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BACKGROUND AND PURPOSE: **MR imaging was performed in very preterm infants by using an MR imager in the neonatal intensive care unit. The aims of this study were to assess the development of myelination in the preterm brain based on MR imaging findings and to compare the ability of T1-weighted conventional spin-echo, inversion recovery fast spin-echo, and T2-weighted fast spin-echo MR imaging to show myelination in these infants.**

METHODS: **MR imaging was performed for 26 preterm infants with a median gestational age of 28 weeks who had normal neurodevelopmental outcomes at 2 years corrected age.**

RESULTS: **Myelin was evident in the gracile and cuneate nuclei and fasciculi, vestibular nuclei, cerebellar vermis, inferior and superior cerebellar peduncles, dentate nucleus, medial longitudinal fasciculus, medial geniculate bodies, subthalamic nuclei, inferior olivary nuclei, ventrolateral nuclei of the thalamus, decussation of the superior cerebellar peduncles, medial lemnisci, lateral lemnisci, and inferior colliculi at ≤28 weeks gestational age. From this gestational age, myelination was not visualized at any new site until 36 weeks gestational age, when myelin was visualized in the corona radiata, posterior limb of the internal capsule, corticospinal tracts of the precentral and postcentral gyri, and lateral geniculate bodies. T2-weighted fast spin-echo MR imaging showed myelin in gray matter nuclei at an earlier gestational age than did T1-weighted conventional spin-echo or inversion recovery fast spin-echo MR imaging. T1-weighted conventional spin-echo MR imaging showed myelin earlier in some white matter tracts in the preterm brain.**

CONCLUSION: **Myelination was evident in numerous gray and white matter structures in the very preterm brain. A knowledge of myelination milestones will allow delays to be detected at an early stage.**

MR imaging is a noninvasive and non-ionizing imaging technique, and the excellent soft-tissue differentiation afforded by MR imaging makes it the modality of choice to show cerebral myelination in vivo. Numerous MR imaging studies describing the post-term development of myelination in neonates have been reported (1–8), and the development of myelination in the preterm brain has been described histologically, with numerous gray matter nuclei and white

matter tracts showing evidence of myelination before 30 weeks gestational age (9, 10). However, little is known regarding the progression of myelination before term as revealed by MR imaging. The few studies of preterm infants to date either were conducted for infants who were ≥30 weeks gestational age at the time of imaging (11) or examined myelination in only a limited number of anatomic sites (12, 13). A detailed knowledge of myelination milestones in preterm infants who have achieved good neurodevelopmental outcomes is essential to detect delays in development at an early stage. The effects of such delays on long-term neurodevelopmental outcome could then be studied.

For this study, we obtained T1-weighted conventional spin-echo, inversion recovery fast spin-echo, and T2-weighted fast spin-echo MR images of a cohort of preterm infants, born at ≤30 weeks gestational age, who were admitted to the neonatal intensive care unit. The images were obtained using a dedicated neonatal MR imager in the neonatal inten-

TABLE 1: Pulse sequence parameters

Pulse Sequence	TR (ms)	TI (ms)	TE (ms)	NSA	Matrix	Section Thickness (mm)	FOV (cm)	Echo Train Length	Inter-echo Spacing (ms)
T1 CSE	600		20	2	192 × 256	4	20		
IR FSE	3695	950	30	4	256 × 256	4	20	16	16
T2 FSE	3500		208	4	256 × 256	4	20	16	16

Note.—TI indicates inversion time; NSA, number of signals acquired; FOV, field of view; T1 CSE, T1-weighted conventional spin-echo; IR FSE, inversion recovery fast spin-echo; T2 FSE, T2-weighted fast spin-echo.

sive care unit equipped with full intensive care facilities, obviating the need to transport very low birth weight preterm infants to the MR imaging department. When possible, serial images were obtained between birth and term. The aims of this study were to assess the development of myelination in the preterm brain from 25 weeks gestational age until term using serial MR imaging and to compare these results with the reference standard of histology and to compare T1-weighted conventional spin-echo, inversion recovery fast spin-echo, and T2-weighted fast spin-echo MR imaging to determine whether there are any differences among these pulse sequences in their ability to show myelination in the preterm brain.

Methods

Patients

For this retrospective study, we analyzed MR images obtained in preterm infants, born at ≤30 weeks gestational age, who were admitted to the neonatal intensive care unit between January 1997 and May 1998. Infants were eligible for this study if they had undergone MR imaging during the first week after birth and if they had a developmental quotient of ≥85 when assessed, with no sign of cerebral palsy, at 2 years corrected age. A total of 58 infants born at <30 weeks gestational age were admitted to the neonatal intensive care unit between these dates. Of these infants, 14 (24%) had a developmental quotient of <85 at 2 years corrected age, four (7%) were lost to follow up, three (5%) had not undergone MR imaging during the early neonatal period, and 11 (19%) died. The remaining 26 (45%) infants were eligible for this study.

The study group consisted of 13 male and 13 female infants, with a median gestational age of 28 weeks (range, 25–30 weeks gestational age) and a median birth weight of 905 g (range, 590–1440 g). The median gestational age of the infants at the time of their initial MR imaging was 28 weeks (range, 25–30 weeks gestational age). Nineteen infants were either ventilated or received continuous positive airways pressure at the time of their initial imaging session. Gestational age was calculated from the date of the last menstrual period and was confirmed by early antenatal sonograms. Ethical permission for this study was granted by the local hospitals' Research Ethics Committee, and written parental consent was obtained for each infant.

MR Imaging

MR imaging was performed on a 1.0-T imager in the neonatal intensive care unit (14). This system allows MR imaging to be performed on extremely preterm infants without compromising their care (15). T1-weighted conventional spin-echo, inversion recovery fast spin-echo, and T2-weighted fast spin-echo MR images were obtained in the transverse plane. In some cases, T2-weighted fast spin-echo MR images were also obtained in the sagittal and coronal planes. Details of the pulse sequence parameters used in this study are illustrated in Table 1.

