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TITLE

Increased liver fat and glycogen stores following high compared with low glycaemic index food: a randomized cross over study

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SHORT RUNNING TITLE

GI Diet Study

WORD COUNT OF ABSTRACT

242

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4,183

LIST OF ABBREVIATIONS

NAFLD – Non-Alcoholic Fatty Liver Disease

NASH – Non-Alcoholic Steatohepatitis

GI – Glycaemic Index

LGI – Low Glycaemic Index

HGI – High Glycaemic Index

MRS – Magnetic Resonance Spectroscopy

SPMIC – Sir Peter Mansfield Imaging Centre

IPAQ – International Physical Activity Questionnaire

COMA – Committee on Medical Aspect of Food Policy

QMC – Queen's Medical Centre

VAS – Visual Analogue Scale (subjective appetite rating)

PRESS – Point Resolved Spectroscopy

GCV – Gastric Content Volume

AUC – Area Under Curve

iAUC – Incremental Area Under Curve

ANOVA – Analysis of Variance

CV – Coefficient of Variance

NIHR – National Institute of Health Research

CLINICAL TRIALS REGISTRY NUMBER AND WEBSITE

This study was registered at clinicaltrials.gov, ID: NCT02482558.

ABSTRACT

Aims

To investigate the acute and longer term effects of low (LGI) v high (HGI) glycaemic index diets on hepatic fat and glycogen accumulation and related blood measures in healthy volunteers.

Methods

Eight healthy males (age=20.1±0.4y, BMI=23.0±0.9 kg/m2) attended a test day before and after a 7-day macronutrient and energy matched HGI or LGI diet, followed by a minimum 4 week wash-out period, and then returning to repeat the intervention with the alternative diet. During test days, participants consumed either a HGI or LGI test meal corresponding to their diet week, and liver fat (^{1}H MRS), glycogen (^{13}C MRS) and gastric content volume (MRI) were measured. Blood samples were obtained regularly throughout the test day for plasma glucose and insulin.

Results

Plasma glucose and insulin peak values and AUC were significantly greater following the HGI test meal compared with LGI test meal as expected. Hepatic glycogen concentrations increased more following the HGI test meal ($P < 0.05$) and peak levels were significantly greater after 7 days of HGI dietary intervention compared to that at the beginning of the intervention ($P < 0.05$). Liver Fat fractions increased significantly following the HGI dietary intervention compared with the LGI dietary intervention (two way repeat measures ANOVA, $P \leq 0.05$).

Conclusions

Compared to an LGI diet, a one week HGI diet increased hepatic fat and glycogen stores. This may have important clinical relevance for dietary interventions in the prevention and management of non-alcoholic fatty liver disease.

INTRODUCTION

Shifts in eating patterns and dietary compositions are believed to be a major contributing factor to the recent rise in obesity and obesity related problems [1, 2]. Type II diabetes, for example, has been thought to be a disease of ectopic fat and the development of non-alcoholic fatty liver disease (NAFLD) as well as non-alcoholic steatohepatitis (NASH) have been considered as key steps in its pathogenesis [3]. Changes in the amount of food consumed and total energy intake influences long-term energy stores such as adipose tissue and intrahepatic triglycerides, but the specific influence of individual macronutrients on ectopic fat in general and accumulation of liver fat in particular are not established.

Recently, glycaemic index has been considered as a potentially important factor influencing these conditions, and low glycaemic index (LGI) dietary interventions have been shown to be effective in lowering total fat mass and increasing lipid utilisation in patient studies [4, 5]. LGI foods have also been linked to more rapid recovery from previous training sessions [6] and improved satiety with less hunger between meals [7]. Whilst these findings are promising with potential clinical relevance, work is needed to investigate a wide range of factors effecting metabolic disorders. This includes both forms of energy storage in the liver, in the longer term as fats, and in the shorter term as glycogen. Gastric emptying also impacts the delivery of foods to the small intestines for absorption of nutrients into the blood stream and previous studies have shown meal timing, volume and fibre content can affect the postprandial response [8, 9].

Magnetic resonance techniques offer a unique method of investigating some of these parameters. ^{1}H MRS measurements of liver fat have been validated and used in many previous studies [10-12] and ^{13}C MRS measurements of glycogen have also been well validated [13, 14] and provides the only non-invasive measure of hepatic glycogen stores *in*

vivo. Fast imaging techniques can also be used to monitor gastric emptying [15, 16]. These magnetic resonance measures can be obtained alongside blood samples to provide a broader picture of metabolic response.

