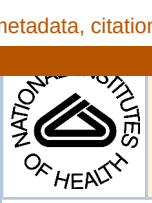



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# D2 Dopamine receptor Taq1A polymorphism, body weight, and dietary intake in type 2 diabetes

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## Abstract

**OBJECTIVE—**Certain D2 dopamine receptor Taq 1A genotypes (A1A1, A1A2) have been associated with obesity and substance abuse. We hypothesized that their presence would be associated with reduced efficacy of dietary interventions in individuals with type 2 diabetes.

**RESEARCH METHODS & PROCEDURES—**In the course of a randomized clinical trial in an outpatient research center in which 93 adults with type 2 diabetes were assigned to a low-fat vegan diet or a diet following 2003 American Diabetes Association guidelines for 74 weeks, Taq 1A genotype was determined. Nutrient intake, body weight, and hemoglobin A1c (A1c) were measured over 74 weeks.

**RESULTS—**The A1 allele was highly prevalent, occurring in 47% of white participants (n = 49), which was significantly higher than the 29% prevalence previously reported in nondiabetic whites (P=0.01). The A1 allele was found in 55% of black participants (n = 44). Black participants with A1 + genotypes had significantly greater mean body weight (11.2 kg heavier, P=0.05), and greater intake of fat (P=0.002), saturated fat (P=0.01) and cholesterol (P=0.02), compared with A2A2 (A1-) individuals; dietary changes during the study did not favor one genotype group. Among whites, baseline anthropometric and nutrient differences between gene groups were small. However, among

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whites in the vegan group, A1+ individuals reduced fat intake (P=0.04) and A1c (P=0.01) significantly less than did A1- individuals.

**CONCLUSIONS—**The A1 allele appears to be highly prevalent among individuals with type 2 diabetes. Potential influences on diet, weight, and glycemic control merit further exploration.

### Keywords

dopamine; DRD2; diabetes; vegetarian diet

## INTRODUCTION

The A1 allele of the Taq1A polymorphism (rs1800497), located ≈10 kb downstream of the D2 dopamine receptor (DRD2) gene (1), has been investigated for possible associations with habitual use of alcohol (2,3), cocaine (4), nicotine (5-8), and opioids (9). Evidence indicates that individuals carrying this allele have reduced brain D2 receptor density, compared with other individuals (10-13). It has been suggested that persistent substance abuse in individuals with the A1 allele may be a form of self-stimulatory behavior that compensates for insufficient dopamine activity (14).

The A1 allele is also associated with obesity (15-17). Food consumption, like use of alcohol and drugs of abuse, increases dopamine concentrations in the nucleus accumbens (18), activating the mesocortiolimbic dopaminergic reward pathways of the brain (19), resulting in the reinforcing effects of euphoria or pleasure.

Among the sequelae of obesity is type 2 diabetes, and altering dietary habits is an important focus of diabetes treatment. Surprisingly, no data are available on the prevalence of the A1 allele or its possible influences on dietary behavior among individuals with type 2 diabetes. We therefore sought to assess the prevalence of the A1 allele among individuals with diabetes and to explore whether individuals with the A1 allele would show differences in dietary habits or be less likely to adhere to therapeutic diets, compared with other individuals. In the course of a dietary trial among individuals with type 2 diabetes, we investigated the distribution of DRD2 genotypes and examined their associations with dietary intake and clinical outcomes.

## MATERIALS AND METHODS

### Participants

The methods for the overall study have been previously described (20). Briefly, individuals with type 2 diabetes mellitus, defined by a fasting plasma glucose concentration ≥126 mg/dl on 2 occasions or a prior physician's diagnosis of type 2 diabetes with the use of hypoglycemic medications for at least 6 months, were recruited through newspaper advertisements in the Washington, D.C., area. Exclusionary criteria included hemoglobin A1c (A1c) values <6.5% or >10.5%, use of insulin for >5 years, tobacco use within the preceding 6 months, alcohol or drug abuse, pregnancy, unstable medical status, and current use of a low-fat, vegetarian diet. Definition of race/ethnicity was required by the National Institutes of Health to ascertain balance in group assignments and assess the degree to which the participant sample reflected the community from which it was drawn. Participants were asked to describe themselves as white; black; American Indian, Eskimo, Aleut; or Asian, Pacific Islander; and describe their ethnicity as either Hispanic or non-Hispanic. The protocol was approved by the George Washington University Institutional Review Board. All participants gave written informed consent.

