Brain Glutamate Proton Transverse Relaxation Time as measured by Spectrally-Selective Refocusing

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INTRODUCTION

Proton MRS offers a noninvasive way to measure the metabolites in human brain. Relaxation times T_1 and T_2 are important for precise evaluation of metabolite concentrations, especially in long-TE MRS methods. They can serve as a diagnostic tool in certain cases. Time evolution of the transverse signal from a coupled-spin system is governed by the J evolution as well as the exponential T_2 decay. Glutamate (Glu), a major excitatory neurotransmitter, has strongly-coupled spins, and consequently signal degradation occurs severely with increasing TE. Moreover, the signal at ~2.35 ppm, which is commonly targeted in conventional MRS, overlaps with the resonances of Gln, NAA, and GSH. Here, we report an apparent Glu T_2, measured by a newly-developed spectrally-selective refocusing method, which enables the selective detection of the Glu C4-proton multiplet with negligible contamination.

METHODS

Spectrally selective refocusing was employed for measuring the relaxation times T_1 and T_2 of the Glu C4-proton multiplet. An 81.9-ms long triple-band 180° RF pulse (T180) was implemented within PRESS, *i.e.*, 90° – 180° – T180 – 180°. The filtering pulse had a single Gaussian RF waveform (truncated at 20%), designed for refocusing at 2.35, 3.02, and 3.92 ppm. The refocusing at 2.35 ppm was for generation of the Glu C4-proton target multiplet. The creatine (Cr) singlets at 3.02 and 3.92 ppm were acquired simultaneously for use as reference in phase correction. The Cr 3.92 ppm resonance was refocused 180° out of phase (see Fig. 2).

Fig. 1 depicts the echo time dependence of the height and area of the Glu filtered multiplet, without T_2 effects, for TE between 128 and 430 ms. Due to the J evolution effects, the Glu signal intensity degrades with increasing TE, exhibiting a sinusoidal pattern. The T_2 measurement was carried out at six echo times: TE = 128, 164, 214, 260, 326, 424 ms, where the Glu peak height is temporally maximal. A density-matrix simulation, using the coupling schemes in Ref. 1, indicates that the Glu filtered multiplet is dominant under the presence of potential contaminants, Gln, NAA (Asp moiety), and GSH (Glu moiety), at all TE. Especially for the shaded region (2.2 - 2.4 ppm), the Glu portion is ~98% of the sum for a concentration ratio of [Glu]:[Gln]:[NAA]:[GSH] = 3:1:3:1. Thus, the peak area of the sum spectrum can be taken as Glu with negligible error, unless the contaminants have substantially different relaxation times than Glu. The T_2 value was extracted by fitting the experimental data to the simulated peak area (in Fig. 1) multiplied by a mono-exponential function, $\exp(-TE/T_2)$. In addition, the T_1 was measured with six inversion recovery delays (TI = 0.19, 0.4, 0.65, 1.0 1.32, and 1.8 s) preceding the filtering sequence. Mono-exponential relaxation was also assumed in the T_1 fitting.

In vivo scans were conducted on eight healthy subjects; six for the prefrontal cortex (30×25×30 mm^3) and two for the motor cortex (25×25×50 mm^3). TR was set at 3 s, with 64 averages for each scan. Experiments were carried out at 3.0 T in an 80-cm bore magnet, interfaced to a SMIS console. A 28-cm diameter quadrature birdcage coil was used for RF transmission and reception. The density-matrix simulation was programmed with Matlab.

RESULTS AND DISCUSSION

Both T_1 and T_2 measurements were performed under a steady-state condition with TR = 3 s, taking advantage of S/N enhancement from increased number of averages for a given measurement time. The longitudinal magnetization immediately prior to the 90° excitation pulse, M_i, to which the observed signal is directly proportional, depended on the flip angles of the RF pulses and their intervals. The M_i was calculated by tracing the longitudinal magnetization over the sequence, and used for the fitting. The M_i for the T_1 fitting was a function of TI and T_1, with constant TR and inter-pulse timings. For the T_2 data, since the echo signal intensity was a function of T_1 as well as T_2, the T_1 fitting was carried out in the first place and subsequently the resulting T_1 value was used for the T_2 fitting.

Fig. 2 presents typical *in vivo* filtered spectra for T_1 and T_2 evaluation and their least-square fitting results. Note that the fitted line for the Glu T_2 data in Fig. 2 (bottom, right) is a combination of the numerically-calculated peak area in Fig. 1 and mono-exponential decay. The estimated T_1 and T_2 values of Glu and Cr for the composite gray-white matter tissues in the prefrontal and motor cortices are tabulated in Table 1, together with the fractions of GM, WM and CSF within the voxel.