Previous studies have focussed on the acute postprandial changes alone, and as such less is known about the longer term effect of well controlled diets with varying glycaemic index. The aim of this study was to investigate both the immediate and cumulative effects of varying glycaemic index on liver metabolic control in healthy volunteers by monitoring hepatic glycogen and lipid levels *in* vivo with MRS [14, 17]. Secondary outcomes were related changes in gastric content volume, blood glucose and insulin and subjective appetite scores.

MATERIALS AND METHODS

Study Design. Eight male participants underwent two 7-day diet periods separated by a minimum four-week washout in a randomized cross-over study. The day before (visit 1) and the day after (visit 2) each diet period, participants attended the Sir Peter Mansfield Imaging Centre (SPMIC) in Nottingham for a test day. Ethical permission was obtained from the University of Nottingham Medical School Research Ethics Committee and all participants provided informed written consent before participation.

Eligibility. Participants were screened for eligibility (male, aged between 18 and 35 years old, with a BMI between 20 and 25 kg/m^2 and no contraindications for MRI). Participants were excluded if they were on any special diets, weight loss programs or strict physical training routine (defined as > 5 hours of intense training per week); if they were heavy drinkers (more than 3 units a day) or smokers; or if they had any metabolic disorders or liver disease. Participants were block randomized to determine the initial intervention (HGI or LGI).

Demographics. Mean age of participants was 20.1 ± 0.4 years with a mean BMI of 23.0 ± 0.9 kg/m^2. The mean weight of participants at the start of visit 1 was 73 ± 3 kg and at the start of visit 2 was 73 ± 3 kg.

Test Day. Prior to the test days the participants were asked to refrain from alcohol and to consume the same evening meal by 9:00 pm the night before visit 1 of both diets. At the end of each dietary period the final meal was consumed before 9:00pm on the evening before visit 2. On the morning of each test day participants arrived fasted at the MR centre between 7:30am and 8:00am, and were weighed. After fasted measurements, participants were given either a high glycaemic index (HGI) or LGI test meal for breakfast (supplementary table 1) depending on their diet week, which was to be consumed within 10 minutes followed by regular measurements for 360 mins.

At the start of the day, participants were cannulated in the forearm and samples were taken at regular intervals throughout the day. Samples were centrifuged, frozen and stored at -80^{0}C for analysis of plasma glucose and insulin (detailed methods in supplementary material).

All MR measurements were acquired using a Philips Achieva 3T system (Philips, Best, The Netherlands).

^{13}C MRS measurements of glycogen were detected with an adiabatic half passage pulse-acquire sequence (MRS bandwidth = 7 kHz, TR = 959 ms). Spectra were acquired using a single loop carbon coil with proton decoupling (Pulseteq, Surrey, UK) as described previously [15, 18, 19] (more details in supplementary material). Measurements were taken at start of day (fasted) and hourly following the test meal.

^{1}H MRS measurements of liver fat were detected with a respiratory triggered point resolved spectroscopy (PRESS) sequence (Bandwidth = 2 kHz; TR = 5 s) with varying TE (40, 50, 60

and 80 ms). Spectra were acquired using a 32 channel Philips XL SENSE torso coil from a $30x30x30mm^3$ voxel in the lower right hepatic lobe, with and without water suppression. T2 was determined and used to correct fat-to-water ratios to determine liver fat fractions [10, 20] at start of day (fasted) and 360 mins after test meal (more detail in supplementary material).

MR Images were also acquired throughout the test day and regions of interest were drawn around the content of the stomach using Analyze9 (Mayo Foundation, Rochester, MN, USA) and summed across slices to determine Gastric Content Volume (GCV) as described previously [15, 16]. GCV was therefore a combined measure of both ingested food and stomach secretion.

Visual analogue scales (VAS) were completed at the same time as blood sampling to assess subjective appetite ratings using five mixed appetite questions [21-23]. On day 1 (start of diet), day 4 (middle of diet) and day 7 (end of diet) participants also filled out subjective appetite ratings. The VAS methods and results are reported in the supplementary material.

Diet Week. Following the test day, participants undertook a 7 day HGI or LGI diet before visit 2, and returned again after a >4 week washout for the alternate diet. During the diet week participants were provided with all the food required as adapted from Morgan et al [24] shown in supplementary table 2. All food was purchased from a single supplier and given directly to participants. They were also given a booklet describing the quantities of each meal to be consumed, along with scales and a measuring jug to measure out the required ingredients for each meal. Participants recorded whether they consumed the full meal, and if not how much was remained.

