

Elevated energy intake is correlated with hyperresponsivity in attentional, gustatory, and reward brain regions while anticipating palatable food receipt^{1–3}

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ABSTRACT

Background: Obese compared with lean individuals show greater attention-, gustatory-, and reward-region responsivity to food cues but reduced reward-region responsivity during food intake. However, to our knowledge, research has not tested whether an objectively measured caloric intake is positively associated with neural responsivity independent of excess adipose tissue.

Objective: We tested the hypothesis that objectively measured energy intake, which accounts for basal needs and the percentage of body fat, correlates positively with the neural response to anticipated palatable food intake but negatively with a response to food intake in healthy-weight adolescents.

Design: Participants ($n = 155$; mean \pm SD age: 15.9 ± 1.1 y) completed functional magnetic resonance imaging scans while anticipating and receiving palatable food compared with a tasteless solution, a doubly labeled water assessment of energy intake, and assessments of resting metabolic rate and body composition.

Results: Energy intake correlated positively with activation in the lateral visual and anterior cingulate cortices (visual processing and attention), frontal operculum (primary gustatory cortex) when anticipating palatable food, and greater striatal activation when anticipating palatable food in a more-sensitive region of interest analysis. Energy intake was not significantly related to neural responsivity during palatable food intake.

Conclusions: Results indicate that objectively measured energy intake that accounts for basal needs and adipose tissue correlates positively with activity in attentional, gustatory, and reward regions when anticipating palatable food. Although hyperresponsivity of these regions may increase risk of overeating, it is unclear whether this is an initial vulnerability factor or a result of previous overeating. This trial was registered at clinicaltrials.gov as NCT01807572. *Am J Clin Nutr* 2013;97:1188–94.

INTRODUCTION

Neuroimaging studies have provided considerable insight into differences in neural responsivity to food stimuli as a function of weight status. Specifically, obese compared with lean individuals have shown greater responsivity in reward-related regions (striatum, pallidum, amygdala, and orbitofrontal cortex) and attention regions (visual and anterior cingulate cortices) to appetizing food images (1–5), anticipated palatable food intake (6, 7), and food odors (8). Obese compared with lean humans have also shown greater activation in the primary gustatory cortex (anterior insula and frontal operculum) and in oral somatosensory

regions (postcentral gyrus and parietal operculum) during exposure to appetizing food images (2, 5) and anticipated palatable food intake (6, 7). These data are consistent with the reward-surficit model, which posits that individuals who experience more reward from food intake are at risk of overeating (9). In juxtaposition, obese compared with lean individuals have shown less activity in reward-related regions during palatable food intake (7, 10, 11), which is consistent with the reward-deficit theory, which asserts that individuals may overeat to compensate for a reward deficit (12). Data have implied that findings differ according to whether the response to food cues relative to food intake is examined, which suggests that it is important to investigate responsivity to both phenomena.

Most neuroimaging research has directly compared obese compared with lean individuals, which has provided little information regarding the etiologic process that underlies initial weight gain. Currently, it is unclear whether obesity-related differences in neural responsivity to food stimuli are driven by altered neuroendocrine functioning that stems from excess amounts of adipose tissue (13, 14) compared with habitual, excess caloric intake as suggested in neuroscience-based etiologic models (9, 12, 15, 16).

To directly examine the effect of typical energy intake (EI)⁴ on neural responsivity to food stimuli, independent of basal needs and adipose tissue, we tested whether doubly labeled water (DLW) estimates of EI were associated with greater responsivity when anticipating palatable food intake and reduced responsivity during intake with the resting metabolic rate (RMR) and the percentage of body fat in healthy-weight adolescents controlled for. We hypothesized that EI would be associated with 1) greater responsivity in reward (eg, striatum), attentional (eg, visual and medial prefrontal cortices), gustatory (eg, anterior insula and frontal operculum), and oral somatosensory

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⁴ Abbreviations used: BOLD, blood oxygen level dependent; DLW, doubly labeled water; EE, energy expenditure; EI, energy intake; MNI, Montreal Neurological Institute; RMR, resting metabolic rate.

