Assessment of Normal Myelination with Magnetic Resonance Imaging

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Abstract

White matter myelination is essential to postnatal neurologic maturation and can be accurately evaluated by magnetic resonance imaging (MRI). Accordingly, MRI pulse sequences should be optimized for detection of myelin in young children. T1-weighted images are most useful during the first year of life. These demonstrate myelin-related white matter hyperintensity consequent to increasing cholesterol and galactocerebroside within myelin membranes. T2-weighted images are most useful in later stages of myelination, during which time elaboration of myelin leads to reduction in brain water content with associated T2 hypointensity. Additional information regarding the status of myelination can be obtained from T2-weighted fluid attenuation inversion recovery (FLAIR) and diffusion tensor imaging (DTI) pulse sequences. Clinically useful milestones for assessment of myelination across all these MRI pulse sequences are available as guidelines to image interpretation. Evaluation of myelination status using a combination of T1- and T2-weighted images should be routine in the interpretation of all pediatric brain MRI exams.

Keywords

► myelination
► development
► brain
► white matter
► infants
► magnetic resonance imaging

Magnetic resonance imaging (MRI) has revolutionized our ability to evaluate myelination in young children. Until the advent of cross-sectional imaging, the in vivo status of myelin development could only be evaluated through clinical history, neurologic exam, or by histology. By the early 1980s, computed tomography allowed gross assessment of myelination through its depiction of white matter density in the pediatric brain.1 However, it was not until the introduction of clinical MRI in the late 1980s that regional or tract-specific myelin maturation could be visualized.2 Myelin assessment has since evolved to become a routine aspect of pediatric neuroimaging. By reviewing a combination of T1- and T2-weighted MRI series, radiologists and clinicians can quickly and reliably determine whether a child’s myelin development is normal, delayed, or abnormal. This capability has greatly enhanced our ability to detect childhood leukoencephalopathies and other disorders of myelin at younger ages, with the attendant benefit of allowing for earlier prognostication and/or treatment. However, effectively detecting abnormalities of myelination is dependent on both proper imaging technique and an understanding of normal, age-related progression of this process. To that end, the MRI techniques that have evolved for the assessment of cerebral myelination will be reviewed. This will be followed by a discussion of both general myelination patterns as well as age-related milestones in myelin development. Finally, we conclude with a brief review of normal variants and imaging pitfalls.

MR Pulse Sequences

The core MRI techniques for myelin assessment in the infant are T1- and T2-weighted pulse sequences. These two forms of MRI contrast are complimentary in that T1-weighting provides information regarding the early stages of myelination, whereas T2-weighting provides insight into later stages of myelination maturation.

For myelin assessment with a 1.5-Tesla (T) MRI scanner, T1-weighted images are generally acquired using conventional spin echo images with a repetition time (TR) of ~500 to 600 milliseconds and an echo time (TE) of less than 20
milliseconds. Due to the significant reduction in T1 relaxation times at 3.0-T field strength, T1-weighted fluid attenuation inversion recovery images (FLAIR) are often employed as a means of improving T1 contrast. Typical 3.0-T T1-weighted FLAIR scan parameters include TR = 2950 milliseconds, TE = full minimum, inversion time (TI) = 890 milliseconds. An alternate means of obtaining excellent T1 contrast at 3.0-T field strength is through the use of a three-dimensional (3D) gradient echo T1-weighted pulse sequence, such as magnetization prepared rapid gradient echo (MP-RAGE). Common scan parameters would include TR = 6.4 milliseconds, TE = full minimum, TI = 900 milliseconds, flip angle = 8 degrees.

T2-weighted images can be acquired using conventional spin echo or fast spin echo (FSE) techniques. However, one must understand that FSE T2 images demonstrate myelin maturation at a slightly earlier age than conventional spin echo images due to increased magnetization transfer effects. In comparison to similar scans in adults, a higher T2-weighting is applied when scanning the brains of infants to compensate for the increased cerebral water content. One means of accomplishing this is using a heavily T2-weighted fast spin echo inversion recovery (FSE-IR) sequence. At our institution, we commonly employ the following parameters for this purpose at 1.5-T field strength: TR = 5000 milliseconds, TE = 101 milliseconds, TI = 133 milliseconds.