Prior to the study, participants completed the international physical activity questionnaire (IPAQ) and their basal metabolic rate was calculated using the Henry modified Schofield formula [25, 26]. This was used to scale the amount of food consumed during diet weeks to

match expected energy expenditure and provide over all energy balance (no weight loss or weight gain). The energy intake and macronutrient content was matched for the HGI and LGI diets (71% carbohydrate, 14% protein, 14% fat per day). Whilst this level of carbohydrate is greater and level of fat is lower than national standards, these proportions were based on previous well defined HGI v LGI intervention in healthy volunteers that show clear glycaemic differences [24], and the diet was deemed suitable for this preliminary proof of concept study exploring carbohydrate glycaemic index. As would be expected and is usually the case, the fibre content was greater during LGI compared with HGI (Fibre: ~22 g/day for HGI and ~42 g/day for LGI) [24] and therefore the term LGI denotes a high-fibre low glycaemic index diet and HGI denotes a lower-fibre high glycaemic index diet.

Sample size. The exploratory nature of this study with few related publications made sample size calculations difficult. However, estimates of effect size were made based on previous studies and used to determine an appropriate sample size using G*power 3.1.5 [27]. An *a priori* two way repeated measures F-test (ANOVA) will find a significance interaction with a power of 0.8 given an effect variance (HGI – LGI) of 2.1% and a within group variance of 2.9% in a sample size of 6 subjects (effect size = 0.84). These variances were based on liver fat changes observed in a previous study [28] assuming changes only observed on HGI diet. There are a number of important differences in the present study, such as increased carbohydrate proportion and iso-energetic intervention, and as such the sample size was increased to 8 subjects. This sample size would also calculate a significant change of 15% hepatic glycogen using a matched pair student's t-test given variability observed in previous studies [13]

Blinding. On completion of all data acquisition, results were blinded by an uninvolved colleague and analysed by the first author. Although the first author was present during scan sessions, spectroscopy data were not viewed in real time and only assessed after blinding.

Blood samples were analysed by uninvolved colleagues and so were not blinded. Following initial analysis a blind review meeting was held before data were unblinded. Deviations from protocol were discussed and data assessed for statistical relevance on a *per* protocol basis.

Data Analysis. Methods of analysis are described in more detail in the supplementary material. Values were calculated for individual time points and hepatic glycogen values were also calculated as percentage baseline. The total area under curve (AUC) across the test visit was also calculated for glucose, insulin and glycogen. In addition, the glycaemic index was calculated using the area above baseline (incremental AUC, iAUC) from t=0 to t=120minutes from plasma glucose results. Homeostasis model assessment of insulin resistance (HOMA-IR) was also calculated from fasted glucose and insulin values using $(GLUCOSE \times INSULIN)/\ 22.5$.

Statistical Analysis. Results are reported as mean with standard error, and mean difference with standard deviation. Parametric testing was performed assuming normal distributions of lipid and glycogen in tissue, as well as postprandial hepatic glycogen and glucose response, which is reasonable given the restrictive selection criteria (healthy, male, sedentary, non-smokers etc.).

To assess differences in the acute response between test meals, Postprandial peaks, AUCs and iAUCs following test meals (HGI v LGI) on visit 1 (prior to diet) were compared using a matched pair Student's t test. Measurements taken across the time course on this visit were also assessed using a two way repeated measures ANOVA and used to evaluate any significant main effect of diet (LGI v HGI) or time of day (across the test day) and/or any significant interaction between diet and time of day.

To assess longer term effects of the dietary intervention, differences in fasted values at each visit were compared using a two way repeated measures ANOVA. Changes across the time

course between visit 2 and visit 1 in LGI and HGI diet arms independently were also assessed using a two way repeated measures ANOVA to evaluate any significant main effect of visit (visit 1 v visit 2) or time of day (across the test day) and/or any significant interaction between visit and time of day.

All significant main effects were followed up by pairwise comparisons using a matched pair two-tail Student's t test and significant interactions were followed up by pairwise comparisons of change from baseline values.

A Bonferroni adjustment was applied for multiple comparisons. In all cases significance was attributed to $P < 0.05$. The statistical package used for analysis was SPSS version 21 for Windows (SPSS, Inc., Chicago, IL).

RESULTS

Participant recruitment and Flow. The first test day was 13th May 2013 and the final test day was on 08th October 2013. One participant dropped out early, and as such his data were removed from analysis and one subject failed to complete the LGI diet week and so his visit 2 data was excluded. For primary outcomes, this gave a sample size of n = 8 for visit 1 HGI v LGI comparisons and n = 7 for visit 1 v visit 2 comparisons. Other difficulties arose for secondary outcomes, such us failure to cannulate, and as such the sample size for each analysis varies as follows - glucose: n=5; insulin: n=6.

Compliance. Participants reported good compliance across the diet week (beside the one exception mentioned above). According to the returned volunteer's booklets, 98 ± 2 % of meals were consumed during the HGI diet and 97 ± 3 % during the LGI diet (reported energy intake was 100 ± 0 % as provided for HGI and 99 ± 1 % for LGI).

