateral prefrontal cortex (dLPFC), the top two peaks were both located in the right hemisphere. To be consistent with how we selected other regions, the left hemisphere was not examined in the dLPFC. In addition, even though the striatum incorporates the caudate and other anatomical/functional regions, we included
these as separate terms since the aforementioned approach created spheres at the peak voxel for each keyword. Thus, the sphere in the striatum might not be located inside the caudate. The co-activation maps in NeuroSynth are generated based on a meta-analysis of activation coordinates commonly reported in the literature. Using an ROI approach allowed us to examine individual differences in brain regions related to reward processing and inhibitory control, where as group differences within a region are not subject to individual variation.
<table>
<thead>
<tr>
<th>Region</th>
<th>Hemisphere</th>
<th>x</th>
<th>y</th>
<th>z</th>
</tr>
</thead>
<tbody>
<tr>
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**Table 3.5** Regions of interest (ROI) coordinates derived from the peak location based on reversed inference maps gathered from the NeuroSynth database (44). MNI coordinates. L = left; R = right.
Contrast values were calculated by subtracting the BOLD response from food reward from the BOLD response to money (e.g., food anticipation – money anticipation; food win – money win). Voxel-wise parameter estimates were extracted for each ROI for each subject and entered into IBM SPSS Statistics for Macintosh V.22.0.0.2 (Armonk, NY: IBM Corp.) for further analyses.

3.4.14 Statistical analyses

Chi-square and independent samples $t$-test were conducted to determine differences between groups in regards to demographics and food intake. Multiple stepwise regressions were conducted in SPSS to determine the association between BOLD responses in the ROIs and laboratory measures of overeating. We included BMI $z$-score, fullness, pubertal status, and total family income as covariates in these models; covariates were eliminated if they were not significant. Correction for multiple comparison testing was performed via the Holm-Bonferroni approach (46). All descriptive statistics are reported as means ± standard deviations unless otherwise noted.

3.5 Results

3.5.1 Descriptive statistics

There were no differences between weight groups by age in years ($\chi^2 (4) = 4.9, p = 0.30$, Pearson chi-square), sex ($\chi^2 (1) = 0.4, p = 0.5$, Pearson chi-square), pubertal status ($\chi^2$
There was a difference between groups in regards to total family income ($\chi^2 (5) = 11.6, p = 0.04, \text{Pearson chi-square}$). Parents of healthy weight children reported higher total family incomes than parents of children who were classified as overweight/obese but both groups had a mean total family income between $51,000 - $75,000.

There were group differences in food intake. Children classified as overweight or obese ate significantly more at the baseline meal ($m = 751 \pm 209$ kcals) compared to healthy weight children ($m = 573 \pm 171$ kcals) ($t(57) = -3.6, p = 0.001, \text{independent samples t-test}$). Children overweight or with obesity ate more at the buffet meal ($m = 1468 \pm 305$ kcals) compared to healthy weight children ($m = 1138 \pm 316$ kcals) ($t(57) = -4.1, p < 0.001$, independent samples $t$-test). No differences by weight status were observed for EAH ($t(44) = -1.3, p = 0.2, \text{independent samples t-test}$). Regardless of weight status, children ate significantly more at the palatable buffet meal ($m = 1295 \pm 350$ kcals) than the baseline meal ($m = 658 \pm 209$ kcals) ($t(57) = -18.2, p < 0.001$, paired $t$-test). There were no differences between child sex and intake at baseline ($t(57) = -0.14, p = 0.9, \text{independent t-test}$) or palatable buffet meal ($t(57) = 1.9, p = 0.06, \text{independent t-test}$). However, boys ate more ($m = 469 \pm 258$ kcals) during EAH than girls ($m = 339 \pm 161$ kcals). Pearson’s correlation revealed that average pubertal status and tanner stage did not correlate with intake at any meals (all $p$’s > 0.05) but child’s age was positively correlated with intake at the palatable buffet meal ($R^2 = 0.31, p = 0.04, \text{Pearson’s Correlation}$). All covariates of interest (e.g., sex, age, puberty) were included in the regression and removed if not significant.
3.5.2 Baseline test meal

*Anticipating food compared to money*

A model that included BOLD response in medial prefrontal cortex (mPFC) along with child BMI z-score predicted 24% of the variance in children’s total intake at the baseline meal ($R^2 = 0.24, F(2,56) = 8.7, p < 0.001$, Linear Regression) (see Figure 3.2). Activation in the mPFC for anticipating food compared to money was associated with increased intake at the baseline meal ($\beta = 0.32, p = 0.009$). However, BMI $z$-score predicted a greater amount of total variance than did BOLD response to anticipating food relative to money ($\beta = 0.35, p = 0.004$).

*Winning food compared to money*

A model that included the BOLD response in the left orbitofrontal (OFC) cortex along with BMI $z$-score and child fullness predicted 29% of total variance in children’s intake at the baseline meal ($R^2 = 0.29, F(3,55) = 7.5, p < 0.001$, Linear Regression) (see Figure 3.2). In the left OFC, greater response to winning food compared to money was associated with increased intake at the baseline meal ($\beta = 0.32, p = 0.008$). Child fullness negatively influenced the model ($\beta = -0.25, p = 0.03$), suggesting that children who were more full ate less. However, BMI $z$-score was a stronger predictor of intake in the model than brain response ($\beta = 0.35, p = 0.004$).
Figure 3.2 Localization of (A) medial prefrontal cortex (mPFC) ($x = 0, y = 52, z = 20$). (B) Partial correlations between intake (kcal) at the baseline meal and BOLD response in the mPFC BOLD for anticipating food vs. money ($\beta = 0.32, p = 0.009$). (C) Localization of the left orbitofrontal cortex ($x = -24, y = 32, z = -14$). (D) Partial correlations between intake (kcal) at the baseline meal and BOLD response in the left orbitofrontal cortex (OFC) for anticipating food vs. money ($\beta = 0.32, p = 0.008$). Partial correlations are adjusted for BMI z-score.
3.5.3 Eating in the absence of hunger

_Anticipating food compared to money_

There were no significant associations between anticipating food relative to money and children’s food intake during EAH in any of the _a priori_ ROIs tested.

_Winning food compared to money_

BOLD responses for the contrast of winning food relative to money in several regions, including the right amygdala, insula, dlPFC, and OFC, were positively associated with EAH, but only the dlPFC survived threshold correction. In the two sites tested in the right dlPFC (see Figure 3.3), BOLD response to winning food relative to money and child fullness level (assessed before EAH) explained 30% and 25% of the variance, respectively (dlPFC R1: \( R^2 = 0.30, F(2,43) = 8.9, p = 0.001 \), Linear Regression; dlPFC R2: \( R^2 = 0.25, F(2,43) = 7.3, p = 0.002 \), Linear Regression). BOLD response in the dlPFC was positively associated with EAH at sites R1 (\( \beta = 0.42, p = 0.002 \)) and R2 (\( \beta = 0.37, p = 0.009 \)), while fullness level was a negative predictor of amount consumed during EAH for both models (R1 model: \( \beta = -0.31, p = 0.021 \); R2 model: \( \beta = -0.28, p = 0.047 \)). BOLD response was the biggest predictor of food intake. This indicates that children who had a greater brain response to winning food relative to money in this cognitive control region ate more palatable foods when not hungry.
Figure 3.3 Localization of the (A) right dorsolateral prefrontal cortex (dlPFC) (R1 x = 44, y = 38, z = 42; R2 x = 36, y = 38, z = -30). (B) Partial correlations between intake (kcal) during EAH and BOLD response in the right (R1) dlPFC for food vs. money ($\beta = 0.42$, $p = 0.002$). (C) Partial correlations between intake (kcal) during EAH and BOLD response in the right (R2) dlPFC for winning food vs. money ($\beta = 0.38$, $p = 0.009$). Partial correlations are adjusted for BMI z-score.
3.5.4 Buffet meal

*Anticipating food compared to money*

BOLD responses in the right caudate, right dlPFC and mPFC for anticipating food compared to money were positively associated with food intake at the buffet meal. However, only BOLD response in the mPFC survived testing for multiple comparisons (see Figure 3.4). Along with BMI z-score, BOLD response in the mPFC predicted 22% of the variance in children’s palatable buffet meal intake ($R^2 = 0.22$, $F(2,56) = 7.8$, $p = 0.001$, Linear Regression). BOLD response in the mPFC positively influenced the model ($\beta = 0.29$, $p = 0.02$), independently of BMI $z$-score, which was also positively associated with food intake ($\beta = 0.35$, $p = 0.005$). This suggests that independently of how much children weighed, those who had greater response in the mPFC for anticipating food compared to money ate more at the palatable buffet meal.

*Winning food compared to money*

BOLD response to winning food compared to money in the bilateral amygdala, right dlPFC and left OFC were all positively associated with children’s intake from the palatable buffet meal ($p’s < 0.001$). However, only the left amygdala and right (R1) dlPFC survived threshold corrections (see Figure 3.4). Together, BOLD response in the left amygdala for winning food compared to money and BMI $z$-score predicted 25% of the variance in buffet meal intake ($R^2 = 0.25$, $F(2,56) = 9.5$, $p < 0.001$, Linear Regression). Children who had a
greater response to winning food relative to money in this reward-related region ate more at the palatable buffet, regardless of body weight ($\beta = 0.36, p = 0.004$). BOLD response in the right (R1) dlPFC to winning food compared to money and BMI $z$-score predicted 28% of the variance in intake ($R^2 = 0.29, F(2,56) = 11.4, p < 0.001$, Linear Regression). BOLD response in dlPFC ($\beta = 0.34, p = 0.004$) positively influenced the model, independently of the effect of child BMI $z$-score ($\beta = 0.39, p = 0.001$). BOLD response in the dlPFC was the biggest predictor in this model. This suggest that children who had a greater BOLD response in an inhibitory control region to winning food compared to money ate more at the palatable buffet meal, regardless of weight status.
Figure 3.4 Localization of the (A) medial prefrontal cortex (mPFC) ($x = 0, y = 52, z = 20$). (B) Partial correlations between intake (in kcals) at the palatable buffet meal and BOLD response in the mPFC for anticipating food vs. money ($\beta = 0.29, p = 0.02$). (C) Localization of the left amygdala ($x = -22, y = -4, z = -18$). (D) Partial correlations between intake (in kcals) at the palatable buffet meal and BOLD response in the left amygdala for winning food vs. money ($\beta = 0.36, p = 0.004$). (E) Localization of the right dorsolateral prefrontal cortex (dlPFC) (R1 $x = 44, y = 38, z = 42$). (F) Partial correlations between intake (in kcals) at the palatable buffet meal and BOLD response in the R1 dlPFC for winning food vs. money ($\beta = 0.39, p = 0.001$). Partial correlations are adjusted for BMI z-score.
3.6 Discussion

This study tested the reward surfeit model of overeating by investigating the relationship between children’s brain response to anticipating and winning food compared to money rewards and laboratory measures of food intake. We hypothesized that independent of child BMI, heightened BOLD response to anticipation of food relative to money in reward regions would positively correlate with overeating. Results showed that BOLD response to anticipation of food compared to money in the mPFC positively associated with children’s intake at the baseline and palatable buffet meal. BOLD responses in other reward processing regions, including the OFC and amygdala, for winning food compared to money were positively correlated with intake at the baseline and palatable buffet meals, respectively. Moreover, BOLD response to winning food compared to money in the right dlPFC, a region associated with inhibitory control, positively predicted consumption of palatable snacks in the absence of hunger, as well as intake at the palatable buffet meal. The overall pattern of results suggests that heightened brain response to food relative to money may increase the vulnerability to overconsume palatable foods when available, regardless of how much a child weighs or how full they report feeling. Our findings show support of the reward surfeit model of overeating in children.

Anticipating food compared to money and food intake

The BOLD response to anticipating milkshake in reward-related regions has been related to BMI (4) and both self-reported and doubly-labeled water, which assesses energy
intake (47). However, it has not been established if these responses relate to overeating. In the present study, greater brain responses to the anticipation of food relative to money in regions of the appetitive brain network were positively associated with several measures of laboratory overconsumption. Importantly, these effects occurred independently of child weight status. This suggests that how the brain responds to anticipating food cues is associated with intake, which has implications for identifying neurological predictors of overeating before the onset of excess body weight.

The present study found that BOLD response to anticipating food rewards in the mPFC positively correlated with intake at both the baseline and palatable buffet meal. We were surprised to find a relationship between BOLD response in the mPFC and intake at the baseline meal. This meal was designed to assess intake of age-appropriate commonly consumed food and overeating at this meal has not been previously observed (27, 28). On the other hand, we expected BOLD response in the mPFC to food rewards to be associated with intake at the palatable buffet meal, which previously has been associated with overconsumption (18). These findings suggest that the mPFC response to anticipating rewards may play a role in food intake behavior. Animal and human studies show that the mPFC is involved in response to food images in a pre-meal state (48) and modulating reward-seeking behavior (49) highlighting its role in appetitive motivation. Thus, how much children eat may be associated with the brain’s processing of the motivational and rewarding properties of food.
There have been mixed findings in the literature examining the receipt of rewards with results demonstrating both a hyper- and hyposensitivity to reward receipt being correlated with increased BMI. The reward surfeit model suggests that increased sensitivity to reward drives intake, possibly due to the rewarding properties of food (10). On the other hand, the reward deficit model suggests that a hyposensitivity to receiving food rewards drives overconsumption as a means to compensate for a reward deficit (50). However, importantly, none of these studies have evaluated how BOLD response to receiving reward relates to actual food intake. The current findings demonstrate that increased BOLD response in reward processing and inhibitory control regions to winning food compared to money positively correlated with consumption, suggesting that a generalized hypersensitivity to receipt of food rewards may be associated with overeating in pre-adolescent children.

There are a few possible explanations as to why we did not find evidence for hyposensitivity. First, studies have suggested that hyposensitivity to reward is moderated by the A1 allele of the Taq1A polymorphism (10, 51, 52), which is associated with decreased dopamine receptor density (53, 54). We did not actively recruit children with this allele. Second, hyposensitivity may develop with age. Therefore, children 7-11-years-old may be too young to have developed reward hyposensitivity. Third, reward processing and inhibitory control regions are still undergoing development (55, 56) and BOLD response to rewards may change throughout brain maturation. Therefore, future studies should assess how the brain response to receiving palatable foods changes throughout development to determine the long-term impact of reward processing on risk for obesity.
Our results showed that BOLD response to winning food compared to money in regions associated with motivation and reward evaluation positively correlated with intake at the baseline and palatable buffet meal. Activation in the OFC, positively correlated with intake at the baseline meal. The OFC is associated with motivation and goal-oriented behavior (57) and monitoring and processing of outcomes, even in non-rewarding contexts (58). On the other hand, BOLD response in the amygdala, a region associated with emotional processing and evaluating the intensity of food rewards, regardless of valence (59), positively correlated with intake at the palatable buffet meal. This suggests that brain processing of motivational value and salience of food relative to money may be associated with increased susceptibility to overconsuming at palatable meals. However, the amygdala is also associated with emotions and memory (60). Therefore, another interpretation is that excess consumption may be associated with increased emotional processing of food rewards.

We also found that brain response to winning food rewards in the dlPFC positively related to overeating at the palatable buffet meal and during EAH but not at the baseline meal. This suggests that brain regions implicated in inhibitory control relate to intake under conditions where children are exposed to large varieties of highly palatable options, but not when presented with fewer choices of lower overall palatability. Prefrontal cortical development is immature in children. Thus, positive relationships between dlPFC and food intake may be indicative of the need to exert greater effortful control when presented with tempting foods. Greater activation in the dlPFC to food images has been observed in children with obesity (61) and in response to food brands relative to nonfood brands in healthy weight children (20). Similar findings were found in adults asked to exercise self-control (62), suggesting that greater activation in the dlPFC reflects an attempt to suppress appetitive behaviors. In our study, children who had the greatest BOLD response to winning
food relative to money rewards in the dlPFC may be conditioned to exert such effortful control in order to moderate their intake as these children showed the greatest overconsumption of highly palatable foods.

*Strengths and limitations*

These results offer a novel contribution to the literature by demonstrating that children’s brain response to food over money positively predicts intake in the laboratory. Intake was measured across three separate protocols giving insight into different facets of eating behavior including: a baseline meal meant to represent typical consumption, overindulgence, and eating when not hungry. Few neuroimaging studies have examined the relationship between BOLD responses to food cues and objectively measured intake, so these findings fill a critical gap in the literature about the neurobiological underpinnings of overeating in children. However, there were also limitations. Intake for each meal was only assessed once and children’s intake is highly variable (63). It would have been beneficial to assess intake across repeated meal visits to better capture the range of eating behaviors exhibited by this age group. In addition, food intake can vary by season (64), but we did not control for the effects of seasonality. Another limitation is that this study evaluated differences in BOLD response using an ROI approach. Other brain regions not included in our analyses could also be related to laboratory intake.
3.7 Conclusion

In conclusion, these findings offer support for the reward surfeit model of overeating by showing that hypersensitivity to anticipating and winning food relative to money was positively associated with objective measures of eating in children. We found that how the brain responds to anticipating food compared to money in reward processing regions was associated with how much children eat, independent of how much they weigh. On the other hand, the brain’s response in inhibitory control regions to winning food rewards correlated with overeating at a highly palatable buffet meal and during eating in the absence of hunger. Results from this study provide critical insight into understanding why some children are more susceptible to overeating than others and may help to clarify the etiology of obesity.
3.8 References


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Chapter 4

Testing the Reflective-Impulsive Dual Processes Model:

Reactive inhibitory control in children is impaired in the presence of reward incentives.

