ORIGINAL ARTICLES

Hypoxic-ischaemic encephalopathy: early and late magnetic resonance imaging findings in relation to outcome

Mary Rutherford, Jacqueline Pennock, Jane Schwieso, Frances Cowan, Lilly Dubowitz

Abstract

Sixteen infants with hypoxic-ischaemic encephalopathy (HIE) were studied using serial magnetic resonance imaging (MRI) up to the age of 2 years. The infants had regular neurological and developmental assessments. An nuclear magnetic resonance (NMR) score was devised to quantify the early and late MRI findings and a neurological optimality score was used to quantify abnormal neurological signs at the time of the final examination. The follow up MRI score was compared with the neonatal MRI score and the outcome of the child.

There was a strong positive correlation between the neonatal and follow up MRI scores and between MRI scores and optimality score. All infants with a normal outcome had patchy white matter abnormalities. All infants with an abnormal outcome had extensive white matter abnormalities. The outcome was most severe in those infants with additional basal ganglia atrophy with or without cyst formation.

Infants with mild HIE who are developmentally normal at the age of 2 years do not have normal MRI scans and may be at risk of minor neurological problems by school age. Bilateral basal ganglia abnormalities are associated with severe developmental delay, but infants with mainly white matter and cortical abnormalities have less severe problems despite extensive tissue loss.

Keywords: hypoxic-ischaemic encephalopathy, magnetic resonance imaging, optimality score, signal intensity.

The neonatal magnetic resonance imaging (MRI) findings in infants with hypoxic-ischaemic encephalopathy (HIE) have been well documented.¹⁻¹⁰ Early neonatal findings include brain swelling and abnormal signal intensity (SI) within the basal ganglia, the periventricular white matter, the subcortical white matter and the cortex.¹⁰ Bilateral abnormal SI within the basal ganglia and thalami that is also detected by ultrasonography is associated with a poor outcome in neonates with HIE.⁸ Cortical highlighting, diffuse loss of grey/white matter differentiation, and abnormal SI along the posterior limb of the internal capsule are associated with structural changes in the brain at 3 months of age,¹⁰ but this is too

early to assess clinical outcome. Magnetic resonance images continue to change in appearance because of normal development, compensatory mechanisms, and secondary degeneration as a result of the initial injury. There are few studies that document both neonatal and late MRI findings in infants with HIE and detailed clinical outcomes are not given.¹⁹

The aim of this study was to document the MRI findings in infants with HIE between 12 and 24 months of age and relate these to: (i) magnetic resonance imaging in the neonatal period; and (ii) the clinical outcome at the time of the final scan.

Methods

Infants were included in the study if they met all the following criteria: (i) term or post-term (37-43 weeks' gestation); (ii) evidence of fetal distress; (iii) neurologically abnormal in the first 48 hours of life, with abnormalities of tone with or without convulsions and altered consciousness. Fetal distress was diagnosed in the presence of cardiotocographic abnormalities of bradycardia (<100/minute or late decelerations (type II dips) with or without meconium stained liquor and with low Apgar scores and the necessity for resuscitation. Hypoxic-ischaemic encephalopathy was classified as mild, moderate, or severe (I, II, or III) according to Sarnat and Sarnat.¹¹

All infants had at least one MRI scan performed within the first 4 weeks of life and one scan between 12 and 24 months of age.

MAGNETIC RESONANCE IMAGING

Magnetic resonance imaging was performed using a Picker HPQ Vista system (Cleveland, Ohio) operating at 1.0 Tesla. T₁ and T₂ weighted spin echo (T₁WSE and T₂WSE) sequences and age related inversion recovery (IR) sequences were used. In some infants a fluid attenuated inversion recovery (FLAIR) sequence was also used.¹² The detailed scanning variables are given in table 1.

