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A Low Glycemic Index Diet Does Not Affect Postprandial Energy Metabolism but Decreases Postprandial Insulinemia and Increases Fullness Ratings in Healthy Women[1–4]

Inger Krog-Mikkelsen,[5,9] Birgitte Sloth,[5,10] Dimiter Dimitrov,[7] Inge Tetens,[5,11] Inger Björck,[8] Anne Flint,[5,10] Jens J. Holst,[6] Arne Astrup,[5] Helena Elmståhl,[8,12] and Anne Raben[5]*

[5]Department of Human Nutrition, University of Copenhagen, Frederiksberg, Denmark; [6]Department of Biomedical Sciences, University of Copenhagen, Copenhagen, Denmark; [7]Department of Endocrinology, Medical University, Varna, Bulgaria; and [8]Department of Applied Nutrition and Food Chemistry, Lund University, Lund, Sweden

Abstract

At present, it is difficult to determine whether glycemic index (GI) is an important tool in the prevention of lifestyle diseases, and long-term studies investigating GI with diets matched in macronutrient composition, fiber content, energy content, and energy density are still scarce. We investigated the effects of 2 high-carbohydrate (55%) diets with low GI (LGI; 79) or high GI (HGI; 103) on postprandial blood profile, subjective appetite sensations, energy expenditure (EE), substrate oxidation rates, and ad libitum energy intake (EI) from a corresponding test meal (LGI or HGI) after consuming the diets ad libitum for 10 wk. Two groups of a total of 29 healthy, overweight women (age: 30.5 ± 6.6 y; BMI: 27.6 ± 1.5 kg/m^2) participated in the 10-wk intervention and a subsequent 4-h meal test. The breakfast test meals differed in GI but were equal in total energy, macronutrient composition, fiber content, and energy density. The LGI meal resulted in lower plasma glucose, serum insulin, and plasma glucagon-like peptide (GLP)-1 and higher plasma glucose-dependent insulinotropic polypeptide concentrations than the HGI meal ($P \leq 0.05$). Ratings of fullness were slightly higher and the desire to eat something fatty was lower after the test meal in the LGI group ($P < 0.05$). Postprandial plasma GLP-2, plasma glucagon, serum leptin, plasma ghrelin, EE, substrate oxidation rates, and ad libitum EI at lunch did not differ between groups. In conclusion, postprandial glycemia, insulinemia, and subjective appetite ratings after a test meal were better after 10-wk ad libitum intake of a LGI compared to a HGI diet. EE and substrate oxidation rates were, however, not affected. These findings give some support to recommendations to consume a LGI diet. J. Nutr. 141: 1679–1684, 2011.

Introduction

Today, obesity and obesity-related complications result in major health problems (1,2). Carbohydrates provide the major source of energy in the Western diet and at present dietary guidelines recommend that 55–60% of our daily EI[13] should come from carbohydrates, mainly from whole grain foods rich in fiber and low in sugar (3–5). The GI, introduced more than 25 y ago, is a method for ranking carbohydrates according to their effect on blood glucose responses (6). An intense debate has been going on for several years about GI and its relevance to diabetes, coronary heart disease, and weight management (7–16). However, it can be difficult to overview, combine, and interpret published results on GI because of the very large differences in design between studies and in participants' characteristics such as lean, overweight, or obese; sedentary or well trained; and diabetic or nondiabetic. Furthermore, the variation in the preparation and composition of the meals and/or diets provided can have a great impact on the results. Quite often, important aspects such as macronutrient composition, fiber content, energy content, and

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[3] This trial was registered at clinicaltrials.gov as NCT00324090.
[4] Supplemental Figures 1–5 and Supplemental Tables 1–3 are available from the "Online Supporting Material" link in the online posting of the article and from the same link in the online table of contents at jn.nutrition.org.
[9] Present address: Aarhus University Hospital, Denmark.
[10] Present address: Novo Nordisk A/S, Denmark.
[11] Present address: Technical University of Denmark.
[12] Present address: Uppsala University, Sweden.
* To whom correspondence should be addressed. E-mail: ara@life.ku.dk.

