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The TaqIA RFLP is associated with attenuated intervention-induced body weight loss and increased carbohydrate intake in post-menopausal obese women[★]

Jameason D. Cameron^a, Marie-Ève Riou^a, Frédérique Tesson^b, Gary S. Goldfield^{a,c}, Rémi Rabasa-Lhoret^{d,e,f}, Martin Brochu^{g,h}, and Éric Doucet^{a,*}

^aSchool of Human Kinetics, University of Ottawa, Ontario, Canada K1N 6N5

^bInterdisciplinary School of Health Sciences, University of Ottawa, Ontario, Canada

^cChildren's Hospital of Eastern Research Institute, Ottawa, Ontario, Canada

^dDepartment of Nutrition, Université de Montréal, Montréal, Canada

^eMontreal Institute for Clinical Research (IRCM), Montréal, Canada

^fMontreal Diabetes Research Center (MDRC) of Centre de Recherche du centre Hospitalier de l'Université de Montréal (CR-CHUM), Montréal, Canada

^gFaculty of Physical Education and Sports, University of Sherbrooke, Sherbrooke, QC, Canada

^hResearch Centre on Aging, Social Services and Health Centre, University Institute of Geriatrics of Sherbrooke, QC, Canada

Abstract

Introduction—Polymorphisms of the dopamine receptor D2 (DRD2) gene have been associated with obesity phenotypes. Our aim was to examine if the genotype of TaqIA Restriction Fragment Length Polymorphism (RFPL) was related to an attenuated weight loss response or to changes in energy expenditure (EE) and food preference before and after weight loss.

Methods—Obese post-menopausal women (age = 57.1 ± 4.6 yr, weight = 85.4 ± 15.4 kg and BMI = 32.8 ± 4.5 kg/m²) were genotyped for TaqIA ($n = 127$) by using PCR-RFLP analysis and categorized as possessing at least one copy of the A1 allele (A1⁺) or no copy (A1⁻). Women were randomized into two groups, caloric restriction (CR) and caloric restriction + resistance training (CRRT) and in this study were further classified as follows: A1⁺CR, A1⁺CRRT, A1⁻CR and A1⁻CRRT. Body composition, total daily EE, physical activity EE, Resting EE (REE), and energy intake were obtained at baseline and post-intervention using DXA, doubly-labeled water, indirect calorimetry, and 3-day dietary records, respectively.

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*Corresponding author. edoucet@uottawa.ca (É. Doucet).

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Results—Overall, all of the anthropometric variables and REE significantly decreased post-intervention ($p < 0.001$). Women in the CRRT group lost significantly more fat mass (FM) than the CR women ($p < 0.05$). There were significant time by group by allele interactions for attenuated body weight (BW), BMI, and FM loss for A1⁺ (vs. A1⁻) in CRRT ($p < 0.05$) and for increased % carbohydrate intake ($p < 0.01$).

Conclusion—TaqIA genotype was associated with body weight loss post-intervention; more specifically, carriers of the A1 allele lost significantly less BW and FM than the A1⁻ and had increased carbohydrate intake in the CRRT group.

Keywords

DRD2/ANKK1; TaqIA RFLP; Obesity; Weight-loss; Diet; Exercise; Post-menopausal women

Introduction

Of late there has been much focus on genotypes thought to be linked with impaired dopamine signaling. The surge in studies of dopamine and the role of its transport and receptor genes in feeding and other reward-driven behaviors such as ethanol consumption, gambling, drug-taking, and obesity strongly points to evidence of reward-related phenotypes (Noble, St. Jeor, et al., 1994). Support for the role of dopamine in human feeding behavior is evidenced in part by the anorexigenic action of dopamine agonists (Goldfield, Lorello, & Doucet, 2007; Leddy et al., 2004; Schertz, Adesman, Alfieri, & Bienkowski, 1996) and by the orexigenic action of dopamine antagonists (Roerig et al., 2005; Ruetsch, Viala, Bardou, Martin, & Vacheron, 2005). Dopamine is also involved in motor control and motivation (Salamone, Correa, Mingote, & Weber, 2005), and there is a body of evidence to suggest that dopaminergic activity in the brain is related to voluntary physical activity (for review see Knab and Lightfoot (2010)). Dopamine availability is dependent on its release, transport (reuptake), metabolism, and receptor binding. Consequently, by looking at the genes involved at any one of these functional stages there is an opportunity to indirectly investigate brain dopamine levels—in effect looking at markers of neurotransmitter activity (Epstein et al., 2007)—and how behavior may be resultantly impacted.

