# Ingestion of Glucose or Sucrose Prevents Liver but not Muscle Glycogen Depletion During Prolonged Endurance-type Exercise in Trained Cyclists

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**Running head:** Carbohydrate ingestion and liver glycogen depletion

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## ABSTRACT

**Purpose:** To define the effect of glucose ingestion compared to sucrose ingestion on liver and muscle glycogen depletion during prolonged endurance-type exercise. **Methods:** Fourteen cyclists completed two 3-h bouts of cycling at 50% of peak power output while ingesting either glucose or sucrose at a rate of 1.7 g/min (102 g/h). Four cyclists performed an additional third test in which only water was consumed for reference. We employed $^{13}C$ magnetic resonance spectroscopy to determine liver and muscle glycogen concentrations before and after exercise. Expired breath was sampled during exercise to estimate whole-body substrate use. **Results:** Following glucose and sucrose ingestion, liver glycogen levels did not show a significant decline following exercise (from 325±168 to 345±205 and 321±177 to 348±170 mmol/L, respectively; $P>0.05$) with no differences between treatments. Muscle glycogen concentrations declined (from 101±49 to 60±34 and 114±48 to 67±34 mmol/L, respectively; $P<0.05$), with no differences between treatments. Whole-body carbohydrate utilization was greater with sucrose (2.03±0.43 g/min) vs glucose ingestion (1.66±0.36 g/min; $P<0.05$). Both liver (from 454±33 to 283±82 mmol/L; $P<0.05$) and muscle (from 111±46 to 67±31 mmol/L; $P<0.01$) glycogen concentrations declined during exercise when only water was ingested. **Conclusion:** Both glucose and sucrose ingestion prevent liver glycogen depletion during prolonged endurance-type exercise. Sucrose ingestion does not preserve liver glycogen concentrations more than glucose ingestion. However, sucrose ingestion does increase whole-body carbohydrate utilization compared to glucose ingestion. This trial was

registered at clinicaltrials.gov as NCT02110836. ***Keywords:*** glucose; hepatic; metabolism; nutrition; sucrose

## Introduction

Carbohydrate and fat are the main substrates oxidized during moderate-intensity, endurance-type exercise (41). In the fasted state, muscle glycogen and plasma glucose are predominant sources of carbohydrate for oxidation (41), the latter continuously replenished by glycogenolysis and gluconeogenesis from the liver, with smaller contributions from the kidneys and intestine (30). Consequently, in the absence of carbohydrate consumption, liver and muscle glycogen concentrations decrease by 40-60% within 90 min of exercise at a workload of 70% of peak oxygen uptake ($\dot{V}O_{2\ peak}$) (6, 37). Given the importance of liver glycogen for metabolic regulation (16), and the close relationship between liver glycogen content and exercise tolerance (6), it is important to understand the impact of carbohydrate ingestion on liver glycogen depletion during exercise.

Carbohydrate feeding during prolonged (>2 h) moderate-to-high intensity, endurance-type exercise enhances endurance performance and capacity (42), attributed to the facilitation of high rates of carbohydrate oxidation, prevention of hypoglycaemia and (under certain conditions) sparing of muscle glycogen (7, 38). Though some support has been provided that carbohydrate ingestion can attenuate muscle glycogen depletion (36, 39, 40), others have failed to confirm these findings (8, 12, 15, 20). Furthermore, prevention of liver glycogen depletion has been suggested (3, 20, 21), but this has never been experimentally assessed. We speculate that carbohydrate ingestion during exercise attenuates the decline in both liver as well as skeletal muscle glycogen contents.

To maximize carbohydrate availability during exercise, carbohydrate digestion and absorption should be optimized. Previous work suggests that exogenous glucose uptake by the gastrointestinal tract during exercise is restricted to ~1 g/min (5, 17, 19), attributed to saturation of the sodium-glucose luminal transporter-1 (SGLT-1). However, combined ingestion of glucose and fructose at ≥1.8 g/min has been shown to result in much higher exogenous carbohydrate oxidation rates (up to 1.75 g/min), compared to the ingestion of equal amount of glucose alone (17, 19). The greater uptake and oxidative capacity of glucose and fructose mixtures has been attributed to fructose being absorbed by the glucose transporter-5 (GLUT-5) in the intestine (11). As sucrose (commonly referred to as table sugar) combines glucose and fructose monomers, and sucrose hydrolysis is not rate limiting for intestinal absorption (14, 43), we hypothesize that sucrose ingestion at a rate exceeding 1 g/min will enhance exogenous carbohydrate availability when compared to the ingestion of an isoenergetic amount of glucose or glucose polymers. Moreover, since fructose appears to be preferentially directed to liver glycogen storage (relative to glucose) (32), sucrose may further prevent liver glycogen depletion during exercise.

The present study aimed to investigate the effect of high rates of glucose and sucrose ingestion on net changes in liver and muscle glycogen contents and intramyocellular lipid concentrations using magnetic resonance spectroscopy (MRS). We hypothesized that high-rates of carbohydrate ingestion would spare liver glycogen during prolonged exercise, and that sucrose ingestion would better maintain liver glycogen relative to glucose ingestion.

## Methods

*Study design*

Participants completed preliminary testing prior to 2 main trials, during which subjects either ingested glucose (GLU) or sucrose (SUC) in a randomized, double-blind, crossover design separated by 7-14 d. Trials were conducted at the Newcastle Magnetic Resonance Centre (Newcastle-upon-Tyne, UK) in accordance with the Second Declaration of Helsinki, and following approval from the Northumbria University Faculty of Health and Life Sciences Ethics Committee. Randomization was performed using online statistical software (http://www.randomizer.org/). Blinding and preparation of the test-drinks was performed by an assistant who was not involved in the exercise tests.

In addition to the two main trials, four participants completed an additional control trial (CON) as a reference to establish the change in liver glycogen concentration without carbohydrate ingestion. This was identical to the SUC and GLU trials, with the exception that only water was ingested during exercise (identical volume to GLU and SUC trials), and blood sampling was not performed.

