Increase of intrahepatocellular lipids (IHCL) during exercise in healthy volunteers

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Introduction

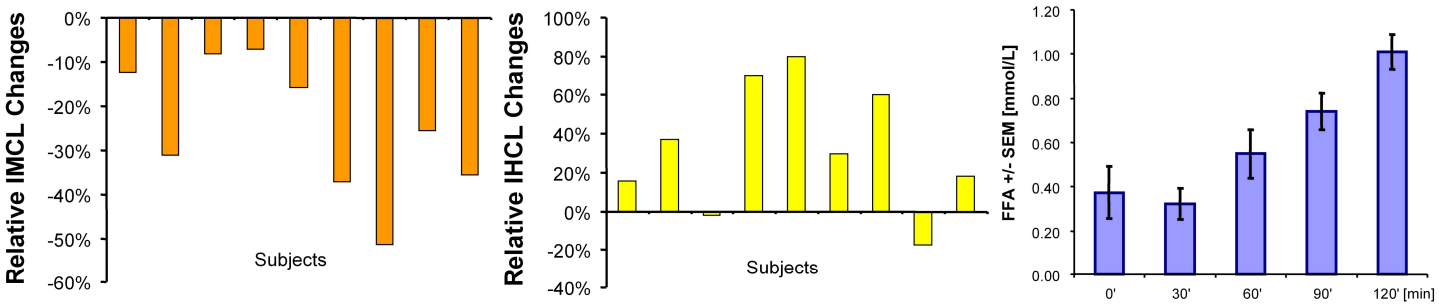
The "metabolic syndrome" represents a cardiovascular risk factor with epidemic dimensions all over the world. Depending on the exact definition and the group of individuals included, up to 40% of the public suffer from that condition, which includes insulin resistance as the major symptom. Because intramyocellular (IMCL) and intrahepatocellular lipids (IHCL) are both related to insulin sensitivity [1], ^{1}H-MR spectroscopy studies of these lipids are of crucial importance to understand the pathophysiology and to follow therapeutic interventions. IMCL are metabolically active and the concentration in skeletal muscle can be changed within several hours with diet and exercise. In contrast, the short-term effects of exercise and diet on IHCL are much less explored. This study investigates the influence of exercise on IHCL and IMCL levels in order to achieve an improved standardization of IHCL measurements and to understand the factors that increase IHCL levels.

Methods

Nine healthy volunteers (age 35 ± 12 years; BMI 22.6 ± 2.7 kg/m^2; VO_2peak 56.1 ± 10.7 ml/kg/min) were enrolled in this study. In order to fill the lipid stores, three days prior to the study, the volunteers did not perform exercise and increased the daily fat intake by additional fat snacks (0.75 g/kg/d). Following a first MR examination with determination of IMCL and IHCL, the volunteers exercised on a treadmill at 50-55% of VO_2peak, followed by a second MR examination. The MR examinations were done on a 3 Tesla system (TIM TRIO, SIEMENS Erlangen) using an extremity coil and a PRESS sequence (TR 3s, TE 30ms, 11x12x18 mm^3, 128 scans) for a determination of IMCL in the m.tibialis anterior, and a body array coil with a STEAM sequence (TR 5s, TE 20ms, 20x30x30 mm^3, average of 8 single acquisitions in expiration) for a determination of IHCL in segment 6 of the liver. Fitting of the spectra was done in jMRUI [2], using published prior knowledge for IMCL [1] and variable lines for water and the methylene groups in IHCL. The unsuppressed water signal served for IMCL and IHCL as an internal standard.

Results

The figure shows (left to right) a significant reduction of IMCL during exercise (mean ± SD: 25% ± 5%, p = 0.006, two-tailed t-test), which contrasts to a significant increase of IHCL (mean ± SD: 32% ± 11%; p = 0.026, two-tailed t-test). During exercise, free fatty acids (FFA) also increased significantly (p < 0.001, two-way ANOVA).



Discussion and Conclusions

The reduction of IMCL during exercise has been expected from several reports in literature (see citations in [1]); however, an increase of IHCL as a consequence of 2 hours exercise has been somewhat surprising. It is well known that during exercise, the skeletal muscle uses IMCL and the body releases FFA. This higher level of FFA seems to stimulate the synthesis of IHCL. On a first glance, it is surprising that exercise reduces insulin resistance and increases IHCL, while higher IHCL levels are related to higher insulin resistance. This apparent paradox can be explained by the different time frame - the increased IHCL level due to exercise measured in this study is a short term effect while exercise improves insulin resistance and thus reduces IHCL levels in the long term. In animals [3], it has been shown that exercise and the subsequent decrease of hydrophobic glycogen leads to a reduction of intracellular water. This effect could not more than partially explain the increase of the fat/water ratio seen in this study, which is much larger (32% ± 11%) than the expected reduction of the water content in the animal study (<10%).

The findings of this study have relevance for our understanding of hepatic lipid metabolism, in particular for correlations of IHCL with insulin resistance.

References

[1] Boesch C, Machann J, Vermathen P, Schick F. NMR Biomed. 19: 968-988 (2006). [2] http://www.mrui.uab.es/mrui/. [3] Latour MG, Brault A, Huet PM, Lavoie JM, Am. J. Physiol. 276, R1258-R1264 (1999).

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