Association of the fatty acid profile of serum lipids with glucose and insulin metabolism during 2 fat-modified diets in subjects with impaired glucose tolerance[1–3]

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ABSTRACT

Background: Both the amount and quality of dietary fat can modify glucose and insulin metabolism.

Objective: The objective was to examine the relation between serum lipid fatty acids and glucose metabolism before and after the consumption of a diet enriched in either monounsaturated (Mono diet) or polyunsaturated (Poly diet) fatty acids.

Design: After consuming a high-saturated-fat run-in diet for 3 wk, 31 subjects with impaired glucose tolerance were randomly counseled to consume the Mono [40% fat; 11%, 19%, and 8% of energy as saturated, monounsaturated, and polyunsaturated fatty acids (S:M:P), respectively] or the Poly (34% fat; S:M:P of 11%:10%:10%) diet for 8 wk. Serum lipid fatty acids were measured, and an intravenous-glucose-tolerance test was performed at baseline and at 8 wk.

Results: At baseline, a higher glucose effectiveness (S_G) was associated with higher proportions of oleic ($r = 0.57$, $P = 0.04$) and α-linolenic ($r = 0.64$, $P = 0.01$) acids in phospholipids. An increase in the proportions of oleic and α-linolenic acids in phospholipids was associated with a decrease in fasting plasma glucose [$r = -0.53$ ($P = 0.002$) and $r = -0.47$ ($P = 0.009$), respectively]. An increase in the S_G was associated with an increase in the proportion of oleic acid ($r = 0.55$, $P = 0.004$) and with a decrease in that of arachidonic acid ($r = -0.40$, $P = 0.04$) in phospholipids.

Conclusions: The beneficial changes in fasting plasma glucose and in the S_G during the Mono diet were associated with alterations in the proportions of oleic, α-linolenic, and arachidonic acids in phospholipids. *Am J Clin Nutr* 2002; 76:331–7.

KEY WORDS Dietary fats, serum fatty acid profile, lipids, glucose metabolism, impaired glucose tolerance, fat-modified diet

INTRODUCTION

Both the amount and quality of dietary fat can modify glucose tolerance and insulin sensitivity (1). In epidemiologic studies, a high amount of fat—especially saturated fat—has been shown to increase the risk of type 2 diabetes or impaired glucose tolerance (2, 3). With respect to monounsaturated fatty acids, the epidemiologic data produce a less clear picture. Some studies indicate that both the effects of monounsaturated fatty acids and saturated fatty acids may be harmful (2, 4) or that all types of fat may be harmful (5). In contrast, experimental studies in patients with type 2 diabetes (6–8) and a meta-analysis (9) suggest a beneficial effect of a high-monounsaturated-fat diet on glycemic control, but this effect has not been shown in all studies of type 2 diabetic patients (10) or in other subject groups (11).

The fatty acid composition of cell membranes has been suggested to be one mediating factor in the interaction of dietary fat and glucose tolerance or insulin sensitivity (1). The fatty acid profile of serum lipids, especially that of phospholipids, reflects the fatty acid composition of cell membranes (12). The fatty acid composition of erythrocytes was associated with insulin metabolism in healthy humans (13). Differences in serum lipid fatty acid composition have been reported between subject groups with different degrees of glucose intolerance (14, 15), which may be due to differences in both fatty acid metabolism and in fatty acid intakes. It has been shown that different types of dietary fat induce different changes in serum fatty acid profiles (12–16). However, there are no previous data regarding the association of changes in serum fatty acid profile due to fat-modified diets with changes in glucose and insulin metabolism. The fatty acid profiles of serum triacylglycerols, cholesteryl esters, and phospholipids were analyzed in a study that investigated the effects of a high-fat, monounsaturated fat–enriched diet and a reduced-fat, polyunsaturated fat–enriched diet on glucose and insulin metabolism in subjects with impaired glucose tolerance (17). The high-fat, monounsaturated fat–enriched diet resulted in a lower fasting plasma glucose concentration and in a better glucose effectiveness index (S_G). The objective of the present investigation was to examine the associations between changes in the fatty acid profile of serum lipids and glucose tolerance.

