Binge-Eating Disorder: Reward Sensitivity and Brain Activation to Images of Food

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Background: The underlying neurobiological mechanisms that account for the onset and maintenance of binge-eating disorder (BED) are not sufficiently understood. This functional magnetic resonance imaging (fMRI) study explored the neural correlates of visually induced food reward and loathing.

Method: Sixty-seven female participants assigned to one of four groups (overweight BED patients, overweight healthy control subjects, normal-weight healthy control subjects, and normal-weight patients with bulimia nervosa) participated in the experiment. After an overnight fast, the participants' brain activation was recorded during each of the following three conditions: visual exposure to high-caloric food, to disgust-inducing pictures, and to affectively neutral pictures. After the fMRI experiment, the participants rated the affective value of the pictures.

Results: Each of the groups experienced the food pictures as very pleasant. Relative to the neutral pictures, the visual food stimuli provoked increased activation in the orbitofrontal cortex (OFC), anterior cingulate cortex (ACC), and insula across all participants. The BED patients reported enhanced reward sensitivity and showed stronger medial OFC responses while viewing food pictures than all other groups. The bulimic patients displayed greater arousal, ACC activation, and insula activation than the other groups. Neural responses to the disgust-inducing pictures as well as trait disgust did not differ between the groups.

Conclusions: This study provides first evidence of differential brain activation to visual food stimuli in patients suffering from BED and bulimia nervosa.

Key Words: Binge-eating disorder, bulimia nervosa, disgust, fMRI, food, pictures

Binge eating has been recognized as a clinically relevant behavior among obese individuals for almost half a century (1). However, the proposal of a provisional mental disorder category, binge-eating disorder (BED), is relatively new (2). The research criteria of BED include the presence of recurrent binge episodes with impaired control and subsequent distress. Unlike bulimia nervosa (BN), in which inappropriate compensatory mechanisms (e.g., vomiting) are employed to counteract the effects of overeating, these regularly reoccurring behaviors are absent in BED. As a consequence, the afflicted individuals are often overweight or even obese. BED is a common mental disorder with a lifetime prevalence of approximately 3% in the general population (3). In samples drawn from weight-control programs, the prevalence is considerably higher (>30%) (2).

The neurobiological factors that account for the onset and maintenance of BED are not yet known in detail. Whereas in BN, dieting nearly always precedes the onset of binge eating, this pattern is typically reversed in BED (4). Here, binge eating usually predates the sporadic dieting attempts. Consequently, food restriction and malnutrition do not qualify as central binge triggers in BED. Negative emotional states (e.g., anger, sadness) have often been reported by BED patients to have preceded overeating episodes (5). It is of note that these triggers are not disorder-specific because they are also present in bulimia. Finally, the type of food seems to be of importance for binging in BED. The afflicted patients prefer high-caloric food with high fat and sugar content (6–8). This preference might be mediated by the reward value of these types of food.

Within this context, it has been suggested, based on the reinforcement sensitivity theory (RST) (9,10), that BED patients might have an elevated sensitivity for primary rewards such as food (11). The differences in sensitivity are mediated by the so-called behavioral approach system. Central underlying neural substrates are the nucleus accumbens, the amygdala, and the orbitofrontal cortex, which are innervated by dopaminergic pathways.

First evidence for a connection between reward sensitivity and overeating was supplied by questionnaire studies (11–13). Here, positive correlations between the degree of binging, the body mass index, and self-reports on reward sensitivity, were observed. Whether this response tendency in BED is mediated by the brain reward system has not yet been addressed and was therefore the focus of this functional magnetic resonance imaging (fMRI) investigation.

Only a few neuroimaging studies have analyzed brain responses to visual food cues in BED patients. To our knowledge, there is only one single photon emission computed tomography (SPECT) study on individuals with clinically relevant BED symptoms (14). After an overnight fast, the female patients were exposed to a freshly cooked lunch and a landscape picture (control condition). Relative to obese and lean nonbinging female subjects, the food presentation provoked increased left prefrontal activation in the patients. This activation was correlated with feelings of hunger. A further investigation (15) analyzed neural responses to pictures of high-caloric foods, low-caloric foods, and nonfood items in obese individuals with subclinical BED. The subjects were scanned after the intake of a standard meal. Compared with lean and overweight nonbingers, the viewing of high-caloric food provoked greater premotor

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Table 1. Characteristics of Study Samples

