Neuroscience Letters 631 (2016) 56–62

Contents lists available at ScienceDirect

Neuroscience Letters

journal homepage: www.elsevier.com/locate/neulet

Research article

Neural correlates of restrained eaters' high susceptibility to food cues: An fMRI study

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HIGHLIGHTS

- To our knowledge, this is the first fMRI study to investigate restrained eaters' susceptibility to food cues.
- Restrained eaters showed special sensitivity (attentional bias) to high-energy food images.
- Restrained eaters were more sensitive (allocated more attentional resources) to low-energy food images.

ARTICLE INFO

Article history:
Received 19 May 2016
Received in revised form 10 August 2016
Accepted 11 August 2016
Available online 11 August 2016

Keywords:
Restrained eating
Functional magnetic resonance imaging
Susceptibility
Attentional bias
Food cues

ABSTRACT

Many studies have reported that specific susceptibility to food cues plays an important role in disordered eating behavior. However, whether restraint status modulates the neural bases of attentional bias to different types of food cues remains unknown. Thus, functional magnetic resonance imaging (fMRI) was conducted in individuals (12 restraint eaters, 12 unrestraint eaters) exposed to high/low-energy food and neutral images while performing a two-choice oddball task. The results indicated that restrained eaters responded more quickly to high-energy food images than to neutral and low-energy food images. More notably, compared with unrestrained eaters, restrained eaters showed faster reaction times, hyper-activation in a much wider array of reward (e.g., insula/orbitofrontal cortex), attention (superior frontal gyrus) and visual processing (e.g., superior temporal gyrus) regions, and hypo-activation in cognitive control areas (e.g., anterior cingulate) in response to high-energy food cues. Furthermore, among restrained eaters, the longest reaction times were found for low-energy food images, and activation of the attention and visual-related cortex (e.g., superior parietal gyrus) in the low–neutral contrast condition was significantly stronger than in unrestrained eaters. These findings contribute to our understanding of susceptibility to food cues: in addition to the special sensitivity (attentional bias) to high-energy food images, restrained eaters may also be more sensitive (allocate more attentional resources) to low-energy food images. These potential neural bases of restrained eaters may help clarify why dieting to lose or maintain weight is so often unsuccessful.

1. Introduction

Dieting has become a very popular means of weight control [1]. Many people try to control their body weight by restricting their food intake, but most fail in the long term [2]. One group that seems particularly unsuccessful in controlling food intake is chronic dieters (i.e., restrained eaters [3]). Restrained eaters are people who are chronically concerned with their weight and are highly motivated to control it by restricting their food intake [3]. Related studies show that dietary restraint can lead to several negative consequences, including weight gain and bulimic symptoms [4,5]. A variety of factors in the development and maintenance of restrained eating are currently being discussed, including psy-

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http://dx.doi.org/10.1016/j.neulet.2016.08.017
0304-3940/

chological [6], behavioral [7] and genetic [8] factors. Among the psychological factors, specific susceptibility to food cues is believed to play an important role. Several studies have found evidence of attentional biases toward high-energy food cues in restrained eaters [9,10]. However, some of the results are contradictory. For example, at least one study did not find any differences in attention bias for food [11], and other studies failed to find exacerbated or blunted responses for food words in restrained eaters [12].

There are many factors that probably contributed to the discrepancy in results other than the methodological differences in the type of samples studied (differing in body mass, age or gender), paradigms used (Stroop or dot-probe tasks), and stimuli presented (words, images or real food exposure) [13]. One explanation of why some results contradict each other according to Coletta was that little research has examined the brain-bases of attentional bias to food stimuli in restrained eaters [14]. There is enough evidence to say that the literature on obesity and disordered eating has shown much more consistent differences in the brain than in behavior [15,16]. A large body of evidence points to the existence of enhanced activity of the amygdala, insula and orbitofrontal cortex in people with obesity/eating disorder vs. normal weight controls [17,18]. However, the brain-bases of restrained eaters' attentional bias to food images remain unclear. Thus, in the current study, we first explored whether restraint status modulated attentional bias to food cues and then explored the different neural activations associated with these responses using functional magnetic resonance imaging (fMRI).