Although T2-weighted FLAIR images are among the most commonly used pulse sequences in contemporary MRI of the brain, the white matter contrast created by these images has traditionally been considered substandard for myelin staging. However, T2-weighted FLAIR images demonstrate signal changes related to the completion of myelination after myelins has already reached its adult appearance on T1- and T2-weighted images. Consequently, this pulse sequence may be of use in assessing the final stages of myelination in various regions of the brain. We employ the following T2-weighted FLAIR imaging parameters at both 1.5- and 3.0-T field strength: TR= 11000, TE = 147 milliseconds, and TI = 2250 milliseconds.

A recently developed tool in the armamentarium for myelin evaluation is diffusion tensor imaging (DTI). This technique uses echo planar pulse sequences to exploit the anisotropic diffusion of water molecules in cerebral tissue and create images that reflect increasing axonal organization in the brain. As areas in the brain with increased axonal organization differentially restrict the movement of water molecules perpendicular to the axon bundles, the fractional anisotropy (FA) of water can be used as a surrogate measure for white matter organization. Several studies have documented the relationship between FA and myelin maturity in infants. In particular, FA values have been useful for assessing the maturation of functional neuronal networks in the brain. Pediatric diffusion tensor imaging may be successfully obtained using the following parameters on a 3-T scanner: echo planar SE pulse sequence, 26 diffusion directions, TR = 8000 milliseconds, TE = minimum b-value = 1000 sec/mm². For the purposes of myelin assessment, raw DTI images can be postprocessed into grayscale FA maps or three-color directionally encoded FA maps where the red, green, or blue color corresponds to the principle axis of anisotropy.

Other advanced MRI techniques have been applied to gauging myelin maturation. These include magnetization transfer, quantitative T2 measurement, functional connectivity mapping, and multiparametric mapping of myelin water fraction. Although none of these methods has yet seen widespread clinical use, they may provide important future contributions to clinical assessment of myelin development.

Finally, it should be stated that appropriate selection of MRI planes can improve one's ability to appreciate age-related changes in myelination. As myelination is mostly centered in the brainstem in neonates, the sagittal plane is particularly useful in that group. During the intermediate stages of myelination, the axial plane is preferred due to its ability to demonstrate major tracts within the brain, such as the corticospinal tracts and optic radiations with bilateral symmetry. In the terminal stages of myelination, coronal images are useful for clear depiction of subcortical U-fibers in the frontal lobes.

General Signal Patterns in Brain Myelination

Despite region-related differences in the timing of myelination development, normal myelination in the brain progresses in a predictable, orderly fashion, both in terms of MRI signal characteristics and neuroanatomic distribution. An understanding of these patterns is critical to image interpretation, both from the standpoint of confirming normal development and for identifying pathologic alterations in the myelination process.

First, consider the general pattern of MR signal progression. In the fully myelinated brain, white matter is hyperintense to cortex on T1-weighted images and hypointense to cortex on T2-weighted images. In the unmyelinated portions of the neonatal brain, this pattern is reversed with the white matter demonstrating T1 hypointensity and T2 hyperintensity relative to cortex. The first of the MR signal changes to occur during myelination is an increase in white matter T1 signal. This alteration of T1 signal is believed to be due to increasing cholesterol and galactocerebroside within the cell membranes of the oligodendrocyte myelin processes. It is thought that these molecules create T1 shortening through their interaction with adjacent free water with associated magnetization transfer effects.