The TaqIA Restriction Fragment Length Polymorphism (RFPL) (rs1800497) is found within the ankyrin repeat and kinase domain containing-1 gene (ANKK1) (Neville, Johnstone, & Walton, 2004), located 10.5 kb downstream of the DRD2 gene in chromosome band 11q23.1 (Manning, Whyte, Martinez, Hunter, & Sudarsanam, 2002). This polymorphism is a single nucleotide C/T change; the T allele is referred to as A1, the C allele as A2, individuals hetero- or homozygous for the T allele are referred to as A1⁺, and individuals homozygous for the C allele are referred to as A1⁻. This polymorphism occurs in ANKK1 exon 8, and results in a glu713-to-lys (E713K) non-conservative substitution; to date, this substitution has not been associated with a change in ANKK1 structural integrity, substrate-binding specificity, or function, however, dopamine-related endophenotypes have been associated with the TaqI RFLP (Rodriguez-Jimenez et al., 2006). Moreover, ANKK1 and DRD2 genes have been shown to overlap, sharing halotypic blocks, and furthermore it was shown that ANKK1 expression was significantly upregulated by the powerful dopamine receptor agonist apomorphine (Hoenicka et al., 2010). Although the precise relationship between

TaqIA RFLP and DRD2 remains uncertain, there is convincing evidence that A1⁺ individuals have a 30–40% reduction in D2 receptor density and availability *in vivo* (Jonsson et al., 1999; Noble, Blum, Ritchie, Montgomery, & Sheridan, 1991; Pohjalainen et al., 1998; Thompson et al., 1997); it must be noted, however, that there are data showing no significant differences in dopamine binding potential between A1⁺ carriers and A1⁻ (Laruelle, Gelernter, & Innis, 1998). Decreased striatal density of dopamine receptors has been shown via PET studies to be related to obesity (Volkow et al., 2008), even proportional to body mass (Wang et al., 2001). In line with the above noted hypo-responsiveness of dopamine transmission, evidence also suggests that the A1⁺ allele is related to body mass (Noble, Noble, et al., 1994; Spitz et al., 2000; Thomas, Critchley, Tomlinson, Cockram, & Chan, 2001) but other groups have failed to find such a relationship (Davis et al., 2008; Jenkinson et al., 2000; Southon et al., 2003).

The TaqIA polymorphism has also been associated with a number of impulsive/addictive behaviors such as alcoholism (Munafo, Matheson, & Flint, 2007), smoking (Noble, 1998), and overeating leading to obesity (Noble, Noble, et al., 1994; Spitz et al., 2000). Another phenotype associated with the TaqIA polymorphism is food preference. In a sample of obese men and women it was shown that 64.3% of those who preferred carbohydrates (as opposed to foods high in fat or protein) were carriers of the A1 allele, compared to the 21.1% of carriers who preferred either high fat or protein foods (Noble, Noble, et al., 1994). What is interesting are the recent findings, using fMRI to measure responsivity of brain reward circuitry to palatable food cues, suggesting that the A1⁺ allele is involved in consummatory and anticipatory feeding behavior. Specifically, individuals identified as having weaker striatal activation post-ingestion of a palatable food (Stice, Spoor, Bohon, Veldhuizen, & Small, 2008) or simply after imagining a palatable food (Stice, Yokum, Blum, & Bohon, 2010) had a greater risk of weight gain at 1 year, but only if they were an A1⁺ carrier (*vs.* A1⁻).