*Participants*

Fifteen trained cyclists were recruited for the study. Inclusion criteria included healthy, endurance trained, male cyclists; $\dot{V}O_{2peak}$ ≥50 mL/min/kg/. Exclusion criteria included the use of medication that could influence substrate metabolism, smokers and any known metabolic disorders. One participant was unable to complete the full 3 h cycling protocol due to nausea on the GLU

trial and was therefore excluded from the analysis. Consequently, 14 participants completed the two main trials.

*Preliminary testing*

An incremental cycling test was performed on an electromagnetically braked cycle ergometer (Velotron, RacerMate Inc., Seattle, WA, USA) to determine peak power output ($W_{peak}$) and peak oxygen uptake ($\dot{V}O_{2peak}$). Following a 5-min warm-up at 100 W, the workload began at 150 W and was increased by 50 W every 2.5 min to voluntary exhaustion (23). Expired gas was sampled continuously to determine oxygen uptake (Oxycon gas analyser, CareFusion corporation, San Diego, CA, USA).

*Main trials*

Participants arrived at Newcastle Magnetic Resonance Centre at 0700-0800 h following a 12 h fast. Strenuous exercise was prohibited for 24 h prior to trials, and participants were asked to record and replicate dietary intake for 24 h prior to trials. The final meal consumed on the evening before the main trials was provided by the investigators to participants to standardize the macronutrient intake across participants for this meal (25 g protein, 51 g carbohydrate and 32 g fat; 2479 kJ; 592 kcal).

MRS was used to determine liver and muscle glycogen and intramyocellular lipid concentrations prior to and following 3 h of cycling. Following a 5 min warm-up at 100 W, power output was increased to 50% $W_{peak}$ for the remainder of the 3 h. Immediately prior to exercise, participants were provided

with 600 mL (86.4 g carbohydrate) of the test-drink, and then a further 150 mL (21.6 g carbohydrate) every 15 min during exercise. Four of the 14 cyclists did not manage to consume all of the carbohydrate on their first trial (which was a GLU trial for two participants, and a SUC trial for the other two participants) and therefore their carbohydrate intake was replicated for their second trial (the carbohydrate intakes for these four cyclists therefore ranged from 238-281 g, mean ± SD: 292 ± 101 g, compared to the 324 g prescribed). This lead to an average rate of carbohydrate intake for the entire group of 1.7 ± 0.2 g/min and 1.7 ± 0.2 g/min (102 ± 12 g/h and 102 ± 12 g/h) during GLU and SUC trials, respectively ($P > 0.05$; **Table 1**).

*Carbohydrate drinks*

Carbohydrate drinks were prepared by mixing 108 g of carbohydrate with 750 mL of water in an opaque bottle. This was replicated two more times to produce 3 bottles, each with 750 ml of a 7% carbohydrate solution; 324 g of carbohydrate in total. Both sources of carbohydrate were from plants that use $C_3$ carbon fixation to minimize differences in the natural abundance of $^{13}C$ (33). Accordingly, the glucose drink was produced with dextrose monohydrate obtained from wheat (Roquette, France) and the sucrose drink was produced with granulated sugar beet (AB Sugar, UK).

*Blood sampling and analysis*

Prior to exercise, an intravenous catheter was inserted into an antecubital vein for regular sampling. Blood samples were obtained prior to the exercise bout, and every 30 min during exercise. Briefly, 10 mL of blood was collected

177 in EDTA-vacutainers and immediately centrifuged at 2000 g for 10 min at 4°C.
178 Plasma was then aliquoted and stored at -80°C for subsequent determination
179 of insulin (IBL International, Hamburg, Germany) and non-esterified fatty acid
180 (NEFA) concentrations (WAKO Diagnostics, Richmond, VA) in duplicate
181 (intra- and inter-assay coefficients of variation all <10%). An additional 20 µL
182 of whole blood was collected in a capillary tube and was used to determine
183 glucose and lactate concentrations immediately (Biosen C_line, EKF
184 Diagnostics, Magdeberg, Germany).
185
186 *Expired gas analysis*
187 Expired breath samples were taken every 30 min throughout exercise using
188 the Douglas bag technique (9) accounting for variance in ambient oxygen and
189 carbon dioxide concentrations (1). A mouthpiece connected to a two-way,
190 non-rebreathing valve (model 2730, Hans Rudolph, Kansas City, Missouri),
191 was used to collect gas samples (60 s sample after a 60 s stabilization
192 phase), analysed for concentrations of oxygen and carbon dioxide using a
193 paramagnetic and infrared transducers, respectively (Servomex 5200S,
194 Crowborough, East Sussex, UK). Sensors were turned on 60 min prior to a
195 two-point calibration (zero: 100% nitrogen; span: 20% oxygen and 8% carbon
196 dioxide) using accuracy certified gas standards (BOC Industrial Gases, Linde
197 AG, Munich, Germany).
198
199 Ambient temperature, humidity and barometric pressure using a Fortin
200 barometer (F.D. and company, Watford, UK) were recorded, and expired gas
201 samples were corrected to standard temperature and pressure (dry). Volume

and temperature of expired gas samples were determined using a dry gas meter (Harvard Apparatus, Edenbridge, Kent, UK) and thermistor (model 810-080, ETI, Worthing, UK), respectively, during gas evacuation. Calibration of the dry gas meter was performed regularly with a 3-L syringe (Series 5530, Hans-Rudolph Inc, Kansas City, Missouri, USA).

*Subjective ratings*

Ratings of gut discomfort were assessed every 30 min during exercise using a 5-point scale, where 1 was anchored at “no discomfort’ and 5 at “maximum discomfort”. Ratings of perceived exertion (RPE) were assessed using the Borg scale (2).

*Measurement of muscle and liver glycogen*

Tissue glycogen concentration was determined from the magnitude of the natural abundance signal from the C-1 carbon of glycogen at a frequency of 100.3 ppm. A Philips 3 Tesla Achieva scanner (Philips Healthcare, Best, The Netherlands) was used with a 6 cm diameter $^{13}C$ surface coil with integral $^{1}H$ decoupling surface coil (PulseTeq, Worton under Edge, UK) to measure muscle glycogen concentration and an in-house built 12 cm $^{13}C/^{1}H$ surface coil used to measure liver glycogen concentration.