Unlike the previously described T1 signal change, T2 signal alteration during myelination is not solely contingent upon specific biochemical changes in the composition of myelin. Rather, growing T2 hypointensity during myelination is largely consequent to generalized reduction in free water content in maturing white matter. As myelin sheaths are elaborated by oligodendrocytes and packed into tight spirals around axons, the increasing volume of myelin simply replaces water in the interstitial space. Additionally, increasing length of hydrocarbon chains in the myelin membranes along with increasing numbers of hydrocarbon double
bonds\textsuperscript{24} contributes to a decrease in T2 times due to resultant increasing hydrophobic properties of the myelin membranes.\textsuperscript{25} Such T2 changes occur days to months after white matter has become hyperintense on the complimentary T1-weighted images\textsuperscript{26} and thus coincide with a later stage in myelin development. Consequently, although T1-weighted images provide the most useful information in the earlier stages of myelination, T2-weighted images are superior in the later stages of the process.

Of the standard MR pulse sequences, T2-weighted FLAIR images demonstrate the most complex signal changes in response to myelination. In general, these images behave as conventional T2-weighted images, with the exception that the conversion from high T2 signal to low T2 signal generally
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 badges behind standard T2-weighted sequences.5,9 This delay is felt to be secondary to partial T1-weighting within the FLAIR pulse sequence9 that partially mitigates the T2 effects. However, unlike the remainder of the brain, the deep hemispheric cerebral white matter demonstrates an unusual triphasic pattern on T2-weighted FLAIR sequences.8,9 This pattern consists of initial neonatal deep white matter hypointensity, followed by gradual signal conversion to hyperintensity. This is eventually followed by reversion to a hypointense appearance during the final stages of myelin development. It is believed that the initial hypointense phase of this FLAIR signal sequence is the result of exceptionally prominent free water in the deep cerebral white matter during the early neonatal period.27 This water lowers the T1 signal to the point that white matter signal is selectively suppressed by the T2 FLAIR pulse sequence in a manner similar to that seen with cerebrospinal fluid.9 As the white matter matures, free water decreases, raising the associated T1 signal to the point that the FLAIR signal suppression is lost, resulting in T2 hyperintense white matter.5,9 Finally, as myelin undergoes further maturation, the free water concentration further declines consequent to increasing volumes of hydrophobic myelin. Eventually, this free water loss leads to the third and final phase of signal change in the deep hemispheric white matter, namely renewed T2 hypointensity. Despite occurring at a later time point, this final phase is entirely analogous to the hypointensity observed on conventional T2 images during the later stages of myelination.

Diffusion tensor imaging for measurement of FA is a more recently introduced tool for the evaluation of myelin; however, this imaging technique is becoming increasingly widespread in clinical practice. As previously mentioned, increasing FA values can serve as a surrogate measure for increasing white matter organization. However, even more interesting is the fact that FA values in the developing infant brain increase in two different distinct phases.28 The first FA rise actually precedes myelination. Consequently, authors have suggested that this may be related to a premyelination state.29 The increase in anisotropy during this early phase is thought to be caused by elaboration of microtubule proteins in the axonal cytoskeleton, increasing axon caliber, increasing activity of sodium ion channels, and proliferation of oligodendrocytes as precursors to myelination.12,21,28,29 The second phase of FA growth coincides with increasing elaboration of myelin28 and reduction in the size of the extracellular space.21 Myelinated axons restrict nonparallel water diffusion leading to a local increase in FA values. Of note, this gradual rise in anisotropy continues beyond the second year of life,30 suggesting that FA values may eventually provide insight into the subtle changes in brain maturation that occur between the second year of life and adulthood.

Contrast Specific Temporal Sequences of Myelination

• Table 1 is a composite outline of normal myelination chronology during the first 2 years of life as described by multiple authors.5,6,9,13,25,36 This table presents the expected appearance of T1- and T2-weighted MRI, T2-weighted FLAIR, and DTI images at specific time points during infancy. There is some inconsistency between authors regarding the timing of some milestones of myelin maturation. This likely exists based on variations in scan technique and image interpretation criteria. Regarding this variability, • Table 1 provides a relatively conservative reference in the sense that most authors agree that myelination of the specific white matter structure should be complete by the ages referenced in the table. Clinical confidence in myelin assessment is increased by employing multiple MRI contrasts. • Figures 1 through 6 illustrate several significant age-related myelination milestones in developing brains. These will be revisited in the following discussion of contrast-specific myelination patterns.

