Investigating Epilepsy: CT and MRI in Epilepsy

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10-20% of all epilepsy is intractable, despite treatment with antiepileptic medications to therapeutic levels. Accurate preoperative localization of the epileptic focus helps significantly in the intraoperative localization of lesion which ultimately determines postoperative control of seizures in a large number of patients treated surgically. Proliferation of cross-sectional imaging techniques over the last several decades has transformed the understanding, evaluation, and management of patients with epilepsy. Commonly applied imaging techniques range from anatomic modalities of computerized tomography (CT) and especially magnetic resonance imaging (MRI) to modalities reflecting metabolism or function including nuclear medicine based examinations as well as MRI based examinations. This article is a review of the application of CT and MRI in the evaluation of epilepsy.

Key Words: computed tomography, epilepsy surgery, magnetic resonance imaging

Proliferation of cross-sectional imaging techniques over the last several decades has transformed the understanding, evaluation, and management of patients with epilepsy. Commonly applied imaging techniques range from anatomic modalities of CT and especially MRI to modalities reflecting metabolism or function including nuclear medicine based examinations as well as MRI based examinations. This article reviews the application of CT and MRI in the evaluation of epilepsy.

Computed Tomography

Although no longer considered a standard for evaluation of the patient with epilepsy, CT is still useful in limited circumstances, notably when speed is paramount or when MRI is contraindicated. Compared to MRI, CT suffers from, by lesser soft tissue contrast, lack of multi-planar capability, and beam hardening artifacts at the skull base.

Despite these limitations, CT readily depicts many of the pathologies which may underlie epilepsy, especially those associated with acute presentations such as hemorrhage, infarction, and mass lesions as well as obvious malformations and calcified lesions. Often CT serves as first line imaging in acute presentation where urgent treatment may be merited. Patients with hemispheric pathology such as Sturge-Weber or with calcified lesions found in tuberous sclerosis may be adequately evaluated with CT. Small tumors, subtle cortical malformations and mesial temporal sclerosis (MTS) may be easily missed with CT. In general patients with normal examinations or with lesions judged incompletely characterized by CT will then proceed to MRI.

MRI

Benefiting from superior soft tissue contrast, multi-planar capability, absence of bone artifact and potential for high resolution, MRI has evolved into the unrivaled imaging standard for routine evaluation of the epilepsy patient. Whereas CT imaging depicts one parameter, x-ray attenuation, MRI reflects a number of independent but related parameters relating to temporal dynamics of proton nuclei responding to changing magnetic fields. The parameters reflected in MRI include T1, T2, susceptibility effects (T2*) and proton density. Most MR sequences attempt to primarily demonstrate a single parameter although the resultant images are generally variably affected by others. Expansive MR development has yielded myriad imaging sequence approaches and options. The choice of optimal sequence and imaging plane depends upon suspected pathology and so is best done with clear communication between radiology and referring service following thorough clinical evaluation.

MR Techniques

MRI protocols attempt to optimize two approaches to lesion detection. In the first, tissue contrast is maximized generally through T2 weighted imaging or related fluid attenuation inversion recovery (FLAIR) imaging. Such imaging increases sensitivity to lesions which exhibit T2 differences from normal brain, most notably MTS. In the second approach to imaging optimization, resolution is enhanced through use of thin slices, especially with 3D imaging acquisition which allows for reformatting in multiple planes. 3D thin slice imaging maximizes evaluation for subtle abnormalities which do not exhibit

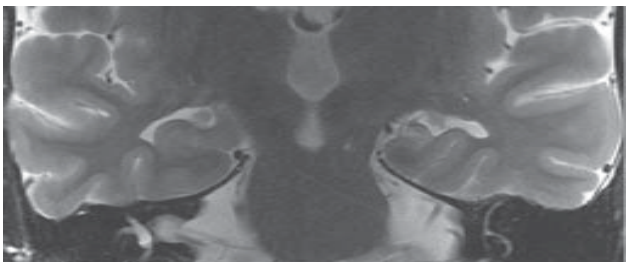

Figure 1. FSE T2 temporal lobe oblique coronal MRI at the level of midbody of hippocampus demonstrates clear hippocampal atrophy and T2 high signal.

T2 changes, most notably MTS. In the second approach to imaging optimization, resolution is enhanced through use of thin slices, especially with 3D imaging acquisition which allows for reformatting in multiple planes. 3D thin slice imaging maximizes evaluation for subtle abnormalities which do not exhibit T2 changes, most notably cortical dysplasia. In this application, the 3D sequence parameters are chosen to augment signal intensity difference between grey and white matter, thereby improving visualization of structural abnormalities. Grey/white differentiation may also be enhanced using a T2 based sequence which includes a magnetization preparation pulse designed to increase tissue signal intensity differences. Sometimes referred to as "white matter inversion recovery" (WMIR), the sequence is similar to short tau inversion recovery (STIR). In STIR, an inversion recovery pulse is used to saturate fat through exploitation of its short T1 relative to other tissues. In WMIR, an inversion recovery pulse is used with a modified inversion time, arrived at empirically, to maximize signal intensity difference between the two tissues.

