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Evening Hyperphagia and Food Motivation: A Preliminary Study of Neural Mechanisms

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Abstract

Evening hyperphagia (EH; consumption of ~25% of total daily calories after the evening meal) is a circadian delay in the pattern of daily food intake and is a core criterion of night eating syndrome (Allison et al., 2010). This preliminary study examined the brain response to food cues using functional magnetic resonance imaging (fMRI) in seven obese adults with EH compared to seven obese adults without EH. When contrasting food to non-food and blurry baseline images pre-meal, groups differed in brain activation in the inferior frontal gyrus, precentral gyrus, cingulate gyrus, superior temporal gyrus and cerebellum. At post meal, groups differed in brain activation in the fusiform gyrus, inferior frontal gyrus, inferior parietal lobule and the cerebellum. Significant interactions between time (pre-meal, post-meal) and group (EH, control) when contrasting food to non-food images were also noted in the inferior frontal gyrus and the superior temporal gyrus. Further research is necessary to replicate these findings and determine if they have a mechanistic role in the development of circadian delayed eating behavior in obese adults with EH.

Keywords

evening hyperphagia; food motivation; disinhibition; inferior frontal gyrus; neural mechanisms; functional magnetic resonance imaging

Introduction 1.1

Evening hyperphagia (EH; consumption of ~25% of one's total daily calories after the evening meal) is a core criterion of night eating syndrome (NES) (Allison et al., 2010;

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Stunkard et al., 1955). The animal literature on limbic system involvement in circadian food entrainment (Escobar et al., 2011) and research on food motivation in obese persons (Carnell, Gibson, Benson, Ochner, & Geliebter, 2012) suggests an intriguing model to explore in the development and/or maintenance of EH: the prefrontal (cognitive control and inhibition) and limbic (motivation and reward) neural systems.

The current study examined the brain response to food cues in obese adults with and without EH. We focused on brain response to food cues mid-day so that comparisons can be made with existing literature using mid-day food cue paradigms. Based on studies showing reduced daytime hunger and food intake in persons with EH compared to weight-matched controls (Boston, Moate, Stunkard, Allison, & Lundgren, 2008; Lundgren et al., 2008; O'Reardon et al., 2004), we hypothesized that obese persons with EH compared to matched controls would show significantly different brain activation in response to food images in prefrontal and limbic regions.

2.1 Methods

2.1.1 Participants

Seven obese adults meeting criteria for EH (mean BMI = 37.9 kg/m², mean age = 33.6 years, 6 female, 5 caucasian) and seven control participants matched for BMI, age, gender, ethnicity, and education level, were selected on the basis of baseline eating patterns and demographic characteristics from a cohort of 80 obese adults enrolled in a study examining the neural predictors of weight loss.

Exclusion criteria included recent weight change, high physical activity, smoking or history of drug abuse/dependence, medications that affect metabolism or appetite, inability to exercise, eating (including binge eating disorder), neurological, or other psychological disorders, metabolic disease, recent or current pregnancy or breastfeeding, and serious medical conditions.

2.1.2. Assessments

Height and weight were measured; BMI was computed. Dietary patterns were assessed with a three-day recall, and participants' percent caloric intake after the evening meal was calculated. Participants were classified as EH positive if either 1) the average percent food intake after dinner was $\geq 25\%$ across the three days or 2) the participant consumed $\geq 25\%$ of total daily food intake after the evening meal on at least two of the three days. Participants were classified as controls if they reported an average of $\leq 5\%$ of their total daily food intake after dinner across the three days, they had no single day with $\geq 15\%$ total daily food intake after the evening meal, and reported the consumption of breakfast, lunch, and dinner during the three recall assessments; their demographic characteristics had to closely match those of the EH participants.

2.1.3. Procedures

All study procedures were approved by the University of Kansas Medical Center Human Subjects Committee.

2.1.4. Food Motivation Paradigm

Participants viewed food, animal (non-food), and blurred baseline images (a) after fasting for four hours (pre-meal) and (b) immediately after eating a small meal (post-meal) standardized for energy [500 kcal] and lunch-specific macronutrient content. The study tasks were counterbalanced to minimize order effects. This well-validated food motivation

paradigm has been described in several reports (Bruce et al., 2010; Bruce et al., 2012; Holsen et al., 2005, 2006, 2009, 2012; Leidy et al., 2011; Martin et al., 2010).

Each scanning session consisted of two functional runs that included three 30-second blocks of each stimulus condition (i.e., food, animal), alternated between blocks of blurred images. Images were never repeated. Stimulus presentation time was 2.5 seconds, and inter-stimulus interval (ISI) was 0.5 seconds. Stimulus condition order was counterbalanced across subjects. Images were back-projected through a projector connected to the stimuli presentation computer using Presentation (Neurobehavioral Systems, Inc., Albany, CA).

