Frequent ice cream consumption is associated with reduced striatal response to receipt of an ice cream–based milkshake[1–3]

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ABSTRACT

Background: Weight gain leads to reduced reward-region responsivity to energy-dense food receipt, and consumption of an energy-dense diet compared with an isocaloric, low-energy-density diet leads to reduced dopamine receptors. Furthermore, phasic dopamine signaling to palatable food receipt decreases after repeated intake of that food, which collectively suggests that frequent intake of an energy-dense food may reduce striatal response to receipt of that food.

Objective: We tested the hypothesis that frequent ice cream consumption would be associated with reduced activation in reward-related brain regions (eg, striatum) in response to receipt of an ice cream–based milkshake and examined the influence of adipose tissue and the specificity of this relation.

Design: Healthy-weight adolescents (n = 151) underwent fMRI during receipt of a milkshake and during receipt of a tasteless solution. Percentage body fat, reported food intake, and food craving and liking were assessed.

Results: Milkshake receipt robustly activated the striatal regions, yet frequent ice cream consumption was associated with a reduced response to milkshake receipt in these reward-related brain regions. Percentage body fat, total energy intake, percentage of energy from fat and sugar, and intake of other energy-dense foods were not related to the neural response to milkshake receipt.

Conclusions: Our results provide novel evidence that frequent consumption of ice cream, independent of body fat, is related to a reduction in reward-region responsivity in humans, paralleling the tolerance observed in drug addiction. Data also imply that intake of a particular energy-dense food results in attenuated reward-region responsivity specifically to that food, which suggests that sensory aspects of eating and reward learning may drive the specificity. *Am J Clin Nutr* 2012;95:810–7.

INTRODUCTION

Basal dopamine concentrations and D2 receptor availability are lower in obese rats than in lean rats and humans (1–4), and obese humans show less striatal activation in response to palatable food receipt than do lean humans (5). Individuals with an A1 *Taq*IA allele, which is associated with lower D2 striatal receptor availability, exhibit less responsivity to palatable food receipt in dopamine target regions (6, 7). Among individuals with an A1 *Taq*IA allele, reduced striatal responsivity to palatable food receipt predicts future increases in BMI (6). These data collectively suggest that reduced signaling capacity of reward circuitry may contribute to overeating.

However, regular intake of energy-dense (ie, high-fat, high-sugar) foods leads to reduced D2 receptor density, D2 sensitivity, μ-opioid receptor expression, and reward sensitivity in rats (8–11). Furthermore, weight gain in humans over a 6-mo period was associated with a reduced striatal response to palatable food receipt relative to baseline and weight-stable women (12), which implies that overeating reduces reward-region responsivity to food receipt. Yet, an energy-dense diet compared with an isocaloric intake of low-energy-dense food resulted in down-regulation of striatal D1 and D2 receptors in rats, implying that intake of energy-dense foods, rather than a positive energy balance per se, induces reward neuroplasticity (8). Weight gain did not differ in rats in these 2 conditions, which suggests that the reduction in dopamine receptor density occurred independently of adipose tissue accumulation. These findings, taken in conjunction with evidence that phasic dopamine signaling to palatable food receipt decreases after repeated receipt of the food (13), suggest that frequent intake of a particular palatable food might produce reduced activation of striatal regions to receipt of that food. This reduced responsivity of reward circuitry may promote subsequent overconsumption in an effort to achieve the degree of satisfaction experienced previously, which contributes to unhealthy weight gain (14).

Thus, we tested the hypothesis that frequent ice cream consumption would be associated with reduced activation in dopamine target brain regions (eg, striatum) in response to receipt of an ice cream–based milkshake. To determine whether results were influenced by adipose tissue, we examined these relations controlling for percentage body fat as well as the correlation between neural responsivity to milkshake receipt and percentage body fat. To explore the specificity of this relation, we examined the association of neural responsivity to reported total energy

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intake, the proportion of energy intake from fat and sugar, and the intake of other energy-dense foods (eg, chocolate candy, cakes/cookies, hamburgers, and French fries).

