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

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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 Magnetom 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 an isotropic 1 mm³ mprage data set with 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 segmentation of the high resolution T1-weighted mprage data into gray matter (GM), white matter (WM) and cerebrospinal fluid (CSF) 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

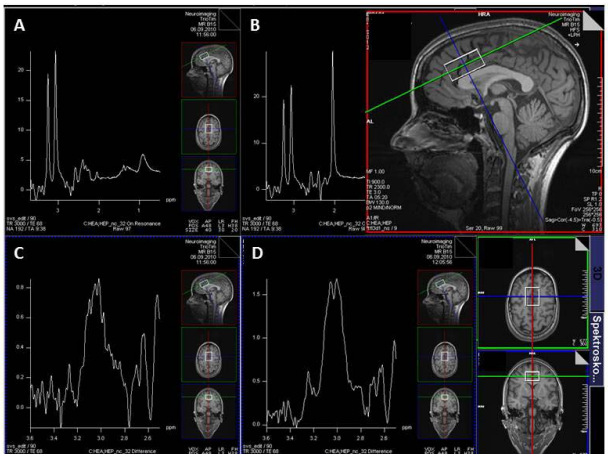

Figure 1: exemplary spectra from a 24 ys old volunteer: A) with editing pulse "on", B) editing pulse "off", C) and D) resulting resonance at 3.0 ppm in the difference spectra, with editing center at 1.7 and 4.7 ppm, respectively.

$$\mathrm{conc}^{\mathrm{iv}}_{\mathrm{GABA}} = \frac{S^{\mathrm{iv}}_{\mathrm{GABA}}}{S^{\mathrm{iv}}_{\mathrm{H2O}}} \frac{S^{\mathrm{ph}}_{\mathrm{H2O}}}{S^{\mathrm{ph}}_{\mathrm{GABA}}} * \mathrm{conc}^{\mathrm{ph}}_{\mathrm{GABA}} * \frac{\rho_{\mathrm{H2O}}}{\rho_{\mathrm{GABA}}}$$

where S^{iv}_{X} and S^{ph}_{X} are the peak areas of the corresponding in vivo and phantom measurement, respectively. $\mathrm{conc}^{\mathrm{ph}}_{\mathrm{GABA}}$ is the GABA concentration of the phantom and the term $\rho_{\mathrm{H2O}}/\rho_{\mathrm{GABA}}$ 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 ± 0.9 and 10.0 ± 1.0, 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.

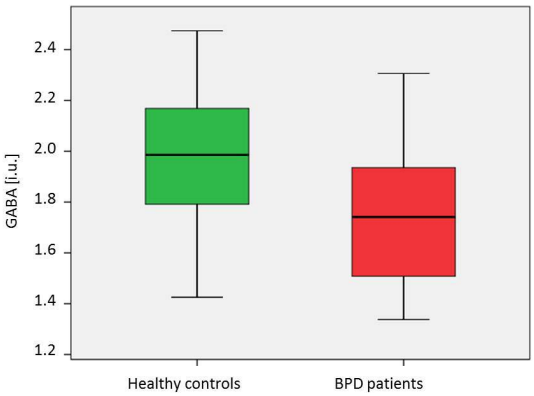

Figure 2: boxplots of GABA values for patients and controls

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