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(eg. postcentral gyrus and parietal operculum) brain regions in response to anticipated palatable food intake and 2) less neural responsivity of reward regions during palatable food intake.

SUBJECTS AND METHODS

The sample ($n = 155$; 75 adolescent males and 80 adolescent females) consisted of 10% Hispanic, 1% Asian, 4% African American, 79% white, and 6% American Indian and Alaska Native participants. Individuals who reported binge eating or compensatory behavior in the past 3 mo, the use of psychotropic medications or illicit drugs, a head injury with a loss of consciousness, or an Axis I psychiatric disorder in the past year (including anorexia nervosa, bulimia nervosa, or binge-eating disorder) were excluded. Parents and adolescents provided informed written consent for this project. Participants arrived at the laboratory after an overnight fast, completed the body composition, anthropometric measurements, RMR assessment, and the first DLW assessment, and returned 2 wk later for the follow-up DLW assessment. fMRI scans took place within 1 wk of DLW assessments. Oregon Research Institute's Institutional Review Board approved all methods.

EI

DLW was used to estimate EI over a 2-wk period. DLW provides a highly accurate measure of intake that is immune to biases associated with dietary recalls or diet diaries (17, 18). DLW uses isotopic tracers to assess total carbon dioxide production, which can be used to accurately estimate habitual caloric expenditure (19). DLW was administered immediately after subjects tested negatively for pregnancy (if applicable). Doses were 1.6–2.0 g H_2^{18}O (10 atom percent)/kg estimated total body water. Spot urine samples were collected immediately before DLW was administered and 1, 3, and 4-h postdosing. Two-weeks later, 2 additional spot urine samples were collected at the same time of day as 3- and 4-h postdosing samples. No samples were the first void of the day. Energy expenditure (EE) was calculated by using equation A6 (19), dilution space ratios (20), and the modified Weir's equation (21) as previously described (22). EI per day was calculated from the sum of EE from DLW and the estimated change in body energy stores from serial body weight measurements performed at baseline (T1) and 2-wk after dosing (T2). This figure was divided by the number of days between the baseline assessment and 2-wk after dosing to calculate the daily source of energy substrates from weight loss or storage of excess EI as weight gain (23). The equation used for each participant was

$$\text{EI} = \text{EE} + [(\text{weightatT2} - \text{weightatT1}) \times 7800] \div (\text{dateofT2} - \text{dateofT1}) \quad (1)$$

The 7800 kcal/kg is an estimate of the energy density of adipose tissue (24). The weight change (weight at T2 – weight at T1) was also used in regression analyses to assess the concurrent validity of EI with basal needs as a proxy of energy balance controlled for.

RMR

The RMR was measured by using indirect calorimetry with a TrueOne 2400 Metabolic Measurement System (ParvoMedics Inc) at the first assessment of DLW. The RMR comprises 60–75% of daily EE and is associated with the maintenance of major physiologic functions of the body (25). For the RMR assessment, participants arrived at the laboratory after an overnight fast (range: 5–15 h) and abstained from exercising for 24 h before testing. The variation was a result of the number of hours slept the previous night. Participants rested quietly in a temperature-controlled room for 20 min, and a transparent plastic hood that was connected to the device was placed over the participant's head. To determine the RMR, the resting gas exchange was measured by using calculations of O_2 consumption (VO_2) and CO_2 production (VCO_2) obtained at 10-s intervals for 30–35 min. Participants remained motionless and awake, and the last 25–30 min of the measurement were used to calculate RMR. The validity and reliability of this method for the assessment of RMR have been established (26, 27).

Percentage of body fat

Air-displacement plethysmography was used to estimate the percentage of body fat with the Bod Pod S/T (COSMED USA Inc) by using recommended procedures on the basis of age- and sex-appropriate equations (28). Body density was calculated as body mass (assessed by direct weighing) divided by body volume. The percentage of body fat estimates has shown test-retest reliability ($r = 0.92$ – 0.99) and correlation with dual-energy X-ray absorptiometry and hydrostatic weighing estimates of the percentage of body fat ($r = 0.98$ – 0.99) (29).