While obesity in general, and weight loss in particular, are no doubt influenced by polygenic factors, to our knowledge there has not been an effort to examine whether polymorphisms of TaqIA may impact the inter-individual variation in weight loss by two separate modalities. Accordingly, our primary objective was to investigate the potential association of the TaqIA RFLP allele with body weight loss in overweight/obese post-menopausal women who completed a 6-month weight loss intervention using caloric restriction (CR) with or without the addition of a resistance training (RT) program. Our secondary objective was to elucidate if there existed genotype associations with energy intake (EI) or energy expenditure variables (EE). It was hypothesized that individuals carrying the A1 allele would respond with reduced body weight loss to the caloric restriction intervention and that individuals carrying the A1 allele would display an enhanced carbohydrate (CHO) preference and attenuated physical activity energy expenditure (PAEE).

Methods

This is a secondary analysis of the Montreal Ottawa New Emerging Team weight loss intervention which was designed to reduce body weight (BW) by 10% and consisted of a 6-month intervention randomising participants to CR with or without resistance training (RT)

(Brochu et al., 2009). The study was conducted according to the guidelines laid down in the Declaration of Helsinki, and all procedures involving human subjects/patients were approved by the Université de Montréal, Comité d'éthique de la Faculté de Médecine. Written informed consent was obtained from all subjects/patients. By design, there were twice as many women randomised in the CR group compared to the CR + RT group, as women who completed the 6-month CR weight loss intervention were asked to participate in a 12-month follow-up with or without RT.

Subjects

A total of 147 Caucasian women aged 46–70 years were included in this study, of which data from 127 were included herein due to missing anthropometric data. Women were eligible to participate if they met the following criteria: (1) body mass index (BMI) ≥ 27 kg/m², (2) cessation of menstruation for more than 1 year and a follicle-stimulating hormone level ≥ 30 U/l, (3) sedentary (<2 h per week of structured exercise), (4) non-smokers, (5) low to moderate alcohol consumption (<2 drinks/day), (6) free of known inflammatory disease and (7) no use of hormone replacement therapy. On physical examination or biological testing, all participants had no history or evidence of: (1) cardiovascular disease, peripheral vascular disease or stroke, (2) diabetes (75 g oral glucose tolerance test), (3) known renal and liver disease, (4) asthma requiring therapy, plasma cholesterol > 8 mmol/L, (5) systolic blood pressure > 160 mmHg or diastolic blood pressure > 100 mmHg, (6) history of alcohol or drug abuse, (7) previous history of inflammation disease or cancer, (8) orthopedic limitations, (9) body weight fluctuation of ± 2 kg in the last 6 months, (10) untreated thyroid or pituitary disease and (11) medications that could affect cardiovascular function and/or metabolism. After reading and signing the consent form, each participant was submitted to a series of tests.

Intervention design and procedure

Caloric restriction intervention (CR)—The women entered a medically supervised weight loss program for 6 months aimed at reducing BW by 10%, as previously described (Brochu et al., 2009). To determine the level of CR, 500–800 kcal were subtracted from baseline resting energy expenditure (REE; determined by indirect calorimetry) multiplied by a physical activity factor of 1.4, corresponding to a sedentary state (Tremblay, Pelletier, Doucet, & Imbeault, 2004). Macronutrient diet composition was prescribed as follows: 55%, 30% and 15% of EI, respectively from carbohydrates, fat and protein. Each participant met with the study dietitian to receive the diet prescription. Also, participants in both study groups were invited to meet bi-monthly with the dietitian for nutrition classes, 1–1.5 h in duration.