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TABLE 1
Composition of the run-in diet; the high-fat, monounsaturated fat–enriched diet (Mono); and the reduced-fat, polyunsaturated fat–enriched diet (Poly)[1]

	Run-in diet (n = 31)	Mono diet (n = 14)	Poly diet (n = 17)
Energy (MJ)	7.4 ± 2.5	7.1 ± 2.0	7.1 ± 2.0
Fat (% of energy)	37 ± 5	40 ± 4[2]	34 ± 5[2,3]
Fatty acids (% of energy)			
Saturated	18 ± 3	11 ± 1[2]	11 ± 2[4]
Monounsaturated	11 ± 2	19 ± 2[4]	10 ± 2[3]
Polyunsaturated	5 ± 2	8 ± 1[4]	10 ± 2[3,5]
Carbohydrates (% of energy)	44 ± 7	42 ± 5[2]	46 ± 5[6]
Protein (% of energy)	17 ± 3	16 ± 3	18 ± 3[6]
Alcohol (% of energy)	2 ± 4	1 ± 4	2 ± 3
Cholesterol (mg/MJ)	42 ± 9	30 ± 6[4]	30 ± 7[2]
Fiber (g/MJ)	3.0 ± 0.7	2.7 ± 0.6	3.2 ± 0.5

[1] Data were derived from a 4-d food record kept during the run-in diet and from three 4-d food records kept during the Mono and Poly diets.
[2,4,5] Significantly different from the run-in diet: [2] $P < 0.05$, [4] $P < 0.01$, [5] $P < 0.001$.
[3,6] Significantly different from the Mono diet: [3] $P < 0.001$, [6] $P = 0.032$.

SUBJECTS AND METHODS

Subjects

Thirty-one moderately obese [mean (±SD) body mass index (BMI; in kg/m^2): 30.0 ± 2.6] subjects, 13 women and 18 men, with a mean (±SD) age of 56 ± 5 y were recruited for the study. Recruitment details were previously reported (17). The primary criterion for inclusion was impaired glucose tolerance in 2 consecutive oral-glucose-tolerance tests according to World Health Organization criteria (1985). Subjects with a history of thyroid, kidney, or liver disease; with previously diagnosed diabetes; or taking lipid-lowering medication were excluded. On entry, all participating women were postmenopausal and 2 were receiving hormonal replacement therapy; 6 of the subjects were taking β-blockers and 3 were taking diuretics for hypertension. The subjects maintained their medication use during the study, and there were no significant differences in the use of different medications between the groups. The subjects provided informed consent to participate in the study, and the study plan was approved by the Ethics Committee of the University of Kuopio, Finland.

Experimental diets and design

On the basis of 12 d of dietary data (4-d food records repeated 3 times during the 8-wk study period), the actual compositions of the 3 test diets were as follows: *1*) run-in diet (37% of energy as fat: 18%, 11%, and 5% of energy as saturated, monounsaturated, and polyunsaturated fatty acids, respectively); *2*) reduced-fat, polyunsaturated fat–enriched diet (Poly diet: 34% of energy as fat; 11%, 10%, and 10% of energy as saturated, monounsaturated, and polyunsaturated fatty acids, respectively); and *3*) high-fat, monounsaturated fat–enriched diet (Mono diet: 40% of energy as fat; 11%, 19%, and 8% of energy as saturated, monounsaturated, and polyunsaturated fatty acids, respectively) (**Table 1**). The study was carried out on an outpatient basis. The fatty acid compositions of the different diets were achieved with the use of different kinds of spreads and oils: butter and a small amount of low–erucic acid rapeseed (LEAR) oil in the run-in diet, sunflower oil and sunflower oil–based margarine in the Poly diet, and LEAR oil and LEAR oil–based margarine in the Mono diet. In addition, salad dressing made of high–oleic acid sunflower oil (Trisun; SVO Enterprises, Eastlake, OH) was used to increase the amount of oleic acid in the Mono diet. The subjects received detailed written and oral instructions about the diets from a dietitian. Butter (Valio Ltd, Helsinki), vegetable oils, margarines, and salad dressings (Van den Bergh Foods, Helsinki) were provided to the subjects free of charge on a single-blind basis. Dietary compliance was monitored by repeated 4-d food records kept before the study visits. Nutrient intakes were calculated with the use of the MICRO-NUTRICA software package for dietary analysis (18).

