Low density lipoprotein receptor related protein 1 variant interacts with saturated fatty acids in Puerto Ricans

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Abstract

Low density lipoprotein related receptor protein 1 (LRP1) is a multi-functional endocytic receptor that is highly expressed in adipocytes and the hypothalamus. Animal models and *in vitro* studies support a role for LRP1 in adipocyte metabolism and leptin signaling, but genetic polymorphisms have not been evaluated for obesity in people. We examined whether dietary fats (eg., saturated, polyunsaturated) modulated the association of *LRP1* variants with anthropometric traits. We studied a population-based sample of Puerto Ricans (n=920, aged 45–74 y) living in the Boston area. In multivariable linear regression models, we dichotomized saturated fat intake and found significant interaction terms between total saturated fatty acids and *LRP1* rs1799986 genotype for BMI (P=0.006) and hip (P=0.002). High intake of saturated fat was associated with higher BMI (P=0.001), waist (P=0.008) and hip (P=0.003) in minor allele carriers (CT+TT) compared to CC participants. Further analysis of dichotomized individual saturated fatty acids revealed that interactions were strongest for two individual longer chain fatty acids. High intake of palmitic acid (C16:0; P=0.0007) and high stearic acid intake (C18:0; P=0.005) were associated with higher BMI in T carriers. Interactions were not detected for polyunsaturated fatty acids. Gene-diet interactions at the *LRP1* locus support the hypothesis that susceptibility to weight gain based on saturated fatty acids is modified by genotype and possibly by chain length. These results may facilitate the development of a panel of genetic candidates for use in optimizing dietary recommendations for obesity management.

Keywords

single nucleotide polymorphisms; saturated fatty acids; fatty acid chain length; Puerto Ricans

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Introduction

Obesity is generally recognized as a multi-factorial condition resulting from dietary, behavioral and genetic contributors. Recent genome-wide association studies (GWAS) have identified new obesity variants using an agnostic approach (1,2). In parallel with GWAS, dietary contributors to obesity continue to be explored, with remaining questions about whether macronutrient composition (eg, fats, carbohydrates, sugars) is relevant to weight maintenance. (3–7). Diets with high fat content are a standard method for producing obese animals experimentally (8) but the role of fat intake in human adiposity is less clear. Although saturated fat, specifically, appears to be more obesogenic in some animal and human studies (3), in others, weight loss is unrelated to any particular macronutrient (9). Similar questions exist for the role of carbon chain length of fatty acids (eg, medium chain vs. long chain), which are inconsistently associated with adiposity and weight loss (10–15). An analytic approach that examines gene-diet interactions may clarify inconsistent results for responses to dietary saturated fat, as well as uncover new obesity candidates.

Gene-diet interaction analysis has typically been performed for candidate genes, which are based on hypotheses reflecting a biological relationship between the gene and the phenotype. One such candidate is *LRP1,* which encodes low density lipoprotein receptor related protein 1. LRP1 is a multi-ligand endocytic receptor that mediates lipoprotein remnant uptake and that is highly expressed in several tissues including adipose and the hypothalamus (16,17). Evidence linking LRP1 to adiposity has been largely limited to animal models. Adipocyte-specific knockout experiments by several groups support a role in adipogenesis, cell signaling, and energy and glucose metabolism (18–21). Animal and *in vitro* studies also demonstrate that fatty acids modulate *LRP1* expression, suggesting that this gene could be responsive to dietary fats (8,22,23).

Although functional evidence for a role of LRP1 in obesity is accumulating, and a single previous study reported an association between *LRP1* genotype and BMI in people (24), studies evaluating relationships between *LRP1* genotype and diet have not been published. Therefore, the objective of the current study is to investigate relationships between *LRP1* genetic variants and dietary fatty acids for adiposity outcomes in a US Puerto Rican population.

