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Corpus callosum thickness on MRI as a surrogate marker of brain volume in children with HIV-related brain disease and its correlation with developmental scores

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2015

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Pediatr Radiol (2015) 45:258–272
DOI 10.1007/s00247-014-2998-9

PICTORIAL ESSAY

Corpus callosum thickness in children: an MR pattern-recognition approach on the midsagittal image

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Received: 12 November 2013 / Revised: 23 February 2014 / Accepted: 3 April 2014 / Published online: 31 August 2014
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Abstract Thickening of the corpus callosum is an important feature of development, whereas thinning of the corpus callosum can be the result of a number of diseases that affect development or cause destruction of the corpus callosum. Corpus callosum thickness reflects the volume of the hemispheres and responds to changes through direct effects or through Wallerian degeneration. It is therefore not only important to evaluate the morphology of the corpus callosum for congenital anomalies but also to evaluate the thickness of specific components or the whole corpus callosum in association with other findings. The goal of this pictorial review is raise awareness that the thickness of the corpus callosum can be a useful feature of pathology in pediatric central nervous system disease and must be considered in the context of the stage of development of a child. Thinning of the corpus callosum can be primary or secondary, and generalized or focal. Primary thinning is caused by abnormal or failed myelination related to the hypomyelinating leukoencephalopathies, metabolic disorders affecting white matter, and microcephaly. Secondary thinning of the corpus callosum can be caused by diffuse injury such as hypoxic–ischemic encephalopathy, human immunodeficiency virus (HIV) encephalopathy, hydrocephalus, dysmyelinating conditions and demyelinating conditions. Focal disturbance of formation or focal injury also causes localized thinning, e.g., callosal dysgenesis, metabolic disorders with localized effects, hypoglycemia, white matter injury of prematurity, HIV-related atrophy, infarction and vasculitis, trauma and toxins. The corpus callosum might be too thick because of a primary disorder in which the corpus callosum finding is essential to diagnosis; abnormal thickening can also be secondary to inflammation, infection and trauma.

Keywords Corpus callosum · White matter thickness · Magnetic resonance imaging · Children

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Introduction

Very little published research specifically addresses the causes, appearances and variations in thickness of the corpus callosum and the implications or diagnoses that should be considered. This pictorial review demonstrates age-related development, primary causes of abnormal thinning and thickening of the corpus callosum and acquired causes of thinning and thickening, both focal and generalized.

Normal anatomy and components

The corpus callosum is the main commissural pathway linking the hemispheres of the brain [1] connecting cortical and subcortical neurons [2]. Four parts are identifiable anatomically: the rostrum and genu anteriorly, the body centrally and the splenium posteriorly (Fig. 1).

The rostral fibers spread laterally, connecting the orbital surfaces of the frontal lobes. The fibers of the genu curve forward as the forceps minor and connect the lateral and medial aspects of the frontal lobes [3]. The fibers of the body course laterally and interconnect with the projection fibers of the corona radiata to connect wide areas of the cerebral

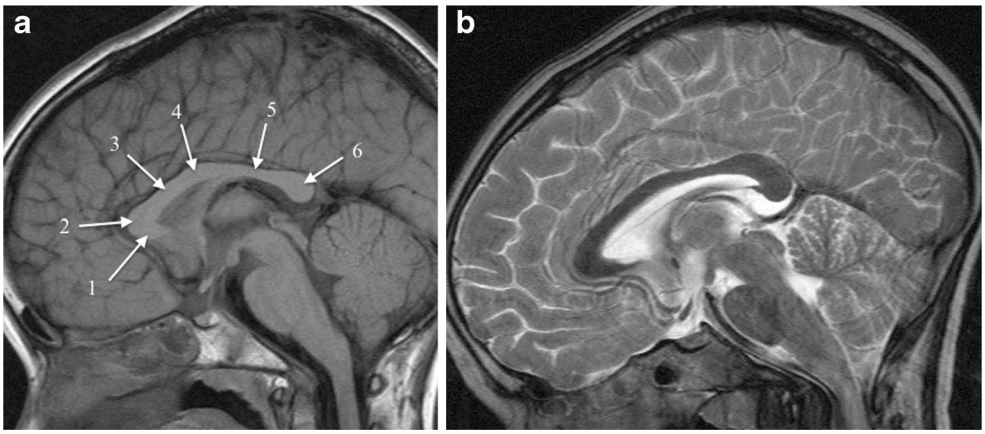


Fig. 1 Midline sagittal MRI demonstrates normal corpus callosum anatomy in a 7-year-old child. **a** T1-weighted MR image shows normal high signal indicating myelination (1=rostrum, 2=genu, 3=anterior body, 4=posterior body, 5=isthmus, 6=splenium). **b** T2-weighted image shows normal low signal of myelin

hemispheres. The fibers of the tapetum/isthmus, which is the junction of the body and the splenium, extend along the lateral surface of the occipital and temporal horns of the lateral ventricle [4]. The majority of the splenial fibers curve posteriorly into the occipital lobes as the forceps major [3].

Diffusion tensor imaging (DTI) and fiber tracking techniques (Fig. 2) have allowed researchers to segment the corpus callosum into bands that correspond to functional units rather than the shape of the corpus callosum [4–7]. The ventral and dorsal prefrontal cortex both project fibers through the genu and rostrum. The superior frontal cortex projects fibers into the posterior body. The parietal lobe and occipital lobe fibers project predominantly through the splenium, while fibers arising from the sensory-motor cortex pass through the isthmus. Dorsal or medial cortical lobes project fibers

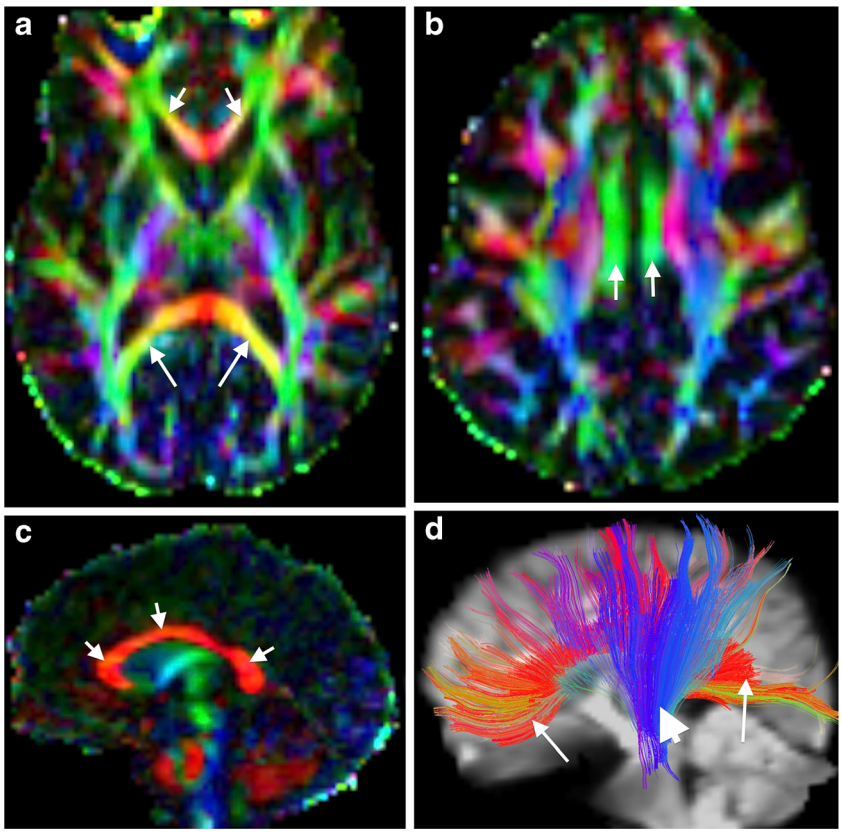


Fig. 2 Diffusion tensor imaging (DTI) of the corpus callosum in a normal child. **a** Axial color-coded directional map demonstrates the forceps minor (*short arrows*) and forceps major (*long arrows*) with *red* indicating the direction of fibers connecting left and right. **b** Axial color-coded directional map demonstrates the cingulate fibers (*arrows*) just superior to the corpus callosum with antero-posterior direction. **c** Sagittal color-coded directional map demonstrates the corpus callosum in a sagittal view with red indicating direction of fibers from side to side. **d** Sagittal fiber tracking generated from the DTI sequences demonstrates callosal fibers (*arrows*) superimposed with corticospinal fibers (*arrowhead*)

through the dorsal region of the corpus callosum, while lateral cortical lobes project fibers through the ventral region of the corpus callosum [8].

There is wide variation in the normal appearance of the corpus callosum both in thickness and in shape (Fig. 3). For example, the splenium can be circular or long and is sometimes separated from the body by an obvious isthmus [9] (Fig. 4).

Normal maturation, myelination, thickening

The appearance of the corpus callosum changes from the fetal stage through infancy and childhood to reach an adult appearance [10]. The thickness of the corpus callosum is reported as reflecting either the number of fibers or the degree of myelination [11, 12], and the signal on MRI relates to myelination.

