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A comparison of the appetite responses to high and low glycemic index post-exercise meals under matched insulinemia and fiber in type 1 diabetes

AUTHORS: Matthew D Campbell, Javier T Gonzalez, Penny LS Rumbold, Mark Walker, James A Shaw, Emma J Stevenson, Daniel J West

AFFILIATION: Department of Sport, Exercise and Rehabilitation, Faculty of Health and Life Sciences, Northumbria University, UK [MDC, JTG, PLSR, DJW, EJS]. Brain, Performance and Nutrition Research Centre, Faculty of Health and Life Sciences, Northumbria University, UK [JTG, EJS]. Institute of Cellular Medicine, Newcastle University, UK [MW, JAS].

CORRESPONDING AUTHIOR

Matthew D Campbell

Department of Sport, Exercise and Rehabilitation, Faculty of Health and Life Sciences, Northumbria University, Newcastle-upon-Tyne, NE1 8ST, UK

Tel: +44 0191 243 4468 Email: matthew.campbell@northumbria.ac.uk

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RUNNING TITLE: Postexercise appetite in Type 1 diabetes

ABBREVIATIONS: GI (glycemic index), LGI (low glycemic index), HGI (high glycemic index), GLP-1 (glucagon-like peptide 1).

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ABSTRACT

Background: Type 1 diabetes patients face a heightened risk of hypoglycemia following exercise. Subsequent overfeeding, as a preventative measure against hypoglycemia, negates the energy deficit following exercise. Patients are also required to reduce the insulin dose administered with post-exercise foods to further combat hypoglycemia. However, insulin dose is dictated solely by carbohydrate content, even though post-prandial glycemia is vastly influenced by glycemic index (GI). With a need to control post-exercise energy balance, the appetite responses following meals differing in GI are of particular interest. **Objective:** This study assessed the appetite response to a low (LGI) and high GI (HGI) post-exercise meal in type 1 diabetes patients. This also offered an opportunity to assess the influence of GI on appetite responses independent of insulinemia, which confounds findings in individuals without diabetes. **Design:** Ten physically-active men with type 1 diabetes completed two trials in a randomized crossover design. Following 45-min of treadmill-exercise at 70% of peak oxygen uptake, participants consumed a low (**LGI**: GI = ~37) or high GI (**HGI**: GI = ~92) meal, with matched macronutrient composition, negligible fiber content, and with insulin dose administration standardized. The postprandial appetite response was determined for 180-min post-meal. During this time, circulating glucose, insulin, glucagon and glucagon-like peptide-1 (GLP-1) concentrations, and subjective appetite ratings were determined. **Results: HGI** meals produced ~60% greater postprandial glucose AUC compared to **LGI** (p = 0.008). Insulin, glucagon and GLP-1 did not significantly differ between trials ($p > 0.05$). Fullness AUC was ~25% greater following **HGI** vs. **LGI** ($p < 0.001$), whereas hunger sensations were ~9% lower following **HGI** vs. **LGI** (p = 0.001). **Conclusions:** Under conditions of matched insulinemia and fiber, a HGI post-exercise meal suppresses feelings of hunger and augments postprandial fullness sensations more so than an otherwise equivalent LGI meal, in type 1 diabetes patients.

INTRODUCTION

Regular exercise brings a vast array of health benefits for patients with type 1 diabetes (1). However, managing diabetes, whilst integrating exercise into the lives of patients, is both complex and challenging. A heightened risk of exercise-induced and iatrogenic hypoglycemia (i.e. a fall in blood glucose concentrations below the normal physiological range) (2), often results in over-consumption of carbohydrate (3), and ultimately excessive energy intake (4) as a preventative measure. This may negate the benefits exercise offers for weight management and body composition, and could potentially contribute to a deterioration in wider diabetes management (5).

Research has shown that insufficient exercise and excessive energy intake can confer detrimental long-term implications for glycemic control and cardiovascular risk in patients (6, 7). Conversely, elevating energy expenditure through regularly exercising, and thus inducing a negative energy balance could be advantageous to glycemic control; reduced energy and carbohydrate intake may assist in the prevention of adiposity accumulation and the associated insulin resistance which occurs following diagnosis of type 1 diabetes (8). However, even in people without diabetes there is a risk of over-compensation of energy intake in response to energy expenditure (9), potentially due to increased appetite (9,10). Indeed, modulating post-exercise appetite through nutritional strategies could be advantageous for type 1 diabetes patients, thus appetite regulation following exercise is emerging as an important component of diabetes care (3, 11).

The composition of the foods consumed following exercise is of importance to type 1 diabetes patients. Work from our group illustrates reduced hyperglycemia in the acute peri- and post-exercise period when low GI (LGI) carbohydrates are consumed before and after

exercise, compared with high GI carbohydrates (HGI) (12-14). This is important, as patients with type 1 diabetes are faced with particular difficulty in normalizing glycemia around the time of exercise and more so following exercise (15). Repeated exposure to severe glycemic variability on a regular basis may be detrimental to diabetes management (5, 16). However, the impact of food composition on appetite in type 1 diabetes is less well understood.

In people without type 1 diabetes, diets that contain LGI carbohydrates are associated with reductions in appetite (17), however this may not be the case when fiber content is matched (18). The acute impact of glycemic index on appetite in a healthy population may be largely driven by insulinemia rather than glycemia, as postprandial insulin concentrations are inversely related to hunger, whereas postprandial glycemia is not (19), and gastrointestinal incretins may also play a role (20-22). Therefore, studying appetite responses following HGI and LGI meals in patients with type 1 diabetes offers a unique insight into the impact of meal glycemic index, whereby insulin-induced satiety is not confounded by dissimilar insulinemia (23), as administration of insulin dose is typically based on carbohydrate amount and not type.

