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REVIEW

MRI of perinatal brain injury

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Abstract MRI is invaluable in assessing the neonatal brain following suspected perinatal injury. Good quality imaging requires adaptations to both the hardware and the sequences used for adults or older children. The perinatal and postnatal details often predict the pattern of lesions sustained and should be available to aid interpretation of the imaging findings. Perinatal lesions, the pattern of which can predict neurodevelopmental outcome, are at their most obvious on conventional imaging between 1 and 2 weeks from birth. Very early imaging during the first week may be useful to make management decisions in ventilated neonates but brain abnormalities may still be subtle using conventional sequences. Diffusion-weighted imaging (DWI) is very useful for the early identification of ischaemic tissue in the neonatal brain but may underestimate the final extent of injury, particularly basal ganglia and thalamic lesions. MR imaging is an excellent predictor of outcome following perinatal brain injury and can therefore be used as a biomarker in interventional trials designed to reduce injury and improve neurodevelopmental outcome.

Keywords Brain · Ischaemia · MRI · Neonate

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Introduction

MR imaging of the brain has an increasingly important role in neonatology with the advent of treatments aimed to decrease perinatally acquired brain injury [1]. The neonatal brain may be injured by many processes including hypoxia-ischaemia, viral and bacterial infection, trauma, haemorrhage and metabolic disorders, acquired conditions such as kernicterus and hypoglycaemia or congenital as in one of the many the inherited disorders of metabolism. It is beyond the scope of this review to cover all aspects of acquired injury and it will focus therefore on the most common cause of perinatal brain injury, hypoxia-ischaemia. In the context of acquired perinatal brain injury MR imaging in the neonatal period will provide information that can:

- Explain neurological symptoms
- Confirm the presence or absence of acquired brain lesions
- Ascertain the timing and aetiology of any brain abnormalities
- Inform clinical management and guide diagnostic investigations

Table 1 Patient preparation

- Check infant suitable and ready for sedation
- Perform metal check prior to sedation
- Sedate infant and monitor as soon as asleep
- Use ear protection
- Perform metal check prior to entry into scanner room
- Connect to MR compatible monitoring
- Swaddle infants to decrease effects of motion
- Ensure trained staff and equipment available for neonatal resuscitation
- Monitor oxygen saturation and heart rate throughout the examination
- Make a neonatal imaging protocol folder on the scanner console

- Monitor the effects of interventions
- Predict outcome and help counsel parents
- Inform critical incident proceedings
- Prevent expensive medico legal proceedings

To achieve these ends it is important to obtain both good quality imaging and a correct interpretation of the imaging findings. Image quality is often impaired by motion artefact, poor signal to noise or inappropriate sequence choice. Good preparation is essential to achieve a successful examination and a good account of the necessary practical issues is provided in a recent review [2]. The protocols in our unit are shown below (Table 1).

Image acquisition

Image quality is governed by the signal to noise ratio (SNR) and the absence of artefact. The SNR is maximised by using a closely fitting coil. In the absence of a dedicated neonatal head coil an adult knee coil may be used. Phased-array coils may provide improved benefit in terms of SNR although lack of homogeneity may be an issue. It is important to place the neonatal head in the centre of the coil to avoid image signal inhomogeneity. Sick infants may be ventilator-dependent in the first few days after delivery and it may therefore be necessary to perform the imaging examination using MR-compatible ventilator equipment. In the absence of this, a neonate can be safely hand bagged during a short MR examination if monitoring is in place. In ventilated neonates a larger adult head coil may be necessary to accommodate the endotracheal tube. Imaging of the neonatal brain may be performed on a 1-, 1.5- or 3-T magnet system but MR sequences need to be adapted for the neonatal brain with its higher water content. An ideal neonatal protocol is listed in Table 2 and sequence parameters are suggested in Table 3. The single most common reason for a failed or poor quality image examination is neonatal motion. If the infant is unsettled it may be necessary to repeat the sequence acquisition or to image with a different approach, whilst this may sacrifice some SNR it will allow interpretable images to be acquired. T1- and T2-weighted imaging sequences from fast brain protocols may be used or motion "correction" sequences e.g., PROPELLER, BLADE. Alternatively a single-shot technique such as the snapshot volume reconstruction (SVR) that has been developed for imaging the mobile fetal brain can provide images of sufficient quality to exclude major pathologies [3].

Diffusion-weighted imaging (DWI) should include as many directions as possible and the generation of at least an apparent diffusion coefficient (ADC) map, which should be possible on most MR consoles. Whilst there have been one or two reports of the useful role of proton-density sequences in early imaging following perinatal brain injury we have acquired it as part of a dual-echo sequence for

Table 2 Neonatal imaging protocol (Fig. 1)

- T1- and T2-W axial images, slice thickness 4 mm (use "neonatal" angle – from inferior frontal lobe to torcula)
- T1-W sagittal images, slice thickness 1.5–3 mm
- T2-W coronal images, slice thickness 4 mm
- DWI axial plane
- Sinus venogram
- MR angiography
- MR proton spectroscopy
- Consider the use of IV contrast if suspect additional acquired infection (check normal renal function)
- Be prepared with suitable sequences to use in presence of motion e.g. BLADE, PROPELLER

Table 3 Suggested MR sequence parameters

Sequence	Roelants-van Rijn et al. [41]			van Wezel-Meijler et al. [2]			Boardman et al. [42]			van Wezel-Meijler et al. [2]			Hammersmith Hospital		
	T2-W TSE	T1-W SE	DWI EPI	T2-W TSE	3-D T1-W TFE	DWI EPI	T2-W TSE	3-D T1-W TFE	DWI EPI	T2 TSE	3-DT1 TFE	DWI EPI	T2 TSE	3-DT1 FFE	DTI EPI
Field strength	1.5T									3 T					
Plane	Trans	Trans	Trans	Trans	Trans	Trans	Trans	Sag	Trans	Trans	Trans	Trans	Trans	Sag	Trans
TR (ms)	5915	512	4000	5327	26	3400	4500	30	6000	6269	9.7	2406	8000	17	8000
TE (ms)	90	15	148	120	12	74	210	4.5	90	120	4.6	64	160	4.6	49
Flip angle (degrees)	90	90	90	90	20	90	90	30	90	90	8	2	90	13	90
Slice thickness (mm)	4	4	5	4	1.5	6	4	1.6	5	2	1	4	2	0.8	2
NSA				3	1	1	2	1	1	2	1	1	1	1	1
b value (s/mm^2)			1000			1000			1000			1000			750
SENSE												×2	×2		×2
Time (mins)				4:05	5:45	0:30	4:30	5:45	0:30	5:38	4:32	0:35	4:40	4:20	3:0+

Trans transverse, *sag* sagittal, *TSE* turbo spin-echo, *TFE* turbo field echo, *EPI* echo- planar imaging, *NSA* number signal averages, *SENSE* sensitivity encoding

years and not found it to add information that was not evident on the T1- and T2-W sequences [4]. Similarly a fluid-attenuated inversion recovery (FLAIR) sequence may accentuate white matter (WM) injury in the neonatal brain but seldom adds new information [5]. In suspected infection the administration of contrast may be considered, the concern being that conventional imaging without contrast enhancement may be negative if performed early in the disease [6]. The majority of neonates with suspected bacterial or viral infection are treated empirically and imaging may not be requested until after the acute illness. At that stage any injury should be established and a negative imaging examination should be truly negative and the administration of contrast would be unnecessary. With the recent discovery of the association between gadolinium-based contrast agents and nephrogenic systemic fibrosis (NSF), the possible advantages of giving contrast at any stage need to be weighed up against the small risk of precipitating NSF [7]. The youngest cases reported to date have been eight years old and all the cases reported have had chronic renal failure. Neonates have an immature renal system and following a hypoxic-ischaemic event often demonstrate both transient renal and hepatic dysfunction placing them at theoretically increased risk of NSF. Where contrast administration is considered the responsible clinician will need to check renal function and for the presence of metabolic acidosis prior to administration. It would seem prudent to keep to the minimum dose, to restrict the use to those neonates with a high suspicion of intracranial infection or those not responding to treatment and to consider contrast agents with a cyclic structure not associated, as yet, with NSF.

The role of susceptibility-weighted imaging (SWI) of the brain has been highlighted recently in the investigation of potential thrombosis [8]. We would recommend a standard MR sinus venogram in every neonate with suspected perinatal brain injury. Many of these neonates have subdural haemorrhage and it can be difficult to differentiate from sinus thrombosis. In term born neonates with haemorrhagic lesions the underlying diagnosis may well be thrombosis of smaller draining veins [9, 10]. In later stage sinus thrombosis the diagnosis may be confirmed by the presence of characteristic cortical and subcortical haemorrhagic lesions. Of interest is the potential role of SWI in detecting calcium [8, 11]. Whilst this is relatively easy with cranial US, MR underdiagnoses the presence of calcium when compared to CT. The presence of calcium may be sought in suspected congenital infection e.g., cytomegalovirus, but many acquired hypoxic-ischaemic lesions may be calcified at some stage during their evolution. As for many sequences in neonatal imaging, optimisation is required because of the small size and altered tissue properties of the immature brain.

