In vivo optimisation of GABA measurements in the Hippocampus using MEGA-PRESS at 3T

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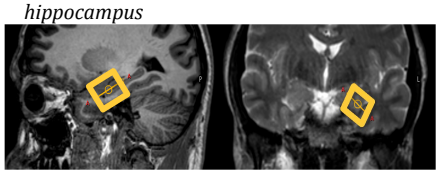
Target Audience: Clinicians and physicists interested in GABA measurements from the hippocampus.
Purpose: Test a spectral editing sequence (MEGA-PRESS) in the hippocampus for quantitative measures of GABA, Glx and NAA.

Introduction GABA is the main inhibitory neurotransmitter in the human brain and has been implicated in a number of neurodegenerative diseases. Non-invasive measures of GABA in the brain have been commonly reported in the occipital lobe, and sensor motor cortex using the MEGA-PRESS editing sequence largely due to the ease of placing large voxels in these areas[1]. However measures in the hippocampus remain elusive. The hippocampus is thought to be affected in a range of neurological disorders including Alzheimer's, Schizophrenia and Multiple sclerosis (MS) due to its role in long and short term memory and cognitive function. ^{1}H MRS measures in the hippocampus are still limited due to the small size of the hippocampus and confounded by strong susceptibility changes from cranial air and bone and the pulsatile flow of cerebrospinal fluid (CSF), which lead to distinct B_0 field distortions that degrade spectral quality. Here we investigate how to overcome these drawbacks using cardiac triggering and careful placement of smaller voxels in order to achieve GABA measures with acceptable Cramer-Rao Lower Bounds (CRLB's) using the MEGA-PRESS sequence at 3T in normal healthy controls.

Figure 1. Sagittal and Coronal images depicting voxel placement in the hippocampus



Method Written informed consent was obtained from 6 healthy male participants.
Data acquisition: All MR experiments were performed on a 3T Achieva system (Philips Medical Systems, Best), with a 32-channel head coil. A survey and T1w sagittal, T2w coronal and axial proton density scans were used for voxel placement (30x19.2x16mm^3 figure 1). Particular care was used to avoid contamination from ventricles and partial volume in the planned voxel. ^{1}H MRS scans were cardiac triggered at 2RR using a Peripheral Pulse Unit (PPU) device, which resulted in a TR of ~2000ms. PB-auto shim was used to achieve linewidths of ~10Hz. GABA is heavily overlapped by other prominent metabolites such as Cr, hence a J-editing sequence (MEGA-PRESS) was used with TE=68ms and editing pulses centered at 1.9 and 7.5ppm[2]. MOIST water suppression was performed and 32 averages collected in 16 blocks leading to a scan time of ~20mins. A water reference scan was also acquired and the water scaled MRS data were quantified for GABA, NAA and Glx using TARQUIN. To have an indication of reproducibility this was repeated in 1 volunteer in a separate scan session.

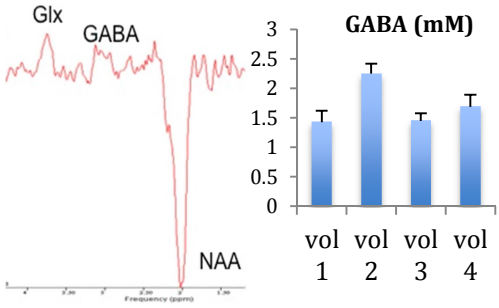


Figure 2. Left: Example MEGA-PRESS spectrum from the hippocampus. Right: GABA concentrations for each volunteer.

Data Analysis: CRLB values provided by TARQUIN were used to assess the reliability of the fit, with poor fits indicated by CRLB values >20%. SNR was also noted in addition to the water linewidths (LW) achieved to assess spectral quality.

Table 1

	Age (yrs)	GABA (mM)	GABA CRLB %	Glx (mM)	NAA (mM)	GABA/Glx	SNR	LW (Hz)
Volunteer 1	32	1.4±0.3	13.7	3.5±1.2	7.4±0.0	0.4±0.3	2.97	10
Volunteer 2	23	2.3±0.2	7.5	2.0±0.4	4.4±0.07	1.1±0.4	2.31	10
Volunteer 3	36	1.4±0.2	9.0	3.4±0.3	4.2±0.06	0.4±0.1	3.30	9
Volunteer 4	30	1.7±0.3	12.1	2.2±0.5	4.6±0.08	0.8±0.3	2.82	11
Mean±SD	30±5	1.7±0.4	10.6±2.8	2.8±1.0	5.2±0.2	0.7±0.6	2.9±0.4	10±0.8

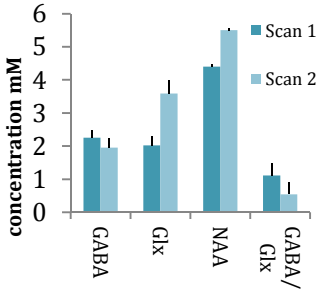


Figure 3. Metabolite concentrations scan 1 and scan 2 (a repeat scan) on the same volunteer

Results Two datasets were rejected due to movement or spurious stimulated echoes contaminating spectra when shims were poor (15Hz). The data for the remaining 4 datasets is shown in table 1. Spectral quality was good in all four spectra as indicated by the SNR (2.9±0.4) and consistent linewidths, and is reflected in acceptable CRLB's for the GABA peak ensuring measures are reliable. Figure 2 shows an example of the MEGA-PRESS spectrum and GABA concentrations found for each volunteer. Mean GABA in the hippocampus was found to be 1.7±0.4mM. Glx and NAA were also measured and found to be 2.8±1.0mM and 5.2±0.2mM respectively. GABA/Glx was found to have a mean of 0.7mM. Concentrations for the repeat scan are shown in figure 3.

Discussion To our knowledge only one report of MEGA-PRESS in the hippocampus exists whereby a larger voxel and non triggered scans were used which may be more susceptible to partial volume effects and dephasing[3]. GABA/Cr ratios were reported but no GABA/Glx or absolute values for comparison. The reported mean GABA/Cr ratios averaged to about 0.2 with data spreading from 0.08-0.25, reflecting a similar spread in GABA values as we found here. Diseases such as MS, though, undergo variations in Cr and so this cannot always be used as a reference measure. Results for GABA/Glx found in our study are similar to previous work by our group in the thalamus[4]. The repeat scan shows good agreement for GABA measurements although other metabolites appear more variable which may reflect the difficulty in positioning a voxel in exactly the same place each time. Larger cohorts would be needed in studies to find significant differences in patient cohorts.

Conclusion Here we have successfully measured GABA in the hippocampus *in vivo* at 3T using cardiac triggered ^{1}H MRS. A mean value of 1.7mM was found. This protocol allows for the first time to assess reliable absolute measures of GABA in the hippocampus.

References 1. Puts NAJ, Prog. in NMR Spec. 2011 2. Mescher M *et al.* NMR Biomed 1998;11:266-272. 3. Stan A. Proc. 19th ISMRM, Stockholm, 2010 4. Graca A, Queen Square Symposium, UK 2012

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