



Citation for published version:

Fuchs, C, Gonzalez, J, Beelen, M, Cermak, N, Smith, F, Thelwall, P, Taylor, R, Trenell, M, Stevenson, E & van Loon, LJC 2016, 'Sucrose ingestion after exhaustive exercise accelerates liver, but not muscle glycogen repletion when compared to glucose ingestion in trained athletes', *Journal of Applied Physiology*, vol. 120, no. 11, pp. 1328-1334. <https://doi.org/10.1152/jappphysiol.01023.2015>

DOI:

[10.1152/jappphysiol.01023.2015](https://doi.org/10.1152/jappphysiol.01023.2015)

Publication date:

2016

Document Version

Peer reviewed version

[Link to publication](#)

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Sucrose ingestion after exhaustive exercise accelerates liver, but not muscle glycogen repletion when compared to glucose ingestion in trained athletes

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Running head: Sucrose for post-exercise recovery

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ABSTRACT

Purpose: To assess the effects of sucrose versus glucose ingestion on post-exercise liver and muscle glycogen repletion. **Methods:** Fifteen well-trained male cyclists completed 2 test days. Each test day started with glycogen-depleting exercise, followed by 5 h of recovery, during which subjects ingested $1.5 \text{ g}\cdot\text{kg}^{-1}\cdot\text{h}^{-1}$ sucrose or glucose. Blood was sampled frequently and ^{13}C magnetic resonance spectroscopy and imaging were employed 0, 120, and 300 min post-exercise to determine liver and muscle glycogen concentrations and liver volume. **Results:** Post-exercise muscle glycogen concentrations increased significantly from 85 ± 27 vs $86\pm 35 \text{ mmol}\cdot\text{L}^{-1}$ to 140 ± 23 vs $136\pm 26 \text{ mmol}\cdot\text{L}^{-1}$ following sucrose and glucose ingestion, respectively (no differences between treatments: $P=0.673$). Post-exercise liver glycogen concentrations increased significantly from 183 ± 47 vs $167\pm 65 \text{ mmol}\cdot\text{L}^{-1}$ to 280 ± 72 vs $234\pm 81 \text{ mmol}\cdot\text{L}^{-1}$ following sucrose and glucose ingestion, respectively (time x treatment, $P=0.051$). Liver volume increased significantly over the 300 min period after sucrose ingestion only (time x treatment, $P=0.001$). As a result, total liver glycogen content increased during post-exercise recovery to a greater extent in the sucrose treatment (from 53.6 ± 16.2 to $86.8\pm 29.0 \text{ g}$) compared to the glucose treatment (49.3 ± 25.5 to $65.7\pm 27.1 \text{ g}$; time x treatment, $P<0.001$), equating to a $3.4 \text{ g}\cdot\text{h}^{-1}$ (95%CI: 1.6 to $5.1 \text{ g}\cdot\text{h}^{-1}$) greater repletion rate with sucrose vs glucose ingestion. **Conclusion:** Sucrose ingestion ($1.5 \text{ g}\cdot\text{kg}^{-1}\cdot\text{h}^{-1}$) further accelerates post-exercise liver, but not muscle glycogen repletion when compared to glucose ingestion in trained athletes.

This trial was registered at clinicaltrials.gov as NCT02344381.

Keywords: ^{13}C magnetic resonance spectroscopy; carbohydrate; recovery; fructose; endurance exercise

New & Noteworthy statement (69 words)

This is the first study to assess both muscle and liver glycogen repletion post-exercise after ingesting different types of carbohydrates in large amounts. We observed that sucrose ingestion accelerates post-exercise liver glycogen repletion compared to glucose ingestion in spite of lower insulinemia and reduced gut discomfort. Therefore, when rapid recovery of endogenous carbohydrate stores is a goal, ingestion of sucrose at 1.5 g/kg/h would be more appropriate than glucose.

1 INTRODUCTION

2 Carbohydrates are a main substrate source used during prolonged moderate to high
3 intensity exercise (35, 42). Both exogenous and endogenous carbohydrate stores
4 can contribute to carbohydrate oxidation during exercise. Endogenous carbohydrate
5 stores include liver and skeletal muscle glycogen, which can provide sufficient
6 energy to sustain 45-60 min of high-intensity exercise (8, 10). However, at longer
7 exercise durations (>60 min) endogenous glycogen stores may become depleted,
8 causing early fatigue (1, 4-6, 9, 16, 20, 39). Due to the apparent relationship between
9 glycogen depletion and exercise capacity (1, 4-6, 9, 12, 19, 20), the main factor
10 determining the time needed to recover from exhaustive exercise is the rate of
11 glycogen repletion. This is particularly relevant when exercise performance needs to
12 be regained within 24 h, for example during tournament-style competitions or in
13 between stages in races such as during the Tour de France.

14 Previous studies have shown that muscle glycogen repletion rates can reach
15 maximal values when glucose (polymers) are ingested in an amount of $1.2 \text{ g}\cdot\text{kg}^{-1}\cdot\text{h}^{-1}$
16 (2, 43), with no further improvements at higher glucose ingestion rates (18). It has
17 been speculated that post-exercise muscle glycogen synthesis rates may be further
18 increased when ingesting multiple transportable carbohydrates (i.e., mix of glucose
19 and fructose). Glucose and fructose are absorbed by several similar (GLUT2, GLUT8
20 and GLUT12) as well as different intestinal transporters (SGLT1 and GLUT5,
21 respectively) (24, 37). Hence, the combined ingestion of both glucose and fructose
22 may augment intestinal carbohydrate uptake and accelerate their subsequent
23 delivery into the circulation (24, 37). To date, only one study investigated this
24 hypothesis, showing no further improvements in post-exercise muscle glycogen
25 repletion rates after the ingestion of $\sim 1.2 \text{ g}\cdot\text{kg}^{-1}\cdot\text{h}^{-1}$ (or $90 \text{ g}\cdot\text{h}^{-1}$) of multiple
26 transportable carbohydrates compared to an equivalent dose of glucose (44).

