

Neural Processing of Food and Erotic Cues in Bulimia Nervosa

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ABSTRACT

Objective: Event-related brain potential (ERP) studies have shown that bulimia nervosa (BN) is associated with facilitated processing of disorder-specific stimuli, visible in altered early components during presentation of food cues and bodies varying in size. Less is known about BN and late ERPs, typically less influenced by perceptual features and regarded as more reliable indices of motivational relevance. The purpose of this study was to use the late positive potential (LPP) to investigate the motivational significance of BN-relevant stimuli.

Methods: Highly salient stimuli, such as pictures of personal binge foods and images that are pleasant, neutral, and unpleasant (e.g., human attacks) were presented to 24 women with bulimia and 24 healthy women (19.7 ± 2.1 and 20.5 ± 2.6 years, respectively). Pictures of erotic couples, previously shown to prompt the greatest appetitive reactions in healthy women, were used as pleasant cues. Based on BN aversion to body cues, we hypothesized that the motivational significance of erotic cues could be increased in bulimic women.

Results: Consistent with the literature, the LPP was modulated by the salience of the pictures ($F(2.8,130.7) = 24.6, p < .001$). An additional interaction with diagnostic group ($F(2.8,130.7) = 2.8, p = .047$) indicated that bulimic women showed a larger LPP than healthy controls during pictures displaying binge foods ($p = .037$) and erotic couples ($p = .031$).

Conclusions: The findings provide objective evidence that BN is characterized by dysregulated emotional processing that is not limited to food cues. The implications are discussed within a transdiagnostic perspective on food-related disorders.

Key words: bulimia nervosa, binge food cues, electrophysiology, emotion, erotic cues, late positive potential.

INTRODUCTION

The lives of women experiencing eating disorders (ED) revolve around food and body cues: believing that their self-worth depends on their body shape, they can fast to self-starvation to adhere to their body ideal (1). Paradoxically, studies on the neural correlates of fasting show that it precisely increases attention toward food cues (2). In healthy adults, food cues are only moderately appetitive (3) but become motivationally relevant as a result of food deprivation and lead to larger early and late event-related potentials (ERPs), i.e., the early posterior negativity (EPN) and late positive potential (LPP) (4,5). Although the initial ERP components are associated with early stimulus detection and processing, the LPP is a reliable biological correlate of motivational relevance and sustained attention (5,6). In the absence of a task, the LPP increases during presentation of stimuli that are intrinsically relevant for being threatening or appetitive, e.g., pictures of attacks, mutilations, or erotica.

Among EDs, bulimia nervosa (BN) alternates food restriction periods—as in anorexia nervosa (AN)—with uncontrolled eating episodes—as in binge EDs (1). In BN, early ERP components are more pronounced during presentation of not only food pictures but also body pictures (7,8), suggesting facilitated processing of food- and body-related cues. Less is known about the late neural correlates of BN. Anorexia nervosa is associated with a larger

LPP to thin bodies (9,10), and binge ED (BED) tends to be related to a larger LPP to food cues (11). Moreover, bulimic women tend to fixate on body cues longer (12) and show a potentiated startle reflex during food cues (13), suggesting that bulimia might be characterized by sustained attention to body cues and aversive processing of food cues. However, there are no studies on how bulimia modulates the LPP, an objective index of motivated attention.

In the present study, to uncover the phenotype of BN during free picture viewing, we needed to identify the stimuli that could acquire the greatest motivational relevance in bulimic women. It has been repeatedly shown that personally significant stimuli—e.g., faces of one's loved ones or cues of personal fears—are associated with high levels of physiological reactivity (14,15). In EDs, personalized cues are especially relevant because binge foods are highly individualized (16) and are the target of treatments based on food cue exposure (17,18). In this study, in addition to highly

AN = anorexia nervosa, ANOVA = analysis of variance, BDI = Beck Depression Inventory, BED = binge eating disorder, BITE = Bulimia Investigatory Test Edinburgh, BMI = body mass index, BN = bulimia nervosa, EAT = Eating Attitude Test, ED = eating disorder, EDE-17 = Eating Disorder Examination, v.17, EPN = early posterior negativity, ERP = event-related potential, IAPS = International Affective Picture System, LPP = late positive potential, OLAF = Open Library of Affective Foods, STAI = State-Trait Anxiety Inventory

SDC Supplemental Content

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appetizing food cues, we asked participants to identify pictures of “foods that you find personally irresistible and that you could keep eating until bingeing.” Thus, in contrast to previous studies, e.g., (19), we used the same instructions for patients and controls. To our knowledge, there are no studies on the late neural correlates of binge food cue processing in BN.

As control cues, we displayed pleasant, unpleasant, and neutral pictures that allow an inference of the motivational relevance that patients assign to food cues (20,21). Because personalized food picture selection would prompt greater familiarity with food compared with other cues, each participant also selected the affective and neutral stimuli. We chose homogeneous affective contents (22), and for pleasant pictures, we chose pictures of erotic content. Erotica consistently prompt great physiological reactivity in both men and women (3). Bulimic women, based on clinical observation and self-reports, seem to be sexually more promiscuous but also experience great body dissatisfaction, even greater than that of anorectic women (23–25). In all women, however, certain erotic cues prompt reactions that indicate aversion—increased corrugator muscle and startle blink reactivity (3). Because we did not want to confound bulimia subjective aversion to body cues with women's mixed motivation toward sexually explicit images, we selected pictures of erotic couples, which in women prompt the greatest startle reflex inhibition, which is indicative of appetitive processing (3). Moreover, because it has been observed that the LPP during erotic cues increases with greater sexual promiscuity (26), we additionally adjusted for the number of sexual partners in the past year. To our knowledge, there are no studies on the neural correlates of erotic stimulus processing in BN.

In sum, this work aims to investigate the motivational salience, as indexed by the LLP, of diverse emotional stimuli in women diagnosed with BN and healthy controls, with a special focus on the impact of individualized food and erotic cues on the late neural components.

METHODS AND MATERIALS

Participants

The study examined 24 healthy women and 24 women with a diagnosis of BN (4/24 with a subthreshold diagnosis, following Stice and colleagues (27)). Participants were recruited from the University of Granada population and received up to €40 for their participation. Physiological data collection took place between May 2015 and March 2017. Exclusion criteria were the following: current pregnancy; past or present drug abuse; visual, auditory, cardiovascular, neurological, or psychotic disorders; and current treatment for eating or weight-related disorders. DSM-5 criteria for eating pathology were evaluated by a trained psychologist using the ED Examination (EDE-17 (28)). The number of sexual partners in the past year was assessed following previous literature (26,29). Furthermore, Spanish-validated scales were used to evaluate disordered eating attitudes and behaviors (30), bulimic symptoms (31), state and trait food cravings (32), generalized anhedonia (33), trait anxiety (34), and depression (35). To qualify as healthy controls, participants had to report no bulimic attitude or symptom (EAT<20; BITE<10). BN patients and healthy controls were matched case-by-case for age and body mass index. Before EEG recording, objective and subjective indices of hunger were collected (36).

