CSI of the brain in guanidinotransferase deficiency syndrome; guanidinoacetate accumulation in the gray matter

P. E. Sijens[1], K. T. Verbruggen[1], L. C. Meiners[2], R. J. Soorani-Lunsing[1], J. P. Rake[1], M. Oudkerk[1]

[1]University Hospital Groningen, Groningen, Groningen, Netherlands, [2]University Hospital Groningen, Groningen, Groningen

Purpose Chemical shift imaging (CSI) and MRI of the brain are used in patients suffering from creatine (Cr) deficiency in order to obtain MRI scans of gray and white matter with the corresponding MR spectra in one overview.

Introduction Cr deficiency syndrome was first defined in 1994 on the basis of a complete lack of brain Cr and phosphocreatine signals as detected by MRS (1). It can be caused by inborn defects of Cr biosynthesis (guanidinoacetate methyltransferase deficiency), arginine:glycine amidinotransferase deficiency or by X-linked creatine transporter defect (2). The ^{1}H MR spectra of the brain in guanidinoacetate methyltransferase (GAMT) deficiency are characterized by a lack of Cr signal (1,3-6) and by the presence of signal of the precursor of Cr, guanidineacetate (GAA) (1,3). The latter compound has to our knowledge not been observed in healthy persons nor in any known pathology other than GAMT deficiency.

Methods Patients suspected of Cr deficiency were examined by MRI and ^{1}H MRS at 1.5 Tesla using the standard head coil of a Magnetom Sonata system (Siemens AG, Erlangen, Germany). The MRI protocol included T2 weighted fast spin echo (TR/TE 4460/105 ms), fluid attenuated inversion recovery (TR/TE/TI 8500/119/2500), inversion recovery (TR/TE/TI 7000/40/350) in the axial plane, coronal T2 weighted FSE (TR/TE 4460/105), sagittal T1 SE (TR/TE 691/15), and axial diffusion weighted images with B = 0, 500 and 1000 sec/mm^2 with an ADC map. PRESS 2D-CSI measurements with TR/TE 1500/135 ms were performed. The T2 weighted MRI series was used as guidance for defining a CSI volume of interest of 8x8 cm^2 (64 spectra) within a 16x16 cm^2 FOV (256 phase encode steps) located cranial to the ventricles, a transverse 2 cm thickness slice in that part of the brain where the white matter is most abundant, for MRS (7). At 1 acquisition per phase encode step the CSI measurements took 7 min.
Automated localized multiple angle projection (MAP) shimming resulted in a water peak line width of up to 5 Hz in the VOI. Excitation with 2.56 ms sinc-Hanning shaped RF pulses preceded by 25.6 ms Gaussian shaped RF pulsess for chemical shift selective excitation (CHESS) and subsequent spoiling of the resultant water signal, was followed by selection of the second spin echo using 1024 data points and a spectral width of 500 Hz Time domain data were multiplied with a Gaussian function (center 0 ms, half width 256 ms), 2D-Fourier transformed, phase and baseline corrected and fitted to Gaussian line shapes.

Results In Cr deficiency the entire MRI investigation is unremarkable with white matter appearing normal on all sequences, the stage of myelination consistent with age and the development of brain structures normal. Results of the CSI examination in a mild case of GAMT deficiency are shown in Figs 1,2. Left in Fig.2 is the MR spectrum of a gray matter voxel showing virtual absence of Cr, as in the patient's white matter (Fig.1), and a distinct GAA peak at 3.8 ppm. Right the spectral map showing all 64 spectra for the 3.7-3.9 ppm region containing the GAA peak. In the gray matter near the separation of both hemispheres the GAA signals are more prominent than in the surrounding white matter.

Discussion That GAA signals were more prominent in gray matter than in white matter contrasts with a single observation that the levels of GAA were similar in two voxels containing parietal white and gray matter respectively (1). Other MRS studies published to date did either not detect GAA in GAMT (4-6) or not offer a comparison between gray and white matter (3).

References

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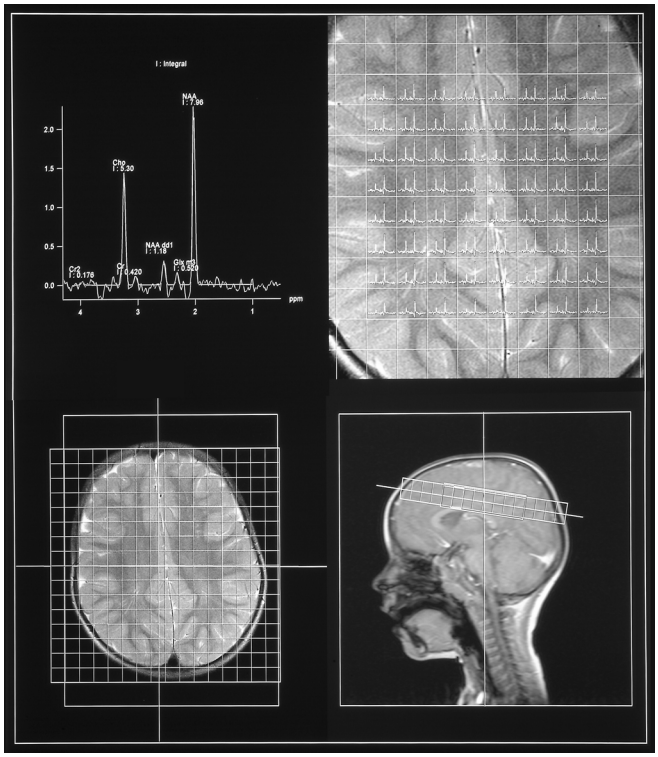

Fig.1 (the figure on the left). ^{1}H MRS of a case of GAMT deficiency. CSI map of 64 spectra shows normal peak intensities for Cho, glutamate (GLx m3) and NAA. Cr (3.0 ppm) is virtually absent. Top: white matter spectrum plus spectral map. Bottom: MRI cross sections showing the localisation of the VOI in the brain.

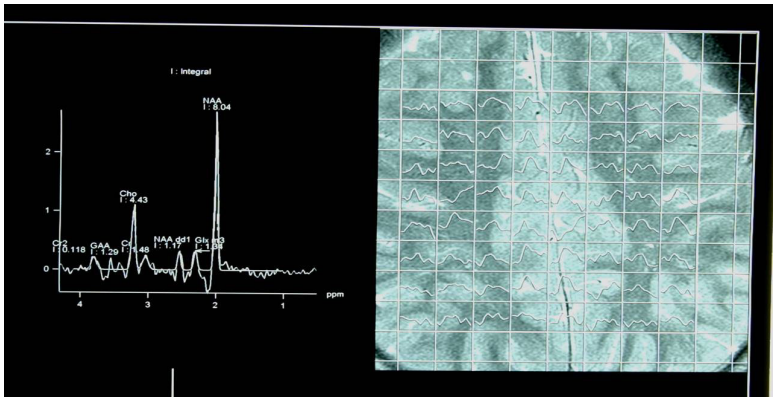

Fig.2 (the figure on the right). Gray matter spectrum (shows a clear GAA peak at 3.8 ppm and the spectral map of Fig.1 after refocussing on the 3.7-3.9 ppm region. GAA is most evident in the gray matter tissue around the separation between both hemispheres.