SUBJECTS AND METHODS

We used fMRI to test whether consumption of ice cream and other energy-dense foods and total energy intake correlated with BOLD activation in response to receipt of an ice cream–based chocolate milkshake compared with a tasteless solution in healthy-weight adolescents (**Table 1**). The sample consisted of 10% Hispanic, 1% Asian, 4% African American, 85% white, and 6% American Indian/Alaska Native participants. Individuals who reported binge eating or compensatory behavior in the past 3 mo, any use of psychotropic medications or illicit drugs, 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. Oregon Research Institute's Institutional Review Board approved all methods. Data collection occurred over 2 y, beginning in July 2009.

Behavioral measures

The 60-item BFFQ[4] (15) inquires about the frequency of consumption of 60 specific food types. Participants are given a definition of a medium portion and asked to indicate the frequency of consumption over the previous 2-wk period. Responses to the question were on a 6-point Likert scale, where 1 = "never in the previous 2-wk period" to 6 = "daily or more in the previous 2-wk period." BFFQ values correlated ($r = 0.57$) with 4-d food record estimates for total energy intake and most nutrients (16) and showed 2-wk test-retest reliability (mean $r = 0.69$) (17). To account for possible effects of underreporting, analyses using reported total intake and percentage of energy from fat and sugar where run with only participants meeting the Goldberg cutoff (reported intake $>$ 1.35 $\times$ resting metabolic rate) for underreporting (18). Resting metabolic rate was measured by indirect calorimetry with the TrueOne 2400 Metabolic Measurement System (ParvoMedics). The FCI (19) was used to assess the craving of a variety of foods, including ice cream. This scale was adapted to also include ratings of how palatable participants found each food (5). Responses were on a 5-point Likert scale for craving (1 = "never crave" to 5 = "always crave") and a 4-point scale for liking (1 = "dislike" to 4 = "love"). The original FCI has shown internal consistency ($\alpha = 0.93$), 2-wk test-retest reliability ($r = 0.86$), and sensitivity to detecting intervention effects (19, 20). The food-frequency item that assessed ice cream intake queried about consumption of "ice cream or frozen desserts" over the previous 2 wk. The FCI items that assessed craving and liking of ice cream were used.

Percentage body fat

Air-displacement plethysmography using the Bod Pod S/T (COSMED Inc) was used to assess percentage body fat. Participants wore tight-fitting swimsuits and swim caps to minimize trapped air mass. Percentage body fat was calculated by using age- and sex-appropriate equations (21). Estimates of percentage body fat show high test-retest reliability ($r = 0.92$–0.99) and correlate with dual-energy X-ray absorptiometry and hydrostatic weighing estimates ($r = 0.98$–0.99), with air-displacement plethysmography estimates of percentage body fat falling an average of only 1.7% relative to dual-energy X-ray absorptiometry estimates (22, 23). Percentage body fat was used as a dependent variable and covariate in fMRI analyses.

fMRI milkshake receipt paradigm

Participants were asked to consume their regular meals, but to refrain from eating or drinking (water was allowed) for 5 h immediately preceding their imaging session to mimic a natural time between meals and for standardization purposes. The fMRI milkshake receipt paradigm examined the BOLD response to receipt of an ice cream–based chocolate milkshake and a calorie-free tasteless solution. The milkshake (270 kcal, 13.5 g fat, and 28 g sugar per 150 mL) was prepared with 60 g vanilla Häagen-Dazs ice cream, 80 mL 2% milk, and 15 mL Hershey's chocolate syrup. The tasteless solution was designed to mimic the natural taste of saliva to avoid activation of the taste cortex (24). Both the milkshake and tasteless solution were kept below ambient temperature at ~45°F. Stimuli were presented in 5 separate randomized scanning runs. Participants were presented with cartoon pictures of either a milkshake or a water glass, which was followed by a jittered time span (1–7 s), administration of the corresponding tastant, another jitter, and subsequently a swallow cue. The jitter allows sampling at multiple points of the hemodynamic response function, thereby increasing design efficiency and decreasing the possible effect of conditioning. Milkshake receipt was followed by a tasteless rinse to cleanse the palate. Visual stimuli were presented with a digital projector/reverse screen display mirror system. The tastants were delivered by using programmable syringe pumps (to ensure consistent timing, delivery, and volume) and tubing leading to a manifold, which fit into the participants' mouths, delivering the taste to a consistent segment of the tongue. (*See* reference 25 for additional detail regarding these methods.) Participants were familiarized with the fMRI paradigm before the imaging session.

fMRI data acquisition and preprocessing

Scanning was performed with a Siemens Allegra 3 Tesla head-only MRI scanner. A birdcage coil acquired 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 mm^2 (64×64 matrix; 192×192 mm^2 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 slice position and orientation as well as to regrid residual volume-to-volume motion in real-time during data acquisition for the purpose of reducing motion-induced effects (26). A high-resolution inversion recovery T1-weighted sequence (MP-RAGE; field of view = 256×256 mm^2, 256×256 matrix, thickness = 1.0 mm, slice number ~160) was acquired.