Fasted Values on visit 1 (prior to diet). HOMA-IR values were similar prior to both diets ($HOMA\text{-}IR_{HGI}$= 1.91 ± 0.12, $HOMA\text{-}IR_{LGI}$ = 1.78 ± 0.05). Fasted liver fat fractions (FF%)

and fasted hepatic glycogen (GLYC) levels were also similar prior to both diets ($FF_{HGI}^{\%}$ = 1.5 ± 0.6 % and FF_{LGI}% = 1.5 ± 0.5 %, P = 0.98; $GLYC_{HGI}$ = 306 ± 37 mmol/l and $GLYC_{LGI}$ = 290 ± 32 mmol/l, P = 0.67) indicating a successful washout period.

Glycaemic and insulinaemic response of diets. Acute changes in plasma glucose and insulin in response to HGI and LGI test meals on visit 1 (prior to diet) are shown in **figure 1a-b**. Plasma glucose rose significantly more following HGI compared with LGI test meal (P < 0.01). Postprandial insulin AUC was significantly more following the HGI compared with the LGI test meal ($INSULIN_{HGI}$ – $INSULIN_{LGI}$: = 19 ± 3 IU/l h, P < 0.05). There was no significant change in HOMA-IR on visit 2 v visit 1 for either diet ($\triangle HOMA\text{-}IR_{HGI}$ = 0.42 ± 0.93; $\triangle HOMA\text{-}IR_{LGI}$ = 0.13 ± 0.43) and there were no significant differences in the glucose and insulin response to the test meal between visit 1 and visit 2.

Study Outcomes

Effect of dietary intervention on liver fat fraction. There was a significant interaction between diet and visit for fasted liver fat fractions ($P \leq 0.05$) with mean values increasing following the HGI dietary intervention and decreasing following the LGI dietary intervention ($\triangle FF_{HGI}$% =1.3 ± 2.0 % and $\triangle FF_{LGI}$% = -0.4 ± 0.7%). In the LGI arm, the main effect of diet on liver fat fraction was significant, and a subsequent pairwise comparison showed a significant reduction in liver lipids at t = 360 minutes on visit 2 compared with visit 1 (FF_{LGI}% Visit 2 – Visit 1 = 0.4 ± 0.1, $P \leq 0.001$) as shown in **figure 2**.

Acute effect of test meal on hepatic glycogen. The main effect of test meal on postprandial glycogen concentration was significant on visit 1 (prior to diet), with values increasing from fasted concentrations for the first 180 minutes and then beginning to decline until the end of the test day, as shown in **figure 3a** ($P \leq 0.01$). In contrast, following the HGI test meal, hepatic glycogen concentrations increased from fasted levels throughout all of the visit, but

the main effect of test meal on glycogen concentration did not reach significance due to increased inter-subject variability. The coefficient of variation (CV) post consumption was significantly greater during the HGI visit compared with LGI (CV_{HGI} = 48%; CV_{LGI}= 20%; p ≤ 0.001). There was no significant interaction between test meal and time of day

Longer term effect of dietary intervention on hepatic glycogen. Figure 3b shows the postprandial changes in hepatic glycogen on visit 2. There was no significant increase following either test meal, and no significant change from visit 1 to visit 2. Figure **3 d, e and f** shows changes in hepatic glycogen at fasted, postprandial peak and AUC between visit 2 and visit 1 for HGI and LGI diets. There was no significant change in fasted glycogen stores between visit 1 and visit 2 (**figure 3c)**, but the main effect of diet on peak glycogen concentration was significant (P ≤0.05) with mean HGI values greater than LGI (**figure 3d**). A subsequent pairwise comparison showed HGI peak glycogen concentration on visit 2 was significantly greater than visit 1 (P = 0.04). The effect sizes of LGI diet on fasted glycogen and peak glycogen values were small (0.06 and 0.38 respectively), whereas the effect sizes of HGI diet on fasted glycogen and peak glycogen values were moderate to large (0.67 and 1.15 respectively). The main effect of diet on hepatic glycogen AUC was also significant, with mean HGI AUC greater than mean LGI AUC (P < 0.02) as shown in **figure 3e**.

Acute effect of test meal on GCV. The main effect of test meal on GCV on visit 1 (prior to diet) was significant (**figure 4**) and a subsequent pairwise comparison showed GCV_{LGI} was significantly greater than GCV_{HGI} at t = 20 minutes (difference = 116 ± 23 ml, P ≤ 0.001).

