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Effect of postprandial modulation of glucose availability: short- and long-term analysis

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Low glycaemic index (LGI) foods have been proposed as potential means to decrease postprandial glucose excursions and thus to improve diabetes management. We modulated glucose availability of cereal products and thus their glycaemic index to study the metabolic effect of LGI foods on daylong glucose control acutely and in the long term following a 5-week GI intervention diet in free-living subjects. In this randomised, parallel trial, two groups of nineteen overweight subjects followed an *ad libitum* 5-week intervention diet in which usual starch was replaced by either LGI or high GI (HGI) starch. During the exploration days (days 1 and 36), subjects ate their assigned ^{13}C-labelled test breakfast (LGI or HGI), and total and exogenous glucose kinetics (using stable isotopes), postprandial concentrations of glucose, insulin, lipid profile and nutrient oxidation were assessed after the test breakfast and a standardised lunch. At day 1, LGI breakfast significantly decreased post-breakfast glycaemic response with a parallel decrease in exogenous and total glucose appearance ($P<0·05$). Post-lunch and post-breakfast glycaemic responses were positively correlated (r 0·79, $P<0·0001$). Following the 5-week diet, difference between the groups in terms of glucose kinetics and response was maintained (no significant interaction group × time) but tended to decrease over time for the post-breakfast glycaemic response. Post-lunch and post-breakfast glycaemic responses remained positively correlated (r 0·47, $P=0·004$). Modulation of postprandial glucose availability at breakfast decreased plasma exogenous glucose appearance and improved glucose control at the subsequent lunch. After 5 weeks, these effects were maintained in healthy subjects but remained to be confirmed in the longer term.

Glucose availability: Glucose kinetics: Stable isotope analysis: Second-meal effect: Short- and long-term analysis

Rising postprandial glucose excursions are associated with greater risk of developing metabolic disorders, CVD and diabetes[1]. There has been a growing interest over recent years in the relation between the consumption of low glycaemic index (GI) or reduced glycaemic load (GL) products and their effect on the management of postprandial glycaemic profile as they have been proposed as potential tools to improve management of diabetes mellitus or to decrease risks of heart disease[2–4]. The intake of low GI (LGI) diets is associated with improved glycaemic control, more particularly among subjects with the poorest glycaemic control[5]. Several studies have shown that low GI diets could enhance glucose tolerance with a corresponding improvement in insulin sensitivity. More particularly, low GI meals have been shown to improve acute postprandial glucose tolerance and reduce insulin response, also at a subsequent meal (the 'second-meal effect')[6–10]. But, evidence is missing as to conclude that the acute reduction in blood glucose response elicited by low GI foods may persist in the long term, as already reported[11]. Some studies showed differences in HbA1c after LGI intervention[12], whereas some other studies did not show any effect on HbA1c in type 2 diabetic subjects with optimal glycaemic control[13]. According to several authors[14,15], the lower glycaemic response effect produced by low GI products could be due to a slower rate of appearance of glucose in the systemic circulation. A classification has been proposed to characterise the different carbohydrate fractions by separating them into rapidly available glucose

Abbreviations: AUC, area under the curve; EGP, endogenous glucose production; GI, glycaemic index; GL, glycaemic load; HGI, high GI; iAUC, incremental AUC; LGI, low GI; SAG, slowly available glucose; RaE, rate of appearance of exogenous glucose; RaT, total rate of glucose appearance.

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and slowly available glucose (SAG), reflecting the rate at which glucose becomes available for absorption in the small intestine[16]. A high correlation has been shown between the GI of a product and the percentage of rapidly available glucose in this product measured *in vitro* [16]. Such SAG-rich products could be considered as lente carbohydrates and thus are candidate tools to regulate daylong glycaemic and insulinaemic profile. The modulation of postprandial metabolic profile and more particularly of insulin response could consequently modify insulin action on fuel partitioning, glucose uptake and carbohydrate and lipid oxidations. Few intervention studies have been undertaken on the effects of dietary GI, GL or SAG on these metabolic parameters in healthy overweight adults, despite the higher relative risk of insulin resistance and type 2 diabetes in this population[17].

Therefore, we investigated the short- and long-term (5 weeks) effects of an *ad libitum* low GI (LGI) or HGI diet on glucose metabolism and nutrient utilisation in overweight subjects. We determined the metabolic effect of GI and its evolution over time (weeks) by thorough analysis of glucose kinetics, insulin and lipid profiles and nutrient oxidation in response to breakfast and subsequent lunch. Preliminary results of the effect of these diets on anthropometric parameters and lipid profile have been previously published showing that the 5-week LGI diet improved weight control and cholesterol profile[18]. Specific cereal processing techniques have been set up in order to produce slowly and rapidly available starchy products with exactly the same nutrient composition but differing in GI only. The follow-up of postprandial glucose kinetics (exogenous and endogenous) was performed using glucose-stable isotope analysis, after the ingestion of a ^{13}C-labelled LGI (SAG-rich) or HGI (rapidly available glucose-rich) breakfast before and after the GI dietary intervention. The metabolic adaptation to a 5-week GI dietary intervention was studied through the postprandial metabolic response to a HGI or a LGI breakfast and to a subsequent lunch in order to detect a potential 'second-meal' effect.

Subjects and methods

Experimental design

This was a parallel, randomised group trial. The two groups of non-diabetic overweight subjects followed an *ad libitum* 5-week dietary intervention in which they were asked to replace all starches in their routine diet by either LGI or HGI starchy foods. Both types of diets were randomly allocated according to the CONSORT guidelines.

One week before the two test days (day 1 and day 36), the subjects were asked to avoid nutrients known to be enriched in ^{13}C (maize starch and oil, cane sugar, tropical fruits and canned foods). Twenty-four hours before D1 and D36, the subjects were asked to limit physical activity, drink no alcohol-containing beverage and eat a normal evening meal.

Subjects came to the Centre de Recherche en Nutrition Humaine de Rhône-Alpes, at Hôpital Edouard Herriot on the test day at 06.30 hours following a 12-h overnight fast.

