New Spectral Filtering Strategy for Detection of the Myo-Inositol 4.06 ppm Resonance: Its Application to Human Prefrontal Brain In Vivo

C. Choi[1], N. J. Coupland[2], C. J. Ogilvie[2], J. T. Ngo[2], M. A. Hartfeil[2], D. Gheorghiu[1], P. S. Allen[1]

[1]Biomedical Engineering, University of Alberta, Edmonton, Alberta, Canada, [2]Psychiatry, University of Alberta, Edmonton, Alberta, Canada

Introduction

Proton MRS offers a noninvasive way to measure metabolites in the human brain. Prior measures of myo-inositol (m-Ins) have focused on the multiplet at ~3.56 ppm because of the strong signal in this region at short TE. However, because of overlapping macromolecule and lipid signals, and the glycine singlet at 3.55 ppm, selective quantification of m-Ins is often uncertain. Here, we propose a new editing strategy for detection of the 4.06 ppm, weakly-coupled resonance of m-Ins. A preliminary result from human prefrontal cortex, obtained within 3 min, is presented.

Backgrounds and Experimental

The spin system of m-Ins can be modeled as AM_2N_2P, where A, M, N and P spins resonate at 4.06, 3.52, 3.61 and 3.27 ppm, respectively. Most of the spins are strongly coupled. However, the coupling between the A spin and the M spins is approximated to be weak at 3T, and this is the only coupling in which the A spin is involved. This coupling characteristic affords an opportunity to detect the A-spin resonance by selective refocusing. When only the A spin is refocused, the J evolution of the A spin evolves back, thereby leading to an in-phase coherence at the onset of the acquisition. This brings about a triplet at 4.06 ppm, with separation of ~3 Hz, and with, neglecting T_2 effects, 100% retention of the triplet following a 90°-acquire sequence (Fig. 3(a)). In practice, the separation within the triplet is so small that, in vivo, the triplet is seen as a singlet-like peak. Fig. 1 depicts the editing sequence. The editing utilizes an 88.4 ms long quadruple-resonance selective 180° pulse (Q180), which is applied between pairs of slice-selection adiabatic pulses. This pulse is a single Gaussian r.f. waveform (truncated at 22%) that incorporates successive r.f. phase variations [1], governed by the frequency separation between four resonances: 4.06, 3.22, 2.01 and 1.31 ppm. The inversion (longitudinal) and refocusing (transverse) profiles of Q180 are shown in Fig. 2, together with the resonances of the potential contaminants. The Q180 gives a refocusing at 4.06 and 2.01 ppm. The former is for generation of the A-spin triplet, and the latter is for detection of the NAA singlet, which is used for reference in measuring the target peak of m-Ins. Contaminants include Cr (3.93 ppm), phophorylethanolamine (PE) (3.98 ppm), Lac (4.01 ppm), and serine (3.98, 3.94 and 3.83 ppm) [2]. These are all coupled systems except Cr. The Cr 3.93 ppm singlet resonance, which is the major obstacle, is not affected ($< 10^{-3}$) by Q180 with a small bandwidth (11.5 Hz), resulting in no signal at acquisition. The contribution from PE and Lac is minimized by allowing the J evolution, which, in general, causes a degradation of the signal. Only an inversion at the resonance (3.22 and 1.31 ppm) of the coupling partner is required, see Fig. 2. Simulation indicates that the signals of PE and Lac are reduced by 6-fold and 3-fold, respectively, with respect to the coedited multiplets without the inversion action. For serine, the strong coupling effect leads to a substantial signal reduction. With these suppression strategies and the low concentration of PE, Lac and serine in human brain [2], it is predicted that the 4.06 ppm resonance of m-Ins can be observed with negligible contamination in vivo (< 3%), as shown in Fig. 3(a). The editing sequence was tested on a 2.5×3×3 cm^3 voxel of a 6-cm diameter spherical phantom (pH = 7.1), containing m-Ins and Cr, both at 50 mM. In vivo tests were performed on four healthy subjects. A 2.5×3×3 cm^3 voxel was selected in prefrontal cortex (Fig. 4). Experiments were carried out at 3.0 T in an 80-cm bore magnet (Magnex Scientific PLC), interfaced to a SMIS console. A 28-cm diameter quadrature birdcage coil was used for r.f. transmission and reception. The density-matrix simulation was programmed with Matlab (The MathWorks, Inc.).

