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Food deprivation and emotional reactions to food cues: implications for eating disorders

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Abstract

Two studies examined emotional responding to food cues. In experiment 1, normal college students were assigned to 0-, 6- or 24-h of food deprivation prior to presentations of standard emotional and food-related pictures. Food deprivation had no impact on responses elicited by standard emotional pictures. However, subjective and psychophysiological reactions to food pictures were affected significantly by deprivation. Importantly, food-deprived subjects viewing food pictures showed an enhanced startle reflex and increased heart rate. Experiment 2 replicated the food deprivation effects from experiment 1, and examined participants reporting either a habitual pattern of restrained (anorexia-like) or binge (bulimia-like) eating. Food-deprived and binge eater groups showed startle potentiation to food cues, and rated these stimuli as more pleasant, relative to restrained eaters and control subjects. The results are interpreted from the perspective that startle modulation reflects activation of defensive or appetitive motivation. Implications of the data for understanding eating disorders are considered. © 2001 Elsevier Science B.V. All rights reserved.

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1. Introduction

The Russian physiologist Pavlov stated early in the last century that 'The most essential connection between the animal organism and the surrounding world is that brought about by certain chemical substances which constantly enter into the composition of the given organism, i.e. the food connection.' (Pavlov, 1909). Subsequently, Pavlov's (1927) classic demonstration of conditioning used the salivary gland reflex of the dog: After a neutral cue was repeatedly paired with food, the gland showed increased flow to subsequent presentations of the cue. Humans may experience the same conditioned salivation when seeing a sign advertising a 'bakery'. Such conditioned reactions to salient food cues (which include other responses — somatic and autonomic) are useful adaptations that generally facilitate survival; however, learning may also modulate appetitive response patterns in less salutary ways that can lead to eating disorders and threaten health.

Since Pavlov's early work, considerable animal and human research has supported the role of conditioning in mediating appetitive reflex modulation and motivation for food intake (e.g. Capaldi et al., 1983; Laberg et al., 1991; Lappalainen et al., 1994; Wooley and Wooley, 1973). In the present study, we sought to investigate normal and pathological forms of food motivation by examining verbal, physiological, and behavioral responses to salient food cues in normal participants systematically deprived of food, and in participants who report habitually deviant eating patterns.

1.1. Motivational priming and the startle reflex

Drawing on ideas developed by Konorski (1967), Lang and coworkers (Lang, 1995; Lang et al., 1990, 1992, 1997) proposed that affects are determined by the individual's motivational state. Two brain circuits are postulated, one determining appetitive responding (e.g. approach, attachment, consumption) and positive, pleasant affects, and the other prompting defense (e.g. avoidance, fight-flight) and unpleasant affects. These systems can be co-active (see Miller, 1944), and the motive significance of cues may be modified by experience. However, emotion and mood (pleasant or unpleasant) at any given time are determined by the dominant motive system (appetitive or defensive).

A feature of this biphasic view is that an individual's affective state (positive or negative valence) can be inferred by evoking a reflex that is consistent or inconsistent with the dominant motive system. Thus, several investigations (e.g. Vrana et al., 1988; Bradley et al., 1990, 1991; Cook et al., 1991) have shown that the defensive startle reflex is potentiated when it is elicited in the context of an unpleasant foreground stimulus. Pleasant foregrounds, on the other hand, prompt an appetitive emotional state that is inhibitory of the defensive startle reflex.

Animal researchers have also consistently shown startle reflex augmentation in an aversive experimental context (see Davis, 1989; Davis et al., 1987). Furthermore, these investigators have elegantly delineated the neural circuitry underlying startle and its potentiation. Thus, the primary, obligatory startle circuit (from the cochlear root neurons through the nucleus reticularis pontis caudalis to the spinal cord) is modulated during aversive cues by projections to reticularis from the central nucleus of the amygdala.

Consistent with the biphasic view, several studies have observed a diminished startle response during presentation of cues that signal food or water (e.g. Armus et al., 1964; Mellgren, 1969; Schmid et al., 1995). Koch et al. (1996) implicated the nucleus accumbens in the circuit mediating this 'pleasure-attenuated startle'. More recently, Yeomans et al. (2000) have shown reflex attenuation to startle probes presented during cue stimuli associated with rewarding hypothalamic brain stimulation.

1.2. Frustrative nonreward

Several researchers studying substance abuse in humans have noted that appetitive cravings can prompt an aversive affective state (e.g. Baker et al., 1987; Drobes and Tiffany, 1997). That is, while reward cues generally prompt positive affect, under conditions of deprivation or denial (frustration) such cues can lead to unpleasant affect, and perhaps, a different pattern of reflex modulation.

The above phenomenon may account for the unexpected results in some animal conditioning studies designed to enhance the salience of appetitive cues through deprivation (e.g. Fechter and Ison, 1972; Ison and Krauter, 1975; Szábo, 1967; Trapold, 1962). In this research, probe startle reflexes sometimes showed diminution, potentiation, or yielded no clear effect, reflecting varying interactions between delay or denial of reward and drive level (deprivation) that were difficult to interpret.

According to frustration theory, an aversive state may be prompted in either of two ways, i.e. direct activation of the defense motivation system, or through blocking of appetitive drive. Regarding the latter, it is proposed that appetitive food cues presented to organisms in a high drive state — when actual consumption is not possible — promote a state of frustrative nonreward (e.g. Amsel, 1958, 1992). Wagner (1969), among others, has emphasized the aversive nature of nonreward in deprived animals. Furthermore, his work showed convincingly that, when food is withheld, food cues potentiate the probe startle response (Wagner, 1963). Frustration has been shown to prompt negative emotional arousal in humans (e.g. Tranel, 1983). Thus, under conditions of food deprivation humans may also show startle potentiation in the context of food cues.

2. The research questions

In the present research, we investigated the impact of food deprivation, as well as binge and restrained eating patterns, on relevant verbal and psychophysiological responses to a broad range of affective and food-related cues in humans. In Study 1, normal college students were randomly assigned to one of three levels of food deprivation. Study 2 included two groups, each composed of subjects with a naturally occurring eating pattern, either binge or restrained eating, that bear a relationship with common eating disorders (i.e. bulimia and anorexia), as well as new groups of food-deprived and non-deprived normal eaters. Stimuli for both studies consisted of pictures selected from the International Affective Picture System (IAPS; CSEA, 1995) that represented one of three valence categories (pleasant, neutral, or unpleasant), or that represented appetitive food items. In addition to the startle eyeblink reflex, visceral measures of autonomic activity (heart rate and skin conductance), affective ratings, and choice picture viewing time were included in both experiments to provide additional indices of attention and emotional response. Each of these measures has been shown to vary systematically according to the affective valence and arousal of picture stimuli (e.g. Bradley et al., 1993; Lang et al., 1993). Furthermore, in study 1, facial EMG measures provided additional information about the emotional valence of the cues, and food consumption was measured to index a relevant behavioral response. Our general prediction was that food deprivation and abnormal patterns of eating would be associated with distinct patterns of reactivity to food cues, but that responding to standard affective picture categories (pleasant, unpleasant, and neutral) would be largely independent of these manipulations.

