Determination of residual dipolar coupling in skeletal muscle of upper extremity

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Introduction: There is great interest in lipid metabolism in skeletal muscle due to the correlation with disorders of glucose homeostasis, including insulin resistance and diabetes. The skeletal muscle spectroscopy is very complex due to the presence of scalar couplings and residual dipolar couplings (1). It is very important to consider the effects of residual dipolar coupling as it can change the spectral pattern and relaxation times. In this study, we demonstrate the feasibility of detecting and quantitating the residual dipolar coupling between the creatine CH_3 and CH_2 along with *J* interactions between the various resonances of IMCL and EMCL lipid pools using two separate pulse sequences, L COSY and 2D *J* PRESS in the upper extremity.

Methods: All measurements were performed at flexor digitorum profundus (forearm) within a single voxel (2.5 x 2.5 x 2.5 cm^3). Two sets of experiments were performed with open and closed fist. Localized L-COSY spectra were acquired with TR=2s, TE_{min}= 30ms, 40 t_1 increments with 0.8ms increment increments, 16 averages/t_1 increment with a total acquisition time of 21 minutes. 2D *J* PRESS experiments were performed with similar parameters, using a t_1 incremental period of 4ms, and 8 averages/t1 increment. All experiments were performed on a 3 Tesla whole body MRI scanner (GE Signa HD) using a 12cm transmit / receive coil (Fig. 1).

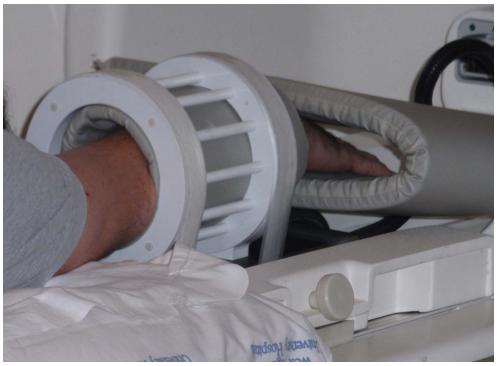

Fig. 1. Orientation of the forearm in the coil

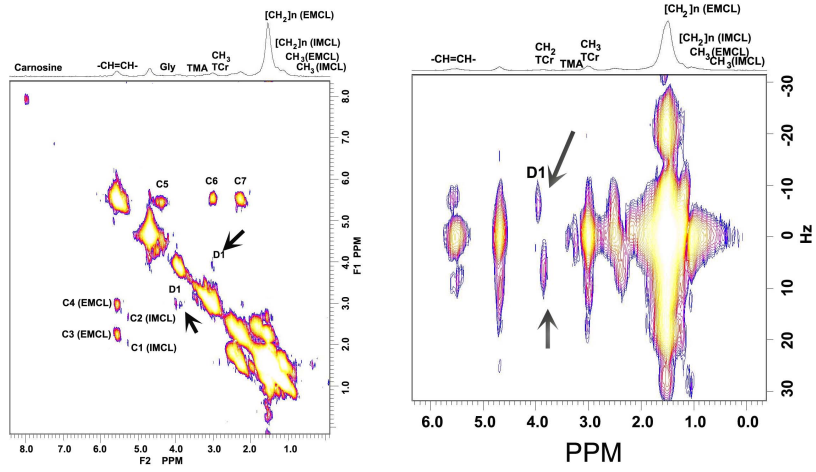

Fig. 2 a) 2D L COSY spectrum b) 2D J PRESS spectrum

Results: Figures 2a, 2b show the L COSY and 2D *J* PRESS spectra acquired from the forearm using a 2.5cm^3 voxel. The spectra display diagonal and cross peaks generated from saturated and unsaturated groups of IMCL, EMCL lipid pools and other metabolites. We also detected a cross peak centered at [3.03, 3.9 ppm] and [3.9, 3.03 ppm] in the L COSY spectrum (Fig. 2a). All assignments were made as described in earlier work (2). The cross peaks labeled as C1-C7 are due to *J* couplings and the cross peak labeled as D1 is due to the residual dipolar coupling (indicated by arrows in the figures). The 2D *J* PRESS spectra (Fig. 2b) also show the various *J* couplings and the residual dipolar coupling (D1) at 3.9 ppm (indicated by arrows). The residual dipolar coupling varied between 12 Hz and 15 Hz for the two positions of the fist. All the measurements were performed from the splitting at 3.9 ppm.

Discussion: The cross peaks in an L COSY spectrum can be generated by either *J* coupling as generally observed in isotropic liquids, or by direct dipole-dipole interaction. The size of the *J* coupling is based on internuclear interactions through fixed bonds, and hence is invariant with respect to molecular orientation. The dipolar coupling, on the other hand, is observable only in oriented media and is diminished when the angle between the internuclear vector and the external magnetic field is close to the magic angle of 54°. Earlier ultrasound experiments have demonstrated that the pennation angle of the muscle fibers in this compartment is ~ 5.5° – 6.5° (3). We observed the residual dipolar coupling with both open (15 Hz) and closed fist position (12 Hz) since the changes in pennation angle is not sufficient to rotate the fibers to magic angle.

Conclusion: We conclude that the peak labeled as D1 in the L COSY and 2D *J* PRESS spectra is generated due to residual dipolar interaction between the CH_3 and CH_2 groups of total creatine. The magnitude of this peak is clearly dependent on muscle fiber orientation with reference to the main magnetic field. Our results are in agreement with an earlier hypothesis that the elongated spaces between actin and myosin chains of muscle hinder the isotropic tumbling of the creatine molecule (4), resulting in residual dipolar coupling.

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