[13] Abbreviations used: CHO-OX, carbohydrate oxidation; E%, percentage energy; EE, energy expenditure; EI, energy intake; F-OX, fat oxidation; GI, glycemic index; GIP, glucose-dependent insulinotropic polypeptide; GLP, glucagon-like peptide; HGI, high glycemic index; HOMA, homeostasis model assessment; LGI, low glycemic index; P-OX, protein oxidation.

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energy density of the LGI and HGI meals/diets are not well matched. Foods with a LGI tend to be rich in fiber and have a low energy density, so these factors should be kept constant when testing the effect of GI per se. The few existing studies where the diets compared are kept similar in macronutrient composition, dietary fiber, and energy density did not have consistent results. Furthermore, diets are often energy fixed. If ad libitum EI and fluctuations in body weight and ensuing changes in health issues are allowed, a more real-life situation is obtained, making results easier to apply to the public. There have been very few long-term intervention studies with diets matched for macronutrient composition, fiber content, energy content, and energy density investigating the effect of GI in healthy participants (8,17), and the evidence of a beneficial effect of longer term diets is inconclusive.

The objective of the present study was to determine if 4-h postprandial plasma glucose, serum insulin, gastrointestinal hormones, EE, substrate oxidation rates, subjective appetite ratings, and ad libitum food intake at lunch differ after 10-wk ad libitum intake of a diet with either LGI or HGI.

Participants and Methods

Experimental design. The study design has been previously described (18). In brief, the study was a parallel, randomized, 10-wk intervention trial, with 2 matched groups receiving either LGI or HGI foods in replacement of their usual carbohydrate-rich foods. In wk 0 and 10, we measured height, blood pressure, heart rate, sagittal height, waist and hip circumference, and body composition (by using DXA scanning) and collected blood samples from fasting participants. In wk 0, 5, and 10, participants completed 7-d weighed dietary records. On the last day of the study, a subgroup underwent a 4-h meal test in which we measured baseline and postprandial EE, substrate oxidation, appetite ratings, and ad libitum EI and took blood samples after a LGI or HGI breakfast meal. The present paper describes the results from the subgroup measurements.

Participants. A total of 55 participants was enrolled in the intervention study. Of these, a subgroup of 30 individuals participated in the present meal test study. The inclusion criteria were: 20–40 y of age, overweight (BMI: 25–30 kg/m^2), body weight fluctuations ≤5 kg in the preceding 2 mo, absence of any physiologic or psychological illnesses that could influence the study results, no regular use of medicine (other than birth control pills), normal to mildly hypertensive blood pressure (≤159/99 mmHg), no food allergies, no special diets (e.g. vegetarian) or particular dislikes, moderate alcohol intake (≤14 alcoholic drinks/wk), nonsmoker (≤1 cigarette/d), not an elite athlete or wishing to change physical activity during the study, not pregnant and with no pregnancy planned, not lactating, premenopausal with regular menstrual cycle, and no blood donation in the 3 mo preceding the study. The recruitment procedure was described earlier in detail (18). All participants gave written consent after receiving verbal and written information about the study. Data from one participant (in the LGI group) was excluded from the analysis, because blood samples revealed pathophysiologic levels of serum insulin (fasting level: 122 pmol/L, peak level: 890 pmol/L). The study was carried out at the Department of Human Nutrition in accordance with the Helsinki-II declaration and was approved by the Municipal Ethical Committee of Copenhagen and Frederiksberg (KF 01–249/01). Characteristics at wk 0 and 10 of the 29 women participating in the meal test are presented in **Supplemental Table 1**.

Experimental diets. The 10-wk experimental diets were previously described in detail (18). To summarize, the test foods were given as fixed carbohydrate-rich supplements providing ~75% of total carbohydrate intake (assuming 55 E% of ingested energy was from carbohydrates). The remaining 25% of carbohydrates was chosen from a list of LGI or HGI foods. Participants were otherwise allowed to choose and consume foods ad libitum.