Previous fMRI studies have shown that when viewing images of highly palatable foods after consuming a meal, participants with high dietary restraint showed comparatively stronger activation than unrestrained eaters in areas implicated in desire, motivation, rewards, and executive functioning, including the orbitofrontal cortex (OFC), prefrontal cortex (PFC), and insula [14,19,20]. On the basis of this evidence, we hypothesized that restrained eaters would show hyper-responsivity in the brain regions associated with food reward. In addition, to study the neural correlates of restrained eaters' susceptibility to food cues, we adopted a two-choice oddball paradigm that has been successfully implemented in studies of attentional bias [21]. In the two-choice oddball task, subjects are instructed to make a standard/deviant distinction by pressing different keys as accurately and rapidly as possible. Because the standard stimulus is presented much more frequently than the deviants, the detection of task-relevant infrequent events (such as high energy-food or cigarette cues) for obese people and active smokers has been associated with a faster P300 latency in event-related potentials (ERP) [22] and a blood oxygenation level-dependent (BOLD) response in the frontal cortex and occipital-temporal regions, representing greater attentional processing for the deviant stimuli [21]. Accordingly, we concluded that restrained eaters may exhibit elevated responsivity of brain attention circuitry to food cues.

2. Materials and methods

2.1. Participants

Participants were recruited from Southwest University (SWU), Chongqing in a pre-screen initially administered to 158 research volunteers two weeks before the imaging study. All participants were selected on the basis of restraint scale (RS) scores and BMI (18.5–24.99 kg/m^2). In accordance with previous research [19], participants who score more than 15 on the Restraint Scale were restrained eaters; participants who score less than 12 were unrestrained eaters. One of the participant was excluded due to excessive artifacts and noise in the imaging data. The final sample includes 12 restrained eaters and 12 unrestrained eaters (see Table 1). We recruited only women because gender differences have been found in how and why they gain and lose weight [23]. Open-ended queries assessed the exclusion criteria including current neurological disease, diagnosis of an eating disorder, binge eating disturbances or a history of these concerns.

Table 1
Demographic and psychological characteristics of restrained eating sample (N = 24).

Variable	Res (N = 12)	UREs (N = 12)	t-Value
Restraint Scale	20.47 (±4.78)	8.93 (±0.79)	8.51***
Age (years)	20.92 (±1.5)	21.83 (±2.33)	1.15
Body mass index	21.14 (±1.92)	20.06 (±1.17)	1.66
Fasting time (hours)	5.17 (±1.3)	5.58 (±2.48)	0.51
Hunger1	59.42 (±15.97)	63.33 (±21.46)	0.51
Hunger2	57.5 (±19.6)	57.08 (±22.81)	0.05
Hunger3	81.67 (±23.29)	68.33 (±29.8)	1.22
Hunger4	40.92 (±25.25)	52.58 (±23.59)	1.17
Menstrual phase (days)	22.42 (±9.9)	17.83 (±7.94)	1.25
Positive Affect	29 (±9.59)	27.67 (±7.57)	0.38
Negative Affect	22.5 (±5.98)	22.92 (±7.67)	0.15

Note: Res = restrained eaters; UREs = unrestrained eaters; Menstrual phase = days from last menstrual cycle; all values are the mean (SD).
*** $p < 0.001$.

2.2. Procedures

The study was approved by the Human Research Ethics Committee at Southwest University. All volunteers provided written, informed consent prior to participation. On the study day, participants were asked to consume their regular meals but to refrain from eating or drinking (except water) for at least 4 h immediately preceding their imaging session for standardization purposes [24]. Fasting status was confirmed by self-report upon arrival. Participants completed a demographics questionnaire, including age, smoking status, current medications, and phase of menstrual cycle, and then rated their hunger and mood on associated measures. Height and weight were measured by an experimenter, and vision tests were completed. Following fMRI data acquisition, women were required to perform a two-choice oddball task. After finishing all tasks, each volunteer received 60 Yuan (equivalent to about $10 USD) and were thanked for their participation.