Accordingly, this study had two main aims: 1) to investigate the appetite and GLP-1 response to HGI and LGI post-exercise meals in type 1 diabetes patients, thereby reflecting a typical daily situation in which exercise recommendations for minimising the risk of hypoglycemia are adhered; 2) to examine the influence of the glycemic index on appetite independent of insulinemia and fiber content.

PARTICIPANTS AND METHODS

Patients

The protocol was approved by local National Health Service Research Ethics Committee (13/NE/0016, ClinicalTrials.gov (NCT02208115). All patients provided written informed consent.

Ten type 1 diabetic men ([mean ± SEM] age 27 ± 1 years, VO_{2peak} 51.3 ± 2.1 $ml.kg^{-1}.min^{-1}$, BMI 25.5 ± 0.3 $kg.m^{-2}$, HbA_{1c} 6.7 ± 0.2%, 49.9 ± 2.4 mmol/mol) attended the Newcastle NIHR Clinical Research Facility on two occasions, separated by a minimum of seven days. All patients had long standing diabetes (duration of diabetes 15 ± 2 years), and were treated on a stable basal-bolus regimen composed of insulin aspart and once-daily insulin glargine. All patients were familiar with carbohydrate counting and were administering 1.0 ± 0.1 units of insulin aspart per 10 g of carbohydrate. Patients were not eligible if taking medication other than insulin, or supplements known to affect appetite or gastrointestinal motor function. Furthermore, patients were free of gastrointestinal disease, had not undergone gastrointestinal surgery, and were free of diabetes-related complications. In addition, all patients were regularly active participating in running-based activities a minimum of 3 times per week for at least 30 minutes on each occasion.

Experimental design

This was a randomised, counter-balanced cross-over design with two experimental arms: a LGI and HGI trial which commenced at ~17:00PM. A schematic of the experimental trial design is presented in **Supplemental Figure 1**. Patients replicated their diet (assessed using weighed dietary recording sheets) and maintained their usual insulin regimen in the 24 hours prior to each main trial. Basal insulin dose was standardised (dose, injection site, and time of injection) across trials. Moreover, real-time continuous glucose monitoring (Paradigm Veo,

Medtronic diabetes, USA) was used prior to main trials to normalise glycemia in the preceding 24 hours (for details see (12)). Patients were asked to replicate activity patterns and refrain from strenuous physical activity 48 hours before each trial. Trials were rescheduled if a patient experienced a symptomatic hypoglycemic episode or periods of severe or prolonged hyperglycemia. On each trial day, patients were provided with two standardised meals which were based on the habitual dietary patterns of type 1 diabetes patients and current recommendations for exercise in diabetic patients (4, 24). This postprandial design allows for greater translation of findings into daily life (25). The meals consisted of a cereal-based breakfast (frosted flakes, semi-skimmed milk, and peaches) equating to 1.3g.carbohdyrate.kg^{-1}BM (549 ± 20 kcal) and a pasta-based lunch (pasta, tomato-based sauce, cheddar cheese, olive oil) equating to 1.3g.carbohdyrate.kg^{-1}BM (968 ± 35 kcal). The breakfast meal was consumed at ~08:00AM, and a lunch meal consumed at ~13:00PM. Both meals were provided to patients by the research team, and consumed at home, with meal times standardised across trials. Carbohydrate intake across the experimental trial day was based on recommendations for exercising type 1 diabetes patients (2), and was calculated to be sufficient to cover the cost of the exercise bout, as determined via indirect calorimetry from predicted VO_2 and VCO_2 concentrations during exercise.

Transport was provided to patients for each laboratory attendance and trial start time was replicated. Following arrival, a resting venous blood sample was taken (see blood sampling and analysis), and patients administered a 75% reduced dose (2.0 ± 0.1 units) of rapid-acting insulin aspart, into the subcutis of the abdomen (12, 13). Injection site was taken as equidistant between the iliac crest and naval as currently recommended (15, 26, 27), and was standardized on each visit using indelible ink. With this insulin administration, patients consumed an exercise carbohydrate-based bolus (frosted flakes, semi-skimmed milk, and

peaches) equating to 1.0g.carbohdyrate.kg^{-1}BM (423 ± 15 kcal), calculated to be of medium GI (GI = 57), as per current pre-exercise recommendations (15). Sixty minutes following rapid-acting insulin administration / carbohydrate bolus ingestion, a blood sample was drawn before patients performed 45 minutes of treadmill running at an intensity to elicit 70% of VO_{2peak}. Running speed was calculated during a preliminary visit where a maximal incremental treadmill test was performed, as previously described by our group (15). For the performance of exercise, ambient temperature and humidity was controlled across trials. Blood samples were taken immediately after exercise and at 60 minutes post-exercise. At 60 minutes post-exercise, patients administered a 50% reduced dose of rapid-acting insulin aspart in anticipation of the test meals (15). Immediately following insulin administration patients consumed one of two test meals matched for energy (**HGI** 1.7 ± 0.1 MJ / 413 ± 16 kcal vs. **LGI** 1.7 ± 0.1 MJ / 409 ± 15 kcal) and carbohydrate content (1.0g.carbohydrate.kg^{-1}BM) but differing in GI (**HGI** = 37 vs. **LGI** = 92) (**Table 1**). Meals were matched for macronutrient content (Table 1), and contained negligible amounts of fiber (**HGI** = 1.0 ± 0.1 vs. **LGI** = 0.5 ± 0.1 g). The order in which test meals were consumed was randomized and counter-balanced, determined using a computer program. We calculated the GI of each meal using methods described by Brouns et al (28) in 10 non-diabetic control participants; meal composition and energy content were determined using a computer software package (Microdiet, Downlee Systems LTD, UK). Following the consumption of each test meal, patients remained rested for 180 minutes with periodic blood sampling every 30 minutes. As each meal composed of food and a beverage (standardised volume), water was withheld during the post-prandial period to control for mechanoreceptor-mediated suppression of appetite. Perceptions of appetite (hunger and fullness) were assessed across the duration of each trial, measured immediately before each blood sample point using visual analogue scales (29).

