Title: Adolescents with versus without parental obesity show greater striatal response to increased sugar, but not fat content of milkshakes.

Abbreviated title: Obesity risk & response to food stimuli

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Abstract

Children of overweight/obese parents are at a high-risk of developing obesity. This study sought to examine the underlying neural factors related to parental obesity risk and the relative impact of sugar and fat when consuming a palatable food, as well as the impact of obesity risk status on brain response to appetizing food images. Using functional MRI, 108 healthy weight adolescents' (BMI 20.9 ± 1.9 ; $n=53$ high-risk by virtue of parental obesity status, $n=55$ low-risk) response to food stimuli were examined. Stimuli included four milkshakes systematically varied in sugar and fat content, a calorie-free tasteless solution, and images of appetizing foods and glasses of water. High risk vs. low risk adolescents showed greater BOLD response to milkshakes (all variants collapsed) > tasteless solution receipt in the primary gustatory and oral somatosensory cortices ($pFWE < 0.05$) replicating a previous report. Notably, high risk adolescents showed greater caudate, gustatory and oral somatosensory response to the high-sugar milkshake > tasteless solution contrast, however an effect of risk status was not seen in the high-fat milkshake contrast ($pFWE < 0.05$). Foods images were not related to obesity risk status. Collectively, data presented here suggests that parental weight status contributes to greater striatal, gustatory, somatosensory response to palatable foods, in particular high-sugar foods in their adolescent offspring, which may contribute to the increased risk for future overeating.

Significance Statement

Healthy weight adolescents with overweight/obese parents versus normal weight parents are at greater risk of becoming obese later in life. Adolescents at high risk for obesity showed greater response to milkshake receipt in areas of the brain regions that are thought to encode aspects of gustatory and reward processing. This effect was more robust when the sugar content was relatively higher than fat. Moreover, this effect was specific to receipt of a palatable food, but not images of appetizing foods. Results indicate that increased neural response to consuming high sugar content may underlie adolescents' obesity risk. Results indicate that parental weight status may bias adolescent offspring neural response to high sugar palatable.

Introduction

Adolescent obesity prevalence has increased from 10.5% between 1988-1994 to over 20% in 2013-2014 in the United States (Singh et al., 2008; Ogden et al., 2016), increasing risk for obesity and comorbid diseases in adulthood (Goran et al., 2003; Attard et al., 2013; Höglström et al., 2015; Llewellyn et al., 2016). Adolescence is a critical developmental period for the examination for obesity risk factors given the increased independence over lifestyle and dietary decisions (Bassett et al., 2008). Evidence consistently indicates that elevated palatability of high-sugar and high-fat laden foods underlies poor dietary decisions and is a known barrier to healthy eating in adolescents (Stevenson et al., 2007; Drewnowski, 2009; Krebs, 2009). However, predisposing risk factors that initiate and perpetuate hedonically motivated food intake are largely unclear.

Functional MRI (fMRI) research has begun to uncover the neural correlates of ingestive behaviors in humans including aberrant eating patterns. Intake of palatable food elicits increased blood flow and blood oxygen level dependent (BOLD) response in the striatum, midbrain, amygdala, and orbitofrontal cortex, regions frequently implicated in hedonically motivated behavior and reward (Small et al., 2001; O'Doherty et al., 2002; Valentin et al., 2007; Page et al., 2013; Stice et al., 2013a; Jastreboff et al., 2016). Moreover, studies in both humans and animals have reported that eating behaviors and weight status influence neural response to palatable food (Johnson and Kenny, 2010a, 2010b; Babbs et al., 2013; Contreras-Rodríguez et al., 2015; Cosgrove et al., 2015). While these studies suggest a strong role of neural functioning impacting hedonically motivated food intake, typically they evaluate differences between weight status and thus are unable draw inference regarding initial obesity risk factors.

