

# Dietary disinhibition modulates neural valuation of food in the fed and fasted states<sup>1–4</sup>

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## ABSTRACT

**Background:** Dietary disinhibition is a behavioral trait associated with weight gain and obesity. Because food choices are made according to the relative value assigned to each option, examination of valuation signals through functional magnetic resonance imaging (fMRI) may elucidate the neural basis for the association between dietary disinhibition and weight gain.

**Objective:** We examined how food valuation signals differ in the fed and fasted states between persons with high dietary disinhibition (HD) and low dietary disinhibition (LD).

**Design:** Sixteen men with HD and 14 with LD underwent fMRI once while fasted and once after being fed in a counterbalanced order. In-scanner preference to consume a test food relative to a neutral-tasting, neutral-health reference food was examined. The slope of magnetic resonance signal change corresponding to these food preferences constituted the food valuation signal that was compared across disinhibition group and satiety state.

**Results:** Both the HD and LD participants reported being less hungry ( $F_{(1,28)} = 113.11$ ,  $P < 0.001$ ) after being fed than when fasted. However, food valuation signals in the ventromedial prefrontal cortex (vmPFC) differed between the groups ( $F_{(1,28)} = 21.34$ ,  $P < 0.001$ ). Although LD participants showed attenuated vmPFC activity after being fed ( $t_{(13)} = 4.11$ ,  $P < 0.001$ ), HD participants showed greater vmPFC activity in the fed than in the fasted state ( $t_{(15)} = -2.56$ ,  $P < 0.05$ ).

**Conclusions:** Despite reporting normal decreases in hunger ratings after being fed, persons with HD have an altered neural valuation of food. This may be a mechanism underlying their propensity to overeat and gain weight. This trial was registered at clinicaltrials.gov as NCT00988819. *Am J Clin Nutr* doi: 10.3945/ajcn.112.053801.

## INTRODUCTION

The rising availability of high-calorie foods and an increasingly sedentary lifestyle have resulted in a growing prevalence of obesity worldwide (1, 2). Nevertheless, individuals differ in their propensity to gain weight (3), and identifying factors that predispose to unhealthy weight gain are of considerable public health interest (4). One fertile avenue of investigation concerns the links across the brain, appetite, and obesity (5). We explored these associations in relation to individual differences in dietary disinhibition.

Dietary disinhibition (6) predicts the tendency to eat regardless of prior food intake, responding instead to food cues, the social environment, and emotional stress. Compared with persons with

low dietary disinhibition (LD)<sup>5</sup>, those with high dietary disinhibition (HD) consume more food (7–9), are more likely to gain weight over time (10–13), and are more likely to be obese (14–17); HD persons also tend to binge eat (18) and to show a stronger preference for high-fat and sweet foods (17, 19–21). Underlying these consummatory behaviors, HD individuals appear to be both hyperresponsive to the rewarding properties of food (22) and to have diminished satiety (21, 23).

Two functional neuroimaging studies have been conducted to investigate how disinhibition might alter responses to food-related stimuli. The first study found that, relative to lean individuals, obese individuals with higher disinhibition scores exhibit increased insular blood flow after consuming a liquid meal (24). A second study found that, in obese participants, food relative to nonfood pictures elicited medial prefrontal responses that were negatively correlated with disinhibition scores (25). Whereas these studies suggest that HD individuals have an altered neural response to food-related stimuli, they do not explain how the observed alterations in neural responses relate to their tendency to overeat. As the decision to eat a given food is made in accordance with the relative value assigned to the options under consideration, examination of neural signals corresponding to food valuation may help explain why HD individuals are predisposed to overconsumption.

Neuroeconomic studies have found that, across a wide range of goods, the magnitude of ventromedial prefrontal cortex (vmPFC) activation reflects the relative value an individual assigns to

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<sup>5</sup> Abbreviations used: HD, high dietary disinhibition; LD, low dietary disinhibition; VAS, visual analog scale; vmPFC, ventromedial prefrontal cortex.