*** INSERT TABLE 1 ***

Blood sampling and analysis

At each sample point a 6-ml venous blood sample was taken of which 20µl was used for the immediate quantification of blood glucose (BG: Biosen C-Line; EKF Diagnostic GmbH, London, UK) and 10 µl analyzed for hemoglobin and hematocrit (Hemo Control; EKF Diagnostic GmbH, UK), which was used to correct for changes in plasma volume following exercise (30). The remaining sample was aliquoted evenly into serum separation (Vacuette, Greiner Bio-One GmBH, Austria) and Lithium-heparin tubes (Vacuette, Greiner Bio-One GmBH, Austria) before being centrifuged at 3000 rev.min^{-1} for 15 minutes at 4˚C and stored at -80˚C for retrospective analysis of serum rapid-acting insulin analogue (Invitron Insulin Assay; Invitron, Monmouth, UK) and plasma glucagon (Glucagon EIA, Sigma-Aldrich, USA) and total GLP-1 (Epitope Diagnostics, San Diego, CA). Further blood samples were taken at 60 minutes following pre-exercise meal / rapid-acting insulin administration (immediately before exercise), at 60 minutes post-exercise (immediately before the post-exercise-meal / rapid-acting insulin administration), and at 30, 60, 90, 120, 150, and 180 minutes following the post-exercise meal / rapid-acting insulin administration. As patients in this study had long-standing diabetes and were solely dependent upon exogenous insulin, the influence of endogenous insulin secretion from residual β-cell function was considered negligible (31). Therefore, any changes in insulin concentrations detected by this assay were considered to be due to changes in the appearance or disappearance of insulin aspart. The coefficient of variation for the biochemical analysis of serum insulin, plasma glucagon and plasma GLP-1 was <10%.

Statistical analysis

All data are presented as mean ± SEM. Data presented as Area Under the Curve (AUC) was calculated using methods described by Wolever and Jenkins (32). Delta changes in AUC

from pre-test meal scores / concentrations were calculated by subtracting subsequent values from pre-test meal scores. PASW *Statistics* software (IBM PASW version 18; IBM, Armonk, NY, USA) was used to analyse data. Within and between condition responses were examined using repeated measures ANOVA on two levels (time*condition). Where significant *p*-values were identified for interaction effects (time*condition), GI was deemed to have influenced the response, and simple main effects analyses were performed. Significant main effects of time were further investigated using Bonferroni adjusted pairwise comparisons. Relationships were explored using Pearson's product moment correlation coefficient. Paired samples t-tests were conducted as relevant. Statistical significance was accepted at $p \leq 0.05$.

RESULTS

Glycemic control was comparable over the 24 hours prior to patients' arrival at the laboratory for both experimental trials (CGM mean glucose: **HGI** 10.4 ± 1.0, **LGI** 9.4 ± 1.1 mmol.l^{-1}; p = 0.534; and total interstitial glucose $AUC_{0\text{-}24hrs}$: **HGI** 11324 ± 1056, **LGI** 10212 ± 1228 mmol.l^{-1} over 24 hours; p = 0.382). In addition, there were no differences in dietary intake, insulin administration, or levels of physical activity during this time (**Table 2.0**).

INSERT TABLE 2

There were no differences in glycemia, serum insulin, plasma glucagon concentrations or appetite scores prior to the consumption of the post-exercise test meals (p > 0.05), such that immediately before administration, patients displayed similar blood glucose (BG: **HGI** 6.2 ± 0.7 vs. **LGI** 5.8 ± 0.5 mmol.l^{-1}, p = 0.169), serum insulin (**HGI** 106 ± 15 vs. **LGI** 102 ± 14 pmol.l^{-1}, p = 0.986), plasma glucagon concentrations (**HGI** 732 ± 99 vs. **LGI** 735 ± 103 pg.ml^{-1}, p = 0.884) and total GLP-1 (**HGI** 1.95 ± 0.21 vs. **LGI** 2.47 ± 0.87 pmol.l^{-1}, p = 0.620). At this time, sensations of hunger (**HGI** 68 ± 3 vs. **LGI** 67 ± 2, p = 0.925) and fullness (**HGI** 60 ± 2 vs. **LGI** 61 ± 2, p =0.791) were similar between conditions.

Following administration of rapid-acting insulin and post-exercise test meals, serum insulin peaked similarly at 30 to 60 minutes under both conditions (**HGI** 181 ± 26 vs. **LGI** 175 ± 30 pmol.l^{-1}, p = 0.773; **Figure 1A**). Temporal changes in serum insulin remained similar beyond this time (p > 0.05), with concentrations returning to periprandial measures at 180 minutes (p > 0.05). Moreover, total insulin AUC were similar between conditions over the postprandial period ($AUC_{0\text{-}180mins}$: **HGI** 49576 ± 6786 vs. **LGI** 43924 ± 6196 pmol.l^{-1} over 180 min, p = 0.332). BG increased from periprandial concentrations over the postprandial period under both conditions, but elevations were significantly more pronounced under **HGI**, with higher

