Original Research

Effects of Acute Chromium Supplementation on Postprandial Metabolism in Healthy Young Men

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Key words: chromium, glycemic index, glycemia, postprandial metabolism, glucose, insulin

Background: Chromium (Cr) potentiates the action of insulin in the cell and improves glucose tolerance after long-term supplementation.

Objective: We hypothesized that Cr may also have acute effects and might be beneficial in lowering the glycemic index of a meal.

Methods: We studied the effects of short-term Cr supplementation using a randomized crossover design. Thirteen apparently healthy, non-smoking young men of normal body mass index performed three trials each separated by one week. Test meals, providing 75 g of available carbohydrates, consisted of white bread with added Cr (400 or 800 μg as Cr picolinate) or placebo.

Results: After addition of 400 and 800 μg Cr incremental area under the curve (AUC) for capillary glucose was 23% ($p = 0.053$) and 20% ($p = 0.054$), respectively, lower than after the white bread meal. These differences reached significance if the subjects were divided into responders (n = 10) and non-responders (n = 3). For the responders AUC after 400 and 800 μg Cr was reduced by 36% and 30%, respectively (Placebo 175 $\pm$ 22, Cr400 111 $\pm$ 14 ($p < 0.01$), Cr800 122 $\pm$ 15 mmol $\cdot$ min/L ($p < 0.01$)). Glycemia was unchanged after addition of Cr in the non-responders. Responders and non-responders differed significantly in their nutrient intake and eating pattern, and total serum iron concentration tended to be lower in the responder group ($p = 0.07$).

Conclusions: Acute chromium supplementation showed an effect on postprandial glucose metabolism in most but not all subjects. The response to Cr may be influenced by dietary patterns.

INTRODUCTION

According to the 1998 World Health Report of the WHO the incidence of non-insulin dependent diabetes mellitus (NIDDM) will more than double from 143 million in 1997 to 300 million in 2025 [1]. Along with other environmental risk factors, nutrition plays an important role in the etiology of NIDDM. The type of carbohydrates and the glycemic response to a meal may be important risk factors, with growing evidence that high-glycemic diets increase the risk of developing insulin resistance and ultimately NIDDM in later life [2,3]. On the other hand, low-glycemic diets may protect against NIDDM [4,5]. Several intervention studies have indicated that low-glycemic diets may improve blood glucose control and insulin sensitivity [6–9]. Also, two large prospective studies have shown associations between low-glycemic diets and a lower risk of NIDDM for women [2] and men [3]. Lowering the glycemic response to a meal or a diet may therefore represent an important preventive approach in delaying the onset of insulin resistance and NIDDM. The trace mineral chromium (Cr) might have an effect on glycemia, since it influences carbohydrate metabolism by potentiating the action of insulin in the cell. Cr has been shown to normalize or improve glucose tolerance in hypoglycemics [10], in hyperglycemics [11], and in subjects with NIDDM [12–14].

Most studies investigating the metabolic effects of Cr used supplementation periods of several weeks or even months. There are only few data on the effects of a short-term

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supplementation on the metabolism [15,16]. Cr is rapidly absorbed and the maximal blood concentration is reached within 90 min after ingestion [17]. An acute effect of Cr may therefore be expected shortly after intake.

Cr functions as a nutrient and will only benefit those with a deficiency [18]. Subjects with normal glucose tolerance and no signs of Cr deficiency do not seem to respond to supplementation [11,19]. The Food and Nutrition Board of the U.S. National Academy of Sciences recently set the Adequate Intake for Cr at 35 μg/d for men and 25 μg/d for women [20]. These recommendations were based on estimated mean intakes, as the Board concluded that there was not enough scientific evidence to set an Estimated Average Requirement. Just one year earlier the Nutrition Societies of Germany, Austria, and Switzerland set the reference intake for adults at 30–100 μg/d [21]. These differing values reflect the existing uncertainty about the exact Cr requirements. As the estimated average Cr intake seems to be on the low side of the recommended intake, there might be individuals with marginal Cr status even in the healthy population and these could possibly benefit from supplemental Cr. We hypothesized that single doses of Cr given to young, healthy men would reduce glycemia after a high-glycemic meal.

