High-fiber rye bread and insulin secretion and sensitivity in healthy postmenopausal women[1–3]

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ABSTRACT

Background: Fiber and whole-cereal intakes may protect against hyperinsulinemia and the risk of type 2 diabetes.

Objective: The aim was to study whether the long-term use of high-fiber rye bread and white-wheat bread modifies glucose and insulin metabolism in healthy postmenopausal women.

Design: The study was a randomized crossover trial consisting of 8-wk test and 8-wk washout periods. The subjects were 20 postmenopausal women [$\bar{x}$ ± SD age: 59 ± 6.0 y; body mass index (in kg/m^2): 27.5 ± 2.9; baseline fasting serum cholesterol: 6.5 ± 0.8 mmol/L], of whom 3 had impaired glucose tolerance as determined by a 2-h oral-glucose-tolerance test. The test breads were high-fiber rye and white-wheat breads, planned to make up ≥ 20% of energy. Fasting blood samples were collected for the measurement of plasma glucose and insulin at the beginning and at the end of both bread periods. The frequently sampled intravenous-glucose-tolerance test was performed at the run-in and at the end of both bread periods. The acute insulin response, insulin sensitivity, and glucose effectiveness were calculated.

Results: The rye bread made up 23.4 ± 4.3% and wheat bread 26.7 ± 8.2% of total energy intake. Compared with that during the run-in period, the acute insulin response increased significantly more during the rye bread period (9.9 ± 24.2%) than during the wheat bread period (2.8 ± 36.3%; $P = 0.047$). Other measured variables did not change significantly during the study.

Conclusions: Modification of carbohydrate intake by high-fiber rye bread did not alter insulin sensitivity in postmenopausal, hypercholesterolemic women. High-fiber rye bread appears to enhance insulin secretion, possibly indicating improvement of b cell function. *Am J Clin Nutr* 2003;77:385–91.

KEY WORDS Rye, wheat, fiber, insulin sensitivity, insulin secretion, glucose, women

INTRODUCTION

Whole-grain cereals have been shown in many recent epidemiologic studies to protect against the development of type 2 diabetes and heart disease, mediated possibly in part through insulin secretion and resistance (1–4). Increasing the intake of dietary fiber may also indirectly protect against hyperinsulinemia by preventing obesity with its associated insulin resistance (5).

Women undergoing menopause display decreased insulin sensitivity (6), insulin secretion (7), and hepatic insulin extraction (8). Loss of ovarian function with consequent effects on hormone metabolism (9) and possible changes in body composition (10) may partly explain why women's susceptibility to diabetes and cardiovascular disease becomes more pronounced after menopause.

We previously showed in healthy individuals that ingestion of whole-kernel rye bread compared with white-wheat bread reduces postprandial insulin, glucose-dependent insulinotropic polypeptide (GIP), and glucagon-like peptide 1 (GLP-1) concentrations (11, 12). Whether these short-term favorable effects on insulin metabolism are reflected in long-term reductions in insulin resistance, enhancement of insulin clearance, or improved insulin secretion has not been previously reported. In the present study, we sought to determine the changes in glucose and insulin metabolism as assessed by a frequently sampled intravenous-glucose-tolerance test (FSIGTT) in response to long-term use of high-fiber rye bread and white-wheat bread by using a randomized crossover design in healthy, postmenopausal women.

SUBJECTS AND METHODS

Subjects

Twenty-two postmenopausal women were recruited into the study. One woman discontinued the study because of a surgical operation. The results of another woman were rejected because of technical difficulties with the FSIGTT at the run-in. Thus, the final number of study subjects was 20. Subjects provided written informed consent for the study, and the study plan was approved by the Ethics Committee of the Kuopio University and Kuopio University Hospital.

Height, weight, systolic and diastolic blood pressure, routine hematologic measures, and serum creatinine, thyroxine, and liver enzyme concentrations were measured before entry into the study (**Table 1**). For the 4 subjects with treated hypothyroidism, concentrations of thyroid-stimulating hormone were normal. All other subjects had normal thyroid function. All women had normal liver and kidney function. The primary inclusion criteria for the study were a serum total cholesterol concentration of 5.0–8.5 mmol/L, a

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TABLE 1
Characteristics of the women at the time of entry to the study[1]

