Five-Week, Low–Glycemic Index Diet Decreases Total Fat Mass and Improves Plasma Lipid Profile in Moderately Overweight Nondiabetic Men

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OBJECTIVE — To evaluate whether a 5-week low–glycemic index (LGI) diet versus a high–glycemic index (HGI) diet can modify glucose and lipid metabolism as well as total fat mass in nondiabetic men.

RESEARCH DESIGN AND METHODS — In this study, 11 healthy men were randomly allocated to 5 weeks of an LGI or HGI diet separated by a 5-week washout interval in a crossover design.

RESULTS — The LGI diet resulted in lower postprandial plasma glucose and insulin profiles and areas under the curve (AUCs) than the HGI diet. A 5-week period of the LGI diet lowered plasma triacylglycerol excursion after lunch (AUC, $P < 0.05$ LGI vs. HGI). These modifications were associated with a decrease in the total fat mass by ~700 g ($P < 0.05$) and a tendency to increase lean body mass ($P < 0.07$) without any change in body weight. This decrease in fat mass was accompanied by a decrease in leptin, lipoprotein lipase, and hormone-sensitive lipase RNAm quantities in the subcutaneous abdominal adipose tissue ($P < 0.05$).

CONCLUSIONS — We concluded that 5 weeks of an LGI diet ameliorates some plasma lipid parameters, decreases total fat mass, and tends to increase lean body mass without changing body weight. These changes were accompanied by a decrease in the expression of some genes implicated in lipid metabolism. Such a diet could be of benefit to healthy, slightly overweight subjects and might play a role in the prevention of metabolic diseases and their cardiovascular complications.

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The insulin-resistance syndrome is a major risk factor for abnormal carbohydrate metabolism and atherosclerotic and coronary heart diseases (1). Recent prospective studies have incriminated the high–glycemic index (HGI) diet in the genesis of insulin resistance and type 2 diabetes (2). High postprandial plasma glucose and insulin excursions are assumed by some authors (3) to be independent predictors of risk for atherosclerotic diseases. Epidemiological evidence shows that the relationship between plasma glucose concentrations and cardiovascular diseases extends well below the glucose level defined for diabetes and even for impaired glucose tolerance. Therefore, interventions to reduce postprandial glycemia in the normal population could reduce the risk of developing atherosclerotic heart disease and/or diabetes. Dietary intervention might be one of the major approaches in diabetic patients' care, but it might even be useful in normal nondiabetic individuals.

In diabetic subjects, the chronic consumption of a low–glycemic index (LGI) diet is generally found to improve plasma glucose and lipid profiles (4). In clinical practice, however, the chronic use of LGI foods is still questioned (5).

In nondiabetic subjects, few data exist on the effects of short- and long-term consumption of LGI foods (6–8). Behall et al. (6) demonstrated that an LGI diet resulted in a decrease in both glycemic area under the curve (AUC) and plasma cholesterol and triacylglycerol levels. Most of these studies, with one exception (8), have demonstrated beneficial effects with regard to plasma glucose and lipid parameters.

Although the main focus in human studies has been on the evaluation of plasma glucose and lipid control, animal study models extend beyond these results to reach underlying cellular and molecular mechanisms. In rats, the chronic consumption of an LGI diet has been shown to increase insulin-stimulated glucose oxidation in isolated adipocytes (9), but to also reduce de novo lipogenesis and adipocyte diameter (10). A 16-week LGI diet also ameliorates whole-body insulin resistance (11). Thus, it is hypothesized that the chronic consumption of LGI foods could decrease adiposity and increase insulin sensitivity.

Therefore, our aim was to evaluate the long- and short-term effects of LGI diets on fat mass distribution and plasma glucose and lipid metabolism in moderately

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Abbreviations: apo, apolipoprotein; AUC, area under the curve; DEXA, dual-energy X-ray absorptiometry; GI, glycemic index; HGI diet, high–glycemic index diet; HOMA, homeostasis model assessment; LGI diet, low–glycemic index diet; LPL, lipoprotein lipase, PPAR-γ, peroxisome proliferator–activated receptor-γ.

A table elsewhere in this issue shows conventional and Système International (SI) units and conversion factors for many substances.