mean peaks (**HGI** +10.2 ± 0.5 vs. **LGI** +3.2 ± 0.6 mmol.l^{-1}, $p < 0.001$; **Figure 1B**) and individualized peaks (**HGI** 15.8 vs. **LGI** 12.9 mmol.l^{-1}). Total BG AUC was significantly greater under **HGI** ($AUC_{0\text{-}180mins}$: **HGI** 2205 ± 90 vs. **LGI** 1437 ± 107 mmol.l^{-1} over 180 min, $p = 0.002$), displaying a significantly greater average change in absolute BG concentrations over the post-meal period compared to the average change under **LGI** (**HGI** +6.6 ± 0.9 vs. **LGI** +1.7 ± 0.4 mmol.l^{-1}, $p < 0.001$). As such, patients under **HGI** were, on average, hyperglycemic (**HGI** 12.8 ± 0.5 mmol.l^{-1}; Figure 1B), whereas patients under **LGI** typically remained within euglycemic ranges (**LGI** 7.6 ± 0.6 mmol.l^{-1}, $p = 0.002$). Glucagon concentrations were significantly increased following the administration of both meals peaking similarly 30 minutes after consumption (**Figure 2A**). Following this, concentrations declined under **HGI** such that at 180 minutes concentrations were significantly lower than pre-meal, whereas the decline under **LGI** was largely attenuated (Figure 2A). However, total glucagon AUC was not statistically different between LGI and HGI ($AUC_{0\text{-}180mins}$: **LGI** 264150 ± 98209 vs. **HGI** 247054 ± 79042 pg.ml^{-1} over 180 min, $p = 0.141$). Temporal increases in total GLP-1 at 60 minutes following the meal were not statistically significant ($p = 0.223$) with concentrations similar to baseline under both conditions throughout the remaining post-prandial period (**Figure 2B**).

INSERT FIGURE 1A-B

INSERT FIGURE 2A-B

INSERT FIGURE 3A-B

Sensations of hunger peaked at 60 minutes following consumption under both conditions, (**Figure 3AB**). Over the remaining 120 minutes hunger sensations decreased under **HGI**, (Figure 3AB). Inversely under **LGI**, no further increases in hunger were apparent, meaning total AUC for feelings of hunger and fullness were significantly higher ($AUC_{0\text{-}180mins}$: **LGI** 7619 ± 1130 vs. **HGI** 6961 ± 1050 $mmol.l^{-1}$ over 180 min, p <0.001) and lower under the **LGI** trial ($AUC_{0\text{-}180mins}$: **LGI** 2669 ± 421 vs. **HGI** 3345 ± 561 $mmol.l^{-1}$ over 180 min, p <0.001).

In the **LGI** trial, a negative relationship was observed between total post-meal BG AUC and hunger AUC (r^2 = 0.420, p = 0.039), but not fullness AUC (r^2 = 0.003, p = 0.910) or serum insulin AUC (r^2 <0.001, p = 0.977), plasma total GLP-1 (r^2 = 0.009, p = 0.543). Neither hunger (r^2 = 0.002, p = 0.900) nor fullness (r^2 = 0.020, p = 0.699) were associated with changes in serum insulin AUC. Glucagon AUC and total GLP-1 were not associated with any other variable under **LGI**. No other correlations were observed between measures under **HGI** (p > 0.05; see **supplemental figure 2AD and 3AD** for correlations).

DISCUSSION

The aims of this study were two-fold, 1) to investigate the influence of manipulating the glycemic index of meals consumed following exercise on appetite responses in patients with type 1 diabetes, and 2) examine the influence of glycemic index on appetite independent of insulinemia and fiber content. We demonstrate for the first time that a HGI meal consumed following exercise elevates subjective feelings of fullness and supresses sensations of hunger in patients with type 1 diabetes, compared to an isoenergetic LGI meal. It is important to note that these responses were observed under comparable insulinemia, plasma glucagon and GLP-1 concentrations, and when meals were matched for macronutrient composition and fiber content.

Work from our group illustrates the clinical utility of consuming meals with a LGI around the time of exercise; specifically, LGI meals before and after exercise offer more favourable postprandial glycemic profiles without increasing risk of post-exercise hypoglycemia in type 1 diabetes patients (12-14). This is important because the inclusion of exercise into the lives of patients is severely hampered by difficulties in managing post-exercise glycemia. From this present study however, we now reveal that patients may experience lower levels of satiety following LGI consumption in the post-exercise recovery period. Although it would be naïve to infer these findings to longer-term observations, our data may indicate likelihood for increased calorie intake following exercise due to increased appetite rather than avoidance of hypoglycemia *per se*. This may have important implications for long-term weight management in this population, and may contrast data in non-diabetic individuals which demonstrate an improvement in weight management following LGI carbohydrate diets (33). Of note however, we did not assess ad libitum energy intake in this present study. Therefore it is possible that perceived ratings of hunger or fullness may not directly translate to changes

in energy intake. However, we provide the first evidence of altered appetite responses to meal GI following exercise in type 1 diabetes.

We have previously demonstrated that with fiber-matched meals, a higher glycemic response is associated with greater postprandial feelings of fullness in a non-diabetic population (18). Based on strong positive correlations of fullness and postprandial insulinemia in humans (19), taken in concert with the acute induction of satiety with intracerebroventricular administration of insulin in baboons (23), we hypothesised that insulin was a confounding factor in their appetite responses. In the present study, we provided HGI and LGI meals in the post-exercise period in people with type 1 diabetes, therefore we were able to manually control for insulin concentrations due to an absolute deficiency in endogenous insulin appearance. Accordingly, insulin concentrations were similar at every time point in the postprandial period (Figure 1A), whereas marked increases in postprandial glucose concentrations were evident with HGI vs. LGI (Figure 1B) as expected. This observation in concordance with pre-trial GI testing confirmed that the meals significantly differed in glycemic index. Therefore the results of the present study indicate that HGI meals induce greater satiety independent of the insulin response that is typical of these meals (34).

