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Perilipin Polymorphism Interacts with Dietary Carbohydrates to Modulate Anthropometric Traits in Hispanics of Caribbean Origin,[1,2]

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Abstract

Perilipin (PLIN) is the major protein surrounding lipid droplets in adipocytes and regulates adipocyte metabolism by modulating the interaction between lipases and triacylglycerol stores. Associations between PLIN gene polymorphisms and obesity risk have been described, but interactions with dietary macronutrients require further attention. We examined whether dietary macronutrients (e.g. carbohydrates and fats) modulated the associations of the common *PLIN* 11482G > A (rs894160) single nucleotide polymorphism with obesity. We studied a population-based sample of Caribbean-origin Hispanics (n = 920, aged 45-74 y) living in the Boston area. Obesity measures (waist and hip circumference, BMI) did not differ between GG subjects and carriers of the A allele (GA and AA). In multivariate linear regression models, we found a significant interaction between complex carbohydrate intake as a continuous variable and *PLIN* 11482 G > A genotype for waist circumference (P = 0.002). By dichotomizing complex carbohydrate intake, we found significantly different effects across *PLIN* 11482G > A genotypes. When complex carbohydrate intake was <144 g/d, waist circumference was larger in *PLIN* 11482G > A carriers (P = 0.024). Conversely, when complex carbohydrate intake was ≥144 g/d, waist and hip circumferences were less in *PLIN* 11482G > A carriers (P < 0.05). These interactions were not found for simple sugars or total carbohydrates. We identified a significant gene-diet interaction associated with obesity at the *PLIN* locus. In subjects with higher complex carbohydrate intake, the minor allele was protective against obesity, whereas in subjects with lower carbohydrate intake, the minor allele was associated with increased obesity. These interactions may be relevant to dietary management of obesity.

Introduction

Obesity is estimated to affect >320 million people globally and is a major risk factor for diabetes and cardiovascular disease (1-3). Obesity is a complex, multifactorial condition and its genetic and environmental contributors continue to be identified and refined; however, these factors often have been mainly evaluated independently of one another.

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The role of macronutrient ratios and dietary composition in modulating obesity risk remains an open question (4-6). Although certain candidate genes have emerged to show consistent effects on obesity, the extent to which manipulation of specific macronutrient intakes may influence genetically based variability in obesity susceptibility remains largely unexplored. Increasing our understanding of the interactions between macronutrients and genetic variants may clarify some of the controversies about obesity and represents a step toward the development of targeted nutritional therapies for obesity management.

One established candidate gene for obesity is *perilipin* (*PLIN*),[5] encoding an adipocyte-associated protein that influences obesity risk and insulin resistance through its regulation of adipocyte metabolism, lipolysis, and body fat accumulation (7-12). PLIN inhibits basal lipolysis and promotes triacylglycerol storage by limiting lipase access to triacylglycerol stores but also participates in catecholamine-stimulated lipolysis through an interaction with lipid droplet-associated hormone-sensitive lipase (13-15). Genetic variants in *PLIN* affect the PLIN protein content and lipolytic rates of adipocytes and also modify obesity risk in White and Asian populations (7-12).

Another candidate gene for obesity is PPARγ (*PPARG*), the gene encoding a nuclear transcription factor, which, like PLIN, plays a major role in adipocyte differentiation and function (16). Several (17-19) but not all (20) studies have reported associations between *PPARG* variants, specifically, the *PPARG* Pro12Ala polymorphism, and obesity. In addition, both PLIN and PPARG share a role in the regulation of lipolysis and adipogenesis and functional linkages between these proteins have been demonstrated. The *PLIN* promoter contains a PPAR-responsive element and *PLIN* mRNA is upregulated by synthetic PPAR agonists such as the insulin-sensitizing agent thiazolidinedione (21). These agents, although used therapeutically to treat diabetes, also cause weight gain (22).

