13 Brain Imaging: Magnetic Resonance Imaging

Arastoo Vossough

Abstract

Imaging plays an important role in elucidating many of the aetiologies of cerebral palsy in children. Magnetic resonance imaging is a particularly powerful tool in the evaluation of the causes of cerebral palsy, both in the acute and chronic phases. We will review the role of MRI in assessment of various aetiologies contributing to cerebral palsies. These categories include congenital malformations, intracranial haemorrhage, hypoxic-ischaemic injury, periventricular leukomalacia and white matter injury of prematurity, perinatal ischaemic stroke and a number of other neonatal encephalopathies. In this chapter, we will review the utility of MRI in the evaluation of cerebral palsy in the young child.

13.1 Introduction

The American Academy of Neurology and the Child Neurology Society have recommended that neuroimaging of the central nervous system be a part of the diagnostic process for all patients with cerebral palsy [1]. While not all experts may agree with this recommendation, there is no doubt that neuroimaging can shed light into the possible aetiologies, extent of brain involvement, potentially better timing of responsible lesions and the complexity of the motor spectrum of disability [2, 3].

Imaging can be important in differentiating various disorders underlying cerebral palsy (CP), with further implications for treatment and prognosis. Most (83%) children with CP have abnormal neuroradiological findings [4]. In the early postnatal period, it may provide diagnosis of the specific brain injury or anomaly. Imaging in this phase of the newborn at risk may be of importance, as some lesions, particularly those of mild-to-moderate degree, may not be visible at a later date when the full-blown clinical picture of CP is apparent. Furthermore, prognostic assessments can be made with regard to the risk of neurodevelopmental disability. Imaging at the time the diagnosis of CP has been made provides information on the type and extent of the end-stage brain damage. The specification of a

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subtype of CP may also be possible on detection of characteristic neuroimaging findings. These can help in providing adjunct data in planning early interventions and treatments tailored to the specific needs of the child.

Hypoxic-ischaemic insults to the brain, neonatal encephalopathies, intracerebral haemorrhage, congenital malformations and congenital infections of the central nervous system are considered among a long list of possible aetiologies to be the leading causes of cerebral palsy (see Chap. 5) [4–6]. The precise aetiologic factor may not be recognised in many cases, but a common risk factor is prematurity [7]. In recent years, substantial improvement in the survival rates of very-low-birth-weight (VLBW) infants has been associated with an increase in the rates of CP [8]. The combination of increasing number of cases and advancements in various neuroimaging modalities has further facilitated the diagnostic imaging studies in CP. These comprise primarily of ultrasonography (US) and magnetic resonance imaging (MRI). The prospective comparison of state-of-the-art brain US with MRI for neonatal encephalopathy has brought to light the real value of US contrary to the relatively poor review of older retrospective studies [9]. In this study the head US and MRI were performed within 2 h in 76 consecutive patients. The comparison of these two modalities with MRI as the reference method revealed the following results for cranial US: sensitivity 100% (CI: 94.1–100), specificity 33.3% (CI: 7.5–70), positive predictive value (PPV) 91% (CI 81.5–96.6), negative predictive value (NPV) 100% (CI: 29.2–100) and accuracy 95.7%. The authors also noted that the parenchymal abnormalities depicted on US are not as florid or conspicuous as on MR, and fewer focal lesions may be detected. Consequently, US might underestimate the degree of injury and just reveal the tip of the iceberg. In light of these findings and particularly of the very high negative predictive value, US remains an excellent screening method, and MRI retains its position as the method of choice to obtain more detailed and accurate information [9, 10].

13.2 Magnetic Resonance Imaging (MRI) for Evaluation of Cerebral Palsy

The advantages of MRI in the imaging assessment of cerebral palsy include the ability to obtain high-resolution imaging in multiple planes, excellent tissue contrast between various structures in the brain and lack of radiation exposure. The disadvantages of MRI include less availability, high cost, long imaging times, sensitivity to patient motion, selective need for sedation, transport of very young or labile patients and problems with MR compatibility of monitoring or indwelling devices. Newer MRI techniques, such as diffusion-weighted imaging (DWI), diffusion tensor imaging (DTI), functional MRI (fMRI), perfusion MRI and magnetic resonance spectroscopy (MRS), have enhanced our capabilities to demonstrate injuries to the brain earlier, distinguish different patterns of brain injury and shed further light into the pathophysiologic mechanisms behind the neurological substrates of CP.

Similar to ultrasound, MRI can also provide prognostic information (see Chap. 12). For example, in analysis of several studies, 50–94% of the infants with changes in the basal ganglia on MRI had developed cerebral palsy, mental retardation and seizures at 1–2 years of age [11]. In a retrospective analysis of MR findings in 40 patients with cerebral palsy [12] found in the prematurely born patients signs of periventricular white matter damage. In those who had been born at term, three major patterns emerged: (1) gyral anomalies, suggestive of polymicrogyria, (2) isolated periventricular leukomalacia and (3) watershed cortical or deep grey nuclear damage.

Furthermore, MRI supports the categorisation of characteristic findings to a specific subtype of cerebral palsy [13]. In some patients with extrapyramidal cerebral palsy, focal high intensity in the posterior putamen and the anterior or posterior thalamus were detected [14]. PVL and posthaemorrhagic porencephaly have been categorised as preterm-type brain injury because

they are often based on immaturity of vascular system. *Border-zone* infarct, bilateral basal ganglia-thalamic lesion, subcortical leukomalacia and multicystic encephalomalacia are seen as more commonly term-type of brain injury due to the fact that these lesions have been more typically seen in asphyxiated term infants.

Okumura et al. [15] found that 84% of those with diplegia were born prematurely and in 88% showed MRI findings compatible with preterm-type brain injury. In the group with quadriplegia, only 33% were preterm-type, and 49% had term-type pathologic findings with 22% having various other brain anomalies. Patients with only hemiplegia had in 65% unilateral findings, and 42% were preterm-type lesions [16].

13.3 Congenital Malformations

A large variety of congenital malformations of the brain can cause CP and present with various functional impairments. These include microcephaly, holoprosencephaly, hemimegalencephaly, lissencephaly, heterotopias, schizencephaly, pachygyria, polymicrogyria, cortical dysplasia and infratentorial malformations, among others. In two large studies, approximately 8% of children with cerebral palsy had a congenital anomaly of the brain [17, 18]. The prevalence of cerebral anomaly was highest in children with ataxic CP (41.7%) and lowest in those with dyskinetic CP (2.1%). Conventional MRI is often crucial in the diagnosis of these entities and shows the severity of brain abnormality. The location and type of brain anomaly affects the incidence and type of cerebral palsy. For example, the location and extent of schizencephaly (Fig. 13.1), type of schizencephalic cleft (open vs. closed) and unilaterality vs. bilaterality of the disease will determine the extent of clinical symptomatology and motor deficit [19]. The use of higher-resolution and volumetric MRI imaging facilitates the detection of subtler cortical and subcortical abnormalities. For example, subtle cases of polymicrogyria may remain undiagnosed on routine

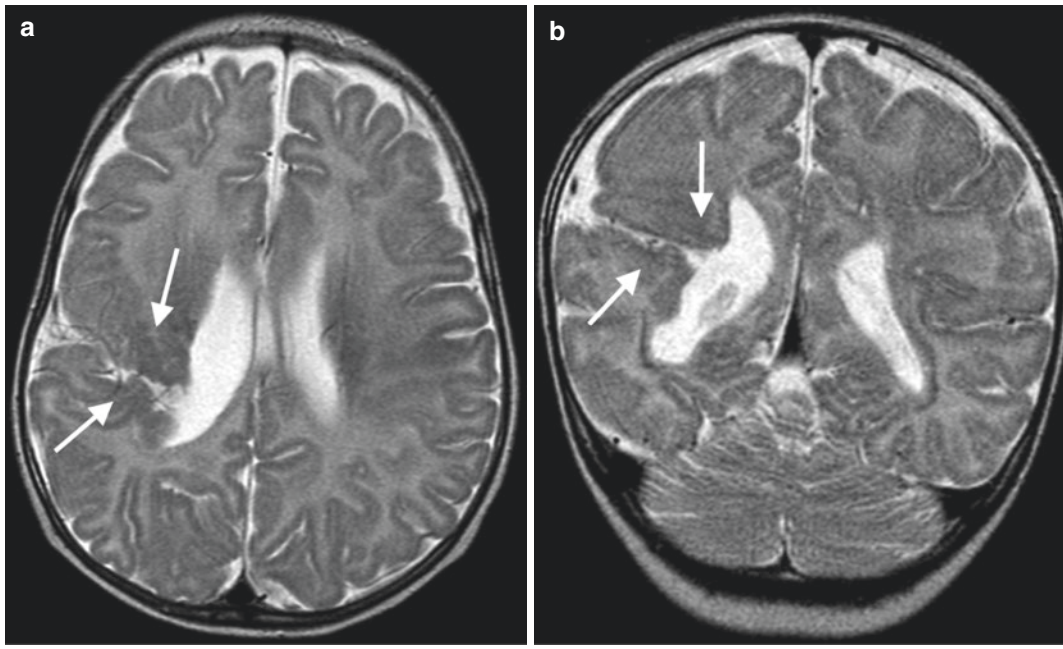

Fig. 13.1 Right-sided schizencephaly shown on axial (**a**) and coronal (**b**) imaging. The margins of the schizencephalic cleft are lined by grey matter (*arrows*)

