Pitfalls and advantages of different T2 correction strategies for the absolute quantification of Choline, Creatine, N-acetil aspartate in human grey matter by 1H-MRS

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Introduction

Cerebral grey matter is affected in many neurological disorders. Proton MRS can be used to investigate metabolic alteration in grey matter, by assessing changes in the Choline (Cho), Creatine (Cr), or *N*-acetyl aspartate (NAA) concentrations. Absolute quantification of Cho, Cr and NAA depends on T1 and T2 relaxation effects and a bias in the evaluation of relaxation times may lead to a substantial error in the assessment of metabolites concentration. Several studies have investigated the influence of T2 effects on absolute quantification of Cho, Cr and NAA (1,2). Results from one of the above studies (1) show that the use of the group mean T2 (T2mean) when performed using long TE values give a better accuracy than the use of individually evaluated T2 (T2ind). In this study we compare different strategies for the metabolite absolute quantification in the cerebral grey matter of 15 healthy control subjects at 1.5T using QUEST (3) algorithm investigating their pitfalls and advantages in detail.

Methods

We investigated fifteen healthy subjects (age , 39 ± 17, males 10 and 5 females), the study was approved by the local ethical committee and all subjects provided informed written consent. We used a 1.5 T General Electric Medical Systems (Milwaukee, Wisconsis) Signa Horizon LX whole-body scanner using a 25 cm diameter quadrature birdcage head coil. PRESS localization sequence was used in all cases by placing the voxel (3×3×2 cm) in the mid-brain parietal-occipital grey matter and spectra 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 and the signal was used as internal standard. For all the spectra data signal amplitudes were calculated using the time domain fitting algorithm QUEST. Prior knowledge based on a metabolites basis set computed by quantum mechanics, simulated with NMR-SCOPE(4), both included in the jMRUI software package was used. In the T2ind protocol Cho, Cr and NAA concentrations were calculated in each subject by best-fitting the mono-exponential decay of signal amplitudes of uncoupled spins as a function of TE values by least-square minimisation algorithm. In the T2mean protocol Cho, Cr and NAA concentrations were calculated in each subject using the group mean T2 relaxation time of each metabolite for each TE value. In both protocols we used T2 water calculated in each subject by best-fitting the bi-exponential decay of water signal amplitude (Individual T2 Water). In the T2mean protocol we also used unsuppressed water at TE= 30 ms corrected for T2 relaxation decay by the mean group water T2 values superimposing a mono-exponential decay (Mean T2 Water mono-exp) or a bi-exponential decay (Mean T2 Water bi-exp).

Table 1. ***T2ind protocol:*** [Cho], [Cr] and [NAA] expressed in mM were calculated in each subject by best-fitting the mono-exponential decay of signal amplitudes. T2 water was calculated in each subject by best-fitting the bi-exponential decay of water signal amplitude. ***T2mean protocol*****:** [Cho], [Cr] and [NAA] expressed in mM were calculated in each subject using the group mean T2 relaxation time of each metabolite for each TE value. *Individual T2 Water:* T2 water was calculated in each subject by best-fitting the bi-exponential decay of water signal amplitude. *Mean T2 Water mono-exp*: uses unsuppressed water at TE= 30 ms corrected for T2 relaxation decay by the mean group water T2 values superimposing a mono-exponential decay. *Mean T2 Water bi-exp:* uses unsuppressed water at TE= 30 ms corrected for T2 relaxation decay by the mean group water T2 values superimposing a bi-exponential decay.

T2ind protocol

	T2(NAA)	T2(Cr)	T2(Cho)	[NAA]	[Cho]	[Cr]
Mean	336	188	351	11.9	1.64	9.5
SD	40	17	46	0.92	0.23	1.09
CV	12%	9%	13%	8%	14%	11%

T2mean protocol

	[NAA]					[Cho]					[Cr]					
TE	**35**	**70**	**100**	**144**	**288**	**35**	**70**	**100**	**144**	**288**	**35**	**70**	**100**	**144**	**288**	
Individual T2 Water	11.9	11.6	11.8	12.4	11.4	1.64	1.61	1.59	1.71	1.57	9.4	9.8	9.3	9.1	9.9	**Mean**
	0.95	0.89	0.80	0.83	0.97	0.23	0.24	0.25	0.25	0.22	1.08	1.00	0.86	0.92	1.13	**SD**
	8%	8%	7%	7%	9%	14%	15%	16%	14%	14%	11%	10%	9%	10%	11%	**CV**
Mean T2 Water mono-exp	9.5	9.2	9.4	9.9	9.1	1.30	1.28	1.26	1.36	1.25	7.4	7.8	7.4	7.2	7.9	**Mean**
	1.00	1.10	1.14	1.22	1.14	0.20	0.17	0.17	0.17	0.18	0.96	0.90	0.83	0.73	0.97	**SD**
	11%	12%	12%	12%	13%	16%	13%	14%	12%	14%	13%	12%	11%	10%	12%	**CV**
Mean T2 Water bi-exp	12.1	11.7	11.9	12.6	11.5	1.65	1.62	1.60	1.72	1.58	9.5	9.9	9.3	9.1	10.0	**Mean**
	1.45	1.58	1.63	1.77	1.71	0.29	0.22	0.23	0.24	0.24	1.39	1.32	1.20	1.11	1.42	**SD**
	12%	13%	14%	14%	15%	17%	14%	15%	14%	15%	15%	13%	13%	12%	14%	**CV**

Results

i) T2ind and T2mean protocols show overlapping results in metabolites concentration and CV values when using individual T2 of water; *ii)* In the T2mean protocol the use of different TE values did not affect metabolites concentration and CV values; *iii)* In the T2mean protocol the use of mean group values of T2 water gave higher CV than using individual values of T2 water, regardless of the water decay mode used (mono- or bi-exponential); *iv)* In the T2mean protocol the use of mean group values of T2 water using the mono-exponential water decay, gave the lowest metabolites concentrations.

Discussion

Our results show that in the grey matter both T2mean and T2ind protocols give similar metabolites concentrations and CV, when using individual T2 of water. Therefore, it is possible reducing the acquisition time by acquiring at single TE. Rutgers et al. (1) showed in their study on white matter that the CV is lower at higher TE. Nevertheless our results on grey matter show no dependence of the accuracy on TE values, indicating a more flexibility of the T2mean protocol and suggesting the possibility to use also short TE with obvious advantages for clinical applications. On the other hand, the use of T2 water mean affects sensibly the accuracy of metabolites quantification discouraging the use of this approach. The differences found in this study compared to that of Rutgers et al. (1) can be explained by the different tissue investigated (grey and white matter respectively) and/or by the different post-processing algorithm used, since QUEST algorithm takes into account metabolites contamination from lipid signals at low TE and proton j-coupling.

References

1) Rutgers et al. *NMR Biomed,* 2002;15:215-221; 2) Brief E. E. et al. *Biomed,* 2005;18:14-18; 3) H. Ratiney et al. *MAGMA*, 2004;16:284-296 ; 4) D. Graveron-Demilly et al. *J. Magn. Reson.*, 1993; A101:233-239