

Gender differences in GABA and glutamate concentrations measured with MEGA-PRESS

R. L. O'Gorman¹, L. Michels¹, R. Edden², and E. Martin¹

¹University Children's Hospital, Zürich, Switzerland, ²Russell H Morgan Department of Radiology and Radiological Sciences, Johns Hopkins University, Baltimore, MD, United States

Introduction: Magnetic resonance spectroscopy (MRS) provides a non-invasive method for quantitatively measuring in vivo concentrations of the major excitatory and inhibitory neurotransmitters glutamate (Glu) and γ -amino butyric acid (GABA). However, the spectral overlap of Glu and GABA with each other and with glutamine (Gln) can confound the reliability of MRS measurements of these neurotransmitter systems. Spectral editing methods like the MEGA-PRESS technique¹⁻² provide a promising approach for spectroscopic evaluation of GABA and glutamate, but few studies have examined the normal inter-subject variability in the measured GABA and Glu concentrations with factors like age and gender.³⁻⁴ The purpose of the present study was to investigate age- and gender-related differences in GABA and glutamate in a group of healthy adults.

Methods: The subject group consisted of fourteen healthy volunteers (7 female, mean age range 25-38) with no history of neurological or psychiatric illness. MR imaging and spectroscopy studies were performed with a 3T GE HD.xt TwinSpeed MRI scanner (GE Healthcare, Milwaukee, WI, USA), using an 8-channel receive-only head coil. Four consecutive resting single-voxel MEGA-edited ¹H MR PRESS spectra were acquired from a 2.5x3x4 cm³ voxel of interest in the left DLPFC with TE/TR = 68/1800 ms and 320 averages (160 pairs). Water-scaled metabolite concentrations were derived using LCModel,⁵ and the metabolite concentrations from the four resting spectra were averaged for each participant. Correlations between neurotransmitter levels and age were examined with a Pearson correlation, and the average GABA and Glx concentrations for the male and female participants were compared using a 2-tailed unpaired t-test. The statistical analysis was performed in SPSS version 14.0 (SPSS inc. Chicago, Illinois, USA).

Results: A representative MEGA-PRESS spectrum is shown in figure 1. The GABA peak at 3.0 ppm and the Glx peak at 3.75 ppm were well visualised for all spectra. GABA, Glu, and Glx (Glu+Gln) concentrations were significantly higher in the male participants, ($p=0.02$, $p=0.001$, and $p<0.001$, respectively, 2-tailed), although no significant gender-differences were detected for Gln ($p=0.1$). No significant age effects were seen, and no significant gender-related differences in the fraction of grey or white matter in the MRS voxel were evident ($p=0.9$).



Figure 1: Representative MEGA-PRESS spectrum showing the GABA peak at 3.0 ppm and the co-edited Glx peak at 3.75 ppm.

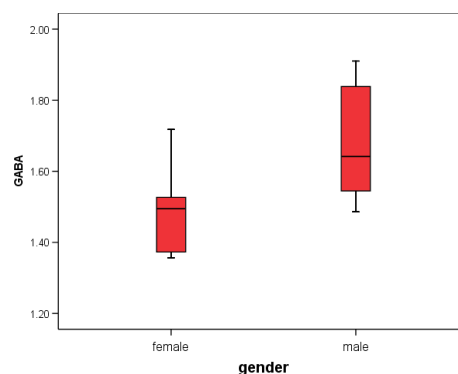


Figure 2: Gender differences in GABA (median and interquartile ranges)

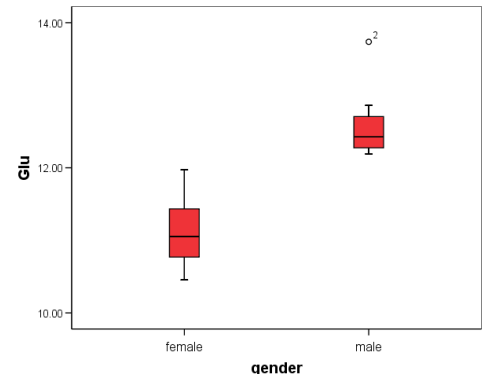


Figure 3: Gender differences in Glu (median and interquartile ranges)

Discussion: Age and gender differences have been reported previously for glutamate³ although a subsequent re-analysis of these results only revealed significant differences in glutamate concentration with age but not gender.⁴ We did not see any significant interactions between glutamate or GABA and age in our sample, possibly due to the relatively limited age range of the participants. However, we did observe strong gender differences in both GABA and glutamate, emphasizing the importance of gender-matching for studies aiming to investigate differences in neurotransmitter concentrations between mixed-cohort subject groups. The lack of any significant difference in grey matter fraction in the MRS voxel between the male and female participants suggests that these gender-related differences in GABA and glutamate are independent of the voxel composition.

References: ¹Thompson and Allen ²Edden & Barker *Magn Reson Med* 58:1276-1282, ³Sailasuta et al. *Magnetic Resonance Imaging* 26: 667-675 ⁴Chang et al. *Magnetic Resonance Imaging* 27: 142-145, ⁵Provencher SW. *Magn Reson Med* 30:672-679