Investigation of Skeletal Muscle Lipid Composition by Localized Correlated Spectroscopy with Weight Loss Intervention: Preliminary results

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Introduction. Fatty acid composition in individuals with insulin resistance and metabolic syndrome is typically characterized by high levels of saturated fatty acids and low levels of polyunsaturated fatty acids [1-3]. Several studies have shown the association between intra- and extra-myocellular lipids (IMCL and EMCL) and insulin sensitivity using 1D MRS approaches. The limitations of 1D MRS include its difficulty to determine the unsaturation components within the lipid pools. Recently, the degree of IMCL unsaturation determined using 2D localized correlated spectroscopy (L-COSY) technique [5] was shown to significantly decrease with BMI in overweight and obese subjects in Caucasian population [4]. However, the saturated and unsaturated components within these lipid pools have not been thoroughly investigated after a weight loss intervention. In this study, we employed L-COSY technique to estimate the degree of unsaturation within IMCL and EMCL lipid pools in overweight Chinese subjects after a weight loss intervention.

Methods. We studied 15 Chinese males, aged 21 to 40 year with BMI ≥ 23 kg/m^2. Each underwent a 16-week weight loss intervention consisting of three 90-min exercise sessions per week with expected calorie expenditure of 500 kcal per session in combination with a diet comprising of a calorie deficit of between 40% estimated total energy expenditure and 1000 kcal. Pre- and post-intervention anthropometry, metabolic profiles and insulin sensitivity index (ISI; determined using hyperinsulinemic euglycemic glucose clamp and adjusted for fat free mass (FFM)) were measured. We implemented the L-COSY sequence on the 3T MR scanner (Tim Trio, Siemens) running on VB17 platform and determined the degree of unsaturation in a voxel volume of 27 ml ($3\times3\times3$ cm^3) located predominantly within the soleus muscle. Parameters included TE/TR = 30/2000 ms, 50 t_1 increments with 8 averages, and a total acquisition time of ~13 minutes.

The 2D L-COSY data were processed using FELIX software (Figure 1). Various resonances from IMCL and EMCL, trimethyl ammonium containing molecules (Choline), glycerol backbone protons, and Carnosine were identified. Cross peaks C1 (from IMCL), C3 (from EMCL) arising due to the scalar coupling between olefinic (-CH=CH-) and allylic methylene protons CH_2CH=CH are due to mono-unsaturated lipids. Cross peaks C2 (from IMCL), C4 (from EMCL) arising from the scalar coupling between the olefinic (-CH=CH-) and diallylic methylene protons (-CH=CH-CH2-CH=CH-) are due to poly-unsaturated lipids. The cross peaks were assigned and their volume integrals were quantified. The peak volume ratios C2/C1 in IMCL and C4/C3 in EMCL are indicative of the degrees of unsaturation within these pools.

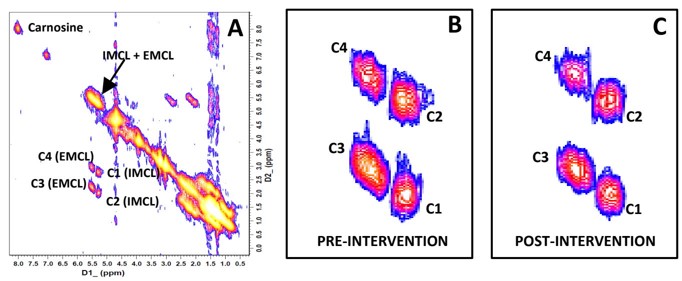

Figure 1. (A) L-COSY spectrum obtained from the soleus muscle. (B-C) Expanded views of the cross peaks pre- and post-intervention.

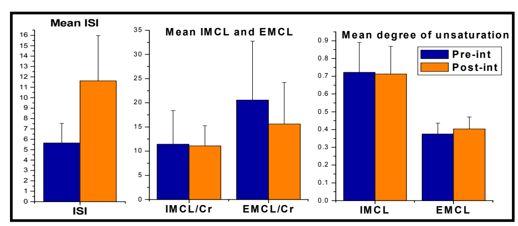

Figure 2. Comparison of mean ISI (left), mean IMCL/Cr and EMCL/Cr (middle) and mean degrees of unsaturation within IMCL and EMCL (right) pre- and post-intervention.

Results. After 16-week of intervention, the mean weight loss was 8.03 kg (p=0.001). Insulin sensitivity improved significantly after intervention (from 5.65 to 11.62 mg/min/kg FFM/microU/mL$\times10^{-2}$, $p<0.0001$), see Figure 2. The mean EMCL/Cr was higher than IMCL/Cr while the mean degree of unsaturation within EMCL was lower than that within IMCL. EMCL/Cr decreased by 25% with intervention but did not reach statistical significance. There was no significant difference in the unsaturation within IMCL and EMCL with intervention. The correlation between the difference in the saturation and unsaturation components (Δ fat) due to weight loss and the increase in insulin sensitivity (Δ ISI) was not statistically significant, see Table 1.

Table 1. Correlation between Δ fat and Δ ISI (* $p < 0.05$)

Fat depot	Correlation coefficient (r)
IMCL	-0.1
Deg. of unsat (IMCL)	0.32
EMCL	0.06
Deg. of unsat (EMCL)	0.19

Conclusion. We investigated the effects of long term weight loss intervention on the saturated and unsaturated components of the IMCL and EMCL lipid pools. The preliminary results of the weight loss program, consisting of exercise and dietary intervention did not alter the lipid composition of IMCL and EMCL.

References. [1] Vesby et al. Annals of NY Acad of Sci 2002; 967:183–195. [2] Warensjo et al. Diabetologia 2005; 48:1999–2005. [3] Sendhil et al. JMRI 2007; 25:192-199. [4] Sendhil et al. AJP Regul Int Comp Phy 2008; 295:R1060-R1065. [5] Thomas et al. MRM 2001;46:58-67.