The MRI studies were carried out with the infant's head placed laterally in a specifically designed 24 cm split, clear receiver coil. Images were obtained in the transverse plane. Immobilisation was achieved by surrounding the head with an air evacuated bag filled with polystyrene balls. Neonates were examined unsedated during natural sleep. Older infants were sedated with chloral hydrate 60-100 mg/kg orally, or rectally as a suppository. All children

Department of
Paediatrics and
Neonatal Medicine,
Hammersmith
Hospital,
Du Cane Road,
London W12 0HS
M Rutherford
F Cowan
L Dubowitz

Robert Steiner MRI
Unit,
Hammersmith
Hospital
Jacqueline Pennock
Jane Schwieso

Correspondence to:
Dr Mary Rutherford.

Accepted
10 September 1996

Table 1 Parameters for MRI sequences

	Repetition time (ms)	Echo time (ms)	Inversion time (ms)
Inversion recovery	3600-3800	30	700-950
FLAIR	6500	160	2100
T ₁ weighted spin echo	860	20	
T ₂ weighted spin echo	3400	120	

were monitored with ECG and pulse oximetry. A paediatrician was present throughout the investigation.

Abnormal SI within the basal ganglia and thalami may predict outcome and a separate detailed score for the basal ganglia and thalami (TBG) was used, as described before.⁸ The maximum score was 18.

The neonatal NMR score was obtained from first week scans.¹⁰ Points were given for the presence of brain swelling and abnormal signal intensities within the cortex, subcortical and periventricular white matter, basal ganglia and thalami (less detailed than in the TBG score) and from the posterior limb of the internal capsule. The maximum score was 17.

The follow up NMR score was adapted from the neonatal scoring system¹⁰ and included points for atrophy and delayed myelination, but not for brain swelling as this was not seen after the first week of life. The IR sequence and the T₂WSE sequence images were assessed visually and a score reached by consensus. A comparison was made with scans of neurologically normal infants of equivalent age. Details of the follow up score are shown in table 2.

The late MRI findings were compared with the neonatal MRI findings and with the clinical outcome of the infant.

FOLLOW UP AND CLINICAL OUTCOME

Infants had a detailed neurological examination¹³ and a Griffiths developmental assessment at three monthly intervals over the first two years of life. All infants were over 1 year of age at their final assessment. Clinical outcome was classified as normal or abnormal. Those infants with an abnormal outcome were divided into groups according to the severity of their developmental delay.

Normal outcome—A normal neurological and developmental assessment, although there may

have been transient disturbances of tone during the first year of life.

Abnormal outcome—These infants had persistent neurological signs consistent with a central motor deficit, with or without developmental delay.

- (a) No developmental delay
- (b) Moderate developmental delay
- (c) Severe developmental delay
- (d) Very severe developmental delay (no discernible development)

The central motor deficit was classified as a hemiplegia, spastic quadriplegia, athetoid quadriplegia or a mixed quadriplegia (spastic with athetoid/dystonic movements).

OPTIMALITY SCORE

A neurological optimality score was given to each child at their last examination to give a quantifiable assessment of their neurological function. This was adapted from a proforma used by Kuenzle.⁷ The optimality score combined both developmental and neurological findings and was easy to complete even in severely abnormal infants. The proforma scored the following areas separately: tone, posture, spontaneous motility, elicited motility, interaction and reflexes. A mean score was given in each area and a total mean score gave the optimality score. The maximum optimality score and therefore a normal result was 21.

Results

The 16 infants had a total of 95 follow up scans, 36 after the age of 6 months. All infants had at least one scan between 1 and 2 years of age. The abnormal imaging findings are given in table 3 and the MRI scores are given in table 4.

All sixteen infants had abnormalities in the white matter on follow up scans. In eight of these infants the changes were mild and patchy and limited to the periventricular white matter (fig 1). One of these eight infants had mild ventricular dilatation, but in the remaining seven the scans were otherwise normal. All eight infants had had signs of brain swelling on their first week scan, but only one had a persistent area of abnormal SI in the white matter (case7).