Table 1—*Clinical characteristics of subjects*

Variables	
n	11
Age (years)	46 ± 3
Body weight (kg)	86 ± 3
BMI (kg/m^2)	28 ± 1
Fasting glycemia (mmol/l)	5.61 ± 0.01
Plasma cholesterol (mmol/l)	5.67 ± 0.23
Plasma triacylglycerols (mmol/l)	1.62 ± 0.17

Data are means ± SEM.

overweight nondiabetic subjects. Furthermore, to understand the underlying mechanisms, we determined the expression of some genes and enzymes implicated in lipid metabolism.

RESEARCH DESIGN AND METHODS

— Clinical characteristics for the 11 male study subjects are given in Table 1. Subjects with abnormal renal, hepatic, or thyroid function were excluded ($n = 5$). None of the subjects was taking any drug that might affect glucose, insulin, or lipid metabolism. The Ethical Committee of Hôtel-Dieu Hospital approved the experimental protocol. The purpose, nature, and potential risks of the study were explained to, and written informed consent was obtained from, each subject.

Study design

The patients were randomly allocated to two periods of 5 weeks of an LGI or HGI diet in a crossover design. The two nutritional periods were separated by a washout interval of 5 weeks. Before the beginning of the study, all subjects were instructed to maintain their usual lifestyle during the experimental period.

At the beginning and end of each nutritional period, subjects were hospitalized for 2 days after an overnight fast. During the first day, a sample of abdominal subcutaneous adipose tissue was obtained by needle biopsy using a 14-gauge needle and a 30-ml syringe under local anesthesia with xylocaine 10% without adrenaline. The tissue obtained was rapidly frozen in liquid nitrogen and stored at −80°C. On the same day, an indwelling cannula was inserted into an antecubital vein for the hourly withdrawal of blood samples during the metabolic day profile. Each subject consumed an LGI or HGI breakfast at 0830 and lunch at 1230. The diet during the 1-day profile had the same high or low glycemic index (GI) percent as did the diet for the chronic period (breakfast mean GI, 75 vs. 38%; lunch mean GI, 73 vs. 41%). Blood samples were collected in the fasting state ($t = 0$) and hourly during the 8-h metabolic day profile. Blood samples were centrifuged, and plasma was frozen (−20°C) for further measurements of plasma glucose, insulin, and lipids. At $t = 0$, plasma fructosamine, leptin, HDL, apolipoprotein (apo)-A1 and apoB levels were also measured. During the first day, body lean and fat mass distributions were also measured by a dual-energy X-ray absorptiometry (DEXA) with a total-body DEXA scanner Holojic QDR-2000, as previously described (12).

During the second day, three blood samples were taken from fasted subjects at 5-min intervals to measure insulin sensitivity and secretion by the homeostasis model assessment (HOMA) using HOMA/continuous infusion of glucose model assessment (CIGMA) software (13).

Glucose turnover and hepatic glucose production

In the morning of the experiment, at 0800, one catheter was placed in an antecubital vein for a primed and continuous [6,6-$^2H_2$] glucose infusion (Mass Trace, Woburn, MA). Another catheter was placed retrogradedly into a lateral wrist vein for blood sampling. After a priming dose of 5 mg/kg of [6,6-$^2H_2$]glucose, the infusion rate of glucose was maintained at 3 mg · kg^{-1} · h^{-1} for 3 h. To determine the [6,6-$^2H_2$] glucose enrichment, blood samples were withdrawn before the isotope infusion and at 10-min intervals during the last 30 min, based on the assumption that the plasma glucose steady state was achieved (14). The calculation of the hepatic glucose production was made according to the formula $Ra = i/Ep$, where Ra is the rate of glucose production, i is the tracer infusion rate, and Ep is the [6,6-$^2H_2$]glucose isotopic enrichment in the plasma.

Dietary follow-up

The GIs ascribed to the foods used were taken from either published data (15) or an unpublished French work (J. Maffré, J.L. Volatier, G. Slama, V. Lang, M. Champ: Measurements of the Glycemic Index of Foods in the French Population, 2000). Values for the special cereals and the LGI cookies used in the study were provided by the suppliers (Nestle, Orbe, Switzerland; Danone Vitapole and Nestle, France). The diet in the two experimental periods consisted of ordinary food items. In the LGI period, carbohydrate items with a GI <45% were recommended, whereas foods with a GI >60% were recommended in the HGI period. This was accomplished by providing each subject with a list of the recommended daily intake of commonly used foods and a substitution list allowing exchanges within food groups.