Methods and Procedures

Study Design and Subjects

Participants were recruited for a prospective two-year cohort study of men and women of Puerto Rican origin aged 45–74 y and living in the Boston, Massachusetts, USA metropolitan area. Individuals were recruited through door-to-door enumeration, using US Census data to locate neighborhoods with a high density of Hispanic residents. Individuals were also invited to participate through flyers and at Hispanic community events and festivals. Eligibility for participation included self-reported Puerto Rican origin, living in the Boston area, and being able to answer interview questions in Spanish or English. Exclusion criteria were limited to age outside of the target range, plans to move away from Boston within two years and a Mini Mental Status Examination Score of <10. Interviews to collect

baseline demographic information, medical history and dietary data were conducted between 2004 and 2009 by trained bilingual staff. (25) 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 techniques used by the National Health and Nutrition Surveys. Blood was collected for biochemical analyses and genetic analysis, plasma was separated within 4 hours in a refrigerated centrifuge and was stored at −70° C.

Genetic analysis

Genomic DNA was isolated from peripheral blood lymphocytes by standard methods. *Low density lipoprotein receptor related protein* 1 single nucleotide polymorphisms (SNP) *LRP1* rs1799986, *LRP1* rs715948 and *LRP1* rs1800191 were genotyped using the ABI TaqMan SNP genotyping system 7900HT (Applied Biosystems, Foster City, California) using standard procedures. These SNPs were chosen for genotyping based on literature documenting associations with health-related phenotypes, including Alzheimer Disease. Linkage disequilibrium (LD) was estimated as a correlation coefficient (r^2) assessed using Haploview software version 4.0 (26).

Population ancestry admixture

The Puerto Rican study participants are characterized by admixture from three ancestral groups, European, Taíno American Indian, and African. In order to reduce confounding related to the population substructure created by multiple ancestries (27, 28), we estimated admixture from one hundred ancestry informative markers using principle components analysis. The calculated first major principle component was added to multivariable regression analysis models as a covariate.

Dietary Assessment

Dietary intake was assessed using a food frequency questionnaire (FFQ) that was adapted from the National Cancer Institute Block FFQ and modified for use in US Hispanics (29,30). The modified FFQ, which includes foods commonly consumed by Hispanics and open-ended portion sizes, more accurately estimated nutrients and energy intake in older Hispanics than the original FFQ based on its improved correlation with dietary recall data (29). Dietary data were linked to the Minnesota Nutrient Data system (NDS, 1999 version 25) for nutrient analysis. Participants with implausible dietary intakes (<600 or >4800 kcal/d) were excluded from analysis as previously established for this population (25). Intakes of saturated fat, polyunsaturated fat, and individual saturated fatty acids (C4:0, C6:0, C8:0, C10:0, C12:0, C14:0, C16:0 and C18:0) were expressed as percentages of total energy intake and were evaluated as categorical variables. To construct categorical variables, intakes were classified into two groups according to the median intake of the population.

Statistical Analyses

The relationship between *LRP1* genotypes, dietary intakes and anthropometric measures was evaluated by analysis of variance techniques. Interactions between dietary macronutrient intakes (including saturated fatty acids, polyunsaturated fatty acids and individual saturated

fatty acids) and polymorphisms were tested in a multivariable interaction model with control for potential confounders including age, sex, alcohol intake (grams/day), smoking (current vs. never and former), physical activity, anti-glycemic medication and ancestral admixture.

The population medians for saturated fat, polyunsaturated fat and individual fatty acids as percentages of total energy were used as cutoffs to dichotomize these variables. QUANTO software was used to estimate the sample size needed to achieve adequate statistical power (30). With R^2 fixed at 0.01, the number of participants needed to detect a relationship for the outcome of BMI with 80% power is 790. SAS (Version 9.1 for Windows) was used to analyze data. Adjustment for multiple testing was based on Bonferroni correction. Three SNPs and two macronutrients were planned for evaluation, and a *P* value of 0.008 (0.05/3×2) was considered statistically significant.