Table 2 Clinical neonatal details and optimality scores

Case No	Gestation	Fetal distress	Apgar score 1,5 minutes	Delivery	HIE grade	Outcome	Optimality score
1	40	ctg/msl	3,7	Ventouse	II	Normal	21
2	40	nil	4,4	nvd	I	Normal	20.7
3	41	ctg/tachy	4,4	nvd	I/II	Normal	20.5
4	40	ctg	2,7	nvd	I	Normal	21
5	41	NR	3,4	nvd	I	Normal	21
6	41	ctg/msl	2,6	Ventouse	I	Normal	20.9
7	43	NR	0,0	nvd	II	Hemisynndrome	20.3
8	39	ctg/msl	2,3	nvd	II	Hemiplegia	20.3
9	40	ctg	1,2	emcs	II	cmd/mdd	16.4
10	38	ctg	2,5	emcs	II	cmd/sdd	14.6
11	40	PA	2,6	emcs	II	cmd/sdd	11.9
12	41	ctg	0,0	Ventouse	II	cmd/sdd	11.7
13	42	ctg	0,0	Forceps	II	cmd/sdd	9.0
14	41	ctg/msl	1,	Ventouse	II	cmd/sdd	8.8
15	41	ctg	2,5	emcs	II	cmd/vsdd	7.6
16	41	ctg/msl	0,4	emcs	III	cmd/vsdd	6.3

CTG = cardiotocograph; msl = meconium stained liquor; emcs = emergency caesarean section; NR = not recorded; PA = placental abruption; cmd = central motor deficit; mdd = moderate developmental delay; sdd = severe developmental delay; vsdd = very severe developmental delay.

Table 3 Abnormal imaging findings

Site	Abnormal neonatal findings	No of infants	Follow up findings	No of infants
Basal ganglia and thalami	High and low SI on both IR and T2WSE sequences	8	Unilateral high SI on T2WSE	1
			Bilateral atrophy of lentiform and thalami with low SI on IR and high SI on T2WSE	5
			Severe atrophy of lentiform, caudate head and thalami with both high and low SI on IR and T2WSE	2
Cortex	Abnormal high SI on IR	6	Low SI on T2WSE, only seen running along interhemispheric fissure	3
Subcortical white matter (1) Corticospinal tracts (2) Adjacent to interhemispheric fissure	High SI on IR	7	High SI on T2WSE, seen in "bats wing" pattern	7
	Low SI on IR	6	High SI on T2 on T2WSE	6
	Focal low SI on IR	1	Patchy high SI on T2WSE	8*
Periventricular white matter	Areas of infarction seen as low SI on IR and high SI on T2WSE	3	Extensive high SI on T2WSE with generalised deficit in myelination	8
	Streaky high and low SI on IR	5		
	High SI in insula cortex on IR	7		
Insula	Infarct involving insula	1	High SI on T2WSE and FLAIR	
Cerebellum	Nil		Deficit in myelination but no atrophy	2
Hippocampus	High SI on IR	4	Atrophy of hippocampus with dilated temporal horns of lateral ventricles	4

* All infants had signs of brain swelling on neonatal scan.

Table 4 MRI and optimality scores

Case No	Neonatal scan score		Follow up scan score		Optimality score
	TBG (max=18)	Total (max=17)	TBG (max=18)	Total (max=46)	
1	0	3	0	4	21
2	0	0	0	2	20.7
3	2	3	0	2	20.5
4	0	2	0	4	21
5	2	4	0	5	21
6	2	3	0	2	20.9
7	0	2	0	3	20.3
8	0	3	0	4	20.3
9	3	7*	2	16	16.4
10	12	14	10	31	14.6
11	12	11	10	28	11.9
12	15	11*	6	20	11.7
13	12	13	16	37	9.0
14	12	9*	14	28	8.1
15	18	12	18	46	7.6
16	18	13	18	45	6.3

* Minimum score.

Eight infants had more extensive abnormal SI in the periventricular white matter associated with a deficit in myelination (fig 2). These eight infants also had abnormalities in the subcortical white matter, with increased T₂ along the corticospinal tracts adjacent to the Rolandic fissure (fig 3C) and increased T₂ running parallel to the interhemispheric fissure (fig 4B). These abnormalities corresponded to increased SI in the corticospinal tracts (fig 3A) and decreased SI in the subcortical white matter (fig 4A), respectively, on the neonatal inversion recovery sequence. Cerebral atrophy with ventricular dilatation and/or widening of the interhemispheric fissure was seen in these eight infants. Focal widening of the interhemispheric fissure (fig 3B) developed in those infants with cortical highlighting and adjacent subcortical breakdown on neonatal scans. These infants had additional changes within the basal ganglia which varied in severity (figs 5 and 6). Bilateral atrophy of the brainstem was seen in two infants with severe basal ganglia changes and unilateral atrophy in one with a parietal infarct.