Dietary factors interact with *PLIN* variants in modulating obesity and insulin resistance. Variation at the *PLIN* 11482G > A locus modulated weight loss in an energy-restricted, low-carbohydrate intervention (12). Furthermore, an interaction between macronutrients and obesity-related insulin resistance for the same *PLIN* variant was observed in a large multiethnic Asian population (11). In both studies, lower carbohydrate intake was associated with adverse metabolic consequences in those individuals carrying this minor *PLIN* allele. Dietary interactions have also been demonstrated for *PPARG* Pro12Ala, although dietary fats, rather than carbohydrates, have been the focus of previous studies (18).

Dietary intervention trials conducted over the past several decades have closely examined the role of carbohydrate and, particularly, specific types of carbohydrate such as complex

[5]Abbreviations used:

DNL de novo lipogenesis

HDL-C HDL cholesterol

LD linkage disequilibrium

PPARG PPARγ

PLIN perilipin

SNP single nucleotide polymorphism

carbohydrate in promoting weight management and improving glycemic control (6,23). Considerable evidence has accumulated in support of complex carbohydrate as a particularly beneficial macronutrient (24-27), while others have emphasized the negative role of carbohydrate, particularly in its refined form, through its effect on glycemic load (28-30). Overall consensus regarding the relative importance of specific macronutrients in the management of obesity does not exist. Collectively, results from dietary trials and previously reported *PLIN*-nutrient and *PPARG*-nutrient interactions suggest that genetic variation might be 1 source of variability in responses to dietary interventions. Therefore, in this study, we examined the interactions between *PLIN* single nucleotide polymorphisms (SNP), dietary composition, and obesity measures in a Caribbean-origin Hispanic population. Secondarily, based on widespread evidence for a role of *PPARG* Pro12Ala in obesity combined with evidence for possible functional relationships between PLIN and PPARG, we also examined these interactions for the *PPARG* SNP Pro12Ala.

Methods

Study design and subjects

Participants were recruited for a prospective 2-y cohort study of men and women of Puerto Rican origin aged 45-74 y living in the Boston, Massachusetts metropolitan area. Interviews to collect baseline demographic information, medical history, and dietary data were conducted between 2004 and 2007 by trained bilingual staff. The Institutional Review Board at Tufts University/New England Medical Center approved the protocol of the current study. Anthropometric data including height, weight, and waist and hip circumference were measured in duplicate consistent with the technique used by the NHANES. Blood was collected for biochemical analyses and genetic analysis and plasma was separated within 4 h in a refrigerated centrifuge and was stored at -70°C. Serum glucose was measured using an enzymatic, kinetic reaction with Olympus glucose reagents (OSCR6121). HDL cholesterol (HDL-C) was analyzed using EDTA plasma with the enzymatic endpoint reaction with Olympus HDL reagents (OSR6156) and triglycerides were analyzed using EDTA plasma with Olympus triglyceride reagents (OSR6033). Glucose, HDL-C, and triglyceride were measured using the Olympus AU400e (Olympus America).

Genetic analysis

Genomic DNA was isolated from peripheral blood lymphocytes by standard methods as previously described (8,10). SNP *PLIN* 6209 T > C (rs2289487), *PLIN* 11482 G > A (rs894160), *PLIN* 13041 A > G (rs2304795), *PLIN* 14995 A > T (rs1052700), and *PPARG* Pro12Ala (rs1801282) were genotyped using the ABI Prism SNapShot multiplex system (Applied Biosystems).

Dietary assessment

Dietary intake was assessed using a FFQ that was designed for and tested in this population (31). Dietary data were linked to the Minnesota Nutrient Data system (1999, version 25) for nutrient analysis. Intakes of total fat, saturated fat, total carbohydrate, complex carbohydrate, and simple sugars were expressed as percentages of total energy intake and were included in analyses as both continuous and categorical variables. To construct categorical variables, intakes were classified into 2 groups according to the median intake of the population.

