ABSTRACT

The study aimed to explore how both sex and dietary restraint impacts brain activation in response to visual food stimuli in young adolescents (12-13 y) under fed and fasted conditions.

Food and non-food images were viewed by 15 boys and 14 girls while functional magnetic resonance images were acquired. The adolescents were either fasted or in a satiated (fed) state following a randomised crossover study design.

When satiation state was not considered, girls showed significantly greater brain activity than boys in regions associated with executive function and decision making, working memory, and self-awareness. In contrast, when either fasted or fed states were considered separately, boys showed significantly increased brain activity in regions linked to executive function, self-awareness and decision making than the girls. When fasted, compared to unrestrained eaters, restrained individuals showed heightened activation in regions connected to executive function and decision making, with areas associated with self-assessment showing increased activity for unrestrained eaters relative to restrained under fed conditions.

These findings highlight important differences in adolescent brain activity and support further investigations to gain greater insight into how these differences might evolve with age.

1. INTRODUCTION

Whether through the media, on screen, in print or via the observation of others eating, individuals are continually exposed to visual food cues. Given the high prevalence of childhood obesity (1, 2), gaining greater insight into the processing of such cues, particularly their impact on energy intake and reward homeostasis, is a key area of interest. Any detection of underlying differences in brain function in children relative to adults in response to cues of unhealthy food being displayed is of particular importance, as it may be indicative of an underlying susceptibility to such cues. Studies subsequently examining such responses have indeed shown greater activation in children than adults in a range of brain areas (3). In addition, children display greater responsiveness to high energy density food cues than low energy density (4, 5) and to larger portion sizes (5), as well as exhibiting a correlation between body composition and the degree of brain response (4).

Specific susceptibility to weight gain differs between individuals (6), making any identifiable predictive factor important to public health research. One proposed variable is dietary restraint, which refers to the conscious restriction of energy intake for the purpose of weight control. It has been suggested that those with high levels of dietary restraint are at an increased risk of obesity (7), binge eating and bulimia nervosa (8). However, assessments of brain activation differences between restrained and unrestrained eaters when exposed to food cues are limited. Coletta, Platek (9) observed increased activity in brain regions associated with desire for food and reward in female fed restrained individuals when compared to unrestrained females. By comparison, unrestrained females showed increased activity in brain regions associated with inhibition and memory (9). Similarly, Burger and Stice (8) reported restrained fasted female eaters displaying increased activation in response to food stimuli in regions associated with food reward. These findings correlate well with the theoretical model of reward circuitry hyper-responsiveness of food intake in restrained

eaters, whereby significantly heightened reward response is observed when food is consumed (10, 11). For example, a study in adults showed a positive associative correlation between dietary restraint scores and dopamine release in the dorsal striatum on presentation of food (12). However, the age at which these distinctions present in response to food stimuli, and whether they represent a cause or a consequence of restrained behaviour are currently unknown and thus warrant further investigation.

When examining neurocognitive functioning and reward processing in response to food stimuli in adults, significant sex differences have also been shown. Females display greater responses to visual food stimuli than males, with increased activation in regions associated with sensory processing, such as the fusiform gyrus (13) and high-level decision making, self–reflection, feelings of hunger and current need status such as the dorsolateral and inferior lateral orbitofrontal cortex, the medial orbitofrontal cortex, and the posterior/middle cingulate gyrus (14). However, similarly to restrained/unrestrained behaviour, the age at which sex distinctions in response to food cues become apparent remains unclear.

The aim of the study was to undertake a small initial exploratory assessment to examine if both participant sex and dietary restraint characteristics impact on brain activity in 12-13 year olds in response to visual food stimuli under both fed and fasted conditions, as determined by functional magnetic resonance imaging (fMRI). As morphology and brain function significantly change during adolescence (15) this study will provide preliminary data examining the response within this age group that will aid subsequent larger studies which aim to investigate at what age brain responses begin to reflect those typically seen in adults, thereby providing further insight into the dynamic nature of eating behaviour.

2. SUBJECTS AND METHODS

2.1 Participants

The study was conducted in accordance with the guidelines of the Declaration of Helsinki, the British Association of Sport and Exercise Sciences (BASES) and the British Education Research Association (BERA). Institutional ethics committee approved all procedures and all participating adolescents provided written informed assent, together with written consent from their parents or caregivers.

A local secondary school in the South West of England gave permission for the researchers to verbally introduce the study to the whole of the year eight year group, (12 – 13 y old adolescents). The 169 adolescents who expressed an interest in the study were asked to complete the Dutch Eating Behaviour Questionnaire for Children (DEBQ-C; (16)) which provides a continuous value for dietary restraint between 1 (strongly unrestrained) and 3 (highly restrained). Thus, from the restrained eating behaviour scores attained, the 16 highest scoring (restrained eaters; scoring between 1.86 to 3) and 16 lowest scoring (unrestrained eaters; scoring between 1 to 1.29) participants were recruited, evenly distributed across sex. Over the course of the data collection period, one boy and two girls dropped out of the study, as a result of a dislike of the scanner environment (1 boy, 1 girl) or a dislike of eating breakfast (1 girl). As a result, groups consisted of eight restrained boys (R-Boy), seven unrestrained boys (UR-Boy), six restrained girls (R-Girl) and eight unrestrained girls (UR-Girl). All participant characteristics are presented in Table 1.

