Original Article

Diets high in carbohydrate may not be appropriate for rs328 G carriers with the metabolic syndrome

Shixiu Zhang PhD[1,2], Yiyi Ma PhD, MD[1,3], Hongwei Guo MD[1], Wentao Wan MD[1], Kun Xue PhD, MD[1]

[1]*Department of Nutrition and Food Hygiene, School of Public Health, Fudan University, Shanghai, China*
[2]*Department of Nutrition and Food Hygiene, School of Public Health, Shandong University, Jinan, China*
[3]*Jean Mayer US Department of Agriculture Human Nutrition Research Center on Aging at Tufts University, Boston, USA*

The objective of this study was to test how the genetic polymorphisms located within the lipoprotein lipase (*LPL*) locus would modulate the relationship between a diet high in carbohydrate and insulin resistance related traits in metabolic syndrome adults. A one year nutritional intervention study focusing on education to increase dietary intake of whole grain, vegetable and fruit, and to reduce the intake of sodium, simple sugar and dietary fat (especially cooking oil and pork lard) was conducted. Two districts in Shanghai, China were randomly selected to be the intervention and control group, and patients (n=235) with metabolic syndrome within these two districts were selected based on a multistage sampling method. Fasting glucose was reduced in rs328 CC homozygotes (p=0.028) but not G carriers (p=0.686) within the intervention group. Also an ancillary study with greater statistical power by combining the baseline measurements across both the intervention and control groups was conducted to test the cross-sectional statistical interactions between carbohydrate/fat and lipoprotein lipase genotypes for homeostasis model assessment of insulin resistance/insulin/fasting glucose. Increased carbohydrate intakes were positively associated with homeostasis model assessment of insulin resistance and insulin in rs328 G carriers but not CC homozygotes (p for interaction was 0.025). These results indicate that diet high in carbohydrate may not be suitable for metabolic syndrome rs328 G carriers, calling for the development of personalized dietary intervention for metabolic syndrome subjects.

Key Words: gene-by-diet interaction, carbohydrate, lipoprotein lipase, metabolic syndrome, insulin resistance

INTRODUCTION

Metabolic syndrome (MS) is a cluster of obesity, high glucose, dyslipidemia and hypertension, and it has been identified as a risk factor of cardiovascular diseases and type 2 diabetes.[1,2] The prevalence of MS in China was 9.8% in men and 17.8% in women in 2001.[3] Though the prevalence of MS in China was lower than that in western countries like United States,[4] the big population determines the huge absolute numbers of people at risk for cardiovascular disease and mortality from related diseases. Furthermore, MS population in China is different from MS in US, in which the Chinese had higher percentage of body fat compared with caucasians of the same body mass index (BMI).[5,6]

Environmental factors, especially dietary factors, play a key role in the development of MS.[7,8] Lifestyle changes could reduce the MS prevalence and type 2 diabetes incidence.[9] But the difference in the dietary response creates a huge challenge for the success of dietary intervention in MS patients,[10] and there is no personalized dietary instructions for MS patients yet. Thus, the study to identify the personalized dietary intervention for MS patients may be of value.[11]

Lipoprotein lipase (*LPL*) gene is a good candidate for personalized dietary intervention for MS patients because of its role in insulin resistance, a major risk factor for MS.[12,13] LPL affects insulin resistance across different types of tissues. For example, skeletal muscle LPL activity and serum LPL mass were reduced in insulin resistance.[14-16] LPL from adipose tissue was also reduced during insulin resistant condition, and weight reduction with increased insulin action could increase adipose tissue LPL activity.[17-19]

As LPL's role in insulin resistance, *LPL* SNPs also have been suggested to be associated with insulin resistance. One haplotype containing rs320 (HindIII) G carrier and rs328 (S447X) G carrier was associated with increased insulin resistance measured by assessment of the glucose infusion rate.[20] *LPL* rs320 and rs285 (PvuII) have also been studied for their relation with insulin resistance in non-diabetic Chinese men with coronary heart

Corresponding Author: Dr Hongwei Guo, Department of Nutrition and Food Hygiene, School of Public Health, Fudan University, 130 Dong'an road, Shanghai, 200032 China.
Tel: (86)-13651730955; Fax: (86)-21-54237320
Email: hwguo@shmu.edu.cn
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disease,[21] and rs320 G carriers were more insulin resistant. Based on their suggested relationships with insulin resistance, we included rs320, rs285, and rs328 into our analysis.

