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Effects of whole-grain cereal foods on plasma short chain fatty acid concentrations in individuals with the metabolic syndrome

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ABSTRACT

Objective: Short chain fatty acids (SCFAs) derived from dietary fiber fermentation by gut microbiota have been identified as one of the mechanisms behind the association between habitual whole-grain intake and a lower risk of cardiometabolic diseases. The aims of the present work are: (1) to evaluate whether a whole-grain wheat-based diet may increase SCFAs concentration, and (2) to identify possible associations between SCFAs and metabolic changes observed after the nutritional intervention.

Methods: Fifty-four subjects participated in the trial. They underwent a 12-wk dietary intervention based on whole-grain or refined cereal products. At baseline and after the intervention, glucose, insulin, triacylglycerol, inflammatory markers (hs-CRP, IL-1 ra, IL-6, and TNF-α), and SCFAs plasma concentrations were evaluated.

Results: After the intervention, in the whole-grain group fasting plasma propionate concentrations were higher than at baseline, whereas a reduction was detected in the control group. The absolute changes (end of trial minus baseline) in fasting plasma propionate concentrations were significantly different between the two groups ($P = 0.048$). The absolute changes of fasting propionate correlated with cereal fiber intake ($r = 0.358$, $P = 0.023$), but no significant correlations with clinical outcomes were found. However, postprandial insulin was significantly decreased in the group having the absolute changes of fasting propionate concentration above the median value ($P = 0.022$ versus subjects with fasting propionate changes below the median value).

Conclusions: A 12-wk whole-grain wheat-based diet increases fasting plasma propionate. This increase correlates with the cereal fiber intake and is associated with lower postprandial insulin concentrations.

Introduction

Whole-grain consumption has been associated with a reduced risk of cardiovascular disease, overweight/obesity and type 2 diabetes [1,2].

One of the proposed mechanisms behind these associations is the colonic fermentation of cereal fiber, leading to the production of short chain fatty acids (SCFAs): acetate, propionate, and butyrate. In fact, many studies have speculated on the role of SCFAs in the modulation of glucose and lipid metabolism [3,4]. Nevertheless, evidence from clinical trials is still scant and

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controversial [5–8]. This may be due, at least in part, to the high variability of fiber fermentation by colonic microbiota. In vitro [9, 10] and in vivo [4] studies have demonstrated that the rate of fiber fermentation depends strictly on the type of cereal; in particular, rye and barley seem to be more fermentable than wheat. Moreover, study duration may also play a role. In fact, Freeland et al. [11] have shown that wheat also increases colonic SCFAs production, even though it takes time to be able to appreciate a significant increase of fiber fermentation products in plasma (9 mo).

Thus, the aim of this study was to evaluate whether a 12-wk consumption of a diet rich in whole-grain products (mainly whole wheat) may influence the production of SCFAs in subjects with the metabolic syndrome. In addition, we hypothesized a role of SCFAs in the modulation of postprandial glucose, insulin, and triacylglycerol concentrations and subclinical inflammation.

Material and methods

Subjects and study design

Fifty-four overweight/obese subjects (23 men and 31 women) with the metabolic syndrome were randomly assigned to an isoenergetic diet based on either whole-grain cereal products (whole-grain group, n = 26) or refined cereal goods (control group, n = 28) for 12-wk.

Details on the study design have been published elsewhere [12]. In short, participants were encouraged not to change their habitual meat, dairy products, eggs, fish, fruit, vegetable, and fat intake during the study. The only difference between the whole-grain and the control diet was the inclusion of a fixed amount of whole-grain or refined cereal products as the main carbohydrate source. Therefore, the two diets were designed to have the same energy intake and nutrient composition (18% protein, 30% fat, 52% carbohydrates); they were different only for cereal-foods consumed and for the cereal fiber intake.

At baseline and at the end of the intervention, fasting blood samples were taken in K2-EDTA tubes for SCFAs measurements and fasting and postprandial blood samples (over 3 h) for the evaluation of glucose, insulin, triacylglycerol, and inflammatory markers (hs-CRP, high-sensitivity C-reactive protein; IL-6, interleukin-6; IL-1 ra, interleukin-1 receptor antagonists; and TNF-α: tumor necrosis factor-α). During the study, all subjects were asked to fill in a 7 d food record every mo to assess dietary compliance.

The design of the trial was approved by the "Federico II" University Ethics Committee and followed the Helsinki Declaration guidelines. All participants provided written informed consent.

The study was registered with ClinicalTrials.gov (identifier NCT00945854).

Experimental procedures

Plasma glucose and triacylglycerol concentrations were assayed by enzymatic colorimetric methods (ABX Diagnostics, Montpellier, France; Roche Molecular Biochemicals, Mannheim, Germany; Wako Chemicals GmbH, Neuss, Germany, respectively) on a Cobas Mira autoanalyzer (ABX Diagnostics, Montpellier, France). Plasma insulin concentrations were measured by an enzyme-linked immunosorbent assay for the specific determination of biologically active insulin (DAKO Insulin, DAKO Diagnostics, Ely, UK). The inflammatory markers (hs-CRP, IL-1 ra, IL-6, and TNF-α) were determined in Germany at the University of Ulm, in the laboratory of the Department of Internal Medicine II-Cardiology, as described by de Mello et al. [13].