In the near-term and term infant, the corpus callosum is usually easily visualized [10] and is thin and flat without the bulbous enlargements characteristic of the genu and splenium [2, 10] (Fig. 5). The first postnatal change is a substantial thickening of the genu, which frequently occurs as early as the 2nd and 3rd months of age [10]. The splenium enlarges slowly until the 4th or 5th postnatal month and then rapidly increases in size [10] (Fig. 5). By the end of the 7th month, the splenium is equal in size to the genu. It then gradually enlarges in proportion with the genu and the rest of the brain, and at about 9–10 months the appearance of the corpus callosum becomes similar to

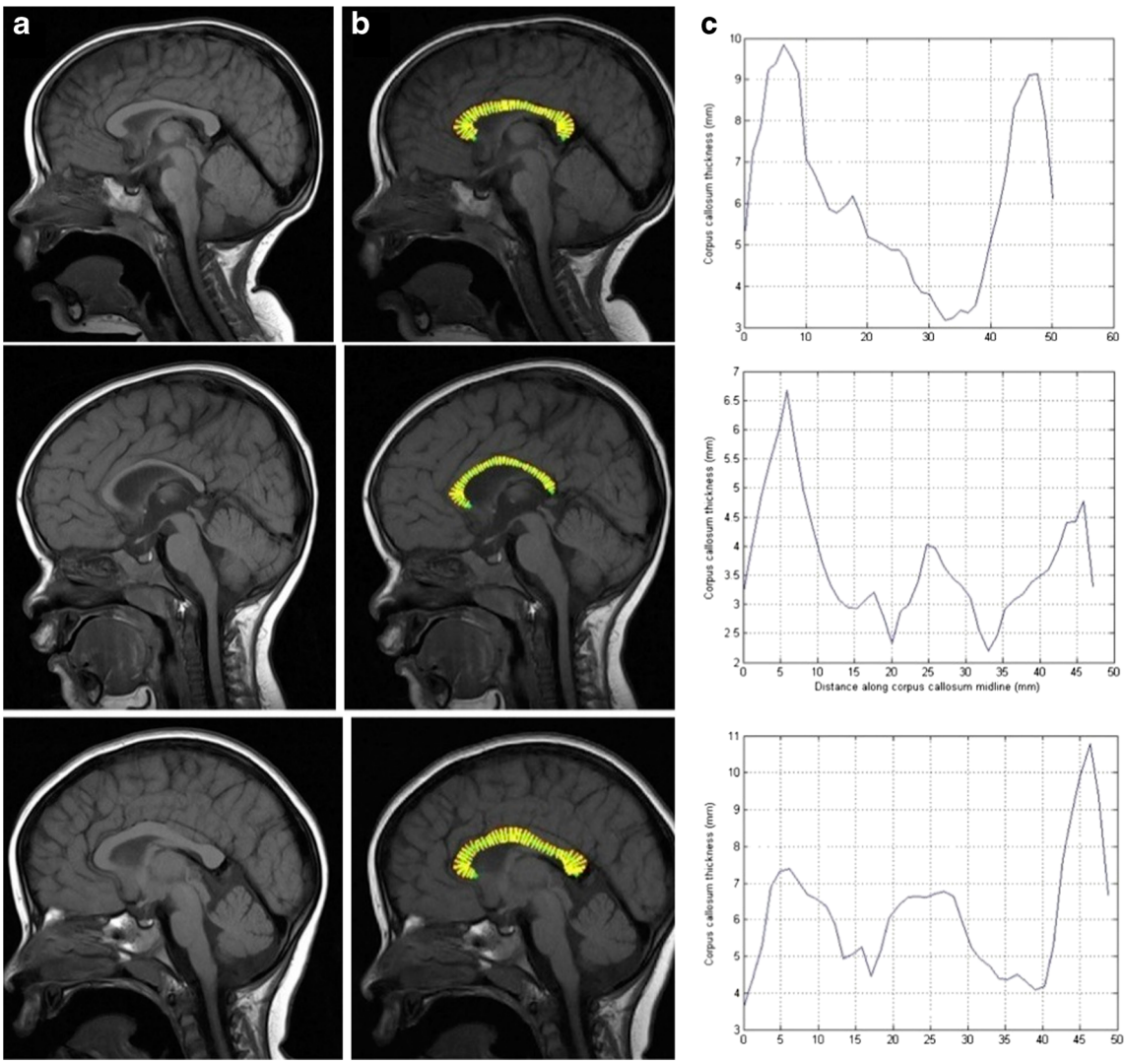


Fig. 3 Corpus callosum variation in three normal children. **a** T1-weighted midsagittal MR images demonstrate variation in thickness and shape of the corpus callosum. **b** Matched semi-automated measurement of thicknesses of the corpus callosum with graphic representation (**c**) of the thickness as a function of location along its length

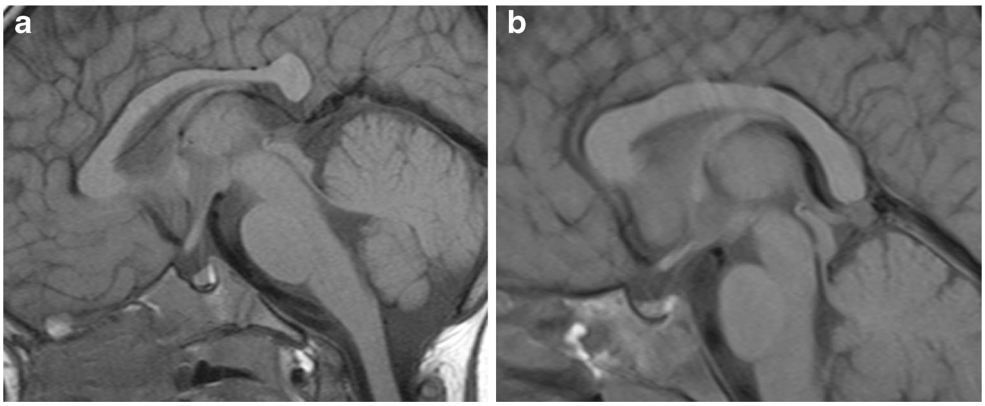


Fig. 4 T1-weighted MRI shows a variety of normal shapes of the genu and isthmus in the midsagittal images. **a** The expected appearance of the corpus callosum includes the presence of a rounded splenium and identifiable isthmus. **b** Normal variation in shape of the corpus callosum includes an elongated and sloping splenium without an obvious isthmus, as in this child

that in the adult [10]. The body of the corpus callosum steadily enlarges throughout childhood without any detectable growth spurts. The size of the body is relatively uniform, except that a focal thinning is frequently seen at the junction of the body and splenium [10].

Luders et al. [13] showed in 190 children that corpus callosum thickening in infancy and childhood was associated with normal development, and demonstrated that the most significant thickening occurred at the splenium and midbody of the corpus callosum, and the least at the rostrum. This suggests that the most reliable rule-of-thumb thickness measure of corpus callosum normality during childhood that is least affected by age would be the rostrum.

More recent morphological data obtained by Garel and colleagues [14] from 622 children using MRI demonstrated that there is rapid growth of the corpus callosum until 3 years of age, after which stabilization of the isthmus-splenial thickness ratio occurs (considered indicative of corpus callosum modeling). This study made available normal values of corpus callosum thickness, on MRI, for children age 1 day to 15 years [14]. Table 1 summarizes rule-of-thumb measures of corpus callosum thickness at each region from this publication [14].

A corpus callosum that is too thin

Primary conditions causing a thin corpus callosum: abnormal or failed myelination

Causes of myelination failure resulting in thin corpus callosum include hypomyelinating conditions, metabolic

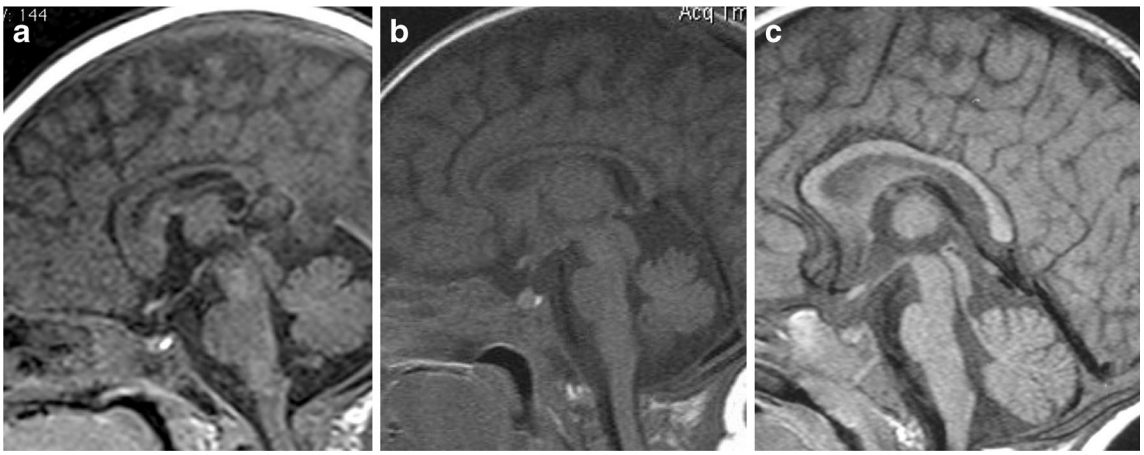


Fig. 5 Progressive thickening and myelination of the corpus callosum with signal change in normal children of different ages. **a** Sagittal T1-W MR image in a newborn shows a thin, fairly flat corpus callosum. It is unmyelinated and of intermediate signal intensity on T1-weighted images. **b** Sagittal T1-W MR image in a 1-month-old shows progressive uniform thickness of the corpus callosum, which is still unmyelinated. **c** Sagittal T1-weighted MR image in a 5-month-old shows thickening and myelination (high T1 signal) of the genu and splenium with early identification of an isthmus