One approach to identifying precursors for overeating is to compare healthy weight adolescents that are at high and low risk for obesity by virtue of parental overweight/obesity status. Parental body mass index (BMI) is a reliable and relatively robust predictor for obesity in their offspring (Faith et al., 2006; Jacobson et al., 2006; Kumar et al., 2010; Rath et al., 2016) as

it reflects both environmental and genetic factors that are thought to impact weight gain (Faith et al., 1999). For example, parental obesity has been shown to increase preference for palatable, high energy foods in their offspring (Birch and Fisher, 1995; Wardle et al., 2001) and preference for these foods increases obesity risk (Salbe et al., 2002; Johnson and Wardle, 2014). In support, preclinical experiments demonstrate the obesity prone versus obesity resistant animals show a greater preference for sweet and fatty foods and increased hedonically motivated behaviors prior the onset of diet induced obesity (Shin et al., 2011; Vogel et al., 2017). Collectively these reports indicate, parental overweight/obese status may increase obesity risk in their offspring via increased hedonically motivated food intake promoting overconsumption.

Utilizing both neuroimaging techniques and parental weight status is, in principle, a strong approach assess the underpinnings of obesity risk factors during adolescents. Previously, healthy-weight adolescents with overweight/obese parents, versus those with healthy weight parents, exhibited a heightened BOLD response to palatable milkshake receipt in regions associated with encoding aspects of gustatory, somatosensory, and reward processes (Stice et al., 2011). While that initial study uncovered possible neural contributors underlying obesity risk stemming from parental weight status, the relative impact of macronutrient content in the tastants consumed and the response to appetizing food images are unknown. Preclinical work suggests the sugar and fat composition of palatable food imparts differential motivation to eat and weight gain (Avena et al., 2009). Moreover, in general, neuroimaging has placed a large emphasis on reliability of results, as such replication of this previous report is merited. The purpose of the present report is to examine a larger sample of adolescents at high versus low risk for obesity by parental obesity, examine response to milkshakes that varied parametrically in fat and sugar content, and examine neural response to images of palatable foods extends results from an initial study.

Materials and Methods

Participants

In total, 133 participants completed the study, of which 108 had parental weight status for both parents. This analysis included 53 male and 55 female healthy-weight adolescents (M age 15.01 ± 0.86). Participants were considered at high risk if they had two overweight/obese parents ($n = 53$), and were considered at low risk if they had an overweight parent and a normal weight parent or two normal weight parents ($n = 55$). We modeled parental overweight status in this manner because it resulted in similar group sizes, putatively increasing sensitivity. Demographic information on the full sample and between risk groups can be found in **Table 1**. Individuals who reported binge eating or compensatory behavior in the past 3 months, any use of psychotropic medications or illicit drugs, head injury with a loss of consciousness, or Axis I psychiatric disorder in the past year (including anorexia nervosa, bulimia nervosa, or binge eating disorder) were excluded. Data were collected in at the Oregon Health Sciences University. All parents provided written informed consent and adolescents provided written assent. Oregon Research Institute's Institutional Review Board approved all methods, registration can be seen at clinicaltrials.gov as DK092468.

Experimental Design

Height was measured to the nearest mm using a stadiometer. Weight was assessed to the nearest 0.1 kg using digital scales with participants wearing light clothing without shoes at each assessment. BMI (kg/m^2) correlates with measures of body fat ($r = 0.80-0.90$) and with biomarkers of health in young adult samples (Dietz and Robinson, 1998; Davis et al., 2009). BMI measures were collected at baseline to confirm the present effects were not driven by differences in weight, and to confirm risk status BMI was tested at 1-year, 2-year and 3-year follow-ups. We recruited adolescents in the healthy weight range to ensure that a history of overeating did not contribute to any differences in BOLD response between groups.