Statistical analyses

All continuous variables were examined for normal distribution. The relationship between *PLIN* and *PPARG* genotypes, dietary intakes, and anthropometric measures was evaluated using ANOVA techniques. The interactions between dietary macronutrient intakes (including

total fat, total carbohydrate, complex carbohydrate, simple sugars) and polymorphisms were tested in a multivariate interaction model with control for potential confounders, including age, sex, alcohol (never, past, current), smoking (never, past, current), physical activity, diabetes medications, and dietary fiber. Total carbohydrate, complex carbohydrate, and simple sugar intakes were each adjusted for total energy intake using a residuals model. Macronutrient intake was regressed on total energy intake by computing residuals to which the predicted nutrient intake for the mean energy intake was added as a constant. The population medians for total carbohydrate, complex carbohydrate, and simple sugar intakes were used as cutoffs to dichotomize these variables. Additional adjustments for appropriate macronutrients were performed for each type of carbohydrate. Complex carbohydrate intake was also evaluated as a continuous variable by computing predicted values for each subject from the adjusted regression model and plotting those predicted values against complex carbohydrate intake depending on the *PLIN* genotype. Men and women were analyzed together to ensure adequate statistical power. SAS (version 9.1 for Windows) was used to analyze data. A *P*-value of 0.05 was considered significant.

Results

Demographic, biochemical, anthropometric, and genotypic data are presented in Table 1. Allele frequencies for the minor alleles of each SNP were 0.49 (*PLIN* 6209T>C), 0.27 (*PLIN* 11482G>A), 0.37 (*PLIN* 13041A > G), 0.22 (*PLIN* 14995A > T), and 0.06 (*PPARG* Pro12Ala). Genotype frequencies of the 5 genotyped SNP did not deviate from Hardy-Weinberg equilibrium expectations. No significant associations between obesity measures (waist and hip circumference, BMI) were observed for the 4 *PLIN* SNP or the *PPARG* SNP in this population. Interactions between dietary intakes and *PLIN* 11482G > A were examined by dichotomizing macronutrients according to the mean population intakes regressed on energy and evaluating their effects on obesity measures (Table 2). Homozygotes and heterozygotes of the variant alleles for *PLIN* 11482 G > A and *PPARG* Pro12Ala SNP were combined and compared with homozygous major allele subjects to increase statistical power. Multivariate adjustments for potential confounders included age, sex, smoking, alcohol, physical activity, diabetes medications, and dietary fiber. We did not find significant interactions between *PLIN* 6209T > C, *PLIN* 13041A > G, and *PLIN* 14995A > T polymorphisms and dietary intake for measures of obesity. Dietary interactions for *PPARG* Pro12ALA were examined for complex carbohydrate only. Results reported below pertain to *PLIN* 11482G > A and *PPARG* Pro12Ala.

Complex carbohydrates were dichotomized based on median intake after energy adjustment using a residuals model into high (≥144 g/d) and low (<144 g/d) daily intakes and interaction terms between complex carbohydrate and genotype were obtained for waist ($P = 0.004$) and hip ($P = 0.009$) circumference and BMI ($P = 0.035$). For the *PPARG* SNP, no significant interaction terms between complex carbohydrate and genotype were obtained for obesity. Adjustment for saturated fat, simple sugars, and alcohol intakes were added to the model but did not alter significance. Analysis was also performed for *PLIN* 11482 G > A using a regression model that did not adjust for extraneous variability in total energy intake but was instead based on a dichotomized percentage of complex carbohydrate intake. Using this 2nd model, interaction terms for *PLIN* were obtained for waist ($P = 0.014$) and hip circumference ($P = 0.048$). Values in Table 2 and Figure 1 reflect the use of the residuals energy-adjusted model. For both high and low intakes of complex carbohydrate, significant differences in measures of obesity were observed for waist circumference between carriers of the *PLIN* variant allele (GA and AA) and noncarriers (GG). However, the direction of the difference depended on the level of complex carbohydrate intake. When daily intake of complex carbohydrate was low (<144 g/d), the presence of 1 or 2 variant alleles was associated with larger waist circumference ($P = 0.024$). Yet, for high daily intake of complex carbohydrate (≥144 g/d), carrier status was associated with lower waist ($P = 0.012$) and hip circumference

($P = 0.016$). Using the same statistical models, we did not find any significant interactions between *PLIN* 11482G > A polymorphism and simple sugar intake when it was dichotomized according to the energy-adjusted population median (111 g/d). Similarly, we did not find any significant interaction between this *PLIN* SNP and total carbohydrate intake when intake was dichotomized according to the median intake (265 g/d). We also examined interactions between the simple sugar:complex carbohydrate ratio, with both macronutrients dichotomized according to the median intake after adjustment for energy using the residuals model, and did not find significant interactions between the *PLIN* 11482 G > A and this ratio for obesity measures. Finally, we examined interactions between dietary fiber, *PLIN* 11482 G > A, and obesity, but did not observe any significant interactions for obesity (data not shown).

