Original Article

Food cravings, food addiction, and a dopamine-resistant (DRD2 A1) receptor polymorphism in Asian American college students

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Background and Objectives: In an era where obesity remains an important public health concern, food addiction has emerged as a possible contributor to obesity. The DRD2 gene is the most studied polymorphism. The aim of this study was to investigate a relationship between food addiction questionnaires, body composition measurements, and a dopamine-resistant receptor polymorphism (DRD2 A1) among Asian Americans. **Methods and Study Design**: A total of 84 Asian American college students were recruited. Participants underwent body composition measurement via bioelectrical impedance, answered questionnaires (Food Craving Inventory and Power of Food Scale), and had blood drawn for genotyping (PCR). **Results**: There was no difference in body composition (BMI, percent body fat) between the A1 (A1A1 or A1A2) and A2 (A2A2) groups. There were statistically significant differences in food cravings of carbohydrates and fast food on the Food Craving Inventory between the A1 and A2 groups (p=0.03), but not for sugar or fat. Among Asian college females, there was also a difference on the Power of Food questionnaire (p=0.04), which was not seen among men. 13 out of 55 women also had >30% body fat at a BMI of 21.4 to 28.5 kg/m^2. **Conclusion**: Greater carbohydrate and fast food craving was associated with the DRD2 A1 versus A2 allele among Asian Americans. Further studies examining the ability of dopamine agonists to affect food craving and to reduce body fat in Asian American are warranted. More studies in food addiction among obese Asian Americans are needed with careful definition of obesity, specifically for Asian women.

Key Words: dopamine, obesity, food addiction, food cravings, Asian American

INTRODUCTION

Food addiction, which involves eating behavior, food choice preference, motivation, and hedonic eating, has been increasingly investigated as a possible contributor to obesity.[1] A frequently investigated polymorphism is DRD2 Taq1A A1 allele (rs1800497). This minor allele of the D2 dopamine receptor gene is associated with food addiction and lower density of dopamine receptor in the brain.[2,3] Altered dopamine receptor expression due to this polymorphism may confer vulnerability to alcohol and drug addiction. The concept of food addiction is that a subset of obese individuals who carry this polymorphism may also overeat to compensate for reduced dopamine signaling.[4] However, there are studies that do not support an association between DRD2 A1 and obesity or food addiction.[5,6] The differences in age, sex, ethnicity, and sample size may contribute to the inconsistencies.

The majority of studies looking at DRD2 and obesity are done in non-Asian populations (mostly Caucasian). The available literature regarding DRD2 gene in Asian population pertains to other forms of addiction including smoking or alcoholism, not specifically food addiction or obesity.

Given the lack of food addiction research in Asian populations, the purpose of this study is to investigate the relationships between DRD2, body measurements, and food addiction questionnaires in an Asian American college student population.

SUBJECTS AND METHODS

Study population

Individuals were recruited from a college nutrition class taught at the University of California, Los Angeles. Recruitment took place in February 2014. Participation in the study was completely voluntary and participants were not randomly selected. Table 1 outlines the study population and demographics. Participants were given written informed consent. IRB approval was obtained from the institution. Participants were given food addiction questionnaires,

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underwent blood draw for genotyping, and had body composition measurements obtained. Exclusion criteria included participants with psychiatric history or who took medications affecting appetite including steroids, cyproheptadine, and antipsychotics. None of the participants were excluded. Participants were compensated for their time with a single movie ticket voucher (valued at less than $10.00).

Body measurements

Participants verbally reported their height in inches and in those that did not know their height, was measured to an accuracy of 1 inch. BMI was calculated with the standard equation: weight (kg) / $(\text{height})^2$ (m^2). Body measurements included weight, lean body mass, and fat body mass which were measured by bioelectrical impedance (Tanita BC-418 segmental body composition analyzer) from which basal metabolic rate and percent body fat (PBF) were calculated. Shoes were removed. Participants were not fasting for weight measurement. Measurement was taken once by clinical research staff on the Tanita analyzer.