Each subject entered a run-in period of 15 days. Subjects received individual counseling by a dietitian concerning food intake. Dietary intake was prescribed individually according to data obtained from dietary questionnaires (3-day recall technique). Total energy and macronutrient intakes of the experimental diets were similar to those of the regular diet for each subject, except for the type of carbohydrate. To assess compliance with the dietary recommendations, patients were asked to complete a food diary on the last 7 days of each dietary period. When subjects returned their records at the end of each dietary period, the dietitian checked the records and clarified any ambiguous information with each subject. Records were analyzed using the computer program Profile Dossier V3 software (Audit Conseil en Informatique Médicale, Bourges, France), whose dietary database is made up of 400 foods or groups of foods representative of the French diet. French food contents were obtained from Ciqual Repertory (16).

Biological assays

Glucose was measured by the glucose oxidase method using a glucose analyzer (Beckman, Fullerton, CA). Insulin was determined by a radioimmunoassay (RIA Diagnostic; Pasteur, Marnes La Coquette, France). The antibody used in the test showed a cross-reactivity of 100% with human insulin. Plasma triacylglycerols and free fatty acids were measured with Biomérieux kits (Marcy-l'Etoile, France), total cholesterol with Labintest kits (Aix-en-Provence, France), and apoA1 and apoB by an immunochemical assay with Boehring kits (Mauburg, Germany). Fructosamine was measured with an adapted Fructosamine Test Plus kit (Roche, Neuilly-sur-Seine, France), and leptin was determined with a Linco kit (St. Charles, MO). Isotopic enrichment

Table 2—*Plasma glucose, insulin, and fructosamine values during the metabolic day profile before (baseline) and after 5 weeks of HGI or LGI diet*

	HGI diet		LGI diet	
	Baseline	5 Weeks	Baseline	5 Weeks
Glycemia				
Fasting (0 min; mmol/l)	5.38 ± 0.06	5.26 ± 0.11	5.43 ± 0.1	5.36 ± 0.11
Morning peak (60 min; mmol/l)	7.74 ± 0.32*	7.7 ± 0.44†	6.04 ± 0.37	6.6 ± 0.28‖
Before lunch (240 min; mmol/l)	4.62 ± 0.14*	4.5 ± 0.13†	5.3 ± 0.19	5.03 ± 0.13‖
Afternoon peak (300 min; mmol/l)	6.37 ± 0.23	6.03 ± 0.34	5.7 ± 0.11	6.36 ± 0.27‡§
Morning AUC (mmol · l^{-1} · 4 h^{-1})	152 ± 22*	187 ± 23†	65 ± 23	109 ± 22¶
Afternoon AUC (mmol · l^{-1} · 4 h^{-1})	188 ± 32*	179 ± 33†	93 ± 23	119 ± 21§
Insulinemia				
Fasting (0 min; pmol/l)	96.5 ± 17.1	228.9 ± 127.7	132.4 ± 134.2	93.9 ± 15.2
Morning peak (60 min; pmol/l)	751.4 ± 129.7	840.1 ± 216.6†	480.1 ± 130.4	497.1 ± 80.6§
Before lunch (240 min; pmol/l)	126.5 ± 34.1	128.9 ± 34.5	163.1 ± 25.1	107.6 ± 18.7‡§
Afternoon peak (300 min; pmol/l)	507.5 ± 94.6	609.9 ± 134.2†	521.2 ± 117.1	501.6 ± 127.9§
Morning AUC (pmol · l^{-1} · 4 h^{-1})	54,159 ± 10,889	72,148 ± 13,995†	35,399 ± 7,566	37,669 ± 6,238§
Afternoon AUC (pmol · l^{-1} · 4 h^{-1})	53,010 ± 8,896*	59,526 ± 12,217†	34,049 ± 9,029	41,347 ± 8,745§
Fructosamine (mmol/l)	1.94 ± 0.07	1.86 ± 0.12	2.01 ± 0.06	1.90 ± 0.07

Data are means ± SEM (n = 11). Values were taken just before (in the fasting state) or after meal. *$P < 0.05$ vs. baseline values of LGI diet; †$P < 0.05$ vs. 5-week values of LGI diet; ‡$P < 0.05$ for changes during the dietary periods (delta: baseline −5 week, HGI vs. LGI); §$P < 0.05$, ‖$P < 0.001$, ¶$P < 0.0001$, by multiple ANOVA.

for [6,6-$^2H_2$]glucose was determined by capillary gas chromatography coupled with electron-ionization mass spectrometry. The incremental AUCs were calculated according to the trapezoidal method, as previously described (17).

