Effective transverse relaxation time of the C4 proton multiplet resonance of glutamate in tissue phantoms and human brain at 3 Tesla

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Introduction

Localized quantification of the excitatory neurotransmitter L-glutamate (Glu) in brain is of extreme importance for the characterization and follow-up of psychiatric and neurological disorders. Reasonably distinct resonance lines of the C4 protons of glutamate can be observed in both conventional spin echo-based spectra and quantum coherence edited spectra. We have recently shown both methods at a field strength of 3 T to be of use for estimation of the Glu level in human brain [1]. However, at longer echo times, namely that of 80 ms found to be optimal for this purpose, knowledge of the T_2 of Glu (as well as other analytes) is indispensable for accurate quantification of its concentration. Since the spectral pattern of multiplets such as the present target group (C4) depends on echo time, referencing to appropriate phantom spectra yields an *effective* T_2 that will be applicable to quantification of in vivo spectra fitted using the same phantom spectra as prior information.

Materials and methods

Measurements were performed on a 3 Tesla scanner (MEDSPEC 30/100, Bruker Biospin, Ettlingen) using a circularly polarized headcoil. Gel phantoms simulating brain tissue [2] were prepared by mixing 0.1 M phosphate buffer, *pH* 7.2, containing metabolites in approximate physiological concentrations (NAA, choline, creatine, Glu, glutamine, *myo*-inositol, glutathione, aspartate, GABA, all from Sigma-Aldrich) and 1 mM NaN_3 with 2 % (w/v) monodisperse glass beads (d = 100 nm, Monospher 100, Merck, Darmstadt) for 60 min in an ultrasonic bath. 2 % (w/v) agarose (Type I-B, Sigma-Aldrich) was added, the mixture was heated to 90 °C and cooled back to 58 °C under continuous stirring, poured into a spherical flask and gelled at room temperature. This type of phantom is stable for at least 3 years. Spherical glass bottles with 0.1 M metabolite in 0.1 M phosphate buffer, *pH* 7.2, at 37 °C were used as single metabolite phantoms.
Spectra were acquired from a 2.5 x 4 x 2 cm^3 voxel including the anterior cingulate gyrus (acc) and from a 2 x 3 x 3 cm^3 voxel including the left hippocampus (hc), from 3 healthy volunteer brains each; and from voxels of the same size in the center of the phantoms contained in an annular load phantom simulating the typical coil loading by a head. For spectroscopy PRESS was employed using Shinnar-LeRoux-optimized excitation and Mao refocusing pulses. Other parameters were T_R = 3 s, n = 128 and n = 8, with and without CHESS water suppression, respectively. Transverse relaxation times were obtained from spectra measured at five echo times (50, 80, 135, 250, 330 ms) and fitted using the TDFD method incorporating phantom spectra of NAA, Glu and glutamine, and prior knowledge as described before [1].

Results and Discussion

The effective transverse relaxation time (in ms, SD in parentheses) of glutamate (C4) is given in the table together with the true T_2 values for the fitted singlets of NAA, total choline, total creatine, and water. Our results for brain at 3 T confirm the expected increase in the transverse relaxation rate with increased B_0, and yield T_2 values for the singlets comparable to published ones [3,4]; to our knowledge no value for the transverse relaxation time of Glu has been published before. The present effective values are suitable for determination of Glu concentrations provided a phantom spectrum acquired at the same echo time as the in vivo spectrum is used for spectral fitting. In the brain-mimicking phantom the combination of agarose gel and monodisperse glass beads permits adjustment of the relaxation properties relatively close to those in vivo, indicating applicability of such phantoms for quantification studies.

	Glu	NAA	tCho	tCr	Water
Acc voxel	194 (37)	278 (31)	282 (45)	179 (9)	69 (5)
Hc voxel	171 (22)	267 (15)	291 (13)	198 (31)	73 (2)
Brain phantom	270 (10)	280 (20)	190 (10)	220 (20)	48 (1)

References

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