Stimuli

Participants viewed 6 repetitions of a set of 16 pictures, belonging to 4 different categories: high-calorie foods ($n = 4$) and nonfood pleasant ($n = 4$),

neutral ($n = 4$), and unpleasant ($n = 4$) cues. Each participant selected her own set of pictures.

Women's ratings obtained in previous Spanish normative studies (37–40) were used as a reference to select an initial pool of 32 pictures. Emotional and neutral nonfood images were taken from the International Affective Picture System (IAPS) (41) and consisted of erotic couples ($n = 8$; IAPS codes: 4643, 4652, 4658, 4668, 4669, 4670, 4672, 4676), neutral objects ($n = 8$; IAPS codes: 5531, 7002, 7009, 7025, 7175, 7224, 7233, 7235), and human attacks ($n = 8$; IAPS codes: 6230, 6231, 6244, 6263, 6312, 6313, 6530, 6571). Food images, sweet or salty, consisted of four images: two high-calorie food pictures, which each participant selected from among 8 that were taken from the Open Library of Affective Foods (OLAF) and ranked the highest in normative ratings (37) (OLAF codes: fat_0018, fat_0037, fat_0224, fat_0655, sug_0013, sug_0072, sug_0096, sug_0157); two personalized high-calorie food pictures, which each participant selected from the web with the assistance of an experimenter. Table S1 (Supplemental Digital Content 1, <http://links.lww.com/PSYMED/A564>) displays normative affective ratings, collected among Spanish women, of the initial pool of IAPS and OLAF images. Before the diagnostic interview, each participant selected, from this set of 32 images, her own set of nonfood pleasant ($n = 4$), neutral ($n = 4$), and unpleasant ($n = 4$) and food ($n = 4$) pictures: All pictures were printed in color on A4 plastic sheets (210 × 297 mm or 8.27 × 11.69 in. and included in 4 folders, one per category, following 4 orders that were randomized across participants. For each category, the participant had to choose and rank the 4 images that made her feel the most “stimulated, excited, frenzied, jittery, wide-awake, aroused” or, for neutral pictures, the pictures that made her feel the most “completely relaxed, calm, sluggish, dull, sleepy, unaroused” (41). Thus, we used the same instructions for food and nonfood images and, for erotica, we avoided the ambiguity in the women's pleasure ratings. Next, the participant was required to identify two “foods that you find personally irresistible and that you could keep eating until bingeing.” The participant then had up to 5 minutes to search the web for naturalistic pictures that best represented such foods. An experimenter assisted, and they ensured that the caloric content was high, that the pictures had a high digital resolution and that the food was displayed on a nonuniform background that matched the perceptual properties of the IAPS pictures (37). The same instructions were used for patients and controls.

Procedure

The University of Granada ethics committee certified that the study complied with the Declaration of Helsinki (IRB # 699). Figure 1 shows the participant selection procedure that led to the two experimental sessions. The first session (i.e., diagnostic interview and picture selection) took place at the UGR CIMCYC Clinical Psychology Unit. After signing the informed consent form, the participant personally selected the pictures. Next, her body mass index was estimated using an electronic body composition analyzer (Tanita Model 300MA, Chicago, IL) and a Leicester height measure stadiometer recorded to the nearest millimeter. The participant was then administered the semistructured ED examination (28) that ended after 1 to 1.5 hours, with standardized questions on the number of sexual partners during the past year (29). Afterward, some prescreening questionnaires (i.e., BITE and EAT) and surveys on depression (BDI) and trait anxiety (STAI) were completed. Finally, the experimenter double-checked the “personally irresistible foods” so that the participant could repeat the picture selection if necessary. The EEG session took place approximately 1 week later, in the morning (9:30 AM–12:00 PM) or in the afternoon (4:30–6:00 PM), at the UGR CIMCYC Laboratory of “Human Psychophysiology and Health.” To control for the impact of hunger on ERPs (2), participants were instructed to have a small snack—toasted bread with butter (1038 kcal) or olive oil (1193 kcal)—2.5 hours before EEG recordings. After arrival at the laboratory, a glucose test assessed if they adhered to the instructions. Participants were rescheduled if they did not comply, or if they were ill, had menstruated, or had been

