PROTON DIFFUSION TENSOR SPECTROSCOPY OF METABOLITES IN HUMAN MUSCLE IN VIVO

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PURPOSE

To study the apparent diffusivity and its directionality for metabolites of skeletal muscle in humans in vivo by ^{1}H MR spectroscopy.

INTRODUCTION

Diffusion characteristics of various metabolites have been investigated by ^{1}H MR spectroscopy (MRS) in brain in order to observe intracellular diffusion and to disentangle disputed compartment effects. In vivo metabolite diffusion rates are also of interest as potential co-determinants of reaction velocities [1]. The prime interest in metabolite diffusion in muscle was originally related to the creatine shuttle hypothesis. Recently, these models have been extended to concepts of "intracellular energy-transducing units", macro-compartments or metabolic compartments [2-3]. Metabolite diffusion in muscle has so far almost exclusively been studied by ^{31}P, rather than ^{1}H MRS. Gabr et al. reported the diffusion tensor-derived properties of PCr [4] in human muscle. Kruiskamp, in his PhD thesis [5], also used proton MRS to investigate the ADC of total creatine (Cr) in rat muscle. Renewed interest in ^{1}H diffusion MRS has recently also been brought up by studies of the diffusion behavior of muscular lipids.

Our main interest for this study was to investigate whether the interactions of metabolites with muscle cell ultrastructure, which cause effects like residual dipolar coupling and limited MR-visibility [6], are reflected in a metabolite-specific way in diffusion properties.

METHODS

Metabolite diffusion tensors were determined on a 3T MR system (Siemens Verio) using optimized acquisition and processing methods including an adapted STEAM sequence (TE 30 ms, TM 250 ms, with and without water presaturation) with orientation-dependent diffusion weighting (6 gradient directions, low b: 176 s/mm^2, high b: 1499 s/mm^2 (metabolite scans), 1117 s/mm^2 (water scans)), pulse-triggering (TR > 1.1 s) with individually adapted delays, eddy-current correction schemes (gradient inversion and use of lipid signals for calibration of residual differences between diffusion directions), median filtering, and simultaneous prior-knowledge fitting of all related spectra. In addition, for ease of peak assignment and spectral fitting, the measurements were done in tibialis anterior with the muscle fibers close to the magic angle, such that dipolar coupling effects are minimized [6]. The typical voxel size was 18x20x25 mm^3. Ten healthy volunteers (35.2 ± 8.4 y) were investigated. For carnosine evaluations, data from 4 subjects were excluded because of insufficient SNR.

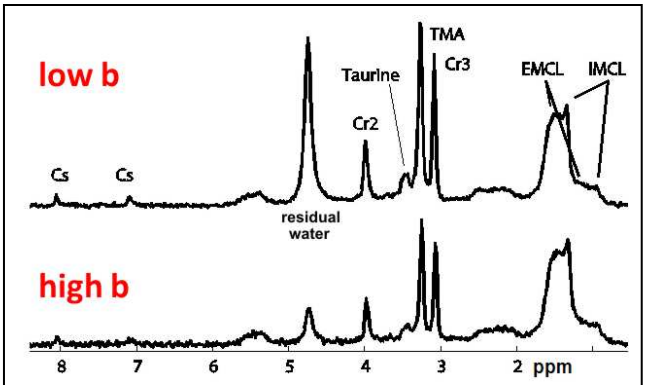

Fig. 1 *Spectra from tibialis anterior aligned at ~54° in one subject with low and high diffusion weighting (single direction)*

RESULTS

Typical spectra for a single subject are plotted in Fig. 1. The average apparent diffusivities (see Fig. 2), as well as the fractional anisotropies (FA) of taurine (ADC=0.74x10^{-3}s/mm^2, FA=0.46), creatine (Cr, ADC= 0.41x10^{-3}s/mm^2, FA=0.33), trimethylammonium compounds (TMA, ADC= 0.48x10^{-3}s/mm^2, FA=0.34), carnosine (Cs, ADC=0.46x10^{-3}s/mm^2, FA=0.47) and water (ADC=1.5x10^{-3}s/mm^2, FA=0.36) were estimated. The diffusivities of most metabolites (all except Cs vs. Cr and Cs vs. TMA) and water were significantly different from each other. FAs did not differ significantly. The correlations between the eigenvectors of all metabolites and water were calculated according to [7] and yielded values close to 1.

DISCUSSION and CONCLUSIONS

Diffusivities, directional dependence of diffusion and fractional anisotropies of ^{1}H MRS-visible muscle metabolites and water are presented. The ADC for "total" Cr (caveat for limited visibility of free Cr in ^{1}H MRS [6]) was found to be similar to the ADC of PCr as determined with ^{31}P MRS [4]. Metabolite and water diffusion in human muscle has proven to be anisotropic and metabolite diffusion tensors showed correlation coefficients to water close to one implying that they are essentially coaligned. The magnitudes of apparent metabolite diffusivities were largely ordered according to molecular weight, with taurine as the smallest molecule (besides water which diffuses twice as fast) diffusing fastest, both along and across the fiber direction.

It appears that this study is the first to report diffusion-tensor properties of taurine, TMA, Cs, and "total" Cr obtained from human muscle in vivo. Metabolites appear to share diffusion directionality with water and have similar fractional anisotropies - hinting at similar diffusion barriers.

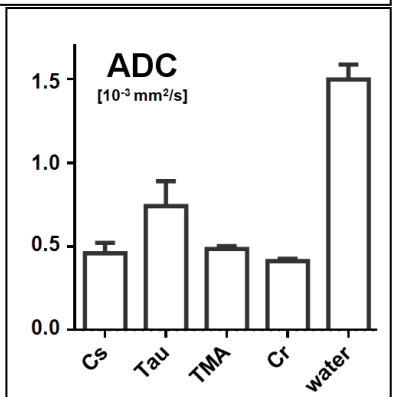

Fig. 2 *Mean (+ 1SD) values for metabolite and water ADCs (10 subjects)*

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