T1-Weighted Images

From birth through 12 months, T1-weighted images provide an excellent window into myelin development. In the
newborn, there is extensive brainstem myelination (►Fig. 1). Myelin-associated T1 signal hyperintensity is noted in the medulla, dorsal pons, brachium pontis, and both the inferior and superior cerebellar peduncles. More superiorly, myelinated white matter is visible in the cerebral peduncles of the midbrain, the ventral lateral thalami, and the posterior limbs of the internal capsules. Additional T1 hyperintense myelin can be identified in the corticospinal tracts extending superiorly in the perisylvian centrum semiovale. The cortex along the central sulci is similarly T1 hyperintense. In the visual pathways, myelin is seen in the optic nerves, optic tracts, and optic radiations.

By 2 to 3 months of age, myelination in the internal capsule has extended to involve the anterior limb (►Fig. 2). Between 2 and 3 months of age, T1 hyperintense myelin progresses peripherally from the deep cerebellar white matter to involve the entire cerebellum. At 4 months, the splenium of the corpus callosum has myelinated. Callosal myelination proceeds in an anterior to posterior direction to involve the genu by 6 months of age (►Fig. 3).

Outside the central sulcus region, initiation of myelination in the subcortical white matter begins at ~3 months of age. Progression of T1 hyperintensity in the supratentorial white matter evolves peripherally from the perirolandic region to...
involve the subcortical U-fibers in the occipital pole by 7 months of age. On the other hand, T1 hyperintensity in the frontal and temporal lobes proceeds more slowly and does not reach the most anterior subcortical U-fibers in these lobes until ~1 year. Despite the fact that there is still active, ongoing cerebral myelination, the brain at this stage has achieved a typical adult T1 contrast pattern. Consequently, T1-weighted images are of little use for myelin assessment beyond the first year.

**T2-Weighted Images**

In the newborn, myelination, as demonstrated by low T2 signal, is anatomically less extensive than the signal changes contemporaneously demonstrated by T1 images. Sites of myelination include the medulla, dorsal pons, superior and inferior cerebellar peduncles, midbrain, and ventral lateral thalamus. The cortex surrounding the central sulcus also demonstrates low signal at the time of birth or shortly thereafter. By 2 months, low T2-signal myelin has extended to involve the brachium pontis, posterior limb of the internal capsule, and the perirolandic component of the centrum semiovale. Also, at about this time, myelin becomes visible in the optic tracts. Progressive myelination of the visual system leads to low T2 signal in the optic radiations and subcortical white matter about the calcarine fissure by 4 months of age.

**Figure 2** A 2-month-old girl imaged at 3 Tesla field strength. (A) Axial T1-weighted image demonstrates prominent high-signal myelination of the posterior limbs of the internal capsules and early myelination within the anterior limbs. (B) Axial T2-weighted fluid attenuation inversion recovery image shows uniform high signal throughout the deep hemispheric white matter. The low-signal regions characteristic of the newborn have resolved by this age. (C) Axial T2-weighted fast spin echo inversion recovery (FSE-IR) image demonstrating low-signal myelin within the posterior limbs of the internal capsules, the anterior thalami, and to a lesser extent, the bilateral optic radiations. (D) Axial T2-weighted FSE-IR image displays myelin involving the brachium pontis bilaterally with early involvement of the deep cerebellar white matter.
T2-signal changes in the corpus callosum lag 1 to 2 months behind the T1-signal changes at this site. Notably, at 6 months, while the entire corpus callosum is hyperintense on T1, the T2-signal changes are just beginning in the splenium (►Fig. 3). The genu of the corpus callosum will not demonstrate T2 hypointensity until 8 months. Concurrent with these callosal signal changes, the anterior limb of the internal capsule achieves T2 hypointensity by 8 months.

Within the posterior fossa, the ventral pons demonstrates T2 hypointense myelin by 6 months and the deep cerebellar white matter becomes hypointense by 12 months (►Fig. 4). The entire posterior fossa white matter is T2 hypointense by 18 months.

