Age effect on intramyocellular lipid composition in db/db mice using *in vivo* ^{1}H-MR spectroscopy.

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Purpose:

In vivo proton NMR spectroscopy (^{1}H-MRS) of intramyocellular lipid (IMCL) became interesting because of the relation between the IMCL level and the insulin resistance both in human and in rat [1, 2]. It has been demonstrated also that IMCL level is influenced by age, obesity, training status [1].
Very recently, ^{1}H-MRS of the IMCL in mice model were investigated in spite of the experimental difficulties due mainly to the small size of muscle, low signal to noise ratio and the strong extramyocellular lipid (EMCL) signal contamination [3,4].
The aim of the present paper is to assess the longitudinal evolution of the IMCL composition in db/db mice and their littermates control mice.

Methods:

Two groups of eight male db/db mice (BKS.Cg-m+/+Lepr<db> (n= 4) and their littermates 57BLKS/j <m+/m+> (n= 4) at 7 and 17 weeks of age were used for this study. Mice were anesthetized during the NMR experiments by inhalation of 1.5 % of isoflurane mixed with N_2O.
MRS experiments were performed on a 7 T horizontal Biospec system (Brucker Biospin, Germany). A birdcage coil with an inner diameter of 72 mm was used for RF excitation and a surface coil of 15 mm for MR signal reception. Legs of mice were fixed to be parallel to the scanner tunnel axe, in order to have an accurate alignment of the tibialis anterior (TA) muscle fibers with the B_0 magnetic field direction. The surface coil was positioned as near as possible to the legs and in front of the TA muscle to increase the MRS sensitivity. After acquiring tree-dimensional scout imaging, localized proton spectra were obtained from the TA using PRESS sequence (TR/TE= 2000/18 ms, 1×1×2 mm^3, 1024 averages). Data were processed using the j-MRUI software and suppression of residual water components was achieved using the HLSVD algorithm. Spectra were corrected for B_0 shift by referencing total creatine (tCr) resonance at 3.02 ppm. Quantification of components was performed using AMARES. Data are presented as means of IMCL-tCr ratio ± SD.

Results:

Figure 1 shows an example of water–suppressed ^{1}H-MR spectra obtained from TA of diabetic mice and their littermates at 7 and 17 weeks. At 7 weeks of age, mean body weights in the control and db/db mice were 23.5±1.1 g and 34± 2.5 g respectively with a significant difference (p<0.01). The IMCL content of diabetic mice TA was significantly different from the IMCL (2.41± 0.5 Vs 1.21± 0.35, p<0.01).

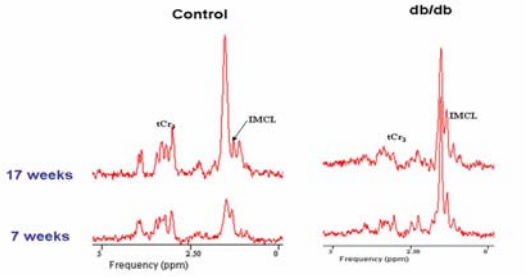

Figure1: Example of 1H NMR spectra taken from a 2µl voxel in tibialis anterior at 7 and 17 weeks

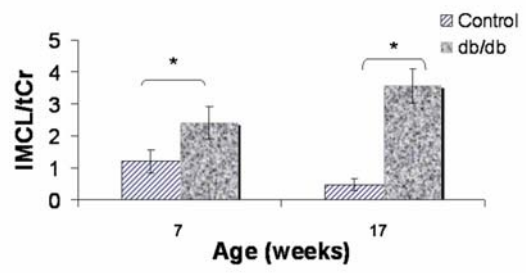

*Figure2: In vivo 1H-MRS data for IMCL/tCr in tibialis anterior muscle in control and db/db mice. Values are means± SD, *p<0.01.*

At 17 weeks of age, a significant difference was observed in the mean weights of the two groups of mice (28.5± 2.14 and 57.6± 1.68 g in the control and diabetic mice respectively, p<0.01) and also in the IMCL level (3.56± 0.53 Vs 0.47± 0.18, p<0.001).
In comparison to mice aged of 7 weeks, the LIMC levels were significantly decreased in control mice at 17 weeks of age (Figure 2, p<0.01). However; in db/db mice the IMCL content was increased between 7 and 17 weeks of age (Figure 2, p<0.05).

Discussion:

In all investigated mice, a higher IMCL-TCr ratio was found in the db/db mice in comparison to their control littermates. These results were observed both at 7 and at 17 weeks. With age, IMCL level is decreased in the control mice in contrast to db/db mice that IMCL is increased. A similar age-related decline in IMCL was observed in normal rats [2]. However, no data was published in mice. In conclusion, this study shows that ^{1}H-MRS can be used to achieve longitudinal evolution of IMCL, and consequently to characterize insulin resistance and drug effects, on mice model.

References:

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