27 The use of multiple transportable carbohydrates is potentially more relevant for liver

28 glycogen repletion, as fructose is preferentially metabolized and retained in the liver
29 (30). Factors that contribute to this are the high first pass extraction of fructose by the
30 liver and the high hepatic expression of fructokinase and triokinase, which are
31 essential enzymes for the metabolism of fructose (30). Furthermore, it has been
32 shown that intravenously administered fructose leads to greater increases in liver
33 glycogen content when compared with intravenous glucose administration (33). Yet,
34 few studies have tried to assess the effects of carbohydrate ingestion on post-
35 exercise liver glycogen repletion (9, 14, 15, 31). This is mainly due to obvious
36 methodological limitations, as liver biopsies are not considered appropriate for
37 measuring liver glycogen concentrations for research purposes *in vivo* in humans
38 (17). With the introduction of ¹³C-Magnetic Resonance Spectroscopy (¹³C-MRS), a
39 non-invasive measurement to study changes in liver and muscle glycogen (40, 41), it
40 has been demonstrated that post-exercise liver glycogen resynthesis is stimulated by
41 carbohydrate ingestion (9, 14, 15). Only two studies assessed the effects of fructose
42 ingestion on post-exercise liver glycogen resynthesis rates. Décombaz *et al.* (14)
43 reported elevated liver glycogen resynthesis rates when co-ingesting fructose with
44 maltodextrin (~0.93 g·kg⁻¹·h⁻¹), whereas Casey *et al.* (9) reported no differences in
45 post-exercise liver glycogen repletion following ingestion of ~0.25 g·kg⁻¹·h⁻¹ glucose
46 versus sucrose (9). No study has assessed the impact of ingesting multiple
47 transportable carbohydrates on both liver and muscle glycogen repletion when
48 optimal amounts of carbohydrate are ingested during post-exercise recovery.

49 We hypothesize that ingestion of large amounts of sucrose leads to higher liver and
50 muscle glycogen repletion rates when compared to the ingestion of the same amount
51 of glucose. To test this hypothesis, 15 well-trained cyclists completed glycogen
52 depleting exercise, after which we applied ¹³C MRS to compare liver and muscle
53 glycogen repletion rates following the ingestion of 1.5 g·kg⁻¹·h⁻¹ sucrose or 1.5 g·kg⁻¹·
54 h⁻¹ glucose during 5 hours of post-exercise recovery.

55 **METHODS**

56

57 *Subjects*

58 Fifteen well-trained male cyclists participated in this study (age: 22±4 y, bodyweight:
59 74.4±7.5 kg, body mass index: 22.6±1.8 kg/m², maximal workload capacity (W_{\max}):
60 350±30 W, peak oxygen uptake ($\dot{V}O_2$ peak): 61.5±5.2 mL·kg⁻¹·min⁻¹). Subjects were
61 fully informed of the nature and possible risks of the experimental procedures, before
62 written informed consent was obtained. Trials were conducted at the Newcastle
63 Magnetic Resonance Centre (Newcastle-upon-Tyne, UK) in accordance with the
64 Second Declaration of Helsinki, and following approval from the Northumbria
65 University Faculty of Health and Life Sciences Ethics Committee.

66

67 *Preliminary testing*

68 All subjects participated in a screening session, which was performed ≥1 wk before
69 the first experiment. Subjects performed an incremental cycling test on an
70 electromagnetically braked cycle ergometer (Velotron, RacerMate Inc., Seattle, WA,
71 USA) to determine maximal workload capacity (W_{\max}) and peak oxygen uptake
72 ($\dot{V}O_2$ peak). Following a 5 min warm-up at 100 W, the workload began at 150 W and
73 was increased by 50 W every 2.5 min to exhaustion (27). Expired gas was sampled
74 continuously to determine oxygen uptake (Oxycon gas analyser, CareFusion
75 corporation, San Diego, CA, USA).

76

77 *Diet and physical activity*

78 All subjects received the same standardized dinner (2797 kJ; 666 kcal; providing
79 23.9 g fat, 83.7 g carbohydrate and 23.9 g protein) the evening before each test day.

80 All volunteers refrained from exhaustive physical activity 24 h before each main trial
81 and kept their diet as constant as possible 2 d before each experimental day. In

82 addition, subjects filled in food intake and physical activity diaries for 2 d before the
83 start of the first and second trial.

84

85 *Study design*

86 Participants performed 2 trials in a randomized, double-blind, crossover design
87 separated by at least 7 d. During each trial, they were first subjected to a glycogen
88 depletion protocol on a cycle ergometer. Thereafter, subjects were studied for 5 h
89 while ingesting only glucose in the control trial (GLU) or sucrose in the SUC trial.
90 During the 5 h post-exercise recovery period, subjects remained at rest in a supine
91 position. Magnetic Resonance Spectroscopy (MRS) was performed immediately
92 post-exercise and after 2 and 5 h of post-exercise recovery to determine liver and
93 muscle glycogen concentrations. In addition, Magnetic Resonance Imaging (MRI)
94 was performed immediately post-exercise and after 2 and 5 h of post-exercise
95 recovery to determine liver volume.