Resistance training intervention (RT)—As previously described (Brochu et al., 2009) each training session included a warm-up of low intensity walking on a treadmill for 10 min. The 6-month RT program consisted of four progressive phases and was performed weekly on three non-consecutive days [phase 1: introduction to training (3 weeks, 15 repetitions, 2–3 sets per exercise, 90–120 s between sets); phase 2 (5 weeks, 12 repetitions, 2–3 sets per exercise, 90 s between sets); phase 3 (9 weeks, 8–10 repetitions, 2–4 sets per exercise, 120–

180 s between sets) and phase 4 (8 weeks, 10–12 repetitions, 3–4 sets per exercise, 60–90 s between sets)]. Each exercise session was individually monitored by qualified trainers.

Measurements

Anthropometric measurements—Body composition (fat mass (FM) and fat-free mass (FFM)) and BW were assessed by dual energy X-ray absorptiometry (DXA) using a daily calibrated GE-LUNAR Prodigy module (GE Medical Systems, Madison, WI). Briefly, subjects laid on an examination table, wearing standard issue hospital gowns, while a low-intensity X-ray scanned their entire body; height (Perspective Enterprises, Michigan, USA) and BW (BWB-800AS Digital Scale; Tanita Corporation of America Inc.) was also measured while wearing standard issue hospital gowns. BMI [body weight (kg)/height (m²)] was also calculated.

Energy intake—To measure free-feeding EI 3-day self-reports (see Strychar et al., 2009) were employed at baseline and then 1-month post-intervention (after completing 1 month of weight stability). Briefly, participants were given detailed instruction on how to report all foods and beverages consumed over a 1-week period represented by 2 weekdays and 1 weekend day. Upon handing in the completed self-reported food records, a registered dietitian reviewed the records with the women and reconciled any ambiguities in reporting or obtained more detailed information of EI.

Energy expenditure—Daily energy expenditure was determined from doubly labeled water (DLW) over a 10-d period (Schoeller & van Santen, 1982). The DLW (²H₂ ¹⁸O) experiments generated five urine samples per subject: a pre-dose sample was collected before administration, two samples (16–24 h later) were obtained after the ²H₂ ¹⁸O dose had initially equilibrated in the body, and two more samples were collected 10 days later, as previously described (Karelis et al., 2010). All samples were measured in triplicate for ¹⁸O-water and ²H-water. An Isoprime Stable Isotope Ratio Mass Spectrometer connected to a Multiflow-Bio module for Isoprime and a Gilson 222XL Autosampler (GV Instruments, Manchester, UK) were used for daily energy expenditure measurements. Data processing was performed with MassLynx 3.6 software. Stability tests were performed each day before testing giving a standard deviation of 0.026% for deuterium and 0.004% for ¹⁸O (Lavoie et al., 2010; St-Onge, Mignault, Allison, & Rabasa-Lhoret, 2007). In addition, REE and PAEE were measured by indirect calorimetry and total daily energy expenditure (TDEE) was then calculated as previously described (Conus et al., 2004).

TaqIA genotyping—The genotyping of TaqIA was done by polymerase chain reaction (PCR) using with forward primer: 5′-GAC GGC TGG CCA AGT TGT CTA-3′ and reverse primer: 5′-GTC GAC CCT TCC TGA GTG TC-3′ to amplify a 304 bp fragment spanning the polymorphic TaqIA site. Analysis of the TaqIA polymorphisms was done as previously described (Spitz et al., 1998). The amplified products were incubated with 1 µl of the TaqI (*Thermus aquaticus* YT-1, *invitrogen*) restriction enzyme for 22 h at 65 °C. The restriction products were visualized on a 2% agarose gel (run for 60 min at 100 V) stained with ethidium bromide. The A1 allele corresponds to the uncut amplicon of 304 bp, the A2 allele is characterized by two fragments of 177 and 127 bp. Of the 127 samples, 119 were

analyzed in duplicate, while eight samples were only analyzed once due to insufficient volume of plasma; all samples run in duplicate verified no difference in allele type (i.e. 100% precision), so it was deemed acceptable to include the 11 non-duplicated samples in the overall analysis.