4.1 Abstract

The Reflective-Impulsive Dual Processes Model suggests maladaptive behavior such as overeating occurs when the temptation to consume rewarding energy-dense foods overrides inhibitory control. Thus, deficits in inhibitory control are theorized to contribute to overeating. However, the relationship between inhibitory control and objectively assessed overeating in children has not been studied. We investigated this by having children (n = 65; 35 females; 31 overweight or obese), 7-11-years-old, complete two versions of a Go/Nogo task: a baseline assessment and a reward incentivized Go/Nogo task that included food, money, and no reward blocks. Objective measures of overeating were assessed in the laboratory at a baseline meal, a meal designed to elicit overconsumption, and with a protocol that assesses eating in the absence of hunger (EAH). Decision-making components of the Go/Nogo data were analyzed using a drift-diffusion model of simple decisions, while the number of errors made measured task accuracy. Repeated measures ANOVA demonstrated inhibitory control performance on the baseline Go/Nogo was not related to weight status or overeating. However, regardless of weight status, children had poorer task accuracy to rewarded blocks (i.e., food and money) on the reward Go/Nogo task. In addition, there was a main effect of weight with Go/Nogo condition showing that compared to healthy weight children, overweight/obese made even more inhibitory control errors on the rewarded Go/Nogo task. In addition, results of a regression revealed that laboratory food intake, regardless of measure, were predicted by increased weight status, but not by inhibitory control performance at baseline or in the rewarded Go/Nogo task. Overall, findings from this study suggest that although heavier children eat more and make more errors on
inhibitory control tasks, there was no relationship between inhibitory control and objectively assessed food intake. More studies are needed to understand the relationship between weight status and inhibitory control deficits in children with obesity, which could have implications for obesity prevention and treatment.
4.2 Introduction

Despite existing prevention and intervention methods, the prevalence of childhood obesity is still alarmingly high (1). Currently, 17% of children in the United States are considered obese, which is associated with serious medical and psychological consequences (2), which have profound implications for health, economic and social outcomes throughout the lifespan (3). The reasons for overeating are multifactorial, however, the current prevalence rates of childhood obesity suggest that resisting the temptation to overeat may be difficult for some children. The Reflective-Impulsive Dual-Processes Model describes the conflict of temptation between self-control and giving into a more pleasurable outcome (4, 5). Based on this theory, it can be proposed that for some children, inhibitory control may be failing to inhibit the urge to eat rewarding foods, and as such, this may be a reason as to why some children overeat. However, this has not been tested with objective measures of food intake. Since childhood is a period marked by dramatic changes in reward and inhibitory control circuitry (6–8), it is important to study these relationships during childhood to understand how changes in these processes may contribute to overeating and subsequent weight gain.

Deficits in inhibitory control have been positively correlated with weight gain and obesity in both adults (9–16) and children (17–19), suggesting that insufficient inhibitory control processes may predispose some to overeat. On the other hand, increased sensitivity to food rewards is also thought to play a role in overeating as reward sensitivity has been positively associated with body weight in adults (20, 21) and children (20, 22–28). However, some findings in adults suggest that reward sensitivity is not food specific as alterations in
reward response extend to other domains, such as money (29, 30), suggesting that a general sensitivity to rewards contributes to excess consumption. In synthesizing the literature, both inhibitory control deficits and increased response to reward are related to obesity, which seems to support the theory of the Reflective-Impulsive Dual-Processes Model suggesting that exposure to highly palatable foods (21, 31) may stress inhibitory control systems. Thus, resisting temptations may be particularly challenging for individuals with inhibitory control deficits and this may pose an increased risk for overeating and obesity. However, to date, no studies have evaluated if reinforcers, such as food or money, affect inhibitory control and how this relates to objective measures of overeating, particularly in children.

The current study will bridge this gap in the literature by measuring inhibitory control with and without the presence of a reward incentive to examine how the ability to stop behavior interacts with reward to predict overeating in children with and without obesity. Generally, inhibitory control incorporates a wide range of cognitive and motor processes (32, 33) involved in stopping or withholding inappropriate actions and behaviors in order to achieve tasks or goals (34). More specifically, inhibitory control is comprised of two processes: proactive and reactive inhibitory control. Proactive inhibitory control is the ability to plan to inhibit a response (35–37) while reactive inhibitory control is the ability to quickly and automatically inhibit an urge with little cognitive regard (37). Thus, proactive inhibitory control may be involved in preparatory inhibitory control such as the plan to stick to a diet and avoid tempting foods, whereas reactive inhibitory control is activated in a just-in-time manner, such as inhibiting the urge to consume donuts that were unexpectedly placed in front of you. Although both of these inhibitory control mechanisms are important, the dual-processes model describes reactive inhibitory control (5). Therefore, proactive inhibitory control will not be discussed further in the present study.
Reactive inhibitory control can be assessed by the Go/Nogo task (18, 38, 39). In this task participants respond to frequent “go” stimuli and withhold responses to an infrequent (and different) “nogo” stimuli. Responding to “go” stimuli sets up a prepotent response tendency (i.e., respond to the urge), which makes it difficult to inhibit “nogo” stimuli (40). In other words, the task measures the ability to stop at an unexpected time following the buildup of a prepotent response. Typically, performance on Go/Nogo tasks are assessed via reaction time (i.e., how quickly or slowly was the task performed), and by how many errors occurred. The type of errors made can be further broken down to look at false alarms (i.e., responding when not supposed to), omission errors (i.e., forgetting to respond), and the total number of errors made throughout the task. However, by using a drift-diffusion model to analyze the data (see below), the reaction times can be further broken down to sub-components including: 1) non-decision time (i.e., the time it takes to visually process what the stimulus is and the time it takes to actually execute the response (i.e., hitting the response button) and 2) time to make a decision. Furthermore, the time to make a decision can be further divided into components, including caution (i.e., the extent to which speed is favored over accuracy) and response bias (i.e., preference to respond or not to respond under certain conditions). Previous studies have not determined the extent to which different components of the decision making processes are related to child weight status. Therefore, we applied a drift-diffusion model of simple decisions to provide clearer insight into the decision-making processes that may affect inhibitory control performance and their relationship to childhood weight status.

In the current study, we had two objectives. First, we investigated how reactive inhibitory control differs between children with and without obesity and how this relates to objective measures of overeating. Second, we tested the Reflective-Impulsive Dual
Processes Model to evaluate how reactive inhibitory control was affected by the presence of rewarding stimuli and how this related to overeating in children with and without obesity. Because it is theorized that obesity in adults is related to impaired reward processing in general (29, 30), the rewarded version of the Go/Nogo task included food and monetary rewards. We applied a drift-diffusion model of simple decisions to provide more insight into the decision-making processes driving reaction time. We hypothesized that 1) deficits in inhibitory control performance as assessed by error rates and decision-making components would positively correlate with weight status and objective measures of overeating; 2) inhibitory control deficits would be exacerbated in the presence of reward incentives such as food or money, and this would correlate with increased weight status and objective measures of overeating.

4.3. Methods

4.3.1 Study design

We conducted a cross-sectional study in children 7-11-years-old. The overall purpose of this study was to determine how behavioral and neurological correlates of decision-making relate to objective measures of overeating and child weight status. This paper focuses on a sub-set of the data analysis examining the relationship between inhibitory control and objective measures of food intake. The larger study had children come to our laboratory for four sessions; each scheduled a week apart, occurring at either lunch (11:00AM-1:00PM) or dinnertime (4:00-6:30PM). Participants were fasted for at least three hours, and satiety
ratings were assessed before and after each test-meal using a validated visual analog scale for children (41). The first three visits included behavioral assessments of decision-making and food intake measurements. On the fourth visit, children underwent functional magnetic resonance imaging (fMRI). The order of the first three visits was randomized. The current study focuses on results from two of the first three visits, which include measures from the Go/Nogo task and meal intake data. The Go/Nogo task was completed prior to eating the buffet meal. The baseline meal and eating during the absence of hunger were collected during a separate visit. Findings from the other measurements are detailed elsewhere (Adise et al., 2017). This study was approved by the Pennsylvania State University Institutional Review Board. Parental consent for child participation and child assent were obtained on the first visit to the laboratory.

4.3.2 Participants and sample size determination

Children were recruited via flyers and postings on popular websites. Eligibility was determined over the phone. The following were conditions or reasons for exclusion from the study, which were assessed by parent report: underweight (i.e., BMI-for-age < 5%), pre-existing food allergies and/or dietary restrictions, use of prescription medications known to effect food intake, major psychiatric diagnoses and neurological illnesses, and learning disabilities. Since this study incorporated an fMRI scan, some additional exclusion criteria were included: left-handedness, common MRI contraindications including metal implants or dental work containing metal, impaired or uncorrected vision, and use of prescription medications known to affect MRI. Children were also not eligible if there was a history of
immediate familial psychiatric problems; therefore, adopted children were not included due to potentially unknown familial medical history.

The goal of the study was to determine how decision-making relates to child weight status and food intake. Therefore, we aimed to recruit an even number of children who were healthy weight (i.e., BMI-for-age < 85th %). and overweight/obese (i.e., BMI-for-age ≥ 85th %). Although parents provided child height and weight over the phone, these measures were confirmed in the laboratory. Sample size for the larger study was determined based on power calculations to observe effects in MRI studies (see Adise et al., 2017 for a detailed description of the power calculation).

We enrolled 71 children in this study. Of those 71 children, four were excluded from the analyses for the following reasons: participant dropout (n = 1), failure to provide accurate eligibility criteria (n = 1), and non-compliance with experimental procedures (n = 4). This resulted in the final sample of 65 children (35 females; 30 males) (see Table 4.1 for participant characteristics). Participants in the final sample included 34 healthy weight children with a BMI-for-age % < 85th (mean ± SD age in years = 8.7 ± 1.4; 15 males) and 31 children classified as overweight or obese with a BMI-for-age % ≥ 85th (mean ± SD age in years = 9.3 ± 1.2; 15 males) (42). Chi-squared and independent samples t-test was conducted to determine if there were differences between weight groups.
### Table 4.1

Descriptive statistics for the participants (n = 65; 54% female). SD = standard deviation; kg = kilograms; m^2 = meters squared. *Body fat percentage was missing for one participant.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Healthy Weight (n = 34)</th>
<th>Overweight/Obese (n = 31)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean ± SD</td>
<td>Range</td>
</tr>
<tr>
<td>Age (years)</td>
<td>8.7 ± 1.4</td>
<td>7 – 11</td>
</tr>
<tr>
<td>Age (months)</td>
<td>111.7 ± 17.5</td>
<td>85 – 143</td>
</tr>
<tr>
<td>BMI Percentile</td>
<td>55.0 ± 18.8</td>
<td>11 – 83</td>
</tr>
<tr>
<td>BMI z-score (kg/m^2)</td>
<td>0.1 ± 0.5</td>
<td>-1.25 – 0.96</td>
</tr>
<tr>
<td>Body Fat Percent*</td>
<td>17.1 ± 2.0</td>
<td>6.4 – 30.6</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>31.6 ± 6.5</td>
<td>21.3 – 51.4</td>
</tr>
<tr>
<td>Puberty Status</td>
<td>1.8 ± 0.7</td>
<td>1.0 – 3.5</td>
</tr>
<tr>
<td>Tanner State</td>
<td>1.6 ± 0.8</td>
<td>1.0 – 4.0</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>15</td>
<td>44.1</td>
</tr>
<tr>
<td>Female</td>
<td>19</td>
<td>55.9</td>
</tr>
<tr>
<td>Ethnicity</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hispanic or Latino</td>
<td>3</td>
<td>9</td>
</tr>
<tr>
<td>Not Hispanic or Latino</td>
<td>31</td>
<td>91</td>
</tr>
<tr>
<td>Race</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Asian</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Black</td>
<td>2</td>
<td>6</td>
</tr>
<tr>
<td>White</td>
<td>32</td>
<td>94</td>
</tr>
<tr>
<td>Total Combined Income</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Less than $20,000</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>$21,000-$35,000</td>
<td>2</td>
<td>6.5</td>
</tr>
<tr>
<td>$36,000-$50,000</td>
<td>5</td>
<td>12.9</td>
</tr>
<tr>
<td>$51,000-$75,000</td>
<td>6</td>
<td>19.4</td>
</tr>
<tr>
<td>$76,000-$100,000</td>
<td>11</td>
<td>32.3</td>
</tr>
<tr>
<td>$100,000+</td>
<td>10</td>
<td>29</td>
</tr>
<tr>
<td>Parent Education Level</td>
<td></td>
<td></td>
</tr>
<tr>
<td>High school</td>
<td>4</td>
<td>11.8</td>
</tr>
<tr>
<td>Associate's Degree</td>
<td>3</td>
<td>8.8</td>
</tr>
<tr>
<td>Bachelor's Degree</td>
<td>15</td>
<td>44.1</td>
</tr>
<tr>
<td>Master's Degree</td>
<td>3</td>
<td>98.8</td>
</tr>
<tr>
<td>PhD/MD/JD</td>
<td>9</td>
<td>26.5</td>
</tr>
</tbody>
</table>

*Body fat percentage was missing for one participant.
4.3.3 Anthropometric measurements and body composition

On the first visit to the laboratory, children were measured in light clothing and stocking feet to the nearest 0.1 cm and 0.1 kg using a standard scale (Detecto model 437, Webb City, MO) and stadiometer (Seca model 202, Chino, CA). Measurements were collected twice, and the average height and weight was converted to child BMI (kg/m$^2$). BMI $z$-score and percentile was calculated based on this information [25], and used to classify children as healthy weight (< 85th %ile) or overweight/obese ($\geq$ 85%ile) (42).

4.3.4 Food Intake Measures

*Baseline meal*

Children’s *ad libitum* intake was assessed at a baseline multi-item test-meal. This meal consisted of common, age-appropriate foods including: macaroni and cheese, garlic bread, broccoli, tomatoes, grapes and water (see Table 4.2 for food descriptions and quantities). These meal items were commonly consumed amongst this age group, as assessed by the continuing survey of food intakes of individuals (43). In addition, this meal has been previously used by our lab and others (44–46) and the foods are well-liked and familiar. Children had 30 minutes to eat until they were full. Most children ate for the entire duration ($m = 21.3 \pm 7.8$ minutes), but this was not required. To serve as a neutral distraction, a researcher read a non-food related book to the child while they ate. Other studies in this age group have used similar methods (44, 47, 48).
Baseline Test Meal

<table>
<thead>
<tr>
<th>Food Items</th>
<th>ED (kcal/g)</th>
<th>Weight (g)</th>
<th>Energy (kcal)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Macaroni &amp; cheese¹</td>
<td>1.05</td>
<td>400</td>
<td>420</td>
</tr>
<tr>
<td>Garlic Bread²</td>
<td>3.44</td>
<td>100</td>
<td>344</td>
</tr>
<tr>
<td>Broccoli with butter and flavoring³</td>
<td>0.31</td>
<td>180</td>
<td>56</td>
</tr>
<tr>
<td>Cherry Tomatoes⁴</td>
<td>0.21</td>
<td>100</td>
<td>21</td>
</tr>
<tr>
<td>Red Seedless Grapes⁵</td>
<td>0.77</td>
<td>200</td>
<td>154</td>
</tr>
<tr>
<td>Angel food cake⁶</td>
<td>2.31</td>
<td>80</td>
<td>185</td>
</tr>
<tr>
<td>Water⁷</td>
<td>0</td>
<td>1000</td>
<td>0</td>
</tr>
</tbody>
</table>

| Total food served                        | 1.35        | 1060       | 1180          |
| Total food & water served                | 1.15        | 2060       | 1180          |

¹Macaroni and Cheese Dinner, Original, Kraft Foods Inc.
²Garlic Bread, Pepperidge Farm Inc.
³Large Broccoli Florets, Birds Eye; Unsalted Whipped Sweet Cream Butter, 45% less salt, Land O'Lakes Inc.; Molly McButter Butter Flavor Sprinkles, B&G Foods Inc.
⁴Wegman’s Super Sweet Cherry Tomatoes.
⁵Wegman’s Red Seedless Grapes.
⁶Angel Food Bundt Cake, Sara Lee Desserts, Hillshire Brands Co.
⁷Tap Water, University Park, PA.

**Table 4.2** Items served at the baseline test meal; amounts in weight (g) and energy (kcal) served are shown. ED = energy density; kcal = kilocalorie; g = grams.
Eating in the Absence of Hunger (EAH)

Eating in the absence of hunger was assessed twenty minutes after consumption of the baseline meal to satiety (49). The EAH paradigm was developed by Fisher and Birch (50). During this paradigm, children were left alone in a room with a range of palatable snacks and treats (e.g., candies, cookies, cakes, chips) (see Table 4.3 for food descriptions and quantities) as well as toys (e.g., books, arts and crafts). Children were instructed that they could play with the toys and/or eat any of the foods while the experimenter did work in the adjacent room. The experimenter left the room for 15 minutes. “Eating in the absence of hunger” was determined by the amount of snacks and treats the child consumed in calories. Only children who had pre-EAH fullness ratings of 75% or greater, on the analog scale were included in data analysis for this measure. This resulted in a sample of 49 children for analyses including EAH.
### Table 4.3

<table>
<thead>
<tr>
<th>Food items</th>
<th>ED (kcal/g)</th>
<th>Weight (g) or serving size</th>
<th>Energy (kcal)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Popcorn¹</td>
<td>5.28</td>
<td>15</td>
<td>79</td>
</tr>
<tr>
<td>Potato Chips²</td>
<td>5.64</td>
<td>58</td>
<td>327</td>
</tr>
<tr>
<td>Pretzels³</td>
<td>5.89</td>
<td>39</td>
<td>230</td>
</tr>
<tr>
<td>Cheese crackers⁴</td>
<td>5.37</td>
<td>6 crackers (~44 g)</td>
<td>236</td>
</tr>
<tr>
<td>Mini-brownies⁵</td>
<td>4.36</td>
<td>4 mini-brownies (~51 g)</td>
<td>222</td>
</tr>
<tr>
<td>Chocolate Chip Cookies⁶</td>
<td>4.97</td>
<td>6 cookies (~66 g)</td>
<td>327</td>
</tr>
<tr>
<td>Fruit candies⁷</td>
<td>4.08</td>
<td>66</td>
<td>269</td>
</tr>
<tr>
<td>Chocolate candies⁸</td>
<td>4.86</td>
<td>66</td>
<td>321</td>
</tr>
<tr>
<td>Cheese-flavored corn chips⁹</td>
<td>5.14</td>
<td>58</td>
<td>298</td>
</tr>
<tr>
<td>Chocolate¹⁰</td>
<td>5.37</td>
<td>66</td>
<td>354</td>
</tr>
<tr>
<td><strong>Total food served</strong></td>
<td>4.89</td>
<td>529</td>
<td>2663</td>
</tr>
</tbody>
</table>