2.2 Study procedure

The study was a randomised crossover-design. On the first visit participants were randomly assigned, in a counterbalanced order, to either the fasted or fed condition, with the reverse condition being completed on their second visit. Following an overnight fast, participants arrived at 0830 h at the Institutes Magnetic Resonance Centre where they verbally confirmed their adherence to the overnight fast before testing procedures began. On visit 1 between

0830 h and 0850 h, participants were visually familiarised with the food images to be used within the testing procedure to ensure they were able to identify them. If a food was not recognised, time was taken to describe it to establish a basic level of familiarity. On visit 2 the same time period was used to collect anthropometric measurements (stature, sitting stature and body mass), which was subsequently used to calculate BMI and peak height velocity (PHV (17)).

Measures of appetite were taken immediately before and after the fMRI protocol using a 100 mm visual analogue scale (VAS (18)). Hunger was assessed by the question 'How hungry are you now?' with participants requested to quantify their response by drawing a line on the VAS, where the left extreme represented 'not at all' and the right extreme 'very hungry'. Similarly fullness was assessed by the question, 'How full do you feel now?' anchored on the left by 'empty' and right by 'very full'. Finally, prospective consumption (desire to eat) was assessed using the question 'How much would you eat right now?' anchored on the left by 'nothing' and on the right by 'lots and lots'.

For the fasted condition, participants entered the MRI scanner at 0850 h with testing completed by 0920 h, before access to an *ad libitum* breakfast (a choice of 5 breakfast cereals and milk). Breakfast intake was weighed covertly (Salter, Electronic Kitchen Scales) and recorded. For the fed condition *ad libitum* access to breakfast was permitted between 0850 h and 0920 h before entering the scanner at 0930 h and the scan was finished by 1000 h.

2.3 Functional imaging procedure

To determine brain activity responses to the food stimuli, participants were scanned in a whole body MR scanner (1.5 Tesla, Philips Gyroscan Intera) with an eight element head coil within which a mirror was mounted allowing participants to view a screen at the end of the

scanner bed onto which images were projected. fMRI data were acquired continuously during stimuli presentation using single shot echo-planar dynamic images (EPI) (TR = 3 s, TE = 45 ms, resolution 2.5 x 2.5 x 3.5 mm, 38 contiguous transverse-oblique slices, scan field of view 230 x 230 mm, 64 x 64 within-plane matrix). Images were presented in a random order using E-Prime version 2 (Psychology Software Tools Inc, Sharpsburg, USA) with 60 food pictures (with an even distribution of high and low energy foods) and 30 non-food pictures. Each image was projected for 5 s, interleaved with a blank screen with a fixation cross at the centre presented for 4 s. In order to ensure participants maintained attention throughout the testing procedure they were given hand-held MR-compatible response buttons and instructed to press the button in their left hand if they liked the presented food or right hand if they did not. For non-food images participants were instructed not to press either button. The total task lasted approximately 14 minutes. For both participant scanning sessions, the same visual images were presented during the fMRI task to ensure no variation in the relative distribution of foods a participant did and did not like. Once the task was completed a high-resolution T1-weighted anatomical image with a resolution of 0.9 x 0.9 x 0.9 mm was acquired.

2.4 Data analysis

2.4.1 Participant characteristics

All statistical analyses were conducted in the Statistical Package for Social Sciences (version 20.0; SPSS Inc., Chicago, USA). Participant characteristics were compared between groups using a one-way ANOVA. VAS scores were compared between conditions over time using repeated measures ANOVA and differences for sex and dietary restraint groups with condition over time examined using a mixed model ANOVA. In addition, VAS scores obtained immediately prior to the fMRI session were compared between groups (males v

females, restrained v unrestrained) via independent paired t-tests to examine whether any of the brain activity differences observed during scanning could be attributed to varying degrees of perceived appetite sensations. Energy intake values were compared between conditions for both sex and dietary restraint using a mixed model ANOVA. Energy intake, carbohydrate, protein and fat intakes were compared between sexes and between dietary restraint groups in the fed condition to elucidate whether the nutrient content of the meal impacted brain activation using a one-way ANOVA. In all cases a Greenhouse-Geisser correction factor was applied if Mauchly's test of sphericity was violated. Any significant differences to the ANOVAs were investigated using post hoc Bonferroni corrected pairwise comparisons. Potential differences between groups for the number of images participants reported showed foods they liked were assessed by performing two-sample t-tests examining restrained v unrestrained, boys v girls and fasted v fed. A value of $P<0.05$ was accepted for statistical significance for all tests. All group data are reported as mean ± SEM.