Analytic plan—A between subjects two-way analysis of variance (ANOVA) was conducted to determine if there were any differences between exercise groups (CR *vs.* CRRT) or genotype (A1⁺ *vs.* A1⁻). Effects of the TaqIA polymorphism on anthropometric (i.e. BW, BMI, FM, and FFM), EI (i.e. mean EI, % CHO, % fat, % protein, and % alcohol), energy expenditure (i.e. TDEE, REE, and PAEE), and variables were analyzed using two (A1⁺ *vs.* A1⁻) $\times$ 2 (caloric restriction *vs.* caloric restriction and resistance training) $\times$ 2 (baseline *vs.* post-intervention) repeated measured ANOVAs. This analysis also allows the determination of how genotype influences changes in EI over time (A1⁺ *vs.* A1⁻) $\times$ (baseline *vs.* post-intervention), as well as which exercise modality was more effective in producing changes in variables of interest [(CR *vs.* CRRT) $\times$ (baseline *vs.* post-intervention)]. Due to the limited data on rs1800497 genotype differences and possible differences in BW or CHO preference, for example, we chose not to control for multiple statistical comparisons so as to not overlook findings that could otherwise help to bring light to better describing this polymorphism. Differences with *p*-values ≤ 0.05 were considered statistically significant and values are presented as means $\pm$ standard deviation unless indicated otherwise. Statistical analyses were performed using SPSS version 17 (Chicago, SPSS Inc.).

Results

At baseline, the average woman was 57.1 ± 4.6 years of age, BW of 86.5 ± 14.5 kg, BMI of 33.1 ± 4.4 kg/m², FFM of 46.2 ± 6.8 kg, FM of 40.4 ± 9.3 kg, and % FM of 46.4 ± 4.5 . There were no significant differences in initial BW or body composition at baseline neither by group nor by genotype.

TaqIA was in Hardy–Weinberg equilibrium and the frequencies of the TaqIA alleles were distributed as follows: six subjects (4.7%) were homozygous for the A1 allele, 60 subjects (47.2%) were heterozygous, and 61 (48.0%) were homozygous for the A2 allele. Due to the low frequency of A1 homozygous subjects, and in order to maintain consistency with previous research (Blum et al., 1996; Epstein et al., 2007), the TaqIA genotypes were dichotomized to A1⁺ and A1⁻.

As seen in Table 1 a significant 3-way interaction of time by group by allele, $F(1,123) = 4.2$, $p = 0.04$, was found for attenuated BW loss whereby A1⁺ carriers lost less BW than non A1 carriers in the CRRT group only (A1⁺CRRT: 81.1 ± 12.0 kg to 76.7 ± 13.4 kg; A1⁻CRRT: 86.1 ± 16.6 kg to 79.1 ± 18.4 kg, $p < 0.05$). Similarly, significant 3-way interactions of time by group by allele were discovered only for the CRRT group for attenuated FM loss, $F(1,123) = 6.0$, $p = 0.01$, whereby A1⁺ carriers lost less FM than non A1 carriers (A1⁺CRRT: 37.2 ± 8.5 kg to 32.8 ± 9.3 kg; A1⁻CRRT: 41.1 ± 10.7 kg to 34.9 ± 13.5 kg, $p < 0.05$), and lastly for an attenuated decrease in BMI, $F(1,123) = 4.7$, $p = 0.03$, whereby A1⁺ carriers lost less BMI than non A1 carriers (A1⁺CRRT: 31.7 ± 3.6 kg/m² to 29.4 ± 4.2 kg/m²; A1⁻CRRT: 32.4 ± 5.2 kg/m² to 31.0 ± 6.0 kg/m², $p < 0.05$) (see Table 1).