For muscle glycogen measurements, the surface coil was placed over the widest part of the *Vastus lateralis* and the leg was held in position with fabric straps to prevent movement. Pulse power was calibrated to a nominal value of 80° by observing the power dependent variation in signal from a fiducial

marker located in the coil housing, containing a sample exhibiting $^{13}C$ signal with short $T_1$ (213 mM [2-$^{13}C$]-acetone and 25 mM $GdCl_3$ in water). Automated shimming was carried out to ensure that the magnetic field within the scanner was uniform over the active volume of the $^{13}C$ coil. The $^{13}C$ spectra were acquired over 15 min using a non-localized $^{1}H$ decoupled $^{13}C$ pulse-acquire sequence (TR 120 ms, spectral width 8 kHz, 7000 averages, WALTZ decoupling). $^{1}H$ decoupling was applied for 60% of the $^{13}C$ signal acquisition to allow a relatively fast TR of 120 ms to be used within the Specific Absorption Rate safety limitations.

For liver glycogen measurements the $^{13}C/^{1}H$ surface coil was placed over the right lobe of the liver. Spectra were acquired over 15 min using non-localized $^{1}H$ decoupled $^{13}C$ pulse acquisition sequences (TR 300 ms, spectral width 8 kHz, 2504 averages, WALTZ decoupling, nominal $^{13}C$ tip angle of 80°). Scout images were obtained at the start of each study to confirm optimal coil position relative to the liver.

Tissue glycogen concentrations were calculated from the amplitude of the C1-glycogen $^{13}C$ signal using Java Based Magnetic Resonance User Interface (jMRUI) version 3.0 and the AMARES algorithm [7] as described in detail previously (25, 26, 28, 37).

*Measurement of intramyocellular lipid*

Intramyocellular lipid content was determined routinely, as described in more detail previously (37). In short, a 12 cm $^{1}H$ transmitter/receiver coil was used

to obtain $^{1}H$ spectra to measure intramyocellular lipid (IMCL) content in the widest part of the *gastrocnemius*. The PRESS (Point Resolved Spectroscopy) (4) sequence was used to acquire $^{1}H$ spectra from a 2×2×2 cm voxel, using an echo time of 25 ms, spectral resolution of 1 Hz and repetition time of 5000 ms with 32 acquisitions. Spectra were analyzed with JMRUI version 3.0 using the least square fitting AMARES algorithm (4, 31). The inter-observer bias was 0.09 mmol/L with a 95% limit of agreement of 0.8 mmol/L ($P > 0.05$).

*Calculations and statistical analysis*

Due to the lack of data regarding exercise-induced changes in liver glycogen concentrations with carbohydrate feeding, a sample size estimation was based on data from exogenous carbohydrate oxidation rates (as a surrogate for carbohydrate availability). Sucrose increases exogenous carbohydrate oxidation during cycling by ~30% (18). Using this figure, along with the 7% intra-individual coefficient of variation of hepatic glycogen content measured by $^{13}C$ MRS (34), the study was designed to provide statistical power above 90% with an alpha level of 0.05 with a minimum sample size of $n = 7$ in a crossover design (10).

Whole-body rates of carbohydrate and lipid utilization were estimated using the following equations assuming negligible protein oxidation (13, 22):

$$\text{Net lipid utilization (g/min)} = \left(1.695 \times \dot{V}O_2\right) - \left(1.701 \times \dot{V}CO_2\right)$$

Net carbohydrate utilization (g/min) = $\left(4.210 \times \dot{V}CO_2\right)$ - $(2.962 \times \dot{V}O_2)$

Units of $\dot{V}O_2$ and $\dot{V}CO_2$ are L/min

Unless otherwise stated, all data were expressed in the text as the mean ± standard deviation (SD) of the mean and the error bars presented in figures are 95% confidence intervals (CI). Data were checked for normal distribution and log-transformed if appropriate prior to statistical analysis.

Liver and muscle glycogen, and IMCL concentrations from the four participants who completed the CON trial were assessed by two-way (trial x time) repeated measures ANOVA with trial (GLU vs SUC vs CON) and time (pre- vs post-exercise) as within-subject factors. Rates of substrate utilization were assessed by a one-way repeated measures (GLU vs SUC vs CON) ANOVA. No further inferential statistics were performed on CON data since this was only a subgroup of the total sample and was only used as a reference for the change in liver glycogen concentration with 3 h of exercise in the absence of carbohydrate ingestion. Accordingly, all other comparisons were made between GLU and SUC only.

Blood, plasma and respiratory variables and subjective ratings were assessed by two-way (trial x time) repeated measures ANOVA with trial (GLU vs SUC) and time (all time points during exercise) as within-subject factors. Liver and muscle glycogen and intramyocellular lipid concentrations were also assessed by two-way (trial x time) repeated measures ANOVA with trial (GLU vs SUC)

and time (pre- vs post-exercise) as within-subject factors. Mean exercise responses in GLU and SUC trials (carbohydrate intake, heart rate, fluid intake and power output) were assessed by paired t-tests. All *P* values are corrected for multiple comparisons (Holm-Sidak). A *P* value of ≤ 0.05 was used to determine statistical significance. All data were analyzed using Prism v5 (GraphPad Software, San Diego, CA).

## Results

*Participants*

Participants' characteristics are provided in **Table 2**. No differences were observed for age, body mass, height, $\dot{V}O_{2\,peak}$, $W_{peak}$, body mass index, systolic or diastolic blood pressure between participants who completed the main trials (GLU and SUC) and the subgroup of participants who also completed the additional CON trial.

*Subjective ratings*

RPE increased during exercise (time effect, $P < 0.001$), but to less of an extent during SUC when compared to GLU (interaction effect, $P < 0.05$; **Figure 1A**), becoming significantly different between trials from 150 min onwards ($P < 0.05$). Similarly, ratings of gut discomfort increased throughout exercise (time effect, $P < 0.001$) but to less of an extent during SUC when compared to GLU (interaction effect, $P < 0.01$), becoming significantly different at 180 min (Figure 1B, $P < 0.05$).