2.4.2 fMRI data processing

The functional images were analysed using SPM8 (The Wellcome Department of Cognitive Neurology, University College London) in MATLAB (Mathworks, inc., Sherborn, MA). Pre-processing steps included slice time correction, spatial processing, and warping to the Montreal Neurological Institute template (MNI305). Images were then convolved with a 3D Gaussian filter with an 8 mm full-width-at-half maximum (FWHM). The fMRI data was analysed based on mass univariate (voxel-by-voxel) testing within the general linear model framework over the whole brain, treating each participant separately and constructing individual maps for each visit based on differences in signal intensity associated with food image presentation and fixation cross images. Group analysis between conditions (fed and fasted), between sexes (boys and girls) and between eating behaviours (restrained and

unrestrained) was subsequently undertaken by combining the individual responses to create contrast maps. Significantly different brain activation between variables (condition, sex or eating behaviour) were defined as arising for a P-value < 0.001, after no corrections had been made for multiple comparisons and for a cluster size equal or greater than 20 voxels. Subsequently, coordinates of activated regions were transformed into the Talariach coordinate system before anatomical location was identified via a Talariach Atlas (19, 20).

3. RESULTS

3.1 Participant characteristics

Participant characteristics are presented in Table 1. There were no significant differences in age, BMI and PHV between the four participant groups. No significant differences were found for restraint scores between the UR-Boy and UR-Girl groups, however the R-Boys scored significantly higher on the restraint scale than the R-Girls (P=0.020). When groups were split based on sex only, no significant differences were found between boys and girls for age, BMI, PHV or restraint scores.

3.2 VAS findings

Feelings of hunger (Figure 1) and prospective consumption (Figure 2) were significantly higher for the fasted condition compared to the fed (P<0.001 and P<0.001 respectively) whereas feelings of fullness (Figure 3) were significantly lower (P<0.001). Hunger and prospective consumption changed significantly over time (both P<0.002); however, there were no significant interactions between condition*time for any of the appetite measures. There were no significant differences over time between the sexes for hunger, fullness or prospective consumption, neither were there any interactions effects of time*sex, condition*sex or time*condition*sex. Similarly there were also no significant differences

over time between restrained and unrestrained eaters for hunger, fullness or prospective consumption or any interactions effects of time*restraint, condition* restraint or time*condition*restraint.

3.3 Energy intake

There were no significant differences in mean energy intake from the breakfast meal consumed prior to the fMRI protocol (fed condition) compared to that consumed after (fasted condition) or any significant differences for mean energy intake between the sexes or between the dietary restraint groups (Figure 4). There were also no significant differences between the sexes and between the dietary restraint groups for the intake of energy, carbohydrate, protein and fat in the fed condition.

3.4 fMRI

No significant differences were found between fed v fasted, boys v girls or restrained v unrestrained groups for the number of images presented during the fMRI experiment which participants reported as foods they liked. Areas showing significant differences in fMRI activation patterns when comparing these same groups are presented in Tables 2-5. Each table presents the Talairach Coordinates (X,Y,Z) of the centre of mass of each identified activated cluster, the t-statistic and the number of voxels within each cluster. In summary, girls showed significantly greater brain activity than boys in response to visual food stimuli, in regions associated with executive function and decision making, working memory, and first-person perspective taking and self-awareness when satiation or dietary restraint was not considered. In contrast, when either fasted or fed states were considered separately, boys showed significantly increased activity than girls in regions linked to executive function, self-awareness and decision making. When fasted, restrained individuals showed heighted activation in regions connected to executive function and decision making and sensory and

motor planning relative to unrestrained eaters. Conversely, under fed conditions unrestrained eaters showed increased activity in similar areas to those displayed by restrained eaters when fasted.

4. DISCUSSION

The current study assessed brain activation in an adolescent population in response to visual food stimuli, examining differences between fasted and fed states, between the sexes and between different dietary restraint characteristics.

4.1 Sex differences

Within the current study in response to food stimuli, increased activation was shown for girls relative to boys within the cuneus, an area associated with basic visual processing and areas associated with executive function and decision making such as the medial frontal gyrus and cingulate (21), working memory, the superior parietal lobule (22) and parahippocampal gyrus (23) and first-person perspective taking and self-awareness, the precuneus (24). In contrast, only the thalamus showed significantly higher activation in boys. Collectively, these findings show that even in early adolescence, females are demonstrating an increased level of control and reflective consideration than males in response to food stimuli. These findings are similar to results found in an adult population when attitudes towards food have been examined. Adult females have been shown to be more likely to diet, have an increased knowledge of food and nutrition and subsequently self-assess their dietary habits more regularly than males (25). Uher (13) suggested differences in attitude towards food seen in adult females relative to males manifested itself in increased levels of brain activity in visual processing areas and those associated with taste responses such as the insula and the

prefrontal cortex, when viewing food cues. Similarly, Killgore and Yurgelun-Todd (14) found significantly increased activity within the frontal and prefrontal cortex's together with the cingulate gyrus suggesting a greater level of self-reflection, response inhibition and planning being exhibited by females. In contrast, either no (14) or very limited (13) numbers of regions demonstrated increased activity in males compared to females.

