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MR Imaging of Neuronal Migrational Disorders

Robin E. Osborn^{1,2}
 Sharon E. Byrd¹
 Thomas P. Naidich¹
 Timothy P. Bohan^{3,4}
 Harold Friedman⁵

Neuronal migrational disorders of the brain represent abnormalities in the formation of the neocortex caused by faulty migration of the subependymal neuroblasts. These migrational anomalies include lissencephaly (agyria/pachygyria), pachygyria, schizencephaly, heterotopias, hemimegalencephaly, and polymicrogyria. We used MR imaging (performed on a 0.5-T or 1.5-T scanner) to evaluate 21 patients who had neuronal migratory anomalies. Four patients had lissencephaly, seven had pachygyria, including one patient with hemimegalencephaly, seven had schizencephaly, and three had heterotopias. All MR scans included T1-weighted spin-echo sequences, and seven also had inversion-recovery sequences. The cortical surface, cortex, and gray-white matter interface were well evaluated with both sequences; however, the inversion-recovery images were superior. All but two patients were imaged in both the axial and coronal planes: both projections demonstrated well the migrational abnormalities.

MR is an excellent method for diagnosing the migrational anomalies of lissencephaly, pachygyria, schizencephaly, heterotopias, and hemimegalencephaly; it appears to be the imaging method of choice for evaluating these disorders.

Neuronal migrational disorders of the brain represent a group of anomalies that result from faulty migration of the subependymal neuroblasts [1–3]. The neuroblasts normally migrate between the sixth and 15th gestational week and in doing so form the six-layered neocortex [4]. When the migration does not occur in a normal fashion the resultant brain anomalies include lissencephaly, pachygyria, schizencephaly, hemimegalencephaly, heterotopias, and polymicrogyria [4–11].

We present and discuss the MR imaging findings in 21 patients with neuronal migrational disorders.

Materials and Methods

Twenty-one patients with neuronal migrational disorders were evaluated with MR imaging and form the basis of the present study.

MR was performed with a Philips Gyroscan or Elscint Gyrex scanner operating at 0.5 T or a 1.5-T General Electric scanner. Each patient was studied with T1-weighted spin-echo (SE) sequences with repetition times (TR) of 500–750 and an echo time (TE) of 30. Seven patients also had inversion recovery (IR) sequences, which were performed with 1200/400/30 (TR/TI/TE). Eighteen patients were also evaluated with T2-weighted SE sequences (2000/30–100). All patients were imaged in the axial plane, 19 were also imaged in the coronal plane, and 12 were also imaged in the sagittal plane.

All but three of the patients required sedation for the MR examination. Sedation was given in the form of chloral hydrate at a dosage of 50–100 mg/kg orally. Each examination required 60–90 min. Each patient's cardiac status was electronically monitored and a nurse or physician was in the scan room during the examination.

Results

The 21 patients with neuronal migratory disorders included four with lissencephaly, seven with pachygyria (including one patient with hemimegalencephaly), seven with schizencephaly, and three with heterotopias (Table 1).

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¹ Department of Radiology, Children's Memorial Hospital, Northwestern University Medical School, Chicago, IL 60614.

² Present address: Department of Radiology, Naval Hospital, San Diego, CA 92134. Address reprint requests to LCDR R. E. Osborn.

³ Department of Pediatric Neurology, Children's Memorial Hospital, Northwestern University Medical School, Chicago, IL 60614.

⁴ Present address: Departments of Neurology and Pharmacology, University of Texas Health Science Center, Houston, TX 77225.

⁵ Department of Radiology, Illinois Masonic Medical Center, Chicago, IL 60614.