On D1 and D36, body weight was measured with a graded scale (SECA©, Valenciennes, France). Intravenous cannulas were inserted into deep forearm veins in both arms for tracer infusion on one side and blood sampling on the other side. A primed, continuous infusion of D-[6,6-$^2H_2$] glucose (0·0570 mg/kg per min) was started 120 min before breakfast was eaten and was maintained for the next 270 min to determine the total rate of glucose appearance (RaT). The priming dose was eighty times the infusion rate over 1 min. At time 0, subjects ate the test breakfast (either LGI or HGI breakfast, composition in Table 1) in 15 min. Blood samples were taken at baseline and sequentially every 15 min until 90 min, then every 30 min until 270 min following ingestion of the meal and were used to determine glucose, TAG, NEFA, insulin and C-peptide concentrations and deuterium and ^{13}C glucose isotopic enrichments. At 270 min, a standardised HGI lunch was served to the subjects and ingested in 30 min (composition in Table 1). Blood samples were taken sequentially every 30 min until 480 min and were used to

Table 1. Macronutrient composition of the high glycaemic index (HGI) breakfast, of the low glycaemic index (LGI) breakfast and of the standardised high glycaemic lunch

	Serving size (g)	Proteins (g)	Lipids (g)	Total CHO (g)	SAG (%)	RAG (%)	Fibre	Energy (kJ)
LGI breakfast (GI 47)								
Half-skimmed milk	180	5·8	2·9	8·1				1468·58
Biscuits (GI 45)	80	7·0	9·8	58·6	26	40	1·6	343·09
Total for LGI breakfast	260	12·8	12·7	66·7	26	40	1·6	1807·00
Energy distribution		12 %	26 %	62 %				
HGI breakfast (GI 66)								
Half-skimmed milk	180	5·8	2·9	8·1				1456·03
Flakes (GI 70)	80	6·9	9·5	58·6	<1	66	1·6	343·09
Total for HGI breakfast	260	12·7	12·4	66·7	<1	66	1·6	1794·94
Energy distribution		12 %	26 %	62 %				
Standardised HGI lunch (GI 71)								
Minced beef (15 % fat)	150	27·0	22·0	27·4				
Instantaneous mashed potatoes	200	4·4	3·4	30·3				
White bread	55	4·4	0·6	0·0				
Camembert cheese	30	6·4	6·6	22·5				
Whole milk yoghurt with fruits	125	4·4	3·4					
Total for HGI lunch	560	46·6	36·0	80·2	–	–	5	3476·90
Energy distribution		22 %	39 %	39 %				

CHO, carbohydrate; SAG, slowly available glucose; RAG, rapidly available glucose.

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determine glucose, TAG, NEFA and insulin and C-peptide concentrations. Blood was collected in tubes maintained at 4°C and immediately centrifuged. Plasma was then stored at −20°C until assay.

V_{O2} and CO_2 production were monitored by indirect calorimetry (Datex Instruments, Helsinki, Finland) after breakfast ingestion (T15–T270 min) and after lunch ingestion (T300–T480 min) in order to calculate total carbohydrate, lipid oxidation and respiratory exchange rate.

Subjects remained in the supine position for the duration of the study except when required to void urine (urinary nitrogen measured three times: at baseline (T120 min); post breakfast (T270 min); post lunch (T480 min)).

Subjects

As described previously, a power calculation based on change in body weight (1 kg, SD = 1 kg) as primary study endpoint was done; seventeen subjects per group provided >80 % power to detect a significant difference in weight loss between groups at the $P<0{\cdot}05$ level[18]. The pre-inclusion tests were performed on sixty-eight volunteers who responded to the recruitment campaign. Each subject underwent a screening inclusion test including measurements of body weight, height, blood pressure, waist and hip circumference; an interview regarding general health; blood sample collections (blood differential count, glycaemia, transaminases, γGT, total cholesterol, HDL and LDL cholesterols and TAG). Eating habits were also explored through dietary surveys, including consultation and advice by a trained dietitian, and dietary records. The inclusion criteria for the study were men and women aged 20–60 years, BMI 25–30 kg/m^2, stable body weight over the previous 3 months, normal results for pre-inclusion biological tests, sedentary or moderate physical activity and routine breakfast representing 10–25 % of the daily energetic intake. Thirty-eight healthy overweight subjects (nineteen men and nineteen pre-menopausal women), aged 38·3 (SD 9·2) years, weighing 77·3 (SD 9·1) kg and with a BMI 27·3 (SD 1·5) kg/m^2 (means and standard deviations) were recruited for the study.

The subjects were randomised into two groups as follows: nineteen subjects in the LGI diet group (nine men and ten women) and nineteen subjects in the HGI diet group (eleven men and eight women).

All the subjects received written and oral information about the protocol and signed an informed consent document. The study was approved by the Scientific Ethics Committee of Lyon (CCPPRB Lyon A) and was in accordance with both the French 'Huriet-Serusclat' law and the Second Declaration of Helsinki. The characteristics of the thirty-eight subjects are presented in Table 2. There were no significant differences between groups at baseline.

Experimental diets

The detailed composition of the 5-week dietary intervention, the test foods and breakfasts was described previously[18]. Briefly, foods were considered as having a low GI whenever GI < 50 % and a high GI whenever GI > 70 %. In the present study, the subjects received individual guidance by a trained clinical dietitian in order to implement their intervention diet, and compliance to diets was strictly controlled by dietary questionnaires. Part of the starchy products was supplied by the CRNHRA and Danone Vitapole©. The food provided consisted in cereal breakfast products (extruded cereals for the HGI group and plain biscuits for the LGI group), and in black bread (Harris© pumpernickel) for the LGI group. According to their diet group, a detailed list was given to the subjects indicating the starches they were allowed to eat and the prohibited ones (Table 3). Subjects were asked to continue eating the same amount of starch as usual. They were also asked not to modify their dietary habits regarding the amount of food eaten, food patterns and the amount of fruits and vegetables eaten. The subjects were instructed to measure and record the exact amount eaten each day by using a 5-day food diary during the pre-inclusion period (D7–D11) and on weeks 3 (D16–D20) and 5 (D31– D35) of the study. Ingested quantities were evaluated by the dietitian using a SU.VI.MAX© dietary photographic support. The macronutrient content of the test foods and 5-day dietary records was calculated using a computerised food database that included specific product–ingredient lists and recipes for test foods (latest release of GENI© software by MICRO 6© using CIQUAL® table). For the mean GI calculation of all meals from food diaries, GI data are based on the international table of GI and GL values[19].

Table 2. Baseline characteristics of the subjects of the low glycaemic index (LGI) diet group and of the high glycaemic index (HGI) diet group (Mean values with their standard errors)

	LGI diet group (*n* 19)		HGI diet group (*n* 19)	
	Mean	SEM	Mean	SEM
Age (years)	36·3	2	40·4	2·2
Weight (kg)	77·2	2·2	77·3	2·1
BMI (kg/m^2)	27·5	0·3	27·2	0·3
Fasting glucose (mmol/l)	5·15	0·15	5·31	0·08
Fasting insulin (pmol/l)	67	9·5	61·4	5·7
C-peptide (nmol/l)	0·67	0·06	0·67	0·05
Total cholesterol (mmol/l)	5·21	0·23	5·2	0·18

Table 3. Allowed starch lists according to diet group

Allowed starch	
LGI group	HGI group
Breakfast biscuits (GI 45)	Breakfast extruded cereals (GI 70)
Black bread (Harris pumpernickel, GI 50)	White bread, whole meal bread (GI 95)
Spaghetti al dente (GI 32)	Mashed potatoes (GI 75), peeled, baked or 35-minute boiled potatoes (GI 70)
Other pastas (GI 48)	French fries, chips (GI 75)
Durum wheat precooked in pouch (Ebly, GI 40)	
Bulgur (GI 48)	Gnocchi (GI 70)
Semolina (GI 55)	Flour contents, pizzas, quiche, etc. (GI 70–80)
Prohibited starch (both groups)	

Rice (GI unpredictable). Starches belonging to the other diet group list.

