Localized Exchange Spectroscopy of Muscle at 3T

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Introduction: The underlying mechanisms for exchange spectroscopy (EXSY) observations of magnetization transfer (MT) between a broad, generally unobservable, resonance and an observable spectral line are thought to be dipolar cross-relaxation involving nuclear spins in the two compartments, or direct chemical exchange of nuclei. In the case of proton MT involving creatine (Cr) and phophocreatine (PCr), previous investigators have hypothesized that the broad pool is due to the binding of Cr to the enzyme creatine kinase (1,2). Here, we have implemented localized EXSY (L-EXSY) (3) on a clinical 3T MRI/MRS scanner in order to monitor intermolecular exchange of water with Cr or PCr, and intramolecular exchange within Cr and PCr in skeletal muscle in vivo.

Methods: Ten healthy subjects (21-30 years) were investigated using a GE 3T MRI/MRS scanner equipped with self-shielded gradients (40mT/m). A transmit / receive extremity coil was used for both excitation and signal reception. Two-dimensional L-EXSY spectra were recorded from a 3x3x3 cm^3 voxel centered in the soleus muscle, using the following parameters: TR=3s + mixing time (TM), 50 t_1 increments, 2048 points along t_2, and TM's of 6ms, 150ms, 300ms, 500ms, 700ms and 1000ms. Post-processing incorporated linear prediction from 50 to 100 t_1 points and zero filling to 128 points using FELIX software.

Results and Discussion: Figure 1 shows a representative 2D L-EXSY spectrum, with TM= 600ms. Strong diagonal peaks from saturated and unsaturated fatty acids are evident from the intramyocellular (IMCL) and extramyocellular (EMCL) lipids. The assignments were: methyl protons (0.8 ppm for IMCL, 0.95 ppm for EMCL), poly-methylene protons ($(CH_2)_n$) at 1.2 ppm for IMCL, 1.35 ppm for EMCL, methyl and methylene protons of Cr/PCr at 3.0 and 3.9 ppm, trimethyl amine protons (TMA) from Ch/PCh at 3.2 ppm, residual water at 4.7 ppm, olefinic protons from (IMCL and EMCL) at (5.5 ppm), and imidazole protons of carnosine at 7.00 and 8.0 ppm. Cross peaks C2 and C3 show the exchange between methyl and methylene groups of Cr/PCr with water. C1 is the intra-molecular exchange cross peak between methyl and methylene groups of Cr/PCr. An intra-molecular exchange cross peak connecting the olefinic and poly-methylene protons was also recorded at longer TMs. Clear demonstration of three exchange cross peaks indicates the increased spectral dispersion at 3T as opposed to 1.5T (3). The build-up curves of the intermolecular and intra-molecular exchange cross peaks as a function of TM were also recorded using multiple TMs (range 6-1000ms). Figure 2 shows this for intermolecular and intramolecular exchange cross peaks as a function of the mixing time. The intermolecular cross peaks between water and creatine/phosphocreatine appear at 150ms mixing time and the intramolecular cross peak appears at around 300ms mixing time. This intramolecular peak builds up more slowly and also decays more rapidly as compared to the intermolecular cross peaks.

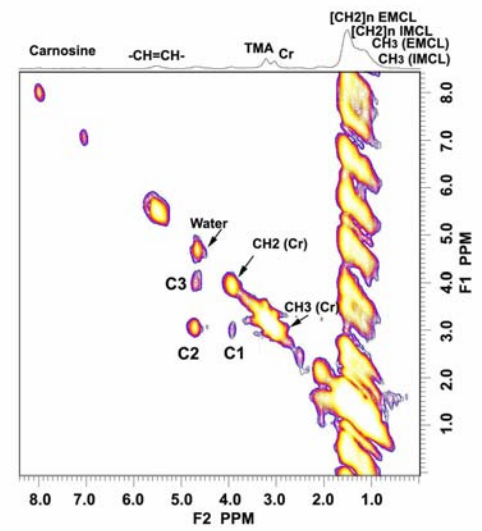

Figure 1

With the availability of this methodology, it would be of substantial interest to evaluate a number of physiologic processes taking place in muscle in terms of their effects on intra- and inter-molecular exchange rates. Such effects are expected to be observed in response to e.g. acute exercise, training, and a variety of pathophysiologic states including the metabolic syndrome and diabetes.

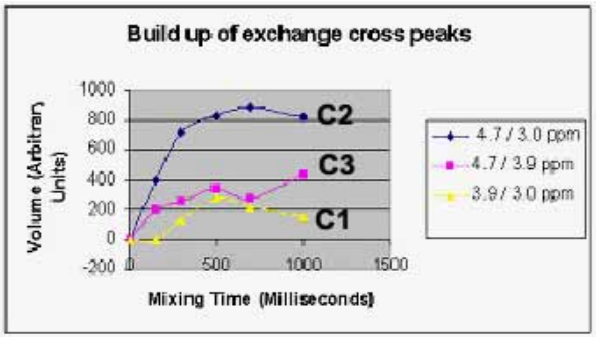

Figure 2

Conclusion: In addition to the previously reported intermolecular exchange between PCr/Cr and water observed at 1.5T (3) the results reported here indicate the potential of L-EXSY to detect inter- and intra- molecular exchange simultaneously in muscle at 3T.

References:

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