Creatine methylene group and PCr observed by interleaved 1H/31P MRS during muscle exercise

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Introduction The time course of phosho-creatine (PCr) during exercise and recovery can be measured with ^{31}P MRS. In ^{1}H spectra, the resonances of creatine are attributed to the total creatine content, (tCr), i.e. the sum of phosphorylated (PCr) and unphosphorylated form of creatine (Cr), which can only be separated in highly resolved MR spectra at ultra high fields. However, an influence of exercise on the spectral appearance of the Cr methylene group's resonance at 4 ppm (Cr2) in skeletal muscle has been described extensively ten years ago by Kreis et al. [1]. They conclude that the Cr2 resonance, a doublet with a coupling constant dependent on the muscle fibres' orientation relative to the magnetic field corellates to PCr rather than total creatine, unlike the methyl resonance at 3 ppm. The experiments for correlation of and data have been conducted subsequently, inhibiting Cr/PCr recovery by inducing ischaemia and measuring a at a static Cr/PCr level.

Here we describe data measured with interleaved dynamic localised ^{1}H and ^{31}P spectroscopy, following PCr and Cr signal during ischaemic rest, exercise and recovery of human calf muscle.

Subjects and Methods Healthy subjects (n =15, aged 25.9±4.7 yrs) performed plantar flexion exercise using a custom built ergometer. Written informed consent was obtained in accordance to the regulations of the local ethics committee. Excitation and reception of RF signals was achieved using a dual tuned loop coil, 10 cm (Rapid Biomedical, Ger) interfaced to a Bruker Medspec S300 DBX whole body MR system. Ischemia in the lower leg was induced by inflating a pneumatic cuff.

The MRS protocol was an interleaved acquisition of double quantum filtered (DQF) localized MR spectra of lactate (data not shown here) and of STEAM localized [31]P- and ^{1}H spectra. Within each full cycle of the interleaved sequence, one ^{31}P STEAM, one ^{1}H STEAM, and two localized DQF acquisitions were performed, yielding effective repetition times of 7.6 s for ^{31}P spectra, 1.6 s for ^{1}H STEAM and 3 s for the double quantum filtered lactate. [31]P- and ^{1}H STEAM spectra were acquired with a short TE = 7.48 ms and TM = 30 ms, employing sinc3 pulses with a duration of 1500 µsec and a resulting excitation bandwidth of 3.7 kHz. ^{31}P MRS data were quantified using AMARES [3] after averaging 8 spectra. ^{1}H MRS data were averaged 16x, lipid and water resonances were removed using an HLSVD filter, after manuall frequency correction, the creatine CH$_2$ doublet at 4 ppm was fitted with AMARES. Then the resulting amplitude time series were shiftet to match the respective end-exercise time points and summed up for display (Fig. 1) and fitting of recovery to a single exponential function.

Results Four of 15 data sets were not included in analysis of the time course, due to convergence issues of the MRS fit routine or obvious outliers in Cr2 amplitude time courses. For the sum of the remaining 11 data sets (See Fig.) the recovery rate constant of the CH$_2$ group was k=0.47±0.12/min or tau=2.11 min starting from a depletion of 65±10 % relative to the recovery value. Corresponding data for the analysis of dynamic localised data are: k=0.59±0.24 /min or tau = 1.97±0.77 min, with a depletion of 87±12 %.

Discussion and Conclusion We show dynamic localised ^{31}P and ^{1}H MRS data acquired interleaved, without keeping metabolite concentrations on a level for the purpose of an MRS measurement, but directly follow the time course of an ischaemic experiment in real time. So far we observed comparable results of fractional creatine depletion and recovery rate constant after ischaemic exercise, for PCr measured in indiviudal ^{31}P spectra and the CH$_2$ group of Cr in ^{1}H spectra, amplitudes fitted individually and pooled for analys of recovery kinetics.

References

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