Two primary questions were addressed in the present research:

First, would food deprivation specifically impact the startle response and other emotional responses to food-related cues, relative to a broad range of affective stimuli with known properties? It was predicted that non-deprived subjects, when presented with appetitive food cues, would exhibit responses that would resemble responses to other appetitive cues. In particular, we expected the startle reflex to both food and non-food pleasant cues to be inhibited, relative to aversive and neutral cues. For food-deprived subjects, food cues presumably have enhanced motivational significance, and two competing predictions are considered. First, food deprivation could increase the appetitive value of food cues, with a corresponding inhibitory effect on the startle reflex. Alternatively, food deprivation may lead to a high level of anxiety or frustration in an experimental context in which salient food cues are presented, but without an explicit opportunity for consumption (e.g. Amsel, 1958; Wagner, 1969). As frustration is an aversive state (see also, Mackintosh, 1974), this scenario predicts startle potentiation to food cues as a function of food deprivation, with non-deprived subjects showing startle inhibition to food cues.

Second, would abnormal patterns of eating involving self-induced food restriction, like those associated with eating disorders such as bulimia and anorexia, result in similar patterns of reactivity to food cues as observed with experimentally-induced food deprivation? We studied two patterns of disturbed eating, binge and restrained eating. We predicted that binge and restrained eaters would show disparate patterns of responding to food cues, due to the different dispositions these groups show towards eating (i.e. indulgent vs. avoidant). It was of particular interest to determine which of these abnormal patterns of eating would produce a response profile more similar to that produced by food deprivation. It was predicted that binge eaters, as a function of an overly indulgent predilection towards food, would be more similar to food-deprived subjects.

3. Study 1

3.1. Method

3.1.1. Subjects and design

One hundred and five undergraduate students were recruited as subjects from the University of Florida Introductory Psychology subject pool. Each subject was contacted by telephone and asked to participate in a study concerning emotional reactions to pictures after 0-, 6- or 24-h of food deprivation, in return for experimental credit or monetary compensation[5]. Subjects who agreed to participate were randomly assigned to one of the three deprivation conditions. The final sample consisted of 35 subjects in the 0-h group (19 males), 31 in the 6-h group (15 males), and 23 in the 24-h group (12 males).

3.1.2. Materials

Forty colored slides were selected from the International Affective Picture System (IAPS; CSEA, 1995). Ten pictures contained explicit food content, and ten were selected from three valence-defined categories (i.e. pleasant, unpleasant, and neutral) based on normative affective ratings (Lang et al., 1995)[6]. The food pictures included candy, ice cream, and other high-calorie, high density foods that were previously rated as highly appetitive. Five blocks of eight pictures were arranged such that each block contained two pictures from each of the four categories. Within each block, picture categories were randomly ordered. A total of four picture orders were created such that, across subjects, each block was presented at least once during each fourth of the series.

The acoustic startle stimulus consisted of a 95 dB (A) white noise burst presented binaurally for 50 ms, with instantaneous rise time, over matched Telephonics TDH-49 headphones. The signal was produced by a Coulbourn S81-02 noise generator and gated through a Coulbourn S82-24 amplifier. A startle probe was presented at a random interval from 2.5 to 5 s after picture onset during 28 of the 40 pictures, such that a probe was presented during seven of the ten pictures within each category. Eight additional probes were presented during a variable 10–20 s inter-trial interval (ITI).

[5] Since many potential subjects had already fulfilled their course research participation requirement when recruitment for the study began, all subjects were given the option to participate for course credit or $US15. The overall rate of agreement was 87%, and approximately 85% of participating subjects received course credit.

[6] The following IAPS numbers correspond to the slide pictures included in study 1: food — 723, 733, 735, 740, 741, 743, 745, 746, 747, 748; pleasant — 144, 208, 466, 468, 819, 820, 837, 847, 849, 851; neutral — 700, 701, 703, 705, 708, 709, 710, 713, 715, 750; unpleasant — 112, 130, 300, 313, 315, 353, 623, 635, 981, 991.

Subjects completed the following questionnaires:

1. Beck Depression Inventory — short form (BDI-S; Bech et al., 1975) — a 12-item version of the full-length BDI, used to measure current depressive symptomatology.
2. Food Craving Questionnaire (FCQ) — a 10-item scale developed for this study to measure current desire and intention to eat food. Items were adapted from the Questionnaire of Smoking Urges (QSU; Tiffany and Drobes, 1991), with specific items selected to represent four content domains: desire to eat, intention to eat, expectation of positive effects of eating, and anticipation of relief from negative mood after eating. The items were also selected based on those that had the highest loadings on two factorial derived subscales of the QSU.
3. EASI (Buss and Plomin, 1984) — a 25-item questionnaire that taps five dimensions of temperament, i.e. activity, sociability, impulsivity, fear and anger.
4. The Restraint Scale (TRS; Herman and Polivy, 1980) — a 10-item form designed to measure concern about weight and chronic weight fluctuation.
5. Food Preference Scale (FPS; Peryam and Pilgrim, 1957) — a form to assess subjective liking of a variety of food items. The form was modified to include the specific food items that would be presented in the behavioral food consumption test.
6. Demographic Questionnaire — this form collected information about age, sex, race, handedness, as well as 24-h food recall data.

3.1.3. Procedure

Subjects in the 6- and 24-h deprivation groups were required to attend a brief ‘pre-session’ at the start of their deprivation interval, either the morning of or the day before the individual experimental session, respectively. At the pre-session, informed consent was obtained and a standard food pre-load was consumed[7]. Each subject was reminded when to return for the experimental session, and told to do their best to avoid eating or drinking for the entire deprivation interval, with the exception of water[8]. Experimental sessions were scheduled to begin between 13:00 and 16:30 h.

Upon arrival at the laboratory for the experimental session, informed consent was obtained for subjects in the 0-h group. All subjects then completed the BDI-S

[7] The pre-load consisted of an 8 oz. nutritional chocolate shake containing 220 calories (Chocolate GO!; Phoenix Advanced Technology, Inc., Gainesville, FL). Further information regarding the nutritional content is available from the first author.

[8] Subjects in the 6- and 24-h deprivation groups were told that physiological and behavioral measures would determine whether or not they had eaten over the deprivation interval. Thus, a ‘bogus pipeline’ effect was utilized to increase overall compliance with deprivation instructions. Furthermore, to increase the likelihood that subjects would accurately report whether or not they had eaten over the deprivation interval, they were told that they would receive compensation for participating in the study whether or not they were able to refrain from eating successfully. As a result, 16 out of 39 subjects who were initially assigned to the 24 h deprivation group reported some eating/drinking over the interval; data for these subjects were not included in analyses.

and the FCQ. Then, the subject was taken to a sound-attenuated room and seated in a comfortable recliner. Electrodes were attached according to established guidelines. The picture series was presented, with each picture presented for 6 seconds each on a screen approximately 1.8 m in front of the subject, using a Kodak Ektagraphic IIIA slide projector stationed in an adjoining equipment room. Subjects were instructed to watch each picture for the entire time it was on the screen, and to ignore occasional noises heard over the headphones.