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TABLE 1: Summary of Patient Data

Patient No.	Age	Gender	Diagnosis	Clinical Presentation	Other
1	18 mo	M	Lissencephaly type 2	Seizures, developmental delay	
2	7 mo	M	Lissencephaly type 2	Seizures, developmental delay	
3	2 mo	M	Lissencephaly type 3	Hypotonia, developmental delay	Callosal agenesis, Dandy-Walker cyst
4	5 mo	M	Lissencephaly type 1	Seizures	
5	1 mo	F	Pachygyria	Hypotonia	
6	13 mo	F	Pachygyria	Failure to thrive, abnormal facies	Miller-Dieker variant
7	18 mo	M	Frontal pachygyria	Developmental delay	
8	9 mo	M	Hemimegalencephaly	Infantile spasms, developmental delay	Congenital CMV encephalitis
9	9 mo	M	Pachygyria	Spastic quadraparesis, developmental delay	Congenital CMV encephalitis
10	12 mo	F	Pachygyria	Seizures, hypotonia, microcephaly	? Toxoplasma encephalitis
11	12 mo	F	Pachygyria	Hypotonia, developmental delay, abnormal facies	
12	1 mo	M	Bilateral fused-lip schizencephaly	Arthrogryposis	
13	11 mo	F	Bilateral fused-lip schizencephaly	Hypotonia, visual disturbance	Bilateral optic nerve hypoplasia
14	2.5 yr	F	Unilateral fused-lip schizencephaly	Seizures, spastic diplegia, microcephaly	? Toxoplasma encephalitis
15	8.5 yr	M	Bilateral fused-lip schizencephaly	Seizures, developmental delay	
16	1 wk	F	Unilateral open-lip schizencephaly	Seizures	
17	14 mo	M	Bilateral open-lip schizencephaly	Seizures, developmental delay	
18	2.5 yr	M	Bilateral open-lip schizencephaly	Spastic quadraparesis, developmental delay	
19	14 yr	M	Single frontal lobe heterotopia	Seizures	Biopsy proved
20	11 yr	M	Periventricular heterotopias	Seizures	
21	22 yr	M	Single occipital region heterotopia	Homonymous hemianopsia	

Note.—CMV = cytomegalovirus.

Of the four patients with lissencephaly only one had a completely smooth brain (Fig. 1); two were nearly completely agyric (Fig. 2); and one had mixed agyria/pachygyria. In three of these cases MR demonstrated a figure-eight appearance with shallow sylvian grooves caused by the lack of opercularization (Fig. 3). In three of these brains the cortex was thick, the white matter was decreased, and the gray-white matter interface was smooth from the lack of white-matter interdigitation. The patient with mixed agyria/pachygyria had hypoplastic opercula and a relatively smooth gray-white matter interface. This patient (patient 3) also had absence of the corpus callosum and a Dandy-Walker cyst.

Seven patients with pachygyria were evaluated with MR. In all seven cases MR delineated broad-based, thickened gyri, thickened cortex, and an abnormal gray-white matter junction (Fig. 4). The gray-white matter interface was delineated in all seven examinations. In six cases there was diffuse involve-

ment of one or both hemispheres. Only the frontal lobes were involved in the remaining case. In two patients (patients 8 and 9) with congenital cytomegalovirus encephalitis, associated white-matter changes were also identified and one of these had hemimegalencephaly (Fig. 5).

Each of the patients with schizencephaly had unilateral or bilateral clefts that were lined by gray matter. These clefts extended from the lateral ventricular wall to the pial surface of the brain (pial-ependymal seam). Four cases had type 1 schizencephaly or the fused-lip form (Fig. 6) and three had type 2 schizencephaly or the open-lip form with an intervening CSF cavity communicating with the lateral ventricle (Fig. 7). Three of the type 1 schizencephalies and two of the type 2 schizencephalies were bilateral.

Three patients had heterotopias. One patient had multiple, bilateral periventricular heterotopias (Fig. 8) and the other two had isolated deep white-matter heterotopias. Pathologic cor-

Fig. 1.—Case 4: Lissencephaly type 1. Spin-echo MR images (750/30) in the axial (A) and coronal (B) planes demonstrate a completely smooth brain surface. Note lack of opercularization and shallow sylvian grooves.