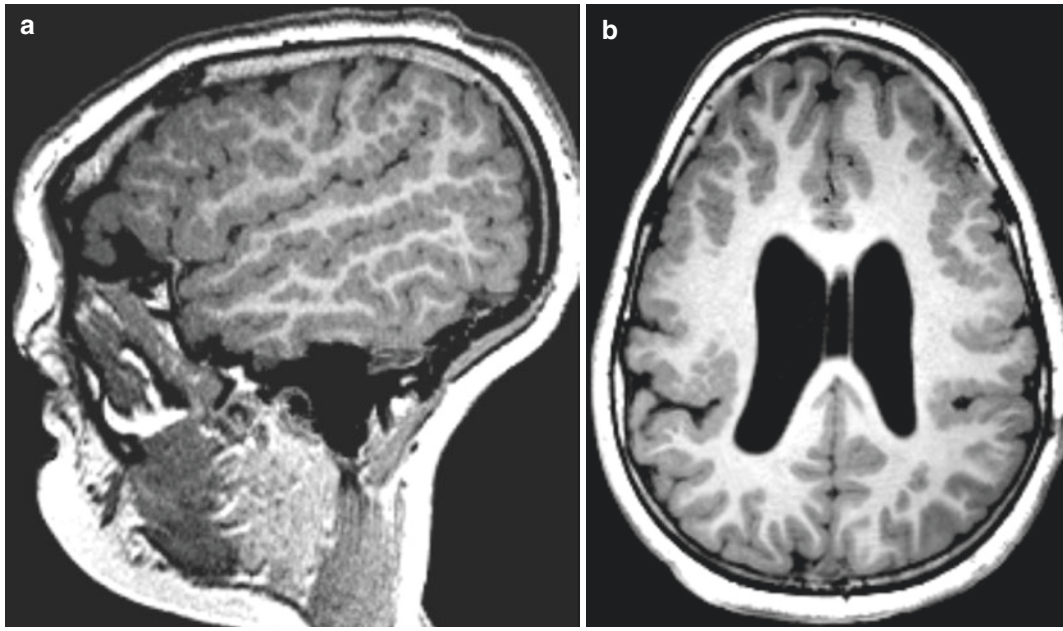

Fig. 13.2 Extensive bilateral perisylvian, frontal and temporal polymicrogyria as demonstrated on high-resolution sagittal (**a**) and axial (**b**) T1-weighted imaging at 3 T. Note the small serrated appearance of the grey-white matter junction due to polymicrogyria compared to a smoother junction in areas of normal cortex in the occipital and frontal poles

MRI exams, whereas higher-resolution scans increase the diagnosis rate. More extensive patterns of polymicrogyria are more easily detected by MRI (Fig. 13.2). Recent advances and more widespread use of foetal MRI result in more accurate diagnosis and characterisation of brain anomalies suspected on prenatal ultrasound; see also Chap. 12 [20].

13.4 Intracranial Haemorrhage

Intracranial haemorrhage is a common cause for cerebral palsy. Neonatal intraparenchymal haematomas are often iso- to slightly hypointense on T1-weighted images and markedly hypointense on T2-weighted images in the acute stage (sometimes up to first 3 days). They gradually turn bright on T1-weighted images while remaining dark on T2-weighted images over the next 3–7 days (Fig. 13.3). Between 7 and 14 days, the haematoma gradually turns bright on T2-weighted images and remains so while slowly turning isointense to CSF on T1-weighted images over the next several months [21]. Note that these timeframes are approximate and typically apply to intraparenchymal bleeds. The use of gradient echo T2* (Fig. 13.3b) or susceptibility-weighted imaging (SWI) sequences shows hypointensity in areas of haemorrhage. These sequences can sometimes increase the conspicuity and sensitivity of detecting small haemorrhages within the brain and may reveal signs of remote prior haemorrhage by demonstrating haemosiderin staining of the margins of the ventricles, cystic areas in the brain or brain surfaces.

The most common clinically important form of intracranial haemorrhage in neonates is intraventricular haemorrhage. The MRI signal of haemorrhage obviously depends on the stage of haemoglobin degradation, but IVH is most commonly seen as T2. T2* sequences can be very helpful for detection of subtle degrees of IVH, both in the acute stage and chronic phase (haemosiderin staining). The severity of neonatal intraventricular and germinal matrix haemor-

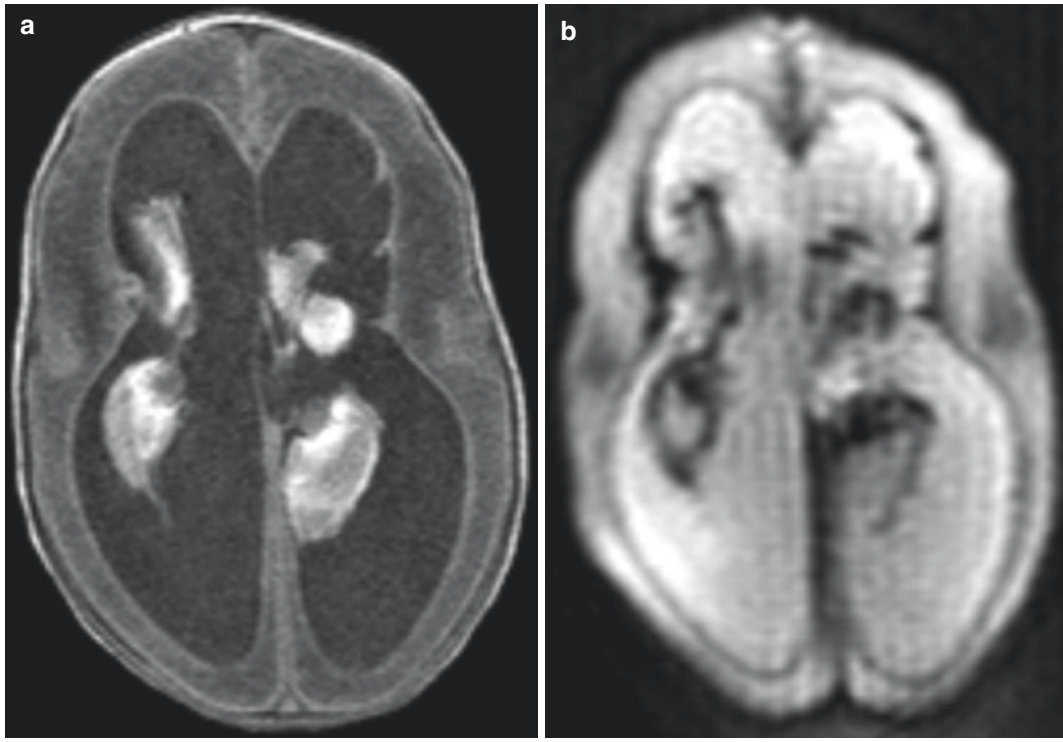

Fig. 13.3 Intraventricular haemorrhage in a 1-week-old neonate as depicted on MRI. (**a**) T1-weighted image demonstrates a hyperintense signal of blood within the ventricles. (**b**) Gradient echo T2* image demonstrates foci of low signal due to haemorrhage. Also note the hypointense staining along the margins of the lateral ventricles secondary to haemorrhage

rhage in the neonate is commonly graded using the classification of Papile et al. [22]. While this is commonly used on ultrasound (see Chap. 12), the same classification can be applied to magnetic resonance imaging as well. IVH encompasses four grades:

Grade 1: Subependymal haemorrhage only. These appear as focal areas of excessive hypointensity along the germinal matrix, most commonly in the region of the caudothalamic groove. The haematoma regresses over a period of days to weeks and may form a subependymal or germinolytic cyst.

Grade 2: Subependymal haemorrhage with blood in nondilated ventricles. Blood is seen extending into the ventricular system on MRI. The normal venous blood of the choroid plexus should not be confused with intraventricular haemorrhage on susceptibility sequences. In the chronic stages, hemosiderin staining of the ependymal margin of the ventricles may persist, but gradually decreases over time.