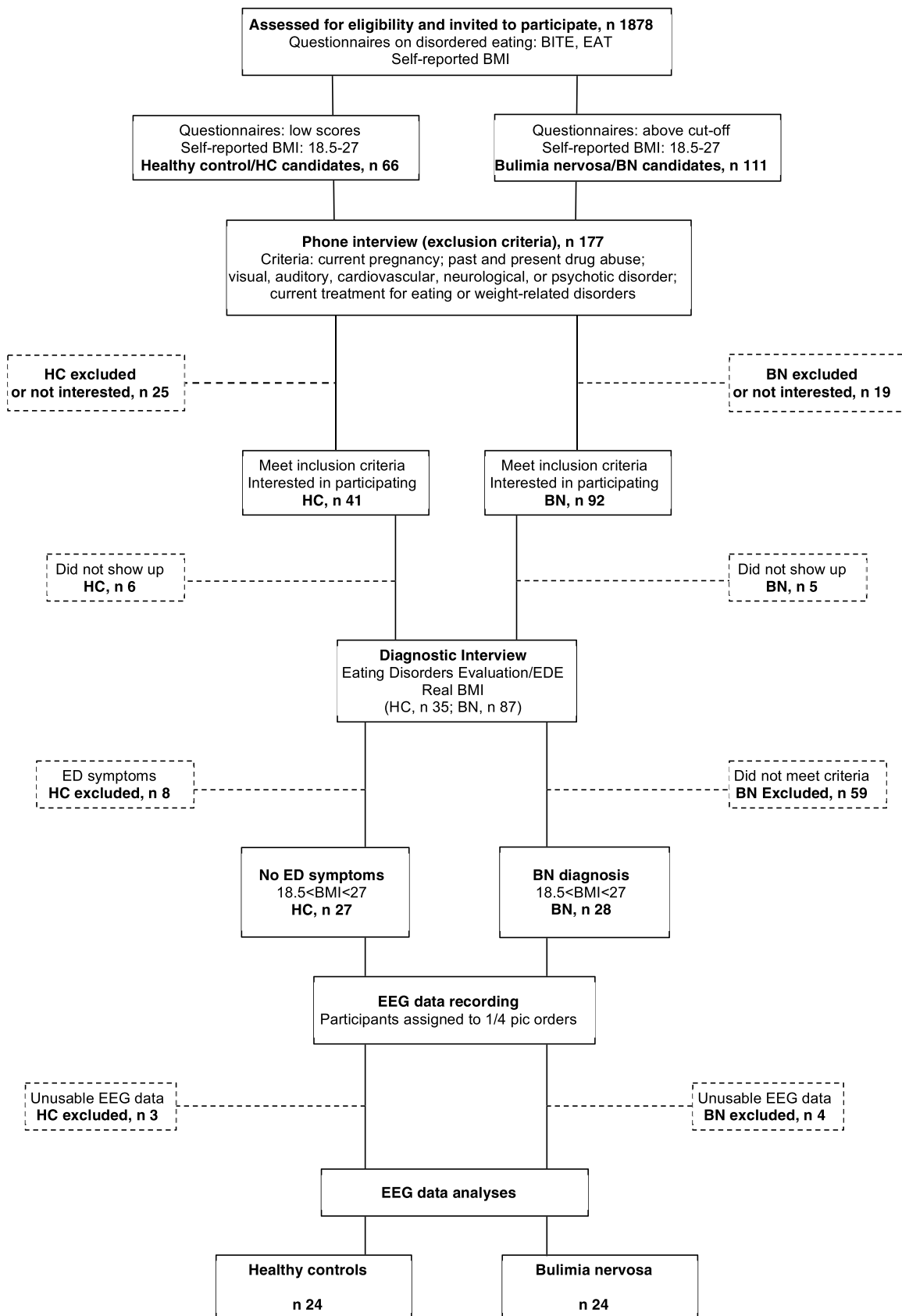


FIGURE 1. Participant flowchart.

involved in extreme physical activity within 24 hours of the session. The EEG sensor net was then attached, while participants were seated in a comfortable recliner in a sound-attenuated, dimly lit room. Next, the experimenter asked questions on current hunger level. After controlling the signal, participants were told that a series of pictures would appear and that they had to view each picture the entire time that it was on the screen, remaining as still as possible. Between pictures, participants had to comfortably focus on a central dot. Picture delivery on a 19" flat screen, situated 60 cm from the participant, was controlled by a computer running Presentation (v.16.3, Neurobehavioral Systems, San Francisco, CA). After a 5-minute baseline, the 96 picture trials were displayed, following this structure: 4-second baseline, 6-second picture viewing, 4-second postpicture, followed by a variable ITI (6–8 seconds). Picture viewing lasted 35 minutes. Four pseudorandomized picture orders, equally distributed across participants, avoided picture repetitions, but allowed a few category repetitions, to decrease predictability. After EEG net removal, participants rated the pictures using a computerized version of the Self-Assessment Manikin (42). The participants then completed some screening questionnaires again (32,43), before being thanked, debriefed, and compensated.

EEG Recording and Analysis

EEG was measured using the ActiveTwo BioSemi system (BioSemi, Amsterdam, the Netherlands) from 64 scalp sensors, organized following the 10/20 system. Two additional sensors served as reference (Common Mode Sense (CMS) active electrode) and ground sensors (Driven Right Leg (DRL) passive electrode). Scalp impedance was kept less than 40 k Ω . EEG was recorded continuously at a sampling rate of 1000 Hz. EEG data were downsampled offline to 512 Hz and digitally filtered from 0.01 to 40 Hz using BioSemi Decimator 85 and a MATLAB-based program (44), respectively. An algorithm performed artifact detection and sensor interpolation (45). On average, 87.0% of trials (for patients) and 86.2% (for controls) were included. Processed EEG data were then referenced to Cz and baseline corrected (200 milliseconds before picture onset) before averaging by participant for statistical analyses. ERPs were averaged independently for each sensor and picture category. To control the affective modulation of early ERPs, the EPN sensor cluster was selected by identifying and grouping occipito-parietal and occipital sensors with the largest microvolt difference between emotional and neutral pictures: PO3, POz, PO4, O1, Oz, and O2. The LPP sensor cluster was selected by identifying and grouping centroparietal and parietal sensors that showed the largest microvolt difference between emotional and neutral pictures: Cp1, Cp2, P1, Pz, and P2. Using Statistica v.13 (Dell Inc, 2015), statistical analyses were run: for the EPN, on the mean amplitude within a 200- to 300-millisecond time window from picture onset; for the LPP, on the mean amplitude within a 500- to 800-millisecond time window.

It must be kept in mind, however, that in the present study, the suitability of interpreting EPN data is challenged by the slow presentation of the stimuli (46), by the presence of faces in some but not all categories (47), and most importantly by the reduced control over the perceptual features of the images, which seem to modulate early ERPs more reliably than their motivational content (48).

STATISTICAL ANALYSIS

Mixed analyses of variance (ANOVAs) were performed that included picture category (food, erotica, neutrals, and unpleasant) and diagnostic group as within- and between-participant variables, respectively. The number of sexual partners during the past year was analyzed as a continuous variable and as a dichotomous variable, based on Binson and Catania's distinction between safe and risky sexual habits (29). First, correlational analyses were run between the number of sexual partners and the LPP amplitude during erotica. Next, risky/safe sexual habits were introduced as a dichotomous variable in a χ^2 test with diagnostic group, to investigate

whether the diagnosis of BN had a strong association with risky sexual habits. Finally, we performed an ANOVA on the mean LPP, introducing diagnostic group and sexual habits as between-participant variables and picture category as a within-participant variable, to investigate whether diagnostic group and risky sexual habits both modulated the mean LPP amplitude during food and nonfood cues. The level of significance was set to 0.05, Greenhouse-Geisser adjustments were applied whenever necessary, and partial η^2 was used to report effect sizes, i.e., the proportion of the variance explained by the factor under study. Significant main effects and interactions were further investigated using pairwise comparisons.

RESULTS

Table 1 shows that the two groups were comparable regarding age and body mass index as well as objective and subjective indices of hunger, whereas they differed in dimensions of psychopathology. Table 2 displays affective ratings of emotional and food pictures for the current sample of bulimic and healthy women.