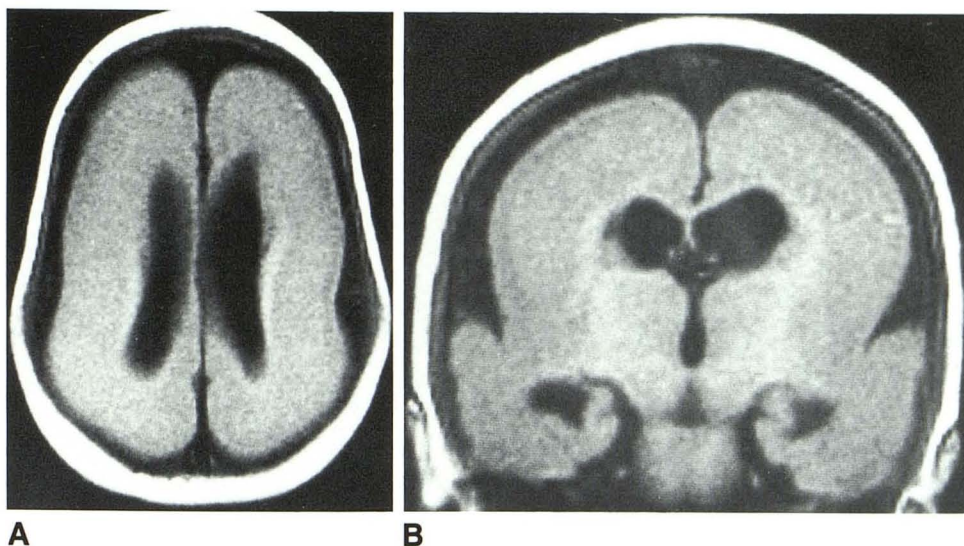


Fig. 2.—Case 1: Lissencephaly type 2. Axial spin-echo MR image (750/30) demonstrates areas of pachygyria. Observe the shallow sylvian grooves, smooth gray-white matter interface (arrows), and thickened cortex.

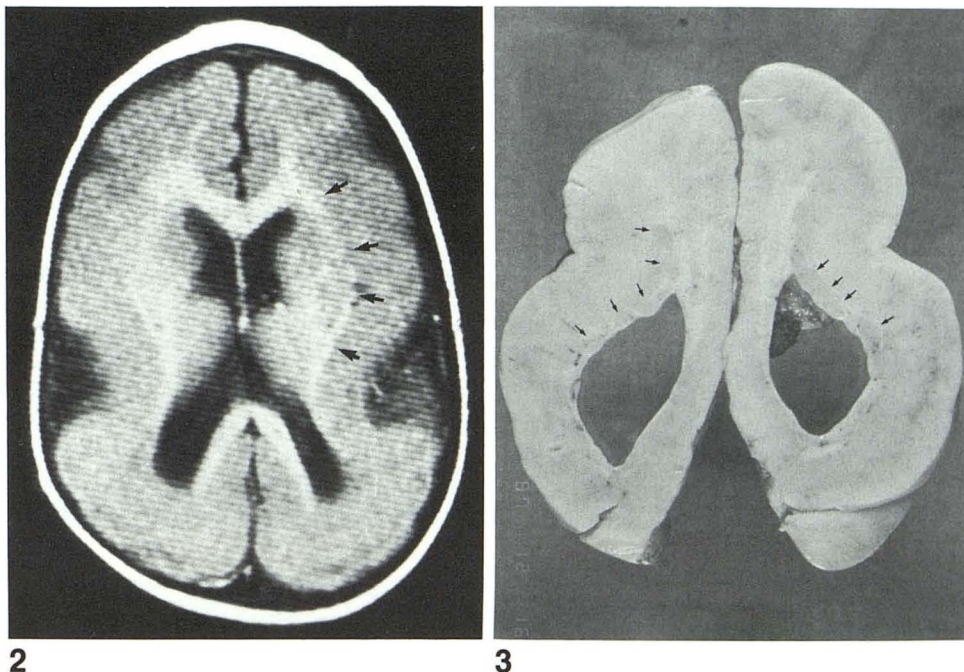


Fig. 3.—Lissencephaly. Neuropathologic specimen not related to present study group illustrates a smooth, thickened cortex and shallow sylvian grooves caused by lack of opercularization, which results in typical figure-eight appearance. This patient also had periventricular heterotopias (arrows) and colpocephaly.

relation was obtained in one patient. The heterotopias were isointense with gray matter on all MR sequences but were best seen on the intermediate-weighted images in all cases.