Grade 3: Subependymal haemorrhage with blood in dilated ventricles. Blood can fill part or all of a dilated ventricle. In the latter case, it may form a cast of the ventricle. Over time, the clot will resolve completely or persist as linear septations or bands within the ventricle. In more than two-third of patients, posthaemorrhagic hydrocephalus develops.

Grade 4: Subependymal haemorrhage with blood in dilated ventricles and intraparenchymal blood. The latter can be the result of haemorrhagic cerebral infarction rather than direct extension of blood from the germinal matrix [23]. This is mostly unilateral and is commonly detected in the frontal and parietal lobes on the same side as the intraventricular haemorrhage (IVH). Mass effect with shift of

the midline structures to the unaffected contralateral side may be present with large haemorrhages. The blood clot liquefies and retracts over several weeks, and in a matter of 2–3 months encephalomalacia develops. This can communicate with the ipsilateral ventricle. As the parenchymal haemorrhage, Grade 4, may be due to a different pathogenetic mechanism, it is sometimes regarded as a separate entity and not part of the original grading system by some authors [24].

Germinal matrix haemorrhage and intraventricular haemorrhage may be complicated by congestion and/or thrombosis of deep medullary veins in the white matter, leading to the white matter injury and periventricular venous infarction (PHVI) (Fig. 13.4). Intraventricular haemorrhage can also be detected in-utero utilising fast foetal MRI sequences targeted at detecting haemorrhage, including higher grades of IVH (Fig. 13.5). Detection of low grades of intraventricular haemorrhage is not uncommon on foetal MRI in our clinical experience. Nevertheless, it is important not to confuse normally prominent germinal matrices and developing deep venous structures in the foetus with IVH, as both may appear hypointense on T2*-weighted or echoplanar sequences.

In a report by the quality standards subcommittee of the American Academy of Neurology and the Practice Committee of the Child Neurology Society based on comprehensive analysis of data from recent literature, Grade 3 and 4 IVH, cystic PVL and moderate-to-severe ventriculomegaly were found to be significantly associated with cerebral palsy at 2–9 years of age in VLBW preterm infants [25]. There was a tenfold elevation in the risk to develop cerebral palsy. The incidences of long-term neurologic sequelae of Grade 1–4 intracranial haemorrhage in the preterm infant are 5, 15, 35 and 90%, respectively [23]. In 90% of term infants with increased parenchymal echogenicity a neurologic sequel is to be expected [11]. Approximately 15% of all infants with IVH will develop PVHI. In 80–90% this develops within the first 96 h after delivery or 24–48 h after the appearance of germinal matrix haemorrhage on US particularly in clinically unstable neonates with metabolic acidosis [26].

Along with aqueductal stenosis, intraventricular haemorrhage is a common cause of

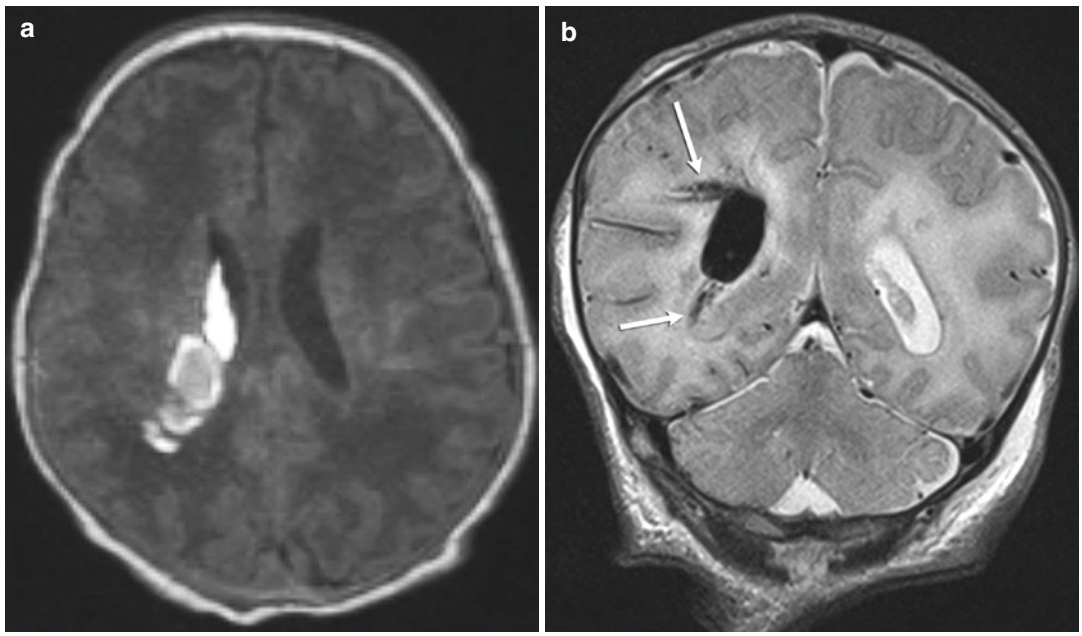

Fig. 13.4 In this patient with intraventricular haemorrhage (**a**), there is adjacent prominence and thrombosis of the medullary veins in the white matter (*arrows* in **b**), leading to periventricular haemorrhagic infarct

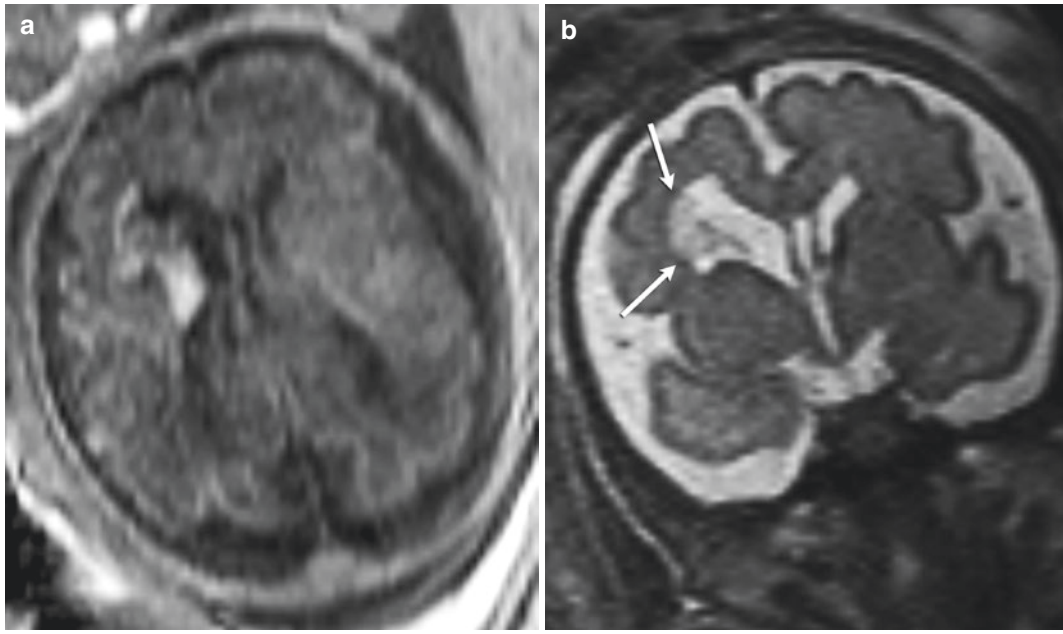

Fig. 13.5 In-utero grade 4 intraventricular haemorrhage on foetal MRI at 28 weeks gestation. (**a**) Axial T1-weighted image shows hyperintense blood within the right lateral ventricle extending into the adjacent parenchyma. (**b**) Coronal single-shot fast spin-echo T2-weighted image shows extension of blood into the brain parenchyma adjacent to the dilated ventricle and a thinned cortical mantle

neonatal hydrocephalus. Haemorrhage may result in obstruction of CSF flow through the ventricular system and CSF resorption at the level of the arachnoid villi, resulting in progressive ventricular dilatation, and both communicating and noncommunicating hydrocephalus. This can be delayed for days to weeks. The temporal horns, trigones and occipital horns often dilate before the frontal horns. The lateral ventricles dilate more than the third or fourth ventricles. Posthaemorrhagic hydrocephalus resolves in over half of the infants. Nevertheless, long-standing extensive ventricular dilatation can lead to white matter damage and atrophy.

Small subdural haemorrhages are extremely common in neonates, but almost cause mass effect or complications. These subdural haemorrhages are typically seen in the posterior fossa, along the tentorium, along the posterior falx and over the occipital regions. They are related to the birthing process. In the term infant, germinal matrix with resultant intraventricular haemorrhage is uncommon. On the other hand, isolated choroid plexus haemorrhage can occur in both the term and preterm neonate. Isolated parenchymal haemorrhage can occur and may be the result of traumatic delivery. The cortical haemorrhages may appear as a focal echogenic mass or cause diffusely increased gyral echogenicity on ultrasound (see Chap. 12). It can be easily detected on MRI. Over time, as the haematoma undergoes lysis and clot retraction, the hematoma mass decreases in size, and encephalomalacia may be a sequel seen on follow-up imaging.