We further examined interactions between complex carbohydrate intake and potential additive effects of the variant allele by evaluating waist circumference for each *PLIN* 11482G > A genotype (GG, GA, and AA) (Fig. 1*A*). In the context of high-complex carbohydrate intake, the presence of each additional variant allele was associated with an incremental decrease in waist circumference ($P = 0.013$) and mean waist circumference differed ($P = 0.008$) between GG and AA subjects. An interaction term was also obtained for dichotomized complex carbohydrate intake and genotype ($P = 0.004$). In contrast, when complex carbohydrate intake was low, the presence of each variant allele was associated with a marginal incremental increase in waist circumference ($P = 0.062$). Significant or almost significant interactions were observed for each *PLIN* genotype group (GG, GA, and AA) for waist circumference but not consistently for hip circumference or BMI (data not shown). When GA and AA were combined into a single group and compared against GG, then statistical power was sufficient to detect differences (Table 2).

We also examined interactions between complex carbohydrate intake as a continuous variable and *PLIN* 11482G > A on waist circumference. Predicted values for waist circumference are plotted against complex carbohydrate intake for carriers and noncarriers of the variant allele for *PLIN* 11482G > A (Fig. 1*B*). For carriers of the variant allele, as complex carbohydrate intake increased, predicted waist circumference decreased ($P = 0.002$). We also obtained an interaction term between genotype and complex carbohydrate for predicted waist circumference ($P = 0.002$).

Discussion

We have identified a significant interaction between *PLIN* 11482G > A polymorphism and dietary intake of complex carbohydrate in which the direction of the genetic effect on obesity is dependent upon intake of complex carbohydrate. When complex carbohydrate intake was ≥144 g/d (energy-adjusted population median intake), carriers of the variant allele exhibited smaller waist and hip circumferences compared with homozygotes for the major allele. In contrast, when complex carbohydrate was <144 g/d, variant allele carriers exhibited larger waist circumference. These associations between a *PLIN* polymorphism and obesity were not apparent when the population was considered in its entirety, independently of complex carbohydrate intake. Further, both the protective effect and the increased risk of obesity demonstrated additive properties; each additional variant allele was associated with an incremental decrease or increase in waist circumference depending on whether complex carbohydrate was high or low, respectively.

The interaction between *PLIN* 11482 G > A and diet for obesity was limited to complex carbohydrates and was not observed for dietary sugar or total carbohydrates. Whereas previous studies have established restricted energy intake as primary in the treatment of obesity, the role of dietary composition in obesity management continues to be debated. Proportions of carbohydrate, fats, and specific classes of these macronutrients have each been shown to

modulate weight loss, but there is no overall consensus on the macronutrient composition that best sustains weight loss or agreement on whether macronutrients modify obesity independently of energy intake (4,6). At the same time, different proportions of carbohydrate, fats, and specific classes of these macronutrients have each been shown to modulate weight gain (5,26) Few studies have examined genetic factors as potential sources of variability in weight loss in response to dietary modifications (12,32). Our observations suggest that incorporating genetic information into dietary trials may help to reduce intra-individual variability in weight loss.

We did not observe an interaction between *PLIN* 11482G > A and obesity (waist, hip, or BMI), which was independent of complex carbohydrate intake. Of the 3 *PLIN* SNP with which obesity risk has been associated in previous studies, the 11482G > A SNP has been most extensively evaluated, both with and without the availability of dietary data. Whereas *PLIN* 11482G > A was shown to be protective against obesity in 2 White populations, carriers of the variant allele in a Mediterranean population were the most resistant to weight loss in an energy-restricted intervention trial (8,9,12). In contrast to the high complex carbohydrate intakes that were protective against obesity in *PLIN* 11482 G > A carriers in the current study, subjects in the weight loss trial consumed a diet that was designed to be lower in carbohydrate and relatively high in mono-unsaturated fats. In a separate study of *PLIN* 11482G > A, carbohydrate intake was shown to be protective against insulin resistance in 3 ethnic groups in a large Asian population (11). Although insulin resistance was not assessed in the current study, links between obesity and insulin resistance suggest that carbohydrate intake may be relevant to both processes (33-35).