Data were preprocessed and analyzed by using SPM8 (27) in MATLAB (Mathworks Inc). Images were manually reoriented to

[4]Abbreviations used: ACC, anterior cingulate cortex; BFFQ, Block food-frequency questionnaire; dlPFC, dorsolateral prefrontal cortex; FCI, Food Craving Inventory.

TABLE 1
Subject characteristics and behavioral measures (n = 151)[1]

	Males (n = 74)	Females (n = 77)	Full sample (n = 151)
Age (y)	14.8 ± 0.6	15.2 ± 0.6	15.1 ± 2.0
BMI (kg/m^2)	20.6 ± 2.4	20.9 ± 1.9	20.9 ± 1.9
Percentage body fat (%)	13.8 ± 5.3	23.8 ± 5.8*	18.4 ± 7.6
Resting metabolic rate (kcal/d)	1624 ± 206	1217 ± 187*	1417 ± 283
Handedness (% right-handed)	88	96	92
Hunger, 0–100[2]	42.2 ± 21.1	37.2 ± 24.7	39.6 ± 23.1
Milkshake pleasantness, 0–100[2]	81.1 ± 9.9	78.8 ± 16.9	79.9 ± 13.9
Tasteless solution pleasantness, 0–100[2]	47.3 ± 14.5	42.0 ± 13.5	44.6 ± 14.2
Average intake (kcal/d)[3]	2993 ± 928	2281 ± 588*	2555 ± 810
Percentage kcal intake from fat and sugar (%)[3]	53.1 ± 2.9	53.8 ± 4.3	53.5 ± 3.7
Ice cream consumption, 1–6[4]	2.5 ± 1.2	2.7 ± 1.2	2.6 ± 1.2
Chocolate candy consumption, 1–6[4]	2.2 ± 1.0	2.4 ± 0.9	2.3 ± 1.1
Cake/cookie consumption, 1–6[4]	2.5 ± 1.1	3.4 ± 3.4	2.5 ± 0.9
Hamburger consumption, 1–6[4]	2.7 ± 1.2	2.1 ± 0.9*	2.4 ± 1.1
French fry consumption, 1–6[4]	2.8 ± 1.1	2.2 ± 0.8*	2.5 ± 1.0
Food craving, 1–5[5]	2.2 ± 0.7	2.0 ± 0.5	2.1 ± 0.6
Food liking, 1–4[6]	2.7 ± 0.4	2.7 ± 0.4	2.6 ± 0.4
Ice cream craving, 1–5[5]	2.5 ± 1.0	2.9 ± 1.2*	2.7 ± 1.1
Ice cream liking, 1–4[6]	3.1 ± 0.8	3.4 ± 0.7*	3.3 ± 0.8

[1] All values are means ± SDs unless otherwise noted. *Significantly different from males, $P < 0.05$.
[2] Scale: 0 = "not at all" to 100 = "extremely."
[3] Subsample consisted of those who met the Goldberg criteria for underreporting (n = 65: 25 M and 40 F).
[4] Consumption over the previous 2 wk; scale: 1 = "never in the previous 2-wk period" to 6 = "daily or more in the previous 2-wk period."
[5] Craving scale: 1 = "never crave" to 5 = "always crave."
[6] Liking scale: 1 = "dislike" to 4 = "love."

the anterior commissure–posterior commissure line and skull stripped by using the brain extraction tool function in FSL [Functional MRI of the Brain Analysis Group (FMRIB; Oxford, United Kingdom) Software Library] (28). Functional images were realigned to the mean and both the anatomic and functional images were normalized to the standard Montreal Neurological Institute T1 template brain (ICBM152). Normalization resulted in a voxel size of 3 mm^3 for functional images and a voxel size of 1 mm^3 for high-resolution anatomic images. Functional images were smoothed with a 6-mm full-width half-maximum isotropic Gaussian kernel. Vectors of the onset time and durations (4 s) for the delivery of tastants were compiled and entered into the design matrix so that responses could be modeled by the canonical hemodynamic response function, as implemented in SPM8. A 128-s high-pass filter was used to remove low-frequency noise and signal drift.