Behavioral measures

The Food Craving Inventory (30) was used to assess cravings for a variety of foods. This scale was adapted to also include ratings of how palatable participants found each food (7). Responses were on a 5-point Likert scale for craving [from 1 (never crave) to 5 (always crave)] and a 4-point scale for liking [from 1 (dislike) to 4 (love)]. The original Food Craving Inventory has shown internal consistency ($\alpha = 0.93$), 2-wk test-retest reliability ($r = 0.86$), and sensitivity to the detection of intervention effects (30). On the fMRI scan, day hunger was assessed before the scan by using A 100-mm cross-modal visual analog scale anchored by 0 (not hungry at all) to 100 (extremely hungry).

fMRI paradigm

The fMRI assessment occurred within 1 wk of the DLW and RMR measurements. On the scan day, participants were asked to consume their regular meals but to refrain from eating or drinking caffeinated beverages for 5 h preceding the scan. The fMRI paradigm assessed the response to intake and the anticipated intake of palatable food [see Stice et al (31) for additional paradigm detail]. Stimuli were 2 images (glasses of milkshake and water) that signaled impending delivery of either 0.5 mL chocolate milkshake or tasteless solution, respectively. The milkshake (270 kcal, 13.5 g fat, and 28 g sugar/150 mL) was prepared with 60 g vanilla ice cream, 80 mL 2% milk, and 15 mL chocolate syrup. The tasteless solution, which was designed to

mimic the natural taste of saliva, consisted of 25 mmol KCl/L and 2.5 mmol NaHCO₃/L. In 40% of trials, the taste was not delivered after the cue to allow for an investigation of the neural response to the anticipation of a taste that was not confounded with the actual receipt of the taste (unpaired trials). There were 30 repeats of both milkshake intake and tasteless-solution intake and 20 repeats of both the unpaired milkshake cue and the unpaired tasteless-solution cue. Tastes were delivered by using programmable syringe pumps. Syringes filled with milkshake and tasteless solution were connected via tubing to a manifold that fit into the mouths of participants and delivered the taste to a consistent tongue segment. Visual stimuli were presented with a digital projector/reverse screen display mirror system. Participants were instructed to swallow when the swallow cue appeared.

Imaging acquisition, preprocessing, and analysis

Scanning was performed with an Allegra 3 Tesla head-only MRI scanner (Siemens Medical Solutions USA Inc). A birdcage coil was used to acquire data from the entire brain. Functional scans used a T2*-weighted gradient single-shot echo planar imaging sequence (echo time: 30 ms; repetition time: 2000 ms; flip angle: 80°) with an in-plane resolution of 3.0 × 3.0 mm² (64 × 64 matrix; 192 × 192 mm² field of view). Thirty-two 4-mm slices (interleaved acquisition; no skip) were acquired along the anterior commissure–posterior commissure transverse oblique plane as determined by the midsagittal section. Prospective acquisition correction was applied to adjust the slice position and orientation as well as to regrid the residual volume-to-volume motion in real time during data acquisition for the purpose of reducing motion-induced effects (32). No participant moved >2 mm or 2° in any direction. A high-resolution inversion recovery T1-weighted sequence (MP-RAGE; field of view: 256 × 256 mm²; 256 × 256 matrix; thickness: 1.0 mm; slice number: ~160) was acquired.

Anatomical and functional images were manually reoriented to the anterior commissure–posterior commissure line and skull stripped by using the brain extraction tool function in FSL (Version 5.0; Functional Magnetic Resonance Imaging of the Brain group). Data were then preprocessed and analyzed by using SPM8 (Wellcome Department of Imaging Neuroscience) in MATLAB (Version R2009b for Mac; The Mathworks Inc). Functional images were realigned to the mean and both the anatomical and functional images were normalized to the standard Montreal Neurological Institute (MNI) T1 template brain (ICBM152). Normalization resulted in a voxel size of 3 mm³ for functional images and a voxel size of 1 mm³ for high-resolution anatomical images. Functional images were smoothed with a 6-mm FWHM isotropic Gaussian kernel. A 128-s high-pass filter removed low-frequency noise and signal drift. Anatomical images were segmented into gray and white matter by using the DARTEL toolbox in SPM (33); a mean of the resulting gray matter was used as a base for an inclusive gray matter mask before the group level analysis.