MR angiography can be used without contrast medium and allows depiction of the proximal cerebral arteries in the neonatal brain. Imaging at 3T improves SNR and therefore

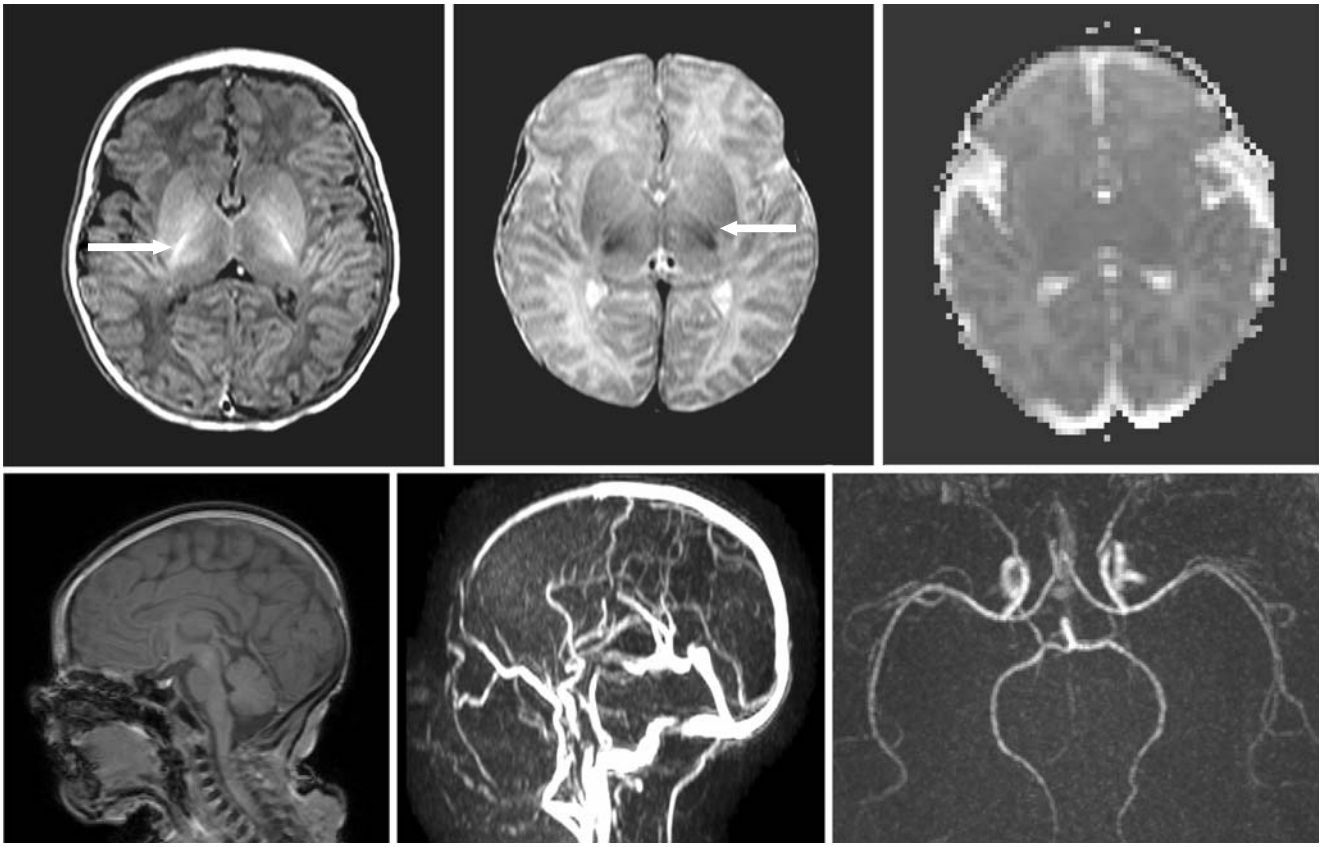

Fig. 1 Normal appearances of the term neonatal brain. Top row: T1-, T2-W and diffusion-weighted ADC map (from *left* to *right*) images in the transverse plane. Myelination within the PLIC is high SI on T1-W and low SI on T2-W images (*arrows*). Bottom row: T1-W, thin-slice image in mid sagittal plane (*left*). The venogram (*middle*) shows normal filling of all the major sinuses. The angiogram (*right*) demonstrates the proximal cerebral arteries and the circle of Willis

the quality of the images (Fig. 1) [12]. Angiography allows the variations of the circle of Willis to be documented, although it remains unclear how these might relate to lesion acquisition and lesion evolution. In neonates with middle cerebral artery infarction there may be transient occlusion of the artery, but in later imaging the vessels on the affected side are often involved within the infarct itself and so an asymmetry in the appearance of the vessels is a common finding.

MR spectroscopy has progressed little in the last ten years compared to imaging and its role in the clinical examination is limited. Following a hypoxic-ischaemic brain insult proton spectroscopy may demonstrate an increased lactate peak; this is useful to confirm the presence of a significant tissue injury, particularly in early examinations before conventional imaging becomes overtly abnormal. Proton spectroscopy has also been used to predict outcome in the research environment and has a good sensitivity and specificity for poor outcomes in neonates with hypoxic-ischaemic encephalopathy (HIE) [13]. However the technique requires the spectra to be processed and the metabolite ratios quantified, which may not be practical in clinical practice. In addition, as will be noted later in this review, important information for determining the nature of the neurodevelopmental impairment is obtained from the site and pattern of the lesions sustained. Occasionally proton spectroscopy may identify the presence of an abnormal peak in a neonate with a metabolic disorder, masquerading as HIE encephalopathy (HIE). Most commonly this is glycine, demonstrated at short echo times, in an infant with non-ketotic hyperglycinaemia [14].

There are few, if any, clinical indications for using perfusion-weighted imaging in suspected perinatal brain injury. There are several reports in the literature using contrast-enhanced methods and one or two exploiting 3T systems to perform arterial spin labelling (ASL) [15, 16]. Both techniques allow the relative differences in perfusion between white and gray matter in both apparently normal and abnormal tissue to be assessed. Absolute quantification is always a problem, where factors such as levels of haemoglobin, blood viscosity and blood carbon dioxide levels need to be addressed prior to quantification. These techniques remain very much in the research arena and may have a role in interventional studies although current

concerns over the use of contrast agents favours developing the ASL approach at higher field strength.

When time is limited, because of heavy demand on the scanner or concerns about the neonate waking up, it is important to prioritise sequences for each neonate depending on the clinical history and the assumed underlying diagnosis.

Image interpretation should be performed by an experienced person, with knowledge of the normal appearances of the term neonatal brain (Fig. 1), although published data with normative values is not prolific, largely because of ethical restrictions on imaging normal term neonates in some centres [17, 18]. The accurate interpretation of image findings also requires information on the antenatal, perinatal and neonatal details, a sound knowledge of the range of lesions seen in perinatal brain injury and the effect of timing from injury on their appearance.

Clinical history

The pattern of injury sustained by a neonate is influenced by the nature of the insult and to some extent the gestational age. The pattern of injury may be predicted by the clinical history and the clinical presentation [21-31]. Term born neonates who sustain perinatal brain injury may present with an encephalopathy or with isolated seizures. HIE describes those neonates who become encephalopathic following an apparent hypoxic-ischaemic event that may be evidenced by signs of fetal distress on cardiotocograph (CTG), a low cord pH and a necessity for resuscitation. In a minority of neonates with HIE there will be a well documented sentinel event, such as a uterine rupture or cord prolapse, but in the majority fetal distress develops without obvious cause. Those neonates with a history of a sentinel event are likely to sustain basal ganglia and thalamic (BGT) lesions (Fig. 2) [28]. These are usually accompanied by abnormalities in the appearance of the intervening posterior limb of the internal capsule (PLIC). In severe cases there may also be brainstem involvement (Figs. 2 and 3). This pattern is seen irrespective of gestational age [29]. Term born neonates with this imaging signature of an acute hypoxic-ischaemic insult may also develop abnormal signal intensity (SI) in specific cortical regions, usually around the central sulcus, the interhemispheric fissure and the insula (Figs. 4 and 5). These cortical changes are most obvious on T1-W images and are usually accompanied by abnormal intensity in the adjacent subcortical WM. Both the cortical and subcortical changes may not be obvious until the end of the first week following birth (Fig. 5). It is unusual to identify isolated cortical lesions in the absence of lesions in the BGT or WM. The presence of isolated cortical lesions should raise suspicion of a sinus thrombosis.