Mechanistic explanations for our observations of complex carbohydrate modulation of obesity for this *PLIN* SNP are unclear. One possibility is that complex carbohydrate modulates postprandial glucose and insulin responses, with subsequent effects on lipolysis and adipocyte energy homeostasis, both of which are regulated by PLIN. Evidence for a connection between PLIN and modulation of postprandial lipemia has been previously demonstrated (36). Early metabolic studies demonstrated increased insulin binding to adipocytes and increased insulin sensitivity in noninsulin-dependent diabetics consuming a high-starch/high-fiber/low-fat diet and more recent studies confirm that modestly increased carbohydrate intake improves insulin sensitivity in obese individuals with diabetes (37,38). Insulin exerts antilipolytic effects that are mediated through hormone-sensitive lipase and PLIN, and dietary interventions that alter insulin metabolism or reduce the hyperinsulinemia associated with type 2 diabetes might be expected to alter PLIN-regulated lipolysis (14,39). An enhanced lipolysis rate has been described for *PLIN* 11482G > A, but the implications of this altered function in response to dietary carbohydrate are unknown (7). Alternative hypotheses can be based on interactions between intake of specific forms of carbohydrate and altered lipid metabolism (40). De novo lipogenesis (DNL), in which lipids are synthesized from excess carbohydrates in the liver or adipose, is sensitive to the proportions of starch and sugar in the diet. A greater starch:sugar ratio is associated with reduced rates of DNL and higher sugar intake is associated with increased DNL (41-43). In the current study, intakes of complex carbohydrate in men and women were high and sugar intake in women was also high relative to average national intakes (NHANES 2003-04 shows complex carbohydrate and simple sugar intakes for 50- to 59-y-old men of 153 and 121 g/d, respectively, and 112 and 95 g/d, respectively, for 50- to 59-y-old women) in a population with a high prevalence of abnormal glucose and lipid metabolism. Although links between DNL and obesity are not clearly established, association of PLIN with adiposity is postulated to be related to its regulation of triacylglycerol storage and lipolysis where these regulatory mechanisms could be responsive to altered carbohydrate ratios (8-10, 12). Ideally, exploration of the mechanisms underlying diet-associated modulation of PLIN and obesity would assess metabolic parameters including insulin sensitivity, plasma fatty acid concentrations, and adipocyte lipolysis rates.

Although mechanisms linking carbohydrate intake, triacylglycerol storage regulation, and obesity to *PLIN* are plausible, the issue of whether functionality can be ascribed to the *PLIN* 11482G > A SNP, as opposed to other *PLIN* SNP, is complicated by the SNP's intronic location. The question of SNP functionality is not limited to the current study but is also implied in studies investigating a variety of obesity-related outcomes with which *PLIN* 11482G > A has been associated, including modulation of insulin resistance by dietary carbohydrate and fat (11), modulation of rosiglitazone-associated weight gain (22), altered weight loss-induced FFA levels (44), decreased adipocyte PLIN protein content, and increased lipolysis rates (7). Although the associations reported above are largely attributed to *PLIN* 11482G > A rather than other *PLIN* SNP, apparently conflicting associations for obesity and *PLIN* 11482G > A may appear to challenge these conclusions. For example, *PLIN* 11482G > A has been associated with increased obesity risk in Malays and Asian Indians (10) but reduced obesity risk in a Spanish population (9). Examination of linkage disequilibrium (LD) patterns in these groups revealed that in the Spanish, *PLIN* 11482G > A was strongly linked to *PLIN* 6209T > C and less strongly linked to *PLIN* 13041A > G and *PLIN* 14995A > T, whereas in the Asian populations, *PLIN* 11482G > A was in positive LD with *PLIN* 13041A > G and *PLIN* 14995A > T but in strong negative LD with *PLIN* 6209T > C. These examples illustrate the difficulties inherent in ascribing functional associations or interactions to particular SNP and as a result, we cannot eliminate the possibility that *PLIN* 11492G > A is a nonfunctional marker for another, functional locus.

