Relation between food reinforcement and dopamine genotypes and its effect on food intake in smokers


ABSTRACT

Background: Food reinforcement and dopaminergic activity may influence food consumption, but research on whether they interact has not been performed.

Objective: We assessed the effects of food reinforcement and the interaction of food reinforcement with the dopamine transporter (SLC6A3) genotype and the dopamine D2 receptor (DRD2) genotype on energy consumption.

Design: We studied food-consumption and reinforcing-value-of-food tasks in 88 smokers of European ancestry before they enrolled in smoking-cessation treatment. In the food-consumption task, subjects tasted and consumed 8 snack foods ad libitum. The reinforcing-value-of-food task assessed how hard subjects would work for food.

Results: Significant interactions between dopamine genotypes and food reinforcement were observed. Subjects high in food reinforcement who lacked an SLC6A3*9 allele consumed significantly more calories (> 150 kcal; P = 0.015) than did subjects low in food reinforcement or those high in food reinforcement who carried at least one SLC6A3*9 allele. Similarly, subjects high in food reinforcement who carried at least one DRD2*A1 allele consumed > 130 kcal more (P = 0.021) than did subjects low in food reinforcement or those high in food reinforcement who lacked a DRD2*A1 allele. There was also a main effect of food reinforcement on energy intake (P = 0.005), with subjects high in food reinforcement consuming 104 kcal (or 30%) more than did subjects low in food reinforcement.

Conclusions: Food reinforcement has a significant effect on energy intake, and the effect is moderated by the dopamine loci SLC6A3 and DRD2.

KEY WORDS Eating, dopamine, food reinforcement, smokers, energy intake

INTRODUCTION

Food is a powerful reinforcer, and individual differences in the reinforcing value of food may help to explain the excess energy intake responsible for obesity (1) and the weight gain after smoking cessation (2). Positive reinforcers such as food and drugs of abuse stimulate the release of brain dopamine (3, 4). Dopamine’s action in the brain depends on the release, transport (reuptake), and receptor binding of synaptic dopamine (5). The dopamine transporter gene (SLC6A3) codes for a dopamine transporter protein (DAT) that influences the amount of synaptic dopamine by rapidly carrying dopamine back into nerve terminals after its release (6), thereby limiting the magnitude and duration of dopamine receptor activation (7). The SLC6A3*10 allele may be related to higher concentrations of DAT protein and, therefore, to lower postsynaptic concentrations of dopamine (8, 9), although this relation is not consistent across all studies (10). Animal (11–14) data suggest that rapid dopamine transport or reduced brain dopamine signaling, or both, may be related to an increase in ingestive behaviors and obesity. Dopamine agonists may reduce the reward value of food and the motivation to eat (15, 16).

Dopamine’s action also depends on the receptor binding of synaptic dopamine. The dopamine D2 receptor (DRD2) genotype has been associated with the density of D2 receptors (17), and obese humans have a higher prevalence of the DRD2*A1 allele, which is associated with lower density of D2 receptors, than do nonobese controls (18). The receptor coded by the D2*A1 allele interacts with the human obesity gene to predict body mass index (BMI: in kg/m2), especially in women (19). Wang et al (20) showed that DRD2 availability was reduced in the striatum of the brains of very obese (BMI > 40) humans in proportion to their BMI.

The mesolimbic dopamine pathway is also involved in the rewarding effects of nicotine (21), and neural activation in response to smoking cues is observed in dopamine-rich brain regions (22). Smoking cessation results in decreased activation of the reward circuitry (23), which may result in a substitution of food for smoking to stimulate the dopamine reward pathway. Smoking cessation is associated with weight gain (24) primarily because of increases in caloric intake (25–27), especially through consumption of snack foods that are high in fat and sugar (28, 29). Consistent with the role of dopamine and food reward in smoking cessation–related weight gain, we found that the effects of the DRD2 genotype on food reward were less in smokers who were...
FOOD REINFORCEMENT AND ENERGY INTAKE

Subjects and Methods

Subjects

Eligible subjects smoked ≥10 cigarettes/d and gave written informed consent for genotyping and treatment. Exclusion criteria included pregnancy, a history of psychiatric disorder as categorized by the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV), seizure disorder, and current use of psychotropic medications. To reduce bias due to racial admixture, the analyses were limited to smokers of European ancestry (n = 88).