¹Butter flavored popcorn, Chester’s by Frito Lays.
²Lay’s Potato Chips, by Frito Lays.
³Rold Gold Tiny Twists Pretzels by Frito Lays.
⁴Ritz Bits Cheese Crackers, Nabisco Foods
⁵Little Bites Fudge Brownies, Entenmann’s
⁶Chocolate Chip Cookies, Original, Chips A’Hoy, Mondelez International.
⁷Skittles, Mars.
⁸M&M’S, Mars.
⁹Doritos by Frito Lay.
¹⁰Chocolate Kisses, The Hershey Company

Items served during eating in the absence of hunger; amounts in weight (g) and energy (kcal) served are shown. ED = energy density; kcal = kilocalorie; g = grams.
Palatable buffet meal

The buffet meal has been previously shown to be positively associated with child weight status (51, 52) and was designed to elicit overconsumption. The meal consisted of three different types of foods: savory-fats (e.g., chicken nuggets, potato chips), sweet-fats (e.g., cupcake, cookies), and sweets (e.g., fruit candies and sugar-sweetened beverage) (see Table 4.4 for food descriptions and quantities). In this meal, children were instructed to eat as much or as little as they wanted during the 30-minute duration; most children ate for the entire duration of the meal (m = 25.8 ± 6.1 minutes). Additional servings were available, if requested. During this meal, the researcher also read to the child.
<table>
<thead>
<tr>
<th>Food Items</th>
<th>ED (kcal/g)</th>
<th>Weight (g) or serving size</th>
<th>Energy (kcal)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Savory Fats</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cheese bagel bites(^1)</td>
<td>2.28</td>
<td>8 pieces (~145 g)</td>
<td>331</td>
</tr>
<tr>
<td>Cheese pizza rolls(^2)</td>
<td>2.51</td>
<td>7 pieces (~85 g)</td>
<td>213</td>
</tr>
<tr>
<td>Chicken nuggets(^3)</td>
<td>2.99</td>
<td>7 nuggets (~105 g)</td>
<td>314</td>
</tr>
<tr>
<td>Mozzarella Sticks(^4)</td>
<td>3.03</td>
<td>4 sticks (~125 g)</td>
<td>379</td>
</tr>
<tr>
<td>Potato Chips(^5)</td>
<td>5.64</td>
<td>28 g</td>
<td>158</td>
</tr>
<tr>
<td>Sweet-fats</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chocolate chip cookies(^6)</td>
<td>4.98</td>
<td>4 cookies (44 g)</td>
<td>219</td>
</tr>
<tr>
<td>Mini-brownies(^7)</td>
<td>4.36</td>
<td>4 brownies (60 g)</td>
<td>262</td>
</tr>
<tr>
<td>Chocolate cupcakes(^8)</td>
<td>4.71</td>
<td>1 cupcake (50 g)</td>
<td>236</td>
</tr>
<tr>
<td>Donut holes(^9)</td>
<td>5.07</td>
<td>4 donuts (58 g)</td>
<td>295</td>
</tr>
<tr>
<td>Whole-fat chocolate milk(^10)</td>
<td>0.83</td>
<td>1 cup (~245 g)</td>
<td>203</td>
</tr>
<tr>
<td>Sweets</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Red licorice(^11)</td>
<td>3.39</td>
<td>50 g</td>
<td>170</td>
</tr>
<tr>
<td>Fruit leather(^12)</td>
<td>4.07</td>
<td>2 pieces (30 g)</td>
<td>122</td>
</tr>
<tr>
<td>Gummy candies(^13)</td>
<td>3.49</td>
<td>105 g</td>
<td>366</td>
</tr>
<tr>
<td>Fruit candies(^14)</td>
<td>4.04</td>
<td>86 g</td>
<td>347</td>
</tr>
<tr>
<td>Fruit punch(^15)</td>
<td>0.09</td>
<td>1 cup (~235 g)</td>
<td>21</td>
</tr>
<tr>
<td>Total food served</td>
<td>3.89</td>
<td>971</td>
<td>3412</td>
</tr>
<tr>
<td>Total food &amp; beverages served</td>
<td>3.43</td>
<td>1451</td>
<td>3636</td>
</tr>
</tbody>
</table>

\(^1\)Cheese Bagel Bites, Three Cheese, H.J. Heinz Company
\(^2\)Cheese Pizza Rolls, Totino’s, General Mills
\(^3\)Chicken Nuggets, Tyson Foods Inc.
\(^4\)Mozzarella Sticks, Friday’s
\(^5\)Lay’s Potato Chips, by Frito Lay
\(^6\)Chocolate Chip Cookies, Original, Chips A’Hoy, Mondelez International.
\(^7\)Little Bites Fudge Brownies, Entenmann’s
\(^8\)Frosted Chocolate Cake with Creamy Filling, Hostess
\(^9\)Pop’ems Glazed Donut Holes, Entenmann’s.
\(^10\)Whole-fat Chocolate Milk, Schneider Farm.
\(^11\)Twizzler’s, Original, The Hershey Company.
\(^12\)Fruit Roll-up, Strawberry, Betty Crocker, General Mills.
\(^13\)Gummy bears, Haribo.
\(^14\)Skittles, Mars.
\(^15\)Kool-aid Bursts, Tropical Punch, Kraft Foods Inc.

**Table 4.4** Items served in the highly palatable buffet meal; amounts of weight and energy served are shown. ED = energy density; Kcal = kilocalorie; g = grams.
4.3.5 Food liking and energy intake measures

Prior to the test-meals, we measured children’s liking of the foods using a 5-point smile face scale (53). Children were asked to taste small samples (~5 grams) of each of the foods. To be consistent with other studies, preference ratings were also gathered for the EAH procedure (54). For all of the food intake measures, intake was determined by calculating the weight (in g) of each food consumed measured from pre- to post- meal to the nearest 0.1 gram. Intake was converted to kilocalories (kcal) using the nutrition facts labels associated with each product.

4.3.6 Inhibitory control measurement: Go/Nogo task

Children completed a child-friendly computerized Go/Nogo task (55) (see Figure 4.1) The Go/Nogo task (55) assesses reactive inhibitory control by having children hit a button when they see “go” stimuli and refrain when they see “nogo” stimuli. Reactive control is primarily assessed by the ability to withhold a response (i.e., percent of successful inhibitions/accuracy rates) and secondarily by the reaction of the response to “go” stimuli (32).
Figure 4.1 A visual presentation of the Go/Nogo task, which was presented via E-Prime 2.0 Professional. Children hit the spacebar to go trials (i.e., pictures of animals) and refrain from responding to nogo trials (i.e., pictures of three orangutans).
Children were informed that they were helping a zookeeper put back all the animals in their cages after someone let them out. Children were instructed to send the animals back to their cages by hitting a space bar when they saw an animal (“go”) but to not hit the space bar when they saw their orangutan friends (“nogo”), who are also helping the zookeeper. To familiarize the children with the procedures, they completed a brief practice session consisting of 12 trials, with nine go trials and three nogo trials. In the actual task (non-practice), each block consisted of 40 trials, which included 10 images of the orangutans and 30 novel zoo animal pictures. Each block consisted of novel sets of animal photographs that were balanced with respect to color, animal type, and size. Each picture was preceded by a fixation cross displayed from a randomized interval ranging between 200 and 300 milliseconds. The stimulus was presented for 750 milliseconds, followed by a blank screen for 500 milliseconds. Responses were allowed during stimuli duration or at any point during the following 500 milliseconds.

Children performed two versions of the Go/Nogo task: one regular version, which served to assess inhibitory control at baseline, and one that contained reward incentives (with three reward trial types [money, food, no reward]) (see Figure 4.2). The regular Go/Nogo (baseline inhibitory control) contained five blocks of 40 trials each. The reward version consisted of eight blocks (three money incentive, three food incentive, and two no reward incentive) of 40 trials. The reward Go/Nogo blocks were fixed in a pseudorandom order. Regardless of task version (baseline inhibitory control or reward version), the instructions remained the same. However, in the reward version of the task, children were told that for blocks when they saw a picture of money or food, they had the chance to earn
additional money or some of their favorite snack based on how quickly and accurately they put the right animals back in the cages. They also were informed that for some blocks, they would not have the chance to earn anything extra (no reward), but they should still try to respond quickly and accurately as they could and put the right animals back in their cages. Earned rewards were delivered at the end of the visit. The total task time was about 20 minutes.
Figure 4.2 A visual presentation of the Go/Nogo task with reward incentives, which was presented via E-Prime 2.0 Professional. In this version, instructions are the same but based on performance, children have the chance to earn additional money, some of their favorite snack or nothing (money, food, no reward blocks).
4.3.7 Go/Nogo analyses

Drift-diffusion analyses

In order to understand the different decision-making components that affect reaction time, a modified drift-diffusion model of simple decisions was fit to reaction time and accuracy data from go trials, and reaction times from commission errors on nogo trials. The drift-diffusion model extracted different facets of the decision-making process such as 1) nondecision time, the time needed for non-decision processes such as motor execution and visual encoding, which is measured in milliseconds. Longer nondecision times indicate slower encoding/motor response processes; 2) response caution, also known as the accuracy vs. speed tradeoff. Higher values of response caution indicate a cautious response style that favors accuracy over speed; 3) response bias, the preference for responding vs. not responding. Values of response bias indicate whether one response option was favored over the other; and 3) drift rate, the quality or strength of evidence from processing the stimulus. Higher values of drift rate indicate better perceptual processing and thus better task performance. The modified drift-diffusion model was run using RStudio V.0.99.893 (56).

The drift-diffusion model (see Figure 4.3) is based on the assumption that it takes time to accumulate evidence to make a decision; evidence can be described as the aforementioned parameters of reaction time (e.g., nondecision time, caution, bias). Once the evidence is accumulated, a response is made or withheld. Responses are scaled to a top and bottom boundary. The top boundary represents go responses where as the bottom boundary represents nogo responses. The rate (magnitude and value of the sign) at which the decision
process approaches a response boundary is known as the drift rate and is driven by the strength of evidence from processing the stimulus. Positive values indicate evidence for the top response (go) while negative values represent evidence for the bottom (nogo). The absolute value of the drift rate relates to task performance, with values closer to zero symbolizing weaker evidence and higher values symbolizing better performance. Caution is measured as the distance between the two boundaries and relates to the total amount of evidence required before a response is committed. Larger values of boundary separation indicate that a lot of evidence is required for the decision, and result in more cautious responding (i.e., favoring accuracy over speed). Bias is measured based on the relative position of the starting point between the two boundaries. If the decision process starts closer to the top (go) boundary, this indicates the participant has a bias for that response option. Bias ratios above 0.5 indicate a bias to respond (go), whereas ratios lower than 0.5 indicate a bias not to respond (nogo). Nondecision time is measured in milliseconds. It is important to note, that the modeled drift-diffusion components provide insight into the decision-making processes that contribute to a response, whereas task accuracy gives insight into inhibitory control performance.
Figure 4.3 Visual representation of the drift-diffusion model for go trials. The process starts along the boundaries (i.e., $\xi$-axis). As evidence is accumulated, the process drifts until a boundary is reached. This corresponds to one of two decisions: to go or not go. The drift rate is the strength of the speed at which the go process hits a boundary. Boundary separation represents the degree of caution of response (i.e., speed/accuracy tradeoff). Nondecision time is calculated as the time it takes for the stimulus to be encoded and the time to execute the motor response. Bias is calculated by examining where along the $\xi$-axis the decision starts (i.e., is the process closer to the “go” or “nogo” boundary). The total reaction time is equal to the time it takes to encode the stimulus, decision time, and motor response time.
The drift-diffusion model was fitted to each participant’s data for each condition, including the proportion of correct and error responses, the RT distribution for correct responses on go trials, and the median RT for incorrect responses on nogo trials (i.e., commission errors). The parameters of the model were adjusted using a SIMPLEX routine to minimize a $X^2$ value based on the misfit between the model predictions and the observed data for each participant and condition (see Ratcliff & Teurlinckx, 2002) (57). The fitting procedure resulted in a set of estimated parameter values for each participant, which was analyzed below.

Results of the drift-diffusion model were entered into IBM SPSS Statistics for Macintosh V.22.0.0.2 (Armonk, NY: IBM Corp.) for further analyses. Higher scores for caution symbolize greater preference for accuracy over speed. Higher scores on the motor execution time reflect slower response times. Higher scores on drift rate reflect better performance. Higher scores on bias indicate greater bias for responding compared to not responding. Task accuracy was measured by omission error (i.e., response failure) and false alarm rate (i.e., incorrect response). Data were assessed for normal distribution. Log transformations were applied to non-normally distributed data.

4.3.8 Go/Nogo baseline assessment statistical analyses

Independent samples-tests were run to determine differences between weight groups and performance on each component of inhibitory control performance. Models that violated Mauchly’s sphericity were corrected with Greenhouse-Gassier. To assess for differences between performance on the reward version, we ran a repeated measures ANOVA in SPSS. A separate mixed linear model was conducted with our covariates of interest, such as fullness rating (assessed after the task), pubertal status, time of day in which
the visits occurred, age and sex. Covariates were entered into the model, but removed if not significant. Interaction effects were tested by running a mixed model with BMI as a group (i.e., healthy weight vs. overweight/obese).

4.3.9 Food intake and Go/Nogo analyses

To assess the relationship between performance on the reward version and laboratory measures of food intake, we created mean difference scores between each reward condition (e.g., food reaction time – money reaction time). Multiple step-wise regressions were conducted in IBM SPSS Statistics for Macintosh V.22.0.0.2 (Armonk, NY: IBM Corp.) to determine the associations between inhibitory control components (at baseline and in the presence of rewards) and laboratory measures of overeating. We included BMI \( z \)-score, fullness rating, pubertal status, time of day in which the visits occurred, age and sex in these models, but then eliminated them if they were not significant. Correction for multiple comparison testing was performed via the Benjamini-Hochberg approach. False discovery rate (FDR) was achieved with a significance level of \( q = 0.05 \) (58). All descriptive statistics are reported as means ± standard deviations unless otherwise noted.
4.4 Results

4.4.1 Descriptive statistics

There were no differences between weight groups by age ($\chi^2 = 4.5, p = 0.3$), sex ($\chi^2 = 0.12, p = 0.7$), total family income ($\chi^2 = 8.5, p = 0.1$), or parent education level ($\chi^2 = 3.9, p = 0.3$). However, there were differences in food intake across weight groups. Children classified as overweight or obese ate significantly more at the baseline meal ($m = 745 \pm 218$ kcals) compared to healthy weight children ($m = 571 \pm 178$ kcals) ($t(63) = -3.5, p = 0.001$). Children with overweight or obesity also ate more at the buffet meal ($m = 1468 \pm 305$) compared to healthy weight children ($m = 1144 \pm 307$ kcals) ($t(63) = -4.2, p < 0.001$).

No differences by weight status were observed for EAH ($t(49) = -1.6, p = 0.12$). Regardless of weight status, children ate significantly more at the palatable buffet meal ($m = 1298 \pm 347$ kcals) than the baseline meal ($m = 654 \pm 215$ kcals) ($t(65) = -19.9, p < 0.001$).

4.4.2 Go/Nogo results at baseline

Children who were overweight/obese ($m = 0.74 \pm 0.01$) were more biased towards go trials than those who were healthy weight ($m = 0.07 \pm 0.02$) ($t(63) = -2.1, p = 0.04$). In other words, children with obesity were more inclined to respond to go trials than children without obesity. There were no differences between child weight status and performance on the baseline inhibitory control Go/Nogo task for caution, nondecision time, drift rate, false alarm, omission error or total number of errors made.
4.4.3 Main effect of reward on performance of the Go/Nogo

Reward condition collapsed across all trials revealed a main effect of false alarm ($F(1.7, 107.9) = 6.6, p = 0.002, d = 0.6$), omission error ($F(2, 128) = 5.4, p = 0.006, d = 0.6$), and total number of errors made ($F(1.7, 110.5) = 9.4, p < 0.001, d = 0.8$) (see Figure 4.4). There were no main effects of reward type for caution, motor execution time, drift rate, or bias ($p$’s > 0.05). Post-hoc tests conducted using the Bonferroni approach showed that children made more false alarm errors (i.e., incorrect responses) for food compared to neutral ($m_{\text{diff}} = 0.13, p = 0.002$) and money compared to neutral ($m_{\text{diff}} = 0.13, p = 0.04$) blocks but no differences were observed between food and money blocks ($m_{\text{diff}} = 0.005, p = 1.0$). Children made more omission errors (i.e., forgot to respond) for money compared to no reward blocks ($m_{\text{diff}} = 0.14, p = 0.005$) but no differences were found between food and money ($m_{\text{diff}} = -0.06, p = 0.3$) or food compared to no reward ($m_{\text{diff}} = 0.08, p = 0.25$) blocks. Children made more total errors for food compared to no reward blocks ($m_{\text{diff}} = 0.13, p = 0.008$) and money compared to no reward ($m_{\text{diff}} = 0.17, p = 0.002$) but there were no differences in total errors made blocks comparing food to money ($m_{\text{diff}} = -0.04, p = 0.8$).
Figure 4.4 Results of the repeated measures ANOVA for the reward version of the Go/Nogo. There was a main effect of reward for the total number of false alarms ($p = 0.002$), omission errors ($p = 0.006$), and the total number of errors made throughout the task ($p < 0.001$). (A) Mean false alarm rates for each condition type. (B) Mean false alarm rates for each condition type. (C) Mean false alarm rates for each condition type. Data were log transformed. * $p < 0.05$. 

[Graphs showing false alarm, omission errors, and total errors for different conditions with statistical significance marked.]

* $p < 0.05$.
4.4.4 Weight effects of the rewarded Go/Nogo

Caution

There was a main effect of child weight status on the level of caution used during the rewarded Go/Nogo task \((F(1, 195) = 4.6, p = 0.03)\). Post hoc tests conducted with the Bonferroni approach showed that regardless of whether the reward was food or money, children who were overweight/obese responded less cautiously (i.e., favored accuracy over speed) (mean = -0.96, SE = 0.006) than healthy weight children (mean = -0.94, SE = 0.006). There were no interactions between weight status and reward condition for caution. There was a main effect of sex for caution on the Go/Nogo \((F(1, 195) = 4.3, p = 0.04)\). Males were more cautious (mean = -0.94, SE = 0.006) than females (mean = -0.96, SE = 0.006). There were no interactions between sex and reward condition.