For *PPARG* Pro12Ala, we did not observe associations with obesity independently of nutrients nor any interaction with complex carbohydrate. This SNP has been associated with obesity in 3 Chinese ethnic groups (Han, Kazaks, and Uygur) (19) and in Amerindians and Mexican Mestizos (17) but was not associated with obesity in a Spanish population (20). Allelic frequency is 1 potential source of variation, because frequencies of 0.12 (European Americans), 0.09 (Hispanics), and 0.04 (African Americans) have been reported (18). Associations of this SNP with obesity in Caribbean Hispanics, as opposed to Hispanic populations that may include non-Caribbeans, have not been previously described, nor have interactions with dietary carbohydrates.

Limitations of the current study include the high prevalence and severity of obesity in this population, particularly with respect to abdominal obesity. These population characteristics, along with a high prevalence of type 2 diabetes, may limit the extrapolation of our results to less obese, metabolically healthier populations. Further, as discussed earlier, variable LD patterns for *PLIN* SNP in different ethnic groups point out the need for additional caution in extrapolating results from this Caribbean Hispanic population to other ethnic groups. Associations between *PLIN* genotype and obesity in Hispanic populations, with or without dietary interactions, have not been previously described. In addition, although we recognize that complex carbohydrates include a wide range of glycemic index foods, which may have differing metabolic effects, we chose to examine complex carbohydrates in relation to *PLIN* based on previous studies suggesting interactions between total carbohydrate, insulin resistance (11), and resistance to weight loss (12) for carriers of the same *PLIN* variant. Interactions between total carbohydrate intake and obesity did not reach significance in the current study; however, sugar intake was high for women in this population and associations between sugar consumption and obesity have been described (45,46). Further, evidence for a relationship between glycemic index and obesity, like that of overall carbohydrate intake and obesity, is inconsistent, with some intervention trials supporting a benefit to low-glycemic diets (47), and others failing to demonstrate any benefit (6,48). Complicating the understanding of the role of glycemic index and obesity in the current population is a high intake of mixed foods (e.g. rice and beans, rice soups, chicken and rice). Combining lower glycemic foods such as beans or fat-containing foods with carbohydrate staples such as bread and rice consistently lowers the glycemic index of these high-glycemic index foods in other populations (49,50). Further

evaluation of the relationships between glycemic index, food patterns, and obesity in the current population is warranted.

In summary, we observed a modulation of the effects of *PLIN* 11482 G > A on several measures of obesity, which became apparent only when evaluated in light of complex carbohydrate intake. A single *PLIN* variant was associated with clinically important and opposite effects in a population exhibiting high rates of obesity and subsequent metabolic disturbance and these effects depended on intake of a specific macronutrient. Consideration of genotype in the evaluation of the effects of dietary factors may help to reconcile disparate results in dietary trials and may suggest more optimal dietary interventions that are based on individual genetic variants. Identifying population subsets that would benefit most from increased complex carbohydrate intake could aid in targeting nutritional advice specifically for these individuals.

