High-Speed GABA Mapping in Human Brain with MEGA-PEPSI at 3 Tesla

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Introduction

As major inhibitory neurotransmitter gamma aminobutyric acid (GABA) plays a decisive role in a variety of nervous system disorders, such as anxiety disorders, epilepsy, schizophrenia, and many others [1]. Being able to non-invasively and quantitatively map its brain concentrations by means of MR spectroscopic imaging is therefore an important asset to study biochemical pathways in such disorders and mechanisms of treatment. While the higher chemical shift dispersion at magnetic field strengths of 7 Tesla and higher allows to assess GABA levels in the human brain with conventional MRS techniques [2], editing techniques are necessary for typical clinical field strengths, such as 1.5 T and 3 T, to separate GABA from overlying resonances. Most GABA measurements have used single voxel GABA editing techniques such as MEGA-PRESS [3-5], except for a few studies who employed spectroscopic imaging [6,7]. However these measurements were very time consuming due to the use of conventional phase encoding. Here we demonstrate the feasibility of combining the MEGA editing scheme with the fast spectroscopic imaging technique PEPSI [8] (MEGA-PEPSI) to achieve clinically feasible acquisition times of less than 10 min. MEGA-PEPSI at 3 T enables mapping of the GABA levels in the human brain with a nominal resolution of 8 ml with measurement times as short as 4:40 min in a 2D slice.

Materials and Methods

MEGA-editing pulses were implemented into a slice-selective spin-echo PEPSI pulse sequence [8], at alternating frequencies of 1.5 ppm and 7.5 ppm. Using a minimum of two averages, frequency alternation of the MEGA pulses and inversion of the excitation pulse for consecutive averages, allows for the measurement of a difference spectrum for each PEPSI voxel, only containing resonances from GABA, co-edited macromolecules (the sum of which will be called 'GABA+'), glutamate/glutamine (Glx), NAA and lipids.

All measurements were performed on 3 T Tim Trio scanners (Siemens Healthcare) equipped with 12- and 32-channel head coils. Phantom measurements of a 20 mm thick axial slice were performed on a 10 cm diameter sphere filled with a solution containing 2 mM GABA and 6 mM creatine using: TR = 2 s, TE = 68 ms, 32x32 matrix, 8 weighted averages, voxel size 2x2x2 cm^3, scan time 4:40 min. *In vivo* data were acquired in several healthy volunteers in axial slices angulated along the AC-PC line and centered above the ventricles using identical parameters. In addition, eight outer volume saturation bands were applied to suppress lipid signals from subcutaneous fat. PEPSI data were reconstructed online on the scanner and displayed on the scanner console. LCModel fitting was performed using analytically computed basis sets simulating the spectral pattern of GABA, glutamate, glutamine and NAA based on known chemical shifts and *J*-couplings [9]. Absolute GABA concentrations were approximated by using the GABA/NAA ratio fitted in the edited spectra assuming an NAA concentration of 11 mM.

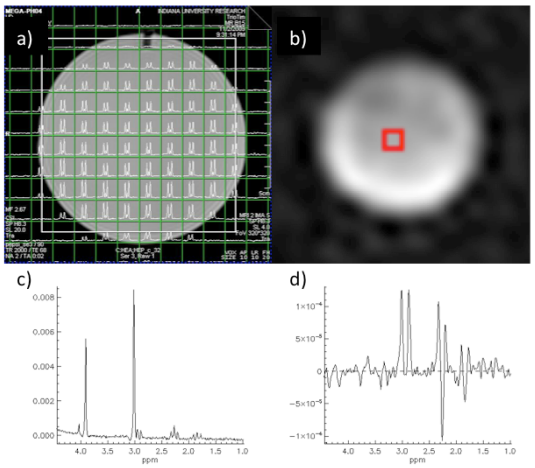

Figure 1: *2D MEGA-PEPSI data acquired in a phantom filled with 2 mM GABA and 6 mM Cr: a) a clear GABA "doublet" (zoomed in at 3 ppm) is achieved throughout the slice. b) GABA metabolite map; c) representative spectrum without MEGA editing (PEPSI, TE=11 ms) showing creatine and GABA signal and d) MEGA-edited spectrum from the same voxel, showing no contamination from creatine.*

Results

Phantom data show that a selective observation of the outer lines of the GABA C4 triplet at 3 ppm is achieved throughout the MEGA-PEPSI slice and that the overlapping creatine resonance is fully removed by the editing scheme (Fig 1). *In vivo*, GABA-edited spectra with spectral peaks from GABA, glutamate, glutamine and NAA were obtained from 8 ml voxels within only 4:40 min using both the 12 and the 32 channel coils. The 'GABA+' signal at 3 ppm, in many cases showing the "doublet" signature as a consequence of the narrow spectral line width within individual voxels (< 0.07ppm), is clearly visible in most spectra throughout the axial slice (Fig 2). For the slice shown, LCModel fitting yielded GABA levels of 2.1±0.4 mM with Cramer Rao lower bounds < 20% for 15 out of 17 voxels within the volume demarcated by the saturation bands.

Discussion

We have demonstrated the feasibility of mapping GABA in the human brain at 3 T using high-speed MRSI with the MEGA-editing scheme. The sensitivity for mapping the *in vivo* 'GABA+' signal with MEGA-PEPSI compares favorably with that of conventional GABA-edited MRSI methods, which is in part due to the use of a slice selective spin-echo excitation scheme. In a next step the absolute GABA concentrations throughout a brain slice will be calculated by correcting for CSF content and using brain water as internal reference. Finally the macromolecular contribution to the 'GABA+' peak needs to be quantified, to obtain pure GABA concentrations. The high sensitivity and fast acquisition speed makes this method suitable for 3D GABA mapping in clinically feasible acquisition times.

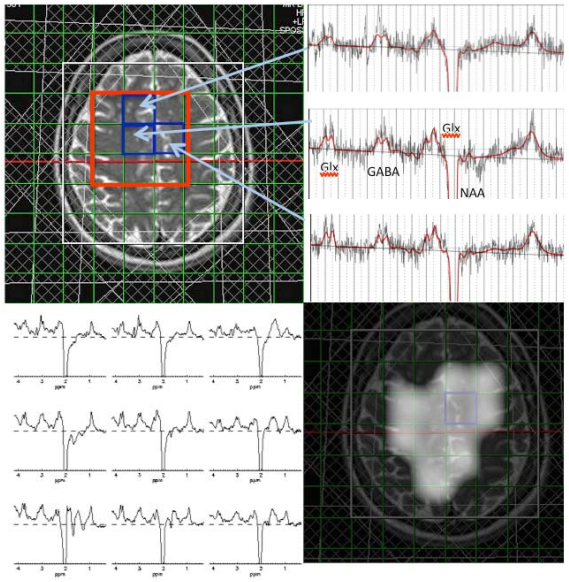

Figure 2: *In vivo 2D MEGA-PEPSI data acquired in 4:40 min. GABA-edited spectra from the voxels outlined in red show a clear 'GABA+' signal at 3 ppm. Representative LCModel fits from three of these voxels are shown on the right. The GABA-map is generated with the LCModel fitting values.*

References:

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Acknowledgements:

M.M. acknowledges support from BTRC P41-RR008079. The authors also would like to acknowledge the help from Edward Auerbach and Pierre-Gilles Henry to generate the MEGA editing pulse. We thank Akio Yoshimoto for support with data analysis tools, Chenguang Zhao for developing the ICE reconstruction program and Ashritha Epur for mixing the phantoms.