Gene expression of ob, peroxisome proliferator–activated receptor-γ, lipoprotein lipase, and HSL

The RNA from adipose tissue (~80–100 mg of frozen tissue) was obtained by using the RNeasy total RNA kit (Qiagen, Courtaboeuf, France), as previously indicated (18). RNA integrity was verified on agarose gel electrophoresis and was similar in all the samples obtained after the LGI and HGI diets. Total RNA was stored at −80°C for <6 months before analysis. Studied genes were quantified by RT-competitive PCR. The RT reactions and the analysis of the amplified products were performed as previously described (19). The construction of the competitor DNA molecules, the sequence of the primers, and the validation of the RT-competitive PCR assay for ob (18), peroxisome proliferator–activated receptor-γ2 (PPAR-γ2) (19), lipoprotein lipase (LPL), and HSL (20) mRNAs have been described elsewhere.

Statistical methods

The validity of the crossover design was tested by ANCOVA of the baseline results of the second period, with the baseline results of the first period as the covariable and the treatment of the first period as the main factor. The effects of the two diets were compared by a multiple ANOVA followed by a post hoc test (least significant differences test). The main factors considered in the analysis were the type of diet (with two values: HGI and LGI), the time of the assay (with two levels: day 0 and 5 weeks), and the order of diets (with two levels). To analyze the acute effects, we compared the effects of a 1-day LGI diet to those of a 1-day diet at the beginning of each dietary period. To analyze the chronic effects, we compared the effects of the two diets at the end of the nutritional periods. Changes during each dietary period (5-week results − baseline results) were also compared (LGI versus HGI). The dietetic evaluations at the beginning and end of each period were compared two by two with a Student's paired t test.

All statistical analyses was performed using a CSS statistical package (StatSoft, Tulsa, OK). Results were considered significant when $P < 0.05$. Data are expressed as means ± SEM.

RESULTS

— The 11 subjects followed the two dietary periods of 5 weeks each without any difficulty, although 3 subjects noted some flatulence with the LGI diet. According to self-report, subjects' lifestyles were unchanged throughout the entire study. There was no effect of the crossover design (LGI or HGI diets) or interaction between diet and period for any of the studied parameters.

Diets and body weight

Results of the 7-day dietary records were unchanged at the end of the two dietary periods with regard to total daily energy (2,462 ± 75 vs. 2,204 ± 65 kcal for HGI vs. LGI), macronutrients (carbohydrate: 42 ± 1 vs. 39 ± 1% of energy; protein: 18 ± 1 vs. 20 ± 1% of energy; fat: 37 ± 1 vs. 38 ± 1%), and alcohol intake. There were no significant changes in total glucose (1.6 ± 0.8 vs. 4.4 ± 1.9 g/day, HGI vs. LGI) or fructose (12.0 ± 5.8 vs. 12.7 ± 6.8 g/day, respectively) content of the diets. The main difference between the two diets was the calculated GI (71.3 ± 1.3 vs. 41.0 ± 1.0% for HGI vs. LGI; $P < 0.0001$). An increase in the fiber content after the LGI diet was also found (19 ± 1 vs. 31 ± 2 g; $P < 0.0001$). Body weight was comparable between the end of the HGI and LGI periods (86.5 ± 2.7 vs. 85.7 ± 2.9 kg).

Metabolic profiles

Glycemic, insulinemic profiles, and fructosamine. As shown in Table 2, postprandial plasma glucose was lower with the LGI than with the HGI diet during the 1-day profile. Plasma glucose

Table 3—*Plasma lipids, plasma lipoproteins and fat mass distribution during the metabolic day profile before (baseline) and after 5 weeks of HGI or LGI diets*