After the run-in diet was consumed for 3 wk, the subjects were randomly assigned to consume the Mono or the Poly diet for 8 wk. Subjects visited the research unit at −3, 0 (baseline), 2, 4, and 8 wk. The main outcome variables were the insulin sensitivity index (S_I), the S_G, the acute insulin response (measured with a frequently sampled intravenous-glucose-tolerance test), and the fatty acid profile of serum cholesteryl esters, triacylglycerols, and phospholipids. The frequently sampled intravenous-glucose-tolerance test was performed and the fatty acid profile of serum lipids was determined at baseline and at 8 wk.

Frequently sampled intravenous-glucose-tolerance test

The frequently sampled intravenous-glucose-tolerance test was performed as previously described (17, 19). First, 2 intravenous catheters were inserted in the antecubital veins of both arms and then fasting blood samples were drawn. Glucose (300 mg/kg body wt) was administered intravenously as a 50% solution over 1.5 min followed by 10 mL of a 0.9% NaCl solution. Thereafter, a 0.9% NaCl solution was slowly infused until a bolus of 0.03 U insulin/kg was rapidly injected 20 min after the administration of glucose. The sodium chloride infusion was continued at full speed for 1.5 min after the insulin dose. For the measurement of plasma glucose and insulin concentrations, venous blood samples were collected before glucose was administered (at −5 and 0 min) and 23 times after its administration (at 2-min intervals until 16 min; at 19, 22, 24, 27, 30, 40, 50, 60, 70, and 90 min; and at 20-min intervals from 100 to 180 min) through a catheter in the contralateral arm. To arterialize venous blood, the arm was kept on an electric pad (50 °C) during the test. The test could not be performed in 4 subjects because of technical reasons.

The plasma glucose concentration was analyzed with a glucose oxidase method (Glucose Auto& Stat, model GA-110; Daiichi, Kyoto, Japan) and plasma insulin by radioimmunoassay (Phadaseph Insulin RIA 100; Pharmacia Diagnostica, Uppsala, Sweden). The data were analyzed by calculating the S_G and S_I with the MINMOD program (20). The S_G is a measure of the ability of glucose to enhance its own disappearance from plasma at the baseline insulin concentration. The S_I is a measure of the ability of the increase in plasma insulin to enhance glucose's ability to accelerate its net disappearance from plasma. In addition, the acute insulin response was determined by calculating the area under the insulin response curve above the baseline value from 0 to 10 min. The acute insulin response is a measure of the incremental insulin response after the intravenous glucose bolus.

Fatty acid profile of serum lipids

Blood samples for the determination of fatty acid profiles for serum triacylglycerols, cholesteryl esters, and phospholipids were stored at −78 °C. Lipids were extracted from 100 μL serum with chloroform:methanol (2:1, vol:vol), and the lipid fractions were

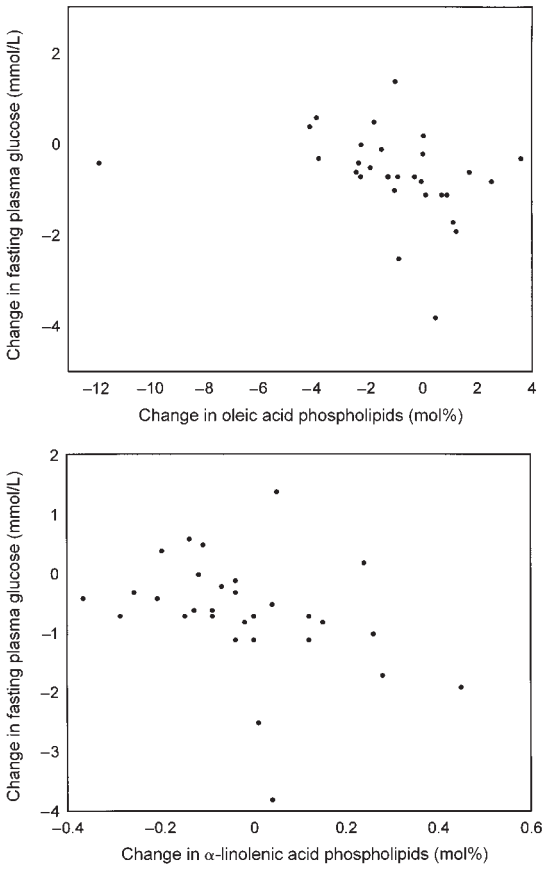

FIGURE 1. Association of changes in the proportions of oleic and α-linolenic acids in phospholipids with changes in fasting plasma glucose concentrations in the Mono-diet (high-fat, monounsaturated fat–enriched diet) and Poly-diet (reduced-fat, polyunsaturated fat–enriched diet) groups combined. Top panel: $r = -0.53$, $P = 0.002$; bottom panel: $r = -0.47$, $P = 0.009$.

separated by solid-phase extraction with an aminopropyl column (21). Fatty acid profiles were analyzed with a Vega 6130 gas chromatograph (Carlo Erba Instruments, Milan, Italy) equipped with an NB-351 silica capillary column (HNU-Nordion Ltd, Helsinki). The standards used to determine recovery and to identify individual fatty acids were purchased from Sigma Chemical (St Louis) and used as previously described in detail (21).

