Reproducibility of *in-vitro* GABA measurements using 2D J-resolved MRS

K. Lymer[1], K. Haga[2], I. Marshall[1], J. Wardlaw[2]

[1]Medical Physics, The University of Edinburgh, Edinburgh, United Kingdom, [2]Clinical Neurosciences, The University of Edinburgh, Edinburgh, United Kingdom

Introduction

MRS studies of GABA are difficult, especially at 1.5T due to low *in-vivo* concentrations and overlapping of higher concentration metabolites of creatine (3.0 ppm) and glutamate (2.35 ppm). Results from previous clinical studies have demonstrated that 2D J-resolved MRS allows GABA to be resolved from these overlapping metabolites at 1.5T [1,2]. Unlike previously published methods, 2D J-resolved is not compromised by patient motion or signal loss, and allows for the simultaneous measurement of GABA and traditional metabolites. Studies using GABA specific spectral editing MRS in depression have reported reductions in GABA levels of approximately 50% [3]. In order to implement 2D MRS to measure GABA changes in healthy and disease states, the reproducibility of the sequence must be sufficient to detect physiological changes. Although studies have shown 2D MRS (COSY) to be highly reproducible for measuring the traditional metabolites seen in 1D MRS, there are no reported reproducibility studies of GABA using this 2D J-resolved sequence [4]. This study presents the results from a series of 150 *in-vitro* experiments across a range of GABA concentrations, using both a standard volume head coil and a 5" general purpose (GP) surface coil to evaluate the reproducibility of GABA measurement using a 2D J-resolved sequence at 1.5T.

Methods

MRS Protocol: All experiments were performed on a 1.5T GE Signa Horizon Scanner. Three phantoms containing physiological concentrations of choline (9mM), creatine (3mM) and GABA (at 2 mM, 1.5 mM or 1.2mM) were scanned 15 times, using either a standard head coil or a 5" GP surface coil. Additional phantoms containing GABA at 5 mM and 10 mM and the same concentrations of choline and creatine were also scanned. Data were acquired from both coils, at each of the GABA concentrations from within-run (no phantom re-positioning, same scanning session), within-session (phantom repositioning, same scanning session) and between-days experiments (phantom scanned across five separate days). 2D J-resolved spectra were acquired from a 30x30x30mm^3 VOI in each experiment [2D PRESS: TR=2000ms, TE_{start}=35ms, NEX=16; 64 increments of $\Delta TE \approx 10$ms, scanning time ≈ 35mins]. Post-processing: The individual FIDs underwent time-domain phase correction and removal of the residual water peak using HLSVD. Apodization was performed in both the F1 and F2 dimensions. After 2D Fourier Transform, magnitude 1D spectra were extracted from J = 7.4Hz and the GABA peak at 3.0 ppm was quantified in MRUI [5]. The choline and creatine peaks in the J= 0Hz extracted row were quantified in the same way. Both absolute GABA values and ratios to creatine were recorded.

Results

The results from the physiologically relevant phantoms are summarised in Table 1. GABA measurements made using the surface coil were generally more reproducible than those obtained with the volume coil. In the phantom with the lowest GABA concentration (1.2mM), the results obtained between scanning days were significantly more reproducible for the surface coil than the volume head coil ($p = 0.005$). In terms of absolute units, the measurements from the surface coil were typically 3-4 times greater than the volume head coil**.** Figure 1 shows a representative spectra obtained from the surface coil at GABA = 1.2 mM.

Table 1 summarises the results from the reproducibility experiments of GABA at 2 mM, 1.5 mM and 1.2 mM. The measured amplitudes of GABA have been normalised to creatine. Values for the Co-efficient of Variation (CV) are provided for the volume head coil (VHC) and 5" GP surface coil.

GABA	Within-run		Within-session		Between-days	
	CV (%)		CV (%)		CV (%)	
	VHC	5" GP	VHC	5" GP	VHC	5" GP
1.2 mM	21.57	21.82	28.18	17.40	67.57	15.47
1.5 mM	12.38	16.89	31.13	11.79	54.99	21.38
2 mM	23.39	16.41	14.43	7.70	28.40	12.32

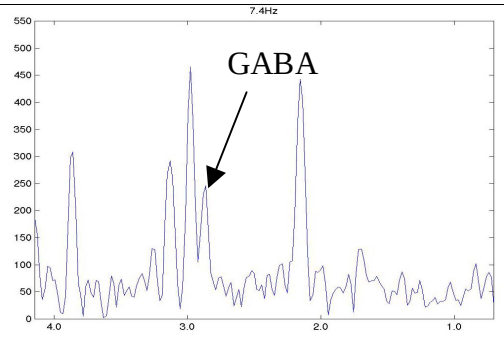

Figure 1 showing extracted magnitude spectrum from 2D contour plot at 7.4 Hz, from the phantom with GABA at 1.2mM phantom using the 5 " GP surface coil

Discussion

Concentrations of GABA similar to those found *in-vivo* can be reproducibly quantified (CV of 15.47%) at 1.5T using the 2D J-resolved PRESS sequence with a 5" GP surface coil and associated in-house post-processing techniques. The results from this study suggest that 2D J-resolved spectra are reproducible, although in translating this work *in-vivo*, slight increases in the CVs are expected due to variation in voxel placement across the brain regions and patient movement. With decreases in cortical GABA of approximately 50% being reported in MRS studies between normal and depressed patients [3], it is possible that such changes may be observed using this method.

Acknowledgements The 2D J-resolved sequence was provided by Dr Napapom Sailasuta of GE Medical Systems.

References;1. Ryner et al, MRI 13:853-869, 1995; 2. Ke et al, Psych Res Neuroimag 100:169-178, 2000; 3. Sanacora et al, Crit Rev Neurobiol 14: 23-45, 2000; 4. Binesh et al, MRM 48:942-948, 2002; 5. http://mrui-web.uab.es/mrui/mrui_homePage.shtml;