^{13}C MRS of muscle and hepatic glycogen metabolism in type I diabetes to investigate muscle exhaustion

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Introduction

Type I diabetes is a common condition, in which patients often find exercise overly exhaustive and may suffer from dangerously low blood glucose. One explanation for this could be insufficient hepatic and muscle glycogen. Many experiments, using either muscle biopsies or ^{13}C MRS, have monitored the glycogen metabolism following both low intensity (1) and high intensity (2) exercise in normal healthy subjects, however, in type 1 diabetics little work has been done to follow glycogen metabolism during exercise. The nature of liver glycogen homeostasis has also been researched post exercise (3) but again not in type I diabetics. This study followed liver and muscle glycogen levels and blood glucose levels in type I diabetics and control subjects before, during and immediately after exercise, using ^{13}C MR spectroscopy and conventional biochemical analysis.

Protocol

A group of type I diabetics (n=7) and a group of control subjects (n=5) were monitored before and during exercise. Each of the subjects followed the same protocol but type 1 diabetics received intravenous insulin continuously throughout the day. All subjects fasted for 12 hours prior to the study and insulin levels of the diabetic subjects were monitored over this period. Baseline (t=0) ^{13}C measurements of liver and thigh muscle glycogen were taken prior to a standard mixed meal. Measurements of hepatic and thigh muscle glycogen were repeated at 2.5h and were followed by 40 minutes of exercise in the form of cycling. Measurements of glycogen were taken at 4, 5.5 and 7h with 40mins of exercise in between.

All glycogen measurements were performed at 3.0T, using a circular ^{13}C surface coil and quadrature ^{1}H coils. A 100μs hard pulse was used to excite ^{13}C with CYCLOPS phase cycling, proton decoupling was achieved with a WALTZ-8 sequence at a power of 55±2W. The repetition time for each acquisition was 360ms, keeping the power deposition within the SAR limits. For each time point 2000 acquisitions were made over 12mins. The C1-glycogen peak at 100.4 ppm was analysed with a MatLab version of MRUI. Quantification of liver and thigh glycogen concentrations was achieved by using a suitably shaped phantom of known glycogen concentration. Blood samples were taken for each subject to measure glucose and insulin levels prior to each glycogen measurement.

Results

Figure 1

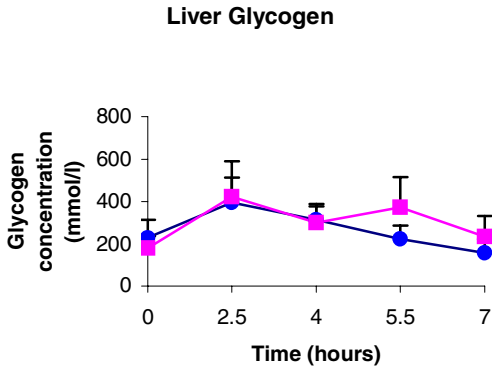

Figure 2

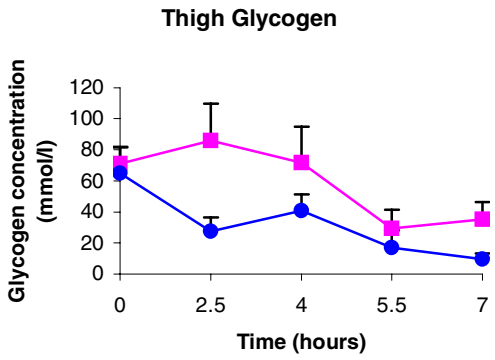

Figure 1 and 2: glycogen concentrations over time for controls (●) and type I diabetics (■) for the liver and thigh respectively

At baseline, controls and diabetics have similar hepatic glycogen levels (fig, 1), which increase after lunch in both groups from 228±84 mmol/l to 395±117 mmol/l and 117±58 mmol/l to 422±169 mmol/l respectively. The hepatic glycogen levels in both groups subsequently decrease and return to baseline after the third bout of exercise.

The baseline glycogen concentrations in the thigh muscle were found to be similar in both groups with concentrations of 65±17 mmol/l and 71±11 mmol/l for controls and diabetic subjects respectively (fig. 2). However, after breakfast the controls exhibited a net decrease in thigh muscle glycogen with levels falling to 28±9mmol/l by 2.5h. Interestingly this recovered after the first bout of cycling (4h) with the glycogen reaching concentrations similar to baseline ($p>0.1$). The level then began to decrease again as two more bouts of cycling were undertaken, and had diverged severely from baseline by 7h ($p<0.02$). In contrast to the control subjects, the diabetic group did not suffer a depletion of glycogen between 0 and 2.5h, and levels, which were higher than in controls, appeared to remain stable between these points ($p>0.1$). However, after the second bout of cycling, depletion occurred with levels falling to 29±12 mmol/m ($p<0.01$). The glycogen concentrations then appeared to stabilise again with no further decrease seen despite exercise ($p>0.1$). At this point (7h) the glycogen was depleted severely from the baseline to 35±11 mmol/l ($p<0.01$), a concentration significantly higher than controls.

Discussion

The liver glycogen concentrations were found to be similar in the controls and the type I diabetic subjects throughout the day ($p>0.1$). This suggests that in situations where insulin levels are controlled hepatic glycogen homeostasis in these subjects is not impaired even when exercise is undertaken.

The baseline levels of glycogen in the thigh muscle are similar for controls and type 1 diabetics. However, there is a significant difference in levels for controls and diabetic subjects after breakfast ($p<0.05$). The similarity in levels is partly restored after the first bout of cycling ($p>0.1$) diverging again only after the third bout of cycling (7h). So in stark contrast to what might have been expected in type I diabetics hepatic glycogen behaves normally with exercise and muscle glycogen, rather then being too low, is actually higher after intense exercise in comparison to controls. The failure of the muscle glycogen levels to decrease at the same rate as in the controls, suggests a possible failure to utilise glycogen in type I diabetes and this may explain why the diabetics experience muscle exhaustion.

References

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