96

97 *Experimental protocol*

98 Participants arrived at Newcastle Magnetic Resonance Centre at 0700-0730 h
99 following a 12 h fast. Liver and muscle glycogen depletion was established by
100 performing an intense exercise protocol on an electromagnetically braked cycle
101 ergometer (26). The exercise protocol started with a 10 min warm-up at 50% W_{max} .
102 Thereafter, subjects cycled for 2-min block periods at alternating workloads of 90%
103 and 50% W_{max} , respectively. This was continued until subjects were no longer able to
104 complete a 2 min, 90% W_{max} exercise period at a cycling cadence of 60 rpm. At this
105 point, the high intensity blocks were reduced to 80% W_{max} after which the same
106 regimen was continued. When subjects were no longer able to complete the 2 min
107 blocks at 80% W_{max} , the exercise intensity of the blocks was further reduced to
108 70%. Subjects were allowed to stop when pedaling speed could not be maintained at

109 70% W_{\max} . Water was provided *ad libitum* during the exercise protocol. Two fans
110 were placed 1 m from the subjects to provide cooling and air circulation during the
111 exercise protocol. After cessation of exercise, gastrointestinal (GI) comfort was
112 assessed using a visual analogue scale. Subsequently, the participants underwent a
113 basal MRS and MRI measurement for approximately 45 min (Fig. 1). After this, they
114 were allowed to take a brief (≤ 15 min) shower before the post-exercise recovery
115 period started. While supine, a catheter was inserted into an antecubital vein of the
116 forearm to allow frequent blood sampling. Following a resting blood sample (10 mL),
117 subjects filled out another visual analogue scale for GI comfort before the first test
118 drink was given ($t=0$ min). Participants were observed for the following 5 h during
119 which they received a drink with a volume of $3.33 \text{ mL} \cdot \text{kg}^{-1}$ every 30 min until $t=270$
120 min. Blood samples were taken at 15 min intervals for the first 90 min of recovery
121 and every 30 min thereafter until $t=300$ min. Further visual analogue scales for GI
122 comfort were completed every 30 min until $t=300$ min. Due to time constraints of the
123 MR measurement it was not possible to acquire a blood sample and collect a visual
124 analogue scale at time point $t=150$ min. At $t=120$ and 300 min in the post-exercise
125 recovery period another MR measurement was performed to assess liver and muscle
126 glycogen concentrations as well as liver volume.

127

128 *GI (dis)comfort*

129 Subjects were asked to fill out computerized visual analogue scales to assess GI
130 comfort. The visual analogue scales consisted of 16 questions. Each question
131 started with "To what extent are you experiencing ... right now?" and was answered
132 by ticking a 100 mm line (0 mm = not at all, 100 mm = very, very much). The
133 questions consisted of six questions related to upper GI symptoms (nausea, general
134 stomach problems, belching, an urge to vomit, heartburn, stomach cramps), four
135 questions related to lower GI symptoms (flatulence, an urge to defecate, intestinal

136 cramps, diarrhea), and six questions related to central or other symptoms (dizziness,
137 a headache, an urge to urinate, a bloated feeling, side aches (left), side aches
138 (right)).

139

140 *Drinks*

141 Subjects received a drink volume of $3.33 \text{ mL}\cdot\text{kg}^{-1}$ every 30 min during recovery to
142 ensure a given dose of $1.5 \text{ g}\cdot\text{kg}^{-1}\cdot\text{h}^{-1}$ glucose (GLU) or $1.5 \text{ g}\cdot\text{kg}^{-1}\cdot\text{h}^{-1}$ sucrose (SUC).

143 To minimize differences in carbon isotope ratio between GLU and SUC, similar plant
144 sources with low natural ^{13}C enrichments (i.e. wheat, potato and beet sugar, all of
145 which use C3 metabolism) were selected for use in this study. The carbohydrates in
146 the glucose drink (GLU) consisted of 60% dextrose monohydrate (Roquette,
147 Lestrem, France) and 40% maltodextrin (MD14, AVEBE, Veendam, The
148 Netherlands). The carbohydrate in the sucrose drink (SUC) consisted of 100%
149 sucrose derived from sugar beet (AB Sugar, Peterborough, United Kingdom). Both
150 drinks contained $20 \text{ mmol}\cdot\text{L}^{-1}$ NaCl (Tesco, Cheshunt, United Kingdom).

151

152 *Measurement of muscle and liver glycogen concentrations*

153 Glycogen concentration was determined from the magnitude of the natural
154 abundance signal from the C-1 carbon of glycogen at a frequency of 100.3 ppm. A
155 Philips 3 Tesla Achieva scanner (Philips Healthcare, Best, The Netherlands) was
156 used with a 6 cm diameter ^{13}C surface coil with integral ^1H decoupling surface coil
157 (PulseTeq, Worton under Edge, UK) to measure muscle glycogen concentration and
158 an in-house built 12 cm $^{13}\text{C}/^1\text{H}$ surface coil used to measure liver glycogen
159 concentration. The intra-individual coefficient of variation of hepatic glycogen content
160 measured by ^{13}C MRS has been shown to be 7% (36).

161 For muscle glycogen concentration measurements, the surface coil was placed over
162 the widest part of the *vastus lateralis* muscle and was held in position with fabric

163 straps to prevent movement. Pulse power was calibrated to a nominal value of 80°
164 by observing the power dependent variation in signal from a fiducial marker located
165 in the coil housing, containing a sample exhibiting ^{13}C signal with short T_1 (213 mM
166 [2- ^{13}C]-acetone and 25 mM GdCl_3 in water). Automated shimming was carried out to
167 ensure that the magnetic field within the scanner was uniform over the active volume
168 of the ^{13}C coil. The ^{13}C spectra were acquired over 15 min using a non-localized ^1H
169 decoupled ^{13}C pulse-acquire sequence (TR 120 ms, spectral width 8 kHz, 7000
170 averages, WALTZ decoupling). ^1H decoupling was applied for 60% of the ^{13}C signal
171 acquisition to allow a relatively fast TR of 120 ms to be used within Specific
172 Absorption Rate safety limitations.