After medical history and physical examination, blood samples were drawn and A1c was assayed using affinity chromatography on an Abbott IMx analyzer (21). Volunteers were then ranked in order of A1c concentrations. Using a computer-generated random-number table, we randomly assigned participants in sequential pairs to a low-fat, vegan diet or a diet following 2003 ADA guidelines (22). Genomic DNA was extracted from participants' blood samples using standard methods. The PCR method for determining DRD2 Taq IA genotypes has been previously described (23). Two alleles were found: A1 [310 b.p.] and A2 [180 b.p. and 130 b.p.] alleles. Participants were considered A1+ if they carried the A1A1 or A1A2 genotype. Participants were considered A1- if they carried the A2A2 genotype. Genotype was not considered in the randomization process.

## Intervention

The vegan diet (approximately 10% of energy from fat, 15% protein, 75% carbohydrate) consisted of vegetables, fruits, grains, and legumes. Animal products were proscribed, and added oils, avocados, olives, nuts, nut butters, and seeds were discouraged to reduce the fat and energy content of the diet. Vegan-group participants were also asked to favor low-glycemic-index foods (24), such as beans and green leafy vegetables. Portion sizes, energy intake, and carbohydrate intake were not limited.

For ADA group participants, dietary energy, carbohydrate, and monounsaturated fat content were individualized, based on each participant's need to reduce body weight and plasma lipid concentrations, following ADA guidelines (22). The diet derived 15-20% of energy from protein and <7% of energy from saturated fats. Carbohydrate and monounsaturated fats together provided 60-70% of energy intake. Dietary cholesterol was limited to 200 mg/day. ADA-group participants with a body mass index >25 $kg/m^2$ were prescribed energy intake limits set at 500-1000 kcal below those estimated as required for weight maintenance. Because the purpose of the overall study was to compare the two diets' effects on glycemia, weight, and lipid control, recognizing that the diets may achieve these ends by different mechanisms, the two diets were not designed to be isocaloric.

All participants were provided a vitamin $B_{12}$ supplement (100 mcg, to be taken every other day). For both groups, alcoholic beverages were limited to 1 drink per day for women, and 2 drinks per day for men.

No meals were provided. Participants were asked not to alter their exercise habits during the initial 22 weeks of the intervention period.

Each participant met with a registered dietitian for 1 hour to establish a diet plan consistent with the assigned diet guidelines. Thereafter, participants attended weekly 1-hour meetings of their assigned groups for nutrition and cooking instruction and group discussions for 22 weeks. For the following 52 weeks, these sessions were biweekly. **A** 3-day dietary record was completed by each participant at weeks 0, 11, 22, and 74 on 2 weekdays and 1 weekend day, using a food scale, after participants had completed a practice record for 3 days. Using the Nutrition Data System for Research software version 5.0, developed by the Nutrition Coordinating Center, University of Minnesota, Minneapolis, MN, Food and Nutrient Database 35 (25), released May 2004, a registered dietitian certified by the Nutrition Coordinating Center analyzed all 3-day dietary records and diet recalls.

Participants were asked to maintain their use of medications as prescribed by their personal physicians prior to the study, except when fasting plasma glucose fell below 4.4 mmol/L (80 mg/dl) or hypoglycemic symptoms were accompanied by a capillary glucose reading <3.6 mmol/L.(65 mg/dl). In such cases, medications were reduced for participant safety by a study endocrinologist, who remained blind to group assignment, following an established protocol.

Body weight was determined at weeks 0, 22, and 74, before breakfast while participants wore hospital gowns, using a digital scale accurate to 0.1 kg. Waist circumference was measured with a tape measure placed 2.5 cm above the umbilicus. Hip circumference was measured at the maximal protrusion of the buttocks. Values were rounded to the nearest 0.5 cm.

A1c was measured with method described above at weeks 0, 11, 22, 35, 48, 61, and 74, after a 12-hour fast, by technicians blind to group assignment.

### Statistical Analyses

Data analyses for the current report were limited to black or white participants, due to small numbers of individuals of other races, and data were analyzed separately for black and white participants. We compared the prevalence of the A1+ genotypes among white participants in the present sample to that previously found among demographically comparable groups of nondiabetic white individuals (26), using a Chi-Square test for proportions. Similar previous comparative data were not available for black participants.

Between-subjects t-tests were calculated for each measure to determine whether baseline characteristics among participants with the A1- genotype differed from those of participants with the A1+ genotypes. The relationship of the A1 genotypes with weight or BMI was assessed using linear regression analysis, controlled for age and sex.

