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

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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 winning 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 both reward processing and inhibitory control. Multiple stepwise regressions were conducted to examine the relationship between intake and BOLD response to rewards. Corrected 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 meals. 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 correlates with laboratory measures of food intake in children.

1. 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) (Dimitropoulos, Tkach, Ho, & Kennedy, 2012; Rothemund et al., 2007; Stoeckel et al., 2008). However, neural processing of food cues is complex and subject to individual differences. BMI has positively correlated with BOLD response in reward regions to *anticipating* (Simon et al., 2014; Stice, Spoor, Bohon, Veldhuizen, & Small, 2008) and *receiving* tastes of a milkshake in the scanner (Geha, Aschenbrenner, Felsted, O'Malley, & Small, 2013; Raaijmakers, Pouwels, Berghuis, & Nienhuijs, 2015; Simon et al., 2015; Stice, Yokum, Burger, Epstein, & Small, 2011). As a result, a reward surfeit model has been proposed, which suggests that overeating is due to a neurobiological hypersensitivity to food rewards (Stice & Yokum, 2016). However, in similar brain regions implicated in reward and motivational processing, BMI has also negatively correlated with the *receipt* of food rewards (i.e., reward outcome) (Babbs et al., 2013; Stice, Yokum, Blum, & Bohon, 2010; Stice et al., 2008). These findings suggest that *hyposensitivity* to reward outcome 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 (Burger & Berner, 2014). 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 is an essential step toward clarifying

Abbreviations: AFNI, Analysis of Functional NeuroImages; BOLD, blood-oxygen-level-dependent; dlPFC, dorsolateral prefrontal cortex; EAH, eating in the absence of hunger; fMRI, functional magnetic resonance imaging; MNI, Montreal Neurological Institute; mPFC, medial prefrontal cortex; OFC, orbitofrontal cortex; ROI, regions of interest

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why some children are more susceptible to obesity than others.

Monetary reward processing has also been positively correlated with weight status in adolescents at risk for developing obesity (Stice et al., 2011) and adults (Balodis et al., 2013; Opel et al., 2015; Simon et al., 2014; Verdejo-Román, Fornito, Soriano-Mas, Vilar-López, & Verdejo-García, 2017). This suggests that heightened brain response for multiple reward types may be a risk factor for obesity. However, behavioral data suggests that heightened response to food *over* alternative rewards, like money, is positively associated with obesity (Epstein, Dearing, Temple, & Cavanaugh, 2008) and may be a risk factor for overeating (Epstein, Salvy, Carr, Dearing, & Bickel, 2010; Rollins, Dearing, & Epstein, 2010) and subsequent weight gain (Epstein, Yokum, Feda, & Stice, 2014). Yet, the neurological mechanisms associated with increased response to food relative to alternative rewards and their relation to overeating is not currently understood, particularly in children. Childhood is a period when cortical pathways implicated in reward processing are rapidly developing (Casey, Jones, & Hare, 2008), which makes understanding this phenomenon critically important to provide insight for intervention and treatment programs.

In a previous report from this cohort, we found that children's brains responded differently to food and monetary rewards, but these responses were not dependent on child weight status. (Adise, Geier, Roberts, White, & Keller, 2018, *Under Review*). BOLD response was increased in motivational and reward-related regions for *anticipating* food versus money, but decreased for *winning* (i.e., outcome) food versus money in similar brain regions. However, a remaining question is how differences in brain response to food versus money are associated with laboratory measures of overeating.

Therefore, in the present study, we tested how the BOLD response to anticipating and winning food compared to monetary rewards relates to laboratory overeating. Food intake was measured with three meals: 1) an *ad libitum* baseline test-meal, 2) a highly palatable buffet designed to elicit overconsumption (Fearnbach, Thivel, Meyermann, & Keller, 2015), and 3) a validated measure of children's intake of palatable snacks when not hungry (i.e., eating in the absence of hunger [EAH]) (Fisher & Birch, 2002). We hypothesized that in line with the reward surfeit model, BOLD response to the anticipation of food versus money in reward processing regions would positively correlate with intake at the palatable buffet and EAH. Because the reward surfeit model of overeating suggests that hypersensitivity to reward relates to overeating, we hypothesized that our findings would be independent of how much children weighed. In addition to the reward surfeit model, other models have suggested that deficits in inhibitory control increase one's vulnerability to overeating (Batterink, Yokum, & Stice, 2010; Francis & Susman, 2009). To test this competing model, we also included several regions implicated in inhibitory control, but made no *a priori* hypotheses about their relationship to food intake. Given the contradictory findings in the literature in regards to theories about reward outcome trials (Babbs et al., 2013; Geha et al., 2013; Raaijmakers et al., 2015; Simon et al., 2015; Stice et al., 2008, 2010, 2011), we also made no *a priori* hypotheses regarding the relationship between reward outcome and laboratory intake.

2. Materials and methods

2.1. 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 response 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. All children were tested individually. 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 (Keller et al., 2006). The first three visits occurred in randomized order and included measures of behavioral decision-making tasks and food intake at test-meals. The fourth visit always included the fMRI scan in order to have time to acclimate the child to the scanning environment on visits two and three. 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., 2018, *Under Review*). This study was approved by the Pennsylvania State University Institutional Review Board (IRB approval number: 674). Parental consent for child participation and child assent were obtained on the first visit to the laboratory. Data collection occurred between April 2015 and September 2016.

2.2. 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 $\geq$ 85th %) (Cole, 2000). Parents provided child height and weight over the phone, but these measures were confirmed in the laboratory. This was the first study in children to evaluate the relationship between BOLD response to multiple rewards and food intake. Power analyses (*a priori*) were estimated for the primary study aim, which was to test for differences in BOLD response to food and monetary rewards between children with healthy weight and those with overweight/obesity. Therefore, to estimate the expected effects sizes needed for our regions of interest, sample size was determined by consulting the food cue literature in children (Black et al., 2014; Bruce et al., 2013; English et al., 2016, 2017). Based on expected effects, we aimed to recruit 80 children who were matched by weight status and sex. This sample size would also allow for 25% loss due to attrition and loss of data due to motion effects in the MRI.