Subjective Ratings

Subjective ratings of pleasure and arousal did not differ between bulimic patients and controls. For valence, a significant main effect of picture category ($F(2.71,124.76) = 222.7, p < .001$, partial $\eta^2 = 0.829$) indicated that in both patients and controls personal foods prompted the greatest feelings of pleasure, followed by erotica, neutrals, and human attacks (all p 's $< .001$). For arousal, a main effect of picture category ($F(2.81,129.47) = 131.6, p < .001$, partial $\eta^2 = 0.741$) showed that both patients and controls were activated the most during erotica, personal foods, and human attacks: these categories did not differ from one another (all p 's $> .95$) and all significantly differed from neutral contents (all p 's $< .001$). In contrast, when dominance/control ratings were examined, in addition to the main effect of image content ($F(2.81,129.35) = 28.4, p < .001$, partial $\eta^2 = 0.381$), a significant interaction between picture category and experimental group ($F(2.81,129.35) = 3.1, p = .030$, partial $\eta^2 = 0.063$) pointed out that bulimic patients felt less in control during personal foods ($p < .001$), whereas they felt as in control as healthy participants during erotica ($p = .91$).

ERPs: Early and Late Components

Early components (EPN) did not differ between bulimic participants and healthy controls. In line with emotion literature (6), a main effect of picture category ($F(2.71,122.42) = 15.7, p < .001$, partial $\eta^2 = 0.255$) indicated that compared with neutrals, erotica prompted the greatest EPN ($p < .001$), followed by personal foods and human attacks ($p = .008$ and $p < .001$, respectively) that did not differ from one another ($p = .58$).

As for the LLP, Figure 2A shows ERP waveforms averaged over centroparietal sensors for emotional, neutral, and food cues. Consistent with the emotion literature, when we examined the late time window (Figure 2B), we observed a significant main effect of picture category ($F(2.8,130.7) = 24.6, p < .001$, partial $\eta^2 = 0.348$) that pointed out that compared with neutral pictures, erotica prompted the largest LLP ($p < .001$), followed by human attacks ($p = .003$); food and neutral objects prompted comparably low neural activity. The main effect of diagnostic group was not significant, indicating that patients and controls did not differ in baseline neural reactivity to the stimuli. However, as seen in Figure 2C and 2D, follow-up tests on the significant interaction between diagnostic group and

TABLE 1. Participant Characteristics

Measure	Healthy Controls (n = 24)	Bulimia Nervosa (n = 24)	Test and p
Demographics			
Age	19.7 (2.1)	20.5 (2.6)	$F(1,46) = 1.5, p = .23$
Body mass index, kg/m ²	22.2 (2.3)	22.7 (3.49)	$F(1,46) = .4, p = .51$
Sexual partners	1.4 (1.3)	1.8 (1.7)	$F(1,46) = .9, p = .35$
European	95.8%	87.5%	$\chi^2(2) = 4.1, p = .39$
Blood glucose, mg/dL ^a	99.2 (13.0)	95.4 (12.6)	$F(1,46) = 1, p = .32$
Questionnaires			
EAT-40	9.2 (5.6)	35.0 (14.7)	$F(1,46) = 64.5, p < .001$
BITE			
Symptom scale	3.0 (2.2)	19.3 (4.8)	$F(1,46) = 225.5, p < .001$
Severity scale	2.3 (1.1)	10.7 (4.1)	$F(1,46) = 95.3, p < .001$
Total	5.3 (2.7)	30.0 (7.6)	$F(1,46) = 223.9, p < .001$
STAI-trait	14.7 (9.9)	34.9 (11.0)	$F(1,46) = 44.3, p < .001$
BDI	3.3 (3.4)	16.8 (8.6)	$F(1,46) = 51.7, p < .001$
FCQ-T	102.2 (28.0)	155.7 (30.7)	$F(1,46) = 39.8, p < .001$
FCQ-S	39.8 (12.7)	52.4 (14.0)	$F(1,46) = 10.8, p = .002$
SHAPS	49.9 (5.0)	46.0 (5.0)	$F(1,46) = 7.3, p = .009$
Questions on current hunger^b			
Are you hungry? (yes/no)	6/18	7/17	$\chi^2(1) = .1, p = .75$
How hungry do you feel? ^c	3.4 (1.8)	3.8 (1.9)	$F(1,46) = .3, p = .56$
How strong is your desire to eat? ^c	3.0 (1.8)	3.5 (2.1)	$F(1,46) = .6, p = .46$
How full do you feel? ^c	4.8 (2.2)	3.9 (2.3)	$F(1,46) = 1.8, p = .19$
How much food do you think you could eat? ^c	4.2 (1.7)	5.3 (2.1)	$F(1,46) = 3.6, p = .066$
How long since your last meal? (in minutes)	184.5 (68.1)	188.7 (57.2)	$F(1,46) = .1, p = .82$

EAT = Eating Attitudes Test-40 (30); BITE = Bulimic Investigatory Test Edinburgh (31); STAI = State-Trait Anxiety Inventory (34); SHAPS = Snaith-Hamilton Pleasure Scale (33); FCQ-T/S = Food Craving Questionnaire-Trait/State (32); BDI = Beck Depression Inventory (35).

Values are presented as M (SD), unless otherwise indicated.

^a Blood glucose level was collected after arrival at the laboratory.

^b Questions on current state of hunger were answered immediately before EEG recordings.

^c Questions on hunger level (36) were measured on a 1–9 Likert scale.

picture category ($F(2.8,130.7) = 2.8, p = .047$, partial $\eta^2 = 0.057$) indicated that compared with healthy controls, women diagnosed with BN showed enhanced LPP amplitude during pictures of binge foods ($p = .037$) and erotic couples ($p = .031$).

Linear correlations, χ^2 tests, and mixed design ANOVAs revealed no relationships among number of sexual partners, diagnostic group, and mean LPP amplitude.

DISCUSSION

In this study, we presented pictures of personally irresistible foods, erotic couples, neutral objects, and unpleasant scenes to women diagnosed with BN and to women with a healthy relationship with food and their own body. The LLP showed a different pattern in women diagnosed with BN compared with the pattern in healthy controls: the amplitude of the LPP was larger

TABLE 2. Affective Ratings of Individually Selected IAPS and Personal/OLAF Pictures for Bulimic and Healthy Women (Current Sample)

	Erotic Couples, M (SD)		High-Calorie, Foods, M (SD)		Neutral Objects, M (SD)		Human Attacks, M (SD)	
	BUL	Contr	BUL	Contr	BUL	Contr	BUL	Contr
Pleasure	7.1 (1.8)	7.3 (1.2)	7.6 (2.0)	8.3 (0.9)	4.5 (2.0)	4.5 (1.7)	2.2 (1.6)	1.8 (1.2)
Arousal	7.1 (1.8)	6.9 (1.6)	7.2 (2.2)	7.2 (1.6)	2.5 (1.8)	2.2 (1.8)	7.0 (1.9)	7.0 (2.1)
Dominance	6.0 (2.1)	6.0 (1.4)	4.1 (2.4)	5.8 (2.1)	6.0 (1.8)	5.7 (1.9)	3.0 (2.0)	3.3 (1.8)

M = mean; SD = standard deviation; BUL = bulimic participants; Contr = healthy controls.