Figure 1 Boy with grade I HIE aged 1 year (case 5). T₂ weighted spin echo sequence (SE 3000/120). Minor bilateral SI is increased in posterior periventricular white matter at 1 year of age (arrow).

Hippocampal atrophy was only seen in infants with severe basal ganglia abnormalities.

There was a positive correlation between the neonatal and follow up TBG scores (Kendall's rank correlation, P=0.0005). There was a

Figures 2 A and B Boy with grade II HIE (case 12). Inversion recovery sequence (IR 3600/30/800) (A) and T₂ weighted spin echo sequence (SE 3000/120) (B). Generalised myelination deficit is evident (A) with increased T₂ most evident in the region of a parietal infarct (arrows) (B).

Figures 3A and B Girl with grade II HIE (case 15). Inversion recovery sequence (IR 3800/30/950) (A), inversion recovery sequence (IR 3600/30/800) (B), and T_2 weighted spin echo sequence (SE 3400/120) (C). There is abnormal increased signal intensity running along the corticospinal tracts in the centrum semiovale adjacent to the Rolandic fissure on the three week scan (arrow) (A) and at 15 months increased T_2 (arrow) (C). There is a generalised myelination deficit with some widening of the interhemispheric fissure (B).

strong positive correlation between the neonatal and follow up NMR scores (Kendall's rank correlation, $P=0.0001$).

NEONATAL AND FOLLOW UP MRI FINDINGS IN RELATION TO CLINICAL OUTCOME

Normal outcome ($n=6$):

Six children had a normal outcome (optimality scores 20.5–21). These children had patchy white matter abnormalities on follow up scan (NMR score 1–2). Five infants had mild brain swelling on the neonatal scan, and two of these also had minor SI changes in the lentiform nuclei. The remaining infant had a subarachnoid haemorrhage.

Abnormal outcome ($n=10$):

Eight infants had a central motor deficit involving all four limbs and two infants had unilateral signs.

Normal development ($n=2$):

Two infants had minor neurological signs and normal development (optimality scores were 20.3). One infant had a mild hemiplegia and one a mild hemisindrome. The T_2 WSE follow up scans showed patchy increased SI in the periventricular white matter in both infants (NMR scores 2, 3). There were no focal lesions or evidence of brainstem asymmetry.

Both infants had brain swelling on the neonatal scans and the infant with the

Figures 4A and B Girl with grade II HIE (case 9). Inversion recovery sequence (IR 3800/30/950) (A) and T_2 weighted spin echo sequence (SE 3000/120) (B). There is bilateral highlighting of the cortex (short arrow), with low signal areas in the adjacent subcortical white matter (long arrow) at 3 weeks of age (A). At 15 months bilateral low signal is seen in the cortex running parallel to the interhemispheric fissure (long arrow). There is bilateral high signal in the subcortical white matter (short arrow) (B).

hemisindrome also had persistent low signal on inversion recovery sequence in the right posterior parietal white matter.

Moderate developmental delay ($n=1$):

One infant had a central motor deficit with moderate developmental delay (optimality score 16.4). The signs consisted of secondary microcephaly, extensor posturing and increased tone in lower limbs. In spite of this at the age of 2 years she was able to cruise around the furniture. She had a vocabulary of several words. Follow up scans showed pronounced

Figures 5A, B, and C Boy with grade II HIE aged 1 year (case 12). Inversion recovery sequence (IR 3600/30/800) (A), T_2 weighted spin echo sequence (SE 3000/120) (B), and FLAIR (fluid attenuated IR 6500/160/2100) (C). There is atrophy of the lentiform nuclei with abnormal low signal intensity in the posterior putamen (long arrow) and in the left thalamus (short arrow) (A). These regions are high signal intensity (B). There is a deficit in myelination posteriorly (A). Abnormal increased SI around the lentiform nuclei and insula cortex is best seen in (C).