Statistical analyses

To identify brain regions showing increases in BOLD activation in response to milkshake receipt, we used the individual-level contrast (milkshake receipt > tasteless solution receipt). To assess reductions in activity in response to milkshake receipt, we used the (tasteless solution receipt > milkshake receipt) individual-level contrast. To assess the main effect of milkshake receipt, we entered the individual-level (milkshake receipt > tasteless solution receipt) contrasts into a second-level, one-sample t test. To study the relation of frequency of intake to BOLD responsivity, the individual contrasts were entered into a second-level regression model with reported intake from the BFFQ as a covariate. We separately examined reported intake of ice cream, total energy intake, percentage of energy from fat and sugar, and consumption of chocolate candy, cakes/cookies, hamburgers, and French fries. To provide a more direct test of the specificity of the relations between ice cream consumption and responsivity to milkshake receipt analyses were also performed including chocolate candy consumption and cakes/cookies consumption as covariates of no interest. Regression analyses were performed with and without including percentage body fat as a covariate of no interest to ensure the observed effects were not driven by adiposity. To further assess the possible relations between adiposity and BOLD responsivity to milkshake receipt, we also preformed a regression directly between the aforementioned contrasts and percentage body fat. To account for possible confounding effects of sex and given the significant differences in percentage body fat between males and females, all fMRI analyses presented include sex as a covariate of no interest. fMRI analyses were also performed with control for menstrual phase in females (data not shown); no differences in results were observed when menstrual phase was statistically controlled.

Whole-brain analyses were used throughout. Activity surviving a threshold of $P < 0.001$, with a cluster (k) ≥ 12 was considered significant. This threshold is the overall significance level of $P < 0.05$ corrected for multiple comparisons across the whole brain based on Monte Carlo simulations of random noise distribution with the use of the 3DClustSim module of the Analysis of Functional NeuroImages (29, 30). All stereotactic coordinates are presented in Montreal Neurological Institute space (31). Pearson's product moment correlation (r) for fMRI data were calculated as ($Z/\sqrt{n}$). Mean parameter estimates from the striatal clusters (and subsequent effect sizes) were calculated by using the MarsBaR region of interest toolbox in SPM8. Tests

of normality of distribution (skewness and kurtosis), descriptive statistics (means and SDs), correlation analyses of self-report data, and testing for differences by sex were performed by using R version 2.13.1 for Mac OS X (The R Foundation for Statistical Computing; 2011).

RESULTS

Average neural responsivity to milkshake receipt

By using the (milkshake receipt > tasteless solution receipt) contrast we observed robust activation throughout brain regions previously associated with food reward and oral somatosensory regions (**Figure 1**, A and B; *see* Figure S1 and Table S1 under "Supplemental data" in the online issue). The peak in largest cluster (k = 14,609) was located in the right oral somatosensory region (45, −13, 37; T = 16.13). This cluster expanded into the bilateral putamen (Figure 1A), caudate (Figure 1B; circles), and thalamus, insula, midbrain, and left oral somatosensory regions (Figure 1B; squares).

Relations between neural responsivity to milkshake receipt and frequency of consumption

To test the hypothesis that frequent ice cream consumption would be associated with reduced striatal responsivity to milkshake receipt, we regressed frequency of ice cream intake to activation from the (tasteless solution receipt > milkshake receipt) contrast. As hypothesized, we observed reduced activation in the bilateral putamen and right caudate (Figure 1, C and D; **Figure 2**; **Table 2**). Ice cream consumption was also significantly associated with reduced activation in the bilateral dlPFC extending into the ACC, and mid and anterior insula (Table 2; *see* Figure S2 under "Supplemental data" in the online issue). These relations were not attenuated when percentage body fat was controlled for. Frequency of ice cream consumption was not significantly related to increases in activation in response to milkshake receipt (ie, milkshake receipt > tasteless solution receipt contrast).