After each picture was presented once, electrodes were removed, and the pictures were presented a second time in the same order. The subject was instructed to view each picture for as long as desired (up to a maximum cut-off of 18 s), and to conclude each picture with a button press; picture viewing times were recorded to the nearest ms as a behavioral measure of interest. After each picture was offset, the subject was instructed to rate that picture along the affective dimensions of valence, arousal, and dominance using a computerized version of the Self-Assessment Manikin (SAM; Hodes et al., 1985). Interest ratings were recorded with a computerized line rating.

Following the picture rating task, a small table was placed in front of the subject with bowls containing an ample supply of each of three target foods (i.e. chocolate M&M's, pretzels, and peanuts), as well as a full glass of water. A 7-item Likert rating form for each food was provided, with items related to taste and palatability (i.e. flavor, odor, sweet, sour, bitter, salty, like). The subject was instructed to consume as much or little of each food as they would need in order to make accurate ratings, and to taste and rate the foods in a particular order identified on the rating forms; the order of foods was counterbalanced across subjects. Upon completion of the ratings, the subject was told that s/he could continue to eat as much of the remaining food as they would like while completing an additional questionnaire (EASI). Subjects were told that, for health reasons, we were not allowed to store and re-use the food for future research participants. A total of 10 min of food access was given, including the taste rating task and subsequent free eating period. Any food remaining at the end of the 10 min was removed and weighed, after giving subjects the option of taking one last handful. The final three questionnaires (TRS, FPS, Post-Session Questionnaire) were then administered, followed by subject debriefing and dismissal.

3.1.4. Experimental control and data collection

Presentation and timing of the picture and startle stimuli, as well as collection of all physiological measures, ratings, and viewing time data was controlled by a Northgate IBM-compatible computer running VPM software (Cook et al., 1987). The eyeblink component of the startle response to the acoustic probes was measured by recording EMG activity from the orbicularis oculi region beneath the left eye using two Beckman miniature Ag–AgCl electrodes, filled with Teca Electrolyte. The raw EMG signal was amplified using a Coulbourn S75-01 bioamplifier (bandpass settings of 90–250 Hz), then filtered with a Coulbourn S76-01 contour following integrator using a 125 ms time constant. The digital sampling rate was 1000 Hz from 50 ms prior to the onset of the startle probe until 250 ms after probe onset. Scoring of the startle response was accomplished off-line using an interactive program designed to score each blink for onset latency and peak amplitude. Trials with clear movement artifact or excessive baseline activity were rejected, and trials with no blink were scored as 0 amplitude. To correct for individual and group differences in startle response magnitudes, each subject's responses were converted to z scores, which were then transformed to T scores (i.e. $[z \times 10] + 50$). All picture and inter-trial interval startle probes were used as the reference distribution for these computations.

Heart rate, skin conductance, and facial EMG indices were monitored throughout the initial picture viewing period and, for each measure, the average deviation for the entire 6-s viewing period (12 half-second values) from a 1-s pre-picture baseline was computed for statistical analyses. For heart rate, the EKG was amplified with a Coulbourn S75-01 bioamplifier, and a Schmitt trigger interrupted the computer to measure each R–R interval to the nearest 1 ms. The data were edited off-line to correct for missed or extra triggers, then converted to change scores for each half-second deviated from a 1-s pre-picture baseline. Skin conductance was measured from a pair of electrodes placed on the left hypothenar eminence, using Beckman standard electrodes filled with unibase conductance medium. The signal was sampled at 50 Hz and recorded on a Coulbourn S71-22 skin conductance amplifier, calibrated to record a range of 0–40 μS. Facial EMG was recorded from the corrugator and zygomatic muscle regions on the left side of the face using guidelines provided by Fridlund and Cacioppo (1986). The EMG signals were amplified using Coulbourn S75-01 bioamplifiers with bandpass settings of 90 to 1000 Hz, then filtered with Coulbourn S76-01 contour following integrators using a 500 ms time constant.

3.2. Data analyses

Verbal, behavioral, and physiological responses during the picture viewing task were initially subjected to mixed-design ANOVAs to evaluate the impact of Group (0-, 6-, 24-h deprivation) and affective picture category (pleasant, neutral, unpleasant). Linear and quadratic trend components were examined across the repeated measure of category, and multivariate statistics were used to assess the significance of each repeated measure effect. If no group or interaction effects were observed, then a second univariate ANOVA was conducted to determine the impact of Group on reactivity to the food pictures. Unless otherwise noted, all effects were evaluated at a 0.05 significance level. Two-way ANOVAs, with Group and Gender as between group factors, were conducted to examine effects on demographic, questionnaire, and food consumption data. Tukey post-hoc tests were used for groupwise comparisons when significant overall group effects were observed.

3.3. Results

3.3.1. Demographic, questionnaire and food consumption differences

There were no significant differences in age or body mass index (BMI) as a function of group, nor were there any differences on the BDI-S, TRS, FPS, or the subscales of the EASI. There was, however, a significant group difference on the FCQ, F (2,76) = 31.91. Post hoc tests showed that the 24-h deprived subjects reported stronger cravings than both of the other groups, and the 6-h deprivation group reported stronger cravings than the 0-h group. In addition, the total amount of food eaten during the consumption test was positively related to the level of food deprivation (linear $P < 0.03$).

Males were significantly heavier, taller, and older than females, and they reported less concern for dieting on the TRS (all P's < 0.01). Males also ate significantly more food than females during the food consumption test, F (1,76) = 31.91. There were no group × gender interaction effects on any of these variables.

3.3.2. Affective self-report and viewing time

There were no significant group differences for any of the picture ratings across the three affective picture categories, nor were there any group × category interactions; these data are presented in Table 1. For each measure, there was a significant main effect for category. Trend analyses revealed that subjects rated pleasant pictures as significantly more pleasant than unpleasant pictures (F linear [1,86] = 304). Subjects rated both pleasant and unpleasant pictures as more arousing than neutral pictures (F quadratic [1,86] = 242), and unpleasant pictures as more arousing than pleasant pictures (F linear [1,86] = 30.82). Dominance ratings were higher for pleasant than unpleasant pictures (F linear [1,86] = 170), suggesting that subjects felt more in control while observing these cues. Finally, subjects rated both pleasant and unpleasant pictures as more interesting than neutral pictures (F quadratic [1,86] = 320).