LPL has been shown to affect lipid metabolism by hydrolyzing core triglycerides in chylomicrons and very low density lipoprotein and it might be susceptible for dietary changes.[22] High carbohydrate intake was reported to increase LPL activity in human adipose tissue.[23] Dietary fat has been shown to markedly blunt the insulin and glucose stimulated response of LPL in adipose tissue.[24]

Although the evidence has been accumulated regarding the potential role of *LPL* in personalized nutrition for MS patients, little has been known about the interaction between *LPL* polymorphisms and diet high in carbohydrate to modulate the insulin resistance in MS patients. Thus, we hypothesized that the effect of diet high in carbohydrate on the status of insulin resistance in MS patients would be different according to different *LPL* genotypes. We tested our hypothesis in an intervention study focusing on the nutritional education to increase the dietary intake of whole grain, vegetable and fruit, and to reduce the intake of sodium, simple sugar and dietary fat (especially cooking oil and pork lard). Further, we conducted an ancillary study with all baseline populations of the intervention study to increase our statistical power to test the interactions between carbohydrate/fat intake and *LPL* genotypes for outcome of insulin resistance.

METHODS

Subjects

Participants included 75 MS men and 160 MS women, aged 31-65 years, living in 2 urban districts of Shanghai, China. Multistage sampling method was used to select MS participants in these two districts. The procedure was described in our previous publication.[25]

All participants provided written informed consents. The protocol was approved by School of Public Health Ethics Committee of Fudan University with eight ethics approvals. MS was defined according to the International Diabetes Federation guidelines for Asian people.[26]

Anthropometric, biochemical measurements

Anthropometric measurements including weight, height, waist circumference, hip circumference and biochemical measurements including fasting glucose (FG), insulin, lipids were measured as previously.[25] FG were determined with an automatic analyzer (Hitachi 7180 Japan) using reagents from Shanghai Fenghui Med-Tech, Inc. Insulin was measured with SN-695 Counter (Shanghai Hesuo Rihuan Photoelectric Instrument Co., Ltd) using radio immune assay kit from Beijing Chemclin Biotech Co. Ltd. Homeostasis model assessment of insulin resistance (HOMA-IR) was calculated as FG times insulin/22.5. Thus insulin resistance was indirectly represented by FG, insulin and HOMA-IR.

Genotyping

Rs285, rs320, rs328 genotypes were analyzed by polymerase chain reaction–restriction fragment length polymorphism as described previously.[27,28] Genomic DNA was extracted from peripheral blood mononuclear cells using phenol-chloroform extraction method.

Lifestyle assessment

Twenty four hour dietary recall interviews were done and data were analyzed as previously described.[25] Food group intakes were given as food to total energy ratios as what SY Nutrition Analysis and Diet Menu Software owned by Fudan University.[25] To exclude other confounding factors that could affect intervention results, medical treatment for hyperglycemia were recorded. Also, physical activity, smoking and drinking status were collected. Physical activities were investigated by "International Physical Activity Questionnaire-Short".[25] Smoking and drinking habits were collected through a "knowledge, attitude and practice" (KAP) questionnaire by asking frequency of smoking/drinking with three degrees of choices: often, sometimes and never.

Nutrition intervention

Two districts were randomly assigned to become intervention and control group. The nutrition intervention was conducted from August 2007 to August 2008. Subjects in the intervention group were given intensive interventions at a frequency of one to two times per month. They were required to follow the diet regime by increasing intake of whole grain, deep colored vegetables, and fruits, and reducing the intake of sodium, simple sugar and dietary fat (especially cooking oil and pork lard). To retain subjects in the control group, control group were given minimally necessary contact. There was one educator responsible for training to eliminate the bias from educator. More detailed information can be found in our previous published study.[25]

Statistical analysis

Pearson chi-square tests were used to evaluate Hardy-Weinberg equilibrium of SNP and to compare enumeration data between groups. Two sample *t* test or Wilcoxon Rank-Sum (Mann-Whitney) test was used to compare continuous variables between genotypes. Pearson chi-square was used to test numeration data changes by time in a certain genotype within a group. Linear mixed-effects model using the XTREG procedure in Stata software was fitted to test differences of change for continuous variables within group.