This experiment was embedded in the design of a larger clinical trial of bupropion, the results of which were reported previously (30, 31). After eligibility screening and provision of written informed consent, subjects provided a blood sample for genotyping, completed self-reported questionnaires on smoking history and nicotine dependence (32), were measured for height and weight, and taste-tested the foods used in the experiment (chocolate cakes, cheese, pretzels, potato chips, milk chocolate candies, gummy bears, fig bars, and shredded wheat squares). Subjects had to indicate that they would eat the snack foods studied. Genotyping for the \( DRD_2 \) Taq1 RFLP (33) and \( SLC6A3 \) gene (34) was performed as described previously. Height was measured with the use of a stadiometer, and weight was measured at baseline with the use of a balance-beam scale, which was calibrated daily. Dietary restraint was measured by using the restraint scale of the Three-Factor Eating Questionnaire, a well-validated measure of dietary restraint (35). Ethics review and approval for the study were provided by the Health Sciences Institutional Review Board of the State University of New York at Buffalo.

Methods

Food intake and the reinforcing value of food were assessed in 2 sessions before initiation of the trial and random assignment to the bupropion or placebo group. Subjects were instructed not to consume any food or caffeine for 4 h before the experiment and to eat normal meals on the days of their testing. Before being tested for food intake, subjects were given an energy bar (290 kcal, 5 g fat, 49 g carbohydrates, 13 g protein; Go-Lean bar; Kashi, Inc, La Jolla, CA) and water to standardize premeal intake and reduce food deprivation. Food intake was assessed in the first baseline session by providing subjects with a tray containing the 8 foods described previously. Subjects were asked to taste-test a bite of food and to rate the 8 foods tasted in screening according to pleasurable taste and sensory characteristics on 9-point Likert scales, and they were given the opportunity to consume as much or as little of each food as desired during a 20-min period after the experimenter left the room. Foods were offered in similar volumes in filled 9-ounce plastic cups, with the caloric values for the foods ranging from 118 (potato chips) to 473 (M & M’s; Mars Inc, Hackettstown, NJ) calories. The total amount of energy available if a person consumed all the snack foods would be 2035 calories. Foods were weighed with the use of an electronic scale (Ohaus, Florham, NJ) that was sensitive to 0.01 g, and total energy and carbohydrate, fat, and protein intakes were calculated on the basis of information provided on the product labels. Hunger level before the taste and consumption session was assessed by using a 9-point Likert scale.

The relative reinforcing value of food was determined at a different baseline session according to how hard a person will work for food or for an alternative reinforcer. We have used these methods in other studies to quantify the relative reinforcing value of food (1, 36, 37). To measure food reinforcement in the present study, we adapted a behavioral choice questionnaire used to quantify smoking reinforcement (38). It was previously shown that the questionnaire is related to choice, as measured by a computer-generated concurrent schedule task we have used to quantify choice of food as a reinforcer (1, 36, 37); the questionnaire is sensitive to food deprivation that changes the reinforcing value of food (GS Goldfield, LH Epstein, M Davidson, FG Saad, unpublished observations, 2003). For the food-reinforcement assessment, subjects chose the snack food they wanted to consume. Before this test, subjects were given an energy bar and water to standardize premeal intake. Reinforcer sensitivity theory hypothesizes that, with sufficient deprivation, all subjects would increase their responses for food on a behavioral choice task (39). To remove deprivation and make the measure more sensitive to those who experience food as very reinforcing, subjects were fed before the food-reinforcement task. Because previous research suggested that weight gain after smoking cessation is mostly attributable to snacking after a meal (29), using snack foods and reducing food deprivation before the task provide an experimental context for snacking. Hunger level was also assessed before the food-reinforcement session with the use of a 9-point Likert scale.

The food-as-reinforcer choice questionnaire provided subjects with 16 choices that differed in the number of button presses needed to obtain 100 g of their chosen snack food or $1. The first choice started with 20 button presses for either alternative, and the values for food increased in 20-response increments, whereas the response requirements for money stayed the same (20 button presses). Thus, by the 16th choice, subjects could have a favorite snack food if they were willing to make 320 button presses, or they could have $1 if they were willing to make 20 button presses. To encourage valid responses, subjects chose 1 of 16 numbered pieces of paper from a hat; the numbers represented the trials (38). For example, if a subject pulled out a paper marked #3, he or she would be asked to carry out the circled choice for item number 3, which would be to perform either 60 button presses to obtain 100 g of the chosen snack food or 20 presses to obtain $1.