2.3. Measures

2.3.1. Hunger ratings

Participants completed a four-item measure of hunger and fullness [14]. With the exception of the third item, responses were rated on a 0–100 scale and included the following: (1) "How hungry do you feel right now?" (ranging from "not at all" to "extremely"); (2) "How strong is your desire to eat right now?" (ranging from "very weak" to "very strong"); (3) "How much food do you think you could eat right now, taking rice as the reference and grams as the unit?"; and (4) "How full does your stomach feel right now?" (ranging from "not at all full" to "very full").

2.3.2. Restraint scale (RS; [3])

The RS measures the degree of eating restraint and identifies women who are chronically concerned with their weight and restrict food intake as a means of weight control. The RS has good internal consistency in normal weight individuals (Cronbach's $\alpha > 0.75$; [14]). Higher RS scores reflect more restrained eating and predict disinhibited eating in laboratory settings [19]. In this study, the alpha coefficients were $\alpha = 0.84$ for restrained eaters and $\alpha = 0.81$ for unrestrained eaters.

2.3.3. Positive and negative affect scale—Chinese (PANAS-Ch; [25])

This scale includes 11 Negative Affect (NA) items and 9 Positive Affect (PA) items. Participants indicated the extent to which they experienced the corresponding emotions in the past 2 weeks on a scale from 1 = not at all to 5 = very much. Past studies have reported alphas between $\alpha = 0.78$ and $\alpha = 0.93$ in eight different samples [24]. In this sample, the alphas were $\alpha = 0.87$ for NA and $\alpha = 0.83$ for PA.

2.4. Materials and paradigm

The present study used a two-choice oddball paradigm that required subjects to make a standard/deviant distinction by pressing different keys, regardless of the energy density of the deviants, to allow cognitive responses in the laboratory setting to more closely resemble nature. Prior to the experiment, all subjects were told that the purpose of the study was to investigate their ability to make a fast response selection and their ability to inhibit the prepotent response to the frequent picture when the deviant appeared. There were 6 blocks of 100 trials, with each block including 70 standard and 30 deviant (grouped into 3 conditions) pictures. The frequent standard stimulus was a picture of a cup, and the deviants were 30 pictures grouped as either high-energy food (e.g., cake, pizza, hamburger, ice cream), low-energy food (e.g., vegetables, fruits), or neutral (e.g., flower, light bulb). High-energy food differed from low-energy food in the dimension of food content [$t(57) = 23.47$, $P < 0.001$], but not in the dimensions of arousal [$F(2, 87) = 0.24$, $P > 0.05$], happiness [$F(2, 87) = 2.16$, $P > 0.05$] or familiarity [$F(2, 87) = 2.77$, $P > 0.05$] [26]. Each block included a single category of pictures as the deviant stimuli, and the sequence of the blocks was counterbalanced across participants. Trials in each block were presented randomly. In each trial, a white fixation appeared for 400 ms on a black screen, followed by 1000 ms of the black screen, a subsequent target picture presented for 800 ms, and finally a black screen for 1000 ms before the next trial. In each group, half of the participants were required to press the “1” key when the standard stimuli were presented and the “3” key when the deviant stimuli were presented; half of the participants were asked to press the opposite keys. Pre-training with 20 practice trials was completed before the formal experiment to familiarize the subjects with the procedure.

2.5. Imaging data acquisition

Images were acquired in a 3 T Siemens TRIO MRI scanner. Functional data comprised 1008 vol acquired with T2*-weighted gradient echo planar imaging sequences. We obtained 32 echo planar images per volume sensitive to blood oxygenation level-dependent contrast (TR = 2000 ms; TE = 30 ms; flip angle = 90°; FoV = $220 \times 220\,mm^2$; matrix size = 64×64; 32 interleaved 3 mm-thick slices; in-plane resolution = $3.4 \times 3.4\,mm^2$; interslice skip = 0.99 mm). High-resolution T1-weighted images were obtained with a total of 176 slices at a thickness of 1 mm and an in-plane resolution of $0.98 \times 0.98\,mm^2$ (TR = 1900 ms; TE = 2.52 ms; flip angle = 9°; FOV = 250).