13.5 Periventricular Leukomalacia and Neonatal White Matter Injury

Periventricular leukomalacia (PVL) is a general pathological description that is used without reference to a particular aetiology, and it is thought to typically affect the premature brain. MRI can detect signal abnormalities in the periventricular white matter early in the course of the injury. There is predilection for periventricular white matter. The MR findings of end-stage PVL are ventriculomegaly with irregular undulated margins of the body and

trigone of the lateral ventricles, reduced quantity of periventricular white matter particularly at the trigones with increased signal intensity on long TR sequences, delayed myelination, thinning of the corpus callosum and deep prominent sulci that abut or nearly about the margin of the ventricle with little or no interposed white matter (Fig. 13.6) [27]. In many cases, necrosis of

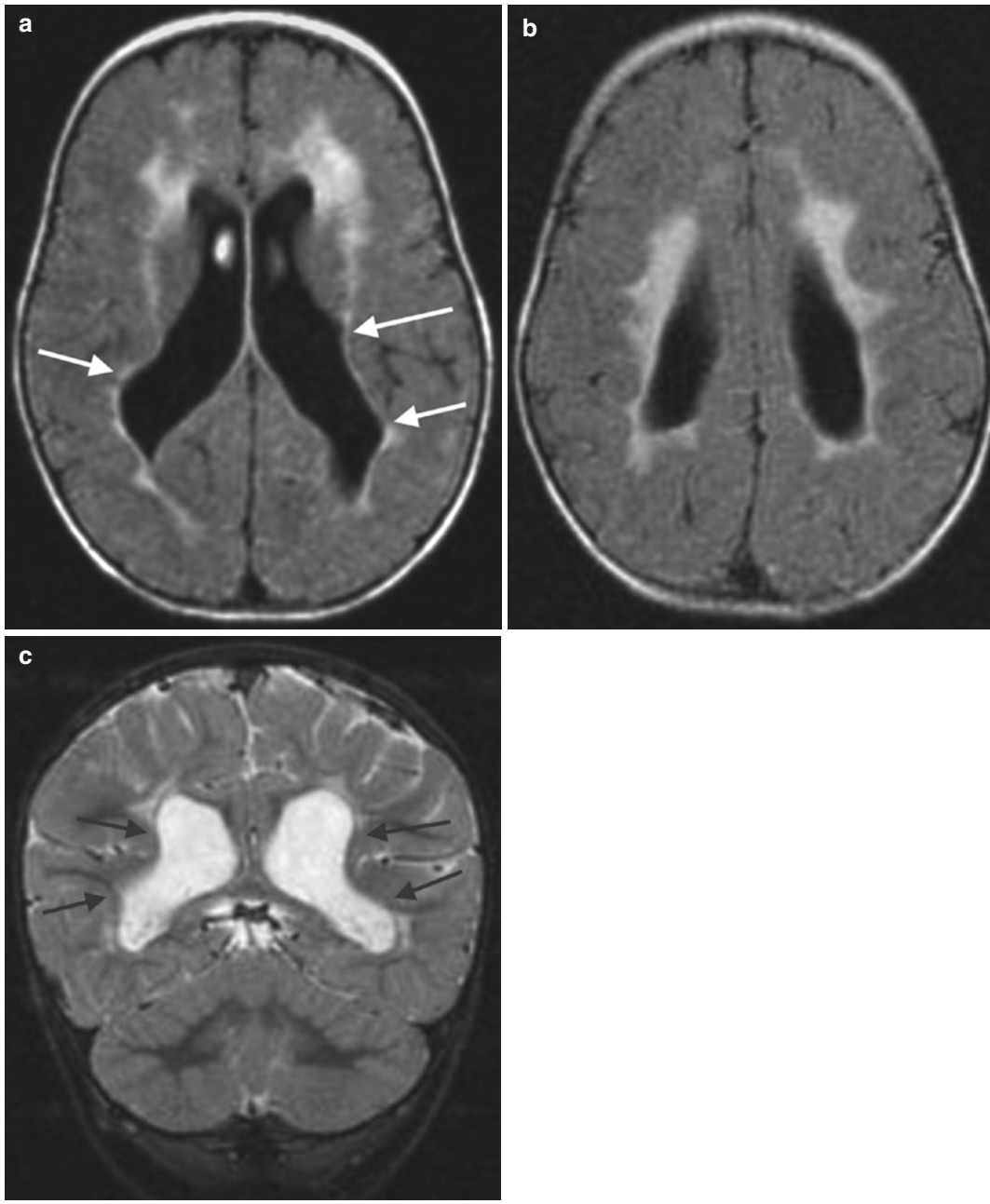

Fig. 13.6 Typical findings of periventricular leukomalacia. (**a**) The posterior lateral ventricles are distended within undulated margin (*arrows*), there is decreased white matter volume and there is periventricular abnormal white matter signal on FLAIR imaging (**a** and **b**). (**c**) Coronal T2-weighted image demonstrates decreased white matter volume, with approximation of the cortex to the margins of the distended lateral ventricles. (**c**) Sagittal T1-weighted image demonstrates associated sending of the corpus callosum

the immediate periventricular tissue occurs and cystic areas develop. The resulting cysts often later collapse or are incorporated into the lateral ventricles and the areas of signal abnormality come to lie closer and closer to the ventricular wall, until they finally disappear (Fig. 13.7). Compared with US performed on the same day, MRI of preterm neonates detects more white matter abnormalities in the first week of life [11, 28]. Contrary to findings in US in term newborns that later developed cerebral palsy, MRI can reveal a high rate of findings compatible with end-stage PVL [29].

There are other patterns of white matter diseases of prematurity as well [26, 28, 30]. Punctate white matter lesions may be seen at any gestational age including both in preterm and term patients. They are commonly seen in term neonates with cardiac disease or neuromuscular disease. Term neonates with severe cardiac anomalies have been shown to have delayed brain maturation [31]. These punctate white matter lesions are T1 hyperintense, often mildly T2 hypointense, and are most frequently detected along the corona radiata, the periventricular and deep centrum semiovale white matter and along the optic radiations [26]. They may occasionally also show restricted diffusion (Fig. 13.8).

Another less well-known pattern is termed diffuse excessive high signal intensity (DEHSI) within the white matter on T2-weighted MR imaging in premature babies at term-equivalent age, with signal intensity approaching that of cerebrospinal fluid [26, 32]. These were initially thought to represent abnormal white matter development without evidence of focal pathology on conventional MRI. However, more recent studies have shown that diagnosis of this entity is highly subjective [33], and there is no neurodeelopmental consequence in neonates with this appearance [34, 35]. On the other hand, cystic encephalomalacia and punctate white matter lesions were significant predictive of motor delay and cerebral palsy.

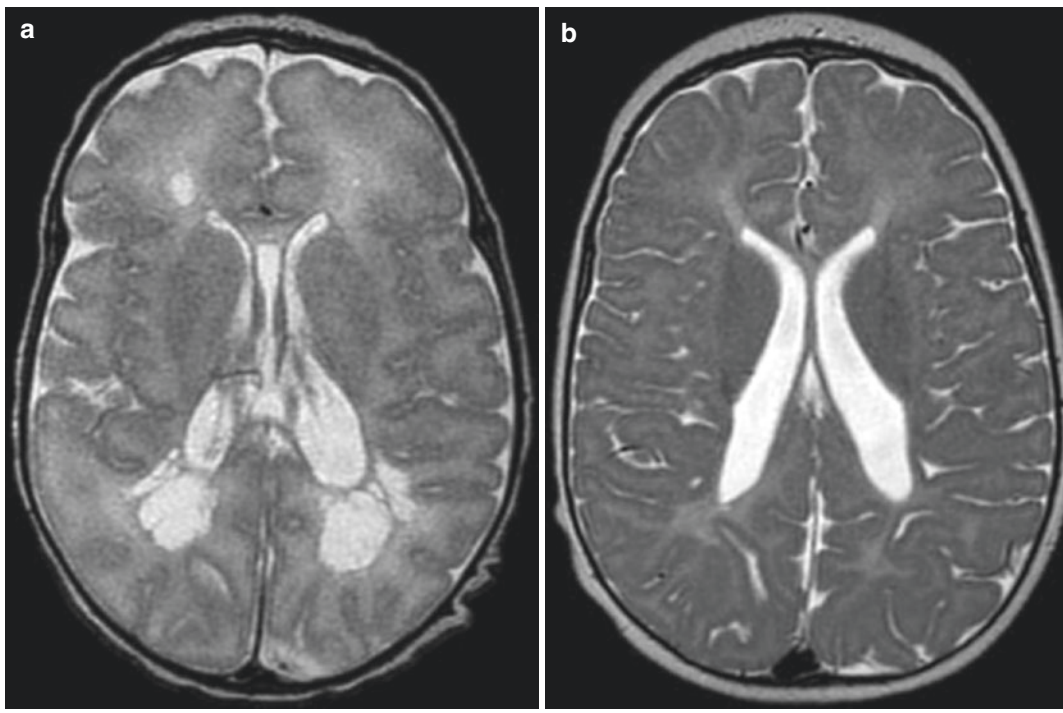

Fig. 13.7 (**a**) Axial T2-weighted image shows multiple foci of cystic periventricular leukomalacia in a 6-week-old infant. (**b**) Six months later, the cystic areas are no longer seen, but now depicted are undulated margins of distended posterior lateral ventricles and associated white matter volume loss