In total, we were only able to screen 195 families during the study period (see Fig. 1). Fifty-five 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, 12 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 (i.e., were not fasted) (n = 2). This resulted in the final sample of

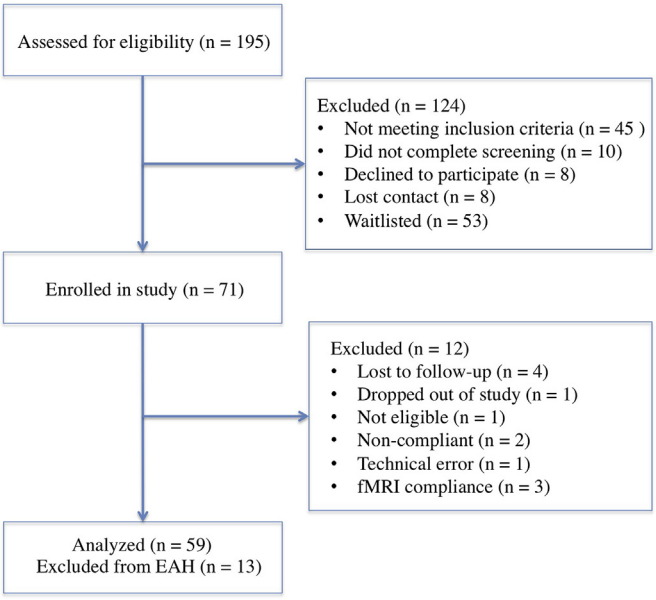

Fig. 1. An overview of study enrollment.

59 children (32 females and 27 males; 2% Asian, 5% Black, and 93% White) (see Table 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).

2.3. 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 twice, 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 (≥85%ile) (Cole, 2000). We measured height and weight for the parent who accompanied the child and had them report approximate weight/height for the second parent who was not at the visit. For some analyses, we also created an obesity risk score for the child, defined as: no-risk (i.e. both parents were not overweight or obese), low-risk (i.e., one parent was overweight or obese), or high-risk (i.e., both parents were overweight or obese). We also collected body fat measures from both the child and accompanying parent using a bioelectrical impedance analysis (Tanita model BF-350, Arlington Heights, IL).

2.4. Pubertal assessment

On the first visit, puberty was assessed via a 5-item pubertal development scale (Petersen, Crockett, Richards, & Boxer, 1988). 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 pubertal development) to four (seems complete). Scoring for this pubertal development scale followed the guidelines outlined in Carskadon and Acebo (1993) (Carskadon & Acebo, 1993). 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 (Bonat, Pathomvanich, Keil, Field, & Yanovski, 2002). 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.

Table 1
Descriptive characteristics for the participants (n = 59; 54% female). SD = standard deviation; kg = kilograms; m^2 = meters squared. *Body fat percentage was missing for one participant.

Characteristic	Healthy Weight (n = 31)		Overweight/Obese (n = 28)	
	Mean ± SD	Range	Mean ± SD	Range
Age (years)	8.7 ± 1.4	7–11	9.4 ± 1.2	7–11
Age (months)	111.0 ± 17.5	85–143	118.8 ± 14.7	85–142
BMI Percentile	53.4 ± 11.8	11–83	94.5 ± 4.0	85–99
BMI *z*-score (kg/m^2)	0.1 ± 0.5	−1.25–0.96	1.7 ± 0.4	1.04–2.57
Body Fat Percent*	17.1 ± 5.5	6.4–30.6	32.9 ± 6.8	19.1–46.7
Weight (kg)	31.5 ± 6.3	21.3–51.4	49.3 ± 10.0	26.9–71.7
Puberty Status	1.8 ± 0.7	1.0–3.5	1.8 ± 0.8	1.0–3.0
Tanner Stage	1.6 ± 0.8	1.0–4.0	1.9 ± 1.1	1.0–4.0
	n	%	n	%
Sex				
Male	13	42	14	50
Female	18	58	14	50
Ethnicity				
Hispanic or Latino	3	10	0	0
Not Hispanic or Latino	28	90	28	100
Race				
Asian	0	0	1	0.036
Black	2	0.065	1	0.036
White	29	93.5	26	92.8
Total Combined Income				
Less than $20,000	0	0	3	10.7
$21,000-$35,000	2	6.5	1	3.6
$36,000-$50,000	4	12.9	4	14.7
$51,000-$75,000	6	19.4	10	35.7
$76,000-$100,000	10	32.3	1	3.6
$100,000+	9	29	9	32.1
Parent Education Level				
High school	3	9.7	6	21.4
Associate's Degree	3	9.7	4	17.9
Bachelor's Degree	14	45.2	10	32.1
Master's Degree	3	9.7	3	10.7
PhD/MD/JD	8	25.8	5	17.8

2.5. Fullness assessment

Children were required to fast for at least three hours before coming to the laboratory. To assess compliance, children reported their fullness before each meal and the fMRI scan. Children were asked to report their fullness using a 150-point validated visual analog scale for children (Keller et al., 2006). This scale has been successfully used in this age group (English et al., 2017, 2016; Fearnbach et al., 2016). Fullness assessments were also conducted after food intake and the fMRI scan. Children who were not hungry and/or reported eating less than 3 h prior to coming into the laboratory were not included in the analyses (n = 2).

Table 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.

Baseline Test Meal			
Food Items	ED (kcal/g)	Weight (g)	Energy (kcal) per serving
Macaroni & cheese[a]	1.05	400	420
Garlic Bread[b]	3.44	100	344
Broccoli with butter and flavoring[c]	0.31	180	56
Cherry Tomatoes[d]	0.21	100	21
Red Seedless Grapes[e]	0.77	200	154
Angel food cake[f]	2.31	80	185
Water[g]	0	1000	0
Total food served	1.35	1060	1180
Total food & water served	1.15	2060	1180

[a] Macaroni and Cheese Dinner, Original, Kraft Foods Inc.
[b] Garlic Bread, Pepperidge Farm Inc.
[c] Large 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.
[d] Wegman's Super Sweet Cherry Tomatoes.
[e] Wegman's Red Seedless Grapes.
[f] Angel Food Bundt Cake, Sara Lee Desserts, Hillshire Brands Co.
[g] Tap Water, University Park, PA.