Statistical analysis

The data were analyzed by using the SPSS 6.0.1 statistical program (22). The data for serum cholesteryl ester composition was missing for one subject and for serum phospholipid composition for one subject. Sum variables for saturated (myristic, palmitic, and stearic acids), monounsaturated (palmitoleic and oleic acids), and n−6 (linoleic, γ-linolenic, dihomo-γ-linolenic, and arachidonic acids) and n−3 (α-linolenic, eicosapentaenoic, and docosahexaenoic acids in cholesteryl esters) polyunsaturated fatty acids were calculated from each lipid fraction. In triacylglycerols and phospholipids, the sum variable for n−3 fatty acids also included docosapentaenoic acid. Before further analysis, the normal distribution of the variables was checked with Shapiro-Wilk's test. Because most of the fatty acids in different serum lipid fractions were not normally distributed and did not become normally distributed after mathematical transformations, nonparametric tests were used in all analyses. Differences in the means and in the absolute and percentage changes (from 0 to 8 wk) between the 2 diet groups were analyzed with the Mann-Whitney *U* test. Wilcoxon's matched-pairs signed-rank test was used for the analysis of the within-group changes in dietary intake. Spearman correlation coefficients were calculated between selected variables. To control the overall α level, Bonferroni adjustment was used. To see whether outliers (*x* and *y* axes, respectively: −12.0 and −0.4 in **Figure 1** (top); 0.01 and −2.5, and 0.04, and −3.8 in Figure 1 (bottom); and −12.0 and −0.1 in **Figure 2**) affected the strength of associations presented in Figures 1 and 2, the correlation coefficients were calculated with and without outliers. The exclusion of outliers did not affect the strength of the associations. The correlation coefficient for the association shown in Figure 1 (top) was −0.53 ($P = 0.002$) when all subjects were included and was −0.54 ($P = 0.002$) when the outliers were excluded from the analysis. For the association presented in the bottom panel of Figure 1, the correlation coefficient was −0.47 ($P = 0.009$) when all subjects were included and was −0.46 ($P = 0.014$) when the outliers were excluded from the analysis. For the association presented in Figure 2, the correlation coefficient was 0.55 ($P = 0.004$) when all subjects were included and was 0.56 ($P = 0.004$) when the outlier was excluded from the analysis. All results are expressed as means ± SDs. A P value < 0.05 was considered statistically significant.

RESULTS

Fatty acid profile of serum lipids

As was expected, the proportions of oleic and α-linolenic acids increased significantly more after consumption of the Mono diet than after consumption of the Poly diet. The proportion of linoleic acid in serum triacylglycerol and cholesteryl ester fractions increased significantly more after consumption of the Poly diet than after consumption of the Mono diet (**Tables 2** and **3**). In the

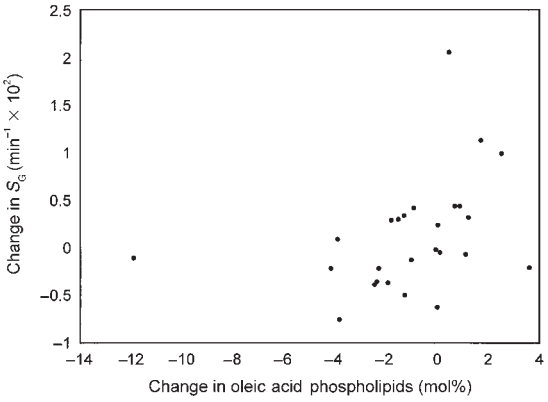

FIGURE 2. Association of the change in proportion of oleic acid in phospholipids with the change in the glucose effectiveness index (S_G) in the Mono-diet (high-fat, monounsaturated fat–enriched diet) and Poly-diet (reduced-fat, polyunsaturated fat–enriched diet) groups combined. $r = 0.55$, $P = 0.004$.