The test foods consisted of wheat bread (LGI: whole grain; HGI: whole meal), rye bread (LGI: whole grain; HGI: whole meal), rice (LGI: long grain; HGI: round grain), and pasta (LGI) or mashed potato powder (HGI). Macronutrient composition was kept similar in the 2 groups of test foods by adjusting protein and fat intake with a low-fat sour milk product (0.3% fat; Fromage Frais; MD Foods) and butter (80% fat; Kærgården; MD Foods). Energy density was kept similar by adding water to the menus. The weighted average GI of the test foods were 79 and 103 for the LGI and HGI foods, respectively.

Meal test protocol. On the last day of the 10-wk study period, participants arrived at 0745 h after traveling to the department using a minimum of physical activity (by car or bus) and after having fasted for at least 10 h. Body weight, height, sagittal height, waist and hip circumference, and blood pressure were measured before participants were DXA scanned for 45 min (19). Participants were then moved to a bed covered with an anti-decubitus mattress and were provided with a pillow and a blanket. Resting EE was measured for 30 min. Subsequently, a venflon catheter (ref. 391467, Becton Dickinson) was inserted in an antecubital arm vein and participants rested for 15 min before fasting blood samples were taken. A breakfast meal was then served (at time −15 min) and participants were instructed to finish the entire meal within 15 min. A total of 1.5 g of paracetamol was added to the yogurt as a marker of gastric emptying rate. Visual analogue scales (20) were used for rating of subjective appetite sensations at −15, 0, 30, 60, 90, 120, 180, and 240 min after completion of the breakfast. A visual analogue scale was also used to assess the palatability (appearance, smell, taste, aftertaste, and overall palatability) of both the breakfast and the lunch (which was consumed ad libitum). Postprandial blood samples were taken 30, 60, 90, 120, 180, and 240 min after finishing breakfast. Postprandial EE was measured continuously for 4 h with a 5-min break every 30 min, where participants were allowed to sit up and to visit the toilet. EE was measured by indirect calorimetry using an open-air-circuit, computerized, ventilated hood system (21,22). The ventilated hood system is regularly validated by an alcohol burn. EE and CHO-OX, F-OX, and P-OX were calculated as previously described (22) from the gas exchange and urinary nitrogen measurements using the formulas of Elia and Livesey (23).

All urine, except morning urine, was collected during the test period for determination of nitrogen content. Water was provided on request with a maximum of 200 mL during the entire test period. After 255 min, a lunch, which participants consumed ad libitum, was served and food intake was registered.

Test meals. The test meal consisted of 2 different rye breads, which were also part of the 10-wk intervention. The bread was served with butter, artificially sweetened strawberry marmalade, cheese, low-fat/low-sugar yoghurt with berries, and water. The energy content of the meal was designed to provide 20% of the participant's daily energy requirement adjusted to the nearest 0.5 MJ. Energy requirements were calculated from body weight, height, age, and physical activity according to the questionnaire of Baecke et al. (24) and the FAO/UNU/WHO formulas (25). The distribution of energy in the test meals was 57.0 E% carbohydrates, 14.0 E% protein, and 29.0 E% fat (**Table 1**). The specific rye breads were chosen because of the nature of the starch. The HGI bread was based on milled whole grain rye flour and the LGI bread contained 35% whole intact kernels. The detailed composition (carbohydrate fractions) and GI of our carbohydrate test foods were determined with 2 in vitro methods (26–30). Furthermore, we measured GI in vivo with the standard method described by FAO/WHO (31) using 10 participants (Table 1).

Acute glycemic responses to the LGI and HGI tests meals was measured in 10 healthy participants (26.8 ± 0.9 y; 22.8 ± 0.4 kg/m^2) by taking ear prick blood samples at 0, 15, 30, 45, 60, 90, and 120 min.

The lunch served to both groups was a salad consisting of pasta, smoked boiled turkey breast, carrots, peas, sour cream, mayonnaise, olive oil, basil, and 200 mL of water. The distribution of energy represented the mean distribution in the Danish diet with 50.0 E% carbohydrates, 13.5 E% protein, and 36.5 E% fat. The dietary fiber content of the lunch was 1.4 g/100 g. All calculations of the nutrient contents of the meals were conducted

TABLE 1 Macronutrient composition of the breakfast test meals (10 MJ energy level) and glycemic index (GI) the rye breads[1,2]