These findings are consistent with previous infusion studies in people with and without type 1 diabetes, whereby hyperglycemic (~14 and ~10 $mmol.l^{-1}$) intravenous infusion reduced hunger sensations compared to euglycemia (~6 $mmol.l^{-1}$) (35, 36). Interestingly, these effects are more apparent in the postprandial state (35), suggesting an interaction with the gastrointestinal tract. Using ^{13}C octanoic acid, Russell et al (35). attempted to assess whether gastric emptying could explain the reduction in hunger seen under postprandial hyperglycemia (35). The gastric emptying coefficient (representing global gastric emptying

rate) tended (p = 0.052, n = 6) to be ~9% greater (i.e. slower gastric emptying) with postprandial hyperglycemia vs. euglycemia (35), which has also been shown by others (37-39). Taken together, hyperglycemic-induced delayed gastric emptying and the associated mechanoreceptor-mediated suppression of appetite (40) could be a possible contributory mechanism to explain the effect we have observed.

Another potential mechanism to explain the reduced hunger sensations with HGI vs LGI could be through portal vein signalling (41). With HGI, high glucose concentrations would likely be present in the portal vein. Since portal glucose infusions in postabsorptive rodents decreases food consumption and increases the number of c-*fos*-like immunoreactive neurons in the arcuate nucleus (41), this suggests that portal glucose enhances the activity of hypothalamic nuclei associated with appetite suppression. Furthermore, this response is attenuated by portal vein denervation (41), demonstrating the importance of this pathway for glucose sensing and appetite. Whilst glucagon displays anorectic properties (42), it is implausible that this explains the appetite response we observed in this study, since glucagon concentrations did not significantly differ between trials.

GLP-1 may play a role in the appetite response to HGI and LGI meals in healthy populations (21, 43), although the evidence for a differential GLP-1 response to HGI vs. LGI mixed-meals in equivocal (17). We chose to measure GLP-1 because it is considered at least partly active in type 1 diabetes patients (22), whereas other incretins such as gastric inhibitory polypeptide are largely absent (44). Postprandial responses in GLP-1 are thought to differ to those elicited by healthy non-diabetic individuals (22), and we now demonstrate that there is no significant difference in the GLP-1 response to HGI vs. LGI meals, consumed following

exercise in type 1 diabetes patients. We encourage further work to explore the wider role that incretins play in modulating appetite responses in this population.

The difference in fiber content between the HGI and LGI meals was small (0.5 g). Meta-analyses indicate that fiber reduces subjective sensations of hunger and subsequent energy intake (45). The difference between meals in the present study however, is not likely to have played a role in the response we have observed, as a 1 g increase in fiber intake suppresses appetite by ~0.18% (45). In the current investigation we observed a ~9% and ~25% difference in the postprandial AUC for hunger and fullness, respectively. Given the ~0.5 g difference in fiber would influence these responses by at least 2 orders of magnitude less (~0.09%) we consider this a negligible difference.

These findings should be considered in the context of more global diabetes care, as LGI post-exercise meals produce more suitable glycemic control than HGI (14), However, we demonstrate that a post-exercise HGI meal acutely induces greater fullness and less hunger, independent of insulin, in patients with type 1 diabetes. The clinical application of these findings should not be underestimated; interventions were carried out in the evening, in a non-fasted state, thereby facilitating greater translation to daily life (46). It is important to consider that our patients were young, physically fit, and well-controlled, and that responses observed herein may not be directly transferable to the wider type 1 diabetes population who may to be less physically active, in poorer glycaemic control and who may be treated on different insulin regimens. Further work is needed to clarify the mechanisms of this effect in well-controlled and physically-active patients and to establish the long-term implications of this response in a wider cohort of patients regularly participating in exercise. In addition we advise that future investigations feature assessment of prospective ad libitum dietary intake to

374 determine whether changes in appetite are matched with increased energy intake. In
375 conclusion, HGI post-exercise meals induce greater postprandial feelings of fullness and
376 lower postprandial hunger sensations in type 1 diabetes patients, under conditions of similar
377 insulinemia and plasma GLP-1 concentrations.
378
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384
385 **AUTHORS' CONTRIBUTIONS**
386 **MDC** designed research, conducted research, analysed data and wrote the manuscript. **JTG**
387 conducted research analysed data and wrote the manuscript. **PLSR** reviewed the manuscript
388 and contributed to its preparation. **MW** conducted research, provided essential materials, and
389 reviewed the manuscript. **JAS** conducted research, provided essential materials, and reviewed
390 the manuscript. **DJW** designed research, conducted research and contributed to the
391 preparation and write up of the manuscript. **EJS** designed research, conducted research,
392 contributed to the preparation and write up of the manuscript, and has responsibility for final
393 content.

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TABLES

Table 1. Meal composition and glycemic index

	GI	Energy (kcal)	CHO (g)	Fat (g)	Protein (g)	Fiber (g)
Evening meal						
LGI	37	409±15	85±1	12±1	2±0.4	0.5±0.1
HGI	92	413±16	85±1	12±1	2±0.4	1±0.1

NOTE: test meals were based on 1.0g.carbohydrate.kg^{-1} body mass (BM). LGI evening meal: basmati rice, tomato-based sauce, turkey breast, isomaltulose orange flavoured drink [10% solution]; HGI evening meal: jasmine rice, tomato-based sauce, turkey breast, maltodextrin orange flavoured drink [10% solution].