Results

Demographic, biochemical, anthropometric and genotypic data are presented in Table 1. Allele frequencies for the minor alleles of each SNP were 0.13 for *LRP1* rs1799986, 0.31 for *LRP1* rs715948, and 0.31 for *LRP1* rs1800191. Frequencies of the three genotyped SNPs did not deviate from Hardy-Weinberg equilibrium expectations (*P*>0.05) and the SNPs were not in LD (r^2<0.1). Following testing of each SNP using an additive model for the outcome of BMI, *LRP1* rs1799986 and *LRP1* rs715948 were evaluated using a dominant model (carriers of one or two copies of the minor allele were combined and compared to homozygous major allele individuals) and *LRP1* rs1800191 was evaluated using a recessive model (homozygous minor individuals were compared to homozygous major and heterozygotes combined). No significant associations for anthropometric traits (BMI and waist and hip circumference) were observed for the *LRP1* SNPs (Table 2).

Interactions between dietary fat intake (saturated and polyunsaturated) and *LRP1* genotype for each of the three SNPs were examined by dichotomizing each type of dietary fat according to the median population intake. Saturated fats were dichotomized into high and low according to the median intake of 9.3 (expressed as a percentage of total energy). Significant interaction terms between saturated fat intake and *LRP1* rs1799986 genotype were obtained for BMI (*P*=0.006) and hip circumference (*P*=0.002; Table 3). Adjustment for total energy intake, total fat, polyunsaturated fatty acids or dietary fiber did not alter significant relationships. Significant differences were observed for BMI (*P*=0.001), waist (*P*=0.008) and hip (*P* =0.003) between carriers of the *LRP1* rs1799986 minor allele (CT +TT) and non-carriers (CC) only when saturated fat intake was high (9.3% of total energy). No differences in anthropometric traits were observed by *LRP1* rs1799986 genotype when saturated fat intake was low (<9.3%). No significant interactions were detected between saturated fat and *LRP1* rs1800191 or *LRP1* rs715948 for anthropometric traits (Table 3). Interactions terms between *LRP1* rs1800191, *LRP1* rs715948 and rs1799986 for polyunsaturated fatty acids (*P*=0.2, *P*=0.1, *P*=0.6, respectively) for the outcome of BMI were not significant. Multivariable adjustments for potential confounders included age, sex, smoking status, alcohol intake, physical activity, anti-glycemic medication and ancestral admixture.

Based on significant interactions between total saturated fats and *LRP1* rs799986 genotype for anthropometric traits, we next evaluated interactions between the single SNP rs799986 and individual saturated fatty acids for BMI (Table 4). Each fatty acid was dichotomized into high and low based on the population median intakes. Based on a Bonferroni adjusted *P* value threshold of 0.008, we detected a significant genotype interaction term with palmitic acid (C16:0; *P*=0.004) for the outcome of BMI. LRP1 rs799986 interaction with stearic acid (C18:0; *P*=0.03) did not reach significance following adjustment for multiple testing. The pattern of interaction was the same for the individual fatty acid as for total saturated fatty acids, in that BMI was greater in carriers of the minor allele (T) for palmitic (C16:0; *P*=0.0007) and stearic (C18:0; *P*=0.005) only when intake of the individual fatty acid was high.

Major food group sources of longer chain fatty acids (eg, those contributing more than five per cent in this population) are identified (Table 5). Whole fat dairy foods and cooking oil are major sources of myristic, palmitic and stearic acids.

Discussion

We have detected an interaction between saturated fat intake and *LRP1* genotype for obesity-related traits in a US Puerto Rican population. Although genotype-based differences were not significant in the overall population, *LRP1* genotype was associated with consistently greater adiposity in the context of high saturated fat intake. Additionally, the gene-diet interactions were not consistent for all saturated fatty acids, and were most apparent for those of longer carbon chain length (e.g., palmitic and stearic). These observations support a role for *LRP1* genetic variation in modulating sensitivity to saturated fat intake. To our knowledge, relationships between genetic variability, fatty acid chain length and obesity have not been previously described. Overall, results from this study may begin to address the challenges of translating animal studies into knowledge that may be applied to the management of obesity in people.