*Respiratory data and whole-body substrate utilization*

$\dot{V}O_2$ and $\dot{V}CO_2$ remained stable during exercise (time effect, $P > 0.05$ for both) and were not different between GLU and SUC (both $P > 0.05$). Respiratory exchange ratio (RER) was higher with SUC vs GLU (trial effect, $P < 05$) for time points 90 min onwards (interaction effect, $P < 0.05$; **Figure 2C**). Whole-body carbohydrate utilization rates were higher during SUC (2.03 ± 0.43 g/min) when compared with GLU (1.66 ± 0.36 g/min; $P < 0.05$), at the

331 expense of fat oxidation rates (SUC: 0.35 ± 0.15 vs GLU: 0.48 ± 0.12 g/min; *P*
332 < 0.05), resulting in energy expenditure rates that did not differ between trials
333 (SUC: 8.8 ± 1.2 vs GLU: 8.6 ± 0.9 MJ; *P* > 0.05; **Figure 3A**). In the subgroup
334 who also completed the CON trial (*n* = 4), whole-body fat oxidation rates were
335 lower during both GLU (0.42 ± 0.10 g/min) and SUC (0.33 ± 0.11 g/min),
336 compared to CON (0.64 ± 0.19 g.min; *P* < 0.05), whilst carbohydrate oxidation
337 rates (SUC: 2.04 ± 0.40 vs GLU: 1.79 ± 0.43 vs CON: 1.20 ± 0.44 MJ) did not
338 significantly differ between trials (*P* > 0.05). Accordingly, energy expenditure
339 (SUC: 8.7 ± 0.6 vs GLU: 8.6 ± 0.8 vs CON: 8.4 ± 0.4 MJ) also did not differ
340 between trials (*P* > 0.05; Figure 3B).
341
342 *Circulating metabolite and insulin concentrations*
343 Blood glucose and plasma insulin concentrations were not significantly
344 different between trials (trial effect, *P* > 0.05; interaction effect, *P* > 0.05 for
345 both variables; **Figure 4A**). In contrast, blood lactate concentrations were
346 higher with SUC vs GLU (trial effect, *P* < 0.01), rising at the onset of exercise
347 (time effect, *P* < 0.001) to a greater extent in SUC vs GLU until 120 min
348 (interaction effect, *P* < 0.01; Figure 4B). Plasma NEFA concentrations fell
349 from ~0.5 mmol/L to ~0.2 mmol/L during the first hour of exercise before rising
350 again (time effect, *P* < 0.001), the latter of which occurred to a greater degree
351 in GLU compared to SUC (interaction effect, *P* < 0.01; Figure 4D).
352
353 *Muscle and liver glycogen concentration*
354 Muscle and liver glycogen concentrations are displayed in **Figures 5A**, 5B,
355 5C and 5D. Pre-exercise, no differences were observed in liver and muscle

356 glycogen concentrations between trials $P > 0.05$ for both variables). The day-
357 to-day coefficients of variation for pre-exercise liver and muscle glycogen
358 concentrations were 12% and 20%, respectively. The between subject
359 coefficient of variation for pre-exercise liver and muscle glycogen were 54%
360 and 41%, respectively. In the subgroup who also completed the CON trial ($n$ =
361 4), liver glycogen concentrations declined during exercise in CON, but not
362 when either glucose or sucrose were ingested (interaction effect, $P < 0.05$;
363 Figure 5B). In contrast to the liver, muscle glycogen concentrations declined
364 during exercise regardless of trial (trial effect, $P > 0.05$; time effect, $P < 0.01$;
365 interaction effect, $P > 0.05$; Figure 5D).
366
367 Post-exercise liver glycogen concentrations did not differ from pre-exercise
368 values when either glucose or sucrose were ingested (time effect, $P > 0.05$;
369 interaction effect, $P > 0.05$). The change in liver glycogen concentrations from
370 pre- to post-exercise was positive with glucose (20 ± 55 mmol/L) and sucrose
371 (27 ± 58 mmol/L; $P > 0.05$ GLU vs SUC) ingestion, but negative in the CON
372 treatment (-171 ± 73 mmol/L).
373
374 Muscle glycogen concentrations were reduced following exercise (time effect,
375 $P < 0.001$). The changes in muscle glycogen concentrations did not differ
376 between trials (trial effect, $P > 0.05$; interaction effect, $P > 0.05$; Figures 5C
377 and 4D). The pre- to post-exercise changes in muscle glycogen concentration
378 did not differ between GLU (-40 ± 37 mmol/L) and SUC (-47 ± 36; $P > 0.05$).
379
380 *Intramyocellular lipid concentration*

No differences were observed in pre-exercise IMCL concentration ($P > 0.05$) between trials. The day-to-day coefficient of variation for pre-exercise IMCL concentration was 21%. The between-subject coefficient of variation for pre-exercise IMCL concentration was 47%. In the full sample ($n = 14$) exercise decreased IMCL concentrations (time effect $P < 0.01$) to a similar extent in both trials (trial effect, $P > 0.05$; interaction effect, $P > 0.05$; Figure 5E). The pre- to post-exercise changes in IMCL concentration did not differ between GLU (-1.5 ± 6.0 μmol/g) and SUC (-1.6 ± 6.4 μmol/g; $P > 0.05$).

In the subgroup who completed the CON trial ($n = 4$), post-exercise IMCL concentrations were not significantly different to pre-exercise values (time effect, $P > 0.05$), and the responses were not significantly different between trials (trial effect, $P > 0.05$; interaction effect, $P > 0.05$; Figure 5F).

## Discussion

In the present study we provide novel data demonstrating that carbohydrate ingestion during endurance type exercise can prevent liver glycogen depletion, and that this effect is independent of the type of carbohydrate (glucose or sucrose) ingested. In contrast, neither glucose nor sucrose ingestion at 1.7 g/min (102 g/h) could attenuate the decline in muscle glycogen following exercise. Sucrose ingestion increased whole-body carbohydrate utilization when compared with glucose ingestion.