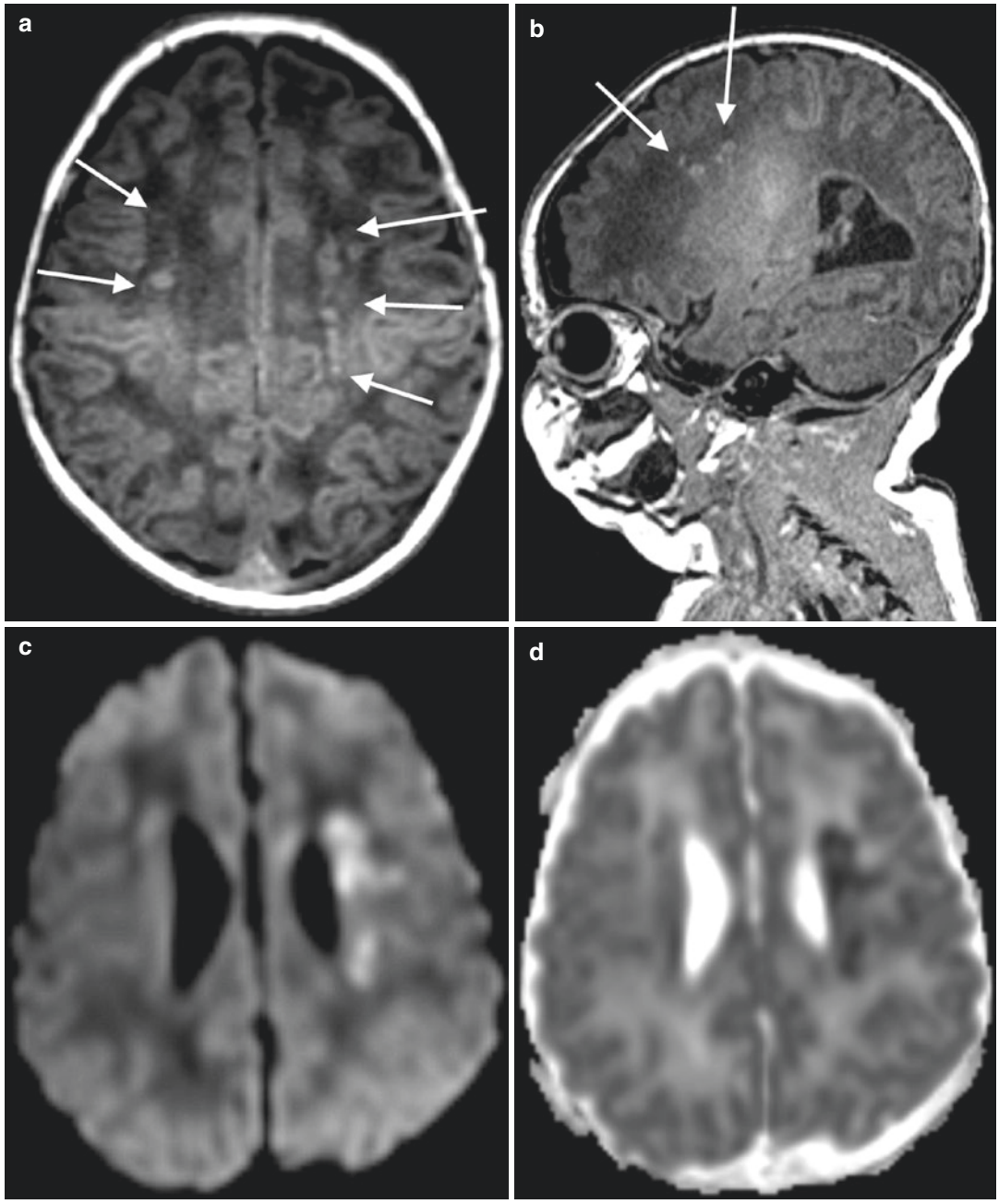

Fig. 13.8 Punctate foci of white matter injury in a term neonate with transposition of the great arteries. Axial (**a**) and sagittal (**b**) images demonstrate multiple small foci of abnormal high T1 signal intensity in the deep white matter. DWI (**c**) and ADC (**d**) images showed that a few of these foci demonstrate acute restricted diffusion

13.6 Hypoxic-Ischaemic Injury

Hypoxic-ischaemic injuries are another *aetiologic* category for CP. The use of MRI has been of great value in trying to determine timing of brain injury and recognition of patterns of injury [10, 36]. Nevertheless, there is some overlap in these patterns and the timing may not be as clear-cut. Presence of very wide subarachnoid spaces and interhemispheric fissure, ventricular dilatation, cystic lesions of the white matter and germinolytic cysts at birth or within the first week are some of the potential signs of prenatal injury (see Chaps. 5 and 12). The use of diffusion imaging has greatly assisted in timing of injuries to the brain. Diffusion-weighted imaging (DWI) assesses the movement of water molecules in tissue. It can detect acute injury to the brain and cytotoxic oedema resulting in reduced motion of water. High signal intensity on trace DWI maps and low signal intensity on the apparent diffusion coefficient (ADC) maps are often indicative of this acute injury. DWI is able to provide evidence of cerebral injury before conventional MRI in newborns with hypoxic-ischaemic encephalopathy [11].

The use of diffusion imaging has helped in assessing various patterns of acute injury to the brain [10]. The patterns of injury depend on the severity of the hypoxic event, presence or severity of hypotension, maturity of the brain, duration of injury and timing of the MRI relative to the acute injury episode. One major pattern of hypoxic-ischaemic injury to the brain in full-term neonates is seen in acute severe hypoxia. Diffusion-weighted imaging often shows restricted diffusion with high DWI and low ADC signal predominantly in the ventral lateral thalami and basal ganglia, putamina (most commonly posterior putamina) and also in the perirolandic cortices. Increased signal intensity in the deep grey structures including the thalamus and basal ganglia can develop on T1-weighted images (Fig. 13.9). There may be involvement of the hippocampi and brainstem. This pattern is usually seen as a result of a catastrophic event such as placental abruption, prolapse uterine court or ruptured uterus. In our experience, arterial spin labelling (ASL) perfusion often shows increased blood flow in the areas of injury by the time the patient is evaluated on MRI, likely as a result of luxury reperfusion. A second common pattern is the watershed predominant pattern of injury. This pattern is commonly seen following prolonged partial asphyxia. Often the watershed or border zone areas are involved, affecting the white matter and at least parts of the overlying cortex (Fig. 13.10). Another severe pattern, which is less common, includes extensive involvement of the cortex and subcortical white matter with relative sparing of the immediate periventricular white matter and central grey matter, referred to as the "*white cerebrum*" on diffusion imaging [10]. This type is often fatal though it may lead to multicystic encephalomalacia.

Hypoxic-ischaemic encephalopathy in the preterm neonate tends to affect the deep white matter at the level of the optic radiations adjacent to the trigones of the lateral ventricles and the frontal horns near the foramen of Monro and can result in periventricular leukomalacia (PVL). The sequel of PVL can be cystic encephalomalacia that can be identified about 2–3 weeks after the ischaemic insult. Only 15% of patients with increased periventricular echogenicity develop periventricular cysts. These can be single or multiple and communication with the ventricular system can occur when there is breakdown of the ependymal lining. PVL can be graded by the characteristics of the periventricular white matter [37].