4.1.1 Sex differences when fasted or fed

There are few studies examining differences between males and females when nutritional status is varied. Previous work assessing differences in brain responses between fasted and fed conditions in adults have either combined groups by sex (26, 27) or examined only female (9, 28) or male participants (29). Leidy, Lepping (28) found fasted adolescent females displayed increased activations in the hippocampus, amygdale and anterior cingulate, relative to the fed condition. Adult males (21–29 y) conversely have been shown to have significantly enhanced brain activity in the left striate and extrastriate cortex, inferior parietal lobe and the orbitofrontal cortices (29) when fasted relative to fed. In the current study, as discussed above where nutritional states were combined, girls demonstrated increased activity in a number of regions relative to the boys. However, when satiation states were examined individually, the boys showed markedly more activation than the girls in both states. Under fasted conditions, areas associated with executive function, self-awareness and decision making (medial frontal gyrus, cingulate gyrus, precuneus), all showed increased activation in boys relative to girls. Similarly, under fed conditions boys showed increased activation in the middlel frontal gyrus and cingulate gyrus, suggestive of a degree of inhibition to any food cue stimulated responses (30). In contrast, when fasted, girls only showed increased activation relative to the boys in a small number of deep lying brain structures and no regions of higher activity when fed. Given that when fasted and fed results

are combined girls showed more activation than boys, the implication of this observation is that girls exhibit more consistent activity in specific brain regions independent of nutritional state in comparison to boys. However, further investigations into the implications of these sex dependent differences are warranted.

4.2 Dietary restraint

The inclusion of male participants when examining restrained eating behaviour has not typically been undertaken in either adult or paediatric studies, as dietary restraint is more commonly associated with females. However, given dietary restraint is not a uniquely female characteristic both sexes were included in the current study. Two previous studies in females have reported brain activation differences between restrained and unrestrained eaters, one with adults (9) and one with older adolescents (mean age 15.5 years) (8). With older adolescents, restraint scores were not significantly associated with any areas of increased neuronal activation in response to appetising visual food stimuli (8). Significant increases in activation of the orbitofrontal cortex, a region associated with reward was however found when highly restrained female adolescents were given a taste of chocolate milkshake, leading the authors to suggest pictures were less salient stimuli than actual food intake (8). In the present study, when fasted and fed states were combined, only a single region showed significantly different degrees of activity between restrained and unrestrained groups. However, this still nevertheless potentially highlights important disparities in response patterns dependent upon behavioural characteristics in adolescents when presented with food cues with unrestrained eaters showed increased activation in the paracentral lobule, a region previously shown to be activated in children presented with food product logos (31) suggesting that unrestrained eaters may be more susceptible to cues of this nature.

4.2.1 Dietary restraint when fasted or fed

When fasted and fed state responses are examined independently it might be anticipated that differences between restrained and unrestrained eaters would become more prominent. Restrained eaters are assumed to discount their hunger signals in pursuit of weight loss or maintaining current weight (32), thereby undermining their ability to generate, recognise or act upon normal hunger signals. In the current study, under fasted conditions, when the ability to overcome hunger stimuli would presumably have been most taxed, restrained eaters showed extensive heightened activation in a number of regions compared to unrestrained participants. These areas were associated with executive function and decision making such as the medial frontal gyrus (21), and other areas typically activated following food cue stimulation which are involved in sensory and motor planning such as the postcentral gyrus (33) and the precentral gyrus (34). Such findings are suggestive of restrained eaters suppressing their hunger in the presence of visually stimulating food cues, with such heightened responses potentially increasing the risk of binge eating. However, in fed conditions no areas of increased activity were seen in the restrained eaters relative to the unrestrained, suggesting the heightened response to food cues present under fasted conditions are quashed when sufficient food has been eaten. In contrast, unrestrained eaters continue to be responsive to food cues despite not being hungry, manifesting itself as increased activity in the precuneus perhaps indicative of a degree of self-assessment in order to determine the degree of hunger and whether subsequent eating was desired.

4.3 Limitations

Overall the study featured a relatively small number of participants, and was thus limited in terms of statistical power. However, given it was generally undertaken to provide initial

findings which would inform future larger-scale studies, this was not regarded as a severe limitation.

