Combined influence of diet and physical activity on intramyocellular lipids (IMCL), glycogen, and insulin resistance

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Introduction: Insulin resistance is a common disorder in western societies and plays an important role in the pathogenesis of numerous affluent diseases, e.g. diabetes. Although the underlying mechanisms are still not fully understood, it has been recognized that lipids and a sedentary lifestyle are often involved in the pathogenesis of insulin resistance. It was the goal of our investigation to use multinuclear $^{1}H/^{13}C$-MR spectroscopy for the observation of IMCL (^{1}H-MRS) and glycogen (^{13}C-MRS) stores in skeletal muscle under the influence of inactivity and different high-fat (HF) and high-carbohydrate (HCH) diets.

Methods: Eight untrained healthy male volunteers (age: 23±1 years; BMI: 21.6±0.8 kg/m^2) participated in this blinded cross over study with a minimal gap of 10 days between the trials. After a 2 day equilibrated preparatory diet (50% carbohydrates CH, 35% fat F & 15% proteins P, 1.6 x basal metabolic rate BMR) and controlled physical activity (2 x 30 minutes on a bicycle ergometer at 70W and ´normal´ physical activity during the day) subjects consumed either an isocaloric HF- or HCH-diet during bed rest (BR) for 60 hours. HF (45% F, 40% CH, 15% P) and HCH (15% F, 70% CH, 15% P). Both diets covered 1.2 x BMR, accounting for the reduced physical activity.

A control trial was performed with six of the eight volunteers where the BR period was replaced by continued controlled physical activity. During this time the subjects were fed an identical HF diet, however covering 1.6 x BMR.

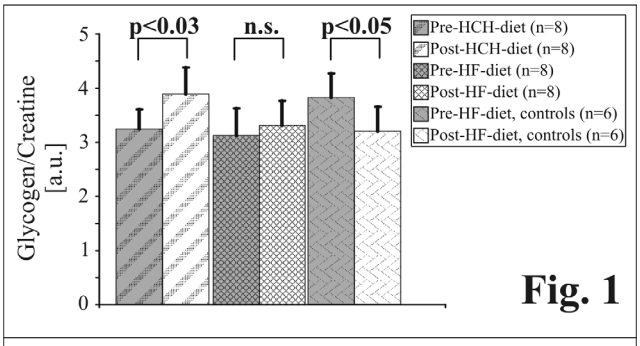

Fig. 1

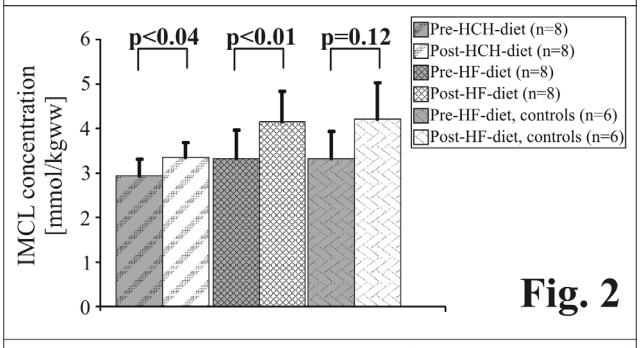

Fig. 2

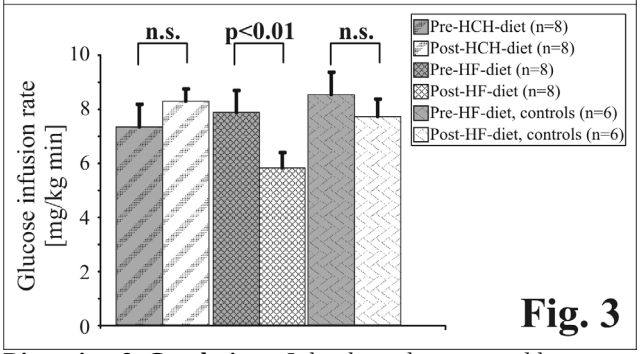

Fig. 3

Immediately before and after the BR- and the control-period (days 2 & 5) insulin sensitivity was measured using the hyperinsulinemic euglycemic clamp technique (90 minutes administration of 1 mU insulin per kg and minute) following a standardized breakfast in the morning. The glucose infusion rate (GIR, [mg/kg·min]) during the last 30 minutes of the clamp served as a measure for insulin sensitivity. Glycogen (in arbitrary units relative to Creatine [a.u.]) and IMCL (in units of mmol per kg wet weight [mmol/kgww]) stores were determined with $^{1}H/^{13}C$-MRS in the right leg's *m. quadriceps femoris* few hours after the clamp.

MRS & signal processing: ^{1}H-MRS: single voxel PRESS, 11×12×18mm^3 placed in the *m. vastus intermedius*, TR=3s, TE=20ms. ^{13}C-MRS: pulse and acquire, adiabatic excitation, decoupling and NOE, TR=165ms (coil was placed above the *m. rectus femoris*).

Following eddy current correction ^{1}H-spectra were evaluated with TDFDFIT [1] using the fully relaxed water signal as internal standard. ^{13}C-spectra were processed using the MRUI software package [2]. After phase correction of the spectra and filtering of the large CH_2=CH_2 signals, peak areas were determined with AMARES.

Statistics: All data are expressed and shown as mean value ± SEM. Statistical significance was assessed using a double-sided paired Student's t-test.

Results: Figures 1 and 2 show relative Glycogen and absolute IMCL concentrations before (bars with a grey background) and after (white background) the distinct dietary and physical activity period (HCH-BR, HF-BR and HF-control). Glycogen levels significantly increased during the HCH-BR trial (19±7%) whereas no significant changes were observed during HF-BR(13±15%). During the control trial – including physical activity at HF-diet – Glycogen levels significantly decreased by 17±7%. Significant increases were found for IMCL levels during BR period independent of the diet (HCH: 17±8%, HF 32±7%. The increase of 31±19% during the control trial did not reach significance. Figure 3 shows the glucose infusion rates during the last 30 minutes of the clamp as a measure for insulin sensitivity. HCH-BR conditions as well as the control trial did not change insulin sensitivity, whereas HF-diet combined with physical inactivity led to a significant decrease of the GIR by 24±6%. Additional tests revealed no statistically significant differences for the pre- and post-trial levels of plasma glucose, insulin and non-esterified fatty acids (NEFA) except for the difference of the NEFA pre-clamp values between HF-BR and HCH-BR ($p<0.05$).

Discussion & Conclusions: It has been demonstrated by means of multinuclear $^{1}H/^{13}C$-MRS that already moderate behavioral changes in diet and physical activity can lead to significant changes of muscular glycogen and IMCL (see Figs. 1 & 2). To our knowledge, this is the first time that a relatively modest increase in dietary fat and a short period of physical inactivity have been combined to investigate a possible interaction of these two factors with insulin sensitivity. Results from the hyperinsulinemic euglycemic clamp (see Fig. 3) suggest that during a very short period of 2½ days, insulin sensitivity decreases if physical inactivity is combined with a diet rich in fat. It seems that BR under the regime of a high carbohydrate diet does not impair insulin sensitivity, neither does a HF-diet modify insulin resistance as long as moderate physical activity is maintained.

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References: [1] Slotboom J, Boesch C, Kreis R. *Versatile frequency domain fitting using time domain models and prior knowledge*. Magn Reson Med 1998;**39**:899-911

[2] http://www.mrui.uab.es/mrui