Questionnaires

Food Craving Inventory (FCI)

The FCI is a validated self-report measure for cravings of different types of foods.[7] Participants rate frequency of cravings over the past month on 28 food items using the five point Likert scale (0, never; 1, rarely (once or twice); 2, sometimes; 3, often; 4, always/almost every day). FCI consist of foods that can be categorized into sweets (brownies, cookies , candy, chocolate, donuts, cake, ice cream, and cinnamon rolls), high fats (fried chicken, sausage, gravy, fried fish, bacon, corn bread, hot dog, and steak), carbohydrates/starches (rolls, pancakes/waffles, biscuits, sandwich bread, rice, baked potato, pasta, and cereal), and fast food (hamburger, french fries, chips, and pizza). An average score was taken (maximum score 4 for each category).

Power of Food Scale (PFS)

The PFS is a validated measure of appetite drive to consume highly palatable food.[8,9] Scores correspond to hedonic ("liking") hunger motivation and patient susceptibility to the food environment. Participants are provided statements like "I find myself thinking about food even when I'm not physically hungry" and "If I see or smell a food I like, I get a powerful urge to have some." On a scale from 1 ("I don't agree") to 5 ("I strongly agree") a composite score is calculated from the 15 statements (maximum score 75).

Genotyping

Five milliliters of peripheral blood was drawn into EDTA Vacutainer tubes (BD Biosciences, Franklin Lakes, NJ, USA). Plasma and buffy coat were separated by centrifugation for 15 minutes at 2060xg. Genomic DNA was isolated from the buffy coat using the GenElute Mammalian Genomic DNA miniprep kit (Sigma-Aldrich, St. Louis, MO, USA) according to manufacturer's instructions. Participants were genotyped for the Taq I A1/A2 alleles of the DRD2 gene using SNP Genotyping Assay for ANKK1/DRD2 (rs1800497) (Applied Biosystems, Foster City, CA, USA). Real-time PCR was performed using 20 ng of DNA in a 5 μL reaction containing Taqman genotyping master mix and SNP genotyping assay mix (Applied Biosystems). In a 384 well plate reaction mixes were heated to 95˚C for 10 minutes followed by 55 cycles of 92˚C for 15 seconds then 60˚C for 1 minute. Alleles were determined using the allelic discrimination plot in the SDS 2.2.2 software genotyping program on a 7900HT Fast Real-Time PCR system (Applied Biosystems). Each sample was performed in duplicate.

Statistical analysis

The non-parametric Wilcoxon Rank-Sum test was conducted to compare continuous data including the four FCI scores and the PFS between subjects who have the A1 allele and those who do not. Categorical variables were compared using the Chi-square test. Partial Pearson correlations controlling for sex were conducted to examine the relationship between body composition (BMI, metabolic rate, body fat) as well as hours of TV watched per week with the FCI and PFS. For variables with significant correlations, multiple linear regression was used to further model these relationships. A p-value less than 0.05 was considered statistically significant. All analyses were conducted in SAS version 9.4.

RESULTS

A total of 84 college Asian students participated. Demographics and characteristics of study population can be found in table 1 and 2.65% of the students were women. All but one participant were nonsmokers.

The prevalence of college students with at least one A1 allele was 63% (Table 3). 37% of students were A2A2 genotype. While the majority of students were not considered obese by BMI standards, some could be classified as obese by PBF. 5 out of the 6 women who were categorized as such had at least one copy of A1.

Among Asian college students, there were no statistically significant differences in the frequency of gender,

Table 1. Demographics and study characteristics

Variable	Characteristic	N (%)
Gender	Men	29 (35)
	Women	55 (65)
Past medical history	Diabetes	4 (5)
	Hypertension	3 (4)
	High cholesterol	5 (6)
	NAFLD	1 (1)
Transportation	Car	8 (10)
	Bus	23 (27)
	Walking	57 (68)
	Bike	5 (6)
	Other: skate boarding, scooter	7 (8)
Smoking	Yes	1 (1)
	No	83 (99)
Exercise	Yes	46 (55)
	No	38 (45)
DRD2 genotype	A1A1	11 (13)
	A1A2	42 (50)
	A2A2	31 (37)

NAFLD: nonalcoholic fatty liver disease; DRD2: dopamine resistant receptor polypmorphism.