Discussion

Neuronal migratory disorders include lissencephaly (agyria/pachygyria), pachygyria, hemimegalencephaly, schizencephaly, heterotopic gray matter, and polymicrogyria [12]. These anomalies result from abnormal migration of the neuroblasts from the subependymal region of the brain between the sixth and 15th gestational weeks [4, 12]. The known or suspected causes of migrational disorders are numerous and

heterogeneous [7, 8, 12–20]. The origin of the migrational anomalies in most of our patients was not known (Table 1).

Patients with neuronal migrational disorders usually present clinically with microcephaly, failure to thrive, developmental delay, hypotonia, hypertonia, and/or seizures. Many of these patients die before the age of two, notably those with the more severe migrational anomalies. The diagnosis of all migrational anomalies is made by imaging studies or at autopsy.

Lissencephaly is the most severe neuronal migrational disorder and presents with a completely or partially agyric brain. Pachygyria represents a disorder wherein the gyri are too few, thick, and coarse. Lissencephaly can be divided into three categories: (1) total agyria, which is most rare; (2) nearly complete agyria; and (3) mixed agyria/pachygyria [4].

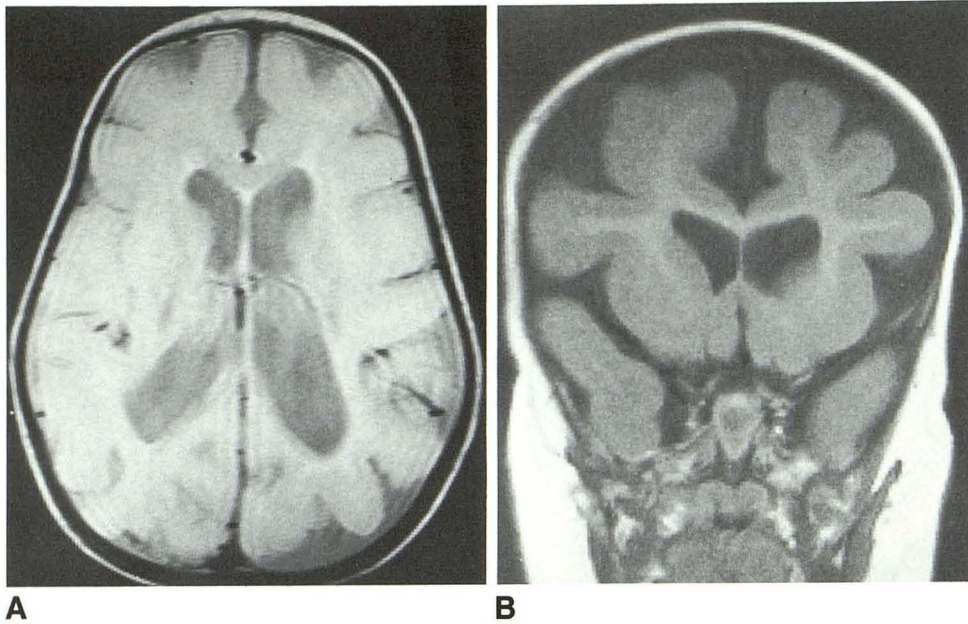


Fig. 4.—Case 11: Pachygyria.
A, Axial spin-echo MR image (2000/30) demonstrates bilateral large gyri.
B, Coronal spin-echo MR image (600/30) demonstrates broad-based gyri and thick cortex.