Age (y)	59 ± 6.0
Body mass index (kg/m^2)	27.5 ± 2.9
Systolic blood pressure (mm Hg)	123 ± 12.9
Diastolic blood pressure (mm Hg)	79 ± 8.0
Serum total cholesterol (mmol/L)	6.5 ± 0.8
Serum HDL cholesterol (mmol/L)	1.6 ± 0.3
Serum triacylglycerol (mmol/L)	1.2 ± 0.4
Plasma glucose (mmol/L)	5.4 ± 0.4
Plasma insulin (pmol/L)	57.9 ± 22.4

[1] $\bar{x}$ ± SD; n = 20.

non-HDL-cholesterol concentration of 3.5–6.5 mmol/L (calculated as serum total cholesterol − serum HDL cholesterol), a serum total triacylglycerol concentration < 2.5 mmol/L, and body mass index (in kg/m^2) of 20–33. Exclusion criteria included the use of lipid-lowering, laxative, or corticosteroid medication and diagnosed or undiagnosed diabetes mellitus. The glucose tolerance of the subjects was screened by use of an oral-glucose-tolerance test (World Health Organization criteria; 13). Only 3 women had impaired glucose tolerance as diagnosed by the 2-h glucose concentration after a glucose load, and none had impaired fasting glucose. Postmenopausal status was confirmed by measuring serum follicle-stimulating hormone concentrations. Thirteen subjects used low-dose postmenopausal medication by mouth, skin, or vagina; 4 subjects taking oral medication also had menstrual flow.

Study design

The first bread period was preceded by a 2–3-wk run-in period. At the beginning of the run-in period, the subjects were advised to maintain their body weight and lifestyle habits, such as exercise, alcohol consumption, and smoking, throughout the study. In addition, they were advised not to change their consumption of regularly used medication during the study unless it was necessary. They also received instructions not to use cholesterol-lowering foodstuffs [such as Benecol, a plant stanol ester margarine (Raisio Group, Raisio, Finland), or Balanssi sausages (Huittisten Lihapojat Oy, Huittinen, Finland)], foodstuffs or preparations that contain probiotics, or foodstuffs that affect bowel function (plums and plum juice, dried fruit, brans and muesli, various seeds, and licorice). During the run-in period, every subject kept a 4-d food record to determine individual energy intake.

After the run-in period, the subjects were randomly assigned into either an 8-wk rye bread or an 8-wk wheat bread period. There was an 8-wk washout period between the bread periods, during which the subjects ate their usual diet. The FSIGTTs were performed during the run-in period and at the end of the rye and wheat bread periods. The mean of 2 measurements (−5 and 0 min) before the FSIGTT was used as the fasting value for plasma glucose and insulin at the end of the bread periods. In addition, one blood sample was taken at the beginning of the bread periods for the measurement of fasting plasma glucose and insulin concentrations. The subjects were weighed every 2 wk. Subjects were asked to record daily exercise during the 2-wk baseline period and the bread periods.

The duration of the test bread periods and the washout period between the bread periods was adjusted to cycle length in those women using low-hormone oral postmenopausal medication and who consequently had menstrual flow. Their blood samples were collected at the same phase of the menstrual cycle, except in one subject as the result of scheduling problems.

Diet

The test breads were intended to cover a minimum of 20% of daily energy intake. The high-fiber rye bread (≈17% dietary fiber) was prepared by increasing the content of rye bran in the bread. To increase compliance with consumption of the high-fiber rye bread during the 8-wk bread period, 2 commercial bakeries (Fazer Bakeries Ltd, Lahti, Finland and Vaasan & Vaasan Oy, Helsinki) made from the basic recipe 4 products varying in appearance but with similar nutrient composition. The rye breads were baked in 2 lots, one for those who started with the rye bread and one for those who ate rye bread during the second bread period. The breads were stored (−18 °C) until given to the subjects at the visits to the study center. Seven different white-wheat breads (≈2.8% dietary fiber) produced from refined wheat flour were offered during the wheat bread period. These freshly baked, commercially used breads were available once a week from the study center. The wheat breads were also supplied from the 2 above-mentioned bakeries.