To identify brain regions activated by anticipation of a food reward, the blood oxygen level dependent (BOLD) response during presentation of the unpaired cue that signaled the impending delivery of the milkshake was contrasted with the response during presentation of the unpaired cue that signaled

the impending delivery of the tasteless solution (anticipated milkshake > anticipated tasteless solution). To identify regions activated by palatable food intake, the contrast of (milkshake intake > tasteless solution intake) was used. These individual level contrasts were used in regression analyses of EI with RMR and percentage of body fat controlled for to best capture the effects of EI that accounted for basal needs and adipose tissue. A cluster-wise threshold of $P < 0.001$ with k (cluster size) >12 was considered significant at $P < 0.05$ corrected for multiple comparisons across the whole brain. This threshold was determined by estimating the inherent smoothness of the gray matter–masked functional data with the 3dFWHMx module in AFNI software (version 05_26_1457) and running 10,000 Monte Carlo simulations of random noise at 3 mm³ through that data by using the 3DClustSim module of AFNI software (34). This method was performed for each independent analysis, and the cluster was rounded to the nearest whole number. In all cases, this was $k > 12$. Results presented were not attenuated when controlled for menstrual phase and sex, handedness, or hunger unless otherwise noted. Stereotactic coordinates are presented in MNI space, and images are presented on the mean anatomical brain image for the sample. On the basis of previous studies that implicated dopamine-mediated reward regions in response to food stimuli (3–8, 10), a more sensitive region of interest analysis was performed on the striatum (caudate and putamen). Variable estimates of the average striatal activity per individual was assessed with the program MarsBaR (35) in response to the main effects of (anticipated milkshake > anticipated tasteless solution) and (milkshake intake > tasteless solution intake). These variable estimates were used in regression models that controlled for RMR and the percentage of body fat with EI. Effect sizes (r) were derived from z values (z/\sqrt{N}).

In parallel with fMRI analyses, we used regression analyses that controlled for RMR and the percentage of body fat to test whether EI was related to the weight change over the 2-wk DLW assessment period, self-reported measures of food craving and liking, and hunger. A non-fMRI statistical analysis, including tests of normality of distribution of descriptive statistics (means ± SDs), and the linearity of relations, regression analyses, and independent sample t tests were performed with SPSS software (for Mac OS X, version 19; SPSS Inc). All presented data were checked for overly influential data points.

RESULTS

DLW estimates of EI resulted in a mean caloric intake of 2566 kcal/d (Table 1). EI was significantly related to reported food cravings (semipartial $r = 0.19$, $P = 0.025$) and food liking (semipartial $r = 0.33$, $P = 0.001$) but not hunger (semipartial $r = -0.12$, $P = 0.14$). Regression analyses revealed a positive relation between EI and weight change over the 2-wk DLW period (semipartial $r = 0.85$, $P < 0.001$), which suggested that EI that accounts for basal needs and the percentage of body fat may serve as a proxy for energy balance. Compared with adolescent females, adolescent males had a significantly higher EI ($P < 0.001$), RMR ($P < 0.001$), and lower percentage of body fat ($P < 0.001$) (Table 1). No other significant differences were observed between adolescent males and adolescent females ($P = 0.09$ – 0.44).