In those neonates who fulfil the clinical criteria for HIE, but without a history of a sentinel event, BGT lesions are still the most prevalent, but these are accompanied by more widespread WM injury in approximately a half of cases (Fig. 6).

Isolated WM and cortical injury with normal BGT is a rare pattern of injury in neonates with HIE and is more likely to be detected in neonates with an atypical clinical course and without the need for major resuscitation following delivery. Neonates with HIE following a history of decreased fetal movements tend to sustain WM injury either in isolation or in combination with BGT lesions (Fig. 7) [30]. Many infants with cortical and WM injury present with isolated seizures rather than HIE. Injury may take the form of a focal WM infarct or "stroke" or bilateral parasagittal infarction (Figs. 7 and 8) [21]. Focal infarction is more likely to occur in infants born to primigravida

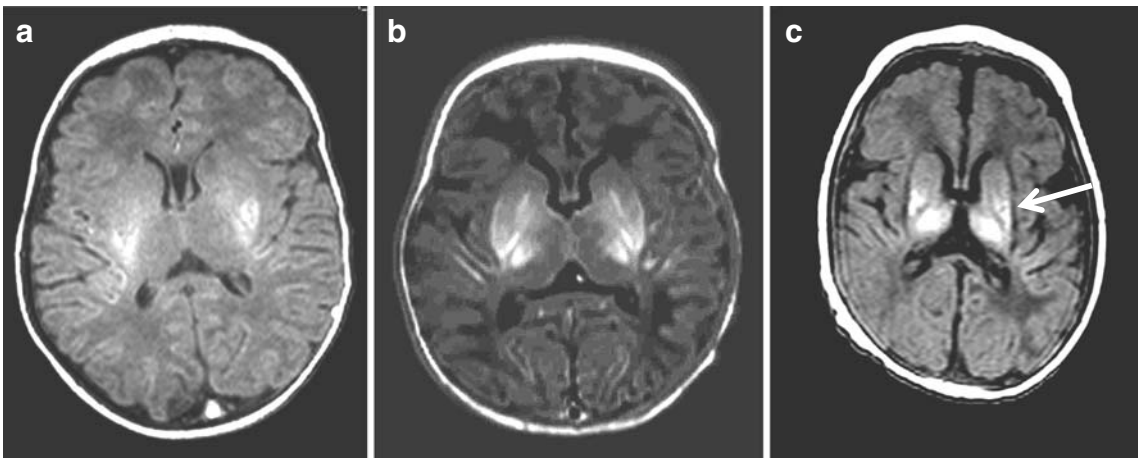

Fig. 2 BGTs. Range of severity of BGTs in term born neonates with HIE. T1-W images show focal regions of abnormal high SI. The severity of BGT can be graded into mild (**a**) moderate (**b**) and severe (**c**). There is already atrophy of the BGT with flattening of the border of the lateral lentiform nucleus (*arrow*, **c**). The more severe the lesions the more severe the motor impairment in the form of cerebral palsy

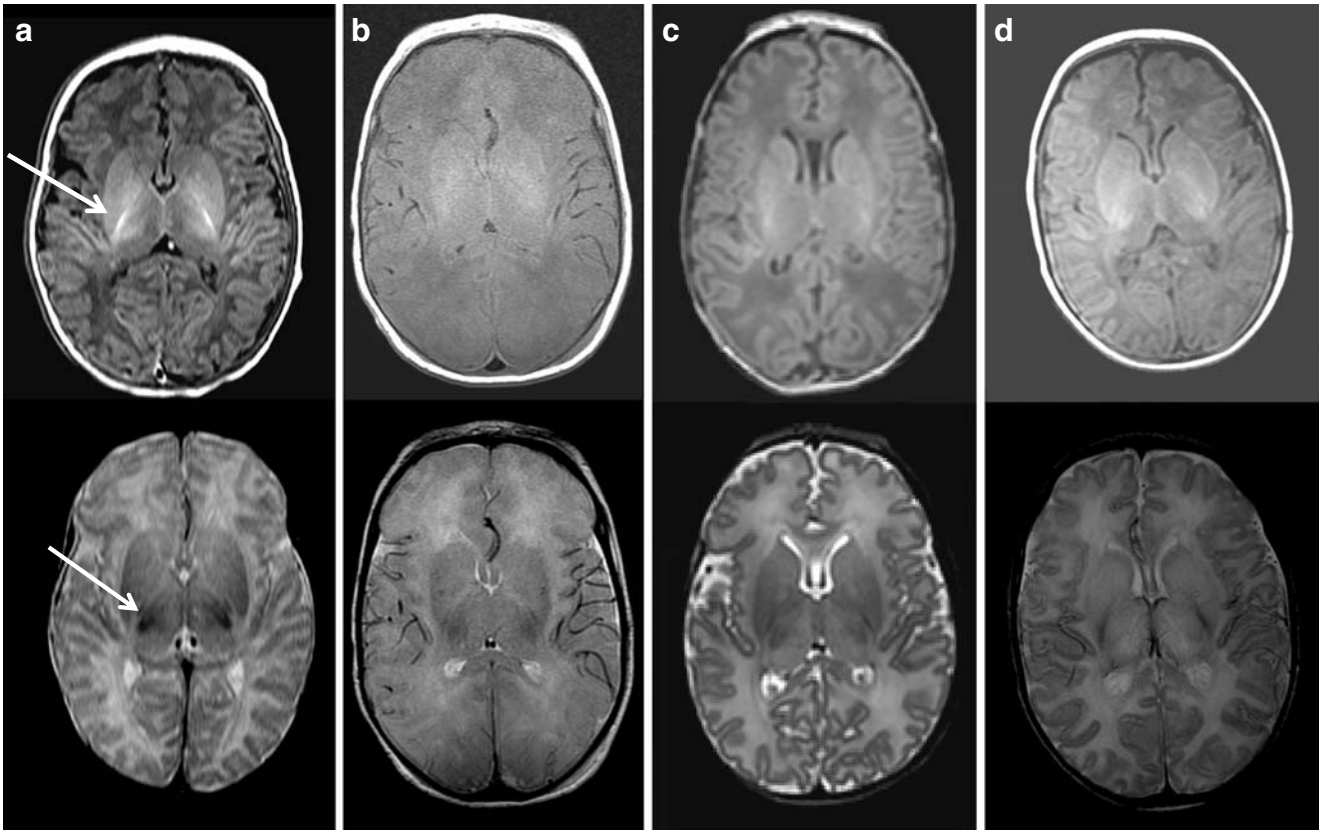

Fig. 3 Appearances of the PLIC on T1-W images (*top row*) and T2-W images (*bottom row*). **a** Normal appearances of the PLIC (*arrows*). Abnormal appearances of paired T1- and T2-W sequences **(b, c, d)** in three different infants with HIE. It is important to use both T1- and T2-W sequences to assess the PLIC

women; delivery may be difficult and some resuscitation may be required but the infant usually recovers sufficiently and does not require admission to neonatal intensive care. Within this group with mainly WM and cortical injury there are also more likely to be neonates with alternative or additional pathologies e.g., cerebral malformations, infection, metabolic disorders, hypoglycaemia (Fig. 9) [23, 31].

The clinical presentation therefore serves as a guide to the lesions that will have been sustained and it is important to obtain all relevant details prior to image interpretation. This should include gestational age, antenatal history, type of delivery, Apgar scores, resuscitation, neonatal course, family history.

Timing of imaging examination

Perinatal brain lesions are at their most visually obvious on conventional MR sequences between 1 and 2 weeks from birth. This is therefore the most useful time to image to assess the extent of injury. In addition, neonates are more likely to be clinically stable and off assisted ventilation by this time and in those infants receiving treatment with hypothermia (that is continued for 72 h) this will have been completed. Earlier imaging, within the first few days, may be required to make a diagnosis or to assist clinical management. Imaging within the first couple of days may demonstrate only subtle abnormalities on conventional sequences in the presence of significant brain injury (Figs. 7 and 10). Early image examinations should always therefore include a diffusion-weighted sequence. DWI, which is available on most modern scanners, should identify ischaemic WM (Figs. 7 and 8) but is not so reliable at detecting significant injury to the BGT, where it may underestimate the extent of the lesions (Fig. 11).

