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Nuclear magnetic resonance imaging of the brain in children

M I LEVENE, A WHITELAW, V DUBOWITZ, G M BYDDER, R E STEINER, C P RANDELL, I R YOUNG

Abstract

A preliminary study of nuclear magnetic resonance imaging of the brains of four normal children (36 weeks' postmenstrual age to 5 years) showed long T_1 areas in the periventricular region of the neonate as well as evidence of progressive myelinisation with increasing age. Study of 18 patients of 40 weeks' postmenstrual age to 4 years showed an apparent deficit in myelinisation in an infant with probable rubella embryopathy and another with ventricular dilatation of unknown cause. Abnormal scans were obtained in an infant with congenital muscular dystrophy, and abnormalities were visualised at the lateral ventricular margins in a case of acute hydrocephalus after shunt blockage. Periventricular regions of increased T_2 were seen in a term infant aged 4 days after severe birth asphyxia and convulsions.

Nuclear magnetic resonance imaging appears to provide a unique demonstration of myelinisation in vivo and shows changes in pathological processes of importance in paediatric practice.

Royal Postgraduate Medical School, Hammersmith Hospital, London W12 0HS
M I LEVENE, MD, lecturer in neonatal medicine
A WHITELAW, MD, consultant paediatrician
V DUBOWITZ, MD, professor of paediatrics and neonatal medicine
G M BYDDER, MRCP, senior lecturer, department of diagnostic radiology
R E STEINER, MD, FRCP, professor of diagnostic radiology
Hirst Research Laboratory, Wembley, Middlesex HA9 7PR
C P RANDELL, MSC, senior scientist
I R YOUNG, PHD, manager, Picker research laboratory

Introduction

Examination of the brain with nuclear magnetic resonance imaging in adults shows several features which may be particularly applicable to paediatric practice. A high level of contrast between grey and white matter is seen,[1] suggesting that progressive myelinisation may be detected and hence delays in this process may be recognised. Also the technique is sensitive to cerebral oedema and ischaemic change in adults[2 3]—conditions difficult to recognise in neonates with *x*-ray computed tomography or ultrasound.

To examine the potential of nuclear magnetic resonance imaging of the brain in infancy we have conducted a preliminary study of four normal children and 18 patients with various neurological conditions and compared the results with ultrasound or *x*-ray computed tomography in most cases.

Subjects and methods

With the approval of the ethical committee of the Royal Postgraduate Medical School we studied four normal infants and 18 patients. In each case the parents gave informed consent. The normal subjects comprised an infant of 5 weeks born after 31 weeks of gestation and children aged 6 months, 20 months, and 5 years. The newborn infant had shown hypotonia, which had disappeared by the time of the nuclear magnetic resonance scan. The 18 patients ranged in age from a full-term neonate to 4 years and had various clinical diagnoses (table I). Six had intraventricular haemorrhage diagnosed by real-time ultrasound[4]; three of these children subsequently developed ventricular dilatation, and one also had a porencephalic cyst. One patient with ventricular dilatation had a cephalhaematoma. Ultrasound examination was performed in 14 patients and *x*-ray computed tomography in two.

All nuclear magnetic resonance examinations conformed to guidelines provided by the National Radiological Protection Board for clinical imaging. Sedation with oral chloral hydrate (75 mg/kg) was given in 20 of the 23 nuclear magnetic resonance examinations

TABLE I—*Clinical diagnoses*

Clinical diagnoses	No of patients	Age* (months)	Proportion with clinical neurological defects†
Severe ventricular dilatation‡	5	3, 9, 11, 12, 21	3/5
Spinal cord transection	1	14, 17¶	0/1
Probable rubella embryopathy	1	17	1/1
Congenital muscular dystrophy	2	10, 48	1/2
Organic acidaemia§	1	3	1/1
Partial agenesis of corpus callosum	1	3 weeks	1/1
Spinal muscular atrophy	1	33	0/1
Posthaemorrhagic porencephalic cyst	1	10	1/1
Asphyxia	2	4 days, 5	2/2
Spastic quadriplegia	2	6, 6	2/2
Severe prematurity	2	4, 4	1/2

*Age corrected for prematurity.
†Excluding spinal cord and neuromuscular abnormalities.
‡Diagnosed with ultrasound.
§3-Hydroxy-3-methylglutamicaciduria.
¶Infant scanned twice.