Table 2. Pre-trial dietary intake, insulin administration, and physical activity

	HGI	LGI	*p* value
Energy intake (MJ)	9.5 ± 0.9	9.4 ± 0.8	0.776
Carbohydrate (%)	49 ± 3	49 ± 3	0.999
Fat (%)	32 ± 3	32 ± 3	0.879
Protein (%)	19 ± 2	20 ± 3	0.887
Rapid-acting insulin (IU)	24 ± 4	25 ± 4	0.803
Levels of activity (steps)	7492 ± 140	7325 ± 129	0.202

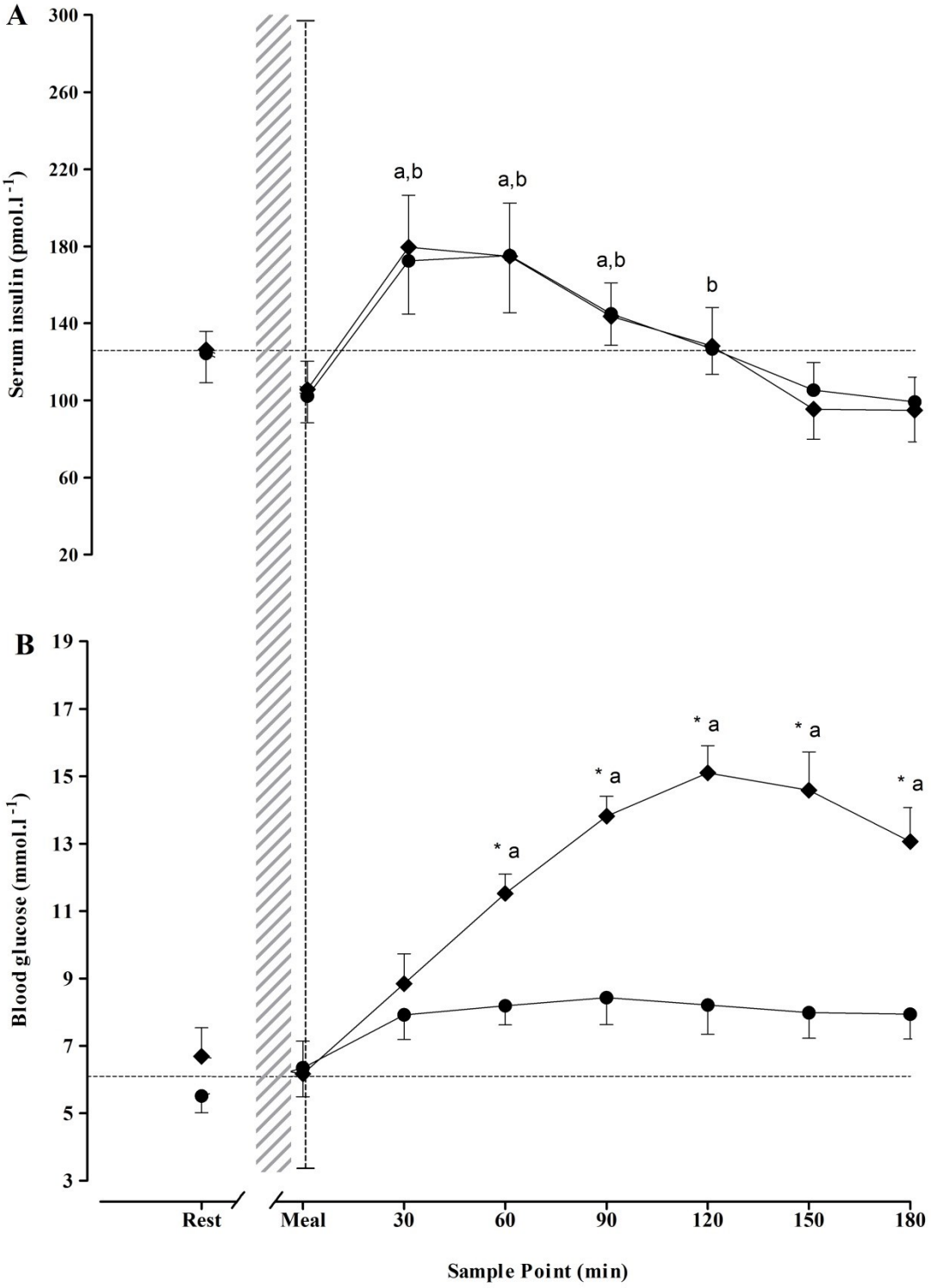
Note: Data collected over 48 hours prior to laboratory attendance and presented as mean ± SEM (n=10). Data were analyzed using paired samples t-tests. IU = insulin units. Steps recorded via pedometer.