The aim of this study was to investigate the effects of acute Cr supplementation (400 and 800 μg) on postprandial carbohydrate metabolism after a high-glycemic meal and to evaluate which amount of Cr would be more beneficial.

SUBJECTS AND METHODS

Subjects

Thirteen seemingly healthy, nonsmoking males aged 24.7 $\pm$ 0.9 years (mean $\pm$ SEM) and with normal body mass indexes (22.5 $\pm$ 0.5 kg/m^2) participated in the study. They had no family history of diabetes and did not use any medication nor take any nutritional supplements for the last two months before and until completion of the study. The subjects performed only moderate amounts of physical activity (exercise volume up to 1–2 h/wk). All participants were informed of the purpose of the study and signed an informed-consent form. The Scientific Ethics Committee of the Swiss Federal Institute of Technology in Zurich approved the study.

Study Design

The study was performed as a placebo-controlled, single-blind crossover experiment. Subjects underwent three different trials in random order. Test meals consisted of white bread with supplemental Cr (Cr400 and Cr800) or placebo (WB), each meal providing 75 g available carbohydrates. Participants were tested at least one week apart to avoid carry-over effects and all three trials were performed within four weeks. Each subject was told to maintain the same dietary habits and physical activity level until completion of the study. On the evening before each trial, subjects consumed a standardized rice meal providing approximately 3.9 MJ energy (180 g carbohydrates, 13 g fat, 23 g protein), and were told not to eat anything else until the next morning. In addition, subjects were asked not to ingest alcohol or caffeine containing drinks and foods, and were requested to avoid heavy physical exercise the day prior to each trial. Subjects were told to use local transport to get to the laboratory in order to avoid any intense physical exertion. They arrived at the laboratory after a 10–12 h overnight fast and then completed a short questionnaire assessing recent food intake and activity patterns. Three people were tested daily, beginning at 7:45, 8:00, and 8:15 a.m., respectively. Following the insertion of an indwelling catheter (Insyte-W, Becton Dickinson, Rutherford, NJ, USA) into an antecubital vein, a fasting blood sample was taken. After assessment of baseline values, test meals were given and eaten within ten minutes. Test meals consisted of commercially available white bread (140 g, 1.8 MJ) and provided 75 g of carbohydrates, 2 g of fat, and 13 g of protein. Postprandial blood samples were taken at 15, 30, 45, 60, 90, and 120 min after beginning of the meal. Finger-prick capillary blood samples for analysis of glucose were taken at the same times than the venous samples. After baseline assessment and 30 min before ingestion of the test meal, 400 or 800 μg Cr as Cr picolinate in pill form (GNC, Pittsburgh, PA, USA) was given with the Cr trials and a placebo (Hänseler AG, Herisau, Switzerland) with the WB trial. Placebo pills contained 120 mg lactose and 50 mg potato starch and could not be distinguished from the Cr pills.

Blood Sampling

Venous blood was collected in different tubes for whole blood (glycosylated hemoglobin (HbA_{1c})), plasma (glucose, insulin) and serum samples (iron, transferrin, ferritin). Tubes with blood for plasma samples were immediately placed on ice and then centrifuged at 3000 g for 15 min at 8° C. Tubes for serum samples were left at room temperature for 30 min to allow coagulation before centrifugation. Plasma and serum samples were stored at -20° C until analysis.