Acetate, propionate, and butyrate acids were evaluated in plasma at baseline and at the end of the dietary intervention. Before the analyses, 400 mL-samples were deproteinated using 50 μL metaphosphoric acid (16% W/V) at 60° C for 30 min and 50 μl of internal standard (isovaleric acid 80 μM) was added to each sample. After centrifugation (8000 rpm for 30 min at room temperature) all samples were filtered. Then, SCFAs concentrations were analyzed by gas-chromatography (Hewlett Packard 5890 Series II), according to Remesey and Demigne [14].

Statistical analyses and calculations

Results were expressed as mean ± SEM. Variables not normally distributed were analyzed after logarithmic transformation or as medians.

To test the effects in each intervention group, 12-wk concentrations were compared to the baseline concentration by a paired sample *t* test. Differences between the two experimental diets, expressed as absolute changes (12-wk value minus baseline value) were evaluated by one-way analysis of variance (ANOVA). Bivariate associations were assessed by Pearson's correlation. A P value <0.05 was considered significant. Statistical analysis was performed according to standard methods using the Statistical Package for Social Sciences software version 21.0 (SPSS, Chicago, IL, USA).

Results

Subjects characteristics and dietary compliance

SCFAs measurement was performed in 40 subjects who were, therefore, included in this analysis: 19 subjects (7 M/12 F) in the control group and 21 subjects (9 M/12 F) in the whole grain group. The two experimental groups were similar at baseline for anthropometric parameters as well as for all clinical and metabolic parameters and inflammatory markers (Table 1). A significant reduction of postprandial insulin and triacylglycerol responses were observed at the end of the intervention in the whole-grain group compared to the control group (postprandial insulin: −17.2 ± 10 versus 13.6 ± 6.7 μU/mL, whole grain and control group respectively, $P < 0.05$; postprandial triacylglycerols: −22.6 ± 13 versus 11.6 ± 8.9 mg/dL, whole-grain and control group respectively, $P < 0.05$) [12].

Table 1
Clinical data, fasting plasma metabolic parameters and inflammatory markers at baseline and after the intervention in the two experimental groups

Parameters	Control group (n = 19)			Whole-grain group (n = 21)			ANOVA for Δ
	Baseline	12 week	Δ	Baseline	12 week	Δ	
Age (years)	58.4 ± 1.6			57.2 ± 1.9			
Sex (M/F)	7/12			9/12			
BMI (kg/m^2)	31.5 ± 1.3	31.3 ± 1.3	−0.20 ± 0.2	32.1 ± 1.4	31.9 ± 1.4	−0.20 ± 0.2	0.992
Fasting glucose (mg/dL)	105 ± 2.8	105 ± 0.2	−0.72 ± 1.5	103 ± 2.2	103 ± 2.7	−0.38 ± 1.7	0.882
Fasting insulin (μU/mL)	11.8 ± 1.3	11.7 ± 1.6	−0.11 ± 1.5	14.1 ± 1.9	13.3 ± 1.1	−0.47 ± 0.9	0.726
HOMA	3.08 ± 0.3	3.09 ± 0.5	0.01 ± 0.4	3.61 ± 0.5	3.36 ± 0.3	−0.25 ± 0.3	0.615
Triacylglycerols (mg/dL)	133 ± 9.5	136 ± 13	2.95 ± 12	153 ± 36	137 ± 15	−16.9 ± 28	0.538
Total cholesterol (mg/dL)	201 ± 8.8	208 ± 7.5	6.47 ± 5.0	200 ± 10	201 ± 10	1.10 ± 5.1	0.457
HDL-cholesterol (mg/dL)	38.7 ± 1.5	39.8 ± 1.5	1.11 ± 1.2	42.9 ± 3.2	42.3 ± 3	−0.62 ± 1.2	0.324
hs-CRP (mg/dL)	2.27 ± 0.4	2.39 ± 0.4	0.12 ± 0.2	2.52 ± 0.5	2.44 ± 0.5	−0.08 ± 0.4	0.693
IL-6 (pg/mL)	1.69 ± 0.3	1.70 ± 0.3	0.01 ± 0.2	1.84 ± 0.2	2.23 ± 0.3	0.39 ± 0.2	0.161
IL-1 ra (pg/mL)	316 ± 73	311 ± 63	−5.17 ± 14	380 ± 61	378 ± 61	−1.40 ± 24	0.897
TNF-α (pg/mL)	1.07 ± 0.4	1.31 ± 0.5	0.24 ± 0.1	1.71 ± 0.6	1.50 ± 0.6	−0.21 ± 0.3	0.232

BMI, body mass index; HDL, high-density lipoproteins; hs-CRP, high-sensitivity C-reactive protein; HOMA, homeostasis model assessment; IL-1 ra, interleukin-1 receptor antagonists; IL-6, interleukin-6; TNF-α, tumor necrosis factor-α; ANOVA, analysis of variance
Data are expressed as mean ± SEM