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ORIGINAL ARTICLE

Opiates, overeating and obesity: a psychogenetic analysis

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Objective: This study provides an original perspective on the associations among endogenous opiates, overeating and obesity. The aim was to assess whether variability in the *OPRM1* gene, as assessed by seven single-nucleotide polymorphisms, relates to individual differences in the preference for sweet and fatty foods. We also anticipated that these food preferences would be positively associated with binge eating, hedonic eating and emotionally driven eating-patterns of overeating that would, in turn, predict higher body mass index (BMI).
Design: Analysis of variance procedures examined genotype differences in food preferences; bivariate correlation coefficients examined the relationships among food preferences and the overeating variables; and a regression analysis tested the combined influences of the overeating variables on BMI. DNA was extracted from whole blood for the genotyping, and measures of food preferences and eating behaviours were obtained from well-validated self-report questionnaires.
Subjects: Participants were 300 healthy adult men and women recruited from the community.
Results: All the predicted associations were supported by statistically significant results. In particular, the G/G genotype group of the functional A118G marker of the *OPRM1* gene reported higher preferences for sweet and fatty foods compared with the other two groups. Food preferences were also related to all overeating measures, which in turn accounted for a substantial proportion of the variance in BMI.
Conclusions: Our findings suggest that some of the diversity in the preference for highly palatable foods can be explained by genotypic differences in the regulation of *mu* opioid receptors. The associations reported in this paper are important from a public-health perspective because of the abuse potential of sweet-fat foods and their strong relationship with obesity.
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Keywords: opioid pathways; overeating; *mu* receptors

Introduction

An emerging theme in the neuropsychology of eating behaviours is that some foods—typically those high in fat, sugar and salt—have an abuse potential similar to other manufactured and concentrated substances like cocaine and alcohol,[1,2] and that compulsive overeating can be viewed as an addiction disorder.[3–5] Central to these arguments is the dominant role of dopamine in both the behavioural pathology of substance abuse disorders,[6] and in the regulation of food reward and the hedonic aspects of appetite.[7,8]

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The endogenous opioid system is also implicated in the pathology of various drug addictions like alcoholism and heroin abuse.[9] Similarly, opioid peptides are known to stimulate food intake,[10] primarily by amplifying the hedonic properties of palatable food[11,12]—or as Berridge[13] has stated so expressively, by 'painting a pleasure gloss' on rewarding sensations. Specifically, opioid circuitry in both the nucleus accumbens and the ventral palladium appear to mediate taste-reactivity responses to palatable events.[14] Of particular interest are the *mu* opioid receptors, especially those in the ventral striatum and amygdala where their activation tends to foster hyperphagia and the preference for a high-fat diet.[15,16] In addition, impulsivity and the tendency to act on cravings rather than to delay gratification have been associated with higher *mu* receptor concentrations and greater opioid system activation.[17] Consequently, some have suggested that higher *mu* receptor levels in the brain may thereby increase the risk for obesity.[18,19]

Genetic vulnerability

A biological propensity to an addiction disorder is, to some degree, reflected in our genetic diversity—that is, those inherent differences which render some of us more susceptible than others to the effects of relevant environmental forces. Indeed, it has been suggested that the increasing rates of obesity may have strong roots in the mismatch between our evolved, and once adaptive, survival mechanisms and the current superfluity of rich and highly palatable food supplies in today's world.[20] To date, considerable research in the biological risk for obesity has focused on variability of dopamine transmission and signalling, and other functional aspects of this brain neural circuitry.[21–23] By contrast, individual differences in opioid pathway functioning have been scarcely considered in the vulnerability profile for overeating, despite its long history in risk-related drug addiction research.