To minimize handling of the infants and to continue monitoring during transport from the incubator to the imager, a specially designed transport trolley was constructed with dimensions similar to those of the incubators on the ward. Using this system, infants were handled only when being moved from their cot or incubator to the trolley and back to their incubator from the trolley after imaging. Infants requiring mechanical ventilation or continuous positive airways pressure underwent imaging with either an MR imaging-compatible ventilator (babyPAC; pneuPac Limited, Luton, England), which could be placed adjacent to the imager, or an SLE 2000 ventilator (SLE, South Croydon, England), which could be placed in an RF-shielded cupboard within the imaging room. The majority of the infants successfully underwent imaging after they were fed or while sedated for ventilation. However, administration of oral chloral hydrate (20–30 mg/kg) was occassionally needed for the more mature infants.

Effective immobilization of the infant was essential to obtain high quality MR images. This was achieved using an Olympic bag, which contains small polystyrene beads, evacuated with suction to fit snugly around the infant's head. The Olympic bag also helps to muffle gradient acoustic noise. Infants were swaddled in blankets to maintain their temperature, and the temperature of the imaging room was set at 27°C, the same as that on the ward. Additional heating for extremely preterm neonates was provided with bubble wrap, woollen hats, and "gel bags" that retain heat once warmed in a microwave oven. Physiological monitoring was performed during each MR imaging examination using a Hewlett Packard Merlin life-monitoring system (Hewlett Packard, Bracknell, Berkshire, England). Oxygen saturation, heart rate, temperature, and, when required, invasive blood pressure were monitored. An experienced neonatologist remained in the imaging room throughout the examination.

The MR images were analyzed by two authors (S.J.C., M.A.R.) who were blinded to the gestational age and birth weight of each infant. Interobserver and intraobserver variabilty were analyzed by calculating the κ statistic, and the following ranges for agreement were used: 0.00, poor; 0.00 to 0.20, slight; 0.21 to 0.40, fair; 0.41 to 0.6, moderate; 0.61 to 0.8, substantial; and 0.81 to 1.0, almost perfect (16). In cases of initial disagreement, the final decision was made by consensus. The images were assessed to determine the gestational age at which myelination was first evident in white and gray matter structures in the brain stem, basal ganglia, and cerebral white matter. Myelination was considered to be present in white matter tracts if the signal intensity was hyperintense to unmyelinated white matter on T1-weighted conventional spin-echo and inversion recovery fast spin-echo MR images or hypointense to unmyelinated white matter on T2-weighted fast spin-echo MR images. Myelination was considered to be present in gray matter structures if the signal intensity was hyperintense to the cerebral cortex on T1-weighted conventional spin-echo and inversion recovery fast spin-echo MR images or hypointense to the cortex on T2-weighted fast spin-echo MR images, as described by Barkovich (8). The identity of the structures was confirmed by consulting a fetal neuroanatomy textbook (17) and a previous study on term neonates (8). Additionally, the results were divided into three age groups: <30 weeks gestational age, 30 to 36 weeks gestational age, and 37 to 42 weeks
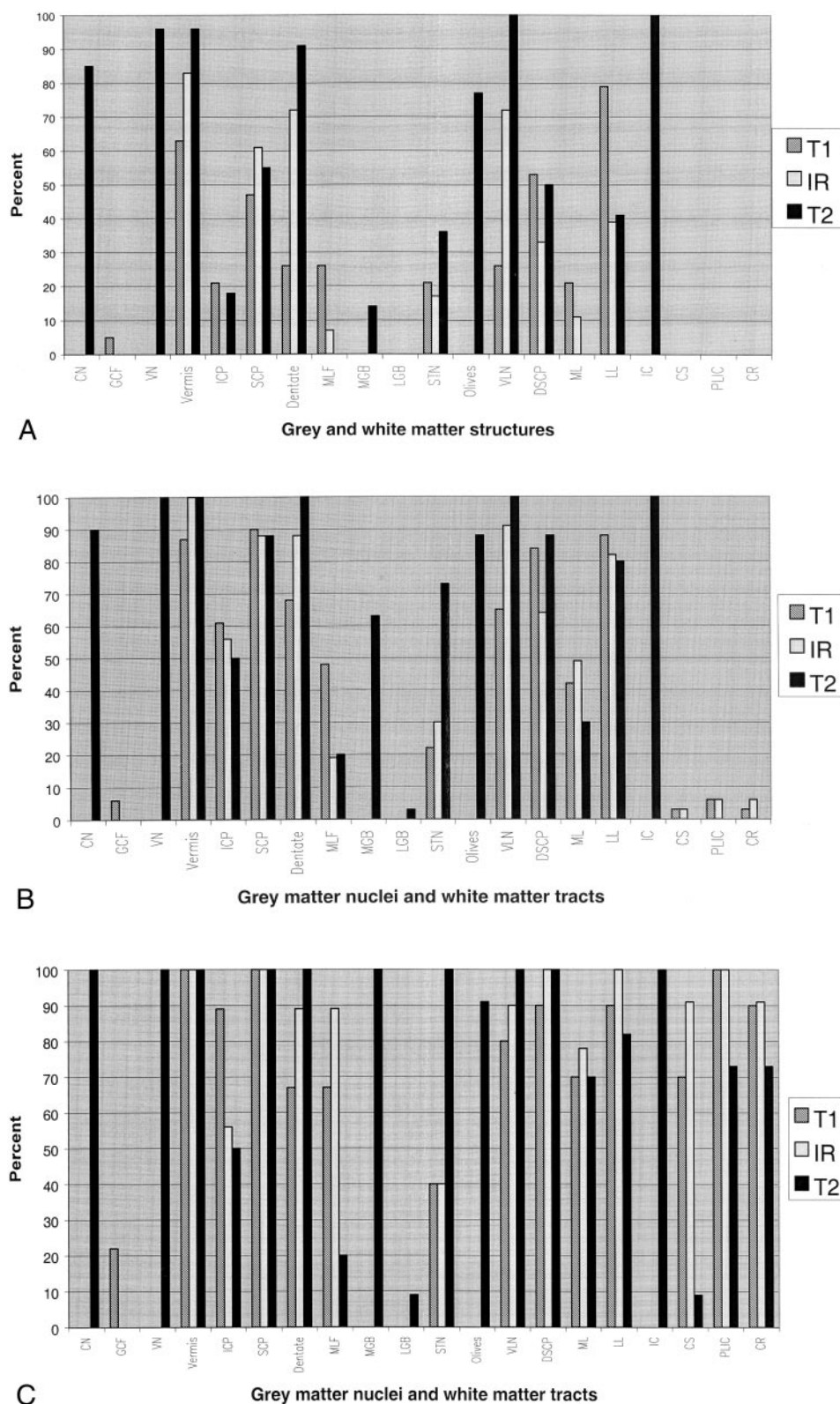
FIG 1. Percentages of different types of images showing myelination in the gray matter nuclei and white matter tracts identified in this study at <30 weeks gestational age, between 30 and 36 weeks gestational age, and between 37 and 42 weeks gestational age. *CN*, region of gracile and cuneate nuclei; *GCF*, gracile and cuneate fasciculi; *VN*, vestibular nuclei; *Vermis*, cerebellar vermis; *ICP*, inferior cerebellar peduncles; *SCP*, superior cerebellar peduncles; *Dentate*, dentate nucleus of the cerebellum; *MLF*, medial longitudinal fasciculus; *MGB*, medial geniculate bodies; *LGB*, lateral geniculate bodies; *STN*, subthalamic nuclei; *Olives*, inferior olivary nuclei; *VLN*, ventrolateral nuclei of the thalamus; *DSCP*, decussation of the superior cerebellar peduncles; *ML*, medial lemnisci; *LL*, lateral lemnisci; *IC*, inferior colliculi; *CS*, corticospinal tracts of the precentral and postcentral gyri; *PLIC*, posterior limb of the internal capsule; *CR*, corona radiata; *T1*, T1-weighted conventional spin-echo MR images; *IR*, inversion recovery fast spin-echo MR images; *T2*, T2-weighted fast spin-echo MR images.