Figure 6 Girl with grade II HIE, aged 15 months (case 15). T_2 weighted spin echo sequence SE 3000/120. There is pronounced bilateral atrophy of the lentiform nuclei, thalami, and head of the caudate nucleus with abnormally high and low signal intensities (arrows).

white matter atrophy with increased T_2 in the centrum semiovale and periventricular white matter. Decreased T_2 was seen in the cortex adjacent to the interhemispheric fissure (NMR score 9). The basal ganglia were of normal appearance. Her neonatal scan showed brain swelling and widespread cortical highlighting.

Severe developmental delay (n=5):

Five infants had a central motor deficit, severe developmental delay, and secondary microcephaly. (The optimality scores ranged from 8.1–14.6.) All had secondary microcephaly.

Three infants had a mixed quadriplegia with athetoid or dystonic movements of the upper limbs, hypotonia of the trunk, and increased tone in the lower limbs (cases 12,13,14). Two of these infants had no hand function, but the third who had milder dystonic posturing was able to transfer objects at 17 months of age (case 12). This infant had no abnormal facial appearances and showed good vocalisation with a vocabulary of two words.

A fourth infant had a generalised increase in tone with dystonic posturing of the right hand (case 10). She was able to sit independently and spoke a few words. The sixth infant with a central motor deficit and severe delay had generally decreased tone with severe visual problems. He was able to sit with minimal support and was able to transfer objects but had no fine hand manipulation at 18 months (case 11).

A follow up MRI scan showed severe basal ganglia changes with atrophy and cyst formation in the three infants with severe dystonic and athetoid movements. They also showed a loss of white matter and an abnormal increase in SI around the primary corticospinal tracts on T_2 WSE scans (NMR scores 16, 21, 31). One infant had a posterior parietal infarct. These

infants had abnormal SI in the basal ganglia and thalami, the cortex, and in the subcortical and periventricular white matter on neonatal scans.

Two further infants (cases 10,11) with severe developmental delay showed a different pattern of abnormalities on MRI.

Follow up MRI showed loss of tissue secondary to infarction in both infants. The basal ganglia were affected in both infants, although these were asymmetrical in case 10. The images did not show any substantial increase in SI on the T_2 WSE scan. Myelination was decreased in both infants but this decrease was extreme in case 11 (NMR scores 20 and 28).

Their neonatal scans showed multiple areas of infarction involving the white matter and cortex and abnormal SI within the basal ganglia and thalami.

Very severe developmental delay (n=2):

Two infants made no discernible development. (Optimality scores were 7.6 and 6.3.) Both had secondary microcephaly, severe extensor posturing, ongoing convulsions, persistent feeding problems necessitating nasogastric or gastrostomy feeding.

On follow up MRI both infants had extensive atrophy of the basal ganglia, a decrease in white matter, and a substantial decrease in myelination. On the T_2 WSE sequence images there was an increase in SI along the primary corticospinal tracts (fig 3C) (NMR scores 39 and 40). Their neonatal scans showed abnormal SI throughout the basal ganglia and thalami with highlighting of the cortex, which was most severe around the central fissure and interhemispheric fissure.

Table 4 shows the details of the follow up optimality score with the neonatal and follow up TBG and total NMR scores. There was a strong positive correlation between the optimality score and the neonatal TBG ($P=0.0004$), the neonatal NMR ($P=0.0034$), the follow up TBG ($P=0.0002$) and the follow up NMR score ($P=0.0012$).

