Unobstructed Measurement of Brain Glutamate using TE-Averaged PRESS at 3T

N. Sailasuta[1], R. Srinivasan[2], D. Vigneron[3], D. Pelletier[3], S. Nelson[2], R. Hurd[1]

[1]GEMS, Menlo Park, CA, United States, [2]U. of California, San Francisco, CA, United States, [3]U of California, San Francisco, CA, United States

Synopsis

A method is introduced to accurately measure the tissue level of brain glutamate at 3T. This method, based on a TE-Averaged PRESS data acquisition, gives an unobstructed single line response for glutamate at 2.38 ppm. A glutamate signal is also observed at 3.82 ppm, which co-resonates with glutamine. The tissue level of glutamate can be estimated using a ratio of glutamate to water or any other known metabolite level, or by external referencing. The method also provides the effective metabolite T2 relaxation rates for uncoupled spins, a measure of the intracellular status. The results from normal volunteer studies demonstrated the feasibility and repeatability of this method. These preliminary findings in 3 MS patients indicate a clinical value for this technique in the study of MS and other brain disorders that affect glutamate/glutamine metabolism.

Introduction

The quantitative measurement of overlapping metabolites in the human brain, in particular glutamate(glu), glutamine(gln),r-aminobutyric acid (GABA) and glutathione(gth) spin systems is a formidable task. These resonances are severely overlapped making it very difficult to separately detect each metabolite accurately even at high field. Numerous data acquisition techniques have been proposed to detect these metabolites, for example the editing technique based on J-coupling for GABA detection (1,2) and the two dimensional technique CT-PRESS for glutamate detection (3). In this communication we demonstrate that glutamate concentration in human brain can be reliably measured using TE-Averaged PRESS, the f1=0 trace in 2DJ spectroscopy (4,5).

Methods

Data were acquired on a GE Medical Systems 3T Signa (Milwaukee WI), using a volume head coil. A total of 18 exams were acquired for 6 volunteers (several repeat exams) and 3 MS patients. A modification of standard asymmetric single voxel PRESS with 64 t1-increments of 2.5ms was used. The TE ranged from 35 to 195ms. Spectra were obtained on basis set solutions for LCModel , 6 normal healthy consenting adult volunteers and 3 relapsing-remitting MS patients. Appropriate informed consent was obtained for all human subjects. The TR is 3s for basis set solutions and 2s for volunteers. A typical voxel size is 8 cc and it is located either in the white and gray parietal for volunteers and at the parietal white for the MS patients. Spectra from 64 FIDS were averaged and analyzed with either LCModel or simply calculating metabolite peak height ratio.

Results and Discussion

A comparison of single voxel PRESS at TE 35ms and the TE-Averaged PRESS, in Figure 1, shows for TE-Averaged PRESS the 2.1-2.9ppm region is greatly simplified. Signals from coupled spins not coincident with chemical shift (f1 = 0) are substantially reduced, even in this limited t1-average. Figure 2 shows spectra of a phantom containing a mixture of brain metabolites and some component spectra from a data acquisition where the data were sampled out to 195ms in t1. The region between 2.1 and 3.0 ppm contains some contribution from NAA, but the glutamate peak at 2.38 ppm is clearly separated, free from contamination from glutamine, NAA, GABA and glutathione. A more dramatic reduction of non-glutamate signals can be achieved by sampling out to 355 msec in t1, but at a cost of 2x in time for the same effective SNR. In addition, myoinositol is also detectable as a well resolved and easy to quantitate pseudo doublet at 3.65 ppm.

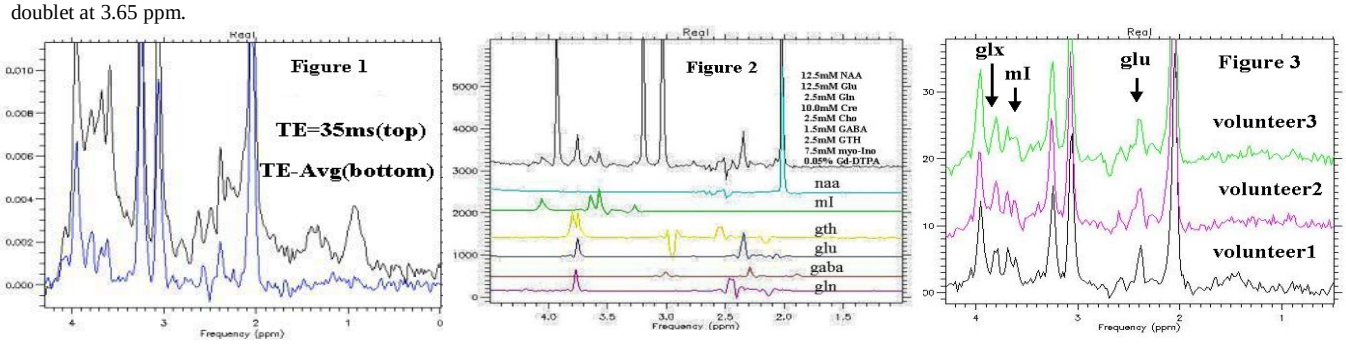

Figure 3 shows representative spectra from the gray matter of three volunteers. For our full volunteer group, the Glu/NAA ratio was 0.11 +/- 0.01 for white matter, and 0.14 +/- 0.01 for gray matter (less than 10% variance). NAA and Glu basis set spectra acquired under identical conditions gave an equimolar NAA/Glu ratio of 8.37. Using literature values for NAA tissue levels (6), the estimated brain glutamate concentration in our adult volunteer group was calculated to be 10.98 and 8.11 mmole per kg tissue for gray and white matter respectively. This data acquisition also provides a measure of uncoupled metabolite T2's. The 6 TE-averaged spectra run in the 3 MS patients showed some interesting trends, a 30% loss in NAA, along with a 16% decrease in NAA T2 relative to our normal volunteers. Although Glu/NAA and total Glx (Glu + Gln) as represented by the 3.82 signal, remained unchanged from normal, the Glu/Glx ratio shifted from 0.82 to 0.62 (shift of 40% of Glu to Gln). These results are clearly preliminary and absolute tissue levels are difficult in the absence of Glu and Gln T2s.

Conclusions

Our preliminary data demonstrate that brain glutamate levels can be reliably measured from the TE-Averaged PRESS technique, which in addition provides potentially diagnostic effective metabolite T2's for uncoupled spins, and reliable measures of NAA, Cho, Cre and mI. In preliminary studies of 3 MS patients, differences in glutamate resonances were observed and thus this method may have value for assessing glutamate levels in these patients.

Acknowledgements

This work was supported by joint funding from General Electric Medical Systems and the Life Sciences and Informatics Program award number lsit01-10107, as part of the University of California Industry University Cooperative Research Program.

References

1. Rothman,DL, et al. Proc.Natl.Acad.Sci.USA,90,5662 (1993).
2. Gruetter,R et.al. Proc. ISMRM, 1217 (1997).
3. D. Myer and D. Spielman, Proc. ISMRM, 785 ,(2002).
4. Hurd, R.et. al. MRM, 40, 343, (1998).
5. Bolan,P., et.al., MRM, 48, 215 (2002).
6. R. Kreis, et.al., J. Mag. Res, seriesB,102, 9, (1993).