To guarantee that the subjects ate the correct amount of the test breads, they were given detailed instructions on how to slice the loaves and how to combine the daily portions of different products. It was easier for the subjects to estimate the amount of test breads to be consumed as slices rather than as grams, and no kitchen scales for estimating the amount of bread to be consumed were used. The portions of rye breads weighed 24.1–28.1 g and those of wheat breads, 20.8–25.0 g. One portion of rye bread contained on average 206 kJ (range: 174–234 kJ) and 4.4 g fiber (range: 4.1–4.6 g); the respective values for wheat bread were 241 kJ (range: 233–249 kJ) and 0.6 g (range: 0.5–0.8 g). Because the energy content of the bread portions varied, the subjects were advised to eat approximately the same amount of each product during the week. A minimum of 4–5 portions of the test breads had to be eaten each day, and the number of portions to be eaten varied according to the daily energy intake of the individual. There was no maximum for the amount of bread to be consumed, but the subjects were advised to eat the bread in amounts corresponding to cereal consumption in their habitual diet.

The dietary advice to the subjects was similar to that in our previous study on the effects of rye bread on lipid metabolism in hypercholesterolemic men and women (14). The only change in the diet was to replace the customarily used breads and baked products with rye breads during the rye bread period and with wheat breads during the wheat bread period. In addition to the test breads, the subjects could eat a piece of sweet pastry or a portion of porridge once a day, but it was not obligatory. The latter products were recommended to be rye-based products during the rye bread period and wheat-based products during the wheat bread period. Pasta and rice could be eaten as part of warm dishes in amounts usually eaten by the subject. Otherwise, the diet was to be maintained unchanged. The subjects were especially advised not to change the amount and type of fat and cold cuts eaten with the breads or the use of fiber-containing foods such as vegetables, fruit, and berries.

Compliance with the diet was checked by daily records on the use of breads and by 4-d food records. The subjects kept daily records of the number of portions of the test rye or wheat breads that were eaten as well as the quantity, quality, and frequency of other cereals that were consumed. Four-day food records that included one weekend day were kept by the subjects during weeks 4–6 in both bread periods.

The clinical nutritionist (KSJ) advised the subjects on the practical management of the diet. All 4-d food records were analyzed by the clinical nutritionist with the MICRO-NUTRICA calcula-

tion program for nutrients (version 2.0; Finnish Social Insurance Institute, Turku, Finland), which included the database of Finnish foods (15). The nutrient composition of the rye and wheat breads used in the study was analyzed at VTT Biotechnology (Espoo, Finland) and added to the database.

Frequently sampled intravenous-glucose-tolerance test

The subjects arrived at the study center in the morning after they had fasted overnight (12 h). Smoking was forbidden on the morning the test was conducted, and the subjects were asked to travel to the laboratory by car or by bus if possible to avoid extra physical activity. After arrival, they were weighed (light clothing, no shoes) on a digital scale.

The minimal model FSIGTT was performed as described by Bergman (16). First, 2 intravenous catheters were inserted into the antecubital veins in both arms. After the catheters were inserted, the patients rested in a supine position for 10 min before the fasting samples were drawn. A glucose dose of 330 mg/kg body wt was given intravenously as a 50% solution in 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 glucose dose. NaCl was then rapidly infused for 1.5 min after the insulin dose. To measure plasma glucose and insulin concentrations, venous blood samples were collected before the glucose dose (−5 and 0 min) and 23 times after the glucose dose (at 2, 4, 6, 8, 10, 12, 14, 16, 19, 22, 24, 27, 30, 40, 50, 60, 70, 90, 100, 120, 140, 160, and 180 min) via a catheter in the contralateral arm. To arterialize the venous blood, the arm was kept in a 50 °C electric pad during the test.

The plasma samples were collected in prechilled tubes containing EDTA for measurement of insulin and in prechilled tubes containing fluoride citrate for measurement of glucose and were centrifuged within 30 min of the time of blood collection for 15 min at 2100 × g and −4 °C. The plasma was separated, and the samples were stored at −20 °C until analyzed. Plasma glucose was analyzed by the enzymatic photometric method (Granutest 100; Merck, Damstadt, Germany) in a Kone Specific Clinical Analyser (Kone Ltd, Espoo, Finland); plasma insulin was analyzed by radioimmunoassay (Phadaseph Insulin RIA 100; Pharmacia Diagnostica, Uppsala, Sweden). The between-assays CVs were 1.80% (n = 39) and 1.48% (n = 39) for the lowest and highest glucose controls, respectively, and 7.22% (n = 21), 3.31% (n = 21), and 4.74% (n = 21) for the lowest, middle, and highest insulin controls, respectively.

Glucose effectiveness (S_G) and insulin sensitivity (S_I) indexes were calculated with the MINMOD program (17). In addition, the acute insulin response (AIR) was determined by calculating the area under the insulin curve above the baseline concentration from 0 to 10 min.