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choices (for a review, see reference 26). Here, we examined individuals with LD or HD to determine how valuation signals associated with food choice differed across the fasted and fed states. We predicted that vmPFC value representations would be higher in the fasted than the fed state for LD individuals, and that this difference would be blunted in HD individuals.

## SUBJECTS AND METHODS

### Participants

Healthy men ( $n = 57$ ) were recruited as part of a larger study investigating endocrine, cognitive, and neural contributions to obesity. The participants were recruited through poster and Web-based advertisements and through a database from a separate metabolism study. They were included if they 1) were between 21 and 45 y of age; 2) were of Chinese ethnicity; 3) had a BMI (in  $\text{kg}/\text{m}^2$ ) between 18.5 and 35 (with  $<5\%$  weight change over the past 6 mo); 4) had no history of psychiatric, neurologic, or long-term medical conditions; 5) were familiar with local foods (having lived in Singapore for  $\geq 5$  y); 6) had no food allergies or restrictive diets; and 7) kept regular sleeping patterns. In addition, participants had to 1) be right-handed, 2) have a girth of  $<120$  cm, 3) smoke  $<5$  cigarettes/wk, 4) consume  $<200$  mg caffeine/d, and 5) consume  $<168$  g alcohol/wk. Of the enrolled participants, 7 failed to complete both visits, 9 were excluded for excessive in-scanner motion (see Data analysis: imaging data), 4 were excluded because of technical issues (eg, faulty response box), 2 were excluded because of insufficient data or spread of data (eg, because of excessive nonresponses), 1 was excluded because of unfamiliarity with the food stimuli, and 1 was excluded because of erratic sleep patterns the night before both scan sessions; the remaining 33 participants were included in the final analyses [mean ( $\pm$ SD) age:  $26.6 \pm 5.33$  y]. All participants provided written informed consent and were financially compensated for their time. The experimental protocol was approved by the National University of Singapore Institutional Review Board.

### Overview of experimental procedure

As part of the larger study protocol, participants first completed baseline anthropometric measurements, questionnaires, computer-based neuropsychological tests, and pre- and post-prandial blood collections. During this visit, participants completed the Three-Factor Eating Questionnaire (6), which was used to group participants on the basis of their disinhibition scores.

With the use of a median split, 14 participants were classified as having LD (score of  $<6$ ) and 16 participants as having HD (score of  $>6$ ). The remaining 3 participants were excluded from further analyses because their disinhibition scores coincided with the median score. Participants were then scheduled for 2 fMRI visits (fasted and fed) with a 1- to 3-wk washout period (Figure 1A); the order of visits was counterbalanced across participants. Twenty-four hours before each visit, participants were asked to refrain from alcohol consumption, smoking, and intense physical activity and to maintain their regular meal and sleep routines.

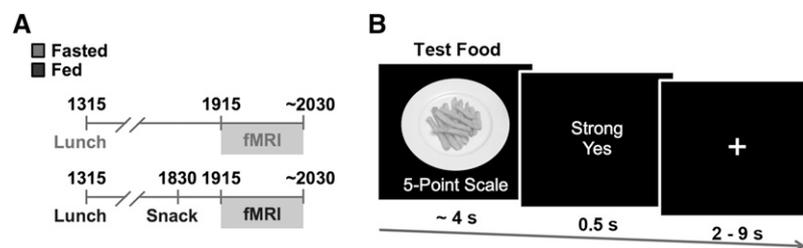
### Study procedure

On the day of each fMRI visit, participants were asked to consume a regular breakfast, matched across both visits. After breakfast, participants fasted from 1030 and arrived at the laboratory at 1230. Compliance with dietary instructions was verified through a 24-h food recall. At 1315, participants were fed a meal (56% carbohydrates, 30% fat, and 14% protein) portioned to provide 25% of the participant's estimated daily energy requirements (495–731 kcal; based on the Schofield equation with an activity factor of 1.3) (27). After lunch, participants were asked to remain in a waiting room, where they were only permitted sedentary activities (eg, reading and watching videos) and were not allowed to consume anything other than plain water. During this waiting period, participants also completed several questionnaires.