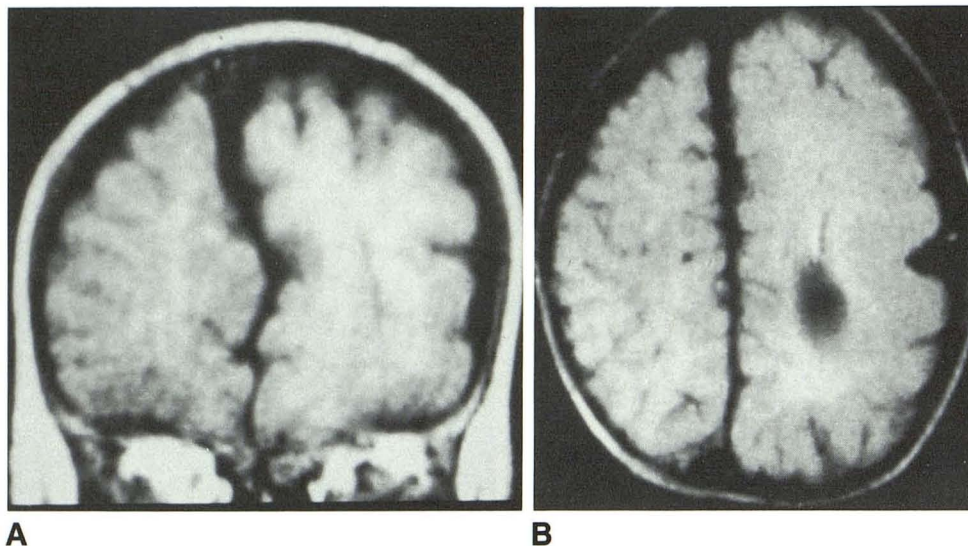


Fig. 5.—Case 8: Hemimegalencephaly. Axial (A) and coronal (B) spin-echo MR images (500/30) demonstrate enlarged left cerebral hemisphere and thickened pachygyric cortex.

The major MR findings in lissencephaly include (1) cerebral contour with a “figure-eight” configuration caused by incomplete or lack of opercularization of the insula, which in turn results in sylvian grooves; (2) thickened cortex; and (3) smooth gray-white matter interface [21].

Pachygyria without associated areas of agyria does not represent lissencephaly but rather a distinct form of migrational disorder. MR imaging of pachygyria demonstrates a thickened cortex with incomplete white-matter digitations. All or only a part of the brain may be involved.

Hemimegalencephaly is a migrational disorder resulting in hemihypertrophy of the brain [22–24]. It may be idiopathic or result from a variety of causes including storage diseases and neurocutaneous syndromes. MR imaging will demonstrate a thickened, pachygyric or agyric cortex, a too-smooth gray-white matter interface, and ipsilateral ventricular enlargement. Heterotopias may also be identified. MR imaging demonstrated abnormal myelination in our patient who also had congenital cytomegalovirus encephalitis.

Schizencephaly consists of a hemispheric cleft extending from the pial to the ependymal surface [10, 11]. This cleft is typically lined by gray matter; however, the gray-matter lining may be incomplete or too thin to identify radiographically. Schizencephaly usually involves the parasylvian area and is most commonly bilateral and symmetrical [10, 11, 25]. In the type 1 or the fused-lip form, the two cortical layers are fused. In the type 2 or open-lip form a CSF-filled cavity is interposed between the two layers of gray matter that line the cleft. Gray-matter heterotopias have also been described in association with schizencephalic clefts [10, 11].

The MR evaluation of schizencephaly delineates the pial-ependymal cleft lined by a thickened cortical layer. The schizencephalic cleft can usually be well evaluated with axial sections. Coronal images assist in delineating more completely the relationship of the cleft to the ventricular wall, especially the open-lip schizencephalies. T1-weighted imaging is usually the best method for evaluating the anatomic anomalies of all migrational disorders; however, we found T2-

Fig. 6.—Case 12: Type 1 schizencephaly. Axial spin-echo MR images (2000/100) (A) and (750/30) (B) demonstrate bilateral fused-lip schizencephaly. Both the T1- and T2-weighted images demonstrate well the gray-matter-lined clefts.