Muscle glycogen and plasma glucose are the main fuel sources during prolonged, moderate-intensity endurance type exercise (41). Plasma glucose is maintained during exercise by glycogenolysis and gluconeogenesis, primarily from the liver. Accordingly, continuous exercise lasting more than 60 min substantially depletes liver glycogen concentrations (37). Given that liver glycogen strongly associates with endurance capacity (6), maintaining liver glycogen concentrations is likely to benefit endurance performance. Previous research using glucose tracers has indicated that high rates of glucose ingestion can suppress endogenous glucose appearance (21), implying that carbohydrate ingestion during exercise may attenuate exercise induced liver glycogen depletion. Here we present the first quantitative evidence of liver glycogen maintenance following carbohydrate ingestion during exercise. We found that 3 h of cycling, in the absence of carbohydrate ingestion reduces liver glycogen concentrations by ~49%, which is consistent with previous findings (37). When ingesting ~1.7 g/min (~102 g/h) glucose or sucrose, liver

418 glycogen concentrations are not lowered during prolonged exercise (Figures
419 5A and 5B).
420
421 Liver glycogen concentrations displayed a relatively high variability between
422 subjects (coefficient of variation: 54%), compared to the day-to-day variability
423 within subjects (coefficient of variation: 12%). This provides an explanation for
424 the relatively higher baseline liver glycogen concentrations in the subgroup
425 that completed the CON trial (*n* = 4; Figure 5B) compared to the entire sample
426 (*n* = 14; Figure 5A).
427
428 Carbohydrate ingestion during exercise increases exogenous carbohydrate
429 oxidation and has been shown to spare net muscle glycogen utilization under
430 some conditions (36), although not typically during the latter stages of more
431 prolonged (> 1 h), cycling exercise. These responses are thought to contribute
432 to the performance benefits of carbohydrate ingestion during prolonged
433 exercise (7). The present data demonstrate that neither the ingestion of
434 glucose nor sucrose are able to attenuate net muscle glycogen utilization
435 during prolonged moderate-intensity cycling, even when large quantities of
436 multiple transportable carbohydrate (~1.7 g/min; 102 g/h) are ingested that
437 augment exogenous carbohydrate availability. In contrast, whole body
438 carbohydrate utilization rates were higher with sucrose vs glucose ingestion,
439 with a concomitant reduction in fat use. Data from the subgroup also
440 demonstrate that both glucose and sucrose ingestion suppress fat utilization
441 relative to CON, although the numerical differences in carbohydrate utilization
442 rates did not reach statistical significance with the subgroup (*n* = 4; *P* = 0.07).

443 At rest, fructose is preferentially stored as liver glycogen rather than muscle
444 glycogen. This has led some to speculate that sucrose, when compared with
445 glucose ingestion may be particularly effective at maintaining or increasing
446 liver glycogen during exercise. In the present study, sucrose ingestion did not
447 preserve liver glycogen concentrations to any greater extent than glucose
448 ingestion. In line with previous observations of substantial declines in
449 endogenous glucose production during exercise when glucose was ingested
450 (21), our data seem to suggest that liver glycogen contents are maintained
451 during exercise when ingesting large amounts (~1.7 g/min; ~102 g/h) of
452 glucose or sucrose. The surplus carbohydrates are shunted towards oxidation
453 rather than storage, at the expense of lipid oxidation.
454
455 The increase in whole-body carbohydrate utilization following sucrose vs
456 glucose ingestion seems to confirm that sucrose ingestion increases
457 exogenous carbohydrate availability and carbohydrate flux. This shift in
458 metabolism is likely due to a number of coordinated factors, including the
459 higher lactate concentrations observed following sucrose ingestion. Higher
460 circulating lactate concentrations are very likely due to the fructose
461 component of sucrose, the majority of which is converted to lactate and
462 glucose upon bypassing the liver. Glucose-fructose co-ingestion during
463 exercise has been shown to increase plasma lactate and glucose turnover
464 and oxidation (24), with a minimal amount of fructose being directly oxidized
465 (24). The greater whole-body carbohydrate utilization rate following sucrose
466 ingestion is therefore likely attributed to a combination of (greater) plasma
467 lactate, glucose and (to a lesser extent) fructose oxidation rates. Lactate also

468 inhibits adipocyte lipolysis via the G-protein coupled receptor GPR81 (27).
469 This is likely one of the factors responsible for the lower plasma NEFA
470 concentrations following sucrose versus glucose ingestion in the presence of
471 similar insulinemia. As there were no differences in muscle lipid content
472 changes between treatments, the greater fat use in the glucose compared
473 with the sucrose trial is likely entirely attributed to greater uptake and
474 oxidation of plasma derived NEFA.
475
476 Lactate formation is associated with hydrogen ion production, which may
477 displace $CO_2$ from bicarbonate stores with consequent implications for
478 estimates of $\dot{V}CO_2$, RER and substrate utilization (13). The ~0.5 mmol/L
479 increase in lactate concentration following SUC vs GLU however, would have
480 a negligible (<0.07 mL/min) effect on $CO_2$ displacement (13). Therefore,
481 values obtained from expiratory gas samples are likely to be a valid
482 representation of net substrate utilization.
483
484 We observed a lower RPE towards the end of exercise following sucrose
485 compared with glucose ingestion. This is in spite of the higher lactate
486 concentrations following ingestion of sucrose compared to glucose, offering
487 additional evidence of the disassociation between lactate concentrations and
488 RPE (29). Exogenous carbohydrate oxidation rates have been shown to
489 correlate with exercise performance during prolonged, moderate-to-high
490 intensity exercise (35). Therefore, the lower RPE following sucrose versus
491 glucose ingestion may be attributed to the greater exogenous carbohydrate
492 uptake and subsequent oxidation rates when co-ingesting fructose (17, 19).

493 The lower RPE may of course also be directly attributed to the lesser
494 occurrence of gastrointestinal discomfort when ingesting large amounts of
495 multiple transportable carbohydrates versus glucose only (Figure 1).
496
497 In conclusion, ingestion of large amounts [~1.7 g/min (~102 g/h), relative to
498 the ~1.5 g/min (90 g/h) recommended for exercise lasting >2.5 h] of glucose
499 or sucrose during prolonged endurance type exercise prevent the exercise-
500 induced decline in liver glycogen content without modulating muscle glycogen
501 depletion.

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**FIGURE LEGENDS**

**Figure 1** Ratings of perceived exertion (A) and gut discomfort (B) during 3 h of cycling with ingestion of glucose or sucrose in trained cyclists (*n* = 14). Data are expressed as means ± 95% CI. * *P* < 0.05, significantly different between GLU and SUC. GLU, glucose; SUC, sucrose.