At 1830 in the fed visit, participants were given an additional meal (57% carbohydrate, 23% fat and 20% protein) that provided 20% of the participant's estimated daily energy requirements (396–585 kcal; based on the Schofield equation with an activity factor of 1.3) (27); this meal commenced 45 min before the fMRI scan. In the fasted visit, participants had fasted from the lunch meal at 1315 until the end of the fMRI scan at  $\sim 2030$ .

### Visual analog scales

Throughout the scan-related visits, participants were asked to provide subjective appetite and mood ratings every hour (except during the fMRI scan). These ratings involved 17 computerized visual analog scales (VASs), anchored on one end with “not at all” (scored as 0) and on the other with “extremely” (scored as 100). To evaluate fullness after a meal, participants were asked to report how “hungry” and how “full” they felt. In addition, participants rated their desire to eat certain food types (4 items; eg, sweet foods, salty foods), several aspects of appetite states



**FIGURE 1.** A: Schematic of study procedure; each participant was scheduled for 2 fMRI visits (fasted and fed). B: Schematic illustration of a typical decision trial. On every trial, one food picture was presented for up to 4 s. During this time frame, participants were required to indicate on a 5-point scale (strong no, no, neutral, yes, strong yes) the strength of their preference to eat the test food relative to the reference food. After a response, the screen would show the chosen value for 0.5 s. Trials were separated by intertrial intervals exponentially distributed between 2 and 9 s.

(5 items; eg, how nauseated they felt, how thirsty they felt), and their mood (6 items; eg, happiness, clear-headedness).

### Functional imaging procedure

For the fMRI scan, participants were taken to the Centre for Cognitive Neuroscience scanner suite and were scanned at 1915. Images were acquired on a 3-Tesla Tim Trio system (Siemens) fitted with a 12-channel head coil. Stimuli were presented by using a projector (Epson EMP 7250) and rearview mirror system, and participants responded using an MR-compatible button box held in the right hand.

Before undergoing functional imaging, participants viewed all 72 food pictures that would be used in the functional imaging paradigm; this was to ensure that participants would be able to identify the foods. Pictures were of local foods that had been evaluated for familiarity by a pilot group of 10 male participants.

The functional imaging paradigm was adapted from a previous study designed to evaluate food valuation signals (28). This involved 8 imaging runs, with 36 trials per run (lasting 5 min and 38 s). In each trial, 1 of the 72 food pictures was presented for up to 4 s. During this period, participants were asked to make a rating on a 5-point scale. After a response, the screen would show the chosen value for 0.5 s. If participants did not respond within 4 s, the screen would show a “?” and the trial was classified as a “miss.” Trials were separated by intertrial intervals exponentially distributed between 2 and 9 s.

In the first 4 imaging runs, participants were asked to rate the food pictures for how healthy or how tasty they were (2 runs for each of health and taste ratings). Both health and taste ratings were made by using a 5-point scale (labels for health scale: unhealthy, fairly unhealthy, neutral, fairly healthy, and healthy; labels for taste scale: bad, fairly bad, neutral, fairly good, good), and the order in which participants made health and taste ratings was counterbalanced across participants.

In the second 4 imaging runs, participants decided which of a pair of foods they would like to eat at the end of the experiment. On the basis of each participant’s health and taste ratings, 2 reference foods were selected for each participant: one neutral in taste and neutral in health (neutral-neutral reference food) and one good-tasting but unhealthy (good-unhealthy reference food). Before each of these runs, participants were presented with one of the reference foods and were asked to remember it for the experimental run (order of neutral-neutral and good-unhealthy reference food presentation was counterbalanced across participants). During the experimental run, participants indicated on a 5-point scale (strong no, no, neutral, yes, strong yes) their preference to eat each of the 72 food items relative to the reference food. A schematic of a typical decision trial is shown in Figure 1B.

