

# Testing the efficacy of therapeutic approaches with in vivo <sup>1</sup>H MRS of intramyocellular lipids in the rat skeletal muscle

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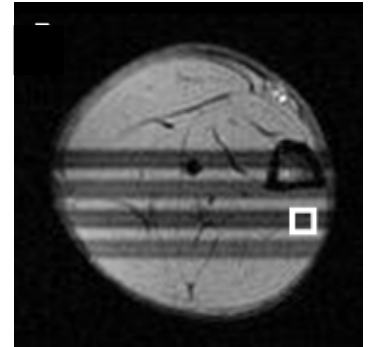
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## Introduction

In recent years, intramyocellular lipids (IMCL) have been identified as important markers for insulin resistance in metabolic disorders, such as type 2 diabetes [1,2]. As a consequence, the non-invasive assessment of such triglycerides by localized proton magnetic resonance spectroscopy (<sup>1</sup>H-MRS) in animal models has evolved to a valuable tool for the characterisation of new therapeutic approaches [3,4]. In addition to IMCL, which accumulates as droplets in the cytoplasm of muscle cells, extramyocellular lipids (EMCL) are stored as interstitial adipocyte triglycerides in sheet-like structures between the muscle fibers [5]. In this contribution, we present the application of in vivo MRS to evaluate the efficacy of Rimonabant treatment on the muscle lipid content and its correlation with biochemical data.

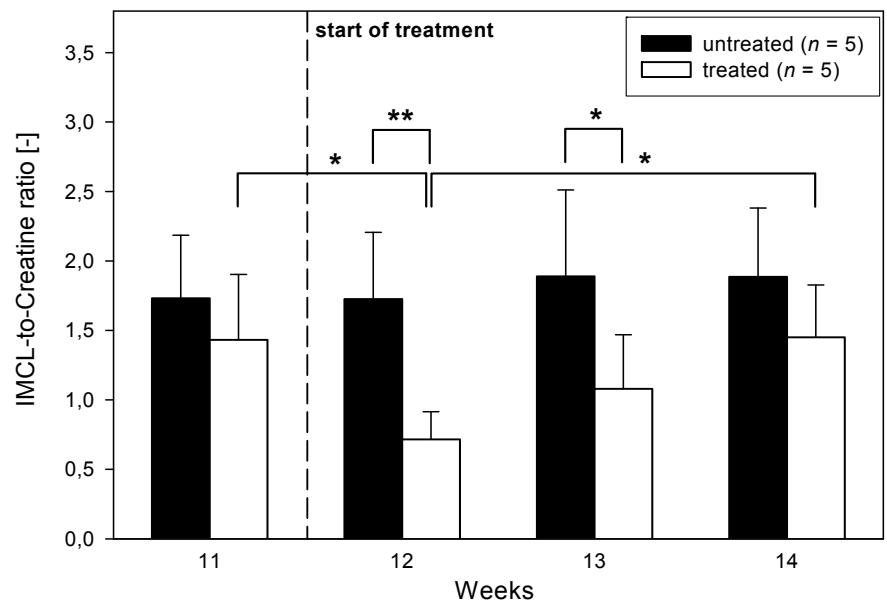
## Methods

MR measurements were performed on a Biospec 47/40 scanner (Bruker BioSpin, Ettlingen, Germany). A bird-cage resonator volume coil was used for excitation, a custom-made Helmholtz coil set-up for signal reception [6]. For positioning the MRS voxel in the tibialis muscle a  $T_1$ -weighted pilot scan (right image) with the following parameters was acquired: TR 100 ms, TE 4 ms, flip angle 55 degrees, NEX 6, field-of-view 3.6 cm x 3.6 cm, slice thickness 1.2 mm, interslice distance 1.5 mm, total measuring time 1 min 55 seconds. Single voxel MR spectra were acquired using a PRESS sequence with following parameters: TR 1300 ms, TE 20 ms, voxel size 1.6 x 1.6 x 3.2 mm<sup>3</sup> (8.13 mm<sup>3</sup>), NEX 512, digital resolution 1024 data points, total measuring time 11 minutes. MR spectra were analyzed by the LCModel software package (Version 6.1) by S. W. Provencher using the built-in basis set for the analysis of muscle spectra [7].



## Results

Fig. 1 shows the IMCL content in the tibialis muscle of obese rats (diet-induced obesity, DIO) before and after treatment with Rimonabant (in week 12) compared to controls. After a significant reduction of IMCL content, the reservoirs almost completely recover within two weeks after the end of Rimonabant treatment (DIO treatment is continued during this time). In addition to significant differences between control and DIO rats, different time points can be distinguished by their respective IMCL content in DIO rats. The IMCL data nicely correlates with body fat content and body weight and other biochemical data, such as blood sugar content. The reduction of IMCL is most likely explained by increased metabolism of lipids induced by Rimonabant treatment.



IMCL-to-creatine ratio after Rimonabant treatment

## References

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