Typical protocols for MRI in imaging the epileptic patient begin with a standard non-contrast brain evaluation. Included are a T1 sagittal, a T1 axial, a T2 axial, and a FLAIR axial. Slice angulation is determined by a common practice which varies by institution. A line drawn on the T1 sagittal from the anterior commisure to the posterior commisure (so called AC-PC line, **Figure 1**) is widely used. Standard slices thickness of 4 to 5mm are employed usually with a skip between slices of 1mm or so. This simple protocol provides significant information but does not optimally evaluate sometimes more subtle abnormalities.

MTS provides an imaging challenge for which MRI is particularly well-suited. In general, T2 or FLAIR sequences are performed in a near coronal plane obliqued, based on the T1 sagittal, so as to be orthogonal to the long axis of the hippocampus (so called "temporal lobe oblique", **Figure 2**). Greater resolution improves visualization of the internal architecture of the hippocampus and thereby enhancing diagnostic sensitivity and confidence. In MRI, higher resolution comes at the cost of signal-to-noise ratio (SNR) and so steps must be taken to improve SNR and thus avoid images unacceptably noisy or grainy. At our institution, we use especially designed surface coils which increase SNR at the level of the hippocampi. The dedicated

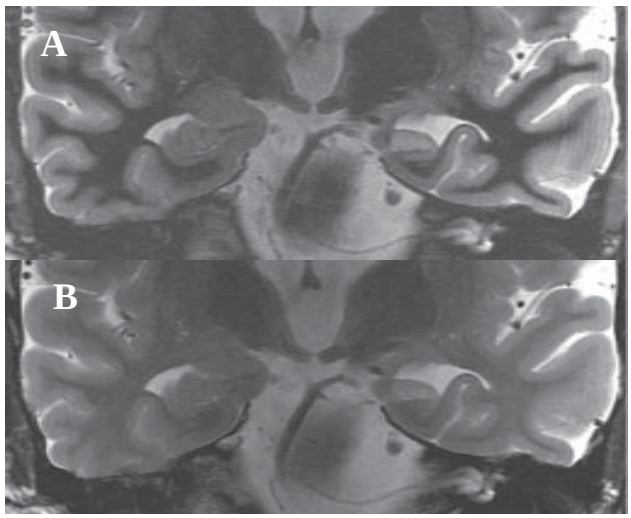

Figure 2. Temporal lobe oblique WMIR (A) and FSE T2 (B) MR scans demonstrate loss of interdigitations along with T2 high signal and atrophy MTS involving pes hippocampus.

coils allow for higher resolution (512 x 384 matrix) T2 fat spin echo (FSE) images and WMIR images with satisfactory imaging times **(Figure 3)**. FLAIR provides improved T2 contrast as well and is useful in the evaluation of MTS when performed using temporal lobe oblique orientation. In the author's opinion, FLAIR has two deficiencies in this specific application. First, the hippocampi may normally appear somewhat bright compared to adjacent brain. Of course, asymmetry in signal intensity will help in detection of the abnormal hippocampus but bilateral MTS does occur in some cases and so may be confused with normal findings. As a second potential FLAIR deficiency, the sequence is not readily performed with high resolution.

As an additional procedure in MTS evaluation, a 3D T1 sequence (see below) may be performed in the temporal lobe oblique orientation. The sequence provides contiguous thinner slices (1 to 1.5 mm) which improve visualization of anatomy, a capabilility sometimes helpful in challenging cases. The T1 sequence lacks sensitivity to T2 changes which are a common and useful finding in MTS but provides superior depiction of atrophic changes. Additionally, the T1 3D sequence is optimally suited to application-quantitative volumetric techniques used commonly in research studies and is gaining increasing acceptance in clinical evaluation.[9]

Cortical dysplasias and migrational disorders range from profound to quite subtle in their imaging manifestations, and often present a greater imaging challenge than that provided by MTS. Sequences which maximize contrast between grey and white matter while providing high resolution are most useful. In this regard, volumetric high resolution T1 gradient echo (GRE) scanning with thin partitions is commonly applied. The sequences vary subtly from one manufacturer to another and unfortunately no uniform system of nomenclature has been adopted.[6,7]