When comparing the restrained and unrestrained groups, it should also be recognized that although restraint scores were significantly different between the groups, the restrained group range was larger (1.89-3) than for the unrestrained (1-1.29), which may result in a reduction in any measured differences between groups. This resulted from only a small number of very highly restrained individuals volunteering for the study, potentially either due to such individuals being less likely to willingly participate in such studies or perhaps because highly restrained eating behaviours might not be fully developed at this age.

5. Summary

For the first time this study has shown significant differences in brain activity between girls and boys dependent upon their hunger state and between restrained and unrestrained eaters. The differences in activity seen in girls relative to boys when fed state is not considered is similar to that seen in adult women, suggestive that such response patterns are initiated early on in life. However, the variations in responses seen between girls and boys when hunger state is included and when participant restraint status is reflected upon for 12-13 year olds illustrate the complexity of the brain's response to food cues and highlight important differences between groups which warrant further investigations to gain insight into how these differences evolve with age.

References

1.	Ogden CL, Carroll MD, Kit BK, Flegal KM. Prevalence of Childhood and Adult Obesity in the United States, 2011-2012. Jama-J Am Med Assoc. 2014;311(8):806-14.

2.	Health Survey for England. Chapter 11: Children's BMI, overweight and obesity. 2012.

3.	van Meer F, van der Laan LN, Charbonnier L, Viergever MA, Adan RAH, Smeets PAM, et al. Developmental differences in the brain response to unhealthy food cues: an fMRI study of children and adults. Am J Clin Nutr. 2016;104(6):1515-22.

4.	Fearnbach SN, English LK, Lasschuijt M, Wilson SJ, Savage JS, Fisher JO, et al. Brain response to images of food varying in energy density is associated with body composition in 7-to 10-year-old children: Results of an exploratory study. Physiol Behav. 2016;162:3-9.

5.	English LK, Fearnbach SN, Lasschuijt M, Schlegel A, Anderson K, Harris S, et al. Brain regions implicated in inhibitory control and appetite regulation are activated in response to food portion size and energy density in children. Int J Obesity. 2016;40(10):1515-22.

6.	Bouchard C. The biological predisposition to obesity: beyond the thrifty genotype scenario. Int J Obesity. 2007;31(9):1337-9.

7.	Stice E, Presnell K, Shaw H, Rohde P. Psychological and behavioral risk factors for obesity onset in adolescent girls: A prospective study. J Consult Clin Psych. 2005;73(2):195-202.

8.	Burger KS, Stice E. Relation of dietary restraint scores to activation of reward-related brain regions in response to food intake, anticipated intake, and food pictures. Neuroimage. 2011;55(1):233-9.

9.	Coletta M, Platek S, Mohamed FB, van Steenburgh JJ, Green D, Lowe MR. Brain Activation in Restrained and Unrestrained Eaters: An fMRI Study. J Abnorm Psychol. 2009;118(3):598-609.

10.	Davis C, Strachan S, Berkson M. Sensitivity to reward: implications for overeating and overweight. Appetite. 2004;42(2):131-8.

11.	Dawe S, Loxton NJ. The role of impulsivity in the development of substance use and eating disorders. Neurosci Biobehav R. 2004;28(3):343-51.

12.	Volkow ND, Wang GJ, Maynard L, Jayne M, Fowler JS, Zhu W, et al. Brain dopamine is associated with eating behaviors in humans. Int J Eat Disorder. 2003;33(2):136-42.

13.	Uher R, Treasure, J., Heining, M., Brammer, M. J., Campbell, I. C. Cerebral processing of food-related stimuli: Effects of fasting and gender. Behav Brain Res. 2006;169(1):111-9.

14.	Killgore WDS, Yurgelun-Todd DA. Sex differences in cerebral responses to images of high versus low-calorie food. Neuroreport. 2010;21(5):354-8.

15.	Giedd JN, Blumenthal J, Jeffries NO, Castellanos FX, Liu H, Zijdenbos A, et al. Brain development during childhood and adolescence: a longitudinal MRI study. Nat Neurosci. 1999;2(10):861-3.

16.	van Strien T, Oosterveld P. The children's DEBQ for assessment of restrained, emotional, and external eating in 7- to 12-year-old children. Int J Eat Disorder. 2008;41(1):72-81.

17.	Mirwald RL, Baxter-Jones ADG, Bailey DA, Beunen GP. An assessment of maturity from anthropometric measurements. Med Sci Sport Exer. 2002;34(4):689-94.

18.   Varley-Campbell JL, Moore MS, Williams CA. The effects of a mid-morning snack and moderate-intensity exercise on acute appetite and energy intake in 12-14-year-old adolescents. British Journal of Nutrition. 2015:1-9.

19.   Lancaster JL, Rainey LH, Summerlin JL, Freitas CS, Fox PT, Evans AC, et al. Automated labeling of the human brain: a preliminary report on the development and evaluation of a forward-transform method. Human brain mapping. 1997;5(4):238-42.

