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Taq1a polymorphism (rs1800497) is associated with obesity-related outcomes and dietary intake in a multi-ethnic sample of children

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Abstract

Background: In adults, the *Taq1a* polymorphism (rs1800497) near the D2 receptor *(DRD2)* gene is associated with body mass index and binge eating and is more prevalent among non-Hispanic Blacks (NHB) and Hispanic-Americans (HA) relative to non-Hispanic Whites (NHW). We hypothesize *Taq1a* polymorphism (rs1800497) risk alleles contribute to paediatric racial/ethnic differences in obesity phenotypes.

Objectives: This study aims to characterize the relationship between the *Taq1a* polymorphism (rs1800497), diet and adiposity in a multi-ethnic cohort of 286 children (98 NHB, 76 HA and 112 NHW), ages 7–12.

Methods: Dual-energy X-ray absorptiometry, computed tomography scans and two 24-h dietary recalls assessed body composition, fat distribution and dietary intakes, respectively.

Results: Children with two *Taq1a* risk alleles (NHB = 50.0%, HA = 43.3%, NHW = 6.7%) reported a 20% increase in total energy intake ($P = 0.0034$) and percent of calories from sugar consumed ($P = 0.0077$) than did children with less than two risk alleles. Children with two *Taq1a* risk alleles demonstrated significantly higher total body fat ($P = 0.0145$), body fat percentage ($P = 0.0377$), intra-abdominal adiposity ($P = 0.0459$), subcutaneous abdominal adiposity ($P = 0.0213$) and total abdominal adiposity ($P = 0.0209$) than did children with one or no *Taq1a* risk alleles.

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Conflict of interest statement

No conflict of interest was declared.

Supporting information

Additional supporting information may be found online in the Supporting Information section at the end of the article.

Conclusions: Our results suggest that having two *Taq1a* risk alleles is associated with an increase in reported calorie and sugar consumption and is a potential risk factor for early development of excess adiposity in multi-ethnic children. These results need to be confirmed in a larger sample.

Keywords

adiposity; dopamine; *DRD2*; SNPs

Introduction

Paediatric obesity affects 17.5% of children ages 6 to 11 in the USA (1). Obesity is a multifactorial disease with identified contributors including genetics (2), poverty (3), low levels of physical activity (4) and adverse eating behaviour (5). Importantly, non-Hispanic Black (NHB) and Hispanic-American (HA) children are disproportionately affected by obesity when than are non-Hispanic White (NHW) children (1); yet potential genetic factors accounting for these differences remain poorly characterized. Limited genomic information has been incorporated into research investigating health disparities, although it has direct relevance to concepts of race/ethnicity, health status, appropriate care and socioeconomic status (SES). Although the molecular mechanisms that contribute to disparities in the risk of paediatric obesity remain largely unknown, interactions among environmental and genetic factors are likely to be relevant.

Reward pathways that modify eating behaviour could partially explain racial/ethnic disparities in paediatric obesity. For example, dopamine reward circuitry includes dopamine receptors, which have been associated with eating behaviour and weight gain (6). Dopamine D2 receptor (*DRD2*) gene polymorphisms have been found to be related to several addictive behaviours, or reward-dependent behaviours, such as alcohol/drug dependence, pathological gambling and motivation (7). The A1 allele of the *Taq1a* polymorphism (rs1800497) is located downstream of *DRD2* and in an exon of the *ANKK1* gene. However, it has been found to be associated with reduced brain D2 receptor density (8), which has been demonstrated to increase the risk for overeating and obesity (6).

Previous work has demonstrated frequency of the *Taq1a* 'risk' allele (A1) varies according to race/ethnicity with 19.4% of NHW, 29.6% of HA and 43% of NHB having at least one A1 risk allele (9). Multiple studies have shown that the presence of at least one A1 risk allele is associated with body mass index (BMI) in adults (10); however, a recent meta-analysis found no relationship between children who are A1+ (defined as having ≥1 A1 risk alleles) and BMI (11). The meta-analysis focused solely on BMI, and only two of the 10 studies included a racially/ethnically diverse group of youth (12,13). Given previous research indicating significant differences in child body composition based on race/ethnicity and genetics (2), the authors of these studies may have missed significant differences in body composition by only focusing on childhood BMI as the outcome. Additionally, the studies did not look at the interplay of relationships based on child genetic or environmental factors (e.g. diet) with more robust measures of obesity. Thus, there is a need to investigate the

relationship between presence of the *Taq1a* risk allele, environmental factors such as diet and obesity-related outcomes in diverse populations.