TABLE 1
Subject characteristics and behavioral measures ($n = 155$)¹

	M ($n = 75$)	F ($n = 80$)	Full sample ($n = 155$)
Age (y)	15.9 ± 1.2	15.7 ± 0.9	15.8 ± 1.0
Percentage of body fat	12.7 ± 5.1	24.1 ± 5.1*	18.6 ± 7.6
BMI (kg/m ²)	20.7 ± 1.9	20.9 ± 1.8	20.8 ± 1.9
Energy intake (average kcal/d)	2999 ± 653	2160 ± 655*	2566 ± 776
Resting metabolic rate (average kcal/d)	1623 ± 201	1202 ± 178*	1406 ± 283
Weight change (kg) ²	0.4 ± 0.97	-0.7 ± 0.93	-0.2 ± 0.95
Hunger (0-100) ³	41.5 ± 21.3	37.4 ± 24.3	39.4 ± 22.9
Food craving (1-5) ⁴	2.3 ± 0.7	2.1 ± 0.5	2.2 ± 0.6
Food liking (1-4) ⁵	2.8 ± 0.4	2.6 ± 0.4	2.7 ± 0.4

¹ All values are means ± SDs. *Significant difference between M and F via independent-sample *t* tests, $P < 0.05$.

² Change in energy stores from serial body weight measurements performed at baseline and 2 wk after doubly labeled water dosing (weight at 2 wk - weight at baseline).

³ Scale ranged from 0 (not at all hungry) to 100 (extremely hungry).

⁴ Scale ranged from 1 (never crave) to 5 (always crave).

⁵ Scale ranged from 1 (dislike) to 4 (love).

EI and BOLD responsivity

For the anticipated contrast of milkshake > anticipated tasteless solution, EI correlated positively with activation in the superior lateral visual cortex located in the parietal lobe and the anterior cingulate cortex (regions associated with visual processing and attention) (Table 2, Figure 1), the frontal operculum (a region of the primary gustatory cortex), and the posterior cingulate cortex (thought to encode the salience of stimuli). Significant activation was also observed in the precuneus and cuneus (which have been associated with attention/imagery), the posterior middle temporal gyrus (which has been associated with semantic memory), and other regions in the lateral parietal lobe (eg, supramarginal gyrus) (Table 2). EI was not significantly related to the BOLD response during milkshake intake.

After determination of average variable estimates by using the region of interest approach previously described, the striatal activity in response to anticipating the milkshake (> anticipating tasteless solution) showed a small, positive relation to EI (semi-partial $r = 0.18$, $P = 0.038$). However, regression analyses indicated that the average striatal activity during milkshake intake (> tasteless intake) was not significantly related to EI (semi-partial $r = 0.04$, $P = 0.61$).

RMR and BOLD responsivity

We thought it prudent to examine whether RMR correlated directly with BOLD responsivity and to test whether the observed effects were driven by individual differences in basal needs. No

TABLE 2
BOLD responsivity during anticipated palatable food intake as a function of energy intake ($n = 155$)¹

		x, y, z	k	Peak z	Peak r^2	Peak P^3
Lateral visual cortex	L	-27, -76, 37	57	4.33	0.35	7.6×10^{-6}
		-21, -73, 43		3.65	0.29	1.3×10^{-4}
Posterior middle temporal gyrus	R	48, -28, -8	86	4.24	0.34	1.1×10^{-5}
		51, -37, -2		4.22	0.34	1.2×10^{-5}
		51, -19, -11		3.71	0.30	1.0×10^{-4}
Precuneus	R	9, -67, 25	203	4.14	0.33	1.7×10^{-5}
		9, -79, 22		4.06	0.34	2.4×10^{-5}
Supramarginal gyrus and middle temporal gyrus ⁴	L	12, -79, 34	29	3.65	0.29	1.3×10^{-4}
		-60, -52, 16		4.06	0.33	2.5×10^{-5}
Frontal operculum ⁴	L	-63, -43, 4	13	3.43	0.28	2.9×10^{-4}
		-45, 23, 1		3.99	0.32	3.3×10^{-5}
Supramarginal gyrus	R	54, -46, 16	33	3.94	0.32	4.1×10^{-5}
		63, -43, 16		3.62	0.29	1.5×10^{-4}
Cuneus	L	-12, -79, 28	27	3.86	0.31	5.7×10^{-5}
Anterior cingulate cortex	L	-12, 38, 25	18	3.84	0.31	6.2×10^{-5}
Posterior cingulate cortex	L	-12, -46, 40	13	3.79	0.30	7.5×10^{-5}
Precuneus ⁴	L	-6, -67, 34	14	3.55	0.29	1.9×10^{-4}

¹ Anticipated palatable food intake > anticipated tasteless solution intake with the resting metabolic rate and percentage of body fat controlled for. BOLD, blood oxygen level dependent; k , cluster size; L, left hemisphere; R, right hemisphere; r , effect size.