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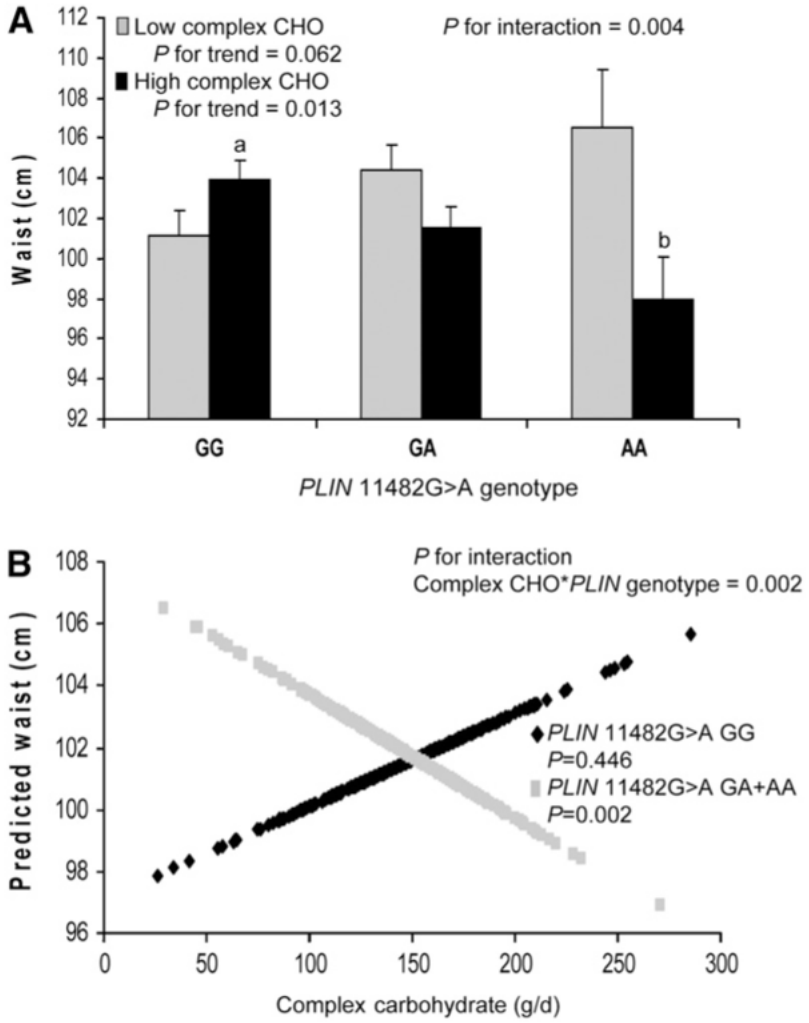

FIGURE 1.

Waist circumference (*A*) by PLIN 11482G > A genotype and complex carbohydrate intake, adjusted for total energy intake using the residuals method. High complex carbohydrate ≥144 g/d. Low complex carbohydrate <144 g/d. Values are means + SE. Means were adjusted for age, sex, smoking, alcohol, physical activity, diabetes medications, saturated fat, dietary fiber, and simple sugars. *P*-values for trend were obtained through comparisons of means for genotype (GG, *n* = 480; GA, *n* = 353; AA, *n* = 71) according to complex carbohydrate intake. *P* for interaction was obtained for the interaction between genotype and complex carbohydrate intake. Means marked with different letters differ, $P < 0.05$. Predicted values of waist (*B*) by PLIN 11482G > A genotype (GG, *n* = 480; GA+AA, *n* = 424) plotted against complex carbohydrate intake (g/d, adjusted for total energy using residuals method) as a continuous variable. Predicted values for waist were calculated from the regression model after adjustment for age, sex, smoking, alcohol, physical activity, diabetes medications, saturated fat, and simple sugars. *P*-value for interaction indicates the significance of the interaction term for complex carbohydrate and PLIN genotype in the adjusted regression model. *P*-values for GG and GG +AA indicate the significance of the regression coefficients in the adjusted regression model.

TABLE 1

Demographic, anthropometric, biochemical, dietary, and genotypic data in Caribbean-origin Hispanics[1]