Longer term effects of dietary intervention on GCV. Visit 1 and visit 2 GCVs are shown on **figure 4**. In the HGI arm, the main effect of diet on GCV was significant (P < 0.03) and a subsequent pairwise comparison showed gastric content values were significantly greater on HGI visit 2 compared with HGI visit 1 at t = 20 minutes (P ≤ 0.05), 140 minutes (P ≤ 0.05)

and 200 minutes ($P < 0.05$). In the LGI arm the main effect of diet on GCV was not significant. There was also no significant interaction between diet and visit.

DISCUSSION

Glycaemic Response. The immediate glycaemic responses were as expected and blood glucose levels were in strong agreement with Morgan *et al* [24] confirming a variation in glycaemic index as intended. Plasma insulin responses were also as expected [29], with greater plasma glucose levels prompting increased insulin secretion. There was no change in fasting insulin resistance following the diet week (HOMA-IR) which is not surprising given the short intervention period. Changes in liver fat are expected to precede insulin resistance, and future studies should explore the longer term impact of HGI and LGI diets on insulin sensitivity.

Liver Fat Fraction. Results from ^{1}H MRS were striking and of high clinical relevance. Hepatic fat fractions increased after 1 week of HGI diet and decreased after LGI, suggesting that reducing dietary glycaemic index has the potential of providing long term health benefits in the prevention and management of NAFLD, obesity and type II diabetes.

Previous HGI v LGI dietary intervention studies have not controlled for macronutrient content or total energy intake and energy balance; as such the present study provides new evidence that glycaemic index and/or fibre content plays an important role in ectopic fat deposition independent of nutritional composition. In a recent cross sectional analysis, Valtuena *et al* reported a strong correlation between steatosis grading and dietary glycaemic index specifically [30]. Whilst the smaller sample size of the present study limits its direct applicability to the general population, it does provide preliminary data that supports the findings of this previous study [30] and suggests that glycaemic index is indeed associated with liver lipid storage even under iso-energetic conditions.

A recent 4 way trial comparing glycaemic index (High v Low) and carbohydrate content (65% v 50%) during a period of weight gain found significant increases in liver fat following a high carbohydrate diet but no association with glycaemic index [31]. However, in this study the refeeding phase included excess energy, whereas the present study used a dietary intervention that provided no energy surplus or deficit in participants and also had a greater proportion of carbohydrates. Further studies should explore if the significant effects of glycaemic index found in the present study are driven by the increased carbohydrate consumption and how this relates to excess energy intake. These results indicate the potential importance of type of carbohydrate consumed in the prevention of metabolic disorders, for example in the pre-diabetic population. Whilst excess energy intake will provide the most significant contribution to fat deposition and metabolic dysfunction [32], glycaemic index should also be seen as relevant.

Glycogen. As far as the authors are aware, this study showed for the first time increased hepatic glycogen storage following a HGI breakfast compared with an iso-energetic LGI breakfast. During the visit prior to the diet, the increase in mean absolute glycogen levels following the HGI test meal accounted for 25% of the ingested intake of carbohydrates, in strong agreement with the literature [33, 34]. In contrast to this, the peak LGI hepatic glycogen response was lower and declined from 180 minutes. Similar findings have been reported in muscle in a number of studies [35, 36] in which HGI test meals prompted a greater storage of muscle glycogen. This relationship may be due to increased insulin levels driving an increased rate of glycogenesis and these effects may differ in patient populations, such as people with insulin resistance or obesity. ^{13}C MRS provides a powerful non-invasive method for monitoring these effects in future studies and provides useful insight into metabolic diseases. Related to this finding was the observation of increased peak glycogen levels on the visit following the 7-day diet, which was only significant after the HGI

intervention, although this may be due to the larger proportion of carbohydrates in the dietary intervention consumed compared with the standard UK diet. Whilst previous studies have shown longitudinal glycogen MRS measurements have considerable variability [20], there was a large effect size in fasted and peak measures following the HGI diet. This may be accounted for by the increased postprandial glycogen levels from the evening HGI meal before visit 2. Greater glycogen stores at the start of the day would seem beneficial to individuals who need a sustained postprandial energy release, for example athletes or other physically active individuals, but have the potential to be broken down through glycogenolysis and enter lipogenesis for longer term energy stores in more sedentary individuals. The significantly greater CV following the HGI compared with LGI test meal also indicates a more variable glycogen response to high glycaemic index food in healthy individuals and may be relevant to the prevention or treatment of patients with glycogen storage disease.

Gastric Contents Volume. The present study also showed evidence of changes in postprandial GCV following the diet week, though could be due to either changes in gastric emptying or gastric secretion which were not distinguished here. During the visit prior to the diet week, gastric content was greater for LGI compared with HGI despite meal volumes being matched, which may be a result of slowed gastric emptying during LGI due to increased fibre content [9]. However, during visit 2 this was reversed and gastric content was significantly smaller for LGI visit 2 compared with LGI visit 1. Further work is needed to establish whether these changes are an adaptive effect of the dietary interventions.

