Proton magnetic resonance spectroscopy reflects metabolic decompensation in maple syrup urine disease

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Abstract. Using localized proton magnetic resonance spectroscopy (1H-MRS), accumulation of branched-chain amino acids (BCAA) and their corresponding 2-oxo acids (BCOA) could be non-invasively demonstrated in the brain of a 9-year-old girl suffering from classical maple syrup urine disease. During acute metabolic decompensation, the compounds caused a signal at a chemical shift of 0.9 ppm which was assigned by in vitro experiments. The brain tissue concentration of the sum of BCAA and BCOA could be estimated as 0.9 mmol/l. Localized 1H-MRS of the brain appears to be suitable for examining patients suffering from maple syrup urine disease in different metabolic states.

Localized proton magnetic resonance spectroscopy (1H-MRS) of the brain allows the non-invasive study of metabolic disorders in vivo [1-3]. Maple syrup urine disease (MSUD; McKusick 24860) is characterized by acute and chronic brain dysfunction due to accumulation of branched-chain amino acids (BCAA) and their 2-oxo acids (BCOA) caused by a defect of the oxidative decarboxylation of leucine, isoleucine, and valine [4, 5].

In this study, we present the results of an MRS examination of the brain of a 9-year-old girl suffering from classic MSUD, during an acute metabolic decompensation. The accumulation of the pathologic metabolites within cerebral tissue was demonstrated non-invasively. The concentration of the sum of BCAA and BCOA could be estimated using in vivo 1H-MR spectroscopy.

Patients and methods

The plasma concentrations of BCAA were determined by automated amino acid analysis, and of BCOA as quinoxalinolone derivatives by a high-performance liquid chromatography (HPLC) method [6]. Image-guided volume-selective 1H-MRS measurements were performed using a clinical 1.5-T whole-body MR system (Gyrosan S 15, Philips, Best, The Netherlands) operating at 63.86 MHz for protons. 1H imaging preceded spectroscopy to define the volume of interest. The spectrum was taken from a 3 x 3 x 7 cm^3 volume located in the parieto-occipital region of the patient's brain (see Fig. 1).

Volume-selective 1H spectra were achieved using a spatially selective 90°-180°-180° spin-echo sequence [7, 8] with water suppression by selective inversion. The applied spin-echo times (TE) of 136 ms resulted in inversion of doublets with spin-spin couplings of about 7.35 Hz (e.g. lactate and amino acids as leucine, isoleucine, valine, and the related 2-oxo derivatives). A repetition time (TR) of 2 s resulted in a total acquisition time of 8 min 32 s for 256 scans.

Spectra were evaluated quantitatively after Lorentzian broadening of 2 Hz and phase correction by comparing peak areas, which were calculated using the product of peak height and full line width at half maximum, assuming Lorentzian line shape.

Spectra from six additional children of between 4.5 and 14.5 years of age, without known metabolic disorders, taken under the same conditions were available for comparison.

Results

The 9-year-old patient presented with high fever, vomiting and moderate ataxia during acute metabolic decompensation of known classic MSUD, diagnosed in the
neonatal period when she suffered from metabolic coma. At the time of admission, the plasma concentrations of BCAA were found to be elevated: Leu, 1023 µmol/l; Val, 692 µmol/l; Ile, 290 µmol/l, compared with normal concentration ranges: Leu, 77-173 µmol/l; Val, 167-265 µmol/l; Ile, 30-71 µmol/l [9]. Oral feeding was stopped, and high-caloric parenteral nutrition was started immediately. During the following days, oral feeding was reintroduced, using a diet extremely reduced in leucine.

Seven days after admission, 1H-MRS of the brain was performed. At that time the patient showed only mild ataxia and she was being fed completely orally. The plas-