Exploratory analyses were conducted for associations between genotype and dietary or clinical changes during the study, but were interpreted cautiously, due to small numbers in some cells. Paired comparison t-tests were calculated to test whether the change from baseline to 74 weeks was significantly different from zero. To assess differences between A1+ and A1- genotype groups in the changes from baseline to 74 weeks, we conducted multiple regression models to examine the effects of race (black or white), diet group (vegan or ADA), and genotype (A1+ or A1-) on nutrient intake changes and on clinical measure changes (SAS PROC GLM). Based on these regressions, we conducted additional t-test comparisons of A1- and A1+ participants within racial and diet groups.

The primary analysis of the main end-point included all participants. Because medication changes influence the dependent measures, A1c changes were also analyzed for changes from baseline to the last value before any alteration in hypoglycemic medications. An alpha of 0.05 was used for all statistical tests, with no adjustment for multiple comparisons.

## RESULTS

Of 1,049 individuals initially screened by telephone, 99 met study criteria and were randomly assigned to the vegan (n = 49) and ADA (n = 50) diet groups. Reasons for exclusion were: A1c values outside the required range (n = 201), failure to meet other participation criteria (n = 279), inability to attend scheduled meetings (n = 187), failure to keep interview appointment (n = 153), reluctance to change diet (n = 72), and other or unspecified (n = 58). Limiting the present study to black or white individuals, the population included 44 black and 49 white participants. The sample was predominantly female, married, and well-educated (Table I). There were no significant demographic differences between A1- and A1+ participants.

Six A1- and 6 A1+ participants failed to complete laboratory assessments at 74 weeks and 9 A1- participants and 7 A1+ participants failed to complete 74-week dietary records. There were no significant differences between these individuals and study completers. During the 74-week study period, 39% (18/46) of A1- participants and 49% (23/47) of A1+ participants altered their diabetes medications, either as prescribed by the study protocol or without investigators' authorization.

### Prevalence of A1+ Genotypes

The A1+ genotypes were highly prevalent among both white and black participants. Among the 49 whites, the overall prevalence was 47%. The genotype distribution was 4 A1A1 (8%); 19 A1A2 (39%); and 26 A2A2 (53%). This prevalence was significantly higher than the 29% prevalence previously reported in whites without diabetes (p=0.01) (26), and was not significantly different from the reported prevalence of these genotypes in white substance abusers (26).

Among the 44 blacks, the A1+ genotype prevalence was 55%. The distribution was 5 A1A1 (11%); 19 A1A2 (43%); and 20 A2A2 (45%) (These numbers sum to less than 100%, due to rounding). Comparison data on the prevalence of the A1+ genotypes among blacks without diabetes are not available. The DRD2 genotype distribution was in Hardy-Weinberg equilibrium in both black (p = 0.88) and white (p = 0.84) participants.

### Diet and Body Weight

Black A1+ participants were, on average, more than 11 kg heavier than A1- participants at baseline (110.4 kg vs 99.2 kg, P = 0.05), and ate significantly more fat, saturated fat, and cholesterol, and less carbohydrate, compared with A1- participants (Table II). Among whites, baseline carbohydrate intake was higher among A1+ participants, but other baseline nutritional and anthropometric differences were not significant.

Among blacks, the A1+ genotypes were identified in 0% (0/2) of participants with BMI <25.0, 40% (2/5) with BMI = 25.0-29.9, 29% (2/7) with BMI = 30.0-34.9, 63% (12/19) with BMI = 35.0-39.9, and 73% (8/11) with BMI >40.0. Among whites, A1+ genotypes were identified in 50% (2/4) of participants with BMI <25.0, 62% (8/13) with BMI = 25.0-29.9, 31% (4/13) with BMI = 30.0-34.9, 38% (5/13) with BMI = 35.0-39.9, and 67% (4/6) with BMI >40.0. The trend of higher A1 prevalence among higher BMI categories did not reach statistical significance.

A series of linear regressions assessed the association of the A1+ genotypes with weight and BMI, while controlling for age and for sex. In the initial models, age, but not sex, was associated with weight and BMI. When the A1+ genotype was added to the models, age continued to be associated with weight and BMI, but there was no association for genotype.

### Exploratory Analyses of Clinical and Dietary Changes

Exploratory analyses examined clinical and dietary changes that occurred during the course of the dietary intervention. For the vegan group, the reduction in A1c was significantly greater among A1-, compared to A1+, white participants (-0.89 vs. -0.02, P=0.01). Other anthropometric and glycemic changes were also generally greater among A1- participants, compared with A1+ participants, for both blacks and whites assigned to the vegan diet (Table III), but subgroup samples were small and most differences did not reach statistical significance. In the ADA diet group, there were no significant differences in anthropometric or clinical variables between A1- and A1+ participants. Using the regression models, neither diet group nor DRD2 genotype status was a significant predictor of A1c change in either blacks or whites.