Previous population-based studies for *LRP1* and adiposity are limited to a single study of US Whites, in which the SNP rs715948 was nominally associated with BMI (24). Although the previous study supports a role for *LRP1* genetic variation in weight-related phenotypes, rs715948 was not associated with anthropometric traits in Boston Puerto Ricans. Supplementing this human study are functional data from animal and *in vitro* models support *LRP1* as a potential obesity candidate. As a cell surface receptor capable of binding more than forty ligands ranging from apolipoprotein E to leptin, *LRP1* is a multifunctional protein that is expressed in many tissues (16). A series of experiments using adipocyte-specific *LRP1* knockout mice demonstrated the role of *LRP1* as a regulator of adipogenesis, fat storage and obesity (18–20). Subsequent *in vitro* studies using *LRP1* deficient pre-adipocytes (murine embryonic fibroblasts) have revealed LRP1 as an essential 'adaptor molecule' that complexes with ShcA (Src homology 2/α-collagen) to regulate insulin-like growth factor 1 mediated switching between adipocyte proliferation and differentiation (21).

Gene expression studies supplement the data gained from knockout and *in vitro* models, suggesting that *LRP1* may be responsive to dietary factors. In the current study we detected

a significant interaction between dietary saturated fat and *LRP1* rs1799986 for adiposity. However, most *in vitro* studies support a role of unsaturated rather than saturated fatty acids in the regulation of *LRP1* expression. For example, the unsaturated fatty acids arachidonic (C20:4) and oleic acid (C18:1) increased *LRP1* expression through activation of peroxisome proliferator-activated receptor gamma (PPARγ) (22). A single intervention in mice documented increased expression of adipocyte *LRP1* in response to high saturated fat (58% saturated fat) intake, and this increase preceded and predicted high weight gain. Although sequence variation was not evaluated in that study because the mice were genetically identical, the authors hypothesize that saturated fat acts epigenetically with *LRP1* and other genes to alter gene expression and adiposity phenotypes (8,32). Whether genetic variation could modify the epigenetic relationship is unknown.

Whereas most functional studies of *LRP1* and adiposity generate hypotheses based on adipocyte metabolism and differentiation, recent research has explored alternative mechanisms that depend on altered energy intake (17). LRP1 binding to leptin was previously demonstrated, with potential effects on the bioavailability of plasma leptin and implications for altered eating behavior (33). More recently, hypothalamic LRP1 was shown to regulate leptin signaling and energy homeostasis in mice, in which deletion of forebrain *Lrp1* caused increased food intake and obesity (17). Specifically, LRP1 binding to leptin was required for activation of Stat3 (signal-transduction-activated-transcript-3), a previously established hypothalamic target of leptin (34). Interestingly, subsequent studies demonstrated that Stat3-knockout mice exhibit increased appetite and weight gain (36). Further, *STAT3* genotype-associated obesity risk is heightened in people with high saturated fat intake (35). Based on observations that a high fat diet or saturated fats have been shown to promote resistance to anorexigenic signaling via stimulation of inflammatory molecules in animal models (37,38), we hypothesize that saturated fat dysregulation of hypothalamic function may be mediated through multiple participants. Joint genetic interaction analyses of *STAT3, LRP1* and other signaling pathway participants could yield potential additional genetic candidates that modulate saturated fat induced weight gain.