Breakfasts

The breakfast products provided during the intervention trial consisted of plain biscuits (LGI) or flakes (HGI). The LGI breakfast consisted of standard biscuits (80 g), semi-skimmed milk (180 ml) and non-energetic hot beverage (max 300 ml). The HGI breakfast consisted of flakes (80 g), semi-skimmed milk (180 ml) and non-energetic hot beverage (max 300 ml). The composition of the two test meals is given in Table 1. Biscuits and extruded cereals contained different quantities of SAG, 26 and 0·4 %, respectively. The two breakfasts represented about 20 % of daily energy intake. They were isoenergetic (about 1803·30 kJ) and contained the same amount of proteins (12 %), lipids (26 %) and carbohydrates (62 %). The only variable parameter was the GI (45 and 70 % for LGI and HGI breakfasts, respectively). Both cereal products were processed by Danone (Danone Vitapole, Paris, France).

Both cereal products (biscuits and flakes) ingested on the test days (D1 and D36) were exactly the same composition as those ingested during the trial, but they were uniformly labelled with stable isotope ^{13}C. For this purpose, they were manufactured with starch coming from a preparation of durum wheat semolina cultivated in a $^{13}CO_2$-enriched atmosphere, mixed with naturally rich ^{13}C sugarcane. ^{13}C enrichment of starch was adjusted to ^{13}C sugarcane enrichment.

D-[6,6-$^2H_2$] glucose (99 mol% excess) was obtained from Eurisotop (Gif-sur-Yvette, France); chemical and isotopic purity was confirmed by selected-ion-monitoring GC MS analysis. It was dissolved in sterile isotonic saline (0·9 % NaCl) and passed through a 0·22-μm millipore filter (Millipore Corp., Bedford, MA, USA) before infusion. The preparation was pyrogen free. The concentration of deuterated glucose in the infusate was determined at the end of each test.

Analytical procedures

Metabolites and hormones. Blood samples were collected in tubes containing lithium heparinate and then centrifuged at 3645 ***g*** and 4°C for 10 min, and the plasma was stored at −20°C until analysis. Glucose, TAG and NEFA concentrations were measured with an enzymatic colorimetric method on a Cary 50 Bio© spectrophotometer (Varian©) using a BioMérieux© Glucose RTU kit (Marcy l'Etoile, France), a BioMérieux© TG PAP 150 kit and a Wako chemicals© NEFA-C kit (Neuss, Germany), respectively. Plasma insulin and C-peptide concentrations were determined by RIA kit (INS-IRMA Biosource, Nivelles, Belgium; Immunotech, Marseille, France, respectively).

Indirect calorimetry. Respiratory exchange measurements were integrated after breakfast ingestion and the non-protein RQ was calculated from VO_2, VCO_2 and measured urinary nitrogen excretion determined by chemiluminescence[20].

Total carbohydrate and lipid oxidation were calculated according to the equation developed by Ferrannini[21].

Isotope analysis. Plasma glucose isotopic enrichments were determined on neutral fractions of deproteinised plasma samples partially purified over sequential anion–cation exchange resins, as previously described[22]. Plasma [6,6-$^2H_2$]glucose was measured by organic GC-MS (Hewlett Packard 5971, Evry, France) on acetyl-bis-butane-boronyl glucose derivative using an electron impact mode and a selective monitoring of *m/z* 297 and 299[23]. Plasma ^{13}C glucose enrichment was measured by GC-combustion-isotope ratio MS (GC-C-IRMS, Isoprime, GV instruments, Lyon, France) after derivatisation to pentacetyl glucose, as previously described[24].

The ^{13}C enrichment of ingested starch (biscuits and cereals) was determined after enzymatic hydrolysis using the Thivend method[25], and the glucose obtained was purified by sequential anion–cation exchange chromatography before derivatisation as glucose pentacetate and analysed as previously described[26]. The ^{13}C enrichment of the derivatised glucose molecule was −34·59 (SD 0·65) $\delta^{13}C$ ‰ (1·07 320 (SD 0·00 071) atom $\%^{13}C$) and −35·72 (SD 0·42) $\delta^{13}C$ ‰ (1·07 196 (SD 0·00 046) atom $\%^{13}C$) for biscuits and cereals, respectively.

Calculations

Mean GI of all meals taken in a day was determined using the following equation:

$$GI_{mean} = \sum((C_{food}/C_{total}) \times GI_{food}),$$

where C_{food} is the amount of carbohydrate (in grams) contained in each ingested food and C_{total} the total amount of total carbohydrate (in grams) ingested during the day. Mean GI targets were defined as <50 for the LGI group and >70 for the HGI group. GL were also determined by multiplying the total amount of total carbohydrate (in grams) by the mean GI for each food and adjusted for energy intake:

$$GL = (GI_{mean} \times C_{total}).$$

The rates of glucose appearance were calculated from plasma [6,6-$^2H_2$]glucose enrichment (RaT; T for total glucose) and from plasma ^{13}C glucose enrichment (RaE; E for exogenous glucose) using Steele's equation for non-steady state[27,28] as previously described[22]. Endogenous glucose production (EGP) was calculated as RaT−RaE.

Postprandial data were also assessed as area under the curve (AUC) calculated using the trapezoidal method and integrated throughout the experiment (0–480 min) and between 0–270 min and 270–480 min. Incremental AUC (iAUC) were calculated using GraphPad Prism (version 4.03; GraphPad Software, San Diego, CA, USA). Glucose peaks were calculated as the maximum glucose concentration following breakfast or lunch ingestion for each subject (consequently it does not correspond to the same time point for each subject).

Statistical analysis

The results are expressed as means with their standard errors. For each parameter, normality was checked before testing. Statistical significance was inferred at $P<0·05$. Differences between groups at baseline and at day 1 were assessed using the Student's unpaired *t* test.

For postprandial responses, a two-way ANOVA, followed by Bonferroni adjustment was used to compare postprandial peaks and nadir values, as well as AUC, between the groups from day 1 to day 36 and evaluate the main effect of group (LGI compared with HGI), the main effect of the time

(before dietary intervention compared with after dietary intervention) and the group × time interaction.

When there was a significant group × time interaction, the difference within group between day 1 and day 36 was analysed using the Student's paired *t* test. When GI, GL and change in body weight over the 5 weeks were used as covariates, same statistical results were obtained for the comparison of metabolic parameters from day 1 to day 36 between the groups. Correlation between variables was studied using the *Z*-test.

All statistical analyses were performed using Statview v 5.0 (SAS Institute, Cary, NC, USA) software.