Table 1 Measures of corpus callosum thickness by region at age 6 months, 1–2 years and 2 years and older in millimeters based on the findings of Garel et al. [14]

Corpus callosum component	6 months		1–2 years		>2–13 years	
	3rd/97th centiles	Median	3rd/97th centiles	Median	3rd/97th centiles	Median
Genu	3.7/8.9	5.8	4.6–5.7/9.7–11	6.9–8.3	6–7.5/11.4–13.5	8.8–10.7
Body	1.8/5.3	3	2.2–2.9/5.7–6.5	3.6–4.5	3.1–3.9/6.8–8.1	4.8–5.9
Isthmus	1.4/4.1	2.2	1.5–1.7/4.3–4.6	2.5–2.8	1.7–2.5/4.8–6.1	3–4
Splenium	3.4/9.2	5.6	4.4–5.6/9.0–10.9	6.7–8.1	6–7.5/11.3–13.7	8.5–10.6

disorders and microcephaly. There are also mimics of failed maturation of the corpus callosum.

Hypomyelinating leukoencephalopathies These disorders are caused by a primary disturbance in the formation of myelin. Pelizaeus–Merzbacher disease is considered the prototype of these [15] and is associated with a thin corpus callosum from delayed myelination of the white matter [10] (Fig. 6). Other hypomyelinating leukoencephalopathies associated with a thin corpus callosum include Cockayne syndrome type II (Fig. 6), sialuria (Salla disease), Tay syndrome, 18q- syndrome, leukodystrophy with trichothiodystrophy and photosensitivity, congenital cataracts with hypomyelination, hypomyelination with atrophy of the basal ganglia and cerebellum, and the recently described cerebral hypomyelination with cerebellar atrophy and callosal hypoplasia [10].

Metabolic disorders affecting white matter Certain metabolic disorders that primarily affect white matter are associated with a thin corpus callosum. These include mucolipidosis type IV (predominantly in Ashkenazi Jews), characterized by diminished white matter volume and central T2 prolongation, a dramatically thin corpus callosum (hypoplasia) and possible absence of the rostrum and splenium (hypogenesis).

Thin corpus callosum associated with microcephaly Microcephalies can be segregated into categories based on their morphological characteristics including the gyral pattern, cortical thickness and presence of callosal anomalies (Figs. 7 and 8). Simplified sulcation, as in classic lissencephaly, is more a general consequence of diminished cell proliferation and therefore is associated with diminished white matter volume [10] as well as anomalies of the corpus callosum, including hypoplasia.

Mimickers of corpus callosum hypoplasia Agenesis of the corpus callosum is usually accompanied by a small anterior commissure and an absent hippocampal commissure [16]. Occasionally, however, the hippocampal commissure is enlarged and can mimic a hypoplastic section of corpus callosum on midline sagittal images (Fig. 9). Review of coronal images in the mammilary-anterior-commissural plane shows that this commissure connects the fornices and not the cerebral hemispheres. Use of DTI fiber tractography in this scenario can confirm the absence of crossing callosal fibers and demonstrate the Probst bundles running in an antero-posterior orientation alongside the medial ventricular margins (Fig. 9).

Secondary or acquired conditions causing a thin corpus callosum: diffuse injury

Thinning of the corpus callosum is determined by inspection of midsagittal images [14, 17]. Corpus callosum thinning correlates with decreased brain volume [12, 17, 18], and therefore the corpus callosum can act as a surrogate marker of cerebral atrophy [9]. This occurs from Wallerian degeneration (a process of antegrade neural disintegration that occurs after injury to the proximal axon or cell body). Digital tools can measure thickness of the corpus callosum to enable correlation with clinical parameters in a number of medical conditions [11, 19] (Fig. 3).

Corpus callosum thinning in hypoxic–ischemic encephalo-pathy Severe, global or advanced cases of hypoxic–ischemic encephalopathy affect the corpus callosum, resulting in generalized thinning [20] (Fig. 10). Fifty percent of children with peri-ventricular leukomalacia have thinning of the corpus callosum in association with white matter volume loss [21].

HIV encephalopathy Decreased brain volume in HIV-infected children usually involves sub-cortical areas including the corpus callosum, amygdala and caudates [22]. Areas adjacent to the ventricles are most affected by the viral penetration by infected mononuclear cells trafficking from cerebrospinal

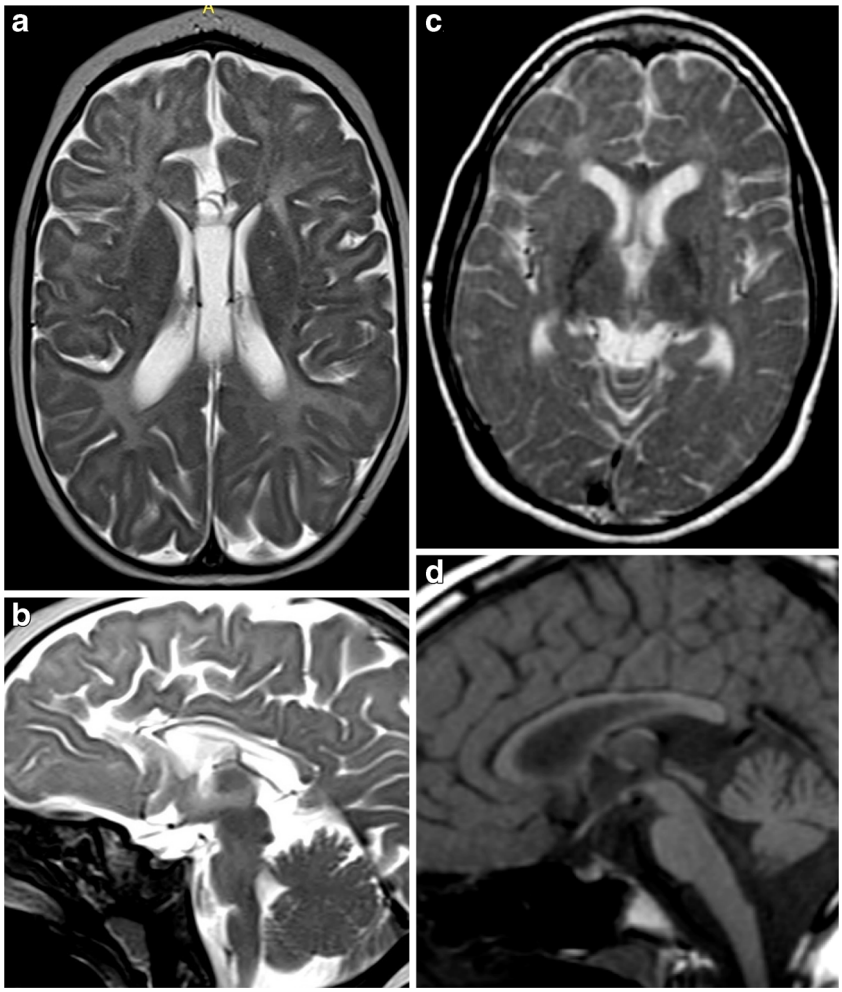


Fig. 6 Hypomyelinating disorders resulting in a thin corpus callosum. **a** Axial T2-weighted MRI in an 8-month-old with Pelizaeus–Merzbacher disease demonstrates a complete lack of visualized myelin in expected parts of the brain, with relatively high signal in all the white matter regions and tracts. **b** Corresponding sagittal T2-weighted image in the same child demonstrates a diffusely thin corpus callosum for age, with relative hyperintensity from failure to deposit myelin. **c** Axial T2-weighted MR image in a 17-year-old with Cockayne disease demonstrates typical bilateral calcification of the globi pallidi and lack of white matter myelination. **d** Sagittal T1-weighted MR image in the patient with Cockayne disease demonstrates the diffusely thin corpus callosum

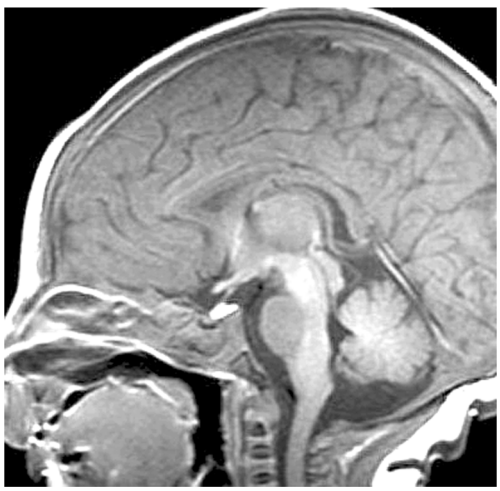


Fig. 7 Sagittal T1-weighted imaging in a 1-year-old with microcephaly demonstrates a thin and hypomyelinated corpus callosum