Statistical analysis

Percentage changes in nutrient intakes from the run-in period to the rye bread period and from the run-in period to the wheat bread period were calculated. Because all values were not normally distributed even after logarithmic transformations, the comparisons were made with Wilcoxon's rank-sum test for dependent data. Because the changes in energy intakes from protein and total fat over the rye bread period were different from the changes over the wheat bread period, the differences in these protein and fat variables were used as covariates in the covariance analysis.

Normal distribution and homogeneity of variance were checked, and logarithmic transformations were made for all the variables included in covariance analysis if needed. However, untransformed values are presented in Tables 4 and 5. The changes in body weight and fasting plasma glucose and insulin concentrations at the beginning and at the end of the bread periods were analyzed by covariance analysis of repeated measures (18).

FSIGTTs were performed at 3 time points rather than 4 because of scheduling reasons on the part of the laboratory and the subjects. To get normally distributed variables for the proportional changes in AIR, the basic values were at first logarithmically transformed, and then the proportional change variables were calculated. The proportional changes in S_G, S_I, and AIR from the run-in period to the rye bread period and from the run-in period to the wheat bread period were calculated and analyzed by covariance analysis of repeated measures (18). Because body weight did not change during the study, it was not used as a covariate in the analyses of the changes in fasting plasma glucose and insulin, S_G, S_I, and AIR.

The comparison in the single measurement points during the FSIGTT and in the frequency of exercise among the run-in, rye bread, and wheat bread periods was made by using the nonparametric Friedman's test for the dependent data. To compare the changes in fasting glucose and insulin, S_G, S_I, and AIR during the rye bread and wheat bread periods according to glucose tolerance, use of thyroid hormone and estrogen replacement therapy, and body weight, the nonparametric Mann-Whitney U test for independent samples was used. In all analyses, P values < 0.05 were considered to be statistically significant. The results are expressed as means ± SDs. Data were analyzed with SPSS for WINDOWS 8.0. (SPSS Inc, Chicago) (19, 20).

RESULTS

The subjects maintained their body weights throughout the study. Mean body weights were 71.2 ± 6.1 kg at the run-in period, 71.6 ± 6.2 and 71.1 ± 6.3 kg at the beginning and the end of the rye bread period, and 71.4 ± 6.6 and 71.4 ± 6.5 kg at the beginning and the end of the wheat bread period. In agreement with these data, energy intake (**Table 2**) and the reported frequency of exercise did not differ significantly between the run-in and bread periods.

Diet

Compliance with the diet in the present study was good. The consumption of the bread portions exceeded the minimum number of portions recommended during both bread periods (**Table 3**). All 4 rye breads and 7 wheat breads were eaten daily or almost daily during the respective periods. Intake of other cereals was less than one portion a day. The rye bread made up 23.4 ± 4.3% and the wheat bread 26.7 ± 8.2% of total energy intake.

No significant differences were found in the percentage changes of nutrient intakes from the run-in period to the test bread periods, except in that of protein (P = 0.007) and total fat (P = 0.033) (Table 2). The intake of protein was greater, and the intake of fat smaller, during the rye bread period than during the wheat bread period. The intakes of total, soluble, and insoluble fiber from the total diet (Table 2) and from the test breads were significantly greater during the rye bread period than during the wheat bread period. The subjects received 35.5 ± 7.3 g total, 5.8 ± 1.1 g soluble, and 29.7 ± 6.3 g insoluble fiber from rye breads, respectively. The respective values for wheat breads were 4.7 ± 1.0, 1.6 ± 0.4, and 3.1 ± 0.6 g.

TABLE 2
Daily energy and nutrient intakes by postmenopausal women during the run-in, the rye bread (RB), and the wheat bread (WB) periods[1]