To make the task incentive compatible, one of the participants’ decisions was selected at random. Participants were given a food item based on their decision (for “strong yes”/“yes” responses, the food item was given; for “strong no”/“no” responses, the reference food was given; for “neutral” responses, either the food item or the reference food was given) and were required to consume the food of their choice before leaving the experimental premises.

Functional images were acquired by using a gradient echo-planar imaging sequence (repetition time: 2000 ms; echo time:

30 ms; interslice time: 55 ms; flip angle: 90°; field of view: 192 × 192 mm; matrix size: 64 × 64; voxel size: 3.0 × 3.0 × 3.0 mm). 36 oblique axial slices (slice thickness: 3 mm; gap: 0.3 mm) were acquired along the anterior commissure-posterior commissure plane (total 166 volumes for each run). Structural images were acquired by using a T1-weighted magnetization-prepared rapid acquisition with gradient echo sequence (repetition time: 2300 ms; inversion time: 900 ms; flip angle: 9°; bandwidth: 240 Hz/pixel; field of view: 256 × 240 mm; matrix size: 256 × 256; number of slices: 192; voxel size: 1.0 × 1.0 × 1.0 mm). Co-planar 2-dimensional anatomical images were acquired by using a T1-weighted sequence to facilitate coregistration between functional and structural images (repetition time: 1470 ms; inversion time: 1100 ms; flip angle: 9°; bandwidth: 150 Hz/pixel; field of view: 192 × 192 mm; matrix size: 256 × 256; number of slices: 36; voxel size: 0.8 × 0.8 × 3.3 mm).

### Imaging data preprocessing

Imaging data were processed by using BrainVoyager QX Version 2.3.0 (Brain Innovation). The first 2 functional volumes were discarded to allow for magnetic saturation. The remaining 164 volumes were subjected to slice time correction, followed by motion correction with realignment to the first volume of the third run. Images were spatially smoothed by using a Gaussian kernel (full-width-half-maximum: 6 mm). Linear trend removal and temporal high-pass filtering (0.009 Hz) were applied. The functional data were then spatially normalized to Talairach space. Participants with excessive in-scanner motion between runs (>3 mm translation or 3° rotation) or within-run (>1 mm translation or >1° rotation) were excluded from the analysis. The functional data were analyzed by using BrainVoyager QX Version 2.3.0 (Brain Innovation), NeuroElf Version 0.9c (<http://neuroelf.net/>), MATLAB R2009a (The Mathworks Inc), and SPSS 20 (SPSS Inc).

### Statistical analysis

VAS and in-scanner behavioral data were analyzed by using separate 2 × 2 repeated-measures ANOVAs with disinhibition group (LD compared with HD) and satiety state (fed compared with fasted) as the factors. For VAS data, dependent variables were participants’ scores on the 17 VAS scales (*P* values, Bonferroni corrected); for in-scanner behavioral data, dependent variables were health ratings, taste ratings, decision ratings, and mean decision task reaction time. All data were analyzed by using MATLAB R2009a (The Mathworks Inc) and SPSS 20 (SPSS Inc).

Only imaging data relating to food decisions were analyzed (*see* Results). For each participant, the fMRI signal was modeled by using a voxel-wise general linear model with 6 regressors, 3 for each satiety state. In each state, the first regressor estimated the average signal associated with any food valuation response. The second regressor was a parametric regressor that estimated how much magnetic resonance signal would vary from the average response depending on the participant’s preference for the test food relative to the neutral-tasting, neutral-health reference food. In constructing this regressor, the 5-point food rating scale described earlier was collapsed to a 3-point scale to increase

power. Thus a “+1” weighting referred to a “strong yes”/“yes” response, “0” referred to “neutral” (no preference), and “−1” referred to a “strong no”/“no” response. Parameter estimates for the parametric regressor indexed the slope of MR signal change corresponding to food preferences. The greater the value of the parameter estimate, the higher the signal would be for a preferred food and the lower it would be for a non-preferred food relative to the signal averaged across all choices. The parameter estimate of this parametric regressor is henceforth referred to as the food valuation signal and constituted the principal imaging measure in this study. A third regressor modeled missed trials. Each regressor consisted of a 1s-boxcar function beginning at the onset of food presentation that was convolved with a canonical double gamma hemodynamic response function.