Changes in energy and fat intake are depicted in Table IV. In the regression model for nutrient intake changes, diet group was associated with changes in fat, saturated fat, cholesterol, protein, carbohydrates, and fiber (all p <0.01 or lower). There was an interaction of race and the A1+ genotype as a predictor of change in fat intake (P=0.02): Blacks with A1+ genotypes reduced fat intake more than did those with the A1- genotype; whites with A1+ genotypes reduced fat intake less than did those with the A1- genotype.

### Comparisons of the 2 Diets within Genotype Groups

The differences between the clinical effects of the vegan and ADA diets were strongly apparent among the individuals with the A1- genotype of both races, but were greatly blunted among those with the A1+ genotypes (Table V).

For both races, among individuals with the A1- genotype, the vegan diet was associated with a greater A1c reduction (from baseline to the final value), compared to the ADA diet. The weight change among black A1- participants associated with the vegan diet was also much greater than in the ADA group (-8.2 kg vs +0.6 kg, p=0.02).

In contrast, among A1+ individuals, the differences in A1c changes between the two diet groups were not significant. In black A1+ participants and white A1- and A1+ participants, differences in weight change between groups did not reach significance.

## DISCUSSION

The A1 allele prevalence was strikingly high in this sample of individuals with type 2 diabetes, being identified in approximately half of all participants. In whites, this prevalence was significantly higher than has been reported among whites without diabetes and was similar to that observed in substance-abusing populations (26). The A1 allele prevalence was high in black participants, as well, although comparison data for blacks without diabetes are not available.

Body weight and intake of fat, saturated fat, and cholesterol were higher among blacks with the A1 allele, compared with A1- participants. This dietary pattern difference was not evident among whites, although A1+ whites ate more carbohydrate, compared with A1- whites, and the A1+ individuals assigned to the vegan group were less successful in reducing fat intake and A1c, compared with A1- individuals.

These findings raise the question as to whether diabetes, or the eating habits and elevated body weight that contribute to it for some individuals, are in part the result of genetic contributors that have commonalities with addictive disorders.

The Taq1A polymorphism is located ≈10 kb downstream of the DRD2 gene (1). The A1 allele has been shown to be associated with low D2 dopamine receptor density in positron emission tomography studies (10) and with a significantly lower mean relative glucose metabolic rate in dopaminergic regions in the human brain (27). The allele has been associated with habitual use of alcohol (2,3), cocaine (4), nicotine (5-7), and opioids (9), although some studies have not supported these findings (8,28,29).

Kidd studied a four-site haplotype system, including three Taq1 restriction site polymorphisms (Taq1A, B, and D) and one dinucleotide short tandem repeat polymorphism, in 28 distinct populations, demonstrating the highest average heterozygosity in Africa, with lower average heterozygosity in Europe, East Asia, and the Americas (30). This pattern suggests that homo sapiens carried the haplotypes out of Africa, with successively less variation as they branched out to the east and eventually to the Americas.

The role of dopamine in the brain's reward and pleasure systems and in addictive behavior—including dietary behavior—has been the subject of extensive research. Dopamine is involved in appetite regulation, and genes regulating its availability influence eating behavior. (31,32) However, the relationship between the DRD2 receptor and body weight is not simple or direct. Evidence suggests that the A1 allele may be associated with an exaggerated reinforcing effect of food or other psychological traits that, in turn, lead to pathological eating behavior. (33,

34) Some have hypothesized that a dopaminergic deficit may lead to overeating as a form of stimulus-seeking behavior (14). In turn, overeating may lead to weight gain and higher risk of diabetes.

Some forms of disordered eating behavior, particularly compulsive eating, have been likened to substance abuse, and there is a substantial comorbidity between these conditions (35). Indeed, some evidence suggests that some foods (sugar, cheese, and meat—which were proscribed on the low-fat, low-glycemic-index, vegan diet) have qualities akin to addictive substances among some individuals (36,37).

If persistent food habits that lead to diabetes have similarities to substance abuse for some individuals, dietary treatments may be more effective to the extent they use approaches that have been helpful for substance abuse. These might include group support, family involvement, and dietary interventions based on elimination of problem foods, rather than attempts to moderate their intake. These considerations suggest that a vegan diet should be more effective than the ADA diet. However, it was only in the A1- individuals where the two diets diverged significantly in their effects on glycemic control.