20.   Lancaster JL, Woldorff MG, Parsons LM, Liotti M, Freitas CS, Rainey L, et al. Automated Talairach atlas labels for functional brain mapping. Human brain mapping. 2000;10(3):120-31.

21.   Rushworth MF, Walton ME, Kennerley SW, Bannerman DM. Action sets and decisions in the medial frontal cortex. Trends in cognitive sciences. 2004;8(9):410-7.

22.   Koenigs M, Barbey AK, Postle BR, Grafman J. Superior Parietal Cortex Is Critical for the Manipulation of Information in Working Memory. J Neurosci. 2009;29(47):14980-6.

23.   Takahashi E, Ohki K, Miyashita Y. The role of the parahippocampal gyrus in source memory for external and internal events. Neuroreport. 2002;13(15):1951-6.

24.   Cavanna AE, Trimble MR. The precuneus: a review of its functional anatomy and behavioural correlates. Brain. 2006;129:564-83.

25.   Davy SR, Benes BA, Driskell JA. Sex differences in dieting trends, eating habits, and nutrition beliefs of a group of Midwestern college students. J Am Diet Assoc. 2006;106(10):1673-7.

26.   Goldstone AP, de Hernandez CGP, Beaver JD, Muhammed K, Croese C, Bell G, et al. Fasting biases brain reward systems towards high-calorie foods. Eur J Neurosci. 2009;30(8):1625-35.

27.   Holsen LM, Zarcone JR, Thompson TI, Brooks WM, Anderson MF, Ahluwalia JS, et al. Neural mechanisms underlying food motivation in children and adolescents. Neuroimage. 2005;27(3):669-76.

28.   Leidy HJ, Lepping RJ, Savage CR, Harris CT. Neural Responses to Visual Food Stimuli After a Normal vs. Higher Protein Breakfast in Breakfast-Skipping Teens: A Pilot fMRI Study. Obesity. 2011;19(10):2019-25.

29.   Fuehrer D, Zysset S, Stumvoll M. Brain activity in hunger and satiety: An exploratory visually stimulated fMRI study. Obesity. 2008;16(5):945-50.

30.   Horn NR, Dolan M, Elliott R, Deakin JFW, Woodruff PWR. Response inhibition and impulsivity: an fMRI study. Neuropsychologia. 2003;41(14):1959-66.

31.   Bruce AS, Bruce JM, Black WR, Lepping RJ, Henry JM, Cherry JBC, et al. Branding and a child's brain: an fMRI study of neural responses to logos. Soc Cogn Affect Neur. 2014;9(1):118-22.

32.   Herman CP, Polivy J. Eating and its Disorders. New York: Raven Press; 1984.

33.   Huerta CI, Sarkar PR, Duong TQ, Laird AR, Fox PT. Neural Bases of Food Perception: Coordinate-Based Meta-Analyses of Neuroimaging Studies in Multiple Modalities. Obesity. 2014;22(6):1439-46.

34.   Carnell S, Gibson C, Benson L, Ochner CN, Geliebter A. Neuroimaging and obesity: current knowledge and future directions. Obesity reviews : an official journal of the International Association for the Study of Obesity. 2012;13(1):43-56.

Table 1. Mean (±SEM) participant characteristics.

R-Boy, restrained boys; UR-Boy unrestrained boys; R-Girl, restrained girls; UR-Girl unrestrained girls.

[a] Measured using the Dutch Eating Behavior Questionnaire for Children; [b] significantly different from UR-Boy, R-Girl and UR-Girl, P<0.02; [c] significantly different from R-Boy and R-Girl, P<0.001; [d] significantly different from R-Boy, UR-Boy and UR-Girl, P<0.02; [e] significantly different from R-Boy, R-Girl, P<0.001.

Characteristic	R-Boy (n = 8)	UR-Boy (n = 7)	R-Girl (n = 6)	UR-Girl (n = 8)
Age (y)	12.8 ± 0.2	12.9 ± 0.2	12.6 ± 0.1	12.8 ± 0.2
Stature (m)	1.59 ± 0.03	1.56 ± 0.03	1.56 ± 0.03	1.58 ± 0.02
Weight (kg)	48.0 ± 2.8	42.1 ± 1.7	55.4 ± 6.7	48.8 ± 4.1
BMI (kg/m^2)	19.1 ± 1.1	17.4 ± 0.3	22.5 ± 2.5	19.5 ± 1.4
Peak Height Velocity (y)	-1.66 ± 0.22	-1.79 ± 0.25	-1.93 ± 0.23	-1.59 ± 0.16
Restraint score[a]	2.47 ± 0.06[b]	1.16 ± 0.05[c]	2.16 ± 0.11[d]	1.14 ± 0.03[e]

Table 2. Regions of the brain showing significantly increased activation ($P<0.001$ uncorrected) when comparing boys (n=15) and girls (n=14), combining data over dietary restraint and satiation condition. BA, Brodmann Area.