The imaging data from individual participants were entered into a group-level random-effects analysis with participants as the random factor to enable the generalization of the imaging findings. The food valuation signal across the whole brain was subjected to a  $2 \times 2$  repeated-measures ANOVA to test for an interaction between state and group. A voxel-level threshold of  $P < 0.001$  was used to generate  $F$  statistical maps. To control for type I error, an iterative cluster size thresholding procedure that takes into account the spatial smoothness of functional imaging maps and its 3-dimensional spatial correlation was used to determine the minimum cluster size corresponding to a probability of family-wise error of  $< 0.05$  (29), accounting for whole-brain volume. Food valuation signals were then extracted from the suprathreshold clusters in every participant and subjected to post hoc  $t$  tests. Finally, Levene’s tests were used to compare the variability of the food valuation signal between the groups in each state.

## RESULTS

### Participant characteristics

Participant characteristics are presented in **Table 1**. HD participants had a higher BMI than did the LD participants ( $t_{(28)} = -3.51$ ,  $P < 0.002$ ). LD and HD participants did not differ in terms of age ( $t_{(28)} = 1.15$ ,  $P = 0.26$ ) or in the interval between the fasted and fed visits ( $t_{(28)} = -0.66$ ,  $P = 0.51$ ). Furthermore, no significant effects of visit order on key dependent variables (smallest  $P = 0.19$ ) was observed; therefore, the subsequent analyses collapsed across this variable.

**TABLE 1**  
Participant characteristics<sup>1</sup>

Characteristic	LD ( $n = 14$ )	HD ( $n = 16$ )
Dietary disinhibition <sup>2</sup>	$3.50 \pm 1.16$	$8.81 \pm 1.60$
Age (y)	$28.2 \pm 6.24$	$25.9 \pm 4.61$
BMI ( $\text{kg}/\text{m}^2$ )	$21.9 \pm 2.13^3$	$26.8 \pm 4.78$
Days between visits (d)	$7.64 \pm 3.13$	$8.56 \pm 4.29$

<sup>1</sup> All values are means  $\pm$  SDs. All participants were men. HD, high disinhibition; LD, low disinhibition.

<sup>2</sup> Measured with the Three-Factor Eating Questionnaire (6).

<sup>3</sup> Significantly different from HD,  $P < 0.005$ .

### VAS findings

A main effect of satiety on perceived fullness ( $F_{(1,28)} = 54.35$ ,  $P < 0.001$ ; **Figure 2A**) and on hunger ( $F_{(1,28)} = 113.11$ ,  $P < 0.001$ ; **Figure 2B**) was observed. Participants were more full and less hungry in the fed than in the fasted state. No significant main effect of group and no group-by-state interaction (LD or HD; smallest  $P > 0.60$ ) were found. Together, these results suggest that the satiety manipulation was equally successful in both groups.

In comparison with the fasted state, participants in the fed state reported being able to eat less at that moment ( $F_{(1,28)} = 40.12$ ,  $P < 0.001$ ), to have a lower desire to eat ( $F_{(1,28)} = 79.88$ ,  $P < 0.001$ ), to be more satisfied ( $F_{(1,28)} = 105.58$ ,  $P < 0.001$ ), and to be more energetic ( $F_{(1,28)} = 11.96$ ,  $P = 0.03$ ). Participants additionally reported a decreased desire to eat salty ( $F_{(1,28)} = 12.22$ ,  $P = 0.03$ ) and savory ( $F_{(1,28)} = 20.80$ ,  $P = 0.002$ ) foods in the fed state. No other main effect of state (smallest  $P = 0.07$ ) or any main effect or interaction involving group (smallest  $P > 0.60$ ) was observed.