On the scan day, participants were asked to fast for 4 hours before the scanning session to standardize feelings of hunger (Stice et al., 2013b). A block milkshake paradigm was used to assess BOLD response to milkshakes with varying fat and sugar content: high-sugar/high-fat,

high-sugar/low-fat, low-sugar/high-fat and low-sugar/low-fat milkshakes, along with a tasteless solution as a control contrast. Details on the block paradigm, scanner acquisition parameters, and the composition of the milkshakes and tasteless solution have been previously published (Stice et al., 2013b). Briefly, milkshake or tasteless solution was delivered into the scanner via a gustometer. A one second cue preceded all milkshake receipt, followed by a fixation cross during the taste administration. Milkshakes were delivered over a 5 second period followed by 3 seconds to swallow. Administration of milkshake and tasteless solution occurred in variable length blocks of 4, 5, or 7 milkshake or tasteless administration events. The order of the milkshake or tasteless blocks was randomized. Subjects received a rinse of tasteless solution between milkshake tastes, followed by a swallow cue and a variable jitter (9-11s). Two runs were preformed, with each run consisting of 3 blocks of each of the 4 milkshake types and tasteless solution in a random order making 6 blocks of each of the 5 tastants (Stice et al., 2013b).

A food picture exposure paradigm was used to assess BOLD response to images of appetizing and unappetizing foods, and to images of glasses of water. To account for the high variability in food preferences a self-rating approached was used at a session prior to scan day. Participants rated 103 food images on a visual analogue scale for how appetizing the food looked (0 - 100). The foods depicted in the pictures varied by macronutrient content and energy density, but were matched on size, brightness, and had a minimum number of pixels. Pictures rated extremely low (0) were eliminated as not to elicit a 'disgust' response. During the fMRI scan, the participants were exposed to the 32 pictures they rated most appetizing and to the 32 pictures they rated as the least appetizing, along with 32 images of glasses of water as a neutral stimulus (which were the same for all participants). All pictures were presented for 4.5 seconds with a 4-11 second (mean 5.5s) inter-stimulus jitter where a fixation cross allowed for BOLD recovery and eliminated random eye-movement.

Scanning was performed using a Siemens Tim Trio 3T MRI scanner. Functional scans used a T2* weighted gradient single-shot echo planar imaging (EPI) sequence (TE = 30ms, TR = 2000ms, flip angle=80°) with an in-plane resolution of 3.0 x 3.0 mm² (64 x 64 matrix; 192 x 192 mm² field of view). Thirty-two 4mm slices (interleaved acquisition, no skip) were acquired along the AC-PC transverse oblique plane, as determined by the midsagittal section.

fMRI preprocessing and statistical analysis

Data was preprocessed and analyzed using FMRIB Software Library (FSL version 5.0.9) (Jenkinson et al., 2012). Brains were skull stripped using FSL's brain extraction tool (BET). Time series were then motion corrected using MCFLIRT, and the 18 motion regressors created and their derivatives were included in first level model. B0 unwrapping was implemented to correct for potential magnetic field inhomogeneities with a signal loss threshold of 10% and slice-timing correction was used with a custom slice order file. Functional data was smoothed with a 5.0mm full width half maximum isotropic Gaussian kernel, and a high pass temporal filter of 90s was used. Functional images were registered to their T1 weighted structural scan and to the standard Montreal Neurological Institute (MNI) template brain using FNIRT with a 10mm warp resolution. Normalization resulted in a voxel size of 2mm³ for functional images, and 1mm³ for structural images.

To test BOLD response to tastant receipt we created a general linear model with regressor and temporal derivatives for receipt of each type milkshake (four regressors) and tasteless solution as regressors of interest. The milkshake cue, the tasteless cue, and the rinse receipt and their derivatives were included as confounds. A similar approach was used for the picture paradigm. All regressors were convolved using the double-gamma hemodynamic response function. The model was prewhitened with FSL's FILM tool (Woolrich et al., 2001). All the milkshakes combined were compared to the tasteless solution (all milkshake > tasteless). In addition, each type of milkshake was compared to the tasteless solution individually (high-sugar/high-fat milkshake > tasteless; high-sugar milkshake > tasteless; high-fat milkshake >

tasteless; low-sugar/low-fat milkshake > tasteless). To assess brain regions associated with viewing appetizing foods, the appetizing food pictures were compared to pictures of water (appetizing food pictures > pictures of glasses of water). This contrast was chosen for the picture paradigm because it most closely resembles the milkshake contrasts used (milkshake receipt > tasteless solution receipt) where a palatable/appetizing beverage/food is contrasted against a water-type control.