gestational age. The percentages of T1-weighted conventional spin-echo, inversion recovery fast spin-echo, and T2-weighted fast spin-echo MR images that showed myelination in each age group were compared to determine whether there was any difference between the pulse sequences at showing myelination.

Results

The infants underwent imaging a median number of three times (range, one to seven times) between birth and term. T1-weighted conventional spin-echo MR images were not obtained in one case, inversion recovery fast spin-echo MR images were not obtained in seven cases, and T2-weighted fast spin-echo MR images were not obtained in one case. Fifteen T1-weighted conventional spin-echo, 13 inversion recovery fast spin-echo, and four T2-weighted fast spin-echo MR images were not analyzed because of motion artifact. A total of 78 sets of images were evaluated. Interobserver and intraobserver variability rates were low ($\kappa = 0.72$ and 0.78, respectively), representing substantial agreement.

No infants had evidence of parenchymal white matter lesions on MR images. On their initial images, 19 infants had normal MR imaging findings and seven had findings indicating small lesions. Of these, two had unilateral germinal layer hemorrhage, one had bilateral germinal layer hemorrhage, two had small unilateral intraventricular hemorrhage, and two had bilateral germinal layer hemorrhage and intraventricular hemorrhage. The cerebral cortex was shown as high signal intensity on T1-weighted conventional spin-echo and inversion recovery fast spin-echo MR images and as low signal intensity on T2-weighted fast spin-echo MR images. Unmyelinated white matter had long T1 and long T2, as described previously (13). Figure 1, A through C, illustrates the percentage of images showing myelination in the gray matter nuclei and white matter tracts identified in this study at <30 weeks gestational age, between 30 and 36 weeks gestational age, and between 37 and 42 weeks gestational age.

<30 Weeks Gestational Age

Myelin was evident in numerous gray matter nuclei and white matter tracts at ≤28 weeks gestational age. These structures were the vestibular nuclei, cerebellar vermis, inferior cerebellar peduncles, superior cerebellar peduncles, dentate nucleus of the cerebellum, medial longitudinal fasciculus, medial geniculate bodies, subthalamic nuclei, inferior olivary nuclei, ventrolateral nuclei of the thalamus, decussation of the superior cerebellar peduncles, medial lemnisci, lateral lemnisci, and inferior colliculi. Additionally, my-

TABLE 2: Gestational age at which myelination was first evident on T1-weighted conventional spin-echo, inversion recovery fast spin-echo, and T2-weighted fast spin-echo imaging

	T1 CSE	IR FSE	T2 FSE
Region of the gracile and cuneate nuclei			25
Gracile and cuneate fascilculi	28		
Vestibular nuclei			25
Cerebellar vermis	25	25	25
Inferior cerebellar peduncle	28	30	28
Superior cerebellar peduncle	28	27	27
Dentate nucleus of the cerebellum	28	25	25
Medial longitudinal fasciculus	25	27	29
Medial geniculate bodies			28
Lateral geniculate bodies			36
Subthalamic nuclei	28	29	28
Inferior olivary nuclei			25
Ventrolateral nuclei of the thalamus	28	26	25
Decussation of the superior cerebellar peduncles	27	27	27
Medial lemnisci	27	28	30
Lateral lemnisci	26	28	27
Inferior colliculi			25
Corticospinal tracts of the pre- and post-central gyri	36	36	42
Posterior limb of the internal capsule	36	36	40
Corona radiata	36	36	40

elination was evident in the region of the gracile and cuneate fasciculi on T1-weighted conventional spin-echo MR images and in the region of the gracile and cuneate nuclei on T2-weighted fast spin-echo MR images, but these two structures could not be clearly separated. Table 2 shows the gestational age at which myelin was first visualized in white matter tracts and gray matter structures on each imaging pulse sequence.