Of the many genetic variants identified on the *mu* receptor gene (*OPRM1*), the single-nucleotide polymorphism (SNP) A118G (rs1799971) has been the most widely studied in relation to alcoholism and opiate addiction. The rarer G118 allele has shown greater affinity for β-endorphins and morphine, but reduced mRNA and protein expression *in vitro*.[24] Although the exact mechanisms remain unclear, *in vivo* evidence supports a 'gain-of-function' for those possessing the G allele.[25] For example, a recent study reported a greater prevalence of the G allele in both alcoholic and opioid addicts in India compared with those in the normal population,[26] in keeping with similar findings from a Swedish study.[27] However, not all studies have found this association in drug addiction research.[28,29]

There are persuasive arguments that *intermediate phenotypes* provide a more sensitive test of gene–disorder associations than the use of a dichotomous variable for conditions (like alcoholism), which have a complex aetiology.[30] In other words, allele-based association studies can be better used to examine dimensional symptoms and traits that are associated with the clinical presentation of a syndrome or disorder. Adopting this paradigm, Miranda *et al*.[31] found that adolescent carriers of the G allele had significantly more alcohol-related problems and reward-focused drinking motives than their non-G counterparts. Similarly, adult G carriers exhibited greater dose-dependent responsiveness to the reinforcing effects of alcohol,[32] and a heightened sensitivity to alcohol cues, as indicated by the activation of mesocorticolimbic brain structures.[33]

There is also evidence that *OPRM1* variation predicts sensitivity to *natural* rewards. For example, in rhesus macaque monkeys, G allele carriers formed stronger attachment bonds with their mothers during infancy, and greater distress during periods of maternal separation.[25] Related to these findings, human G carriers showed greater sensitivity to social rejection, and greater reactivity in neural regions involved in processing social pain as well as the unpleasantness of physical pain.[34]

The present study

Supported by the positive links among body mass index (BMI), overeating and a predilection for highly palatable food identified in previous research,[35,36] we propose that a promising *intermediate phenotype* for obesity is the preference for sweet and fatty foods. We are unaware of any previous allele-based association study of the *OPRM1* gene in relationship to food preferences. Therefore, the present study provides an original perspective on the links between endogenous opiates and food palatability. Our aim was to test the series of associations depicted in Figure 1. Our first hypothesis is that variation in the *OPRM1* gene will relate to differences in the preference for sweet and fatty food in a group of adults who vary in BMI from lean to morbidly obese. In particular, we predict that carriers of the 'gain-of-function' G allele of the A118G marker will report a stronger preference for sweet and fatty foods. With respect to the other *OPRM1* SNPs (of unknown functional significance), our investigation should be viewed as exploratory. In a second set of hypotheses, we anticipate that preferences for sweet and fatty foods will correlate positively with measures of overeating, such as binge eating, hedonic eating and emotionally driven eating. Our final hypothesis is that collectively the overeating variables will contribute unique variance, in a positive direction, to the variability in BMI.

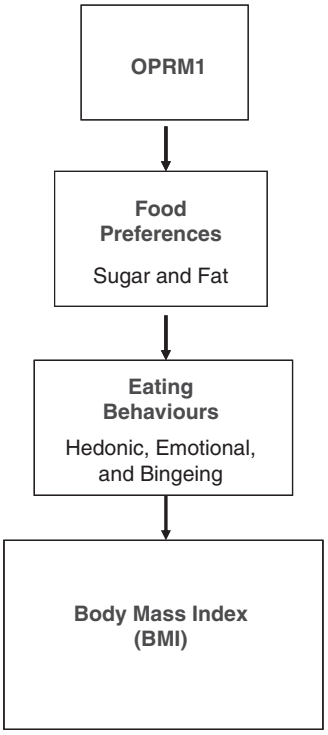

Figure 1 Path diagram predicting that markers of the *OPRM1* gene are associated with sweet-fat food preferences; that food preferences relate to overeating; and that overeating is associated with BMI.

Participants and methods

Participants
Three hundred women ($n=238$) and men ($n=62$) between the ages of 24 and 50 years took part in the study. Participants were required to be fluent in English and to have lived in North America for at least 5 years before their enrolment. All female participants were also pre-menopausal as identified by the self-reporting of regular menstrual cycles. Exclusion criteria included a current diagnosis of any psychotic disorder, substance abuse, alcoholism or a serious medical/physical illness, such as cancer, heart disease or paralysis. Female participants with a pregnancy within the previous 6 months were also ineligible. The sample comprised a broad range of BMI values, with a distribution representative of the general adult population.[37] In all, 35% had a BMI $<25\,kg\,m^{-2}$ while the remainder was classified as overweight or obese according to the World Health Organization[38] criteria. In total, 80% of the sample was Caucasian and 13% were of African descent.