The questionnaire can be scored to provide a either dichotomous measure of whether the subject chose money or food reinforcement when both choices carried equal behavioral requirements (20 presses) or a measure of the switchpoint at which subjects who chose food when the response requirements were equal switched from choosing food to choosing money. Examination of the response
patterns showed that most subjects \((n = 57)\) never chose food, in part because of the experimental prefeeding, and the dichotomous measure was used. Subjects who chose money rather than food when the response requirements were equal were categorized as low in food reinforcement \((n = 57)\), and subjects who chose food rather than money after the experimental prefeeding were categorized as high in food reinforcement \((n = 31)\).

**Statistical analysis**

We used analysis of covariance (ANCOVA) to compare energy intake as a function of food reinforcement and the dopamine genotypes. Between-group differences as a function of food reinforcement and the dopamine genotypes were first assessed. To evaluate differences in energy intake as a function of the reinforcing value of food or the genotypes, an ANCOVA was conducted with food reinforcement and genotypes as between-subject variables and with energy intake as the dependent variable. To control for variables that conceptually could be related to energy intake, we used sex, cigarettes/d, hunger before the food-consumption task, and BMI as covariates.

In addition to analysis of total energy intake, an ANCOVA was conducted with food reinforcement and the 2 dopamine genotypes as between-subject variables and with energy intake associated with carbohydrate, fat, and protein as the within-subject variable. Interactions for both ANCOVAs were probed by using 3 post hoc linear contrasts. Contrasts for the \(SLC6A3\) genotypes included those comparing the energy intakes or macronutrient intakes between participants high in food reinforcement and participants low in food reinforcement, both groups of whom lacked the \(SLC6A3^{*}9\) allele; in participants high in food reinforcement and participants low in food reinforcement, both groups of whom had the \(SLC6A3^{*}9\) allele; and in participants high in food reinforcement who lacked the \(SLC6A3^{*}9\) allele and participants high or low in food reinforcement who had the \(SLC6A3^{*}9\) allele.

Similarly, contrasts for the \(DRD_2\) genotypes included contrasts comparing the energy intakes or macronutrient intakes in participants high in food reinforcement and participants low in food reinforcement who had the \(DRD_2^{*}A1\) allele; in participants high in food reinforcement and participants low in food reinforcement who lacked the \(DRD_2^{*}A1\) allele; and in participants high in food reinforcement who had the \(DRD_2^{*}A1\) allele and participants high or low in food reinforcement who lacked the \(DRD_2^{*}A1\) allele. Bonferroni corrections were used to correct \(P\) values for multiple comparisons \((0.05/3 = 0.017)\). Statistical analyses were performed with SYSTAT software \((40)\). All tests of significance were two-tailed.

**RESULTS**

The sample included 88 smokers of European ancestry, 56% of whom were female and 38.6% of whom were college graduates. Subjects categorized as being low or high in food reinforcement and according to the 2 dopamine genotypes are shown in Table 1. The mean (\(\pm SD\)) age of subjects was 43.5 (\(\pm 10.7\)) y, the smoking rate was 22.3 (\(\pm 7.7\)) cigarettes/d, the BMI was 27.1 (\(\pm 4.8\)), the hunger rating on the day of the food-consumption task was 3.2 (\(\pm 2.1\)), and the dietary restraint score was 4.9 (\(\pm 3.2\)). Three subjects (3.4%) had the \(DRD_2^{*}A1/A1\) genotype, 38 (43.2%) had the \(DRD_2^{*}A1/A2\) genotype, and 47 (53.4%) had the \(A2/A2\) genotype.

Because there were so few subjects with the rare \(DRD_2^{*}A1/A1\) genotype, subjects with the \(DRD_2^{*}A1\) allele were combined for all analyses, as in previous research \((30)\). Forty-one subjects \((46.6\%)\) had the \(SLC6A3^{10/10}\) genotype, whereas 16 \((18.2\%)\) had the \(SLC6A3^{9/9}\) genotype, and 31 \((35.2\%)\) had the \(SLC6A3^{9/10}\) genotype. The number of subjects with the \(SLC6A3^{*}9/9\) genotype was too small for separate analysis.

**Table 1**: Characteristics of subjects by food reinforcement, dopamine transporter \((SLC6A3)\) genotype, and dopamine \(D_2\) receptor \((DRD_2)\) genotype.