	LGI[2]	HGI
Energy, *kJ*	2040	2000
Carbohydrate, *g*	67.8	67.6
Fat, *g*	15.7	15.1
Protein, *g*	16.8	16.4
Dietary fiber, *g*	12.1	13.1
Energy density, *kJ/g*	6.59	6.48
Rye bread predicted GI[3] (% of HGI)	55 (83)	66 (100)
Rye bread in vivo GI[4] (% of HGI)	82 ± 12 (77)	107 ± 16 (100)

[1] The values in the table correspond to a participant with a daily energy requirement of 10 MJ.
[2] HGI, high glycemic index; LGI, low glycemic index.
[3] GI values predicted from in vitro determination and multiplied by 0.7 to facilitate comparison with the in vivo GI values obtained with glucose as reference food.
[4] Values are mean (± SEM), $n = 10$.

using the computer database of foods from The National Food Agency of Denmark (Dankost 2000) (32).

Laboratory analyses. Blood was sampled without stasis through an indwelling catheter. Samples were centrifuged for 15 min at 2800 × *g* and 4°C within 60 min of sampling, and the supernatant fluid was stored at −20°C until analysis. Blood for glucose analysis was collected in iced tubes containing EDTA prepared with sodium fluoride. Blood for determination of plasma GIP, GLP-1, GLP-2, and glucagon was collected in iced tubes containing EDTA. Blood for analysis of serum insulin, serum leptin, plasma ghrelin, and serum paracetamol was collected in plain tubes.

Plasma glucose and serum insulin concentrations were measured as previously described (18). Leptin was determined in serum with a human leptin RIA (catalog no. RIA-1624/RIA-2997, DRG Instruments). Paracetamol in serum was analyzed by fluorescence polarization immunoassay technology according to the AxSYM system, acetaminophen (list no. 3B35, 68–1920/R2, Abbott Laboratories, Diagnostics Division). GIP, glucagon, and GLP-1 concentrations in plasma were all measured by RIA after extraction of plasma with 70% ethanol as previously described (22,33). The GLP-2 concentration in 75% ethanol-extracted plasma was measured by using RIA as previously described (22,33). Ghrelin was determined in plasma with a Ghrelin (Human) RIA kit RK-031–30 (Phoenix Pharmaceuticals).

The urinary nitrogen concentration was measured by the method of Dumas (34) using a nitrogen analyzer (NA 1500,Carlo Erba Strumentazione).

Statistical analyses and calculations. All results are reported as means ± SEM. Results are considered significant at $P < 0.05$. Differences between groups in participant characteristics, fasting blood values, and meal evaluations were analyzed using ANCOVA with baseline values as covariates. The mean daily energy and macronutrient intakes (from food diaries at baseline and wk 5 and 10) and body weight of the 2 groups were analyzed as described elsewhere (18). Following exclusion of one participant from the LGI group, total body weight significantly differed between groups at wk 10. For this reason, postprandial changes were analyzed with total body weight at wk 10 as a covariate. P-OX and ad libitum EI were analyzed using ANCOVA with body weight as covariate. Postprandial response curves were evaluated by comparing Δ-AUC (or area over the curve) using ANCOVA with fasting values and body weight as covariates. Δ-AUC (or area over the curve) was calculated as previously described (22). Postprandial response curves were analyzed by repeated measurements 2-way ANCOVA testing the effects of diet, time, and the diet × time interaction with fasting values and body weight as covariates. When the diet × time interactions were not significant ($P > 0.10$), the model was reduced. Residual plots of data were examined to consider homogeneity of variance and Shapiro-Wilk test performed for normal distribution of data and logarithmic transformation was used when required. Tukey-Kramer adjusted post hoc tests were applied where appropriate. All statistical analyses were performed using Statistical Analysis Package version 8.02 (SAS Institute). Insulin sensitivity was calculated by the HOMA-R (insulin resistance) and HOMA-β (β cell function) (35) and the Matsuda index (36).

Results

At baseline (wk 0), dietary intake in the 2 groups was well matched in energy and macronutrient content (**Supplemental Table 2**). During the intervention, we observed a shift toward a lower energy density ($P = 0.02$) and a tendency to a lower EI ($P = 0.06$) in the LGI group compared to the HGI group (Supplemental Table 2).