Measures
Genotyping. DNA extraction from whole blood was completed by the non-enzymatic, high-salt procedure as described by Lahiri and Nurnberger.[39] We tested seven OPRM1 SNPs: A118G, rs510769, rs495491, rs563649, rs675026, rs9322447 and rs558948. The functional A118G polymorphism causes a missense amino acid change from an aspartate residue to an asparagines residue, thus potentially removing an N-glycosylation site.[40] The rs495491 marker in intron 1 was selected because of its association with alcohol/drug dependence[29] and pain sensitivity.[41] The rs563649 marker was recently reported to affect the translational efficiency of novel isoforms of the *mu* opioid receptor through a structurally conserved internal ribosomal entry site.[42] The other SNPs were selected from the five tag SNPs reported by Zhang *et al*.,[29] which included rs9322447 and rs648893 (that we have replaced with rs558948 because of assay availability) in addition to rs1799971 and rs495491. The rs3823010 marker from Zhang *et al*.[29] was excluded from this study because of relatively low minor allele frequency. We have instead added two common polymorphisms, rs510769 and rs675026, to capture additional variability within the *OPRM1* gene. All seven SNPs were genotyped using commercially available genotyping assays (Applied Biosystems Inc., Foster City, CA, USA). Genomic DNA (20 ng) was amplified in 10-μl reactions by polymerase chain reaction with the following conditions: 95 °C 10 min, followed by 50 cycles of 92 °C 15 s, 60 °C 1 min. The Allelic Discrimination Program on ABI7000 Prism Sequence Detection System was used to determine the genotypes of each individual.

Genotypes were tested for fitness to Hardy–Weinberg equilibrium using Haploview version 4.1.[43] Single-marker analyses employed analysis of variance procedures in SPSS version 17 (SPSS for Windows, 2010, SPSS Inc., Chicago, IL, USA). Haplotype analyses with the quantitative variables used the QTPHASE algorithm within the UNPHASED software version 2 (see ref. 44) and those with $<5\%$ frequency were excluded.

Food preferences. Three variables from the *Food Preference Questionnaire*[45] were used in the analyses. This 72-item scale was designed as a 2 (FAT: high vs low) by 3 (CARBOHYDRATE: high simple, high complex, low carbohydrate/high protein) measure of preference for various kinds of macronutrients. Respondents indicate their preference for each food on a nine-point Likert scale. The *high fat preference* score comprises the mean of 36 items (for example, onion rings and barbeque chicken); the *high sugar preference* score the mean of 24 items (for example, canned pears and dried dates); and the *high fat and high sugar preference* score the mean of 12 items (for example, chocolate layer cake and pecan pie). The investigators report good reliability and validity of these measures, and the α-coefficients for these scales in our study were 0.95, 0.89 and 0.88 consecutively.

Eating behaviours. (i) Binge eating was assessed by the *Binge Eating Questionnaire*,[46] which obtains information about the frequency and severity of symptoms associated with binge eating (such as, loss of control over eating, and negative affect following a binge) and with purging (for example, self-induced vomiting). Binge eating was quantified by summing the responses to five (yes–no) questions tapping aspects of the behaviour (for example, 'Are there times when you feel you cannot voluntarily stop eating?'). The α-coefficient of the scale in this study was 0.87.

(ii) Hedonic eating was assessed by the *Power of Food Scale*,[47] which is a 21-item self-report questionnaire that assesses individual differences in the appetitive responsiveness to food in environments replete with highly palatable food—independent of their actual consumption of them. In other words, it differentiates the *motivation* and appetitive drive to obtain food from the tendency to *(over)eat* food (for example, 'If I see or smell a food I like, I get a powerful urge to have some'). On the basis of a factor analysis of the items, Lowe *et al*.[47] concluded that a one-factor solution was most appropriate. Accordingly, the Cronbach α-coefficient in this study was very high (0.96).

(iii) Emotional eating was assessed by the same-named 10-item subscale of the *Eating Behaviour Patterns Questionnaire*,[48] which describes how eating is prompted by emotional states like tension and worry rather than by hunger (for example, 'My emotions affect what and how much I eat'). The α-coefficient in this study was 0.88.

(4) BMI (weight(kg)/height(metres^2)) was calculated from height and weight measured with the participant wearing indoor clothing and standing in stocking feet.