Our study objective was to explore the relationships between *Taq1a* polymorphism (rs1800497), diet and obesity-related measures in a multi-ethnic cohort of children. We hypothesize that (i) there will not be a significant relationship between being A1+ and childhood BMI, (ii) we will observe increased reported energy intake and higher adiposity in children who have two *Taq1a* risk alleles relative to those who have less than two risk alleles and (iii) allele frequency differences will vary by child race/ethnicity.

Methods

Study protocol

Participants were 286 children aged 7–12, self-identified as NHB ($n = 98$), NHW ($n = 112$) or HA ($n = 76$) from the Birmingham, Alabama, area. Children were recruited at schools, churches and health fairs and through newspapers, magazines and participant referrals. The children were peripubertal (pubertal stage ≤ 3 as assessed by a paediatrician according to the criteria of Marshall and Tanner) (14,15) and had no medical diagnosis or medications contraindicated for study participation (i.e. medication known to affect metabolism and body composition). Prior to study participation, the children and parents provided informed assent and consent, respectively. Protocol for the AMERICO study was approved by the Institutional Review Board for Human Subjects at the University of Alabama at Birmingham. Subjects participated in two study visits. On the first visit, pubertal status, anthropometrics, questionnaire data, dietary recall and body composition by dualenergy X-ray absorptiometry (DXA) and/or computed tomography (CT) scanning were completed and/or measured. Within 30 days, the children and parents returned for the second visit, where buccal samples for genetic admixture analysis were taken and a second dietary recall was performed.

Anthropometrics

The same registered dietitian obtained anthropometric measurements for all participants. Participants were weighed (Scale-Tronix 6702W, Welch Allyn, Skaneateles Falls, NY, USA) to the nearest 0.1 kg (in minimal clothing without shoes). Height was recorded to the nearest 0.1 cm without shoes using a digital stadiometer (Heightronic 235; Measurement Concepts, Snoqualmie, WA). Children's BMI-for-sex-and-age percentiles (BMI percentile) were calculated as indicated by the Centers for Disease Control and Prevention guidelines (16).

Body composition and fat distribution

Body composition (fat mass, lean mass, body fat percentage [%BF]) was measured by DXA using a GE Lunar Prodigy densitometer (GE LUNAR Radiation Corp., Madison, WI). Participants were scanned in light clothing, lying flat on their backs with arms at their sides. DXA scans were performed and analysed with paediatric software version 1.5e (GE Luna Radiation Corp., Madison, WI, United States of America). DXA has been found to be highly reliable for body composition assessment in children (17). Owing to financial limitations, CT scanning was used to quantify distribution of abdominal adipose tissue as total

abdominal adipose tissue (TAAT), intra-abdominal adipose tissue (IAAT) and subcutaneous abdominal adipose tissue (SAAT) in a subsample of children (n = 209). There were no significant differences in demographic variables between children who were assessed with CT and children who were not assessed via CT. A HiLight/Advantage scanner (General Electric, Milwaukee, WI) was used to perform a single-slice (5-mm) scan of the abdomen at the level of the umbilicus. Scans were analysed for cross-sectional area (cm^2) of adipose tissue using the density contour programme with Hounsfield units for adipose tissue set at –190 to –30. CT has been shown to provide reliable measurements of body fat distribution in children (18).

Dietary recall

Two 24-h diet recalls were administered and analysed by a registered dietitian using the 'multiple pass' method, which provides a cup and bowl to help estimate portion sizes (19). A parent/guardian was present for, and assisted with, each recall, and all 24-h diet recalls were conducted on weekdays. A registered dietitian coded and entered the data into Nutrition Data System for Research version 2006 (Nutrition Coordinating Center, University of Minnesota, Minneapolis, MN). Total energy intake (kcal d^{-1}), carbohydrate (g), % of energy from carbohydrate, protein (g), % of energy from protein, fat (g), % of calories from fat, % of calories from saturated fatty acids, total sugar (g) and % of energy from total sugar were among the variables analysed. It is important to note that we are aware of non-trivial errors associated with self-reported estimates of energy intake and we recognize that this limits the definitive conclusions that can be made from this report alone (20). Rather, we believe this study provides a unique opportunity to explore our hypothesis of interest and to identify, on the basis of our results, potential future hypotheses directed toward the understanding of the physiological differences of individuals who are A1 + (have one or two A1 risk alleles) versus A1 – (have zero A1 risk alleles).

Physical activity assessment

Given that physical activity is inversely associated with weight in children, we examined differences in physical activity between the groups (21). Children wore an MTI ActiGraph accelerometer (GT1M, ActiGraph Health Services, Pensacola, FL) on their waist over the right hip for 7 days to objectively measure physical activity levels (removal was limited to times when the child was sleeping, bathing or swimming). Epoch length was set at 1 min, and physical activity data were expressed as counts per minute (counts min^{-1}). As previously described, the daily counts per minute > 1952 were summed and analysed as the average time children spent in moderate and vigorous physical activity (MVPA) (22).