From Table 2, it can be seen that myelin was shown in the ventrolateral nuclei of the thalamus on T2-weighted fast spin-echo MR images before it was evident on T1-weighted conventional spin-echo or inversion recovery fast spin-echo MR images. Furthermore, myelin was identified only in the region of the gracile and cuneate nuclei, vestibular nuclei, medial geniculate bodies, inferior olivary nuclei, and inferior colliculi on T2-weighted fast spin-echo MR images. However, myelin was shown in the white matter tracts of the medial longitudinal fasciculus, medial lemnisci, and lateral lemnisci on T1-weighted conventional spin-echo MR images before it was evident on inversion recovery fast spin-echo or T2-weighted fast spin-echo MR images; myelin was visualized only in the the gracile and cuneate fasciculi on

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A, Graph illustrates the percentages of T1-weighted conventional spin-echo, inversion recovery fast spin-echo, and T2-weighted fast spin-echo MR images showing myelination at <30 weeks gestational age.

B, Graph illustrates the percentages of T1-weighted conventional spin-echo, inversion recovery fast spin-echo, and T2-weighted fast spin-echo MR images showing myelination between 30 and 36 weeks gestational age.

C, Graph illustrates the percentages of T1-weighted conventional spin-echo, inversion recovery fast spin-echo, and T2-weighted fast spin-echo MR images showing myelination between 37 and 42 weeks gestational age.
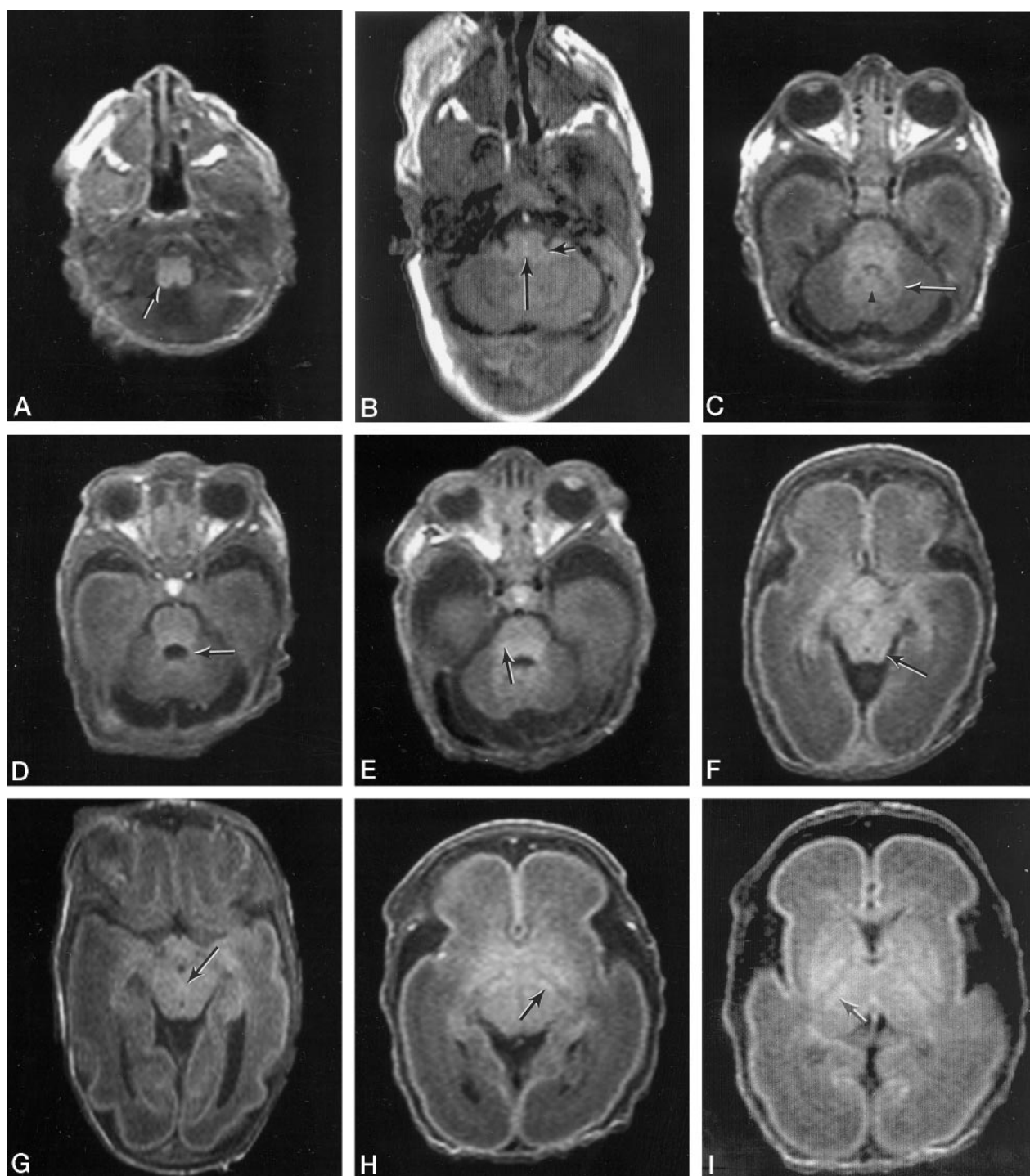
FIG 2.   Myelin is shown in numerous gray and white matter structures in the preterm brain on T1-weighted conventional spin-echo images.

A, Transverse T1-weighted conventional spin-echo image of an infant at 28 weeks gestational age shows myelin in the gracile and cuneate fasciculi (*arrow*) as high signal intensity.

B, Transverse T1-weighted conventional spin-echo image of an infant at 28 weeks gestational age shows myelin in the medial longitudinal fasciculus (*long arrow*) and in the inferior cerebellar peduncles (*short arrow*) as high signal intensity.