TABLE II—*Nuclear magnetic resonance imaging sequences*

Sequence	Duration of scan cycle (ms)	τ (ms)	Principal image parameters
Repeated free induction decay	1000		Proton density
Inversion recovery	1800	600	T_1, proton density
Spin echo	1080	40	T_2, proton density
	1160	80	
	1240	120	

(including one repeat), though no sedation was used in the other three. An oesophageal stethoscope was used to monitor the heart and respiratory rate in the infants. No child became distressed during the procedure.

The scanner and basic pulse sequences have been described.[1 5] Table II summarises the particular sequences used in this study. Up to 10 slices were performed in each case, including at least one of each type of sequence (repeated free induction decay, inversion recovery, and spin echo). No adverse effects were observed in any examination.

Results

NORMAL APPEARANCES

In the normal subjects aged 6 months, 20 months, and 5 years repeated free induction decay images showed the ventricular system but were otherwise relatively featureless. In the neonate repeated free induction decay scans showed a darker area in the periventricular region. Inversion-recovery images in this infant also showed bilateral symmetrical long T_1 (dark) regions in these areas (fig 1). In the normal infant of 6 months inversion-recovery images showed symmetrical short T_1 (white) areas within the posterior limb of the internal capsule and thalamo-occipital radiation (fig 2). In the child of 20 months there were more extensive short T_1 areas in both limbs of the internal capsule, forceps major and minor, margins of the lateral ventricles, and external capsule with extension into the periphery of both hemispheres. The 5-year-old showed further short T_1 areas but fewer than those seen in adults.

Spin-echo scans showed the periventricular region as darker than the rest of the brain in the neonate, but otherwise these scans were relatively featureless and showed no evidence of contrast between grey and white matter.

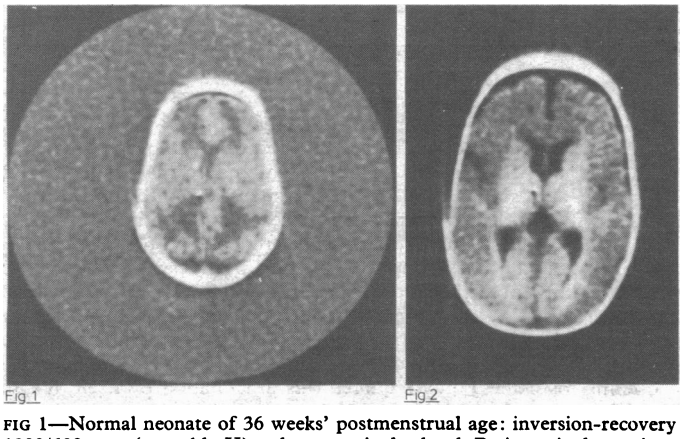

FIG 1—Normal neonate of 36 weeks' postmenstrual age: inversion-recovery 1800/600 scan (see table II) at low ventricular level. Periventricular regions within frontal and occipital lobes appear darker owing to their long T_1. (Central black-and-white spot represents machine artefact.) FIG 2—Normal infant aged 6 months: inversion-recovery 1800/600 scan (see table II) at low ventricular level. Short T_1 (white) regions shown within posterior limb of internal capsule and in thalamo-occipital radiation but not elsewhere.

ABNORMAL APPEARANCES

Ventricular dilatation (fig 3), a porencephalic cyst, and partial agenesis of the corpus callosum were visualised in a similar manner to ultrasound and *x*-ray computed tomography. The cephalhaematoma was well shown with repeated free induction decay, inversion-recovery, and spin-echo scans.

Evidence of apparent deficit in myelinisation (based on the inversion-recovery scans) were seen in two infants. The first was an 18-month-old with probable rubella embryopathy (fig 4), and the second was an infant of 21 months with grossly dilated ventricles of unknown cause. Both these children were developmentally retarded.