With moderate or severe oedema, there may be poorly defined gyral-sulcal interfaces and slit-like ventricles. Later parenchymal atrophy,

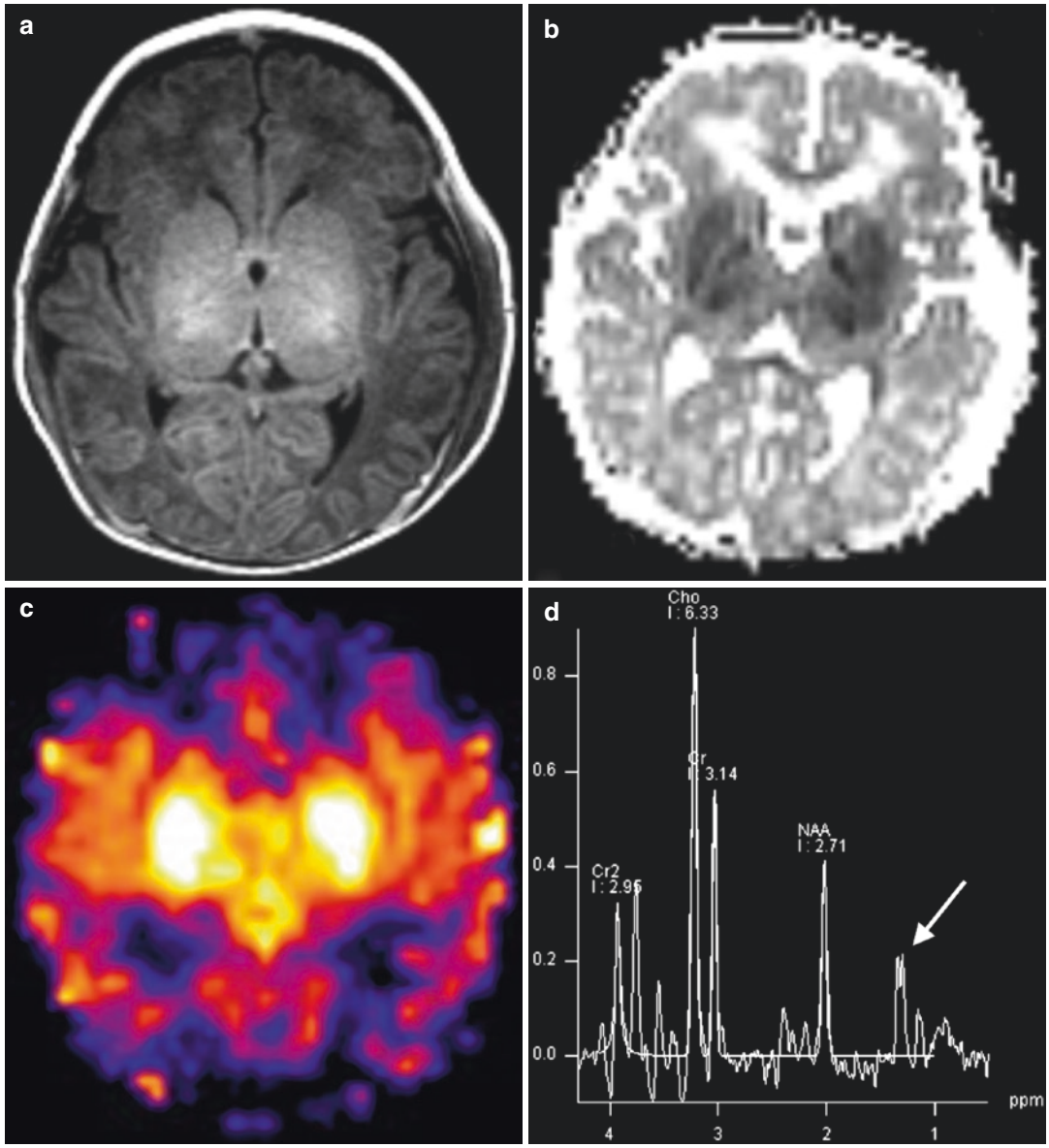

Fig. 13.9 Neonate with seizures after emergency caesarean section delivery due to close on full abruption, showing a deep profound pattern of hypoxic injury. (**a**) T1-weighted image demonstrates subtle increased signal in the basal ganglia and parts of the thalamus. Differentiating abnormal signal from normal myelination in the lateral thalamus and posterior limb of internal capsule may be difficult. (**b**) Apparent diffusion coefficient (ADC) map shows abnormally reduced diffusion in the basal ganglia and parts of the thalamus. (**c**) Arterial spin labelling (ASL) perfusion imaging demonstrates markedly elevated blood flow in the basal ganglia, corresponding to the areas of hypoxic injury on diffusion imaging. (**d**) Magnetic resonance spectroscopy demonstrates abnormally elevated lactate (*arrow*)

ventricular enlargement and cystic encephalomalacia may develop (Siegel et al. 1984). The cysts are mostly in the frontal and occipital lobes. In the term newborn, the thalamus and basal ganglia are vulnerable to hypoxic damage and if affected can be focally or diffusely echogenic on US [38] or

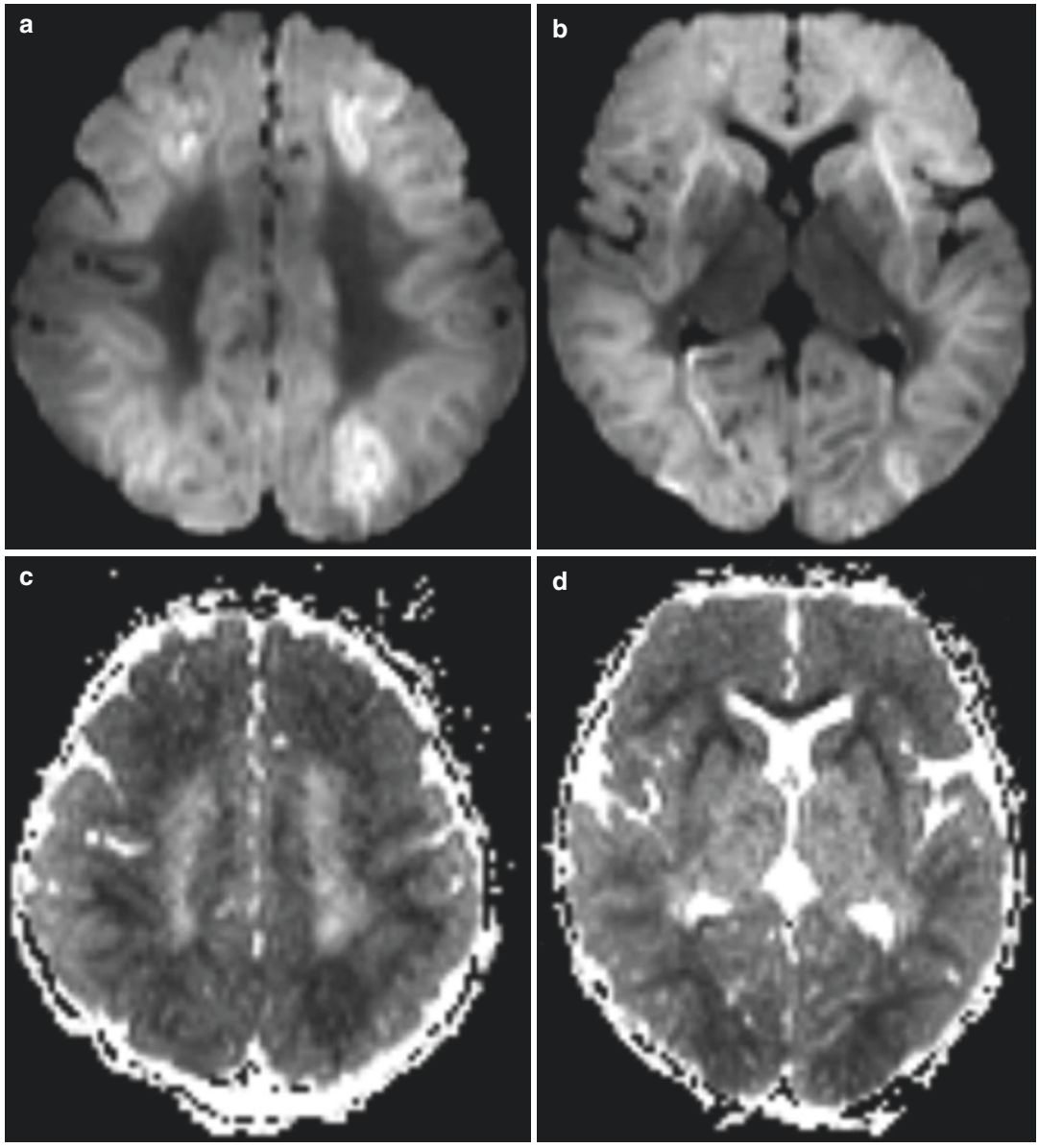

Fig. 13.10 DWI (**a** and **b**) and ADC (**c** and **d**) maps demonstrating a watershed-type injury to the brain, also involving white matter and parts of the cortex with relative sparing of the basal ganglia, thalami and other parts of the cortex

have abnormal signal on MRI (also see Chaps. 5 and 12). It should be noted that there may be cases of overlap between the different patterns of hypoxic-ischaemic brain injury. In the chronic phases after various types of injury, there may be cortical thinning and diminution of the underlying white matter with ex vacuo dilatation of the lateral ventricles. The affected areas of brain are shrunken and show high signal intensity on T2-weighted images compared to normal brain tissue.