Fig. 8 Sagittal T1-weighted MRI in a 7-month-old with pachygyria demonstrates a thin corpus callosum, which is also hypogenetic at the rostrum and splenium

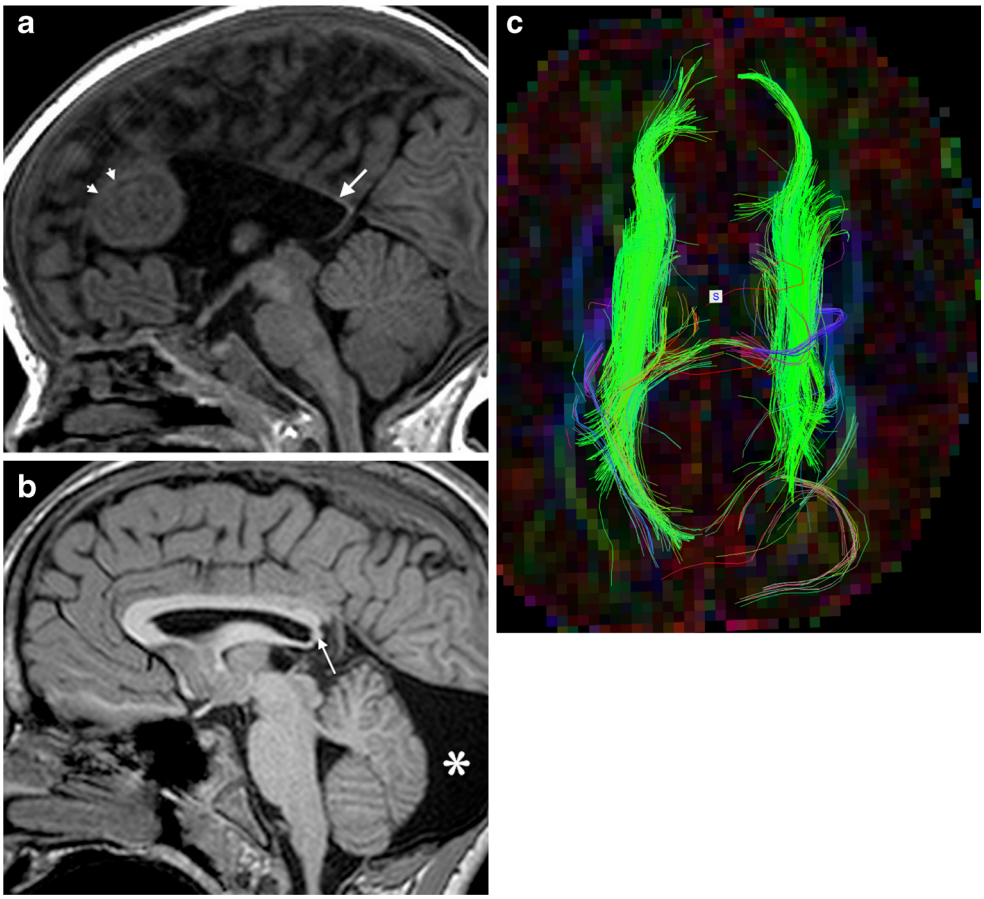


Fig. 9 Enlargement of the hippocampal commissure mimicking a thinning corpus callosum. **a** Sagittal T1-weighted MR image in a child with complete agenesis of the corpus callosum demonstrates an enlarged hippocampal commissure (*arrow*), mimicking a hypoplastic section of corpus callosum. The vertically radiating gyri and non-visualization of a horizontally oriented cingulate gyrus are clues to the diagnosis. The anterior mass-like lesion (arrowheads in a) represents the medial aspect of the asymmetrical right frontal lobe, which is herniating across the midline. **b** A different patient demonstrating a focally defective splenium which is replaced by an enlarged hippocampal commissure (*arrow*). There is also a posterior fossa arachnoid cyst (*asterisk*) displacing the cerebellum anteriorly. **c** Fiber tractography from axial diffusion tensor imaging in a with agenesis of the corpus demonstrates Probst bundles (*green*) running in an antero-posterior orientation along medial aspects of the lateral ventricles

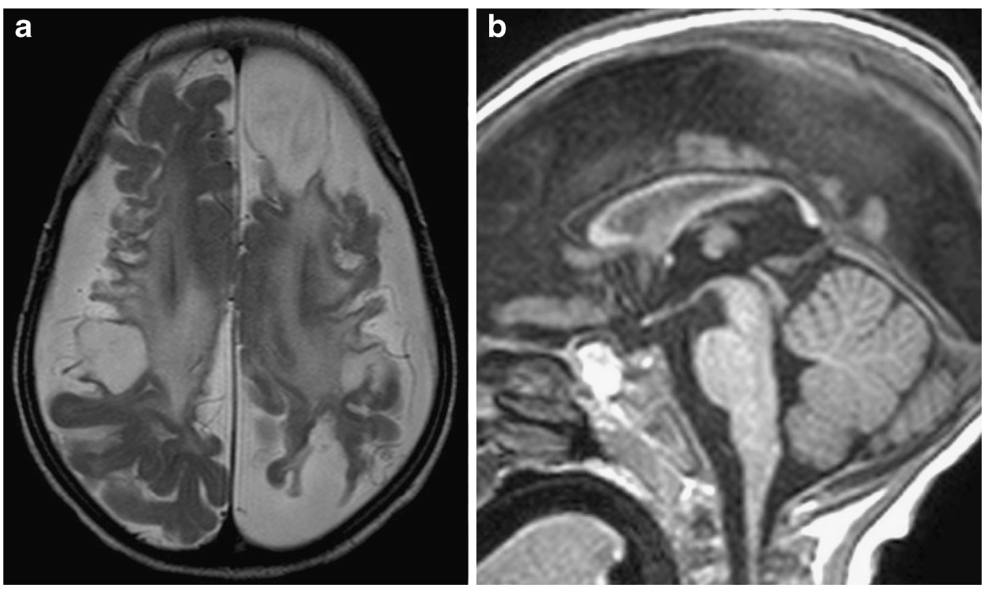


Fig. 10 MR imaging in a term newborn child who sustained severe global hypoxic–ischemic injury perinatally with resultant generalized thinning of the corpus callosum. **a** Axial T2-weighted MRI demonstrates the chronic changes of hypoxic–ischemic encephalopathy, including global atrophy, cystic encephalomalacia and prominent sub-arachnoid spaces. **b** Midsagittal T1-weighted MRI demonstrates diffuse corpus callosum thinning proportional to the degree of white matter volume loss. There is also incidental sphenoid sinus fluid

fluid [22, 23]. Decreased corpus callosum thickness is sometimes caused by inhibited development [18], by direct effects of the HIV virus [22], or through Wallerian degeneration (Fig. 11).

Hydrocephalus Hydrocephalus results in diffuse thinning of the corpus callosum even after ventricular shunting (Fig. 12). Possible causes include edema, ischemia and demyelination [24] related to a relatively long-standing compression of the fibers of the corpus callosum against the rigid under-surface of the falx [24].

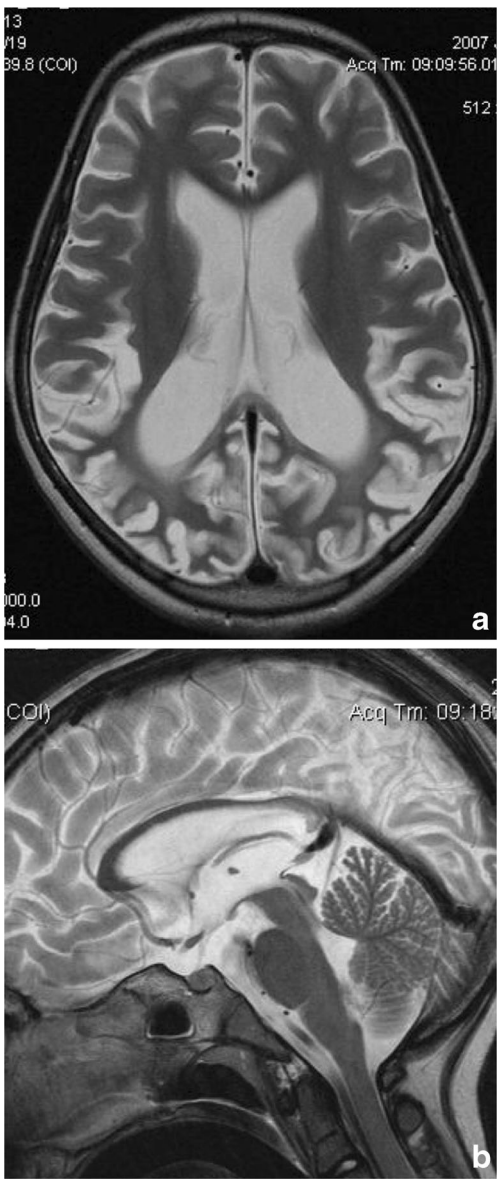


Fig. 11 MR imaging in a child with HIV encephalopathy and corpus callosum thinning. **a** Axial T2-weighted MRI demonstrates bilateral symmetrical subcortical white matter volume loss, predominantly in the posterior parietal areas. **b** Midsagittal T2-W MRI demonstrates diffuse corpus callosum thinning and prominent subarachnoid spaces. *HIV* human immunodeficiency virus

Corpus callosum thinning in dysmyelinating and demyelinating conditions Metachromatic leukodystrophy is the most common hereditary disorder of myelin formation and maintenance that results in diffuse symmetrical demyelination, with increased signal on T2-W fluid-attenuated inversion recovery (FLAIR) MR images, global cerebral atrophy and a thin corpus callosum. Adrenoleukodystrophy is another cause of demyelination, which typically progresses from the parieto-occipital to fronto-temporal lobes and involves the corpus callosum from posterior to anterior. Other hereditary leukoencephalopathies affecting the corpus callosum include Alexander disease (Fig. 13), Krabbe disease and Sudanophilic leukodystrophy [20].

