

## **<sup>13</sup>C-magnetic resonance spectroscopy; a viable technique to study overnight liver glycogen depletion and response to feeding in 8–12-year-old children**

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Owing to its role in maintaining glucose homeostasis, liver glycogen content can be an important marker of altered metabolism seen in disorders which impact health of children. Although <sup>13</sup>C-magnetic resonance spectroscopy (<sup>13</sup>C-MRS) has been used extensively in research to non-invasively assess liver metabolites in adult health and disease, similar measurements in children are lacking. There is a paucity of normative data for liver glycogen concentration ([LGly]) in children to allow comparison with patient cohorts, and time-course assessment of [LGly] in response to feeding has not been reported. The present study quantified the depletion of [LGly] after an overnight fast, and subsequent response to consuming a mixed-macronutrient test drink (Milo®; Nestlé S.A.), using a randomised, controlled, open-label, crossover design. Sixteen (9F:7M) healthy, normal-weight prepubescent children (8–12y) were recruited. Following screening, a 4-day dietary record and accelerometry recording were made to estimate daily energy requirement and indicate dietary preferences. Participants subsequently attended the University on 4 occasions; 2 evening visits, each separated by ≥5days, and each directly followed by a morning visit. An individually tailored meal providing 35% daily energy requirement (60% of energy as carbohydrate, 20% protein, 20% fat) was consumed 3 h prior to evening assessments, with participants remaining fasted from this meal until the morning visit. [LGly] was assessed once in the fed (20:00hrs) and fasted state (08:00hrs) using <sup>13</sup>C-MRS; Spectra acquired on a Philips 3T Achieva MRI system with a single-loop carbon surface coil (with integral proton decouple coils) placed over the liver for 15-minute acquisition (4096 averages). The glycogen peak area was normalised to an external reference and quantified by comparison with signal from a volume with known glycogen concentration. On morning visits, 200 ml Milo® containing 16 g carbohydrate (402kJ), or water was consumed within 10 min, with <sup>13</sup>C-MRS measurements made hourly for the next 4 h. Data are expressed as the mean (SD). Fifteen children completed the study (10.0 (1.1) y, BMI percentile 34.4 (25.0), with 1 male dropping out after screening.

Children aged 8–12y tolerated the MR scanning protocol well, making it an acceptable technique to use in this age group. [LGly] decreased from 687.2 (161.4) to 503.9 (144.5) mmol·l<sup>-1</sup> overnight (-24.7 (22.5) %), with between visit coefficient of variation for fasting [LGly] being 174.0 (13.8) %. The mean incremental responses of [LGly] to the test drink and water were significantly different (time-trend difference P < 0.001), with net iAUC being -85.7 (303.4) and -383.4 (369.8) mmol·l<sup>-1</sup>·240 min respectively (P < 0.01). Comparison with adult data<sup>(1,2)</sup> indicated that [LGly] may be higher in children, but percentage depletion overnight was of a similar magnitude<sup>(1)</sup>. These data indicate that consumption of 16 g of carbohydrate after an overnight fast maintained fasting [LGly] for 2 h and delayed the decrease in [LGly] seen with continued fasting.

### References

1. Taylor R, Magnusson I, et al. (1996) *Clin Invest* **97**, 126–132.
2. Bawden SJ, Stephenson MC, et al. (2014) *Food & function* **5**, 2237–2242.