Body weight decreased in both groups from wk 0 to 10 ($P < 0.01$), but the changes were not significantly different between the LGI (2.5 ± 0.6 kg) and HGI (1.2 ± 0.4 kg) groups.

Fasting blood concentrations at baseline (wk 0) of serum insulin, plasma GLP-1, plasma GLP-2, plasma GIP, serum leptin, and plasma ghrelin did not differ between the groups, but at wk 10, the increase in plasma glucose was greater in the LGI group (0.17 ± 0.07 mmol/L) than in the HGI group (−0.1 ± 0.07 mmol/L) ($P < 0.05$) (Supplemental Table 3).

Changes during the meal test

Blood profile. The plasma glucose postprandial peak was greater ($P = 0.05$) in the HGI group (6.8 ± 0.2 mmol/L) than in the LGI group (6.3 ± 0.2 mmol/L), as was the serum insulin response ($P = 0.045$) (**Fig. 1**). Even so, there were no differences in insulin sensitivity assessed using HOMA-R and HOMA-β (Supplemental Table 3) or the Matsuda index between the LGI (18.5 ± 2.4) and HGI (15.1 ± 1.7) groups ($P > 0.05$). Plasma glucagon responses also did not differ between the groups (Fig. 1). None of the Δ-AUC values differed between groups (data not shown).

The acute test meal whole blood glucose Δ-AUC was higher in the HGI (109 ± 18.5 mmol·min/L) compared to the LGI (64.9 ± 19.5 mmol·min/L) group ($P < 0.05$).

The postprandial responses of serum leptin and plasma ghrelin did not differ between the groups (**Supplemental Fig. 1**). None of the Δ-AUC values differed between groups (data not shown).

For plasma GIP, a diet × time interaction was observed ($P = 0.02$). However, post hoc testing revealed that the groups did not differ at any time point tested (**Supplemental Fig. 2**). The HGI group had a higher response in plasma GLP-1 ($P = 0.046$) than the LGI group (Supplemental Fig. 2). There were no significant differences in plasma GLP-2 (Supplemental Fig. 2). None of the Δ-AUC values differed between the groups (data not shown).

EE and substrate oxidation. Postprandial EE, CHO-OX, and F-OX did not significantly differ between the groups (**Supplemental Fig. 3**). P-OX also did not differ between the LGI (1.0 ± 0.1 kJ/min) and HGI (1.2 ± 0.1 kJ/min) groups ($P = 0.11$). None of the Δ-AUC values differed between groups (data not shown).

Appetite, EI, and meal evaluations. There were no significant differences in fasting or postprandial sensations of hunger, satiety, prospective food consumption (**Supplemental Fig. 4**), and desire for something sweet (**Supplemental Fig. 5**) between the 2 groups. However, there was a diet × time interaction in ratings of fullness, with fullness being higher in the LGI group