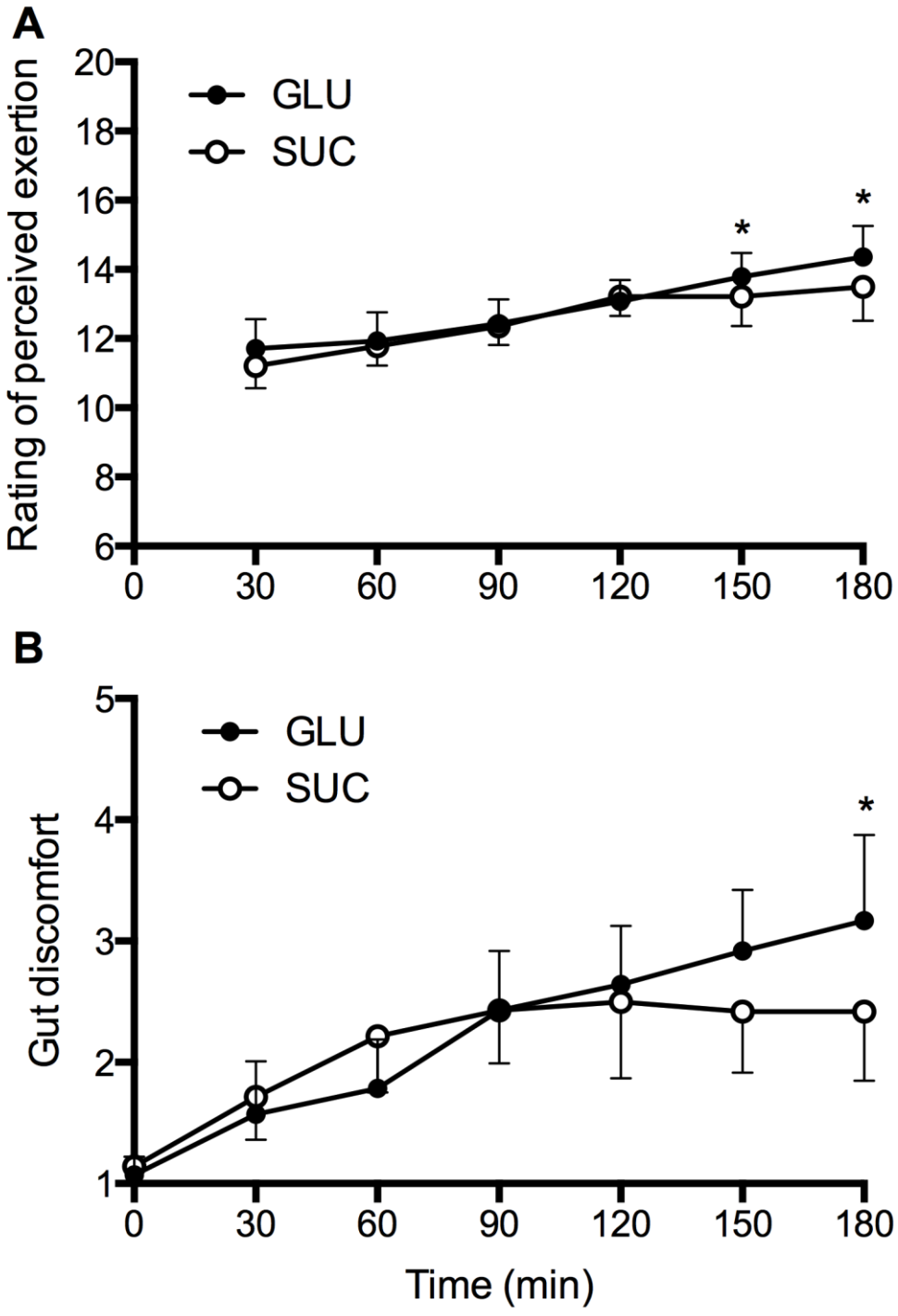


**Figure 2** $VO_2$ (A), $VCO_2$ (B) and respiratory exchange ratio (C) during 3 h of cycling with ingestion of glucose or sucrose in trained cyclists (*n* = 14). Data are expressed as means ± 95% CI. * *P* < 0.05, significantly different between GLU and SUC. GLU, glucose; SUC, sucrose; $VCO_2$, rate of carbon dioxide production; $VO_2$, rate of oxygen consumption.