	HGI diet		LGI diet	
	Baseline	5 Weeks	Baseline	5 Weeks
Total cholesterol				
Fasting (0 min; mmol/l)	5.52 ± 0.42	5.30 ± 0.39	5.30 ± 0.27	4.90 ± 0.38#
Morning AUC (mmol/min)	886 ± 61	824 ± 55	845 ± 47	762 ± 55‡
Afternoon AUC (mmol/min)	897 ± 68	782 ± 0	874 ± 61	768 ± 57
Triacylglycerols				
Fasting (0 min; mmol/l)	1.33 ± 0.15	1.37 ± 0.22	1.59 ± 0.25	1.50 ± 0.42
Morning AUC (mmol · l^{-1} · 4 h^{-1})	292 ± 40	272 ± 47	336 ± 38	336 ± 62
Afternoon AUC (mmol · l^{-1} · 4 h^{-1})	334 ± 43	376 ± 55	413 ± 49	335 ± 36¶*
FFA (0 min; mmol/l)	0.31 ± 0.02	0.32 ± 0.04	0.32 ± 0.03	0.39 ± 0.06
HDL cholesterol (mmol/l)	1.06 ± 0.09	1.06 ± 0.01	0.98 ± 0.08	1.01 ± 0.08
LDL cholesterol (mmol/l)§	4.01 ± 0.26	3.74 ± 0.21	3.71 ± 0.16	3.35 ± 0.32
ApoA (g/l)	1.5 ± 0.09	1.45 ± 0.08	1.45 ± 0.08	1.44 ± 0.09
ApoB (g/l)	1.28 ± 0.08	1.2 ± 0.07	1.21 ± 0.07	1.14 ± 0.06†
Total fat mass (kg)	19.54 ± 1.52	19.52 ± 1.57	19.27 ± 1.69	18.75 ± 1.59‖¶*
Trunk fat (kg)	9.32 ± 0.86	8.92 ± 0.88	8.70 ± 0.93	8.41 ± 0.86‖**

Data are means ± SEM. Values taken just before (in the fasting state) or after meal. §LDL was calculated using the Friedewald formula. Tendency between the end of each period: 5 week data (HGI vs. LGI): #$P = 0.065$, †$P = 0.076$, ‡$P = 0.085$, ‖$P < 0.05$ between the end of each period: 5-week data (HGI vs. LGI) by multiple ANOVA; ¶significant changes during the dietary periods (delta: baseline −5 week, HGI vs. LGI) global results: *$P < 0.05$, **$P < 0.0001$, by multiple ANOVA.

peaks (at 60 min) were lower with the LGI breakfast than with the HGI breakfast. The incremental AUCs for plasma glucose after the LGI breakfast and lunch were consistently lower than those with the HGI meals. A decrease in plasma glucose levels was observed 4 h (240 min) after the HGI breakfast. These results were found at the beginning and end of each experimental period and validated the experimental diets. However, there was no difference for the same diet between the baseline and 5-week metabolic 1-day profile.

Postprandial plasma insulin was consistently lower after the LGI than after the HGI diet (Table 2). At the end of the two dietary periods, the insulin morning peaks (60 min) and the morning insulin incremental AUCs were lower with the LGI than with the HGI breakfast. Likewise, at the end of the two dietary periods, the afternoon insulin peaks (300 min) and the insulin afternoon incremental AUCs were low with the LGI lunch. When the two diets were compared, there was no modification in fasting plasma glucose insulin or fructosamine levels between the two chronic dietary periods.

Plasma lipid profiles. As shown in Table 3, 5 weeks of the LGI diet tended to decrease fasting total cholesterol ($P = 0.065$) as well as apoB ($P = 0.076$). The incremental AUC for total cholesterol after breakfast also tended to be lower after the LGI than after the HGI diet. Moreover, the change (baseline versus 5-week data) in the incremental AUCs of plasma triacylglycerols after lunch was gerater with the LGI diet than with the HGI diet ($P < 0.05$). There was no change in fasting or postprandial triacylglycerol excursions after breakfast between the two dietary periods.

Plasma leptin. Fasting plasma leptin levels did not change significantly during the study (baseline: 6.76 ± 1.45 vs. 6.90 ± 1.39 ng/ml; 5 weeks: 6.29 ± 1.27 vs. 5.85 ± 1.29 ng/ml, HGI vs. LGI).

Fat and lean mass distribution measured by DEXA

Five weeks of the LGI diet, compared with the same period of the HGI diet, induced a reduction of ~700 g of total fat mass for eight subjects and >1 kg for five subjects (Table 3). The change in adiposity (baseline versus 5-week data) during the LGI period was significantly different from that during the HGI period (Table 3). This reduction was mainly attributable to a 500-g decline in trunk fat for eight subjects and was >500 g for five subjects. In parallel to these changes, total lean mass tended to increase during the LGI period compared to during the HGI period (baseline versus 5-week data; $P = 0.07$). During the LGI diet, there was a gain of 430 ± 143 g of lean mass.