Procedures
Participants were recruited from posters placed at universities, local hospitals and other public institutions.

Advertisements were also placed in local newspapers and online sites like CraigsList. The procedures employed in this study were approved by the three Research Ethics Boards relevant to the institutional affiliations of the investigators, and were carried out in accordance with the Declaration of Helsinki. An initial telephone screening was carried out to ascertain eligibility.

On the day of testing, informed consent was obtained, and all relevant demographic information obtained in a face-to-face interview. A structured clinical interview was also carried out to confirm eligibility. Height and weight were measured and the blood sample was taken. The questionnaire package was completed at home and returned at a later date. All subjects were paid a stipend for their participation.

Results

Descriptive statistics

Means and s.d. for all quantitative variables are listed separately for men and women in Table 1. Tests of significance using independent *t*-test procedures indicated no differences between women and men on any of these variables. Consequently, all further analyses used the full sample.

Table 2 gives the allele and genotype frequencies for the seven *OPRM1* SNPs. Some studies have shown that the allele frequencies—at least for the functional A118G SNP—are somewhat different across ethnic groups.[26] We have chosen to analyze data for the entire sample—as many others have done—because the majority of our sample is Caucasian, and because the frequency of the G allele in our full sample is very similar to other Caucasian samples listed in the review by Deb *et al*.[26]

Table 1 Means and s.d. for all quantitative variables listed separately for women and men

Variable	*Women*		*Men*	
	Mean	*S.d.*	*Mean*	*S.d.*
Age	33.5	6.6	35.2	6.7
BMI	31.9	10.0	32.2	9.8
Hedonic eating	59.7	21.1	54.8	22.6
Binge eating	2.2	2.0	1.8	1.9
Emotional eating	36.0	8.4	34.2	9.0
High sugar food preferences	6.2	1.3	6.3	1.2
High-fat food preferences	6.1	1.3	6.4	1.3
High-fat and sugar food preferences	6.3	1.6	6.5	1.5

Abbreviation: BMI, body mass index.

Genotype differences in relation to food preferences

A series of one-way analysis of variance procedures was carried out separately for each SNP with the three genotype groups as the independent variable and the three food preference variables as the dependent variables. For A118G and rs495491 there were significant group differences on all the dependent variables—except in the latter case where there was only a trend for the high sugar variable ($P = 0.072$). As the variance in the three genotype groups were significantly different for the high fat and sugar preference variable, we also calculated a non-parametric Kruskal–Wallis test, which was statistically significant, but produced a somewhat smaller *P*-value (0.006) than the parametric analysis of variance procedure ($P = 0.02$). There were no significant genotype differences for the remaining five SNPs.

Post hoc comparisons using the least significant difference test indicated, for A118G, that the homozygous GG 'gain-of-function' group reported stronger preferences on all three food variables compared with the other two genotype groups, who did not differ from each other. For rs495491, the homozygous GG group reported lower fat preference compared with GA and AA. With respect to food high in fat and sugar, GA reported a lower preference than the AA genotype group. Table 3 presents the summary statistics for these two genotypes.

We next performed a two-marker haplotype analysis in a sliding-window approach to capture variations across the *OPRM1* gene. This involves testing allele combinations of adjacent SNPs, or haplotypes, in a systematic fashion across a gene region (for example, SNP1–SNP2, SNP2–SNP3, SNP3–SNP4) for possible association with the phenotype of interest. In other words, this method interrogates the gene region in more detail by exploring combinations of adjacent SNPs instead of testing only individual SNPs. SNP combinations tend to give us more information on whether there are additional markers in the region covered by the adjacent SNPs that may be more significantly associated with the

Table 2 Allele and genotype frequencies for the seven *OPRM1* SNPs

	Allele		*Genotype*		
A118G	G 86 (14%)	A 514 (86%)	GG 12 (4%)	GA 62 (21%)	AA 226 (75%)
rs495491	G 164 (27%)	A 436 (73%)	GG 26 (9%)	GA 112 (37%)	AA 162 (54%)
rs563649	T 58 (10%)	C 524 (90%)	TT 4 (1%)	TC 50 (17%)	CC 237 (82%)
rs510769	T 140 (29%)	C 344 (81%)	TT 19 (6%)	TC 102 (35%)	CC 171 (59%)
rs558948	T 134 (22%)	C 464 (78%)	TT 16 (5%)	TC 102 (34%)	CC 181 (61%)
rs675026	G 422 (73%)	A 78 (27%)	GG 150 (52%)	GA 122 (42%)	AA 28 (6%)
rs9322447	G 307 (52%)	A 289 (48%)	GG 80 (27%)	GA 147 (49%)	AA 71 (24%)

Abbreviation: SNP, single-nucleotide polymorphism.

