Single-voxel proton MRS at 1.5 Tesla significantly correlates with hypofrontality in schizophrenia

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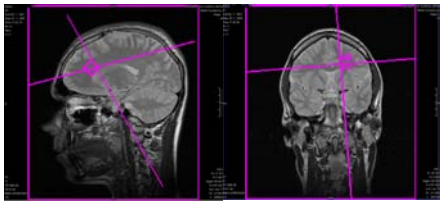
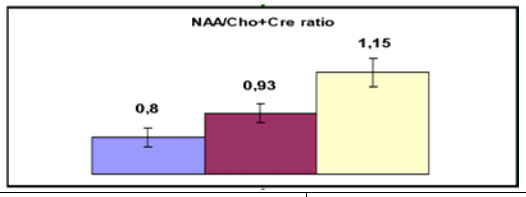
Introduction: Reduction in N-acetylaspartate is generally thought to represent loss of neurons and/or axons, as well as neuronal or axonal dysfunction or damage. Previous investigations with 1H-MRS in schizophrenic patients suggested for neuronal loss in the prefrontal area of schizophrenic patients with negative symptoms (1, 2, 3). The voxels in the previous studies contained various proportions of gray and white matter, which complicated the interpretation of any observed changes in the metabolite concentrations (4).
The aim of this study was to find out whether routine scanner ^{1}H single-voxel MRS can be significantly correlated with hypofrontality in schizophrenia.

Method: ^{1}H-MRS has been performed on a Siemens Symphony 1.5 Tesla MR system in 21 patients with schizophrenia and 9 healthy controls. The patients were evaluated for the occurrence of schizophrenic symptoms using the Positive and Negative Syndrome Scale questionnaire and, based on the number of points scored, 12 of them were found to have dominant positive and 9 dominant negative symptoms. Prior to the measurement, both patient groups were treated with atypical antipsychotics (multireceptor antagonists, ref. 5). Two single-voxel spectra of each subject (TE/TR 135/1600ms PRESS, (1.5cm)^{3}, 256 averages) were obtained bilaterally from voxels in the dorsal frontal white matter. Localization of the voxel was chosen precisely to include the axons from the mesocortical pathway.

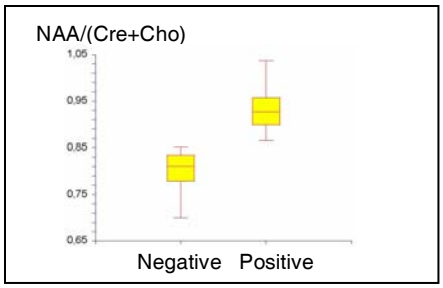


Data evaluation of all the patients was performed on the measuring console using standard spectroscopy software.
All subjects were evaluated with the same protocol, which was substantially customized to avoid misinterpretation of the spectra.

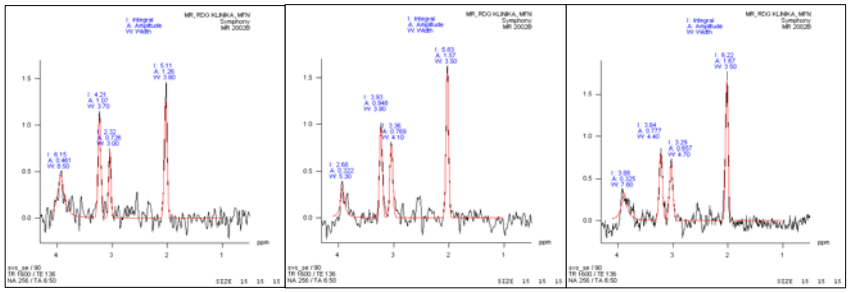
Results: We found bilateral reduction in the NAA/(Cho+Cre) ratio in the patients with schizophrenia in comparison with healthy volunteers. In every subject, the reduction was more evident in the nondominant hemisphere, which was true for all right-handed and left-handed patients. Moreover, the reduction was higher in the patients with dominant negative symptoms compared to the group of dominant positive symptoms, and the values of both groups were significantly different at $p<0.001$, and this significance level was valid comparing any two out of the three groups (dominant positive, dominant negative, healthy).



Subject	*NAA/(Cho+Cre) in the nondominant hemisphere*
patients with dominant negative symptoms	0,80 ± 0,05
patients with dominant positive symptoms	0,93 ± 0,05
control subjects	1,15 ± 0,08



Above: a box plot of the distribution of the patients in the groups with dominant negative and dominant positive symptoms



Above: Typical examples of spectra from the non-dominant hemisphere of a patient with dominant negative symptoms (left), dominant positive symptoms (middle), and a healthy volunteer (right).

Conclusion: In contrast to previous works, we have chosen our voxel embedded entirely in the frontal white matter, and we have found significant correlation between dorsal prefrontal neuronal pathology and negative symptoms in patients with schizophrenia. Compared to healthy volunteers, the value of the metabolite ratio decreases in patients with dominant positive (and mild negative) symptoms and yet significantly more in patients with dominant negative symptoms.
More pronounced reduction of the metabolite ratio in the non-dominant hemisphere of all the patients is in accordance with the laterality theory of schizophrenia.
Our results suggest that this MRS measurement design, easily performed on a clinical scanner, is sensitive to non-invasive monitoring of hypofrontality and therefore might be used in further interesting applications, including potential drug therapy effect in schizophrenic and depressive patients.

References:

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