Optimization of MEGA-PRESS for the simultaneous detection of Glutamate and Glutamine, and GABA

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Target audience: This study will be of interest to researchers concerned with the quantitation of γ-aminobutyric acid (GABA), glutamate (Glu) and glutamine (Gln) in the human brain.

Purpose: The inhibitory neurotransmitter GABA is often measured at 3T using the 'MEGA-PRESS' spectral-editing technique [**1,2**]; although primarily designed to detect the GABA peak at 3.0 ppm, glutamate (Glu) and glutamine (Gln) are also effected by the editing pulse, so that a Glx (=Glu+Gln) resonance also appears in the edited spectrum at 3.75 ppm **(Fig 1)**. Although not optimally edited, this peak is sometimes used to estimate Glx concentrations **[3]**. This abstract investigates modifications of the MEGA-PRESS experiment in order to simultaneously detect both Glx and GABA with high editing efficiency.

Methods: All experiments were performed on a Philips 3T 'Achieva' scanner equipped with a 32-channel head coil. For conventional (*i.e.* non-macromolecule (MM) suppressed) experiments a MEGA-PRESS sequence with TR/TE 2000/68 ms was used with 14 ms Gaussian editing pulses. For MM-suppressed experiments, TE 80 ms and 20 ms editing pulses were used. Experiments were performed in a 20 mM solution of GABA and Glu, and *in vivo* in the mesial posterior gray matter (**Fig 1**). 'On' editing pulse frequencies were varied from 1.9 to 2.15 ppm in 0.05 ppm increments, 'off' = 8.0 ppm, while for MM-suppressed experiments 'on'/'off' frequencies were 1.9/1.5, 1.95/1.45, 2.0/1.4, 2.05/1.35, 2.1/1.3, 2.15/1.25 ppm. Simulations were performed using the VESPA software [**4**], with chemical shift and coupling constant values taken from the literature [**5,6**]. Simulation parameters were matched closely to the experiments, including the actual experimental pulse waveforms, and spatial displacement effects.

Results: **Fig 2A** shows simulations of GABA, Glu and Gln as a function of editing pulse frequency; the corresponding experiments in GABA and Glu phantoms are shown in **fig 2B**. Maximum GABA signal occurs at approximately 2.0 ppm, Glu at 2.1 ppm, and Gln at 2.2 ppm. **Fig 3** shows results of the *in vivo* experiments in 3 volunteers for the non-MM suppressed GABA+ experiment. There is a large (~50%) increase in the Glx signal as the 'on' frequency increases from 1.9 to 2.15 ppm, while GABA+ is relatively stable between 1.9 and 2.0 ppm. As the editing pulse moves downfield, the GABA+ peak has a greater relative contribution from GABA and less from MM. **Fig 4** shows the corresponding *in vivo* MM-suppressed results (n=1). A large increase (~200%) in Glx again occurs, with a maximum at 2.15 ppm, while GABA is relatively flat from 1.9 to 2.1 ppm, with a maximum at about 1.95 ppm.

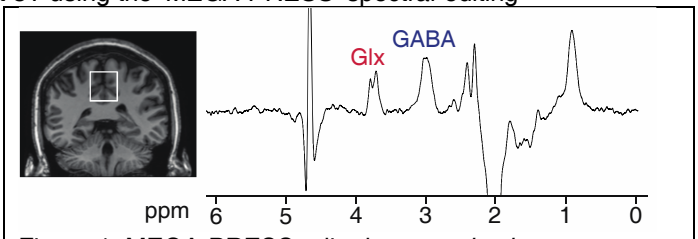

Figure 1. MEGA-PRESS edited spectra *in vivo*

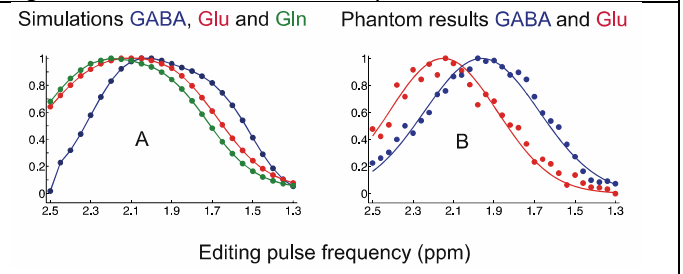

Figure 2. Simulations and phantom results, 'off' = 8.0 ppm

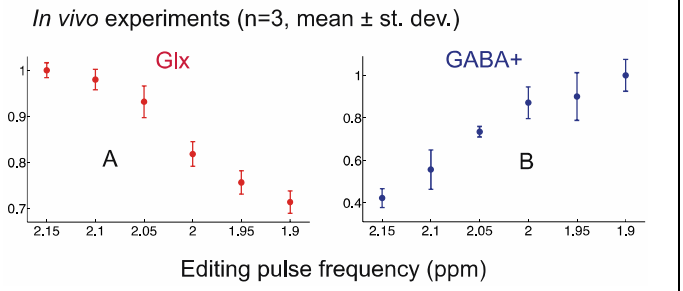

Figure 3. *In vivo* results, 'off' = 8.0 ppm

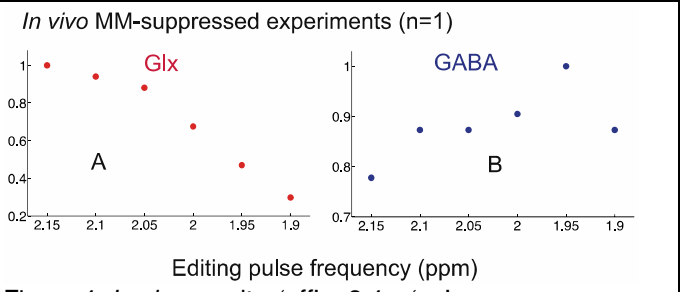

Figure 4. *In vivo* results, 'off' = 3.4 – 'on' ppm

Discussion: Improved Glx editing can be obtained by moving the 'on' editing pulse to 2.15 ppm, particularly for the MM-suppressed experiment, which has more selective editing pulses. However, the increase in Glx has to be balanced against a loss of GABA, which particularly occurs beyond 2.1 ppm. Further optimization of the simultaneous detection of Glx and GABA may also be possible by varying TE and other sequence parameters.

Acknowledgements: Supported by NIH R01MH096263 and P41EB015909. References: 1. Mescher M, et al., NMR in biomedicine 1998;11(6):266-72, 2. Puts NA, Edden RA. Prog NMR Spec 2012;60:29-41, 3. Kegeles LS, et al., Arch Gen Psych 2012;69(5):449-59, 4. Soher BJ, et al., JMR 2007;185(2):291-9, 5. Govindaraju V, et al., NMR Biomed 2000;13(3):129-53, 6. Near J, et al., MRM 2013;70(5):1183-91.