Socioeconomic status

Socioeconomic status has been associated with body composition in children (3); therefore, SES was used as a covariate in all models related to child adiposity. SES was measured with the Hollingshead four-factor index of social class (23), which combines the educational attainment and occupational prestige for working parents in the child's family. Scores range from 8 to 66, with higher scores indicating higher social status.

Pubertal status and sex

Both pubertal stage and biological sex play a role in adiposity accrual and distribution and were included as covariates in the analysis. Tanner staging is an objective measure of pubertal development and a better predictor of body composition than age (14,15). Direct observation for assessment of pubertal stage by the same paediatrician was used for differentiating among the five stages of maturity, and children at pubertal stage ≤ 3 were included in this study (14,15). Based on the criteria of Marshall and Tanner, pubertal staging was assessed according to both breast and pubic hair development in girls and genitalia and pubic hair development in boys. One composite number is assigned for Tanner staging, representing the higher of the two values defined by breast/genitalia and pubic hair development (14,15).

Genetic admixture

Previous work from our group has demonstrated that ancestral genetic background is associated with fat mass and lean mass in children (2). African admixture (AFADM) and European admixture (EUADM) estimates were used to adjust for the genetic contribution to underlying population variability in body composition (2). Genetic admixture estimates were obtained from genotyping of ~142 ancestry informative markers across the human genome that provide information about European, African and Amerindian parental ancestry for each participant. Genotyping was performed at PreventionGenetics (www.preventiongenetics.org) using the Melting Curve analysis of SNPs (McSNP) method and agarose gel electrophoresis, as previously described (2,24). Individual admixture estimates were derived using maximum likelihood method, which estimates the proportion of genetic ancestry for an individual, using a range of proportions from 0 to 1 and identifies the most probable value of admixture on the basis of the observed genotypes, as previously described (2).

Taq1A genetic variation

Given our hypothesis that we would observe increased reported energy intake and higher adiposity in children who have two *Taq1a* risk alleles relative to those who have less than two risk alleles, each single-nucleotide polymorphism was individually tested using a recessive model for association with each trait, adjusting for age, Tanner stage, sex, MVPA, SES and genetic admixture.

Statistical analysis

Demographic and outcome variables are summarized as mean ± standard deviation for continuous variables, or *n* (%) for categorical variables. Residual analyses were conducted for each outcome to check independence and normality assumptions using the Kolmogorov-Smirnov test. Outcomes that were non-normally distributed were transformed using Box–Cox transformation. General linear regression models were used to assess the association between the predictor of interest and the outcomes, adjusting for covariates including age, sex, MVPA, SES, Tanner stage, AFADM and EUADM. For BMI-for-sex-and-age percentile, age and sex were not included as covariates because BMI percentile is a BMI score already adjusted for age and sex. The recessive model of *Taq1A* polymorphism was tested with variables of interest. The parameter estimate (regression coefficient), standardized parameter

estimate, type I semi-partial ΔR^2 and corresponding *P*-values were reported. Power analyses conducted in QUANTO software indicate 84% power to detect an effect size of $r^2 \geq 3\%$, assuming a recessive genetic model, an allele frequency (A allele) of 33% and a 5% type 1 error rate (25). All analyses were conducted using SAS 9.4 (SAS Institute, Cary, NC). Significance was set at $P \leq 0.05$, two tailed.

Results

The baseline characteristics for participants by race/ethnicity are provided in Table 1. Significant racial/ethnic differences were observed in SES, Tanner stage and BMI percentile. HA children had higher total fat mass, %BF, IAAT, SAAT and TAAT than had NHW and NHB children. There were no significant differences in reported total energy, carbohydrate, fat or sugar consumption between races/ethnicities; however, per cent of energy from carbohydrate and protein consumption and per cent of energy from fat were significantly different by race/ethnicity. Table 2 shows unadjusted baseline characteristics by *Taq1a* polymorphism genotype (AA, AG, GG). Children with two risk alleles have lower SES and higher mean BMI percentile than have children with no risk alleles. With regard to dietary intakes, children with two risk alleles had higher energy, carbohydrate and fat consumption than had children with no risk alleles.

Tables S1 and S2 includes *Taq1a* allele frequency by sex, weight classification and race/ethnicity. AA is indicative of the presence of two risk alleles, AG represents the presence of one risk allele and GG represents zero risk alleles. In the total sample, 12.9% of participants are AA, 39.5% of participants are AG and 47.5% of participants are GG. There were marked differences in weight status depending on *Taq1a* genotype, with 40% of AA, 28% of AG and 20.7% of GG having overweight/obesity. Once stratified by race/ethnicity, 3.6% of NHW, 17.4% of NHB and 21.1% of HA were AA, whereas 96.4% of NHW, 82.7% of NHB and 79% of HA were either AG or GG.