Component	Run-in period	RB period	WB period
Energy (MJ)	7.2 ± 1.5	7.4 ± 1.4	7.4 ± 1.7
Protein (% of energy)[2]	17 ± 3.2	19 ± 2.8	17 ± 1.9
Total fat (% of energy)[2]	31 ± 6.1	27 ± 4.7	30 ± 5.5
Fatty acids (% of energy)			
SFA	12.7 ± 2.9	11.2 ± 2.6	12.0 ± 3.2
MUFA	10.6 ± 2.4	8.7 ± 2.2	9.0 ± 2.5
PUFA	5.2 ± 1.1	3.4 ± 0.8	3.6 ± 1.2
Carbohydrates (% of energy)	50 ± 7.2	53 ± 5.9	51 ± 7.6
Fiber (g)[2]	23.3 ± 7.3	45.5 ± 8.8	14.4 ± 4.1
Soluble (g)[2]	5.6 ± 1.7	9.0 ± 1.8	4.7 ± 1.6
Insoluble (g)[2]	10.5 ± 3.5	32.6 ± 6.2	5.8 ± 1.3
Cholesterol (mg)	220 ± 110.4	212 ± 81.5	192 ± 83.4
Alcohol (g)	4.6 ± 5.0	3.8 ± 5.4	6.2 ± 9.5

[1] $\bar{x}$ ± SD; n = 20. Intakes were calculated from 4-d food records. SFA, saturated fatty acids; MUFA, monounsaturated fatty acids; PUFA, polyunsaturated fatty acids.

[2] Change from run-in period to RB period significantly different from change from run-in period to WB period, $P < 0.05$ (Wilcoxon's test).

Fasting plasma insulin and glucose

The fasting plasma glucose and insulin values are shown in **Table 4**. Even though the plasma insulin values seemed to decrease during both the rye bread and the wheat bread periods, the changes were not significant ($P = 0.993$). Bread type had a significant effect ($P = 0.006$) on overall insulin concentrations during the study. There was no significant interaction with time, however, indicating that there was no significant effect of bread type on the changes in insulin during the periods. Overall, plasma glucose concentrations also did not change during the bread periods ($P = 0.958$), nor did bread type affect the changes in plasma glucose during the bread periods. Dietary protein and total fat had a significant association with plasma glucose ($P = 0.028$ and $P = 0.048$, respectively), although no significant changes in plasma glucose occurred during either the rye bread or the wheat period.

Frequently sampled intravenous-glucose-tolerance test

The plasma glucose and insulin curves during the FSIGTT are shown in **Figure 1**. There were no consistent differences at single measurement points in either glucose or insulin during the FSIGTT: plasma glucose concentrations were different at 2 ($P = 0.035$) and 140 ($P = 0.016$) min, and insulin concentration at 50 min ($P = 0.019$) among the run-in and the test bread periods. The values of the S_G, S_I, and AIR at the run-in and at the end of the rye and wheat bread periods are shown in **Table 5**. The differences in S_G and S_I between the rye bread and the wheat bread periods were not significant ($P = 0.522$ and $P = 0.170$, respectively). Protein had a significant association with S_I ($P = 0.008$), although S_I did not significantly change during the study.

The increase in AIR during the rye bread period (9.9 ± 24.2%) was greater than that during the wheat bread period (2.8 ± 36.3%; $P = 0.047$ for the difference in the respective proportional changes in covariance analysis), and the result was independent of the difference in energy intakes from protein and total fat and the order of the bread periods. In addition, the differences in the changes in fasting glucose and insulin, S_G, S_I, and AIR during the rye bread and wheat bread periods were analyzed taking into consideration glucose tolerance, use of thyroid hormone and estrogen replacement therapy, and the body weight of the subjects. No significant effects by these factors were found.

TABLE 3
Daily intakes of rye bread (RB), wheat bread (WB), and other cereals by postmenopausal women[1]

	RB period	WB period
Minimum amount of test breads to be consumed (portions/d)	7.5 ± 1.4	6.2 ± 1.2
Consumption of test breads		
(portions/d)	8.1 ± 1.6	7.7 ± 1.6
(g)	208 ± 38.3	170 ± 36.4
Consumption of other cereals (slices, pieces, or platefuls/d)	0.8 ± 0.3	0.7 ± 0.3

[1] $\bar{x}$ ± SD; n = 20. Each subject recorded daily consumption of test breads and other cereals during the RB and WB periods. Consumption of RB and WB was recorded as test bread portions, which were 24.1–28.1 g for RB and 20.8–25.0 g for WB. One portion of RB contained on average 206 kJ (range: 174–234 kJ) and 4.4 g fiber (range: 4.1–4.6 g). Respective values for WB were 241 kJ (range: 233–249 kJ) and 0.6 g fiber (range: 0.5–0.8 g).

DISCUSSION

In the current randomized crossover study, we modified the intake of carbohydrates from cereals by replacing nearly all cereals consumed by healthy postmenopausal women with either high-fiber rye breads (17% dietary fiber) or white-wheat breads (2.8% dietary fiber). The main finding was that rye bread increased the acute insulin response more than did wheat bread; furthermore, the acute insulin response increased significantly only with rye bread. No significant changes were seen in insulin sensitivity or glucose effectiveness during the study.

