Feasibility of in vivo metabolites diffusion tensor assessment

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Introduction

During the past fifteen years, diffusion tensor imaging (DTI) has shown a great utility in clinical exam and a great reliability. This technique is based on the study of the diffusion process of water molecules restricted by cell membranes. However, water molecules are present in both intra- and extra-cellular spaces and have a high exchange rate which may complicate the interpretation of the results. On the other hand, metabolites are mostly restricted to the intra-cellular space and their concentrations are quantifiable by localized proton magnetic resonance spectroscopy (^{1}H-MRS). Metabolites can be used as diffusion markers by combining MRS with diffusion weighting (DW) technique and to provide information limited to the intra-cellular compartment. The fibers structure of the corpus callosum make this region very interesting for the investigation of metabolite diffusivity as it presents only one fiber orientation. Additionally, CC has never been studied by ^{1}H-MRS in the rodent brain so far. Therefore the aim of this study was to implement a DW-MRS sequence and to characterize the *in vivo* neurochemical profile and to study the diffusion behavior of metabolites in the rat CC at 14.1T.

Materials and Method

All experiments were performed on a 14.1T/26cm scanner (Varian/Magnex Scientific) with 12 cm gradients (400 mT/m in 120 µs) with quadrature transmit-receive 12-mm surface RF coil. Localized spectroscopy was performed with a short echo time STEAM sequence with asymmetric RF pulses for slice selection as previously published [1] (TE/TM/TR = 2.9/20/4000 ms). Localization was done in the corpus callosum (CC) with a voxel (VOI) of 1.5x3x3 mm^3 (c.f. figure 1) based on the DWI with a diffusion gradient applied along the CC fibers bundles. First and second shim was done with FASTMAP on a region centered in the VOI of 2x4x4 mm^3 leading to a water linewidth of 15Hz. Signal from the outer volume was suppressed by four blocks of slice selective pulses as well as the water signal by the VAPOR. DW-MRS was performed with the STEAM sequence (TE/TM/TR = 22/120/2500 ms) with a voxel (VOI) of 1.5x3x3 mm^3 and of 1x2x2 mm^3 (c.f. figure 1). Diffusion weighting was applied with a δ/Δ = 8/121.6 ms and a gradient strength of 60 mT/m giving b-value of 3.99 ms/µm^2. Gradients were applied along 6 directions based on the scheme called DUAL [baser 1998] and their opposite to cancel the cross-term due to the spectroscopy gradients. DW-MRS was done by acquiring four blocks of 32 averages per gradient direction repeated 5 times for a total of 640 averages per spectrum. Metabolites signals intensities were assess with LCModel [2] and the metabolites' diffusion tensors were reconstruct with a homemade Matlab (Mathworks, Natick, MA) program.

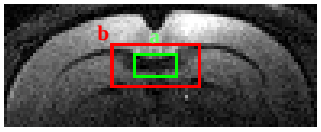

Figure 1 : DW-MRS VOI localized in the CC in the adult rat brain. a) 4µl (green) b) 13.5 µl (red).

Table 1: Metabolites concentration, FA and ADC. (*): metabolites quantify in both voxel.

Met.	Conc. [mmol/kg]	FA	ADC [µm²/ms]
Mac	1.3	0.69	0.032
Asp	2.6	-	-
Cr	4.3	0.38	0.136
PCr	4.1	0.11	0.117
Glu	8.3	0.39	0.138
GSH	1.3	0.63	0.129
Ins *	6.4	0.19	0.110
4 µl		*0.58*	*0.107*
Lac	1.4	0.40	0.137
NAA *	9.6	0.31	0.131
4 µl		*0.57*	*0.137*
Tau	5.9	0.19	0.171
Glc	3.9	0.44	0.187
NAAG	0.8	0.68	0.069
PE	-	0.74	0.140
NAA+NAAG *	10.4	0.33	0.122
4 µl		*0.55*	*0.122*
Glu+Gln *	10.7	0.34	0.144
4 µl		*0.70*	*0.171*
GPC+Pcho	0.8	0.47	0.107
Cr+PCr *	8.4	0.21	0.126
4 µl		*0.48*	*0.118*

Results and discussion

The neurochemical profile show a very good spectral resolution (c.f. figure 1) resulting from the quality of the shimming due to the homogenous and highly organized structure of the CC. Compared to a previous study [3] in the cortex, glutamine (Gln) and glutamate (Glu) are lower and aspartate (Asp) and N-Acetylaspartate (NAA) higher (c.f. table 1). The diffusion tensor reconstruction was possible for 17 metabolites in the VOI of 13.5 µl and 5 metabolites for the 4µl VOI. The mean diffusivity (ADC), calculated from the tensor trace, show results in excellent agreement with a previous study [4] for both VOI (c.f. Table 1). The principal diffusion directions of the metabolites were aligned to the water along the CC fibers (c.f. Figure 3). The fractional anisotropy (FA) computed in the smaller VOI ranged from 0.48 for tCr to 0.68 for Glu+Gln approaching the FA of water (0.8). In the bigger VOI, the FA was lower probably due to partial volume effects.

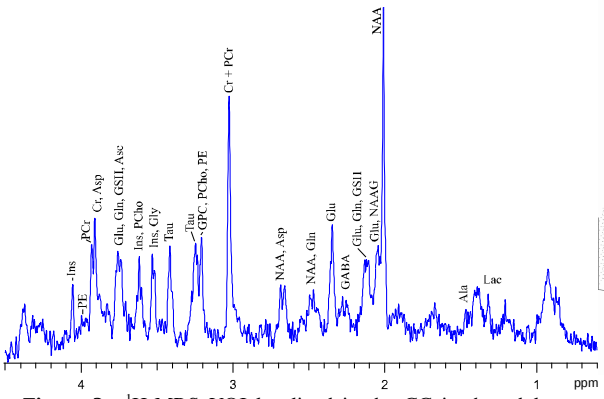

Figure 2 : ^{1}H-MRS VOI localized in the CC in the adult rat brain in a VOI of 13.5 µl with metabolites name labelled. Postprocessing: with Gaussian filtering (gf = 0.11, gfs = 0.06)

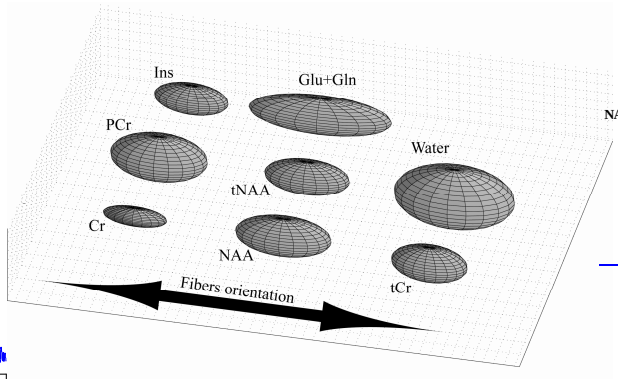

Figure 3: Metabolites diffusivity represented by ellipsoid, reconstructed with the 4 µl VOI data. The water ellipsoid has been rescaled. Ellipsoid are well aligned with the fibers orientation

Conclusions

These preliminary results demonstrate the feasibility of *in vivo* DW-MRS experiment including the reconstruction of the diffusion tensor for several metabolites. Such studies are likely to shed light on the nature of the diffusion signal.

References: [1] Tkáč I et al., MRM 1999; [2] Provencher S., NMR Biomed 2001; [3] Mlynarik V et al., JMR 2008; [4] Pfeuffer J et al., JCBFM 2000;

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