Results

Dietary survey data, mean glycaemic index and mean glycaemic load

These results have been described previously[18]. In summary, the diets were well accepted and tolerated by the subjects, and the dietary surveys indicated good compliance of subjects in both the groups. In comparison with the HGI group, the LGI group presented a trend to increased satiety before lunch, but this was not significant.

While there were no significant differences in GI and GL between groups at baseline, after a 5-week nutritional intervention, the LGI group reached the defined LGI target (46·5 (SEM 0·3) for <50) with a significant decrease in mean GI ($P=0·001$). In the HGI group, the defined HGI target (66·3 (SEM 0·6) for >70) was not reached; GI remained high and was not significantly different to baseline value. The difference in mean GI between the LGI and HGI groups was significant after 5 weeks of diet ($P=0·0001$). There was no significant variation in energy intake, protein, fat and carbohydrate distributions in both the groups during the trial or between groups at baseline and after 5 weeks of nutritional intervention. There was no difference in dietary fibre intake between groups at baseline. However, the dietary surveys did show a significant increase in dietary fibre intake in the LGI group ($P=0·0001$), while no significant difference was noticed in the HGI group. No subject was reported as underreporting when using Goldberg's cut-off limits[29].

Comparison of the acute postprandial responses to a low glycaemic index or high glycaemic index breakfast and a standardised lunch

Metabolites and hormones. There was a significant difference in glycaemic response between the HGI and the LGI groups over the 270 min after ingestion of the two kinds of breakfasts (Fig. 1(a)). In fact, glucose peaks and glycaemia curves between T30 and T180 min were significantly lower in the LGI group than in the HGI group (glucose peak: 7·06 (SEM 0·29) mmol/l in the LGI group *v.* 7·85 (SEM 0·17) mmol/l in the HGI group). Consequently, the glucose AUC and the glucose iAUC following LGI breakfast were significantly lower (8 and 33 %, respectively, $P=0·01$).

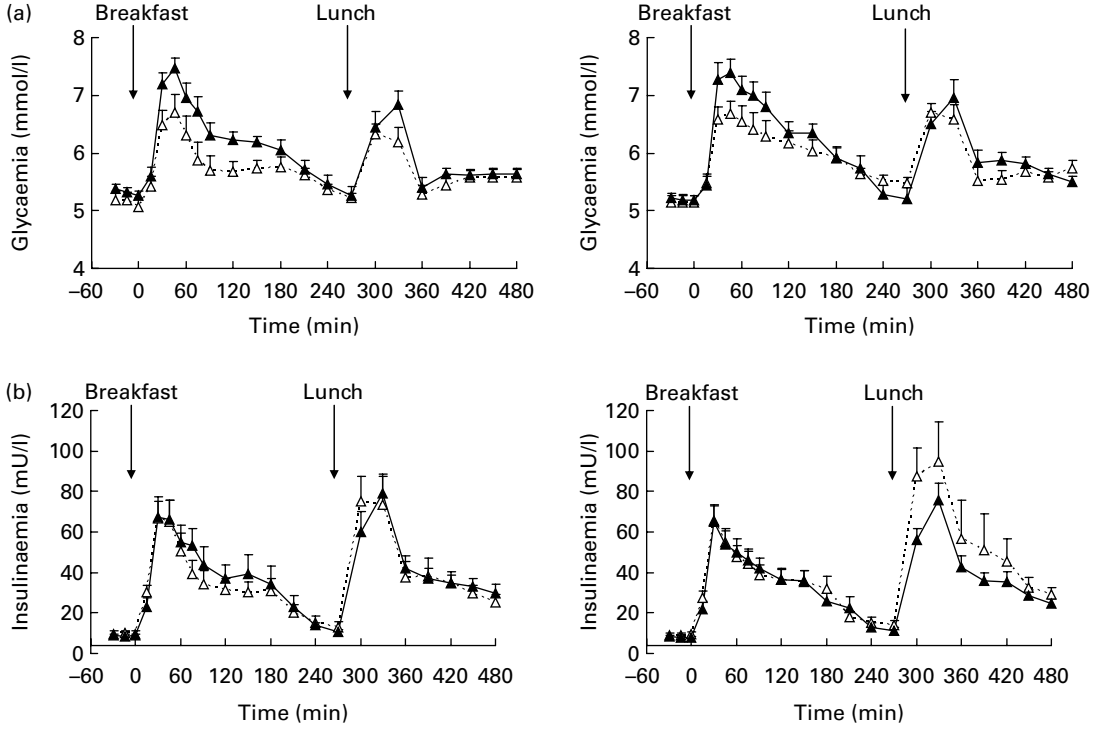

Fig. 1. Means with their standard errors plasma glucose concentration and (a) and plasma insulin (b) for 480 min after subjects ingested either a low glycaemic index breakfast (△, *n* 19) or a high glycaemic index (HGI) breakfast (▲, *n* 19) at days 1 and 36 following GI intervention. A standardised HGI lunch was ingested at $t=270$ min. At day 1, an unpaired *t* test showed a significant difference between groups for the post-breakfast glucose peak and 0–270 min glucose area under the curve (AUC; * $P<0·05$) but no difference between groups for post-lunch glycaemic response or insulinaemic response. Using a two-way ANOVA, a significant main effect of group for the post-breakfast glycaemic peak ($P=0·01$) and a significant interaction group × time for the post-lunch insulin peak ($P=0·02$) and insulin AUC ($P=0·05$) were seen throughout the 5-week intervention.

Before the standardised HGI lunch, there was no significant difference between the groups in glucose concentration, which had returned to baseline. Following lunch ingestion, there was a trend to reduced glycaemic response in the LGI group when compared with the HGI group, but this was not significant when considering either the glycaemic peak or the glucose AUC or iAUC (using post-breakfast AUC as covariate). The post-lunch glucose AUC was positively correlated to the post-breakfast glucose AUC and to the T270-min glucose concentration just before lunch (r 0·79, $P<0·0001$ and r 0·38, $P=0·02$, respectively). There was also a significant positive correlation between the post-breakfast glucose AUC and the postprandial glucose peak at lunch (r 0·51, $P=0·002$; Table 4).

Plasma insulin response tended to be lower after the LGI breakfasts but this was not significant when considering insulin peak and AUC. Insulin concentration was not different between the groups at T270 min and insulinaemic response to the lunch was similar for both the groups. Concerning plasma C-peptide concentration, response to the LGI breakfast was lower than that of the HGI breakfast, but the difference was not significant (data not shown).

There was no difference between the groups in lipid profile in response to breakfast and subsequent lunch. Plasma NEFA as well as TAG concentrations during the trial (data not shown) were not altered by the type of breakfast ingested. At T270 min, just before lunch ingestion, there were no significant difference between NEFA concentrations in either group; these parameters had not returned to baseline values at T480 min.