2.6. Food intake measures

2.6.1. 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 2 for food descriptions and quantities). Items for the meal were selected based on the Continuing Survey of Food Intakes of Individuals (Harnack, Walters, & Jacobs, 2003); these foods have previously been used by our laboratory and others (English et al., 2017; Leahy, Birch, & Rolls, 2008; Spill, Birch, Roe, & Rolls, 2010). For the baseline meal, children were instructed that they had 30 min to eat until they were full. Children were not required to eat for the entire 30 min; 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 (English et al., 2017, 2016; Fearnbach et al., 2016).

2.6.2. Eating in the absence of hunger (EAH)

Twenty minutes after children ate the baseline meal to satiety we assessed EAH using a paradigm developed by Fisher and Birch (1999) (Fisher & Birch, 1999; Francis, Granger, & Susman, 2013). To assess EAH, children were exposed to a range of palatable snacks and treats (e.g., candies, cookies, cakes, chips) (see Table 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 min, and therefore, the child was left alone with the toys and snacks. Amount consumed (in calories) was considered "eating in the absence of hunger". As this paradigm is intended to capture non-homeostatic eating, 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.

Table 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.

Eating the Absence of Hunger Meal			
Food items	ED (kcal/g)	Weight (g) or serving size	Energy (kcal) per serving
Popcorn[a]	5.28	15	79
Potato Chips[b]	5.64	58	327
Pretzels[c]	5.89	39	230
Cheese crackers[d]	5.37	6 crackers (~44 g)	236
Mini-brownies[e]	4.36	4 mini-brownies (~51 g)	222
Chocolate Chip Cookies[f]	4.97	6 cookies (~66 g)	327
Fruit candies[g]	4.08	66	269
Chocolate candies[h]	4.86	66	321
Cheese-flavored corn chips[i]	5.14	58	298
Chocolate[j]	5.37	66	354
Total food served	4.89	529	2663

[a] Butter flavored popcorn, Chester's by Frito Lays.
[b] Lay's Potato Chips, by Frito Lays.
[c] Rold Gold Tiny Twists Pretzels by Frito Lays.
[d] Ritz Bits Cheese Crakers, Nabisco Foods.
[e] Little Bites Fudge Brownies, Entenmann's.
[f] Chocolate Chip Cookies, Original, Chips A'Hoy, Mondelez International.
[g] Skittles, Mars.
[h] M&M'S, Mars.
[i] Doritos by Frito Lay.
[j] Chocolate Kisses, The Hershey Company.

2.7. Palatable buffet meal

Children's intake at a highly palatable buffet meal was measured on a separate visit from the baseline/EAH procedures. 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 (Fearnbach et al., 2015; Keller et al., 2014). 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 for food descriptions and quantities). Children were instructed to eat as much or as little as they wanted during a 30-min meal period. 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.

2.8. 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).

2.9. Food liking

Before each meal, children tasted and rated samples (~5 g) of each food and rated liking using a 5-point smiley face scale (Chen, Resurreccion, & Paguio, 1996). To be consistent with other studies that have assessed EAH (Fisher & Birch, 1999, 2002; French, Epstein, Jeffery, Blundell, & Wardle, 2012), children also ranked their

Table 4
Items served in the highly palatable buffet meal; amounts of weight and energy served are shown. ED = energy density; Kcal = kilocalorie; g = grams.

Palatable buffet meal			
Food Items	ED (kcal/g)	Weight (g) or serving size	Energy (kcal) per serving
Savory Fats			
Cheese bagel bites[a]	2.28	8 pieces (~145 g)	331
Cheese pizza rolls[b]	2.51	7 pieces (~85 g)	213
Chicken nuggets[c]	2.99	7 nuggets (~105 g)	314
Mozzarella Sticks[d]	3.03	4 sticks (~125 g)	379
Potato Chips[e]	5.64	28 g	158
Sweet-fats			
Chocolate chip cookies[f]	4.98	4 cookies (44 g)	219
Mini-brownies[g]	4.36	4 brownies (60 g)	262
Chocolate cupcakes[h]	4.71	1 cupcake (50 g)	236
Donut holes[i]	5.07	4 donuts (58 g)	295
Whole-fat chocolate milk[j]	0.83	1 cup (~245 g)	203
Sweets			
Red licorice[k]	3.39	50 g	170
Fruit leather[l]	4.07	2 pieces (30 g)	122
Gummy candies[m]	3.49	105 g	366
Fruit candies[n]	4.04	86 g	347
Fruit punch[o]	0.09	1 cup (~235 g)	21
Total food served	3.89	971	3412
Total food & beverages served	3.43	1451	3636

[a] Cheese Bagel Bites, Three Cheese, H.J. Heinz Company.
[b] Cheese Pizza Rolls, Totino's, General Mills.
[c] Chicken Nuggets, Tyson Foods Inc.
[d] Mozzarella Sticks, Friday's.
[e] Lay's Potato Chips, by Frito Lay.
[f] Chocolate Chip Cookies, Original, Chips A'Hoy, Mondelez International.
[g] Little Bites Fudge Brownies, Entenmann's.
[h] Frosted Chocolate Cake with Creamy Filling, Hostess.
[i] Pop'ems Glazed Donut Holes, Entenmann's.
[j] Whole-fat Chocolate Milk, Schneider Farm.
[k] Twizzler's, Original, The Hershey Company.
[l] Fruit Roll-up, Strawberry, Betty Crocker, General Mills.
[m] Gummy bears, Haribo.
[n] Skittles, Mars.
[o] Kool-aid Bursts, Tropical Punch, Kraft Foods Inc.

preference for the foods used in the EAH procedure from most to least liked.

2.10. Mock training

Children underwent three mock training sessions before the fMRI. In brief, across the first two sessions, children were trained to remain still, respond to questions without moving their heads and to use a button press to respond to the task requirements. Children were also familiarized with the sounds of the scanner. During the third session, children were familiarized with and allowed to practice the task and were informed about the types and quantities for each of the rewards used in the fMRI paradigm.