The possible confounding effects were minimized by study design, with each subject serving as her own control. Body weight, energy intake, alcohol consumption, and the frequency of exercise also remained constant during the study. In addition, the greater percentage increase in protein intake and the greater percentage decrease in fat intake during the rye bread period than during the wheat bread period were taken into account by using these as covariates. Glucose tolerance, use of thyroid hormone or hormone replacement therapy, and body mass index did not significantly affect the results.

We have considered 2 possible mechanisms for the increased acute insulin response after the rye bread period. The most obvious explanation for this finding is that the lente properties of rye fiber modify the digestion and absorption of carbohydrates in the small intestine and consequently the secretion of insulin from the pancreas. Second, rye may contain specific compounds that enhance the acute phase of insulin secretion. Such compounds may include phenolic acids and tannins, which are benzoic acid and phenylalanine derivatives (21, 22). The latter compounds have recently been described as short-acting prandial drugs that stimulate insulin secretion (23, 24), in contrast with the slower-onset and long-acting sulfonylureas. The mechanism of action of these compounds includes enhancing the function of potassium channels in pancreatic β cells, which play a decisive role in the generation of the acute insulin response (25).

The high-fiber content of the rye products may explain their lente effects after ingestion. Soluble fibers produce viscous solutions that may interfere with hydrolysis by binding enzymes and

TABLE 4
Fasting plasma glucose and insulin concentrations at the beginning and the end of the rye bread (RB) and wheat bread (WB) periods in postmenopausal women[1]

	Beginning of RB period	End of RB period	Beginning of WB period	End of WB period
Plasma glucose (mmol/L)	5.39 ± 0.47	5.43 ± 0.34	5.47 ± 0.41	5.41 ± 0.34
Plasma insulin (pmol/L)	59.3 ± 28.3	52.4 ± 30.3	58.9 ± 25.8	49.0 ± 20.3

[1] $\bar{x}$ ± SD; n = 20. There were no significant changes in plasma glucose or insulin concentrations during the study, P = 0.958 and P = 0.993, respectively (repeated-measures analysis of covariance).

nutrients to the fiber, reducing the surface area of the food particles available for digestion, altering the intraluminal mixing and contractability, and reducing the rate of diffusion through the intraluminal contents of the small intestine to enterocytes (26, 27). In addition, the end products of fiber fermentation in large bowel, such as propionic and butyric acids, may have insulinotropic effects (28).

It is possible that lower postprandial insulin responses after consumption of rye bread than after wheat bread (11, 12) occurring repeatedly over longer periods of time result in "relief" of overstimulation of β cells and correction of β cell dysfunction (29). The loss of the acute insulin response is one of the earliest defects in the development of type 2 diabetes, and it is found already in subjects at high risk (25). It is therefore tempting to speculate in light of the present results and our earlier postprandial studies that long-term ingestion of rye bread could protect the pancreatic β cells from exhaustion or even enhance β cell function.

Insulin sensitivity can be measured in many different ways. As a more sophisticated method, calculations of S_I and S_G from the minimal model FSIGTT were used in the present study. Although S_I seemed to be affected by the intake of protein, no significant differences either in proportional changes of S_I during the rye bread and the wheat bread periods compared with the run-in period or in the pairwise comparisons between the run-in and the end of the bread periods were observed. S_G was also unaltered during the rye bread and wheat bread periods. Earlier studies of the long-term effects of different cereal foods on indexes modifying insulin action and glucose metabolism in peripheral tissues in healthy elderly women are lacking. There is one earlier study with fat-carbohydrate modification of the diet in postmenopausal women (30), but the different study design and diets do not allow us to compare those results with those of the present study.

