A proton magnetic resonance spectroscopy study of the brain metabolite changes after antipsychotic treatment

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INTRODUCTION

- The most replicated proton magnetic resonance spectroscopy (^{1}H MRS) finding in schizophrenia is lower NAA (N-acetylaspartate) level in the dorsolateral prefrontal cortex, hippocampal area, temporal cortex and thalamus. These results are consistent with morphological findings of volume reductions of these regions.
- Some authors, on the other hand, did not show any differences in the described areas in brain metabolite levels between patients with schizophrenia and healthy individuals.
- The influence of antipsychotic medication on brain alterations observed in ^{1}H MRS in schizophrenia can be the explanation of many discrepancies observed in the previous studies.
  - NAA reductions are probably not an effect of prior medication exposure
  - some studies revealed that patients on atypical antipsychotics showed significantly higher level of NAA/Cr in the left frontal lobe, superior and anterior cingulate cortex in relation to patients on typical medication.
  - higher NAA in the dorsolateral prefrontal cortex levels in patients after neuroleptic treatment
  - the significant increase in NAA level in thalamus after the risperidone therapy
  - decrease of the complex of GABA and glutamate in the prefrontal lobes of schizophrenic patients after neuroleptic treatment and a significant correlation between this measure and BPRS results.
  - decreased glutamine level in the left dorsolateral prefrontal cortex after neuroleptic treatment
  - increased glutamate level in cingular cortex after treatment with olanzapine only among patients, who showed improvement in negative symptoms
  - some authors didn't report any antipsychotic influence on brain metabolites in ^{1}H MRS studies

OBJECTIVE:

The aim of the study was the evaluation of antipsychotic medication effect on the metabolite levels in the brain of schizophrenic patients based on ^{1}H MRS examination.

SUBJECTS AND METHODS:

- 47 patients (33 men and 14 women) with the diagnosis of schizophrenia (ICD-10)
  - mean age 32.2±5.9 years
  - mean duration of illness 9.2±4.6 years, mean number of hospitalisations 6.9±4.3.
- Two evaluations: one while drug free (after minimum 7 days period without medication) and the other while on drugs (after at least 4 weeks of being on stable dose).
  - mean time without antipsychotics was 9.4±3.2 days
  - mean period of treatment was 55.8±15.2 days.
  - 21 patients received risperidone, 11 - olanzapine, 5 clozapine, and 5 typical neuroleptics.
  - The results of 5 patients after the treatment were not available
- The clinical evaluation included PANSS (The Positive and Negative Syndrome Scale for Schizophrenia) and CGI scales (all patients improved significantly in the clinical symptoms - **Table 1**) and also WCST (Wisconsin Card Sorting Test).

Table 1. The clinical characteristics of the patients before and after the treatment.

Scale	Before the treatment (N=42)	After the treatment (N=42)	p
PANSS Total score	94.7±13.4	77.3±14.0	<0.05
PANSS Positive scale	18.5±4.8	14.3±4.7	<0.05
PANSS Negative scale	26.1±3.4	21.8±3.9	<0.05
PANSS General psychopathology	49.8±8.6	41.4±7.7	<0.05
CGI	4.5±0.6	3.7±0.5	<0.05

SUBJECTS AND METHODS:

- MRI and MRS procedures: The same procedure was used for all the scans. Proton resonance spectroscopy was performed on a 1,5 MR scanner. The ^{1}H MRS procedure involves PRESS sequence, TR=1500 ms, TE=35 ms, number of repetition=192 and includes suppression of water by MOIST sequence. Each volume element (voxel) has dimension of 2x2x2 cm and was localised in the left frontal lobe, in the left temporal lobe and in the left thalamus (**Fig.1**). To produce metabolite maps, location and integration of the signal strength of metabolites were automatically computed. Metabolite ratios:. NAA, Cho (choline), mI (myo-Inositol) and Glx (GABA, glutamine and glutamate) to creatine (Cr) and unsupressed water signal (H2O) were analysed. (**Fig. 2 a, b**)