	BED M (SD)	BN M (SD)	C-NW M (SD)	C-OW M (SD)	Group Differences[a]
Age (years)	26.4 (6.4)	23.1 (3.8)	22.3 (2.6)	25.0 (4.7)	
BMI	32.2 (4.0)	22.1 (2.5)	21.7 (1.4)	31.6 (4.7)	BED, C-OW > BN, C-NW
Education (years)	13.0 (1.5)	12.7 (.8)	13.2 (.9)	12.5 (1.9)	
Blood glucose level (mg/dL)	92.5 (7.8)	83.2 (7.0)	86.9 (6.6)	92.8 (10.4)	BN < BED, C-OW
BDI	12.1 (4.6)	15.0 (8.8)	2.3 (2.4)	4.3 (2.7)	BED, BN > C-NW, C-OW
BAS	3.4 (.4)	2.7 (.6)	2.8 (.6)	2.8 (.4)	BED > C-NW, C-OW, BN
BIS	3.1 (.5)	2.7 (.9)	2.8 (.5)	2.6 (.5)	
QADS—total	2.3 (.6)	2.2 (.7)	2.3 (.4)	2.3 (.6)	
EDI—binging	14.4 (2.0)	15.8 (2.0)	.80 (1.4)	.65 (1.2)	BED, BN > C-NW, C-OW

BDI, Beck Depression Inventory; BED, binge-eating disorder; BAS, Behavioral Activation Scale; BIS, Behavioral Inhibition Scale; BMI, body mass index; BN, bulimia nervosa; C-NW, normal-weight control subjects; C-OW, overweight control subjects; EDI, Eating Disorder Inventory, subscale: binging; QADS, Questionnaire for the Assessment of Disgust Sensitivity.

[a]Statistically significant group differences: *t* tests, all $p < .05$, uncorrected.

activation in the obese bingers. The authors suggested that this activation reflects mouth movement preparation for food ingestion.

Up until now, reactivity to visual food stimuli has been primarily studied in healthy individuals without eating disorders. Some of these neuroimaging studies contrasted brain activation to food versus nonfood pictures. Activated regions included the orbitofrontal cortex (16–20), the ventral striatum (17), the amygdala (21), and the insula (16,18). Other investigations examined cerebral responses to foods differing in caloric content (22–24). These fMRI studies showed that high-caloric foods provoked greater activity of the medial prefrontal cortex and the dorsal striatum than low-caloric foods. A subsequent analysis of the data showed that the degree of positive affect induction while viewing high-caloric food was positively correlated with orbitofrontal cortex (OFC) activation (23). Correlation approaches had also been applied in other investigations in which hunger/appetite ratings were positively associated with insular and OFC activation (14,16,18).

Few studies have focused on food-motivation-relevant trait factors, such as reward sensitivity, that might also influence affective and neural responses to food. An exception is the study by Beaver *et al.* (17), who demonstrated that subjects' reward sensitivity scores significantly predicted activation of the ventral striatum, the amygdala, and the OFC while they looked at food pictures.

Based on reinforcement sensitivity theory (9), this fMRI study explored whether BED patients would be characterized by an elevated reward sensitivity and increased activation in reward-processing brain areas (e.g., OFC, ventral striatum) while viewing pictures depicting high-caloric food. Further, we investigated whether BED patients would display lowered disgust responsiveness. Because food does not develop aversive qualities for BED patients when eating beyond satiety during binging (25), we hypothesized that this inhibited aversion development might be mediated by decreased trait disgust. This was the second exploratory question for this investigation.

Methods and Materials

Participants

Females suffering from BED ($n = 17$), BN (purging type, $n = 14$) according to DSM-IV (2), and healthy control subjects with no previous history of eating disorders (normal-weight [C-NW]; $n = 19$; overweight [C-OW]; $n = 17$) participated in this study. We restricted the sample to women because they are more likely to suffer from BED (1.5 times) and BN (10 times) than men (2). The subjects had been recruited through announcements in local newspapers and at the university campus. Written informed consent was obtained from each subject before entry. All subjects were nonmedicated and right-handed. The groups had a comparable mean age [$F(3,63) = 2.6$, $p = .07$] and education duration [$F(3,63) = .7$, $p = .56$; see Table 1]. The majority of participants were students. The BED patients and C-OW subjects were obese and had a comparable mean body mass index [BMI; $t(32) = .3$, $p = .76$]. Bulimic and C-NW subjects had a comparable mean BMI [$t(31) = .6$, $p = .54$]. Clinically relevant depression led to exclusion from the study. However, the groups differed in their BDI scores [$F(3,63) = 26.8$, $p < .001$]. Post hoc *t* tests showed that the patient groups had higher scores than the control groups (all pairwise comparisons, $p < .001$; all *p* values for self-report data are not corrected for multiple comparisons).

