Degree of unsaturation: A potential biomarker for investigating human obesity

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Introduction: Intramyocellular lipids (IMCL) and extramyocellular lipids (EMCL) have been measured extensively by localized one-dimensional ^{1}H MRS in diabetes and exercise physiology (1-4). However, the saturated and unsaturated components within these lipid components have not been clearly distinguished. In this study we employed a localized 2D MRS (L-COSY) technique to separate the saturated and unsaturated components within IMCL and EMCL. The degree of unsaturation may be useful as a metabolic biomarker that can be estimated non-invasively ***in vivo***.

Methods: 15 subjects with moderate BMI (range 18 - 25 kg/m^2) and 5 overweight and obese subjects (BMI range 28 - 32 kg/m^2) participated in this study. All measurements were performed on a 3.0 T whole-body clinical MRI/MRS scanner using an extremity coil. The degree of unsaturation was determined using L-COSY within a single voxel (3x3x3 cm^3) located predominantly within the soleus muscle. Parameters included TR=2s, minimum TE=30ms, 50 t_1 increments with 8 averages, and a total acquisition time of ~ 13 minutes.

Results:

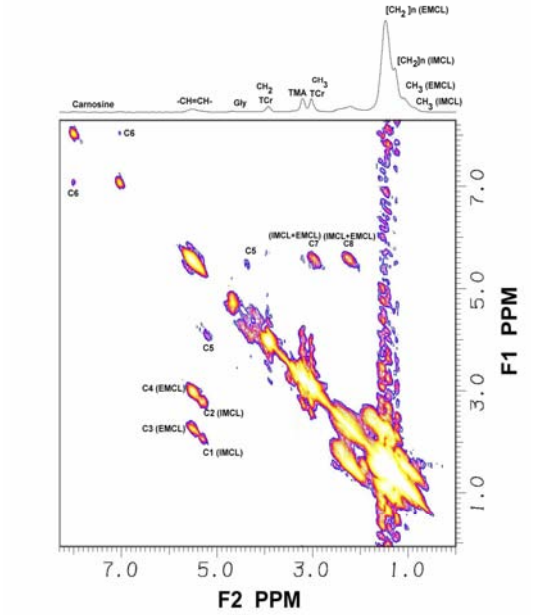

Figure 1 shows a 2D L-COSY spectrum recorded in the soleus muscle of a healthy subject. Various resonances from IMCL and EMCL, trimethyl ammonium containing molecules (choline), glycerol backbone protons, and carnosine were identified. Note that the creatine (3.9 ppm) and carnosine (7.00, 8.00 ppm) exhibit residual dipolar couplings (5). 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-). They occur if there are at least two unsaturated sites between which the methylene protons are located. The peak volumes under C2 and C4 increase as the number of unsaturated sites increases. Thus, the peak volume ratios C2/C1 in IMCL and C4/C3 in EMCL are indicative of the degree of unsaturation within these pools. The values of these ratios from the subjects with moderate BMI were 1.2 ± 0.13 and 0.89 ± 0.11. Corresponding values from the overweight subjects were 0.71 ± 0.20 ($p < 0.01$ compared to moderate BMI group) and 0.76 ± 0.094 ($p < 0.05$ compared to moderate BMI group).

Fig.1. A 2D L-COSY spectrum recorded in the soleus muscle.

Discussion: The desaturation of fatty acids is an oxidative reaction catalyzed by desaturase enzymes that convert -CH_2-CH_2- to -CH=CH-. These enzymes function abnormally in diabetes mellitus, obesity, metabolic syndrome and other lipid disorders (6). This preliminary study indicates a substantial (41%) and statistically significantly decreased degree of unsaturation in overweight and obese subjects within IMCL. A much smaller (15%) decrease was seen within the EMCL pool. The reduction in unsaturation can be attributed to reduced effectiveness of desaturase enzymes to introduce double bonds within muscle cells, particularly within the IMCL.

Conclusions: The degree of lipid unsaturation indicates the effectiveness of desaturase enzymes within IMCL and EMCL, and our data indicate that this measurement might serve as a potential biomarker for obesity. Further, based on the known relationship between obesity and other physiologic states, this index may also serve as a biomarker for metabolic syndrome and diabetes, and possibly correlate with therapy as well.

References:

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