2.11. 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 (Sweitzer et al., 2014). We modified the task to include food reward trials instead of the cigarette puff trials (Adise et al., 2018, *Under Review*). 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 min and 38 s. The task was presented using E-Prime (version 2.0 Professional). Rewards were earned by guessing (duration 4 s) if a computer-generated number was higher or lower than the number five. After 6 s, 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 s) followed by feedback (win, no win; duration 1 s). A 9-s 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 min.

For each "won" trial, participants earned $0.50 or a few pieces of Skittles or M&M's. 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). Similarly to other studies (Opel et al., 2015; Sweitzer et al., 2014), participants were told that the total reward amounts earned were based on task performance. Preferred candy was selected before undergoing fMRI in attempt to ensure salience. 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. Since no previous studies had modified this task to include a food reward, Skittles and M&M's were chosen as the food reward because it was a discrete unit food that was not only similar in shape but could be distributed in similar increments as monetary rewards. In addition, similar amounts of these exact rewards have been used in an fMRI studies in adults (Levy & Glimcher, 2011).

2.12. 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 × 1.0 × 1.0 mm voxel size. The MPRAGE sequence was approximately 4 min 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 = 2000ms, TE = 24 ms, flip angle = 90°, matrix 64 × 64, FOV = 220 mm, slice thickness = 3 mm, AC-PC transverse, oblique plane determined by the mid-sagittal section, and 3.0 × 3.0 × 3.0 mm voxel size. Thirty-eight oblique sagittal slices were acquired in an interleaved and descending fashion. Each block consisted of 196 vol.

2.13. fMRI preprocessing

Functional images were preprocessed using Analysis of Functional NeuroImages (Cox, 1996). FMRIB Software Library's (FSL) brain extraction tool (BET) (Smith, 2002; Smith et al., 2004; Woolrich et al., 2009) 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 (Burgund et al., 2002), therefore aligning to an adult template would pose minimal differences in our data. In addition, 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

(Silverman, Jedd, & Luciana, 2015).

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. Of note, for reward outcome, trials with missed guesses were excluded from the analyses (n = 241, 5.6% of all trials across participants).

2.14. 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, pp. 1–102). 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. For each subject, the first-level model (i.e., 3ddeconvolve) 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 s (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. We report outcome data for exploratory purposes, since we may have been underpowered to assess differences. In addition, for the reward outcome, the analyses only focused on win trials between conditions.

2.15. Regions of interest

To test our primary hypotheses, we selected regions that have been previously associated with food-cue reactivity in reward, motivation, and inhibitory control. We focused on regions that had previously been implicated in processing of food rewards in children (Bruce et al., 2010; Holsen et al., 2005) and adolescents (Stice & Yokum, 2016; Stice et al., 2011; Yokum, Ng, & Stice, 2011). We selected these regions prior to the experiment based on advice recommended for conducting a 'brain-as-predictor' approach outlined by Berkman and Falk (Berkman & Falk, 2013). The final regions selected included those implicated in reward and motivation [ie., amygdala, caudate, insular cortex, medial prefrontal cortex (mPFC), nucleus accumbens, orbitofrontal cortex (OFC), striatum, and ventromedial prefrontal cortex (vmPFC)] and those implicated in inhibitory control [ie., dorsolateral prefrontal cortex (dlPFC) and inferior frontal gyrus]. Six mm spheres were drawn based on peak voxels on reverse inference functional co-activation masks generated from NeuroSynth (Yarkoni, Poldrack, Nichols, Van Essen, & Wager, 2011) using the term names for each ROI (e.g., caudate) as a keyword (see Table 5 for coordinate locations and a list of ROIs); similar approaches have been used in the literature (Chung, Paulsen, Geier, Luna, & Clark, 2015). The top two peak voxels were selected in order to have ROIs in both the left and right hemispheres. However, in the dlPFC, the top two peaks were both located in the right hemisphere. To be consistent with how we selected other regions, the left hemisphere of the dlPFC was not examined. 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 associated with 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 between weight status groups would not provide insight into individual differences.

Table 5
Regions of interest (ROI) coordinates derived from the peak location based on reversed inference maps gathered from the NeuroSynth database (Yarkoni et al., 2011). MNI coordinates. L = left; R = right.

Region	Hemisphere	*x*	*y*	*z*
Amygdala	L	−22	−4	−18
	R	24	−4	18
Caudate	L	−10	10	6
	R	12	10	14
Dorsolateral Prefrontal Cortex	R	44	38	32
	R	36	38	30
Insular Cortex	L	−40	12	−6
	R	40	6	6
Inferior Frontal Gyrus	L	−48	14	18
	R	54	14	20
Medial Prefontal Cortex		0	52	20
	R	4	56	26
Nucleus Accumbens	L	−10	8	−12
	R	12	10	−10
Orbitofrontal Cortex	L	−24	32	−14
	R	6	36	−20
Dorsal striatum	L	−12	10	−6
	R	14	10	−6
Ventral Striatum	L	−12	8	−10
	R	12	10	−6
Ventromedial prefrontal cortex	L	−4	42	−8
	R	4	26	−14

Contrast values were calculated by subtracting the BOLD response from food reward trials from the BOLD response to money trials (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 Mactinosh V.22.0.0.2 (Armonk, NY: IBM Corp.) for further analyses.

2.16. Statistical analyses

Chi-square and independent samples *t*-tests were conducted to determine differences between weight groups in regards to demographics and food intake. Multiple stepwise regressions were conducted in SPSS to determine the association between BOLD responses in our ROIs and laboratory measures of overeating. Covariates of interest were selected if they were likely to be related to our independent variables (i.e., food intake) such as: BMI *z*-score, liking for study foods, pre-meal fullness, pubertal status, age, sex, total family income, and obesity risk. Covariates were entered into the model and removed if they were not significant. Correction for multiple comparison testing was performed via the Holm-Bonferroni approach (Holm, 1979). All descriptive statistics are reported as means ± standard deviations unless otherwise noted.