Hepatic glucose production

Basal hepatic glucose production was similar during the two dietary periods at the beginning (baseline: 1.53 ± 0.13 vs. 1.68 ± 0.17 mg · kg^{-1} · min^{-1}, HGI vs. LGI) and at the end (5 weeks: 1.56 ± 0.16 vs. 1.78 ± 0.16 mg · kg^{-1} · min^{-1}, HGI vs. LGI).

Insulin secretion and sensitivity

Insulin secretion and sensitivity determined by HOMA remained unchanged during the two dietary periods. No significant difference in the insulin secretion index was detected (baseline: 111 ± 10 vs. 117 ± 10%; 5 weeks: 111 ± 9 vs. 111 ± 8%, HGI vs. LGI) and insulin-sensitivity index (baseline: 81 ± 18 vs. 64 ± 5%; 5 weeks: 77 ± 12 vs. 87 ± 10%, HGI vs. LGI).

Gene expression of ob, PPAR-γ2, LPL, and HSL

Results of expression of ob, LPL, and HSL genes in abdominal subcutaneous adipose tissue measured by competitive RT-PCR are given in Fig. 1. Because the main results found concerned lipid metabolism and fat mass, we focused on genes involved in adipocyte differentiation and lipid metabolism. During the LGI diet, mRNA values of *ob* decreased (Fig. 1*A*) from 17.7 ± 3.4 to 12.3 ± 3 amol/μg total RNA (baseline vs. 5-week data, re-

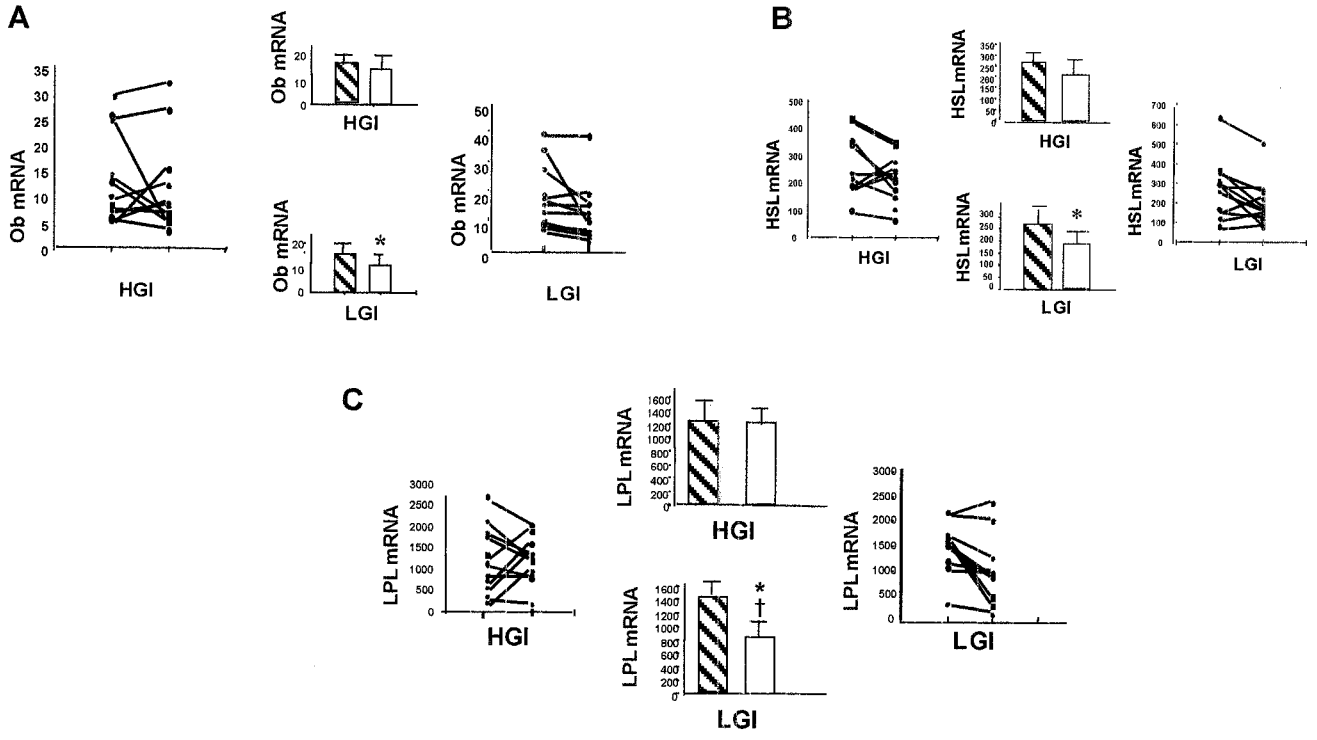

Figure 1—*Levels of ob* (A)*, HSL* (B)*, and LPL* (C) *mRNAs in abdominal subcutaneous adipose tissue before (baseline: left column) and after 5 weeks (right column) of HGI and LGI diets.* *P < *0.05 for ob, HSL, and LPL gene expression during the LGI period (baseline vs. 5 weeks);* †P < *0.01 for increased changes during the dietary periods (delta: baseline to 5 weeks, LGI vs. HGI) for LPL.*