The visual appearances of infarcted tissue on DWI are obvious very early and last for 7–14 days (Fig. 12) [17]. By this time conventional imaging should be overtly abnormal. Occasionally visual analysis of the DWI is unremarkable or difficult to interpret particularly in the presence of widespread injury where there is no normal tissue for comparison. Most scanners have the software necessary to obtain ADC values from the trace diffusion images. Several studies have reported their own centres values for ADC within the normal term brain (Table 4) [17, 18]. It is

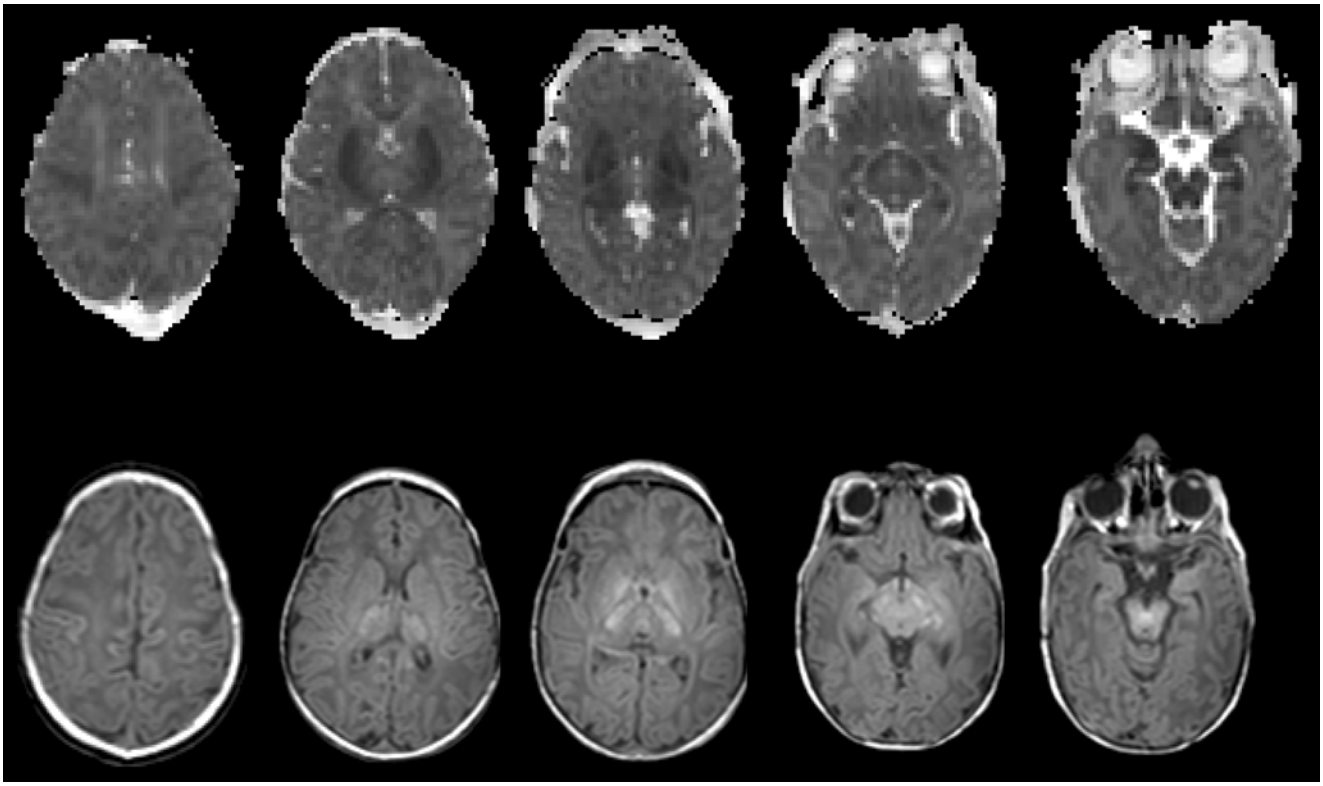

Fig. 4 Acute hypoxic-ischaemic injury. Lesion sites in a term born neonate with HIE following an acute sentinel event. Top row: diffusion-weighted images (ADC map) acquired on day 5 shows abnormal low SI in the cortex of the central sulcus, central grey matter, medial temporal lobe and brainstem (from *left* to *right*). These are characteristic sites for an acute hypoxic-ischaemic injury. Bottom row: by day 11 in the majority of sites these abnormalities have become obvious as high SI on T1-W images

recommended that ADC values are measured in all infants even when the DWI appears unremarkable (Fig. 13). During the first week from injury ADC values are usually decreased in the presence of ischaemic WM and then show pseudonormalisation. In clinically significant BGT lesions however, ADC values may be reduced, normal or elevated (Fig. 11) [17]. In addition, abnormalities consistent with restricted diffusion appear to involve different regions within the BGT over time (Fig. 12) [19]. Any single diffusion examination is therefore likely to underestimate

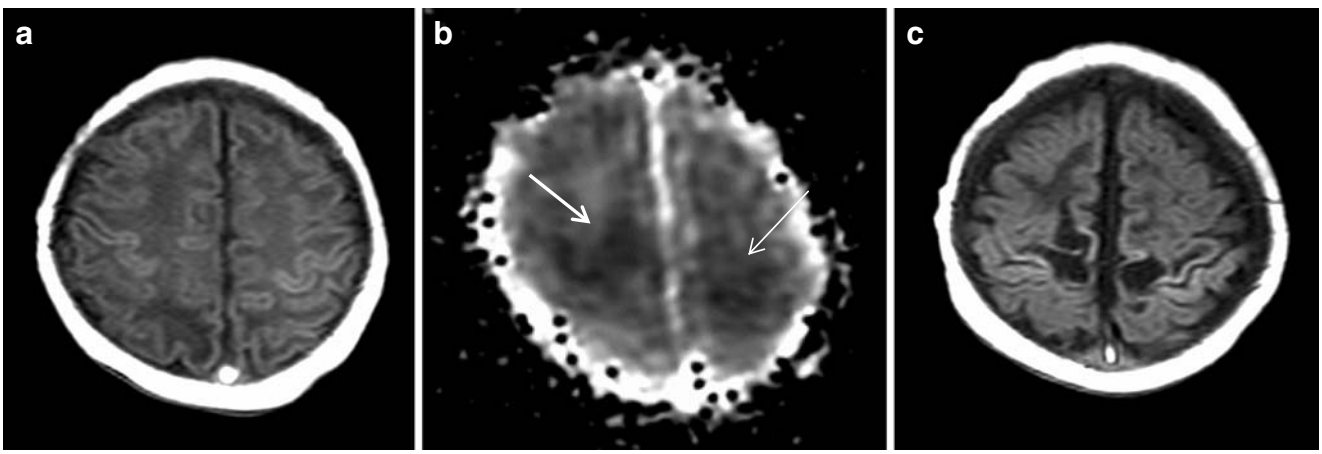

Fig. 5 Cortical and subcortical WM lesions in a term born neonate with HIE. T1-W images at the level of the central sulcus (**a, c**) and ADC map (**b**) at 3 days show minimal highlighting of the cortex of the central sulcus on conventional images (**a**) but marked restriction of diffusion with low SI on the ADC map (**b**). By day 14 there is overt cortical highlighting and abnormal low SI in the adjacent subcortical WM (**c**). This pattern of injury is usually present in neonates with moderate and severe basal ganglia lesions