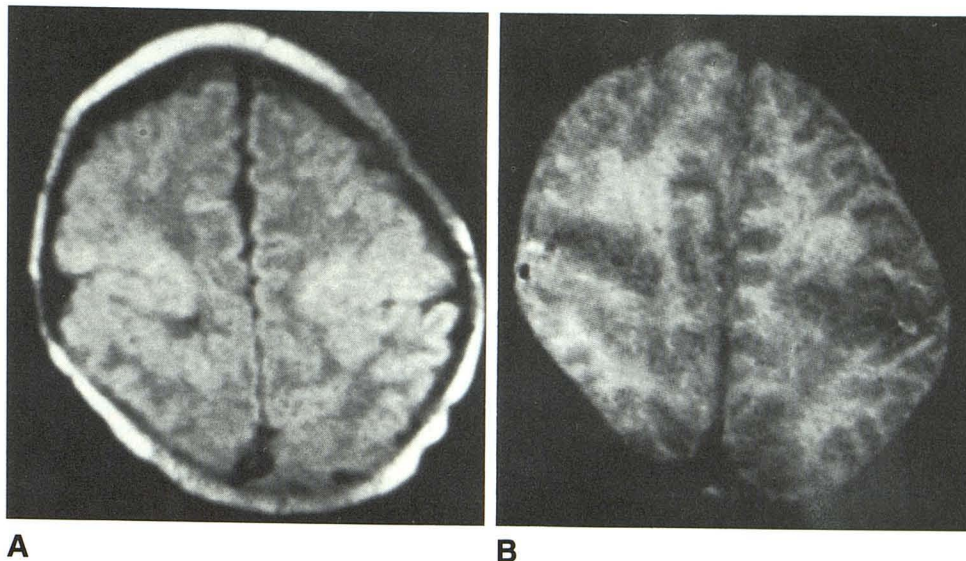


Fig. 7.—Case 18: Type 2 schizencephaly. Axial (A) and coronal (B) inversion-recovery images (1200/400/30) demonstrate bilateral open-lip schizencephalic clefts, which are lined by gray matter (closed arrows) and communicate freely with the dilated lateral ventricles. A septum separates part of the right cavity from the ventricle (open arrow in B).

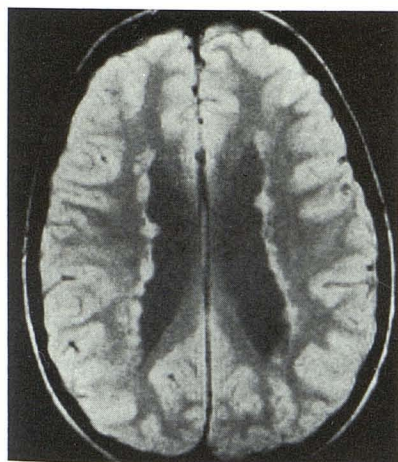
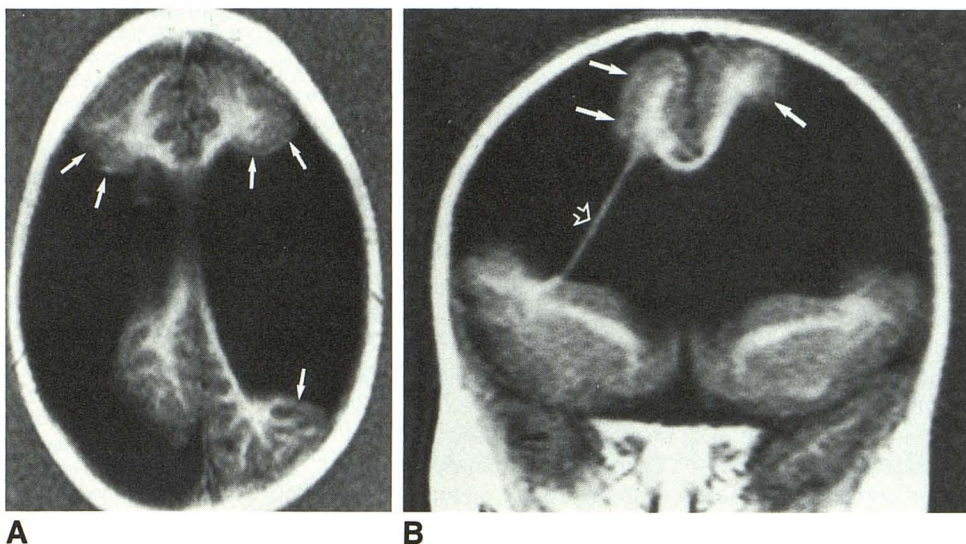


Fig. 8.—Case 20: Heterotopia. Spin-echo MR image (2000/30) demonstrates multiple bilateral periventricular nodules that correspond in signal intensity to the normal cortex.