173 For liver glycogen measurements the $^{13}\text{C}/^1\text{H}$ surface coil was placed over the right
174 lobe of the liver. Spectra were acquired over 15 min using non-localized ^1H
175 decoupled ^{13}C pulse acquisition sequences (TR 300 ms, spectral width 8 kHz, 2504
176 averages, WALTZ decoupling, nominal ^{13}C tip angle of 80°). Scout images were
177 obtained at the start of each study to confirm optimal coil position relative to the liver.
178 Tissue glycogen concentration was calculated from the amplitude of the C1-glycogen
179 ^{13}C signal using Java Based Magnetic Resonance User Interface (jMRUI) version 3.0
180 and the AMARES algorithm [7]. For each subject the separation between RF coil and
181 muscle / liver tissue was measured from ^1H images, and ^{13}C coil loading assessed
182 from ^{13}C flip angle calibration data. Tissue glycogen concentration was determined
183 by comparison of glycogen signal amplitude to spectra acquired from liver- and leg-
184 shaped phantoms filled with aqueous solutions of glycogen (100 mM) and potassium
185 chloride (70 mM). Phantom data were acquired at a range of flip angles and
186 separation distances between coil and phantom. Quantification of each human ^{13}C
187 spectrum employed a phantom dataset matched to body geometry and achieved flip
188 angle so that account differences in coil sensitivity profile and loading were taken into
189 account for each subject.

190

191 *Measurement of liver volume*

192 A turbo spin echo (TSE) sequence was used to obtain T₂-weighted axial images of
193 the liver with a repetition time (TR) of 1687 msec. The matrix size was 188x152 mm,
194 with a field of view of (303x240x375) mm. The body coil was used for both
195 transmission and reception. Slice thickness was 10 mm with a 0 mm gap. Scans
196 were obtained on expiration. The total number of liver slices used for volume analysis
197 differed between subjects due to anatomical differences but numbered on average
198 20 slices. Liver volumes were measured in the open source Java image processing
199 program ImageJ (38).

200

201 *Calculation of liver glycogen content*

202 Total liver glycogen content was calculated by multiplying liver volume with liver
203 glycogen concentration. Subsequent conversion from mM to g was performed by
204 using the molar mass of a glycosyl unit (i.e., 162 g·M⁻¹).

205

206 *Plasma analysis*

207 Blood samples (10 mL) were collected in EDTA-containing tubes and immediately
208 centrifuged at 3000 rpm for 10 min at 4°C. Plasma was then aliquoted and stored at -
209 80°C for subsequent determination of glucose and lactate concentrations (Randox
210 Daytona spectrophotometer, Randox, Ireland), insulin (IBL International, Hamburg,
211 Germany) and non-esterified fatty acid concentrations (WAKO Diagnostics,
212 Richmond, VA).

213

214 *Statistics*

215 Sample size estimation was based on previous data on liver glycogen content (14).
216 Based on this, the expected effect size was calculated from the difference in post-

217 exercise liver glycogen content after ingesting a mixture of maltodextrin with fructose
218 vs glucose (polymer) (52 ± 23 vs 23 ± 9 g, respectively). A sample size of $n=10$ in a
219 crossover design would provide statistical power above 90% with an α -level of 0.05.
220 We therefore recruited 15 participants to ensure adequate power and ample data
221 sets.

222 Unless otherwise stated, all data are expressed as mean \pm SD. Differences between
223 primary outcomes in the text and the data in the figures are presented as mean \pm 95%
224 confidence interval (CI). All data were analyzed by two-way repeated measures
225 ANOVA with treatment (GLU vs SUC) and time as within-subject factors. In case of a
226 significant interaction, Bonferroni post hoc tests were applied to locate the
227 differences. For non-time-dependent variables, a paired Student's t-test was used to
228 compare differences between treatments. A P value <0.05 was used to determine
229 statistical significance. All calculations were performed by using the SPSS 21.0.0.0
230 software package.

231

232

233 **RESULTS**

234

235 *Glycogen depletion protocol*

236 Maximal workload capacity measured during preliminary testing averaged 350 ± 30 W
237 (4.75 ± 0.6 W/kg). Consequently, average workload settings in the depletion protocol
238 were 315 ± 27 , 280 ± 24 , 245 ± 21 , 175 ± 15 W for the 90, 80, 70, and 50% W_{\max} workload
239 intensity respectively. On average, subjects cycled a total of 21 ± 7 and 19 ± 5 high-
240 intensity blocks, which resulted in a total cycling time of 93 ± 27 and 89 ± 21 min in the
241 SUC and GLU experiments, respectively. Total cycling time did not differ between
242 trials ($P=0.434$).

243

244 *Drink ingestion and gastrointestinal complaints*

245 The total amount of drink ingested in both treatments was 2.48 ± 0.25 L. The first
246 drinks were ingested 75 ± 7 min after cessation of exercise, due to timing of the MR
247 measurements. Subjects reported upper GI issues following ingestion of the glucose
248 drink only, and these issues included nausea, general stomach problems, belching
249 and urge to vomit. These symptoms all displayed significant differences over time
250 and between treatments (time x treatment, $P < 0.05$; data not shown) and for every
251 symptom the sucrose drink was better tolerated than the glucose drink.