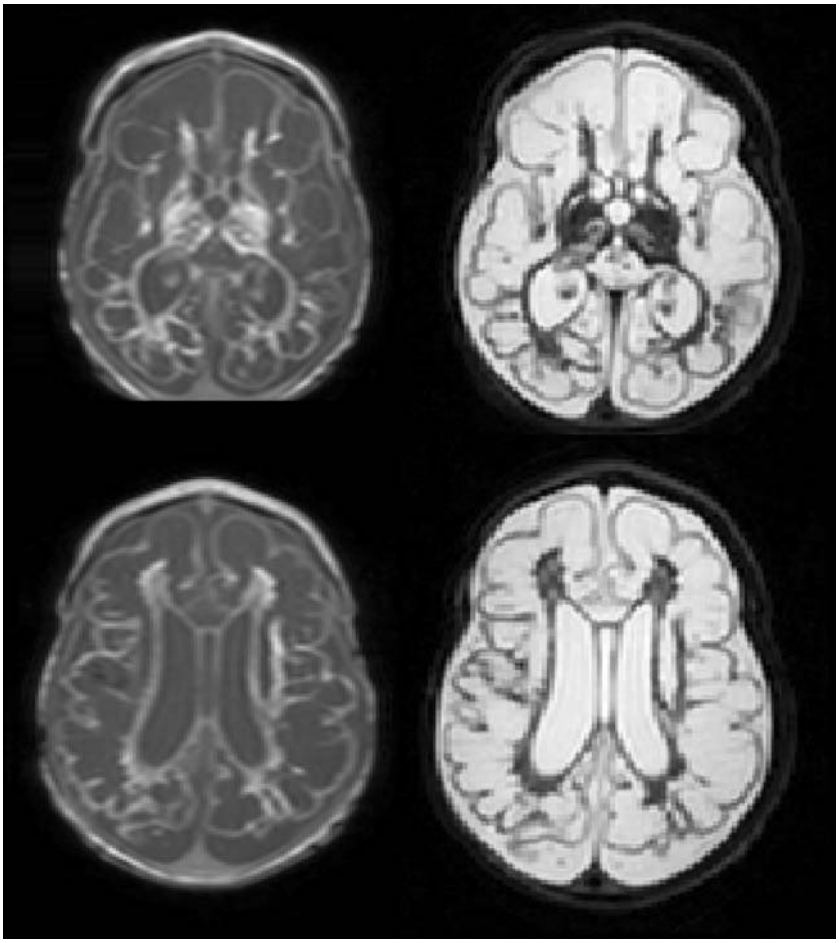

Fig. 6 Widespread injury in a term born neonate with severe brain injury and multiple aetiological factors (delivered by emergency caesarian section for antepartum haemorrhage, low Apgar scores, hypoglycaemia on day 1, seizures on day 3 and herpes positive). T1- (*left*) and T2-W (*right*) images at 4 weeks of age. There is widespread infarction with abnormal signal intensities throughout the brain

the total lesion load in the BGT. We take a value of $<1\times10^{-3}$/mm^2/s in term WM to be consistent with impending infarction. The range of abnormal values for ADC within the BGT is much narrower and therefore it is less easy to predict irreversible infarction but levels $<0.7\times10^{-3}$/mm^2/s are associated with significant lesions (Table 4). In addition, because values within the central grey matter can be both abnormally low and abnormally high in adjacent

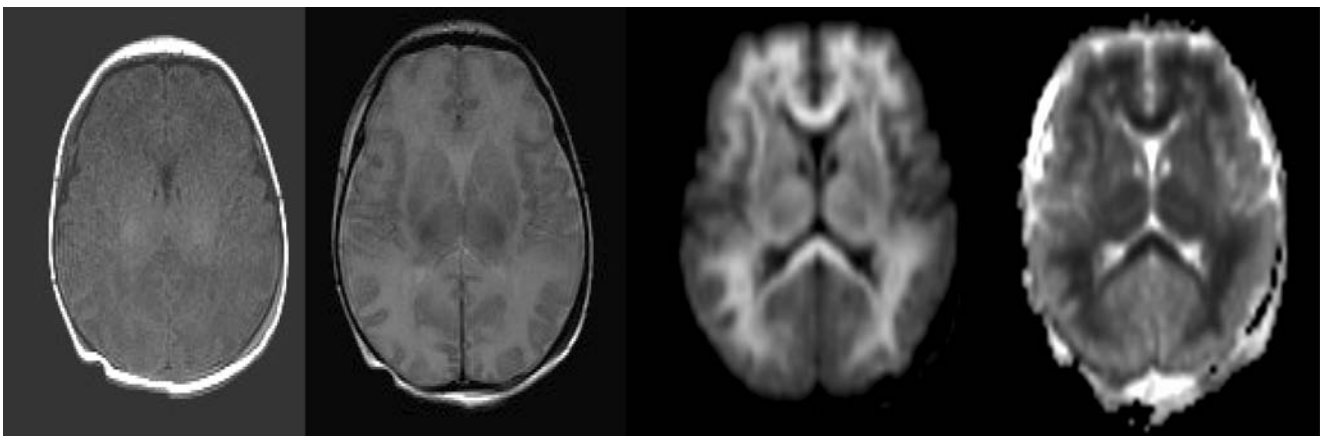

Fig. 7 WM lesions. Term born neonate with HIE following a history of decreased movements after 48 h. Images taken on day 2 with T1-W, T2-W, diffusion-weighted sequences and an ADC map (left to right) show some loss of grey-white matter differentiation on the conventional T1- and T2-W images. There is widespread abnormal SI throughout the WM and some thalamic involvement on DWI and the ADC map. Extensive WM involvement with no basal ganglia injury is an uncommon pattern of injury in neonates fulfilling criteria for HIE and is very unusual in infants with HIE and a history of a sentinel event e.g., uterine rupture

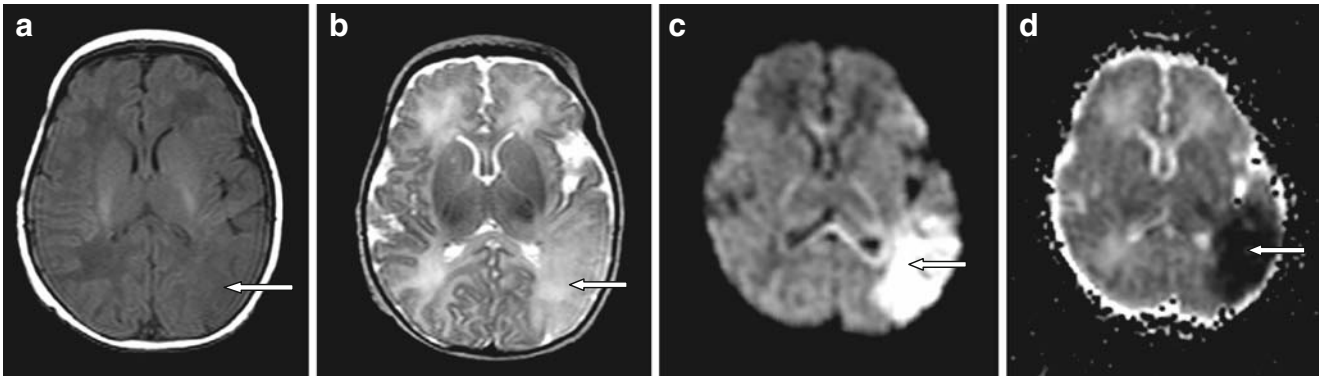

Fig. 8 Middle cerebral artery infarct. Five-day-old term born infant with left middle cerebral artery infarct (*arrows*). The abnormalities are quite subtle on the T1-W images (**a**), more obvious on the T2-W images (**b**) but most obvious on the DWI (**c**) and ADC trace map (**d**)

tissue, an ADC value may be measured as within the normal range because of partial volume effects. Measures of fractional anisotropy (FA) may be useful in detecting persistent abnormalities within tissue after the first week from injury. FA values have been shown to continue to decrease in abnormal tissue that shows pseudonormalisation of the ADC value [20].

Serial imaging provides information about the secondary effects of an acute hypoxic-ischaemic insult. In neonates with BGT lesions the WM may show initially normal ADC values that increase over time as part of a secondary WM injury. The WM then shows signs of atrophy on subsequent scans and the infant shows poor head growth (Fig. 11).

There has been speculation that treatment with hypothermia will delay the appearance of abnormalities on MRI.

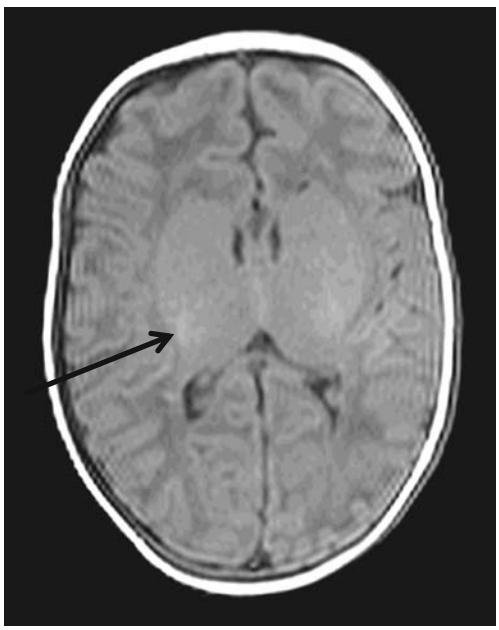

Fig. 9 Near normal imaging in HIE. Term born neonate with hypotonia and seizures. T1-W image shows slight delay in myelin in the PLIC (*arrow*). There was no evidence of any acquired lesions. The final diagnosis was non-ketotic hyperglycinaemia