Individual-level data (fixed-effects) were averaged and taken to group-level (mixed effects) analysis to assess the difference between the high and low risk for obesity groups. Between group T-Tests were used to test differences in the aforementioned contrasts between the high and low obesity risk groups using FSL's FLAME 1. Nonparametric permutation testing was preformed using FSL's randomize using the threshold free cluster enhancement (TFCE) algorithm with 5000 permutations (Smith and Nichols, 2009). Clusters after randomization were considered significant if a cluster had $pFWE < 0.05$ and a cluster $k > 10$ (Lieberman and Cunningham, 2009; Roiser et al., 2016). All stereostatic coordinates are presented in MNI space. Analyses of all non-imaging data were performed in R (v. 3.3.1, Vienna, Austria).

Confirmatory analyses of risk status

The purpose of this report was to examine obesity risk status. To confirm obesity risk status two tests were used; hierarchal linear modeling and a T-test at the last point of BMI data collection. Individual change in BMI was modeled using a mixed-effects model with visit (baseline, year-1, year-2, and year-3) and participant as a random slope and intercept respectively (lme4, v. 1.1-12). These models offer a flexible and powerful technique for modeling change in continuous variables and use maximum likelihood estimation to accommodate missing data (Singer, 1998). To build these models we: a) examined plots; b) fit a conditional means model; c) fit a conditional linear slope model; and d) fit spline models of 2 and 3. We compared the linear and spline models for model fit quality using a likelihood ratio test.

Post-hoc unpaired T-Tests were used to assess risk dependent differences in BMI at the year 3 follow-up.

Results

Impact of risk status on brain response to palatable food receipt

Brain regions where high-risk adolescents showed significantly greater BOLD response during receipt the various milkshake contrasts relative to their low risk counterparts are summarized in **Table 2**. High vs. low risk adolescents exhibited increased BOLD response during receipt when collapsing across all 4 milkshakes versus tasteless solution in the insula (**Figure 1A** $r = 0.29$, $p_{FWE} = 0.04$), lateral orbital frontal cortex (**Figure 1B**, $r = 0.39$, $p_{FWE} = 0.03$), postcentral gyrus ($r = 0.42$, $p_{FWE} = 0.02$), and the precentral gyrus ($r = 0.39$, $p_{FWE} = 0.04$). When using the high-sugar milkshake versus tasteless solution contrast, high risk versus low risk adolescents showed greater BOLD response in the caudate (**Figure 1C**, $r = 0.35$, $p_{FWE} = 0.03$), central operculum (**Figure 1D**, $r = 0.37$, $p_{FWE} = 0.04$), superior temporal gyrus ($r = 0.42$, $p_{FWE} = 0.03$), juxapositional lobule ($r = 0.28$, $p_{FWE} = 0.03$), and the thalamus ($r = 0.30$, $p_{FWE} = 0.03$).

No significant effect of obesity risk status was observed when testing the high-sugar/high-fat milkshake versus tasteless solution contrast, the high-fat milkshake vs. tasteless solution contrast or the low-sugar/low-fat versus tasteless solution contrast.

Impact of risk status on brain response to appetizing food images

No significant differences between risk groups was observed when viewing pictures of self-selected appetizing foods versus pictures of glasses of water. Of note, appetizing foods were selected by each individual, rather than some other standardized characteristic of the food presented, e.g., fat/sugar density, food phase or typical eating occasion. This was done intentionally as food preferences are highly variable between individuals and the purpose of this paradigm was to examine neural response to food images rated as highly palatable across the sample.

