Comparing methods for absolute quantification of brain metabolites in grey and white matter

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Introduction

Absolute quantification of brain metabolites by ^{1}H-MRS can be used to investigate metabolic alteration in grey and white matter, by assessing changes in their concentrations[1]. A rigorous quantification requires the consideration of T_1 and T_2 relaxation effects. Nevertheless, a sufficiently long repetition time and short echo time can minimize the effect of relaxation times on metabolite concentrations. Here we compare two quantification protocols based on LCModel[2] analysis of spectra to assess whether the use of mean T_2 relaxation times of metabolites (MP, mean protocol) in grey and white matter of healthy subject gives metabolite concentrations comparable to those obtained using each subject own T_2 (IP, individual protocol). The MP allows us to halve the acquisition time of a full spectroscopic exam.

Methods

We investigated 13 healthy subjects (age 40±17, mean ± standard deviation, 7 males) for the spectroscopic acquisition in grey matter and 12 healthy volunteers (age 40±16, 9 males) for acquisition in white matter. The study was approved by the local ethical committee and all subjects provided written informed consent.

All ^{1}H-MRS spectra were acquired with a 1.5 T General Electric Medical Systems Signa Horizon LX whole-body scanner using a 25 cm diameter quadrature birdcage head coil. Using a single-voxel PRESS localization sequence, a voxel of 3x3x2 cm^3 was placed in the mid-brain parietal-occipital grey matter and a voxel of 2x2x2 cm^3 in left-parietal-occipital white matter. Spectra were collected at 5 echo times (TE = 35, 70, 100, 144, 288 ms), TR = 4000 ms, and 32 FIDs. We also collected unsuppressed water spectra at 11 echo times (TE = 25, 30, 40, 50, 60, 80, 100, 300, 600, 900, 1000 ms) TR = 15000 ms to be used as internal standard. Both suppressed and unsuppressed water spectra were processed with the fitting program LCModel which analyzes spectra in the frequency domain as a linear combination of a basis set of complete model spectra of metabolite solutions in vitro.

The T_2 of Cho, Cr and NAA were calculated by fitting the decay of their signal in the water-suppressed PRESS spectra at different TEs as monoexponential; water T_2 relaxation times were calculated by fitting the decay of unsuppressed water using a bi-exponential equation assuming a two-compartment model. We set up two quantification protocol: the individual (IP) and the mean protocol (MP). T_2s of water were estimated for both protocols to calculate metabolite concentrations (namely [Cho], [Cr], [NAA]) using water as an internal standard. In the IP, [Cho], [Cr], [NAA] were assessed by calculating each subject own T_2 of metabolites. In the MP, [Cho], [Cr], [NAA] were assessed at TE=35 ms using the mean value of T_2 for each metabolite. Statistical analysis was done using SPSS (version 14.0). Descriptive statistics were calculated for T_2 and concentrations of each metabolites separately for the two groups of volunteers (grey and white matter). A full factorial ANOVA was performed including three factors which might influence the analysis: tissue, protocol and the specific metabolite.

Table 1. Mean T_2 times (ms) using IP protocol

	white matter (n.12)			grey matter (n.13)		
	Cho	**Cr**	**NAA**	**Cho**	**Cr**	**NAA**
	300	213	750	340	199	530
SD	(33)	(17)	(118)	(37)	(13)	(103)
CV	11%	8%	15%	11%	7%	19%
R^2	0.97	0.98	0.94	0.98	0.98	0.98
SD	(0.03)	(0.02)	(0.05)	(0.01)	(0.01)	(0.01)

Table 2. Mean concentrations (mM)

	IP, white matter (n.12)			IP, grey matter (n.13)		
	[Cho]	**[Cr]**	**[NAA]**	**[Cho]**	**[Cr]**	**[NAA]**
Conc	2.28	6.99	10.95	1.34	8.29	9.29
SD	(0.25)	(0.61)	(0.75)	(0.19)	(0.89)	(0.95)
CV	11%	9%	7%	14%	11%	10%
	MP, white matter (n.12)			**MP, grey matter (n.13)**		
	[Cho]	**[Cr]**	**[NAA]**	**[Cho]**	**[Cr]**	**[NAA]**
Conc	2.27	6.96	10.93	1.34	8.28	9.26
SD	(0.24)	(0.56)	(0.71)	(0.19)	(0.85)	(0.90)
CV	10%	8%	6%	14%	10%	10%

Results and Discussion

Table 1 shows T_2 of metabolites calculated by LCModel which are in agreement with literature, with the exception of T_2-NAA which is substantially higher[1,3]. Possible explanations have to be found even though the means of the coefficient of determination R^2 of the mono-exponential fitting is largely over 0.9. In Table 2 metabolite concentrations are reported both for IP and MP: each metabolite showed similar CV values in both grey and white matter. IP and MP concentrations are very similar. In fact, ANOVA analysis (Table 3) suggests that the use of the different protocols does not significantly affect concentrations values. Our analysis showed that it is possible to use the MP protocol to calculate absolute concentration values which are not significantly different from those calculated using the individual T_2 of metabolites derived for each subject. This means that it is possible to have an accurate quantification while halving the acquisition time for both white and grey matter spectroscopic exams.

Table 3. Main effects of full factorial ANOVA

Factor	p	Level	Mean	SD
Tissue	<0.001	white matter	6.729	3.607
		grey matter	6.300	3.625
Protocol	N.S.	IP	6.521	3.630
		MP	6.508	3.616
Metabolite	<0.001	Cho	1.807	0.515
		Cre	7.630	0.983
		NAA	10.107	1.167

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