252

253 *Liver glycogen concentration*

254 No significant differences in baseline liver glycogen concentrations were found
255 between SUC and GLU ($P=0.210$; Table 1). Liver glycogen concentrations increased
256 significantly over time during post-exercise recovery in both SUC and GLU
257 ($P < 0.001$). Liver glycogen repletion rates during 5 h of post-exercise recovery in SUC
258 and GLU were 19 ± 8 versus 14 ± 12 $\text{mmol} \cdot \text{L}^{-1} \cdot \text{h}^{-1}$, respectively ($P=0.052$). Differences

259 in liver glycogen repletion rates between SUC vs GLU were $5.8 \text{ mmol}\cdot\text{L}^{-1}\cdot\text{h}^{-1}$ (95%CI:
260 0.4 to $11.2 \text{ mmol}\cdot\text{L}^{-1}\cdot\text{h}^{-1}$).

261

262 *Liver volume*

263 Liver volume data are shown in Table 1. Over the 5 h post-exercise recovery period,
264 liver volume increased significantly in SUC ($P=0.036$), whereas no significant
265 changes were observed in GLU ($P=0.151$). A significant time x treatment interaction
266 was found between SUC and GLU ($P=0.001$).

267

268 *Liver glycogen content*

269 Liver glycogen content increased over time in both treatments ($P<0.01$; Fig. 2). Over
270 time, liver glycogen content increased significantly more in the SUC compared to the
271 GLU treatment (time x treatment interaction, $P<0.001$). Liver glycogen repletion rates
272 during 5 h of post-exercise recovery in SUC and GLU were 6.6 ± 3.3 versus 3.3 ± 3.0
273 $\text{g}\cdot\text{h}^{-1}$, respectively ($P=0.002$). Differences in liver glycogen repletion rates between
274 SUC vs GLU were $3.4 \text{ g}\cdot\text{h}^{-1}$ (95%CI: 1.6 to $5.1 \text{ g}\cdot\text{h}^{-1}$), leading to a 17 g difference
275 (95%CI: 8 to 26 g) over the 5 h recovery period.

276

277 *Muscle glycogen concentration*

278 No significant differences in baseline muscle glycogen concentrations were observed
279 between SUC and GLU ($P=0.940$; Fig. 3). Muscle glycogen concentrations increased
280 significantly over the 5 h recovery period in both SUC and GLU ($P<0.001$). No
281 significant differences were observed between treatments (time x treatment,
282 $P=0.673$). Muscle glycogen repletion rates during 5 h of post-exercise recovery in
283 SUC and GLU were 11 ± 3 versus $10\pm 5 \text{ mmol}\cdot\text{L}^{-1}\cdot\text{h}^{-1}$, respectively ($P=0.558$).
284 Differences in muscle glycogen repletion rates between SUC vs GLU were 0.9
285 $\text{mmol}\cdot\text{L}^{-1}\cdot\text{h}^{-1}$ (95%CI: -1.9 to $3.6 \text{ mmol}\cdot\text{L}^{-1}\cdot\text{h}^{-1}$).

286

287 *Plasma analyses*

288 In both experiments, plasma glucose concentration increased during the first 45 min
289 of post-exercise recovery, after which concentrations gradually declined to baseline
290 values (Fig. 4A). Plasma glucose concentrations were significantly higher at $t=60, 75$
291 and 90 min in the GLU compared to SUC treatment ($P<0.05$), whereas they were
292 significantly higher in the sucrose treatment at time point 270 min ($P<0.05$). Plasma
293 lactate concentrations increased significantly after 15 min in the SUC trial compared
294 to GLU and remained significantly higher over the entire post-exercise recovery
295 period ($P<0.01$; Fig. 4B). Plasma insulin concentrations increased during the first 120
296 min of post-exercise recovery. Thereafter, plasma insulin concentrations decreased
297 but remained elevated compared to baseline values during the entire post-exercise
298 recovery period (Fig. 4C). Plasma insulin concentrations were significantly higher in
299 the GLU compared with the SUC treatment at $t=45, 75$ and 90 min ($P<0.05$). Plasma
300 NEFA concentrations decreased immediately after carbohydrate ingestion and
301 remained low over the entire recovery period, with no differences between
302 treatments (Fig. 4D).

303

304

305 **DISCUSSION**

306 In this experiment we observed that sucrose ingestion ($1.5 \text{ g}\cdot\text{kg}^{-1}\cdot\text{h}^{-1}$) during recovery
307 from exhaustive exercise results in more rapid liver glycogen repletion, despite lower
308 plasma insulin levels, when compared with the ingestion of glucose. Ingestion of
309 sucrose or glucose did not result in differences in post-exercise muscle glycogen
310 repletion rates.