<table>
<thead>
<tr>
<th>Age (y)</th>
<th>Cigarettes/d</th>
<th>Baseline hunger</th>
<th>BMI (kg/m²)</th>
<th>Dietary restraint</th>
<th>Average food liking</th>
<th>Energy intake (kcal)</th>
<th>Diet. restraint</th>
<th>Education</th>
<th>SLC6A3</th>
<th>DRD2</th>
</tr>
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<tbody>
<tr>
<td>Low ((n = 25 M, 32 F))</td>
<td>High ((n = 14 M, 17 F))</td>
<td>9/9 and 9/10 ((n = 16 M, 31 F))</td>
<td>10/10 ((n = 23 M, 18 F))</td>
<td>A1/A1 and A1/A2 ((n = 19 M, 22 F))</td>
<td>A2/A2 ((n = 20 M, 27 F))</td>
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<tr>
<td>43.2 ± 10.5 (\pm SD)</td>
<td>44.2 ± 11.2</td>
<td>42.2 ± 11.4</td>
<td>43.7 ± 10.4</td>
<td>43.4 ± 11.1</td>
<td>275.6 ± 144.4</td>
<td>367.0 ± 241.7</td>
<td>283.8 ± 167.8</td>
<td>335.2 ± 208.3</td>
<td>342.5 ± 225.0</td>
<td>277.5 ± 145.2</td>
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<td>22.2 ± 8.1</td>
<td>22.4 ± 7.1</td>
<td>22.4 ± 7.2</td>
<td>22.1 ± 8.4</td>
<td>20.8 ± 5.5</td>
<td>5.1</td>
<td>3.9</td>
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<td>5.5 ± 2.6</td>
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<td>5.4 ± 2.7</td>
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<td>27.4 ± 4.6</td>
<td>26.4 ± 5.3</td>
<td>26.5 ± 5.0</td>
<td>27.8 ± 4.6</td>
<td>26.7 ± 5.2</td>
<td>225.0 ± 277.5</td>
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<td>4.6 ± 3.0</td>
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<td>4.7 ± 3.4</td>
<td>5.0 ± 2.8</td>
<td>4.6 ± 3.1</td>
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<td>6.1 ± 0.8</td>
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1 Significant difference in \(SLC6A3\) genotype between the sexes, \(P < 0.05\) (chi-square test).
2 \(\bar{x} \pm SD\) (all such values).
3 Rated on 9-point Likert scales; 1 = not at all pleasurable; 9 = extremely pleasurable.
4 Derived from the Three-Factor Eating Questionnaire (35).
5 Significantly different from low food reinforcement, \(P < 0.03\) (\(t\) test).
when subjects in this group were considered in relation to food reinforcement and the DRD$_2$ genotype. Subjects with the SLC6A3 genotypes were divided into those with (9/9 + 9/10) or without (10/10) the SLC6A3$^{9}$ allele, as in previous research (30).

Comparison of subjects by categories of food reinforcement and by SLC6A3 and DRD$_2$ genotypes found that those with the SLC6A3 genotype differed by sex ($P = 0.037$): those with the 9 allele were more likely to be female (31) than male (16), and those who lacked the 9 allele were more likely to be male (23) than female (18). Sex was related to energy intake—males consumed more calories (389.7 ± 219.5 kcal) than did females (242.5 ± 128.0 kcal, $P < 0.001$)—and cigarette smoking was related to energy intake ($r = 0.26, P = 0.016$) at baseline. Both sex and cigarettes/d were used as covariates in the ANCOVA. In addition, although hunger at the beginning of the food-consumption task and BMI did not differ significantly between groups, they are conceptually related to food intake and were added as covariates to control for their influence on food intake.