With respect to the hemispheric white matter, signal changes commence in the central occipital white matter by 7 months, with progressive involvement of the central frontal white matter by 11 months and the central temporal white matter by 12 months. As this process is completing, peripheral extension of T2 hyperintensity into the subcortical U-fibers is beginning with early involvement of the occipital lobes around the 1-year mark. Occipital subcortical white matter signal changes should be complete by 15 months (►Fig. 5). However, the anterior aspect of the frontal and temporal lobes will not achieve a similar state of myelination until around 24 months (►Fig. 6).

T2-Weighted FLAIR Images
Assessing myelination on the basis of T2-weighted FLAIR imaging is controversial with some authors advocating this pulse sequence, and other authors considering it to be of minimal utility. Regardless of one’s opinion on the matter, familiarity with the appearance of myelination on FLAIR...
images is important as this pulse sequence is frequently encountered in clinical imaging.

At birth, areas of low T2 signal are noted in the deep white matter of the occipital, frontal, and temporal lobes (►Figs. 1 and 7).5,9 As previously discussed, this is the result of a large amount of free water in these regions with consequent FLAIR signal suppression. By 1 month of age, this low FLAIR signal will have converted to high signal in the occipital lobe. By 2 months of age, this same deep white matter signal conversion will be complete in the frontal and temporal lobes (►Figs. 2 and 7).9

On FLAIR imaging, familiar myelination landmarks generally lag behind conventional T2-weighted images, with the posterior limb of the internal capsule and brachium pontis first demonstrating low T2 signal ~3 months.5 Low myelin-related signal in the dorsal pons is not seen on FLAIR images until ~4 months of age,5 a site that appears myelinated at birth on both T1- and T2-weighted images. Visualization of myelin in the supratentorial motor and visual systems is similarly delayed, with the periolandic centrum semiovale demonstrating myelin by ~5 months and the optic radiations demonstrating myelin by ~6 months (►Fig. 3).5

Figure 4 A 12-month-old boy imaged at 3 Tesla field strength. (A) Coronal T1-weighted three-dimensional gradient echo image demonstrates an adult pattern of myelination with high-signal myelin extending into the subcortical U-fibers of the frontal and temporal lobes as well as throughout the cerebellum. (B) Axial T2-weighted fluid attenuation inversion recovery image shows early low-signal myelin in the deep white matter of the anteromedial occipital lobes best seen on the right (arrow). (C) Axial T2-weighted fast spin echo inversion recovery (FSE-IR) image demonstrates low-signal myelin in the deep white matter of the cerebellar hemispheres. (D) Axial T2-weighted FSE-IR image at a more superior level demonstrating early hypointense myelination of the occipital subcortical U-fibers. There is low-signal myelin in the deep temporal white matter; however, the subcortical white matter of the temporal lobes demonstrates persistent high signal.
Of interest, there is minimal, if any, delay in myelin-related signal changes in the corpus callosum with respect to T2-weighted images. Authors describe callosal myelination to be complete on FLAIR between 5 and 7 months,\(^5,9\) which minimally lags behind reported callosal myelination on FSE T2-weighted images.\(^5\) However, this FLAIR signal change may slightly precede the time of callosal myelination as reported by conventional spin echo T2-weighted images.\(^25\) Similarly, the appearance of myelin in the anterior limb of the internal capsule at 8 months on FLAIR imaging\(^5,9\) is contemporary with similar signal changes reported on conventional spin echo T2-weighted images, but apparently lags behind those seen on FSE T2 pulse sequences.