2.6. Imaging data analyses

All preprocessing steps were carried out using the Data Processing Assistant for Resting-State fMRI V2.0 (DPARSF, http://www.restfmri.net/forum/DPARSF) [27]. Slice timing was used to correct slice order, the data were realigned to estimate and modify the six head movement parameters, and the first six volumes of the functional runs were discarded to achieve magnet-steady images. These images were then normalized to MNI space in $3 \times 3 \times 3\,mm^3$ voxel sizes. The normalized data were spatially smoothed with a Gaussian kernel; the full width at half maximum (FWHM) was specified as $6 \times 6 \times 6\,mm^3$.

After preprocessing, Statistical Parametric Mapping software (SPM12; Wellcome Department of Cognitive Neurology, London, UK) was used to analyze the imaging data. Three main contrasts were specified per single-participant analysis: (1) high-energy foods vs. neutral, (2) low-energy foods vs. neutral and (3) high-energy foods vs. low-energy foods activity. A general linear model generated statistical parametric maps. The resulting single participant contrast images were then entered into second-level random-effects group analyses for each of the corresponding contrasts. Following other published accounts [28], the statistical threshold was set at a whole-brain false discovery rate of $P < 0.05$ for main effects combined with an extent threshold of at least 10 voxels for all reported clusters. Across participants, statistical parametric maps were calculated using a hierarchical random-effects model and a random-effects (RFX) two-way 2×3 analysis of variance; Restraint Status was the between-groups factor, and Image Type was the within-subjects variable. For specific interaction effects, an uncorrected statistical threshold criterion of $P < 0.005$ was adopted with a minimum cluster size of 10 voxels [12].

3. Results

3.1. Behavioral results

The false responses and responses exceeding the time limit were rare, as nearly all subjects achieved more than 97% accuracy rates in this experiment. The repeated measures ANOVA (Image Type as the repeated factor and Restraint Status as the between-subjects factor) showed a significant main effect of image type [$F(2, 24) = 5.23$, $P < 0.05$] and a significant image type × restraint status interaction effect [$F(2, 24) = 14.8$, $P < 0.001$] [Fig. 1]. Further analysis of the image type × restraint status interaction effect showed a significant image type effect in restrained eaters [$F(2, 24) = 15.42$, $P < 0.001$]; the RTs were significantly shortest for high-energy food, followed by neutral, while the longest RTs were for low-energy food images. Moreover, the RTs for high-energy food were significantly shorter in restrained eaters than in unrestrained eaters [$t(22) = 2.29$, $P < 0.05$], whereas the two groups exhibited comparable RTs for neutral [$t(22) = 0.8$, $P > 0.05$] and low-energy food images [$t(22) = 0.22$, $P > 0.05$]. Finally, we ran a correlation analysis within the entire sample and revealed a negative correlation between restraint scores and RTs in the high-energy food condition ($r = -0.535$, $P < 0.01$, Fig. 1). No other associations with RTs were significant (all $Ps > 0.05$).

3.2. fMRI results

3.2.1. Main effects of image type

Although peripheral to the main research focus, numerous differences in main effects emerged for Image Type within the entire sample (Table 2). We found greater activation in the (i) left superior frontal gyrus, left hippocampus, right amygdala, left fusiform gyrus and right middle occipital gyrus in response to high-energy food images vs. low energy food images, (ii) right middle frontal gyrus, right superior frontal gyrus and right superior temporal gyrus in response to high-energy food images vs. neutral images, and (iii) right superior temporal gyrus, left fusiform gyrus and left middle occipital gyrus for low-energy food images vs. neutral images. These regions have all been implicated in attentional resources allocated to and encoding the reward value of food [29]. These data suggest that the two-choice oddball task was suitable for studying susceptibility to food cues.