Glucose turnover. Fig. 2 shows the changes in RaE (Rate of appearance of Exogenous glucose), RaT (Rate of appearance of Total glucose) during the 270-min test after the ingestion of the HGI or of the LGI breakfast. RaE kinetics was dramatically altered by the kind of breakfast ingested, as seen in Fig. 2(a). After the HGI breakfast, the rate of exogenous glucose appearance reached a peak at T30 min (4·08 (SEM 0·25) mg/kg per min) and then decreased slightly. After the LGI breakfast, the RaE increased to T45 min and then remained steady (<2·5 mg/kg per min). The overall rate of exogenous glucose appearance integrated over 270 min (AUC) was also significantly different between the groups: 58·5 (SEM 3·2) g/270 min of exogenous glucose appeared in plasma after the HGI breakfast *v.* 38·3 (SEM 1·9) g/270 min after the LGI breakfast ($P<0·0001$). The kinetics of disappearance of exogenous glucose was parallel to the RaE kinetics, and there was also a significant difference in the rate of disappearance of exogenous glucose AUC between the groups ($P<0·0001$, data not shown).

The RaT increased in parallel in the two groups following breakfast ingestion with a peak at T30 min. Then RaT decreased until T270 min in both the groups, but remained steadier in the LGI group. After integration of the area under the RaT curve, we calculated the estimated quantity of total glucose which appeared in plasma over the 270 min following breakfast ingestion. The quantity of total glucose appearing in plasma following LGI breakfast was significantly lower than that following HGI breakfast (RaT AUC: 62·2 (SEM 2) g/270 min in the LGI group *v.* 68·4 (SEM 2) g/270 min in the HGI group, $P=0·03$).

Similarly, the overall rate of disappearance of total glucose was significantly lower in the LGI group ($P=0·03$; data not shown) and the RdT kinetics remained parallel to RaT kinetics in all the groups (data not shown).

EGP was calculated by subtracting RaE from RaT at each time point. As a consequence, EGP appeared to be significantly less inhibited after the ingestion of the LGI breakfast ($P<0·003$). Over the 270 min of the test, the quantity of EGP was 24·8 (SEM 1·8) g/270 min for the LGI breakfast, whereas it was 16·4 (SEM 1·9) g/270 min for the HGI one (data not shown).

Substrate oxidation. There was significant lower total carbohydrate oxidation after the LGI breakfast (39 (SEM 2) in the LGI group *v.* 45 (SEM 3) in the HGI group). But no significant differences were found between breakfasts with regard to total lipid oxidation. There were no differences between the groups in total carbohydrate and lipid oxidation after lunch ingestion (270–480 min; data not shown).

Effect of a 5-week low glycaemic index or high glycaemic index diet on postprandial responses to a low glycaemic index or high glycaemic index breakfast and a standardised lunch

Metabolites and hormones. When considering glucose response to breakfast, there was no significant group × time interaction for the post-breakfast glucose AUC and glucose iAUC, no main effect of time or of group for the glucose AUC. There was a significant main effect of group and of time for the glucose iAUC (between day 1 and day 36, + 31 % in the LGI group and +15 % in the HGI group, $P=0·01$). There was a significant effect of group for the post-breakfast glycaemic peak (glucose peak at day 36: 7·37 (SEM 0·21) mmol/l in the LGI group *v.* 7·92 (SEM 0·28) mmol/l in the HGI group, $P=0·01$). At day 36, post-breakfast glucose AUC and glucose iAUC were lower in the LGI group compared with the HGI group but this was not significant ($P=0·4$ and 0·06, respectively). Following lunch ingestion, there was no main effect of group and no significant group × time interaction for glucose response, but there was a

Table 4. Correlation in the whole study group between post-breakfast glucose response and post-lunch glucose response at days 1 and 36

	Day 1		Day 36	
	r	*p*	*R*	*p*
AUC glycaemia post-lunch × AUC glycaemia post-breakfast	0·79	<0·0001	0·47	0·004
AUC glycaemia post-lunch × glycaemia T270	0·38	0·02	*0·19*	*0·24*
Glucose peak at lunch × AUC glycaemia post-breakfast	0·51	0·002	0·33	0·04

r, correlation coefficient; AUC, area under the curve.

