The longitudinal relaxation time of GABA in vivo at 3T

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Target audience: This research will be of interest to spectroscopists with an interest in GABA and the potential for quantification of GABA in vivo.

Purpose: The inhibitory neurotransmitter GABA is present in the brain at low millimolar levels. It is possible to measure GABA concentration with MRS by tailoring the MRS experiment to isolate GABA signals from other stronger, overlapping signals from other molecules in the spectrum. The most widely used method for doing this is MEGA-PRESS (1), a J-difference editing technique. J-difference editing of GABA works by using frequency-selective RF pulses ('editing' pulses) to modulate the evolution of the coupling between spins at 1.9 ppm and spins at 3 ppm. GABA-edited MRS is now being widely applied in clinical and basic neuroscience. The GABA signal acquired using MEGA-PRESS at 3T usually suffers from a significant contamination due to co-edited macromolecular (MM) signals, because MM signals at 3 ppm are coupled to MM signals at 1.7 ppm that are affected by editing pulses at 1.9 ppm. By placing editing pulses symmetrically around MM spins at 1.7 ppm, so that both editing pulses affect the MM signal equally, it is possible to minimize the MM signal in the difference spectrum, which allows for the measurement of the relaxation times of GABA signals *in vivo* without MM contamination. In this abstract, a saturation-recovery (multi-TR) approach to measure the longitudinal relaxation time (T_1) of MM-suppressed GABA at 3T. The measurement of *in vivo* relaxation times is an important pre-requisite for measuring absolute concentration, which is expected enhance the site-to-site and scanner-to-scanner comparability of quantitative results.

Methods: J-difference edited single-voxel MRS was used to isolate GABA signals. An increased echo time (80 ms) acquisition was used, accommodating the longer, more selective editing pulses (20 ms) required for symmetric editing-based suppression of co-edited MM signal (Figure 1)[2]. In ON experiments, editing pulses were applied to the GABA spins at 1.9 ppm to selectively refocus the evolution of couplings to spins at 3 ppm. In the OFF experiment, these couplings are allowed to evolve for the duration of the echo time. The difference between these two subsets only contains those signals that are affected by the editing pulse at 1.9 ppm, including the 3 ppm GABA signal. CHESS water suppression; $B_{1,max}$ 13.5 uT; slice-selective excitation and refocusing bandwidth 2.3 kHz and 1.4 kHz respectively; 1024 datapoints sampled at 2 kHz. Edited GABA measurements at a range of relaxation times were made in 1) a one litre 10 mM GABA phantom (TR = 1s, 2s, 3s, 5s and 10s; 64 averages per TR; and 2) in 10 healthy participants (5 female; aged 35.4 ± 8.8 years) from a $(3.5cm)^3$ voxel in the posterior cortex (TR = 1s, 2s, 3s and 5s; 256 averages per TR). All MR spectra were processed in csx3 (http://godzilla.kennedykrieger.org/csx) and baseline fitted. A saturation-recovery equation was used to model the integrated data: $S(TR)/S_0 = 1-\exp(-TR/T_1)$, where S(TR) is the integral at a given TR, S_0 is an amplitude scaling factor (corresponding to the signal acquired at infinite TR), and T_1 is the longitudinal relaxation time constant to be measured. This equation was implemented within a non-linear fitting algorithm (nlinfit) in Matlab with S_0 and T_1 as variable parameters.

Results: Phantom spectra for each TR are shown in Figure 2 and show increased prominence of the central peak of the multiplet at 80 ms compared to 68ms (note that this is not a subtraction error, but rather an expected behavior of the multiplet at this echo time). The fitted T_1 relaxation time for edited GABA signal in the phantom was 2.77 ± 0.22 s. Figure 3 shows the difference spectra for each TR for a single participant. Figure 3b shows the normalised GABA integral for each TR overlaid with the fitted T_1 relaxation curve for 5 participants. The *in vivo* average T_1 = 1.31 ± 0.16 s, a coefficient of variation of approximately 12%. *Discussion:* A multiple-TR method to determine the T_1-value of the edited GABA signal was used both in a phantom and in vivo in the brain with macromolecular suppression at a field strength of 3 T. The value of T1 = 1.31 s may be used in future work to determine the absolute GABA concentration in vivo. *Conclusion:* Being able to validate absolute GABA concentration will provide a more quantitative measure of GABA, as well as allowing for more direct comparison of GABA concentration across studies and research sites.

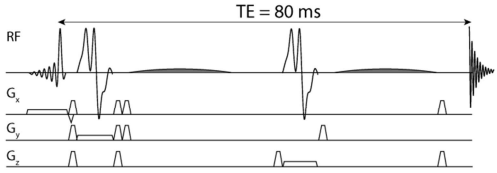

Figure 1

Figure 1. MM-suppressed MEGA-PRESS sequence using 80 ms TE.

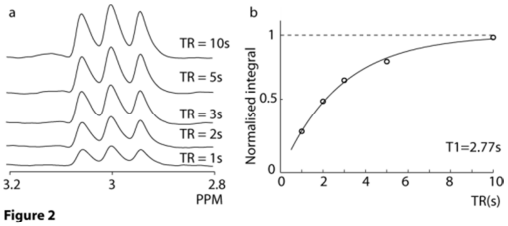

Figure 2

Figure 2. 10 mM GABA phantom. Left shows an increase with increasing TR. Right panel shows fitted increase in normalised integral of the GABA peak and calculated T1 of 2.77.

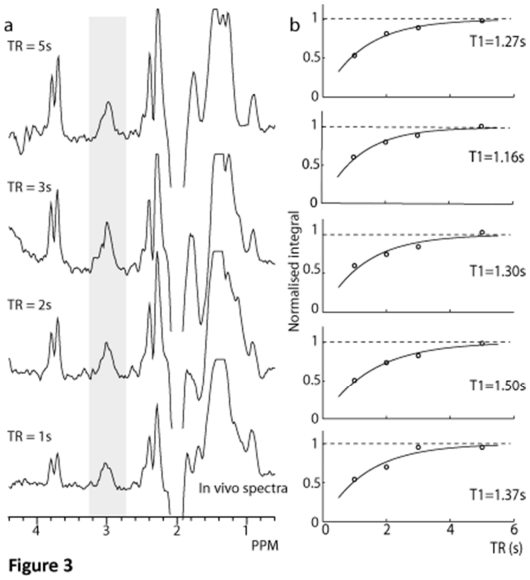

Figure 3

Figure 3. In vivo GABA spectrum. Left panel shows an increase in the GABA peak with increasing TR for 1 participants. Right panel showss the normalised GABA integral for each TR overlaid with the fitted T1 relaxation curve for 5 participants (avg. T1 = 1.31s).

1. Mescher and Garwood *NMR Biomed* 1998. 11(6):266-72 2. Edden et al. *MRM* 2012 68(3):657-61. This work was funded by NIH P41 EB015909.