Multiple sclerosis is the commonest demyelinating disorder [20] and typically affects young women [25]. The presence of subcallosal striations or callosal-septal interface lesions is highly sensitive and specific for this condition [20, 25]. Corpus callosum lesions have been reported in up to 93% of patients and atrophy of the corpus callosum can occur in long-standing cases, making the identification these lesions difficult [25]. Acute disseminated encephalomyelitis (ADEM) can mimic multiple sclerosis and commonly involves subcortical white matter and deep gray matter nuclei [26] (Fig. 14).

Hereditary spastic paraplegias are another cause of slowly progressive cerebral white matter and cortical atrophy with T2 prolongation of the periventricular white matter and thinning of the corpus callosum on MRI [10].

Secondary or acquired conditions causing a thin corpus callosum: focal injury

Regardless of etiology, focal white matter volume loss can result in focal thinning of the corpus callosum.

Mimickers of focal corpus callosum thinning

A slightly off-midline sagittal section can lead to apparent focal thinning of the corpus callosum (Fig. 15). Even on a true sagittal section there is often focal thinning at the junction between the posterior body and splenium in normal patients corresponding to the isthmus. Variations of normal can cause diagnostic dilemmas if not considered in relation to other findings such as cerebral atrophy (Fig. 16). Enlarged perivascular spaces can also mimic focal defects or thinning of the corpus callosum but are isointense to cerebrospinal fluid on all sequences [27].

Callosal hypogenesis vs. dysgenesis Callosal hypogenesis is incomplete formation of the corpus callosum and dysgenesis refers to defective development. Callosal hypogenesis from abnormal development affects formation of the posterior body, splenium and rostrum, resulting in a well-recognized

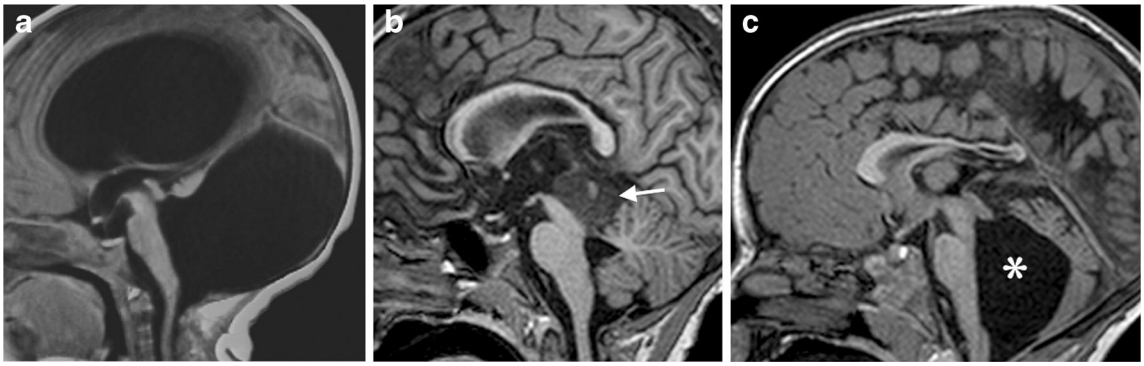


Fig. 12 Corpus callosum thinning in children with different causes for long-standing hydrocephalus. **a** Midsagittal T1-weighted MRI demonstrates features of a Dandy–Walker malformation with resultant diffuse thinning of the corpus callosum by long-standing hydrocephalus. **b** Sagittal T1-weighted image demonstrates corpus callosum thinning and signal alteration as a result of hydrocephalus developing from a tectal glioma (*arrow*). **c** Sagittal T1-weighted image of a patient after shunting for severe chronic hydrocephalus demonstrates thinning of the posterior corpus callosum. Note the isolated (encysted) 4th ventricle (*asterisk*)

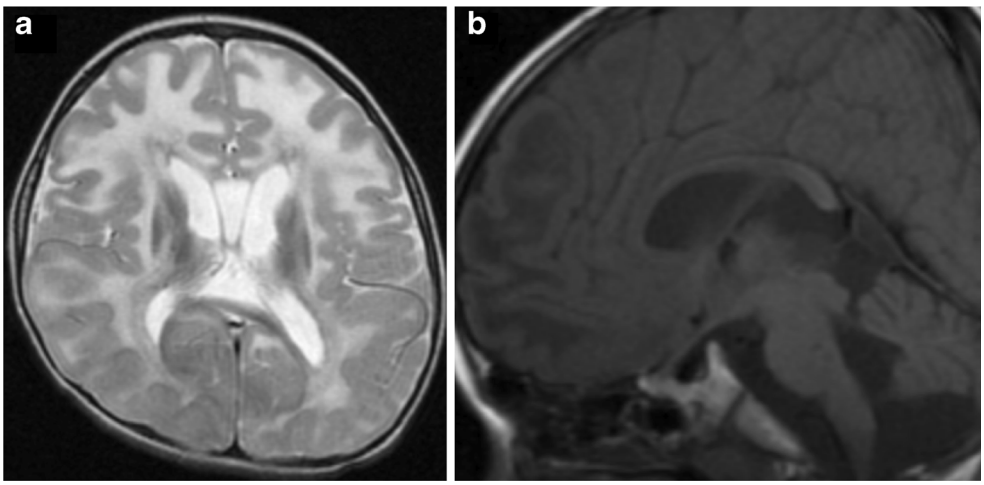


Fig. 13 Alexander disease. **a** Axial T2-weighted MRI demonstrates the severe involvement of the frontal white matter typical of Alexander disease. **b** Sagittal T1-weighted MRI demonstrates the loss of myelin signal and thinning of the rostrum, genu and body of the corpus callosum associated with the frontal white matter signal changes

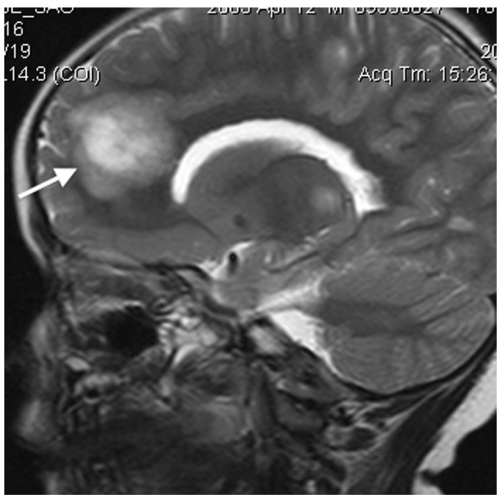


Fig. 14 Parasagittal T2-W image demonstrates a large inflammatory mass involving the left side of the forceps minor of the corpus callosum and the thalamus in a child with HIV who was diagnosed with acute disseminated encephalomyelitis, or ADEM. *HIV* human immunodeficiency virus

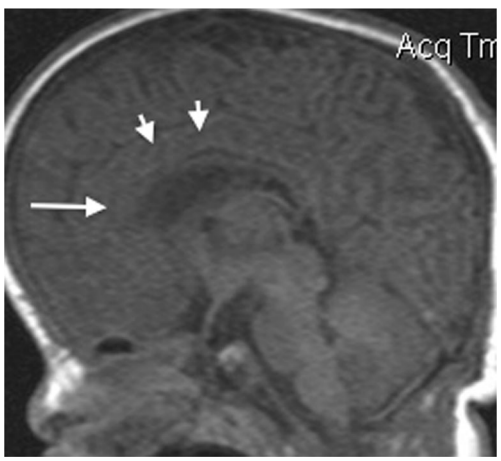


Fig. 15 T1-weighted MRI in a newborn has been performed obliquely rather than in the true sagittal plane with resultant poor visualization of the anterior corpus callosum (*long arrow*). Other than the fact that hypogenesis would present with absence of the splenium in addition to the rostrum, the cingulate gyrus is also present (*short arrows*) and points toward the presence of the corpus callosum