Confirmatory analyses of risk status

Confirmatory analyses to insure fMRI results were not driven by current weight status or other confounds revealed that baseline BMI ($p = 0.28$) and demographic characteristics did not vary by risk status (**Figure 2A**; Table 1). BMI trajectory analyses of risk status revealed that over the 3-year follow-up high risk adolescents linear slope of BMI did not differ from low risk adolescents (**Figure 2B**; $p = 0.21$). Likelihood ratio test of the linear slope relative to spline models indicated that the splines did not fit the data significantly better than a linear slope (2-spline $p = 0.07$; 3-spline $p = 0.36$). However, in support of the obesity risk status definition herein, a post-hoc test revealed that high obesity risk participants were significantly heavier than low risk participants at the 3-year follow-up visit (**Figure 2C**, $p = 0.02$).

Discussion

Adolescents at high risk of developing obesity showed elevated BOLD response to intake of palatable milkshake in brain regions associated with encoding gustatory and reward processing when compared to those at lower obesity risk independent of current BMI. Further, higher sugar content in the milkshake consumed elicited a more robust response in regions that are thought encode gustatory processing and hedonically motivated behaviors/reward. The finding that higher sugar elicits a greater striatal response dovetails a previous report from a subsample of these participants showing when calories were consistent across milkshakes, higher sugar content elicited a stronger BOLD response compared to higher fat content (Stice et al., 2013b). Preclinical work further supports these results, with sugar, but not fat, increasing and maintaining hedonically motivated eating behavior e.g., compulsive like eating (Avena et al., 2009; Johnson and Kenny, 2010b). This potent capacity of sugar to elicit a strong response in hedonically motivated behaviors has led some research to draw parallels to neural response to substances of abuse (Avena et al., 2009; Johnson and Kenny, 2010b).

A viable alternative interpretation of the relative contribution of sugar compared to fat is that fat content, at a certain threshold, acts to dampen the striatal, gustatory, and

somatosensory response. While fat and sugar both provide calories, and are associated with high palatability, they are fundamentally different in terms of hedonic sensation (Drewnowski, 1993). Ingestion of sugar is more readily associated with hedonic aspects of taste and fat is more associated with texture and mouth feel. Therefore, it is possible that repeated exposure to high fat milkshakes over the course of the experiment decreased striatal response due the creamy and thick texture of fat imparting sensory specific satiety (Rolls et al., 1981; Yeomans et al., 2017). The dampening effects of high fat content may have also contributed to the lack of impact of risk status seen when testing the high-sugar/high-fat milkshake. In contrast, we did see an effect when collapsing across all milkshakes. This could be a result of the aggregate tastant containing high amounts of sugar and greater power given the increased number of events tested. No effect of risk was seen when directly contrasting the high sugar and high fat milkshakes, which would be the most direct test of our abovementioned hypotheses around sugar and fat. These milkshakes were the same flavor and eucaloric, and thus only varied on macronutrient composition. The lack of effect here may be a function the highly conservative nature of the milkshake versus milkshake comparison, a concept supported by the null finding when testing against the low-sugar/low-fat milkshake. Further, both the high-sugar and high-fat milkshakes did contain the disparate macronutrient, i.e., the high sugar contained fat and vice versa, an approach selected to best mimic foods found in the natural environment. As such, presenting and comparing tastants that only contain sugar to a tastant that only contains fat may be the ideal in future work.

In general, results presented here replicate previous findings demonstrating the relationship of parental overweight status on greater striatal region response to tastes of a palatable food, but not to visual cues signaling impending high-calorie food tastes (Stice et al., 2011). The present results are from an independent sample, examined on a different magnet, using a different paradigm, and a different analytic approach. Thus, this study meets the replication criteria that has been suggested for full generalizability/conceptual replicability