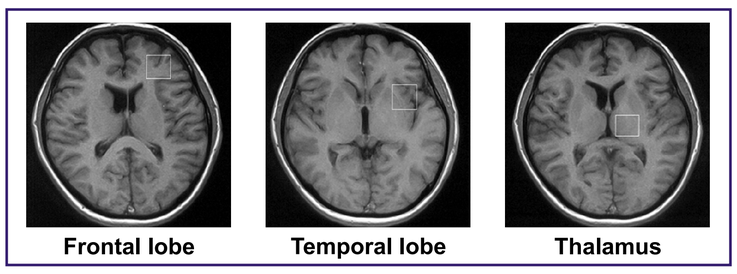

Figure 1. Voxel localization

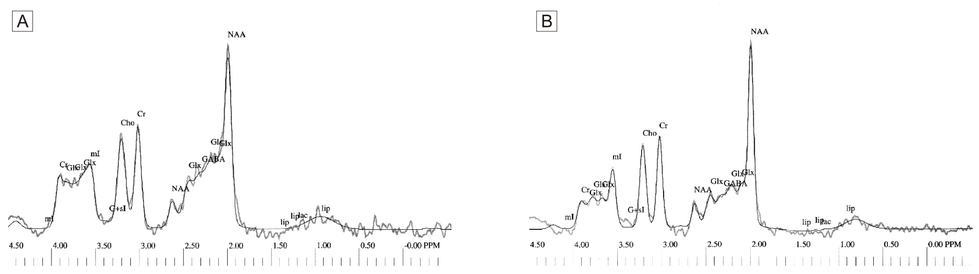

Figure 2. ^{1}H MRS spectra from the frontal lobe in the schizophrenic patient before (2a) and after (2b) clozapine therapy. Increase in NAA concentration observed after the treatment.

RESULTS:

- Significant elevation of the NAA/Cr level after the treatment in thalamus (t test, p=0.029)
- A trend toward higher NAA/Cr level after the treatment in the left frontal lobe
- Significant decrease of the Glx/Cr level in the temporal lobe (t test, p=0.006)
- Risperidone and clozapine therapy seemed to be the most effective in the process of the NAA level elevation in thalamus (**Figures 3-5**)

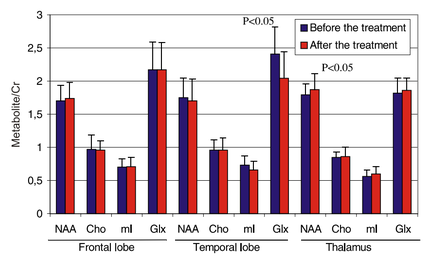

Figure 3. Metabolite/Cr ratios before and after the treatment

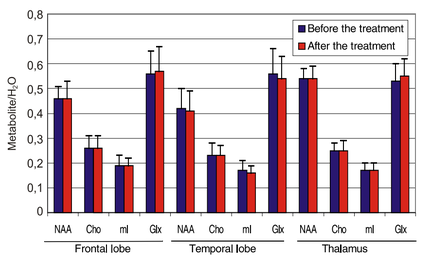

Figure 4. Metabolite/H2O ratios before and after the treatment

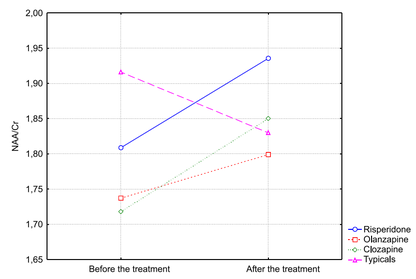

Figure 5. The influence of different drugs on the NAA/Cr level in thalamus

CONCLUSION:

Our results confirm that the neuroleptic drugs, especially atypicals, modify brain metabolism measured by ^{1}H MRS. The pattern of the changes suggest neuroprotective influence of the antipsychototic treatment in schizophrenic patients.

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