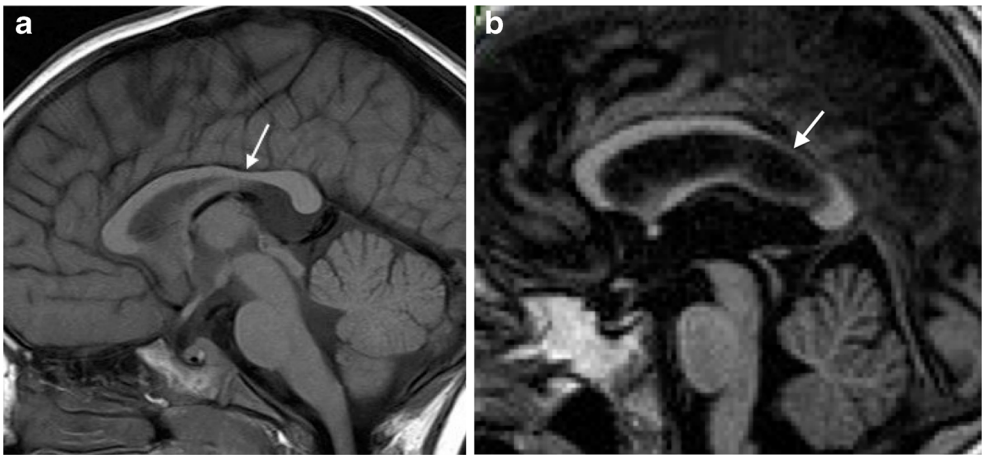


Fig. 16 Thinning of the corpus callosum at the isthmus can be normal or pathological and must be considered in relation to associated findings. **a** The isthmic thinning (*arrow*) in this child with no symptoms is a variation of normal. **b** The exaggerated isthmic thinning (*arrow*) in this child with significant cortical loss is pathological

appearance [28] (Fig. 17). In callosal dysgenesis occurring with holoprosencephaly, there is deficiency in the anterior and middle portions, which may be misinterpreted as a corpus callosum defect [28] (Fig. 17).

Inherited metabolic disorders with focal thinning of the corpus callosum

X-linked adrenoleukodystrophy in its classic childhood form shows a typical pattern of involvement that originates in the splenium of the corpus callosum and progresses to the peritrigonal white matter and corticospinal tracts, fornix, commissural fibers, visual and auditory pathways [27] (Fig. 18). Urea cycle disorders cause atrophy of affected areas, which in turn cause areas of focal thinning in the corpus callosum [27]. Cobalamin C deficiency is a treatable disorder that causes marked volume loss of the corpus callosum body and hypomyelination [27]. Hereditary spastic paraplegia with thin corpus callosum is associated with progressive cerebral and cerebellar atrophy and a thin corpus callosum predominantly involving the genu and body [29, 30].

Hypoglycemia

In newborns severe hypoglycemia results in T2 hyperintensity and restricted diffusion is seen in the occipital and parietal lobes and splenium of the corpus callosum. If untreated, localized thinning of the corpus callosum can occur at the splenium [26] (Fig. 19).

Encephalomalacia and white matter injury of prematurity

Focal thinning of the corpus callosum is common in late imaging of pre-term neonates with periventricular leukomalacia and in term infants with prenatal or perinatal brain injury. There is usually disproportionate involvement of the posterior corpus callosum [27] (Fig. 20) but when there is predominantly peri-rolandic injury, the corpus callosum is disproportionally thinner in its mid-portion [31] (Fig. 21).

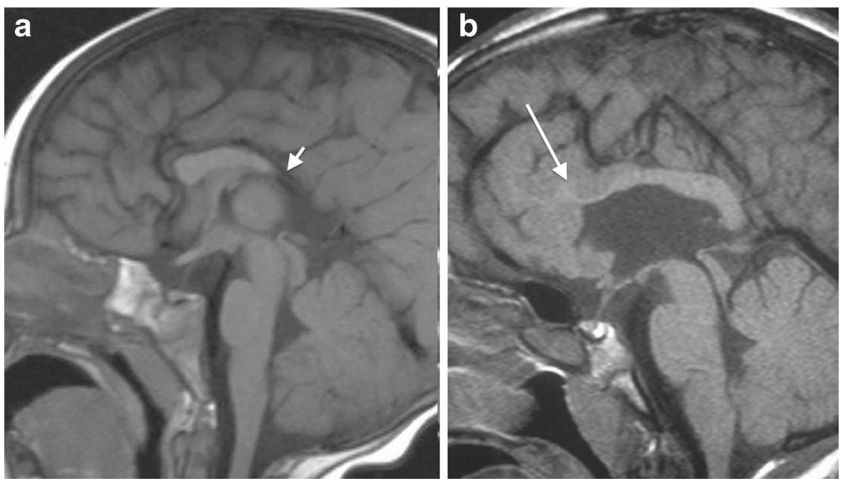


Fig. 17 Callosal hypogenesis vs. dysgenesis. **a** Sagittal T1-W MR image shows hypogenesis with completely absent posterior corpus callosum and rostrum (*arrow*). Note the "sun-ray radiation" of the adjacent parieto-occipital gyri, which differentiates this from posterior corpus callosum thinning. **b** Sagittal T1-W MR image shows holoprosencephaly, the only developmental cause of absence of the anterior and middle portions of the corpus callosum

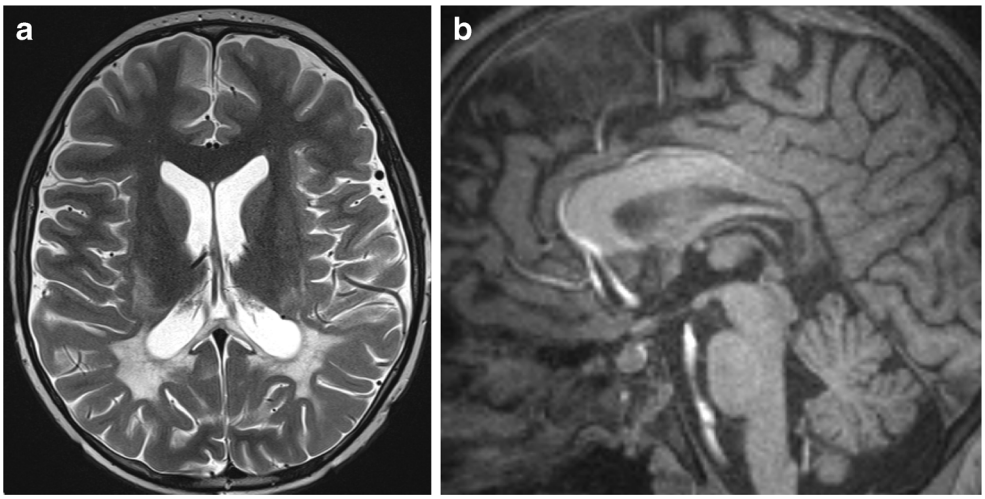


Fig. 18 Adrenoleukodystrophy. **a** Axial T2-weighted MR imaging demonstrates high signal from demyelination typically involving the parieto-occipital lobes. **b** Sagittal T1-weighted MR imaging of the classic childhood form shows a typical pattern of involvement that involves thinning of the splenium of the corpus callosum

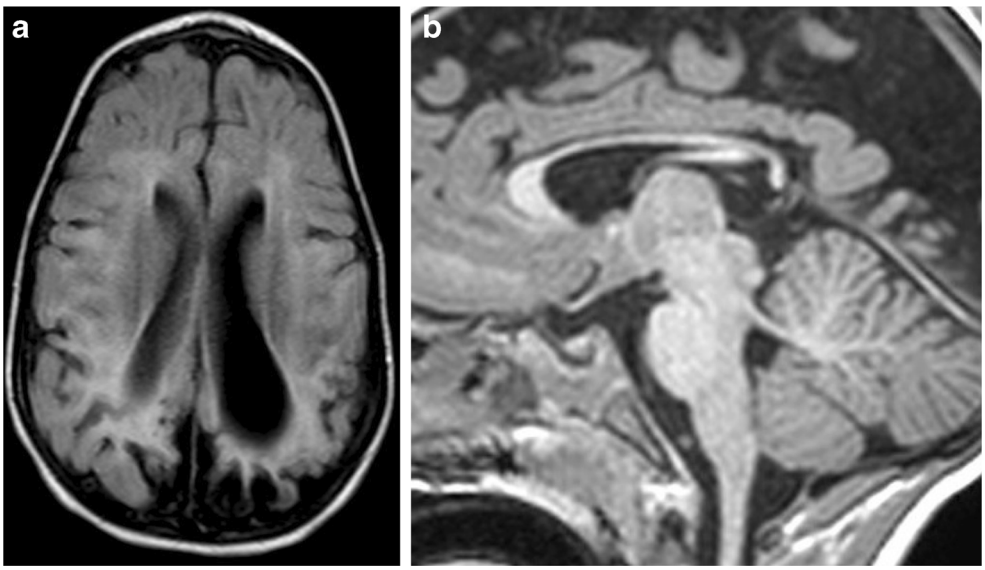


Fig. 19 Hypoglycemia occurring in the neonatal period with late imaging. **a** Axial FLAIR MR image shows bilateral parieto-occipital white matter high signal and volume loss affecting both gray and white matter as a result of hypoglycemia. **b** Sagittal T1-weighted MRI demonstrates resultant associated localized thinning of the middle and posterior corpus callosum. *FLAIR* fluid-attenuated inversion recovery