All ratings are from adult women.

Boldface indicates significant difference between bulimic and healthy participants.

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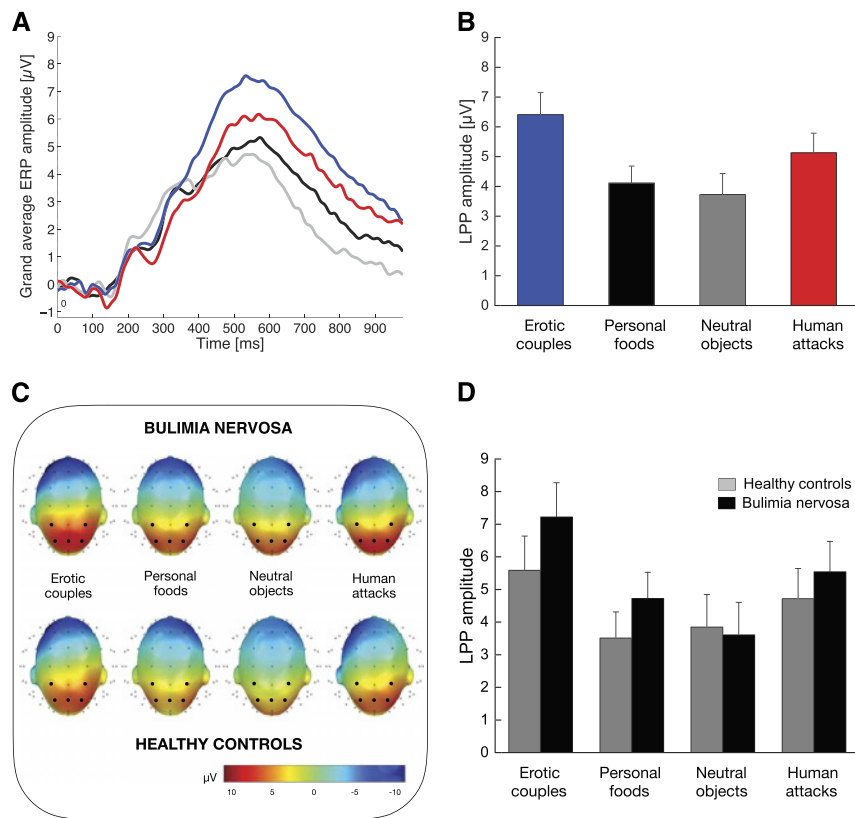


FIGURE 2. A, Grand average ERP waveforms over centroparietal sensors (CP1, CP2, P1, Pz, and P2) during images displaying erotic couples (blue line), personal foods (black line), human attacks (red line), and neutral objects (gray line). B, Mean ERP amplitudes for erotic, personal food, neutral, and unpleasant cues in the LLP time window (500–800 milliseconds). As expected, the LPP was larger during pictures displaying content with greater motivational significance (erotica and human attacks). Error bars represent 95% confidence intervals. C, For each picture category and for each experimental group, scalp topography (top view) represents ERP amplitudes in the LPP time window. Black dots display the centroparietal sensor cluster used for statistical analysis: CP1, CP2, P1, Pz, and P2. D, Mean LPP amplitudes for erotic, personal food, neutral, and unpleasant cues for bulimic women and healthy controls. In bulimic women, pictures displaying erotic couples and personal food cues elicited larger LPP amplitudes. Error bars represent 95% confidence intervals. Color image is available only in online version (www.psychosomaticmedicine.org).

during binge food and erotic cues. Previous investigations focused on the early neural correlates of BN and observed facilitated processing of food and body cues (7,8). The current data are the first findings on the late neural correlates of BN. The LPP is regarded as a reliable indicator of motivational significance because, unlike early components, it is less influenced by perceptual features, e.g., brightness, contrast, and complexity (6,48), and it has been shown to reflect the activity of cortical and subcortical structures involved in emotional picture perception (49). The observed results, therefore, provide physiological evidence of the undue relevance that bulimic women assign to food and erotic cues.

The early stages of picture processing, reflected in the EPN, can also be modulated by the motivational salience of the stimuli (see, e.g., (6,46)). In the current study, each participant selected her own pictures, and as a result, we could not control perceptual features that could have modulated the EPN (48). Thus, although the EPN seemed to be modulated by picture content and not by experimental group, the findings might be blurred by perceptual processing rather than motivational salience, e.g., erotica, that prompted the largest EPN, included faces, and displayed easily recognizable naked bodies that could have biased EPN results.

The presentation of personally selected irresistible binge food cues was successful in prompting subjective feelings of arousal that were, as expected, higher than those observed using nonpersonally selected high-calorie foods (compare Table 2 and Table S1, Supplemental Digital Content 1, <http://links.lww.com/PSYMED/A564>) and, most importantly, in differentiating the neural correlates of bulimic women and controls. In a previous study, finger pulse amplitude during binge food cues did not differ between bulimic patients and controls (18). The LPP could possibly differentiate ED patients from controls because its affective modulation, in contrast to peripheral measures, shows limited habituation across trials (50,51).

Recent advances in mental health (52) propose a wider, dimensional look at mental disorders, focusing on specific processes with known neural bases, rather than diagnostics (e.g., see (53)). Within this transdiagnostic perspective, food-related disorders can be examined as a function of their specific neural correlates during food cue processing. Studies that examined the LPP in obesity repeatedly observed that obese individuals do not differ from healthy controls in their overall neural response to food and non-food stimuli (4,21). Therefore, the data suggest that excessive food

intake is not by itself clearly associated with a larger LPP during food cues. However, recent investigations ran additional cluster analyses on obese and healthy participants' average LPP during food and nonfood cues: the cluster analyses uncovered a healthy endophenotype—characterized by reduced neural responses to food cues and increased neural responses to erotica—and an aberrant endophenotype—characterized by exaggerated neural reactions to food cues and blunted neural reactions to erotica. The latter cluster consisted predominantly of obese individuals (21). In the present study, to rule out the presence of such healthy/aberrant endophenotypes, we ran further statistics that verified that these patterns were not present in BN. Thus, BN, similarly to binge ED (11), is associated with exaggerated late neural reactions to food cues, suggesting that the loss of control or excessive control over food could prompt pathological brain reactions to food cues. Interestingly, studies that ran cluster analyses on the late neural correlates of obesity (21) did not investigate the presence of binge eaters among obese participants. Taken together, the data suggest that pathological control/no control over food could be a key factor underlying exaggerated late neural correlates of disordered food cue processing. The possible association between diametrically opposed feeding behaviors is in line with recent animal studies on the etiology of food-related disorders (54,55), suggesting that in rats specific gene mutations combined with environmental changes alternatively prompt AN-like or BN/BED-like behaviors.