In spite of increased understanding of the actions of saturated fatty acids at the level of cell signaling, whether additional properties of saturated fatty acids alter obesity risk is unknown. Fatty acid chain length, for example, differentially affects transport and oxidation with potential implications for energy metabolism. (39). Whereas medium chain fatty acids are transported via the portal vein to the liver for oxidation, long chain fatty acids are absorbed via the lymphatic ducts and transported in chylomicrons to the thoracic duct and into systemic circulation. Results from clinical trials investigating the role of fatty acid chain length in weight loss have been inconsistent. In some, but not all studies, intake of medium-chain triacylglycerols or fatty acids have been associated with reduced body weight compared to longer chain fatty acids (10,11,13–15). In a cross-over, inpatient trial designed to evaluate the specific effect of saturated fatty acid chain length, obese women consuming 67% of fat as medium chain fatty acids (octanaote (C8:0) and decanoate (C10:0)) demonstrated increased energy expenditure and fat oxidation compared to those consuming fat derived exclusively from beef tallow (long chain saturated fatty acids) (11). In spite of rigorous methodology in that study, considerable interindividual variability was reported in

changes in adipose tissue volume in response to chain length differences, suggesting the possibility of genetic modulation of these responses.

In the current study, after adjustment for multiple testing, we detected significant interactions between *LRP1* rs1799986 genotype and the longer chain fatty acid, palmitic (C16:0), with a tendency for similar interaction for stearic acid (C18:0). Whole fat dairy foods and corn oil were important sources of longer chain saturated fatty acids in this population. Although the predominant fatty acids in corn oil are polyunsaturated, corn oil contains a proportion of saturated fatty acids. A previous study in a Boston population of Puerto Rican and Dominican elders documented high consumption of corn oil, identifying cooking oils as the second highest source of energy in those with high rice consumption (30). Several mechanisms can be proposed to account for the observed statistical interactions of *LRP1* with longer chain fatty acids. As a member of the LDL receptor family, LRP1 functions as a chylomicron remnant receptor, and may therefore be expected to functionally interact with long chain fatty acids that are transported in chylomicrons. Alternatively, investigation of the peroxisome proliferator-activated receptor gamma response element (PPRE) in human adipocytes demonstrated that palmitic and stearic acids, but not lauric (C12:0) acid, increased PPRE activity compared to basal levels (40). Theoretically, the rs1799986 SNP, although not yet shown to be functional, could be linked to a "loss of function" variant that does not respond appropriately to long-chain fatty acid exposure, resulting in dysregulation of *LRP1* expression. Based on adipocyte-specific *LRP1* silencing in mice, which results in a lean phenotype, we might hypothesize that the variant is associated with overexpression of *LRP1* and increased adipogenesis in response to long chain saturated fatty acids. In the current population, we note that palmitic and stearic acids represent the greatest sources of saturated fatty acids, which may facilitate detection of interactions. However, these interactions may also suggest that susceptibility to weight gain based on saturated fatty acid chain length may be modified by genotype.

Limitations of the current study suggest the need for a range of additional studies of *LRP1*. Most importantly, evaluation of replication of these results in independent populations of additional ethnic groups is critical. Similarly, evaluation of additional SNPs is needed, particularly because functionality for *LRP1* rs1799986 has not been established. Finally, the population in the current study is characterized by a high prevalence and severity of obesity and high prevalence of diabetes, which could limit the generalizability of our results to healthier populations.

In summary, we have detected gene-diet interactions that may help to explain apparent differences in susceptibility to the high saturated fat intake that characterize the Western diet. The dual roles of LRP1 in both adipocyte metabolism and hypothalamic leptin signaling increase its appeal as a potential obesity candidate. Expansion of our knowledge of obesity candidates and their modifiers not only adds to biologic understanding, but also facilitates the development of a panel of candidates whose genotypes may be applied to optimize dietary recommendations for obesity management.