C, Transverse T1-weighted conventional spin-echo image of an infant at 28 weeks gestational age shows myelin in the cerebellar vermis (*arrowhead*) and in the dentate nucleus of the cerebellum (*arrow*) as high signal intensity.

D, Transverse T1-weighted conventional spin-echo image of an infant at 30 weeks gestational age shows myelin in the superior cerebellar peduncles (*arrow*) as high signal intensity.

E, Transverse T1-weighted conventional spin-echo image of an infant at 28 weeks gestational age shows myelin in the medial lemnisci as high signal intensity (*arrow*).

F, Transverse T1-weighted conventional spin-echo image of an infant at 28 weeks gestational age, obtained at the level of the mesencephalon, shows myelin in the lateral lemnisci (*arrow*) as high signal intensity.

T1-weighted conventional spin-echo MR images (Fig 1A). Figures 2 and 3 show myelin in numerous gray and white matter structures in the preterm brain on T1-weighted conventional spin-echo and T2-weighted fast spin-echo MR images.

30 to 36 Weeks Gestational Age

Between 30 and 36 weeks gestational age, there was an increase in the percentage of images showing myelin in the gray matter nuclei and white matter tracts that had been identified before 30 weeks gestational age (Fig 1B). However, myelin was not visualized at any new site from 28 weeks gestational age until 36 weeks gestational age, when it was shown in the posterior limb of the internal capsule, corona radiata, and corticospinal tracts of the precentral and postcentral gyri on T1-weighted conventional spin-echo and inversion recovery fast spin-echo MR images and in the lateral geniculate bodies on T2-weighted fast spin-echo MR images.

37 to 42 Weeks Gestational Age

At 40 weeks gestational age, myelin was shown in the posterior limb of the internal capsule and the corona radiata, and at 42 weeks gestational age, myelin was visualized in the corticospinal tracts of the precentral and postcentral gyri on T2-weighted fast spin-echo MR images. Therefore, myelination in these white matter tracts was evident on T1-weighted conventional spin-echo and inversion recovery fast spin-echo MR images before it was evident on T2-weighted fast spin-echo MR images (Table 2). The percentage of images showing myelin in numerous white and gray matter structures increased (Fig 1C). Figure 4 shows myelination in the sites that myelinate at term-equivalent age.

The dorsal brain stem was shown as diffuse high signal intensity on T1-weighted conventional spin-echo and inversion recovery fast spin-echo MR images and as low signal intensity on T2-weighted fast spin-echo MR images. This signal intensity probably represents a combination of nuclei and myelinated tracts, but it was not possible to delineate specific structures. Additionally, the dorsal globus pallidus and putamen were visualized as diffuse high signal intensity on T1-weighted conventional spin-echo and inversion recovery fast spin-echo MR images and as low signal intensity on T2-weighted fast spin-echo MR images before term. By term-equivalent age, these areas became isointense to the rest of the basal ganglia on T1-weighted conventional spin-echo and inversion recovery fast spin-echo MR images and

much less hypointense on T2-weighted fast spin-echo MR images.

Discussion

This study showed myelination in numerous white and gray matter structures on MR images of the very preterm brain. Although the percentage of MR images showing myelination in most structures increased with increasing gestational age, myelin was not visualized in any new sites from 28 to 36 weeks gestational age, when it was shown in the posterior limb of the internal capsule, corona radiata, corticospinal tracts of the precentral and postcentral gyri, and lateral geniculate bodies.

The changes in signal intensity that are associated with myelination on T1- and T2-weighted images are due to changes in the lipid and water content of developing myelin. Myelination is probably shown as high signal intensity on T1-weighted images because of T1 shortening caused by an increase in cholesterol and glycolipids in the myelin sheath (3). Galacterocerebroside, in particular, has been shown to cause T1 shortening in vitro (18). The hypointense appearance of myelination on T2-weighted images corresponds to the time of tightening of myelin around the axon and the saturation of polyunsaturated fatty acids within the myelin membrane. The reduction in signal intensity on T2-weighted images is probably due to a reduction in the number of aqueous protons due to the development of the hydrophobic inner phospholipid layer (3).

Myelination has been shown histologically to occur in a systematic fashion beginning with the peripheral nervous system before 20 weeks gestational age, with myelination of motor roots occurring before myelination of sensory roots. In the CNS, myelination begins in the spinal cord and proceeds cranially, with sensory nerve fibers myelinating before motor nerve fibers (9). Myelination is predominantly a post-term process, and myelin is evident only in certain structures in the preterm brain.

The numerous white and gray matter structures that showed evidence of myelination in the very preterm brain in this study concur with those areas that would be expected to show histologic evidence of myelination at this gestational age (9, 10). Histologically, myelin has been shown in the white matter tracts of the medial longitudinal fasiculus at 20 weeks gestational age, in the medial lemnisci at 23 weeks gestational age, in the lateral lemnisci and the inferior cerebellar peduncles at 24 weeks gestational age, and in the superior cerebellar peduncles at 26 weeks gestational age (10). The hypointense signal of gray matter nuclei on T2-weighted fast spin-echo MR images

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G, Transverse T1-weighted conventional spin-echo image of an infant at 28 weeks gestational age shows myelin in the decussation of the superior cerebellar peduncles (*arrow*) as high signal intensity.

H, Transverse T1-weighted conventional spin-echo image of an infant at 28 weeks gestational age shows myelin in the subthalamic nuclei (*arrow*) as high signal intensity.