The BED and the bulimic group reported a similar degree of binging (Eating Disorder Inventory) (26): binging subscale, $t(29) = 1.95$, $p = .06$ (Table 1). Also, the duration of the eating disorder was comparable (BN: M = 7.3 years, SD = 3.6, BED: M = 6.8 years, SD = 4.0; $t(29) = .5$, $p = .66$). Those patients interested in treatment were assisted with referrals. The study had been approved by the ethics committee of the German Society for Psychology.

Stimuli and Design

The participants passively viewed pictures depicting high-caloric food (e.g., French fries, ice cream, cake, chips), disgust-inducing items (e.g., dirty toilets, maggots), and neutral items (household articles), which had been matched for complexity, brightness, and color composition. Each picture category consisted of 15 pictures. The scenes were shown for 4 sec each in an event-related design. The presentation was pseudo-randomized with the restriction that two pictures of the same category were not allowed to follow each other. In addition, a null condition was introduced, where a fixation cross was shown for an interval ranging between 3.5 and 6 sec. This was done to ensure design orthogonality. The design was repeated once. The duration of the total experiment was 19 min including functional pre- and postscans.

Procedure

The study was conducted on 2 days. After a telephone screening, the participants were invited to a diagnostic session

where they were interviewed with a standardized clinical interview for mental disorders (27). Also, they answered a set of questionnaires (Eating Disorder Inventory) (26), Beck Depression Inventory (BDI) (28), Questionnaire for the Assessment of Disgust Sensitivity QADS (29), and Behavioral Inhibition/Behavioral Activation Scales (BIS/BAS) (30).

The original BAS construct (31) includes three subscales (Drive, Reward Responsiveness, Fun Seeking). The BIS (Sensitivity to Punishment) is represented by a single scale. Possible mean scores range from 1 to 4. Because data for the German questionnaire version (30) revealed a two-factor solution consisting of one BIS and one BAS factor, we did not further consider the subscales. The QADS assesses subjects' disgust proneness. The self-rating instrument describes situations referring to, for example, death/deformity, body secretions, and poor hygiene, which have to be judged with regard to the degree of disgust induction. Possible mean scores range between 0 and 4. The BDI is one of the most widely used instruments for measuring the severity of depression. Total scores can range from 0 to 63. We report data for the EDI subscale binging, which assesses the urge to binge. Possible sum scores range from 0 to 18.

Patients of the eating-disordered groups were additionally interviewed with a disorder-specific interview (32) to obtain data about the frequency and duration of binge eating, the type of consumed food, compensatory behaviors (type, frequency), and associated mood. All subjects were weighed to determine the BMI. The diagnostic session ended with an anatomic scan to familiarize the subjects with the scanner.

The fMRI experiment was conducted in a second session, always in the morning (between 8 and 10 AM) following an overnight fast. (The subjects had been instructed not to eat after 8 PM.) Before the scanning, subjects underwent a blood glucose test. All groups had a normal fasting blood glucose level below 100 mg/dL (see Table 1) but differed significantly in their values [$F(3,63) = 4.6$, $p = .005$]. Post hoc t tests indicated that bulimic patients had lower levels than BED patients ($p = .002$) and overweight control subjects ($p = .004$). After the scanning, subjects rated the pictures on 9-point Likert scales for the dimensions appetite, disgust, arousal, and valence.

Brain Imaging

Brain images were acquired using a 1.5-Tesla whole-body tomograph (Magnetom Symphony, Siemens, Erlangen, Germany) with a standard head coil. For the functional imaging, 380 volumes were registered using a T2*-weighted gradient echo-planar imaging sequence (EPI) with 30 slices covering the whole brain (slice thickness = 4 mm; 1-mm gap, interleaved, repetition time = 3000 msec; echo time = 50 msec, flip angle = 90°, field of view = 192 mm × 192 mm; matrix size = 64 × 64). The orientation of the axial slices was parallel to the anterior commissure–posterior commissure line. The first six volumes of the time series were discarded to account for saturation effects. Preprocessing (SPM2; Wellcome Trust Centre for Neuroimaging, University College London, United Kingdom) included slice-time correction, realignment, normalization to the Montreal Neurological Institute (MNI) brain coodinates, smoothing (isotropic three-dimensional Gaussian filter, full width at half maximum = 8 mm, high-pass filter = 128 sec).