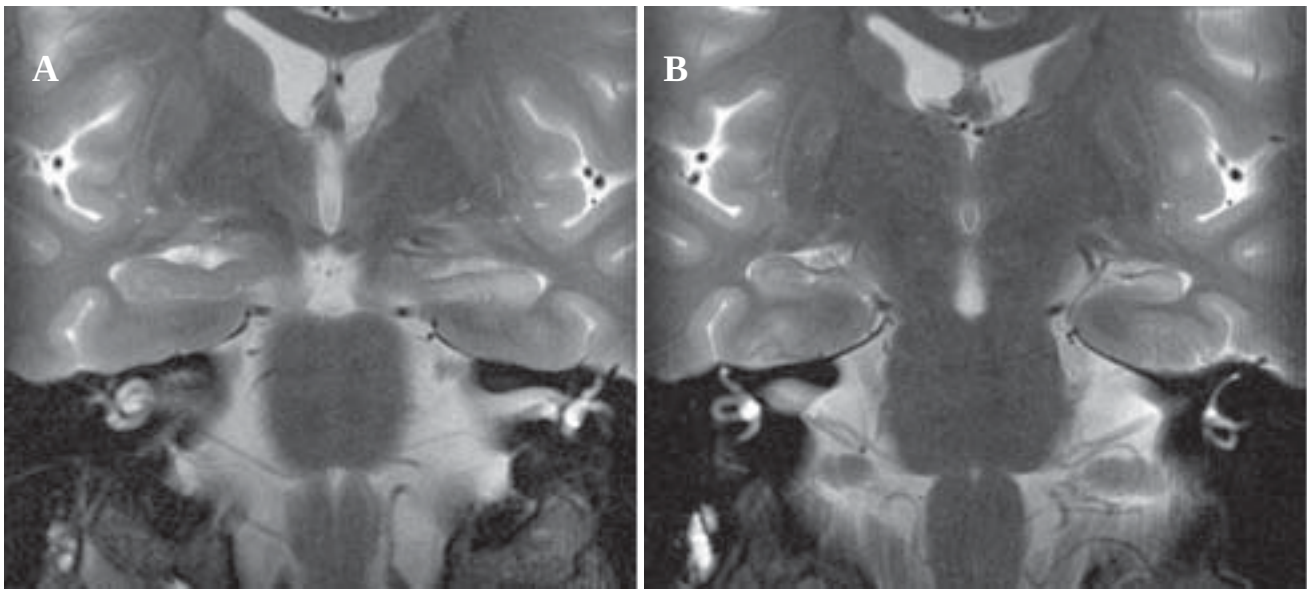

Figure 3. FSE T2 temporal lobe oblique coronal MR scans at the level of pes (A) and hippocampal body (B) demonstrate MTS exhibiting mainly high signal with more subtle atrophy. In this case, the distinction between grey and white matter signal is diminished, another finding in MTS.

MRI protocol choice

Specific choice of MRI protocol depends on the technology available, the preferences and experience of the interpreter, and critically the suspected type and location of epileptogenic lesion. The type of pathology likely to underlie a given patient's epilepsy depends on multiple factors especially age and duration of disease process. The reader is referred to **Table 1.** Although a general protocol designed to evaluate all epilepsy patients is an option, the patient's interests will be better served through crafting the protocol to specific lesion possibilities. Commonly, MTS is a prime consideration in which case the MRI protocol should consist of a basic screening exam with additional temporal oblique sequences especially a high resolution T2 FSE and at least one of WMIR, FLAIR, and 3D T1 gradient exam. If cortical dysplasia is a main possibility, then a screening exam followed by a T1 3D gradient is a good start. Ideally, the T1 3D exam is positioned to evaluate the area of brain suspected as an epileptogenic focus as suggested by seizure semiology and EEG. Sometimes a WMIR sequence favorably oriented to the cortex will improve diagnostic confidence in subtle cases. On occasion, findings detected after review of the initial imaging exam merit a second more focused MRI evaluation.

Use of Gadolinium

In general, gadolinium is not necessary in patients with chronic epilepsy. In patients who have a lesion suspicious for neoplasm, then contrast is certainly helpful in further characterizing the lesion. However, gadolinium is not helpful in evaluating MTS, cortical dysplasia, or most atrophic processes. At our institution, contrast is not part of the initial evaluation for patients with chronic epilepsy. In patients with a more recent epilepsy presentation, especially older adults, the likelihood of tumor as a cause for the symptoms is higher. So contrast may be useful in the initial evaluation. Note that in this subgroup, a dedicated epilepsy imaging study may not be needed.

Imaging of specific epileptogenic disease processes

MTS

Mesial temporal or hippocampal sclerosis is characterized pathologically by pyramidal and granule cell neuronal loss in the cornu ammonis and gyrus dentatus often with hippocampal reorganization and evidence for changes in energy metabolism.[19] It is the most common pathology associated with temporal lobe epilepsy, especially those refractory to medial therapy.The

Causes	Age of onset (years)				
	0-2	3-20	21-40	41-60	>60
Cerebral anoxia	X				
Metabolic	X				
Congenital	X	X			
Infection	X	X			
Phacomatoses	X	X			
Primary generalized epilepsy		X			
Hippocampal sclerosis		X			
Vascular malformation		X	X		
Post-traumatic		X	X	X	X
Tumor			X	X	X
Stroke				X	X

Table 1. Age of onset and the the likely underlying pathology (adapted from Bronen RA. Epilepsy: the role of imaging. AJR 1992, 159(6); 1165-74).

