Assessment of acetylcarnitine in individuals with type 1 diabetes after exercise in eu- and hyperglycemia using $^1$H MR spectroscopy in skeletal muscle

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Introduction / Background

$^1$H magnetic resonance spectroscopy (MRS) of the skeletal muscle allows for the non-invasive assessment of acetylcarnitine (AC) accumulation during and after exercise. AC increases when the production of acetyl-CoA by the pyruvate dehydrogenase complex exceeds its utilization by the TCA-cycle. The transfer of the acetyl-group to carnitine regenerates free CoA which allows intramitochondrial CoA-dependent reactions to proceed. This was shown with muscle biopsies that different diets and thus altered substrate availability not only affect PDC-activity but also AC-concentrations. So far, $^1$H-MRS has not been used to follow the influence of substrate availability upon the concentration of AC. Therefore, we reanalyzed muscle spectra of a study set up to investigate the effects of euglycemia vs. hyperglycemia on substrate metabolism during prolonged exercise in type 1 diabetic subjects, where the original endpoints had been intramyocellular lipids (IMCL) and glycogen.

Methods

Details of this randomized, single-blinded cross-over trial have been described before. Briefly, 7 physically active type 1 diabetic males (33.5 ± 2.4 years, BMI: 24.3 ± 0.4 kg/m²) performed prolonged ergometer exercise (120min, 55 - 60% VO₂max) twice; on one occasion in euglycemia (5 mmol/L), on the other in hyperglycemia (11 mmol/L). Insulin infusion was kept constant and equal during both conditions (median: 7mU m⁻² min⁻¹). Fuel metabolism before and during exercise was assessed by a combination of indirect calorimetry and tracer methods (D-[U-¹³C]glucose, D-[6-6-²H₂]glucose). Furthermore $^1$H-MRS and $^{13}$C MRS (1.5T SIGNA, GE Medical) were applied for the assessment of exercise-induced depletion of IMCL and glycogen.

For the present evaluations, $^1$H-MRS spectra obtained from vastus intermedius (ROI: 11 x 12 x 18 mm³, PRESS localization, TR=3s, TE=20ms, 2000 IMCL and glycogen.

Results

With factors: eu- vs. hyperglycemia, pre- vs. post-exercise, and the mutual interaction.

Discussion

We have shown that the influence of substrate availability upon exercise-induced AC accumulation can be assessed non-invasively by $^1$H-MRS. In particular, post-exercise AC in vastus intermedius of type 1 diabetic subjects was found to be more elevated in euglycemia than in hyperglycemia. This was accompanied by increased fat oxidation and IMCL use during euglycemia. This is contrary to initial expectations, where we had speculated that AC production would be higher in hyperglycemia, because a presumed increased glycolytic flux and pyruvate availability should stimulate pyruvate dehydrogenase complex activity. However, AC production in muscle is multifactorial and, for instance, it has been shown in biopsies from resting muscle that high levels of AC coincide with high rates of β-oxidation. In order to follow glycerogen metabolism, $^1$H-MRS spectra were acquired after $^{13}$C-MRS in this study, resulting in a delay of about 60 minutes after exercise for the measurements of AC. Therefore, it can be speculated that either AC accumulated differently after exercise, or that AC might have decreased more rapidly after exercise in hyperglycemia. From the MR-methodological point-of-view, it should be mentioned that the consistent observation of a TMA peak in the difference spectra confirms the idea that the carnitine moiety becomes more NMR-visible upon acetylation. This demonstrates the importance of local molecular environment for the understanding of $^1$H MRS of muscle.

References


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Fig. 1

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Fig. 2

Fig. 1

Fig. 2

Δ Acetylcarnitine [n.a.u.]

Euglycaemia Hyperglycaemia

Euglycaemia Hyperglycaemia

Mean Individuals