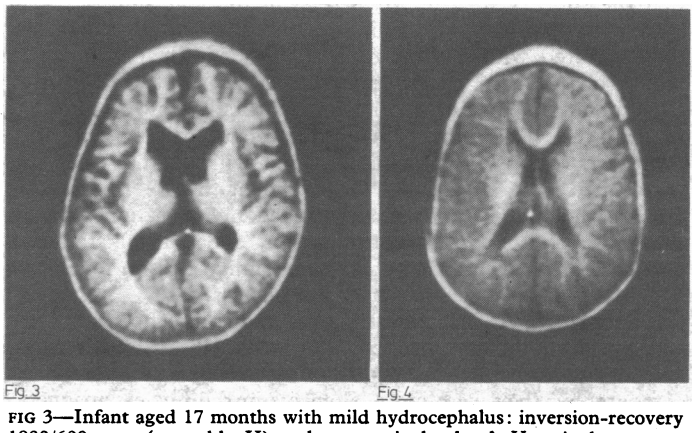

FIG 3—Infant aged 17 months with mild hydrocephalus: inversion-recovery 1800/600 scan (see table II) at low ventricular level. Ventricular system slightly dilated. Much more extensive short T_1 areas evident, including regions of forceps major and minor and external capsule. FIG 4—Infant aged 17 months with probable rubella embryopathy: inversion-recovery 1800/600 scan (see table II) at low ventricular level. Brain shows fewer short T_1 regions than infant in fig 3.

Long T_1 (dark) areas and long T_2 (light) areas were seen in the periventricular regions of an infant with congenital muscular dystrophy. Bilateral but less extensive lesions of low attenuation were seen in the corresponding positions with *x*-ray computed tomography.

In an infant of 11 months with hydrocephalus and acute Holter valve failure spin-echo 1160/80 scans (see table II) displayed an increased T_2 (light) area at the margins of both lateral ventricles consistent with the development of acute hydrocephalus (fig 5). This was not seen in other infants with chronic hydrocephalus.

An infant of 41 weeks' gestation scanned two days after convulsions due to severe birth asphyxia (Apgar score 1 at one minute) showed increased T_2 regions in both hemispheres anterolateral and posterolateral to the lateral ventricles (fig 6), though no increase in T_2 was seen in these regions in the normal infant of 36 weeks' postmenstrual age or in the older normal children.

Discussion

Progressive myelinisation of the brain during infancy has been described in pathological specimens.[6 7] Rapid myelinisation within the first two years of life with a slower rate thereafter has been reported from brain cholesterol measurements, though

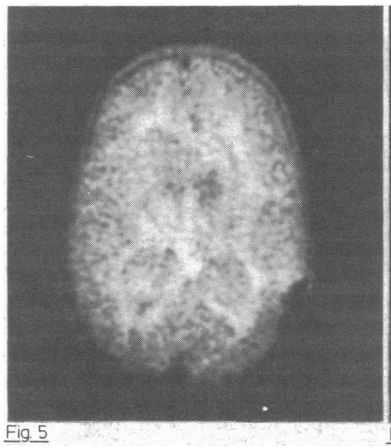

Fig 5

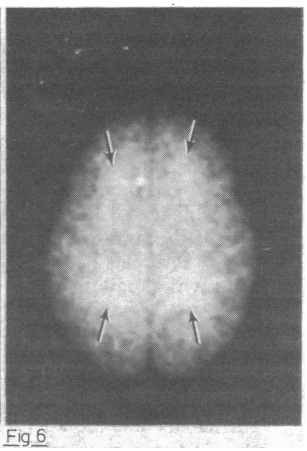

Fig 6

FIG 5—Infant aged 11 months with acute hydrocephalus: spin-echo 1160/80 scan (see table II) at low ventricular level. Lighter regions (increased T_2) shown at margins of dilated lateral ventricles. With this sequence (spin-echo 1160/80) approximately equal signal received from brain and cerebrospinal fluid. FIG 6—Severe birth asphyxia in 4-day-old infant of 41 weeks' gestation: spin-echo 1240/120 scan (see table II) at low ventricular level. Diffuse lighter areas (increased T_2) shown in periventricular regions (arrows).