3. Results

3.1. Descriptive statistics

There were no differences between weight groups by age in years (χ^2 (4) = 4.9, p = 0.30), sex (χ^2 (1) = 0.4, p = 0.5), pubertal status (χ^2 (5) = 5.2, p = 0.4), tanner stage (χ^2 (4) = 2.6, p = 0.6), or parent education level (χ^2 (4) = 3.1, p = 0.5). There was a difference between weight groups in regards to total family income (χ^2 (5) = 11.6, p = 0.04). 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 (m = 751 ± 209 kcals) and buffet meals (m = 1468 ± 305 kcals) compared to healthy weight children (baseline: m = 573 ± 171; buffet: m = 1138 ± 316 kcals) (all p's < 0.001). No differences by weight status were observed for EAH (t(44) = −1.3, p = 0.2). Regardless of weight status, children ate significantly more at the palatable buffet meal (m = 1295 ± 350 kcals) than the baseline meal (m = 658 ± 209 kcals) (t(57) = −18.2, p < 0.001). There were no differences between child sex and intake at baseline (t(57) = −0.14, p = 0.9) or the palatable buffet meal (t(57) = 1.9, p = 0.06). However, boys ate more (m = 469 ± 258 kcals) during EAH than girls (m = 339 ± 161 kcals). Pearson's correlations showed 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).

3.2. Baseline test meal

3.2.1. Anticipating food compared to money

A model that included BOLD response in the 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) (see Fig. 1). Even though BMI z-score positively predicted food intake (β = 0.35, p = 0.004), activation in the mPFC for anticipating food compared to money was independently associated with increased intake at the baseline meal (β = 0.32, p = 0.009). No other covariates of interest influenced the model.

3.2.2. Winning food compared to money

A model that included the BOLD response in the left orbitofrontal cortex (OFC) 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) (see Fig. 2). In the left OFC, greater response to winning food compared to money was associated with increased intake at the baseline meal (β = 0.32, p = 0.008). Child fullness negatively influenced the model (β = −0.25, p = 0.03), suggesting that children who were more full ate less. However, BMI z-score also positively influenced the model (β = 0.35, p = 0.004) and was a stronger predictor of intake in the model than brain response in the OFC. No other covariates of interest influenced the model.

3.3. Eating in the absence of hunger

3.3.1. 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.

3.3.2. 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 Fig. 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; dlPFC R2: (R^2 = 0.25, F(2,43) = 7.3, p = 0.002). BOLD response in the dlPFC was positively associated with EAH at sites R1 (β = 0.42, p = 0.002) and R2 (β = 0.37, p = 0.009), while fullness level was a negative predictor of amount consumed during EAH for both models (R1 model: β = −0.31, p = 0.021; R2 model: β = −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 region implicated in cognitive control ate more palatable foods when not hungry. No other covariates of interest influenced the aforementioned models.

3.4. Buffet meal

3.4.1. Anticipating food compared to money

BOLD responses in the right, 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 Fig. 4). Along with BMI z-score, BOLD response in the mPFC predicted 29% of the variance in children's palatable buffet meal intake (R^2 = 0.29, F(3,55) = 7.5, p < 0.001). BOLD response in the mPFC positively influenced the model (β = 0.25, p = 0.03), independently of BMI z-score and age, which was also positively associated with food intake (BMI z-score: β = 0.32, p = 0.008; age: β = 0.28, p = 0.02). This suggests that independently of how much children weighed or how old they were, those who had greater response in the mPFC for anticipating food compared to money ate more at the palatable buffet meal. No other covariates of interest influenced the model.

3.4.2. 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 Fig. 4). Together, BOLD response in the left amygdala for winning food compared to money, BMI z-score and age predicted 32% of the variance in buffet meal intake (R^2 = 0.32, F (3,55) = 8.7, p < 0.001). Children who had a greater response to winning food relative to money in the amygdala ate more at the palatable buffet (β = 0.32, p = 0.008), regardless of body weight (β = 0.42, p = 0.001) or age (β = 0.27, p = 0.02). BOLD response in the right (R1) dlPFC to winning food compared to money, BMI z-score, and age predicted 36% of the variance in intake (R^2 = 0.36, F(3,55) = 10.4, p < 0.001). BOLD response in dlPFC (β = 0.37, p = 0.001) positively influenced the model, independently of the effect of child BMI z-score (β = 0.31, p = 0.006) or age (β = 0.27, p = 0.02). BOLD response in the dlPFC was the strongest predictor in this model. This suggests that children who had a greater BOLD response in this region to winning food compared to money ate more at the palatable buffet meal, regardless of weight status or age. No other covariates of interest influenced the aforementioned models.

4. Discussion

This study tested the reward surfeit model of overeating by investigating the relationship between children's brain response to anticipating 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