ANCOVA showed a significant interaction of food reinforcement with the SLC6A3 genotype ($P = 0.015$) and with the DRD$_2$ genotype ($P = 0.021$). The main effects of food reinforcement and the interactions of food reinforcement with the genotypes on total energy intake across macronutrients are shown in **Figure 1**. As shown in Figure 1B, the interaction of food reinforcement with the SLC6A3 genotype was due to greater energy intake in participants high in food reinforcement than in participants low in food reinforcement who lacked the SLC6A3$^{9}$ allele ($P = 0.001$); no difference in energy intake between participants low in food reinforcement and participants high in food reinforcement who had the SLC6A3$^{9}$ allele ($P > 0.05$); and greater intake in participants high in food reinforcement who lacked the SLC6A3$^{9}$ allele than in participants high or low in food reinforcement who had the SLC6A3$^{9}$ allele ($P < 0.003$). Interactions of the DRD$_2$ genotype with food reinforcement are shown in Figure 1A. Greater energy intake was observed in participants high in food reinforcement than for participants low in food reinforcement who had the DRD$_2^{*}$A1 allele ($P < 0.001$); no difference in energy intake between participants low in food reinforcement and participants high in food reinforcement who lacked the DRD$_2^{*}$A1 allele ($P > 0.05$); and greater intake in participants high in food reinforcement who had the DRD$_2^{*}$A1 allele than in participants high or low in food reinforcement who lacked the DRD$_2^{*}$A1 allele ($P = 0.002$). In addition to the interactions of food reinforcement with genotype, there was a significant main effect of food reinforcement on energy intake ($P = 0.005$). Subjects high in food reinforcement consumed 379.9 ± 241.7 kcal, and those low in food reinforcement consumed 275.9 ± 144.4 kcal. There were no statistically reliable main effects of SLC6A3 or DRD$_2$ genotypes on energy intake. Neither the two-factor interaction of SLC6A3 × DRD$_2$ genotypes or the three-factor interaction of SLC6A3 × DRD$_2$ genotypes × food reinforcement was significant.

ANCOVA for macronutrients using covariates of sex, cigarettes/d, BMI, and baseline hunger showed significant interactions of food reinforcement with SLC6A3 ($P = 0.015$) and DRD$_2$ ($P = 0.022$) genotypes across the macronutrient (carbohydrates, fat, protein) groups, which confirms the previous ANCOVA on total energy intake. However, there were no significant interactions of either genotype with macronutrients or of food reinforcement with genotypes that resulted in effects on macronutrient intake. The same pattern of response was observed across macronutrients as was observed for energy intake: participants high in food reinforcement had greater intakes than did participants low in food reinforcement of carbohydrates (193.0 ± 133.2 compared with 144.3 ± 91.1 kcal), fat (149.6 ± 92.7 compared with 106.4 ± 58.8 kcal), and protein (37.6 ± 22.9 compared with 26.0 ± 17.0 kcal). Participants high in food reinforcement consumed 33%, 41%, and 44% more energy as carbohydrates, fat, and protein, respectively, than did participants low in food reinforcement.
DISCUSSION

The results provide support for the hypothesis that genotypes that influence dopamine transport or the density of dopamine receptors moderate the relation between the food-reinforcement behavioral phenotype and energy intake. A moderating variable (41) is one that can influence how a variable relates to an outcome, just as, in the present study, genotypes moderated the effect of food reinforcement on energy intake. The influence of food reinforcement on energy intake was greater in subjects with a DRD2*A1 allele or without an SLC6A3*9 allele than in subjects without the former or with the latter.

Many genes have been identified with obesity, but genes associated with dopaminergic activity may be central to motivations to eat. Dopaminergic activity influences food intake (42), and identification of the genes that moderate food reinforcement may provide important information about individual differences that influence the regulation of body weight. The DRD2 and SLC6A3 genes discussed here represent genes that influence dopaminergic activity, and they are good candidates as genes that influence food intake. The influence of the food-reinforcement behavioral phenotype on energy intake was moderated by the absence of the SLC6A3*9 allele or the presence of the DRD2*A1 allele. Significant differences were observed across the macronutrients, which suggests that the moderating effect of the genotypes on food reinforcement is a general effect and not one that is specific to types of foods.

The results of this investigation also support the hypothesis that food reinforcement is related to food intake: in the present study, subjects high in food reinforcement consumed 104.8 (or 33.2%) more calories during the food-consumption task than did subjects low in food reinforcement, and subjects high in food reinforcement consumed more of each macronutrient than did those low in food reinforcement. These findings support our previous findings that obese nonsmokers find food more reinforcing than do nonobese nonsmokers (1) and that smokers high in food reinforcement gain more weight after smoking cessation than do those low in food reinforcement (2). Individual differences in the reinforcing value of food may suggest mechanisms relevant to understanding obesity as well as weight gain after smoking cessation. Food reinforcement may relate to differences in energy intake, but more information is gained by considering both the food-reinforcement phenotype and either of the dopamine genotypes than by considering only the behavioral phenotype of food reinforcement.