Acknowledgments

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Table 1

Demographic, biochemical, lifestyle and genotypic characteristics.[1]

Age, y	57.2 ± 7.8
Female, n (%)	676 (71.5)
Height, cm	159 ± 9
Weight, kg	80 ± 17
BMI, kg/m^2	31.9 ± 6.6
Obese, n(%)[2]	546 (58.5)
Waist, cm	102 ±15
Hip, cm	109 ±14
Total energy intake (kcal)	2117.6 ± 876.9
Total fat intake, % total energy	31.2 ± 5.2
Saturated fat intake, % total energy	9.5 ± 2.2
Butyric acid (C4:0) intake, % total energy	0.19 ± 0.11
Caproic acid (C6:0) intake, % total energy	0.11 ± 0.06
Caprylic acid (C8:0) intake, % total energy	0.09 ± 0.05
Capric acid (C10:0) intake, % total energy	0.15 ± 0.08
Lauric acid (C12:0) intake, % total energy	0.21 ± 0.12
Myristic acid (C14:0) intake, % total energy	0.76 ± 0.33
Palmitic acid (C16:0) intake, % total energy	5.4 ± 1.11
Stearic acid (C18:0) intake, % total energy	2.2 ± 0.6
Polyunsaturated fat intake, % total energy	7.7 ± 1.8
Current alcohol use, n (%)	359 (38.1)
Current smoker, n (%)	217 (23.2)
Diabetes medication, n (%)	309 (32.7)
LRP1 rs1799986, n(%)	
CC	735 (82.7)
CT	144 (16.2)
TT	10 (1.1)
LRP1 rs715948, n(%)	
CC	484 (54.4)
CT	355 (39.9)
TT	51 (5.7)
LRP1 rs1800191, n(%)	
GG	330 (36.8)
GA	424 (47.3)
AA	142 (15.9)

[1] Values are mean±SD or n(%)

[2] Obesity=BMI 30 kg/m^2

Table 2

Associations for *LRP1* SNPs in Boston Puerto Rican Health Study[1,2]

LRP1 rs1799986	CC (n=735)	CT+TT (n=154)	P
BMI (kg/m^2)	31.2 ± 0.3	32.3 ± 0.6	0.06
Waist (cm)	102 ± 0.7	104 ± 1.3	0.12
Hip (cm)	108 ± 0.6	110 ± 1.2	0.05
LRP1 rs1800191	GG+GA(n=754)	AA (n=142)	P
BMI (kg/m^2)	31.4 ± 0.3	30.6 ± 0.6	0.2
Waist (cm)	102 ± 0.7	101 ± 1.3	0.5
Hip (cm)	108 ± 0.7	106 ± 1.2	0.1
LRP1 rs715948	CC (n=484)	CT+TT(n=406)	P
BMI (kg/m^2)	31.6 ± 0.3	31 ± 0.4	0.2
Waist (cm)	103 ± 0.8	102 ± 0.9	0.4
Hip (cm)	108 ± 0.7	108 ± 0.8	0.4

[1]Values are mean±SEM

[2]Adjusted for age, sex, physical activity, smoking status, anti-glycemic medication, alcohol intake, ancestral admixture

Table 3

Interactions between *LRP1* variants and saturated fat intake for adiposity traits in the Boston Puerto Rican Health Study [1,2]

LRP1 **rs1799986**

Saturated fat intake(% energy intake/d)		CC (n=735)	CT+TT (n=154)	*P*	*P* interaction
<9.3	BMI (kg/m²)	31.0 ± 0.4	31.3 ± 0.4	0.5	0.006
9.3		30.5 ± 0.8	33.9 ± 0.8	0.001	
<9.3	Waist (cm)	101 ± 0.9	100 ± 1.8	0.6	0.02
9.3		103 ± 0.9	108 ± 1.7	0.008	
<9.3	Hip (cm)	107 ± 0.8	106 ± 1.6	0.4	0.002
9.3		108 ± 0.8	114 ± 1.6	0.003	