Table 3 : Means, s.d. and ANOVA results for genotype differences on three food preference variables

	GG	*GA*	*AA*	*F*	P⩽
A118G					
High sugar	7.14 $(0.66)_{a,b}$	5.99 $(1.34)_{a}$	6.20 $(1.22)_{b}$	4.28	0.015
High fat	7.18 $(0.64)_{a,b}$	5.89 $(1.37)_{a}$	6.15 $(1.29)_{b}$	5.00	0.007
High sugar and fat	7.49 $(0.64)_{a,b}$	6.10 $(1.51)_{a}$	6.33 $(1.59)_{b}$	3.99	0.020
rs495491					
High sugar	5.78 (1.50)	6.10 (1.10)	6.33 (1.28)	2.66	0.072
High fat	5.53 $(1.57)_{a,b}$	6.10 $(1.10)_{a}$	6.27 $(1.34)_{b}$	3.64	0.027
High sugar and fat	5.92 $(2.00)_{a}$	6.13 $(1.59)_{b}$	6.33 $(1.44)_{b}$	3.09	0.047

Abbreviation: ANOVA, analysis of variance. Means in a row sharing the same subscript are significantly different ($P<0.05$). For all measures, higher means indicate greater preference.

phenotype of interest than the individual SNPs. In addition, some SNPs may affect the function of the gene within haplotypes. In this study, only the haplotypes containing rs495491 and rs563649 were associated with food preferences. Specifically, the A–C haplotype was associated with stronger sweet and fatty food preference than the other two common haplotypes. Results with other two-marker haplotype windows across the *OPRM1* gene were not significant. Figure 2 presents a *P*-value graph for all the genotype and haplotype analyses.

The genetic analyses were rerun using only the data for the Caucasian participants. Essentially, there were no changes to the finding except for the expected increase in the *P*-values because of the reduced sample size. For the A118G SNP and all food-preference differences remained statistically significant ($P=0.03$–0.05). For the rs495491, the *P*-values ranged from $P=0.04$ to 0.06. As with the full sample, there were no significant food-preference differences with the remaining five SNPs.

Food preferences in relation to eating behaviours

The three food preference variables were highly inter-related with pairwise correlation coefficients ranging from 0.84 to 0.88. Consequently, the variance inflation factors were elevated (4.8–6.0) when they were simultaneously added as independent variables to the regression models with each eating behaviour as the dependent variable. Therefore, to avoid issues of multicollinearity, we are only reporting the bivariate correlation coefficients among the food preference and eating variables. It can be seen in Table 4 that sugar preference was weakly, or not at all, related to the eating variables. Although fat and fat/sugar preferences were significantly related to all the eating variables, these associations were relatively weak.

Eating behaviours in relation to BMI

Regression analysis was used to assess the influence of the three eating variables on BMI. As the simple correlations between BMI and the three eating variables were virtually identical (binge eating: 0.40; hedonic eating: 0.41;