From a wider perspective for ED treatment, it has been put forward that the focus be not only on disorder-specific cues—food and bodies varying in shape—but also on stimuli that are regarded as pleasant in the general population (56). Several recent studies have included nonfood affective cues as controls (7,13,56,57). However, most studies chose low-arousing cues with diverse content as pleasant control cues, such as landscapes, families, and puppies. Some authors suggest that the absence of potent appetitive stimuli, such as erotica, resulted in reduced physiological reactivity to pleasant cues that limited the scrutiny of appetitive activation in ED patients and controls (57). In the present study, pictures of erotic couples were chosen as control cues, because in women, based on startle reflex reactivity, they are associated with strong appetitive processing and cause less subjective aversion than images displaying opposite-sex erotica, i.e., naked men (3).

There is surprisingly scarce research on ED women's sexuality, and to our knowledge, it is exclusively based on clinical observations and self-reports (25,58,59). The current findings therefore provide objective evidence that bulimic women, compared with healthy controls, assign undue significance to erotic cues displaying naked bodies. However, participants' LPP during erotica was not modulated by the number of sexual partners during the past year. The results are probably related to our selection of low-arousing erotica, because in healthy controls the LPP modulation by past sexual partners was observed during highly explicit erotic pictures rather than less arousing IAPS images (26). Our goal was to select erotic stimuli that were highly appetitive for women, who subjectively tend to report a certain degree of avoidance toward sexually explicit material, which is physiologically visible in the slightly larger amplitude of the startle reflex (3). Our selection of IAPS erotic couples, associated in women with the largest startle reflex inhibition that is indicative of appetitive motivation (*idem*), allowed us to confirm that the stimuli were highly positive, at least for healthy controls. We can speculate that bulimic women's neural

overreaction to pictures displaying erotic couples could reflect the characteristic aversion to body cues (1) and pathological body dissatisfaction (23) seen in BN but also the context of social intimacy that bulimic women tend to find less gratifying than healthy controls (60). In our study, as typically observed, bulimic patients scored high in anxiety and depression. Anxiety scores have been related to the size of the LPP mostly during negative cues (e.g., (61,62)), whereas during rewarding cues, the association with LPP amplitude seems less clear (63,64). As for depressive symptoms, it is more consistently accompanied by reduced LPP to pleasant cues (65,66). Thus, we can hypothesize that bulimic women's overreaction to binge foods and erotic couples might be disorder-specific rather than related to depressive symptoms. However, as mentioned earlier, pleasant stimuli typically consist of low-arousing cues (e.g., landscapes, families, puppets...), whereas erotic stimuli are less commonly used in clinical populations (57). It will therefore be especially informative to use the LPP in addition to food cues to investigate how erotic cues are processed in different food- and nonfood-related pathologies.

The LPP is an index of stimulus salience (6) that, unlike other physiological measures, does not differentiate appetitive and aversive motivation. As in AN (56,57), future studies that include physiological measures that are modulated by the emotional content of the images—such as the startle reflex, facial electromyography, and heart rate—could clarify whether the pronounced neural reactions to erotic and food cues in BN signify exaggerated pleasure, aversion, or a combination of both. In our study, bulimic women reported feeling less in control during personal food cues, whereas they felt equally in control as healthy participants during erotic cues. Thus, based on subjective ratings, food cues were perceived by bulimic patients as more unsettling than pleasant/erotic cues. Interestingly, in a previous study from our laboratory, bulimic patients felt less in control during food as well as erotic cues (67). We hypothesize that this divergence stemmed from the current selection of erotic couples, which women experienced as more pleasant compared with other explicit erotic content (3). However, it must be kept in mind that ratings are known to diverge from physiology (e.g., (67)), even more so when patients are concerned (e.g., (68)), and that erotic cues have seldom been used as pleasant cues in clinical populations (57). Accordingly, further studies on the physiological correlates of BN are needed to clarify the valence associated with food cues and erotica.

Previous studies (13,69) suggest that bulimia might be characterized by coactivation of approach and avoidance that result in affective ambivalence toward disorder-relevant cues (70), with an additional mismatch between the subjective and physiological measures (69). In contrast to late neural data that suggest exaggerated motivational relevance of food and erotic cues, ambivalent peripheral physiological data could therefore confirm the mixed nature of BN that, more than any other ED, might be characterized by coactivation of approach and avoidance (13,71,72).