For the ancillary analysis, iteratively reweighted least squares robust regression was used to test interactions between *LPL* SNPs and carbohydrate/fat intake which was classified into tertiles. We created tertiles of carbohydrate, fat, fibre and energy intake at baseline. Carbohydrate/fat to total energy ratio and food to total energy ratio were also divided into tertiles. There were relatively low completion rate for other lifestyles, like smoking, drinking and physical activity, completion rate were 90.6%, 85.1%, 76.2%, respectively. So, covariates adjusted in the regression model were gender, age, BMI, and drug treatment for hyperglycemia. Energy was also adjusted if the analysis were for carbohydrate, fat, and fibre. Statistical analysis was performed using Stata Co. Stata 8.0. Significance was defined at the level of $p<0.05$.

Haploview 4.2 software was applied to evaluate pairwise linkage disequilibrium between SNP.

RESULTS

General population characteristics

General population characteristics are shown in Table 1. Minor allele frequencies for rs285, rs320, rs328 were 0.29, 0.20, 0.06, respectively, and all of them were similar to those shown in HapMap for Han Chinese. All three SNPs were consistent with Hardy-Weinberg equilibrium expectations (p>0.05). According to linkage disequilibrium test in Figure 1, there was high linkage between rs285 and rs320 (R^2=0.98) and some linkage between rs328 and rs285 (rs320) (R^2=0.64). Thus rs285 and rs328 were used for the following analysis.

Table 1. General population characteristics in Shanghai MS subjects

	Control group	Intervention group
Male/female	41/79	34/81
Age, years	53±6	56±6
Genotype		
Rs285 (PvuII), CC\CT\TT	50\41\14	64\41\9
Rs320 (HindIII), TT\TG\GG	77\26\2	64\41\9
Rs328(S447X),CC\CG\GG	103\15\0	102\11\1

Effects of nutrition education on lifestyles changes

After one-year intervention with the nutritional education (Table 2 and 3), subjects within the intervention group changed their dietary habits. For food items, they increased their intake of vegetables and fruits, and decreased their intake of other food items represented mainly by cooking oil, after one year intensive nutritional education. For nutrients, subjects in intervention group increased their gram intake of carbohydrate, but decreased their intake of dietary fat represented by the percentage of total energy intake.

Effects of nutrition education on lifestyles changes by LPL genotypes

Subjects with rs285 CC genotype but not with rs285 T carriers in intervention group increased their cereal, fibre