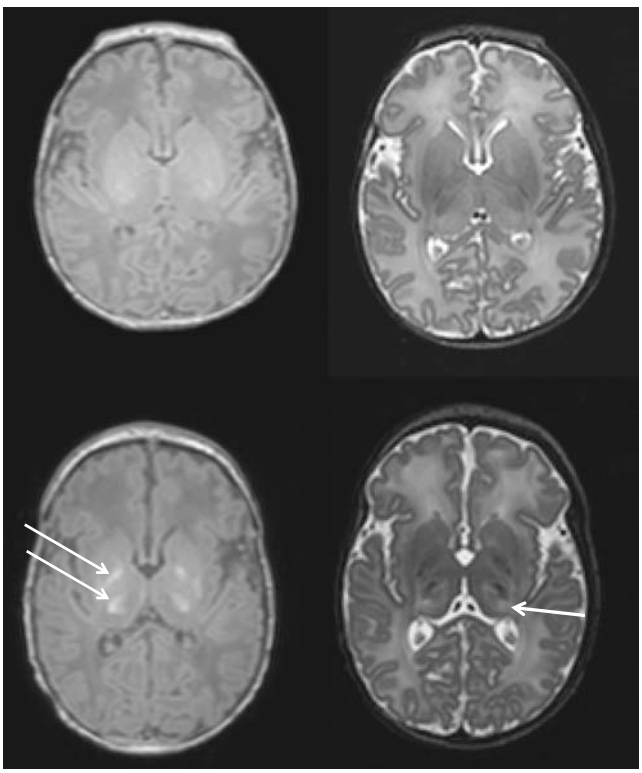

Fig. 10 Evolution of BGTs. Term born neonate with HIE. T1- (*left*) and T2-W (*right*) images. Top row: imaging on day 4 shows subtle changes within the BGT. The PLIC does not have a normal appearance. The T1-W images show a reduction in the high SI from myelin for a term infant. On the T2-W images there is an excessive amount of low SI. Normal myelination in the PLIC is usually more obvious on T1-W sequences. The basal ganglia are also slightly swollen and homogeneous in appearance. Bottom row: imaging on day 14 shows the abnormalities within the BGT are now more prominent with obvious foci of increased SI on T1-W images (*arrows*). The BGT appear smaller due probably to a reduction in initial swelling but they may also have started to atrophy. There are corresponding foci of abnormal low SI on the T2-W image (*right*) with additional regions of high SI (*arrows*)

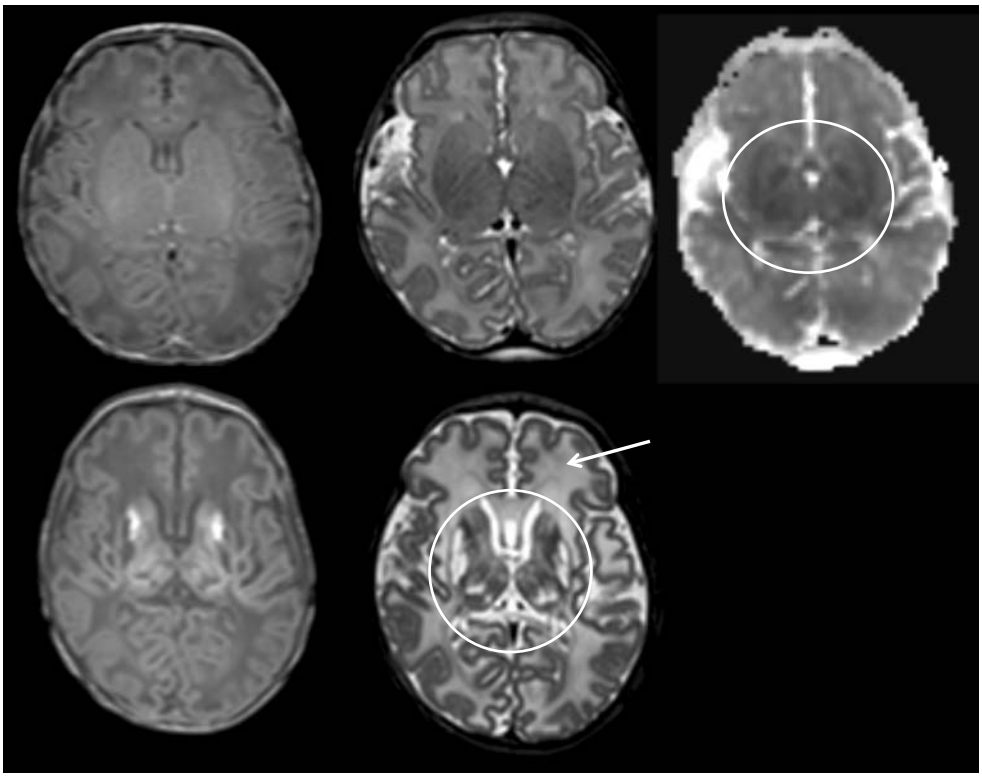

Fig. 11 DWI in the BGT. Top row: T1- (*left*) and T2-W (*middle*) images and ADC map (*right*) acquired on day 3. The original ADC map shows several regions of abnormal low SI within the BGT that look relatively subtle (*circular region of interest*). Bottom row: day 22. T1- (*left*) and T2-W (*right*) images show BGT abnormalities are very severe with no normal looking tissue within the BGT (*circular region of interest*). Any abnormality within the BGT on an early ADC map is likely to be clinically significant and any one diffusion-weighted examination is likely to underestimate the final lesion load. By day 22 the WM SI (*arrow*) has become abnormally high and there has been no head growth

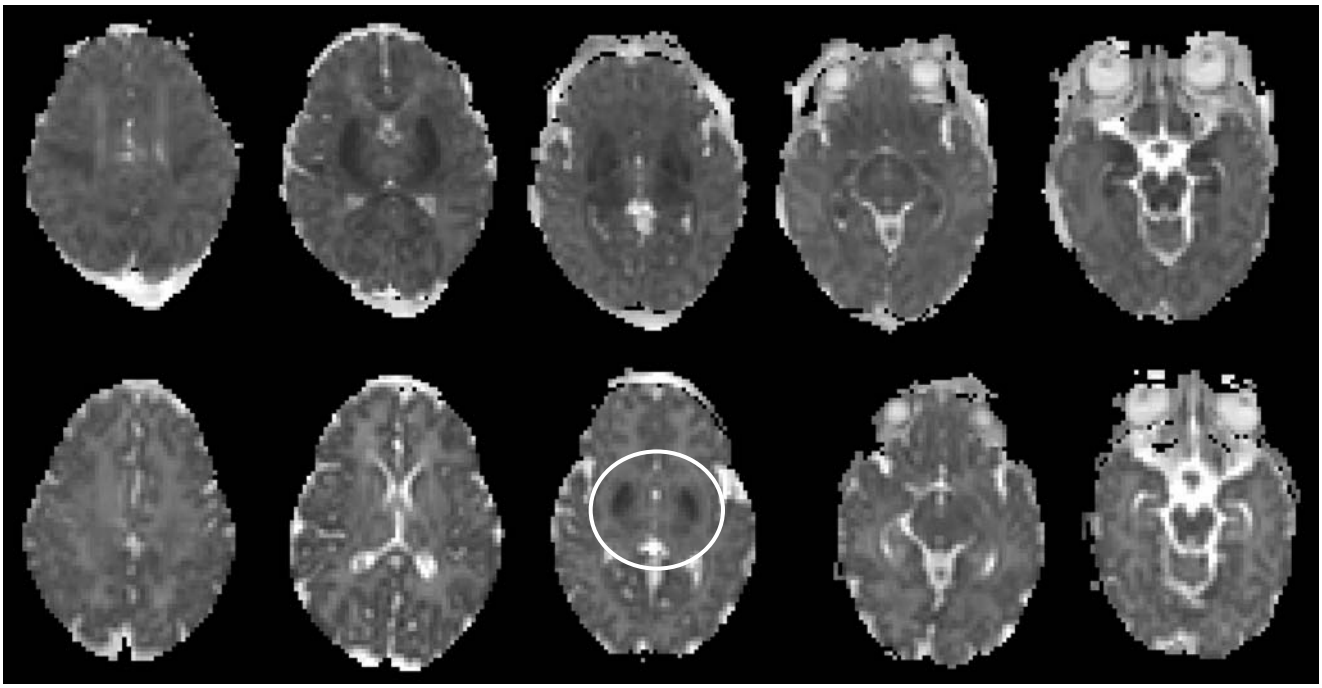

Fig. 12 Evolution of abnormalities on diffusion ADC maps. Top row: imaging at day 5 shows abnormal low SI in the cortex of the central sulcus, central grey matter, medial temporal lobe and brainstem (from *left* to *right*). Bottom row: imaging at day 11 shows areas of abnormal low SI consistent with restricted diffusion and ischaemia disappear in many areas. Appearances on an ADC map evolve over time between day 5 and day 11. Within the BGT (*circular area of interest*), abnormalities may move from one region to another

Table 4 ADC Values (median [range]) in different brain regions in term controls and neonates with HIE (taken from Rutherford et al. [17])