If individuals with the A1 allele are prone to overeating, this may suggest that a caloric restriction may be helpful in limiting this behavior. However, our results provide no clear support for such an intervention. Among A1+ participants, weight loss was not significantly greater in the ADA group, which included an energy restriction for overweight individuals, compared with the vegan group, which did not. It remains an open question whether individuals with disordered eating behavior are better able to conform to a quantitative restriction on food intake, such as the calorie limit used in the ADA group, or to qualitative restrictions, such as the exclusion of certain types of food as was required by the vegan diet.

Although the strikingly high prevalence of the A1+ genotypes in our study population supports the possibility that variations in dopaminergic activity may influence the likelihood that diabetes will manifest in genetically predisposed individuals, this finding does not settle the question as to whether this relationship is mediated by dietary differences. Factors other than diet may contribute to the apparent relationship between dopaminergic activity and diabetes. Dopamine plays a key role in the central regulation of insulin action; bromocriptine, a D2 dopamine receptor agonist, significantly reduces A1c in individuals with type 2 diabetes (38).

Despite abundant prior research on associations between the A1 allele and substance abuse and eating disorders, this is, to our knowledge, the first report of A1 allele prevalence in individuals with diabetes. However, the present study has several limitations. Because the overall study was designed to assess the effect of therapeutic diets on glycemic control, genetic factors were not considered in either the determinations of sample size or the randomization process. While this was less of a problem for baseline determinations, sample size was small for specific racial and genetic groups after randomization to diet assignments. Because randomization was done before genotyping, the two diet groups did not have equal distributions of the represented genotypes. Dietary intake was determined based on 3-day dietary records, which rely on self report. Finally, while we asked participants to avoid medication changes, many participants altered their diabetes medications due to hypoglycemia or other reasons. This is an inherent problem in diabetes research, and, in the present study, necessitated analyses accounting for medication changes.

## CONCLUSION

The A1 allele of the Taq1A polymorphism appears to be highly prevalent in individuals with type 2 diabetes, similar to its prevalence in substance-abusing populations. The possibility that

this allele may influence eating habits, body weight, or response to dietary treatment for diabetes merits further investigation in larger populations.

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## TABLE I

BASELINE DEMOGRAPHICS

| | | A1- | A1+ | P-value |
|---|---|---|---|---|
| **Black Participants** | | | | |
| **N** | | 20 | 24 | |
| **Mean age, range (years)** | | 51.1 | 51.4 | 0.92 |
| **Sex** | | | | 0.51 |
| | Male | 6 | 8 | |
| | Female | 14 | 16 | |
| **Marital status** | | | | 0.37 |
| | Not married | 12 | 12 | |
| | Married | 8 | 12 | |
| **Education** | | | | 0.13 |
| | High school, partial or graduate | 0 | 4 | |
| | College, partial or graduate | 13 | 12 | |
| | Graduate degree | 7 | 8 | |
| **Occupation** | | | | 0.28 |
| | Service occupation | 4 | 2 | |
| | Technical, sales, administrative | 5 | 10 | |
| | Professional or managerial | 9 | 7 | |
| | Retired | 2 | 5 | |
| **White Participants** | | | | |
| **N** | | 26 | 23 | |
| **Mean age, range (years)** | | 59.8 | 57.9 | 0.52 |
| **Sex** | | | | 0.66 |
| | Male | 12 | 11 | |
| | Female | 14 | 12 | |
| **Marital status** | | | | 0.63 |
| | Not married | 11 | 9 | |
| | Married | 15 | 14 | |
| **Education** | | | | 0.29 |
| | High school, partial or graduate | 3 | 2 | |
| | College, partial or graduate | 15 | 9 | |
| | Graduate degree | 8 | 12 | |
| **Occupation** | | | | 0.38 |
| | Service occupation | 3 | 1 | |
| | Technical, sales, administrative | 11 | 6 | |
| | Professional or managerial | 7 | 9 | |
| | Retired | 5 | 7 | |

