Quantitative proton MRS in a clinical setting for diagnosis and collection of reference data for children

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Introduction: Magnetic resonance spectroscopy (MRS) is an appropriate technique to non-invasively measure tissue metabolite levels. However, although *in vivo* MRS has been used in research for several decades, its clinical use is still limited. This is probably partly due to its low sensitivity and partly because of unfamiliarity with the technique. With the advent of clinical MR systems with higher magnetic field strengths, the development of better coils, and the design of optimized radio-frequency pulses, sensitivity has been considerably improved. In addition, software has been developed to facilitate automatic shimming and MRS data acquisition. Therefore, *in vivo* MRS is becoming more and more a technique suitable for routine use in the clinic. In our hospital, MRS has been used for a long time both in a research setting and for diagnosis or follow-up in specific patient groups, but not in routine cerebral MR screening of children. The **aim of the present study** was to evaluate the addition of a simple ^{1}H MRS acquisition block to the routine MRI protocol of pediatric patients to obtain cerebral metabolic information. For this purpose also reference cerebral metabolite levels for children were determined.

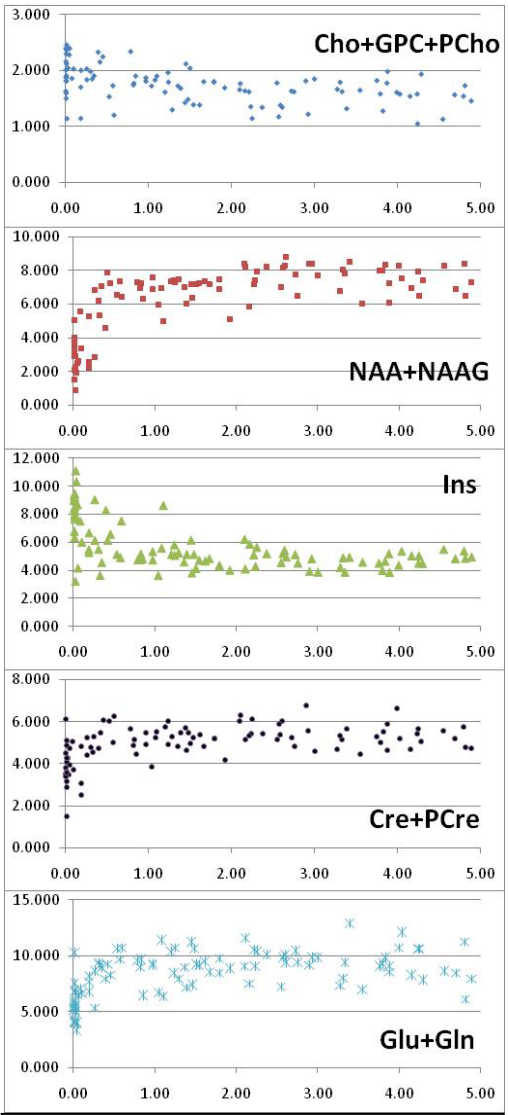

Fig. 3 Metabolite concentrations (mM) as function of age (yrs) over the first five years.

Methods: The standard cerebral screening MRI protocol for pediatric patients performed by technicians at a 1.5T MR system (Siemens 1.5T Avanto, Erlangen, Germany) was extended with one short single-voxel MRS acquisition. A metabolite proton MR spectrum was obtained from a voxel positioned in periventricular occipital white matter (see Figure 1) using a PRESS localization scheme [1] with water suppression (TE/TR=30/2000ms, 128 acq). In addition, a spectrum without water suppression was acquired (TE/TR=30/2000ms, 8 acq) to be used for eddy current correction and quantification. Metabolite concentrations were obtained by fitting the metabolite spectrum to simulated spectra of model compounds using the LCModel software package [2]. Absolute metabolite concentrations were obtained by water scaling assuming 35.88 M water content in the voxel and (average) T1 relaxation times for water and metabolites of 985 and 1255 msec, respectively.

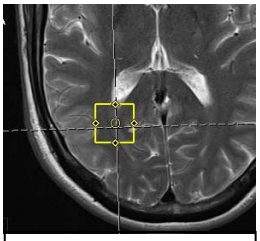

Fig. 1 Voxel position

Results: Up till now MR spectra of 140 children have been collected. All spectra were evaluated by an experienced MR spectroscopist and a neuroradiologist. Less than 5% of the spectra were discarded because of technical failures. The spectral pattern was pathological in 13% of the cases, which was mainly caused by hypoxia (for example by asphyxia during birth), tissue degeneration like gliosis, and inborn errors of metabolism [3]. See figure 2 for an example of a pathological spectrum. The spectra with an obvious pathological pattern were removed from the data set and the rest was used to determine metabolite concentrations as a function of age. In particular during the first months after birth, metabolite tissue contents and thus the spectral pattern changed, e.g. choline and myo-inositol decreased and NAA, creatine and the sum of glutamine and glutamate increased (see Figure 3).

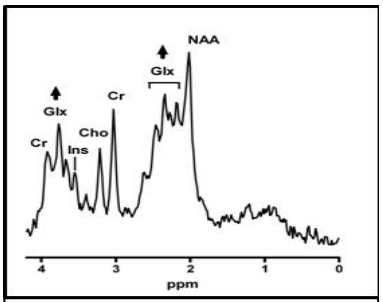

Fig. 2 Pathological MRS spectrum showing severe increased glutamine during acute hyperammonemia in a 3yr-old male patient with a urea cycle defect.

Discussion and Conclusion: This study shows that addition of only one short single-voxel MRS measurement has additional diagnostic value in cerebral MR screening in 13% of the patients. Simultaneously, more technicians and radiologists were trained in MRS data acquisition and interpretation. Further, MRS data of young children could be obtained to be used as reference values in the future. As visible in Figure 3 the data show quite some variation, which could be caused by biological variability or by differences in tissue content in the voxel, e.g. variations in the ratio white/gray matter or water content. In this study, only periventricular occipital white matter was assessed to limit the extra time requested by the additional MRS measurement, but a similar study may be performed in other areas of the brain. In conclusion, a short MRS measurement can be considered to be a valuable add-on to cerebral MR screening in daily clinical practice.

References: **[1]** Ordidge RJ, Bendall MR, Gordon RE, Connelly A (1985) Volume selection for in-vivo biological spectroscopy. In: Govil G, Khetrapal CL, Saran A (eds) Magnetic resonance in biology and medicine, Tata McGraw-Hill, New Delhi, 387-397; **[2]** Provencher SW (1993) Estimation of metabolite concentrations from localized in vivo proton NMR spectra. Magn Reson Med 30:672-679**; [3]** Engelke UFH, Moolenaar SH, Hoenderop SMGC, Morava E, van der Graaf M, Heerschap A and Wevers RA (2007) Handbook of 1H-NMR spectroscopy in inborn errors of metabolism: body fluid NMR spectroscopy and in vivo MR spectroscopy, 2nd edition; Heilbronn: SPS Verlagsgesellschaft (Publisher), ISBN 3-936145-49-0.