In vivo Simultaneously detecting glutamine (Gln), glutamate (Glu), and g-aminobutyric acid (GABA) at 4T

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Introduction: Enormous effort has been put into the *in vivo* detection of glutamate (Glu), glutamine (Gln) and γ-aminobutyric acid (GABA), because of their importance in neurochemistry. Although tremendous progress and important milestones have been achieved with various new techniques and high magnetic field strengths [1-4], simultaneous detection of Glu, Gln and GABA without spectrally overlapping has remained unconquered thus far. Detection of Gln, Glu, and GABA is challenging because of the similarity in structure of the molecules and strong coupling of their spin systems. These properties result in closely overlapping resonances and complicated spectral patterns. Moreover, spectral patterns for Glu, Gln and GABA vary with different experimental condition. We report here a novel approach to simultaneously detecting Gln, Glu, and GABA at 4 Tesla

Method and Material: All experiments were performed in a 4T system with a standard 1H STEAM pulse sequence. The key concept is that by taking the advantage of the high field magnet and the previous unfavorable spectral properties, such as the similarity in the structure of the molecules and spectral patterns varying with experimental condition, we can sufficiently and simultaneously suppress the two outlet peaks of the triplet signals around 2.4 ppm for Gln, Glu, and GABA.

Results: Figure 1A is a spectrum of a phantom containing 20mM Glu, 5 mM Cho and 5mM tCr acquired with the optimized TE (80 ms) and TM (50 ms) at 4T with a shimming of 4 Hz (the width at the half-height of the water peak). As illustrated with the optimized parameters, the two outlet peaks of the Glu2 triplet are suppressed to the point that the original triplet pattern of the Glu2 (data not shown) by the shortest TE/TM(10/10 ms) virtually become singlet. Figure 1B is the spectra from the same phantom with the same experimental parameters except that the shimming was 11 Hz, respectively. The best shimming of the human brain we have achieved so far at the 4T imager is 10 Hz. 15 Hz to 25 Hz is the typical result depending on the location. As illustrated, the spectral pattern of Glu2 apparently becomes singlet at a normal *in vivo* shimming condition. Figure 1C is the spectrum from a phantom containing 5mM Cho, 5mM tCr, 20 mM Gln, 20 mM Glu, and 20 mM GABA acquired with the optimized TE/TM with a shimming of 16 Hz. As illustrated, there is no overlap between Gln2, Glu2 and GABA2 signals in a typical shimming condition. Figure 1D is a spectrum from a patient with trauma brain injury (TBI). The patient data was acquired in 21 minutes with a spatial resolution of 3 cm^3. This first *in vivo* simultaneous detection of Gln, Glu and GABA without spectral overlapping in the human brain clearly demonstrates elevated Gln, Glu and GABA levels for the patient.

Discussion: Our results illustrate the capability of simultaneous detection of Gln, Glu and GABA with a standard 1H STEAM sequence at 4 Tesla. It worthy note that the signals around 2.4 ppm for Gln, Glu, and GABA also offers the highest SNR (data not shown) compared to other signals (around 4 ppm and 2ppm for Gln and Glu; 3ppm and 2ppm for GABA). In summary, this novel MRS approach has several advantages compared to existing techniques: 1) the capability of separating Gln, Glu and GABA in typical *in vivo* shimming conditions; 2) no loss of other metabolites, such as NAA, Cho, tCr; 3) facilitating accurate quantification, because of little baseline distortion and no strong overlap among Gln, Glu and GABA signals; 4) Applicable to any 4T magnet with 1H MRS capability.

Reference: [1] Rothman *et al* PNAS USA 81, 5662(1993); [2] Shen *at al*, Magn. Reson. Med. 41(1999); [3] Thompson and Allen, Magn. Reson. Med. 39, 762(1998); [4] Hanstock *et al*, Magn. Reson. Med. 48, 617(2002).