Neurotransmitter profiling at 3T using GABA optimized PRESS sequence

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Introduction: GABA is the major inhibitory neurotransmitter in mammalian brain and GABAergic alterations have been implicated in several psychiatric and neurological disorders. GABA was also proposed to underlie DFM modulation (1). Because of this growing interest in understanding physiology and pathophaysiology of cerebral GABA homeostasis, there is a need for robust measurement of in vivo GABA levels. On the other hand, spectroscopic detection of GABA is still challenging due to its low concentration, and the fact that all GABA peaks are overlapped by much stronger metabolite resonances at the field strength accessible for clinical studies. Our aim is to simultaneously detect GABA as well as Glu, Gln using a standard PRESS localization pulse sequence with optimized timing parameters. This approach exploits the dependence of the spectra of the strongly coupled spin systems on the partial echo times TE1 and TE2 at 3 T to find an optimized sequence parameter set {TE1, TE2} (2).

Methods: The study was divided into different parts: first spectra simulations were conducted to optimize and find the best sequence parameter set and second in vivo experiments were carried out for verification. The simulations were exploited by Spinevolution software and the same software was used to create the exact basis-dataset for the in vivo analysis. The simulations were focused on the C3 and C4 protons of GABA. Essentially all the protons of GABA are hidden by other metabolites, even so, in the case that NAA peak is reasonable narrow, the C3 protons are visible enough to be fitted. The numerical simulations spanned different TE1s and TE2s at long echo time in order to avoid any fitting problems due to unavoidable macromolecules at short TE. Data apodization was employed to emulate more the real linewidth and then the amplitude of peak was maximized. The in vivo experiment was part of larger test-retest study approved by local ethic committee. 6 healthy volunteers participated in the study after giving written informed consent. A 3T Philips Achieva scanner (software release 2.5.3) with 8 channel sense coil was used and each subject underwent two different sessions separated by 10 minutes. In order to reproduce completely technical between scan variability, each subject was taken out the scanner between the sessions. A 25x25x25 mm^3 voxel was positioned in the prefrontal cortex and PRESS sequence TE1=15 ms and TE2=37.5 ms, TR=3000ms, NA=128 was used. All concentrations were estimated by LcModel software and the intra-subject coefficients of variation (CV) were computed as the absolute variation in concentration between scan 1 and scan 2 divided by the average concentration of them for each metabolite.

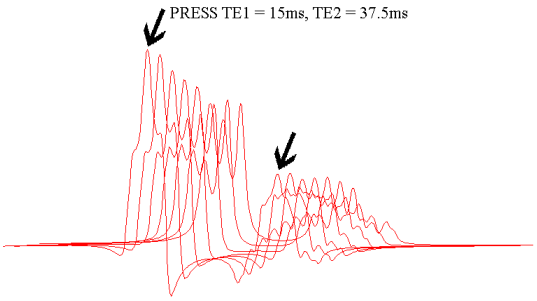

Fig.1: Some of simulations showing the reduction of the C3 and C4 peaks' amplitude

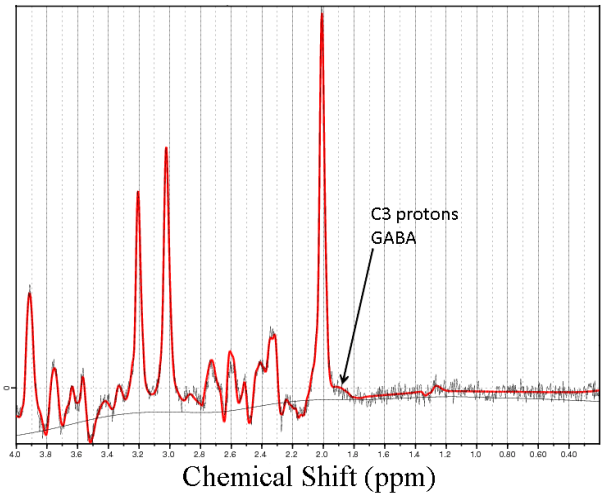

Fig.2: LcModel fittig example

Results and Discussion: The simulations have showed that the parameters TE1=15 ms and TE2=37.5 ms correspond to a maximum value for the peak heights of C3 and C4 protons. For 11 out of 12 in vivo spectra, this yielded CRLB values below 19%. The mean CRLB was 16% which is largely consistent with also reasonable reproducibility reflected by a mean GABA CV of 18%. Head repositioning and manual voxel repositioning may have added to this slightly higher retest variation. Editing sequences allow better accuracy for GABA fitting, but the proposed protocol retained accurate estimation of other metabolites also for Glu CV = 5% (mean CRLB Glu =3.5%) and Gln CV =16% (mean Gln CRLB =14%).

Discussions: The MEGA-PRESS (3) protocol is the most prevalent method for detecting and measuring GABA. It is also capable of providing reasonable levels of intra-subject reproducibility (13%) (4). Nevertheless for *in vivo* studies where the duration of the protocol is time constrained the use of MEGA-PRESS might be not feasible. In fact it needs two acquisitions which make the experimenting time longer. Furthermore, it is known that the optimized MEGA-PRESS employs a TE=68 ms, which may reduce the chances of reliably quantifying Glu and Gln. In the present study we optimised a standard PRESS protocol optimisation allowing neurotransmitter profiling at 3T with mean CRLB and CV <18% for GABA, <10% for Gln and =5% for Glu. This paves the way for wider application for characterisation of GABAergic pathology in clinical cohorts.

1. Northoff G. et al. Nat Neurosci. 2007 Dec; 10(12):1515-7. 2. G. Gambarota et al. Journal of Magnetic Resonance 2005; 177: 299–306. 3. Mescher M, et al., NMR Biomed 1998;11(6):266–72. 4. Bogner W., et al. In vivo quantification of intracerebral GABA by single-voxel 1H-MRS—How reproducible are the results? Eur J Radiol (2009) (in press).