TABLE 2
Fatty acid composition of serum triacylglycerols in the high-fat monounsaturated fat–enriched (Mono) and reduced-fat polyunsaturated fat–enriched (Poly) diet groups during the study[1]

	Diet group			
	Mono diet (n = 14)		Poly diet (n = 17)	
Fatty acid	0 wk	Δ0–8 wk	0 wk	Δ0–8 wk
	mol% of total			
Myristic	3.40 ± 0.93	−0.73 ± 0.69	3.28 ± 0.88	−0.59 ± 0.92
Palmitic	29.33 ± 3.18	−4.13 ± 3.30	28.81 ± 3.90	−1.18 ± 3.14[2]
Palmitoleic	5.72 ± 1.21	−0.51 ± 1.33	6.76 ± 2.85	−0.83 ± 2.27
Stearic	3.95 ± 0.53	−0.83 ± 0.78	4.07 ± 0.97	−0.32 ± 0.86
Oleic[3]	37.53 ± 2.46	3.01 ± 5.53	38.17 ± 3.06	−2.71 ± 3.85[4]
Linoleic	14.77 ± 3.41	2.65 ± 10.01	13.36 ± 3.97	5.29 ± 4.09[4]
γ-Linolenic	0.41 ± 0.13	0.09 ± 0.17	0.44 ± 0.21	0.07 ± 0.18
α-Linolenic	1.64 ± 0.61	0.41 ± 0.84	1.29 ± 0.44	−0.09 ± 0.44[5]
Dihomo-γ-linolenic	0.37 ± 0.17	−0.04 ± 0.17	0.42 ± 0.34	0.09 ± 0.29[6]
Arachidonic	1.12 ± 0.39	−0.06 ± 0.31	1.30 ± 0.59	0.17 ± 0.56
Eicosapentaenoic	0.42 ± 0.20	0.17 ± 0.38	0.50 ± 0.30	0.04 ± 0.41
Docosapentaenoic	0.42 ± 0.18	0.02 ± 0.26	0.46 ± 0.14	0.03 ± 0.11
Docosahexaenoic	1.13 ± 0.86	−0.02 ± 0.90	1.36 ± 0.80	0.09 ± 0.89

[1] $\bar{x}$ ± SD.
[2,4–6] Significantly different from the Mono diet (Mann-Whitney U test): [2] $P = 0.012$, [4] $P \leq 0.001$, [5] $P = 0.039$, [6] $P = 0.035$.
[3] Includes octadecenoic acid.

phospholipid fraction, the proportion of oleic acid decreased after consumption of both study diets but significantly more after the Poly diet (**Table 4**). The proportion of α-linolenic acid in the phospholipid fraction increased after the Mono diet and the proportion of linoleic acid in the phospholipid fraction increased after consumption of the Poly diet. The proportion of eicosapentaenoic acid in the cholesteryl ester and phospholipid fractions increased in the Mono-diet group, whereas the proportion decreased in the Poly-diet group (Tables 3 and 4). As for the other fatty acids, the proportion of dihomo-γ-linolenic acid increased significantly more in the Poly-diet group than in the Mono-diet group in the triacylglycerol fraction (Table 2). In the same fraction, the proportion of palmitic acid was reduced in both groups but significantly more so in the Mono-diet group.

Frequently sampled intravenous-glucose-tolerance test

No significant differences were found in the variables of glucose metabolism between the 2 diet groups at baseline or in the changes in these variables during the study (**Table 5**; 17). However, there was a tendency toward a greater reduction in fasting plasma glucose in the Mono-diet group than in the Poly-diet group ($P = 0.053$). Furthermore, at the end of the study, the S_G was higher in the Mono-diet group than in the Poly-diet group (1.64 ± 0.49 compared with 1.11 ± 0.54 $min^{-1} \times 10^2$; $P = 0.013$).

Associations between the fatty acid profile of serum lipids and indexes of glucose and insulin metabolism

A higher S_G at baseline was associated with higher proportions of oleic ($r = 0.57$, $P = 0.04$) and α-linolenic ($r = 0.64$, $P = 0.01$) acids in phospholipids. A higher S_I at baseline was associated with a lower proportion of saturated fatty acids in triacylglycerols ($r = -0.55$, $P = 0.04$). For individual saturated fatty acids, there tended to be an inverse correlation between the S_I and the proportion of palmitic acid in triacylglycerols ($r = -0.54$, $P = 0.052$). The S_I tended to be higher in subjects with higher proportions of docosapentaenoic acid in the triacylglycerol fraction ($r = 0.54$, $P = 0.09$) and of docosahexaenoic acid in both the triacylglycerol ($r = 0.54$, $P = 0.09$) and cholesteryl ester ($r = 0.51$, $P = 0.10$) fractions.