The ratings for the food pictures are also displayed in Table 1. Analyses revealed significant group differences for arousal, dominance, and interest ratings, but not for valence. For the arousal rating, post hoc tests indicated that each of the food-deprived groups rated the food pictures as more arousing than the non-deprived group, consistent with an increase in appetitive drive strength. Similarly, both food-deprived groups gave lower dominance ratings to food pictures than non-deprived subjects. Evidently, either 6- or 24-h of food deprivation was sufficient to promote a diminished sense of control while they viewed pictures of food (for a full discussion of the control dimension of affective self-report, see Bradley and Lang, 1994 or Mehrabian and Russell, 1974). Finally, the 24-h deprivation group rated their interest in food pictures as higher than the 6-h deprived and non-deprived subjects.

As with the ratings data, there was no group effect on choice viewing times for the affective pictures, nor was there a group × category interaction. There were significant differences as a function of category (F [2,85] = 15.02), with subjects viewing pleasant and unpleasant pictures longer than neutral pictures (F [1,86] = 30.39), and unpleasant pictures longer than pleasant pictures (F [1,86] = 7.55). Although 24-h deprived subjects tended to view food pictures longer than 6-h deprived subjects (3.20 vs. 2.44 s), this effect was not statistically reliable ($P = 0.10$).

3.3.3. Startle reflex

There were few ratings differences between the 6- and 24-h deprivation groups, in that both of these groups differed from the non-deprived subjects. Similarly, there

Table 1
Picture rating means (and standard deviations) for each group: study 1

Measure	Group			Trend test (*P*)
	0 h	6 h	24 h	
Valence ratings				
Pleasant	14.49	14.37	14.36	Linear, 0.001
	(3.55)	(2.40)	(2.07)	Quadratic, ns
Neutral	9.97	9.69	9.47	
	(1.67)	(1.58)	(1.65)	
Unpleasant	4.50	4.92	5.24	
	(3.20)	(2.73)	(3.51)	
Food	12.95_a	12.23_a	13.60_a	
	(2.97)	(3.65)	(4.16)	
Arousal ratings				
Pleasant	12.03	12.53	12.03	Linear, 0.001
	(4.51)	(2.70)	(2.92)	Quadratic, 0.001
Neutral	4.82	4.46	5.49	
	(3.68)	(3.83)	(3.77)	
Unpleasant	13.67	14.61	13.68	
	(5.16)	(2.92)	(2.53)	
Food	9.42_a	12.71_b	14.24_b	
	(4.49)	(3.11)	(2.85)	
Dominance ratings				
Pleasant	11.95	11.24	11.85	Linear, 0.001
	(2.83)	(3.12)	(1.93)	Quadratic, 0.001
Neutral	12.03	12.32	11.97	
	(3.68)	(3.84)	(3.71)	
Unpleasant	5.69	5.96	6.61	
	(3.53)	(4.13)	(3.47)	
Food	12.12_a	9.66_b	8.01_b	
	(4.18)	(4.13)	(3.51)	
Interest ratings				
Pleasant	13.60	13.38	13.96	Linear, 0.01
	(4.14)	(3.24)	(3.26)	Quadratic, 0.001
Neutral	4.77	3.29	3.50	
	(3.23)	(3.43)	(3.50)	
Unpleasant	11.96	13.50	12.42	
	(5.46)	(3.75)	(2.51)	
Food	10.37_a	11.53_a	14.27_b	
	(3.20)	(3.46)	(3.15)	

Note: all ratings were recorded on a 0–20 scale. Trend tests for affective category (pleasant, neutral, unpleasant) effects are indicated. Group differences for pleasant, neutral, and unpleasant pictures are not statistically significant. For food pictures, means in the same row that do not share subscripts differ at $P<0.05$.

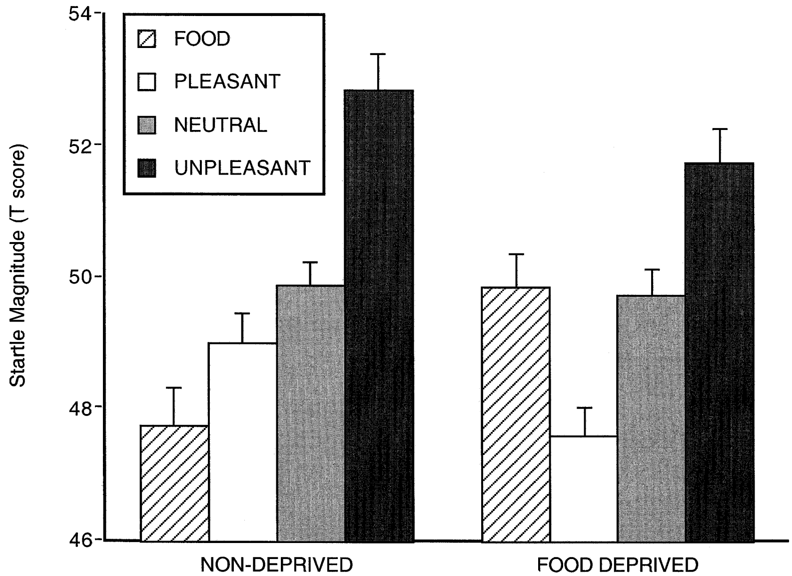

Fig. 1. Standardized startle magnitude (with standard error bars) for food and affective pictures for non-deprived and food-deprived subjects.

were no differences in startle responding to any of the picture categories between the two food-deprived groups ($F < 1$); accordingly, these two groups were combined in a simple comparison between non-deprived and deprived subjects with respect to startle responding. The startle findings for each picture category for non-deprived and deprived subjects are presented in Fig. 1. As with the ratings data, there was no group effect or group × category interaction while viewing the affective pictures. Consistent with previous findings, there was a significant linear trend for affective pictures (F linear [1,75] = 10.17), with enhanced startle during aversive, relative to appetitive pictures.

Food-deprived, but not non-deprived, subjects showed an enhanced startle response during presentations of food cues, relative to non-food pleasant pictures ($F = 10.43$). Furthermore, the startle response exhibited during food cue trials was significantly higher among deprived, relative to non-deprived, subjects (F [1,75] = 7.05).