There were a number of limitations with this study. First, the study group was small; given the multifactorial nature of the study, it would have been preferable to have allowed more for non-compliance and cannulation difficulties while calculating sample size. Whilst eight participants could be analysed for the proposed primary outcomes, problems with blood samples and

incomplete response to survey limited our ability to assess some of the secondary outcomes. Secondly, it was difficult to account for the effect of the variation in fibre content between diets and this cannot be ruled out as a factor independent of glycaemic index that influenced some of the outcomes. In addition, obtaining information about eating habits of participants prior to entry into the study would allow the investigators to more directly compare changes seen in both diets rather than our assumption that intake reflected average UK dietary intakes. This could also be used to exclude those with unusual eating habits or to normalize intake in a pre-diet period. Thirdly, we recruited young healthy Caucasian males with the intention to limit metabolic and hormonal variability and to improve statistical power given a small sample size. However, this limits the generalisability of our findings and further work should explore if the results can be extrapolated to a wider population.

In conclusion, this study provides preliminary data that suggest that iso-energetic HGI diets compared with LGI diets lead to significant accumulations of liver fat without changes in body weight. Therefore, low glycaemic index high fibre foods offer significant health benefits in reducing liver fat fractions compared with high glycaemic index foods, and should be considered in dietary interventions in NAFLD, obesity and related metabolic disorders. Future studies should explore the impact of glycaemic index over a longer period, and also in patients with obesity or metabolic syndromes to assess whether the findings of this study can be used in the prevention and management of these conditions.

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FIGURE LEGENDS

Figure 1. (a) Plasma glucose (n=5) and (b) plasma insulin (n = 6) results on visit 1 for high (▲) and low (●) glycaemic index test days; Values are means, with SEMs represented by vertical bars. *P < 0.05 between diets, † P < 0.005 between diets using matched pair Student's t-test.

Figure 2. Liver fat fractions at fasted state and end of day (t = 360 minutes) on visit 1 and visit 2 for HGI (■) and LGI (□) dietary interventions (n=7). Values are means, with SEMs represented by vertical bars. * P < 0.05 between diets using a two way repeat measures ANOVA; ‡ P < 0.05 FF% at t = 360 min on visit 2 compared with visit 1 using matched pair Student's t-test.

Figure 3. Hepatic glycogen concentration (% baseline) across the time course on (a) visit 1 (n=8) and (b) visit 2 (n=7) for HGI (visit 1 =▲, visit 2 =△) and LGI (visit 1 = ■, visit 2 = □) test days; (c), (d) and (e) are fasted, postprandial peak and AUC respectively (n=7). Values are means, with SEMs represented by vertical bars. * P ≤ 0.05 between visits using matched pair Student's t-test, † P ≤ 0.05 significant mains effect of diet using two way repeat measures ANOVA.

Figure 4. Gastric contents volume across the time course on visit 1 and visit 2 for HGI (visit 1 =▲, visit 2 = △) and LGI (visit 1 = ●, visit 2 = ○) test days; x and y-axis are scaled equally for both visits and grid lines are included to compare absolute values. † P ≤ 0.001 between diets using matched pair Student's t-test $^{\$}$ P < 0.05 between visit 1 and visit 2 HGI using matched pair Student's t-test.