The three experimental conditions, Food, Disgust, and Neutral, were modeled by a function convolved with a hemodynamic response function in the GLM. The six movement parameters of the rigid body transformation applied by the realignment procedure were introduced as covariates in the first-level general linear model. Different contrasts (Food > Neutral, Disgust > Neutral) were calculated for each subject (first level) and then used in the second-level analyses. We studied within group effects via

Table 2. Brain Activation While Viewing Food Pictures (Contrast: Food > Neutral) in Binge-Eating Disorder Patients (BED), Bulimic Patients (BN), Normal-Weight Healthy Control Subjects (C-NW), and Overweight Healthy Controls Subjects (C-OW)

Region	Hem	Cluster Size[a]	x	y	z	*t*	*p*
BED ($n = 17$)							
Middle occipital gyrus	**L**	**2792**	**−15**	**−96**	**0**	**10.3**	**<.001**
Middle frontal gyrus	**L**	**569**	**−24**	**30**	**−21**	**8.1**	**<.001**
Insula	L	44	−36	6	−15	5.6	<.001
Insula	R	37	39	0	−3	5.0	<.001
ACC	L	117	−9	39	−3	4.7	<.001
ACC	R	11	15	36	15	4.8	<.001
Lat OFC	L	119	−24	30	−21	8.1	<.001
Lat OFC	R	60	21	27	−21	5.2	<.001
Med OFC	L	60	0	36	−15	4.9	<.001
Med OFC	R	38	3	36	−15	4.9	<.001
BN ($n = 14$)							
Lingual gyrus	**R**	**5563**	**15**	**−84**	**−9**	**18.9**	**<.001**
Insula	**L**	**834**	**−39**	**6**	**−9**	**8.2**	**.050**
Insula	R	82	39	3	−3	6.8	<.001
ACC	L	163	−3	18	21	6.3	<.001
ACC	R	98	6	18	21	7.0	<.001
Lat OFC	L	101	−27	33	−12	4.7	<.001
Lat OFC	R	8	24	24	−18	3.2	.004
Amygdala	L	28	−30	3	−18	3.6	.002
Ventral striatum	R	17	12	9	−6	4.5	<.001
C-NW ($n = 19$)							
Lingual gyrus	**R**	**3153**	**9**	**−93**	**−6**	**15.6**	**<.001**
Inferior frontal gyrus	**R**	**403**	**27**	**27**	**−18**	**7.8**	**.013**
Insula	**L**	**577**	**−36**	**−6**	**6**	**7.2**	**.038**
Insula	R	57	30	24	−21	4.9	<.001
ACC	L	157	−3	39	9	5.5	<.000
ACC	R	67	3	33	12	4.3	<.001
Lat OFC	L	147	−27	33	−15	5.4	<.001
Lat OFC	R	121	27	27	−18	7.8	<.001
Med OFC	L	15	−9	63	−3	4.3	<.001
Amygdala	L	15	−18	−3	−21	4.7	<.001
Amygdala	R	10	27	0	−27	3.5	.001
Ventral striatum	L	9	−9	9	−6	3.4	.002
C-OW ($n = 17$)							
Calcarine Fissure	**L**	**2864**	**−9**	**−90**	**−12**	**15.8**	**<.001**
Insula	L	99	−36	−3	12	5.1	<.001
Insula	R	116	33	24	−21	6.1	<.001
ACC	L	58	0	36	12	3.6	.001
ACC	R	35	3	33	12	3.6	.001
Lat OFC	L	100	−21	33	−18	6.5	<.001
Lat OFC	R	139	33	27	−24	6.0	<.001
Med OFC	L	5	−9	63	−3	3.5	.001
Amygdala	L	9	−18	−3	−21	3.7	.001
Amygdala	R	6	33	3	−21	3.8	.001

ACC, anterior cingulate cortex; Hem, hemisphere; Lat, lateral; Med, medial; OFC, orbitofrontal cortex; x, y, z, Montreal Neurological Institute coordinates.

Bold text indicates exploratory tests (family-wise error corrected). Nonbold text indicates region of interest tests (p = uncorrected).

[a]Cluster size is number of voxels.

one-sample *t* tests; group comparisons were performed through two-sample *t* tests. We report whole-brain corrected *p* values for exploratory analyses ($p < .05$; family-wise error-corrected; FWE) and uncorrected *p* values ($p < .005$) for region of interest (ROI) effects (33). The cluster size threshold was set to $k = 5$. On the basis of previous research on the processing of visual food stimuli and the RST, we selected the following ROIs: lateral/medial OFC, anterior cingulate cortex (ACC), amygdala, insula, and ventral striatum. For the disgust contrast, we chose the lateral OFC, the amygdala, and the insula as ROIs because these regions were activated in previous studies (34). ROIs were based on the parcellation (35) and were created with MARINA (36). Further, we separately computed simple regression analyses (with constant) using SPM2 (contrast Food > Neutral) for the two eating-disordered groups and related state–trait measures to the brain activation. Contrast values for statistically significant peaks in the simple regression models were extracted, and Pearson Product–Moment Correlation Coefficients were computed outside SPM.