Omission errors

There was a main effect of age on rate of omission error \((F(4, 195) = 4.7, p = 0.001)\) during the rewarded Go/Nogo task. Seven-year-olds made more omission errors than 9-year-olds \((m_{\text{diff}} = 0.29, p = 0.004)\), 10-year-olds \((m_{\text{diff}} = 0.27, p = 0.01)\), and 11-year-olds \((m_{\text{diff}} = 0.32, p = 0.003)\). However, there were no differences in omission error rate between 7- and 8-year olds \((p = 0.3)\). There were no interactions with age and omission error rate.
There was a main effect of weight status ($F(1,195) = 11.9, p = 0.001$) (see Figure 4.5) and age ($F(4,65) = 5.7, p < 0.001$) on the total number of errors made on the rewarded Go/Nogo task. Heavier children made more total task errors (mean = 1.06, SE = 0.03) than healthy weight children (mean = 0.91, SE = 0.03, $p = 0.001$). Seven-year-old children made more errors than 9-, 10- and 11-year-old children, respectively ($m_{\text{diff}} = 0.27, p = 0.001; m_{\text{diff}} = 0.27, p = 0.001, m_{\text{diff}} = 0.26, p = 0.003$). There were no differences between 7-year-olds and 8-or 10-year-olds, respectively ($m_{\text{diff}} = 0.15, p = 0.17, p = 0.1$). There were no interactions with total error rate and weight or age.
Figure 4.5 Results of a mixed model ANOVA for the reward Go/Nogo. There was a main effect of weight on the total number of errors made ($p = 0.001$). Mean number of total errors made on the reward version of the Go/Nogo task. Children with overweight/obesity made more total errors than healthy weight children. OW = overweight/obese; HW = healthy weight; Data were log transformed. ** $p < 0.001$. 
4.4.5 Food intake and performance on the Go/Nogo

*Baseline meal*

Child BMI \( z \)-score predicted 12\% of the variance in intake at the baseline meal (\( R^2 = 0.12, F(1,63) = 9.0, p = 0.004 \)). No other covariates of interest or measures on the baseline or reward Go/Nogo predicted food intake.

*Buffet meal*

A model that included BMI \( z \)-score and age predicted 21\% of the total variance in intake at the buffet meal (\( R^2 = 0.21, F(2,62) = 8.5, p = 0.001 \)). Both BMI \( z \)-score (\( \beta = 0.34, p = 0.004 \)) and age (\( \beta = 0.29, p = 0.01 \)) were positive influences on this mode. No other covariates of interest or measures on the baseline or reward Go/Nogo predicted food intake at the palatable buffet meal.

*Eating in the absence of hunger*

Pre-meal fullness predicted 9\% of the total variance in intake (\( R^2 = 0.09, F(1,44) = 4.5, p = 0.04 \)). No other covariates of interest or measures on the baseline or reward Go/Nogo predicted food intake.
4.5 Discussion

The current findings demonstrate support for the Reflective-Impulsive Dual-Processes Model that suggests that rewarding stimuli may interfere with inhibitory control abilities. Regardless of weight status, children made more errors during rewarded blocks compared to non-rewarded blocks, suggesting that reward incentives may interfere with the ability to successfully stop motor execution behavior. In addition, these effects were exacerbated by weight status. In comparison to healthy weight children, children who are overweight/obese showed greater deficits in reactive inhibitory control, as evidenced by increased error rates, when a reward incentive was present. However, there were no differences between weight status groups and performance on the baseline assessment of inhibitory control. Moreover, regardless of condition, inhibitory control performance did not predict laboratory measures of food intake at a baseline meal, a palatable buffet, or during EAH. The overall pattern of results demonstrates that child weight status is independently associated with both laboratory food intake and inhibitory control, and deficits in inhibitory control do not mediate the relationship between laboratory overeating and weight status.

In the present study, we found evidence that the processes that affect decision-making differed by weight status. Specifically, results from the drift-diffusion model revealed that at the baseline assessment, children who were classified as overweight/obese were more biased towards go trials than their healthy weight counterparts. However, there were no observed differences between groups in regards to overall task accuracy, suggesting that weight status was not associated with baseline inhibitory control performance at baseline. This finding is contrary to the literature showing that in comparison to healthy weight
children and those who were classified as overweight, obese children make more errors on this task (19, 59). In our study, weight groups were dichotomized, and the heavier weight group consisted of both overweight and obese children. This current study was not designed to assess inhibitory control performance across three weight groups, and therefore, may have been underpowered to detect differences driven by the extremes.

Furthermore, the Reflective-Impulsive Dual-Process Model proposes that behavioral outcomes are achieved based on a competition between reward and inhibitory control processes. Thus, it has been theorized that rewarding properties of food may interfere with the ability to inhibit temptations to overindulge (60–62). To test this, we had children complete a second Go/Nogo task that included reward incentives, in which before the start of each block, children were told that they could earn some of their favorite snack or extra money based on how well they performed on each respective block of the task. Overall, regardless of weight status, children made more errors for blocks that included reward incentives compared to no rewards. In addition, there were no differences between the numbers of errors made for food or money blocks. This finding supports the Reflective-Impulsive Dual-Process Model by suggesting that the presence of a reward, in general, interferes with inhibitory control performance. Additionally, children with overweight or obesity responded less cautiously (i.e., they favored speed over accuracy), and they made more total errors on the reward version of the Go/Nogo than healthy weight children. This suggests that in the presence of a reward, regardless of whether it is food or money, the ability to successfully stop behavior may be impaired in children with obesity.

Contrary to our hypothesis, inhibitory control performance was not related to objective measures of overeating. Because studies have found that obesity was related to
inhibitory control performance (19, 59), it was commonly assumed that this relationship would explain why some children have difficulties controlling the ability to resist tempting food and/or overeating. However, no studies have tested how inhibitory control relates to actual eating behavior, particularly in children. Here we showed that weight status was related separately to how much children ate and overall inhibitory control performance in the presence of a reward. This suggests that although weight status correlates with difficulties in stopping behavior in the presence of a reward, this deficit did not correlate with laboratory measures of overeating, at least not of the test-foods used in the current study. On the other hand, the Go/Nogo task measures reactive inhibitory control, which is a fast and automatic, impulsive process. Therefore, it may be that deficits in proactive inhibitory control, which is a slow, controlled, and planned process, may offer additional insight into food intake behavior.

Strengths and limitations

This was the first study to assess inhibitory control performance in the presence of rewarding stimuli and relate this performance to not only weight status, but also objective measures of food consumption in children. To date, no studies have assessed how inhibitory control relates to actual food intake behavior, so this study filled a critical gap in the literature. However, there were some limitations. The sample size was relatively small compared to other studies that have assessed inhibitory control in children (18, 19). Therefore, we may have been underpowered to detect differences between weight groups and interactions for decision-making processes that contribute to behavior (e.g., motor execution time, bias). Although we observed medium effect sizes, our study did not actively
recruit an equal number of overweight and obese children, which did not allow us to conduct comparisons across the three weight groups. Another limitation is that we did not ask children to rate whether they preferred to receive food or monetary rewards. Therefore, we do not know if children were more affected by one reward or another. However, results showed that inhibitory control performance did not differ based on the reward contingency, which suggests that in general, rewards interfere with performance.

4.6 Conclusion

In conclusion, this was the first study to assess how reward sensitivity and inhibitory control relate to food intake and body weight in children. For the first time, we showed that inhibitory control performance was affected by the presence of rewarding stimuli, and overweight children exhibited increased deficits on this task that were independent of reward type. However, inhibitory control performance did not relate to overeating in the laboratory. Therefore, our results suggest that inhibitory control may relate to weight status, but these relationships did not extend to overconsumption in short-term, laboratory feeding protocols. The present study provides critical insight about how rewards interfere with inhibitory control in a pediatric sample varied by weight status. The results highlight potential components of the inhibitory control process that may be targeted by interventions to moderate excess weight gain during youth.
4.7 References


36. Criaud M, Boulinguez P. Have we been asking the right questions when assessing


Discussion

Figure 5.1 A conceptual model of the summary of the main findings for how reward and inhibitory control relate to food intake. We found negative associations between the brain response to winning food compared to money in the posterior cingulate and appetitive traits, such as food responsiveness and emotional overeating, and this was independent of the child’s body mass index (BMI). Appetitive traits were positively associated with both overconsumption and increased weight status. Independent of child weight status, the brain response to winning food compared to monetary rewards in the amygdala and medial prefrontal cortex was positively correlated with overconsumption. We propose that this occurs via an increased response to reward. Overconsumption had a positive influence on BMI and was increased in children with obesity. The brain response to winning food compared to monetary rewards in the dorsolateral prefrontal cortex positively associated with overconsumption. Reactive inhibitory control response on a behavioral task was negatively associated with child BMI but only in the presence of rewarding stimuli.
The goal of this dissertation was to begin to elucidate some of the neural and behavioral mechanisms that contribute to overeating in children 7-11-years-old. This was the first study to evaluate how the brain responds to food and money rewards using the same experimental paradigm. In addition, this was also the first study to relate how the brain responds to food and money rewards to objectively measured food intake across different facets of eating behavior. Collectively, the three papers presented in this dissertation highlighted several risk factors for obesity development that may be driven by brain response to food rewards in key decision-making regions such as reward and inhibitory control. Deficits in decision-making have been associated with increased body weight in adults and children (1–7), suggesting one reason for overeating. However, no previous studies have evaluated how differences in decision-making relate to objectively measured food intake in children. For the first time, we showed that brain response in regions associated with emotion and reward processing to food compared to money rewards was associated with appetitive traits and objectively measured overeating. These findings were independent of how much the child weighed. This dissertation also provided evidence to suggest that brain response to winning food compared to money in an inhibitory control region may also play a role in overeating. Behaviorally, inhibitory control performance was affected by the presence of rewards and this was associated with increased weight status. Decreased performance on the reactive inhibitory control task did not relate to overeating. Since weight status was correlated with performance, reactive inhibitory control may relate to overeating, but not under controlled laboratory settings. Therefore, more studies are needed to better understand how reactive inhibitory control relates to overeating. Together, findings from papers one and two provide insight into how neurological correlates of decision-making predict different facets of eating behavior in children. Results from paper three shed light on behavioral decision-making impairments and the relationship to weight status in children. Understanding how
basic decision-making circuitry relates to food intake and weight status may provide insight for current obesity prevention and intervention programs.

Based on the findings from all three dissertation papers, we propose a conceptual model to summarize the relationship between the brain response to rewards and obesity (see Figure 5.1). This dissertation highlights the role of the brain in maladaptive food intake behavior, which may lead to obesity development in children. Paper one found that independent of weight status, decreased BOLD response in the posterior cingulate to winning foods compared to money correlated with a greater parental report of their child’s susceptibility to emotional overeating and food responsiveness. In our study, these appetitive traits also positively related to weight status. In addition, emotional overeating was related to greater intake at the baseline and palatable buffet meal, whereas food responsiveness related to how much children ate at the buffet meal (see Supplemental Material Table S.5.5.1). It is important to note that food responsiveness and emotional overeating are stable traits associated with childhood obesity (8–12). Therefore, hyposensitivity in the posterior cingulate to food vs. money may predict overeating and future weight gain but this should be tested with a longitudinal study. Therefore, brain response to winning food compared to money in a region associated with emotional regulation may identify children who may not currently be obese but exhibit appetitive traits and eating behaviors that may predict future weight gain. These findings have implications for identifying targets for future interventions aimed at the prevention of weight gain.

The proposed conceptual model also highlights the role of the brain response in regions associated with reward processing and inhibitory control in relation to overeating, and over time, the development of obesity. Results from paper two suggested that laboratory measures of overeating were positively associated with child brain response to food relative to money rewards, independent
of how much a child weighs. It is important to note that child weight status was also correlated with overeating. However, hypersensitivity to anticipating and receiving food compared to money in brain regions associated with reward processing and motivation also positively associated with how much children ate at both the baseline and palatable buffet meal. This suggests that how the brain responds in motivational regions may play a role in determining how much children eat at a meal. On the other hand, hypersensitivity to food compared to money rewards in the dorsolateral prefrontal cortex (dlPFC), a brain region implicated in inhibitory control, positively correlated to objective measures of overeating at the palatable buffet meal and during eating in the absence of hunger (EAH), but not at the baseline meal. Notably, the brain response to winning food compared to money in the dlPFC correlated with overeating completely independent of child weight status. Moreover, children who overate during the EAH protocol also ate more at the palatable buffet and baseline meal (see Supplemental Material Table S.5.5.2). This highlights the potential role of inhibitory control response as a risk factor for overeating at a meal and during intake of palatable snacks when not hungry in children who are not yet obese. Furthermore, these findings suggest that although body weight is related to food intake, the brain response to rewards independently predicts how much food children eat. Along with paper one, this highlights the importance of brain response to food rewards in predicting risk factors for developing obesity (see Supplemental Material Table S.5.5.3 for a summary of brain regions and possible interpretations).

The Reflective-Impulsive Dual-Processes Model proposes that sensitivity to rewards may interfere with inhibitory control (13). This model implies that overeating occurs when inhibitory control mechanisms are weak and cannot act to stop consumption of a tempting (food) reward. Although results from paper two suggest that both inhibitory control and reward sensitivity are important components to overeating, fMRI results do not provide insight into the directionality of these findings. Results from paper three, which tested reactive inhibitory control showed that
inhibitory control performance was impaired in the presence of rewarding stimuli in children with obesity but this did not relate to objective measures of overeating. Results of paper three may appear to contradict results from paper two which showed that activation in the dLPCF, an inhibitory control region, was positively associated with objectively measured overeating. However, it is important to highlight that reactive inhibitory control measures the ability to stop a response. Reactive inhibitory control is associated with activation in the inferior frontal gyrus (IFG) and not specifically the dLPCF (14). The dLPCF is associated with top-down cognitive control, which stops behavior based on information and values in order to adhere to task-appropriate behaviors (15). Therefore, inhibiting excess food intake may reflect a more complicated cognitive control process, which could explain differences between results from these two papers.

The finding that reactive inhibitory control performance in the presence of reward stimuli was related to weight status supports the theory guiding the Reflective-Impulsive Dual Processes Model. However, we did not find that inhibitory control performance was related to laboratory measures of overeating. In support of the Reflective-Impulsive Dual Processes Model, results of paper two suggest that brain response in inhibitory control regions may be important for understanding overeating. Therefore, the proposed model suggests that brain response in inhibitory control regions might have been affected by the presence of rewarding stimuli but this was not directly tested. Based on the results from paper two and three, the proposed conceptual model of overeating proposes that inhibitory control may be an important risk factor for obesity development but this needs to be further explored. Future studies should continue to investigate the relationship between reward and inhibitory control processes and overeating.

Taken together, the proposed conceptual model of overeating represents a simplistic model of some of the factors that contribute to excess food consumption. Most importantly, results from
this dissertation provide evidence for individual differences in susceptibility for overeating and weight gain. Here, we showed that a child’s current weight status might not be the only predictor for overconsumption as the brain response to reward independently predicted laboratory measures of overeating. Moreover, child weight status did not correlate with overconsumption during EAH. However, brain response in the dIPFC for winning food compared to money predicted excess calorie intake when children were not hungry and was the best predictor of overconsumption at the highly palatable buffet meal. These two findings highlight the importance of the brain’s role in food intake in order to identify children who are more susceptible for overeating when highly palatable foods are available. In addition, overeating at a highly palatable buffet meal was associated with both reward and inhibitory control response, while intake during EAH was only associated with brain response in an inhibitory control region. This suggests that the mechanisms that contribute to each of these facets of eating behavior are different. Therefore, results from this dissertation stress that it is inappropriate to assume that a one size fits all treatment approach for obesity prevention and intervention would be successful for everyone. Collectively, the findings in this dissertation exemplify the importance of investigating the individual differences in brain response to food rewards to understand the complex drivers of overeating and weight gain in children.

This dissertation marks a first step toward understanding the mechanisms that contribute to overeating. This was the first study to evaluate the neural mechanisms related to overeating in children. Although the reasons for overeating are multifactorial, we showed that independent of how much a child weighs, the brain response to rewards may play an important role in predicting risk factors that may contribute to overeating and obesity risk in children 7-11-years-old. Hyposensitivity to winning food rewards in a region associated with emotion was positively associated with food approach behaviors, independent of child weight status. Similarly, although weight status was related to objective measures of overeating, how the brain responded to
anticipating and receiving food compared to money was also associated with overeating, regardless of how much a child weighed. This suggests that the brain response to rewards may play a crucial role in maladaptive eating behavior. In summary, findings from these papers may identify potential risk factors for developing obesity, which may have substantial impacts on prevention and intervention programs.

5.1 Implications

This dissertation helped to identify neurophenotypes that may be associated with obesogenic behaviors, which may be targets for interventions. For example, the neural pathways associated with emotional overeating are distinct from those associated with hypersensitivity to reward. Thus, some intervention programs may develop strategies focused on decreasing the rewarding value of food, while others may incorporate emotion regulation techniques. Additionally, this dissertation showed that neural responses to reward are distinct for different facets of ingestive behavior (e.g., overeating at a meal versus eating when not hungry). This finding further highlights the complex relationship between decision-making and overeating. Since the neural mechanisms associated with overeating differ for each facet of eating behavior, it is inappropriate to assume that a standard approach to obesity prevention and intervention would be successful for all individuals. Overall, findings from this dissertation provide more concrete information about how key decision-making components relate to food intake and weight status during a critical period in development. Thus, intervention and prevention programs may use this information to incorporate better decision-making strategies to reduce childhood obesity.
In addition, findings from this dissertation support fMRI as a tool that can be used for identifying neural mechanisms that may contribute to maladaptive eating behaviors. However, fMRI can also be used to validate if neural responses can be altered based on obesity intervention methods and if these changes in the brain coincide with long-lasting behavioral outcomes. Currently, the success rates of obesity prevention and intervention remain low (16–18), suggesting that existing efforts might not be considering the different aspects of decision-making that contribute to overeating. Most prevention and intervention methods have been created based on data gathered from behavioral tasks and questionnaires. Although studies that use these assessment tools are useful, they provide little insight into how decision-making contributes to the behavioral outcomes. Without understanding how the decision-making process maps onto appetite traits or behaviors, it is difficult to design intervention programs aimed at strengthening specific cognitive functions. Therefore, it is imperative to understand the neural mechanisms guiding behavior.