13.7 Perinatal Ischaemic Stroke

Perinatal arterial ischaemic stroke and venous thrombosis can also be causes for damage to the brain leading to development of cerebral palsy. The incidence of perinatal stroke is between 2300 and 5000 births [39, 40]. As such, the neonatal period carries the highest risk for paediatric ischaemic stroke among all paediatric age groups. It is classified into arterial ischaemic stroke (confirmed by neuroimaging showing parenchymal infarct corresponding to an arterial territory) and neonatal cerebral sinovenous ischaemic stroke (confirmed by imaging showing thrombosis in the cerebral venous system and infarct corresponding to a venous territory). The aetiology of arterial ischaemic stroke in the neonate often remains unknown although placental factors are thought to be contributory [41].

Approximately half of neonates with a perinatal infract will develop hemiplegia [39]. The anatomic location and the size of infarct are obviously related to outcome. The presence of restricted diffusion along the descending corticospinal tracts is a sign of pre-Wallerian degeneration (diaschisis) (Fig. 13.11). The presence of pre-Wallerian degeneration at the time of acute arterial ischaemic stroke is a poor motor prognostic sign and often results in long-term motor weakness and signs of cerebral palsy [42].

The neonatal period is also a high-risk period for the development of cerebral sinovenous thrombosis (CSVT) [43]. These may involve the superficial or deep venous system. Adverse outcomes include postnatal epilepsy, cerebral palsy, visual deficits, cognitive impairments, posthaemorrhagic hydrocephalus requiring shunting and death. Outcome will be highly dependent on the location and extent of venous structures involved

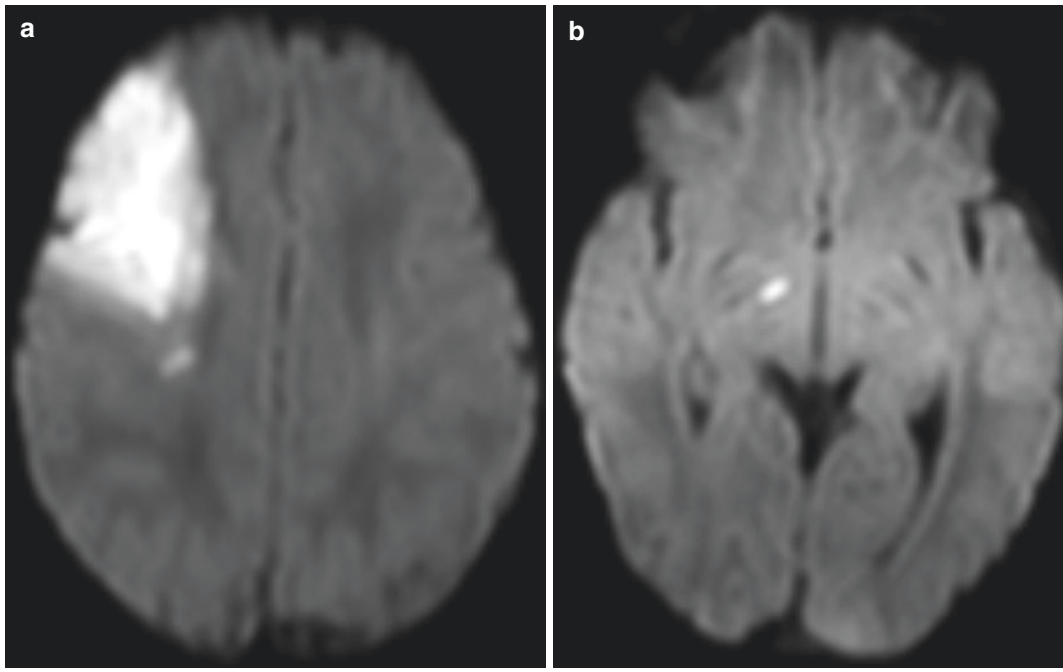

Fig. 13.11 Neonatal arterial ischaemic stroke (AIS) in a term infant. Diffusion imaging shows a large area of restricted diffusion in the right cerebral hemisphere in keeping with an infarct in the right middle cerebral artery territory (**a**). On a lower slice distant from the infarct zone (**b**), there is also focal restricted diffusion coursing along the descending corticospinal tract, in keeping with acute pre-Wallerian degeneration. The presence of this finding is a poor prognostic risk factor for motor outcome in neonatal arterial ischaemic stroke

and whether there are associated venous infarcts. Diagnosis can be made by detecting of abnormal signal intensity within the dural venous sinuses or cortical veins, demonstration of lack of flow on various magnetic resonance venographies (MRV) or filling defects within the dural venous sinuses on postcontrast MRI or CT studies. Of note, a number of artefacts and slow or turbulent flow may cause false positive or false negative results on various magnetic resonance imaging techniques.

In a subset of children, perinatal stroke may not be detected in the neonatal period for a variety of reasons [44]. They may present later with signs such as asymmetry in the use of an extremity and grasp, failure to reach normal developmental milestones, seizures and congenital hemiplegia. In these children, the diagnosis of presumed perinatal arterial ischaemic stroke (PPAIS) is made based on imaging appearance of a chronic arterial territory infarct (Fig. 13.12).

13.8 Advanced MRI Techniques

Newer MRI imaging methods have been utilised in evaluation of patients with brain disorders leading to cerebral palsy. These include metabolic imaging (MR spectroscopy, see Chap. 14), diffusion tensor imaging, volumetric MR imaging and functional connectivity MRI. These techniques have the ability or potential to provide additional pathophysiological insight into the biomolecular, cellular and systems processes that underlie development and outcome in children with cerebral palsy [45].

Widespread use of high-field magnetic resonance system and advances in MRI pulse sequences design has enabled acquisition of robust high-resolution 3D volumetric images of the brain. These images can be utilised in assessment of both global and regional brain volumes after segmentation. Thus, correlation of various

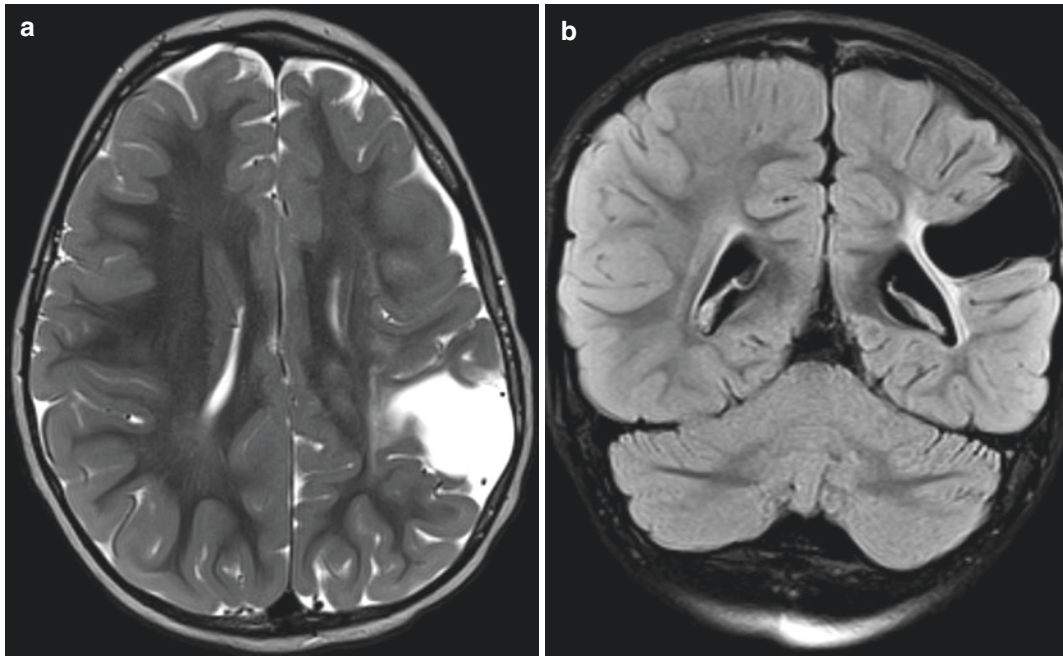

Fig. 13.12 Presumed perinatal arterial ischaemic stroke (PPAIS). A 15-month-old patient without a significant past medical history is brought to neurology clinic with preferred use of the left hand and shows some gait abnormality, with increased tone and reflexes in the right extremities. MRI shows chronic encephalomalacia in the left middle cerebral artery territory on axial T2-weighted (**a**) and coronal fluid-attenuated inversion recovery (**b**) sequences, with some surrounding gliosis. This is likely the result of a prior undiagnosed infarct, presumably in the perinatal period

brain segmental volumes with injury and outcome can be performed. The same data can be used for calculation of focal cortical thickness and analysis of the relationship with various diseases. The total brain and cerebellum volumes in children with cerebral palsy have been shown to be significantly reduced in comparison to controls [46]. In patients with periventricular leukomalacia, including those with spastic diplegia, cortical volume of the pre- and postcentral gyri and the paracentral lobule has been shown to be negatively correlated with motor function [47].