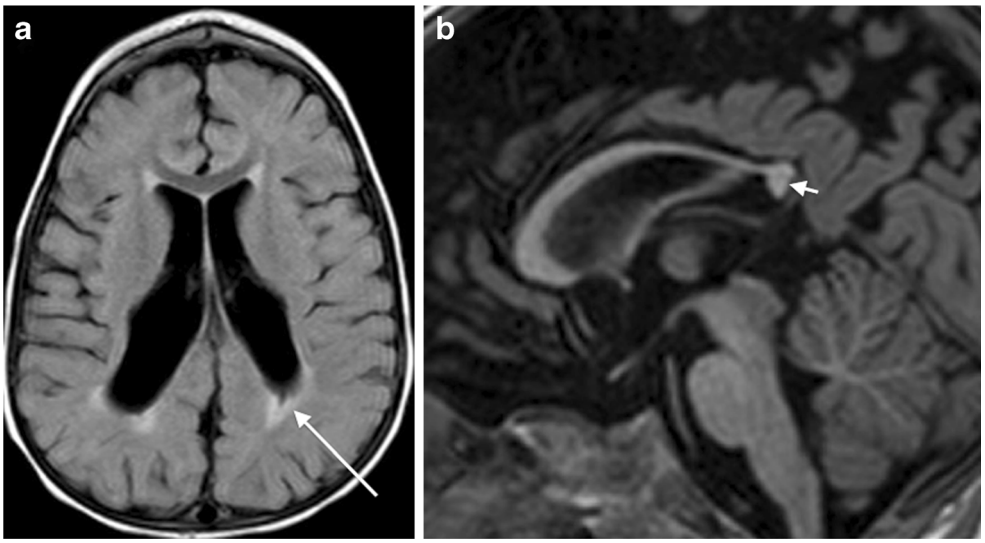


Fig. 20 Imaging in an infant born prematurely with posterior corpus callosum thinning as a result of hypoxic–ischemic encephalopathy. **a** Axial fluid-attenuated inversion recovery (FLAIR) MR image demonstrates white matter high signal with volume loss predominantly affecting the posterior periventricular (parietal and occipital) white matter (*arrow*). **b** Corresponding sagittal T1-weighted MR image shows associated focal thinning of the posterior corpus callosum (*arrow*)

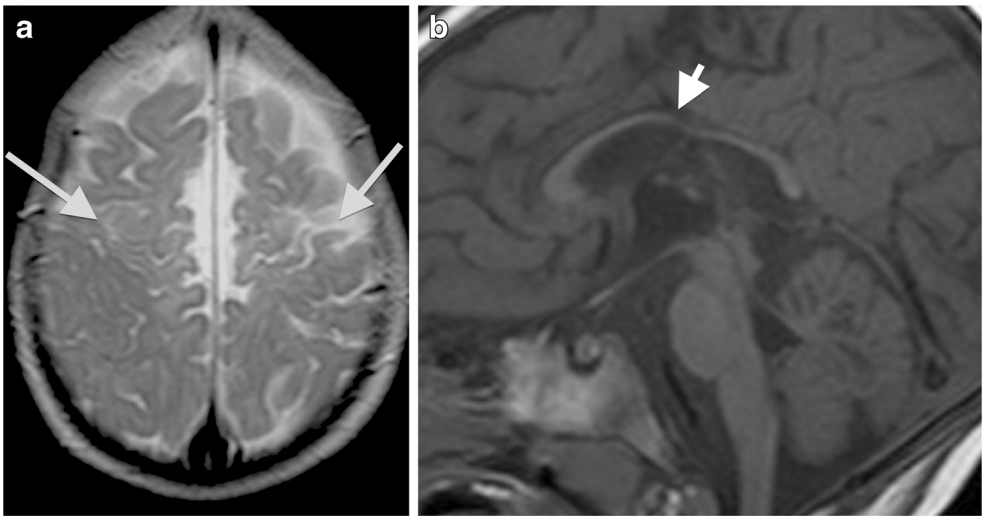


Fig. 21 MR shows thinning of the mid-corpus callosum in an infant as a result of white matter volume losses from hypoxic–ischemic encephalopathy affecting the parietal lobes and peri-rolandic regions. **a** Axial T2-W MR image demonstrates peri-rolandic white matter high signal (*arrows*) with volume loss. **b** Corresponding sagittal T1-W MRI demonstrates associated localized thinning of the middle corpus callosum (body) (*arrow*)

HIV-related atrophy

In HIV-associated atrophy, segmental cortical volume loss causes focal corpus callosum thinning. This occurs anteriorly when the frontal lobes are involved and in the middle portion of the corpus callosum with sensorimotor cortical loss [23].

Infarction and vasculitis

The corpus callosum communicates with the anterior artery, pericallosal artery and the posterior pericallosal artery. Infarction of the corpus callosum is therefore rare because of the rich blood supply [26]. Anterior cerebral artery vasculitis can occur with tuberculous meningitis, resulting in corpus callosum infarction (Fig. 22). With bilateral cerebral infarction, Wallerian degeneration of the commissural fibers can cause atrophy of the intervening corpus callosum [20].

Trauma

In 20% of cases of diffuse axonal injury, there is involvement of the corpus callosum, usually affecting the splenium (Fig. 23) or the undersurface of the posterior body. Focal encephalomalacia resulting in a corpus callosum "hole" is a sequela of this type of injury [2, 26].



Fig. 22 MRI in a child with confirmed tuberculous meningitis. Sagittal T2-W image demonstrates multiple infarcts involving the corpus callosum and the brainstem

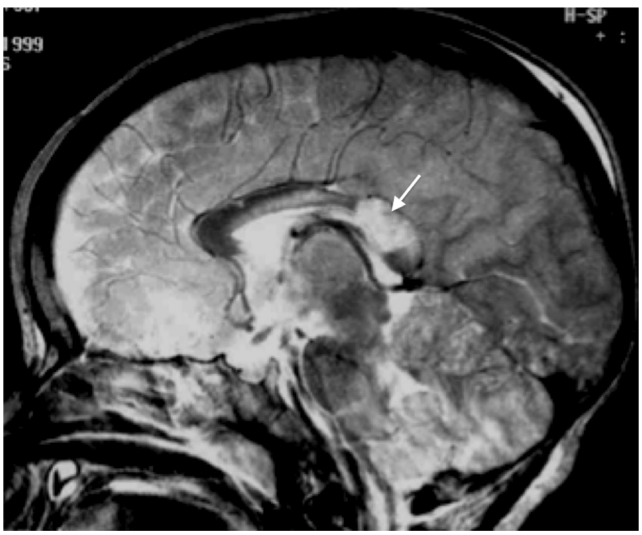


Fig. 23 MRI in a child who sustained diffuse axonal injury in a car accident. Sagittal T2-W image shows a hyperintense expansile lesion in the typical location of the splenium of the corpus callosum (*arrow*). There was associated cytotoxic edema on diffusion-weighted images (not shown)

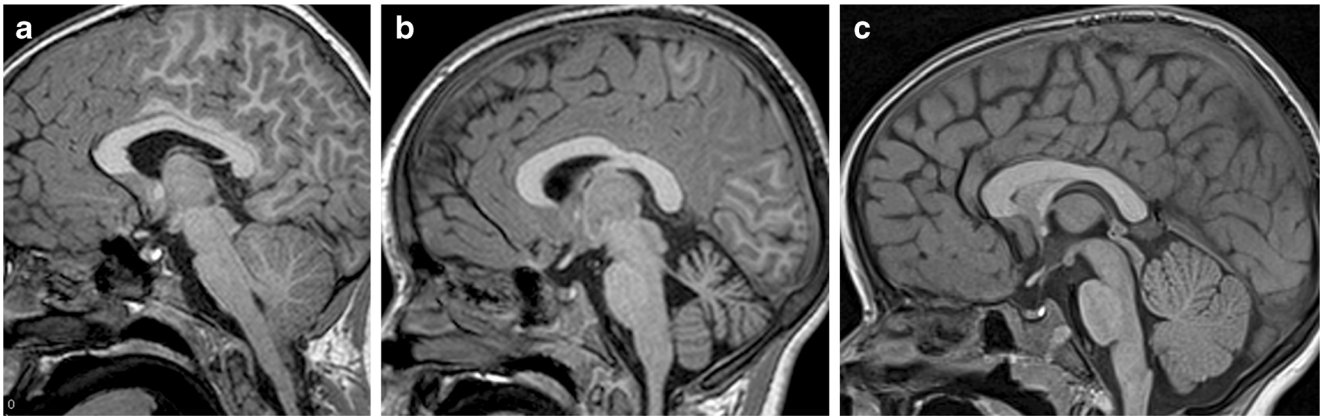


Fig. 24 Incidental non-inflammatory thickened corpus callosum. **a** Sagittal T1-weighted MRI shows borderline thick anterior corpus callosum in this patient with a Chiari II malformation associated with a myelomeningocele. **b** Sagittal T1-weighted MRI shows an incidental finding of thick corpus callosum and mild atrophy of the vermis in this patient imaged for refractory headaches. **c** Sagittal T1-weighted MRI demonstrates a relatively thick corpus callosum and no other pathological findings in this child with autism

Toxic causes: fetal alcohol syndrome

Various reports have shown that prenatal alcohol exposure has an adverse effect on callosal growth, resulting in localized thinning of the corpus callosum. A South African cohort of children showed this most prominently at the anterior third of the corpus callosum [32].