Brain Regions	Talairach Coordinates			t	Cluster extent (voxels)
	X	Y	Z		
Boys to Girls					
Thalamus	6	-23	5	4.51	24
Girls to Boys					
Posterior Cingulate	14	-46	21	3.83	86
Frontal Lobe-Medial Frontal Gyrus (BA 8)	6	49	42	5.08	88
Parahippocampal Gyrus	-32	-43	-6	5.03	31
Occiptal Lobe-Cuneus (BA18)	12	-82	28	4.50	39
Occiptal Lobe-Cuneus (BA19)	-28	-80	28	4.30	61
Parietal Lobe-Superior parietal Lobule (BA 7)	14	-52	56	4.77	27
Parietal Lobe-Precuneus (BA 7)	14	-70	37	4.43	88
Cingulate Gyrus	14	-45	26	4.33	121

Table 3. Regions of the brain showing significantly increased activation (P<0.001 uncorrected) when comparing boys (n=15) and girls (n=14) over satiation conditions combining over dietary restraint. BA, Brodmann Area.

Brain Regions	Talairach Coordinates			t	Cluster extent (voxels)
	X	Y	Z		
Boys to Girls FED					
Caudate	-4	15	-2	5.10	37
Frontal Lobe-Inferior Frontal Gyrus (BA 47)	24	25	-13	4.78	32
Frontal Lobe-Middle Frontal Gyrus (BA 8)	26	35	41	4.11	21
Cingulate Gyrus (BA 31)	10	-55	27	3.95	38
Cingulate Gyrus	16	-49	25	3.61	38
Boys to Girls FASTED					
Occipital Lobe-Cuneus (BA19)	-26	-80	26	4.12	66
Parietal Lobe-Precuneus (BA7)	16	-68	35	4.40	66
Parietal Lobe-Precuneus (BA 7)	-14	-40	50	4.12	33
Frontal Lobe-Medial Frontal Gyrus (BA 8)	6	47	42	4.27	24
Cingulate Gyrus	12	-31	42	4.13	23
Girls to Boys FASTED					
Thalamus	6	-23	4	4.42	130
Parahippocampal Gyrus	-20	-35	2	6.20	64

Table 4. Regions of the brain showing significantly increased activation (P<0.001 uncorrected) when comparing restrained (n =14) and unrestrained (n = 15) eaters, combining data over sex and satiation condition. BA, Brodmann Area.

Brain Regions	Talairach Coordinates			t	Cluster extent (voxels)
	X	Y	Z		
Unrestrained to Restrained					
Frontal Lobe-Paracentral Lobule (BA 5)	-6	-44	59	5.00	85

Table 5. Regions of the brain showing significantly increased activation when comparing restrained (n=14) and unrestrained (n=15) eaters over fed and fasted conditions combining over sex characteristics. BA, Brodmann Area.

Brain Regions	Talairach Coordinates			t	Cluster extent (voxels)
	X	Y	Z		
Unrestrained to Restrained FED					
Parietal Lobe-Precuneus (BA 7)	-6	-47	61	4.77	232
Parietal Lobe-Precuneus (BA 7)	-12	-70	40	4.28	49
Restrained to Unrestrained FASTED					
Frontal Lobe-Medial Frontal Gyrus (BA 10)	32	42	26	4.55	84
Frontal Lobe-Middle Frontal Gyrus (BA 9)	36	37	33	4.12	84
Parietal Lobe-Postcentral Gyrus (BA 3)	-44	-17	45	4.49	41
Frontal Lobe-Precentral Gyrus (BA 4)	-36	-19	47	3.67	41
Frontal Lobe-Middle Frontal Gyrus (BA 11)	-30	42	-12	4.35	28

Figure Legend

Figure 1 Reported feelings of hunger for both the fed (dark bar) and fasted (light bar) over time as determined via a visual analogue scale (VAS). Each point represents group mean ± SEM (n=29). *denotes a significant differences between conditions, P<0.001

Figure 2 Reported feelings of prospective consumption for both the fed (dark bar) and fasted (light bar) over time as determined via a visual analogue scale (VAS). Each point represents group mean. Mean ± SEM (n=29). *denotes a significant differences between conditions, P<0.001

Figure 3 Reported feelings of fullness for both the fed (dark bar) and fasted (light bar) condition over time as determined via a visual analogue scale (VAS). Each point represents group mean. Mean ± SEM (n=29). *denotes a significant differences between conditions, P<0.001