2.1.5. fMRI Methods

Image acquisition—Scanning was performed on a 3 Tesla Siemens Allegra (Siemens, Erlangen, Germany) fitted with a quadrature head coil. Following automated scout image acquisition and shimming procedures to optimize field homogeneity, a T1-weighted anatomic image was acquired with a 3D magnetization prepared rapid acquisition gradient echo (MPRAGE) sequence (TR/TE = 2300/3.06 ms, flip angle = 8°, FOV = 192 × 100 mm, matrix = 192 × 192, slice thickness = 1 mm). Next, two gradient echo blood oxygen level dependent (BOLD) scans were acquired in 43 contiguous oblique axial slices at a 40° angle (repetition time/echo time [TR/TE] = 3000/30 ms, flip angle = 90°, field of view [FOV] = 220 mm, matrix = 64 × 64, slice thickness = 3 mm, in-plane resolution = 3 × 3 mm, 130 data points). Participants were positioned in the scanner so that the angle of the anterior commissure-posterior commissure (AC-PC) plane was between 17° and 22° in scanner coordinate space, verified with a localization scan.

Data analysis—Pre-processing and statistical analyses were performed using BrainVoyager QX (Brain Innovation, Maastricht, Netherlands, 2004). Pre-processing steps included trilinear 3D motion correction, sinc-interpolated slice scan time correction, 3D spatial smoothing with 4-mm Gaussian filter, and high pass filter temporal smoothing. Functional images were co-registered to the anatomic images obtained within each session and normalized to Talairach and Tournoux's (1988) stereotaxic atlas. Runs were discarded if motion exceeded 3 mm along any axis (*x*, *y*, or *z*).

A whole brain statistical analysis approach was used. Activation maps were analyzed using statistical parametric methods (Friston et al., 1995) contained within the BrainVoyager QX software. Regressors representing the experimental conditions of interest, with the motion parameters included as regressors of no interest, were modeled with a hemodynamic response filter and entered into the multiple regression analysis using a random effects general linear model (GLM). The resulting GLMs, run separately for pre-meal and post-meal, were entered into second level analyses: t-tests comparing EH and Control group activation to food vs. blurred baseline images and a Group (EH, Control) × Stimulus Type (food, animal) ANOVA.

Resulting statistical parametric maps were overlaid on three-dimensional renderings of an averaged-group brain. Based on Monte Carlo simulations implemented by BrainVoyager's cluster level threshold estimator plugin (Forman et al., 1995; Goebel, Esposito, & Formisano, 2006), voxel values were considered significant if the activation survived a statistical threshold of $\alpha < .05$, whole-brain corrected. Activation clusters were identified and verified by mapping Talairach coordinates onto two atlases (Mai, Paxinos, & Voss, 2008; Talairach & Tournoux, 1988). For each participant, mean percent signal change (food vs. nonfood in percentage of baseline) in the maximally activated voxel from the group analyses of each hypothesized region was extracted to clarify the direction of activation.

3.1 Results

3.1.1 Food vs. Blurry Baseline Comparisons

Pre-meal—There were no regions in which the EH group showed greater activation than Controls to food images versus blurry baseline images. The Control group relative to the EH group, however, showed greater activation to food versus blurry baseline images in the left cingulate gyrus, right precentral gyrus, and right inferior parietal lobule (Table 1).

Post-meal—The EH group relative to the Control group showed greater activation to food versus blurry baseline images in left fusiform gyrus (Table 1). The Control group relative to the EH group showed greater activation to food versus blurry baseline images in the right inferior frontal gyrus and the right inferior parietal lobule.

Group (EH, Control) by Time (Pre-meal, Post-meal) Interaction—There were no areas of greater activation when examining this interaction for the food versus blurry baseline image contrast.

3.1.2. Food (F) vs. Non-food (NF; animal) Comparisons

Pre-meal—A significant interaction was found in the left inferior frontal gyrus (Table 2), driven by a group difference in activation to non-food images (EH>C) with no difference in activation to food images. Significant interactions were also found in the left superior temporal gyrus (STG), left middle temporal gyrus (MTG), and cerebellum. Inspection of these data revealed that the interaction in the STG was driven by the EH group showing a greater difference in activation to food vs. non-food images, compared with the Control group. The interaction in the MTG was driven by a group difference in activation to non-food images (EH>C), with no significant difference in activation to food images.

Post-meal—A significant interaction was found in the right inferior frontal gyrus (Table 2), driven by a group difference to non-food images (EH>C) with no difference in activation to food images. Significant interactions were also found in the cerebellum bilaterally.

Group (EH, Control) by Time (Pre-meal, Post-meal) by Stimulus (F, NF)

Interaction—A significant interaction between time and group when contrasting food to non-food images was found in the right inferior frontal gyrus (BA 45; $x, y, z = 42, 20, 13$). The EH group showed *decreased* activation pre- to post-meal for food images, but *increased* activation pre- to post-meal when viewing animal images. The control group showed the opposite pattern. A significant interaction between time and group when contrasting food to non-food images was also found in the superior temporal gyrus (BA 42; $x, y, z = -60, -31, 19$). Both the EH and Control groups increased activation pre- to post-meal when viewing food cues, but the pattern of activation pre- to post-meal was opposite when viewing animal cues: the EH group increased activation and the Control group decreased activation.