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REFERENCES

- Fairburn CG, Harrison PJ. Eating disorders. *Lancet* 2003;361:407–16.
- Stockburger J, Weike AI, Hamm AO, Schupp HT. Deprivation selectively modulates brain potentials to food pictures. *Behav Neurosci* 2008;122:936–42.
- Bradley MM, Codispoti M, Sabatinelli D, Lang PJ. Emotion and motivation II: sex differences in picture processing. *Emotion* 2001;1:300–19.
- Nijs IM, Franken IH, Muris P. Food cue-elicited brain potentials in obese and healthy-weight individuals. *Eat Behav* 2008;9:462–70.
- Stockburger J, Schmäzle R, Fleisch T, Bublatzky F, Schupp HT. The impact of hunger on food cue processing: an event-related brain potential study. *Neuroimage* 2009;47:1819–29.
- Schupp HT, Fleisch T, Stockburger J, Jungho M, Junghoefer M. Emotion and attention: event-related brain potential studies. *Prog Brain Res* 2006;156:31–51.
- Blechert J, Feige B, Joos A, Zeeck A, Tuschen-Caffier B. Electrocutaneous processing of food and emotional pictures in anorexia nervosa and bulimia nervosa. *Psychosom Med* 2011;73:415–21.
- Mai S, Gramann K, Herbert BM, Friederich H, Warschburger P, Pollatos O. Electrophysiological evidence for an attentional bias in processing body stimuli in bulimia nervosa. *Biol Psychol* 2015;108:105–14.
- Homdasch S, Heinrich H, Kratz O, Moll GH. The late positive potential as a marker of motivated attention to underweight bodies in girls with anorexia nervosa. *J Psychosom Res* 2012;73:443–7.
- Homdasch S, Kratz O, Van Doren J, Graap H, Kramer R, Moll GH, Heinrich H. Cue reactivity towards bodies in anorexia nervosa – common and differential effects in adolescents and adults. *Psychol Med* 2017.
- Svaldi J, Tuschen-Caffier B, Peyk P, Blechert J. Information processing of food pictures in binge eating disorder. *Appetite* 2010;55:685–94.
- Blechert J, Nickert T, Caffier D, Tuschen-Caffier B. Social comparison and its relation to body dissatisfaction in bulimia nervosa: evidence from eye movements. *Psychosom Med* 2009;71:907–12.
- Altman SE, Campbell ML, Nelson BD, Faust JP, Shankman SA. The relation between symptoms of bulimia nervosa and obsessive-compulsive disorder: a startle investigation. *J Abnorm Psychol* 2013;122:1132–41.
- Guerra P, Campagnoli RR, Vico C, Volchan E, Anllo-Vento L, Vila J. Filial versus romantic love: contributions from peripheral and central electrophysiology. *Biol Psychol* 2011;88:196–203.
- McTeague LM, Lang PJ, Laplante MC, Cuthbert BN, Shumen JR, Bradley MM. Aversive imagery in posttraumatic stress disorder: trauma recurrence, comorbidity, and physiological reactivity. *Biol Psychiatry* 2010;67:346–56.
- Bulik CM, Lawson RH, Carter FA. Salivary reactivity in restrained and unrestrained eaters and women with bulimia nervosa. *Appetite* 1996;27:15–24.
- Jansen A, Van Den Hout MA, De Loof C, Zanderbergen J, Griez E. A case of bulimia successfully treated by cue exposure. *J Behav Ther Exp Psychiatry* 1989;20:327–32.
- Nederkooom C, Smulders F, Havermans R, Jansen A. Exposure to binge food in bulimia nervosa: finger pulse amplitude as a potential measure of urge to eat and predictor of food intake. *Appetite* 2004;42:125–30.
- Carter FA, Bulik CM, Lawson RH, Sullivan PF, Wilson JS. Effect of mood and food cues on body image in women with bulimia and controls. *Int J Eat Disord* 1996;20:65–76.
- Versace F, Schembre SM. ‘Obesogenic’ oversimplification. *Obes Rev* 2015;16:702–3.
- Versace F, Kyriotakis G, Basen-engquist K, Schembre SM. Heterogeneity in brain reactivity to pleasant and food cues: evidence of sign-tracking in humans. *Soc Cogn Affect Neurosci* 2016;11:604–11.
- Weinberg A, Hajcak G. Beyond good and evil: the time-course of neural activity elicited by specific picture content. *Emotion* 2010;10:767–82.
- Cash TF, Deagle EA. The nature and extent of body-image disturbances in anorexia nervosa and bulimia nervosa: a meta-analysis. *Int J Eat Disord* 1997;22:107–25.
- Higgins MK, Choukas-Bradley S, Crowder EE, Bardone-Cone AM. Examining moderators of the relation between body consciousness during sexual activity and disordered eating. *Adv Eat Dis* 2016;4:31–46.
- Wiedeman MW, Pryor T, Don Morgan C. The sexual experience of women diagnosed with anorexia nervosa or bulimia nervosa. *Int J Eat Dis* 1996;19:109–18.
- Prause N, Steele VR, Staley C, Sabatinelli D. Late positive potential to explicit sexual images associated with the number of sexual intercourse partners. *Soc Cogn Affect Neurosci* 2015;10:93–100.
- Stice E, Marti CN, Rohde P. Prevalence, incidence, impairment, and course of the proposed DSM-5 eating disorder diagnoses in an 8-year prospective community study of young women. *J Abnorm Psychol* 2013;122:445–57.
- Fairburn C, Cooper Z, O'Connor M. Eating disorder examination (Edition 16.0D). In: Fairburn C, editor. *Cognitive Behavior Therapy and Eating Disorders*. New York, NY: Guilford Press; 2008:265–308.
- Binson D, Catania JA. Respondents' understanding of the words used in sexual behavior questions. *Public Opin Q* 1998;62:190–208.
- Castro J, Toro J, Salameró M, Guimerá E. The eating attitudes test: validation of the Spanish version. *Evaluación Psicológica* 1991;7:175–89.
- Rivas T, Bersabé R, Jiménez M. Fiabilidad y validez del Test de investigación bulímica de Edinburgo (BITE) en una muestra de adolescentes españoles [Reliability and validity of bulimic investigatory test Edinburgh (BITE) in a sample of Spanish adolescents]. *Psicología Conductual* 2004;3:447–62.
- Cepeda-Benito A, Gleaves DH, Fernández MC, Vila J, Williams TL, Reynoso J. The development and validation of Spanish versions of the State and Trait Food Cravings Questionnaires. *Behav Res Ther* 2000;38:1125–38.
- Fresán A, Berlanga C. Traducción al español y validación de la Escala de Placer Snaith-Hamilton para Anhedonia (SHAPS) [Spanish translation and validation of the Snaith-Hamilton Anhedonia Pleasure Scale]. *Actas Esp Psiquiatr* 2013;41:227–31.
- Seisdedos N. Cuestionario de Ansiedad Estado-Rasgo [State-Trait Anxiety Inventory]. Madrid: TEA Ediciones; 1982.
- Sanz J, Vázquez C. Fiabilidad, validez y datos normativos del Inventario para la Depresión de Beck. *Psicothema* 1998;10.
- Hill AJ, Magson LD, Blundell JE. Hunger and palatability: tracking ratings of subjective experience before, during and after the consumption of preferred and less preferred food. *Appetite* 1984;5:361–71.
- Miccoli L, Delgado R, Guerra P, Versace F, Rodríguez-Ruiz S, Fernández-Santaella MC. Affective pictures and the Open Library Of Affective Foods (OLAF): tools to investigate emotions toward food in adults. *PLoS One* 2016;11–13.
- Vila J, Sanchez M, Ramirez I, Fernandez MC, Cobos P, Rodriguez S, Munoz MA, Tormo MP, Herrero M, Segarra P, Pastor MC, Poy R. El Sistema Internacional de Imágenes Afectivas (IAPS): Adaptación española. Segunda parte. *Rev Psicol Gen Apl* 2001;54:635–57.
- Molto J, Montañés S, Poy R, Segarra P, Pastor MC, Tormo MP, Ramírez I, Hernández MA, Sánchez M, Fernández MC, Vila J. Un nuevo método para el estudio experimental de las emociones: El “International Affective Picture System” (IAPS). Adaptación española. *Rev Psicol Gen Apl* 1999;52:55–87.
- Moltó J, Segarra P, López R, Esteller A, Fonfría A, Pastor MC, Poy R. Adaptación española del International Affective Picture System (IAPS). Tercera parte *Anales de psicología* 2013;29:965–84.
- Lang P, Bradley M, Cuthbert B. International Affective Picture System (IAPS): Affective Ratings of Pictures and Instruction Manual. In: Technical Report A-8. University of Florida. Gainesville, FL: University of Florida; 2008.
- Bradley MM, Lang PJ. Measuring emotion: the Self-Assessment Manikin and the semantic differential. *J Behav Ther Exp Psychiatry* 1994;25:45–59.
- Snaith RP, Hamilton M, Morley S, Humayan A, Hargreaves D, Trigwell P. A scale for the assessment of hedonic tone the Snaith-Hamilton Pleasure Scale. *Br J Psychiatry* 1995;167:99–103.
- Peyk P, De Cesarei A, Junghöfer M. ElectroMagnetoEncephalography Software: Overview and Integration with Other EEG / MEG Toolboxes. *Comput Intell Neurosci* 2011;2011:861705.
- Junghöfer M, Elbert T, Tucker DM, Rockstroh B. Statistical control of artifacts in dense array EEG/MEG studies. *Psychophysiology* 2000;37:523–32.
- Fleisch T, Häcker F, Renner B, Schupp HT. Emotion and the processing of symbolic gestures: an event-related brain potential study. *Soc Cogn Affect Neurosci* 2010;6:109–18.
- Wiens S, Sand A, Olofsson JK. Nonemotional features suppress early and enhance late emotional electrocortical responses to negative pictures. *Biol Psychol* 2011;86:83–9.
- Bradley MM, Hamby S, Low A, Lang PJ. Brain potentials in perception: picture complexity and emotional arousal. *Psychophysiology* 2007;44:364–73.
- Sabatinelli D, Lang PJ, Keil A, Bradley MM. Emotional perception: correlation of functional MRI and event-related potentials. *Cereb Cortex* 2007;17:1085–91.
- Codispoti M, Ferrari V, Bradley MM. Repetitive picture processing: autonomic and cortical correlates. *Brain Res* 2006;1068:213–20.
- Ferrari V, Bradley MM, Codispoti M, Lang PJ. Repetitive exposure: brain and reflex measures of emotion and attention. *Psychophysiology* 2011;48:515–22.
- Insel TR, Cuthbert BN. Medicine. Brain disorders? Precisely. *Science* 2015;348:499–500.
- Crocker LD, Heller W, Warren SL, O'Hare AJ, Infantolino ZP, Miller GA. Relationships among cognition, emotion, and motivation: implications for intervention and neuroplasticity in psychopathology. *Front Hum Neurosci* 2013;7:1–19.
- Bulik CM, Breen G. Solving the eating disorders puzzle piece by piece. *Biol Psychiatry* 2017;81:730–1.
- Lutter M, Khan MZ, Satio K, Davis KC, Kidder IJ, McDaniel L, Darbo BW, Pieper AA, Cui H. The eating-disorder associated HDAC4A778T mutation alters feeding behaviors in female mice. *Biol Psychiatry* 2017;81:770–7.
- Racine SE, Forbush KT, Wildes JE, Hagan KE, Pollack LO, May C. Voluntary emotion regulation in anorexia nervosa: a preliminary emotion-modulated startle investigation. *J Psychiatr Res* 2016;77:1–7.
- Erdur L, Weber C, Zimmermann-Viehoff F, Rose M, Deter HC. Affective responses in different stages of anorexia nervosa: results from a startle-reflex paradigm. *Eur Eat Disord Rev* 2017;25:114–22.