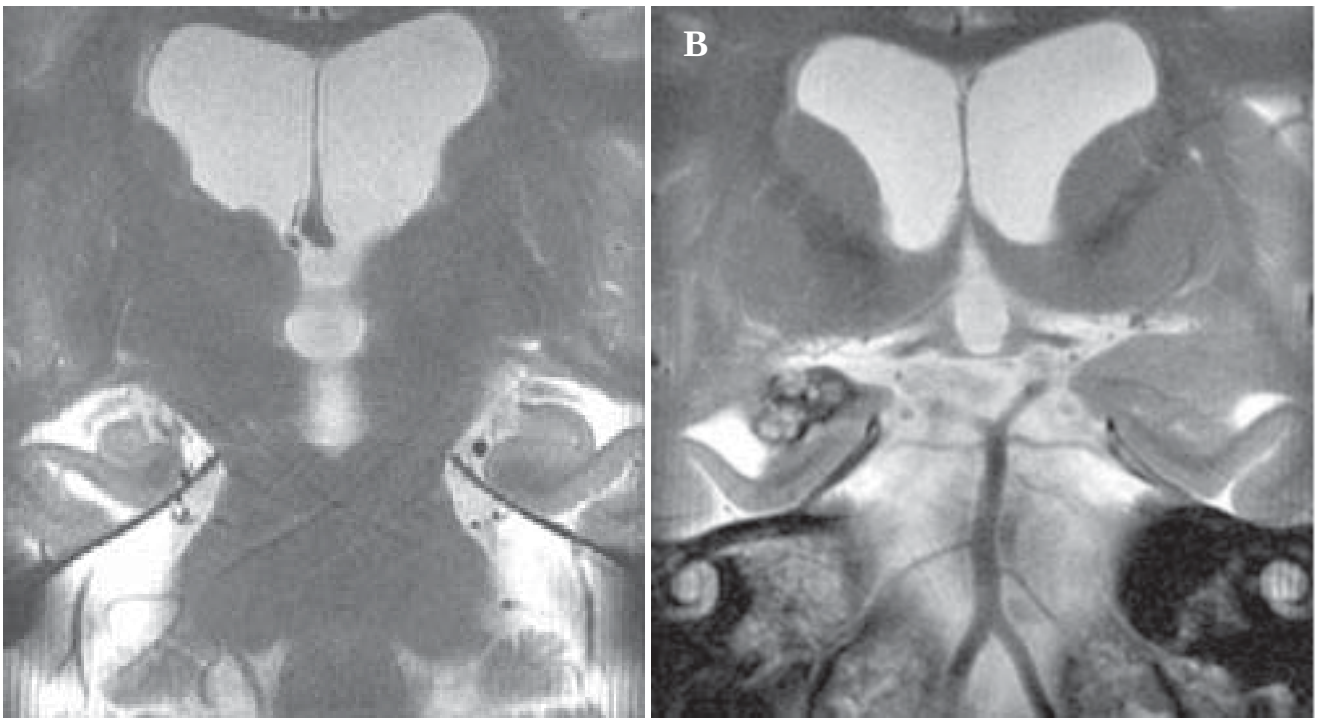

Figure 4. FSE T2 temporal oblique coronal (A) MR scan shows MTS in midbody of the hippocampus in this patient with a cavernous malformation adjacent to the pes and amygdala (B).

identification of MR abnormality in such patients, when correlated with EEG serves as useful prognosticator for successful surgical treatment. It should be noted that MTS in and of itself does not prove the existence of refractory epilepsy as it has been observed in patients successfully medical treated.[10]

Primary findings seen on MRI in MTS are T2 high signal and atrophy of the hippocampus.[3] Such findings may be quite subtle and so a concerted effort at obtaining the highest quality temporal lobe MR study should be made in all cases. Other findings have been described in MRI as well, notably diminished grey-white matter differentiation, often referred to as loss of internal architecture. Secondary findings include ipsilateral atrophy of the fornix and of the mamillary body. One may also note ipsilateral atrophy of the hippocampal collateral white matter as well as atrophy of the ipsilateral temporal lobe. These secondary findings are in general less helpful as they tend to be seen only in the more advanced MTS cases and may be misleading without the observation of the primary abnormality. As a manifestation of atrophy, ipsilateral enlargement of the temporal horn has been described. Asymmetric temporal horns sometimes occur normally so this nonspecific finding should be used with caution. Findings essentially never seen in MTS include enhancement and mass effect. Of course, the presence of mass effect should raise concern for underlying neoplasm.

Patients with MTS may have more than one lesion relevant to their epilepsy. The so-called dual pathology occurs in up to 15% of cases. Associated pathologies include cortical dysplasias, tumors, and vascular malformations. Further evaluation, management and potential surgical treatment will be directly altered by the presence of a second relevant lesion so the search for pathology does not end with the observation of MTS. In general, the finding of dual pathology decreases the likelihood of successful surgical treatment. In most cases, both lesions merit consideration of resection.