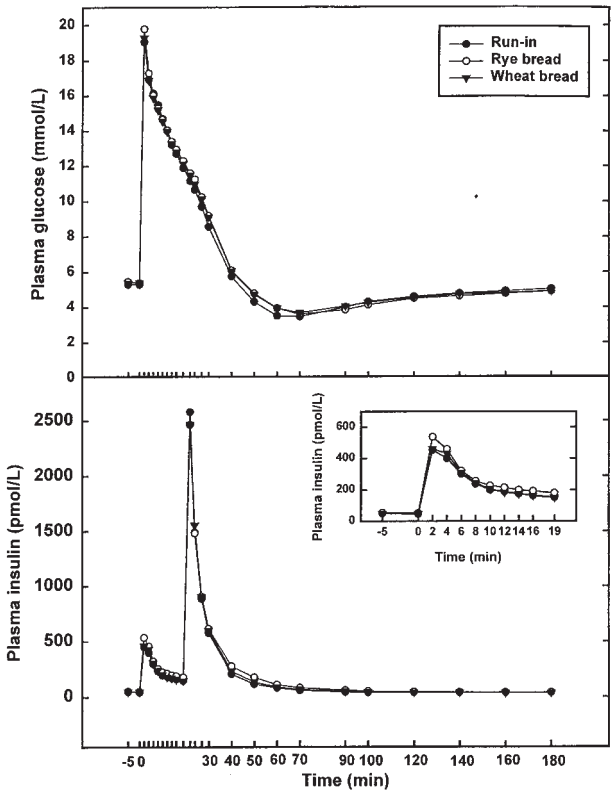

FIGURE 1. Plasma glucose and insulin concentrations during the frequently sampled intravenous-glucose-tolerance tests (0 to 180 min). Glucose (330 mg/kg) was given at 0 min and insulin (0.03 U/kg) at 20 min.

No significant changes in fasting glucose and insulin concentrations, which are crude measures of insulin sensitivity, were found in the present study. Although bread type seemed to have some effect on insulin, and the intakes of protein and total fat had some interaction with plasma glucose, these findings are of questionable importance because insulin and glucose concentrations remained unchanged throughout the study. The finding of unchanged fasting glucose and insulin concentrations confirms our earlier finding in hypercholesterolemic men and women who ate commercial rye and white-wheat breads for 4 wk in random order (14). One previous study showed that consumption of a high-carbohydrate, high-fiber diet compared with the usual ad libitum diet could decrease both fasting glucose and insulin in elderly men and women (31). However, in that trial, the intakes of carbohydrates and fiber were considerably greater than in the present study (68% compared with 53% of energy and 68 compared with 46 g/d, respectively). In agreement with our results, no alteration of the fasting glucose or insulin concentrations was observed after consumption of a high-carbohydrate diet (60% of energy) by elderly men and women with impaired glucose tolerance for 12 wk (32), after consumption of a low-glycemic-index diet by elderly men and women with coronary heart disease for 4 wk (33), and after supplementation of the diet with guar gum (15 g/d) in perimenopausal women for 6 mo (34).

The lack of effect of the dietary carbohydrate and fiber modifications on fasting glucose and insulin concentrations remains unexplained. Some studies have consistently shown postprandially improved glycemic and insulinemic responses with the consumption of low-glycemic-index foods (35), whole-grain bread (36), and increased amounts of fiber from naturally high-fiber foodstuffs (37). In addition, epidemiologic evidence suggests that the consumption of foods with a low glycemic index and high in dietary fiber and whole-grain cereals may prevent diabetes (2, 4). It is possible that modification of carbohydrate and fiber intake alters fasting insulin and glucose concentrations and insulin sensitivity only after much longer time periods in nondiabetic individuals.

Rye bread increased the acute insulin response to a minimal model glucose tolerance test in postmenopausal women,

TABLE 5
Glucose effectiveness (S_G), insulin sensitivity (S_I), and acute insulin response (AIR) at the run-in and at the end of the rye bread (RB) and wheat bread (WB) periods in postmenopausal women[1]

	Run-in period	RB period	WB period
S_G (min^{-1})	0.025 ± 0.004	0.022 ± 0.005	0.023 ± 0.006
S_I (10^{-4} min^{-1} × μU^{-1} × mL^{-1})	4.6 ± 2.0	4.1 ± 2.1	3.9 ± 1.8
AIR (pmol·min/L)[2]	2561 ± 1373	2904 ± 1749	2651 ± 1632

[1] $\bar{x}$ ± SD; n = 20.
[2] The proportional changes from the run-in period to the end of the RB period were significantly greater than the changes from the run-in period to the end of the WB period, P = 0.047 (repeated-measures analysis of covariance).

suggesting that high-fiber rye bread may have favorable long-term effects on the maintenance of normal β cell secretion or on the improvement of pancreatic β cell dysfunction. Further studies should, however, confirm these results and evaluate the mechanism and the components in rye that are responsible for this effect.

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