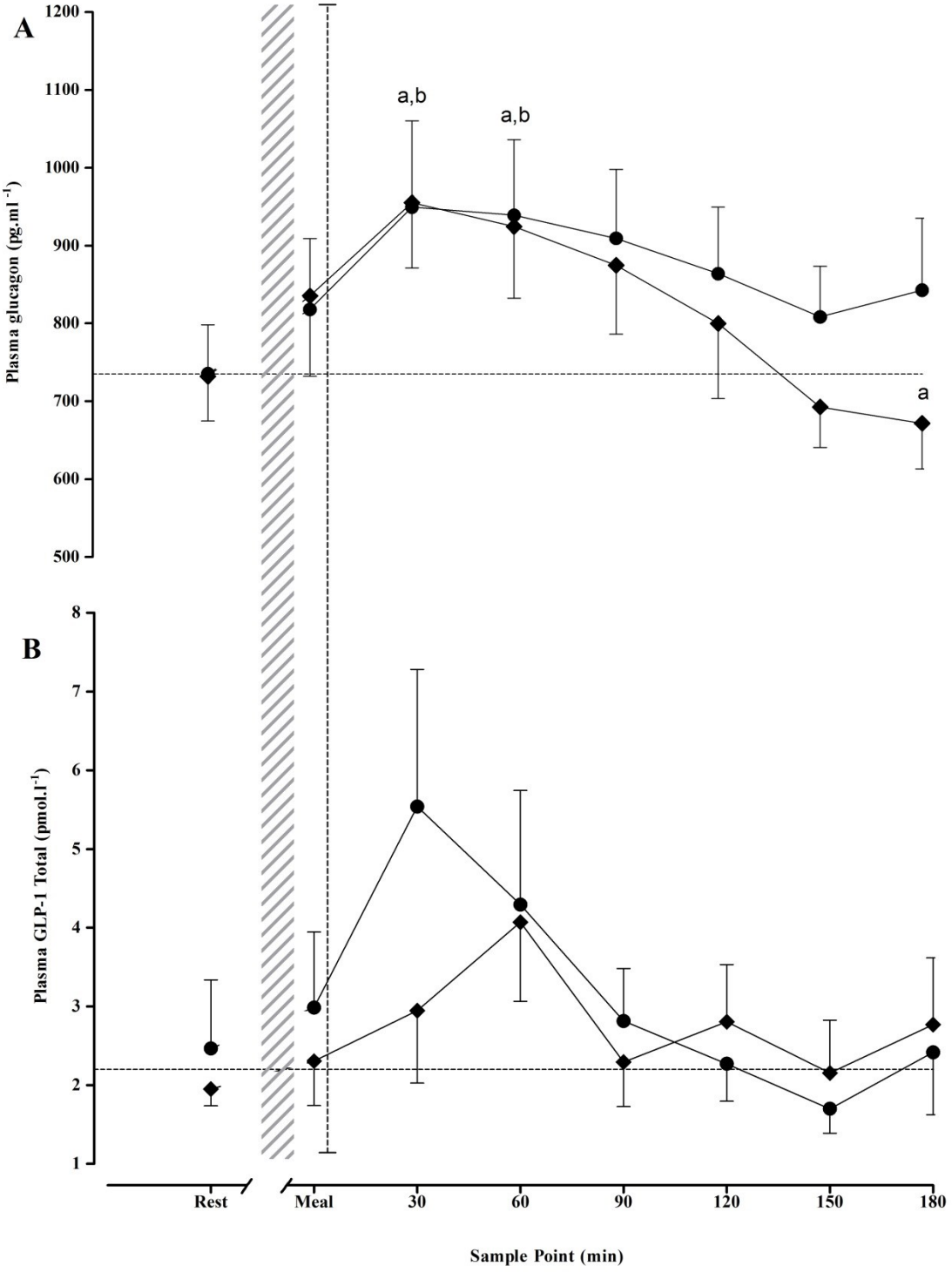
FIGURES

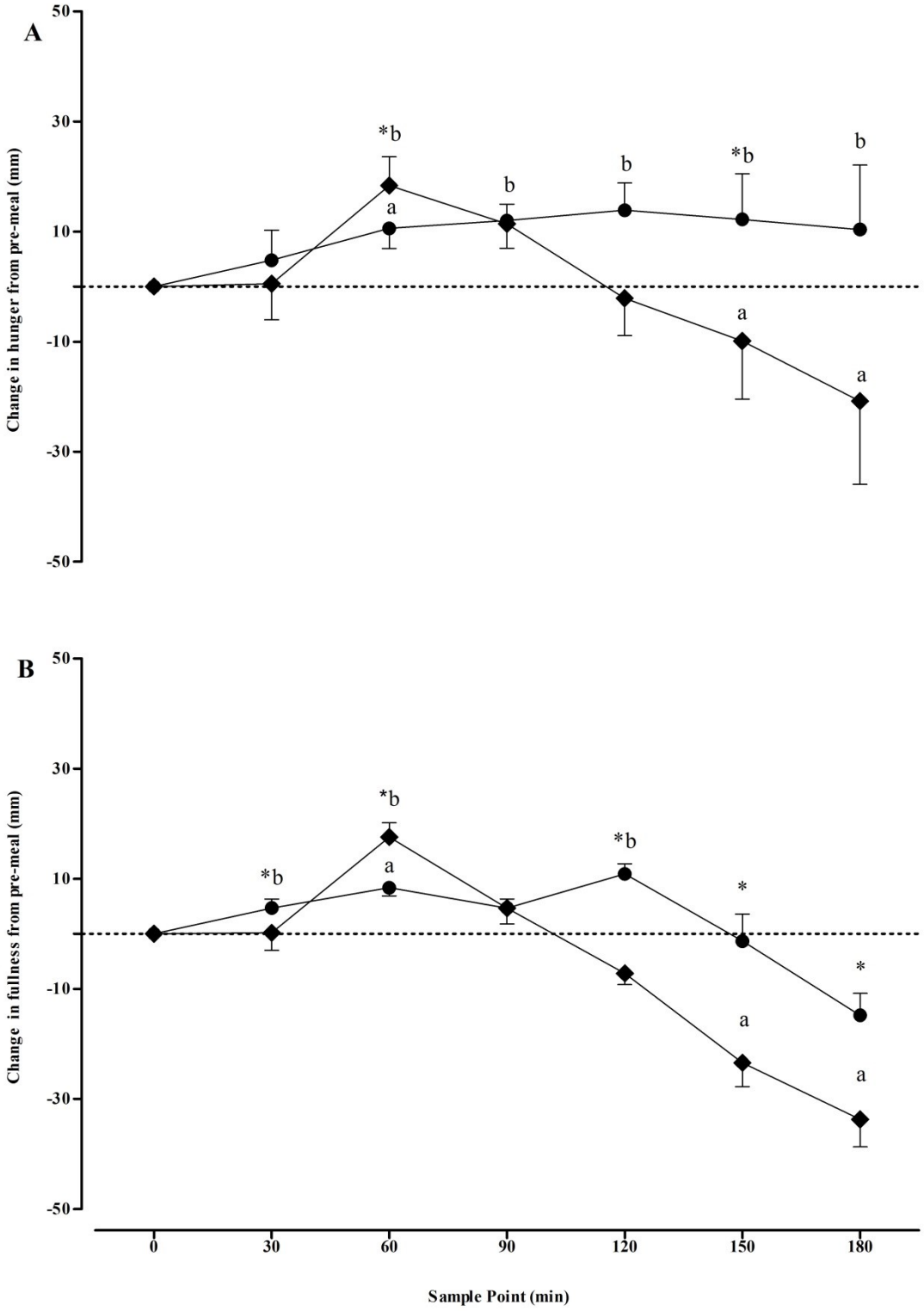
Figure 1 A-B. Time-course changes in (**A**) serum insulin and (**B**) blood glucose. Data presented as mean ± SEM (n=10). Data were analysed using repeated measures ANOVA and subsequent Bonferroni adjusted pairwise comparisons. Black diamonds = **HGI**, black circles = **LGI**. * indicates a difference between **LGI** and **HGI** ($p \leq 0.05$). *a* indicates a significant difference from pre-test meal concentrations under **HGI**, *b* indicates a significant difference from pre-test meal concentrations under **LGI**. Vertical dashed line break indicates post-exercise intervention, which occurred 60 minutes post-exercise. Thatched area indicates exercise.