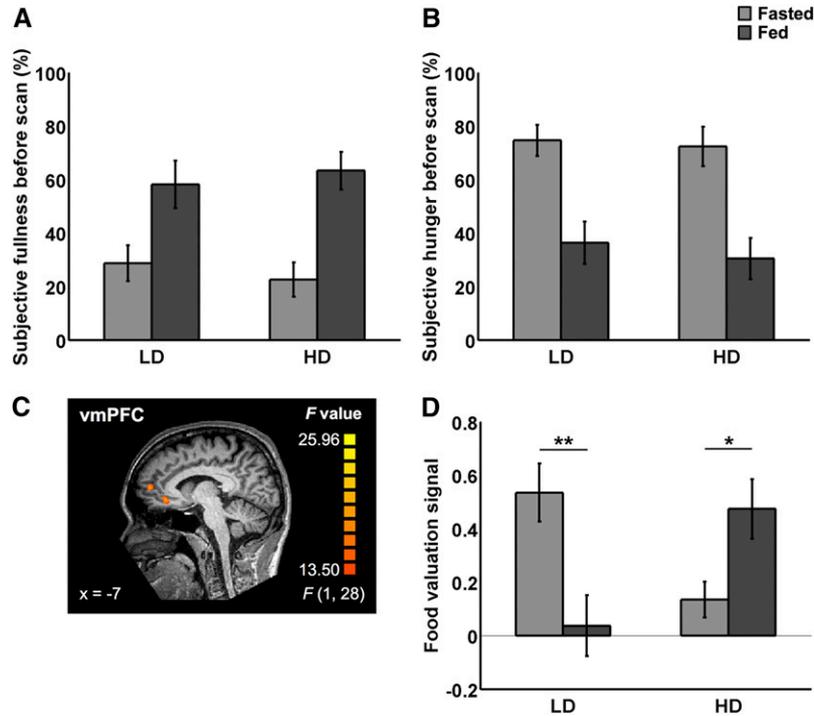
### Behavioral findings

There were no main or interaction effects of state or group on health (smallest  $P = 0.07$ ) and taste ratings (smallest  $P = 0.42$ ) of food stimuli in the in-scanner task. Similarly, there were no significant effects involving state or group on decision ratings about which food to eat (smallest  $P = 0.68$ ) or for mean reaction time to respond during the decision task (smallest  $P = 0.25$ ).

Unlike in the original study (28), on which the current experiment was based, we found that health ratings for food were inconsequential to participant food choices [regression coefficient for LD:  $-0.09$  (fasted),  $-0.08$  (fed); regression coefficient for HD:  $-0.08$  (fasted),  $-0.03$  (fed)]. Instead, choices were driven by taste considerations [regression coefficient for LD:  $0.58$  (fasted),  $0.52$  (fed); regression coefficient for HD:  $0.63$  (fasted),  $0.57$  (fed)]. Because participants in both groups did not factor health in food choices in either state, we confined the data analysis to the second set of imaging runs relating to food decisions.

### fMRI findings

At the whole-brain level of analysis, the fMRI signal in 3 brain regions showed a significant interaction of disinhibition group and satiety state (**Table 2**). Two of these regions lay in the vmPFC region (**Figure 2C**), denoted in some previous studies as the medial orbitofrontal cortex (30). These regions are in close proximity to the region identified in a prior experiment using a similar paradigm (28). The more posterior vmPFC region showed a significant state-by-group interaction in the parametric food valuation signal ( $F_{(1,28)} = 21.34$ ,  $P < 0.001$ ; **Figure 2D**). In LD participants, this signal was lower in the fed state than in the fasted state ( $t_{(13)} = 4.11$ ,  $P < 0.001$ ). In contrast, the food valuation signal in HD participants was higher in the fed than in the fasted state ( $t_{(15)} = -2.56$ ,  $P < 0.05$ ). There was a significant negative correlation between disinhibition score and the corresponding shift in food valuation signal between states ( $\rho = -0.57$ ,  $P < 0.001$ ; **Figure 3**). The variability in signals for the fasted and fed states did not differ between the groups (smallest  $P = 0.10$ ).