Regression analyses showed that percentage body fat, total energy intake, percentage of energy from fat and sugar, chocolate candy consumption, cakes/cookie consumption, hamburger consumption, and French fry consumption were not associated with neural responsivity to milkshake receipt with either the (milkshake receipt > tasteless solution receipt) or (tasteless solution receipt > milkshake receipt) contrasts. The observed effects between ice cream consumption and reduced responsivity to milkshake receipt in the striatum, dlPFC, ACC, and insula were not attenuated when chocolate candy or cakes/cookie consumption was controlled for. Furthermore, no relations between reported total energy intake and neural responsivity to milkshake receipt were observed, with

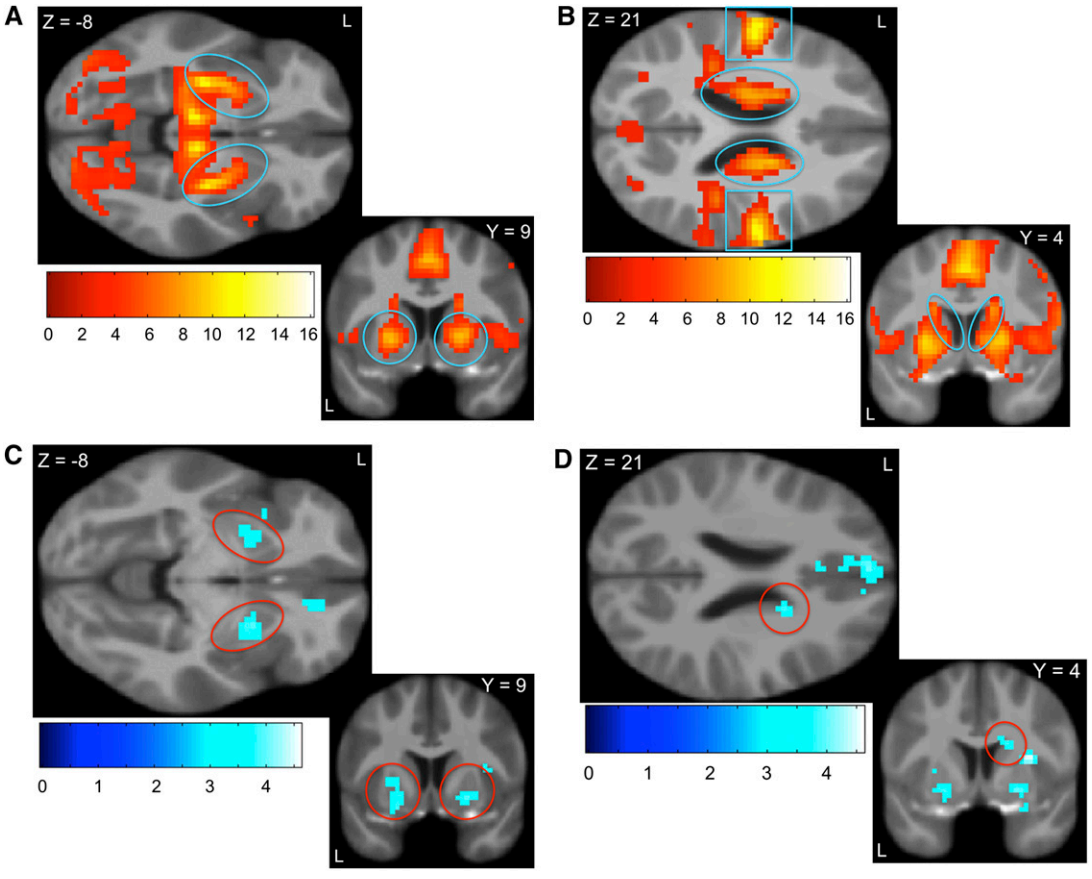

FIGURE 1. A and B: Widespread activation in response to milkshake receipt (milkshake receipt > tasteless solution receipt contrast) in the bilateral putamen (circles; A) and the bilateral caudate (circles; B) and oral somatosensory regions (squares; *see* Table S1 and Figure S1 under "Supplemental data" in the online issue for additional details). C and D: Reduced striatal responsivity to milkshake receipt as a function of frequency of ice cream consumption (tasteless solution receipt > milkshake receipt contrast). Participants' frequency of ice cream intake was associated with reduced responsivity to milkshake receipt in the bilateral putamen (A) and right caudate (B). Additional details are presented in Table 1. Both the axial (upper left) and coronal (lower right) views are presented, and color bars indicate the T value of the activation.

