Test-retest Reliability of Dorsolateral Prefrontal Cortical GABA Measurement using an 8-Channel Phased-Array Head Coil with the J-editing Technique at 3T

L. S. Kegeles[1,2], X. Mao[3], J. Dyke[3], R. Gonzales[1], T. N. Soones[1], D. C. Shungu[1,3]

[1]Psychiatry, Columbia University, New York, NY, United States, [2]Radiology, Columbia University, New York, NY, United States, [3]Radiology, Weill Medical College of Cornell University, New York, NY, United States

Introduction: Evaluation of brain GABA and glutamate concentrations is of major interest in many neuropsychiatric conditions including stroke, epilepsy, substance abuse, depression, anxiety disorders, and schizophrenia. Recent studies using spectroscopic editing measurements of occipital lobe GABA have found significant deficits in depression [1] and in anxiety disorders. Postmortem studies have found pre- and postsynaptic alterations in schizophrenia in the dorsolateral prefrontal cortex (DLPFC) consistent with GABA transmission deficits [2]. Recent work has shown high reliability of GABA and glutamate/glutamine ("Glx") measurements in DLPFC with a single-channel standard GE quadrature volume head coil and a fairly large acquisition volume (19.5 cc) [3], as well as significant signal-to-noise (SNR) gains with a phased-array multichannel coil in the same brain region [4]. The goal of the present study was to evaluate the potential for utilizing this improved SNR to reduce the acquisition volume by comparing test-retest reliability of the two configurations (single-channel with 19.5 cc voxel as previously reported [3], vs. multiple-channel with 9 cc voxel) with the same acquisition time.

Methods: We studied 6 young adult healthy volunteers, 4 females and 2 males, to determine test-retest reliability of measurements of GABA and Glx concentrations in the DLPFC. All spectra were recorded in 26 minutes on a 3T GE 'EXCITE' MR system using an 8-channel phased-array head coil. Using internal landmarks on T1-weighted MRI scans, a voxel was reproducibly placed in the left DLPFC (middle frontal gyrus), angled parallel to the brain surface, with dimensions 1.0 cm x 2.0 cm x 4.5 cm (Fig. 1). The J-edited spin echo difference technique [5, 6] followed by a frequency-domain nonlinear least-squares spectral fitting procedure were used to determine GABA and Glx in this DLPFC voxel (Fig. 1), which were normalized both to the creatine-containing compounds (Cr) and to the internal water signal recorded simultaneously. Test-retest reliability of the measurements was assessed with the Pearson correlation coefficient R (Fig. 2), with the percent coefficient of variation (%CV), and with the intraclass correlation coefficient (ICC), a statistic that compares within- to between-subjects variance such that a maximum ICC of 1.0 indicates identity between test and retest values.

Results: Test-retest reliability using this methodology was found to be very high. The Pearson correlation coefficient of test vs. retest for GABA normalized to internal water was R = 0.993 (R^2 = 0.986, p = < 0.0001, Fig. 2). Percent coefficient of variation was %CV = 5.2%, and ICC was 0.84. Similar reliability was found for Glx to internal water ratios, as well as for both GABA and Glx ratios to Cr.

Conclusions: These data show that DLPFC GABA and Glx can be measured with high reliability under the conditions of our study. Use of the improved SNR of the multichannel system to reduce voxel volume allows a more purely gray matter volume to be sampled. Test-retest reliability was comparable to the single-channel configuration with larger voxel size, suggesting that the greater SNR of the 8-channel configuration can be used for voxel volume reduction without degradation of signal reliability.

Acknowledgments: We are indebted to J.W. van der Veen, Ph.D. (NIH), R. Hurd, Ph.D. (GE) and S. Kohler, Ph.D. (GE) for assistance in porting the editing sequence from the GE 'LX' to the 'EXCITE' platform. Funding: Weill Cornell Medical College New Faculty Development Funds (DCS), NIMH K08 MH01594-01 (LSK), and Lieber Center for Schizophrenia Research.

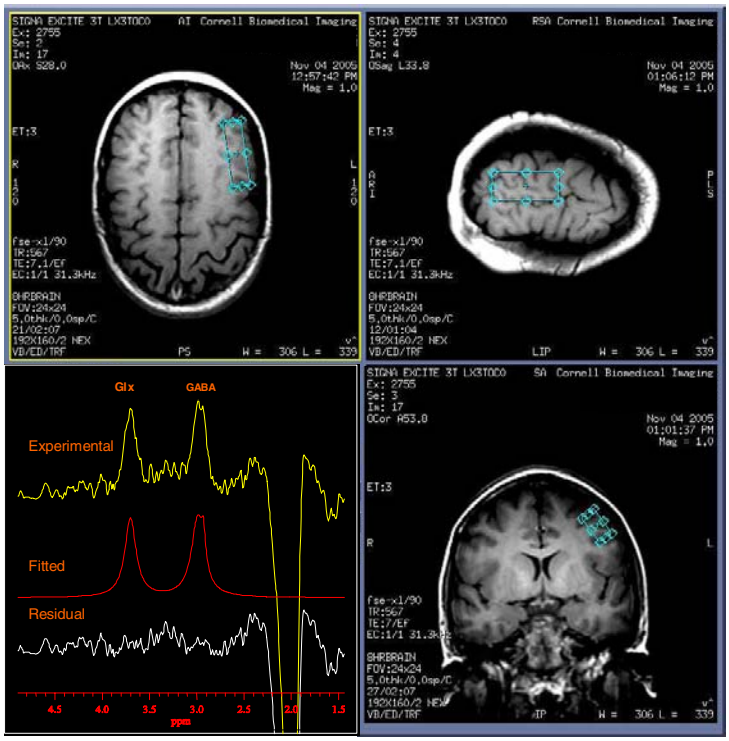

Figure 1. Panels clockwise from upper left: oblique axial (parallel to Sylvian fissure), sagittal, and coronal slices showing voxel size and orientation; and difference spectrum showing GABA and Glx peaks with best-fit model curves.

References:

1. Sanacora G, Mason GF, Rothman DL, et al., *Arch Gen Psychiatry* 56, 1043-1047 (1999)
2. Volk DW, Pierri JN, Fritschy JM, et al., *Cereb Cortex* 12, 1063-1070 (2002)
3. Kegeles LS, Dyke J, Mao X, et al., *ISMRM Workshop on MR Spectroscopy for Neuropsychiatric Disorders* (2005)
4. van der Veen JW and Shen J, *Proc. ISMRM* 13, 214 (2005)
5. Rothman DL, Petroff OA, Behar KL, Mattson RH, *Proc Natl Acad Sci USA*. 90, 5662-5666 (1993)
6. Sailasuta N, LeRoux P, Hurd R, et al., *Proc Intl Soc Magn Reson Med* 6, 1011 (2001)

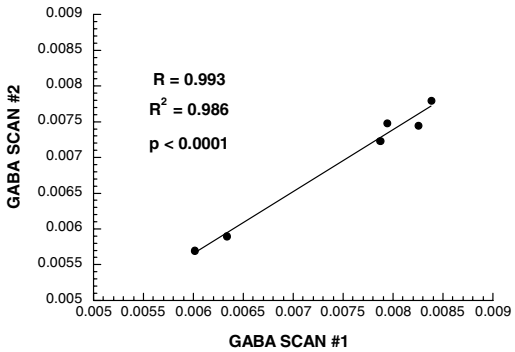

Figure 2. Regression fit for plot of GABA ratio to internal water signal from first versus second scan for each of 6 healthy subjects.