Similarly, the 3-way interaction on CHO intake was significant ($p = 0.019$) whereby $A1^+$ carriers exhibited an increase in % CHO intake over time ($A1^+CRRT$: pre-intervention $46.2 \pm 5.1\%$ to post-intervention $52.5 \pm 8.5\%$, $p < .05$) in the CRRT group, and the $A1^-$ exhibited a significant decrease in % CHO intake over time in the CRRT group ($A1^-CRRT$: pre-intervention $51.4 \pm 6.7\%$ to post-intervention $47.6 \pm 9.9\%$, $p < 0.01$), $F(1, 33) = 7.93$, $p = 0.008$ (see Table 1). No significant differences in % CHO were found over time between carriers of the $A1^+$ and $A1^-$ genotypes.

In the entire sample, all of the anthropometric variables and REE significantly decreased post-intervention ($p < 0.001$). No significant effects of allele were noted for REE, PAEE, or TDEE (see Table 1).

Discussion

This study utilized a theoretically driven approach to elucidate possible relationships between the rs1800497 genotype believed to alter dopaminergic activity and the predisposition to respond differently to standardized weight loss modalities. Overall there was a significant association between the TaqIA genotype and BW loss, FM loss, and decrease in BMI post-intervention, but only for the women in the CRRT group. Regarding the secondary hypotheses, there was an association between the TaqIA genotype and macronutrient intake, whereby $A1^+$ individuals in the CRRT group demonstrated an increase in CHO intake whereas $A1^-$ carriers showed a decrease in CHO intake post-weight loss. There was no difference by genotype pre- and post-intervention in CHO intake in the CR group. $A1^+$ individuals exhibited smaller reductions in BW, FM, and BMI pre- and post-intervention in the CRRT group compared to the $A1^-$ participants, whereas no interactive effects were found in the CR group.

Ongoing research on the genetics of obesity has found more than 430 genes, markers, and chromosomal regions discovered to be related to obesity phenotypes (Snyder et al., 2004) and estimates of the heritability of BMI are between 40% and 70% (Barsh, Farooqi, & O'Rahilly, 2000). Strong evidence also suggests that changes in FM and fat distribution, especially during negative energy balance (vs. overfeeding) (Bouchard & Tremblay, 1997), are largely determined by genetic factors. In a study examining the potential role of TaqIA polymorphism in "neurobesigenics", a clinical subtype of Reward Deficiency Syndrome, 122 non-Hispanic Caucasian obese subjects (17 males and 105 female, mean age 42.3 yr) with age matched non-obese controls were genotyped for TaqIA polymorphism (Chen et al., 2012). It was found that the $A1^+$ genotype was present in 67% of the obese and only in 33% of the controls and that there was a significant positive association with percent body fat. Furthermore, a recent study demonstrated that parent-child concordance of the TaqIA genotype predicts similar parent-child weight loss response to a diet/exercise intervention (Epstein, Dearing, & Erbe, 2010). Specifically, if parent and child were concordant for the $A1$ allele, the child showed double the zBMI change at 6 months into the intervention and over four times the change at 12 months in comparison to a child who was not concordant for the $A1$ allele. In our sample of obese/overweight post-menopausal women we report similar findings whereby individuals with the $A1^+$ genotype had a lesser change in BMI (vs. $A1^-$) in the CRRT group (see Table 1). A similar significant finding was also noted in our

group for concordance of the A1⁺ allele and overall weight loss, but again only in the CRRT group.

