# Localised in vivo measurement of GABA and glutamate in the rat brain at 4.7T

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## Target audience

Clinicians/scientists using animal models of psychiatric disorders or performing spectroscopy in rodents

## Purpose

γ-aminobutyric acid (GABA) is the chief inhibitory neurotransmitter in the brain and dysfunction of the GABAergic system is suspected in a range of important neurological and psychiatric conditions. The spectral-editing sequence MEGAPRESS [1] has seen a rise in popularity in human studies, but there are no reports in the literature of its use in rodents to date. Here we applied the technique to rats at 4.7T to establish its feasibility and measure variability in GABA measurements across subjects.

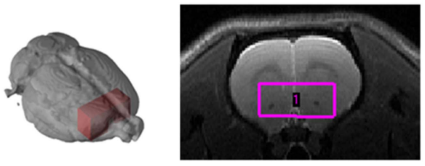

**Figure 1** Spectra were acquired in a large voxel centred on the ventral striatum covering both hemispheres.

## Methods

Ten adult male Lister Hooded rats were anaesthetised with isoflurane maintained at 1-3% in 1l/min $O_2$ throughout. A Bruker BioSpec 47/40 system at 4.7T was used with a manufacturer provided 4ch head array for reception and a 72mm birdcage for excitation. 2D RARE images (1mm slice thickness, 160μm resolution) were used for voxel placement in the ventral striatum. For GABA measurements, two editing pulses (Gaussian, 20ms/130Hz BW) were incorporated within a PRESS sequence symmetric about the final refocusing pulse. Water suppression was achieved with VAPOR with manually adjusted RF pulses to minimise water signal. Shimming was achieved using field mapping with the Bruker MAPSHIM method. A large voxel spanning both sides of the brain (7×5×4mm$^3$) was acquired with outer volume suppression, eddy current correction and retro frequency lock enabled (Figure 1). TR/TE were 2000/68ms and 256 transients were recorded in 8.5 minutes, with MEGA pulses applied at 1.9ppm and 7.8ppm in alternating acquisitions. An unsuppressed water reference scan was acquired for the same voxel for quantification.

LCModel was used to fit the mean 'off' spectra for measurement of major brain metabolites. For GABA concentrations, spectra were processed using Matlab. After manual phase correction, spectra were manually phase-corrected and subtracted followed by line broadening of 10Hz. A Gaussian peak was fitted to the signal at 3.0ppm and the GABA$^+$ to water peak area ratio was adjusted for T1 and T2 differences between GABA and water, the visibility of water with correction factors for macromolecule contamination and editing efficiency following [2]. Values are reported in institutional units (mM).

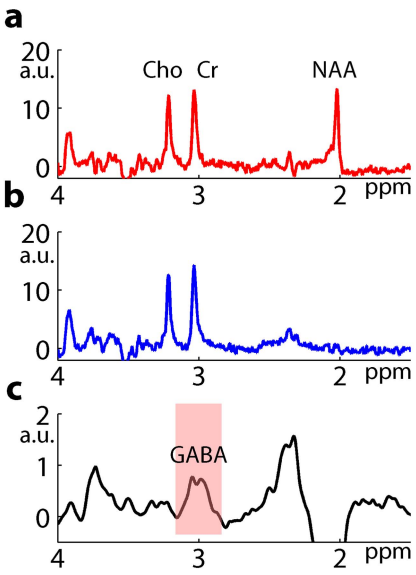


**Figure 2** Representative results a) MEGAPRESS 'off', b) MEGAPRESS 'on' and c) edited spectrum showing GABA. Line broadening is 1 Hz for a-b and 10 Hz for c.

## Results and discussion

Representative spectra for one subject are shown in figure 2 and are similar in appearance to those seen in human data [2]. The mean GABA concentration measured was 1.7±0.5mM (mean ± SD) across subjects. The spectra were of good quality, with line widths for water reference spectra at 7.1±0.4Hz. Table 1 shows mean concentrations of metabolites with standard deviations of each calculated between subjects.

| Metabolite | Concentration (IU) | Population variation (IU) |
|---|---|---|
| **GABA** | 1.75 | 0.51 (29%) |
| **Glu** | 5.95 | 1.05 (18%) |
| **Gln** | 4.40 | 1.40 (32%) |
| **Cr** | 6.62 | 1.27 (19%) |
| **Cho** | 2.97 | 0.29 (10%) |
| **NAA** | 9.18 | 0.52 (6%) |

**Table 1**
Ventral striatum metabolites with intersubject variability. Concentrations are scaled relative to water in mM.

## Conclusion

We have shown that localised measurements of GABA and glutamate are feasible in the rat brain with MEGAPRESS and report the population variability. We are currently measuring intrasubject variability and investigating how modifications to the pre-processing approach used can refine the precision of the measurement.

**References** [1] Mescher M *et al.* (1998) NMR Biomed. [2] Mullins PG *et al.* (2013) Neuroimage