Sensitivity of single shot multiple J-coupled metabolite detection using Dual Sel-MQC (D-Sel-MQC) editing

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Introduction: The single scan J-coupled metabolite editing scheme, Sel-MQC (**Sel**ective **M**ultiple **Q**uantum **C**oherence), proposed by He et al.[1] enables editing of a single J-coupled resonance with simultaneous suppression of water and other resonances. The sequence was developed for robust one-scan lactate (Lac) detection and co-resonant lipid suppression in tumors[1]. In the last decade the Sel-MQC scheme was modified in several ways to edit additional uncoupled metabolites[2], J-coupled drugs[3], glucose (Glc)[4], or γ-aminobutyric acid (GABA) and glutamate (Glu) in the rodent brain[5]. The detection of these metabolites is often complicated, because of co-resonant macromolecule resonances and strong signals from overlapping uncoupled metabolites (N-acetylaspartate (NAA), 2.01ppm, Creatin (Cr), 3.02ppm). A number of methods have been proposed for detection of hidden or overlapped J-coupled metabolites in vivo, including J-difference spectroscopy, 2D spectroscopy, and multiple-quantum spectroscopy. The last group of methods can be used to perform single scan editing and is very robust against motion artefacts, but suffers from signal loss of the coherence pathway selection. In this study, the Sel-MQC editing scheme was extended by an additional frequency selective pulse (Dual Sel-MQC) to increase the number of detectable J-coupled metabolites in one scan. The editing and the sensitivity of the sequence were evaluated with simulations and phantom experiments.

Material and Methods: The Sel-MQC editing scheme was extended with an additional frequency selective pulse to enable optimal multiple J-coupled metabolite detection in one scan. The pulse sequence of the Dual Sel-MQC (D-Sel-MQC) editing scheme in shown in Figure 1: The first selective 90° pulse is applied on the alanin (Ala, 1.48 ppm) and lactate (Lac, 1.33 ppm) CH_3 resonances. The second frequency selective pulse excites Glu (2.05 ppm / 2.12 ppm), Gln (2.13 ppm / 2.14 ppm) and GABA (1.89 ppm) resonances. The metabolites evolve under J-coupling and after τA and τB (depending on J of the edited metabolites) the third selective pulse is applied at 2.7-4.5 ppm on the corresponding coupling groups (Ala CH (3.78 ppm), Lac CH (4.11 ppm), Glu CH (3.75 ppm), Gln CH (3.77 ppm), GABA CH_2 (3.01 ppm)), creating a mixture of MQCs. The 180° slice selective pulse refocuses the chemical shift evolution, B_0 inhomogeneities and interchanges the MQCs. The coherence is selected by gradients G1 and G2, which are applied in a ratio -1:2 to filter the double-quantum pathway. The last 90° frequency selective "read" pulse is placed on the 2.7-4.5ppm region and converts the labeled MQCs in transverse magnetization. The editing principle and the efficiency of the D-Sel-MQC were evaluated by simulating the sequence on a number of brain metabolites at 750 MHz proton resonance frequency using the Bruker NMR-SIM 3.5 software package[6] (Fig.2 and Tab.1). For the frequency selective 90° pulses hermite shaped pulses with 12 ms duration were used, resulting in a spectral bandwidth of 450 Hz (FWHM). The duration of the selective 90° pulses on the 2.7-4.5 ppm area were 4 ms, resulting in a 1350Hz FWHM bandwidth. The slice selective refocusing pulse duration was 1 ms and the t1-period of the pulse sequence was kept as short as possible. The phantom experiments were carried out at 17.6 T (750 MHz proton resonance), using the same pulse parameters as for the simulations. The phantom consists of a 5 mm diameter glass tube containing Lac, GABA, Glu and NAA, each at 100 mM in aqueous solution. Spatial localization was incorporated by 2D phase encoding at the end of the MQC editing period (Fig.1). The sensitivity of the sequence was evaluated by comparing the signal intensity of the edited metabolites to the signal intensity of the corresponding conventional spin echo experiment.

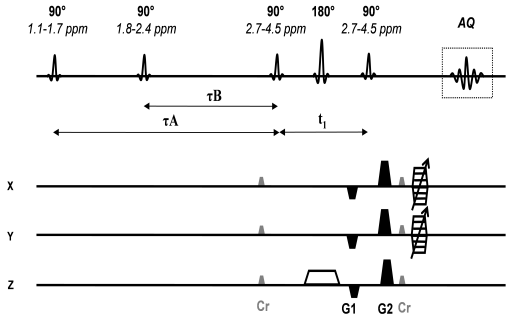

Fig. 1. D-Sel-MQC pulse sequence

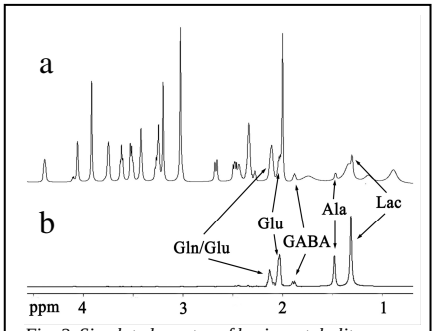

Fig. 2. Simulated spectra of brain metabolites:
(a) Single pulse acquisition
(b) D-Sel-MQC edited metabolites (zoomed scale)

Metabolite	Chemical Shift [ppm]	Simulated Intensity	Experimental Intensity
Lac	1.33	42%	41%
Ala	1.48	42%	41%
GABA	1.89	16%	13%
Glu	2.05	23%	20%

Tab. 1. Percentage of D-Sel-MQC signal intensity compared to conventional spin-echo intensity

Results and Discussion: Fig. 2a shows the spectrum of the simulated metabolites with the main resonances occurring in the mammalian brain. The D-Sel-MQC edited spectrum of the metabolites is shown in Fig 2b. Only resonances from the J-coupling metabolites Lac, Ala, GABA, Glu and Gln are passing the coherence filter, proofing the editing principle of the sequence. The simulations of the D-Sel-MQC sequence on the spin systems show a signal reduction of about 58% for the Lac and the Ala resonance, and a signal loss of 77% and 84% for the GABA and Glu resonances. The phantom experiments confirm the sensitivity of the sequence compared to a conventional spin echo experiment. The signal loss results from the selective double quantum coherence pathway and from J-coupling effects in the t1-period, which are not refocused by the slice selective 180° pulse.

Conclusion: By extending the Sel-MQC sequence with a selective pulse and adjusting the timing of the sequence several J-coupled metabolites in the 1.2-2.2 ppm area can be detected in a one scan. The D-Sel-MQC editing on the Glu and GABA resonances cause an increased signal loss compared to the conventional spin echo experiment, but the sequence can be advantageous when metabolite editing is needed and single scan editing is important for minimizing respiratory motion artefacts.

References: [1] He Q et al. J Magn Reson B 1995, 106: 203-211. [2] He Q et al. J Magn Reson B 1996, 112: 18-25. [3] He Q et al. Magn. Reson. Med. 1995; 33: 414-416. [4] de Graaf RA et al. Magn. Reson. Med. 2000; 43: 621-626. [5] Shungu DC et al. Proc. Intl. Soc. Mag. Reson. Med. 2003; 1140 [6] Bruker NMR-SIM 3.5; http://www.bruker.com.