In a recent study examining the efficacy of a vegan diet intervention and the potential impact of the TaqIA polymorphism on outcome variables it was found that relative to individuals with the A1⁻ genotype, Caucasian A1⁺ carriers demonstrated significantly more CHO intake (Barnard et al., 2009). Though there was no genotype interaction with weight loss in the overall sample, when race was considered, however, African American A1 carriers did experience significantly less weight loss than the A1⁻ individuals TaqIA genotype (Barnard et al., 2009). Although the vegan diet intervention was by caloric restriction alone the negative energy balance (500–1000 kcal/day) was very close to that prescribed in our intervention. Accordingly, these results dovetail nicely with our findings and those of previous groups (Noble, 2000; Noble, Noble, et al., 1994). Another very likely candidate phenotype that could have operated concurrently with CHO preference is a food reinforcement phenotype. Literature shows that acute (2–4 h) and chronic (2 months) energy deprivation can increase the reinforcing value of palatable foods (Cameron, Goldfield, Cyr, & Doucet, 2008; Saelens & Epstein, 1996); what is more, studies have revealed that food reinforcement can not only be a good predictor of *ad libitum* EI, but the presence of the A1 allele can interact with obesity to influence food reinforcement (Epstein et al., 2004, 2007). Subjects identified as high in food reinforcement who were carriers of the A1 allele consumed more food than participants high in food reinforcement without the A1 allele and participants low in food reinforcement with or without the A1 allele (Epstein et al., 2007). In our sample of women we did not, however, have access to any measure of food reinforcement or reward, but given no study has examined how the chronic effects of energy deprivation involved in an intervention impacts food reinforcement in those with the A1 allele, this remains a fruitful area of inquiry as it may provide a mechanism for the current finding of increased CHO intake in these polygenetic individuals.

Another of our secondary hypotheses was that the TaqIA polymorphism would be related to lower levels of EE. Existing literature clearly demonstrates that dopamine deficient mice are hypoactive and dopamine receptor knockout mice demonstrate significantly less spontaneous movement (Baik et al., 1995). Further, there is considerable evidence to show that genetic variation contributes to the inter-individual variation in responsiveness to exercise training and that genotype-by physical activity interactions may play a measurable role in following health-related outcomes (Rankinen & Bouchard, 2012). In this light and in concert with findings that lower levels of Nonexercise Activity Thermogenesis (NEAT) can contribute to BW gain (Levine et al., 2005), it was hypothesized that lower EE in A1⁺ individuals would account for part of the attenuated weight loss. Although there was no association between genotype and EE variables (see Table 1), this finding is to our knowledge novel and is the first to examine the potential for a energy expenditure-related phenotype using well validated measures of EE (i.e. doubly-labeled water).

The current study is among the first study to examine how variants of the TaqIA allele influence changes in body composition and EI in a 6-month weight loss trial in obese adults. Also, we are the first to show that the TaqIA genotype was associated with attenuated BW and FM losses in a group receiving diet and exercise interventions. Consistent with our

hypotheses and with previous research, we also found that being a carrier of the A1 allele was associated with an increase in CHO intake (only in the CRRT group) compared to non A1 carriers. Limitations of the study include the fact that although overweight or obese, the studied population was a homogeneous population of “healthy” non-diabetic Caucasian women, thus we are uncertain if our results generalize to all obese women in the targeted age range. Also, due in part to the significant differences in allele frequency and genotype prevalence that generally occur due to racial/ethnic variation (Chang et al., 2009), there is also a need to be mindful of ethnic variation (or lack thereof) when interpreting the Taq1 A genetic data. Regarding the EI variables, there exists the limitation of self-reporting and the well-known under-reporting phenomenon (Karelis et al., 2010). Finally, our observed associations between rs1800497 and FM and CHO intake must be interpreted recalling the less-stringent analysis of multiple comparisons.

In summary, in support of the main hypothesis there was an association between Taq1A polymorphism and the amount of BW loss; more specifically, there were group by genotype interactions where carriers of the A1 allele (*vs.* A1⁻) lost significantly less BW, FM and BMI in the CRRT group. The secondary hypothesis was partially confirmed, whereby a post-weight loss increase in CHO intake emerged for A1⁺ carriers in the CRRT group; however, there were no significant effects on any measure of EE. Future research should be directed at longitudinally examining the interplay of dopamine-related polymorphisms, nutritional status, and food reward in order to have a better understanding of potential gene-environment interactions and how each of these variables may differentially affect feeding behavior and obesity at large.

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Table 1

Subjects' characteristics by weight loss modality and TaqIA genotype.