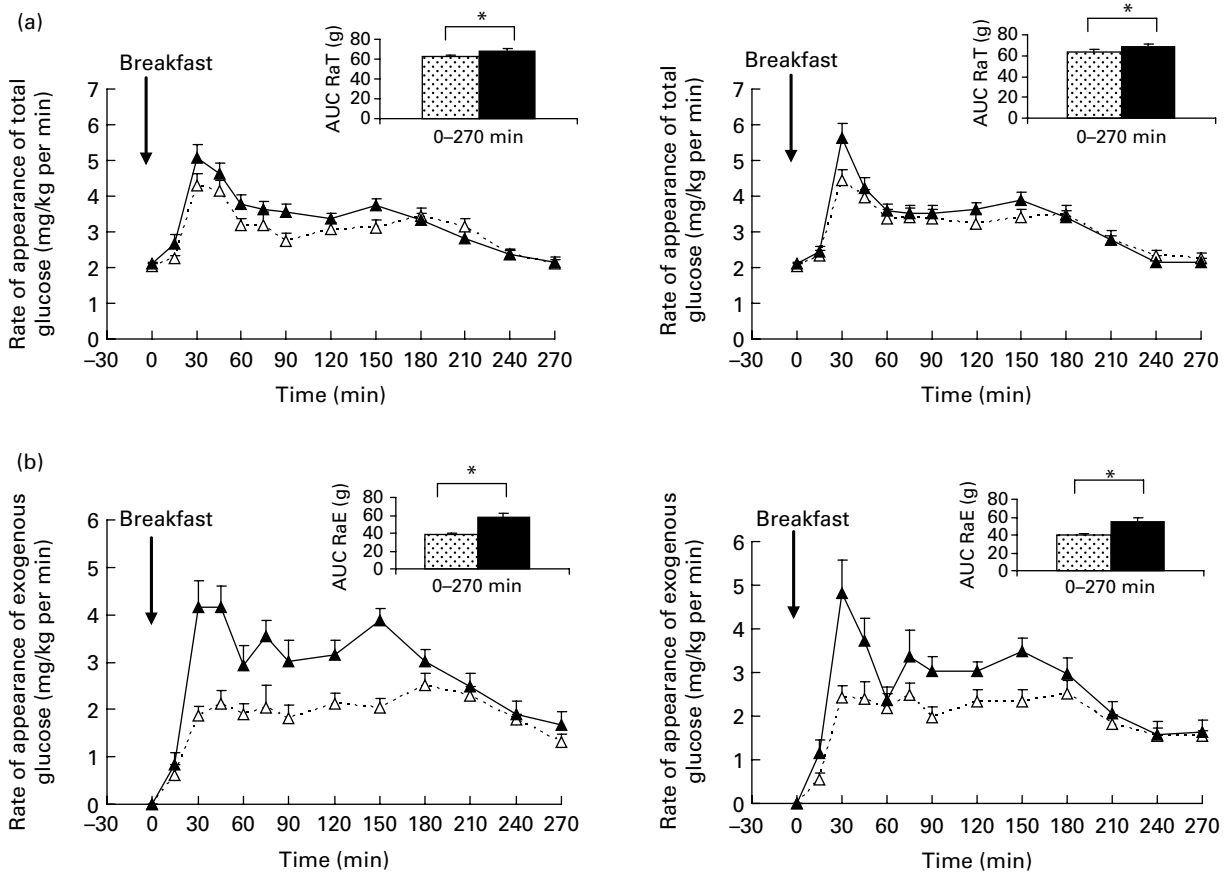

Fig. 2. Means with their standard errors rate of appearance and 270-min plasma appearance (area under the curve, AUC) of total glucose (RaT, (a)), of exogenous glucose (RaE, (b)) after subjects ingested either a low glycaemic index breakfast (△, *n* 19) or a high glycaemic index (HGI) breakfast (▲, *n* 19) at days 1 and 36 following GI intervention. At day 1, an unpaired *t* test showed a significant difference between groups for the post-breakfast rate of appearance of exogenous glucose (RaE) area under the curve (AUC) and rate of total glucose appearance (RaT) AUC (* $P<0{\cdot}05$). Using a two-way ANOVA, a significant main effect of group for the RaE AUC, RaT AUC and endogenous glucose production AUC was seen throughout the 5-week intervention ($P<0{\cdot}0001$, 0·0001, $P=0{\cdot}01$, respectively).

significant time effect for the post-lunch glucose peak and for the post-lunch glucose AUC and iAUC ($P=0{\cdot}04$, 0·01 and $P<0{\cdot}0001$, respectively). On day 36, post-breakfast glucose AUC was positively correlated to post-lunch glucose AUC (r 0·47, $P=0{\cdot}004$), as well as to the postprandial glucose peak at lunch (r 0·33, $P=0{\cdot}04$).

With respect to insulin response to breakfast, there was no significant group × period interaction and no main effect of group or time, either for the insulin peak or the post-breakfast insulin AUC. After lunch ingestion, there was a significant group × period interaction for the insulin peak ($P=0{\cdot}02$) and for the post-lunch insulin AUC ($P=0{\cdot}04$). For the LGI group, post-lunch insulin peak and post-lunch insulin AUC were significantly higher at day 36 when compared with day 1 ($P=0{\cdot}04$ and 0·01, respectively). But there was no difference in post-lunch insulin peak or post-lunch insulin AUC between the groups at day 36.

No group × time interaction and no main effect of group or time were found for C peptide, NEFA and TAG concentrations (baseline concentrations and postprandial responses, data not shown).

Glucose turnover. No significant group × time interaction and no main effect of time were found for the RaE and rate of disappearance of exogenous glucose, but a significant main effect of group appeared over the 5-week intervention dietary trial ($P<0{\cdot}0001$). At day 36, the RaE and rate of disappearance of exogenous glucose curves and associated AUC were still significantly lower in the LGI group ($P=0{\cdot}0004$). In the same way, there were no significant group × time interaction for the RaT and RdT and no main effect of time, but there was a significant main effect of group ($P=0{\cdot}06$ and 0·05, respectively). The RaT and RdT curve remained lower in the LGI group at days 1 and 36, but the difference between the groups at day 36 was no longer significant ($P=0{\cdot}1$). As for EGP, no significant group × time interaction and no main effect of time was found, but a significant main effect of group ($P=0{\cdot}01$) remained. Following the 5-week dietary intervention trial, EGP in the LGI group tended to remain less inhibited at day 36, but this was no longer significant ($P=0{\cdot}07$; data not shown).

Substrate oxidation (data not shown). There was no main effect of group or of time and no significant group × period interaction, when considering carbohydrate or lipid oxidation (baseline and following breakfast and lunch). Carbohydrate oxidation decreased in the two groups after the 5-week diet, but the differences between day 1 and day 36 in each group

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were not significant. In parallel, lipid oxidation was significantly increased in the HGI group between day 1 and day 36 ($P=0{\cdot}04$); the increase in the LGI group was not significant.

Discussion

In the present study in healthy subjects, a LGI breakfast rich in SAG decreased acute postprandial glucose availability and metabolic response compared with a HGI breakfast. The postprandial glucose response to the breakfast appeared to determine glucose response to the subsequent lunch. This effect of the LGI breakfast on glycaemic response was not accentuated by the 5-week LGI intervention diet.

The cereal products ingested for breakfast did not differ in macronutrient distribution and quantity but differed in term of SAG composition and thus in term of GI as previously shown[16,30,31]. These properties are correlated to *in vitro* starch digestibility and are dependent of processing[32]. This way, the observed effect could not be attributed to a modification in protein or lipid content. The present study, thanks to the monitoring of glucose kinetics, provides evidence that the SAG content of the LGI breakfast induced a significant decrease in exogenous glucose appearance, which contributed to the LGI effect. In parallel, EGP was less inhibited and balanced the total glucose response. Indeed, differences in EGP, due to the physiological glucose regulation in healthy subjects, lowered the final impact on glycaemia. This compensatory effect may not be observed in diabetic subjects, and this could explain the improvement in glucose control with low GI diets in diabetic subjects or in subjects with poor glycaemic control. In the present parallel study, the subjects consume either the LGI or the HGI breakfast. Thus, to adjust for inter-individual differences, iAUC was calculated and the same statistical results were obtained. Previous studies using glucose-stable isotope analysis have tried to explain the moderate glycaemic response associated to low GI products in term of plasma glucose appearance and disappearance. Comparing the ingestion of breakfasts with different GI, Schenk *et al.*[15] showed that the different GI of breakfast cereals could be partially related to the different rates of glucose removal from blood by tissue as a result of stimulation of insulin secretion and not to the difference in glucose appearance in plasma. But in another study, in which exogenous and endogenous glucose kinetics were measured, the addition of β-glucan to a polenta meal did prolong insulin secretion and reduced glycaemic response and the rate of appearance of exogenous and total glucose, with no significant alteration in the rate of glucose disposal[33]. In the present study, the ingestion of the LGI breakfast induced a decrease in both the appearance and removal of exogenous and total glucose, suggesting that different GI could be related to both metabolic mechanisms.