HbA_{1c} samples were analyzed within 24 h on a Cobas Integra 700 (Roche, Basel, Switzerland) using a Cobas Integra Hemoglobin A_{1c} kit. Plasma metabolites were analyzed enzymatically with a Cobas Mira analyzer (Roche, Basel, Switzerland) using commercial kits: glucose, iron and transferrin (Roche, Basel, Switzerland). Insulin was assessed by a standard radioimmunoassay kit (Pharmacia AB, Uppsala, Sweden). Capillary blood glucose concentrations were determined with a glucose oxidoreductase method with photometric end-point measurement using the Glucotrend® 2 system (Roche Diagnostics, Rotkreuz, Switzerland).

Diet Diary

The subjects were asked to take home and complete an open-ended estimated 5-day diet diary. A diet diary booklet containing instructions and four sets of color photographs was explained and then given to them. Each set of photographs showed three portion sizes of a common food item. They were provided to help the subjects estimate portion sizes. The instructions indicated that the participant should record the name, food brand, and amount of all foods eaten. The quantity of food eaten was estimated either in common household measures (e.g. tablespoons, cups), in whole units (e.g. number of apples, slices of bread), or in portion sizes (i.e. small, medium or large). Nutrient intake was calculated using the EBISpro software (University of Hohenheim, Hohenheim, Germany).

Insulin Sensitivity

The quantitative insulin sensitivity check index (QUICKI = 1/[log (fasting insulin) + log (fasting glucose)]) was used to assess insulin sensitivity [22].

Statistical Analysis

All results are expressed as means ± SEM and/or range. The general linear model (analysis of variance) was used to compare the pattern of the postprandial changes in blood variables between treatments. For significant overall differences between treatments, the data were further analyzed with Tukey's *post hoc* comparisons. Calculation of correlation coefficients between variables were performed by using the Pearson product-moment test. Glucose and insulin responses were calculated as incremental areas under the curve (AUC) using the trapezoidal method [23] and then compared between trials using paired *t*-tests with Bonferroni correction. The level of significance was set at $p < 0.05$. Data were analyzed by using the statistics software SYSTAT 9.01 (SPSS Inc., Chicago, IL, USA).

RESULTS

The HbA_{1c} concentration was normal for all subjects and ranged from 4.8% to 5.7% (5.4% ± 0.1%). We observed no significant differences between trials in the fasting concentration of all measured indexes and all fasting values were within the normal range for healthy people.

Glucose

There was a main effect of treatment for capillary ($p < 0.05$) but not venous ($p = 0.31$) glucose measurements (Fig. 1). Capillary glucose peak values were reached at 30 min for Cr400 and at 45 min for WB and Cr800, and were higher for WB then for Cr400 and Cr800 (7.4 ± 0.2 compared with 6.9 ± 0.2 ($p < 0.05$) and 7.0 ± 0.3 mmol/L ($p = 0.13$), respectively).

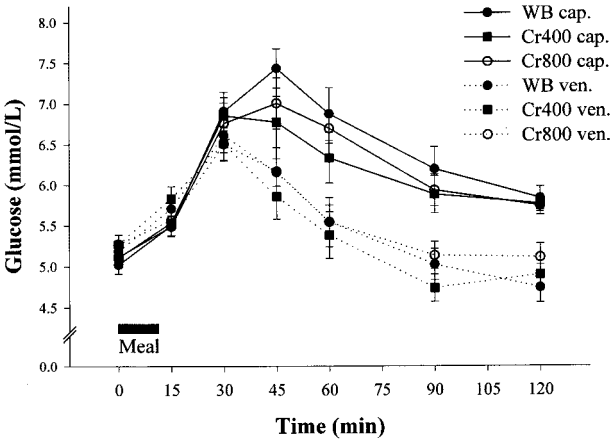

Fig. 1. Capillary and venous glucose concentrations after test meals providing 75 g available carbohydrates. Test meals were eaten within 10 min and consisted of white bread with placebo (WB, ●), white bread with 400 μg chromium (Cr400, ■) and white bread with 800 μg chromium (Cr800, ○). Values are means for thirteen subjects with standard errors of the means shown by vertical bars.