311 Carbohydrate ingestion during 5 h of post-exercise recovery allowed substantial
312 increases in muscle glycogen concentrations (Figure 3). This represents muscle
313 glycogen repletion rates of $10\pm 5 \text{ mmol}\cdot\text{L}^{-1}\cdot\text{h}^{-1}$ after glucose ingestion and 11 ± 3
314 $\text{mmol}\cdot\text{L}^{-1}\cdot\text{h}^{-1}$ after sucrose ingestion. Assuming a skeletal muscle mass density of
315 $1.112 \text{ g}\cdot\text{cm}^3$ (46) and a wet-to-dry mass ratio of 4.28 (22), our muscle glycogen
316 repletion rates assessed using ^{13}C MRS would translate to glycogen repletion rates
317 of 39 ± 20 and $42\pm 11 \text{ mmol}\cdot\text{kg}^{-1} \text{ dw}\cdot\text{h}^{-1}$, respectively. These values are in line with
318 previously published data on post-exercise muscle glycogen resynthesis rates when
319 ingesting ample amounts of carbohydrate ($\sim 1.2 \text{ g}\cdot\text{kg}^{-1}\cdot\text{h}^{-1}$), based upon muscle
320 biopsy collection and concomitant muscle glycogen analyses, showing values
321 ranging between $30\text{--}45 \text{ mmol}\cdot\text{kg}^{-1} \text{ dw}\cdot\text{h}^{-1}$ (3, 23, 43, 44). We did not observe
322 differences in muscle glycogen repletion rates following ingestion of either sucrose or
323 glucose (polymers) during the 5 h post-exercise recovery period ($P=0.558$). Hence,
324 muscle glycogen resynthesis rates are not limited by exogenous carbohydrate
325 availability when large amounts of glucose, glucose polymers and/or sucrose (≥ 1.2
326 $\text{g}\cdot\text{kg}^{-1}\cdot\text{h}^{-1}$) are consumed. This supports the contention that ingestion of $\geq 1.2 \text{ g}$
327 $\text{carbohydrate}\cdot\text{kg}^{-1}\cdot\text{h}^{-1}$ maximizes post-exercise muscle glycogen synthesis rates. This
328 also implies that the limitation in exogenous carbohydrate oxidation rates residing in
329 the rate of intestinal glucose absorption does not impose a restriction for post-
330 exercise muscle glycogen synthesis in a post-exercise resting condition.

331 After exhaustive exercise, the ingestion of glucose and sucrose resulted in liver

332 glycogen repletion rates of 14 ± 12 and 19 ± 8 $\text{mmol} \cdot \text{L}^{-1} \cdot \text{h}^{-1}$, respectively. These liver
333 glycogen repletion rates together with our observed liver glycogen content values
334 (Figure 2) are comparable to previous observations made by Décombaz and
335 colleagues (14). However, we extend on previous work by showing a doubling of liver
336 glycogen synthesis rates during recovery from exercise when sucrose as opposed to
337 glucose (polymers) were ingested (6.6 ± 3.3 versus 3.3 ± 3.0 $\text{g} \cdot \text{h}^{-1}$, respectively:
338 $P=0.002$). When looking at the present data together with the results of Décombaz *et*
339 *al.* (14), it can be concluded that ingestion of both submaximal (~ 0.93 $\text{g} \cdot \text{kg}^{-1} \cdot \text{h}^{-1}$) and
340 maximal amounts (1.5 $\text{g} \cdot \text{kg}^{-1} \cdot \text{h}^{-1}$) of multiple transportable carbohydrates further
341 accelerate post-exercise liver glycogen repletion compared to the ingestion of
342 glucose (polymers) only. These observations can be attributed to the differential
343 effects that glucose and fructose exert on hepatic carbohydrate metabolism. Glucose
344 is a relatively poor substrate for hepatic glycogen synthesis (14, 32, 33) and much of
345 it seems to be released into the systemic circulation to be either oxidized or stored as
346 muscle glycogen (7, 10, 11). In contrast, fructose is primarily taken up by the liver
347 where it can be phosphorylated and converted to glycogen or metabolized to lactate
348 and glucose (28, 29). Lactate will subsequently be released into the bloodstream for
349 oxidation in extrahepatic tissues or can be used as substrate for muscle glycogen
350 synthesis (via gluconeogenesis) (45). In agreement, we observed substantial
351 differences in circulating plasma lactate concentrations between treatments (Figure
352 4B).

353 With liver glycogen contents returning to 66 and 87 g it seems that hepatic glycogen
354 stores were not fully replenished within the 5 h recovery period, despite ingesting
355 large amounts of glucose and sucrose. Liver glycogen content was significantly
356 greater and closer to a normal liver glycogen content of ~ 100 g (21) following
357 sucrose ingestion when compared to glucose ingestion. Since a significant
358 relationship has been found between liver glycogen content at the end of post-

359 exercise recovery and subsequent exercise time-to-exhaustion (9), sucrose as
360 opposed to glucose ingestion may be of benefit for those athletes who need to
361 maximize performance during a subsequent exercise task. To put this into
362 perspective, the difference in liver glycogen content (15-20 g; 57-76 kJ assuming
363 22% efficiency) could provide enough energy to sustain an additional 3-5 minutes of
364 exercise at 75% W_{max} . This difference is by no means negligible for trained cyclists
365 as it represents a 7-14% difference in time to exhaustion (9). Future research should
366 aim to prove the ergogenic benefit of accelerating liver glycogen repletion on
367 subsequent performance in various (laboratory) exercise settings.

368 Besides the benefits of sucrose over glucose (polymer) ingestion to maximize liver
369 glycogen repletion, we also observed much better tolerance to the ingestion of large
370 amounts ($1.5 \text{ g}\cdot\text{kg}^{-1}\cdot\text{h}^{-1}$) of sucrose when compared with glucose (polymers). In the
371 present study we found considerably lower subjective ratings of upper gastro-
372 intestinal complaints (including nausea, general stomach problems, urge to vomit
373 and belching) after sucrose as opposed to glucose ingestion ($P<0.05$). These
374 findings are not surprising, as after ingesting large amounts ($\geq 1.2 \text{ g/kg/h}$) of a
375 multiple transportable carbohydrate source (i.e., sucrose) more transporters in the
376 gastrointestinal tract will be utilized, thereby decreasing water retention, enhancing
377 absorption and subsequently causing less upper abdominal discomfort when
378 compared to the ingestion of glucose (polymers) only (13). The form in which these
379 carbohydrates are ingested may be of lesser importance, as previous work has
380 shown no differences in post-exercise muscle glycogen repletion when ingesting
381 carbohydrate in either liquid or solid form (25, 34).