Recessive model results of general linear regression analyses for body composition and dietary characteristics, adjusting for covariates including age, sex, MVPA, SES, Tanner stage, AFADM and EUADM, are shown in Table 3. Children with two risk alleles (AA) had significantly higher BMI percentile ($P = 0.0387$), lean mass (0.0107), fat mass ($P = 0.0145$), %BF ($P = 0.0377$), IAAT ($P = 0.0459$), SAAT ($P = 0.0213$) and TAAT ($P = 0.0209$). Being AA, relative to the AG or GG genotype, was also significantly associated with consuming more energy ($P = 0.0034$) and per cent of total calories from sugar ($P = 0.0077$), equating to an approximately 20% increase in energy and per cent total sugar.

Discussion

The *Taq1a* allele has been implicated in obesity in adults, but questions in children remain regarding its influence on diet and obesity-related outcomes beyond BMI percentile, particularly in racially/ethnically diverse populations. Our results demonstrate that children with two *Taq1a* risk alleles (AA), relative to children with less than two *Taq1a* risk alleles, report consuming a diet significantly higher in total energy intake and per cent of calories from sugar, which could influence obesity-related outcomes. Specifically, having two *Taq1a*

risk alleles, relative to having one or zero *Taq1a* risk alleles, is positively associated with all measures of body composition (including BMI percentile, lean mass, total body fat, %BF, IAAT, SAAT and TAAT). This suggests that children homozygous for the *Taq1a* polymorphism (rs1800497) have reduced body fat and central adiposity, even after controlling for demographic, lifestyle and population genetic factors known to contribute to child body composition. We hypothesize that a reported dietary pattern composed of increased energy intake and a higher percentage of calories derived from sugar may contribute to the less healthy phenotype observed in multi-ethnic children with two *Taq1a* risk alleles.

Children with two *Taq1a* risk alleles reported a 20% increase in total energy intake and per cent of calories from sugar consumed than had children with less than two risk alleles. This is consistent with previous research demonstrating that when adults with type 2 diabetes are randomized to a dietary intervention, small differences are observed in eating behaviour based on *Taq1a* genotype (10). The presence of *Taq1a* risk alleles has also been associated with binge eating in adults (26). The A1 allele of the *Taq1a* polymorphism (rs1800497) is located downstream of *DRD2* and is associated with reduced brain D2 receptor density (8). Relative to lean individuals, individuals with obesity have reduced dopamine D2 receptors (6). The hypothesized mechanism underlying the relationship between eating behaviour and the *Taq1a* polymorphism is that individuals with reduced brain D2 receptor density have hypofunctioning reward circuitry, which leads them to overeat to compensate for a hypofunctioning dopamine reward system (6). Thus, previous work supports our findings that children with two *Taq1a* risk alleles may be more likely to report an energy-dense and sugar-dense diet, increasing their risk for obesity, than are children with one or zero *Taq1a* risk alleles.

Although the *Taq1a* polymorphism may exert some effects through the *DRD2* gene, it is important to note that it is located in exon 8 of the *ANKK1* gene and may thus exert its effect through this gene (27). Further-more, in the Genotype-Tissue Expression (GTEx) data on tissue-specific expression quantitative trait loci (eTLs) data, this polymorphism is most strongly associated with expression of another nearby gene, *TTC12,* in subcutaneous adipose tissue as well as other tissues (27). Further work is thus needed to elucidate the mechanisms linking this polymorphism to dietary behaviour and obesity.

As mentioned in the, a recent meta-analysis including 10 studies on children and adolescents found no relationship between childhood BMI and the *Taq1a* allele (11). However, the objective of four of these studies was not to look at the relationship between childhood BMI and the *Taq1a* allele (28–31). Additionally, two studies only included youth with overweight or obesity (29,32), and only two included racial/ethnic minorities in the study sample (12,13). Our study included a larger sample that was appropriately powered to detect the relationships between *Taq1a* and obesity than did eight out of the 10 included studies in the meta-analysis. Moreover, our analysis included robust measures (DXA and CT scans) to assess body composition and fat distribution. Although the meta-analysis concluded that the presence of *Taq1a* risk alleles in children is not associated with obesity (as measured by BMI), our findings suggest otherwise. Our data add significantly to the literature by demonstrating that having two *Taq1a* risk alleles is associated with increased risk for

increased total body fat and fat deposition in undesirable abdominal regions, which have been associated with increasing a child's cardiometabolic risk. Additionally, we tested these relationships in a multiethnic cohort of children after having controlled for known biological, genetic and environmental factors known to contribute to body composition, of which none of the 10 studies comprehensively controlled for. Regardless, further research should be conducted in larger and more diverse populations of children to confirm our study findings.