## TABLE II

BASELINE DIETARY AND CLINICAL CHARACTERISTICS*

| | | A1- | A1+ | P-value† |
|---|---|---|---|---|
| **Black Participants** | | | | |
| **N** | | 20 | 24 | |
| **Dietary Intake (per day)** | Energy (kilocalories) | 1644 (100) | 1909 (115) | 0.10 |
| | Fat (% energy) | 34.7 (1.5) | 41.7 (1.5) | 0.002 |
| | Saturated fat (% energy) | 10.5 (0.6) | 12.7 (0.6) | 0.01 |
| | Carbohydrate (% energy) | 47.6 (1.7) | 41.4 (1.8) | 0.02 |
| | Protein (% energy) | 18.5 (1.3) | 17.0 (0.6) | 0.30 |
| | Sugar (% energy) | 18.4 (1.2) | 16.1 (1.2) | 0.20 |
| | Fiber (g/1000 kcal) | 11.0 (1.0) | 9.5 (0.8) | 0.24 |
| | Cholesterol (mg/1000 kcal) | 144 (13) | 197 (16) | 0.02 |
| **Weight (kg)** | | 99.2 (4.8) | 110.4 (3.1) | 0.05 |
| **BMI (kg/m$^2$)** | | 36.1 (2.0) | 38.7 (1.2) | 0.28 |
| **Waist circumference (cm)** | | 111.3 (3.7) | 118.2 (2.5) | 0.12 |
| **Hip circumference (cm)** | | 120.6 (3.6) | 128.3 (2.4) | 0.07 |
| **A1c (%)** | | 8.15 (0.3) | 7.86 (0.2) | 0.36 |
| **White Participants** | | | | |
| **N** | | 26 | 23 | |
| **Dietary Intake (per day)** | Energy (kilocalories) | 1793 (97) | 1871 (131) | 0.63 |
| | Fat (% energy) | 36.3 (1.4) | 32.8 (1.5) | 0.09 |
| | Saturated fat (% energy) | 12.0 (0.7) | 11.0 (0.7) | 0.31 |
| | Carbohydrate (% energy) | 44.7 (2.0) | 50.7 (1.6) | 0.03 |
| | Protein (% energy) | 20.0 (1.0) | 17.9 (0.6) | 0.09 |
| | Sugar (% energy) | 17.3 (1.3) | 17.8 (1.5) | 0.82 |
| | Fiber (g/1000 kcal) | 11.6 (0.9) | 11.0 (1.0) | 0.63 |
| | Cholesterol (mg/1000 kcal) | 179 (16.7) | 151 (22.9) | 0.32 |
| **Weight (kg)** | | 94.8 (4.4) | 92.2 (5.0) | 0.70 |
| **BMI (kg/m$^2$)** | | 33.3 (1.3) | 32.5 (1.5) | 0.70 |
| **Waist circumference (cm)** | | 110.3 (3.7) | 107.5 (3.6) | 0.59 |
| **Hip circumference (cm)** | | 117.5 (3.0) | 114.8 (3.3) | 0.55 |
| **A1c (%)** | | 8.03 (0.20) | 8.02 (0.25) | 0.97 |

*Mean values. Standard error of the mean is indicated in parenthesis

†P-values for between-group (A1- vs A1+) differences.