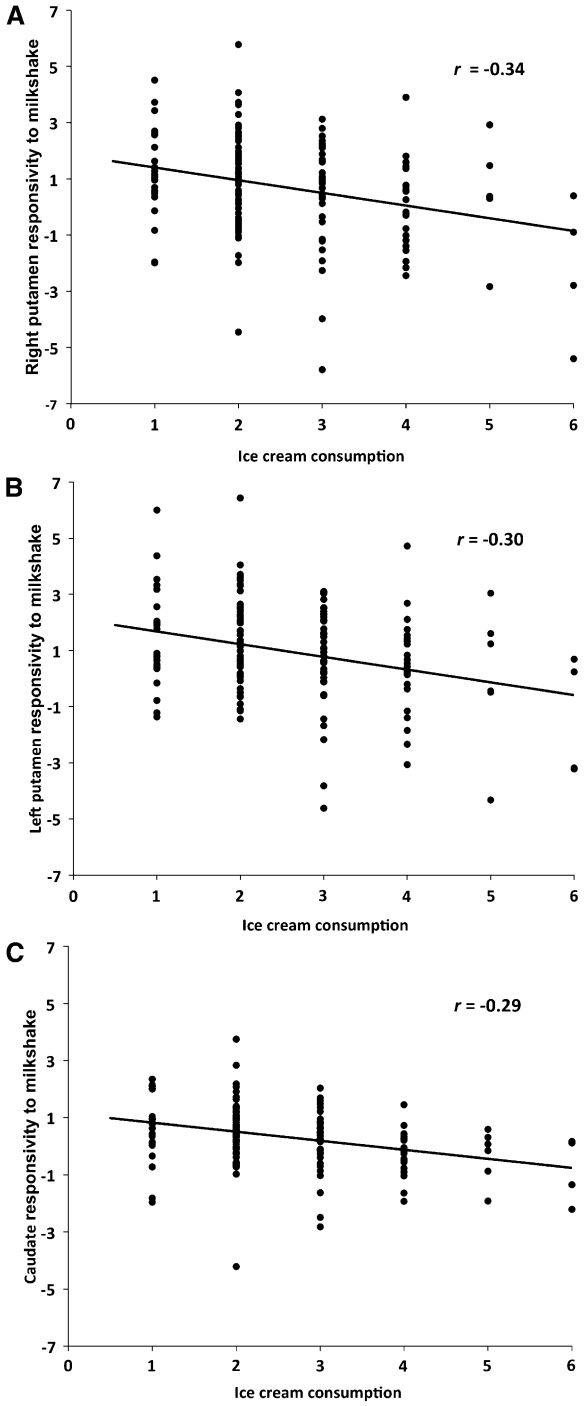

FIGURE 2. Striatal responsivity to milkshake receipt as a function of ice cream consumption. Frequency of ice cream consumption relations to the average cluster parameter estimates of the right putamen (A), left putamen (B), and left caudate (C).

and without control for resting metabolic rate (thereby accounting for variability in basal energy needs).

Relations between participant characteristics and behavioral measures

Compared with males, females had a significantly greater percentage body fat, had a lower resting metabolic rate, and reported consuming fewer total calories (Table 1). Frequency of ice cream consumption correlated positively with total energy intake, ice cream craving, and ice cream liking (r = 0.40–0.51; **Table 3**). Milkshake pleasantness ratings were not significantly related to ice cream intake, craving, or liking (Table 3). Pearson's correlations among consumption of energy-dense foods are shown elsewhere (*see* Table S2 under "Supplemental data" in the online issue).

DISCUSSION

The finding that healthy-weight adolescents who report frequent ice cream consumption show less striatal response to an ice cream–based milkshake receipt provides novel evidence that regular intake of an energy-dense food may reduce reward-region responsivity to that food, independent of total energy intake and excess adipose tissue. The current data extend results from animal experiments that found isocaloric intake of energy-dense compared with standard low-energy-density foods leads to reduction in dopamine signaling capability (8) and previous work in humans that found reduced striatal responsivity to palatable food intake in individuals who gained weight compared with those who did not (12). Collectively, these data suggest that the reduced striatal D2 receptor density (3, 4) and the reduced striatal response to palatable food receipt (5) in obese relative to lean individuals may be a consequence of habitual intake of energy-dense foods rather than to an initial vulnerability factor. The evidence that regular intake of energy-dense foods may reduce striatal responsivity, independent of general caloric intake or excess adipose tissue, is a novel contribution to the literature. These findings suggest that intake of energy-dense foods may contribute to down-regulation of reward circuitry, echoing the effects of frequent drug use (32).