In the meta-analysis conducted by Livesey *et al.*[5], the available carbohydrate content was shown to have an impact on glycaemic control, even if it was weaker than GI or GL. In the present study, the lower glycaemic response at lunch associated to the lower glycaemic response at breakfast is consistent with results from previous studies[6–8,14,34]. A study comparing the effect of the GI and indigestible carbohydrate-resistant starch and dietary fibre content of cereal-based breakfasts on day-long glucose tolerance at a second meal (lunch) concluded that the content of fermentable carbohydrates *per se* did not influence second-meal glucose tolerance[7]. This beneficial effect has been allocated for some part of the ability of certain carbohydrates to produce slow and sustained glycaemia. This could be compared to the present study in which the reduced glycaemic response was associated with the decreased appearance of exogenous glucose. The significant positive correlation found between glucose response to the breakfast (T0–270 min AUC) and glucose response to the standardised lunch (T270–480 min AUC) showed that the kind of breakfast ingested can impact on the glucose tolerance in the short term. This is in accordance with results from a previous study by Nilsson *et al.*[34]. The authors tested glucose tolerance and response to breakfasts differing in GI and indigestible carbohydrate and found a positive correlation between the glucose response to breakfast and the glucose response to lunch, as in the present results, but a negative correlation between glucose before the start of the lunch and the glucose response to lunch. They concluded on the major input of GI on this second-meal effect, with an independent effect of colonic fermentation. The GI was in fact a major determinant of second-meal effect in both Nilsson's and our own study, but we did not find the same impact of glucose concentration just before the second meal.

In the present study, the metabolic effect of LGI *v.* HGI diet was investigated over 5 weeks. Interestingly, after the 5-week dietary intervention, a significant decrease in GI was obtained in the LGI group, by replacing usual starchy products in diet by LGI products. This showed that it is possible to implement such a dietary intervention based on simple dietary advice and a few LGI products. These modifications in the mean GI of diet in the two groups did not affect the intake of other nutrients, either in quantity or proportion. It should be noted that in the LGI group there was also a trend to a decrease in hunger sensation between meals[18]. This effect may be due to the consumption of food richer in dietary fibre and thus more satiating in this group[35]. The mean GL of food in the LGI group decreased in parallel to the mean GI and it is difficult to distinguish the effects due to GI and/or GL, as already underlined in other studies[5]. Following the 5-week dietary intervention, no significant effect was noticed on baseline glucose and insulin concentrations. This is consistent with conclusions of Livesey's[5] meta-analysis, in which the authors concluded that LGI products could have an effect on baseline glucose tolerance parameters in subjects with baseline glycaemia >5 mM or with poor glucose control. Concerning the post-breakfast glycaemic response, the difference between the groups (LGI *v.* HGI) was maintained over the 5 weeks (no significant group × time interaction) but tended to decrease over time. Indeed, at day 36, post-breakfast AUC and iAUC were lower in the LGI group but this was not significant. The two cereal products still differed significantly in term of exogenous glucose appearance in plasma, but the endogenous production was not significantly different between the groups. However, at day 36, the glycaemic response to lunch remained correlated to the glycaemic response to breakfast. But in the LGI group, insulin response to the lunch was significantly higher. Thus, the lowest glycaemic response at lunch associated to the lowest glycaemic response at breakfast (potential second-meal effect) was maintained over weeks but this seems to be at the expense of the insulin profile. One hypothesis could be that

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the LGI group may present an improvement in β-cell function, as it has been demonstrated by Wolever *et al.* [13]. But, when assessed by homeostasis model assessment β-cell function, no difference was found in β-cell function between the groups and over time (data not shown). Several papers have reported long-term beneficial effects of low-GI foods on glucose metabolism and insulin sensitivity in type 2 diabetic subjects and healthy subjects[5,36–38]. Moreover, the reduced glycaemic response induced by LGI products could present a potential beneficial effect on oxidative stress with a reduction of glucose excursion, as already shown[39]. In the present study, the 5-week dietary intervention may have equalised glycaemic profiles by regularising breakfast intake in both the groups and thus tended to balance the difference between LGI and HGI metabolic effects.

LGI foods were thought to potentially promote fat oxidation compared to carbohydrate oxidation, through their action on insulin response[40,41]. But the present results did not show any major change of nutrient oxidation and of respiratory exchange rate following GI modification. Reviewing the GI effects on nutrient oxidation (short-, mid- and long-term), Diaz *et al.* came up with the statement that fuel partitioning was not affected by different glycaemic features[42]. The metabolic changes induced by a LGI intervention seemed insufficient to initiate a significant effect on lipid oxidation.

In conclusion, modulation of postprandial glucose availability at breakfast is shown to be an important factor in day-long metabolic control in healthy subjects, as it decreases plasma exogenous glucose appearance and improves glucose control at subsequent lunch. After 5 weeks, such acute effects on glucose metabolism were maintained but remain to be confirmed in the longer term.

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References

1. Coutinho M, Gerstein HC, Wang Y, *et al.* (1999) The relationship between glucose and incident cardiovascular events. A metaregression analysis of published data from 20 studies of 95,783 individuals followed for 12·4 years. *Diabetes Care* **22**, 233–240.
2. Jenkins DJ, Kendall CW, Augustin LS, *et al.* (2002) Glycemic index: overview of implications in health and disease. *Am J Clin Nutr* **76**, 266S–273S.
3. Salmeron J, Manson JE, Stampfer MJ, *et al.* (1997) Dietary fiber, glycemic load, and risk of non-insulin-dependent diabetes mellitus in women. *JAMA* **277**, 472–477.
4. Augustin LS, Franceschi S, Jenkins DJ, *et al.* (2002) Glycemic index in chronic disease: a review. *Eur J Clin Nutr* **56**, 1049–1071.
5. Livesey G, Taylor R, Hulshof T, *et al.* (2008) Glycemic response and health – a systematic review and meta-analysis: relations between dietary glycemic properties and health outcomes. *Am J Clin Nutr* **87**, 258S–268S.
6. Wolever TM, Jenkins DJ, Ocana AM, *et al.* (1988) Second-meal effect: low-glycemic-index foods eaten at dinner improve subsequent breakfast glycemic response. *Am J Clin Nutr* **48**, 1041–1047.
7. Liljeberg HG, Akerberg AK & Bjorck IM (1999) Effect of the glycemic index and content of indigestible carbohydrates of cereal-based breakfast meals on glucose tolerance at lunch in healthy subjects. *Am J Clin Nutr* **69**, 647–655.
8. Liljeberg H & Bjorck I (2000) Effects of a low-glycaemic index spaghetti meal on glucose tolerance and lipaemia at a subsequent meal in healthy subjects. *Eur J Clin Nutr* **54**, 24–28.
9. Nilsson A, Granfeldt Y, Ostman E, *et al.* (2006) Effects of GI and content of indigestible carbohydrates of cereal-based evening meals on glucose tolerance at a subsequent standardised breakfast. *Eur J Clin Nutr* **60**, 1092–1099.
10. Brighenti F, Benini L, Del Rio D, *et al.* (2006) Colonic fermentation of indigestible carbohydrates contributes to the second-meal effect. *Am J Clin Nutr* **83**, 817–822.
11. Miles JM (2008) A role for the glycemic index in preventing or treating diabetes? *Am J Clin Nutr* **87**, 1–2.
12. Brand-Miller JC, Petocz P & Colagiuri S (2003) Meta-analysis of low-glycemic index diets in the management of diabetes: response to Franz. *Diabetes care* **26**, 3363–3364.
13. Wolever TM, Mehling C, Chiasson JL, *et al.* (2008) Low glycaemic index diet and disposition index in type 2 diabetes (the Canadian trial of carbohydrates in diabetes): a randomised controlled trial. *Diabetologia* **51**, 1607–1615.
14. Jenkins DJ, Wolever TM, Taylor RH, *et al.* (1982) Slow release dietary carbohydrate improves second meal tolerance. *Am J Clin Nutr* **35**, 1339–1346.
15. Schenk S, Davidson CJ, Zderic TW, *et al.* (2003) Different glycemic indexes of breakfast cereals are not due to glucose entry into blood but to glucose removal by tissue. *Am J Clin Nutr* **78**, 742–748.
16. Englyst KN, Englyst HN, Hudson GJ, *et al.* (1999) Rapidly available glucose in foods: an *in vitro* measurement that reflects the glycemic response. *Am J Clin Nutr* **69**, 448–454.
17. McMillan-Price J, Petocz P, Atkinson F, *et al.* (2006) Comparison of 4 diets of varying glycemic load on weight loss and cardiovascular risk reduction in overweight and obese young adults: a randomized controlled trial. *Arch Intern Med* **166**, 1466–1475.
18. de Rougemont A, Normand S, Nazare JA, *et al.* (2007) Beneficial effects of a 5-week low-glycaemic index regimen on weight control and cardiovascular risk factors in overweight non-diabetic subjects. *Br J Nutr* **98**, 1288–1298.
19. Foster-Powell K, Holt SH & Brand-Miller JC (2002) International table of glycemic index and glycemic load values: 2002. *Am J Clin Nutr* **76**, 5–56.
20. Arock M, Desnault H, Viars P, *et al.* (1985) Determination of total nitrogen in biological milieux by chemoluminescence: a comparison with the reference method. *Ann Biol Clin (Paris)* **43**, 872–874.
21. Ferrannini E (1988) The theoretical bases of indirect calorimetry: a review. *Metabolism* **37**, 287–301.

