# 1H MR Spectroscopy of Mild form of Canavan disease: *Role of NAA in neuron-oligodendrocyte interaction*

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***Introduction:***

N-acetyl-aspartate (NAA) gives most pronounced peak measured with proton spectroscopy of the normal brain in vivo. NAA is accepted as neuronal marker, and the loss of NAA is commonly correlated to the degree of neuronal loss in the brain tissue. The function of this brain metabolite remains not completely understood. In recent review(s) [1], the role of NAA in vertebrate brain was primarily considered to be an osmolyte present mostly in neurons. Canavan disease is caused by the lack of function of aspartoacylase, with gene of localized on the short arm of the chromosome 17 (17p-13-ter)[2]. Aspartoacylase, found in oligodendrocytes, is responsible for hydrolysis of NAA.

***Patient and Methods***::

17 year old girl with Canavan disease (lack of aspartoacylase enzymatic activity confirmed at the age of 6 using cultured fibroblasts) and with high NAA concentration in urine (see fig.1.) was presented with slight mental retardation, dysmetria and dysphasia, was examined on 1.5T MR scanner (Magnetom Vision and Sonata, Siemens Erlangen, Germany). 3D – MPRAGE T1w (TR=9.7ms,TE=4ms, FA=10$^o$,isotropic resolution 1mm) was made in order to perform GM, WM and CSF tissue segmentation, and DTI weighted images (19 slices 5 mm thick with interslice gap of 0.3, matrix resolution 128x128, FOV 230 mm, b=0 and 6 volumes with different gradient orientations b=1000 s/mm$^2$) were made additionally to standard MR imaging protocol, out of which fractional anisotropy (FA) maps are created.

1H single voxel spectroscopy was performed using PRESS (TE=135 ms; TR=1500 ms) and STEAM (TE=20 ms and TR=1500) sequences were performed using voxels positioned in parietal white matter, basal ganglia, and occipital grey matter NACQ 256 voxel size (15x15x15 mm) CSI using hybrid PRESS-CSI sequence (8x8 voxel dimensions 10x10 mm 12 mm thickness with TE=135 ms and TR=1500 ms, NAcq=12). External reference was used for absolute metabolite quantification[4]. Urine sample was analyzed using BRUKER AMX 400 MHz spectrometer.

***Results:***

Fig. 1. Presents spectroscopy of urine in patient, showing the presence of NAA peak at 2.0 ppm.

1H-SVS spectra of voxels positioned in occipital cortex (STEAM and PRESS) are shown on fig. 2a and 2b. Spectra acquired in parietal white matter is shown on fig. 2c and 2d and spectra in the region of basal ganglia are presented on fig. 2e and 2f. NAA metabolic map is presented on fig. 3 and FA image is shown on fig 4.

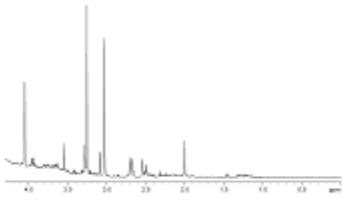

Fig 1.

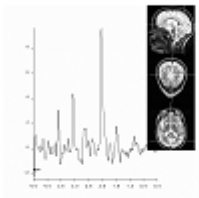

Fig 2a.

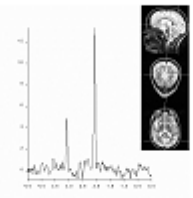

Fig 2b.

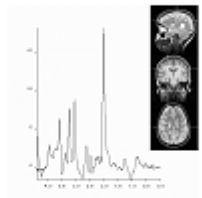

Fig 2c.

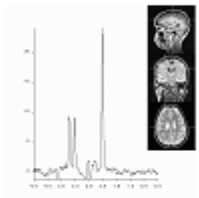

Fig 2d.

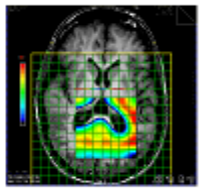

Fig 3.

**Table 1.** Metabolic concentrations in different brain regions

| Metabolite\Region | Parietal WM | Occipital GM | Basal Ganglia |
|---|---|---|---|
| NAA | 10.95 | 11.5 | 9.48 |
| Cho | 1.61 | not present | 1.9 |
| Cre | 5.54 | 6.5 | 7.37 |

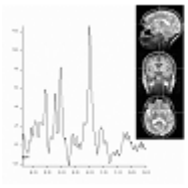

Fig 2e.

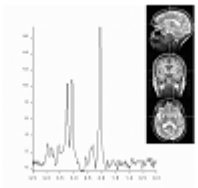

Fig 2f.

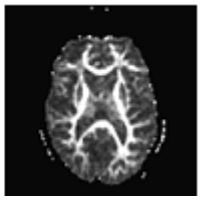

Fig 4.

***Discussion:***

Common to “standard presentation” of Canavan disease we found lack of choline in grey matter, and increased myo-inositol in all brain regions. NAA presence in extracellular spaces in Canavan spongiform leukodystrophies has as a consequence increased level of myo-inositol as a response of astrocytes on changed osmolyte conditions. In white matter, disfunction of aspartoacylase in Canavan leukodystrophies leads to the massive swelling of oligodendrocytes, which is not present in this case. However, NAA is accumulated in white matter as shown on fig 3. This leads to the hypothesis that mutation of aspartoacylase, a membrane bounded enzyme, present in this case does not hydrolyze NAA, but allows transport of NAA into the oligodendrocytes and therefore prevents them from swelling. In this case, a slow process of grey matter loss is present, followed by the enlargement of CSF spaces.

***Conclusion:***

Spectroscopic findings in mild form of Canavan disease presented here, support the role of NAA as an important osmolyte in the brain. Lack of hydrolysis of NAA does not significantly affect myelination in this case, which is in agreement with the finding [3] in which lack of NAA synthesis did not led to deteriorating leukodystrophy. However, slow loss of grey matter is present, which in cases of Canavan leukodystrophy, is masked by the main presentation as a white matter disease.

***Literature:***

1.Baslow M: Functions of ***N***-Acetyl-L-Aspartate and *N*-Acetyl-Laspartylglutamate in the Vertebrate Brain: Role in Glial Cell-Specific Signaling *J. Neurochem.* 75**,** 453–459 (2000).

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4. Helms G: A precise and user-independent quantification technique for regional comparison of single volume proton MR spectroscopy of the human brain *NMR Biomed.* 13, 398–406 (2000)