This study had many strengths, including a multiethnic sample of children, with a larger sample size than the majority of studies conducted in this area of research. Additionally, Table S1 provides a race-by-genotype display of the study sample that supports previous research results (9), which indicated a significant difference in *Taq1a* genotype by race/ethnicity. Additionally, the majority of previous studies have used anthropometrics (BMI and/or waist circumference) to examine relationships between obesity and *Taq1a* allele in children; hence, our robust measures utilizing DXA and CT scan expand on previous findings. In addition, our analysis accounted for demographics that have been shown to independently contribute to body composition (3). Given the established role of genetics in paediatric body composition, an additional strength of this study includes adjusting for ancestral genetic background (2). The limitations of this study include its cross-sectional design, thus requiring further verification in a longitudinal analysis. Thus, we do not ascribe causality to the relation observed between *Taq1a* allele presence, diet or body composition. Additionally, although we had 84% power to detect an effect size of $r^2 \geq 3\%$, assuming a recessive genetic model, we acknowledge that the sample size is relatively small and further studies are needed to confirm the associations observed in this study.

In summary, our results found that children with two *Taq1a* risk alleles report a diet higher in total energy intake and % of calories from sugar and demonstrate significantly higher total and abdominal body fat than do children with one or no risk alleles. Thus, children with two *Taq1a* risk alleles may be at risk for a more energy-dense and sugar-dense diet and early development of excess adiposity.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgements

MIC, DJL, YCK and JRF designed the research (project conception, development of overall research plan and study oversight). MIC and JRF conducted the research (hands-on conduct of the experiments and data collection). MIC, DJL, YCK and TH analyzsd data or performed statistical analysis. MIC, DJL, AML, DRM, YCK and JRF interpreted data findings. MIC, DJL, AML, DRM and JRF wrote paper. MIC and JRF had primary responsibility for final content. All authors have read and approved the final manuscript.

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Abbreviations:

%BF	body fat percentage
%SFA	% of calories from saturated fatty acids
AFADM	African admixture
BMI percentile	body mass index percentile for age and sex
BMI	body mass index
CT	computed tomography
DRD2	dopamine D2 receptor gene
DXA	dual-energy X-ray absorptiometry
EUADM	European admixture
FM	fat mass
HA	Hispanic-American
IAAT	intra-abdominal adipose tissue
LM	lean mass
MVPA	moderate and vigorous physical activity
NHB	non-Hispanic Black
NHW	non-Hispanic White
SAAT	subcutaneous abdominal adipose tissue
SES	socioeconomic status
SNP	single-nucleotide polymorphism
TAAT	total abdominal adipose tissue

References

1. Ogden CL, Carroll MD, Lawman HG, et al. Trends in obesity prevalence among children and adolescents in the United States, 1988–1994 through 2013–2014. JAMA 2016; 315: 2292 10.1001/jama.2016.6361. [PubMed: 27272581]
2. Cardel M, Higgins PB, Willig AL, et al. African genetic admixture is associated with body composition and fat distribution in a cross-sectional study of children. Int J Obes (Lond) 2011; 35: 60–65. 10.1038/ijo.2010.203. [PubMed: 20877287]
3. Cardel M, Willig AL, Dulin-Keita A, Casazza K, Mark Beasley T, Fernández JR. Parental feeding practices and socioeconomic status are associated with child adiposity in a multi-ethnic sample of children. Appetite 2012; 58: 347–353. 10.1016/j.appet.2011.11.005. [PubMed: 22100186]