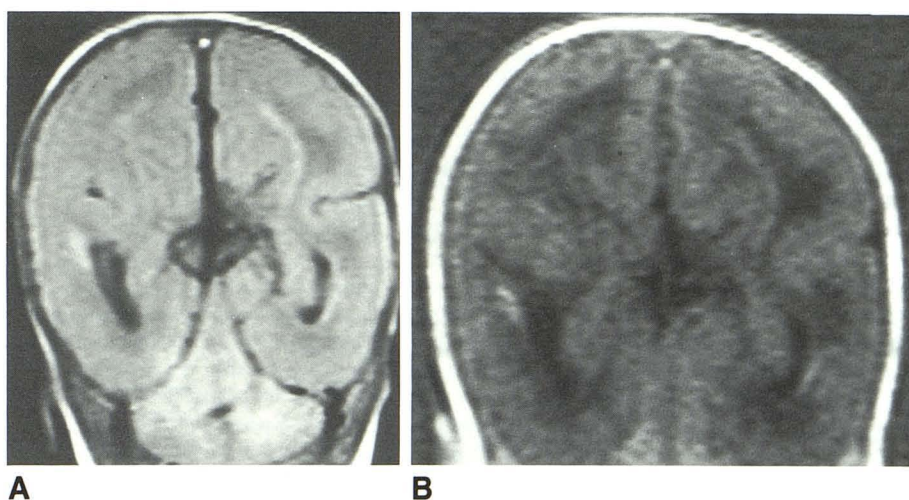


Fig. 9.—Case 3: Lissencephaly type 3. Coronal spin-echo (750/30) (A) and inversion-recovery (1200/400/30) (B) MR images. Gray-white matter interface is better delineated by inversion-recovery image.

weighted images helpful for delineating the fused-lip form (Fig. 6).

Heterotopias may be found as an isolated anomaly or in association with other congenital brain malformations [10, 11, 26]. They represent the least clinically symptomatic type of neuronal migrational anomaly and usually present later in life. They may be single, multiple, unilateral, bilateral, periventricular, or located deep within the white matter. Most heterotopias are microscopic but occasionally they may be identified radiographically. When periventricular they must be differentiated from tuberous sclerosis [9]. The periventricular hamartomas in tuberous sclerosis and heterotopias may not be differentiated reliably on the basis of signal intensities alone [27]. Tuberous sclerosis has been shown to have abnormal hemispheric signal intensities, which have been shown to represent tubers. Also in our three cases of heterotopias the signal intensities correlated exactly with those of normal gray matter whereas this does not always appear to be the case with tuberous sclerosis [27].

Seven of our patients were evaluated with inversion recovery (IR) sequences. Five of these patients were 9 months old or older and therefore had a significant degree of white-matter myelination. In these patients the gray-white matter interface was demonstrated with both SE and IR images; however, IR was significantly better for gray-white matter differentiation. Of two patients aged 2 months and 5 months, respectively, the gray-white matter interface was not delineated in one (Fig. 1), probably because of a similar degree of hydration of the gray and white matter [28]. In the remaining patient the gray-white matter interface was demonstrated but was not seen as well as in the older patients. The interface was only slightly better delineated with IR (Fig. 9).

Both SE and IR sequences allowed adequate evaluation of the migrational anomalies in this study. Initially, all our patients were evaluated only with SE sequences whereas in the most recent studies we also used IR imaging. Most patients were evaluated in all three imaging planes and also had T2-weighted imaging. The axial images were usually adequate for evaluation and diagnosis. Coronal images usually resulted in more complete delineation of the anatomic anomalies but were usually not necessary for diagnosis. They were most helpful for evaluating open-lip schizencephaly in that they allowed a better understanding of the relationship of the cleft to the lateral ventricle. Sagittal images are necessary for adequate evaluation of the midline structures if an abnormality is suggested on axial or coronal images.

The T1-weighted images were best for delineating the anatomic anomalies present. T2-weighted images were helpful in evaluating fused-lip schizencephaly and for identifying white-matter abnormalities. Intermediate-weighted images resulted in the best delineation of heterotopias.

Owing to time constraints, not all T1-weighted images were IR sequences. IR required approximately 15 min per sequence while the short SE sequences required only 6–9 min. These shorter scan times were preferable in some of the more neurologically impaired patients.

In summary, MR imaging is an excellent method for evaluating neuronal migrational disorders. MR allows delineation of both the abnormal cortex and underlying gray-white matter interface. It permits multiplanar imaging without patient manipulation and demonstrates associated abnormalities such as midline anomalies and white-matter diseases. MR appears

to be the imaging method of choice for the evaluation of neuronal migrational disorders.

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