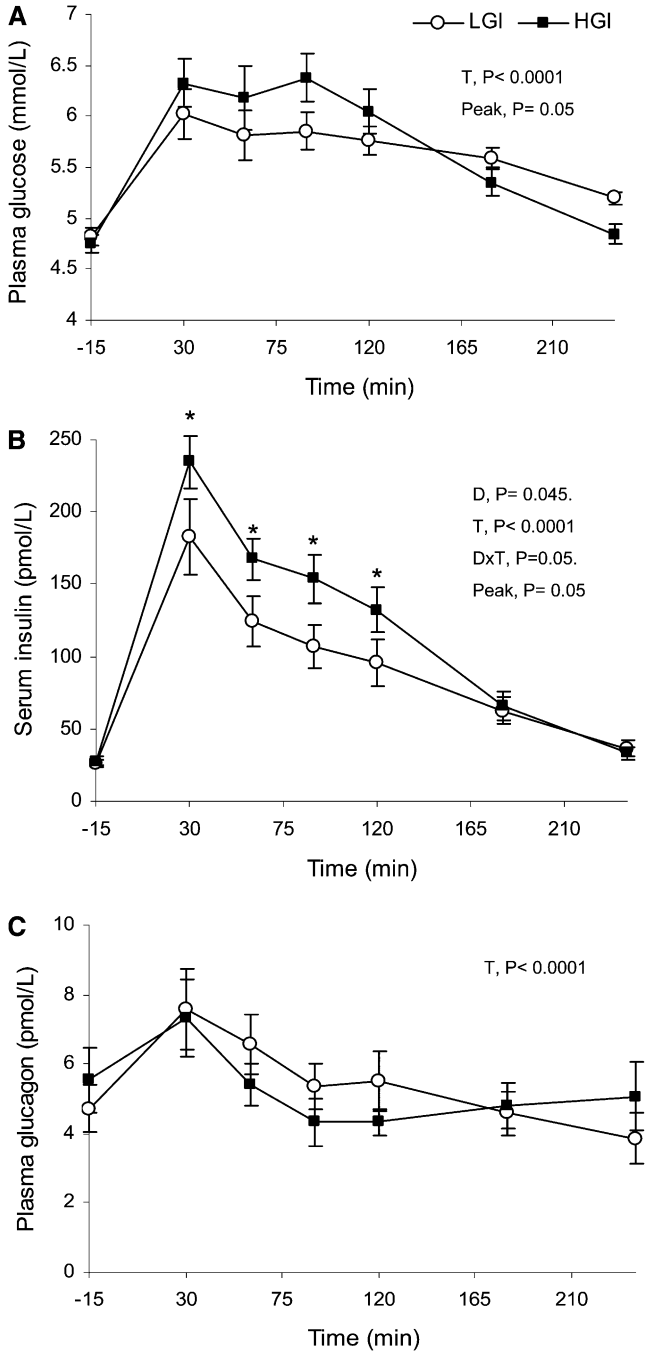

FIGURE 1 Concentrations of plasma glucose (*A*), serum insulin (*B*), and plasma glucagon (*C*) after a low glycemic index (LGI) or high glycemic index (HGI) test meal in 29 healthy, overweight women who had consumed an LGI or HGI diet, respectively, for 10 wk. Data are means ± SEM, n = 14 (LGI) or 15 (HGI). *Different from LGI at that time, $P < 0.05$. Significant effects ($P < 0.05$) of D, T, and D × T are shown. Postprandial responses were analyzed by repeated-measures 2-way ANCOVA with fasting values and body weight as covariates. Peak concentrations were analyzed by ANCOVA with fasting values and body weight as covariates. D, diet; D × T, diet × time interaction; T, time.

(P = 0.01) (Supplemental Fig. 4). None of the Δ-AUC values differed between groups (data not shown). Furthermore, the LGI group had a lower desire to eat something fatty than the HGI group (P = 0.01) (Supplemental Fig. 5) and Δ-AUC differed between the LGI (269 ± 134 mm·min) and HGI (−46.5 ± 79.4 mm·min) groups (P = 0.03).

There was no difference in ad libitum EI at lunch between the LGI (1.9 ± 0.2 MJ) and HGI (HGI: 2.1 ± 0.3 MJ) groups (P = 0.62).

The questionnaire, given to the participants immediately after they consumed the test meals and lunch, revealed that the 2 groups evaluated all meals alike (data not shown).

Gastric emptying (paracetamol). Serum paracetamol postprandial responses did not differ between the LGI (16.8 ± 1.26 mmol · min/L) and HGI (16.7 ± 3.5 mmol · min/L) groups.

Discussion

We observed lower postprandial plasma glucose, serum insulin, and plasma GLP-1 responses in the LGI group compared to the HGI group after 10-wk ad libitum intake of the LGI or HGI diet. We also observed higher plasma GIP and ratings of fullness and a lower desire to eat something fatty in the LGI group. Postprandial EE and substrate oxidation rates did not differ.

The observed differences in plasma glucose and serum insulin after 10 wk of intake confirm that the 2 diets also maintained their effects on glycemia and insulinemia after quite a lengthy exposure. Although we did not conduct the same meal test study at baseline (wk 0), we did measure the acute in vivo whole blood glucose response after consumption of the test products in question. Here, we found the expected differences in GI and glucose Δ-AUC. Our data are supported by middle- and long-term studies that have shown lower postprandial glucose and insulin responses after consumption of LGI diets (37–42). However, a recently published crossover intervention study found no difference in plasma glucose and serum insulin responses between groups after 12 wk of consuming a LGI or HGI diet ad libitum (43). Similarly, in an earlier crossover study, there was a lower postprandial plasma glucose response after the LGI diet on the first day of the study but no difference between the LGI and HGI diet groups after 30 d (44). This was also the case for the postprandial serum insulin response, where an initial difference in serum insulin response between the LGI and HGI groups disappeared after 30 d of consuming the diets (44).