Vascular malformations

Some vascular malformations may present with epilepsy. The most noteworthy example is the cavernous malformation (CM) **(Figure 4)** for which most common presentation is seizures.[8,15] Arteriovenous malformations may occasionally cause seizures although more typically they will present with hemorrhage or other symptoms referable to mass effect. Although, in general, specialized MRI techniques are not needed to detect these lesions, MR does assist in lesions characterization and in many cases may be used to make a definitive diagnosis preoperatively. Key findings to detect in characterizing a CM on MRI include the presence of a complete hemosiderin ring, best seen with T2 sequence. Other characteristic findings include lack of adjacent edema (except in the setting of recent overt hemorrhage), reticulated internal architecture, and blooming of blood products on T2 (T2 GRE) sequence. The T2 sequence may also be used to identify lesions too small to detect without the benefit of susceptibility effects. Also, with gadolinium, one may identify developmental venous malformations often associated with CMs, thereby aiding further in pre-operative planning.

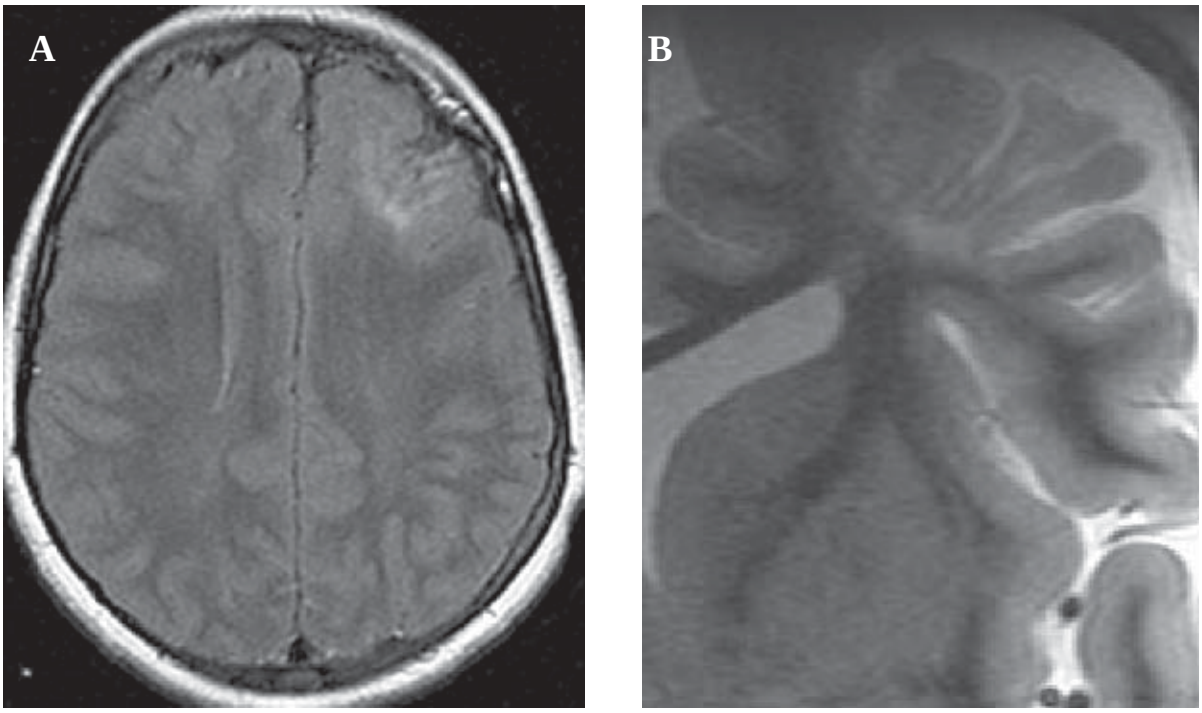

Figure 5. FLAIR axial (A) and high resolution T2 FSE coronal (B) MR scans in a patient with ulegyria.

Destructive lesions associated with epilepsy

Trauma and stroke are major causes of epilepsy in young to older adults. In general, such lesions do not represent a dilemma either in detection or in diagnosis. However, in select cases, the MRI may assist in lesion characterization and management. In **Figure 5A**, a routine FLAIR axial demonstrates an area of abnormal signal in a 10-year-old with chronic epilepsy. Based on the FLAIR, the lesion is fairly nonspecific with differential considerations including gliosis, encephalomalacia, encephalitis and less likely tumor. In this case, a high resolution T2 coronal FSE was performed using surface coils positioned immediately over the abnormality. The superior resolution provided by the examination allowed by detailed morphologic evaluation including identification of gyri which were thinned more so at the base than at the apex. This observation along with the presence of volume loss and of high T2 signal in adjacent white matter led to the specific diagnosis of ulegyria, a characteristic pattern seen with perinatal ischemic injury. Subsequent surgical resection confirmed the preoperative diagnosis.

Developmental abnormalities

Developmental abnormalities represent a most challenging diagnosis in patients with epilepsy. In addition to enhancing detection, MRI has greatly expanded our understanding of such pathology.[1] Indeed, much of current classification is based largely on MRI findings.[11] Resolution, grey-white matter contrast and multi-planar capability afforded by MRI again enhances evaluation. Although MRI detected lesions are often sources of epilepsy, the actual epileptogenic zone may differ from or be more extensive than the anatomic lesion. As such, even with an MRI detected lesion, surgical management demands invasive electrophysiologic monitoring in most cases. In the following, a few representative developmental abnormalities and their MRI appearance are presented.