The behavioral phenotype associated with a high reinforcing value of food may develop because of various conditions. One way in which neutral stimuli become reinforcing is by being paired with other positive events. People who find food very reinforcing may have many positive associations that are paired with eating and food ingestion, such as social interactions (43). The reinforcing value of a stimulus can also shift as a result of food deprivation. Food deprivation can sensitize a person to the reward value of food (44), and in humans food deprivation increases the immediate reinforcing value of food (36, 45). Chronic food deprivation may also sensitize a person to the reward value of food or increase the reinforcing value of food, because developmental research has shown that dieting during development leads to later obesity (46, 47), which may be mediated by an increase in the reinforcing value of food.

Food consumption may be influenced by factors in addition to the reinforcing value of food. Berridge (43) suggested that the consumption of many types of reinforcers, including food, is influenced by wanting as well as liking a substance. Research suggests that wanting is mediated by dopaminergic pathways, whereas liking is mediated by opioid pathways (42). Liking particular foods, or food preference, is probably important in the acquisition of wanting food, but, after food becomes wanted, liking and wanting can be separated. For example, animals will usually choose more palatable foods to maintain body weight when given the choice of both palatable foods and chow, but, when the opioid system and food preference are altered by opioid antagonists, animals do not prefer more palatable foods but rather eat to maintain body weight, which suggests that the antagonists block the hedonic response to food but not the wanting of food. Likewise, blocking the wanting of food does not alter liking of food, as assessed by taste reactivity in rats (42). We also showed in humans that increasing the reinforcing value of food with the use of food deprivation has little effect on liking selected foods (45). Thus, the concept of food reinforcement may be useful in understanding when a person will eat, and food preference may determine what is consumed. Both motivation to eat and preferences for the foods that are available may be relevant to an understanding of how much food is consumed in a meal.

The relation between dopamine genotypes and food intake should be replicated in nonsmokers, obese persons, and persons of different racial and ethnic groups. Dopamine pathways are involved in the reinforcing effects of both food and nicotine (21, 22), and dopamine transport reuptake inhibitors may be useful in the treatment of smoking (31) and the treatment of obesity in nonsmokers (48). Smoking may stimulate pathways similar to those that food stimulates, and food reinforcement may be greater in nonsmokers who do not obtain regular stimulation of these pathways. Our observation that food reinforcement predicts weight gain in currently abstinent smokers, but the fact that weight gain is less in smokers receiving bupropion (2), a dopamine transport reuptake inhibitor, suggests that maintaining higher concentrations of synaptic dopamine may reduce energy intake. This possibility is consistent with a hypothesis presented by Wang et al (20).

It is possible that study methods may have influenced food reinforcement and the interaction of food reinforcement with dopamine genotypes. Subjects were given a tray of 8 snack foods in the eating task, and they could eat as much or as little of the foods as they liked. Research suggests that variety influences intake, and there is greater intake in conditions of variety than in conditions of nonvariety (49, 50). Subjects who find food more reinforcing also respond more to variety than do subjects who do not find food reinforcing; thus, providing a less varied array of foods might have limited the effect of food reinforcement. The preload provided before the food reinforcement task to reduce initial deprivation may not have reduced deprivation or food reinforcement to similar degrees across all groups, although hunger measured after consumption of the preload was similar in all groups. The reinforcing value of food is sensitive to the alternatives provided, and using an alternative to food other than money in the reinforcement task (eg, reinforcing sedentary alternatives) may have differentially influenced food reinforcement and produced a different pattern of responses. In the food-reinforcement task, subjects chose how hard they would work for a single snack food of their choice, whereas, in the food-consumption task,
subjects were provided with a standard set of 8 foods. The use in the food-reinforcement task of more foods or of standard foods rather than the food of the subjects’ choice may influence the relation between food reinforcement and food consumption.

This study shows that food reinforcement should be considered when factors that could influence energy intake are studied and that the food-reinforcement behavioral phenotype may be moderated by dopamine genotypes to influence energy intake. Studying dopamine genotypes that could influence dietary intake without including food-reinforcement or similar phenotypes may reduce the opportunity to assess the influence of genotypes on dietary intake. Additional research on the interplay between behavioral phenotypes and genotypes is needed for better understanding of the factors that may influence food reinforcement and energy consumption.

We thank Angela Pinto and E Paul Wileyto for data management. SC-M, CL, and LHE contributed to the study design; SMW, RAP, and LHE contributed to the data analysis; and LHE and SMW assumed responsibility for drafting and revising the manuscript. FGS and JLJ were involved in data collection and contributed to the Methods sections of the manuscript; other authors contributed to the revisions. LHE is a consultant to Kraft foods. None of the other authors had any conflicts of interest.

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