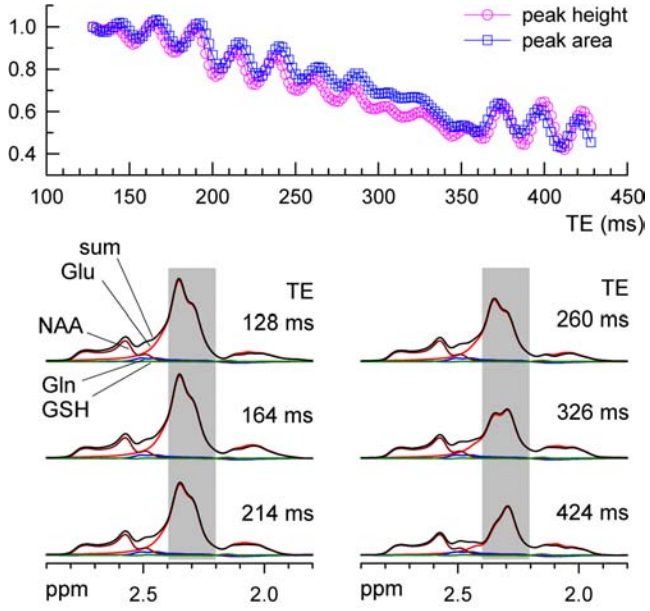

FIG. 1. (Top) Echo time dependence of the Glu filtered peak height and area, without T_2 effects. (Bottom) Calculated spectra of Glu (red), Gln (blue), NAA (Asp moiety) (brown), GSH (Glu moiety) (green), and sum (black) at six selected TE, for their relative concentration of 3:1:3:1. For the shaded region, the Glu portion is ~98% of the sum. The spectra are broadened to 9 Hz.

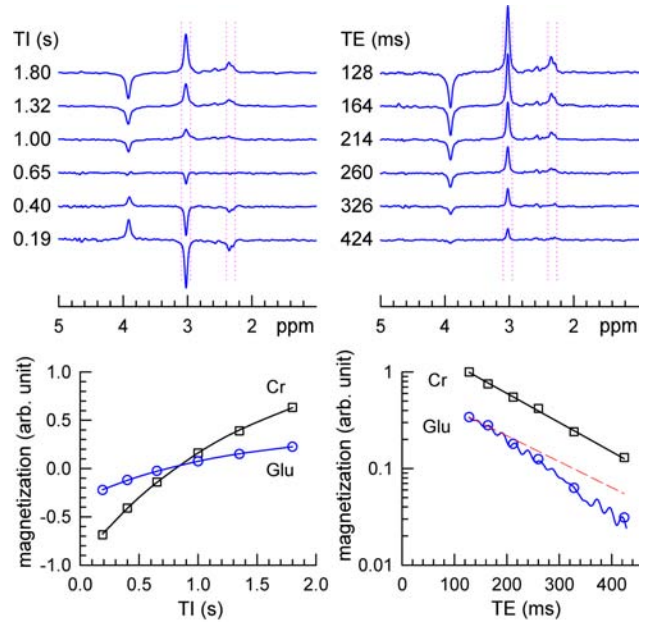

FIG 2. (Top) *In vivo* prefrontal spectra for evaluation of Glu T_1 (left) and T_2 (right). (Bottom) T_1 (left) and T_2 (right) fitting for the peak area obtained between the dotted vertical lines in the spectra. For the Glu T_2 data, the J evolution brings about signal degradation shown in Fig. 1, and, combined with a T_2 exponential signal decay indicated by a dashed line, leads to the fitted line. TR was 3 s for both T_1 and T_2 measurements.

Table 1. Relaxation times T_1 and T_2 of Glu and Cr are tabulated together with the fractions of GM, WM and CSF within the voxel. The data are mean±SD.

	T_1 (s)		T_2 (ms)		GM (%)	WM (%)	CSF (%)
	Glu	Cr	Glu	Cr			
Prefrontal (n=5)	1.23±0.08	1.41±0.05	168±11	149±4	63±3	23±2	14±3
Motor (n=2)	1.22±0.05	1.38±0.03	163±14	142±3	41±4	42±2	17±2

REFERENCE

1. V. Govindaraju *et. al.*, NMR Biomed **13**, 129 (2000).

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