Table 2. Participant study characteristics

Variable	Range	Median (IQR)
Age	20-26	21 (1)
BMI	16.1-31.1	22.4 (4.2)
% body fat – women	10.3-37.2	25.9 (9.0)
% body fat – men	2.1-21.2	21.5 (12.4)
Metabolic rate (kcal)	1069-2451	1488 (509)
FCI – high fat	0-2.9	0.6 (0.8)
FCI – high sugar	0.1-3.8	1.4 (0.9)
FCI – high carbs	0-3	1.0 (1.0)
FCI – fast food	0-4	1.8 (1.3)
PFS	19-74	42 (17)

BMI: body mass index; FCI: food craving inventory; PFS: power of food scale.

past medical history, transportation usage, exercise behavior, TV watching time, or body composition (BMI) between A1 and A2 groups (Table 4).

The A1 group had significantly higher scores for FCI – carbohydrates and fast food (p=0.03) (Table 5). There was no difference in PFS between groups (p=0.06). The data was further examined by looking for gender differences. Wilcoxon rank sum analysis was conducted on each sex separately to determine if there were significant differences in PFS between A1 status groups within each sex. For Asian men, mean (SD) PFS was 43 (14) in the A1 group vs 43 (17) in A2 group (no difference, p=0.39), however among Asian women, mean (SD) PFS was 46 (12) in the A1 group vs 41 (13) in the A2 group (significant difference, p=0.04).

The relationship between BMI and PBF among Asian men and women is graphed in figure 1. Both showed a positive linear trend. This supports that there is a correlation between BMI and PBF. Interestingly, none of the women had BMI greater than 30, yet many had PBF >30%.

There was no correlation between body composition measurements (i.e. PBF or BMI) and questionnaires (PFS and FCI). There was also no correlation between body composition measurements and genotype.

DISCUSSION

The majority of food addiction research is performed in Caucasian study participants and the studies on Asian Americans specifically are lacking. It is plausible we did not detect a significant correlation between genotype and FCI for high fat and high sugar because the foods chosen for the FCI may be ethnicity dependent. The validation studies for the FCI questionnaire included mostly African American and white participants. For example, culture differences may prevent fried fish, fried chicken, gravy, and cinnamon rolls to be craved among Asian Americans. The studies regarding food addiction utilize these questionnaires routinely. There needs to be consideration regarding the ethnic population being studied prior to making conclusions about food addiction in different populations.

In addition to ethnic considerations, this study also raises the concern of gender differences for food addiction questionnaires. We detected a difference in the PFS score for Asian women between genotype groups (A1 vs A2) but not for men. The reason for this is unclear but a

Table 3. Genotype distribution

	n	A1A1/A1A2 n (%)	A2A2 n (%)
All Asians students	84	53 (63)	31 (37)
Women	55	35 (64)	20 (36)
Obese by % body fat >33	6	5 (83)	1 (17)
Men	29	18 (62)	11 (38)
Obese by % body fat >19	4	2 (50)	2 (50)

Table 4. Subject characteristics by genotype

Variable	A1A1/A1A2 (n=53)	A2A2 (n=31)	p-value
Gender – men, n (%)	18 (34)	11 (35)	0.887
Past medical history[†]			
Diabetes	2 (4)	2 (6)	0.624
Hypertension	1 (2)	2 (6)	0.552
High cholesterol	3 (5)	2 (6)	0.999
Fatty liver	1 (2)	0 (0)	0.999
Transportation, n (%)			
Car	7 (13)	1 (3)	0.248
Bus	15 (28)	8 (26)	0.805
Walking	36 (68)	21 (68)	0.986
Bike	3 (6)	2 (6)	0.999
Other	5 (9)	2 (6)	0.999
Exercise – yes, n (%)	32 (60)	14 (45)	0.176
Television hours – total	3.4 (2.7)	3.7 (4.5)	0.955
Body mass index, mean (SD)	22 (3)	22 (3)	0.613
Metabolic rate, mean (SD)	1494 (287)	1523 (342)	0.763
% body fat, mean (SD)	19.7 (8.7)	21 (7.9)	0.306