For venous glucose peak values were attained at 30 min and no differences in peak height between treatments were observed. For WB and Cr800 peak values were lower in venous compared with capillary glucose (both $p < 0.01$).

The AUC were lower for Cr400 and Cr800, respectively, than for the WB trial for capillary (23% and 20%) and venous glucose (29% and 15%). But these differences were not significant (Table 1). The differences reached significance for capillary glucose if the subjects were divided into a responder and a non-responder group. Responders were defined as subjects who showed a lower postprandial glycemia after both Cr trials compared with the WB trial, and non-responders as those who displayed no change or an increase after supplementation. Postprandial capillary glycemia and the glycemic indexes (GI) were significantly reduced after both Cr supplements for the responder group (n = 10, Cr400: $p = 0.04$, Cr800: $p = 0.03$, Table 1). The non-responders tended to show larger capillary glucose AUC after the Cr trials than after placebo, but these differences were not significant (Table 1, Cr400: $p = 0.14$, Cr800: $p = 0.15$). No differences between trials were observed for venous glucose (Table 1).

There was a positive correlation between the capillary glycemic response to WB and the extent of the glycemic response shown after supplementation with Cr400 ($r = 0.70$, $p = 0.008$) or Cr800 ($r = 0.67$, $p = 0.011$). That is, individuals with large glucose AUC after the WB trial showed large reduction in glycemia after Cr intake (Fig. 2).

Insulin

Insulin concentrations after the Cr trials were not significantly different from concentrations after the WB trial at all

Table 1. Capillary and Venous Glucose Area under the Curve (mmol · min/L), and Glycemic Index (in Parentheses) Values after Test Meals Consisting of White Bread with Placebo (WB), White Bread with 400 μg Cr (Cr400) and White Bread with 800 μg Cr (Cr800) for All Subjects, Responders and Non-Responders

	WB	Cr400	Cr800
All (n = 13)			
Capillary	163 ± 19 (100)	123 ± 14* (82)	130 ± 14* (86)
Venous	62 ± 9 (100)	44 ± 7 (84)	53 ± 8 (99)
Responders (n = 10)			
Capillary	175 ± 22 (100)	111 ± 14** (66**)	122 ± 15** (72**)
Venous	64 ± 12 (100)	39 ± 5* (79)	46 ± 5 (90)
Non-responders (n = 3)			
Capillary	121 ± 16 (100)	164 ± 26 (135)	158 ± 24 (130)
Venous	56 ± 11 (100)	61 ± 21 (101)	77 ± 24 (132)

* $p < 0.1$, ** $p < 0.01$: Cr400 and Cr800 compared with WB, value in the same row; mean ± SEM.