Results

Reward Sensitivity and the Processing of Food Pictures

Scores from the self-report measures were compared between the four groups using one-way analyses of variance. We observed significant group effects for the BAS [$F(3,63) = 2.6$, $p = .05$]. Post hoc *t* tests indicated that BED patients reported greater reward sensitivity than all other groups (all $p < .05$; Table 1). The BIS group effect was nonsignificant [$F(3,63) = 2.2$, $p = .09$].

Ratings of valence [$F(3,63) = .8$, $p = .46$] and appetite [$F(3,63) = 1.5$, $p = .22$] for the food picture did not differ between the groups, whereas arousal ratings did [$F(3,63) = 3.7$, $p = .02$]. Post hoc *t* tests showed that bulimic patients had experienced these pictures as more arousing than the other groups (all $p < .01$) (Supplement 1).

Neural Responses to Food Pictures

Within-Group Effects. The contrast Food > Neutral showed occipital activation (exploratory effects) as well as ROI activation of the OFC, the ACC, and the insula in all groups (Table 2, Figure 1).

Between-Group Effects. We focused on the comparisons between the eating-disordered groups with all other groups. The BED patients were characterized by greater ROI activation in the medial and lateral OFC than the bulimic patients. Relative to the overweight and normal-weight healthy control subjects, BED patients showed greater medial OFC involvement (Table 3). None of the comparisons revealed significant exploratory effects.

Bulimic patients were characterized by stronger responses in the insula and the ACC than the three other groups (Table 3).

Correlation Analyses. Positive correlations for the BED

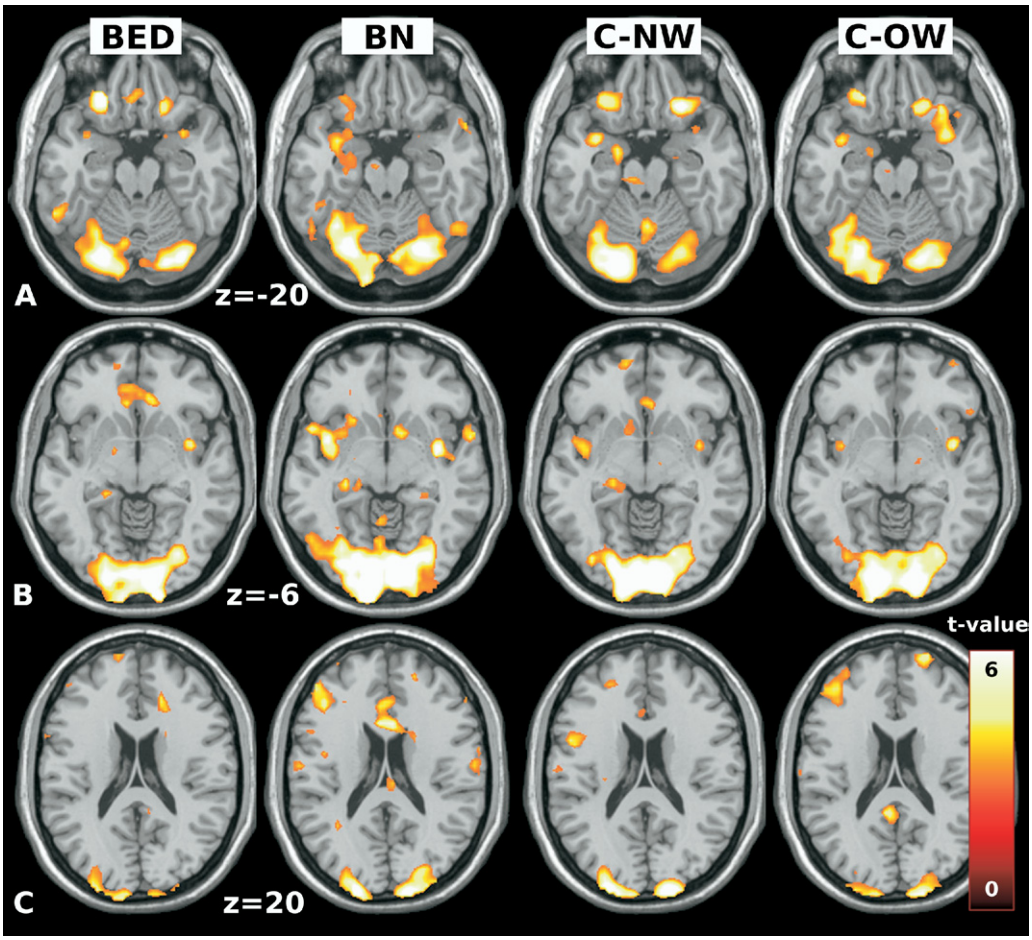

Figure 1. Brain activation to viewing high-caloric foods (contrast: Food > Neutral) in binge-eating disorder patients (BED), bulimic patients (BN), normal-weight healthy control subjects (C-NW), and overweight healthy control subjects (C-OW). Axial slices were chosen to show activation of the orbitofrontal cortex **(A)**, the ventral striatum **(B)**, and the anterior cingulate cortex **(C)**.