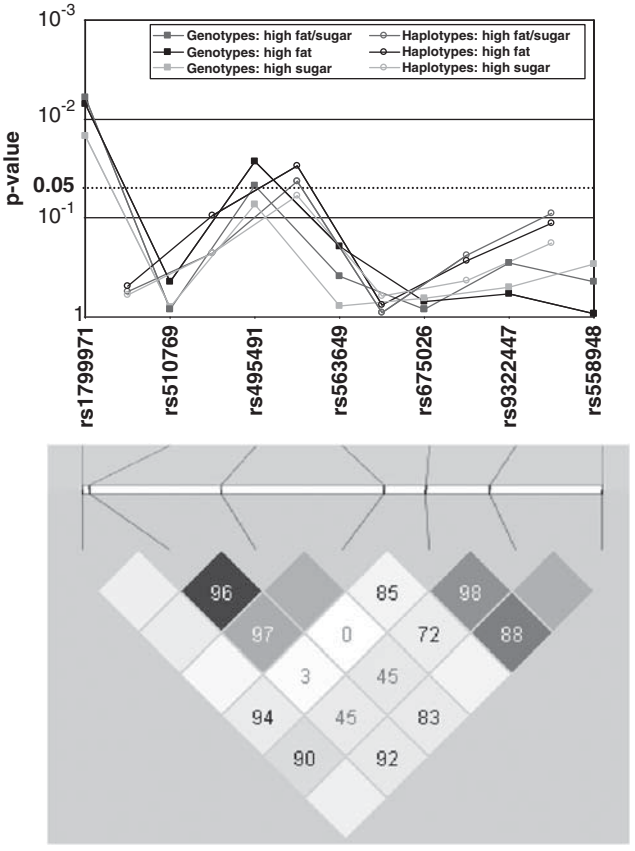

Figure 2 Summary graph of *P*-values from the analyses of food preference with the seven tested SNPs and their haplotypes across the *OPRM1* gene. Results from genotypic, and two-marker sliding-window haplotypic analyses are shown. The significance threshold of 0.05 is indicated by the dotted line. The schematic diagram showing the relative position of the polymorphisms, followed by linkage disequilibrium structures derived from the entire sample, are shown below the graph.

Table 4 Correlation matrix of all bivariate correlation coefficients among food preference and eating behaviours

Measure	*1*	*2*	*3*	*4*	*5*	*6*
1. High-fat preference	___					
2. High sugar preference	00.84**	___				
3. High-fat and sugar preference	0.88**	0.88**	___			
4. Binge eating	0.17**	0.06	0.15*	___		
5. Hedonic eating	0.28**	0.18**	0.30**	0.76**	___	
6. Emotional eating	0.26**	0.14*	0.27**	0.68**	0.73**	___

*$P<0.05$, **$P<0.01$.

emotional eating: 0.46), we entered each one consecutively in the model beginning with the emotional eating variable, which had the largest correlation coefficient with BMI, followed by hedonic eating, and then binge eating. Only the first two variables reached statistical significance, accounting for 22% of the variance in BMI. The binge eating variable failed to contribute any additional variance to the regression model after accounting for emotional eating and hedonic

Table 5 Regression model with BMI as the dependent variable

Variable	*β*	t	P
Constant		6.00	<0.0001
Emotional eating	0.33	4.30	<0.0001
Hedonic eating	0.17	2.18	0.030

Abbreviation: BMI, body mass index. $R^2 = 0.22$.

eating. Table 5 presents the summary statistics for the model with the significant effects.

Discussion

Our data were very supportive of the associations we specified in Figure 1. Although there are presently many indications that the incentive value of food is regulated by activation of the endogenous opiate system,[49,50] this is the first study to demonstrate *mu* receptor genotype differences in relation to the liking of sweet and fatty foods. Of the seven *OPRM1* SNPs included in the study, only two reached statistical significance—most notably the functional A118G marker. The homozygous GG group reported higher scores on all three food preference variables compared with the other two groups. In addition to the originality of these findings, they reinforce the view of G as a 'sensitivity' allele in response to opioid stimulation, and are in accord with other very recent data. For instance, G-carrier macaque monkeys showed a greater preference for alcohol than non-carriers,[51] and human G carriers were more sensitive to pre-operative pain and they consumed more analgesia post-operatively than their counterparts.[52] However, our results do not suggest a dominant or dose-dependent response. Rather, we found a recessive pattern of G transmission because only the homozygous group had elevated preference scores. Nevertheless, these findings must be viewed as preliminary because of the small number of observations in the GG group relative to the other genotypes.

Reinforcement learning models provide a good explanation for the links between response sensitivity and food preferences because it is well established that emotion is tightly connected to behaviour at several points.[53] When a pleasurable experience first occurs, a positive affective value is assigned to the stimulus. In order for goal-directed behaviour to ensue when the stimulus occurs again, the individual must call on, and hold on to, this affective value, and use it to determine a course of action through a series of choices.[54] It seems that GG individuals are innately prone to assigning an exaggerated pleasure value, which in turn promotes a strong appetitive response to highly palatable food—a biological liability that is easily exploited in our 'fast food' culture and toxic food environment.