We analyzed the associations between the changes in the proportions of fatty acids in serum lipid fractions and indexes of glucose and insulin metabolism during the study. An increase in the proportion of oleic and α-linolenic acids in phospholipids was associated with a decrease in the fasting plasma glucose concentration: $r = -0.53$ ($P = 0.002$) and -0.47 ($P = 0.009$), respectively (Figure 1). Similar but weaker associations were found between the change in fasting plasma glucose and the change in the proportions of oleic acid ($r = -0.33$, $P = 0.07$) and α-linolenic acid ($r = -0.35$, $P = 0.05$) in cholesteryl esters. An increase in the S_G was associated with an increase in the proportion of oleic acid ($r = 0.55$, $P = 0.004$) (Figure 2) and with a decrease in the proportion of arachidonic acid ($r = -0.40$, $P = 0.04$) in phospholipids. The decrease in insulin concentration was associated with a decrease in the proportion of palmitoleic acid in triacylglycerols ($r = -0.57$, $P = 0.04$).

DISCUSSION

In the present study, the Mono diet resulted in beneficial changes in fasting glucose concentrations and in the S_G in subjects with impaired glucose tolerance (17). There was also a beneficial change in lipid metabolism. Substituting monounsaturated or polyunsaturated fat for saturated fat is known to reduce serum lipid concentrations by 10–15% (23). In the present study, the change from the high–saturated fat run-in diet to either the monounsaturated fat–enriched diet (Mono diet) or the polyunsaturated fat–enriched diet (Poly diet) reduced serum total cholesterol concentrations by 11% and 6%, respectively, and serum triacylglycerol concentrations by 16% and 9%, respectively (17). To adjust for the variation in the total amount of serum lipids, the fatty acid data used in the analyses were proportions of the total amount of lipid in each fraction (triacylglycerols, cholesteryl esters, and phospholipids). A higher S_I at baseline was associated with a low proportion of saturated fatty acids in the triacylglycerol

TABLE 3
Fatty acid composition of serum cholesteryl esters in the high-fat monounsaturated fat–enriched (Mono) and reduced-fat polyunsaturated fat–enriched (Poly) diet groups during the study[1]

	Diet group			
	Mono diet (n = 13)		Poly diet (n = 17)	
Fatty acid	0 wk	Δ0–8 wk	0 wk	Δ0–8 wk
	mol% of total			
Myristic	1.35 ± 0.29	−0.11 ± 0.49	1.26 ± 0.27	−0.24 ± 0.27
Palmitic	12.17 ± 0.85	0.32 ± 2.78	11.63 ± 1.39	−0.34 ± 1.27
Palmitoleic	4.32 ± 0.97	−0.48 ± 0.96	5.04 ± 1.86	−0.63 ± 1.11
Stearic	1.08 ± 0.24	0.03 ± 0.61	1.09 ± 0.18	−0.08 ± 0.22
Oleic[2]	18.52 ± 1.63	3.58 ± 6.25	20.18 ± 2.56	−3.33 ± 2.15[3]
Linoleic	52.36 ± 3.65	−4.07 ± 9.4	50.72 ± 4.56	5.51 ± 4.81[3]
γ-Linolenic	0.79 ± 0.33	−0.08 ± 0.29	0.81 ± 0.36	0.03 ± 0.21
α-Linolenic	0.73 ± 0.23	0.47 ± 0.65	0.69 ± 0.21	−0.22 ± 0.24[3]
Dihomo-γ-linolenic	0.87 ± 0.30	−0.19 ± 0.24	0.95 ± 0.63	−0.19 ± 0.63
Arachidonic	5.73 ± 1.42	−0.25 ± 1.44	5.55 ± 1.37	−0.32 ± 1.05
Eicosapentaenoic	1.43 ± 0.58	0.55 ± 1.48	1.47 ± 0.70	−0.23 ± 0.86[4]
Docosahexaenoic	0.74 ± 0.24	0.13 ± 0.23	0.65 ± 0.17	0.01 ± 0.27

[1] $\bar{x}$ ± SD.
[2] Includes octadecenoic acid.
[3,4] Significantly different from the Mono diet (Mann-Whitney U test): [3] $P < 0.001$, [4] $P = 0.015$.

fraction and a higher S_G was associated with higher proportions of oleic and α-linolenic acids in the phospholipid fraction.