5.2 Strengths and limitations

5.2.1 Strengths

Overall, there are several strengths to the work of this dissertation. First, the same cohort of children was used for papers one through three, which gives insight into the brain response to rewards, food intake, weight status, and measures of inhibitory control in the same population. It is rare that studies include all of these measures within the same cohort of children. Second, the overall study had high retention rates and the sample size for an fMRI study was substantial. Third, the dissertation had high fMRI scan success rates and a low dropout rate. Therefore, this dissertation
demonstrated the feasibility of conducting a study with fMRI in children 7-11-year-old. Finally, we also controlled for several covariates of interest that might have affected our data, such as parental income and education level, obesity risk, pubertal status, the child’s reported level of fullness, sex, age, and the time of day that the study was conducted. None of these covariates of interest had an affect on the data.

5.2.2 Limitations

Although the dissertation work had several strengths, it also posed some weaknesses. First, the fMRI task did not assess inhibitory control, which makes our interpretations of the relationship between the dLFC and overeating limited. Second, this study did not include extensive measures aimed at assessing eating disorders in children. Binge eating was assessed by parental report, while loss of control eating was assessed via an interview style questionnaire. However, loss of control was measured by a single question (dichotomous response). No measures were collected in regards to potentially harmful eating behaviors (e.g., bingeing and purging). Therefore, it is unknown if children in this study exhibited disordered eating tendencies. Third, no measures were included to assess usual food intake (outside the laboratory) or any other measures that might counteract obesity such as exercise. Future studies should aim to incorporate these measures into the study protocol. Fourth, although we assessed parental income, we did not measure food insecurity or if children were a part of the school lunch program. This information would have provided additional insight into whether children were overeating due to a lack of availability of food at home. Finally, this study was cross-sectional and does not provide insight into whether these findings correlate with weight gain and excess consumption outside the laboratory. Therefore, future studies should aim to develop longitudinal studies within a pediatric population.
5.2.3 Neuroimaging methods: defining regions of interest

Regions of interests (ROIs) can be defined via various methods. Meta-analyses can be used to determine commonly reported $xyz$ coordinates for each region and is termed a coordinate-based ROI approach. This method is not subject to multiple comparison corrections. However, ROIs can be defined functionally within anatomical boundaries, by using an anatomical mask. The latter approach provides a study-specific location of peak activation within a region, which may more accurately delineate task-specific BOLD activation in a particular sample. In this approach, multiple comparison testing is conducted within the masked region to determine the number of voxels (i.e., size of the activation cluster) needed in order to pass threshold correction testing. This method of correction is called small volume correction and, restricts correction to a particular region (i.e., masked ROI) instead of correcting on the entire brain. When there are a priori hypotheses about particular ROIs, small volume correction may be appropriate, especially when evaluating BOLD response in small anatomical regions such as the amygdala.

The results from chapter two were initially analyzed using a coordinate-based and functionally defined ROI approaches. Small volume correction was applied to the functionally defined ROIs for reward anticipation. However, there was ample push back from reviewers who suggested that because this paradigm was novel, a whole-brain approach would have been more appropriate. Therefore, we reanalyzed the results for both reward anticipation and outcome with a whole-brain approach. Once corrected for multiple comparisons testing, activation in reward-processing regions did not survive correction testing for reward anticipation (see section 5.2.3 for an additional explanation). The reviewers had suggested reporting results that were uncorrected. However, given the recent discussions in the fMRI community in regards to threshold correction (see section 5.2.2), we decided to forgo reporting uncorrected results.
5.2.4 Changes in the field of neuroimaging methods

In 2016, a research article published by Eklund and colleagues (19) tested the ability of three software packages (e.g. AFNI, FSL, SPM) to correctly control for family-wise error (FWE) rates. FWE is the probability of making one or more false positive discoveries. The results of the research concluded that across all of the three major fMRI software packages, family-wise Type I errors were inflated. This revelation also brought forefront a 15-year-old error in AFNI’s 3dClustSim program, which is used for cluster correction. Specifically, 3dClustSim largely underestimated the smoothness estimates needed for cluster correction, which in turn, underestimated the size of the cluster needed to survive threshold correction. In addition, AFNI, amongst other software packages, used Gaussian random-field theory to correct for FWE to determine cluster sizes. This theory assumes that the 1) smoothness of the fMRI signal is constant throughout the entire brain and 2) spatial autocorrelation shape is known (20). However, results from Eklund and colleagues suggested a Gaussian shape was not appropriate for estimating smoothness, and thus, this method further exacerbated false positive rates. In response to Eklund and colleagues, AFNI fixed the bug in 3dClustSim. In addition, smoothness estimates are now fit to a mixed function (exponential and Gaussian shape), which greatly reduced the number of false positives (21).

5.2.5 Changes in the field of neuroimaging methods: impacts on the findings from chapter 2

The change in fMRI cluster correction occurred during preparation of this dissertation. Therefore, the results of Chapter 2 were reanalyzed using the most current fMRI methods and used the updated 3dClustSim as outlined in Cox 2017 (21). When implementing these new methods on
our data, it was revealed that a cluster at least 68 voxels in size was needed in order to survive threshold correction. Since our voxels were 3mm x 3mm x 3mm, this converted to a cluster size that was 1.84 cm$^3$, which is larger than some of the regions associated with reward processing, such as the amygdala. For example, the average size of the amygdala in children (mean age = 11.6) is between 1.04 ± 2.10 cm$^3$ (22). In Chapter 2, we did not find significant clusters of activation in reward processing regions, which is not surprising given the above cluster calculations. Therefore, small volume correction within our ROIs would have been an appropriate method to analyze the brain response to reward anticipation. However, for aforementioned reasons, these analyzes were not published.

5.3 Future Directions

This dissertation work provided knowledge into some of the mechanisms driving overeating in children. However, much more work is needed. Although a few future directions were discussed in the preceding paragraphs, other areas of interest are described below:

5.3.1 Assessing if there is a critical window for obesity development

Evidence from food-cue reactivity (i.e., passive viewing tasks) shows a positive relationship between BOLD response to food images and weight status (23–25). However, active tasks that assess anticipatory and consummatory responses to rewards and the relationship to weight status exhibit mixed results (26–31). Findings in adults show that anticipatory and consummatory
responses to food positively correlated with weight status (29–31). Yet, a positive relationship between BOLD response to anticipating food rewards and weight status is only observed in obese adolescents (26). In children with obesity and youth at risk for developing obesity, a greater BOLD response in reward-related regions was correlated with reward receipt, but not anticipation (32). Contrary to the literature, our study did not observe differences between weight statuses for anticipating and receiving rewards. This suggests that a critical window may exist for in which development may directly affect BOLD response. Therefore, longitudinal studies are necessary to determine if changes in functional brain responses coincide with physical structural changes.

5.3.2 Network communication and overeating

Previous studies have shown that children with obesity showed altered connections between reward and inhibitory control regions at rest and during passive viewing tasks when compared to healthy weight counterparts (25). This suggests that connectivity between brain regions may relate to overeating, though this has not been tested. Findings from this dissertation demonstrated that the brain response to winning food rewards positively correlated with overeating independent of child weight status. However, we did not evaluate how these regions communicate with each other. Studies of this nature will provide insight into how differences in network communication at rest versus under cognitive demands are associated with food intake. Findings may be useful for intervention programs by providing insight into how changes in connectivity may be affected by food stimuli.
5.4 Conclusions

The predominant factor contributing to obesity is overeating highly palatable high-energy-dense foods. Yet, little is known about the mechanisms that drive overeating, which subsequently leads to obesity development. In this dissertation, we identified several potential neural mechanisms that were associated with risk factors for obesity development. How the brain responded to anticipating and receiving rewards was not related to child weight status. However, brain response to food vs. money in regions associated with emotion, reward, and inhibitory control correlated with different aspects of maladaptive eating behavior. Brain response to reward in regions associated with emotion, reward processing, and inhibitory control was related to appetitive traits and objectively measured overeating. This suggests that the brain response to rewards may play a crucial role in food intake and subsequent weight gain. Additionally, we also found that the impairment of reactive inhibitory control in the presence of rewarding stimuli was related to child weight status, but not overeating. Although reactive inhibitory control was not related to overeating in a controlled environmental setting, weight status differences suggest that inhibitory control may still be an important component of food intake regulation. However, this dissertation highlights some of the neural correlates associated with eating behavior and it provides evidence that fMRI can potentially be used to predict individual variations in child eating behavior. The extreme variation of behaviors that contribute to overeating suggests that individualized treatment focused on strengthening specific decision-making processes may be more appropriate for the success of interventions. Taken together, this dissertation provides the groundwork for understanding mechanisms contributing to eating behavior in children.
5.5 Supplementary Material

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<table>
<thead>
<tr>
<th></th>
<th>Emotional Overeating</th>
<th>Food Responsiveness</th>
</tr>
</thead>
<tbody>
<tr>
<td>Emotional Overeating</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Food Responsiveness</td>
<td></td>
<td>1</td>
</tr>
<tr>
<td>Baseline Meal</td>
<td>0.30*</td>
<td>0.14</td>
</tr>
<tr>
<td>EAH**</td>
<td>0.09</td>
<td>0.30*</td>
</tr>
<tr>
<td>Palatable Buffet Meal</td>
<td>0.28*</td>
<td>0.30*</td>
</tr>
</tbody>
</table>

**Table S.5.5.1.** Pearson’s correlations between subscales of the Child’s Eating Behaviour Questionnaire (CEBQ) and meal intake across the three conditions. EAH = eating in the absence of hunger; * \(p < 0.05\); ** \(n = 46\).

---

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>Palatable Buffet Meal</th>
<th>EAH</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline Meal</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Palatable Buffet Meal</td>
<td>0.65**</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>EAH</td>
<td>0.39*</td>
<td>0.45*</td>
<td>1</td>
</tr>
</tbody>
</table>

**Table S.5.5.2.** Pearson’s correlations between intake at each of the meal conditions. Children who ate more during eating in the absence of hunger (EAH) ate more at the baseline and palatable buffet meal. Data shown is for 46 children. * \(p < 0.05\); ** \(p < 0.001\).
<table>
<thead>
<tr>
<th>Brain region</th>
<th>Literature findings</th>
<th>Study finding(s)</th>
<th>Possible interpretation(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Amygdala</strong></td>
<td>Involved in evaluation food reward intensity, regardless of valence (33)</td>
<td>✸ response to winning food vs. money correlated with ✸ intake of highly palatable foods, regardless of child WS</td>
<td>Increased valuation of food rewards in the amygdala may be associated with overeating and subsequent future weight gain</td>
</tr>
<tr>
<td></td>
<td>✸ response to receiving sucrose in children with obesity (32)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>✸ response to milkshake when not hungry is associated with weight gain in adults (29)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>dlPFC</strong></td>
<td>✸ response to food cues vs. nonfood cues in children with obesity (34)</td>
<td>✸ response to winning food vs. money correlated with ✸ intake of highly palatable foods and eating in the absence of hunger, regardless of child WS</td>
<td>Regions involved in self-control, such as the dlPFC, may play a role in overeating and eating when not hungry, which may lead to future weight gain</td>
</tr>
<tr>
<td></td>
<td>✸ response correlated with ✸ self-control efforts in adults (35)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>IFG</strong></td>
<td>✸ response in children to large vs. small potions of food, regardless of energy density (36)</td>
<td>✸ response to winning money vs. food, regardless of child WS</td>
<td>The IFG is involved in how the brain responds to winning food cues, and to large portions of food.</td>
</tr>
<tr>
<td></td>
<td>✸ response to food vs. nonfood logos in children with obesity (37)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>LN</strong></td>
<td></td>
<td>✸ response to winning money vs. food, regardless of child WS</td>
<td>The lentiform nucleus is involved in how the brain responds to winning food.</td>
</tr>
<tr>
<td><strong>MFG</strong></td>
<td>✸ response to food cues vs. nonfood cues in children with obesity (37)</td>
<td>✸ response to winning money vs. food, regardless of child WS</td>
<td>The MFG may play a role in how the brain responds to food cues.</td>
</tr>
</tbody>
</table>
† resting state connectivity in children with obesity between the MFG and mPFC and the lateral OFC (38)

<table>
<thead>
<tr>
<th><strong>mPFC</strong></th>
<th>† response to food images in a pre-meal state (39)</th>
<th>† response to anticipating food vs. money correlated with † intake at a baseline and highly palatable buffet meal, regardless of child WS</th>
<th>The mPFC may play a role in general food intake.</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Modulation of reward-seeking behavior (40)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>OFC</strong></th>
<th>† response to food vs. nonfood logos in children with obesity (37)</th>
<th>† response to winning food vs. money correlated with † intake at a baseline meal, regardless of child WS</th>
<th>The OFC may play a role in overeating, regardless of child weight status</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Involved in motivation and goal directed behavior (41) and monitoring outcomes even in nonrewarding contexts (42)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>PCG</strong></th>
<th>Involved in emotion processing (43)</th>
<th>† response to winning food vs. money was correlated with higher prevalence of appetitive traits, such as food responsiveness and emotional overeating, regardless of child WS</th>
<th>The PCG may be important for mediating the relationship between appetitive traits and food intake in children, regardless of weight status</th>
</tr>
</thead>
</table>

**Table S.5.5.3.** Summary of brain regions that were found to associated with the brain response to food in this dissertation and the literature. Suggested interpretations of function are listed. dlPFC = dorsolateral prefrontal cortex; IFG = inferior frontal gyrus; LN = lentiform nucleus; MFG = middle frontal gyrus; mPFC = medial prefrontal cortex; OFC = orbitofrontal cortex; PCC = posterior cingulate gyrus; WS = weight status.
5.6 References


APPENDIX A:

Telephone Screening Questionnaire

Study 1, 2, 3
DECISION-MAKING KIDS STUDY RECRUITMENT FORM

Parent’s Name: ________________________________________________

Phone: (home) __________________  (work/cell) ____________________

Address:______________________________________________________

Email: _______________________________________________________

Date Call Received: ____________  Date Call Returned: ___________

What is your relationship to the child? ______________________________

Child’s Sex: boy  girl

Child’s Name ____________________________  Age: _______ (if under 7 or above 11 they are not eligible)

Child’s DOB: __________  Height (in):_______  Weight (lb):_______

Height (cm):

Weight (kg):_______

Tanner Stage: __________  BMI zscore: _____  BMI %-ile: __________

Mother’s Height: ________  Weight:_______  BMI:_______

Father’s Height: ________  Weight:_______  BMI:_______

1. Is your child right-handed? YES  NO

2. Is your child on any prescription medications?  *YES  NO
   a. If yes, please specify what medications:

   b. How often does your child take this medication?

3. Does your child take any over the counter medications? If yes, what are they and how often does your child take these?

4. Does your child have any dietary restrictions? YES  NO
   a. If yes, please specify: (ineligible if vegetarian, vegan, or fasts for religious reasons)

5. Does your child have any food allergies?  *YES  NO
   a. If yes, please specify:
6. Does your child have any learning disabilities?  
   YES  NO

7. Does your child read at or above grade level?  
   YES  NO

8. Is English your child’s native language?  
   YES  NO

9. Does anyone in your child’s immediate family (parents, siblings) have a diagnosed psychiatric illness, such as depression, anxiety, and bipolar disorder?  
   YES  NO

10. Does your child have any medical problems?  
    a. If yes, please specify:  
    *YES  NO

11. Is your child red/green color blind?  
    YES  NO

12. Has your child ever had an MRI before?  
    YES  NO

13. Does your child have any metal in or on his or her body that cannot be removed (like a metal plate or pin, or dental work which may contain metal)?  
    a. If yes, please specify:  
    *YES  NO

14. Does your child have any medical devices that may contain metallic parts (like an insulin pump or pacemaker)?  
    a. If yes, please specify:  
    *YES  NO

15. Has your child ever had an injury to the eye involving a metallic object or fragment?  
    *YES  NO

16. Does your child have any body piercings?  
    a. If yes, would he or she be willing to remove them?  
    *YES  NO

17. Is your child comfortable in small spaces?  
    YES  *NO

18. For the fMRI visit, we will be providing a snack of apple juice and a granola bar to your child. Will your child eat these foods?  
    YES  *NO

19. We will be asking you and your child to answer questions pertaining to pubertal assessment. Would you and your child be willing to answer these questions?  
    YES  *NO
20. It is very important that you are able to participate in this study for four weeks in a row, at the scheduled time. Will you be able to do this?  

YES ☐  NO ☐

Subject is ineligible if any bolded responses are selected. For the starred responses, check with Shana to discuss eligibility. If any starred responses are selected, politely inform them you will get back to them shortly with information regarding eligibility.

**Eligibility:** YES ☐  NO ☐

May we keep your information to contact you for further studies? YES ☐  NO ☐

How did you hear about our study?

Could you please tell us your child’s favorite foods?

Could you please tell us a list of your child’s least favorite foods?

Do they like these foods (circle all that apply). This is not an exclusion criteria.

Macaroni and Cheese ☐  Tomatoes ☐
Pizza Rolls ☐  Garlic Bread ☐
Bagel bites ☐  Chicken fingers ☐
Broccoli ☐  Mozzarella sticks ☐

Comments:
"Puberty Assessment Questionnaire" to determine the child's Tanner Stage.

**TCS (PDS)**

**Introduction:** The next questions are about changes that may be happening to your child’s body. These changes normally happen to different young people at different ages. Please do your best to answer the questions carefully. If you do not understand a question or do not know the answer, just say “I don’t know.”