(Condon et al., 2017). Behaviorally, these findings may contribute to parental overweight status increasing preferences for energy dense foods (Wardle et al., 2001; De Cosmi et al., 2017). Further, this analysis is in accord with the broader field of parental impact on hedonically motivated behaviors (Gilman et al., 2007; Bjork et al., 2008; Heitzeg et al., 2008; Hill et al., 2009; Andrews et al., 2011; Stice and Yokum, 2014). For example, substance abuse research has reported that adolescent children of parents with alcoholism show altered reward processing (e.g., decreased sensitivity to loss in the striatum and increased impulsivity), as well as increased risk of developing alcoholism later in life compared to children from parents without alcoholism (Gilman et al., 2007; Bjork et al., 2008; Heitzeg et al., 2008; Hill et al., 2009; Andrews et al., 2011). Specifically, increased BOLD response was found in the caudate of adolescents at risk for alcoholism (Heitzeg et al., 2010) similar to an increased BOLD response found in the caudate of individuals at risk for obesity responding to sugar presented here. Additionally, adolescents of parents with versus without a history of parental substance use disorder showed greater BOLD response to milkshake versus tasteless solution in the right orbital frontal cortex (Stice and Yokum, 2014), similar to the result of greater BOLD response in right orbital frontal cortex to the aggregate milkshake in high obesity risk adolescents compared to low obesity risk. Furthermore, elevated response to a monetary reward was associated with increased risk of substance abuse at a one-year follow up in adolescents (Stice et al., 2013c), suggesting that parental maladaptive reward learning behaviors may be passed to their children across rewarding modalities.

On a theoretical level, the present report and previous work supports tenants of the dynamic vulnerability model of obesity, suggesting parental obesity may underlie the initial obesity risk factors (Burger and Stice, 2011a; Stice et al., 2011). As reported here, we observed a hyper-responsivity in striatal and gustatory regions to intake of palatable foods, particularly those high in sugar, but not to appetizing food images. As seen in the dynamic vulnerability model, the initial stage is associated with greater striatal response to taste that potentiates

overeating and a lack of response to food cues. Where the decreased striatal response and heightened response to food cues, as seen in obesity, develop as a function of habitual overeating and weight gain (Burger and Stice, 2011a; Stice et al., 2011). Multiple theories of obesity, based on several reports, support the tenants of this model (Wang et al., 2001; Stice et al., 2008a, 2008b; Volkow et al., 2008; Burger and Stice, 2011b, 2012, 2013; Yokum et al., 2012; Demos et al., 2012; Geha et al., 2013; Cosgrove et al., 2015; Burger, 2017). Though, it is noteworthy that the null finding associated with the response to the appetizing food images could be a function of the manner in which the stimuli were selected. Specifically, the images were selected on individual preference, not as a function of food characteristics, e.g., fat content, where the latter would be a closer analog to the tastants presented. Given the nature of the paradigm design, attempting to analyze the data by macronutrient content is not viable as participants would have a varied number of exposures. Lastly, given the above findings, sugar's robust ability to elicit reward circuitry and the knowledge that fat provides more energy density (kcal/g), it is reasonable to suggest that sugar is more associated with creating and maintaining habitual overeating and the fat typically paired with sugary foods more readily contributes to excess calories (Avena et al., 2009; Johnson and Kenny, 2010b). This 'synergistic input' of fat and sugar content to overeating and weight gain notion, is relatively parsimonious from a public health standpoint, but it may provide additional information of the relative neural impact of macronutrients, and thus is worth further investigation.

The period of adolescences is a critical time point in the development of dopaminergic systems resulting in over-performance of hedonically motivated behaviors (Galvan et al., 2006). An increase in risk taking, impulsivity, and reward seeking is commonly reported throughout adolescences (Ernst et al., 2006; Ernst and Luciana, 2015). Preclinical studies have shown that dopamine levels in the striatum peak in adolescences and cortical and subcortical dopamine receptors (both 1 and 2) increase in density (Lidow and Rakic, 1992; Teicher et al., 1993; Reichelt, 2016). Together this suggests that during adolescences, the brain is primed to learn

rewarding behaviors, but is also predisposed towards hedonically motivated and impulsive behaviors (Blakemore and Choudhury, 2006; Galvan, 2010). Adolescence is also a period of increased autonomy in both lifestyle and dietary decisions (Bassett et al., 2008). Thus, in theory, adolescence may be a critical period for developing and establishing habits around hedonically motivated behaviors such as repeated consumption of high-sugar, high-fat palatable foods.