**FIGURE 2.** Subjective VAS ratings for fullness (A) and hunger (B) immediately before the fMRI scan: both LD and HD individuals were more full ( $F_{(1,28)} = 54.35, P < 0.001$ ) and less hungry ( $F_{(1,28)} = 113.11, P < 0.001$ ) in the fed than in the fasted state. C: Statistical parametric map showing the ventromedial prefrontal region, where food valuation signals showed a significant state  $\times$  disinhibition group interaction (voxel threshold:  $P < 0.001$ ; cluster corrected to  $P_{FWE} < 0.05$ ). D: Signals sampled from the posterior vmPFC region were subject to post hoc  $t$  tests (\*\* $P < 0.001, *P < 0.05$ ). Error bars indicate SEMs. HD, high disinhibition ( $n = 16$ ); LD, low disinhibition ( $n = 14$ ); VAS, visual analog scale; vmPFC, ventromedial prefrontal cortex.

The more anterior region similarly showed a significant state-by-group interaction in the food valuation signal ( $F_{(1,28)} = 22.25, P < 0.001$ ). In LD participants this signal was lower in the fed state than in the fasted state ( $t_{(13)} = 4.95, P < 0.001$ ). HD participants showed a trend toward a higher food valuation signal in the fed than in the fasted state ( $t_{(15)} = -2.02, P = 0.06$ ). No main effects of state or group were found in either of these 2 regions (smallest  $P = 0.10$ ). The variability in signals for the fasted and fed states did not differ between the groups (smallest  $P = 0.54$ ).

**DISCUSSION**

We explored how dietary disinhibition modulates the neural representation of food value as a function of satiety. As hypothesized, LD participants showed lowered vmPFC food valuation signals after being fed. In contrast, HD participants

showed no attenuation of this valuation signal after being fed and instead showed a higher signal than in the fasted state.

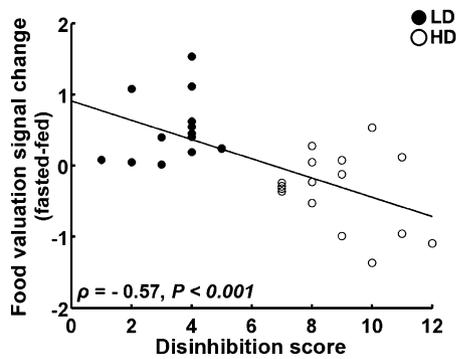
Our observations regarding LD participants are consistent with behavioral evidence regarding devaluation of food with satiety (31). Prior neuroimaging studies have shown that the vmPFC, sometimes referred to as the medial orbitofrontal cortex (30), tracks food valuation (32–34) and that feeding reduces vmPFC responses to food stimuli (35–37). Furthermore, vmPFC signals associated with food decisions are attenuated when a food is devalued by selective satiation (38). LD participants therefore exhibited the expected response to feeding.

In contrast, HD participants reported a tendency to eat regardless of hunger and satiety, eating instead as a response to food cues, the social environment, and emotional stress (6). In the current study, HD participants were indistinguishable from LD participants in reporting increased fullness when fed. However, instead of showing attenuated vmPFC value signals after being

**TABLE 2**  
Regions exhibiting significant state (fed or fasted) by group (LD or HD) interaction in food valuation signal<sup>1</sup>

Region <sup>2</sup>	Talairach coordinates <sup>3</sup>					F value	Cluster size (3 × 3 × 3 mm voxels)
	BA	x	y	z			
Ventromedial prefrontal cortex (anterior)	10	-10	52	12	23.30	271	
Ventromedial prefrontal cortex (posterior)	32	-7	34	-3	21.40	253	
Angular gyrus	39	-25	-53	33	22.68	122	

<sup>1</sup> BA, Brodmann area; HD, high disinhibition; LD, low disinhibition.  
<sup>2</sup> All regions listed were identified in the left hemisphere.  
<sup>3</sup> Coordinates correspond to the peak voxel within each cluster.