FIGURES

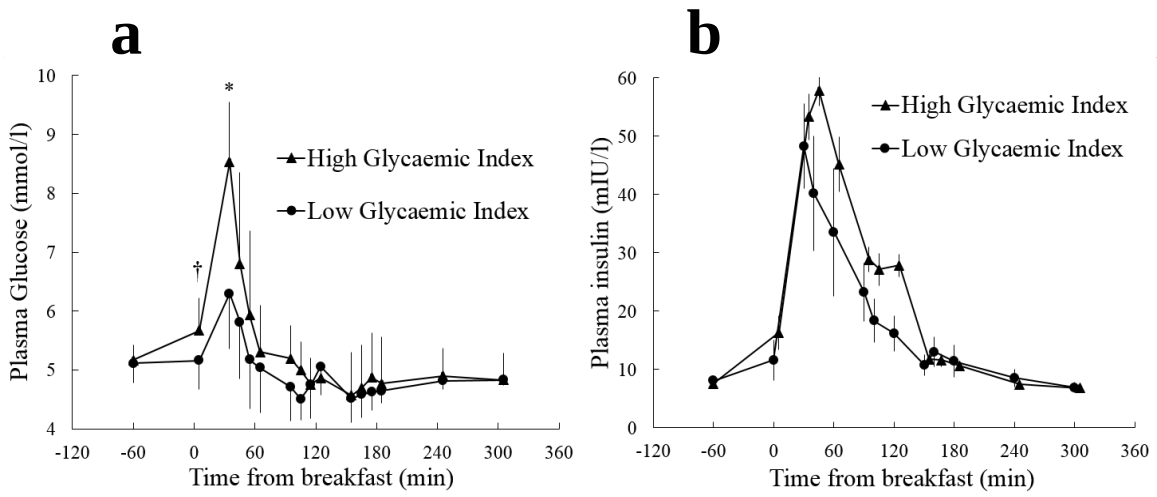

Figure 1

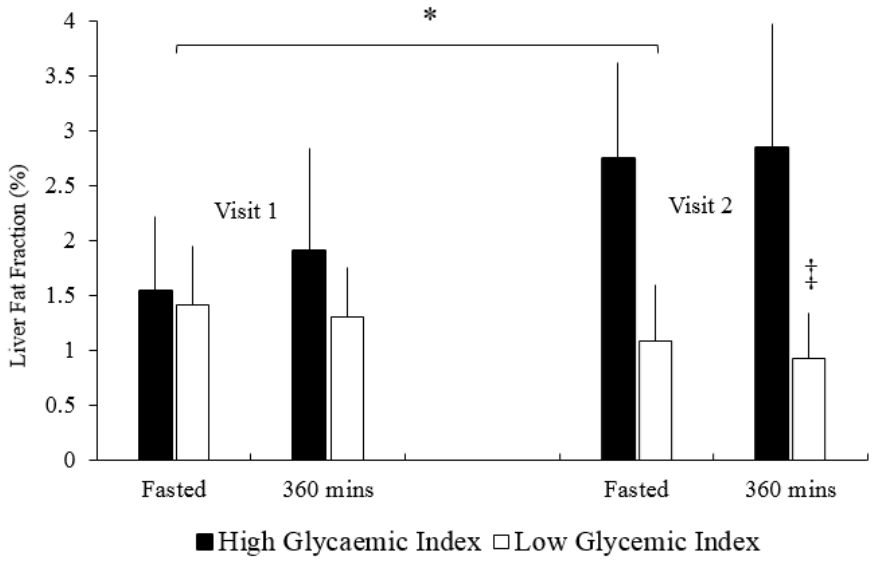

Figure 2

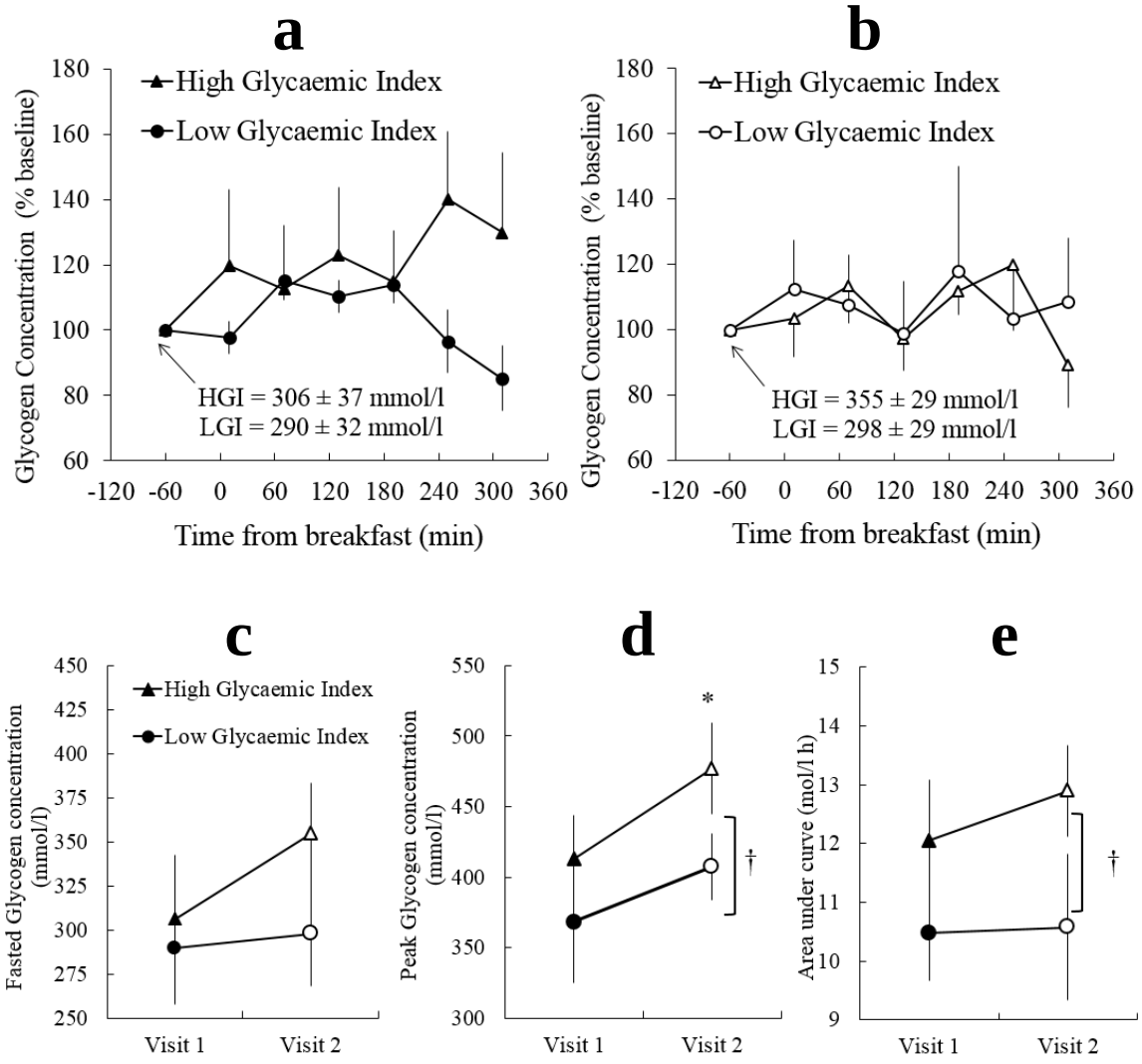
a
High Glycaemic Index
Low Glycaemic Index
Glycogen Concentration (% baseline)
HGI = 306 ± 37 mmol/l
LGI = 290 ± 32 mmol/l
Time from breakfast (min)
b
High Glycaemic Index
Low Glycaemic Index
Glycogen Concentration (% baseline)
HGI = 355 ± 29 mmol/l
LGI = 298 ± 29 mmol/l
Time from breakfast (min)