In conclusion, results indicate that parental weight status was associated with greater BOLD response to high-sugar and high-fat milkshakes, with sugar being more robustly implicated in regions thought to encode hedonically motivated behavior. Where images of individually preferred foods did not differ by risk status. As such the present report provides data supporting the initial tenants of the dynamic vulnerability model of obesity, which suggests that individual differences in reward region response to high-calorie food plays a role in the etiology of overeating and obesity.

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Figure Legends.

Figure 1. Greater activation in the left insula (A: 46,-4,-2 $Z = 2.99$, $pFWE = 0.04$, $k = 30$) and left orbital frontal cortex (40, 22, 8, $Z = 4.07$, $pFWE = 0.03$, $k = 257$) in the high risk group compared to the low risk group during receipt of all milkshakes – tasteless solution. Greater activation in the left caudate (C: 10, 10, 14 $Z = 3.68$, $pFWE = 0.03$, $k = 11$) and left central opercular (44, 8, 6, $Z = 3.86$, $pFWE = 0.04$, $k = 40$) in the high risk group compared to the low risk group during receipt of high-sugar milkshake – tasteless solution.

Figure 2. No difference in BMI was seen between the high and low risk groups at baseline (A: $p=0.28$). Trend analysis did not a difference by risk status over the course of the 3-year follow period (B: $p=0.21$). However, post hoc analysis showed at the 3-year follow up visit, the high risk compared, to low risk subjects, had significantly higher BMI (C: $p=0.02$).

Table 1. Sample demographics by obesity risk status

	Full sample	High Risk N=53	Low Risk N=55
Participant BMI ^a	20.9± 1.9	21.1± 1.8	20.7± 2.0
Mom BMI ^a	27.0± 5.8	31.2± 5.1	22.9± 2.9
Dad BMI ^a	28.17± 4.4	29.6± 4.0	26.8± 4.3
Age ^a	15.01± 0.86	14.91± 0.81	15.11± 0.9
Sex (m/f)	53/55	29/24	24/31
Race ^b			
Non-Hispanic White	75%	34%	40%
Non-Hispanic Black	2%	1%	1%
Hispanic	12%	11%	1%
Asian/Pacific Islander	6%	2%	4%
Native American	3%	0	3%
Multirace/other	3%	1%	2%

^aMean±SD; ^bPercentage of the sample

Table 2. Brain regions with significantly greater BOLD response to milkshake stimuli in adolescents at risk for obesity compared to those at low risk for obesity

Contrast and Regions	k	P-1	Z-value	r	x	y	z
High risk > Low risk							
<i>All Milkshakes > Tasteless Solution</i>							
Postcentral gyrus	2003	0.98	4.34	0.42	68	-8	24
Central Opercular Cortex			4.09	0.39	50	-18	20
Parietal operculum			4.04	0.38	50	-30	20
Orbital frontal cortex	257	0.97	4.07	0.39	40	22	-8
Precentral gyrus	63	0.96	4.20	0.39	48	0	40
Insula	30	0.96	2.99	0.29	46	-4	-2
<i>High-Sugar Milkshake > Tasteless Solution</i>							
Superior temporal gyrus	3133	0.97	4.37	0.42	70	-50	6
Planum temporal gyrus			4.12	0.39	50	-34	16
Parietal operculum			4.00	0.28	46	-26	22
Central Opercular Cortex	40	0.96	3.86	0.37	44	8	6
Juxtapositional lobule	24	0.96	2.91	0.28	6	-2	64
Thalamus	13	0.97	3.16	0.30	12	-10	6
Caudate	11	0.97	3.68	0.35	10	10	14
k = cluster size at 2x2x2							
$r = Z/\sqrt{n}$							
P values and clusters were generated using threshold free cluster estimation through FSL's randomize, and then parcellated to better probe independent clusters, local maxima were calculated with FSL's cluster tool in randomise. Local maxima are listed under the cluster they fall within. Coordinates are presented in MNI space.							

Figure 1.

Figure 2.