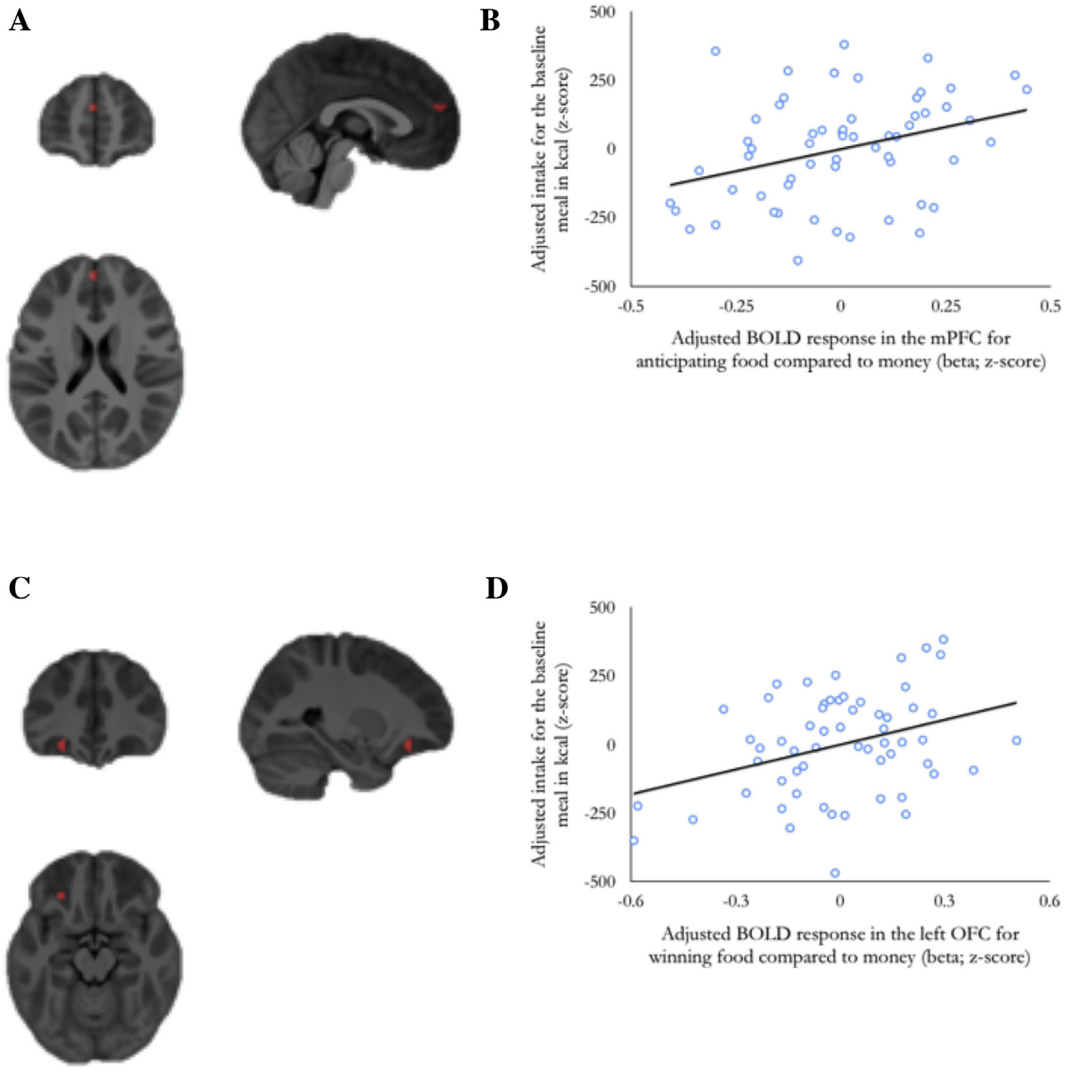

Fig. 2. Localization of (***A***) medial prefrontal cortex (mPFC) ($x = 0$, $y = 52$, $z = 20$). (***B***) Partial correlations between intake (kcal) at the baseline meal and BOLD response in the mPFC BOLD for anticipating food vs. money ($\beta = 0.32$, $p = 0.009$). (***C***) Localization of the left 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.

and palatable buffet meals. We also tested the relationship between children's brain response to winning food compared to money and laboratory measures of food intake. Given that research has stated conflicting theories in regards to reward outcome (i.e., reward surfeit vs. deficit), no *a priori* hypotheses were made. Results showed that 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. However, we also found that 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. This is the first study, to our knowledge, to provide support for the reward surfeit model of overeating using objective measures of food intake.

4.1. Anticipating food compared to money and food intake

In adolescents, BOLD response to anticipating milkshake in regions associated with reward and gustation, such as the caudate and frontal operculum, have been related to BMI (Stice et al., 2008) and measures of energy intake from both self-report and doubly-labeled water (a measure to assess daily metabolic rate) (Burger & Stice, 2013). However, the relationship between how the brain responds to anticipating food rewards and laboratory assessed overeating has not been determined. In the present study, greater brain response to the anticipation of food relative to money in regions of the appetitive brain network such as the amygdala, mPFC, and OFC, 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 did not expect 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 (Leahy et al., 2008; Spill et al., 2010). On the other hand, we expected BOLD response in the mPFC to food relative to

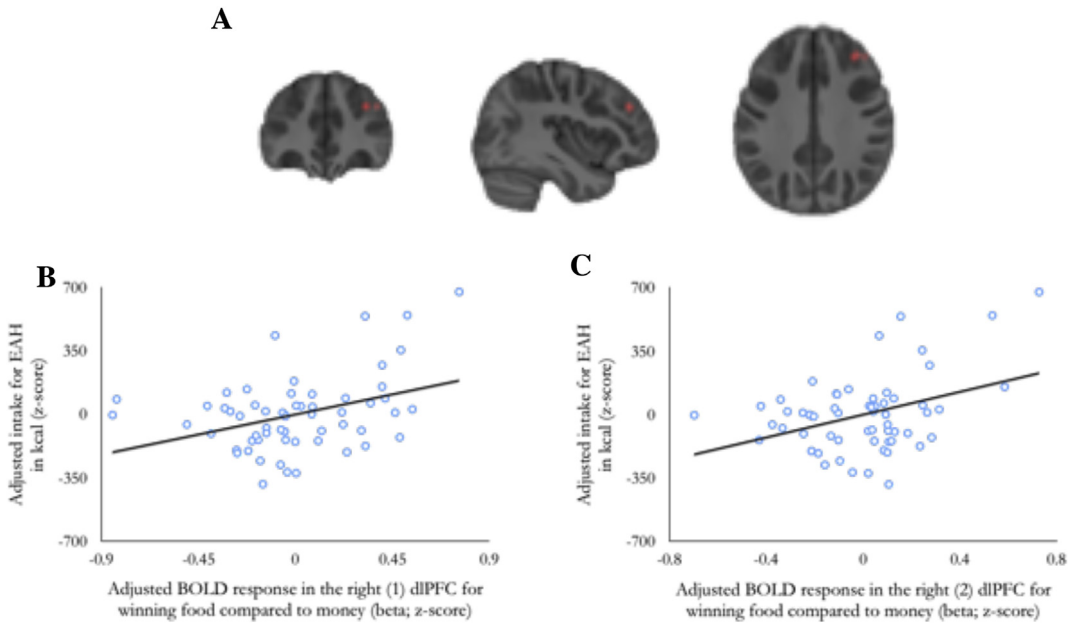

Fig. 3. Localization of the (***A***) right dorsolateral prefrontal cortex (dlPFC) (R1 $x = 44$, $y = 38$, $z = 42$; R2 $x = 36$, $y = 38$, $z = -30$). (***B***) Partial correlations between intake (kcal) during EAH and BOLD response in the right (R1) dlPFC for food vs. money ($\beta = 0.42$, $p = 0.002$). (***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.