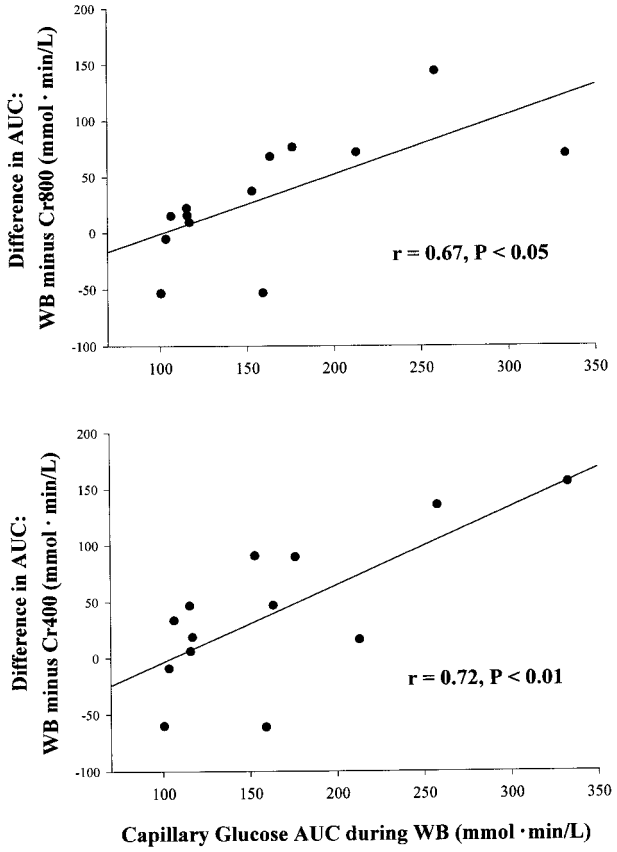

Fig. 2. Significant positive correlations were shown between the extent of the capillary glycemic response after the WB trial and the reduction in glycemia during the Cr400 and the Cr800 trial. The dots above zero (y-axis) represent the subjects having shown a decrease in glycemia after chromium supplementation (i.e. the responders), while the dots below zero symbolize the non-responders. AUC = area under the curve.

time points (Fig. 3). Accordingly, we observed no differences for the AUC (WB: 13520 ± 920, Cr400: 12840 ± 1240 (p = 0.53), and Cr800: 12600 ± 1330 (p = 0.34) pmol · min/L). Insulin sensitivity (QUICKI) was similar for responders and non-responders (0.68 ± 0.02 and 0.66 ± 0.01, p = 0.69).

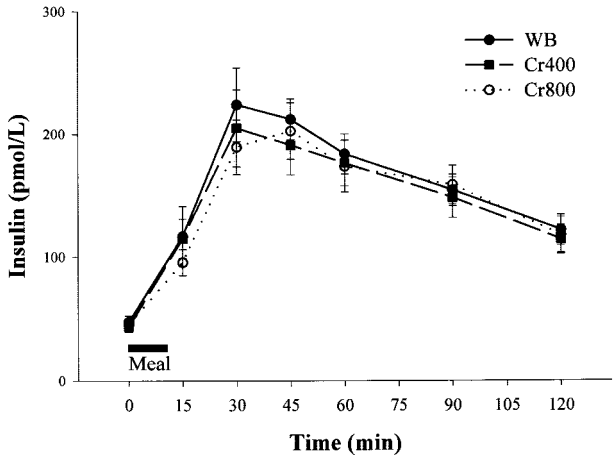

Fig. 3. Plasma insulin concentrations after test meals providing 75 g available carbohydrates. Test meals were eaten within 10 min and consisted of white bread with placebo (WB, ●), white bread with 400 μg chromium (Cr400, ■) and white bread with 800 μg chromium (Cr800, ○). Values are means for thirteen subjects with standard errors of the means shown by vertical bars.

Diet Records

Non-responders had a higher consumption of milk and meat products but tended to eat less fruit and vegetables than responders. This reflects itself in higher intakes of fat, protein, disaccharides, vitamin B_2 and B_{12} but lower intakes of fiber, folate and vitamin C for the non-responders compared with the responders (Table 2).

Iron Variables

Non-responders had significantly higher iron and transferrin concentrations in the blood compared with responders, while ferritin concentration and transferrin saturation were similar for both groups (Table 3).

Table 2. Comparison of Estimated Energy and Nutrient Intake in Responders and Non-Responders

