

1H magnetic resonance spectroscopy studies of cerebral metabolism in children

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This article summarizes some applications of 1H magnetic resonance spectroscopy in the investigation of children with brain disease. Studies are described of children with inborn errors of metabolism, including lactic acidoses and mitochondrial disorders, ornithine carbamoyl transferase deficiency (a disorder of the urea cycle), and Canavan’s disease (a disorder of N-acetylaspartate metabolism). Applications in epilepsy are also discussed.

Key words: magnetic resonance spectroscopy, brain, metabolism, metabolic disease, epilepsy.

INTRODUCTION

Over the last 4 years, we have been using 1H magnetic resonance spectroscopy (MRS) to investigate cerebral metabolism in children with brain disease, and in this article we briefly summarize some of our main findings.

Our observations fall into two broad categories: (i) the accumulation of brain metabolites in children with inherited metabolic disease and (ii) spectral changes (more specifically a loss of signal from N-acetylaspartate) that are attributed to selective neuronal loss or damage. Examples are given from both of these categories to illustrate the scope and limitations of this noninvasive approach to the investigation of brain metabolism.

METHODS

All the clinical studies were carried out using a 1.5-T Siemens whole-body system, with a standard quadrature head coil. Most of the children were examined under sedation according to the protocol of the Hospital for Sick Children, Great Ormond Street, London, UK, as previously described [1]. Full diagnostic magnetic resonance imaging (MRI) was carried out together with the spectroscopy in each examination.

RESULTS AND DISCUSSION

The dominant contributions to the spectra are normally from N-acetylaspartate (NAA), creatine + phosphocreatine (Cr), and choline-containing compounds (Cho). The relative intensities of these signals show both age dependence [4, 5] and regional dependence [5, 6], which must be taken into account when making comparisons.

Figure 1 shows a number of 1H spectra obtained from children with brain disease. Figures 1A and 1B
show spectra from two patients with epilepsy, in one of which there are reduced NAA/Cho and NAA/Cr ratios. Fig. 1C shows a lactate signal in the spectrum of a patient with a lactic acidosis, and Fig. 1D-F shows two spectra from a child with ornithine carbamyl transferase deficiency, together with a spectrum from a solution containing creatine and glutamine. The roles of such spectra in the investigation of these children is discussed below.

Inherited metabolic diseases

Lactic acidosis and mitochondrial disorders

Congenital lactic acidoses form a large group of disorders that are commonly associated with profound neurological dysfunction. Difficulties are frequently encountered in establishing a precise diagnosis, and the mechanisms underlying brain damage are poorly understood. It has been shown that in several disorders of the brain, lactate can be seen by MRS at elevated concentrations [7-10]. We have performed $^1$H MRS on 24 patients under investigation for suspected metabolic disorder and have compared the MRS observations of brain lactate with measurements of cerebrospinal fluid (CSF) lactate [11].

Spectra were obtained from the basal ganglia in all 24 children, and from occipital white matter in 16 of the children. There was good concordance between the MRS and CSF investigations, in that all of the 9 children with CSF lactate concentrations of 2.5 mmol L$^{-1}$ or less gave no detectable lactate signal on spectroscopy, whereas the 13 children with CSF lactates above 4 mmol L$^{-1}$ all showed an inverted doublet signal characteristic of lactate (see Fig. 1C). This concordance proves to validate both types of measurement and suggests that $^1$H MRS may have a role in the investigation of those children who have neurological dysfunction in whom screening of blood or urine may not be adequate to establish a diagnosis.

Of further interest is the distribution of lactate in different areas of the brain. It is well recognized that the basal ganglia are particularly susceptible to damage in disorders of lactate metabolism, this being the hallmark of mitochondrial cytopathy and Leigh's disease. Eleven of 13 patients with CSF lactate concentrations above 4 mmol L$^{-1}$ all showed the peak in the basal ganglia, but lactate was also detected in the occipital white matter in all of the 8 examinations in which the spectra could be interpreted unambiguously. Regional variations in the lactate signal were observed in some cases. Further investigations of such variations, and of their relationship to focal brain damage, preferably using metabolic imaging methods [11], should help to explain the neurological patterns that are observed in these disorders.

Fig. 1. (A) and (B): Spectra from the medial temporal regions of two age-matched children with epilepsy. In comparison with (A) and with the spectra of control subjects, (B) shows reduced NAA/Cho and NAA/Cr ratios. (C): Spectrum showing lactate (Lac) in occipital white matter, in a child aged 6 months with CSF lactate of 5.7 mmol L$^{-1}$. (D) and (E): Spectra of a child with OCT deficiency from an infarcted region (E) and from the contralateral hemisphere (D). On comparison with (F), it is clear that both spectra show signals that are characteristic of glutamine; (E) also shows very low NAA, Cr, and Cho signals, indicating a major loss of cellularity. (F): Spectrum of a solution containing 10 mM creatine and 40 mM glutamine, obtained with the same TE value (135 ms) as spectra (A)–(E).