	Men	Women
n	256	664
Age, *y*	57.6 ± 7.7	58.0 ± 7.2
BMI, *kg/m*^{2}	29.7 ± 5.3	33.1 ± 7.1
Obese,[2] %	45.3	66.1
Morbidly obese,[2] %	4.2	15.8
Waist circumference, *cm*	102 ± 14	102 ± 16
Abdominal obesity,[3] %	46.5	84.8
Plasma HDL-C, *mmol/L*	1.04 ± 0.32	1.21 ± 0.32
Plasma triglycerides, *mmol/L*	2.06 ± 1.83	1.77 ± 1.15
Serum glucose, *mmol/L*	6.99 ± 3.11	6.72 ± 2.83
Energy intake,[4] *kcal/d*	2370 ± 855	2023 ± 855
Total fat, *% of energy*	31.8 ± 5.3	30.7 ± 5.2
Saturated fat, *% of energy*	9.9 ± 2.4	9.5 ± 2.3
Carbohydrate, *% of energy*	50.2 ± 7.5	52.5 ± 7.6
Complex carbohydrate, *g/d*	176.3 ± 64.9	148.0 ± 63.2
Complex carbohydrate, *% of energy*	30.2 ± 5.9	29.9 ± 6.0
Simple sugars, *g/d*	119.2 ± 65.6	115.1 ± 68.9
Simple sugar, *% of energy*	20.0 ± 7.7	22.6 ± 9.0
Fiber, *g/d*	19.9 ± 7.9	17.7 ± 8.0
Alcohol user, *%*	50.6	33.2
Current smoker, *%*	31.8	20.0
Diabetes,[5] *%*	42.2	41.2
Diabetes medications, *%*	32.8	34.3
PLIN 11482 > A, *n(%)*		
GG	126 (50.0)	354 (54.2)
GA	106 (42.1)	247 (37.9)
AA	20 (7.9)	51 (7.8)
PPARG Pro12Ala, *n(%)*		
CC	599 (88.1)	232 (85.93)
CG	78 (11.5)	38 (14.07)
GG	3 (0.44)	0 (0)

[1] Values are means ± SD, %, or n(%).

[2] Obese, BMI ≥30 kg/m^2. Morbidly obese, BMI ≥40 kg/m^2.

[3] Abdominal obesity, waist circumference ≥102 cm in men; waist circumference ≥88 cm in women.

[4] 1 kcal = 4.184 kJ.

[5] Diabetes, fasting blood glucose ≥7 mmol/L or taking diabetes medications.

TABLE 2

Interactions between PLIN 11482G > A and carbohydrate intake in association with obesity-related measures in Caribbean-origin Hispanics[1]

	GG	GA+AA	*P*-trend	*P*-interaction
Complex CHO intake,[3] *g/d*				
Waist, *cm*				
<144[2]	101 ± 1	105 ± 1	0.024	0.004
≥144	104 ± 1	101 ± 1	0.012	
Hip, *cm*				
<144	107 ± 1	110 ± 1	0.060	0.009
≥144	109 ± 1	107 ± 1	0.016	
BMI, *kg/m*^{2}				
<144	30.9 ± 0.5	32.0 ± 0.5	0.069	0.035
≥144	32.0 ± 0.4	31.2 ± 0.4	0.143	
Total CHO intake,[4] *g/d*				
Waist, *cm*				
<265[2]	103 ± 1	105 ± 1	0.093	0.065
≥265	102 ± 1	100 ± 1	0.242	
Hip, *cm*				
<265	109 ± 1	110 ± 1	0.267	0.096
≥265	108 ± 1	106 ± 1	0.233	
BMI, *kg/m*^{2}				
<265	31.7 ± 0.5	32.5 ± 0.5	0.210	0.265
≥265	31.2 ± 0.5	31.0 ± 0.5	0.744	
Simple sugars intake,[5] *g/d*				
Waist, *cm*				
<111[2]	104 ± 1	104 ± 1	0.894	0.821
≥111	101 ± 1	101 ± 1	0.762	
Hip, *cm*				
<111	110 ± 1	109 ± 1	0.861	0.822
≥111	107 ± 1	107 ± 1	0.909	
BMI, *kg/m*^{2}				
<111	32.0 ± 0.4	32.2 ± 0.4	0.811	0.764
≥111	31.0 ± 0.5	31.3 ± 0.6	0.591	

[1] Data are means ± SE.

[2] Dichotomized values for nutrients are adjusted for energy using the residuals method.

[3] CHO = carbohydrate. Adjusted for age, sex, smoking, diabetes medication, physical activity, alcohol, saturated fat, sugar and dietary fiber.

[4] Adjusted for age, sex, smoking, diabetes medication, physical activity, alcohol, saturated fat, and dietary fiber.

[5] Adjusted for age, sex, smoking, diabetes medication, physical activity, alcohol, saturated fat, complex carbohydrate and dietary fiber. Simple sugars consist of sucrose, glucose, maltose, fructose, and lactose.