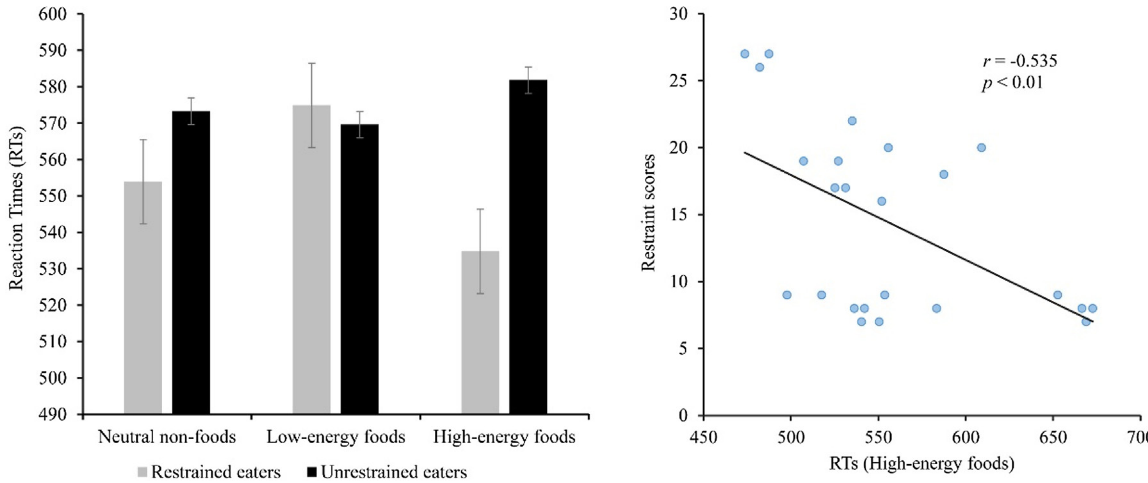

Fig. 1. Behavioral data (reaction times) obtained on the two-choice oddball task. The left panel shows the reaction times of correct responses in high/low-energy food and neutral conditions. The right panel shows the corresponding partial correlation scatterplots of restraint scores and RTs for the high-energy food condition adjusted for age, BMI, fasting time, hunger, phase of menstrual cycle and mood for illustration purposes only.

Table 2
Neural activation differences between food image contrasts for the entire sample ($n = 24$).

Contrast	Region	Hem	BA	x	y	z	t	Cluster
High > Low	Superior Frontal Gyrus	L	9	−15	48	36	4.53	27
	Hippocampus	L		−30	−12	−15	9.19	68
	Amygdala	R		27	−6	−18	5.83	21
	Fusiform Gyrus	L	19	−36	−81	−21	6.42	81
	Middle Occipital Gyrus	R	18	33	−87	−3	5.04	44
High > Neutral	Middle Frontal Gyrus	R		39	39	0	6.47	129
	Superior Frontal Gyrus	R		21	21	57	4.95	19
	Superior Temporal Gyrus	R	22	66	−36	12	5.42	25
Low > Neutral	Superior Temporal Gyrus	R		69	−36	15	5.01	33
	Fusiform Gyrus	L		−42	−45	−21	8.07	26
	Middle Occipital Gyrus	L		−51	−78	6	5.22	50

Note: High = high-energy food; Low = low-energy food; Hem = Hemisphere; L = left brain; R = right brain; BA = Brodmann's area; Cluster = number of voxels in a cluster. Remaining conventions as in Tables 2 and 3. Analyses used a whole-brain false discovery rate of P < 0.05 and a minimum cluster size of 10 voxels (Talairach coordinates).

Table 3
Neural activation differences for image contrasts between restrained and unrestrained groups ($n = 24$).