Table 3. Group Comparison of Brain Activation (Contrast: Food > Neutral)

Group/Region	Hem	Cluster Size	x	y	z	*t*	*p* (ROI)
BED > BN							
Lat OFC	R	14	36	33	−12	2.8	.005
Med OFC	R	8	12	27	−12	2.8	.005
BED > C-OW							
Med OFC	L	54	0	33	−18	3.6	.001
Med OFC	R	87	6	36	−12	3.8	<.001
BED > C-NW							
Med OFC	R	32	6	33	−24	2.9	.004
BN > BED							
ACC	L/R	58	0	15	21	4.1	<.001
ACC	R	30	3	15	24	4.3	<.001
Insula	R	16	39	−3	−12	4.5	<.001
BN > C-OW							
ACC	L	7	−6	21	−6	3.3	.001
ACC	R	10	6	15	21	2.7	.005
Insula	R	6	38	−3	−9	2.7	.005
BN > C-NW							
ACC	R	25	12	42	21	2.8	.004
Insula	L	8	−36	−6	−9	2.7	.005
Insula	R	11	39	−3	−9	2.7	.005

ACC, anterior cingulate cortex; BED, binge-eating patients; BN, bulimia nervosa patients; C-OW, overweight control subjects; C-NW, normal-weight control subjects; Hem, hemisphere; L, left; Lat, lateral; Med, medial; OFC, orbitofrontal cortex; R, right; ROI, region of interest; x, y, z, Montreal Neurological Institute coordinates.

group were found among reward sensitivity (BAS), experienced arousal, and ACC/medial OFC activation (Table 4, Figure 2). A similar correlation pattern characterized the bulimic group with a positive relationship between BAS scores and activation of the ACC, the medial OFC, and the insula. The insular activation was further positively associated with the degree of binge eating and negatively with the blood glucose level (after the overnight fast).

Disgust Sensitivity and the Processing of Disgust Pictures

On self-report, the four groups had a comparable overall disgust sensitivity [$F(3,63) = .2$, $p = .87$; Table 1]. The disgust pictures obtained similar disgust ratings [$F(3,63) = .4$, $p = .76$] and arousal ratings [$F(3,63) = 2.4$, $p = .07$] by the groups (Supplement 1). Differences were observed for the valence ratings [$F(3,63) = 3.8$, $p = .01$]. Normal-weight control subjects gave lower valence ratings than bulimic patients and overweight-control subjects (post hoc *t* tests: both $p < .01$). Neutral pictures were similarly rated by the groups (Supplement 1) with regard to valence [M = 6.1, SD = 1.6; $F(3,63) = 1.1$, $p = .35$] and arousal [M = 1.7, SD = 1.1; $F(3,63) = .3$, $p = .81$].

Neural Responses to Disgust Pictures

Within-Group Effects. The disgust pictures (contrast: Disgust > Neutral) provoked significant activation in the defined ROIs (amygdala, insula, lateral OFC) in all subject groups. Exploratory effects referred to the visual cortex (see Supplement 1).

Between-Group Effects: The exploratory tests (Contrast: Disgust > Neutral) were statistically nonsignificant. The ROI analyses detected greater insula activation in bulimic patients relative to overweight control subjects [MNI coordinates x,y,z: −27,30,6, $t(29) = 4.2$, $p < .001$]. Normal-weight females displayed stronger responses of the insula [MNI: −45,9,0; $t(34) = 3.9$, $p < .001$] and the lateral OFC [x,y,z: 39,45,−18; $t(34) = 4.0$, $p < .001$] than BED patients.

Discussion

This study was designed to investigate differences between patients suffering from binge-eating syndromes and healthy individuals in their neural response to visual food stimuli. After an overnight fast of 12 hours, the four samples (patients with BED, bulimia nervosa, lean and obese healthy females) rated the food pictures as very pleasant and appetizing. This positive affective experience was accompanied by activation of the ACC, the OFC and the insula across all participants, which points to a

Table 4. Simple Regressions Between State–Trait Measures and Brain Activation (Contrast: Food > Neutral) for BED and BN Patients