We observed a lower plasma GLP-1 response in the LGI group than in the HGI group. Conversely, the plasma GIP response was initially higher in the LGI group. Our breakfast test meals were matched for macronutrient composition, fiber content, energy content, and density, as well as composition of fatty acids and single sugars, so the meals were identical except for the GI. A meal test study investigating test foods with rapidly or slowly available glucose found no difference in plasma GIP incremental AUC between meals and a higher plasma GLP-1 incremental AUC from 120 to 240 min after the slowly available glucose test meal (45). In acute studies by Juntunen et al. (46,47), lower plasma GIP and GLP-1 responses were observed after intake of different rye breads compared to white bread. We were able to reproduce these results for only the plasma GLP-1 response.

In the present study, no significant differences between the LGI and HGI groups were observed in postprandial EE or substrate oxidation rates. A review of the literature on EE and GI found that the majority of studies have been performed with single sugars (14). Of these studies, 9 of 15 found a higher EE when LGI sugars were consumed (fructose or sucrose) compared to HGI sugar (glucose) or starch (14). In one later study using real foods (48), the acute effect of GI on EE was investigated in a crossover design including 12 obese females. Test meals either low or high in GI and matched for macronutrient composition,

fiber content, energy content, and density were provided, and EE and substrate oxidation were measured for 10 h. This study found no difference between LGI or HGI meals in their effects on EE and substrate oxidation. Keogh et al. (49) performed a cross-over study including 14 healthy females consuming meals containing either wheat (HGI) or barley (LGI). They measured EE and substrate oxidation for 3 h after a test lunch and found no differences between the effects of HGI compared to LGI on EE and substrate oxidation. Finally, one long-term investigation by Howe et al. (50) tested the difference between the effects of amylose (LGI) and amylopectin (HGI) for 14 wk. Plasma glucose and serum insulin responses were reduced after high amylose consumption, but no difference in EE was found. The hypothesis of LGI meals/diets increasing EE or F-OX and decreasing CHO-OX (51) is so far supported only by exercise studies with well-trained participants (52–54). No clear conclusion can be drawn as yet, which is further supported by a recent review (55). It could be speculated that if GI does indeed have an impact on body weight regulation, this would derive primarily from an effect on hunger/satiety and EI and not from a significant effect on EE and substrate oxidation.

We observed a later increase in postprandial feelings of fullness and reduced desire to eat something fatty in the LGI group compared with the HGI group. Several appetite regulatory hormones were also measured in this study, but among these neither plasma ghrelin nor serum leptin revealed postprandial differences in support of a satiating effect of either GI diet.

In contrast, plasma GLP-1 had a higher response in the HGI group but apparently was not sufficient to promote a difference in appetite and EI, which would then have been in favor of the HGI meal. In the meal test study by Keogh et al. (49), no differences were found in effects on appetite of the wheat- and barley-containing meals, and ad libitum EI was higher after consumption of the barley (LGI)-containing meals. Recently published results (43) from a 12-wk crossover intervention including 19 overweight females who consumed LGI or HGI diets revealed no differences in appetite measures and EI between diets. Thus, our results on appetite and EI are consistent with some studies (43,49,56) but not others (57–59). However, differences in study design and meal composition can probably explain some of these discrepancies. As mentioned earlier, to examine whether GI per se has a positive effect on appetite and EI, all other factors in meals and diets must be kept constant, and this is often not the case.

In conclusion, postprandial glycemia, insulinemia, and subjective appetite ratings after a test meal were better after 10-wk ad libitum intake of a LGI compared to a HGI diet. EE and substrate oxidation rates were, however, not affected. Further long-term studies are needed to clarify if GI is a useful tool for preventing disease and body weight management.

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