Simultaneous Quantification of γ-aminobutyric acid, Glutamate, and Glutamine at 3T

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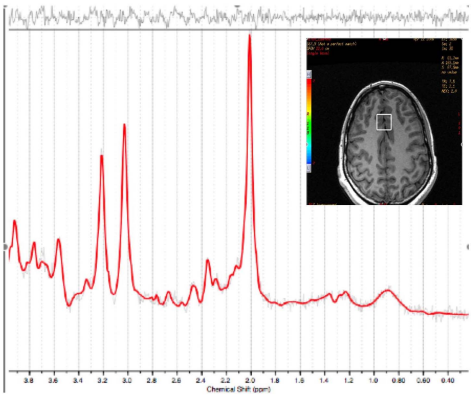

Figure 1. LCmodel analysis from optimized STEAM acquisition. Glx and GABA were significant (SD%<20%): [GABA]=3.494mM, [Glu]=11.415mM, [Gln]=5.768mM (FWHM=0.033ppm, S/N=35). Inset shows acquisition ROI containing anterior cingulate gyrus (8cc volume).

BACKGROUND: γ-Aminobutyric acid (GABA), glutamate (Glu) and glutamine (Gln) are three important neurochemicals comprising a tightly coupled spin system. The coupling of this system and their low concentrations in brain typically render GABA MRS-invisible and Glu/Gln indistinguishable (and represented as the composite peak Glx) on standard clinical PRESS scans. Investigations by Hu *et al.* **[1]** have demonstrated the differentiability of these peaks at 4.7T using a TE/TM optimized STEAM sequence. Our investigation extends their method to the more common field strength of 3.0T, and demonstrates the stability of the approach through repeated scanning.

METHODS: As per Hu *et al.* **[1]** STEAM acquisition was optimized such that the outer multiplet wings of Glu C4 (2.35ppm), Gln C4 (2.45ppm), and GABA C2 (2.28ppm) are suppressed to leave resolvable singlets. Optimization was at echo time (TE) of 72ms and mixing time (TM) 6ms **[1]**. LCmodel basis sets were constructed for this parameter set **[2]**. Subsequent phantom studies indicated the optimal TR for GABA/Glu/Gln differentiation to be in the ≥3000ms range to allow more complete T1 recovery. In a study approved by our institutional review board optimized STEAM acquisition (8cc volume; 512 NEX; TR=3s, scan time=25.6min) of the anterior cingulate cortex (ACC; **fig.1**) was performed in 7 healthy male volunteers using a GE Healthcare 3T HD Signa MRI, and 8 channel phased array RF coil (GE Healthcare, Milwaukee WI). Two of the 7 subjects were subsequently scanned four times in a day (2x in AM, with a repositioning between scans 1 and 2, and 2x in PM, with same) to assess stability. Absolute quantization of metabolite concentrations was determined through the use of LCModel's water-scaling algorithm.

RESULTS: Significant levels (defined as SD≤20%) of Glutamate were detected in all subjects (n=7). Concentrations trending towards significance (defined as 20>SD%≥30) of GABA were detected in two (n=2) subjects, with significant Gln (n=2) detected in two different subjects. No significant differences existed between subjects' overall, absolute metabolite concentrations (p=0.998). No significant temporal differences were observed across four time points for 2 subjects (p=0.9909, and p=0.9995) indicating the stability of the approach. However, some fluctuations in individual time points for each Glx and GABA appeared to be approaching significance.

in vivo Concentrations of GABA, Glu, and Gln (mM)		
GABA	Glu	Gln
2.323 ± 1.538	8.861 ± 1.360	1.595 ± 0.893

Table 1. *in vivo* concentrations of neurochemicals of interest, reported with 95% confidence intervals about the mean.

DISCUSSION: These results demonstrate simultaneous quantification of GABA, Glu, and Gln *in vivo* is feasible and consistent using a standard STEAM sequence at 3T. The ability to differentiate Glu from Gln in the 'Glx' signal would be of profound benefit case of hyperelevation of the excitotoxic processes were occurring in a in assessing whether or not patient; being able to differentiate one from the other while also capturing information about inhibitory (GABAergic processes) could be of use in the study of OCD **[3]** and depression **[4]**. Presently used clinical scans (i.e. PRESS) do not enable this. The only drawback to this approach is the acquisition time (25.6min) required due to the low concentration of these metabolites. Lastly, although the approach appears to give consistent results for Glx and GABA, there may be some normal variations occurring over the course of a day. This, if true, would be in agreement both with the concentrations predicted *in vivo* from other MR imaging studies **[5,6,7]**, and from research in circadian neurotransmitters fluctuations **[8]**. We are currently investigating any circadian effects.

References: ***[1]*** *Hu, et al. (2007) JMR 185:204-213.* ***[2]*** *Provencher (2008) LCModel and LCMgui User's Manual.* ***[3]*** *Ebert, et al. (1997) Psych. Res. 74:173-176.* ***[4]*** *Block et al. (2008) Int. J. Neuropsychopharm. 10:1-8.* ***[5]*** *Keltner, et al. (1996). MRM 36:458-461.* ***[6]*** *Pouwels, et al. (1998) 39:53-60.* ***[7]*** *Knorle, et al. (1997) Neurosci. Lett. 221:169-172.* ***[8]*** *Soreni, et al. (2006) MRI 24:187-194.*