LRP1 **rs1800191**

Saturated fat intake(% energy intake/d)		GG+GA (n=754)	AA (n=142)	*P*	*P* interaction
<9.3	BMI (kg/m²)	31 ± 0.4	29.8 ± 0.7	0.1	0.4
9.3		31.6 ± 0.4	31.4 ± 0.8	0.8	
<9.3	Waist (cm)	101 ± 0.9	100 ± 1.7	0.5	0.7
9.3		103 ± 0.9	103 ± 2	1	
<9.3	Hip (cm)	107 ± 0.9	104 ± 1.6	0.1	0.4
9.3		109 ± 0.8	109 ± 1.8	0.8	

LRP1 **rs715948**

Saturated fat intake(% energy intake/d)		CC (n=484)	CT+TT (n=406)	*P*	*P* interaction
<9.3	BMI (kg/m²)	31.1 ± 0.5	30.6 ± 0.5	0.4	0.9
9.3		32 ± 0.5	31.4 ± 0.5	0.3	
<9.3	Waist (cm)	101 ± 1.1	101 ± 1.2	0.7	0.7
9.3		104 ± 1	103 ± 1.1	0.4	
<9.3	Hip (cm)	107 ± 1	107 ± 1.1	1	0.4
9.3		110 ± 1	108 ± 1	0.2	

[1] Values are mean±SEM

[2] Adjusted for age, sex, physical activity, smoking status, alcohol intake, anti-glycemic medication, ancestral admixture

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Table 4

Interactions between *LRP1* rs1799986 and individual fatty acids for BMI in the Boston Puerto Rican Health Study[1,2]

Fatty acid intake (% energy intake/d)		CC (n=735)	CT+TT (n=154)	P	P interaction
Butyric acid (C4:0)	<0.17	31.1 ± 0.4	31.6 ± 0.7	0.5	0.3
	0.17	31.2 ± 0.4	33.0 ± 0.8	0.04	
Caproic acid (C6:0)	<0.10	31.1 ± 0.4	31.3 ± 0.7	0.8	0.1
	0.10	31.2 ± 0.4	33.4 ± 0.8	0.01	
Caprylic acid (C8:0)	<0.08	31.5 ± 0.4	31.5 ± 0.8	1.0	0.1
	0.08	30.9 ± 0.4	33.1 ± 0.8	0.008	
Capric acid (C10:0)	<0.14	31.2 ± 0.4	31.5 ± 0.7	0.8	0.1
	0.14	31.1 ± 0.4	33.1 ± 0.8	0.02	
Lauric acid (C12:0)	<0.18	31.1 ± 0.4	31.7 ± 0.8	0.5	0.3
	0.18	31.2 ± 0.4	32.9 ± 0.8	0.04	
Myristic acid (C14:0)	<0.71	31.2 ± 0.4	31.3 ± 0.8	0.9	0.1
	0.71	31.1 ± 0.4	33.3 ± 0.8	0.009	
Palmitic acid (C16:0)	<5.44	31.1 ± 0.4	30.6 ± 0.7	0.5	0.004
	5.44	31.2 ± 0.4	34.0 ± 0.8	0.0007	
Stearic acid (C18:0)	<2.23	31.0 ± 0.4	30.7 ± 0.8	0.8	0.03
	2.23	31.3 ± 0.4	33.6 ± 0.7	0.005	

[1] Values are mean±SEM

[2] Adjusted for age, sex, physical activity, smoking status, alcohol intake, anti-glycemic medication, ancestral admixture

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Table 5

Major contributors to longer chain saturated fatty acids in the Boston Puerto Rican Health Study[1]

Source of saturated fatty acid	% of intake supplied by food group
Myristic acid (C14:0)	
Cheese, processed	16.2
Cheese, natural	13
Milk, whole	12.2
Palmitic acid (C16:0)	
Oils, corn	11.4
Cheese, processed	6.9
Cheese, natural	5.4
Milk, whole	5.1
Stearic acid (C18:0)	
Cheese, processed	7.1
Milk, whole	5.5
Cheese, natural	5.2

[1]Foods contributing at least 5% of total intake are included.