A second *OPRM1* marker (rs495491), of unknown functional significance, also showed significant genotype differences with the GG group reporting *lower* preference for fatty foods than the other two groups, and a lower preference for foods high in both fat and sugar compared with the AA group. In addition, the haplotypes encompassing rs495491 and rs563649 were as similar in significance as the single marker association found with rs495491, with those carrying allele 2(G) reporting lower fat/sugar preference. Thus, the haplotype association appears to be driven largely by the rs495491 marker. To date, we have only located a few allele-based association studies for rs495491. One found that the G allele was a risk factor for both alcohol and opiate dependence, and that it exerted its effect on susceptibility via a recessive mode of action.[29] Another reported an association of the G allele with negative mood.[41] According to recent authorities, both these conditions are consistent with a low level of opioid receptor activity.[42] Such an explanation could also be compatible with a lower preference for palatable foods.

Together, the genetic findings from this study suggest there may be a dual pathway related to opioid functioning, which affects rewarding stimuli via different motivational processes. For example, low opioid signalling could foster overeating (and drug use) in some individuals as a form of 'self-medication', while in others, enhanced opioid signalling could promote greater intake of palatable food (and drug use) because of the heightened pleasure experienced from these substances. Indeed, there is substantial evidence that both high and low reward sensitivity is associated with risk for addiction disorders, and for obesity.[21] For example, in a recent study we found that significantly more obese adults with binge eating disorder had the 'gain-of-function' G allele of the A118G marker compared with their non-binge eating disorder obese counterparts, who, in turn, were significantly more likely than the binge eating disorder group to have a 'loss-of-function' allele related to the dopamine D2 receptor.[55]

In accord with our second set of predictions, preferences for sweet and fatty foods were positively correlated with all three eating variables. These associations are concordant with a body of research showing that for many individuals, foods high in fat and sugar tend to promote overeating and weight gain, both in humans and in animals, and that such foods are selectively preferred by obese individuals.[56] In addition, a recent study demonstrated that high intake of palatable food was a good predictor of binge eating in animals independent of their susceptibility to gain weight.[57] There is also evidence that satiety regulation of fat intake is less efficient than it is for other macronutrients, suggesting another mechanism whereby a fat preference contributes to overconsumption.[58]

Our final hypothesis was also supported by the data. Results indicated that each (over)eating measure made virtually the same contribution to BMI (approximately 17%), suggesting that individually, their predictive utility is roughly equivalent even though each assesses a different dimension of eating. In combination, both emotionally driven eating and hedonic eating contributed uniquely to the variation in BMI, while binge eating failed to make a further significant contribution.

Summary and conclusions

Although the human preference for fat and sugary foods is a universal phenomenon, there are large individual differences on the dimension of its strength, with some people reporting a very 'sweet tooth' and others rather indifferent to the tasty pleasures of life. Our findings suggest that some of this diversity may be explained by genotypic differences in the regulation of *mu* opioid receptors. We also found that food preferences related positively to various forms of overeating, all of which correlated, in the positive direction, with BMI.

Although these are novel findings, it is important to emphasize the need for replication because of the low frequencies in some of the rare-allele genotype groups. Studies with larger, culturally diverse, samples would also allow for stratified analysis to determine whether the pattern of results is similar across ethnic groups that differ in the allele frequency of important markers like A118G. In addition, it is important to consider more ecologically valid assessments of food preferences—for example, by assessing macronutrient intake via daily food diaries. It would also behove future researchers to examine the gene–food preference relationships in children and adolescents to test the generalizability of our findings.

Current evidence suggests that excess body weight is, in large part, the result of high fat consumption, while high sugar intake is responsible for producing addictive-like behaviours, such as cravings, withdrawal and compulsive intake.[59] Therefore, the associations described in this paper are especially important from a public-health perspective because of the abuse potential of sweet-fat foods, and their strong relationship with obesity.[4] As a society, we regularly consume, in quantity, foods that contain substantially more fat and sugar than is ever found in any natural source of energy. Our food environment is especially health aversive for those with an innate predisposition to overeat.

Conflict of interest

The authors declare no conflict of interest.

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