Magnetic resonance spectroscopy in patients with Fabry and Gaucher Disease.

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Introduction:

Fabry (FD) and Gaucher Disease (GD) are progressive, inherited disorders of glycosphingolipid metabolism that affect multiple organ systems [1,2]. Both disorders are considered rare with an estimated incidence of 1:50,000 although a recent study suggested that the incidence of FD may be as high as 1:3,100 male life births in Northern Italy [3]. Involvement of the central nervous system is most prominent in the neuronopathic forms of GD (GD2 and GD3). Interestingly neurological involvement has also been reported in single cases of non-neuronopathic GD (GD1) and also reported using ^{1}H-MRSI [4]. On the other hand storage of glycosphingolipids in vascular endothelium in FD may lead to white matter disease and cerebro-vascular events. Aim of this study was to investigate central nervous system involvement in Fabry- and GD1-patients using two dimensional ^{1}H-Magnetic resonance spectroscopic imaging (^{1}H-MRSI).

Methods and Materials:

In total, 7 Fabry- (42 ± 11.4 yo) and 8 GD1- (42.7 ± 18 yo) patients were scheduled for measurement on a Bruker (S30/80) 3 Tesla whole body scanner (Bruker Medical, Ettlingen, Germany) using a standard birdcage head coil. For comparison, age- and sex-matched healthy subjects were studied with the same protocol. MRIs of all subjects showed no pathological findings. Written informed consent, according to the guidelines and approval of the local review board was obtained from all subjects prior to the study. All subjects were measured with two dimensional ultra short echo time (TE) ^{1}H-MRSI (TE/TR=11/1600ms, acquisition time=27 min) [5]. One 1.8 cm thick single slice was positioned in the centrum semiovale caudal to the ventricles. The 24 cm × 24 cm field of view (FOV) in the LR-AP direction was phase encoded into 32 × 32 matrix resulting in a nominal resolution of 1.35 cm^3. To perform absolute quantification via internal water calibration, the same experiment was performed without water suppression, using a short TR (600 ms), which added approx. 10 minutes measurement time. In average 31 voxels per subject were selected from the white matter and quantified using LCModel, based on internal water [6]. Results were corrected for T1- and T2-relaxation times [7]. Additionally, metabolic concentrations were tested for age dependence.

Metabolite	Gaucher (n=8)	Fabry (n=7)	Vol. (n=7)
NAA	10.21 ± 1.59	10.65 ± 1.86	9.87 ± 2.0
Cr	6.34 ± 1.30	6.56 ± 1.39	6.08 ± 1.39
Cho	2.16 ± 0.36	2.27 ± 0.40	2.05 ± 0.38
mI	5.25 ± 1.49	5.43 ± 1.41	5.52 ± 1.58

Table 1. Concentrations of the metabolites are given in mMol/kg wet weight ± one standard deviation for GD1-, Fabry patients and healthy subjects.

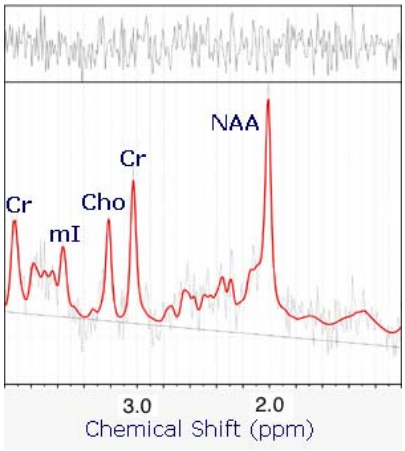

Fig. 1. Typical spectra from the semiovale (thin line) overlayed with the model spectrum obtained by LCModel. On top the residuum, i.e., the difference between in vivo data and the model spectrum, is given.

Results: Fig. 1 shows a representative spectra from a Fabry patient. Table 1 gives the absolute values in mMol/kg wet weight of NAA, Cr, Cho and myo-Inositol (mI). We could not find any significant differences between patients or healthy subjects.

In Fig. 2 the NAA to Cho ratio (Top) and total Cr (bottom) is plotted over the birth year of the subjects. Total Cr didn't changed with age. On the other hand, NAA/Cho decreased significantly with age ($p<0.01$, 2-tailed Pearson correlation) in all three goups measured. In particular NAA/Cho decreased 6%, 5% and 8 % per decade in GD1 patients, Fabry patients and healthy subjects, respectively.

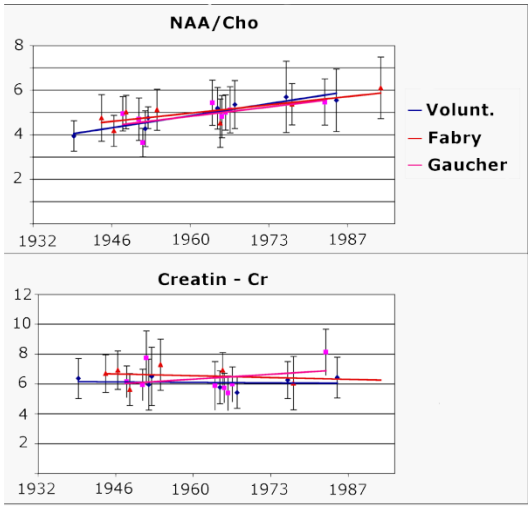

Fig. 2.: Total Cr (bottom) given in Mmol/kg per wet weight and NAA/Cho in dependence of age.

Discussion and Conclusion:

We performed 2D-^{1}H-MRSI with ultra short echo time using internal water calibration to obtain absolute metabolite values. Our measurements yielded excellent data quality in all patients and no significant differences regarding brain metabolite concentrations among study groups. The difference to previous study where, increased Cho in GD1 patients compared to healthy control was reported [4], can be explained by using different echo time (135 ms) and inappropriate control group. As already shown elsewhere [5], comparison with age- and sex-matched control group is of great importance due to potential increase of Cho with age. In accordance with this finding, we have found significantly decreasing NAA/Cho with age in patients and healthy controls. In Fabry patients, significant changes of the mean apparent diffusion coefficient could be reported, but no significant changes of metabolites could be revealed in the same study [8]. In summary, we could not detect central nervous system involvement in Fabry- and GD1 patients using 2D ^{1}H-MRSI.

References:

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