Identification of distinct patterns of fat metabolism in skeletal muscle of male and female human subjects using localized 2-dimensional correlated spectroscopy

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Introduction: Fatty acid metabolism plays a central role in the development of disorders of glucose metabolism, such as insulin resistance and diabetes, leading to significant interest in the detection of intramyocellular (IMCL) and extramyocellular (EMCL) pools in skeletal muscle (1). In order to define pathophysiology based on these measurements, it is necessary to determine parameters of fat metabolism under normative conditions. The current study was designed to assess the effect of gender on lipid metabolism using localized 2-dimensional correlated spectroscopy (L-COSY).

Methods: Untrained males and females (n=8 in both groups; BMI range 20-24.5 kg/m^2; age range 25 ± 5 years; no known metabolism-related disorders) participated in this study. Age and BMI were matched between males and females. All measurements were performed on a 3.0 T whole-body clinical MRI/MRS scanner (GE Signa HD) using an extremity coil. The IMCL/Cr, EMCL/Cr, and degree of unsaturation were determined within a single voxel (3x3x3 cm^3) centered within the soleus muscle using the L-COSY technique (2), with TR=2s, minimal TE=30ms, 50 t_1 increments and 8 averages per t_1. In addition five experiments were performed on one female subject at different time points of the menstrual cycle.

Results: Figure 1 shows a typical 2D L-COSY spectrum obtained. Various resonances from IMCL and EMCL, trimethyl ammonium containing molecules (choline), glycerol backbone protons, and carnosine were identified. Cross peaks C1 (from IMCL) and 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) and C4 (from EMCL) arise from the scalar (*J*) coupling between the olefinic (-CH=CH-) and diallylic methylene protons (-CH=CH-C*H*$_2$-CH=CH-). These peaks appear if there are at least two unsaturated sites with methylene protons located between unsaturated site protons. The volumes of C2 and C4 increase as the number of unsaturated sites increases, so that the degree of unsaturation can be estimated from the volume ratios C2 / C1 and C4 / C3 within IMCL and EMCL, respectively (2). Figures 2 and 3 show mean IMCL/Cr, EMCL/Cr and degree of unsaturation for male and female subjects. The IMCL/Cr and EMCL/Cr were 5.9 ± 1.7 and 18.4 ± 2.64 for male subjects and 7.8 ± 1.6 and 22.5 ± 3.6 for female subjects respectively ($p < 0.05$ male vs female for both comparisons). The degree of unsaturation within IMCL and EMCL was 1.5 ± 0.08 and 1.12 ± 0.03 for male subjects and 1.3 ± 0.075 and 1.04 ± 0.06 for female subjects respectively ($p < 0.05$ male vs female for both comparisons). In measurements obtaining on a menstruating subject, the IMCL/Cr increased by 10% in the luteal phase compared to follicular phase.

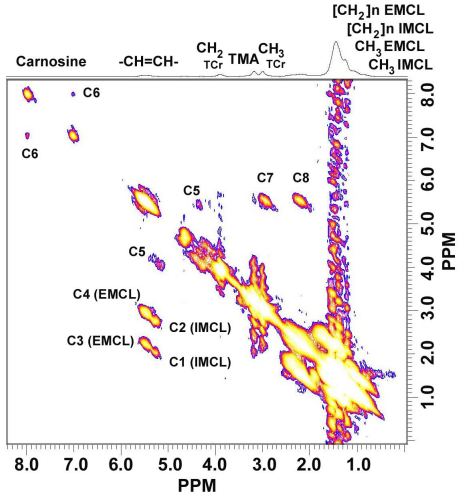

Fig 1. L COSY spectrum from soleus muscle

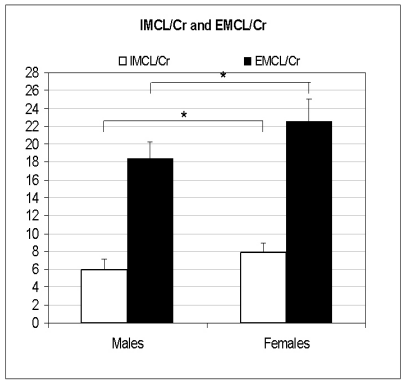

Fig 2. IMCL/Cr and EMCL/Cr content in male and female subjects

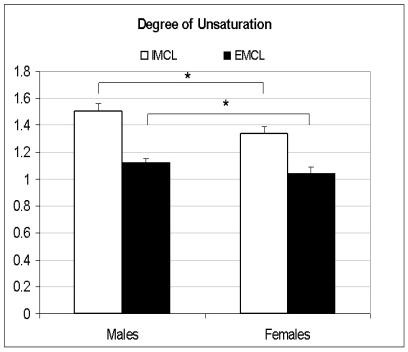

Fig 3. Degree of unsaturation within IMCL and EMCL of male and female subjects

Discussion: The IMCL/Cr and EMCL/Cr was found to be higher in female than in male subjects. It is known that women have a greater adipose body weight fraction than men; this is consistent with our finding of greater IMCL/Cr and EMCL/Cr in women compared to men. Changes in IMCL/Cr during the menstrual cycle are presumably related to the known changes that occur in circulating hormone levels and their effects on fatty acid metabolism (3). The degree of lipid unsaturation is higher in IMCL compared to EMCL for both men and women, indicating higher efficiency of desaturase enzymes within the IMCL pools.

Conclusion: We have established gender differences in skeletal muscle lipids in a group of male and female human subjects, consistent with the notion that endocrine status plays a critical role in fat metabolism. The influence of hormonal factors was further underscored by observed changes during the menstrual cycle.

References:

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