I, Transverse T1-weighted conventional spin-echo image of an infant at 28 weeks gestational age, obtained at the level of the basal ganglia, shows myelin in the ventrolateral nuclei of the thalamus (*arrow*) as high signal intensity.
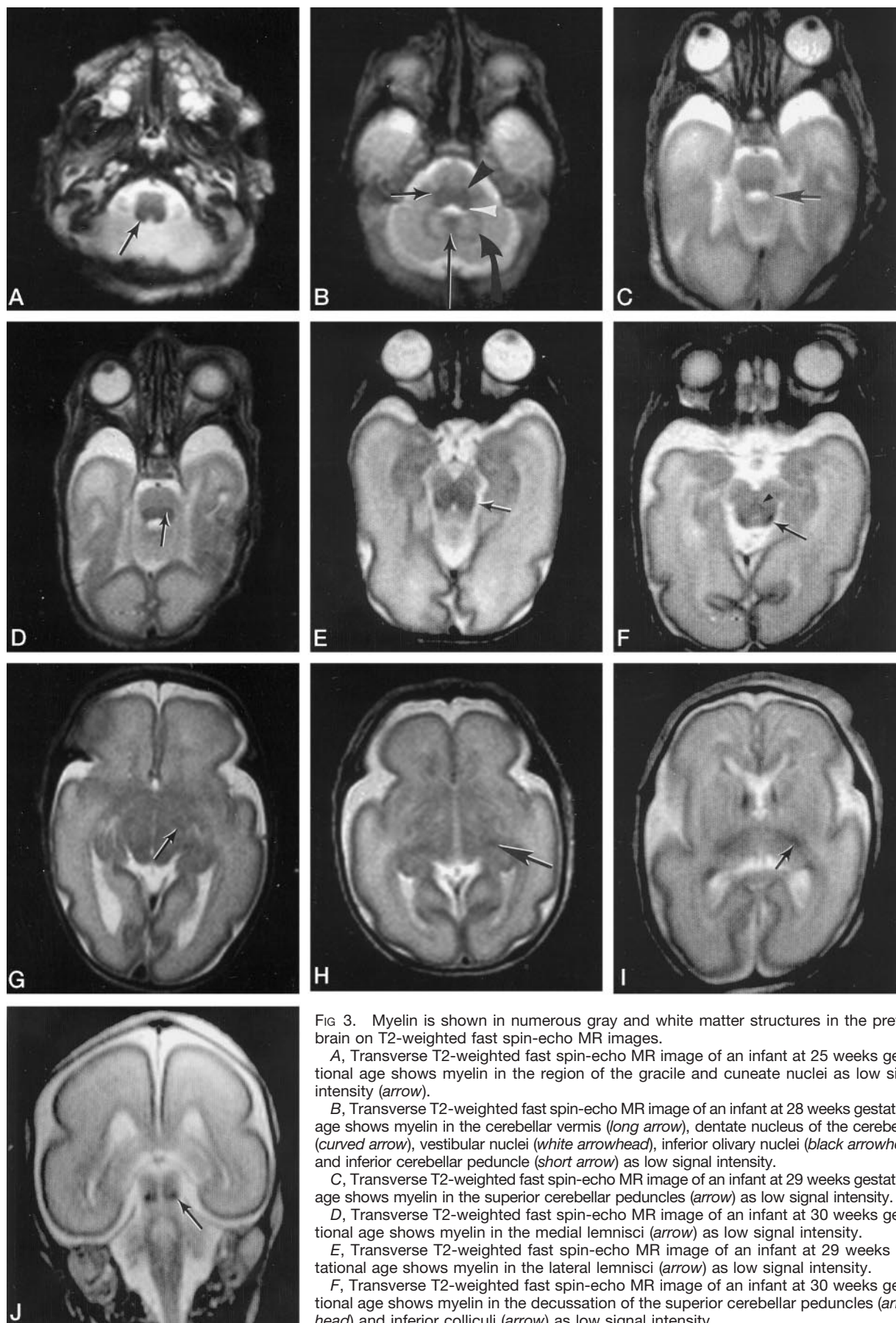
Fig 3. Myelin is shown in numerous gray and white matter structures in the preterm brain on T2-weighted fast spin-echo MR images.

A, Transverse T2-weighted fast spin-echo MR image of an infant at 25 weeks gestational age shows myelin in the region of the gracile and cuneate nuclei as low signal intensity (*arrow*).

B, Transverse T2-weighted fast spin-echo MR image of an infant at 28 weeks gestational age shows myelin in the cerebellar vermis (*long arrow*), dentate nucleus of the cerebellum (*curved arrow*), vestibular nuclei (*white arrowhead*), inferior olivary nuclei (*black arrowhead*), and inferior cerebellar peduncle (*short arrow*) as low signal intensity.

C, Transverse T2-weighted fast spin-echo MR image of an infant at 29 weeks gestational age shows myelin in the superior cerebellar peduncles (*arrow*) as low signal intensity.

D, Transverse T2-weighted fast spin-echo MR image of an infant at 30 weeks gestational age shows myelin in the medial lemnisci (*arrow*) as low signal intensity.

E, Transverse T2-weighted fast spin-echo MR image of an infant at 29 weeks gestational age shows myelin in the lateral lemnisci (*arrow*) as low signal intensity.