Interestingly, reduced striatal activation correlated with frequency of ice cream consumption, but not with frequency of chocolate candy, cakes/cookies, hamburger, or French fry consumption or the general energy density of the diet (the proportion of total energy from fat and sugar) suggesting a marked specificity in the observed relation. The null finding with chocolate candy intake is particularly striking given that both a chocolate milkshake and chocolate candy are palatable, energy-dense foods with similar flavors. However, the fat and sugar content, food form, texture, and temperature of ice cream are most similar to the milkshake delivered in the scanner, which suggests that sensory aspects of the eating experience play a role in neural adaptation and imply a learning explanation for this effect. In addition to hedonic responsivity, the sensory attributes and postingestive consequences influence eating behavior (33); eg, fat content drives conditioned food preferences (34), and texture, not flavor, affects the expected satiation of foods (35). It is feasible that the inverse relation between intake and striatal responsivity is a function of repeated consumption of cold food; unfortunately, the current data cannot address this notion.

Theories of reward responsivity and obesity have hypothesized that either a general reward surfeit (36) or a reward deficit (14) response to food underlies excess weight gain, yet the finding that reduced striatal response to food appeared to be specific to energy-dense foods that are consumed on a frequent basis seems incompatible with these models of general signaling capacity of reward regions. However, the specificity of the current results

TABLE 2
Reduced neural responsivity to milkshake receipt as a function of the frequency of ice cream consumption (n = 151)[1]

				r	
	x, y, z	*k*	Peak *z* value	Peak	Controlled for %BF
dlPFC					
R	33, 35, 37	497	−4.60	−0.37	−0.36
ACC					
L	−6, 38, 16		−4.37	−0.36	−0.36
R	9, 29, 31		−4.16	−0.34	−0.34
Insula (mid)					
R	33, 5, 13	61	−4.35	−0.35	−0.35
R	39, 11, 13		−3.47	−0.28	−0.28
Caudate					
R	18, 5, 22		−3.61	−0.29	−0.29
Insula (anterior)					
L	−33, 14, −14	14	−3.98	−0.32	−0.32
Putamen					
L	−24, 11, 1	48	−3.73	−0.30	−0.30
L	−21, 8, −14		−3.63	−0.30	−0.30
R	24, 8, −8	27	−3.64	−0.30	−0.30
dlPFC					
L	−33, 32, 37	21	−3.36	−0.27	−0.27
L	−21, 32, 40	12	−3.31	−0.27	−0.27

[1] Results using the tasteless solution receipt > milkshake receipt contrast. Values were significant at $P < 0.05$ (whole brain corrected for multiple comparisons). ACC, anterior cingulate cortex; dlPFC, dorsolateral prefrontal cortex; *k*, cluster size; L, left hemisphere; R, right hemisphere; *r*, effect size; %BF, percentage body fat.

converge with data that show that overeating induces adaptations in dopamine functioning and reward sensitivity (6, 8–12) and support models of food-reward neuroplasticity (25, 37), which implies that the relations observed in the current study are a function of repeated intake of ice cream, rather than of a predisposition to hyper- or hyporesponsivity of reward circuitry. Dopamine signaling theoretically plays a key role in reward learning, specifically encoding receipt of novel rewards (13, 38). Striatal dopamine signaling initially occurs in response to receipt of a rewarding stimulus (eg, palatable food), yet after repeated exposure to receipt of the rewarding stimuli and a paired cue, the dopamine firing then occurs in response to cues that predict future receipt of the reward, not during reward receipt (13). Thus, we theorize that participants who rarely consume ice cream show strong striatal activation in response to receipt of an ice cream–based milkshake, whereas participants who regularly consume ice cream show a very weak striatal response to the taste of the ice cream–based milkshake. It is possible that, in those who frequently consume ice cream, the reduced striatal responsivity to milkshake receipt is a function of a discrepancy between elevated expected reward that exceeds the actual reward, because these types of negative prediction errors are associated with reduced dopamine signaling in the midbrain on reward receipt (39). However, the BOLD response to the cue predicting impending milkshake receipt in our paradigm was not correlated with frequency of ice cream consumption (data not shown), which suggests that the current findings were not a result of reward-related prediction error signaling.