4.1 Discussion

Our hypothesis that obese persons with and without EH would demonstrate different brain activation in response to food cues in prefrontal and limbic regions before and after a mid-day test meal was partially supported. We did not find group differences in limbic regions, but did find group differences in prefrontal and other important brain regions both before and after a mid-day test meal.

When considering the pre-meal differences in brain activation between groups, these data suggest that when fasted mid-day, people with EH are less reactive to food cues in brain

areas typically associated with sensorimotor integration and cognitive attention and processing. Post-meal analyses demonstrated that the EH group showed greater brain activation than Controls when viewing food vs. blurry baseline images in the left fusiform gyrus, an area associated with the visual processing of food cues (Tang, Fellows, Small, & Dagher, 2012; van der Laan, de Ridder, Viergever, & Smeets, 2010). In contrast, the Control group's greater activation in the right inferior frontal gyrus and right inferior parietal lobule suggest the occurrence of an inhibitory process, potentially involving task switching and suppression of a situationally inappropriate response set (e.g., Aron, Robbins, & Poldrack, 2004). Similarly, the significant interaction of group, time, and stimulus (food vs. non-food) demonstrated a decrease in inferior frontal gyrus activation from pre- to post-meal in the EH group, but the opposite pattern among the Controls. Together, these post-meals findings suggest that there are group differences in mid-day brain activation in response to food cues in regions previously implicated in cognitive control and behavioral inhibition.

This is a preliminary report, in need of replication with a larger representative sample of obese and non-obese adults with EH. These results, nonetheless, build on findings of aberrant circadian eating patterns previously documented (O'Reardon et al., 2004, Boston et al., 2008) and warrant further exploration and validation. Because obese adults with EH demonstrated *decreased* brain activation in areas associated with inhibition and *increased* activation in areas associated with visual attention after a mid-day meal, one possibility is that a mid-day meal disrupts dietary restraint exhibited during the first half of the day. Alternatively, differences in brain activation might reflect reductions in the EH group's necessity for inhibition mid-day because of reduced motivation to eat until later in the evening. Both hypotheses are consistent with behavioral data showing decreased food intake until later in the afternoon/evening in persons with EH (Boston et al., 2008).

5.1. Conclusion

This preliminary study suggests that there are mid-day differences in brain activation to food cues between people with EH and Controls, but whether or not these differences are the cause or the result of EH are unknown. Future research is necessary to validate these findings and to understand better the neural underpinnings of evening hyperphagia, an aberrant circadian eating pattern common among obese individuals (Gallant et al., 2012).

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Highlights

- We examined neural response to food cues in evening hyperphagic (EH) obese adults.
- EH vs. controls showed less post-meal brain activation in the inferior frontal gyrus.
- EH participants had decreased inferior frontal gyrus activation pre to post-meal.
- EH is associated with decreased activation of inhibitory brain regions.

Table 1

Regions Reaching Significance During GLM Contrasts of EH vs. Control, Food vs. Blurry Baseline

			<u>Peak Talairach Coordinates</u>				
Region and contrast	L/R	BA	X	Y	Z	Voxels	t
Pre-meal							
<hr/>							
<i>EH>C</i>							
<hr/>							
None							
<hr/>							
<i>C>EH</i>							
<hr/>							
Inferior parietal lobule	R	40	39	−52	46	269	−5.67
Precentral gyrus	R	4/6	24	−16	52	311	−4.89
			18	−4	46	212	−5.22
			4	−25	58	190	−4.97
Cingulate gyrus	L	31	−15	−55	28	494	−4.37
<hr/>							
Post-meal							
<hr/>							
<i>EH>C</i>							
<hr/>							
Fusiform gyrus	L	18/19	−42	−67	−11	220	4.21
<hr/>							
<i>C>EH</i>							
<hr/>							
Inferior frontal gyrus	R	45/47	39	32	1	197	−4.59
Inferior parietal lobule	R	40	39	−52	46	288	−5.03

Note. L = left; R = right; BA = Brodmann Area; all ps <0.01

Table 2

Regions Reaching Significance During GLM Contrasts of EH vs. Control, Food vs. Nonfood (Animal)

		Peak Talairach Coordinates					
Region and contrast	L/R	BA	X	Y	Z	Voxels	F
Pre-meal							
Inferior frontal gyrus	L	46	−39	32	7	328	21.91
Superior temporal gyrus	L	38	−39	−1	−14	563	22.96
Middle temporal gyrus	L	21	−60	−13	−8	218	28.22
Cerebellum	L		−24	−52	−17	282	25.49
Post-meal							
Inferior frontal gyrus	R	45	45	20	13	267	20.33
Cerebellum	R		24	−52	−26	198	50.36
			18	−43	−42	273	30.24
			15	−67	−26	280	29.94
			−9	−58	−32	199	24.45
	L		−24	−31	−29	260	52.34

Note. L = left; R = right; BA = Brodmann Area; all ps <0.01.