Proton MR spectroscopy (^{1}H–MRS) is an MR technique that has been applied extensively in the neuroimaging of newborns (see Chap. 14). This technique is most commonly applied by utilising single-voxel point-resolved spectroscopy (PRESS) or stimulated echo acquisition mode (STEAM) in evaluation of select predefined metabolites in the brain [10, 11]. Normally in the developing neonatal brain, there are higher concentrations of choline and lower concentrations of *N*-acetyl aspartate (NAA) compared to an adult or older paediatric brain, given the higher cell membrane turnover (choline) and lower neuronal concentration (NAA). Abnormally elevated lactate is commonly seen in patients with hypoxic-ischaemic injury to the brain (Fig. 13.7d) or in patients with certain metabolic diseases. The presence of elevated lactate may persist for days or weeks after the hypoxic event [10]. Lactate/creatine ratios of >1 in the first 18 h are more common in those infants with later neurologic findings consistent with hypoxic-ischaemic encephalopathy. Elevated lactate/NAA, lactate/creatine and lactate/choline ratios in the first 2 postnatal weeks have been found to be more common in infants with suspected neonatal encephalopathy than in age-matched controls [11]. Changes in metabolite ratios have been shown to correlate with neurodevelopmental outcomes [48].

Another recent advanced neuroimaging technique is diffusion tensor imaging (DTI) which utilises multidirectional diffusion information to reconstruct various quantitative parameters in regard to directionality of water diffusion, which is different in normal white matter and grey matter and in areas of brain injury. DTI is able to detect subtle changes not apparent on conventional MR imaging. DTI data could also be used in the depiction of white matter tracts using various tractography algorithms (Fig. 13.13). On a quantitative basis, alteration in various diffusion parameters in the corticospinal tract and corpus callosum are related to motor outcome [49]. Diffusion tensor imaging has been applied for identification of specific white matter tract injury in children with cerebral palsy and in association with periventricular leukomalacia [50]. In a more recent study, DTI parameters of the motor tract were shown to correlate with future motor function at mean age of 28 months [51]. DTI is being intensely investigated as a tool for assessment of brain function subsequent to various types of injury. The notion of structural connectivity as evaluated by diffusion tensor imaging can shed light into the extent of damage and pathophysiology in children with cerebral palsy [52]. In patients with periventricular leukomalacia, it has been shown although the fractional anisotropy DTI measure within most of the major white matter tracts were significantly lower than that of age-matched healthy controls, fractional anisotropy mainly within the bilateral corticospinal tracts and posterior body and isthmus of the corpus callosum showed more significant correlation with motor dysfunction than thalamocortical pathways [47].

Functional MRI is also being used in the evaluation of neonatal brain injury. Classically, fMRI involves performing certain tasks and observing the change in the blood-oxygen-level-dependent signal that results from vascular changes related to neuronal activation. These task-based methods are generally infeasible in the neonatal and infantile periods. However, it has been shown that even during periods of rest (no task), there is a temporal correlation between different parts of the brain that appear to function as different correlated networks. The method of analysis and characterisation in uncovering these correlated networks is known as resting state functional connectivity MRI. Patterns of aberrant functional

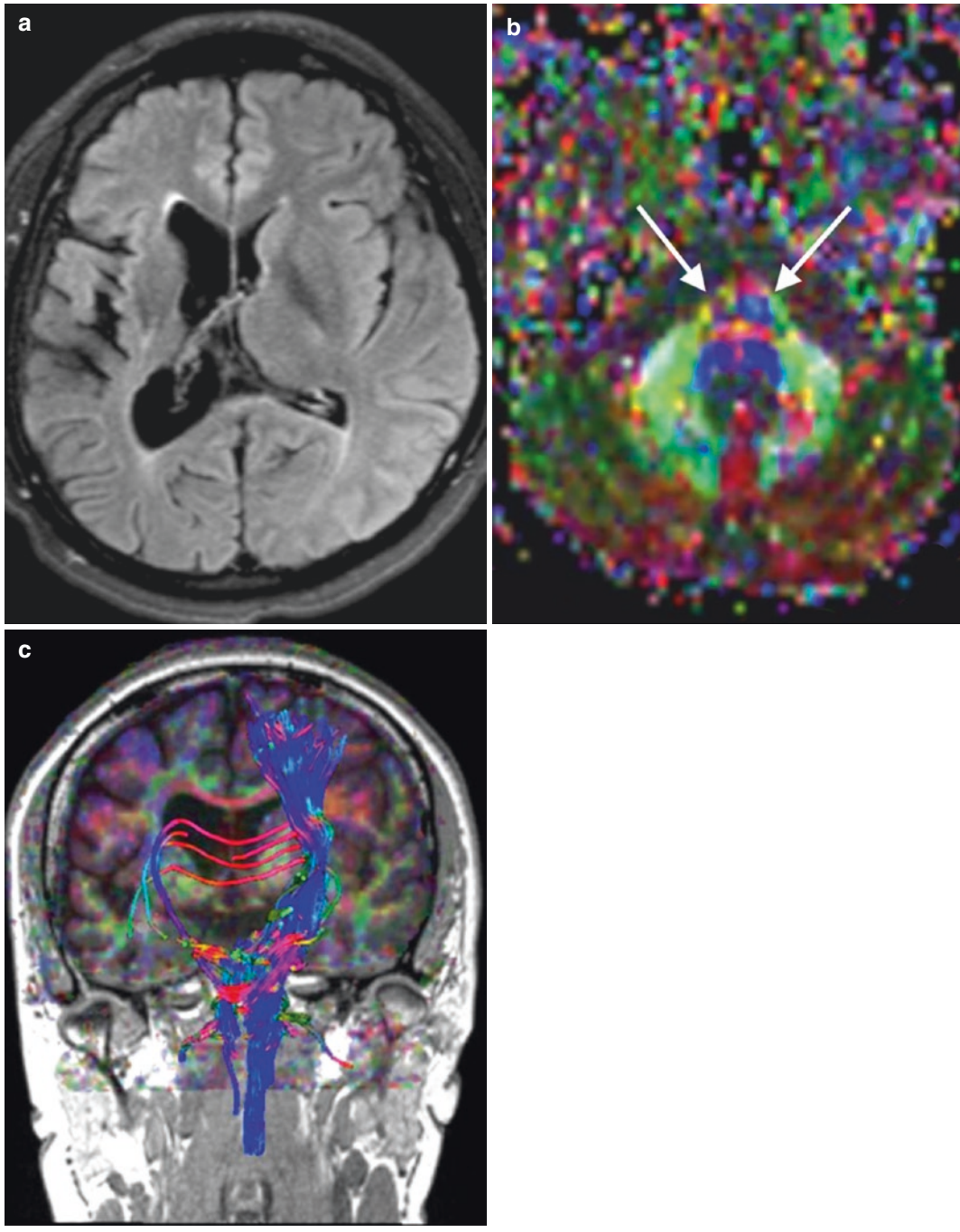

Fig. 13.13 Diffusion tensor imaging (DTI) in a patient with left hemiplegic cerebral palsy. Child with previous right-sided haemorrhage, with resultant volume loss and dilatation of the right lateral ventricle (**a**). (**b**) Colour-coded fractional anisotropy maps through the brainstem demonstrate markedly diminished right corticospinal tract (*blue*) compared to the left (*arrows*). (**c**) Tractography derived from diffusion tensor imaging superimposed on coronal anatomical images also shows markedly asymmetric and diminished right corticospinal tract compared to the left side

connectivity have been observed in premature neonates with white matter injury and depended upon injury severity [53]. In patients with PVL, the motor cortical connectivity was diminished mainly within the bilateral somatosensory cortex, paracentral lobule, cingulate motor area and visual in those with spastic diplegia [47]. More studies are required to assess the role of functional network derangements in patients with cerebral palsy due to a variety of aetiologies.

In conclusion, neuroimaging plays an important role in the evaluation of brain injury in preterm and term neonates and also as a tool in the investigation of motor and cognitive dysfunction. Further advances in neuroimaging have the potential to shed light on the pathophysiology of various types of injury and functional impairment in patients with cerebral palsy. In the combination of advanced techniques with conventional MR imaging techniques, the imaging findings have potential to be utilised beyond routine diagnostic and prognostic tools. They can be potentially employed as biomarkers of long-term motor and neurodevelopmental outcome and means to evaluate the efficacy of neuroprotective strategies and interventions.

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