4. Schwartz C, King NA, Perreira B, Blundell JE, Thivel D. A systematic review and meta-analysis of energy and macro-nutrient intake responses to physical activity interventions in children and adolescents with obesity. Pediatr Obes 2017; 12: 179–194. 10.1111/ijpo.12124. [PubMed: 26916833]
5. Dunford EK, Popkin BM. 37 year snacking trends for US children 1977–2014. Pediatr Obes May 2017 10.1111/ijpo.12220.
6. Stice E, Yokum S, Zald D, Dagher A. Dopamine-based reward circuitry responsivity, genetics, and overeating. Curr Top Behav Neurosci 2011; 6: 81–93. 10.1007/7854_2010_89. [PubMed: 21243471]
7. Blum K, Thanos PK, Gold MS. Dopamine and glucose, obesity and reward deficiency syndrome. Front Psych 2014; 5 (8). 10.3389/fpsyg.2014.00919.
8. Noble EP, Noble RE, Ritchie T, et al. D2 dopamine receptor gene and obesity. Int J Eat Disord 1994; 15: 205–217. 10.1002/1098-108X(199404)15:3<205::AD-EAT2260150303>3.0.CO;2-P. [PubMed: 8199600]
9. McGuire V, Van Den Eeden SK, Tanner CM, et al. Association of DRD2 and DRD3 polymorphisms with Parkinson's disease in a multiethnic consortium. J Neurol Sci 2011; 307: 22–29. 10.1016/j.jns.2011.05.031. [PubMed: 21663922]
10. Barnard ND, Noble EP, Ritchie T, et al. D2 dopamine receptor Taq1A polymorphism, body weight, and dietary intake in type 2 diabetes. Nutrition 2009; 25: 58–65. 10.1016/j.nut.2008.07.012. [PubMed: 18834717]
11. Benton D, Young HA. A meta-analysis of the relationship between brain dopamine receptors and obesity: a matter of changes in behavior rather than food addiction. Int J Obes (Lond) 2016; 40: S12–S21. 10.1038/ijo.2016.9. [PubMed: 27001642]
12. Hardman CA, Rogers PJ, Timpson NJ, Munafò MR. Lack of association between DRD2 and OPRM1 genotypes and adiposity. Int J Obes (Lond) 2014; 38:730–736. 10.1038/ijo.2013.144. [PubMed: 23917806]
13. Duran-Gonzalez J, Ortiz I, Gonzales E, et al. Association study of candidate gene polymorphisms and obesity in a young Mexican–American population from South Texas. Arch Med Res 2011; 42: 523–531. 10.1016/j.arcmed.2011.10.010. [PubMed: 22056417]
14. Marshall WA, Tanner JM. Variations in pattern of pubertal changes in girls. Arch Dis Child 1969; 44: 291–303 http://www.ncbi.nlm.nih.gov/pubmed/5785179. Accessed October 23, 2017. [PubMed: 5785179]
15. Marshall WA, Tanner JM. Variations in the pattern of pubertal changes in boys. Arch Dis Child 1970; 45: 13–23 http://www.ncbi.nlm.nih.gov/pubmed/5440182. Accessed October 23, 2017. [PubMed: 5440182]
16. Kuczmarski RJ, Ogden CL, Grummer-Strawn LM, et al. CDC growth charts: United States. Adv Data 2000; 314: 1–27 http://www.ncbi.nlm.nih.gov/pubmed/11183293. Accessed October 23, 2017.
17. Elberg J, McDuffie JR, Sebring NG, et al. Comparison of methods to assess change in children's body composition. Am J Clin Nutr 2004; 80: 64–69 http://www.ncbi.nlm.nih.gov/pubmed/15213029. Accessed October 23, 2017. [PubMed: 15213029]
18. Fox KR, Peters DM, Sharpe P, Bell M. Assessment of abdominal fat development in young adolescents using magnetic resonance imaging. Int J Obes (Lond) 2000; 24: 1653–1659. 10.1038/sj.ijo.0801464.
19. Johnson RK, Driscoll P, Goran MI. Comparison of multiple-pass 24-hour recall estimates of energy intake with total energy expenditure determined by the doubly labeled water method in young children. J Am Diet Assoc 1996; 96: 1140–1144. 10.1016/S0002-8223(96)00293-3. [PubMed: 8906138]
20. Schoeller DA, Thomas D, Archer E, et al. Self-report-based estimates of energy intake offer an inadequate basis for scientific conclusions. Am J Clin Nutr 2013; 97: 1413–1415. 10.3945/ajcn.113.062125. [PubMed: 23689494]
21. Chaput JP, Lambert M, Mathieu ME, Tremblay MS, O'Loughlin J, Tremblay A. Physical activity vs. sedentary time: independent associations with adiposity in children. Pediatr Obes 2012; 7: 251–258. 10.1111/j.2047-6310.2011.00028.x. [PubMed: 22461356]