Characteristics	Pre				Post				Time	Group	Allele	Time * Group	Time * Allele	Time * Group * Allele	
	A1 ⁺		A1 ⁻		A1 ⁺		A1 ⁻								
	CR	CRRT	CR	CRRT	CR	CRRT	CR	CRRT							
Anthropometric															
<i>n</i>	49	17	44	17	49	17	44	17							
Body Weight (kg)	86.1 ± 15.6	81.1 ± 12.0	86.8 ± 15.3	86.1 ± 16.6	80.5 ± 15.0	76.7 ± 13.4	82.3 ± 14.3	79.1 ± 18.4	.001	.28	.41	.47		.44	.04
BMI (kg/m ²)	32.9 ± 4.7	31.1 ± 3.6	33.1 ± 4.3	32.4 ± 5.2	30.8 ± 4.5	29.4 ± 4.2	31.4 ± 4.2	31.0 ± 6.0	.001	.41	.17	.38		.42	.03
Fat Mass (kg)	39.4 ± 9.8	37.2 ± 8.5	39.9 ± 9.2	41.1 ± 10.7	34.9 ± 9.9	32.8 ± 9.3	37.1 ± 9.7	34.9 ± 13.5	.001	.51	.27	.03		.97	.01
Lean Free Mass (kg)	46.6 ± 7.7	43.9 ± 4.9	46.6 ± 7.3	44.9 ± 7.2	45.6 ± 6.6	43.9 ± 5.1	45.1 ± 6.4	44.1 ± 6.0	.001	.19	.88	.06		.20	.74
Energy expenditure (kcal/day)															
<i>n</i>	35	15	30	17	35	15	30	17							
TDEE	2458 ± 395	2561 ± 296	2493 ± 392	2551 ± 476	2380 ± 360	2435 ± 410	2446 ± 365	2484 ± 345	.06	.38	.63	.69		.58	.87
REE	1352 ± 216	1332 ± 157	1367 ± 232	1287 ± 157	1280 ± 200	1262 ± 169	1309 ± 230	1245 ± 183	.001	.26	.91	.60		.28	.72
PAEE	905 ± 295	953 ± 225	905 ± 275	1009 ± 299	898 ± 274	915 ± 263	916 ± 295	991 ± 279	.73	.21	.44	.69		.80	.99
Energy intake															
<i>n</i>	15	8	5	9	15	8	5	9							
Mean 3-day (kcal/day)	1822 ± 398	1671 ± 421	2198 ± 494.7	23010 ± 772	1670 ± 421	1777 ± 292	1780 ± 367	1748 ± 448	.002	.349	.256	.415		.297	.901
% CHO	49.6 ± 4.9	46.2 ± 5.1	43.8 ± 6.4	51.4 ± 6.6	49.9 ± 6.7	52.5 ± 8.5	50.5 ± 6.1	47.6 ± 9.9	.115	.264	.420	.448		.407	.019
% Fat	30.8 ± 3.7	33.7 ± 4.4	34.9 ± 5.4	30.9 ± 6.2	29.8 ± 6.3	27.3 ± 4.6	29.5 ± 5.5	28.9 ± 3.5	.005	.448	.622	.704		.991	.082
% Protein	17.9 ± 3.8	15.8 ± 1.9	17.7 ± 2.5	15.1 ± 1.7	18.1 ± 3.1	17.1 ± 2.2	18.4 ± 2.5	19.8 ± 1.5	.005	.192	.539	.034		.233	.374
% Alcohol	1.6 ± 2.4	4.2 ± 5.1	3.5 ± 6.7	2.5 ± 2.9	2.1 ± 3.9	2.9 ± 5.7	1.6 ± 3.3	3.7 ± 6.5	.549	.409	.951	.595		.973	.045

TDEE is total daily energy expenditure; REE is resting energy expenditure; and PAEE is physical activity energy expenditure; values are Mean ± SD.

n = 48 for A1⁺ in CR for FM, FFM and REE; *n* = 43 for A1⁻ in CR for FM, FFM and for REE in this group *n* = 44.

n = 17 for A1⁺ and A1⁻ in CRRT for REE.