F, Transverse T2-weighted fast spin-echo MR image of an infant at 30 weeks gestational age shows myelin in the decussation of the superior cerebellar peduncles (*arrowhead*) and inferior colliculi (*arrow*) as low signal intensity.
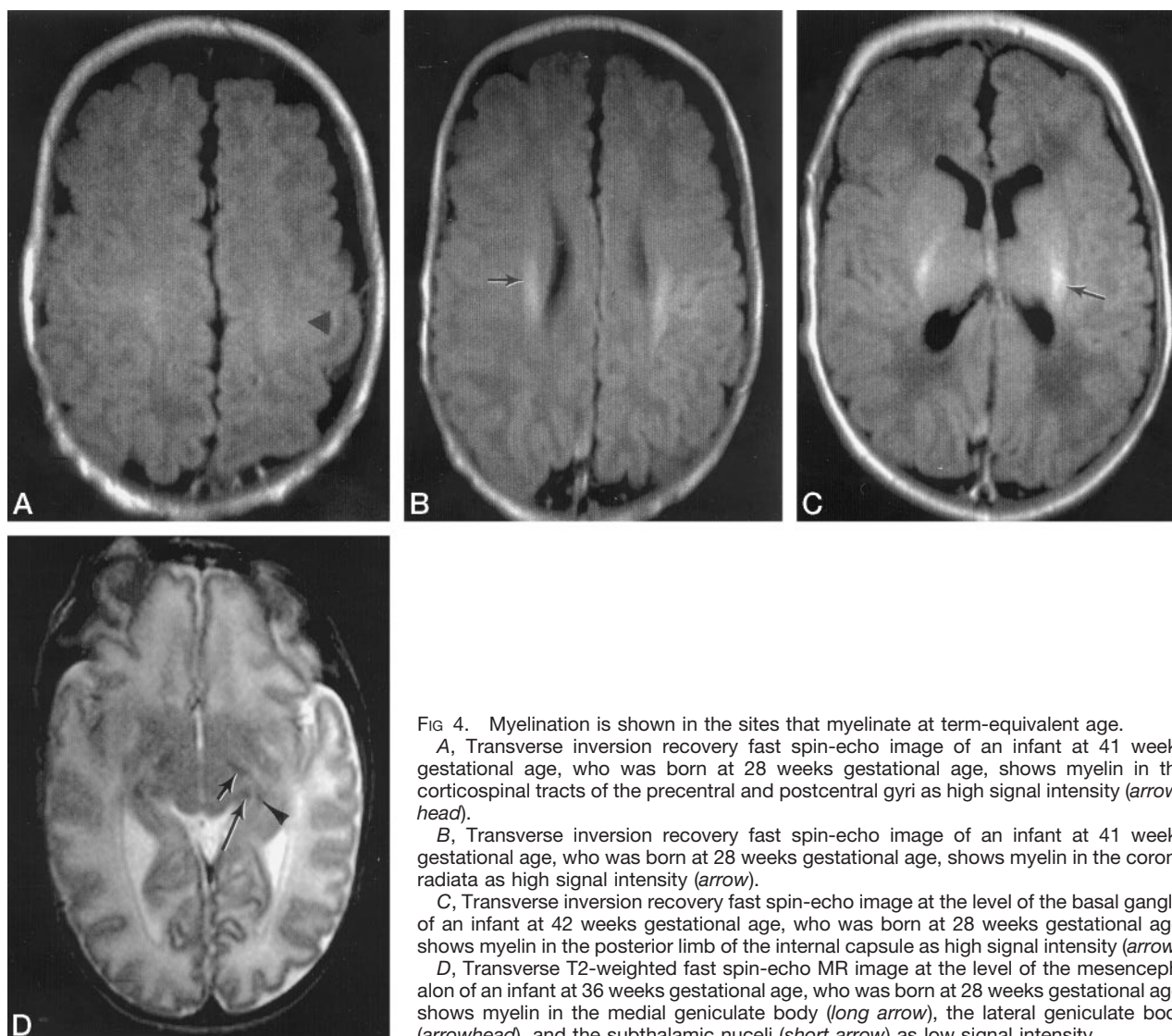
Fɪɢ 4. Myelination is shown in the sites that myelinate at term-equivalent age.

A, Transverse inversion recovery fast spin-echo image of an infant at 41 weeks gestational age, who was born at 28 weeks gestational age, shows myelin in the corticospinal tracts of the precentral and postcentral gyri as high signal intensity (*arrowhead*).

B, Transverse inversion recovery fast spin-echo image of an infant at 41 weeks gestational age, who was born at 28 weeks gestational age, shows myelin in the corona radiata as high signal intensity (*arrow*).

C, Transverse inversion recovery fast spin-echo image at the level of the basal ganglia of an infant at 42 weeks gestational age, who was born at 28 weeks gestational age, shows myelin in the posterior limb of the internal capsule as high signal intensity (*arrow*).

D, Transverse T2-weighted fast spin-echo MR image at the level of the mesencephalon of an infant at 36 weeks gestational age, who was born at 28 weeks gestational age, shows myelin in the medial geniculate body (*long arrow*), the lateral geniculate body (*arrowhead*), and the subthalamic nuclei (*short arrow*) as low signal intensity.

may in part be due to the relatively high cellular density of these structures (19), which have inherently shorter T2 than do white matter structures. However, histologic studies show evidence of myelination in the inferior colliculi from 20 weeks gestational age (9), in the ventrolateral nuclei of the thalamus at 25 weeks gestational age (20), and in the subthalamic nuclei between 24 and 28 weeks gestational age (9). Furthermore, the superior colliculi, which do not show histologic evidence of myelination before term (9), were not shown as hypointense on T2-weighted fast spin-echo MR images. We therefore think that this signal intensity may, at least in part, be attributed to myeli-

nation. Other maturational changes, such as glial cell multiplication, increases in synaptic density, and dendrite formation occur at the same time as myelination in gray matter nuclei and may reduce the amount of free water at these sites, thereby contributing to the hypointense signal on T2-weighted MR images (21).

At 36 weeks gestational age, myelin was visualized in the posterior limb of the internal capsule, corona radiata, corticospinal tracts of the precentral and postcentral gyri, and lateral geniculate bodies. Again, these findings are supported by histologic studies, which show myelin in the posterior limb of the internal capsule at 32 weeks gestational age, in the corona

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G, Transverse T2-weighted fast spin-echo MR image of an infant at 29 weeks gestational age shows myelin in the subthalamic nuclei as low signal intensity (*arrow*).

H, Transverse T2-weighted fast spin-echo MR image of an infant at 29 weeks gestational age shows myelin in the medial geniculate bodies (*arrow*) as low signal intensity.

I, Transverse T2-weighted fast spin-echo MR image of an infant at 27 weeks gestational age shows myelin in the ventrolateral nuclei of the thalamus as low signal intensity (*arrow*).