Scale	Region	Hem	Cluster Size[a]	x	y	z	*t*	*p* (ROI)[b]
BED								
BAS (+)	ACC	L	101	−6	30	15	4.3	<.001
	Med OFC	R	85	6	54	−9	4.7	<.001
Arousal (+)	ACC	L	8	−15	−15	42	4.4	<.001
	ACC	R	33	3	48	12	3.4	.002
	Med OFC	L/R	84	0	51	−18	4.4	<.001
BN								
BAS (+)	Insula	L	24	−39	12	6	4.1	.001
	Insula	R	15	45	6	0	4.5	<.001
	ACC	L	56	−9	−6	33	3.5	.002
	ACC	R	25	6	−12	42	3.1	.005
	Med OFC	L	111	−12	33	−18	4.0	.001
	Med OFC	R	146	12	30	−21	4.7	<.001
EDI binging (+)	Insula	R	88	48	15	−3	4.4	<.001
Blood Glucose Level (–)	Insula	L	6	−42	15	6	3.1	.005
	Insula	R	64	39	15	−6	4.1	.001

−/+, negative/positive correlations; ACC, anterior cingulate cortex; BAS, Behavioral Activation Scale; BED, binge-eating patients; BN, bulimia nervosa patients; EDI, Eating Disorder Inventory—subscale binging, experienced arousal while viewing food pictures; Hem, hemisphere; L, left; Lat, lateral; Med, medial; OFC, orbitofrontal cortex; R, right; ROI, region of interest; x, y, z, Montreal Neurological Institute coordinates.

[a]Cluster size is number of voxels.

[b]Region of interest (ROI) tests, *p* = uncorrected.

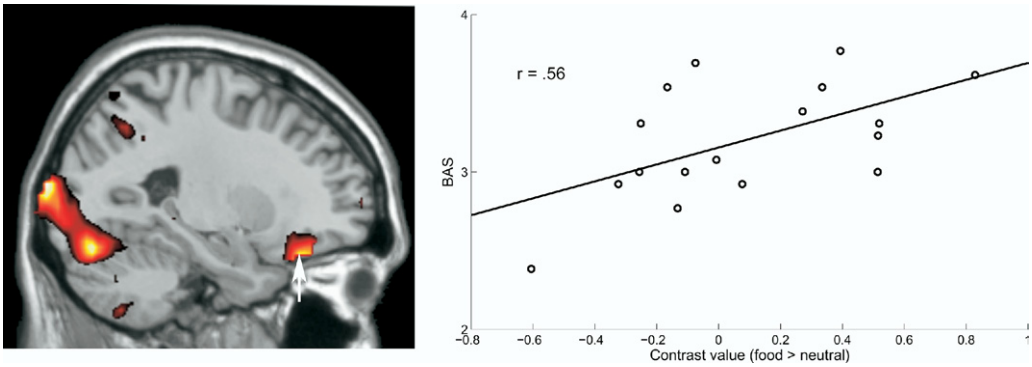

Figure 2. Correlation between Behavioral Activation Scales (BAS) scores and medial orbitofrontal cortex activation (Montreal Neurological Institute coordinates [x,y,z] = 6,54,−9) in binge-eating disorder patients.

very basic appetitive response pattern. Similar findings have been obtained in other neuroimaging investigations in which healthy subjects were exposed to real or pictorial food stimuli after several hours of fasting (16,18) or in a satiated state (17,19,22). The aforementioned studies also consistently detected insula and OFC activation.

An involvement of the insula in food processing seems plausible because this brain region holds somatosensory, visceral, and visceromotor functions. Food reactivity in particular is expected because the anterior part of the insula forms the primary gustatory cortex (37).

The OFC has been identified as a secondary gustatory cortex (38). Experiments in animals demonstrated that some of the neurons in this region reflect the hedonic value of food (39). There is also evidence that parts of the human OFC represent reward relevance of food stimuli (40). In an fMRI study by O'Doherty *et al.* (41), the anticipation as well as the actual experience of a pleasant taste induced OFC activity. Small *et al.* (42) observed that the right OFC responded preferentially to pleasant compared with unpleasant taste. Other neuroimaging studies showed that ratings of taste pleasantness were positively correlated with OFC activation (43,44).

The observed differential effects during food exposure referred to the previously mentioned brain regions—namely, the OFC, the insula, and the ACC. Relative to all other groups, BED patients showed the greatest medial OFC activation. This strong OFC recruitment together with the self-reported elevated reward responsiveness (elevated BAS scores) is in line with our hypothesis of an increased reinforcement sensitivity in BED. Further support of this assumption came from the correlation analysis that indicated a positive association between the degree of reward sensitivity and food-related medial OFC involvement. This differential medial effect is in line with the assumption of a mediolateral distinction in OFC function, whereby medial parts are related to the processing of reward value of many reinforcers (45). Thus, our data support and extend the findings by Beaver *et al.* (17), who reported that higher BAS scores of healthy subjects went along with increased OFC activity during visual food stimulation.