Focal cortical dysplasias (FCD) consist of abnormal neurons and glial cells abnormally arranged in areas of cerebral cortex.[2,5]

When certain abnormal neurons are present, balloon cells, the FCD represents anomalous neuronal and glial proliferation. When balloon cells are not present, then the FCD is the result of abnormal cortical organization. Findings described with FCDs include obscuration of the grey-white junction, thickened cortex, abnormal sulcation, and cortical dimple with overlying CSF cleft.[4] In the balloon cell variant of cortical dysplasia, often T2 high signal is present in involved subcortical areas. **Figure 6** is provided as an illustrative example.

Schizencephaly differs from FCD in that a CSF lined cleft, usually lined by polymicrogyric cortex, connects pial surface to ependymal.[12,14] As with FCDs, the abnormality may be bilateral and is seen commonly in the peri-Rolandic regions. Schizencephalies are subdivided into open- or closed-lip variants. Closed-lip lesions exhibit polymicrogyric walls which appose each other at one or more points whereas in the open-lip form the walls are always separated. In the closed-lip form, a "dimple" along the wall of the ventricle provides a clue to diagnosis. **Figure 7** is provided as an illustrative example.

A disorder of both neuronal and glial proliferation, hemimegalencephaly results in enlargement of all or part of a cerebral hemisphere (**Figure 8**).[13,20] Patients present early in life usually with intractable epilepsy, followed in childhood by hemiparesis and mental retardation. The disorder may be associated with neurofibromatosis type 1 as well as other syndromes. MRI confirms hemispheric enlargement along with ipsilateral enlargement of the ventricular atrium and classic straightening of the frontal horn. Ipsilateral white matter usually exhibits T2 high signal representing gliosis. Cortex in the affected hemisphere is

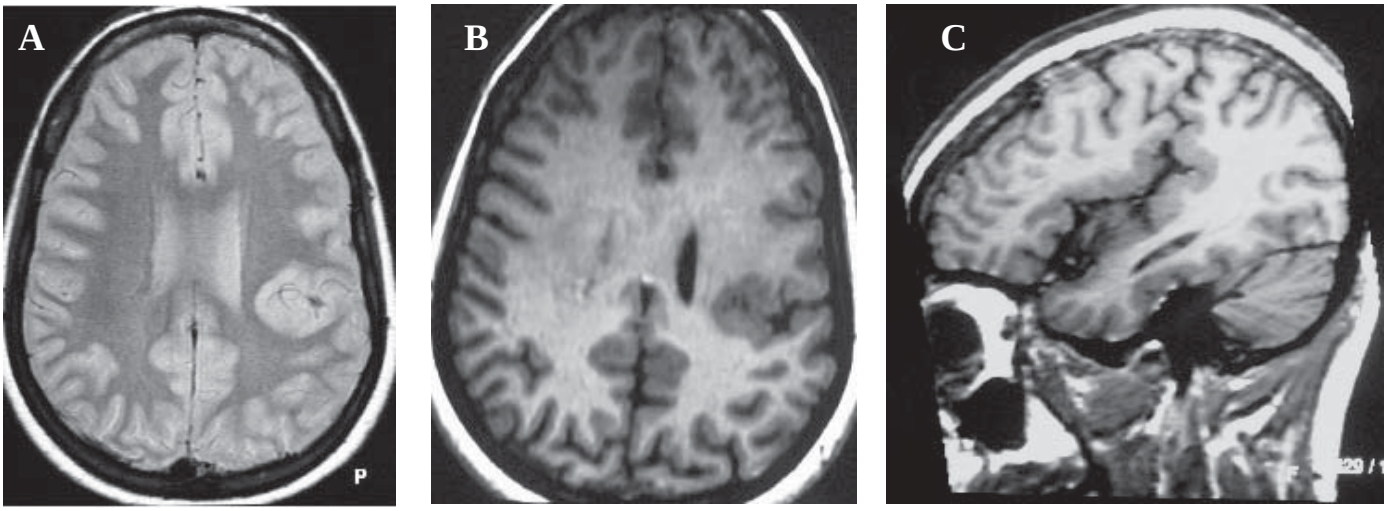

Figure 6. In (A), a proton density axial MR scan shows an abnormality in the left fronto-parietal region. Images reformatted in axial (B) and sagittal (C) plane from 3D T1 GRE sequence show the abnormality to consist of an area of thickened cortex adjacent to the Sylvian fissure associated with an anomalous deep sulcus, consistent with cortical dysplasia.

dysplastic, variously exhibiting polymicrogyria, pachygyria, and/or agyria.

Abnormal radial neuronal migration results in grey matter heterotopias. Depending on the timing of migration interference, the heterotopias may be subependymal or subcortical in location. Presentation is highly variable with patients ranging from asymptomatic to mildly retarded. Seizure, usually partial, is the most common symptom. Patients with the periventricular form may exhibit concomitant abnormalities especially related to development of the corpus callosum and of the cerebellum. The hallmark on imaging is simply grey matter where it does not belong. Imaging may be quite subtle as single foci of ectopic grey matter occur (heterotopion). As such, a 3D T1 GRE sequence is the most useful for reasons previously described.