Iatrogenic causes: surgery and radiation

Surgery might account for localized thinning or defect in the corpus callosum. A focal defect can follow the removal of a corpus callosum tumor or epileptogenic focus, transcallosal surgery or ventricular shunting [26]. Localized Wallerian degeneration can follow surgical removal of a portion of the hemisphere or radiation [26].

A corpus callosum that is too thick

Garel et al. [14] provided updated biometric measurements for corpus callosum thickness and length dependent on age (Table 1), making determination of a thick corpus callosum more objective. A large corpus callosum can be incidental and it can also be associated with certain conditions (childhood schizophrenia, musicians) (Fig. 24), and occur secondary to inflammation or recognized non-inflammatory primary conditions.

Primary conditions associated with thickening of the corpus callosum

Conditions associated with megalencephaly These include megalencephaly, mega corpus callosum and complete lack of motor development [33–35]; megalencephaly, mega corpus callosum polymicrogyria (Fig. 25) [36]; macrocephaly-

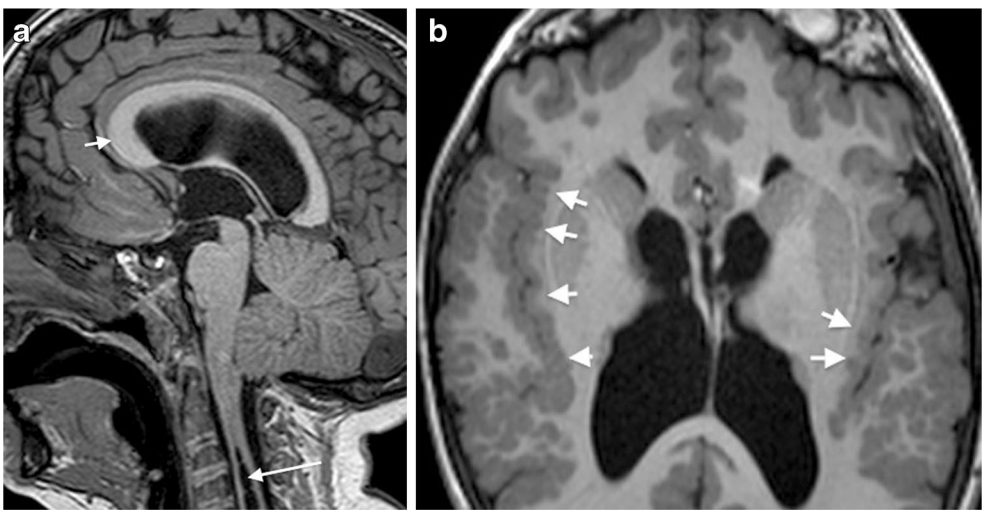


Fig. 25 MRI in a child with megalencephaly, mega corpus callosum polymicrogyria syndrome. **a** Sagittal T1-wegihted MR image demonstrates a Chiari I malformation (cerebellar tonsillar decent and syringomyelia (*long arrow*) and thick anterior corpus callosum (*short arrow*). **b** Axial T1-weighted MR image demonstrates associated peri-Sylvian polymicrogyria (*short arrows*)

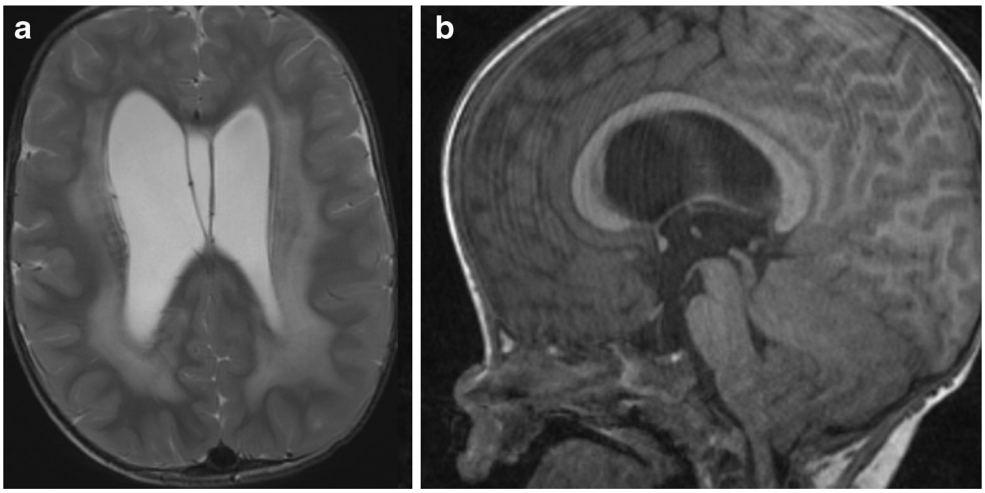


Fig. 26 Macrocephaly-capillary malformation syndrome. **a** Axial T2-weighted MR image demonstrates bilateral deep white matter high signal with enlarged ventricles. **b** Sagittal T1-weighted MR image demonstrates the corpus callosum where the thickness is masked by the presence of hydrocephalus. There is also crowding of the posterior fossa structures and cerebellar tonsillar descent (Chiari I malformation)

capillary malformation (Fig. 26) [37]; syndrome of mega corpus callosum and caudate nuclei with bilateral hippocampal malformation.

Thick corpus callosum associated with a normal head size Thick corpus callosum associated with a normal head size is reported with neurofibromatosis type I and syndrome of hypertrichosis, hyperkeratosis, abnormal corpus callosum and mental retardation; and it can be incidental, e.g., upper range of normal [38].

Thick corpus callosum associated with microcephaly A thick corpus callosum in children with microcephaly has been observed in association with Cohen syndrome [39].

Secondary or acquired conditions associated with thickening of the corpus callosum

Inflammatory thickening of the corpus callosum (Fig. 27) is more common than non-inflammatory enlargement and may be a precursor to thinning of the corpus callosum. These causes include acute ischemia (hypoxic–ischemic encephalopathy), acute trauma (diffuse axonal injury), infection (viral inflammation; ADEM) or demyelination (multiple sclerosis).

Conclusion

Increasing thickness of the corpus callosum is an important feature of development. Failure to gain thickness or patholog-

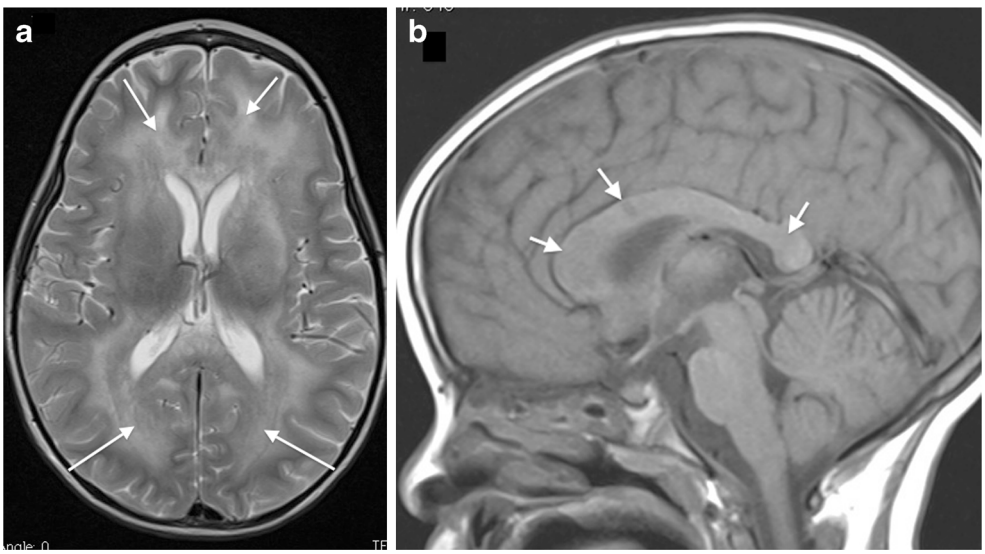


Fig. 27 Diffuse white matter inflammatory condition involving the corpus callosum. **a** Axial T2-W MR image demonstrates diffuse high signal of the deep white matter (*arrows*) with sparing of the subcortical U fibers. **b** On sagittal T1-weighted imaging the corpus callosum shows diffuse thickening with multiple focal low-signal areas (*arrows*)

ical thinning or thickening of the corpus callosum can be the result of a number of disease processes. The thickness also reflects the volume of the cerebral hemispheres, which occurs through Wallerian degeneration. It is therefore not only important to evaluate the morphology of the corpus callosum for congenital anomalies but also to evaluate the thickness of specific components or the whole corpus callosum in association with other cerebral findings.

Conflicts of interest None

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