As an interim resumé, it can be stated that our data provide first evidence that a heightened medial OFC reactivity to food cues might translate reward drive into compulsive overeating in BED patients. Similar mechanisms might be relevant in other reward-dependent mental disorders. An important role of the OFC has been implicated in drug-addictive states, especially in drug craving (46,47). This suggests that the same brain regions that control individuals' desire for natural rewards (food) is also concerned with drug reward.

It remains an open question why BED patients did not display stronger responses in other structures of the brain reward system. We did not detect differential activation in the ventral striatum or in the amygdala. Within this context, it has been suggested that orbitofrontal regions are involved in the processing of hedonic aspects of reward, whereas ventrostriatal and amygdala systems are concerned with motivational aspects of reward (48). Because our design consisted of passive viewing and the subjects knew that they would not be able to eat the depicted food items, the picture presentation had little direct behavioral relevance. Other neuroimaging studies that used anticipation coupled with receipt of taste rewards were able to detect such activation of the amygdala and the striatum (20,21,41).

The second eating-disordered group, the bulimic subjects, differed in their neural responses from their nonpurging counterparts. Relative to all other groups, the bulimic patients showed increased insula involvement during food exposure relative to the other groups. As previously mentioned, the insula is concerned with gustatory processing (37). However, insular functions are not limited to this type of stimuli. The insular cortex is also activated more generally by interoceptive stimulation, and this activation is correlated with autonomic activity. There is empirical evidence (49) that the insula supports the interaction of perceived signal salience and bodily states of arousal, leading to subjective emotional experiences. In this sense, the increased insula involvement in bulimic patients might reflect somatic arousal. This interpretation is in line with the affective ratings for the food pictures by the bulimic patients, which included augmented arousal estimates. It would be of interest for future investigations to record physiological arousal indicators, such as electrodermal responses, simultaneously. This could add empirical evidence to the assumption that patients' reports of experienced emotional pressure when confronted with pleasant but "forbidden" foods are indeed associated with increased somatic arousal.

The strong ACC response by the bulimic subjects is most likely a result of their heightened selective attention for food stimuli. From the therapeutic context, it is known that bulimic patients complain that the environment is full of food cues that are warning signals for a possible loss of control and the occurrence of the next binge episode (32). In healthy subjects, involvement of the ACC, especially of its rostral part, has been repeatedly described during emotional evaluation, attentional control and response selection (for a review, see 50). Further-

more, the ACC has also been implicated in the elicitation and control of sympathetic autonomic arousal (49). Thus, the combined activation of the insula and the ACC in bulimic patients might reflect their attempts to counterregulate the increased arousal and food desire.

The results from the correlation analysis for the bulimic patients pointed to disorder-specific as well as general food-processing-related mechanisms. As in the BED patients, medial OFC activity was positively correlated with self-reported reward responsiveness. This further supports the role of the OFC in the mediation of reinforcement sensitivity. Moreover, differential effects regarding insular involvement were detected. The greater the degree of binge eating and the lower the fasting blood glucose level, the greater the insular involvement in bulimic patients. This finding is in good accordance with clinical observations. Food restriction in BN is linked to elevated attention for food cues, experienced arousal during food exposure, and binging probability (32).

Considering the differential responding toward visual food cues, an important question arises: are specific new therapy approaches required for BED? Classical treatment is directed to obesity (weight-loss programs) and interpersonal functioning. These approaches may be misplaced. Instead, a focusing on the alteration of food reward value or the offer of reward alternatives seems to be more promising. This could be achieved in the context of psychotherapy or with drugs that are able to modulate the brain reward circuitry. Different pharmacologic substances with effects on dopaminergic, γ-hydroxybutyric acid–ergic, or endogenous opiod/cannabinoid systems in the forebrain, basal ganglia, and mesolimbic areas have been identified as to alter the reward value of food (46,51).

To gather further information about relevant binge factors in BED, we explored the disgust sensitivity and reactivity. Patients' self reports on trait disgust, as well as state disgust, did not differ from the other three subject groups. Moreover, the disgust-induced brain activation was comparable in the four samples as indicated by the exploratory tests. Also, the ROI analyses found no systematic differential effects. Accordingly, an altered disgust processing does not seem to play an important role in BED.

Although the implications of this study extend the understanding of neurobiological mechanisms of food reward in BED, some limitations must be acknowledged. We only included female participants, although a substantial portion of BED sufferers is male. Some possibly moderating variables relevant for food processing were not controlled, for example, hormonal fluctuations associated with the menstrual cycle, that influence appetite. Finally, the eating-disordered groups differed from the control groups not only with regard to the specific diagnosis. For example, the patients scored higher on the BDI. This finding is directly linked with the suffering due to the disorder, but, may, however, have influenced the responding.

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Supplementary material cited in this article is available online.

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