In the second year, the deep white matter completes its triphasic FLAIR signal progression by reverting again to low signal as myelin matures (\(\rightarrow\text{Fig. 7}\)). This occurs first in the deep occipital white matter at 12 months (\(\rightarrow\text{Fig. 4}\)), followed by the deep frontal white matter at \(\sim\)14 months (\(\rightarrow\text{Fig. 5}\)), and the deep temporal white matter at \(\sim\)22 to 25 months (\(\rightarrow\text{Fig. 6}\)).\(^5,9\) Low FLAIR signal in the peripheral white matter of the cerebral hemispheres occurs later than the deep white matter changes at each respective location. Subcortical low FLAIR signal is present in the occipital lobes at 14 months and in the frontal lobes at 20 months.\(^7\) On T2-weighted FLAIR sequences, white matter in the subcortical U-fibers of the temporal lobes commonly remains hyperintense beyond 24 months (\(\rightarrow\text{Fig. 6}\)).\(^9\)

**Figure 5** An 18-month-old girl imaged at 1.5 Tesla field strength. (A) Axial T2-weighted fluid attenuation inversion recovery (FLAIR) image shows early low-signal myelin in the subcortical white matter of the occipital lobes (arrows). (B) Coronal axial T2-weighted FLAIR image demonstrating low-signal myelin in the deep white matter of the frontal lobes. (C) Axial T2-weighted fast spin echo inversion recovery (FSE-IR) image demonstrates prominent subcortical white matter myelination posteriorly and significantly less subcortical myelination in the frontal lobes. (D) Axial T2-weighted FSE-IR image demonstrates complete peripheral myelination in the cerebellum.
Diffusion Tensor Imaging

In 2006, Hermoye and colleagues published an analysis of DTI obtained from 30 infants and children ranging in age from 0 to 54 months using a 1.5-T MRI scanner. Their qualitative analysis of the associated FA maps and color-encoded FA directional maps provide guidelines for assessment of such images in the clinical setting. The following is an abbreviated summary of their findings.

In contrast to T1- and T2-weighted imaging, the majority of the major white matter tracts in the brain are visible at birth on FA maps. However, while the central portions of these tracts demonstrate increased anisotropy, the peripheral portions of these tracts have relatively low FA that is difficult to distinguish from gray matter. Structures that are well seen at birth include the superior and inferior cerebellar peduncles, as well as the brachium pontis. In the brainstem, a composite dorsal tract that includes the medial longitudinal fasciculus, medial lemniscus, and reticular formation is evident. Visible components of the motor system include the corticospinal tracts, cerebral peduncles, internal capsules, and corona radiata. Within the limbic system, the cingulum and fornix are discernible. In addition, several association tracts demonstrate increased anisotropy, including the corpus callosum, anterior commissure, and uncinate fascicules.

**Figure 6** A 28-month-old boy imaged at 1.5 Tesla field strength. (A) Axial T2-weighted fluid attenuation inversion recovery (FLAIR) image demonstrating near complete low signal white matter myelination with the exception of the anterior temporal poles. Persistent high signal in the occipital lobes adjacent to the occipital horns of the lateral ventricles represents a normal FLAIR variant. (B) Axial T2-weighted FLAIR image confirms complete low-signal myelination of the frontal and parietal lobes with terminal zones of high signal in the periatrial regions as a normal variant. (C,D) Axial fast spin echo T2-weighted images demonstrate complete low-signal myelination throughout the brain with the exception of the periatrial terminal zones.
By the fourth month, the peripheral portions of the previously demonstrated tracts demonstrate increasing anisotropy. Increased FA is also visible in subcortical U-fibers. Newly visible white matter tracts include the inferior frontal occipital fasciculus and the inferior longitudinal fasciculus. The forceps minor and forceps major can now be identified. However, the forceps major demonstrates an immature inverted V shape at 4 months that will convert to an inverted U shape by 6 months.

At 1 year of age, the superior longitudinal fasciculus becomes the last major white matter tract to become conspicuous. White matter landmarks unique to DTI, the so-called crossing areas, demonstrate increased FA at this time (Fig. 8). The term “crossing areas” refers to the four white matter locations where the forceps minor and forceps major meet with the internal capsules along the lateral aspect of the corpus callosum. Prior to 12 months, these are low anisotropy structures. Beyond the first year, there is gradual, progressive increase in FA as well as tract thickness throughout the brain. However, unlike T1- and T2-weighted images that have a relatively mature appearance by 2 years, color-encoded directional FA maps do not achieve a mature appearance until about 4 years of age. Despite the adult-like appearance of FA maps, quantitative analysis demonstrates gradual increasing anisotropy throughout the white matter throughout the first decade of life.