22. Willig AL, Hunter GR, Casazza K, Heimburger DC, Beasley TM, Fernandez JR. Body fat and racial genetic admixture are associated with aerobic fitness levels in a multiethnic pediatric population. Obesity 2011; 19: 2222–2227. 10.1038/oby.2011.109. [PubMed: 21546928]
23. Hollingshead A Four Factor Index of Social Status. Yale University: New Haven, CT, 1975.
24. Fernández JR, Shiver MD. Using genetic admixture to study the biology of obesity traits and to map genes in admixed populations. Nutr Rev 2004; 62: S69–S74. 10.1301/nr.2004.jul.S69-S74. [PubMed: 15387470]
25. Gauderman WJ, Morrison JM. QUANTO 1.1: a computer program for power and sample size calculations for genetic-epidemiology studies. 2006; Available from: http://hydra.usc.edu/gxe.
26. Davis C, Levitan RD, Yilmaz Z, Kaplan AS, Carter JC, Kennedy JL. Binge eating disorder and the dopamine D2 receptor: genotypes and sub-phenotypes. Prog Neuro-Psychopharmacology Biol Psychiatry 2012; 38: 328–335. 10.1016/j.pnpbp.2012.05.002.
27. Consortium GT. Genetic effects on gene expression across human tissues. Nature 2017; 550: 204. [PubMed: 29022597]
28. Stice E, Spoor S, Bohon C, Small DM. Relation between obesity and blunted striatal response to food is moderated by TaqlA A1 allele. Science (80-) 2008; 322: 449–452. 10.1126/science.1161550.
29. Epstein LH, Dearing KK, Erbe RW. Parent–child concordance of Taq1 A1 allele predicts similarity of parent–child weight loss in behavioral family-based treatment programs. Appetite 2010; 55: 363–366. 10.1016/j.appet.2010.06.006. [PubMed: 20561550]
30. Stice E, Yokum S, Bohon C, Marti N, Smolen A. Reward circuitry responsivity to food predicts future increases in body mass: moderating effects of DRD2 and DRD4. Neuroimage 2010; 50: 1618–1625. 10.1016/j.neuroimage.2010.01.081.
31. Yokum S, Marti CN, Smolen A, Stice E. Relation of the multilocus genetic composite reflecting high dopamine signaling capacity to future increases in BMI. Appetite 2015; 87: 38–45. 10.1016/j.appet.2014.12.202. [PubMed: 25523644]
32. Roth CL, Hinney A, Schur EA, Elfers CT, Reinehr T. Association analyses for dopamine receptor gene polymorphisms and weight status in a longitudinal analysis in obese children before and after lifestyle intervention. BMC Pediatr 2013; 13: 197 10.1186/1471-2431-13-197. [PubMed: 24283216]

Table 1

Sample demographics by race/ethnicity (mean, standard deviation)

Characteristic	Total sample	Non-Hispanic White	Non-Hispanic Black	Hispanic-American	*P*-value
n (%)	286 (100.0)	112 (39.2)	98 (34.3)	76 (26.6)	
Age (years)	9.6 (1.6)	9.7 (1.6)	9.6 (1.5)	9.4 (1.6)	0.4497
Male (*n*, %)	152 (53.1)	59 (52.7)	53 (54.1)	40 (52.6)	0.9768
Socioeconomic status	38.7 (14.1)	49 (9.5)	36.9 (11.0)	25.8 (11.6)	<0.0010
Tanner stage	1.5 (0.8)	1.4 (0.6)	1.8 (0.9)	1.4 (0.7)	0.0006
BMI percentile	66.1 (26.4)	59.6 (26.7)	63 (27.9)	79.7 (18.2)	<0.0001
Lean mass (kg)	25.8 (5.3)	25.5 (5.0)	26.9 (5.5)	24.8 (5.1)	0.0312
Fat mass (kg)	8.9 (5.8)	8.3 (5.2)	7.8 (5.9)	11.2 (5.9)	<0.0001
Body fat (%)	22.9 (9.2)	21.9 (8.5)	19.6 (9.0)	28.2 (8.1)	<0.0001
IAAT (cm^2)	33.4 (22.7)	34.8 (22.7)	26.6 (18.6)	42.9 (25.1)	<0.0001
SAAT (cm^2)	92.6 (75.7)	87.1 (74.4)	78.1 (78.8)	123.1 (64.2)	<0.0001
TAAT (cm^2)	126.2 (95.0)	121.9 (94.9)	104.7 (94.1)	166 (85.8)	<0.0001
Total energy (kcal d^{-1})	1883.4 (463.3)	1876.3 (404.8)	1893.1 (528.4)	1881.2 (460.1)	0.8988
Carbohydrate (g)	241 (68.5)	248.7 (60.3)	234.8 (74.6)	237.6 (71.3)	0.1849
% of energy from carbohydrate	51.2 (7.7)	53 (6.7)	49.8 (8.2)	50.5 (8.2)	0.0095
Protein (g)	69.6 (20.8)	66.2 (18.2)	67.6 (20.7)	77.4 (22.6)	0.0012
% of energy from protein	15 (3.3)	14.3 (3)	14.5 (3.3)	16.6 (3.4)	<0.0001
Fat (g)	73.7 (23.9)	71.3 (20.6)	78.2 (28)	71.4 (22.4)	0.1352
% of energy from fat	35 (6.2)	34.1 (5.6)	36.7 (6.2)	34.0 (6.5)	0.0086
% of energy from SFA	12.5 (2.6)	12.5 (2.7)	12.4 (2.4)	12.6 (2.7)	0.9046
Total sugar (g)	111.8 (42.6)	116.2 (36.7)	108.8 (46.3)	109.2 (45.6)	0.1384
% of energy from total sugar (g)	5.9 (1.7)	6.2 (1.5)	5.8 (1.8)	5.8 (1.8)	0.0980