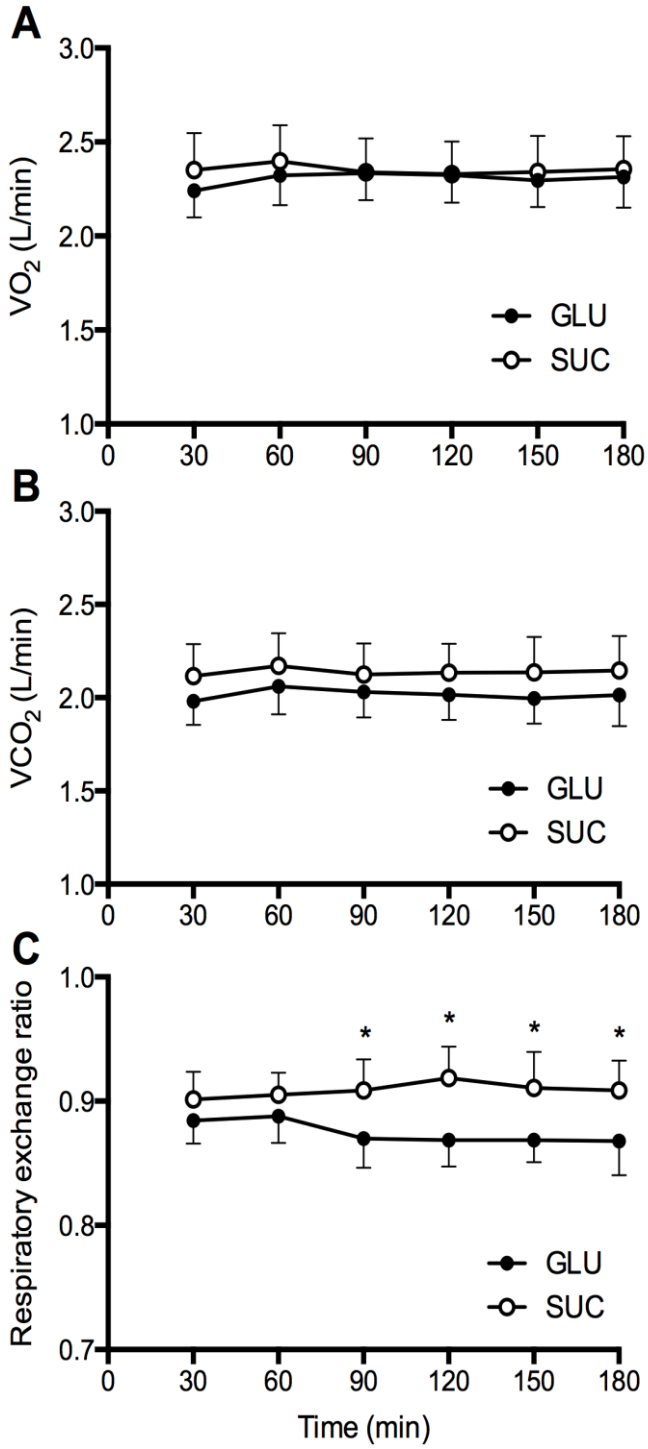


**Figure 3** Substrate utilization during 3 h of cycling with ingestion of glucose or sucrose in trained cyclists (A; *n* = 14) and in the subgroup of trained cyclists (B; *n* = 4). Data are expressed as means ± 95% CI. * *P* < 0.05, significantly different from CON. CHO, carbohydrate; GLU, glucose; SUC, sucrose; CON, water control.

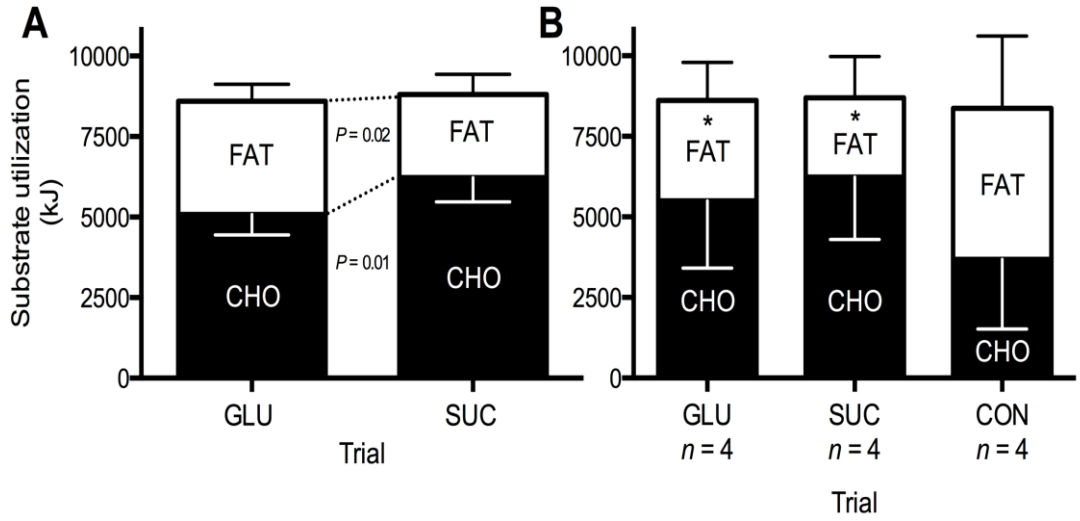
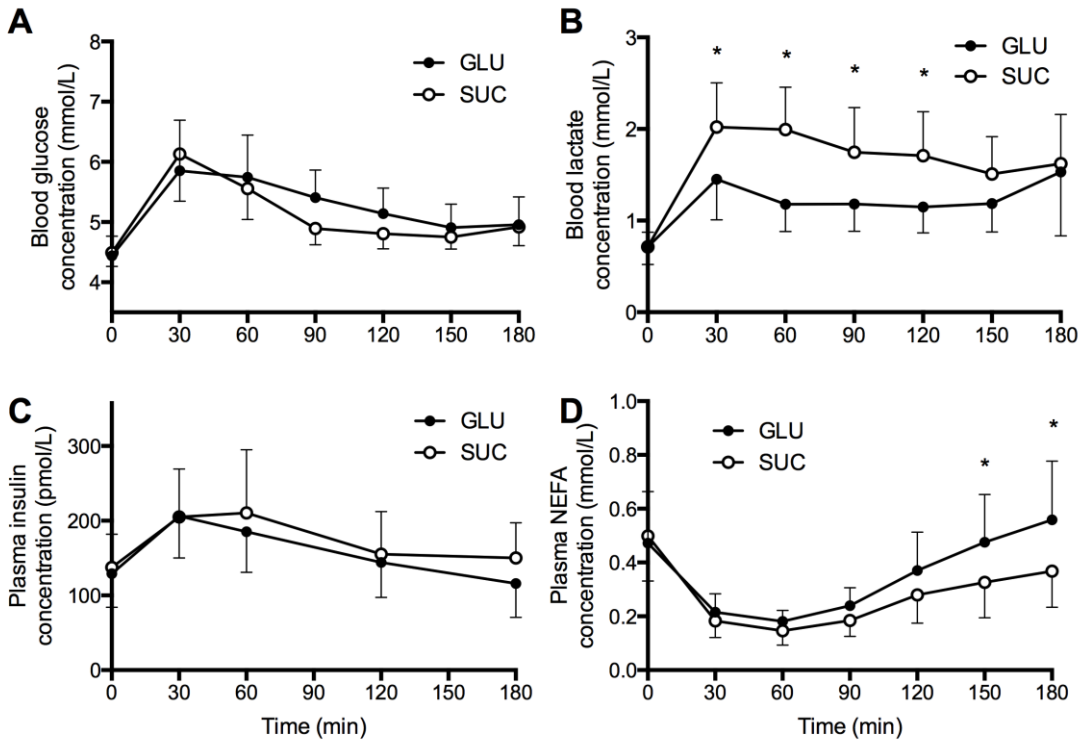


**Figure 4** Blood glucose (A) and lactate (B), and plasma insulin (C) and NEFA (D) concentrations during 3 h of cycling with ingestion of glucose or sucrose in trained cyclists (*n* = 14). Data are expressed as means ± 95% CI. * *P* < 0.05, significantly different between GLU and SUC. GLU, glucose; NEFA, non-esterified fatty acid; SUC, sucrose.