<table>
<thead>
<tr>
<th>Question</th>
<th>Response Options</th>
<th>Point Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Would you say that your child’s growth in height:</td>
<td>has not yet begun to spurt</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>has barely started</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>is definitely underway</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>seems completed</td>
<td>4</td>
</tr>
<tr>
<td></td>
<td>I don’t know</td>
<td></td>
</tr>
<tr>
<td>2. Would you say that your child’s body hair growth:</td>
<td>has not yet begun to grow</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>has barely started to grow</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>is definitely underway</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>seems completed</td>
<td>4</td>
</tr>
<tr>
<td></td>
<td>I don’t know</td>
<td></td>
</tr>
<tr>
<td>3. Have you noticed any skin changes, especially pimples?</td>
<td>skin has not yet started changing</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>skin has barely started changing</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>skin changes are definitely underway</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>skin changes seem complete</td>
<td>4</td>
</tr>
<tr>
<td></td>
<td>I don’t know</td>
<td></td>
</tr>
<tr>
<td><strong>FOR BOYS:</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4. Have you noticed a deepening of your voice?</td>
<td>voice has not yet started changing</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>voice has barely started changing</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>voice changes are definitely underway</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>voice changes seem complete</td>
<td>4</td>
</tr>
<tr>
<td></td>
<td>I don’t know</td>
<td></td>
</tr>
<tr>
<td>5. Have you begun to grow hair on your face?</td>
<td>facial hair has not yet started growing</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>facial hair has barely started growing</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>facial hair growth has definitely started</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>facial hair growth seems complete</td>
<td>4</td>
</tr>
<tr>
<td></td>
<td>I don’t know</td>
<td></td>
</tr>
</tbody>
</table>
FOR GIRLS:
6. Have you noticed that your breasts have begun to grow?
   - have not yet started growing 1
   - have barely started growing 2
   - breast growth is definitely underway 3
   - breast growth seems complete 4
   - I don’t know

7a. Have you begun to menstruate (started to have your period)?
   - Yes 4
   - No 1

7b. If yes, how old were you when you started to menstruate?
   age in years:______

7c. If yes, what was the first day of your last menstrual period? ____________________________

7d. If yes, how many days does your cycle usually last (i.e. how many days are typically between the start of one period to the start of your next period)? _________________

SCORING:

For Items 1 through 4 on the girls’ version and all items on the boys’ version, response options were: not yet started (1 point); barely started (2 points); definitely started (3 points); seems complete (4 points); I don’t know (missing). Yes on the menstruation item = 4 Points; no = 1 point. Point values are averaged for all items to give a Pubertal Development Scale (PDS). Puberty Category Scores are computed using the criteria of Peterson et al., (1988). Puberty Category Scores for boys used body hair growth, voice change, and facial hair growth as follows: Prepubertal = 3; early Pubertal = 4 or 5 (no 3-point responses); Midpubertal = 6,7, or 8 (no 4 points; Late pubertal = 9-11; Postpubertal = 12. For girls, Puberty Category 5 scores used body hair growth, breast development, and menstruation as follows: Prepubertal = 3; Early Puberty = 3 and no menarche; Midpubertal = 4 and no menarche; Late Puberty = 5 - 7 and menarche; Postpubertal = 8 and menarche.

Let the parents know that you will review the eligibility form with your supervisor and call them back shortly to let them know if they are eligible and set up an appointment.

First visit scheduled:  Date: _______________   Time: ______________

Remind Caller: A Parent or Legal Guardian **MUST** be at the first visit to sign consent forms.

Dates and Times of other visits:

Second Visit: ___________________
Third Visit: _____________________
Fourth Visit: ____________________
APPENDIX B:

Consent Form

Study 1, 2, 3
CONSENT FOR RESEARCH
The Pennsylvania State University

Title of Project: Understanding Decision-Making and Reward for Food Choice in Children

Principal Investigator: Shana Adise
Ph.D. Candidate
Department of Nutritional Sciences
110 Chandlee Laboratory
University Park, PA 16802
814-865-4404

Advisor: Kathleen Keller, Ph.D., Assistant Professor
Department of Nutritional Sciences and
Department of Food Sciences
(814) 863 – 2915

Other Investigators:
Charles Geier, Ph.D., Assistant Professor of Human Development and Family Studies
Nicole J. Roberts, MS

Print your name here: ____________________________. This form may contain words that you do not understand. Please ask the study personnel to explain any words or information you do not clearly understand.

We are asking you to be in a research study.

Whether or not you take part is up to you. You can choose not to take part. You can agree to take part and later change your mind. Your decision will not be held against you.

This form gives you information about the research. Please ask questions about anything that is unclear to you and take your time to make your choice.

Some of the people who are eligible to take part in this research study may not be able to give consent because they are less than 18 years of age (a minor). Instead we will ask their parent(s)/guardian(s) to give permission for their participation in the study, and we may ask them to agree (give assent) to take part. Throughout the consent form, “you” always refers to the person who takes part in the research study.

Please read every page carefully and initial the bottom of each page when you have had all of your questions answered to your satisfaction.

Participant Initials ________________
**Purpose of study:**

Our study asks how decision-making and reward influence eating behaviors. We want to know why some children are more likely to overeat than others. We are studying how children make decisions about food, particularly for foods that they find rewarding. We will try to understand how these factors relate with the types of foods your child likes and eats the most. This study will help us learn more about how children make food-based decisions, and this may help us teach children to eat more nutritious diets. We will also use magnetic resonance imaging to understand what areas of the brain are important for decision-making and rewarding value of food.

This study will use questionnaires, eating behavior tests and performance-based computer game tasks, as well as a brain imaging session. For the brain imaging, we use Magnetic Resonance Imaging (MRI). It is a tool that lets us look at your child’s brain activity. In the MRI scanner your child will complete a game.

The MRI scans will assist us in understanding the structure and function of different parts of the body. In this research study, MRI scans of your child will be taken. There are two types of scans that may be done. Anatomy scans are used to image the structure of the body. Scans of function are used to image areas of activity when your child is resting or performing different tasks. In this study, we will only be scanning the brain. NONE of the scans done during this study are designed to detect or evaluate any medical condition your child may have. They are intended solely for research purposes.

Approximately 40 children and their parents will take part in this research study at The Pennsylvania State University.

**Procedures to be followed:**

Visits 1-4: You and your child will attend four visits at Chandlee Laboratory. We ask that your child fast for at least three hours prior to your arrival for each visit. Visits 1-3 will take place in the Children’s Eating Behavior Laboratory and the Decision-Making Laboratory, both in Chandlee. The fourth visit will be conducted at the Penn State’s Imaging Center in Chandlee Laboratory.

You will fill out various computer-based questionnaires that relate to your child’s eating habits, methods used for food preparation, and household characteristics. You will also fill out a survey about how much your child eats of different foods and beverages. In addition, you and your child will be shown line drawings of same-sex genitalia and asked to circle the one that looks most like them and will also be asked about the development of secondary sex characteristics such as breast development and pubic hair. This is being done to assess your child’s pubertal development.

On the first visit only, you will complete the consent form, and both you and your child will complete some computer-based questionnaires. We will also take height and weight measurements for you and your child. Your child will also play video-game-like computer tasks.

On visits two and three, your child will eat a meal of common foods that we make in our kitchen. The meal will last for 30 minutes and your child can eat as much or as little as they want. We would like to video record your
child as they participate in this activity. In addition, your child will also answer computer-based questionnaires and play video-game-like tasks to assess decision-making.

On the fourth visit, we will ask your child to fast for at least three hours prior to your arrival. This visit will take place at the Penn State’s Imaging Center in Chandlee Laboratory. In order to help your child better understand the MRI, we will tell them that they will be helping us explore “Nittany Lion Inner Space”. Inner space is the space inside of your child’s head. Inner space scientists use a special machine – a scanner- to take pictures of the brain’s inner space. We will provide a snack for your child to eat.

The MRI facility at Penn State has a mock scanner, which is like the real MRI Scanner, only without the magnet. Before going into the MRI room, we will ask your child to lie in the mock scanner in order to see if he or she is comfortable and able to be still. It is very important that your child does not move when we are scanning so that we can get the best pictures of your child’s brain. In the mock scanner we will also show your child how they will look at the pictures they will see in the real scanner and introduce your child to the sounds that he or she will hear in the scanner. Through all these procedures, our goal is to make your child feel very comfortable while in the MRI scanner.

To date, 150 million MRI studies have been performed around the world. We will be following standard MRI procedures and safety guidelines. MRI has been shown to be extremely safe as long as proper safety precautions are taken. MRI uses strong magnetic fields and radio waves to make pictures of the body. There is no exposure to x-rays or radioactivity during an MRI scan. Levels of energy used are within safety limits established by the U.S. Food & Drug Administration (FDA). This study will use a 3.0 Tesla MRI scanner.

You and your child will be asked to leave metal objects and personal belongings in lockers provided in the prep room of the MRI center. Articles of clothing with metal inserts or clasps must be removed before entering the MRI room. Please ask us if you are unsure about any items.

Next, we will ask your child to complete a set of simple vision screening tests in order to fit your child with special glasses that are safe to use in the scanner. The glasses will partially correct your child’s vision so that he/she can see things we will display in the scanner. If your child wears contacts or has normal vision the special glasses will not be needed.

Your child will be asked to lie on a bed that slides into the long tube of the scanner. Your child will be given earphones and/or earplugs for hearing protection since the MRI scanner makes loud noises during normal operation. Your child will be asked to remain very still at these times. For scans of the head, we may put cushions around your child’s head and we may lightly tape the head to help keep it from moving. Your child will be able to talk to the MRI technologist by an intercom, and you and the technologist will be able to see and hear your child at all times. Your child will also be given a squeeze-ball signaling device. If at any time your child would like to discontinue the study, he/she can tell the investigators over the intercom or press the squeeze-ball signaling device to be removed immediately from the scanner. You or your child can choose to discontinue the study at any time without penalty.
Discomforts and risks

We will be providing foods for your child to eat. The foods used in the meals are all common foods made with ingredients that you would find at the supermarket. It is possible that your child may not like the taste of these foods and this would result in some psychological distress.

The foods used in this study will be made fresh each day using safe food preparation protocols. However, there is always a chance of food borne illness or uncovering an allergy in your child due to food exposure causing a physical risk.

We will be asking your child some sensitive questions about eating behaviors such as laxative use, vomiting, and other behaviors that are sometimes related to eating problems. These questions may make your child feel uneasy. He/she does not have to answer them. If we are concerned about your child’s responses, we may speak with you and provide a name of a specialist who deals with these issues. We may also ask your child to talk to you about this or speak with a trusted health professional (e.g. school nurse, teacher).

Your child will fill out a pubertal assessment questionnaire. Your child may feel uncomfortable answering some of the questions that are sensitive in nature. In order to minimize the risk, your child will be told that he/she does not have to complete any questions that make him/her uncomfortable.

Risk of injury is very low during an MRI scan. However, MRI is not safe for everyone. It may not be safe for your child to have an MRI scan if there is any metal containing iron in or on your child’s body. This is because metal containing iron can pose a safety risk when in the presence of strong magnetic fields. Radio waves may also heat the body and metallic objects within or on the body, possibly resulting in burns. Before you or your child is allowed in the scanner room, you will be asked a set of questions to determine if it is safe for your child to have an MRI scan at this time. You will also be asked to answer the questions to determine if it is safe for you to enter the scanner room with your child. For you and your child’s safety, it is very important that you answer all questions truthfully.

It is possible that your child may feel uncomfortable or confined once inside the scanner. This feeling usually passes within a few minutes after the study begins. It is possible that your child might experience dizziness, mild nausea, or see tiny flashing lights. These sensations are mostly due to movement while inside the magnet and can be minimized by holding still. All of these sensations should stop shortly after your child leaves the magnet.

As with any study that collects personal data, there is a risk of loss of confidentiality. We have set in place many guidelines to avoid this, as outlined below.

There are no other foreseeable discomforts and risks, other than what is listed above.

Benefits

You will not benefit from this research study. However, you or your child may enjoy the activities during the study, or feel it is good to contribute to scientific study. Furthermore, this study may also benefit the community. That is because we know very little about how children respond to different foods. Now we can learn from how
children make decisions to what foods they actually consume. What we learn in this study will help us come up with ways to help children eat better diets.

**Voluntary participation:**

Participation in this research study is voluntary. Therefore, you may choose to not be in this study. In addition, you or your child can choose to stop at any time. You do not have to answer any questions that you do not want to answer. Refusal to take part in or withdrawing from this study will involve no penalty or loss of benefits you would otherwise receive.

**Duration/ time of the procedures and study:**

If you agree to take part in this study, it involves four total visits, in which you and your child will return to The Children’s Metabolic Kitchen and Eating Behavior Laboratory or the Smoking Laboratory at Penn State. Typically, these visits will be scheduled 1 week apart but all 4 visits can be completed between 3-6 weeks. All visits will last no longer than 2 hours.

**Statement of confidentiality:**

Your child’s participation in this research is confidential. All possible steps have been taken to assure your child’s privacy. Efforts will be made to limit the use and sharing of your personal research information to people who have a need to review this information. Your child will be assigned a code number that will be used throughout the study. Only this code (and never your child’s name) will be used when analyzing or reporting the data. Any identifying information will be kept in a locked location and password protected electronic files.

This consent and any other identifying information will be kept in a locked file in Dr. Kathleen Keller’s (co-investigator) locked office. All questionnaires that you and your child complete will be identified only by your child’s code and stored separate from any identifying information. Only the PI (Shana Adise) and study coordinators will have access to your identifying information. All other project staff who are approved by the Penn State IRB will only have access to data files without your name.

Penn State’s Office for Research Protections, the Institutional Review Board, and the Office for Human Research Protections may review records related to this research study.

In the event of any publication or presentation resulting from the research, no personally identifiable information will be shared. The results of the research, including but not limited to your child’s results, may be published and presented at lectures and professional meetings, but your child will not be identified in any such publication or presentation.

We will do our best to keep your participation in this research study confidential to the extent permitted by law. However, it is possible that other people may find out about your participation in this research study. For example the following/people/groups may check and copy records about this research.

- The Office for Human Research Protections in the U. S. Department of Health and Human Services
- The Institutional Review Board (a committee that reviews and approves research studies) and

Participant Initials ____________________________
The Office for Research Protections.
Some of these records could contain information that personally identifies you. Reasonable efforts will be made to keep the personal information in your research record private. However, absolute confidentiality cannot be guaranteed.

We would like to video record your child as they participate in one of our tasks. However, children will be unaware that they are being recorded during the task. The video recordings will be stored on secure, networked servers in the College of Health and Human Development until three years after the study’s completion, when they will be destroyed. Only research staff on this study will have access to the recordings. With permission from you and your child, we may share segments of audio, video, or photographs with students or other scientists. Once segments have been chosen, the remainder of the recordings will be destroyed three years after the study is complete.

**Right to ask questions:**

Please contact Shana Adise at (814) 865-4404 with any question, concern or comment about the research. Dr. Kathleen Keller, who can be reached via phone at (814) 863-2915, is supervising this study. You can also call these numbers if you feel this study has harmed you or your child in any way. If you have any questions, concerns, or comments about you or your child’s rights as research participants or would like to offer input, please contact Penn State University’s Office for Research Protections (ORP) at (814) 865-1775. The ORP cannot answer questions about research procedures. All questions about research procedures can be answered by Shana Adise and the research team.

**Injury Clause:**

In the unlikely event that you or your child is injured as a result of your participation in this study, medical care is available. It is the policy of this institution to provide neither financial compensation nor free medical treatment for research-related injury. By signing this document, you are not waiving any rights that you have against The Pennsylvania State University from negligence of the University or its investigators.

**Incidental findings:**

The investigators for this project are not trained to perform medical diagnosis, and the scans to be performed in the study are not optimized to find abnormalities. On occasion, a member of the research team may notice a finding on a scan that seems abnormal. When a finding is noticed, the investigator or designate may consult a physician specialist, such as a radiologist or neurologist, as to whether the finding merits further investigation. If the specialist recommends further follow-up, the investigator or another designate will contact you within **48 hours** of the recommendation and suggest that you contact your private medical provider for follow-up. To facilitate follow-up care, you may be given a copy of your child’s images upon request. Being told about a finding may cause anxiety as well as suggest the need for additional tests and financial costs. Medical insurance may be affected whether or not the finding is ultimately proved to be of clinical significance. Costs for clinical follow-up are not covered in the cost of research. The decision as to whether to proceed with further examination or treatment lies with you.
Abnormal test results:

Please provide contact information so that you can be reached in the event of an incidental finding and/or abnormal test results. You will be notified within 48 hours of an incidental or abnormal finding that is determined to need further investigation. This includes the MRI scan and the language test.

Address______________________________________________

Phone_______________________________________________

Payment for participation:

The total compensation possible for this study is $160. For visit 1, you will receive $30 ($20 for you and $10 for your child) reimbursement for your time. For visit 2 and 3, you will receive $40 ($25 for you and up to $15 for your child) reimbursement for your time. For visit 4, you will receive $50 ($30 for you and up to $20 for your child) reimbursement for your time. We use the wording ‘up to’ because in some of our tasks your child has the chance to earn additional money based on performance. If you leave before completing the study, compensation will be provided on a pro-rated basis at the rate of $10 per hour completed.

Consent:

By consenting to participate, you agree to:

☐ Answer questionnaires we provide for you that relate to your household, parenting styles, and methods you use, or have used in the past, to feed your child. If you feel uncomfortable with any item on a questionnaire, you may leave it unanswered.
☐ Answer the SLEIC 3T MRI Participant Safety & Screening questions accurately for both yourself and your child,
☐ Tell the investigators about all metallic devices in/on you and your child’s body, and
☐ Not bring any metal devices (e.g., pens, coins, keys, credit cards) into the scanning room without staff approval.
☐ Participate in weekly sessions and try your best to follow the researcher’s requests.
☐ Talk to the researchers if there is a problem with the study.

If you agree to take part in this research study and the information outlined above, please sign your name and indicate the date below.

You will be given a copy of this signed and dated consent form for your records.

May the researchers video record your child while he or she is participating in the research?

☐ Yes, researchers may record my child while he/she is participating in the research.
☐ No, researchers may NOT record my child while he/she is participating in the research.

Participant Initials ________________
Sharing Video or Photographs With Scientists or Students: We will be recording one of the procedures using video, audio recording, and photographs, which will help us more accurately analyze data. Other scientists or students learning about science may find the video, audio recordings, and photographs useful, too. So we have some questions about whether it’s ok for us to share segments of the video, audio, or photographs.

Please select one of the following options:

_____ Recordings of my child's participation in this research may be shown in scientific presentations

_____ I do not want recordings of my child’s participation in this research shown in scientific presentations.

Please select one of the following options:

_____ Recordings of my child's participation in this research may be shown in scientific publications.

_____ I do not want recordings of my child’s participation in this research shown in scientific publications.

Please select one of the following options:

_____ Recordings of my child's participation in this research may be used for education and training of students.

_____ I do not want recordings of my child’s participation in this research used for education and training of students.

I consent to participate in this study and to have my child participate in this research study.