**TABLE III**

ANTHROPOMETRIC AND GLYCEMIC MEASURES BY RACE AND GENOTYPE*

| | A1- (A2A2) | | | A1+ (A1A1 or A1A2) | | | |
|---|---|---|---|---|---|---|---|
| **Variable** | **Baseline** | **Final** | **Change** | **Baseline** | **Final** | **Change** | **P-Value†** |
| **Black, Vegan Diet (n = 9 A1-, 13 A1+)** | | | | | | | |
| **Weight (kg)** | 93.5 (7.1) | 85.3 (6.4) | -8.2 (3.3)‡ | 108.0 (4.5) | 107.1 (4.5) | -0.9 (1.1) | 0.07 |
| **Body Mass Index (kg/m$^2$)** | 32.1 (2.2) | 29.3 (2.0) | -2.8 (1.1)‡ | 37.6 (1.9) | 37.2 (1.9) | -0.3 (0.4) | 0.06 |
| **Waist Circumference (cm)** | 105.3 (5.5) | 97.1 (4.9) | -8.2 (3.8) | 117.7 (4.0) | 115.3 (4.0) | -2.3 (1.3) | 0.17 |
| **Hip Circumference (cm)** | 114.2 (5.4) | 108.7 (5.4) | -5.6 (1.9) | 126.0 (4.2) | 125.8 (3.9) | -0.2 (1.0) | 0.01 |
| **A1c (%)** | 8.49 (0.40) | 7.77 (0.40) | -0.72 (0.41) | 8.15 (0.30) | 7.75 (0.33) | -0.40 (0.27) | 0.50 |
| **White, Vegan Diet (n = 9 A1-, 16 A1+)** | | | | | | | |
| **Weight (kg)** | 103.9 (10.2) | 98.6 (11.3) | -5.3 (2.5) | 86.0 (5.3) | 81.5 (5.5) | -4.5 (1.0)‖ | 0.77 |
| **Body Mass Index (kg/m$^2$)** | 35.1 (3.1) | 33.2 (3.5) | -1.9 (1.0) | 30.7 (1.9) | 29.1 (2.0) | -1.7 (0.4)‖ | 0.81 |
| **Waist Circumference (cm)** | 117.3 (8.3) | 111.6 (8.8) | -5.7 (2.2)‡ | 103.0 (4.2) | 100.4 (4.6) | -2.6 (1.4) | 0.21 |
| **Hip Circumference (cm)** | 121.4 (7.2) | 117.3 (7.9) | -4.2 (2.0) | 111.8 (4.5) | 107.5 (4.3) | -4.3 (0.8)¶ | 0.95 |
| **A1c (%)** | 8.11 (0.33) | 7.22 (0.24) | -0.89 (0.27)‡ | 7.80 (0.29) | 7.78 (0.28) | -0.02 (0.18) | 0.01 |
| **Black, ADA Diet (n = 11 A1-, 11 A1+)** | | | | | | | |
| **Weight (kg)** | 103.8 (6.4) | 104.3 (6.4) | +0.6 (1.4) | 113.3 (4.2) | 110.6 (4.6) | -2.7 (1.4) | 0.11 |
| **Body Mass Index (kg/m$^2$)** | 39.4 (2.9) | 39.6 (3.0) | +0.3 (0.6) | 39.9 (1.1) | 39.0 (1.1) | -1.0 (0.5) | 0.10 |
| **Waist Circumference (cm)** | 116.1 (4.7) | 115.1 (4.3) | -1.0 (1.6) | 118.7 (3.0) | 119.0 (2.9) | +0.3 (1.0) | 0.48 |
| **Hip Circumference (cm)** | 125.7 (4.4) | 124.6 (4.4) | -1.1 (1.3) | 131.0 (1.7) | 128.6 (1.7) | -2.3 (0.8) | 0.44 |
| **A1c (%)** | 7.87 (0.34) | 8.37 (0.38) | +0.50 (0.38) | 7.52 (0.19) | 7.51 (0.31) | -0.01 (0.25) | 0.28 |
| **White, ADA Diet (n = 17 A1-, 7 A1+)** | | | | | | | |
| **Weight (kg)** | 90.0 (3.9) | 84.4 (4.4) | -5.5 (1.7)§ | 106.4 (9.3) | 103.4 (9.8) | -3.0 (1.5) | 0.38 |
| **Body Mass Index (kg/m$^2$)** | 32.4 (1.1) | 30.3 (1.3) | -2.0 (0.6)§ | 36.7 (1.7) | 35.5 (1.9) | -1.1 (0.5) | 0.36 |
| **Waist Circumference (cm)** | 106.6 (3.6) | 103.5 (3.6) | -3.1 (1.8) | 117.6 (5.4) | 114.4 (6.3) | -3.3 (1.4) | 0.94 |
| **Hip Circumference (cm)** | 115.4 (2.6) | 111.6 (2.5) | -3.8 (1.5) | 121.6 (2.5) | 120.9 (2.8) | -0.6 (1.1) | 0.21 |
| **A1c (%)** | 7.99 (0.25) | 7.86 (0.27) | -0.13 (0.16) | 8.53 (0.49) | 8.06 (0.49) | -0.47 (0.30) | 0.30 |

*Mean values. Standard error of the mean is indicated in parenthesis.

All entries represent 74-week or last available values, except A1c, which represents last value before any change in hypoglycemic medication.

†P- Values for between-group (A1- vs A1+) comparisons of changes from baseline to final values