Phakomatoses

Several of the phakomatoses result in epilepsy with tuberous sclerosis and Sturge-Weber the most noteworthy examples. Although well described clinical signs of these syndromes exist, they can be subtle or sometimes not present and so diagnosis relies on imaging. Both disorders can be diagnosed definitively with MRI.

Cortical tubers and subependymal nodules dominate the intracranial manifestations of tuberous sclerosis.[17,18] The cortical tubers are characterized by broad, flat gyri with subcortical white matter signal abnormality. The signal abnormality varies with the stage of myelination. In neonates, the white matter exhibits T1 high signal and T2 low signal. This pattern reverses with myelination. The number and size of cortical tubers varies greatly. Subependymal nodules are recognized as rounded contour abnormalities lining the ventricles. They should be distinguished from grey matter subependymal heterotopias which follow grey matter on all sequences. In contrast, the subependymal nodules of tuberous sclerosis usually exhibit T1 hyper- and T2 hypointensity. Calcification is present in the subependymal nodules of older patients and may be detected with MRI by using a T2* sequence. Of course, CT is more useful for this specific imaging need.

Sturge-Weber or encephalotrigeminal angiomatous is characterized by leptomeningeal angiomatous proliferation associated with a facial port-wine stain in distribution of the trigeminal nerve.[16] The angioma enhances with contrast and is readily identified with MRI. Associated findings include ipsilateral cortical atrophy with compensatory calvarial thickening. White matter subjacent to the leptomeningeal angioma exhibits T2 hypointensity until calcification alters this characteristic. In a third of cases, either the sclera and/or the ocular choroid exhibit a plexus of dilated small vessels.

Tumors

Although many neoplasms may cause seizures, a subset may present with chronic epilepsy and so fall into the pre-imaging differential diagnosis with cortical dysplasias, CMs, and MTS. Highly epileptogenic tumors occur most often in the temporal lobe in or adjacent to cortex. The indolent tumors yielding chronic epilepsy include ganglioglioma, low-grade glioma and dysembryoplastic neuroepithelial tumor (DNET). These tumors tend to be small and well localized with little edema or mass effect. FLAIR and T2 imaging tends to be the most helpful, at first inspection, in detection of such lesions. The use of additional imaging planes and of gadolinium contrast is often helpful in further characterization. **Figure 9** is provided as an illustrative example.

Conclusions

Neuroimaging, especially with MRI, has evolved into standard evaluation along with EEG in patients with unexplained seizures. In the majority of cases, MRI provides definitive imaging characterization of lesional epilepsy. In order to maximize the potential of the