In addition to hypothesized activity in the striatal regions, ice cream consumption was also significantly associated with reduced activation in the dlPFC, ACC, and insula, which are all regions that receive dopaminergic projections from the striatum. Receipt of palatable food activates regions of the cingulate, prefrontal cortex, and insula in addition to responsivity in the dorsal striatum, and the degree of activation of these regions correlates with food pleasantness (40, 41). The dlPFC, ACC, and insula have also been associated with encoding acute taste habituation; specifically, responsivity to taste stimuli in these regions is dependent on the frequency and regularity of stimulus administration, and it has been theorized that these effects can play a role in reinforcement of eating (42). Although this evidence centers on acute neural adaptations as a function of frequency (relative to the habitual intake focus of the current investigation), the similarity in the activation patterns is noteworthy. Collectively, these data suggest that activity in these brain regions not only moves in concert, but also may play a role in the neuroplasticity of both short- and long-term taste habituation. In addition to its aforementioned role in taste habituation, the dlPFC has frequently been associated with executive functioning and inhibitory signaling (43). Interestingly, data show that inhibitory region responsivity to food stimuli responds similarly with activity in reward-related regions (5, 44); this is particularly relevant given that a reduction in inhibitory signaling could contribute to increases in intake.

The current sample was very large for neuroimaging studies and presents results that extend data from both human and animal research. One limitation of this study was the delivery of only one food in the scanner. Although the milkshake was highly palatable and elicited responsivity in reward-related brain regions, it is only one food item with distinct characteristics (eg, high-fat, high-sugar, and colder than ambient temperature). Therefore, one cannot draw conclusions regarding the individual effect of these food characteristics on the observed relations. It would be useful if future studies investigated the effects of beverages that vary in fat and sugar content as well as solid foods, although there are challenges

TABLE 3
Pearson's correlations between percentage body fat and reported eating behaviors (n = 151)

	Milkshake pleasantness	Total energy intake (kcal/d)	Energy intake from fat and sugar (%)	Ice cream consumption	Ice cream craving	Ice cream liking
Percentage body fat	0.02	−0.09	0.10	0.08	0.10	0.09
Milkshake pleasantness		0.03	−0.06	0.03	0.13	0.06
Total energy intake (kcal/d)			−0.08	0.46*	0.26*	0.11*
Energy intake from fat and sugar (%)				0.26*	0.08	0.11
Ice cream consumption					0.51*	0.40*
Ice cream craving						0.52*

*$P < 0.01$.

to delivering solid food during fMRI scans (eg, chewing-related head motion). A second limitation was the use of only one item to assess frequency of ice cream intake and query about only the recent eating behavior. However, additional questions from the FCI provide convergent validity, as evident in the significant relations observed between frequency of consumption, craving, and liking of ice cream. Because the intake measure queried only about intakes over the previous 2 wk, we were unable to determine whether the observed effects were a function of recent or habitual behavior. Directly examining the permanence of these types of effects is necessary to gain a better understanding of food-reward neuroplasticity. Last, participants from the current sample were in the healthy weight range. This limited range may have attenuated out ability to detect a relation between percentage body fat and neural responsivity to a milkshake.

Past research found that weight gain leads to reduced reward region responsivity to energy-dense food receipt (12), consumption of an energy-dense diet versus an isocaloric low-energy-density diet leads to reduced dopamine receptors, independent of weight gain (8), and that phasic dopamine signaling in response to palatable food receipt decreases after repeated receipt of the food (13). The current data extend these findings by providing novel evidence that the regular consumption of an energy-dense food may reduce reward-related neural processes during receipt of that particular food, independent of total energy intake and excess adipose tissue. Gaining a better understanding of how dopamine encodes food reward over long-term repeated exposure and how food characteristics moderate this relation could elucidate neural adaptations that perpetuate excess intake of rewarding energy-dense foods that contribute to the development and maintenance of obesity.

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