Results and Discussion

An edited, phantom spectrum is shown in Fig. 3(b), together with PRESS and STEAM spectra with optimized timings, all obtained from an identical voxel. The height of the 3.56 ppm peaks from PRESS and STEAM is about the same at this linewidth. When the line broadens in vivo, however, STEAM, with the zero-quantum filtering characteristic, becomes the better option. It is should be emphasized that editing gives a 4.06 ppm peak height ~30% greater than the STEAM multiplet at 3.56 ppm, Fig. 3(b). The STEAM multiplet has larger area, however this is rather regarded as a shortcoming, since resolution is a key issue in spectroscopy. In addition, a phantom test indicates that it is not until TE is less than 70 ms that the peak height of the STEAM output exceeds that of the editing (TE = 154 ms) (data not shown). The increase of the STEAM output in this short TE range is of course substantiated by the reduced T_2 decay. An edited spectrum from the human prefrontal cortex is presented in Fig. 4, together with a PRESS spectrum obtained, from the same voxel, at the same echo time. The target peak at 4.06 ppm is clearly measured with 2.6-min. measurement time. An advantage of this editing method is that the absence of neighbouring interferences enables the use of high-order filtering during post-acquisition processing to enhance SNR. Assuming similar T_1 and T_2, from the m-Ins to NAA peak area ratio of 0.22±0.02, the m-Ins concentration in prefrontal cortex is estimated as 6.6±0.6 µmol/g, with respect to NAA at 10 µmol/g.

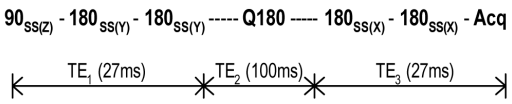

FIG 1. Overview of the spectral editing sequence. Localization is attained with a 90° pulse (T_p = 3.2 ms, BW = 3.5 kHz, and two pairs of adiabatic 180° pulses (T_p = 5ms, BW = 4.6 kHz). Q180 denotes an 88.4 ms long quadruple-resonance selective 180° pulse.

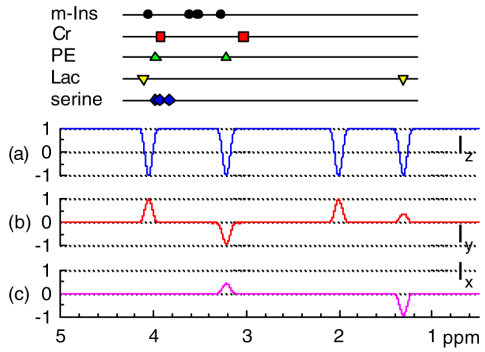

FIG 2. (top) Resonances of five metabolites: m-Ins, Cr, phosphorylethanolamine (PE), Lac and serine. (bottom) (a) Inversion and (b)(c) refocusing profiles of the Q180 pulse. Bloch simulation for the action of Q180 was made (a) on M_z and (b)(c) on M_y.

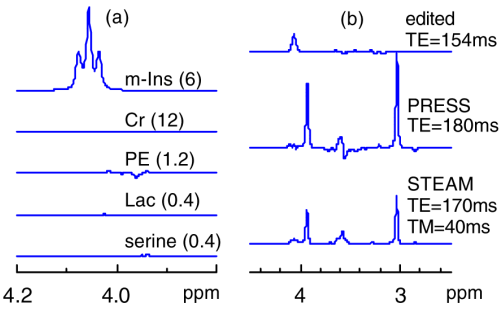

FIG 3. (a) Simulation of the editing sequence for five metabolites. The concentration in brain [2], adopted for scaling, is shown on the right. (b) Phantom spectra (FWHM = 3 Hz). The timings used, gave the largest peak height in simulation and phantom tests for the range 100 – 350 ms.

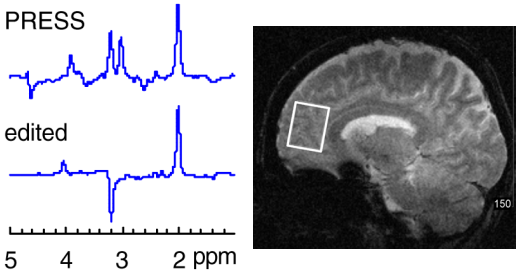

FIG 4. PRESS and edited spectra obtained from a voxel positioned as shown in the image, both with TE = 154 ms and TR = 2.4 s. NEX was 32 and 64, respectively. A 2-Hz exponential and 4-Hz Gaussian filtering was used.

References

1. H. Green *et. al.*, J Magn. Reson. **81**, 646 (1989).
2. V. Govindaraju *et. al.*, NMR Biomed. **13**, 129 (2000).

Acknowledgments

Supported by Canadian Institutes for Health Research & Alberta Heritage Foundation for Medical Research.