3.3.4. Heart rate and skin conductance

The deviations from baseline for heart rate, skin conductance, and the facial EMG measures from study 1 are displayed in Table 2. For the affective picture categories, there were no significant group effects for either the heart rate or skin conductance change scores, nor were there any significant group × category interactions. However, there were significant valence effects for both measures, multivariate F's = 15.7 and 3.1, respectively. For heart rate, there was a clear linear trend across picture categories in which unpleasant pictures consistently elicited more heart rate deceleration than pleasant pictures, F linear = 23.64. There was also a

Table 2
Visceral and electromyographic response means (and standard deviations) for each group: study 1

Measure	Group		
	0 h	6 h	24 h
Heart rate			
Pleasant	−0.46	−0.59	−1.07
	(1.6)	(1.5)	(0.9)
Neutral	−0.84	−0.07	−0.39
	(1.8)	(1.6)	(1.3)
Unpleasant	−1.83	−1.73	−2.08
	(1.8)	(1.9)	(1.7)
Food	−0.19	−0.21	−0.33
	(1.6)	(1.4)	(2.4)
Skin conductance			
Pleasant	0.045	0.030	0.008
	(0.15)	(0.08)	(0.08)
Neutral	0.015	0.000	0.000
	(0.07)	(0.05)	(0.06)
Unpleasant	0.138	0.062	0.003
	(0.40)	(0.13)	(0.06)
Food	0.002	0.001	0.000
	(0.08)	(0.06)	(0.06)
Corrugator EMG			
Pleasant	−0.139	0.135	−0.123
	(0.58)	(0.35)	(0.80)
Neutral	0.216	0.138	0.181
	(0.51)	(0.32)	(0.52)
Unpleasant	0.411	0.490	0.157
	(0.69)	(0.87)	(0.66)
Food	−0.001	−0.108	−0.212
	(0.59)	(0.33)	(1.07)
Zygomatic EMG			
Pleasant	0.441	0.496	0.048
	(1.89)	(1.74)	(1.17)
Neutral	−0.154	−0.112	0.220
	(1.05)	(1.19)	(1.25)
Unpleasant	−0.484	0.102	−0.076
	(1.41)	(1.14)	(1.68)
Food	−0.213	−0.260	0.713
	(1.23)	(2.06)	(3.03)

Note: all responses are deviations from baseline; units of measurement are as follows: heart rate, beats/min; skin conductance, μS; corrugator and zygomatic EMG, μV.

significant quadratic trend, indicating that heart rate decelerations for both pleasant and unpleasant pictures were larger than for neutral pictures, F quadratic = 8.89. Similarly, there were significantly greater skin conductance changes for the pleasant and unpleasant pictures than for neutral pictures, F quadratic = 6.22. Interestingly, there was a trend in which skin conductance changes across all the picture categories were suppressed with increasing levels of food deprivation, F (2,86) = 0.085. Indeed, while the quadratic pattern was evident in both the 0- and 6-h deprivation groups, the 24-h deprived subjects did not show any appreciable skin conductance responses for any of the picture categories. This suggests that 24 h of food deprivation may have generally inhibited sweating reactivity.

As with the startle reflex, heart rate differences between food-related pictures and non-food pleasant pictures were significant only for the 24-h deprived group, with these subjects showing significantly less deceleration for the food pictures, F (1,22) = 5.20. For skin conductance, the food cues did not evoke a response for any of the groups.

3.3.5. Facial EMG

For corrugator and zygomatic EMG, there were significant overall category effects for the affective pictures, F's = 12.77 and 3.19, respectively. In addition, there were significant linear trends for both measures. Specifically, unpleasant pictures elicited larger corrugator responses than pleasant pictures, and pleasant pictures elicited larger zygomatic responses than unpleasant pictures, F's = 19.25 and 5.05, respectively. There were no significant group main effects or group × category interactions for these measures.

In comparing food and non-food pleasant pictures, there was a significant group × category interaction for corrugator activity ($F = 5.40$). Simple effects tests indicated significantly lower corrugator activity in response to food cues for 6- and 24-h deprived subjects, relative to non-deprived subjects. There was also a marginally significant group × category interaction for zygomatic activity ($F = 2.37$, $P < 0.10$). Zygomatic activity was clearly augmented in the presence of food cues for 24-h food-deprived subjects, but not for the other groups. In contrast with the startle data, the overall pattern of EMG findings suggests that food cues activated pleasant motivation for food-deprived subjects.

3.4. Discussion

The self-report and psychophysiological responses to the valence spectrum of affective pictures replicated previous studies, and these findings appear to be independent of food deprivation. In contrast, deprivation did have a clear impact on several responses to food pictures. Compared to the non-deprived, food deprived subjects displayed an enhanced startle response while viewing appetizing pictures of food. Furthermore, only food-deprived subjects showed greater startle magnitude during food cues than during other pleasant pictures. In addition, deprived subjects reported greater arousal, interest, and lack of control (low dominance) while viewing food cues, and showed an elevated heart rate response.

The enhanced startle response for food-deprived subjects suggests that, to some extent, food cues elicited an aversive motivational reaction. Given that the present experimental context did not allow immediate consumption, this corresponds to a state of frustrative nonreward (Amsel, 1992; Wagner, 1969). Frustration generally involves heightened anxious arousal; hence, negative affect. The reports of greater arousal and loss of control from food-deprived subjects are consistent with this interpretation. Capaldi (1990) has discussed evidence that food-deprived rats, given food cues separately from feeding, also show decreased 'pleasure' as a function of hunger.

In contrast to evidence of an aversive reaction, these same subjects showed a facial action pattern associated with positive valence (i.e. increased zygomatic, decreased corrugator) particularly enhanced in the 24-h group. Furthermore, deprived subjects rated food pictures as pleasant, and as significantly more interesting than did the non-deprived.

These mixed findings for food deprived subjects are consistent with a state of motivational ambivalence: food pictures activated appetitive approach responses; however, in the absence of imminent reward, they also prompted unpleasant affect and associated defensive reflexes. From this perspective, the relatively faster heart rate response to food cues of these subjects could be attributed to increased activation prompted by an approach–avoidance conflict. It is curious, however, that most food-deprived subjects (24 h) did not show skin conductance increases. Skin conductance is typically seen to be an index of sympathetic activation — and could thus be expected to increase with frustration. However, as Guyton and Hall (1996) point out, although sweat glands are innervated by sympathetic fibers, they are primarily stimulated by centers in the hypothalamus that are considered parasympathetic. Given the role of the hypothalamus in determining feeding and digestive processes, it is possible that these centers were disregulated by the more prolonged hunger state (24 h). Alternatively, given that synaptic mediation at the sweat gland is cholinergic, neural transmission might be inhibited under higher drive conditions, when there is presumably more circulating norepinepherine.

4. Study 2

Highly indulgent and/or restrictive eating patterns are naturally occurring forms of eating disturbance in our culture. When these patterns become excessive, formal eating disorders such as bulimia or anorexia are diagnosed, with serious consequences that require treatment. Food cues clearly have particular motivational salience for these overly indulgent and/or restrictive eaters. Study 1 showed that the picture paradigm is sensitive to variations in affect, as they relate to experimental manipulation of the hunger state. Study 2 extends this research, examining possible differences in reactivity to food cues in participants with unique, habitual dietary patterns that can potentially lead to serious consequences for human health.

Highly indulgent (binge) and highly restrictive (restrained) eaters participated in Study 2, in addition to new groups of food-deprived and non-deprived normal eaters. It was expected that binge and restrained eaters would show disparate patterns of reactivity to food cues, since the approach/indulgent and avoidant/restrictive tendencies, respectively exhibited by each group, are in sharp contrast. In addition, it was expected that binge eaters would respond similarly to food-deprived subjects, since both groups might have an enhanced approach-oriented bias towards food.