A high fat intake was associated with lower insulin sensitivity in several studies (4, 5, 24) and with a higher risk of type 2 diabetes in one study (3). In a recent study by Vessby et al (25), an interesting interaction between the total fat intake and the fatty acid composition of the diet was reported: the favorable effect of substituting monounsaturated fat for saturated fat was lost in subjects who consumed > 37% of energy as fat. In the present study, the fat content of the Mono diet was 40% of energy and that of the Poly diet was 34% of energy. On the basis of previous data, it can be speculated that the effects of the Mono diet on glucose and insulin metabolism, especially on insulin sensitivity, might have been even more beneficial had the fat content of the diet been somewhat lower.

The positive association of insulin sensitivity with long-chain polyunsaturated fatty acids was reported previously (26). In addition, published data suggest that a high proportion of saturated fatty acids in cholesteryl esters is associated with a greater risk of type 2 diabetes (27). This finding agrees with our finding of an inverse association between the S_I and the proportion of saturated fats in the triacylglycerol fraction. Because palmitic acid is metabolized to palmitoleic acid, the observed association between the reduction in the proportion of palmitoleic acid and the reduction in fasting insulin concentrations also probably reflects the negative association of saturated fat with insulin sensitivity.

To our knowledge there are no previous data showing that the proportion of oleic or α-linolenic acid is related to the fasting glucose concentration or to the S_G in subjects with impaired glucose tolerance. In the present study, higher proportions or an increase

TABLE 4
Fatty acid composition of serum phospholipids in the high-fat monounsaturated fat–enriched (Mono) and reduced-fat polyunsaturated fat–enriched (Poly) diet groups during the study[1]

	Diet group			
	Mono diet (n = 13)		Poly diet (n = 17)	
Fatty acid	0 wk	Δ0–8 wk	0 wk	Δ0–8 wk
	mol% of total			
Myristic	0.74 ± 0.22	−0.09 ± 0.17	0.61 ± 0.14	−0.05 ± 0.10
Palmitic	31.15 ± 3.13	−1.29 ± 4.03	31.80 ± 1.61	−1.16 ± 1.65
Palmitoleic	1.31 ± 0.68	−0.09 ± 0.74	1.15 ± 0.45	−0.10 ± 0.41
Stearic	12.22 ± 3.27	1.43 ± 3.53	12.96 ± 1.52	0.26 ± 1.24
Oleic[2]	12.67 ± 3.54	−0.51 ± 3.80	11.55 ± 1.54	−1.54 ± 1.55[3]
Linoleic	21.79 ± 2.61	−0.81 ± 2.83	21.20 ± 2.78	2.49 ± 2.79[4]
γ-Linolenic	0.18 ± 0.10	−0.02 ± 0.06	0.15 ± 0.08	−0.01 ± 0.04
α-Linolenic	0.36 ± 0.22	0.09 ± 0.20	0.31 ± 0.11	−0.11 ± 0.10[5]
Dihomo-γ-linolenic	3.83 ± 0.97	−0.32 ± 0.90	3.88 ± 0.92	0.20 ± 0.80
Arachidonic	7.59 ± 1.87	−0.11 ± 1.22	7.22 ± 0.82	0.04 ± 0.77
Eicosapentaenoic	1.36 ± 0.50	0.61 ± 1.14	1.46 ± 0.74	−0.11 ± 0.74[6]
Docosapentaenoic	0.70 ± 0.16	0.07 ± 0.30	0.72 ± 0.18	−0.14 ± 0.18
Docosahexaenoic	3.97 ± 1.10	0.46 ± 0.60	3.91 ± 0.93	0.12 ± 0.95

[1] $\bar{x}$ ± SD.
[2] Includes octadecenoic acid.
[3–6] Significantly different from the Mono diet (Mann-Whitney U test): [3] $P = 0.025$, [4] $P = 0.004$, [5] $P = 0.001$, [6] $P = 0.022$.

