^{13}C MRS study of postprandial glycogen storage to investigate the second meal effect

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Introduction

The rise in blood glucose after an initial meal following an overnight fast is much greater than the rise after a secondary meal. It has been suggested that this may be due to more efficient storage of glucose as glycogen in muscles and the liver after the second meal [1]. We used ^{13}C spectroscopy to investigate this effect by observing postprandial glycogen levels in the liver and thigh muscles, and conventional biochemical methods to measure blood glucose levels.

Method

We studied 5 healthy volunteers on 2 separate days. The subjects fasted overnight before each study day. On the first day, an unlabelled breakfast (21.9g protein, 21.9g fat, 124.7g carbohydrate and 768kcal) was consumed at t=0min followed 240min later by lunch (35.6g protein, 47.3g fat, 102.8g carbohydrate and 967kcal) labelled with 3g U[^{13}C]-glucose. Baseline ^{13}C glycogen measurements were taken in the liver and thigh at t=-75min on both days. Further measurements were taken every 2 hrs. After two weeks, the subjects were studied again using the same protocol without the preceding breakfast.

Blood glucose measurements were taken at t=-15, 0, 60, 120, 240, 270, 300, 360 and 480min using a Hemocue photometer analyser.

Glycogen measurements were recorded at 3T using a surface probe containing a ^{13}C coil and quadrature ^{1}H coils. The flip angle 2cm in from the centre of the coil was optimised to be 90º. A 100µs hard pulse was used to excite ^{13}C with phase cycling performed using CYCLOPS. Decoupling was achieved using a WALTZ-8 pulse sequence with a peak power of 55±2W. For each scan 3000 acquisitions were made with a repetition time of 360ms, taking 18 minutes altogether. Spectra were analysed using a MATLAB version of MRUI. Quantification was performed using a phantom with a known glycogen concentration which was positioned appropriately for liver and thigh quantification.

Results

Baseline blood glucose concentrations were comparable for both groups (Fig 1a). The breakfast plus lunch group's blood glucose levels rose after breakfast to 7.43±1.05mmol/l at t=60min, which was significantly higher than in the lunch only group. This remained higher up until t=240min. After lunch the blood glucose concentrations rose in both groups with the concentration in the lunch only group rising above that of the breakfast plus lunch group to 6.61±0.87mmol/l at t=300min. The differences between the concentrations then converged and were comparable in both groups at t=480min.

In the breakfast plus lunch group liver glycogen fell from 157.8±93.7mmol/l at baseline to 119.0±42.6mmol/l 3.5 hours after breakfast (Fig 1b). During the same interval the baseline liver glycogen concentration in the lunch only group dropped from 223.6±53.4mmol/l to 54.3±21.0mmol/l. At t=510min the concentration in the lunch only group had risen significantly to a maximum 282.5±98.1mmol/l ($p<0.05$), with a greater increase in the group which had consumed breakfast (484.2±197.3mmol/l). However, the difference in the glycogen increment from t=210min to the peak at t=510min between the groups fell short of significance ($p<0.11$).

The thigh glycogen concentration in the lunch only group was 65.9±32.2mmol/l at baseline and then fell to 61.5±15.6mmol/l before lunch as expected (Fig 1c). Glycogen concentration reached a maximum of 99.3±28.1mmol/l at t=540min. This trend did not differ between groups and concentrations remained steady during the first 4 hours. However, after lunch we recorded a greater increment in concentration to the maximum of 135.2 ±46.6mmol/l at 540min ($p<0.17$).

Discussion

The blood glucose concentrations were comparable in both groups up until t=60min when the concentration was higher in the group that had breakfast.

The hepatic glycogen concentrations were also comparable in both groups up until 2 hours after breakfast time when the group that had eaten breakfast had a significantly higher glycogen concentration than the group that hadn't. This corresponds with a drop in the blood glucose and occurred at the time where a rise in glycogen levels due to ingested carbohydrates is expected. It also appears in Figure 1c that the glycogen concentration in the thigh muscle rose in the breakfast plus lunch group 120min after breakfast.

The increase of liver concentration following lunch was 61% higher in the breakfast plus lunch group (368.8±154mmol/l vs 228.14±85mmol/l). A similar trend was observed in the thigh glycogen concentrations the increment being 50% greater. This corresponds with a lower blood glucose level after lunch for the breakfast plus lunch group than the in lunch only group after lunch.

These findings support the hypothesis that the second meal attenuation in glucose rise is a consequence of priming of glycogen synthesis in muscle and liver. This is an important phenomenon and has considerable implications for the management of diabetes. If the priming of glycogen synthesis rates could be achieved by non-glucose stimulation of insulin secretion prior to the first meal of the day a major decrease in hyperglycaemia will be possible.

Figure 1a

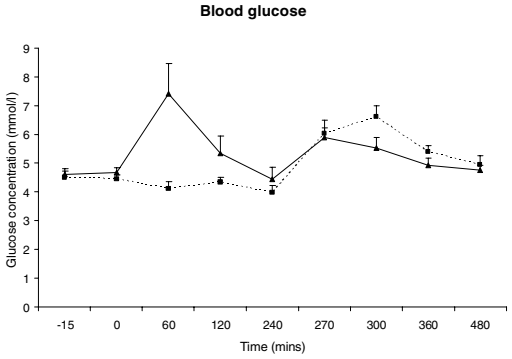

Figure 1b

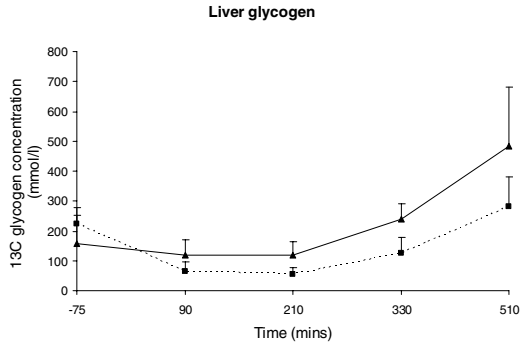

Figure 1c

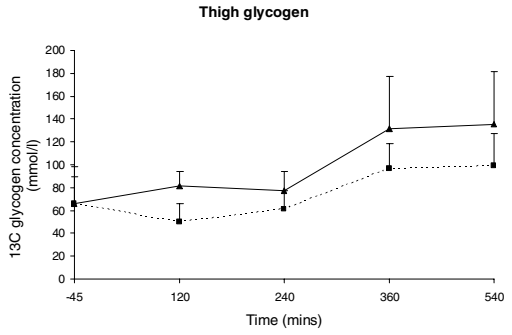

Fig 1: Blood glucose (a), liver glycogen (b) and thigh glycogen (c) concentration as a function of time for a group having just lunch (■) and a group having breakfast plus lunch (▲).

References

1. Carey P.E et al, AMJ Physiol-Endoc M 284, E688-E694, 2003