Contrast	Region	Hem	BA	x	y	z	t	Cluster
RE > uRE: High > Low	Insula	L		−33	−21	24	4.14	29
	Superior Frontal Gyrus	R	9	18	54	36	3.98	18
	Superior Temporal Gyrus	R	41	42	−36	15	3.64	33
	Middle Occipital Gyrus	R		30	−75	9	4.75	33
RE > uRE: High > Neutral	Orbitofrontal Cortex (OFC)	R		45	24	−9	3.98	40
	Orbitofrontal Cortex (OFC)	L	47	−36	30	−15	4.63	25
	Superior Frontal Gyrus	R		21	57	18	3.68	32
	Middle Temporal Gyrus	L		−54	−66	−3	3.95	29
RE > uRE: Low > Neutral	Superior Parietal Gyrus	L		−24	−48	72	4.61	29
	Superior Temporal Gyrus	L	40	−63	−51	21	3.41	23
uRE > RE: High > Neutral	Anterior Cingulate	R	32	18	33	24	4.33	11
	Precuneus	L	7	−9	−66	57	4.28	25

Note: RE = restrained eaters, uRE = unrestrained eaters, $P < 0.005$ uncorrected for multiple comparisons using a minimum cluster size of 10 voxels (Talairach coordinates).

3.2.2. Restraint status and image type contrast interactions

In the second-level random-effects group analyses (Fig. 2, Table 3), the restrained group showed significantly stronger activation in the right superior frontal gyrus, left insula, right superior temporal gyrus and right middle occipital gyrus compared with the unrestrained group in the high- vs. low-energy food contrast condition. The high energy food vs. neutral contrast conditions also corresponded to greater activation in the left and right orbitofrontal cortex (OFC), right superior frontal gyrus, and left middle temporal gyrus and significantly weaker activation in the right anterior cingulate and left precuneus in the restrained vs. the unrestrained group. Furthermore, for the low-energy food vs. neutral activity contrast, greater activation of the left superior parietal gyrus and left superior temporal gyrus was observed in restrained compared with unrestrained eaters. No other restraint status group effects were significant for the other contrasts (all $Ps > 0.005$).