58. Pinheiro AP, Raney TJ, Thornton LM, Fichter MM, Berrettini WH, Goldman D, Halmi KA, Kaplan AS, Strober M, Treasure J, Woodside DB, Kaye WH, Bulik CM. Sexual functioning in women with eating disorders. *Int J Eat Disord* 2010;43:123–9.
59. Castellini G, Lelli L, Sauro Lo C, Fioravanti G, Vignozzi L, Maggi M, Faravelli C, Ricca V. Anorectic and bulimic patients suffer from relevant sexual dysfunctions. *J Sex Med* 2012;9:2590–9.
60. Tchanturia K, Davies H, Harrison A, Fox JR, Treasure J, Schmidt U. Altered social hedonic processing in eating disorders. *Int J Eat Disord* 2012;45:962–9.
61. MacNamara A, Hajcak G. Anxiety and spatial attention moderate the electrocortical response to aversive pictures. *Neuropsychologia* 2009;47:2975–80.
62. Chronaki G, Broyd SJ, Garner M, Benikos N, Thompson MJJ, Sonuga-Barke EJS, Hadwin JA. The moderating effect of self-reported state and trait anxiety on the late positive potential to emotional faces in 6–11-year-old children. *Front Psychol* 2018;9:1–14.
63. Weinberg A, Perlman G, Kotov R, Hajcak G. Depression and reduced neural response to emotional images: distinction from anxiety, and importance of symptom dimensions and age of onset. *J Abnorm Psychol* 2016;125:26–39.
64. Rutherford HJV, Byrne SP, Austin GM, Lee JD, Crowley MJ, Mayes LC. Anxiety and neural responses to infant and adult faces during pregnancy. *Biol Psychol* 2017;125:115–20.
65. Hajcak Proudfit G, Bress JN, Foti D, Kujawa A, Klein DN. Depression and event-related potentials: emotional disengagement and reward insensitivity. *Curr Opin Psychol* 2015;4:110–3.
66. Weinberg A, Sandre A. Distinct Associations between low positive affect, panic, and neural responses to reward and threat during late stages of affective picture processing. *Biol Psychiatry Cogn Neurosci Neuroimaging* 2018;3:59–68.
67. Rodríguez S, Mata JL, Lameiras M, Fernández-Santaella MC, Vila J. Dyscontrol evoked by erotic and food images in women with bulimia nervosa. *Eur Eat Disord Rev* 2007;15:231–9.
68. Lang PJ. Emotion's response patterns: the brain and the autonomic nervous system. *Emotion Rev* 2014;6:93–9.
69. Mauler BI, Hamm AO, Weike AI, Tuschen-Caffier B. Affect regulation and food intake in bulimia nervosa: emotional responding to food cues after deprivation and subsequent eating. *J Abnorm Psychol* 2006;115:567–79.
70. Cacioppo JTJ, Berntson GGG. Relationship between attitudes and evaluative space: a critical review, with emphasis on the separability of positive and negative substrates. *Psychol Bull* 1994;115:401–23.
71. Harrison A, Treasure J, Smillie LD. Approach and avoidance motivation in eating disorders. *Psychiatry Res* 2011;188:396–401.
72. Racine SE, Hebert KR, Benning SD. Emotional reactivity and appraisal of food in relation to eating disorder cognitions and behaviours: evidence to support the motivational conflict hypothesis. *Eur Eat Disord Rev* 2018;26:3–10.