Discussion

In neonates with HIE early MRI may show evidence of brain swelling. This clears during the first week of life as signs of permanent damage become more obvious. Abnormal signal intensities may be seen in the basal ganglia and thalami, the internal capsule, the periventricular and subcortical white matter and in the cortex.¹⁰ We have shown that in term infants with HIE there may be late MRI abnormalities within the basal ganglia, the cortex, the white matter, the hippocampi, the insulae and the brainstem. There were no normal follow up scans and infants with a normal outcome showed patchy abnormal SI within the periventricular white matter, which was most noticeable posteriorly. Persistent basal ganglia abnormalities were always associated with an abnormal outcome, the severity and character of which were related to the degree of abnormality seen. Infants with extensive white matter abnormalities all had an abnormal outcome, but those without pronounced basal ganglia abnormalities had less severe problems. There was a strong correlation between the

neonatal and late NMR and TBG scores and the outcome of the child, as measured by the optimality score.

Infants with a normal outcome all showed patchy white matter changes on their follow up scans. These changes were only detectable on T₂ weighted images and were difficult to distinguish from unmyelinated white matter before 1 year of age. It is not possible to say whether these changes will persist with time or whether they will be associated with more minor neurological dysfunction at school age. Mild or grade I HIE is always considered to be a benign disorder, but to our knowledge there have been no published studies that have looked at the fine motor function in these children at 5 years plus.

Byrne documented the development of cerebral palsy in three children with normal scans at 3 months of age, but abnormal scans at 8 months of age, with the development of delayed myelination and cortical atrophy.³ We did not see this type of deterioration in any of our infants. Deterioration of a previously normal scan may imply that subtle but clinically important changes—that is, in the cortex or white matter—may have been difficult to identify early on. This could be because the changes were time dependent or because the imaging sequences used were not optimal. We have shown that infants with patchy periventricular white matter changed on T₂WSE scans at 1 year of age may have only had signs of brain swelling on neonatal T₁WSE sequence scans.¹⁰ The signs of swelling were only visible for a few days. Alternatively, a child with an abnormal outcome but a normal early scan may have an additional diagnosis, such as a metabolic problem, giving rise to ongoing damage within the brain. Isolated delay in myelination may be one of the earliest MRI changes in children with a metabolic disorder.¹⁴ We have seen isolated deficit in myelination in infants with neurological problems not due to HIE, although they may have had fetal distress and abnormal deliveries in addition to their primary problem. In this study a deficit in myelination was only seen in association with other structural changes within the brain.

The basal ganglia are a common site for abnormalities in the neonatal period, but only the more severe and persistent lesions seem to be associated with a central motor deficit. Atrophy or cysts in the basal ganglia have been reported in retrospective studies of children with cerebral palsy and are felt to be good evidence in support of the occurrence of significant perinatal injury, as opposed to pre-existing prenatal abnormalities.^{15,16} The type of motor deficit may depend on the exact site and extent of basal ganglia injury and whether there is extension into the midbrain and damage in other parts of the brain. We have shown that severe basal ganglia injury is associated with severe spastic quadriplegia with pronounced feeding difficulties and ongoing convulsions. The feeding difficulties are probably related to involvement of the midbrain which is more difficult to assess on MRI but is associated with severe basal ganglia injury on

necropsy specimens.¹⁷ In this study generalised atrophy with or without cyst formation in the basal ganglia was also associated with abnormal SI within the hippocampus, a pattern of injury that has been attributed to a period of total asphyxia using animal models.¹⁸

Less severe damage with atrophy and cyst formation within the lentiform nuclei was seen in three infants, all of whom had a mixed quadriplegia with athetoid and or dystonic movements. A further infant with asymmetrical basal ganglia abnormalities had dystonic movements in the contralateral arm only. Localised cysts in the posterior part of the putamen without generalised atrophy are strongly associated with the development of athetoid quadriplegia.^{19,20} Interestingly, all three infants in this study with a mixed quadriplegia with athetoid movements had microcephaly and severe early feeding problems, with no suck and poor swallow. This contrasts to our previous findings in three infants with a purer athetoid quadriplegia all of whom maintained a normal head circumference and all of whom were bottle feeding by 2 weeks of age.¹⁹

White matter atrophy is a common finding on the follow up scans of infants with HIE. Areas of white matter atrophy were distinguished because of the lack of myelin and the collapsing down of cortical gyri on IR sequences, but it was not possible to differentiate atrophy of the subcortical white matter from the periventricular white matter using the IR sequence alone. Abnormally increased T₂ probably representing secondary gliosis was, however, easily seen on the T₂WSE sequences and permitted a more accurate localisation of white matter damage. A delay or deficiency in myelination was easiest to identify on IR sequence scans, which was also the finding in Byrne's study.³ Although NMR is the imaging method of choice for assessing myelination, the patterns seen only grossly approximate the complex process of central nervous system development.

