Decreased GABA in the anterior cingulate cortex of female borderline personality disorder patients

Gabriele Ende1, Markus Sack1, Nuran Tunc-Skarka1, Wolfgang Weber-Fahr1, Mareen Hoerst1, Anne Krause-Utz2, Anne-Christine Reitz2, Sylvia Cackowski2, and Christian Schmahl2

1Neuroimaging, Central Institute of Mental Health, Mannheim, Germany, 2Psychosomatic Medicine and Psychotherapy, Central Institute of Mental Health, Mannheim, Germany

Introduction

Dysfunction and deficits in the structure of the anterior cingulate cortex (ACC) as well as increased impulsivity have been reported in borderline personality disorder (BPD) [1-3]. γ-Aminobutyric acid (GABA) is the main inhibitory neurotransmitter in the human cerebral cortex. Loss or dysfunction of GABAergic neurotransmission is associated with many neurological and psychiatric conditions, e.g. decreased GABA was found in schizophrenia by Yoon [4]. We are not aware of any study investigating GABA in BPD.

Methods

In vivo single voxel 1H MRS was performed at a 3.0 T MR scanner with a thirty-two channel head coil (Siemens Magneton TIM Trio) in 20 female patients with BPD (26.9 ± 5.2ys) and 24 female age matched healthy controls (27.9 ± 6.9ys). The ACC voxel (40x30x20mm³) was placed based on the reconstructed coronal and transverse planes aligned with the shape of the corpus callosum (see Fig. 1). Approval for this study had been obtained from the local ethics committee.

Spectra were acquired with a Point Resolved Spectroscopy (PRESS) Sequence using the following parameters: TE = 68ms, TR = 3000ms, 96 averages, 2048 acquisition points. Measurements of GABA were obtained using a MEGA-PRESS editing sequence which uses the J-coupling between the GABA-H4 resonance at 3.01 ppm and GABA-H3 resonance at 1.89 ppm to reveal the GABA resonance [5] (see Fig. 1).

Two subsequent editing acquisitions were made. First with the frequency of the editing pulse switching between 1.9 ppm and 7.5 ppm (editing center 4.7 ppm) and second switching between 1.9 and 1.5 ppm (editing center 1.7 ppm). The latter diminishes contamination by nearby macromolecule (MM) resonances [6, 7]. For quantification of GABA the acquired spectra were analyzed using the JMRUI-Software. For the other metabolites, LCModel was used. A fully automated quantification of GABA the acquired spectra were processed using SPM 5 algorithms and MATLAB 7.9 was performed to determine the composition of each spectroscopic voxel [8]. All metabolites were corrected for CSF content and scaled with the water signal at TE = 30ms. The GABA signal was quantified based on GABA phantom measurements. The calculation of the GABA concentration in vivo is as follows:

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\text{conc}^{\text{GABA}} = \frac{S_{\text{GABA}}^p S_{\text{H2O}}^{\text{ph}}}{S_{\text{GABA}}^p S_{\text{H2O}}^{\text{ph}} \cdot \text{conc}^{\text{GABA}} \cdot \frac{\rho_{\text{H2O}}}{\rho_{\text{GABA}}}}
\]

where \(S_{\text{GABA}}^p\) and \(S_{\text{H2O}}^{\text{ph}}\) are the peak areas of the corresponding in vivo and phantom measurement, respectively. \(\text{con}^{\text{ph}}_{\text{GABA}}\) is the GABA concentration of the phantom and the term \(\frac{\rho_{\text{H2O}}}{\rho_{\text{GABA}}}\) describes the density correction for water and GABA, respectively, due to the voxels tissue content. Since no relaxation corrections were applied the values are to be regarded as semi-quantitative.

Results

The mean GABA value obtained with the editing center at 1.7 ppm was significantly reduced in BPD patients compared to controls (1.75 ± 0.3 [i. u.] vs. 2.0± 0.3 [i. u.], p = 0.003 t-test). No significant difference could be found for the mean GABA plus MM value obtained with the editing center at 4.7 ppm, neither for any other metabolite value. Quantification of all other metabolites was excellent. A mean glutamate of 10.2 ± 0.3 and glutamine of 2.1 ± 0.4 vs. 2.0± 0.3 and glutathione of 2.1 ± 0.4 vs. 1.9 ± 0.4 all i. u. was determined in BPD and controls, respectively.

Discussion

These preliminary results suggest a decreased GABA concentration in female BPD patients compared to healthy females which would have been missed if only the “GABA plus MM” signal were acquired. As the ACC is a key region to emotional control, and is strongly connected to the limbic system, decreased GABA concentration may be related to disturbed control mechanisms in these patients. Further analysis in regard of personality trait questionnaires is ongoing.

References