² r values were derived from z values (z/\sqrt{N}) of the peak voxel.

³ Data presented are corrected for multiple comparisons across the whole brain ($P < 0.05$) on the basis of Monte Carlo data simulations.

⁴ k was <12 when controlled for self-reported hunger.

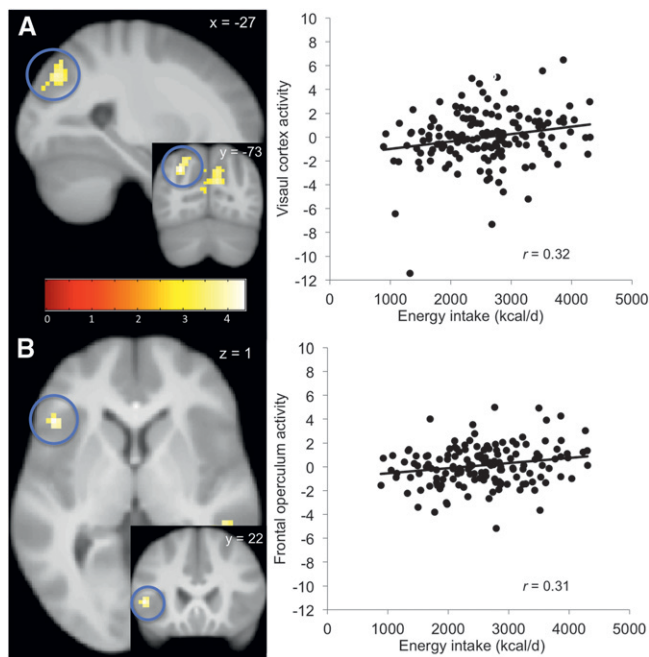


FIGURE 1. Blood oxygen level–dependent response during anticipated palatable food intake (> anticipated tasteless intake) as a function of energy intake (kcal/d) with the resting metabolic rate and percentage of body fat controlled for in the lateral visual cortex ($P = 7.6 \times 10^{-6}$) (A) and the frontal operculum ($P = 3.3 \times 10^{-5}$) (B) and parameter estimates from those peaks. The color bar indicates the T value of the activation ($n = 155$; $P < 0.05$ corrected for multiple comparisons). Additional details are shown in Table 2.

significant relations were observed between RMR and BOLD responsivity during milkshake or anticipated milkshake intakes.

DISCUSSION

The finding that EI that accounts for basal needs and adipose tissue was positively related to attention, gustatory, and reward response when subjects anticipated food intake echoed results seen when the neural responsivity of obese and lean individuals to this event was compared (6, 7). To our knowledge, the current study provided novel evidence that increased EI rather than excess adipose tissue may drive this hyperresponsivity. Specifically, we observed a heightened activity during anticipation in regions associated with visual processing and attention [lateral visual cortex, precuneus, and anterior cingulate (36)], gustatory processes [frontal operculum (37)], and a region thought to encode the salience of stimuli [posterior cingulate (38)]. A small but positive relation was also observed between activity in a reward or incentive region (striatum) and EI during anticipation.

In support of the current results, increases in fat mass over a 6-mo period were associated with increases in responsivity to palatable food images in visual processing/attention and gustatory regions relative to baseline (39). In addition, behavioral data indicated that individuals randomly assigned to consume energy-dense foods for 2–3-wk periods showed an increased willingness to work (ie, incentive for those foods) (40, 41). These results indicated that excess EI may contribute to a hyperresponsivity of attention, gustatory, and reward regions to cues for future food intake. This interpretation accords with the incentive-sensitization theory (16), which posits that the reward from intake and anticipated intake operate in tandem with the development of the

reinforcing value of food, but after repeated pairings of food reward and cues that predict this reward, the anticipatory reward increases. The current results are also in line with the dynamic vulnerability model of obesity (31, 42), which suggests that an elevated responsivity in attentional, gustatory, and reward regions to food cues may increase the susceptibility to these cues, which promotes additional intake in a feed-forward fashion. Because of the cross-sectional nature of the current results, it is also possible that individuals with an innate hyperresponsivity of these brain regions when they anticipate food are more likely to overeat. Such an interpretation is consistent with reward-surfeit theories of obesity (9). Therefore, it is imperative for future research to test whether the elevated responsivity observed in the current study predicts future weight gain over a long-term follow-up.