676 **Figure 5** Liver glycogen (A), muscle glycogen (C) and intramyocellular lipid
677 (E) concentrations prior to (Pre) and immediately following (Post) 3 h of
678 cycling with ingestion of glucose or sucrose in the full sample of trained
679 cyclists (*n* = 14), and in the subgroup of trained cyclists (B, D and F; *n* = 4).
680 Data are expressed as means ± 95% CI. * *P* < 0.05, significantly different
681 when compared with pre-exercise values. GLU, glucose; SUC, sucrose; CON,
682 water control.

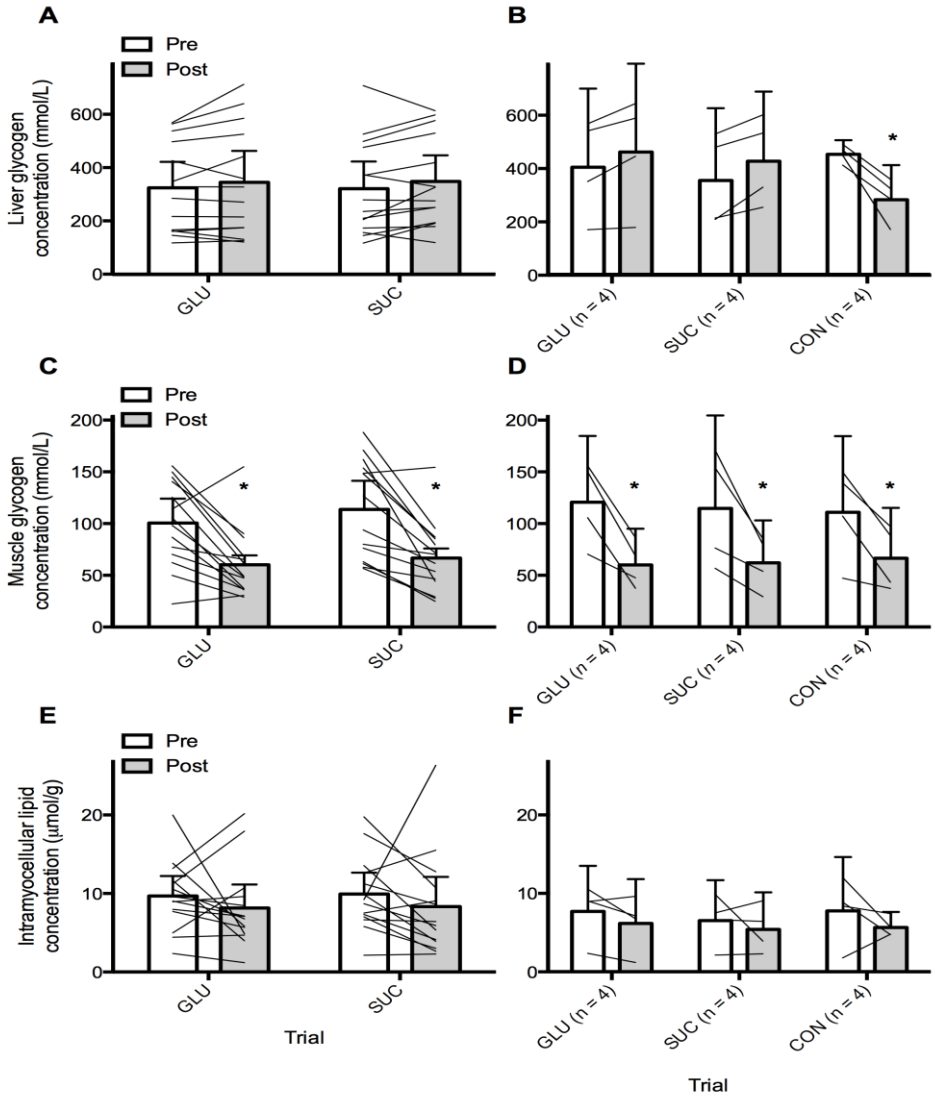



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**Table 1** Carbohydrate intake and physiological variables of trained cyclists during 3 h of cycling with ingestion of glucose, sucrose or water.

| | GLU (*n* = 14) | SUC (*n* = 14) | CON (*n* = 4) |
|---|---|---|---|
| Carbohydrate intake (g/min) | 1.7 ± 0.2 | 1.7 ± 0.2 | 0 ± 0 |
| Fluid intake (L) | 2.1 ± 0.2 | 2.2 ± 0.2 | 2.3 ± 0.0 |
| Power output (W) | 165 ± 17 | 165 ± 17 | 158 ± 7 |
| Mean heart rate (beats/min) | 145 ± 14 | 146 ± 12 | 122 ± 8 |

Data are expressed as means ± SEM. GLU, glucose; SUC, sucrose; CON, water control.

**Table 2** Characteristics of trained cyclists who completed GLU, SUC and CON trials.

| | GLU and SUC ($n$ = 14) | CON ($n$ = 4) |
|---|---|---|
| Age (y) | 25 ± 5 | 26 ± 6 |
| Body mass (kg) | 73.1 ± 9.3 | 75.3 ± 10.7 |
| Height (m) | 1.78 ± 0.08 | 1.75 ± 0.09 |
| $\dot{V}O_{2peak}$ (mL/min/kg) | 58 ± 5 | 60± 7 |
| $W_{peak}$ (W) | 330 ± 35 | 316 ± 27 |
| BMI (kg/m$^2$) | 23.0 ± 1.9 | 24.5 ± 1.8 |
| Systolic blood pressure (mmHg) | 133 ± 11 | 129 ± 6 |
| Diastolic blood pressure (mmHg) | 74 ± 8 | 71 ± 8 |

Data are expressed as means ± SD. GLU, glucose; SUC, sucrose; $\dot{V}O_{2peak}$, peak oxygen uptake; CON, water control; $W_{peak}$, peak power output.