[†]Self reported questionnaire

Table 5. Food craving and food addiction questionnaires by genotype

Variable, mean (SD)	A1A1/A1A2 (n=53)	A2A2 (n=31)	*p*-value
FCI - high fat	0.69 (0.81)	0.53 (0.81)	0.19
FCI - high sugar	1.29 (0.77)	1.29 (1.15)	0.33
FCI - carbohydrates	1.03 (0.93)	0.69 (0.96)	0.03*
FCI - fast food	1.85 (0.88)	1.47 (1.02)	0.03*
Power of food scale	45 (13)	42 (14)	0.06
Power of food scale women only	46 (12)	41 (13)	0.04*
Power of food scale men only	43 (14)	43 (17)	0.39

*p-value <0.05, statistically significant

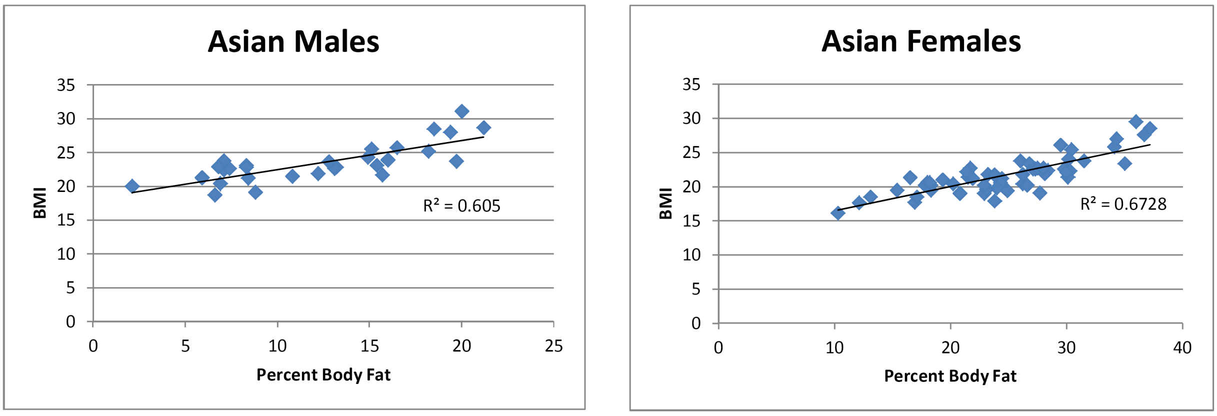

Figure 1. Relationship between BMI and percent body fat among Asian American men and women.

possibility is that Asian women specifically are more vulnerable to food addiction tendencies if they carry at least one A1 allele. It will be important to confirm this with a larger study, particularly among obese Asian women.

Among Asian college students, there was no difference in body composition (BMI, PBF) between the A1 (A1A1 or A1A2) and A2 (A2A2) groups. Despite not finding a difference, we would like to bring awareness to ethnic differences in defining obesity (classically defined as BMI >30). In this study, none of the Asian women had BMI great than 30, yet many had PBF >30%. It has also been previously reported that BMI may be a poor marker for true obesity among Asian American women. Young Asian women may have normal BMI but actually high PBF.[10] For the same PBF, Chinese subjects have lower BMI than Caucasians.[11] In another study using DEXA to measure PBF, BMI underestimated prevalence of overweight and obesity in Asian-Indian men and women, Asian women, and Hispanic women, whereas BMI overestimated overweight and obesity for African American men and women.[12] This finding was again seen in Vietnamese women[13] and in Asian (Chinese and Korean) children in both China and the United States.[14] In this study, we did not select participants based on BMI or percent body fat. The majority of participants were non-obese as all but one Asian participant had BMI less than 30. However, PBF was higher than 30% in 12 Asian women. All of the Asian men had PBF less than 25%. It should also be pointed out that while none of the Asian women had BMI in the obese range (greater than 30), many had PBF greater than 30%. Future studies should be designed to examine only obese Asians that meet criteria for obesity by PBF and BMI, as criteria solely based on BMI may misclassify participants. More importantly, controls should be chosen by strict criteria as well.