We also observed an EI-related activity in the posterior middle temporal gyrus, which is typically associated with semantic memory (43, 44). However, obese compared with lean individuals showed greater responsivity in this region when shown images of appetizing foods (3) in accordance with the current findings. This region has also been activated in paradigms that assessed the responsivity to cues thought to induce craving in habitual substance users. For example, in current smokers, smoking cue-induced cravings were related to middle temporal gyrus activity (45), and similar results were observed in current cocaine users (46). Accordingly, we observed a small but significant relation with reported food craving and EI. The current results hint that the generic milkshake cue may elicit memories of the sensory properties of impending high-fat, high-sugar food intake and may prompt a greater craving or craving-related brain activity for individuals with an elevated intake.

We previously reported that frequent ice-cream consumption, but not total caloric intake, was associated with reduced response to ice-cream–based milkshake intake in dopamine-mediated reward-related brain regions in this sample (47). The current study used an objective measure of EI and also showed no relation. Theoretically, after repeated intake of a particular type of palatable food, reward-learning dopamine signaling shifts from occurring on intake of that food to occurring in response to cues that predict potential food availability, which is a process that has been documented in animal experiments (48). Current imaging techniques and costs limit the ability to assess the neural responsivity to multiple foods. The previous use of food frequency allowed for a specified analysis into the intake of specific foods, with a focus on the food administered in the scanner. Although the DLW measure used in this study provided an objective and more-accurate measure of EI, it did not assess the energy density or macronutrient content of food consumed. To date, there is a lacuna in the literature regarding an interaction between neural effects of the habitual consumption of foods and the macronutrient content, although acute differences in the neural responsivity to foods varied by macronutrient content have been reported (49).

It is important to consider the limitations of this study when interpreting the findings. As noted, the cross-sectional design was a key limitation because we could not determine whether the pattern of neural responsivity increased risk of future overeating or was a consequence of overconsumption. The current sample is being followed longitudinally, and associations with weight change will provide insight into this question; however, an experiment that manipulates intake is necessary for firm causal

inferences that could not be driven by potential confounds. The current measure of EI can serve as a proxy of energy balance of the 2-wk period assessed but cannot simultaneously account for EI and expenditure nor can it be considered a direct measure of overeating in all participants. For example, compared with adolescent females, adolescent males showed a higher EI and RMR but similar BMI and lower body fat, which suggested that adolescent males expend more energy. Future studies should consider objective activity measures such as accelerometers to better capture EE if DLW is used to estimate EI. Despite this limitation, EI provided an objective measure of intake that occurred in the participant's natural setting over a 2-wk period that was immune from self-presentation biases.

In conclusion, hyperresponsivity during anticipated food intake and when exposed to appetizing food cues have been reported in obese compared with lean individuals (1–8). The current investigation extends these findings by providing novel evidence, to our knowledge, that an objective measure of habitual intake is related to hyperneural responsivity when anticipating palatable food intake independent of basal energy needs and adipose tissue amounts. Because of the cross-sectional nature of the study, the temporal precedence of the results is unclear. Attainment of a better understanding of innate, individual difference factors that contribute to overeating would provide additional insight into the development and maintenance of obesity as well as provide critical information in the development of obesity-prevention programs.

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The authors' responsibilities were as follows—KSB and ES: were responsible for manuscript writing and revisions. KSB: assisted in data collection and performed the data analysis; and ES: was responsible for the study design and significantly contributed to the data analysis. Neither author had a conflict of interest.

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