MEGA-PRESSing onward for more metabolites: aspartate, lactate, and PE

James B. Murdoch[1], Andrew J. Wheaton[1], and Robert Anderson[1]
[1]*Toshiba Medical Research Institute USA, Mayfield Village, Ohio, United States*

The MEGA-PRESS editing sequence [1] has proven to be a robust technique for quantifying GABA levels in the brain [2]. The J-coupling between GABA C3 methylene protons (which resonate at 1.9 ppm) and C4 methylene protons (which resonate at 3.0 ppm) is utilized to pick out a small GABA signal amidst much larger peaks. Two spectrally selective inversion pulses are added to a PRESS sequence – one on either side of the second slice-selective refocusing pulse. For "edit-ON" shots, the selective inversion frequency is set to 1.9 ppm, flipping the C3 spins and thereby inhibiting J-modulation of the C4 spins. For "edit-OFF" shots, the selective frequency is set elsewhere, and the C4 J-modulation is unperturbed. Taking a difference spectrum cancels out the bystanders and yields a modified but resolved GABA C4 peak at 3.0 ppm. The usual TE choice for MEGA-PRESS GABA editing at 3T is 68 ms, but Edden *et al.* [3] have recently shown that TE 80 works well too and permits the use of longer selective pulses with narrower bandwidths.

The MEGA-PRESS sequence has also been used to edit the aspartate moieties of NAAG and NAA, providing a means of resolving the similar spectra of these two related metabolites [4]. Such MEGA-successes inspired us to search for additional applications. One possibility is aspartate itself, a nonessential (but not inconsequential) amino acid that is present in the brain at 1-2 mM and acts as an excitatory neurotransmitter [5]. It can be fit as an overlapped component of normal short-TE PRESS spectra with an analysis program like LCModel [6], but MEGA-PRESS provides a cleaner alternative.

The aspartate amino acid side chain has three spins: a CH proton at 3.89 ppm J-coupled to two methylene protons at 2.65 and 2.80 ppm [7]. With this arrangement, an edit-ON frequency of 3.89 ppm can be used to mess with the modulation of the CH_2 multiplet. (One possibility for an edit-OFF frequency is 5.45 ppm – symmetric with respect to water.) We used 20 ms sinc-center-lobe pulses for selective inversion and experimented with a series of TE values from 80 ms to 140 ms. Spectra were acquired from 15.6 ml and 24.4 ml voxels in the parietal cingulate cortex (PCC) region of a normal volunteer. Simulated individual metabolite spectra for visual comparison and LCModel fitting were generated with a refurbished version of an old EDSEL (Exact Dynamics of SELection) program [8].

TE 80 (the same value suggested for GABA editing) proved to be a good choice. Figure 1 shows resulting edit-ON and edit-OFF spectra from a 24.4 ml PCC voxel (128 shots each, acquired individually at TR 2000 and then phase- and frequency-aligned using the residual water peak). Figure 2 shows the LCModel fit of the difference spectrum (OFF – ON). A well-resolved Asp CH_2 peak a 2.74 ppm is apparent, but also inverted peaks for lactate at 1.33 ppm and *probably* phosphorylethanolamine (PE) at 3.23 ppm. These metabolites appear in the difference spectrum because they too have J-coupled resonances near 3.89 ppm. LCModel results of interest for this spectrum are as follows: Asp/Cr = 0.175 (%SD=12), Lac/Cr = 0.087 (%SD=11), PE/Cr = 0.209 (%SD=14). Similar PCC results were obtained from a smaller 15.6 ml voxel in the same volunteer but on a different day: Asp/Cr = 0.186 (%SD=14), Lac/Cr = 0.087 (%SD=13), PE/Cr = 0.321 (%SD=10).

Conclusion: With only minor modifications, the MEGA-PRESS sequence used for GABA editing can be unleashed on aspartate too, yielding bonus edited peaks for lactate and PE as well. These are only preliminary results, however; additional sequence tweaks (perhaps to the edit-ON frequency) plus refinement of the LCModel basis set and control parameters will no doubt be needed for more robust performance.

References

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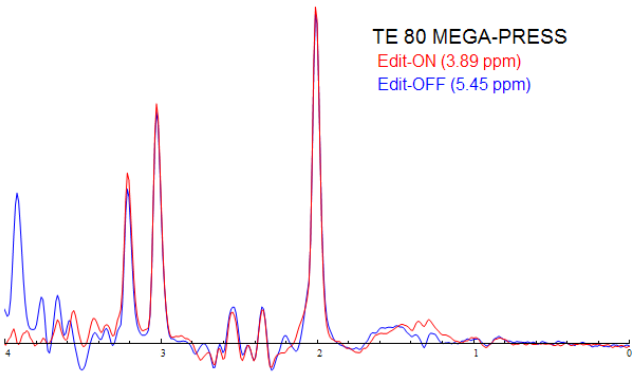

Fig 1. MEGA-PRESS edit-ON and edit-OFF spectra, with a 1.0 Hz Gaussian filter applied for aesthetic purposes

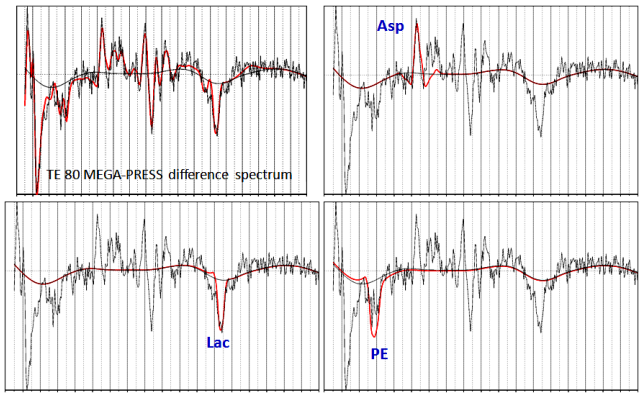

Fig 2. LCModel fit, including the individual Asp, Lac, and PE components (fitted range: 3.8 – 0.2 ppm)