Table 2. Food and nutrient intakes by rs285 genotype†

			Control group			Intervention group		
			Baseline	One year	*p2*§	Baseline	One year	*p2*§
Food group intakes, (food to total energy ratio, %)	Cereal	TT/TC	47.2 (2.0)	48.1 (2.0)	0.730	49.4 (1.8)	50.0 (1.9)	0.776
		CC	45.1 (1.6)	49.2 (1.6)	0.082	45.3 (1.8)	51.1 (1.5)	0.004
		p1‡	0.417	0.691		0.267	0.670	
	Bean	TT/TC	3.2 (0.6)	3.4 (0.9)	0.860	2.5 (0.7)	2.1 (0.7)	0.722
		CC	3.3 (0.9)	3.3 (1.0)	0.998	2.5 (0.6)	2.1 (0.5)	0.652
		p1‡	0.557	0.962		0.665	0.416	
	Vegetable	TT/TC	3.0 (0.3)	3.5 (0.4)	0.437	2.8 (0.3)	4.3 (0.8)	0.032
		CC	3.7 (0.6)	2.9 (0.4)	0.206	3.0 (0.4)	4.2 (0.5)	0.037
		p1‡	0.648	0.120		0.959	0.639	
	Fruit	TT/TC	1.4 (0.3)	1.8 (0.4)	0.309	1.0 (0.3)	2.2 (0.3)	0.003
		CC	1.1 (0.2)	1.9 (0.4)	0.057	1.1 (0.3)	3.0 (0.4)	<0.001
		p1‡	0.465	0.828		0.644	0.190	
	Meat and fish	TT/TC	12.8 (1.4)	11.0 (1.2)	0.261	10.9 (1.4)	11.9 (1.2)	0.557
		CC	13.0 (1.5)	12.3 (1.2)	0.612	11.2 (1.1)	10.4 (0.9)	0.589
		p1‡	0.883	0.385		0.589	0.500	
	Egg	TT/TC	1.2 (0.3)	1.5 (0.3)	0.621	1.9 (0.5)	2.3 (0.5)	0.442
		CC	1.7 (0.4)	2.3 (0.4)	0.317	2.1 (0.4)	2.1 (0.3)	0.893
		p1‡	0.183	0.178		0.425	0.988	
	Milk	TT/TC	2.8 (0.5)	2.9 (0.5)	0.928	1.5 (0.4)	2.3 (0.7)	0.245
		CC	3.4 (0.5)	4.0 (0.7)	0.434	2.4 (0.5)	3.1 (0.7)	0.370
		p1‡	0.385	0.319		0.222	0.506	
	Other food¶	TT/TC	28.2 (1.5)	27.7 (1.8)	0.799	30.0 (1.4)	24.8 (1.5)	0.017
		CC	28.5 (1.7)	24.1 (1.3)	0.039	32.2 (1.8)	24.1 (1.3)	<0.001
		p1‡	0.911	0.355		0.528	0.679	
Nutrient intakes	Fibre, g/d	TT/TC	6.6 (0.5)	8.0 (0.6)	0.124	7.9 (0.9)	8.4 (0.6)	0.545
		CC	9.1 (2.3)	7.3 (0.9)	0.306	7.1 (0.7)	10.5 (0.8)	0.027
		p1‡	0.720	0.239		0.467	0.116	
	Carbohydrate intake, g/d	TT/TC	199 (10.0)	221 (10.9)	0.078	203 (10.6)	251 (9.6)	<0.001
		CC	213 (10.5)	219 (10.6)	0.625	187 (8.8)	259 (8.3)	<0.001
		p1‡	0.338	0.997		0.524	0.528	
	Fat intake, g/d	TT/TC	70.0 (3.6)	69.9 (4.0)	0.987	66.5 (3.5)	71.1 (4.0)	0.321
		CC	73.9 (4.2)	63.3 (3.1)	0.025	70.1 (3.5)	68.6 (3.9)	0.726
		p1‡	0.639	0.334		0.640	0.519	
	Carbohydrate to total energy ratio, %	TT/TC	47.6 (1.5)	50.2 (1.6)	0.153	50.2 (1.5)	53.5 (1.3)	0.076
		CC	48.5 (1.2)	51.9 (1.3)	0.047	46.8 (1.5)	54.9 (1.1)	<0.001
		p1‡	0.654	0.422		0.334	0.431	
	Fat to total energy ratio, %	TT/TC	38.4 (1.4)	35.8 (1.4)	0.126	37.4 (1.4)	33.4 (1.2)	0.020
		CC	38.0 (1.4)	34.0 (1.1)	0.017	39.5 (1.3)	31.4 (1.0)	<0.001
		p1‡	0.815	0.315		0.432	0.222	

†Data are means(SE); ‡*p1* for comparison between genotypes; §*p2* for comparison within group; ¶Other food is the food group that does not belong to cereal, bean, vegetable, fruit, meat and fish, egg and milk, and we think cooking oil is the main contributor for other food.

intake and carbohydrate to total energy ratio. Subjects with rs285 CC genotype but not with rs285 T carriers in the control group increased their carbohydrate to total energy ratio and decreased their other food, fat intake, and fat to total energy ratio. However, the statistical test did not show different intakes between the subjects with these two genotypes.

Subjects with rs328 CC genotype but not with G carriers in intervention group increased their vegetable and fibre intake. Also, the statistical test did not show difference between subjects with these two genotypes.

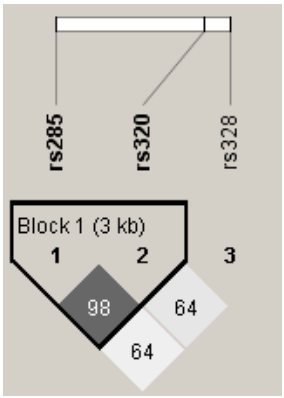

Figure 1. Linkage Disequilibrium of *LPL* SNPs in MS†. †Data shown are R^2 of the linkage disequilibrium analysis between SNPs.