4.1. Method

4.1.1. Subjects and design

Seventy-six female undergraduates were recruited for participation in this study[9]. Subjects were selected from a screening of over 2000 introductory psychology students based on their responses to five items from the Eating Disorders Inventory (EDI; Garner et al., 1983). Subjects scoring within one standard deviation from the sample mean on these items were eligible for either the control or deprivation group. Subjects who scored in the upper 10% on items related to dietary restraint and in the bottom two-thirds on items related to binge-purge behavior were eligible for the Restrained group, and subjects who scored in the upper 10% on binge-purge items and in the bottom two-thirds on dietary restraint items were eligible for the binge group.

4.1.2. Materials

The stimulus materials were 44 IAPS pictures distributed across the same categories as in study 1[10]. Four blocks of 11 pictures were arranged such that each block contained three unpleasant and three neutral pictures, and at least two pleasant and two food pictures; two of the blocks contained two pleasant and three food pictures, and two of the blocks contained three pleasant and two food pictures. Picture categories were randomly ordered within each block, and six orders of picture presentation were developed such that, across subjects, each block occurred during each fourth of the presentation at least once.

The acoustic startle stimulus was the same as that used in study 1. The startle probe was presented during 32 of the 44 pictures, such that a probe was presented during eight of the pictures within each block and within each of the four picture categories. As in study 1, eight ITI probes were presented.

[9] This study was conducted on females only due to vast gender difference in the rates of restrained and binge eating patterns among college students. Food-deprived and non-deprived groups were also exclusively female in order to match gender across all four groups.

[10] To avoid a relative overrepresentation of appetitively-oriented pictures in the overall set due to the inclusion of food and non-food pleasant picture categories, we opted to add two pictures each in the neutral and unpleasant categories for this study. The following IAPS numbers correspond to the pictures included in study 2: food — 720, 733, 735, 740, 741, 743, 745, 746, 747, 748; pleasant — 208, 447, 450, 452, 466, 468, 803, 808, 820, 851; neutral — 219, 550, 700, 701, 705, 708, 709, 710, 713, 715, 717, 750; unpleasant — 107, 112, 130, 212, 300, 301, 310, 313, 315, 602, 619, 623.

Subjects completed the same questionnaires as in Study 1, with the exception of the TRS and the FPS. The following two questionnaires were added:

1. The Eating Disorder Inventory (EDI; Garner et al., 1983) — a 64-item scale that measures cognitive, behavioral, and personality characteristics of eating disorders.
2. Rosenberg Self-Esteem Scale (RSE; Rosenberg, 1979) — a 10-item unidimensional scale of self-esteem.

4.1.3. Procedure

Eligible subjects were contacted by telephone and asked to participate in a study concerning physiological responding to affective pictures. Subjects meeting the criteria for the control or deprivation groups were told about the possibility of being assigned to a food deprivation group, and only those who agreed to be assigned randomly to one of these conditions were included. Deprivation subjects ($n = 21$) were instructed to refrain from eating prior to their two-h session on the day of the experiment (average reported length of deprivation was 16.8 h; range = 10–20 h), and control subjects ($n = 23$) were instructed to eat normally prior to their session. Subjects recruited for the binge ($n = 19$) and restrained ($n = 13$) groups were not given any explicit instructions regarding pre-session food intake[11]. All sessions were scheduled to occur between 12:00 and 18:00 h.

Informed consent, electrode attachment, picture presentation, physiological recording, picture ratings, and data reduction procedures were identical to study 1, except that facial EMG was not recorded, and there was no food consumption test.

4.1.4. Data analysis

Questionnaire scores and demographic variables were subjected to one-way analyses of variance (ANOVA) to determine group differences. The overall data analytic strategy was similar to that employed in study 1, in which initial analyses focused on affective picture categories and subsequent analyses focused on group differences to food and non-food comparison pictures. Based on our primary predictions for this study, the subsequent analyses compared the combined binge and deprived groups with the combined restrained and control groups. Certain tests predicated on the results from study 1 were conducted as one-tailed tests.

4.2. Results

4.2.1. Questionnaire measures

Table 3 displays demographic and questionnaire averages for each group. There were no significant group differences in age or BMI. However, there were several

[11] One subject initially assigned to the control group reported not eating prior to her session, and two subjects initially assigned to the deprivation group reported prior eating; these subjects were reassigned to the appropriate conditions. Due to equipment malfunction, physiological data were lost for two control subjects. In addition, 13 subjects failed to show a measurable startle response on more than 25% of the trials; thus, the sample for examining startle reactivity was reduced to 63 subjects.

Table 3
Demographic and questionnaire means (and standard deviations) for each group: study 2

Measures	Group				*P*
	Control	Restrained	Binge	Deprivation	
Age	18.7_a (1.3)	18.5_a (.8)	19.1_a (2.3)	18.3_a (0.9)	ns
BMI	22.18_a (3.9)	21.75_a (2.6)	22.04_a (3.5)	21.00_a (2.4)	ns
BDI-S	4.96_{ab} (3.4)	7.85_{ab} (5.0)	7.95_a (5.4)	4.25_b (3.7)	0.05
RSE	16.58_a (4.3)	19.15_a (5.9)	20.68_a (5.1)	16.75_a (5.4)	0.05
Last eaten (h)	2.61_a (1.5)	3.76_{ab} (1.5)	5.13_b (4.8)	16.77_c (2.8)	0.001
FCQ	32.04_a (13.6)	31.92_a (12.1)	36.37_{ab} (16.5)	46.79_b (11.8)	0.01
Hunger Rating	3.88_a (1.8)	3.77_a (1.7)	4.42_a (2.0)	6.00_b (1.2)	0.001
% Time dieting this past year	18.33_a (24.1)	44.46_b (40.4)	28.21_{ab} (30.9)	10.10_a (19.6)	0.01
EDI — total score	33.38_a (16.6)	58.54_b (29.0)	55.47_b (26.6)	32.00_a (20.6)	0.001
EDI — drive for thinness	5.00_a (4.5)	12.54_b (4.6)	8.47_{ab} (6.1)	4.30_a (5.4)	0.001
EDI — body dissatisfaction	10.79_a (6.7)	19.00_b (6.0)	17.47_b (7.9)	10.75_a (6.8)	0.001
EDI — interoceptive awareness	2.42_a (3.2)	5.08_{ab} (4.8)	7.32_b (5.9)	2.15_a (4.0)	0.001
EDI — bulimia	1.04_a (1.6)	1.31_{ab} (1.7)	3.68_b (5.1)	0.90_a (1.5)	0.05

Note: BMI, body mass index (weight in kg/height in m^2). For variables in which there was a significant group difference, means in the same row that do not share subscripts differ at $P<0.05$.

significant group differences on measures related to eating habits, dietary concerns, and psychopathology. Post hoc tests revealed that Restrained eaters obtained a higher overall EDI score, as well as drive for thinness and body dissatisfaction subscale scores than did control and deprivation subjects, and they reported spending a greater percentage of time dieting over the past year. Binge eaters also obtained significantly higher EDI total and body dissatisfaction scores than control and deprivation subjects, and these subjects also scored higher on the Bulimia and Interoceptive Awareness subscales. In addition, binge eaters reported significantly more depression (BDI-S), marginally lower self-esteem (RSE), and less anger (EASI-Anger subscale) than deprivation and/or control subjects. The questionnaire results for the binge and restrained eaters confirmed the a priori group assignments, and the levels obtained were consistent with those reported in previous studies as representing significant eating disturbances (e.g. Button and Whitehouse, 1981; Lowe, 1994; Pertschuk et al., 1986). There were no differences between deprivation and control subjects on any of these measures. Finally, deprivation subjects reported a greater interval since last food intake, as well as more hunger and food cravings than the other groups; there were no differences among the three non-deprived groups on these measures.