	Responders (n = 10)		Non-Responders (n = 3)		*p*-value	DRI
	Mean	SEM	Mean	SEM		
Energy (MJ)	10.2	0.5	11.9	0.7	0.14	11.9
Protein (g)*	86 (14%)	3.2	100 (14%)	7.6	0.05	58
Fat (g)*	98 (36%)	6.3	120 (37%)	5.9	0.10	<30%
Carbohydrate (g)*	292 (49%)	16	336 (48%)	31	0.26	>55%
Monosaccharide (g)	43	8	39	15	0.86	—
Disaccharide (g)	75	5.7	114	5.0	0.01	—
Starch (g)	160	14	180	20	0.66	—
Fiber (g)	27	1.9	19	1.4	0.06	—
Vitamin B1 (mg)	1.5	0.1	1.5	0.1	0.89	1.2
Vitamin B2 (mg)	1.7	0.1	2.3	0.04	0.01	1.3
Vitamin B12 (μg)	2.5	0.3	4.7	0.9	0.02	2.4
Vitamin C (mg)	110	14	66	16	0.14	90
Folate (μg)	140	6.1	130	13	0.44	400
Vitamin E (mg)	14	1.0	12	1.9	0.42	15
Sodium (mg)	3400	310	2800	370	0.44	<2400
Potassium (mg)	3200	180	3000	150	0.58	—
Calcium (mg)	1200	110	1300	80	0.76	1000
Magnesium (mg)	420	17	360	24	0.16	400
Iron (mg)	15	0.7	13	1.5	0.30	10

* values in parentheses: percentage of energy; DRI: Dietary Reference Intake (Reference values of the German, Austrian and Swiss Nutrition Societies [21].

Table 3. Fasting Iron, Ferritin and Transferrin Concentrations and Transferrin Saturation in Responders and Non-Responders

	Responders (n = 10)		Non-Responders (n = 3)		*p*-value
	Mean	SEM	Mean	SEM	
Iron (μmol/L)	24	1.0	30	1.6	0.01
Transferrin (g/L)	2.4	0.07	2.7	0.03	0.04
Transferrin saturation (%)	37	2.2	42	3.5	0.27
Ferritin (μmol/L)	100	9.4	95	11	0.78

DISCUSSION

We tested the hypothesis that an acute single dose Cr supplementation would decrease glycemia after a high-glycemic meal in young, apparently healthy adults. A substantial reduction in postprandial glycemia was observed after addition of 400 as well as 800 μg Cr to a white bread meal compared with the white bread meal supplemented with a placebo (−23% and −20% for the incremental AUC, respectively). The reductions in glycemia were similar for both Cr trials suggesting that 400 μg are a sufficient amount to induce a beneficial effect and that there is no additional improvement when supplementing 800 μg of Cr. In a previous study performed at our laboratory using the same experimental procedure we could not detect any effects on glucose response after a high-glycemic meal and supplementation with 200 μg Cr (Frauchiger, Colombani, and Wenk, unpublished). This suggests that, when given as a single dose, 200 μg of Cr might be insufficient to influence postprandial metabolism in healthy young men and that a larger amount of Cr is needed to affect glucose metabolism acutely. To our knowledge there are no other data on the effects of an acute single dose intake of Cr on postprandial metabolism. However, there are similar findings in longer-term studies. In a review by Anderson [24] it is reported that studies showing beneficial effects of supplemental Cr in people with diabetes usually involve 400 μg or more of Cr.

The absorption of Cr seems to be quite rapid as blood concentration peak within 90 minutes after intake [17]. We expected that Cr would show its effect on the cells rapidly and gave the supplement just 30 minutes before the meal. In a recent paper by Vincent and his group [35] it was proposed that Cr picolinate enters tissues intact and is then degraded in the cells. This may suggest that even if absorption is rapid a longer time period would be needed to release Cr in its active form. Therefore, it is well possible that effects on glucose metabolism would be more pronounced if the Cr supplement were given a few hours before the test meal.

There was no significant correlation between the glucose and insulin responses in both venous and capillary blood. The smaller glycemic responses after Cr supplementation were not associated with larger insulin responses. This suggests that another mechanism than stimulation of insulin secretion was responsible for the decreased glycemia after supplemental Cr and supports the proposed mechanism of Cr action. It has been

reported that Cr potentiates the action of insulin by activating the tyrosine kinase activity of the insulin receptor and thereby amplifies insulin signaling [25], but to have no effect on insulin secretion. In our study the effects on blood glucose were more apparent in capillary than in venous blood. This possibly indicates that Cr enhances glucose uptake by peripheral tissue.