Normal Variants and Pitfalls

TERMINAL ZONES

A point of confusion that frequently arises in reviewing the T2-weighted conventional images and T2-weighted FLAIR images in the brains of children and young adults are the presence of small, bilaterally symmetric foci of high signal occurring in the white matter dorsolateral to the atria of the lateral ventricles. These most commonly represent so-called terminal zones of incompletely myelinated brain. These small areas of signal hyperintensity are considered to be a normal developmental variant and at times are even identifiable in the young adult population. Although early histopathologic studies have documented unmyelinated brain in these regions, more recent literature has suggested that prominent perivascular spaces may also be contributing to this signal hyperintensity (Fig. 9). When these periatrial hyperintensities are seen in a young child, it is important to differentiate normal terminal zones from pathologic periventricular leukomalacia associated with prematurity. The two conditions can be distinguished from each other by looking for small bands of low signal, normally myelinated brain separating the high signal regions from the ventricles. This finding will be present with terminal zones of myelination, but will be absent in periventricular leukomalacia where the high signal intensity will commonly extend all the way to the ventricular ependyma. Another helpful clue is that terminal zones have a triangular appearance in the coronal plane with the tip of the triangle oriented superiorly. Finally, periventricular leukomalacia typically occurs more inferolaterally along the atria, near the optic radiations.

In addition to the periventricular regions, persistent unmyelinated areas of white matter are occasionally seen in the anterior frontal lobes and anterior temporal lobes beyond 2 years of age. Consequently, when bilaterally symmetric white matter T2 signal hyperintensities are identified in the frontotemporal regions in young children, consideration should be given to this developmental variant. Generally, these sites of terminal myelination will convert to a normal myelinated appearance by the age of 40 months.

Figure 7 Triphasic evolution of myelin signal in the deep hemispheric white matter on T2-weighted fluid attenuation inversion recovery images. (A) In this 3-week-old boy, there is patchy low signal in the deep white matter due to high cerebrospinal fluid-like content with signal suppression. (B) In this 4-month-old boy, deep white matter signal has converted to a uniformly hyperintense appearance. (C) In this 2½-year-old girl, myelination has caused the deep white matter to again become hypointense with the exception of the periatrial terminal zones.
Frequently, brain imaging is performed on children that have a history of premature birth, and the question arises as to whether assessment of myelination should be based on the child’s birth age or an age adjusted to account for prematurity. Although some authors advocate using the adjusted age, others argue that rapid acceleration of brain growth during the first 2 postnatal months due to endogenous steroid secretion eliminates the need for such an adjustment after 2 months of age. Finally, it should be noted that research has been performed on normal myelination in fetuses and very preterm infants. This literature can be used to guide myelination assessment for infants imaged at less than 40 weeks gestational age.

**Conclusion**

In the young infant, brain myelination is a crucial component of neurologic development that correlates with increasing sensory, motor, and cognitive ability. Consequently, a direct evaluation of myelination should be conducted on each pediatric brain MRI. Both supratentorial and infratentorial...
white matter should be scrutinized for signal changes of myelination and compared against age-appropriate milestones. At the present time, T1- and T2-weighted images continue to provide the most important information regarding cerebral myelination. T1-weighted images are most useful during the first year. As T1-weighted images approach a mature appearance, T2-weighted images become superior for continued surveillance of ongoing myelination. As our understanding of the later stages of myelination increases, particularly beyond the first two years of life, other techniques, such as FLAIR and DTI, are gaining increasing clinical relevance. Additionally, quantitative MRI techniques for evaluation of myelin may become clinically useful in the near future. As knowledge of normal myelination advances, our ability to both recognize and address conditions of abnormal myelination is enhanced.

References
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