Differences in skeletal muscle lipid metabolism in upper and lower extremities by localized correlated spectroscopy

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Introduction: Skeletal muscle is an important tissue for the maintenance of glucose and fatty acid homeostasis in the body, and being a prime target for insulin action is therefore linked to insulin resistance. Intramyocellular lipids (IMCL) and extramyocellular lipids (EMCL) have been measured extensively by Magnetic Resonance Spectroscopy (MRS) in diabetes and exercise physiology (1). However, the differences in lipid metabolism in upper and lower extremity skeletal muscles have not been investigated. In this study we employed localized 2D MRS (L-COSY) technique to investigate the lipid composition in flexor digitorum profundus in the forearm and soleus muscle compartment in lower extremity respectively.

Methods: Five male subjects with BMI ranging from 20 ± 5 kg/m^2 in the age group of (25 ± 5 years) participated in this study. All measurements were performed on a 3.0 T whole-body clinical MRI/MRS scanner using a 12cm T/R coil for forearm (Fig. 1a) and the T/R extremity coil (Fig. 1b) for lower extremity. 3mm thick slices of gradient echo images of forearm (Fig. 1c) and leg (Fig. 1d) was obtained for MRS localization. The IMCL content was determined within a single voxel (2.5 x 2.5 x 2.5 cm^3) in respective muscle compartments by L-COSY technique (TR=2s, minimal TE=30ms, 40 t_1 increments with 16 averages) with the total acquisition time of ~ 21 minutes.

Fig.1 (a) (b) (c) (d)

Results:

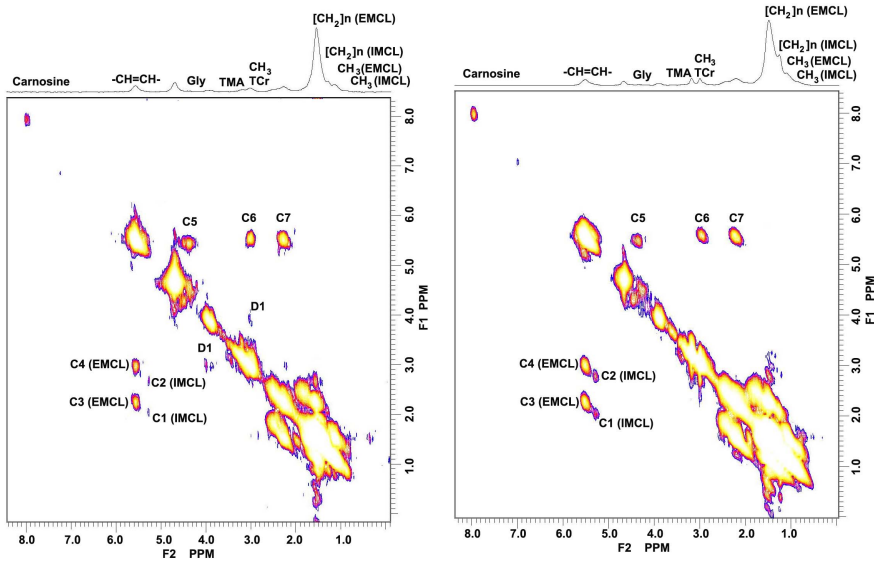

Figure 2 shows the 2D L-COSY spectrum recorded from the forearm (a) and in the soleus muscle (b) of a healthy subject. Various resonances from IMCL and EMCL, trimethyl ammonium containing molecules (choline), glycerol backbone protons, and carnosine were identified. Note that the creatine resonances (3.9,3.02 ppm) exhibit residual dipolar couplings D1 in the forearm. Cross peaks C1 (from IMCL), C3 (from EMCL) arise due to the scalar coupling between olefinic (-CH=CH-) and allylic methylene protons C*H*$_2$CH=CH and thus appear if the methylene protons are adjacent to only one unsaturated site. Cross peaks C2 (from IMCL), C4 (from EMCL) arise from the scalar coupling between the olefinic (-CH=CH-) and diallylic methylene protons (-CH=CH-C*H*$_2$-CH=CH-). All assignments were made based on the earlier 2D MRS studies in calf muscle (2). The average IMCL / Cr estimated from the forearm (upper extremity) and soleus muscle (lower extremity) were 2.6 ± 1.3, 5.8 ± 1.5 respectively.

Fig 2. L-COSY spectrum recorded in the forearm (a) and soleus muscle (b)

Discussion: The skeletal muscle lipids accumulate from either increased uptake of fatty acid, or alternatively, from diminished fat oxidation. Given the different roles of arm and leg muscles and their different activation in daily life, it is possible that the skeletal muscle fatty acid kinetics is not equal in arms and legs. Our studies indicate a heterogeneity in the distribution of intramyocellular lipids in upper extremity compared to lower extremity.

Conclusions: We have demonstrated the differences in accumulation of intramyocellular lipids in upper and lower extremity. The forearms have lower accumulation of IMCL compared to lower extremity thereby being less prone to the development of insulin resistance.

References: 1. Boesch C., J Magn Reson Imaging, 25: 321 (2007).
2. Velan SS, Durst C, Lemieux SK, et al., J Magn Reson Imaging, 25: 192 (2007).