Do Cortical GABA Levels Correlate with Age?

Z. Long[1,2], J. B. Murdoch[3], A. W. Goddard[2,4], and U. Dydak[1,2]

[1]School of Health Sciences, Purdue University, West Lafayette, IN, United States, [2]Department of Radiology and Imaging Sciences, Indiana University School of Medicine, Indianapolis, IN, United States, [3]Toshiba Medical Research Institute USA, Mayfield Village, OH, United States, [4]Department of Psychiatry, Indiana University School of Medicine, Indianapolis, IN, United States

Introduction

γ-Aminobutyric Acid (GABA) is a major inhibitory neurotransmitter in the human brain and plays a critical role in many neurological, psychiatric and neurodegenerative disorders. A deficit in GABA is also suggested to be involved in the degradation of cortical function during aging [1]. In this study we pooled adult healthy control groups from three different studies to investigate the effect of age on GABA levels in the anterior cingulate cortex (ACC), occipital cortex (OCC) and thalamus, using an LCModel approach to fit the GABA signal in spectra acquired with the MEGA-PRESS sequence.

Materials and Methods

MEGA-PRESS GABA-edited data from a total of twenty five healthy adults (seventeen male, eight female, age range 22-59) were evaluated for this study. Written informed consent was obtained from all subjects prior to their participating in any of the studies. ACC data was obtained from eleven subjects (n=11, seven male and four female), OCC data was obtained from eleven subjects (n=11, four male and seven female), and thalamus data was obtained in ten different subjects (n=10, ten male). MEGA-PRESS spectra from ACC and OCC voxels were acquired on a 3T Siemens Tim Trio scanner (Siemens Healthcare, Erlangen, Germany) equipped with a 32-channel head coil. Thalamus experiments were performed on a 3T Philips Achieva scanner (Philips Healthcare, The Netherlands) equipped with an 8-channel head coil. Parameters used for GABA detection with the MEGA-PRESS sequence [2] were as follows: TR=1500ms, TE=68ms, VOI=20.8ml for ACC; TR = 1500ms, TE = 68ms, VOI = 18.8ml for OCC; TR=2000ms, TE=68ms, VOI = 26ml for thalamus measurements. For the ACC and OCC experiments, 196 averages were acquired with the editing pulse centered at 1.9 ppm and 196 averages with the pulse centered at 7.5 ppm in an interleaved fashion, whereas for the thalamus experiments, 128 averages were acquired per pulse location. Data processing and quantification of all spectra were performed with LCModel [3] using basis sets generated from density matrix simulations of the MEGA-PRESS sequence with an exact treatment of evolution during the two frequency-selective MEGA inversion pulses used on the respective scanners [4]. An extra Gaussian peak at 3.0 ppm was added to the LCModel calculation to explicitly fit the macromolecular contribution to the GABA signal at this frequency. Correlation analysis was conducted and Spearman coefficients were obtained using PASW Statistics 18 software.

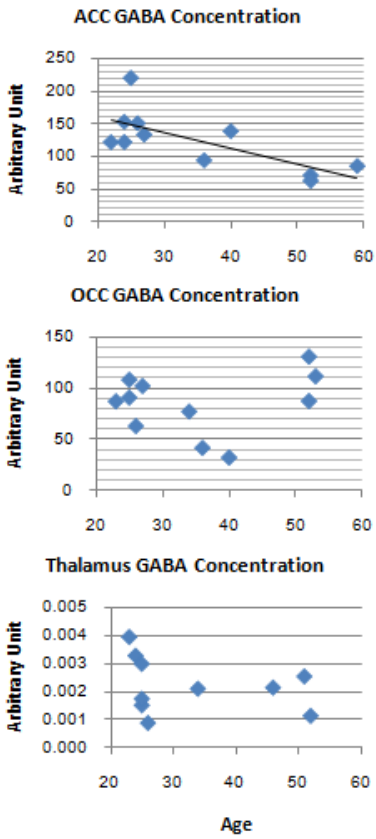

Figure 1. GABA concentration for ACC, OCC and thalamus areas as a function of age.

Results

The mean Cramer-Rao Lower Bounds (CRLB) of the GABA values fitted by LCModel were 17%, 25% and 40% for ACC, OCC and thalamus, respectively. Figure 1 shows the GABA concentrations plotted against age for the ACC, OCC and thalamus VOIs. The GABA concentration was found to be significantly correlated with age in ACC ($R= -0.725$, $p<0.05$). No correlation of GABA levels with age was found in the OCC or the thalamus VOI.

Discussion

Electrophysiological and morphological studies have shown decreased GABAergic inhibition and reduced density of GABA neurons in senescent monkeys and cats [1][5]. However, there is little evidence to date for GABA changes with age in humans. It has been suggested that aging affects brain volume differently in different brain regions [6]. Our study suggests that brain GABA levels decrease with age in certain cortical brain regions, which may relate to altered brain function in elderly people. However, further studies, conducted in more subjects across a wider range of ages, are necessary to confirm these results.

References: 1, Leventhal, A. G., Wang Y., et al, Science 300(5620): 812-815 (2003); 2, Mescher M, et al, NMR Biomed 11:266-272 (1998); 3, Provencher SW, NMR Biomed 14(4):260-264 (2001); 4, Dydak U., et al, Environ Health Perspect (2010) doi:10.1289/ehp.1002192; 5, Hua T., et al, Brain Research Bulletin 75(2008)119-125; 6, Raz N., Cognitive Neuroscience of Aging: Linking Cognitive and Cerebral Aging. Oxford University Press, New York, pp.17-55.

Acknowledgments: The authors acknowledge financial support by NIH/NIEHS ES017498, and Indiana CTSI Collaboration in Biomedical/ Translational Research (CBR/CTR) Pilot Program