In our study fasting capillary and venous glucose concentrations were similar but postprandial values between 45 and 120 min as well as peak values were significantly higher for capillary measurements. These findings are in accordance with those of other studies that found that glucose concentrations approximate arterial values in capillary blood and that fasting concentrations are similar in venous and arterial blood [26,27]. Postprandial glucose concentrations are higher in capillary than in venous blood because of insulin-induced glucose uptake in peripheral tissues. These differences were reported to be as much as 2 mmol/L [28]. The higher concentrations reflect themselves in larger glycemic responses in capillary blood. Because of the greater differences in incremental AUC, Wolever & Bolognesi [27] suggested that using capillary rather than venous blood was a more precise way to assess glycemic responses to foods.

In our study ten out of thirteen subjects, i.e. about 80%, responded to Cr supplementation with a decrease in postprandial glycemia. Other studies [11,14] have also reported that some but not all subjects responded to longer-term supplementation. The reasons why beneficial effects are only visible in a part of the study population are not clear. Ravina *et al.* [14] found no clinical signs indicating which patient may positively respond to the addition of Cr. It has been proposed that individuals with normal glucose tolerance and who are not Cr deficient will not respond to Cr supplements [19]. But as it is still not possible to measure Cr status directly it is difficult to predict who will benefit from supplemental Cr. Offenbacher *et al.* [29] observed that subjects consuming well balanced diets did not respond to additional Cr. It has also been suggested that 30 to 40 μg of Cr per day would be adequate if balanced diets high in fruit and vegetables and low in simple sugars were consumed [24]. We estimated usual dietary intake of our subjects from 5-day diet records. The subjects responding to Cr ate more vegetables and dietary fibers but less disaccharides, meat and meat products, and milk and milk products than the others. The high consumption of vegetables and low intake of sugar for the responders seems to be in contrast to the findings of Anderson [24] and Offenbacher [29]. However, as only three subjects in our study did not respond to Cr, these differences, even if statistically significant, need verification. Another interesting observation is that the responder and non-responder group differed in parameters of iron metabolism. Non-responders tended to have higher serum iron and transferrin concentrations than responders. As Cr is probably transported in the blood by transferrin [30,31] this observation may be important and could possibly explain the differing response to Cr intake. Again, because of the low number of subjects, these results need to be confirmed before any conclusion can be drawn.

All our subjects were apparently healthy and showed normal glucose tolerance. Still, there was a correlation between the extent of postprandial glycemia after the WB trial and the glucose response observed after addition of Cr. The individuals with "poorer" glucose tolerance showed greater reductions in glycemia after supplemental Cr than those with "better" glucose tolerance. This suggests that people with impaired glucose tolerance may benefit even more from acute Cr supplementation than individuals with normal glucose tolerance. Similarly, Anderson *et al.* observed a decreased glucose response after three months of Cr supplementation only in individuals with slightly impaired glucose tolerance [32].

Low-glycemic diets may play an important role in the prevention of insulin resistance and even NIDDM. Unfortunately, lowering the GI of a diet may be difficult to achieve as many low-glycemic foods are not very popular and changing eating habits is not an easy task. Additionally, there is a lack of low-glycemic foods particularly for breakfast, as bread and ready-to-eat cereals have high GI [33]. Therefore, a substance able to lower the glycemic response to a food would be beneficial and especially useful for breakfast foods. After supplementation with 400 and 800 μg Cr the GI of white bread was reduced from 100 to 66 and 72, respectively. That is, the high-glycemic food white bread was "transformed" to a food of moderate to low GI, like oat bran (72) or parboiled rice (66) [34].

In conclusion, an acutely administered single dose of Cr (400 or 800 μg) improved glycemia after a high-glycemic meal in about 80% of young, healthy subjects, without visible effects on insulin concentration. These results seem to support the potentiating role of Cr on insulin action. However, additional studies are required to examine further the effects of acute Cr supplementation in humans.

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