BMI, body mass index; IAAT, intra-abdominal adipose tissue; SAAT, subcutaneous abdominal adipose tissue; SFA, saturated fatty acids; TAAT, total abdominal adipose tissue.

Table 2

Sample demographics by *Taq1a* polymorphism (rs1800497) of the D2 receptor (*DRD2*) gene, unadjusted results (mean, standard deviation)

Characteristic	AA	AG	GG	*P*-value
n (%)	37 (12.9)	113 (39.5)	136 (47.6)	
Age (years)	9.4 (1.5)	9.6 (1.7)	9.6 (1.5)	0.5854
Male (*n*, %)	21 (56.8)	59 (52.2)	72 (52.9)	0.9182
Socioeconomic status	33.9 (14.6)	36.3 (14.3)	41.9 (13.2)	0.0007
Tanner stage	1.4 (0.7)	1.6 (0.8)	1.5 (0.7)	0.2613
BMI percentile	76.2 (20.4)	64.8 (26.9)	64.4 (27.1)	0.034
Lean mass (kg)	26.9 (5.7)	25.5 (5.4)	25.7 (5.0)	0.461
Fat mass (kg)	10.4 (6.4)	8.4 (5.3)	8.9 (6)	0.1136
Body fat (%)	24.9 (8.6)	22.2 (8.8)	22.8 (9.7)	0.2077
IAAT (cm^2)	39.4 (30.3)	28.7 (16.1)	36 (24.3)	0.0543
SAAT (cm^2)	113.2 (102.2)	80.8 (57)	96.5 (79.7)	0.2596
TAAT (cm^2)	152.6 (126.4)	109.5 (69.6)	132.5 (101.5)	0.2096
Energy (kcal d^{-1})	2107 (562.0)	1871 (453.7)	1832.8 (426.2)	0.0091
Carbohydrate (g)	275.4 (91.4)	235.7 (62.9)	236 (63.3)	0.0285
% of energy from carbohydrate	51.8 (7.6)	50.6 (7.9)	51.6 (7.7)	0.632
Protein (g)	75.7 (21.1)	70.8 (21.2)	67 (20.1)	0.0391
% of energy from protein	14.8 (3.4)	15.4 (3.5)	14.8 (3.2)	0.684
Fat (g)	81.1 (24.2)	74.1 (25.2)	71.4 (22.4)	0.035
% of energy from fat	34.7 (5.7)	35.2 (6.3)	34.8 (6.2)	0.7878
% of energy from SFA	12.5 (2.4)	12.6 (2.7)	12.4 (2.6)	0.7626
Total sugar (g)	125.5 (59.4)	110.2 (39.6)	109.5 (39.0)	0.3166
%Energy from total sugar	5.9 (1.8)	5.9 (1.7)	6.0 (1.7)	0.7116

BMI, body mass index; IAAT, intra-abdominal adipose tissue; SAAT, subcutaneous abdominal adipose tissue; SFA, saturated fatty acids; TAAT, total abdominal adipose tissue.

Table 3

Association of the *Taq1a* polymorphism (rs1800497) with body composition and dietary characteristics

Dependent	SE	Standardized estimate	*P*-value
Body composition			
BMI percentile	9.2	0.1	0.0387
Lean mass (kg)	0.0	0.1	0.0107
Fat mass (kg)	0.1	0.1	0.0145
Body fat (%)	0.1	0.1	0.0377
IAAT (cm^2)	0.2	0.1	0.0459
SAAT (cm^2)	0.2	0.2	0.0213
TAAT (cm^2)	0.2	0.2	0.0209
Dietary			
Energy (kcal d^{-1})	27.8	0.2	0.0034
%Carbohydrate	1.4	0.1	0.2532
%Protein	0.1	−0.1	0.2271
%Fat	0.0	0.0	0.5399
%SFA	0.1	0.0	0.9712
%Total sugar	7.8	0.2	0.0077
Total sodium	0.1	0.1	0.1074

BMI, body mass index; IAAT, intra-abdominal adipose tissue; SAAT, subcutaneous abdominal adipose tissue; SFA, saturated fatty acids; TAAT, total abdominal adipose tissue.