4.2.2. Affective self-report and viewing time

There were no group differences in picture ratings or viewing times for the affective picture categories. As in study 1, subjects rated pictures from most to least pleasant as expected (linear: F (1,70) = 835, $P < 0.0001$). For arousal, interest, and viewing time, significant quadratic trends over valence categories (quadratic: F's (1,70) = 806, 571, and 79.24, P's < 0.0001, respectively) indicated that pleasant and unpleasant pictures elicited higher arousal and interest ratings, as well as longer viewing times, than neutral pictures.

Valence, arousal, and interest ratings of food and non-food pleasant pictures for each group are provided in Table 4. Binge and deprived subjects rated food pictures as significantly more pleasant than these pictures were rated by control and restrained subjects, F (1,72) = 6.08. In addition, deprived subjects rated food pictures as more arousing and interesting than these pictures were rated by the other groups, F's (1,72) = 5.11 and 7.49, respectively.

Table 4
Food and non-food pleasant picture rating means (and standard deviations) for each group: study 2

Measure	Group			
	Control	Restrained	Binge	Deprived
Valence ratings				
Pleasant	15.91	16.52	15.77	15.56
	(2.1)	(2.0)	(2.2)	(1.9)
Food	14.55	14.29	15.96	16.23
	(2.6)	(4.2)	(2.9)	(2.1)
Arousal ratings				
Pleasant	13.70	14.25	13.50	13.61
	(3.3)	(4.9)	(4.1)	(2.9)
Food	10.86	11.65	11.27	14.01
	(4.2)	(5.2)	(5.3)	(4.8)
Interest ratings				
Pleasant	14.24	15.28	14.72	14.86
	(2.4)	(2.2)	(2.5)	(2.1)
Food	11.72	12.10	11.69	14.42
	(3.0)	(3.9)	(4.7)	(3.2)

Note: all ratings were recorded on a 0–20 scale.

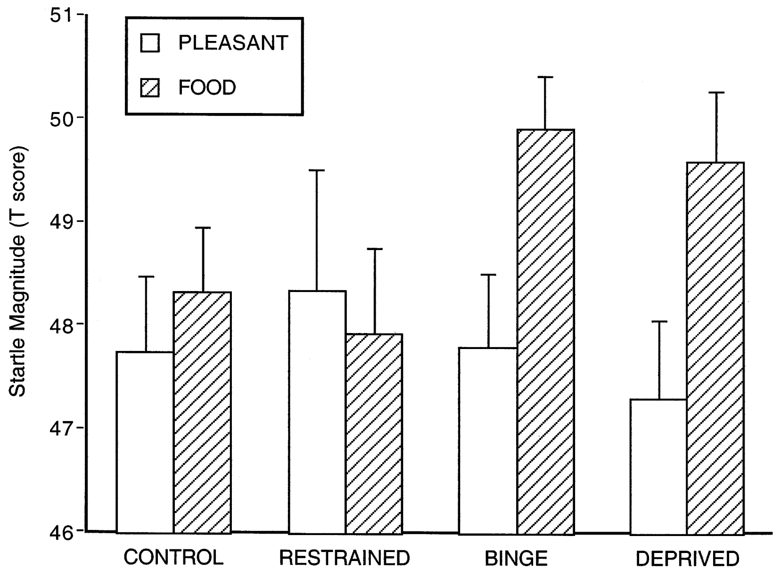

Fig. 2. Standardized startle magnitude (with standard error bars) for food and non-food pleasant pictures for control, restrained, binge and food-deprived groups.

4.2.3. Startle reflex

As in study 1, analyses revealed no group differences in startle responding to the affective picture categories, nor was there a group × category interaction. There was a strong linear trend across the valence categories, with larger responses observed for the unpleasant, relative to the pleasant pictures, F linear $[1,59] = 48.74$.

Startle responding to the food and non-food pleasant pictures are displayed in Fig. 2. Control and restrained subjects showed no differences in responding during food and other pleasant pictures ($F < 1$). However, binge and deprivation subjects exhibited significantly larger startle responses during food pictures, $F\,(1,32) = 7.06$. Further analyses revealed that the binge and deprivation subjects showed larger startle responses during food pictures than shown by the control and restrained subjects, $F\,(1,61) = 5.61$. There were no differences in responding to the non-food pleasant pictures ($F < 1$).

4.2.4. Heart rate and skin conductance

The heart rate and skin conductance data from study 2 are displayed in Table 5. There were significant quadratic trends across the affective picture categories for heart rate and skin conductance, F's $(1,69) = 13.11$ and 16.41, indicating that pleasant and unpleasant pictures elicited greater heart rate decelerations and higher skin conductance levels than neutral pictures. There was also a significant linear trend for skin conductance, $F(1,69) = 7.77$, with unpleasant pictures eliciting greater increases than pleasant pictures. There were no group or group × category interaction effects for either heart rate or skin conductance in response to affective pictures.

Restrained and deprivation subjects demonstrated a relatively faster heart rate in response to food pictures, $F\ (1,31) = 10.31$, despite no group differences in heart rate responding to non-food pleasant pictures, $F\ (1,71) = 1.50$, $P > 0.23$. For skin conductance, there was a greater overall increase in response to the standard pleasant pictures than to food pictures, $F\ (1,69) = 9.84$. An exception was the food-deprived group, which did not show this effect ($F < 1$), indicating a relative elevation of skin conductance in the presence of food cues.

5. General discussion

Food deprivation and deviant eating patterns significantly modulate psychophysiological reactions to food cues. Specifically, when food-deprived subjects and binge eaters view food pictures they show augmented probe startle reflexes. In contrast, reactions to a broad range of pleasant, neutral, and unpleasant pictures (unrelated to food) are largely unaffected by either experimentally induced deprivation or abnormal patterns of eating.