spectively; $P < 0.05$). Changes (baseline to 5 weeks) during the LGI period (−36%) tended to be lower than in the HGI period (+12%; $P \leq 0.07$).

Similarly, HSL decreased during the LGI (271 ± 46 vs. 191 ± 35 amol/μg total RNA; $P < 0.05$), but this decrease was not significantly different from changes during the HGI period (Fig. 1*B*). LPL (Fig. 1*C*) was also decreased at the end of the 5-week LGI diet (1,415 ± 153 vs. 959 ± 202 amol/μg total RNA; $P < 0.05$). Changes during the LGI period (−38%) were significantly ($P < 0.03$) different from changes during the HGI period (+48%). However, PPAR-γ2 mRNA quantity was not modified by the type of diet (HGI: 20.7 ± 3.4 vs. 18.0 ± 2.7; LGI: 21.8 ± 4.1 vs. 22.1 ± 4.0, baseline vs. 5 weeks).

CONCLUSIONS — An LGI diet taken for 5 weeks induced improvement in plasma lipid profile and fat mass, with no detected effect on glucose control or insulin sensitivity when compared with an HGI diet.

The LGI diet resulted in low plasma glucose and insulin responses during the metabolic 1-day profile before and after the 5-week nutritional periods. This result is consistent with that from other studies in diabetic (21–24), hyperinsulinemic (7), and healthy subjects (6), with the exception of Kiens and Richter's study (8), who demonstrated that 30 days of an LGI diet might increase insulin and glucose responses in healthy subjects. The daily decreased plasma glucose and insulin responses in the present study after the 5-week LGI diet were not associated with any decrease in chronic glucose control, as estimated by plasma fructosamine or hepatic glucose production. Similarly, both insulin secretion and sensitivity indexes measured by HOMA were not significantly changed. Thus, the 5-week LGI diet was not able to increase whole-body insulin action or sensitivity in nondiabetic, slightly overweight subjects. One study in the literature, in a special type of older nondiabetic patient with coronary heart disease (25), showed that an LGI diet improves insulin sensitivity both in vivo, during an oral glucose tolerance test, and in vitro in isolated adipocytes. In rats, an LGI diet increases insulin-stimulated glucose oxidation in adipocytes (9) and lowers whole-body insulin resistance (11). However, the dynamics and changes observed in rats could be different from those in humans.

Concerning lipid metabolism, the 5-week LGI diet in the present study tended to decrease fasting plasma cholesterol and decreased triacylglycerol excursions after the lunch meal (as was shown during the 1-day profile). Most studies in diabetic (21–24) and nondiabetic subjects (6,7) have found a reduction in some plasma lipid parameters with an LGI diet.

Surprisingly, this study demonstrated for the first time that the simple replacement of HGI carbohydrates by LGI carbohydrates during only 5 weeks can result in decreased body fat mass. Indeed, we believe that negative energy balance is probably necessary to obtain a reduction in body fat. In the present study, although body weight did not differ significantly between the two dietary periods, a tendency to increase lean body mass was found with the LGI diet. This suggests that fat tissue was replaced by a roughly equal amount of lean tissue. Such a change in body composition, however, might imply a negative energy balance. A

slight decrease in energy intake was found, but it did not reach significant levels. Carbohydrate intake (expressed as percent of energy) was similar in the two dietary periods and might not have contributed to the observed effect. However, the decreased absorption of carbohydrates in the LGI foods, which would be fermented in the colon, might contribute to the observed results. Unfortunately, short-chain fatty acids were not measured in the present study to confirm this hypothesis. Another cause of this imbalance could be due to greater satiety, resulting in a reduced intake. Recently, Ludwig et al. (26) demonstrated that a single LGI meal given to obese teenage boys is more satiating than HGI foods and hence reduces appetite and food intake. In the present study, plasma leptin, the satietogenic factor, did not change significantly between the two chronic nutritional periods; in fact, a reduction of ob gene expression in abdominal adipose tissue ($P < 0.05$) was found. Although we agree that the high postprandial plasma glucose and insulin levels after a high-carbohydrate diet could be associated with decreased satiety and increased appetite independent of any effect of this diet on leptin levels (27), the results of the present study did not confirm a significantly decreased intake. However, the failure to detect significant differences in diet intake might be attributable to the relative insensitivity of that measure as well as the limited number of times it was done.