382 In conclusion, post-exercise sucrose ingestion ($1.5 \text{ g}\cdot\text{kg}^{-1}\cdot\text{h}^{-1}$) accelerates liver, but
383 not muscle glycogen repletion when compared with glucose (polymer) ingestion.
384 Ingestion of large amounts of sucrose are better tolerated than glucose (polymers),

385 making sucrose a more practical carbohydrate source to ingest during acute, post-
386 exercise recovery.

ACKNOWLEDGEMENTS The authors wish to thank the volunteers for their time and effort in participating in this study. We also thank J Maessen for data acquisition, R Veasey, J Forster and T Eschle for blinding and test-drink preparation, and L Ward, D Wallace and T Hodgson for assistance with magnetic resonance examinations.

DISCLOSURES

This study was co-funded by Sugar Nutrition UK and Kenniscentrum Suiker en Voeding Nederland.

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Figure legends

Figure 1. Schematic representation of the experiment. The initial glycogen depletion exercise protocol was followed by three ^{13}C MRS & MRI measurements at $t=0$, $t=120$ and $t=300$ min of post-exercise recovery. The test drink was ingested every 30 min from $t=0$ to $t=270$ min in the post-exercise recovery period as indicated in the figure. Blood samples were obtained every 15 min during the first 90 min of post-exercise recovery. Thereafter they were obtained every 30 min. Visual analogue scales of gastrointestinal (GI) comfort were obtained immediately post-exercise and every 30 min thereafter. At $t=150$ min, no blood sample and visual analogue scale were obtained due to MR scanning.

Figure 2. Liver glycogen contents during 5 h of post-exercise recovery while ingesting glucose or sucrose in well-trained cyclists ($n=15$). # $P<0.05$, significantly different when compared with baseline values; @ $P<0.05$, significantly different when compared to values at 120 min; * $P<0.05$, significantly different from the glucose treatment.

Figure 3. Muscle glycogen concentrations during 5 h of post-exercise recovery while ingesting glucose or sucrose in well-trained cyclists ($n=15$). # $P<0.05$, significantly different when compared with baseline values; @ $P<0.05$, significantly different when compared to values at 120 min. No significant differences between treatments ($P=0.673$).

Figure 4. Plasma glucose (A), lactate (B), insulin (C) and NEFA (D) concentrations during 5 h of post-exercise recovery with ingestion of glucose or sucrose in well-trained cyclists ($n=15$). * $P<0.05$, significantly different between glucose and sucrose treatment. NEFA, non-esterified fatty acid.

Table 1. Liver glycogen concentration, liver volume and liver glycogen content

		Time (min)		
		0	120	300
Liver glycogen concentration (mmol·L ⁻¹)	GLU	167±65	191±66 #	234±81 #@
	SUC	183±47	219±63 #	280±72 #@
Liver volume (L)	GLU	1.79±0.28	1.70±0.24 #	1.72±0.24
	SUC	1.80±0.26	1.78±0.24 *	1.89±0.28 #@*

Values are mean±SD. Liver glycogen concentration (mmol·L⁻¹) and Liver volume (L) at *t*=0, 120 and 300 min post-exercise, after ingesting 1.5 g·kg⁻¹·h⁻¹ glucose (*n*=15: GLU) or sucrose (*n*=15: SUC). Mean values were significantly different from baseline values: # *P*<0.05; 120 min: @ *P*<0.05; and significantly different from GLU: * *P*<0.05. GLU, glucose; SUC, sucrose.