Intervention interaction results on insulin resistance related traits

FG, insulin and HOMA-IR changes by different genotypes are shown in Table 4. Subjects of rs285 CC homozygotes in the control group increased their measurements of insulin (p=0.005) and HOMA-IR (p=0.027) after one year, while those biochemical measurements in subjects of rs285 T carriers within the control group did not change. Within the intervention group, FG was improved in subjects of rs328 CC homozygotes (p=0.028) but not G

Table 3. Food and nutrient intakes by rs328 genotype†

			Control group			Intervention group		
			Baseline	One year	*p2*§	Baseline	One year	*p2*§
Food group intakes, (food to total energy ratio, %)	Cereal	GG/GC	48.6 (2.8)	50.0 (2.7)	0.657	51.5 (4.2)	58.1 (3.0)	0.061
		CC	46.1 (1.3)	48.9 (1.3)	0.102	46.6 (1.4)	49.7 (1.2)	0.054
		p1‡	0.443	0.738		0.251	0.015	
	Bean	GG/GC	3.2 (1.1)	6.0 (2.2)	0.056	2.9 (1.2)	4.3 (1.5)	0.395
		CC	3.1 (0.5)	2.9 (0.6)	0.711	2.5 (0.5)	1.8 (0.4)	0.400
		p1‡	0.346	0.199		0.445	0.066	
	Vegetable	GG/GC	4.1 (0.6)	4.6 (0.8)	0.511	2.2 (0.5)	2.3(0.8)	0.944
		CC	3.5 (0.3)	3.1 (0.3)	0.486	3.0 (0.3)	4.5(0.5)	0.002
		p1‡	0.164	0.056		0.539	0.055	
	Fruit	GG/GC	1.2 (0.4)	0.9 (0.4)	0.584	0.2 (0.1)	2.7 (0.6)	<0.001
		CC	1.4 (0.2)	2.0 (0.3)	0.051	1.1 (0.2)	2.6 (0.3)	<0.001
		p1‡	0.955	0.081		0.110	0.534	
	Meat and fish	GG/GC	13.6 (2.4)	9.0 (1.5)	0.086	12.1 (3.1)	11.7 (2.7)	0.883
		CC	12.9 (1.0)	12.3 (0.9)	0.570	10.9 (0.9)	11.0 (0.8)	0.971
		p1‡	0.713	0.284		0.882	0.828	
	Egg	GG/GC	1.7 (0.5)	2.2 (0.6)	0.508	1.1 (0.7)	1.5 (0.6)	0.664
		CC	1.6 (0.2)	1.7 (0.2)	0.707	2.1 (0.3)	2.3 (0.3)	0.764
		p1‡	0.509	0.159		0.355	0.549	
	Milk	GG/GC	3.8 (1.0)	3.2 (1.0)	0.455	1.4 (0.6)	0.4 (0.4)	0.214
		CC	3.4 (0.4)	3.9 (0.4)	0.355	2.1 (0.4)	3.0 (0.5)	0.086
		p1‡	0.647	0.680		0.912	0.016	
	Other food¶	GG/GC	23.7 (2.4)	23.9 (2.3)	0.920	28.6 (2.6)	19.0 (2.0)	0.002
		CC	27.8 (1.2)	25.1 (1.2)	0.077	31.6 (1.3)	25.0 (1.1)	<0.001
		p1‡	0.244	0.609		0.545	0.071	
Nutrient intakes	Fibre, g/d	GG/GC	6.8 (0.8)	7.7 (1.1)	0.438	6.0 (1.0)	7.3 (0.9)	0.351
		CC	7.8 (1.1)	7.6 (0.5)	0.821	7.6 (0.6)	9.9 (0.6)	0.026
		p1‡	0.864	0.575		0.491	0.162	
	Carbohydrate Intake, g/d	GG/GC	201 (16.4)	205 (18.8)	0.850	189 (19.5)	255 (28.1)	0.004
		CC	207 (7.2)	221 (7.5)	0.141	195 (7.3)	255 (6.3)	<0.001
		p1‡	0.742	0.381		0.786	0.586	
	Fat Intake, g/d	GG/GC	63.8 (6.4)	54.5 (4.3)	0.168	64.0 (6.4)	55.6 (7.5)	0.270
		CC	71.7 (2.7)	68.1 (2.6)	0.272	69.0 (2.7)	71.4 (2.9)	0.479
		p1‡	0.199	0.007		0.654	0.041	
	Carbohydrate to total energy ratio, %	GG/GC	49.4 (2.1)	51.3 (2.8)	0.539	49.5 (3.8)	58.3 (3.0)	0.012
		CC	48.3 (1.0)	51.0 (1.0)	0.031	48.2 (1.1)	53.8 (0.9)	<0.001
		p1‡	0.826	0.911		0.879	0.104	
	Fat to total energy ratio, %	GG/GC	35.3 (2.0)	31.8 (2.2)	0.230	38.8 (3.8)	28.8 (2.6)	0.002
		CC	38.1 (1.0)	35.4 (0.9)	0.025	38.6 (1.0)	32.7 (0.8)	<0.001
		p1‡	0.381	0.141		0.950	0.129	