Some mechanisms could be considered to understand why the LGI diet compared to the HGI diet induced a selective decrease in fat with an increase in lean mass. One factor could be the difference in nitrogen balance and protein metabolism. The implication of nitrogen balance in the regulation of fat and lean mass with HGI and LGI diets is supported by some arguments in the literature. In a recent study, Agus et al. (28) demonstrated a greater negative nitrogen balance with an HGI than an LGI diet, suggesting that fat tissue was oxidized to a lesser degree and muscle to a greater degree with the HGI diet. The authors attributed these results to an increase in the proteolytic counterregulatory hormones, some of which have proteolytic actions that might favor the catabolism of lean body tissue with the HGI diet. A decrease in the counterregulatory hormones, on the other hand, might increase muscle protein synthesis, as with the LGI diet. Another possible mechanism might be the relative shift in substrate utilization. Wee et al. (29) demonstrated that after an LGI test meal, carbohydrate oxidation was 12% lower and fat oxidation was 118% higher than after an HGI test meal.

Another option is that some proteins and genes specific to adipose tissue might be active in this regulation of fat mass by LGI diets. The first gene to be considered is the ob. In the present study, however, there was a decrease in ob gene expression that might be attributable to low postprandial insulin levels following the LGI meals. Otherwise, this decrease is likely to be the consequence rather than the cause of decreased fat mass. Nevertheless, the decreased fat mass could not be due to a decrease in adipose tissue differentiation, as in the present study, PPAR-γ2 gene expression was found to be the same during and between the two diets. Increased lipolysis could be another possible pathway that might mediate the decreased fat mass. To evaluate the part of cellular lipolysis in the reduction of fat mass, the level of HSL gene expression in the adipose tissue was determined. The activation of this enzyme is inhibited by insulin and is involved in abdominal obesity, insulin resistance, and type 2 diabetes (30). In our study, 5 weeks of LGI diet decreased HSL gene expression in abdominal adipose tissue. Therefore, the observed reduction of fat mass with the LGI diet could not be a consequence of increased HSL-mediated lipolysis.

Alternatively, changes in LPL enzyme activity could also be considered in the observed low fat mass in the present study. Current research on metabolic activities of human adipocytes has focused on plasma triacylglycerol hydrolysis and the uptake of fatty acids in adipose tissue by LPL. One possible pathway by which alterations in insulin sensitivity might alter lipid metabolism is through the action of insulin on LPL. Actually, the LPL level in adipose tissue is positively correlated with insulinemia (31). Consistent with the reduction of postprandial insulinemia and triacylglycerol, we found that after an LGI diet, there was a significant reduction in LPL expression in adipose tissue, which could have induced a reduction in fat depot.

The decreased fat mass and the tendency to increase lean body mass with a 5-week LGI diet might be attributable to multiple factors: increase in the proteolytic counter regulatory hormones, shift of substrate utilization, and reduction of LPL. Additional factors, however, might be considered, such as the diminished adipose tissue lipogenesis, which has been previously demonstrated in rat models (9,10). A decrease in carbohydrate absorption, great satiety, and a reduced intake are reasonable possible causes for the differences in energy balance.

Thus, LGI diets resulting in low plasma glucose and insulin peaks are able to decrease some plasma lipid parameters as well as total fat mass, with a tendency to increase lean body mass in nondiabetic, slightly overweight subjects. Although the HGI diet was not associated with increased food intake and body weight, in the conditions of the present study (5-week period), the possibility cannot be excluded that these parameters could be increased after longer periods than in the present study. Such a diet might be considered useful in the prevention of obesity, diabetes, and cardiovascular diseases. Thus the choice of LGI foods should be recommended, as a whole diet, even in healthy men. More data are clearly needed with diets with equal fiber content to justify the claim of LGI carbohydrates. Many factors are implicated in the regulation and control of body fat and lean mass that could be controlled by simple and easy dietary modifications.

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