Printed Name of Child ___________________________ Date of Birth ___________________________ Date

Parent’s Printed Name ___________________________ Parent’s Signature ___________________________ Date

Printed Name of Person Obtaining Consent ___________________________ Signature of Person Obtaining Consent ___________________________ Date

Participant Initials ________________
APPENDIX C:

Assent Form

Study 1, 2, 3
This is a research study that you may choose to join and help. We are trying to figure out why kids like and eat the foods they do. This study requires that you come to our lab for four visits. We want to tell you today what will happen in each of the visits.

We ask that before you come to each visit, you do not eat anything for at least three hours. On each visit, we will play a few games with you, which are similar to video games. On one of the visits, you will be able to eat a few snacks. We will ask you to tell us how much you like the foods you are eating. While you are eating, we will read you a story and you will eat a meal until you're full. You don't have to eat anything that you don't want.

We will also ask you and your mom or dad to answer some questions on a computer. You don’t have to answer any questions that make you feel uncomfortable. This may be something that you have done before at school. It will be a short test, and we ask that you try your hardest on it. There are no right or wrong answers.

On the fourth visit, will explore Inner Space with you. Instead of studying planets and outer space, we study Inner Space. Inner space is inside your head: your brain! We want to know what goes on in kids’ brains when they are playing games. We will use a special camera called an MRI to take pictures of your brain. It's special because you lie on a bed inside the camera to take the pictures. The MRI is a big tube that kind of looks like a spaceship. It is safe and has been used by many doctors to help see people's brains.

We will ask you to lie very still so we can get the best pictures of your brain. Like a real spaceship the MRI can make loud sounds. You will wear our special headphones so you can hear us in Mission Control. Your mom or dad will be watching you the whole time from Mission Control. You'll be able to tell us to stop at any time if you want.

We want you to have fun while helping us out! Any time you have a question, please ask us.

You choose to help with our research study. If you feel like you want to stop, you can tell us at any time.

Does this all make sense to you? If not, we can go over it again.

Do you want to help?
APPENDIX D:

Demographics Questionnaire

Study 1, 2, 3
Demographic Questionnaire

Please answer the following questions about your child:
1. Date of birth (MM/DD/YYYY): ________________
2. Birth weight: _____________
3. Birth length: _____________
4. Was your child born premature?  YES  NO
   a. If yes, by how many weeks? ________
5. Was your child primarily breast-fed or primarily formula-fed?
   a. Breast-fed
   b. Formula-fed
6. If your child was breast-fed, for how many months was he/she exclusively (only) fed breast milk? ______
7. What ethnicity is your child (please check only one)?
   a. Hispanic or Latino
   b. Not Hispanic or Latino
8. What race is your child (please check only one)?
   a. American Indian/Alaskan Native
   b. Asian
   c. Black or African American
   d. White
   e. Hawaiian/Pacific Islander
   f. Mixed:
   g. Other:

Please answer the following questions about yourself and your family:
1. What is your relationship to the child?
   a. Mother
   b. Father
   c. Other (please specify): ________________
2. What is your date of birth (MM/DD/YYYY)? ________________
3. How old are you? ________________
4. What is your ethnicity (please check only one)?
   a. Hispanic or Latino
   b. Not Hispanic or Latino
5. What is your ethnicity (please check only one)?
   a. American Indian/Alaskan Native
   b. Asian
   c. Black or African American
   d. White
   e. Hawaiian/Pacific Islander
   f. Other
   g. Mixed (please describe)
6. Please indicate who lives in your household, and if applicable how many (i.e. Sibling 2).
   a. Mother  ________
   b. Father  ________
   c. Sibling  ________
   d. Uncle   ________
   e. Aunt   ________
   f. Grandmother  ________
   g. Grandfather  ________
   h. Cousin  ________
   i. Others, describe _____________________________________________
7. What is your marital status?
   a. Married
   b. Single (never married)
   c. Widowed
   d. Divorced
   e. Separated
   f. Remarried
   g. Living together (not married)
8. What is your total or combined family income, before taxes?
   a. Less than $20,000
   b. $21,000 - $35,000
   c. $36,000 - $50,000
   d. $51,000 - $75,000
   e. $76,000 - $100,000
   f. $100,000 +

9. What is your highest level of formal education?
   a. High school (12 years)
   b. Associates (14 years)
   c. Technical/Vocational School (14 years)
   d. Bachelor’s Degree (16 years)
   e. Master’s Degree (16 years)
   f. PhD (20 years)
   g. MD (20 years)
   h. JD (20 years)
   i. Other, describe _____________________

10. If applicable, what is your partner’s highest level of formal education?
   a. High school (12 years)
   b. Associates (14 years)
   c. Technical/Vocational School (14 years)
   d. Bachelor’s Degree (16 years)
   e. Master’s Degree (16 years)
   f. PhD (20 years)
   g. MD (20 years)
   h. JD (20 years)
   i. Other, describe _____________________

11. Are you currently employed?  YES  NO
12. Are you currently retired?  YES  NO
13. How many hours per week are you at work (not traveling to & from)? __________
14. Is your partner currently employed?  YES  NO  N/A
15. Is your partner currently retired?  YES  NO  N/A
16. How many hours per week is your partner at work (not traveling to & from)? __________

17. Who is primarily responsible for feeding your child?
   a. You
   b. Your partner
   c. Both
   d. School
   e. Other, please specify: _______________

18. Who is primarily responsible for buying food in your household?
   a. You
   b. Your partner
   c. Both
   d. Other, please specify: _______________

19. On average, how frequently does your family eat out or get delivery/take-out for dinner?
   a. Once a month or less
   b. Twice a month
   c. Once a week
   d. Two times a week
   e. Three times a week
   f. Four or more times a week

20. On average, how many nights a week does your family eat dinner together as a group (with most family members present)?
   a. 1
   b. 2
   c. 3
   d. 4
   e. 5
   f. 6
   g. 7
APPENDIX E:

Anthropometrics Data Sheets

Study 1, 2, 3
Date: __________  
ID#______  
Time: __________  

Anthropometric Measures  
Measure weight and height twice; we will then take the mean of the numbers in SPSS.  

Child:  
Height 1: _________  Height 2:_________  
Weight 1:_________  Weight 2: ________  
Body Fat %: __________  
Sex: __________  Age: __________  DOB: __________  

Parent 1:  
☐ Mother  ☐ Father  
Height 1: _________  Height 2:_________  
Weight 1:_________  Weight 2: ________  
☐ Measured  ☐ Self-reported  
Body Fat %: __________  
Sex: __________  Age: __________  DOB: __________  

Parent 2:  
☐ Mother  ☐ Father  
Height 1: _________  Height 2:_________  
Weight 1:_________  Weight 2: ________  
☐ Measured  ☐ Self-reported  
Body Fat %: __________  
Sex: __________  Age: __________  DOB: __________
APPENDIX F:

Pubertal Status Assessment Data Sheets and Scripts

Study 1, 2, 3

Reference:

Script for BOYS:

Introduction: All boys change and develop physically, mentally, and emotionally in the process of “growing up.” The growth and development of your body is an especially important part of this process of becoming a grown up. Since it is normal for different boys to go through these physical changes at different times, we are interested in learning about what changes are usually happening in boys when they are your age. We would like to ask you to help us get this information by answering some questions about how you are currently growing and developing. Do your best to answer carefully. If you do not understand a question or do not know the answer, just mark “I don’t know.”

When you are answering these questions, it is important to remember that no one will see your answers. The project staff will not be able to match the answers you put into the computer with your name. Therefore, please be as honest as possible since your honest answers will help us learn about boys your age.

REMEMBER- ALL ANSWERS YOU GIVE WILL BE KEPT PRIVATE

HOW TO ANSWER THE QUESTIONS

One on sheet, you will see directions that will ask you to select the number in front of the answer that best describes what is happening to you. Please choose only one answer for each question. The other sheet will show you diagrams and you will be asked to circle the one that looks most like you. When you are done, please put the sheets back into the sealed envelop. I will leave the room for a few minutes so that you may answer these questions privately.

Script for GIRLS:

Introduction: All girls change and develop physically, mentally, and emotionally in the process of “growing up.” The growth and development of your body is an especially important part of this process of becoming a grown up. Since it is normal for different girls to go through these physical changes at different times, we are interested in learning about what changes are usually happening in girls when they are your age. We would like to ask you to help us get this information by answering some questions about how you are currently growing and developing. Do your best to answer carefully. If you do not understand a question or do not know the answer, just mark “I don’t know.”

When you are answering these questions, it is important to remember that no one will see your answers. The project staff will not be able to match the answers you put into the computer with your name. Therefore, please be as honest as possible since your honest answers will help us learn about girls your age.

REMEMBER- ALL ANSWERS YOU GIVE WILL BE KEPT PRIVATE

HOW TO ANSWER THE QUESTIONS

One on sheet, you will see directions that will ask you to select the number in front of the answer that best describes what is happening to you. Please choose only one answer for each question. The other sheet will show you diagrams and you will be asked to circle the one that looks most like you. When you are done, please put the sheets back into the sealed envelop. I will leave the room for a few minutes so that you may answer these questions privately.
Introduction: All boys change and develop physically, mentally, and emotionally in the process of “growing up.” The growth and development of your body is an especially important part of this process of becoming a grown up. Since it is normal for different boys to go through these physical changes at different times, we are interested in learning about what changes are usually happening in boys when they are your age. We would like to ask you to help us get this information by answering some questions about how you are currently growing and developing. Do your best to answer carefully. If you do not understand a question or do not know the answer, just mark “I don’t know.”

When you are answering these questions, it is important to remember that no one will see your answers. The project staff will not be able to match the answers you put into the computer with your name. Therefore, please be as honest as possible since your honest answers will help us learn about girls your age.

REMEMBER- ALL ANSWERS YOU GIVE WILL BE KEPT PRIVATE

HOW TO ANSWER THE QUESTIONS

To answer each question, please select the number in front of the answer that best describes what is happening to you. Please choose only one answer for each question.

1. Would you say that your growth in height:
   1. has not yet begun to spurt (“spurt” means more growth than usual)
   2. has barely started
   3. is definitely underway (happening)
   4. seems completed
   5. I don’t know

2. And how about the growth of your body hair? (“Body hair” means hair any place other than your head, such as under your arms.)
   Would you say that your body hair has:
   1. has not yet begun to grow
   2. has barely started to grow
   3. is definitely underway (happening)
   4. seems completed
   5. I don’t know

3. Have you noticed any skin changes, especially pimples?
   1. skin has not yet started changing
   2. skin has barely started changing
   3. skin changes are definitely underway (happening)
   4. skin changes seem complete
   5. I don’t know
4. Have you noticed a deepening of your voice?
   1. voice has not yet started changing
   2. voice has barely started changing
   3. voice changes are definitely underway (happening)
   4. voice changes seem complete
   5. I don’t know

5. Have you begun to grow hair on your face?
   1. facial hair has not yet started growing
   2. facial hair has barely started growing
   3. facial hair has definitely started
   4. facial hair growth seems complete
   5. I don’t know

6. Do you think your development is any earlier or later than most other boys your age?
   1= much earlier
   2= somewhat earlier
   3= somewhat later
   4= much later
   5= I don’t know

SCORING:

For Items 1 through 4 on the girls’ version and all items on the boys’ version, response options were: not yet started (1 point); barely started (2 points); definitely started (3 points); seems complete (4 points); I don’t know (missing). Yes on the menstruation item = 4 Points; no = 1 point. Point values are averaged for all items to give a Pubertal Development Scale (PDS). Puberty Category Scores are computed using the criteria of Peterson et al., (1988). Puberty Category Scores for boys used body hair growth, voice change, and facial hair growth as follows: Prepubertal = 3; early Pubertal = 4 or 5 (no 3-point responses); Midpubertal = 6,7, or 8 (no 4 points; Late pubertal = 9-11; Postpubertal = 12. For girls, Puberty Category 5 scores used body hair growth, breast development, and menstruation as follows: Prepubertal = 3; Early Puberty = 3 and no menarche; Midpubertal = 4 and no menarche; Late Puberty = 5 - 7 and menarche; Postpubertal = 8 and menarche.
Introduction: All girls change and develop physically, mentally, and emotionally in the process of “growing up.” The growth and development of your body is an especially important part of this process of becoming a grown up. Since it is normal for different girls to go through these physical changes at different times, we are interested in learning about what changes are usually happening in girls when they are your age. We would like to ask you to help us get this information by answering some questions about how you are currently growing and developing. Do your best to answer carefully. If you do not understand a question or do not know the answer, just mark “I don’t know.” When you are answering these questions, it is important to remember that no one will see your answers. The project staff will not be able to match the answers you put into the computer with your name. Therefore, please be as honest as possible since your honest answers will help us learn about girls your age.

REMEMBER- ALL ANSWERS YOU GIVE WILL BE KEPT PRIVATE

HOW TO ANSWER THE QUESTIONS

To answer each question, please select the number in front of the answer that best describes what is happening to you. Please choose only one answer for each question.

1. Would you say that your growth in height:
   1. has not yet begun to spurt (“spurt” means more growth than usual)
   2. has barely started
   3. is definitely underway (happening)
   4. seems completed
   5. I don’t know

2. And how about the growth of your body hair? (“Body hair” means hair any place other than your head, such as under your arms.)
   1. has not yet begun to grow
   2. has barely started to grow
   3. is definitely underway (happening)
   4. seems completed
   5. I don’t know

3. Have you noticed any skin changes, especially pimples?
   1. skin has not yet started changing
   2. skin has barely started changing
   3. skin changes are definitely underway (happening)
   4. skin changes seem complete
   5. I don’t know
4. Have you noticed that your breasts have begun to grow?
   1. have not yet started growing
   2. have barely started growing
   3. breast growth is definitely underway (happening)
   4. breast growth seems complete
   5. I don’t know

5. Do you think your development is any earlier or later than most other girls your age?
   1= much earlier
   2= somewhat earlier
   3= somewhat later
   4= much later
   5= I don’t know

6a. Have you begun to menstruate (started to have your period)?
   yes(4)  no (1)

6b. If yes, how old were you when you started to menstruate? ________________________age in years

6c. If yes, what was the first day of your last menstrual period? ________________________

6d. If yes, how many days does your cycle usually last (i.e. how many days are typically between the start of one period to the start of the next period)? ________________

SCORING:

For Items 1 through 4 on the girls’ version and all items on the boys’ version, response options were: not yet started (1 point); barely started (2 points); definitely started (3 points); seems complete (4 points); I don’t know (missing). Yes on the menstruation item = 4 Points; no = 1 point. Point values are averaged for all items to give a Pubertal Development Scale (PDS). Puberty Category Scores are computed using the criteria of Peterson et al., (1988). Puberty Category Scores for boys used body hair growth, voice change, and facial hair growth as follows: Prepubertal = 3; early Pubertal = 4 or 5 (no 3-point responses); Midpubertal = 6,7, or 8 (no 4 points; Late pubertal = 9-11; Postpubertal = 12. For girls, Puberty Category 5 scores used body hair growth, breast development, and menstruation as follows: Prepubertal = 3; Early Puberty = 3 and no menarche; Midpubertal = 4 and no menarche; Late Puberty = 5 - 7 and menarche; Postpubertal = 8 and menarche.
Please circle either the number or the diagram which represents your development as of right now.
ID: ______  Date: ______

Please circle either the number or the diagram which represents your development as of right now.
APPENDIX G:

“Freddy Fullness” Visual Analog Scale and Script

Study 1, 2, 3

Reference:

Freddy Fullness Script

Introduction: “I have a doll here whose name is Freddy. You can use Freddy to tell how full your stomach feels after eating food or a meal, like breakfast, lunch, or dinner. For example, if you hadn’t eaten anything and your stomach felt empty, you’d put the slider at the very bottom. If you ate so much and were so full that you felt like you could burst and you couldn’t possibly eat anymore, you’d put the slider at the top. Why don’t you try to move the slider to get a feel for it? “

(Allow child to demonstrate how the slider can move up and down Freddy’s tummy.)

“Now, I have a few questions for you, and I want you to move the slider up and down Freddy’s tummy to tell me how full you think you would be. Okay?”

“Imagine if you ate just a little bit, like one cookie, how full do you think your stomach would feel?”
(If child moves the slider more than 25%, ask whether he/she is sure that’s really a little bit. – Moving the slider too far for a little may indicate the child doesn’t understand).

“Now, imagine that you ate a few more cookies, how full do you think your stomach would feel?”
(Any response between the last one and the top is acceptable.)

“Now imagine that you ate so many cookies that you didn’t want any more, but you could still eat something else, how full do you think your stomach would feel?”
(Child should put the slider between 60 and 80% of the distance.)

“Now, if you ate so much that you couldn’t possibly eat anymore of ANY food, how full do you think your stomach would feel?”
(Child should use the maximum.)

“Do you understand how Freddy works?”
(Allow child to respond. If child is still unclear, go through explanation again.)

Fullness Determination and Study Meal

“Can you use Freddy to show me how full your stomach feels right now? Remember, if your stomach feels empty, you push the rectangle to the bottom of the page like this.”
(Push the slider to the bottom of the page).

“If you have eaten a lot and you can’t possibly eat anymore, you push the rectangle all the way to the top like this.”
(Push the slider to the top of the page).

“Do you understand? Great! Move the rectangle to show me how you feel right now.”
(Let child use Freddy to rate how full he/she feels. Mark it on the Pre-Meal Freddy sheet.)
APPENDIX H:

Card-guessing Task Script

Study 1 & Study 2
Card-Guessing Task Script

**IMPORTANT NOTE:** when using the microphone/speaker in the scanner room, you have to press down the microphone button to speak and **RELEASE THE MICROPHONE BUTTON IN ORDER TO HEAR THE CHILD RESPOND.** If you do not release the microphone button when you are done speaking, you WILL NOT be able to hear the child! When the child is in the scanner, hearing a familiar voice may help them relax. So please make sure to sound calm, enthusiastic, and reassuring!

Hi *(child’s name)*, how are you doing? *(Wait for child’s response)*  
Good! Are you ready to get started with today’s task? *(Wait for child’s response)*  
Great!

Today, you will be playing a guessing game. You will be guessing if you think a random number will be higher or lower than the number 5. When you see the white question mark on the screen, you will make your guess. If you think the number will be higher than 5, press the top button with your thumb. If you think the number will be lower than 5, press the trigger button with your pointer finger. Do you understand how to make your guess? *(Release the microphone button and wait for child’s response)* Great!