‡P < 0.05,

§P < 0.01,

‖P < 0.001,

¶P < 0.0001 for within-group changes

**TABLE IV**

REPORTED ENERGY AND FAT INTAKE*

| | A1- (A2A2) | | | A1+ (A1A1 or A1A2) | | | |
|---|---|---|---|---|---|---|---|
| | **Week 0** | **Week 74** | **Change 0-74** | **Week 0** | **Week 74** | **Change 0-74** | **P-value †** |
| **Black, Vegan (6 A1-, 11 A1+)** | | | | | | | |
| Energy (kcal) | 1775 (202) | 979.9 (109.4) | -794.8 (209.5) | 1790.2 (133.6) | 1450.1 (178.4) | -340.1 (195.1) | 0.16 |
| Fat (% energy) | 32.8 (2.8) | 22.4 (3.5) | -10.4 (4.9) | 43.9 (1.9) | 27.2 (3.5) | -16.6 (4.3)§ | 0.38 |
| **White, Vegan (6 A1-, 15 A1+)** | | | | | | | |
| Energy (kcal) | 1890.8 (204.0) | 1328.8 (211.3) | -562.0 (153.3) | 1813.9 (121.3) | 1412.5 (118.7) | -401.3 (95.1) | 0.38 |
| Fat (% energy) | 39.2 (2.9) | 17.7 (3.5) | -21.4 (5.6)‡ | 32.8 (1.7) | 21.3 (1.7) | -11.4 (1.9) † | 0.04 |
| **Black, ADA (9 A1-, 9 A1+)** | | | | | | | |
| Energy (kcal) | 1635.2 (152.2) | 1383.4 (197.6) | -251.9 (221.5) | 2148.3 (219.3) | 1544.9 (139.1) | -603.4 (134.1) | 0.19 |
| Fat (% energy) | 34.5 (1.8) | 37.7 (3.3) | +3.1 (4.3) | 39.2 (3.0) | 34.8 (2.8) | -4.5 (3.5) | 0.19 |
| **White, ADA (16 A1-, 5 A1-)** | | | | | | | |
| Energy (kcal) | 1816.0 (128.9) | 1303.1 (67.9) | -512.9 (94.1) | 2037.9 (444.0) | 1660.7 (246.5) | -377.1 (325.9) | 0.58 |
| Fat (% energy) | 35.1 (1.7) | 31.8 (1.9) | -3.3 (2.5) | 34.2 (3.9) | 32.4 (4.4) | -1.9 (4.9) | 0.79 |

*Mean values. Standard error of the mean is indicated in parenthesis. Data are limited to individuals with records at both time points.

†P- Values for between-group (A1- vs A1+) comparisons of changes from baseline to 74 weeks

‡P < 0.05,

§P < 0.01,

‖P < 0.001,

¶P < 0.0001 for within-group changes

**TABLE V**

COMPARISON OF WEIGHT AND A1C CHANGES BETWEEN DIET GROUPS*

| | Vegan Group | | | ADA Group | | | |
|---|---|---|---|---|---|---|---|
| | **Week 0** | **Final** | **Change** | **Week 0** | **Final** | **Change** | **P-value †** |
| **Black, A1- (A2A2; 9 vegan, 11 ADA)** | | | | | | | |
| Weight (kg) | 93.5 (3.1) | 85.3 (2.7) | -8.2 (1.4)‡ | 103.8 (3.0) | 104.3 (3.0) | +0.6 (0.7) | 0.02 |
| A1c | 8.49 (0.17) | 7.77 (0.17) | -0.72 (0.18) | 7.87 (0.16) | 8.37 (0.18) | +0.5 (0.18) | 0.04 |
| **White, A1- (A2A2; 9 vegan, 17 ADA)** | | | | | | | |
| Weight | 103.9 (4.4) | 98.6 (4.9) | -5.3 (1.06) | 90.0 (2.3) | 84.4 (2.6) | -5.5 (1.0)§ | 0.94 |
| A1c | 8.11 (0.14) | 7.22 (0.10) | -0.89 (0.11)‡ | 7.99 (0.15) | 7.86 (0.16) | -0.13 (0.10) | 0.02 |
| **Black, A1+ (A1A1 or A1A2; 13 vegan, 11 ADA)** | | | | | | | |
| Weight | 108.0 (2.3) | 107.1 (2.3) | -0.9 (0.5) | 113.3 (2.0) | 110.6 (2.2) | -2.7 (0.6) | 0.30 |
| A1c | 8.15 (0.15) | 7.75 (0.17) | -0.40 | 7.52 (0.09) | 7.51 (0.15) | -0.01 (0.12) | 0.30 |
| **White, A1+ (A1A1 or A1A2; 16 vegan, 7 ADA)** | | | | | | | |
| Weight | 86.0 (3.0) | 81.5 (3.2) | -4.5 (0.6) ¶ | 106.4 (3.5) | 103.4 (3.7) | -3.0 (0.6) | 0.40 |
| A1c | 7.80 (0.16) | 7.78 (0.16) | -0.02 (0.11) | 8.53 (0.18) | 8.06 (0.18) | -0.47 (0.11) | 0.20 |

*Mean values. Standard error of the mean is indicated in parenthesis. Final weight measurements are last available values. Final A1c values are last available values before any change in diabetes medications.

†P-Values for between-group (vegan vs ADA) comparisons of changes from baseline to final values

‡P < 0.05,

§P < 0.01,

‖P < 0.001,

¶P < 0.0001 for within-group changes