Lateralization of Glx and GABA metabolic changes in anterior cingulate for Ultra High Risk Schizophrenia patients.

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Target audience: Neuroscientists and clinicians interested in schizophrenia neurobiology and pathogenesis.

Purpose It was reported[1-2] that GLX is reduced in anterior cingulate (AC) for chronic schizophrenia patients medicated with antipsychotics; GABA level is decreased only for older medicated patients. GABA and GLX metabolism remains unclear for schizophrenia metabolic disorders. The aim of the study is to compare GABA and GLX levels in right and left AC of never medicated young patients with ultra-high risk of schizophrenia.

Methods

Participians: 16 patients with ultra-high risk of schizophrenia aged 16 to 25 and 15 age matched healthy control subjects participated in this study. All of the subjects were right-handed men. For inclusion into the group with high risk of schizophrenia following factors required: manifestation of one or more positive symptoms in SOPS scale[3-4] at least one hour per day, four times a week in the period of last month or more, with the absence of concomitant clinically significant mental pathology (previously transferred psychotic episodes, organic mental disorder, mental retardation).

MR acquisition: All investigations were performed Phillips 3.0T Achieva TX MRI scanner using an 8–channel receive head coil. GABA-edited spectra were obtained using MEGA-PRESS sequence[5]. (TE=68ms TR=2000ms, Samples - 1024, Spectral BW (Hz) – 2000, NSA – 8, 14ms editing pulse applied at 1.9 ppm and 7.5 ppm [6], 40 averages). Voxels of 30×30×30mm were located in the left and right AC (fig. 1). The acquisition time was 10 min 40 s.

Quantification and statistical analysis: Processing of the spectra was performed by jMRUI using the Amares algorithm (ver. 5.1 Alpha). The residual water signal was removed by HSLVD Propack. In the edited spectrum GABA and GLX peaks were modeled as a Gaussian singlet (phase 0°) after manually defining of the center frequency and halvewidth of peaks. Baseline was adjusted automatically.

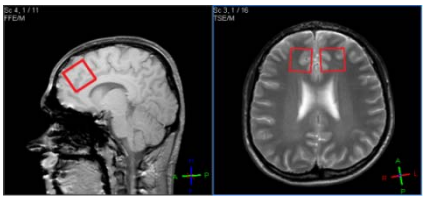

Fig. 1 ROI in the right and left AC

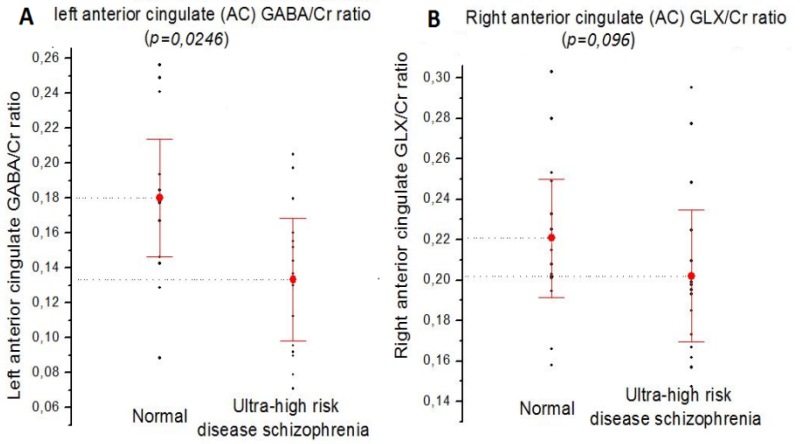

Fig.2 A: Patients show lower GABA/Cr in the left AC (p=0.0246) B: lower GLX/Cr in the right AC as compared to the control (p=0.096)

NAA was modeled as a single inverted Lorentzian peak (phase 180°). GABA/NAA and GLX/NAA ratios were obtained from J-edited spectrum. In reference unedited spectrum Cr and NAA peaks were modeled by Lorenzian singlet (phase 180°) and NAA/Cr ratio was obtained. GABA/Cr (GLX/Cr) was calculated by multiplying GABA/NAA (GLX/NAA) by NAA/Cr [7].

Results: No statistically significant difference of NAA/Cr was obtained for right and left AC in patients and control group. The right AC GLX/Cr was reduced (Fig 2B) relative to the corresponding value in the control group, whereas no GABA/Cr changes were found in right AC for patients and control. For the left hemisphere AC GABA/Cr is lower in the patients group than in group of healthy subjects, GLX is the same in both groups (Fig 2A).

Discussion: Reduction of GLX in AC in schizophrenia was revealed earlier on chronic old and young medicated patients [1]. Therefore reduction of GLX in right hemisphere in our study reflects changes in the metabolic system as a consequence of the illness itself, without influence of treatment with antipsychotics or age changes. The duration of the disease is also irrelevant. We assume also that left AC GABA reduction observed in our study is typical for schizophrenia development - previously reported unchanged GABA in AC of young chronic medicated patients [1] could be associated with an effect of antipsychotic medication.

Conclusion: The obtained results reveal a different role of the left and right hemispheres in regulation of basic inhibitory and excitatory neurotransmitters balance in the psychopathology associated with high risk of schizophrenia.

References: Peter B. Barker et al. 2012, Schizophrenia Bull; 2. Olbrich HM et al. 2008, World J Biol Psychiatry; 3. Miller et al. 1999; 4. McGlashan et al. 2001; 5. Puts, Edden. 2012, Progress in NMR Spectroscopy; 6. M. Mescher et al. 1998, NMR in Biomedicine; 7. Paul G. Mullins et al. 2013, NeuroImage.

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