money rewards to be associated with intake at the palatable buffet meal, which previously has been associated with overconsumption (Fearnbach et al., 2015). These findings suggest that the mPFC response to anticipating rewards may play a role in food intake behavior. Human studies show that the mPFC is involved in response to food images in a pre-meal state (Martin et al., 2010) while animal studies show that this region is involved in modulating reward-seeking behavior (Ferenczi et al., 2016) and reward processing (Perry et al., 2011), 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 relative to alternative reinforces, like money. Furthermore, increased activation in the mPFC has been associated with vulnerability to drug-related cues (Kober et al., 2016) and attenuation of mPFC activity via transcranial magnetic stimulation (TMS) has been shown to reduce craving in cocaine users (Hanlon et al., 2015). Therefore, another interpretation of our results is that children who have increased mPFC activity may be overeating due to a reward surplus in response to food cues and/or craving. Since our study was not designed to test these associations, future research is needed.

4.2. Winning food compared to money and food intake

There have been mixed findings in the literature examining the receipt of rewards (i.e., outcome) with results demonstrating both a hyper- and hyposensitivity to reward outcome trials 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 (Stice & Yokum, 2016). On the other hand, the reward deficit model suggests that a hyposensitivity to receiving food rewards (e.g., tastes of a milkshake) drives overconsumption as a means to compensate for a reward deficit (Blum, Cull, Sheridan, & Braverman, 1996). However, importantly, none of these studies have evaluated how BOLD response to receiving reward (i.e., positive reward outcome notification) relates to actual food intake. The current findings demonstrate that increased BOLD response in reward processing (e.g., amygdala, OFC) and inhibitory control (e.g., dlPFC) regions to winning food compared to money positively correlated with consumption, suggesting that a generalized *hyper*sensitivity to positive outcomes of winning food relative to money 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 (Mathew-Fenn, Das, & Harbury, 2008; Stice & Yokum, 2016; Sun et al., 2015), which is associated with decreased dopamine receptor density (Noble, 1998; Pohjalainen et al., 1998). 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 (Killgore & Yurgelun-Todd, 2005; Padmanabhan, Geier, Ordaz, Teslovich, & Luna, 2011) 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 (Rothkirch, Schmack, Schlagenhauf, & Sterzer, 2012) and monitoring and processing of outcomes, even in non-rewarding contexts (Schnider, Treyer, & Buck, 2005). In addition, BOLD response in the OFC has been associated with sensory-specific-satiety (i.e., decreased pleasantness of food after eating to satiation) (O'Doherty et al., 2000). Therefore, one interpretation of our results is that children who have an increased BOLD response in this region may overeat due to impaired sensory specific satiety. Moreover, the OFC is one of the most consistently identified regions of the appetitive network (Dagher, 2009; van Meer, van der Laan, Adan, Viergever, & Smeets, 2015) and we have previously found it to be associated with overeating among children in response to increases in portion size (Keller et al., 2018). 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 (Small et al., 2003), 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