Figure 4 Breakfast energy intake (mean ± SEM) when participants in both the fed (eating pre scanning represented by the dark grey bar and eating post scanning by the black bar) and fasted (light grey bar) conditions. R = restrained, UR = unrestrained. *denotes a signficant difference between conditions, P>0.05
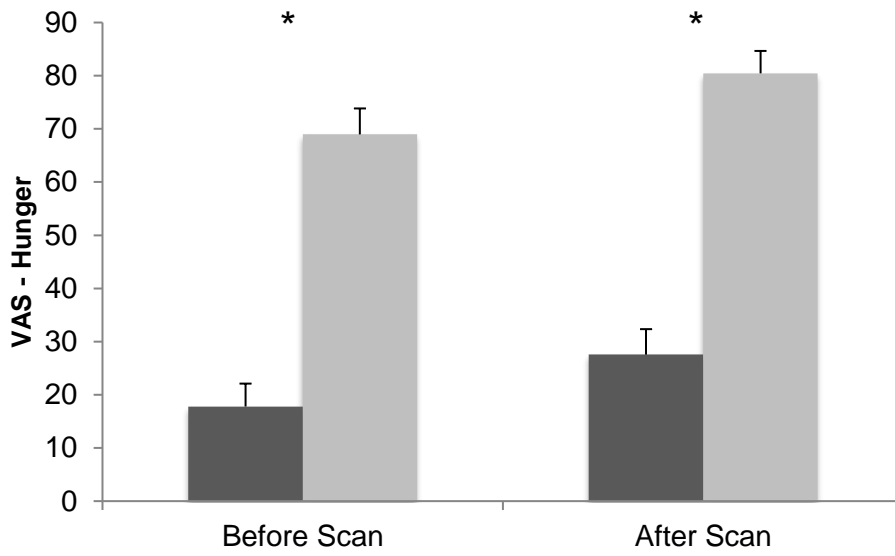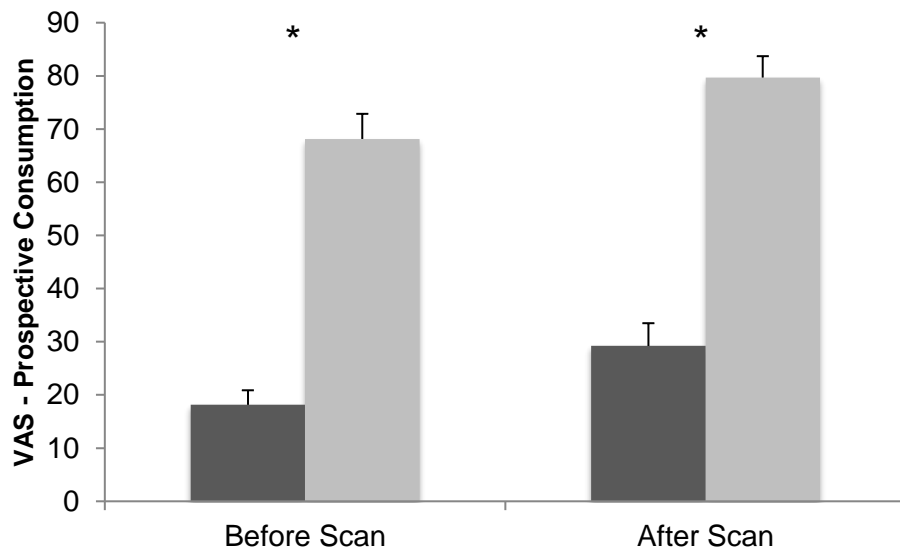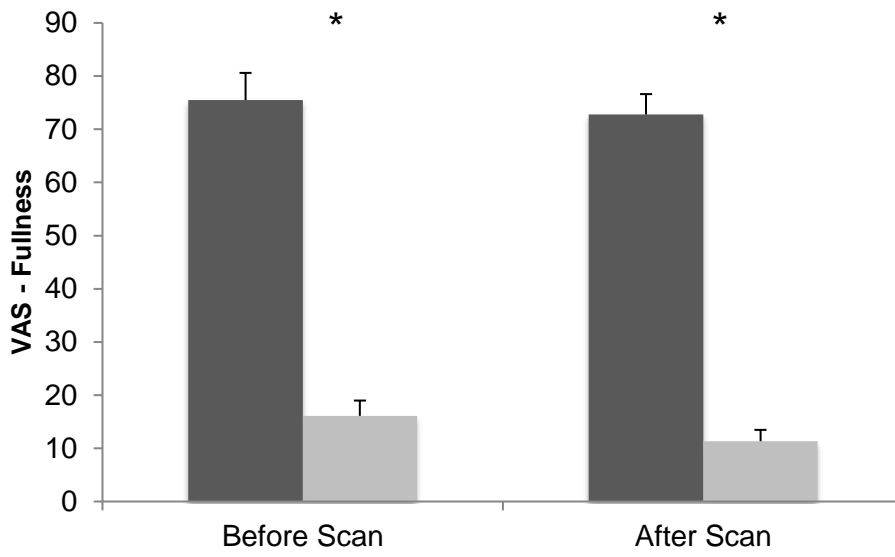
Figure 1

Figure 2

Figure 3

Figure 4