Figure 2 A-B. Time-course changes in (**A**) plasma glucagon and (**B**) plasma GLP-1 total. Data presented as mean ± SEM (n=10). Data were analysed using repeated measures ANOVA and subsequent Bonferroni adjusted pairwise comparisons. Black diamonds = **HGI**, black circles = **LGI**. * indicates a difference between **LGI** and **HGI** ($p \leq 0.05$). *a* indicates a significant difference from pre-test meal concentrations under **HGI**, *b* indicates a significant difference from pre-test meal concentrations under **LGI**. Vertical dashed line break indicates post-exercise intervention, which occurred 60 minutes post-exercise. Thatched area indicates exercise.

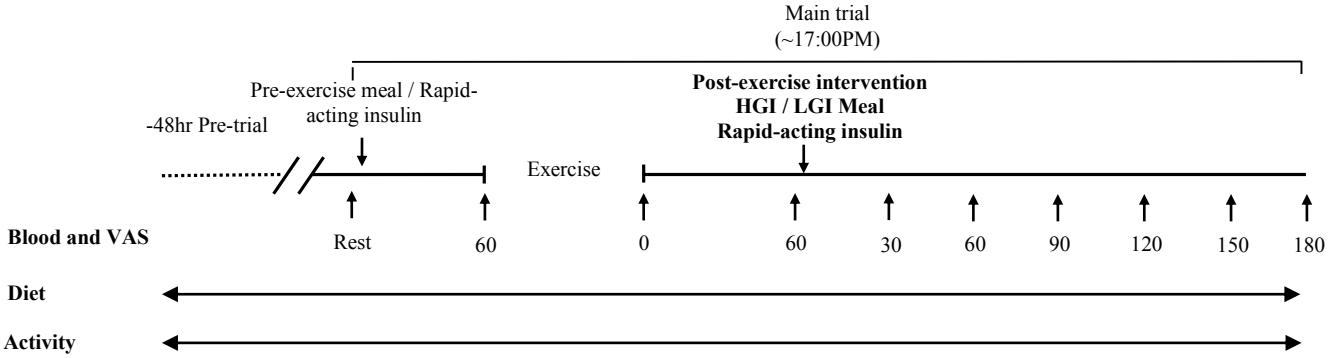
Figure 3A-B. Time courses in (**A**) hunger and (**B**) fullness following the consumption of the post-exercise test meals. Data presented as mean ± SEM (n=10). Data were analysed using repeated measures ANOVA and subsequent Bonferroni adjusted pairwise comparisons. Black diamonds = **HGI**, black circles = **LGI**. * indicates a difference between **LGI** and **HGI** ($p \leq 0.05$). *a* indicates a significant difference from pre-test meal concentrations under **HGI**, *b* indicates a significant difference from pre-test meal concentrations under **LGI**.


A
Serum insulin (pmol.l-1)
300
260
220
180
140
100
60
20
a,b
a,b
a,b
b
B
Blood glucose (mmol.l-1)
19
17
15
13
11
9
7
5
3
* a
* a
* a
* a
* a
Rest
Meal
30
60
90
120
150
180
Sample Point (min)


A
B
Plasma glucagon (pg.ml-1)
Plasma GLP-1 Total (pmol.l-1)
a,b
a,b
a
Rest
Meal
30
60
90
120
150
180
Sample Point (min)


A
Change in hunger from pre-meal (mm)
50
30
10
-10
-30
-50
*b
a
b
b
*b
b
a
a
B
Change in fullness from pre-meal (mm)
50
30
10
-10
-30
-50
*b
*b
a
*b
*
*
a
a
0
30
60
90
120
150
180
Sample Point (min)

SUPPLEMENTAL Figure 1.



Suppl. Figure 1 Schematic of trial design. Note: Blood glucose, serum insulin, plasma glucagon, plasma GLP-1, and VAS were analyzed at each respective blood sample time point.