†Data are means(SE); ‡*p1* for comparison between genotypes; §*p2* for comparison within group; ¶Other food is the food group that does not belong to cereal, bean, vegetable, fruit, meat and fish, egg and milk, and we think cooking oil is the main contributor for other food.

Table 4. FG, insulin and HOMA-IR response to nutrition intervention by rs285 and rs328 genotype[†]

		Control group				Intervention group			
		n	Baseline	One year	$p^{‡}$	n	Baseline	One year	$p^{‡}$
Rs285	FG, mmol/L								
	TT/TC	55	5.8 (0.3)	5.6 (0.2)	0.429	50	5.4 (0.2)	5.2 (0.2)	0.217
	CC	50	5.6 (0.2)	5.5 (0.2)	0.481	64	5.2 (0.2)	5.1 (0.2)	0.315
	Insulin, μIU/L								
	TT/TC	54	11.4 (0.7)	10.9 (0.5)	0.618	50	11.6 (0.9)	13.1 (1.2)	0.180
	CC	50	11.8 (0.8)	14.8 (1.6)	0.005	63	11.5 (1.0)	11.6 (0.7)	0.982
	HOMA-IR								
	TT/TC	54	3.0 (0.3)	2.7 (0.2)	0.586	50	3.1 (0.5)	3.1 (0.3)	0.978
	CC	50	3.1 (0.3)	3.8 (0.5)	0.027	63	2.7 (0.3)	2.7 (0.2)	0.662
Rs328	FG, mmol/L								
	GG/GC	15	5.9 (0.7)	5.8 (0.5)	0.887	12	5.5 (0.8)	5.8 (0.5)	0.686
	CC	103	5.6 (0.2)	5.5 (0.1)	0.171	102	5.3 (0.1)	5.0 (0.1)	0.028
	Insulin, μIU/L								
	GG/GC	15	11.5 (0.9)	12.5 (1.0)	0.708	12	14.4 (3.3)	14.1 (2.4)	0.922
	CC	102	11.7 (0.5)	12.9 (0.8)	0.081	101	11.2 (0.7)	12.0 (0.7)	0.297
	HOMA-IR								
	GG/GC	15	3.2 (0.7)	3.3 (0.4)	0.983	12	4.5 (2.1)	4.0 (1.1)	0.781
	CC	102	3.0 (0.2)	3.2 (0.3)	0.207	101	2.7 (0.2)	2.7 (0.2)	0.887

[†]Data are means (SE); [‡]p for self-comparison before and after intervention.
FG: fasting glucose; HOMA-IR: homeostasis model assessment of insulin resistance.

carriers (p=0.686). These observed effects in the dietary response were not associated with changes in other life-style factors (data not shown), including smoking, drinking, physical activity and medical treatment.

Ancillary baseline interaction analysis

For carbohydrate, rs328 showed a significant interaction for HOMA-IR (p=0.025) and insulin (p=0.040) (Table 5). In minor allele carriers (GG+GC), those with higher carbohydrate intake had significantly greater HOMA-IR (p=0.021) and insulin (p=0.045) than those with lower carbohydrate intake. This association attenuated in the homozygotes of the major C allele. For fibre, fat, carbohydrate/fat to total energy ratio and food to total energy ratio, interaction terms were not significant for HOMA-IR, insulin or FG (data were not shown). No interactions were found for rs285.

DISCUSSION

In this study, FG was not improved in subjects of rs328 G carriers, but was improved in subjects of rs328 CC homozygotes of the intervention group after following the diet with relatively higher proportion of carbohydrate. Furthermore, the ancillary study showed that increased intake of carbohydrate was positively related with increased insulin/HOMA-IR in subjects of *LPL* rs328 G carriers. These results indicated an interaction between rs328 and a diet high in carbohydrate and indicated that diets high in carbohydrate may not be suitable for rs328 G carriers with MS.