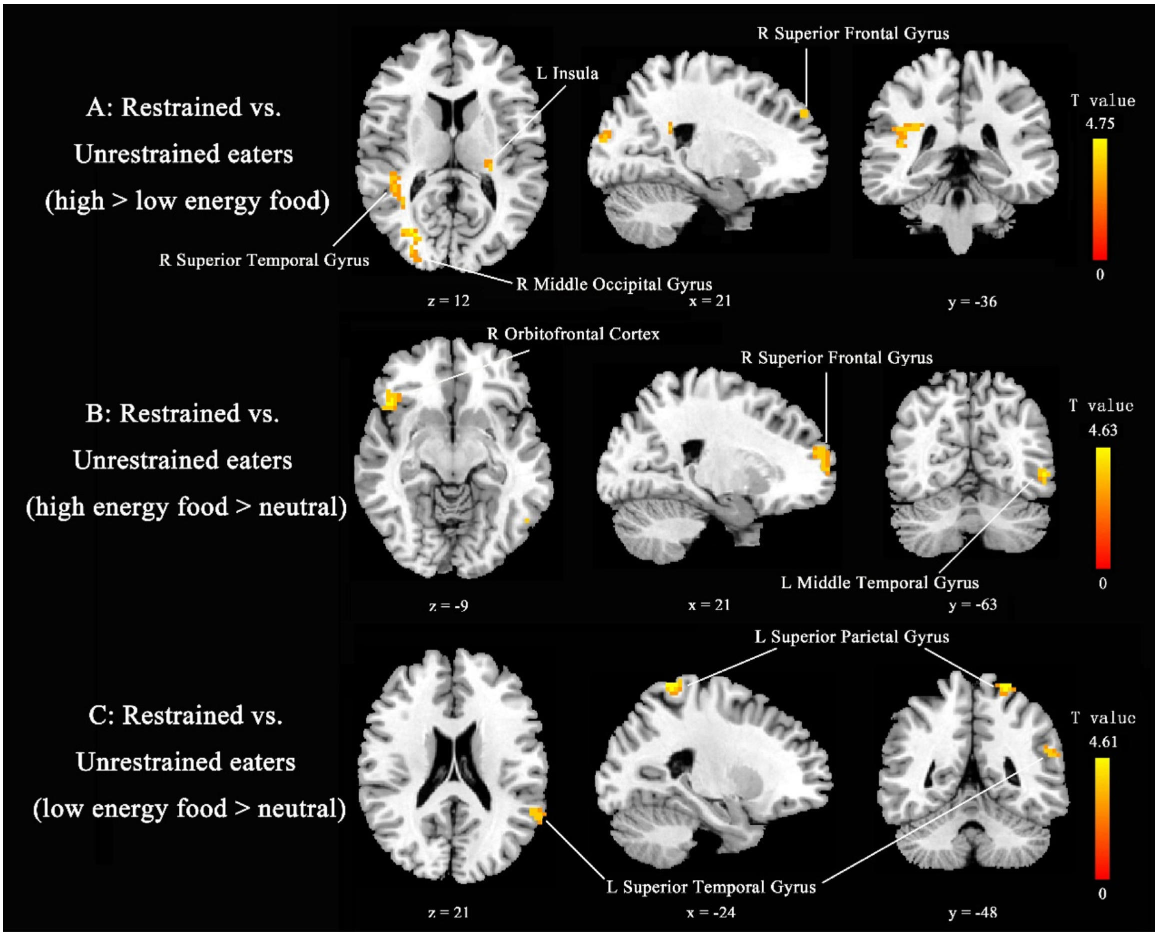

Fig. 2. Contrast maps comparing restrained eaters' response to high- versus low-energy food (A), high versus neutral (B) and low energy food versus neutral (C) condition with unrestrained eaters.

4. Discussion

To our knowledge, this study may be the first to use fMRI to examine the neural bases of attentional bias in food cues among restraint eaters. Consistent with our hypotheses and in line with numerous behavioral studies [10], restrained eaters responded more quickly to high-energy food images, but no difference between response to neutral and low-energy food images was found. These results dovetail with the analysis of related data which shows that restraint scores are negatively correlated with behavioral response to high-energy food images. In a visual attention task, restrained eaters responded more quickly to pictures of high-energy food than unrestrained eaters [18], implying that an attentional bias toward high-energy food cues does exist in restrained eaters. In support of these findings, numerous studies have shown that obese individuals orient more quickly toward food pictures than lean individuals [30]. More notably, restrained (vs. unrestrained) eaters show a hyper-activation in a much wider array of reward (e.g., insula/OFC), attention (superior frontal gyrus) and visual processing (e.g., superior temporal gyrus) regions, as well as hypo-activation in cognitive control areas (e.g., anterior cingulate), in high–low/neutral and low–neutral contrasts [14,19,21]. These results provide new insight into the specific neural mechanisms underlying restrained eaters' increased risk of weight gain and bulimic symptoms.

The goal conflict theory of hedonic eating proposes that people have problems with weight because their eating is overly influenced by hedonic rather than homeostatic hunger [31]. According to Papies and Houben, most restrained eaters fail in the long term mainly because dietary restraint is associated with more positive implicit attitudes and hedonic thoughts about high energy, palatable foods [32,33]. Previous functional imaging studies have demonstrated that both the insula (food craving) and orbitofrontal cortex (encoding of reward, desire for food and expectation of reward), are critically involved in processing food stimuli and motivating appetitive behavior [34–36]. For example, Burger and Stice used a consumption and anticipation paradigm and revealed that dietary restraint scores were positively correlated with activation in the OFC in response to receiving a milkshake [20]. Using a preload paradigm, Coletta et al. also found an association between insula/OFC activation and palatability of food stimuli in restrained eaters [14]. Thus, this relative hyper-activation of the insula and OFC could suggest that restrained eaters have elevated activation of reward circuitry compared to unrestrained eaters.