**FIGURE 3.** Correlation between disinhibition scores and differences in food valuation signal from the fasted to the fed state. There was a significant negative correlation (Spearman's  $\rho = -0.57$ ,  $P < 0.001$ ). HD, high disinhibition ( $n = 16$ ); LD, low disinhibition ( $n = 14$ ).

fed (as shown by LD participants), they demonstrated an increase in valuation signal in the vmPFC.

Our findings parallel those of other neuroimaging studies that have found positive associations between vmPFC responses to food cues and other related behavioral measures, such as dietary restraint (39) and external eating (40). This pattern of findings is reminiscent of the “priming” phenomenon reported in drug addiction research (41), where the presence rather than the absence of the drug in the body activates motivational mechanisms for drug-seeking behavior. Thus, whereas feeding HD individuals may lower homeostatic hunger (as reflected in decreased subjective hunger and increased fullness ratings), feeding may increase hedonic hunger, leading HD individuals to seek food regardless of energy requirements (42).

Previous neuroimaging studies have found that HD and LD individuals differ in their responses to food or food cues (24, 25). Our findings extend these observations by showing that valuation signals associated with food choice are altered in HD, which may in turn underlie the tendency of HD individuals to eat beyond satiety and gain weight. Although we did not measure food intake directly, the prediction concerning weight gain is supported by a significant correlation between disinhibition scores and BMI in the current study ( $r = 0.44$ ,  $P < 0.02$ ). Nonetheless, future studies should test this directly by exploring whether the change in vmPFC valuation signal after satiety is associated with actual food intake.

The current study was founded on the notion that the decision to eat a given food depends on the subjective value assigned to the choices under consideration and that neural signals carrying this information can be detected by using fMRI. In deciding on a given food, 2 considerations that could contribute to valuation are taste and health: eg, we might avoid eating a tasty but unhealthy food because we are concerned about maintaining good health. Earlier work has shown that when participants consider the healthiness of their food choices (in addition to taste considerations) (28), these food choice trials are associated with elevated lateral prefrontal self-control activation. In the current study, perhaps reflecting the recruitment of young adult males (in contrast with reference 28), both HD and LD participants overwhelmingly made food choices according to taste only (see Online Supplemental Material under “Supplemental data” in the online issue). As such, we were unable to evaluate how health considerations affected food valuation.

Interestingly, when participants do factor in health in their food choices, the manner in which they respond to food pictures is amenable to cognitive modulation. Explicitly requiring participants to focus on healthy aspects of foods can elicit lateral prefrontal self-control signals (43). This supports the utility of training individuals to make healthier food choices. Because disinhibition has been shown to decrease with weight loss (44–47), it would be of interest to examine the extent to which food valuation signals in HD participants may be altered by successful intervention in future studies.

One limitation of our study was that we were unable to isolate whether altered valuation signals were related to disinhibition independent of weight status. Our observation that disinhibition scores correlated with BMI provides strong support that this pattern of eating behavior results in weight gain; however, future studies should compare LD and HD participants who are matched in BMI. Also, considering the fasted state alone, the lower food valuation signal in HD than in LD participants was unexpected. This finding merits replication and further exploration in future studies.

In summary, the current study used food picture cues to demonstrate how dietary disinhibition can affect the neural valuation of food depending on whether the participant is fasted or fed. Although both groups of participants reported subjective fullness after feeding, a significant interaction between group and state was found in the food valuation signal. These findings suggest neural underpinnings of how disinhibition may lead to weight gain.

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The authors' responsibilities were as follows—MWLC, YSL, CL, JGG, MF-FC, and MJM: designed the research; YL, JCJL, MZ, SC, and TW: conducted the research; VT, MF-FC, and SC: provided the essential materials; YL, CL, MF-FC, and JCJL: analyzed the data; YL, MF-FC, JCJL, and MWLC: wrote the manuscript; and YL, MF-FC, JCJL, YSL, and MWLC: had primary responsibility for the final content. All authors read and approved the final manuscript. None of the authors declared a conflict of interest.

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