LPL rs328 or a haplotype including rs328 has been shown to promote insulin resistance.[29,30] Rs328 G allele reduced apolipoprotein A-I/A-II ratio[29] and increased very low density lipoprotein (VLDL) diameter[30] while both apolipoprotein A-II[31,32] and VLDL diameter (or large VLDL particle concentrations)[33] were shown to induce insulin resistance.

To our knowledge, there have not been studies showing how rs328 modulates the effect of diet or nutrients on insulin resistance. Our previous intervention study showed that a diet with a relatively higher proportion of carbohydrate helped improve health status but not FG, insulin or HOMA-IR.[25] However, our further analysis indicated that the beneficial effects of a diet high in carbohydrate may not be suitable for all the MS patients.

The sterol regulatory element in the promoter and insulin response element in the 3' untranslated region of *LPL* gene may explain the underlying mechanism of the relationship between LPL and diet high in carbohydrate.[34-37] LPL activity within human adipose tissue was increased after feeding with high carbohydrate.[23]

Genetic variations may play a role in modifying the effect of carbohydrate on LPL. One study showed that those with increased adipose tissue LPL activity after high carbohydrate diet were predicted to have more body fat gain.[38] Our ancillary study may indicate differential HOMA-IR response to carbohydrate due to rs328. *LPL* rs285 may also play a role in differential response to carbohydrate or to a diet high in carbohydrate. Insulin and HOMA-IR increased in subjects of rs285 CC homozygotes but not in subjects of rs285 T carriers of the control group.

Our study was limited by its difficulty in distinguishing the effect of the specific nutrient (carbohydrate) or the effect of the overall diet. Subjects in the intervention group followed a diet with a high carbohydrate content but the sources of carbohydrate were varied. However, our study did point out that it was the nutrient of carbohydrate in total rather than the specific food sources for the carbohydrate that had significant interactions with *LPL* genotypes. Second, the sample size for the ancillary study was relatively small. However, because of the low prevalence of MS patients, the numbers included in the current study were selected from two thousand and eight hundred residents within two districts in Shanghai. Further replication in other bigger populations is needed. Finally,

Table 5. Ancillary study of interaction test between macronutrient intakes and *LPL* rs328 for FG, insulin and HOMA-IR in Shanghai MS subjects[†]

			CC		GG+GC		$p1^{‡}$
			$\overline{X}$ (SE)	n	$\overline{X}$ (SE)	n	
HOMA-IR	Total energy intake (kcal/d)[¶]	Male, <1640 kcal/d Female, <1333 kcal/d	2.8 (0.2)	68	1.9 (0.2)	7	0.260
		Male, <2172 kcal/d, ≥1640 kcal/d Female, <1661 kcal/d, ≥1333 kcal/d	2.9 (0.2)	63	2.8 (0.3)	12	
		Male, ≥2172 kcal/d Female, ≥1661 kcal/d	2.9 (0.3)	70	7.0 (3.2)	8	
		$p2^{§}$	0.658		0.185		
	Carbohydrate Intake (g/d)[††]	Male, <207 g/d Female, <151 g/d	2.8 (0.2)	66	2.0 (0.2)	9	0.025
		Male, <284 g/d, ≥207 g/d Female, <208 g/d, ≥151 g/d	3.0 (0.3)	66	5.2 (2.8)	9	
		Male, ≥284 g/d Female, ≥208 g/d	2.7 (0.2)	69	4.1 (1.1)	9	
		$p2^{§}$	0.884		0.021		
Insulin	Total energy intake (kcal/d)[¶]	Male, <1640 kcal/d Female,<1333 kcal/d	11.3 (0.7)	68	9.0 (0.7)	7	0.074
		Male, <2172 kcal/d, ≥1640 kcal/d Female, <1661 kcal/d, ≥1333 kcal/d	11.8 (0.6)	63	12.0 (1.4)	12	
		Male, ≥2172 kcal/d Female, ≥1661 kcal/d	11.3 (0.9)	70	17.3 (4.4)	8	
		$p2^{§}$	0.589		0.040		
	Carbohydrate intake (g/d)[††]	Male, <207 g/d Female,<151 g/d	10.8 (0.6)	66	10.0 (1.3)	9	0.040
		Male, <284 g/d, ≥207 g/d Female, <208 g/d, ≥151 g/d	12.5 (1.1)	66	14.6 (4.1)	9	
		Male, ≥284 g/d Female, ≥208 g/d	10.9 (0.5)	69	13.8 (1.7)	9	
		$p2^{§}$	0.739		0.045		
FG	Total energy intake (kcal/d)[¶]	Male, <1640 kcal/d Female, <1333 kcal/d	5.5 (0.2)	68	4.6 (0.2)	7	0.208
		Male, <2172 kcal/d, ≥1640 kcal/d Female, <1661 kcal/d, ≥1333 kcal/d	5.4 (0.2)	66	5.3 (0.3)	12	
		Male, ≥2172 kcal/d Female, ≥1661 kcal/d	5.5 (0.2)	71	7.5 (1.6)	8	
		$p2^{§}$	0.615		0.244		
	Carbohydrate intake (g/d)[††]	Male, <207 g/d Female, <151 g/d	5.7 (0.2)	66	4.7 (0.5)	9	0.216
		Male, <284 g/d, ≥207 g/d Female, <208 g/d, ≥151 g/d	5.2 (0.1)	69	6.1 (1.0)	9	
		Male, ≥284 g/d Female, ≥208 g/d	5.4 (0.2)	70	6.4 (1.2)	9	
		$p2^{§}$	0.366		0.393		