Figure 1

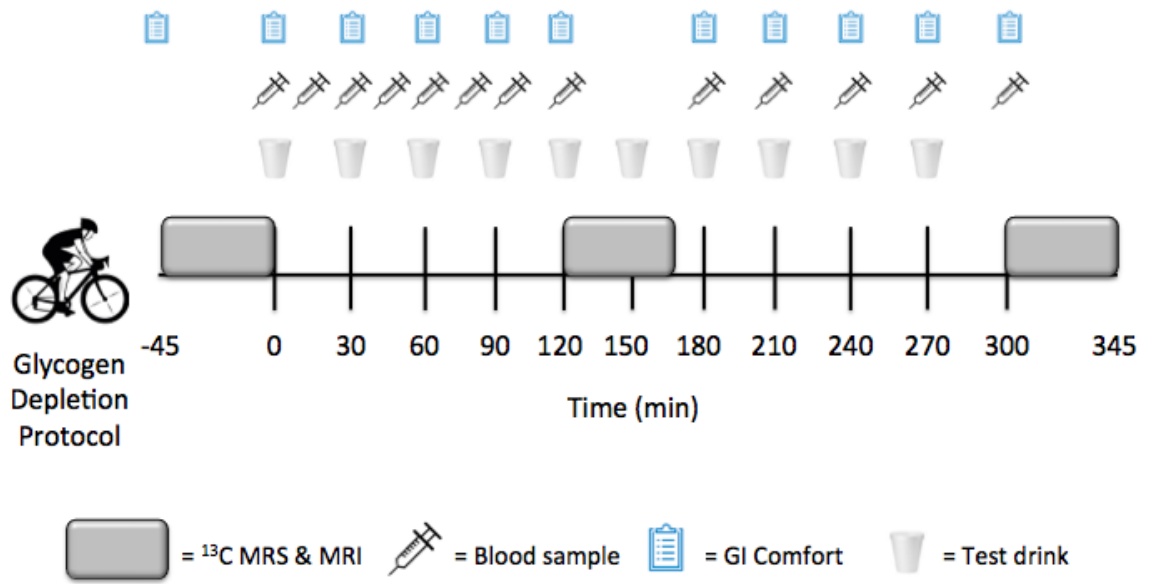


Figure 2

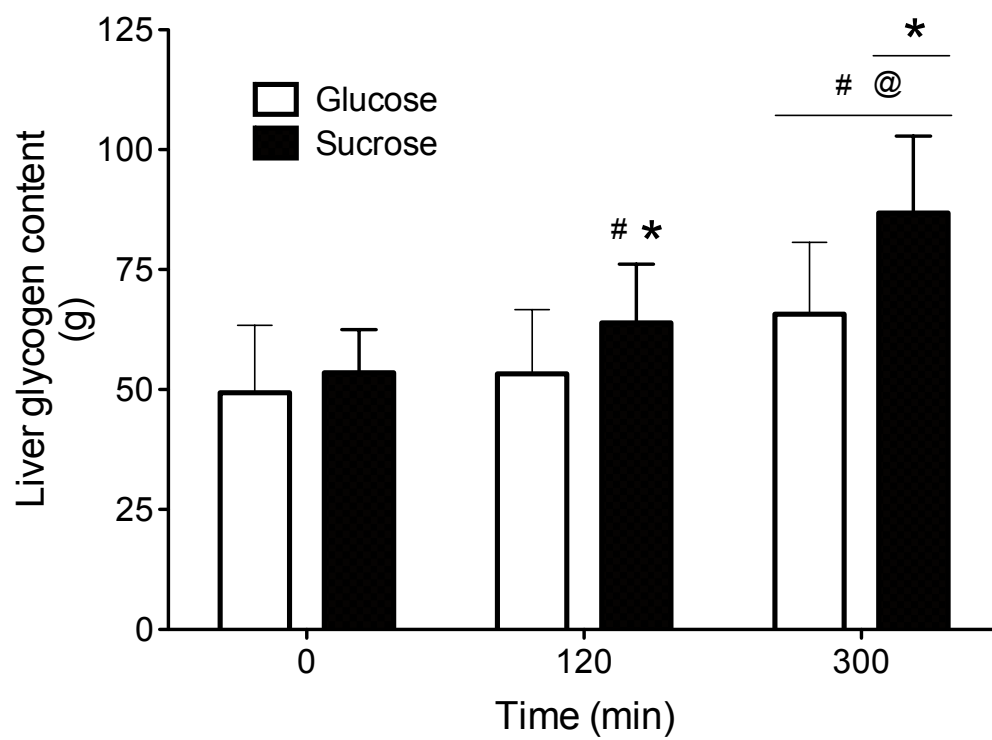


Figure 3

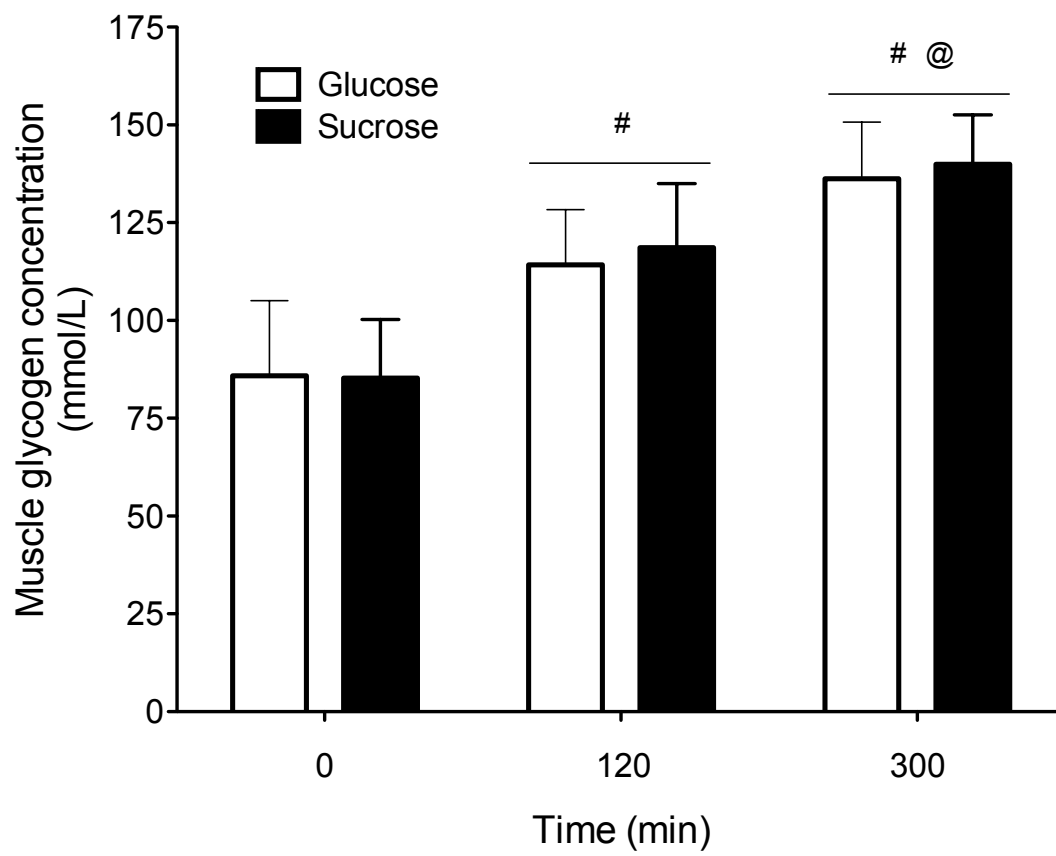


Figure 4