British Journal of Nutrition

22. Tissot S, Normand S, Guilluy R, *et al.* (1990) Use of a new gas chromatograph isotope ratio mass spectrometer to trace exogenous ^{13}C labelled glucose at a very low level of enrichment in man. *Diabetologia* **33**, 449–456.
23. Bier DM, Arnold KJ, Sherman WR, *et al.* (1977) *In vivo* measurement of glucose and alanine metabolism with stable isotopic tracers. *Diabetes* **26**, 1005–1015.
24. Dejongh DC & Hanessian S (1965) Characterization of amino sugars by mass spectrometry. *J Am Chem Soc* **87**, 3744–3751.
25. Thivend P MC & Guilbot A (1972) Determination of starch with glucoamylase. In *Methods in Carbohydrate Chemistry*, pp. 100–105 [RL Whisler, editor]. New York/London: Academic Press.
26. Normand S, Pachiaudi C, Khalfallah Y, *et al.* (1992) ^{13}C appearance in plasma glucose and breath CO_2 during feeding with naturally ^{13}C-enriched starchy food in normal humans. *Am J Clin Nutr* **55**, 430–435.
27. De Bodo RC, Steele R, Altszuler N, *et al.* (1963) On the hormonal regulation of carbohydrate metabolism: studies with ^{14}C glucose. *Recent Prog Horm Res* **19**, 45–48.
28. Proietto J, Rohner-Jeanrenaud F, Ionescu E, *et al.* (1987) Non-steady-state measurement of glucose turnover in rats by using a one-compartment model. *Am J Physiol* **252**, E77–E84.
29. Goldberg GR, Black AE, Jebb SA, *et al.* (1991) Critical evaluation of energy intake data using fundamental principles of energy physiology: 1. Derivation of cut-off limits to identify under-recording. *Eur J Clin Nutr* **45**, 569–581.
30. Englyst KN, Hudson GJ & Englyst HN (2000) Starch analysis in food. In *Encyclopedia of Analytical Chemistry*, pp. 4246–4262 [R Meyers, editor]. Chichester: John Wiley & Sons Ltd.
31. Seal CJ, Daly ME, Thomas LC, *et al.* (2003) Postprandial carbohydrate metabolism in healthy subjects and those with type 2 diabetes fed starches with slow and rapid hydrolysis rates determined *in vitro*. *Br J Nutr* **90**, 853–864.
32. Garsetti M, Vinoy S, Lang V, *et al.* (2005) The glycemic and insulinemic index of plain sweet biscuits: relationships to *in vitro* starch digestibility. *J Am Coll Nutr* **24**, 441–447.
33. Nazare J-A, Normand S, Triantafyllou AO, *et al.* (2007) Modulation of the postprandial phase by beta-glucan in overweight subjects: effects on glucose and insulin kinetics. *Mol Nutr Food Res* **53**, 361–369.
34. Nilsson AC, Ostman EM, Granfeldt Y, *et al.* (2008) Effect of cereal test breakfasts differing in glycemic index and content of indigestible carbohydrates on daylong glucose tolerance in healthy subjects. *Am J Clin Nutr* **87**, 645–654.
35. Howarth NC, Saltzman E & Roberts SB (2001) Dietary fiber and weight regulation. *Nutr Rev* **59**, 129–139.
36. Jenkins DJ, Wolever TM, Buckley G, *et al.* (1988) Low-glycemic-index starchy foods in the diabetic diet. *Am J Clin Nutr* **48**, 248–254.
37. Brand JC, Colagiuri S, Crossman S, *et al.* (1991) Low-glycemic index foods improve long-term glycemic control in NIDDM. *Diabetes Care* **14**, 95–101.
38. Wolever TM, Jenkins DJ, Vuksan V, *et al.* (1992) Beneficial effect of low-glycemic index diet in overweight NIDDM subjects. *Diabetes Care* **15**, 562–564.
39. Food and Drug Administration (2006) Food labeling: health claims; soluble dietary fiber from certain foods and coronary heart disease. Final rule. *Fed Regist* **71**, 29248–29250.
40. Brand-Miller JC, Holt SH, Pawlak DB, *et al.* (2002) Glycemic index and obesity. *Am J Clin Nutr* **76**, 281S–285S.
41. Wee SL, Williams C, Tsintzas K, *et al.* (2005) Ingestion of a high-glycemic index meal increases muscle glycogen storage at rest but augments its utilization during subsequent exercise. *J Appl Physiol* **99**, 707–714.
42. Diaz EO, Galgani JE & Aguirre CA (2006) Glycaemic index effects on fuel partitioning in humans. *Obes Rev* **7**, 219–226.

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