A Novel Approach to Spectral Editing of Glutathione at 7 Tesla using Echo-Time Independent Signal Modulations in PRESS sequence

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Introduction

Various MR methods have been developed, in the last decade, to detect resonances of coupled spin systems which lie underneath singlets [1]. Recently, a novel and simple approach to spectral editing has been proposed for the AB spin system of citrate [2]: this approach exploits the signal J-modulations which occur in PRESS at a constant echo time (TE). In the present study, we investigated with density matrix simulations and experimentally the spectral shape of glutathione at 7 Tesla, with the goal of applying this novel method of difference spectroscopy editing to the protons (ABX spin system) of the cysteine moiety of glutathione.

Methods

Briefly, the editing method is the following: in general, the spectral shape of a strongly coupled spin system under PRESS excitation (90° – [t_1/2] – 180° – [t_1/2] – [t_2/2] – 180° – [t_2/2] – Acq) depends on the first interpulse delay [t_1/2]. In particular, at certain TEs, changes in [t_1/2] result in a complete inversion of the spectral multiplet. Thus, by subtracting one spectrum from the other, resonances of strongly coupled spin systems which lie underneath singlets can be resolved, since the shape and intensity of singlets depend exclusively on TE and not on the interpulse delay t_1/2. The TE-independent J-modulation of the signal of glutathione at 7 Tesla was assessed by simulations, based on the density matrix formalism [3] and published values of coupling constants J and chemical shifts δ [4]. In particular, we focussed our investigation on the protons of the glutathione cysteine moiety, which form an ABX spin system. In order to identify the optimal echo time and interpulse delays for difference editing, 3D plots of the spectral area as a function of t_1/2 and TE were generated. Spectral lineshapes were then simulated at the optimal timings. MRS experiments were performed at 7 T on a phantom containing glutathione, pH-balanced at 7.1, at the temperature of 37°.

Results

Figure 1 shows the simulated signal intensity (spectral area) of the AB protons (2.9-3.1 ppm) of the cysteine moiety of glutathione, under PRESS excitation at 7 T. Substantial modulations, at certain TEs (e.g. TE ~ 160 ms), in the signal intensity as a function of t_1/2 were predicted by the density matrix simulations. Simulated and experimental spectra, acquired at the same TE (TE = 167 ms) with different interpulse delays t_1/2, show the TE independent modulation of the spectral shape of the AB protons of the cysteine moiety. The best parameters to achieve the highest difference in spectral area were: TE = 167 ms, t_1/2 = 18, 47 ms.

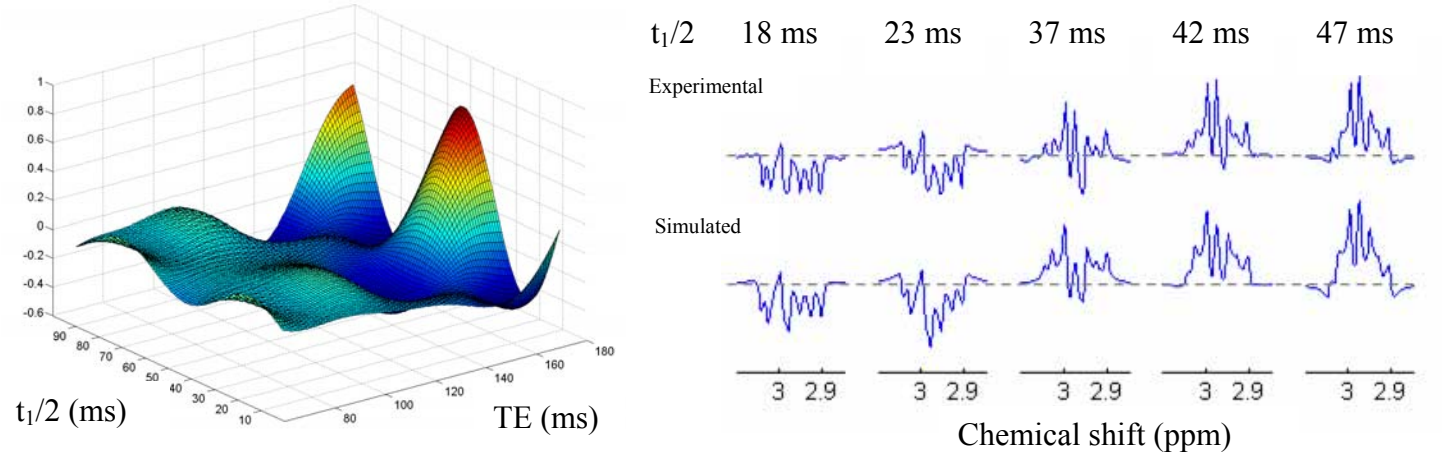

Figure 1. Signal modulations of the AB protons of the ABX cysteine moiety of glutathione at 7 T. **Left panel**. The simulated spectral area. The maximum amplitude of the oscillations occur at ~ TE = 160 ms. The scale of the signal intensity is normalized to value of signal at TE = 0. **Right panel**. Experimental (top) and simulated (bottom) spectral lineshape, at the fixed TE = 167 ms and different interpulse delays t_1/2 (indicated on top of each spectrum).

Discussion

Substantial TE-independent modulations in the signal intensity of the cysteine moiety of glutathione, under PRESS excitation at 7 T, were predicted from density matrix simulations. An excellent agreement between simulations and results of the in vitro experiments was observed. In particular, the two interpulse delays of 18 and 47 ms result in two spectra with negative and positive phase. The phenomenon observed in this study for the ABX spin system is similar to that observed *in vivo* in a previous work [2], for the AB strongly coupled spin system of citrate at 1.5 and 3 Tesla. In both cases, the modulations stem from the non-secular terms ($J^*A_xB_x$ + $J^*A_yB_y$, originating from the J coupling) which do not commute with the primary MR Hamiltonian. Since the singlet resonances are not affected by the changes in t_1/2, this method should be applicable to selectively observe in brain the cysteine resonances at 2.9 ppm from the major overlapping singlet resonance of creatine, just using a PRESS sequence at two different t_1/2 values and the same TE. The results of this study show the feasibility of extending to the ABX coupled spin system the novel approach of spectral editing by TE-independent J-modulations which has already been demonstrated *in vivo* for the AB spin system of citrate.

References

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