Furthermore, the superior frontal gyrus is known to be involved in attention and executive function [21], and the superior/middle temporal gyrus and middle occipital gyrus have been associated with visual processing particularly in response to food images and are also involved in the performance of the oddball task [21,29]. Images of high-energy food elicited greater activation of the visual-attention network, which might mean that restrained eaters orient more readily to the spatial location of high-energy food cues [9]. Consistent with this theory, the results of this study indicate that dietary restraint is associated with greater attentional bias and stronger positive attitudes toward high-energy food cues. Finally, restrained eaters show significantly weaker activation within the anterior cingulate (e.g., monitoring, controlling; [18,21]) and precuneus (e.g., motor planning; [21,29]) regions for the high vs. neutral contrast than unrestrained eaters, which might reflect that restrained groups engage in less cognitive control of high-energy food than unrestrained groups.

Interestingly, in addition to the prominent attentional bias to high-energy food images, restrained eaters also showed significantly stronger activation than unrestrained eaters in the superior parietal gyrus and superior temporal gyrus for the low–neutral contrast. Previous functional imaging studies have indicated that activation in these regions is known to be modulated by attention [14]; for instance, Yokum et al. revealed that BMI correlated positively with activation in the superior parietal gyrus during initial orientation to food cues, and the superior parietal gyrus has been shown to be activated during orientation toward the spatial location of visual signals [18]. In another study exploring the interaction between weight (obese, overweight and lean) and stimuli (e.g., food cues), participants also exhibited greater activation of the superior parietal lobe in response to food cues compared with non-food cues [37]. Thus, the results of our study suggest that food cues in general trigger greater attention in restrained vs. unrestrained eaters. This interpretation is consistent with our behavioral evidence, which showed that among restrained eaters, the longest RTs were found for low-energy food images. This finding extends the results of previous studies that demonstrated that exposure to high-energy food images results in increased activation of reward- and attention-related areas [19,29]; our results suggest that restrained eaters may also show more visual area activity in response to low-energy food images.

Aside from these findings, the main limitations of this study should be mentioned. First, although the sample sizes were similar to those used in most fMRI studies (12–15 participants per group), the recruitment of larger samples in future studies may facilitate the evaluation of related research questions. For example, although the assessment of the differences in neural bases between restrained and unrestrained groups was a sensible initial line of investigation, there is evidence that restrained eaters can be further divided into successful and unsuccessful subgroups [6]. Given the clear differences between general groups of restrained and unrestrained eaters, a logical focus of future studies would be to include the assessment of differences in neural bases between these two restrained eating subgroups and unrestrained eaters. Second, the participants in this study were matched on BMI, and we specifically excluded individuals with a history of psychopathology, including eating disorders. Consequently, these findings may not be generalizable to individuals with eating disorders or problems with obesity. Further research in these populations would be an important extension of this work. Third, while college-age women are a high-risk group for dieting and disordered eating, the inclusion of men and/or other age groups (e.g., adolescents) in future work would help clarify whether these findings can be generalized to other restrained eating groups.

5. Conclusion

To our knowledge, this study is the first to use fMRI to demonstrate differences in patterns of neural activation associated with attentional bias to food cues by restraint status. Restrained eaters showed hyper-activation in a much wider array of reward, attention and visual processing regions, as well as hypo-activation in cognitive control areas, in response to high-energy food cues. Furthermore, the contrast between low-energy and neutral images revealed greater visual area activity in the restrained group. These findings contribute to our understanding of individual's susceptibility to food cues: in addition to the special sensitivity (attentional bias) to high-energy food images when compared with unrestrained eaters, restrained eaters may also be more sensitive (allocate more attentional resources) to low-energy food images. These potential neural bases of restrained eaters may help clarify why dieting to lose or maintain weight fails so often.

Acknowledgements

This research was supported by grants from the National Nature Science Foundation of China (31170981 and 31371037) and"the Fundamental Research Funds for the Central Universities (SWU1509340)".

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