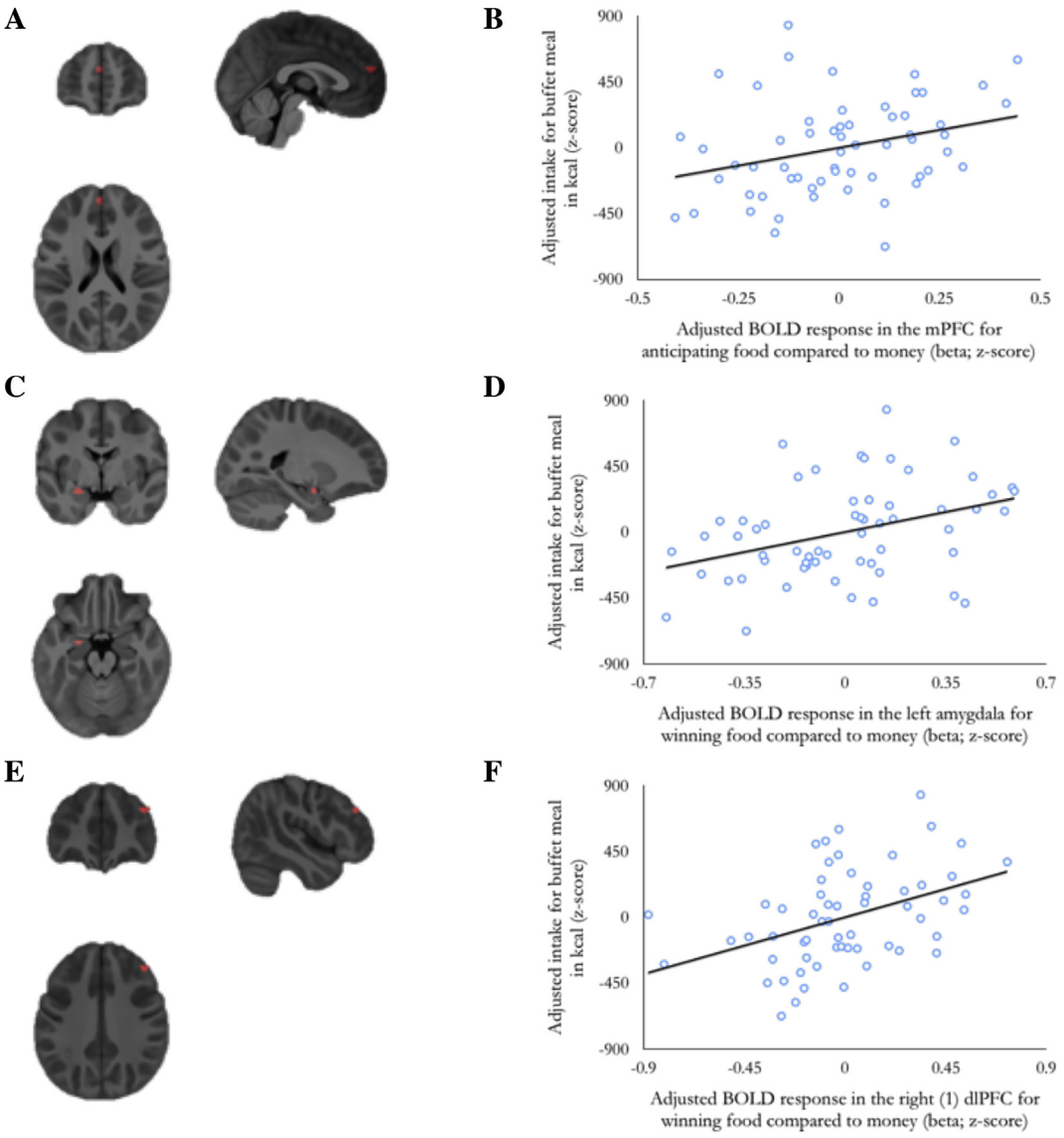

Fig. 4. Localization of the (***A***) medial prefrontal cortex (mPFC) ($x = 0, y = 52, z = 20$). (***B***) Partial correlations between intake (in kcals) at the palatable buffet meal and BOLD response in the mPFC for anticipating food vs. money ($\beta = 0.29, p = 0.02$). (***C***) Localization of the 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 adjusted for BMI z-score.

meals. However, the amygdala is also associated with emotions and memory (Rolls, 2017). Therefore, another interpretation is that excess consumption may be associated with increased emotional processing of food rewards relative to alternative reinforcers. Both of these interpretations require additional investigation.

We also found that brain response to winning food compared to money 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 BOLD response in the dlPFC (an area associated with inhibitory control) may 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 (Davids et al., 2009) and in response to food brands relative to nonfood brands in healthy weight children (Masterson et al., 2017). Similar results were found in adults asked to exercise self-control (Hare, Camerer, & Rangel, 2009), suggesting that greater activation in the dlPFC reflects an attempt to suppress appetitive behaviors. Similarly, exposure to drug-related cues in addicted individuals results in greater dlPFC activation that is associated with craving (Brody et al., 2002), which suggests that heightened activation in this region more generally may correlate with an enhancement in 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.

4.3. Cross-study comparisons

Previous studies have found that in adults and adolescents anticipation and receipt of palatable milkshake evokes BOLD responses in the caudate, putamen, and nucleus accumbens (Babbs et al., 2013; Stice

et al., 2008). In children, reward receipt is also associated with engagement of the insula, operculum, and posterior cingulate (Bohon, 2017). Together, these findings have proposed a network of brain regions implicated in reward processing. In the present study, food intake was associated with BOLD response to food compared to money in some of these regions (e.g., caudate, insula), although these results were not robust enough to surpass multiple comparisons corrections. However, we did find that BOLD responses in the OFC, mPFC, and amygdala for anticipation of food compared to monetary rewards were positively related to food intake. Increased BOLD response in the OFC has been linked to increased BMI in adults (Dong, Jackson, Wang, & Chen, 2015), and this region is thought to be an important contributor to the reward surfeit model (Stice & Yokum, 2016). Although previous studies testing this model have not included discussion of the amygdala and mPFC, these regions are associated with reward processing in adolescents (Silverman et al., 2015). Thus, our findings are generally supportive of the reward surfeit model of overeating. However, it is also important to note that all of the regions discussed have numerous other proposed functions, beyond reward processing. Therefore, one should not rule out other possible interpretations of the brain's role in eating behavior, and additional hypothesis driven studies are needed to further refine our understanding.

4.4. 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 (Birch, Johnson, Andresen, Peters, & Schulte, 1991). 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 (Ma et al., 2006), but we were not powered to evaluate the effects of seasonality on intake in our study. Although children were required to fast for at least three hours before the study, we did not collect measures of the number of hours that had lapsed between the last consumed meal and the start of the study. However, the average starting reported fullness across all visits was only 26% of the scale, indicating that most children were hungry. Moreover, fullness did not affect the relationship between BOLD response to food compared to money and food intake. We also explored whether the child's risk for developing obesity was correlated with food intake and brain response, but found no relationship. However, nearly all of our participants had at least one parent who was classified as overweight or obese, which limits the variability we have in this measure. Lastly, due to time constraints and avoiding child fatigue, meal consumption was assessed on a different visit than the fMRI, which limits the ability to make predictive models of the brain's role in eating behavior.

There were also some limitations regarding our fMRI analyses and experimental design. One 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. Another limitation is that our fMRI paradigm had a relatively long intertrial interval, which may have diminished our BOLD responses between trials. Lastly, our experimental paradigm used money as an alternative reward, and although monetary rewards are popular in children of this age range, they may not be as salient as other reward types such as toys etc. Furthermore, this was a cross-sectional study, which offers limited insight into the longer-term behaviors. Although insight into the mechanisms driving overeating would benefit from a longitudinal design, there are currently few fMRI studies conducted with this age group. Thus, this study served to establish correlational relationship to gather pilot data for longitudinal studies.

5. 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 the amygdala, mPFC, and OFC was associated with how much children eat, independent of how much they weigh. On the other hand, the brain's response in the dlPFC 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.

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Clinical trials registration

The study is registered on www.ClinicalTrials.gov (NCT02855398).

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The authors' responsibilities were as follows - SA: wrote the manuscript; SA, NJR, CFG, and KLK designed the research project (project conception, development, research plan, and study oversight). SA performed the analysis with the guidance of CFG and KLK. SA conducted the research (hands-on conduct of experiments, data collection, and analysis). CNW contributed to study design. All authors contributed feedback, and read and approved the final manuscript. No authors report any conflicts of interest.

Appendix A. Supplementary data

Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.appet.2018.06.014.

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