Just like in the Zoo game, you will be able to win some extra money or some candy based on how well you play this game. If you see a picture of dollar bills after you make your guess, you will win 50 cents if your guess is correct! If you see a picture of a piece of candy after you make your guess, you will win a few, extra pieces of candy if your guess is correct! Sometimes, you will see a picture of a blue book. This means that you won’t win anything extra, even if your guess was correct. No matter if you’re playing for money, food, or nothing at all, make sure that you are making your best guess each time! Do you understand how this works? *(Release the microphone button and wait for child’s response)* Great!

After you’ve made your guess and learned what you are playing for, you will get to see if you guessed correctly! The actually number will appear on the screen, and either a green arrow or a yellow circle. A green arrow means you guessed correctly! A yellow circle means you did not guess correctly.

You will get to take three short breaks throughout the game, but it’s extremely important to keep still and not move, even during these breaks. Are you ready to get started? *(Release the microphone button and wait for child’s response)* Okay, get ready! Remember, try to be as still as possible!

**CHECK IN WITH THE CHILD AFTER EACH RUN**

Hi *(child’s name)*, you’re doing great! How are you doing? *(Wait for child’s response)*  
Good! Are you ready to keep going? *(Wait for child’s response)*  
Remember, try to be as still as possible! Here we go!
APPENDIX I:

Go/Nogo Script

Study 3
Go/No-Go Zoo Task Script

NEUTRAL TASK: (to be done first)

Slide 1: Welcome to the Zoo! Have you ever been to visit the zoo? Do you know what a zookeeper’s job is? Well this is a picture of a zookeeper we know. Her name is Melissa!

In this game we will be helping Melissa the zookeeper. She has had a crazy day at the zoo because someone has opened up all of the cages and let out all of the animals! Melissa wants to make sure that she gets all of the animals back to their cages as quickly as she can and she needs your help!

(PRESS SPACE BAR to transition to next slide)

Slide 2: You and Melissa are in luck because you will also have the help of her 3 orangutan friends. Do you know what an orangutan is? (wait for the child to respond – they are big monkeys, big like a gorilla, but they have orange fur) Each of these orangutan friends is helping her put the animals back in their cages. Let’s meet them!

This is the orangutan family. Fred, his sister Sally, and their mom Molly. Because these are Melissa’s orangutan friends, they don’t need to be put back into their cages. Pay close attention as we look at their picture so we can remember who they are.

Slides 3 - 5: Click through the slides of each orangutan and introduce them.

Slide 6: This is a map of the zoo – it is pretty big! We are going to work our way through the zoo and make sure that the animals in each are back in their cages. Our first stop will be (point to the stops as you go) Koala Cove!!

Slide 7: You can help Zookeeper Melissa catch all of the animals by pressing the button when you see them. Just remember, the orangutans are helping, so don’t press a button when you see an orangutan friend!

I think that you are going to be a great zoo helper! Now let’s practice. But before we begin, can you tell me how we are going to play this game?

Wait for the child to respond that they have to press the space bar every time they see an animal, but not an orangutan friend. If they seem unsure say: Your job is to press the button when you see an animal, but not when you see an orangutan friend!

Slide 8: Are you ready to help Melissa? That’s great!

Slide 9: Remember, these are your helpers, Fred, Sally, and Molly!

Slide 10: Now for this game, you want to try and go as fast as you can!

Practice Block

Have the child complete the practice run. Give the child feedback as to whether or not he or she should speed up or pay greater attention to the orangutans.

Zoo Task

Tell the child that they are doing a great job and advance to the next slide of the Zoo Map. Say,
You did a great job with that! Now let’s help Melissa find even more animals. Remember, just like before, don’t press the button when you see an orangutan friend. Try to go as fast as you can! Next stop, Koala Kove!

Are you ready? Let’s go!” Press the SPACE bar.

Rewarded Task:

You’re doing a great job! Now we’re going to be completing the same task with our friend Melissa, but this time you’ll have a chance to win additional money or some of your favorite snack based on how well you play the game. If you see a picture of money, for that next part of the game you have the chance to win extra money based on how quickly you put the right animals back in their cages. If you see a picture of candy, for that section of the game you have a chance to win candy. There will also be times where you won’t be playing to earn anything extra. No matter if you’re playing for money, food, or nothing at all, don’t forget that Melissa needs your help getting the animals back in their cages! So try and put the right animals back in their cages as quickly as you can with the help of your orangutans friends!
APPENDIX J:

Child Eating Behaviour Questionnaire

Study 1

Reference:

**Child Eating Behaviour Questionnaire (CEBQ)**

Please read the following statements and tick the boxes most appropriate to your child’s eating behaviour. If you cannot answer a question for any reason, feel free to leave it blank.

<table>
<thead>
<tr>
<th>Statement</th>
<th>Never</th>
<th>Rarely</th>
<th>Sometimes</th>
<th>Often</th>
<th>Always</th>
</tr>
</thead>
<tbody>
<tr>
<td>My child loves food</td>
<td>□</td>
<td>□</td>
<td>□</td>
<td>□</td>
<td>□</td>
</tr>
<tr>
<td>My child eats more when worried</td>
<td>□</td>
<td>□</td>
<td>□</td>
<td>□</td>
<td>□</td>
</tr>
<tr>
<td>My child has a big appetite</td>
<td>□</td>
<td>□</td>
<td>□</td>
<td>□</td>
<td>□</td>
</tr>
<tr>
<td>My child finishes his/her meal quickly</td>
<td>□</td>
<td>□</td>
<td>□</td>
<td>□</td>
<td>□</td>
</tr>
<tr>
<td>My child is interested in food</td>
<td>□</td>
<td>□</td>
<td>□</td>
<td>□</td>
<td>□</td>
</tr>
<tr>
<td>My child is always asking for a drink</td>
<td>□</td>
<td>□</td>
<td>□</td>
<td>□</td>
<td>□</td>
</tr>
<tr>
<td>My child refuses new foods at first</td>
<td>□</td>
<td>□</td>
<td>□</td>
<td>□</td>
<td>□</td>
</tr>
<tr>
<td>My child eats slowly</td>
<td>□</td>
<td>□</td>
<td>□</td>
<td>□</td>
<td>□</td>
</tr>
<tr>
<td>My child eats less when angry</td>
<td>□</td>
<td>□</td>
<td>□</td>
<td>□</td>
<td>□</td>
</tr>
<tr>
<td>My child enjoys tasting new foods</td>
<td>□</td>
<td>□</td>
<td>□</td>
<td>□</td>
<td>□</td>
</tr>
<tr>
<td>My child eats less when s/he is tired</td>
<td>□</td>
<td>□</td>
<td>□</td>
<td>□</td>
<td>□</td>
</tr>
<tr>
<td>My child is always asking for food</td>
<td>□</td>
<td>□</td>
<td>□</td>
<td>□</td>
<td>□</td>
</tr>
<tr>
<td>My child eats more when annoyed</td>
<td>□</td>
<td>□</td>
<td>□</td>
<td>□</td>
<td>□</td>
</tr>
<tr>
<td>If allowed to, my child would eat too much</td>
<td>□ □ □ □ □</td>
<td>FR</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>My child eats more when anxious</td>
<td>□ □ □ □ □</td>
<td>EOE</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>My child enjoys a wide variety of foods</td>
<td>□ □ □ □ □</td>
<td>FF*</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>My child leaves food on his/her plate at the end of a meal</td>
<td>□ □ □ □ □</td>
<td>SR</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>My child takes more than 30 minutes to finish a meal</td>
<td>□ □ □ □ □</td>
<td>SE</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>Never</th>
<th>Rarely</th>
<th>Sometimes</th>
<th>Often</th>
<th>Always</th>
</tr>
</thead>
<tbody>
<tr>
<td>Given the choice, my child would eat most of the time</td>
<td>□ □ □ □ □</td>
<td>FR</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>My child looks forward to mealtimes</td>
<td>□ □ □ □ □</td>
<td>EF</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>My child gets full before his/her meal is finished</td>
<td>□ □ □ □ □</td>
<td>SR</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>My child enjoys eating</td>
<td>□ □ □ □ □</td>
<td>EF</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>My child eats more when she is happy</td>
<td>□ □ □ □ □</td>
<td>EUE</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>My child is difficult to please with meals</td>
<td>□ □ □ □ □</td>
<td>FF</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>My child eats less when upset</td>
<td>□ □ □ □ □</td>
<td>EUE</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>My child gets full up easily</td>
<td>□ □ □ □ □</td>
<td>SR</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Behavior</td>
<td>Codes</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>-------------------------------------------------------------------------</td>
<td>-------</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>My child eats more when s/he has nothing else to do</td>
<td>EOE</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Even if my child is full up s/he finds room to eat his/her favourite food</td>
<td>FR</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>If given the chance, my child would drink continuously throughout the day</td>
<td>DD</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>My child cannot eat a meal if s/he has had a snack just before</td>
<td>SR</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>If given the chance, my child would always be having a drink</td>
<td>DD</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>My child is interested in tasting food s/he hasn’t tasted before</td>
<td>FF*</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>My child decides that s/he doesn’t like a food, even without tasting it</td>
<td>FF</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>If given the chance, my child would always have food in his/her mouth</td>
<td>FR</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>My child eats more and more slowly during the course of a meal</td>
<td>SE</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
### SCORING OF THE CEBQ

(Never=1, Rarely=2, Sometimes=3, Often=4, Always=5)

<table>
<thead>
<tr>
<th>Measure</th>
<th>Formula</th>
</tr>
</thead>
<tbody>
<tr>
<td>Food responsiveness</td>
<td>item mean FR</td>
</tr>
<tr>
<td>Emotional over-eating</td>
<td>item mean EOE</td>
</tr>
<tr>
<td>Enjoyment of food</td>
<td>item mean EF</td>
</tr>
<tr>
<td>Desire to drink</td>
<td>item mean DD</td>
</tr>
<tr>
<td>Satiety responsiveness</td>
<td>item mean SR</td>
</tr>
<tr>
<td>Slowness in eating</td>
<td>item mean SE</td>
</tr>
<tr>
<td>Emotional under-eating</td>
<td>item mean EUE</td>
</tr>
<tr>
<td>Food fussiness</td>
<td>item mean FF</td>
</tr>
</tbody>
</table>

*Reversed items*
APPENDIX K:

Laboratory Test-meal Photos

Study 2 & Study 3
Baseline Meal

Eating in the Absence of Hunger Snacks

Palatable Buffet Meal
APPENDIX L:

Food Liking Assessment Data Collection Sheet

Study 2 & Study 3
**VAS- Buffest Meal**

Participant ID:  
Visit #:  
Date:  

*Explanation of Five-point Scale*

I am going to give you some fun foods to taste and I want you to taste each one and use these smiley faces to tell me how they taste, okay?

![Smiley Faces]

- **Hate It**
- **Dislike It**
- **It's Okay**
- **Like It**
- **Love it**

Example:

1. How much do you like this **(INSERT FOOD NAME HERE)** ?

![Smiley Faces]

- **Hate It**
- **Dislike It**
- **It's Okay**
- **Like It**
- **Love it**
APPENDIX M:

Food Intake Data Sheets

Study 2 & Study 3
Subject ID: ______________    Date: ___________________

*Intake Sheets: Standard (Baseline) Lab Test Meal*

Serving #:_______

Check 1: __________    Time: __________________

Check 2: __________    Visit #: ________________

<table>
<thead>
<tr>
<th>Lunch Food</th>
<th>Pre-Weight</th>
<th>Post-Weight</th>
<th>Amount Consumed</th>
</tr>
</thead>
<tbody>
<tr>
<td>Macaroni &amp; Cheese (2 cups ~400g)</td>
<td>(w/o plate)</td>
<td>(w/plate)</td>
<td></td>
</tr>
<tr>
<td>Garlic bread (4” piece)</td>
<td>(w/o plate)</td>
<td>(w/plate)</td>
<td></td>
</tr>
<tr>
<td>Broccoli (180g)</td>
<td>(w/o bowl)</td>
<td>(w/bowl)</td>
<td></td>
</tr>
<tr>
<td>Cherry Tomatoes (100g)</td>
<td>(w/o plate)</td>
<td>(w/plate)</td>
<td></td>
</tr>
<tr>
<td>Red grapes (200g)</td>
<td>(w/o bowl)</td>
<td>(w/bowl)</td>
<td></td>
</tr>
<tr>
<td>Angel Food Cake (80g)</td>
<td>(w/o plate)</td>
<td>(w/plate)</td>
<td></td>
</tr>
<tr>
<td>Water (1L)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Freddy Fullness pre-meal: _______________

Freddy Fullness post-meal: _______________
Intake Sheets: EAH Snacks
Serving #:_______

Check 1: _________          Time: ________________
Check 2: _________          Visit #: ______________

<table>
<thead>
<tr>
<th>Lunch Food</th>
<th>Pre-Weight</th>
<th>Post-Weight</th>
<th>Amount Consumed</th>
</tr>
</thead>
<tbody>
<tr>
<td>Popcorn (15g)</td>
<td>(w/o plate)</td>
<td>(w/plate)</td>
<td></td>
</tr>
<tr>
<td>Potato chips (58g)</td>
<td>(w/o plate)</td>
<td>(w/plate)</td>
<td></td>
</tr>
<tr>
<td>Pretzels (39g)</td>
<td>(w/o bowl)</td>
<td>(w/bowl)</td>
<td></td>
</tr>
<tr>
<td>Ritz Bitz (44g)</td>
<td>(w/o plate)</td>
<td>(w/plate)</td>
<td></td>
</tr>
<tr>
<td>Brownies (51g)</td>
<td>(w/o bowl)</td>
<td>(w/bowl)</td>
<td></td>
</tr>
<tr>
<td>Chocolate chip cookies (66g)</td>
<td>(w/o plate)</td>
<td>(w/plate)</td>
<td></td>
</tr>
<tr>
<td>Starbursts (66g)</td>
<td>(w/o plate)</td>
<td>(w/plate)</td>
<td></td>
</tr>
<tr>
<td>M&amp;M'S (66g)</td>
<td>(w/o plate)</td>
<td>(w/plate)</td>
<td></td>
</tr>
<tr>
<td>Doritos (58g)</td>
<td>(w/o plate)</td>
<td>(w/plate)</td>
<td></td>
</tr>
<tr>
<td>Hershey’s Chocolate Kisses (66g)</td>
<td>(w/o plate)</td>
<td>(w/plate)</td>
<td></td>
</tr>
</tbody>
</table>

Freddy Fullness pre-meal: ________________
Freddy Fullness post-meal: ________________
<table>
<thead>
<tr>
<th>Lunch Food</th>
<th>Pre-Weight</th>
<th>Post-Weight</th>
<th>Amount Consumed</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cheese bagel bites (~145g; 8 pieces)</td>
<td>(w/o plate)</td>
<td>(w/plate)</td>
<td></td>
</tr>
<tr>
<td>Cheese pizza rolls (~80 g; 7 pieces)</td>
<td>(w/o plate)</td>
<td>(w/plate)</td>
<td></td>
</tr>
<tr>
<td>Chicken nuggets (~105g; 7 nuggets)</td>
<td>(w/o bowl)</td>
<td>(w/bowl)</td>
<td></td>
</tr>
<tr>
<td>Mozzarella sticks (~100g; 4 sticks)</td>
<td>(w/o plate)</td>
<td>(w/plate)</td>
<td></td>
</tr>
<tr>
<td>Potato Chips (28 g)</td>
<td>(w/bowl)</td>
<td>(w/bowl)</td>
<td></td>
</tr>
<tr>
<td>Chocolate chip cookies (~43.6 g; 4 cookies)</td>
<td>(w/o plate)</td>
<td>(w/plate)</td>
<td></td>
</tr>
<tr>
<td>Mini-brownies (~60g; 4 mini-brownies)</td>
<td>(w/o plate)</td>
<td>(w/plate)</td>
<td></td>
</tr>
<tr>
<td>Chocolate cupcakes (~50g; 1 mini-cupcake)</td>
<td>(w/o plate)</td>
<td>(w/plate)</td>
<td></td>
</tr>
<tr>
<td>Donut holes (~58.4g; 5 donuts)</td>
<td>(w/o plate)</td>
<td>(w/plate)</td>
<td></td>
</tr>
<tr>
<td>Whole-fat chocolate milk (245g; 1 cup)</td>
<td>(w/o plate)</td>
<td>(w/plate)</td>
<td></td>
</tr>
<tr>
<td>Red Twizzlers strawberry (~50g; 4 pieces)</td>
<td>(w/o plate)</td>
<td>(w/plate)</td>
<td></td>
</tr>
<tr>
<td>Fruit rollups (~30g; 2 packages)</td>
<td>(w/o plate)</td>
<td>(w/plate)</td>
<td></td>
</tr>
<tr>
<td>Gummy bears (105g)</td>
<td>(w/o plate)</td>
<td>(w/plate)</td>
<td></td>
</tr>
<tr>
<td>Skittles (86g)</td>
<td>(w/o plate)</td>
<td>(w/plate)</td>
<td></td>
</tr>
<tr>
<td>Fruit punch (235g; 1 cup)</td>
<td>(w/o plate)</td>
<td>(w/plate)</td>
<td></td>
</tr>
</tbody>
</table>

Freddy Fullness pre-meal: __________  Freddy Fullness post-meal: ________
Curriculum Vitae
Shana Adise, BS

------------ Education

2017  Ph.D.  Nutritional Sciences, The Pennsylvania State University
2012  B.S.  Psychology, The City College of New York

------------ Selected Awards

2016  Society for Neuroscience Trainee Professional Development Award
2016 – 2017  Kligman Graduate Fellowship
2016  Nutritional Sciences Graduate Student Teacher and Mentor Award
2016 – 2017  SLEIC Dissertation Award
2016 – 2017  USDA Childhood Obesity Prevention Training Fellowship
2013  Excellence in Graduate Recruitment Award

------------ Selected Grants

2016 – 2017  The Role of Reward and Inhibitory Control Pathways in Overeating in Healthy and Overweight Children, Principal Investigator

2016 – 2017  Examining the relationship between puberty and reward sensitivity in Overweight and healthy weight adolescents, Co-Investigator

2014 – 2017  Understanding Decision-Making and Reward for Food Choice in Overweight and Healthy Weight Children, Principal Investigator

------------ Selected Publications