[†]Data are means(SE); [‡]$p1$ p for interaction between diet and SNP; [§]$p2$ p for trend for the association between dietary intake and insulin resistant related traits within each genotype group; [¶]Adjusted by gender, age, BMI, hypoglycemic medication; [††]Adjusted by gender, age, BMI: hypoglycemic medication, and energy intake.
FG: fasting glucose; HOMA-IR: homeostasis model assessment of insulin resistance.

mechanistic studies are needed. This study provides potential evidence for the personalized dietary guidelines.

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AUTHOR DISCLOSURES

There was no relationship that may pose a conflict of interest.

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Original Article

Diets high in carbohydrate may not be appropriate for rs328 G carriers with the metabolic syndrome

Shixiu Zhang PhD[1,2], Yiyi Ma PhD, MD[1,3], Hongwei Guo MD[1], Wentao Wan MD[1], Kun Xue PhD, MD[1]

[1]*Department of Nutrition and Food Hygiene, School of Public Health, Fudan University, Shanghai, China*
[2]*Department of Nutrition and Food Hygiene, School of Public Health, Shandong University, Jinan, China*
[3]*Jean Mayer US Department of Agriculture Human Nutrition Research Center on Aging at Tufts University, Boston, USA*

高碳水化合物的饮食可能不适合携带 rs328 G 等位基因的代谢综合征患者

本研究旨在探讨代谢综合征人群脂蛋白脂酶基因多态性在调节高碳水化合物饮食与胰岛素抵抗相关参数中的作用。通过多阶段抽样的方法，在上海市的两个城区筛选出代谢综合征患者，并将筛选出的研究对象按照区域划分为对照组和干预组（n=235）。营养干预期为一年，旨在教育研究对象增加全谷类食物、蔬菜、水果的摄入，减少钠、单糖和膳食脂肪（尤其是烹调油和猪油）的摄入。干预组 rs328 CC 基因型患者空腹血糖降低（p=0.028），而 rs328 G 等位基因携带者血糖没有显著变化（p=0.686）。同时，本文还对合并了干预组和对照组的基线资料进行了一个横断面研究分析，分析碳水化合物或脂肪与脂蛋白脂酶基因多态对稳态模型评估的胰岛素抵抗指数/胰岛素/空腹血糖的交互作用。碳水化合物摄入量与稳态模型评估的胰岛素抵抗指数在 rs328 G 等位基因携带者中呈正相关，而在 CC 基因型患者中没有关联（交互作用 p=0.025）。上述分析结果表明，高碳水化合物饮食可能不适合携带 rs328 G 等位基因的代谢综合征患者，不同基因型的代谢综合征患者可能需要不同的饮食方案。

关键词：基因膳食交互作用、碳水化合物、脂蛋白脂酶、代谢综合征、胰岛素抵抗