Region	Controls (ADC [$\times 10^3$/mm^2/s])	All HIE patients (ADC [$\times 10^{-3}$/mm^2/s])
Thalami	1 (1–1.15)	1 (0.5–1.4)
VLN	0.88 (0.76–0.95)	0.85 (0.39–1.2)
Lentiform	1.1 (1–1.3)	1.05 (0.5–1.65)
PLIC	1 (0.83–1.2)	0.9 (0.48–1.5)
WM CSO	1.5 (1.3–1.7)	1.43 (0.5–2.0)
WM anterior	1.6 (1.5–1.7)	1.5 (0.6–1.95)
WM posterior	1.55 (1.35–1.85)	1.5 (0.5–1.9)
Cerebellar		
Hemispheres	1.1 (1–1.25)	1 (0.8–1.3)
Vermis	0.97 (0.8–1.2)	0.98 (0.7–1.2)
Brainstem	0.98 (0.86–1.1)	0.92 (0.5–1.25)

VLN ventrolateral nucleus, *CSO* centrum semiovale

As the evolution and pattern of lesions may be very variable between individual infants, any potential effect on the evolution of abnormalities would need to be studied in large numbers of infants. It is possible that with the routine use of hypothermia as a treatment strategy in clinical practice we will be in a better position to assess the effect of hypothermia on imaging appearances. With or without hypothermia the second week from delivery is the ideal time to detect the extent of acquired lesions on conventional imaging. In the recently published TOBY trial the presence of hypothermia did not influence the ability of a neonatal MRI (median 8 days) to predict neurodevelopmental outcome [1].

There is a predictable evolution of perinatal brain lesions and so serial imaging may allow the timing of injury to be assessed. Repeat imaging may also be useful to identify atypical evolution of imaging abnormalities, particularly when an additional or different diagnosis such as a metabolic disorder is suspected. In some metabolic disorders there are additional congenital malformations of the brain

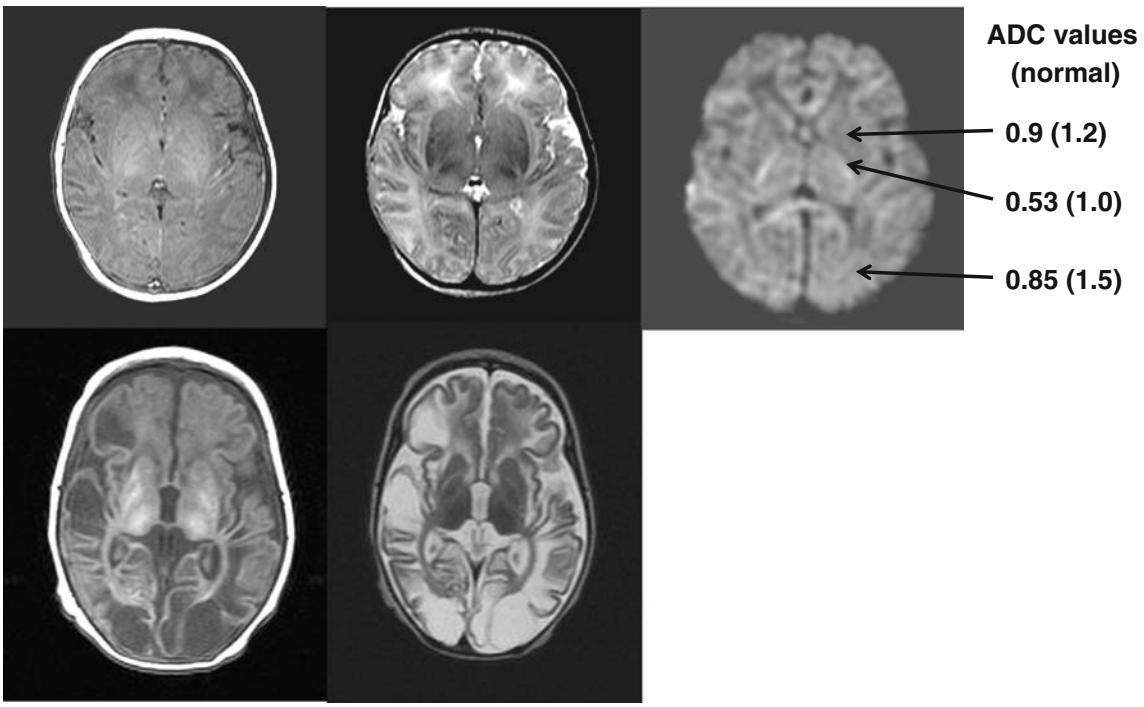

Fig. 13 Widespread lesions in a term born neonate with HIE. Top row: T1- (*left*) and T2-W (*middle*) and diffusion-weighted (*right*) images acquired on day 2 show loss of anatomical detail throughout the brain on the T1-W image but the changes are quite subtle. There is some WM high SI on the T2-W image. The DWI shows linear areas of increased SI mainly in the cortex but no larger focal lesions of altered SI. However, on the ADC map all regions of the brain showed marked reduction in ADC. Bottom row: at 15 days there has been widespread infarction throughout the hemispheres with abnormal SI and some atrophy of the BGT seen on both T1- (*left*) and T2-W (*right*) images

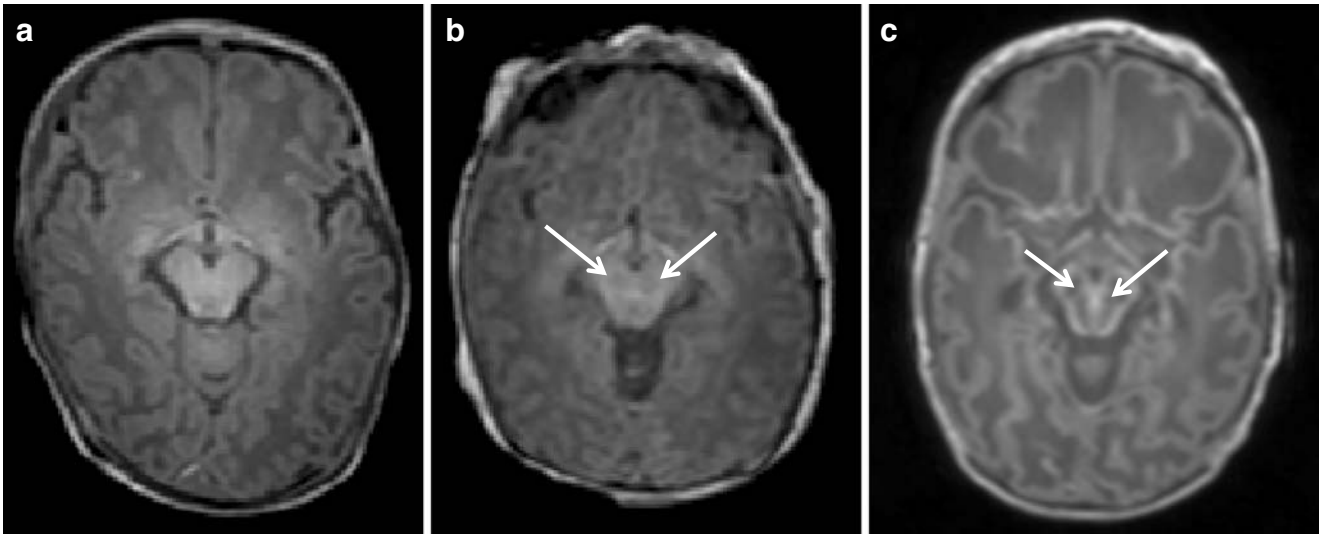

Fig. 14 Brainstem lesions. T1-W images at the level of the mesencephalon shows normal (**a**), moderately abnormal with low SI regions (**b**, *arrows*) and severely abnormal appearances with widespread low SI (**c**, *arrows*)

such as agenesis of the corpus callosum in non-ketotic hyperglycinaemia. A normal scan or an isolated delay in myelination in a neonate with persisting seizures should raise the possibility of a metabolic disorder (Fig. 9).

Patterns of injury and prediction of outcome

MR imaging provides detailed information about the pattern of lesions following perinatal brain injury and conventional sequences may provide excellent predictions of outcome.