J, Coronal T2-weighted fast spin-echo MR image of an infant at 27 weeks gestational age shows myelin in the inferior colliculi (*arrow*) as low signal intensity.

radiata at 34 weeks gestational age (10), and in the corticospinal tracts of the precentral and postcentral gyri at 35 weeks gestational age (20). Therefore, in many of the structures identified in this study, myelination was visible on MR images within 4 weeks gestational age of myelin being revealed by histologic examination.

T2-weighted fast spin-echo MR imaging showed myelin at an earlier gestational age than did T1-weighted conventional spin-echo or inversion recovery fast spin-echo MR imaging in numerous gray matter nuclei in the preterm brain. Additionally, T2-weighted fast spin-echo MR imaging showed myelin in gray matter nuclei in a greater percentage of images than did T1-weighted conventional spin-echo and inversion recovery fast spin-echo imaging combined. The vestibular nuclei, medial geniculate bodies, lateral geniculate bodies, inferior olivary nuclei, and inferior colliculi were identified only on T2-weighted fast spin-echo MR images (Fig 1A–C). However, T1-weighted conventional spin-echo MR imaging showed myelin earlier than did inversion recovery fast spin-echo and T2-weighted fast spin-echo MR imaging in the white matter tracts of the medial longitudinal fasciculus, medial lemnisci, and lateral lemnisci. Gracile and cuneate fasciculi were identified only on T1-weighted conventional spin-echo MR images. These results concur with studies of the post-term neonatal brain, in which T2-weighted conventional spin-echo MR imaging was superior at showing myelin in deep gray matter nuclei and T1-weighted conventional spin-echo MR imaging was better at showing myelin in white matter tracts (8). In the age range of 31 to 36 weeks gestational age, T2-weighted fast spin-echo MR imaging was better than T1-weighted conventional spin-echo and inversion recovery fast spin-echo MR imaging at showing myelin in the decussation of the superior cerebellar peduncles; however, it is possible that the low signal intensity in this region may include some contribution from the oculomotor nucleus.

With the exception of the superior cerebellar peduncles, myelination was better visualized on either T1-weighted conventional spin-echo or T2-weighted fast spin-echo MR images than on inversion recovery fast spin-echo images of the preterm brain before 30 weeks gestational age (Fig 1A). However, at term-equivalent age, inversion recovery fast spin-echo imaging was superior to both T1-weighted conventional spin-echo and T2-weighted fast spin-echo MR imaging at showing myelination in the corona radiata and the corticospinal tracts of the precentral and postcentral gyri. T2-weighted fast spin-echo MR imaging remained superior to T1-weighted conventional spin-echo and inversion recovery fast spin-echo MR imaging at showing myelination in gray matter nuclei at term. These results suggest that age-modified protocols may be useful for assessing myelination in these patients. In the preterm brain, T1-weighted conventional spin-echo and T2-weighted fast spin-echo MR imaging is most useful, and at term-equivalent age, inversion recovery fast spin-echo and T2-weighted fast spin-echo MR imaging may be more appropriate.

It has been suggested that the high signal intensity on T1-weighted conventional spin-echo and inversion recovery fast spin-echo MR images and low signal intensity on T2-weighted fast spin-echo MR images of the dorsal globus pallidus and putamen is indicative of myelination (11). However, as this signal intensity becomes isointense on T1-weighted conventional spin-echo and inversion recovery fast spin-echo MR images and much less hypointense on T2-weighted fast spin-echo MR images at term-equivalent age, it is unlikely that it represents myelin. Pathologic studies have not related these areas to regions of high cellular density (19), and the reason for this change in signal intensity in the dorsal globus pallidus and putamen at term remains unclear.

One caveat is that we examined myelination in the brain of very preterm infants. Although these infants had good neurodevelpmental outcomes at 2 years corrected age, the preterm brain is vulnerable to injury from numerous causes (22, 23), and previous MR imaging studies of preterm infants have shown that the brain develops differently in the ex utero environment (24–26). Furthermore, MR imaging has shown abnormalities in structures that myelinate later than term-equivalent age in preterm infants (eg, in the corpus callosum) (27). It is possible, therefore, that the development of myelination in utero differs from that described in this study. Fetal MR imaging may be of use in determining any differences between the development of myelination on MR images of the in utero and ex utero preterm brain.

Conclusion

Using a specially designed MR system in a neonatal intensive care unit, serial MR imaging can be safely performed for preterm infants as young as 25 weeks gestational age to assess the development of myelination in the preterm brain. A knowledge of myelination milestones in the very preterm infant will allow more accurate assessment of the developing preterm brain and allow delays to be detected at an early stage. The effects of such delays on long-term neurodevelopment can then be assessed.

Myelination was shown in the region of the gracile and cuneate nuclei and fasciculi, vestibular nuclei, cerebellar vermis, inferior cerebellar peduncles, superior cerebellar peduncles, dentate nucleus of the cerebellum, medial longitudinal fasciculus, medial geniculate bodies, subthalamic nuclei, inferior olivary nuclei, ventrolateral nuclei of the thalamus, decussation of the superior cerebellar peduncles, medial lemnisci, lateral lemnisci, and inferior colliculi in the very preterm brain. Myelin was first visualized in the posterior limb of the internal capsule, corona radiata, corticospinal tracts of the precentral and postcentral gyri, and lateral genicualte bodies at 36 weeks gestational age.

Using the pulse sequence parameters described herein, T2-weighted fast spin-echo MR imaging was better

at showing myelin in gray matter structures and T1-weighted conventional spin-echo MR imaging was superior at showing myelination in white matter tracts in the preterm brain. At term-equivalent age, T2-weighted fast spin-echo MR imaging remained superior at showing myelin in gray matter structures and inversion recovery fast spin-echo MR imaging was better at showing myelin in the corona radiata and corticospinal tracts of the precentral and postcentral gyri.

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