TABLE 5
Fasting plasma glucose and insulin, acute insulin response (AIR; 0–10 min), insulin sensitivity (S_I), and glucose effectiveness (S_G) in the high-fat monounsaturated fat–enriched (Mono) and reduced-fat polyunsaturated fat–enriched (Poly) diet groups during the study[1]

	Diet group			
	Mono diet (n = 13)		Poly diet (n = 14)	
Fatty acid	0 wk	Δ0–8 wk	0 wk	Δ0–8 wk
Plasma glucose (mmol/L)	6.4 ± 1.2	−0.9 ± 1.1	6.3 ± 0.7	−0.3 ± 0.8[2]
Plasma insulin (mU/L)	15.9 ± 8.1	−5.5 ± 7.7	14.3 ± 7.2	−4.4 ± 9.3
AIR (mU/L · min)	117 ± 243	60 ± 128	137 ± 263	−29 ± 123
S_I ($\times 10^{-4}$ min^{-1} · μU^{-1} · mL^{-1})	1.37 ± 0.78	0.33 ± 0.93	1.90 ± 1.04	0.06 ± 0.56
S_G (min$^{-1} \times 10^2$)	1.36 ± 0.53	0.27 ± 0.65	1.14 ± 0.65	0.02 ± 0.51

[1] $\bar{x}$ ± SD. Some of these data were published previously by Sarkkinen et al (17).
[2] Significantly different from the Mono diet, $P = 0.053$ (Mann-Whitney U test).

in the proportions of these fatty acids were associated with a higher S_G and with lower fasting plasma glucose both at baseline and after consumption of the study diets. The beneficial effects of high-fat, monounsaturated fat–enriched diets on fasting (28) and postprandial (7) plasma glucose concentrations were reported in type 2 diabetic subjects. In contrast with the results of Parillo et al (7), of Espino-Montoro et al (28), and of the present study, population studies have shown that high intakes of monounsaturated fatty acids are associated with high 2-h postload glucose concentrations (2) and with low insulin sensitivity (5). However, it should be noted that the monounsaturated fatty acids in the Western diet are not derived from vegetable oils but to a large extent from other sources, such as meat and milk products. Thus, the negative effects of a high intake of monounsaturated fatty acids reported in some observational studies (2, 5) may have been due to the strong intercorrelation between saturated and monounsaturated fat intakes from the Western diet (2). Enrichment of the diet with vegetable oil–derived monounsaturated fat could lead to different results. Data concerning the S_G and monounsaturated fats are scarce. In a Danish study, no changes in either the S_G or in other indicators of glucose tolerance were seen in the first-degree relatives of type 2 diabetic patients after the consumption of a diet high in monounsaturated fat (11). However, all of these subjects had normal results from an oral-glucose-tolerance test. In the present study, all of the subjects had impaired glucose tolerance and therefore may have been more susceptible to changes in glucose metabolism as a result of changes in dietary fatty acid composition. The variation in how the proportion of arachidonic acid changed among subjects in response to the diet was large. In the present study, an increase in the proportion of arachidonic acid was associated with a decrease in the S_G. This finding does not agree with the findings of an earlier study in which the proportion of arachidonic acid in serum phospholipids was reported to be lower in diabetic than in nondiabetic subjects (15). Furthermore, the percentage of arachidonic acid in muscle has been reported to be positively correlated with insulin sensitivity (26). However, recent data from a cross-sectional study indicate that the proportion of arachidonic acid in serum cholesteryl esters is inversely associated with the insulin-glucose ratio during an oral-glucose-tolerance test (29). The proportion of different fatty acids in serum lipids was evaluated in the present study. When the proportion of a fatty acid increases or decreases as a result of dietary enrichment, the proportion of other fatty acids automatically changes as well. The observed negative association between arachidonic acid and the S_G in the present study may also have been due to this phenomenon.

In conclusion, higher insulin sensitivity at baseline was associated with a lower proportion of saturated fatty acids and with a higher proportion of long-chain unsaturated fatty acids in serum lipid fractions. Interestingly, indicators of glucose metabolism were related to the proportions of oleic and α-linolenic acids in serum lipid fractions both at baseline and after the study diets were consumed. The results of the present study strengthen the view that dietary fatty acids have a significant effect on glucose and insulin metabolism in subjects with impaired glucose tolerance and emphasize the importance of dietary fat quality in the prevention and treatment of disturbed glucose metabolism. Furthermore, a reduction in saturated fats and a moderate increase in unsaturated fats in the diet are beneficial in the prevention of atherosclerotic vascular diseases.

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