this technique detects lipids other than myelin.[8] We believe that the short T_1 (white) areas seen in the inversion-recovery scans reflect degrees of myelinisation and that this process can be monitored with nuclear magnetic resonance. The long T_1 region observed in the inversion-recovery scans of neonates corresponds in position to the periventricular low-attenuation region seen with *x*-ray computed tomography and probably represents regions of white matter which will eventually become myelinated with progressive development. There is evidence from pathological studies that retarded myelinisation may be seen in malnutrition, hypothyroidism, and phenylketonuria[9] and comparison with other children of similar ages in this study suggests that this occurred in two of our cases.

Lesions on both inversion-recovery and spin-echo scans were seen in an infant with congenital muscular dystrophy; though also shown in areas of low attenuation on *x*-ray computed tomography, they were more extensive in the nuclear magnetic resonance scans, suggesting that this technique may be of value in recognising the leucodystrophies.

The ability of spin-echo scans to detect oedema at the ventricular margin may be of value in diagnosing shunt malfunction leading to acute hydrocephalus.

Diagnosing neonatal asphyxial cerebral damage by *x*-ray computed tomography is complicated by the normal occurrence of low-attenuation lesions in the subject areas.[10] Nuclear magnetic resonance may therefore provide a new approach, though considerable care will be required to ensure that the normal range of appearances in this age group is accurately defined before conclusions are made in abnormal babies.

Currently available imaging techniques such as ultrasound and computed tomography give little or no information on abnormal myelinisation, periventricular oedema, or asphyxial injury. Hopefully nuclear magnetic resonance will provide an important new approach to these problems in an age group where its lack of known hazard[11 12] is of particular importance.

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Guidelines for nuclear magnetic resonance examinations issued by the National Radiological Protection Board and entitled "Exposure to nuclear magnetic resonance clinical imaging 1980" may be obtained from: The Secretary, National Radiological Protection Board, Chilton Didcot, Oxon OX11 0RQ.

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LOOSENING MEDICINES—By loosening here, I do not mean purging, nor that which is opposite to astringency; but that which is opposite to stretching: I knew not suddenly what fitter English name to give it, than loosening or laxation, which latter is scarce English. The members are distended or stretched divers ways, and ought to be loosened by as many, for they are stretched sometimes by dryness, sometimes by cold, sometimes by repletion or fullness, sometimes by swellings, and sometimes by some of these joined together. I avoid terms of art as much as I can, because it would profit my country but little, to give them the rules of physic in such English as they understand not. I confess the opinion of ancient physicians hath been various about these loosening medicines. *Galen's* opinion was, that they might be referred either to moistening, or heating, or mollifying, or evacuating medicines, and therefore ought not to be referred to a chapter by themselves. It is likely they may, and so may all other medicines be referred to heat, or coldness, or dryness, or moisture: but we speak not here of the particular properties of medicines, but of their joined properties, as they heat and moisten. Others, they question how they can be distinguished from such as mollify, seeing such as are loosening, and such as are emolient, are both of them hot and moist. To that, thus: stretching and loosening are ascribed to the moveable parts of the body, as to the muscles and their tendons, to the ligaments and *Membranæ*; but softness and hardness to such parts of the body as may be felt with the hand: I shall make clear by a similitude, Wax is softened, being hard, but Fiddle-strings are loosened being stretched. And if you say that the difference lying only in the parts of the body is no true difference, then take notice, that such medicines which loosen, are less hot, and more moistening, than such as soften, for they operate most by heat, these by moisture. The truth is, I am of opinion the difference is not much, nay, scarce sensible, between emolient and loosening medicines; only I quoted this in a chapter by itself, not so much because some authors do, as because it conduceth to the increase of knowledge in physic, for want of which, this poor nation is almost spoiled. The chief use of loosening medicines is in convulsions and cramps, and such like infirmities which cause distention or stretching. They are known by the very same marks and tokens that emolient medicines are. (Nicholas Culpeper (1616-54) *The Complete Herbal*, 1850.)