c
High Glycaemic Index
Low Glycaemic Index
Fasted Glycogen concentration (mmol/l)
Visit 1
Visit 2
d
Peak Glycogen concentration (mmol/l)
*
†
Visit 1
Visit 2
e
Area under curve (mol/l h)
†
Visit 1
Visit 2

Figure 3

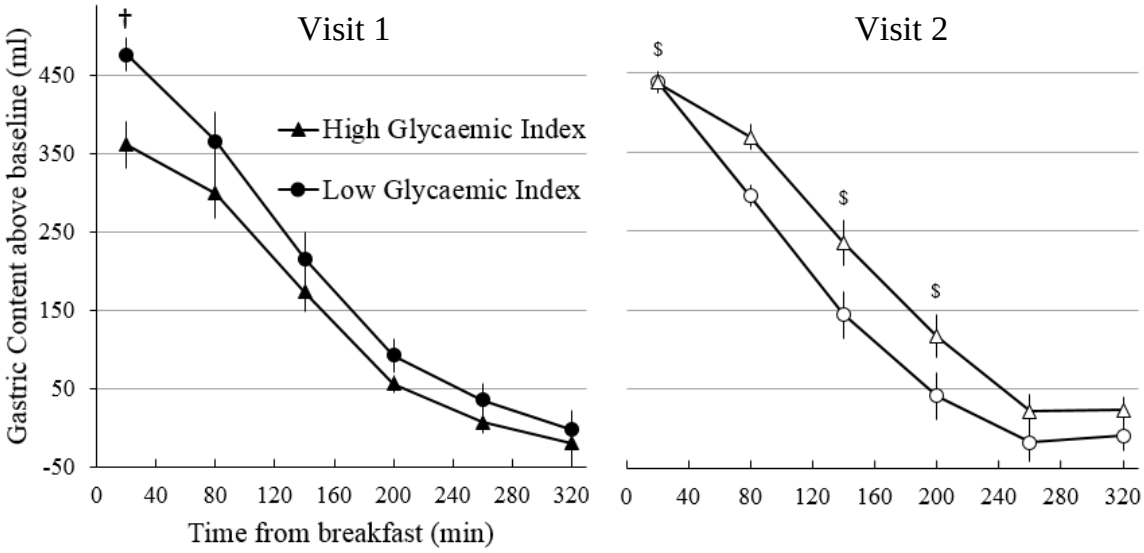
Visit 1
Visit 2
†
$
$
$
High Glycaemic Index
Low Glycaemic Index
Gastric Content above baseline (ml)
450
350
250
150
50
-50
0
40
80
120
160
200
240
280
320
Time from breakfast (min)

Figure 4