In neonates with a global hypoxic-ischaemic insult, lesions are usually detected within the BGT with abnormal SI in the intervening posterior limb of the internal capsule (PLIC) (Fig. 3). Abnormal SI within the PLIC is an excellent predictor of abnormal motor outcome in term infants with HIE [32]. BGT lesions give rise to motor impairment in the form of cerebral palsy. The severity of the BGT lesions dictates the severity and nature of the cerebral palsy (Fig. 2) [28]. Lesions within the brainstem are usually found in those neonates with the most severe form of BGT injury and are often associated with early death (Fig. 14) [33]. In those neonates that survive,

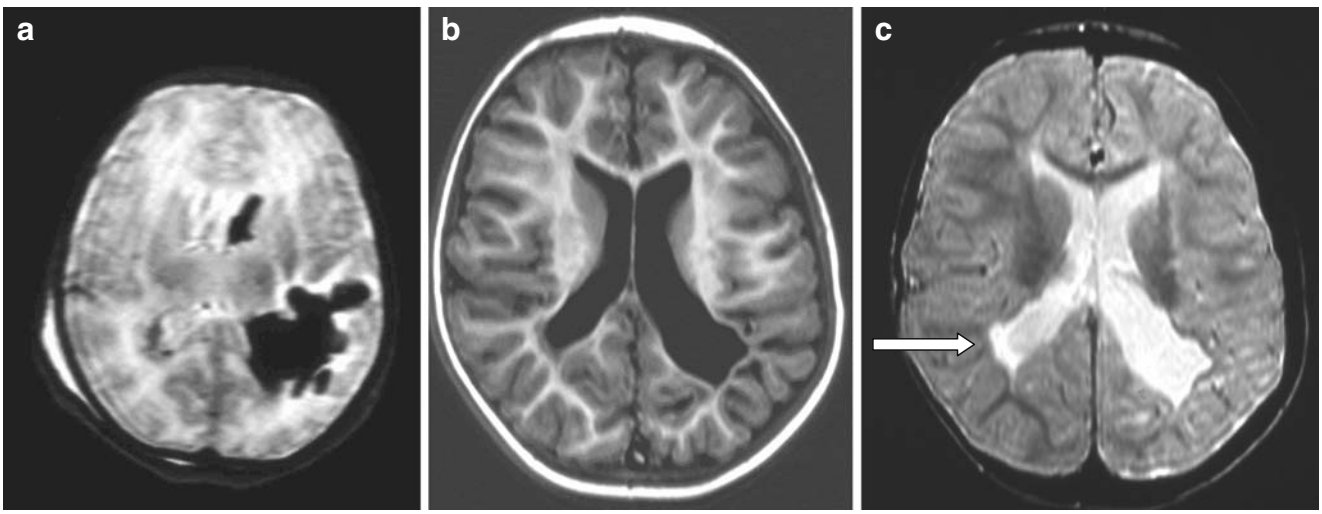

Fig. 15 Haemorrhagic WM lesions in a term born neonate presenting with encephalopathy. Neonatal imaging T2-W sequence (**a**) shows a large haemorrhagic lesion in the WM of the left parietal lobe with additional haemorrhage in the right posterior periventricular WM and in the left caudate head. Follow-up imaging at 16 months. Inversion recovery (**b**) and T2-W sequence (**c**) show posterior WM loss, decreased posterior myelination and glial tissue seen in the right periventricular WM (*arrow*). The ventricles show irregular dilatation. These image findings are very similar to those found in preterm infants with a diagnosis of PVL

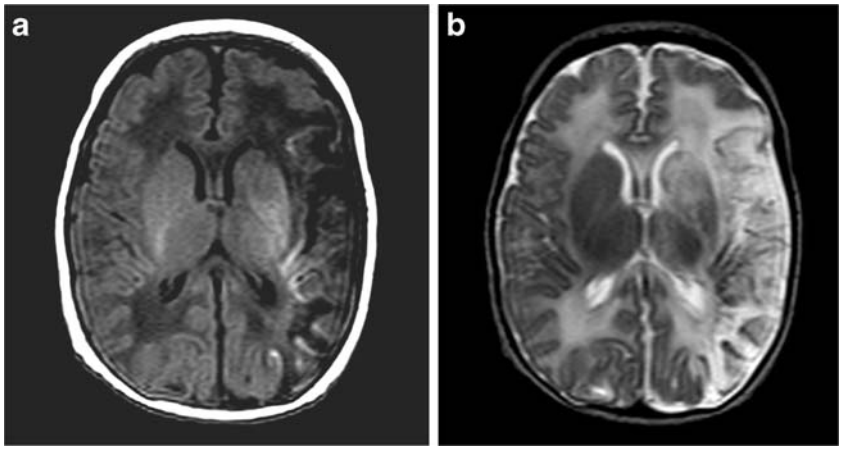

Fig. 16 Left-side middle cerebral artery infarction. Three site involvement in a term born infant presenting with seizures. T1- (**a**) and T2-W (**b**) images at 10 days of age show abnormal SI within the hemisphere, lentiform nucleus, thalamus and internal capsule on the left. This triple site involvement is strongly predictive of a later hemiplegia [37]

persisting feeding difficulties and a necessity for gastrostomy are common. In the presence of severe BGT injury there are usually secondary WM changes with subsequent atrophy, poor head growth with the development of a secondary microcephaly and cognitive impairment [34]. In approximately 50% of neonates with BGT lesions there will be more extensive WM abnormalities seen on the initial scan consistent with a primary injury (Figs. 6 and 13) [23, 24]. The motor outcome for these children is still dictated by the BGT lesions but the more severe WM involvement may exacerbate any cognitive deficit and results in very poor head growth [34].

In some neonates who present with what is thought to be HIE there is no BGT involvement but only WM lesions (Fig. 7). These may be haemorrhagic (Fig. 15). These lesions give rise to tissue atrophy, poor head growth and the development of a secondary microcephaly and are associated with later cognitive impairment. The more severe the WM lesions the worse the cognitive outcome and the greater the likelihood of some motor impairment [35, 36]. In neonates who have a term perinatally acquired WM injury, follow-up imaging may be indistinguishable from what would normally be called periventricular leucomalacia (PVL), an injury thought specific to the more preterm brain (Fig. 15). Without knowledge of the clinical neonatal history, the injury may therefore be wrongly attributed to antenatal damage at an earlier gestation. However in an infant with signs of PVL, on imaging and/or clinically, who was born at term it is probably only reasonable to implicate perinatal events if there were neonatal symptoms such as encephalopathy or seizures.

Focal infarction usually involves the territory of the middle cerebral artery, the left side being more commonly affected than the right (Fig. 16). The outcome following an MCA infarct depends on the extent and sites involved. If there are abnormalities within the parenchyma, BGT and PLIC then the child is likely to develop a later hemiplegia (Fig. 16) [37].

The relationship between ADC values and outcome is complicated. Detection of WM infarction may not relate closely to later outcome as it depends how this is defined and when it is measured [38]. Abnormally low ADC values within the PLIC or the BGT are more likely to predict the development of a significant motor impairment that will be detectable within the first two years [13, 38, 39]. Neonates with reduced ADC values within the WM consistent with acute infarction may have a good short term outcome as in the presence of normal BGT and a normal PLIC, motor development may be normal. Poor head growth should raise suspicion and these children may present in early childhood with neurocognitive and behavioural impairments.

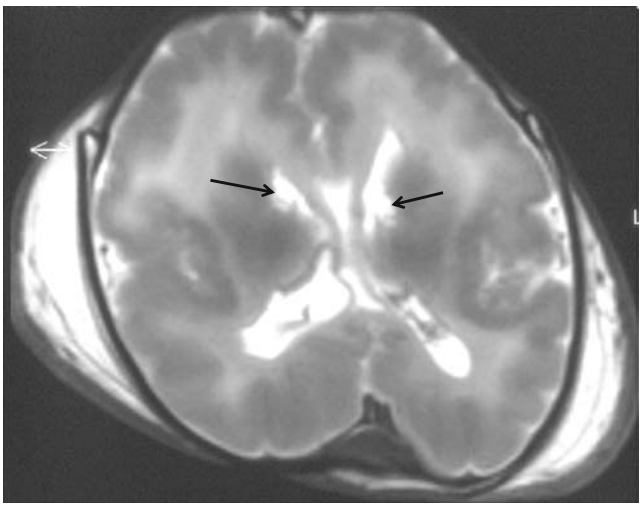

Fig. 17 Alternative diagnosis. Term neonate diagnosed with HIE. Post mortem imaging, T2-W sequence. There is extensive polymicrogyria of the cortex and bilateral subependymal cysts. A final diagnosis of the perioxisomal disorder, Zellweger syndrome, was made by tissue biopsy

Post mortem imaging

Infants with severe encephalopathy should always have brain imaging. This may be difficult and it may not be possible to perform before an infant dies. In such circumstances and particularly if no autopsy is performed post mortem MR imaging should be considered. The usual neonatal protocol can be followed; increasing the signal averages will improve the SNR. T2-W images are usually of better quality than T1-W images. Post mortem imaging may allow confirmation of abnormalities consistent with a hypoxic-ischaemic insult or suggest an alternative diagnosis (Fig. 17) [40]. This would clearly have important genetic counselling and medicolegal considerations.

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