

# The effect of galactose and fructose intake on synthesis of liver glycogen: a <sup>13</sup>C-MRS study

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## Introduction

Prolonged, strenuous exercise is often associated with liver glycogen depletion (hence hypoglycemia) as well as muscle glycogen depletion. Hepatic glycogen synthesis may play an important role in the post exercise period. The limited available evidence suggests that liver glycogen resynthesis is a priority in the hours after exercise [1]. Glucose, fructose and galactose from diet all serve as substrates for glycogen synthesis, but both galactose and fructose need to be converted into glucose before they can be stored as glycogen. As the major hexose derived from the diet, glucose is quantitatively the most important precursor of liver glycogen. Fructose is transported passively across the intestinal membrane by a facilitative hexose transporter (GLUT5) and is then mainly taken up by the liver and converted to glucose. Small amounts of fructose stimulate glucokinase and glycogen synthase, the two rate limiting enzymes of liver glycogen synthesis. The absorption of fructose is facilitated when it is co-ingested with glucose [2] and indirect evidence suggests that total intestinal carbohydrate delivery may also be augmented with co-ingestion [3]. Galactose, an isomer of glucose, is actively absorbed by the small intestine through the sodium coupled glucose co-transporter (SGLT1), taken up and metabolized in the liver and may stimulate glycogen synthesis in the presence of glucose. Furthermore, galactose would appear to be absorbed faster by the small intestine when combined with glucose [4]. Considering that maltodextrin is easily converted to glucose, the facilitating effects of fructose or galactose may increase the synthesis.

**Hypothesis:** The ingestion of large amounts of maltodextrin-based drinks containing added fructose or added galactose results in faster post-exercise liver glycogen synthesis than an iso-osmolar drink with added glucose.

## Methods

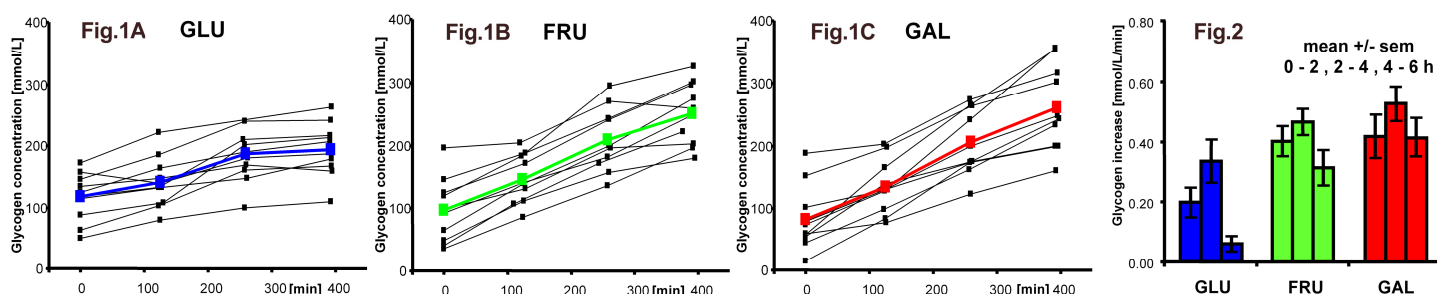
Design: Double blind, randomized cross-over study including 10 well-trained male cyclists (mean  $\pm$  SD: weight 74  $\pm$  8 kg; age 29  $\pm$  5 y; VO<sub>2</sub>max 64  $\pm$  3 ml/min/kg; W<sub>max</sub> 373  $\pm$  42 W). Volunteers were depleted of glycogen by an exhausting exercise [5] consisting of alternated 2-min cycling at 50% and 90% W<sub>max</sub> (exhaustion time 118  $\pm$  8 min; average exercise intensity 59  $\pm$  3 %W<sub>max</sub>; total workload 1564  $\pm$  281 kJ).

Following exhaustion, the volunteers consumed 1 out of 3 experimental drinks (GLU, FRU, GAL) during 6-h recovery in a cross-over design with: MD = maltodextrin; GLU: MD + glucose; FRU = MD + fructose; and GAL = MD + galactose. MD was mixed with one of the 3 monosaccharides in the ratio 2:1, resulting in a total amount of 450g CHO in 3L water (1.25 g CHO/min).

MR images and <sup>1</sup>H decoupled natural abundance <sup>13</sup>C-MR spectra were recorded on a standard 1.5 Tesla MR system (GE SIGNA, GE Milwaukee WI) equipped with a home-built second channel for decoupling and Nuclear Overhauser effect build-up. A double-tuned flexible surface coil (Medical Advance, Milwaukee WI, square-like <sup>13</sup>C circuit 11.3 cm x 11.3 cm, Helmholtz-type <sup>1</sup>H circuit approx. 16 cm diameters) was used for localizer <sup>1</sup>H-imaging, <sup>13</sup>C signal excitation and reception, and for <sup>1</sup>H-decoupling. Based on a calibration curve, rectangular <sup>13</sup>C pulses were set such that the creatine signals from the abdominal muscles, and hence signals from muscular glycogen, were minimized. Four spectra acquired with TR = 165 ms and 4096 scans each were added together. A liver shaped phantom with a known glycogen concentration was used to determine absolute values [mmol/L]. The distance between <sup>13</sup>C coil and liver surface was measured in the localizer images of each individual volunteer and the glycogen phantom was placed accordingly for the calibration measurements. Spectra were fitted in jMRUI [6,7] after removal of the large lipid signals.

## Results

Mean 0-6h replenishment rates  $\pm$  SD for the drinks (Figures 1A-1C) were GLU 0.20  $\pm$  0.08 mmol/L/min, FRU 0.39  $\pm$  0.20 mmol/L/min (p<0.001 against GLU), and GAL 0.45  $\pm$  0.21 mmol/L/min (p<0.001 against GLU). The corresponding peak rates at 2-4h (Fig.2, bars represent time periods 0-2h, 2-4h, and 4-6h) were GLU 0.33  $\pm$  0.22 mmol/L/min, FRU 0.47  $\pm$  0.13 mmol/L/min, and GAL 0.53  $\pm$  0.18 mmol/L/min. An univariate analysis of variance of Fig.2 shows significant differences between drinks (FRU vs. GLU p<0.001; GAL vs. GLU p<0.001) and period 2-4h vs. 4-6h (p=0.0015).



## Discussion and Conclusions

Consumption of the FRU or the GAL drinks during post-exercise recovery led to significantly higher rates of liver glycogen replenishment over 6 hours than when the iso-osmolar GLU drink was consumed, with twice faster net rates of replenishment over 6h. The higher liver glycogen synthesis rates in FRU and GAL compared to GLU might be due, in part, to increased intestinal carbohydrate absorption (hence more carbohydrate might be available for liver glycogen synthesis) and to synergic effects of the different hexoses at hepatic level. Assuming a homogenous glycogen distribution in the liver and an average liver volume of 1.5 L, about 35-40g glycogen may have been stored in the liver with the test drinks (only 17g with the glucose based drink) in 6h, i.e. approximately one half of the average total liver storage capacity.

## References

[1] Casey A et al. Am.J.Physiol. 278:E65 (2000); [2] Truswell AS et al. Am.J.Clin.Nutr. 48:1424 (1988); [3] Jeukendrup A et al. J.Appl.Physiol. 100:1134 (2006); [4] Williams CA. Prog.Biochem.Pharmacol. 21:219 (1986); [5] Kuipers H et al. Pflügers Arch. 410:652 (1987); [6] <http://www.mruj.uab.es/mruj/>; [7] Overloop K et al. NMR Biomed. 9:315 (1996).

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