Three changes on neonatal scans were associated with the subsequent appearance of white matter atrophy, areas of infarction, a streaky appearance in the white matter of the centrum semiovale, and subcortical low signal on IR sequence. Infants with a streaky appearance in the white matter during the first week of life did not develop cysts and the aetiology of the eventual white matter atrophy remains obscure. Low signal in the subcortical white matter was associated with cortical highlighting. The cortical highlighting appeared in the first week of life but the adjacent areas of white matter low signal did not appear for at least another seven days.¹⁰ The timing of the subcortical changes reflects either a primary ischaemic process in the tissue with cyst formation appearing 10 to 14 days later, or alternatively, it may be secondary to the damage within the cortex. The cortex and subcortical white matter around the central fissure in the region of the primary corticospinal tracts were most frequently involved and at follow up detected as increased T₂. This region may be more sensitive to asphyxial damage at term when it is actively myelinating.²

The clinical relevance of the cortical highlighting seen on neonatal IR scans is uncertain. The SI changes observed are in keeping with a haemorrhagic lesion. The MRI appearance of cortical highlighting may correspond to the increased cortical echogenicity identified using cranial ultrasonography in infants with HIE. This increased echogenicity corresponded to areas of cortical laminar necrosis on histological examination.²¹

On follow up MRI scans it was possible to identify persistent low signal on T₂WSE sequence within the cortex along the inter-hemispheric fissure. This would be consistent with old haemorrhage. Cortical laminar abnormalities, giving abnormal SI on T₂ weighted images have been described by other workers on late MRI scans in children with a history of perinatal hypoxic-ischaemic brain injury and spastic quadripareses.²²

Only one of our infants had pronounced cortical and subcortical white matter changes with relatively preserved basal ganglia and she has done remarkably well (case 9). The clinical importance of early and late cortical and subcortical changes following HIE are poorly understood and further insight may be gained with more sophisticated imaging combined with specific electrophysiological studies in children with no evidence of basal ganglia abnormalities.

The dentate nuclei of the cerebellum are sensitive to hypoxic-ischaemic damage in animal models but there are few reports of cerebellar abnormalities following hypoxic-ischaemic injury in neonates.^{23,24} The cerebellum may be damaged along with the thalami and hippocampus as part of the injury following severe total asphyxia. In Eken's study of infants with HIE, histological cerebellar lesions were seen in 11 of 20 infants,²¹ but it is not clear what pattern of injury these infants had sustained.

As all infants in our study survived, the insults they sustained may have been insufficient to cause major lesions within the cerebellum. The only abnormality seen in this study was a deficit in myelination within the cerebellum, and this was associated with a generalised deficit of myelin throughout the brain. Although mild degrees of atrophy may have been present but difficult to identify, the cerebellum seems to remain intact when the rest of the brain is grossly damaged.

MRI permits the detection of exact patterns of early and late damage in infants with HIE. Some correlations with different patterns of damage can be made. In most cases, however, we are still not able to correlate accurately specific areas of damage with specific clinical sequelae. This is partly because in infants with HIE few areas are damaged in isolation. The imaging techniques used did not measure function and while severe degrees of atrophy are identifiable, these could not be measured and less severe atrophy may well have gone undetected. Further studies using a combination of electrophysiological and MRI techniques will allow us to answer some of the questions on the functional relevance of specific abnormalities.

Registration and subtraction of serial volumetrically acquired images should help in measuring and detecting even mild degrees of atrophy, and in detecting milder deficiencies and abnormalities in the progression and patterns of myelination.²⁵

Mary Rutherford was supported by Scope (formerly the Spastics Society). We are grateful to Professor Graeme Bydder for his guidance and support.

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