Food cues appear to prompt a state of motivational ambivalence in food-deprived and binge subjects. That is, some self-report and psychophysiological responses are consistent with an appetitive reaction to these cues; however, other

Table 5
Visceral response means (and standard deviations) for each group: study 2

Measure	Group			
	Control	Restrained	Binge	Deprived
Heart rate				
Pleasant	−1.83	−1.59	−2.09	−1.18
	(2.30)	(2.35)	(2.54)	(1.83)
Neutral	−1.56	−0.08	−1.42	−0.52
	(2.04)	(1.68)	(1.49)	(1.91)
Unpleasant	−1.96	−1.78	−2.34	−1.48
	(1.99)	(2.76)	(2.55)	(1.82)
Food	−1.66	0.27	−1.12	−0.23
	(2.32)	(1.10)	(1.86)	(2.24)
Skin conductance				
Pleasant	0.029	0.057	0.029	0.018
	(0.08)	(0.09)	(0.09)	(0.07)
Neutral	0.004	−0.001	−0.018	−0.007
	(0.06)	(0.03)	(0.05)	(0.03)
Unpleasant	0.101	0.118	0.068	0.034
	(0.29)	(0.21)	(0.20)	(0.14)
Food	0.012	−0.014	−0.003	0.011
	(0.06)	(0.09)	(0.10)	(0.06)

Note: all responses are deviations from baseline; units of measurement are as follows: heart rate, beats/min; skin conductance, μS.

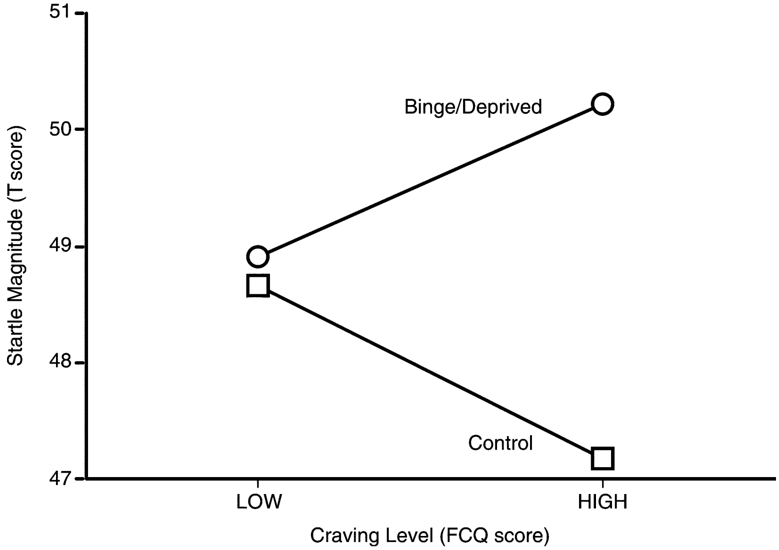

Fig. 3. Standardized startle magnitude for food pictures, based on a median split on initial food craving ratings, for control subjects vs. binge and food-deprived subjects.

responses (e.g. augmented startle reflex) are consistent with an aversive emotional reaction, as in a state of frustrative nonreward. The data suggest that opposing motivational circuits (and evaluative systems) were co-active (see Cacioppo and Berntson, 1994; Miller, 1944; Lang, 1995).

Consistent with the present findings, Mauler et al. (1997) found enhanced probe startle responses during food pictures both in bulimics and in food-deprived normal eaters. Parallel effects have also been observed in nicotine dependent subjects: Elash et al. (1995) found significant startle potentiation in smokers processing imagery scripts that contained explicit smoking urge content. Thus, the weight of evidence suggests that startle is potentiated during appetitive cues if drive is strong and there is no immediate opportunity for consumption.

The presumption that enhanced startle responding among food-deprived and binge eaters represents activation of an aversive motivational state is consistent with Tiffany's (1990) cognitive theory of drug motivation. The theory states that cravings occur when automatized drug-use action sequences are impeded, either due to environmental constraints, or due to one's desire to avoid consuming a substance. Cue-elicited cravings are thought to involve negative affect, due to either frustration (when desired consumption is blocked) or approach-avoidance conflict (when attempting to avoid consumption). Interestingly, the enhanced startle response to food pictures exhibited by binge and deprived subjects in study 2 was associated with self-reported craving. Subjects who reported stronger food cravings at the start of the session exhibited relative elevations in startle responding during food cue presentations, $F\ (1,21) = 6.60$ (see Fig. 3). Thus, for these subjects, it appears that craving was associated with the activation of an aversive affective state that mediated the enhanced startle response to food cues.

The binge and restrained eaters studied here reported attitudes and behaviors regarding food and weight similar to other sub-clinical eating disorder groups (e.g. Button and Whitehouse, 1981; Garner et al., 1984). In particular, binge eaters reported significantly higher scores on the bulimia and interoceptive awareness subscales of the EDI subscale, and restrained eaters reported higher scores on the drive for thinness subscale — relative to normal controls and food-deprived subjects. Both binge and restrained eaters also reported greater body dissatisfaction than controls, and higher depression and lower self-esteem ratings. The evidence of trait negative affect is consistent with previous findings on eating disorders (e.g. Dunn and Ondercin, 1981; Pertschuk et al., 1986).

The present results define distinctly different psychophysiological patterns for binge and restrained groups. Bingers were similar to deprived subjects. They reported the food pictures to be highly positive, but exhibited larger startle responses in the context of these food cues. Frustration and associated aversive arousal may have been further facilitated in bingers by this groups tendency to depression and lower self-esteem.

In contrast, the responses of restrained eaters were more similar to normal, non-deprived subjects. Thus, the Restrained group showed relative startle inhibition during food cues. Overduin et al. (1997), reported a similar absence of differences between restrained and non-restrained eaters viewing food pictures. The only response linking the two sub-clinical groups is the food-cue-induced elevated heart rate response, shown here by both bingers and restrained eaters. This suggests that food cues were salient for both groups; however, there is no corroborating evidence that food-restrained subjects responded to food cues with other than normal affect.

The present findings are heuristic, but need to be extended to a larger sample. Although there was good internal evidence of compliance in the present research (e.g. increased craving and hunger ratings, increased food consumption, a distinct response profile among food-deprived groups), future studies should assess compliance directly by measuring food metabolism (cf. Mauler et al., 1997). Ideally, the experiment could be conducted under controlled conditions in a clinical research unit. Most important of all, the research paradigm needs to be extended to a substantial sample of diagnosed patients, bulimics and anorexics, to determine definitively if these psychophysiological patterns have clinical significance.

In conclusion, the present research tells us much of interest about the motivational-emotional substrate of food cue reactivity in humans, showing the effects of experimental deprivation, highlighting parallels with the animal conditioning literature, and providing a novel perspective on naturally occurring dietary patterns of binge and restraint. In general, physiological reactions in food deprivation and binge eating were associated with a more aversive response to food cues, but still co-activated with the appetitive response set. Binge and restrained eating patterns differed in psychophysiological responses and evaluative report, suggesting that these sub-clinical groups interact in unique ways with the relevant environmental cues. Finally, given that binge and restrained eaters show unique response patterns, it is suggested that the methodology has potential value for assessment in clinical settings. The paradigm might help in matching patients to treatment modalities, and perhaps find further application in predicting and evaluating clinical outcome.

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