The prevalence of A1 allele depends not only on ethnicity but also characteristics of the population being examined. Blum et al summarizes the vast differences in A1 frequency, citing Yemenite Jews (A1 frequency=0.09), "white controls" (0.19), Chinese (0.47), and Cheyenne (0.8).[15] The prevalence of A1 in whites without diabetes is 29%.[16] In white and black adults with diabetes, the prevalence of A1 is closer to 50%.[17] Among non-Asian (mostly Caucasian) adults with obesity, the A1 allele was present in about 45%.[18] In a study looking at DRD2 in Chinese middle age adults (half of the study participants were obese), there were 70% of individuals with at least one copy of A1.[19] A1 allele appears to be more prevalent in Asian populations. In our study, the prevalence of A1 (A1A1 or A1A2) was 63%. Moreover, when it is further broken down by gender, the obese women (by PBF) have a high prevalence of 83% with at least one copy of A1. This further supports and suggests that the prevalence of A1 depends not only on ethnicity but perhaps also gender.

This study has several limitations. We are only studying one single polymorphism, albeit which has been the most studied "food addiction" gene. Obesity is polygenic, and genes affecting cravings and eating behavior are complex. In this study, the majority of participants had normal BMI. It will be important to further understand the relationship between DRD2, body composition, and food addiction questionnaires among an entirely homogeneous obese Asian population. Another limitation is the population studied is in general healthy without significant proportion of obesity related comorbidities. Nearly all of the students did not meet criteria for obesity by

BMI and only a handful did by PBF. We did not find a correlation between questionnaires and body composition perhaps because of the study population. However, it remains plausible that the presence of at least one copy of A1 may predispose to obesity, and that genotype and questionnaire score may be utilized as a marker of food addiction. Additional study limitations include the relatively small sample size and potential selection bias given that students self-selected to be in the study. Future larger studies of obese Asians are needed to investigate food addiction and DRD2.

Obesity rates continue to rise. A recent study showed that the prevalence of overweight and obesity has increased in children and adolescents in developed countries. Also, China now follows the United States as the country with the second highest number of overweight or obese individuals.[20] There is a need for further studies examining the ethnic and gender differences in food addiction.

In conclusion, while there remains much to be investigated about the role of genetic polymorphisms in an obesogenic food environment, there may exist differences among genders and different ethnic populations. These factors need to be taken into consideration when conducting research studies in food addiction. Further studies to explore the potential role of dopamine agonists to alter food craving and hopefully reduce body fat are warranted.

AUTHOR DISCLOSURES

No conflicts to disclose. The authors have no financial relationships relevant to this article to disclose.

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Original Article

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亚裔美国大学生食物渴求、食物成瘾和抗多巴胺（DRD2 A1）受体基因多态性

背景与目的：在肥胖仍然是一个重要的公共健康问题的时代，食物成瘾已经成为导致肥胖的一个可能因素。DRD2 基因多态性目前研究广泛。该研究的目的是探讨亚裔美国人食品成瘾、身体成分和抗多巴胺受体基因多态性（DRD2 A1）的关系。**方法与研究设计**：共招募 84 名亚裔美国大学生,通过生物电阻抗方法对受试者进行身体成分测量，同时进行问卷（食物渴求库存和食物规模有效性）调查，并抽血进行基因分型（PCR）。**结果**：A1（A1A1 或 A1A2）和 A2（A2A2）两组人群身体成分（BMI、体脂百分比）差异无统计学意义。根据食物渴求库存，A1 和 A2 组间在碳水化合物和快餐食品的渴求方面差异有统计学意义（p=0.03），但不包括糖或脂肪。在亚裔美国女大学生中，还发现食物问卷效能不同（p=0.04），但男性中并未发现差异。55 名女性中有 13 名 BMI 在 21.4 至 28.5 kg/m^2 之间，身体脂肪成分>30%。**结论**：亚裔美国人对更多碳水化合物和快餐食品的渴求与 DRD2 A1 和 A2 等位基因有关。有必要进一步研究亚裔美国人多巴胺受体激动剂在影响食物渴求和减少身体脂肪方面的功能，需要更多的研究肥胖亚洲裔美国人对食物的渴求，谨慎定义肥胖的概念，特别是亚洲女性。

关键词：多巴胺、肥胖、食物成瘾、食物渴求、亚裔美国人