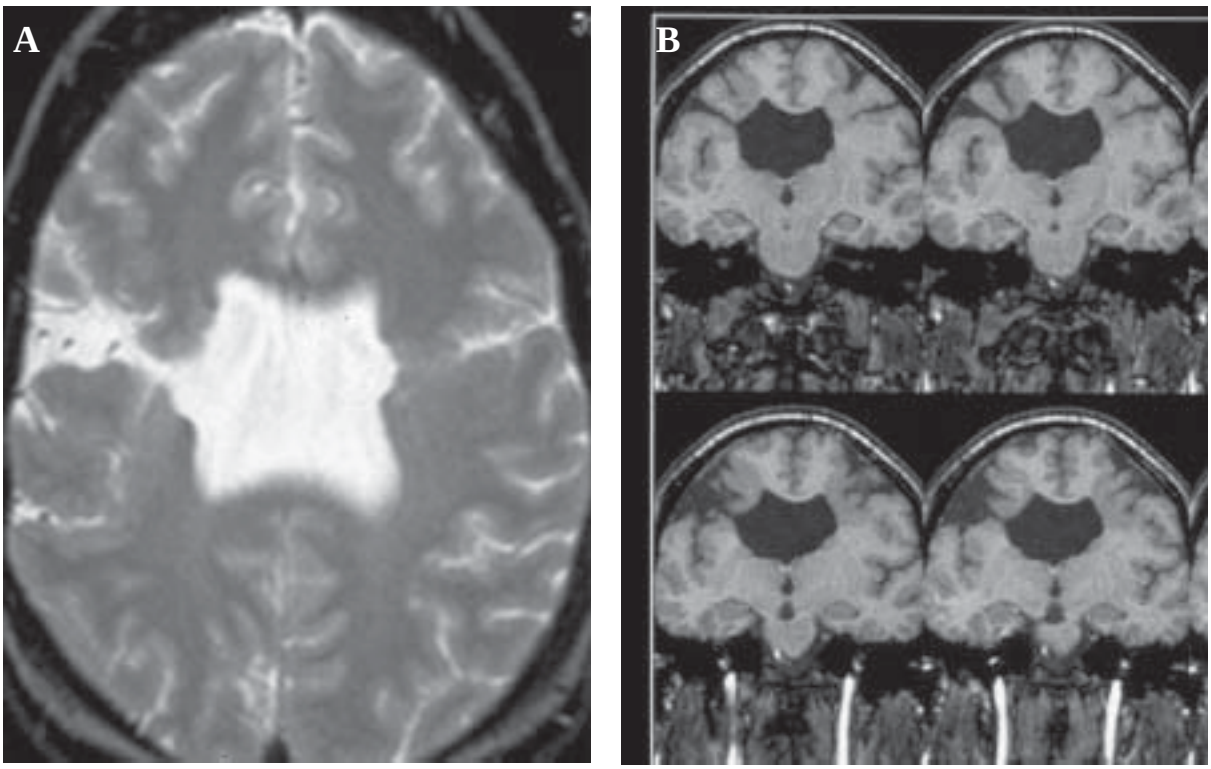

Figure 7. In (A), a T2 axial MR scan shows abnormal cortex bilaterally with that on the patient's right exhibiting a CSF lined cleft in direct communication with the ventricle (open-lip schizencephaly). In (B), series of contiguous partitions from a 3D T1 GRE sequence are presented. The presence of an CSF lined cleft is confirmed. No such cleft in present on the patient's left. However, grey matter clearly extends from the cortex to the ventricle. On the T2 axial, a focal outpouching at the ventricle, represents a "dimple" — as seen with closed-lip form of schizencephaly. If the "dimple" were not present, then the abnormality would be more consistent with focal cortical dysplasia (transmantle cortical dysplasia).

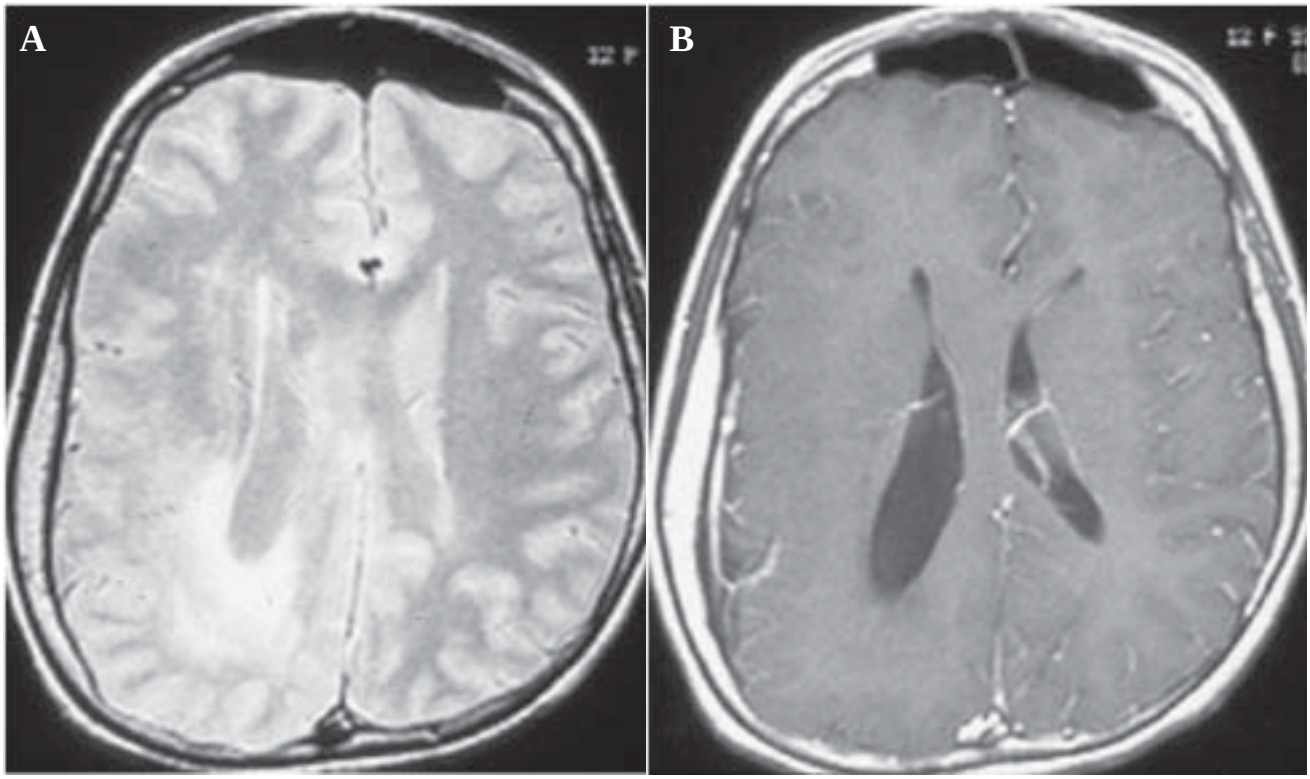

Figure 8. Proton density (A) and post-contrast T1 axial (B) MR scans show typical features of hemimegalencephaly. The patient's right cerebral hemisphere is enlarged and the cortex thickened and disorganized (polymicrogyria). High T2 signal in subcortical white matter is consistent with gliosis. The right lateral ventricle is enlarged and the anterior horn somewhat straightened.

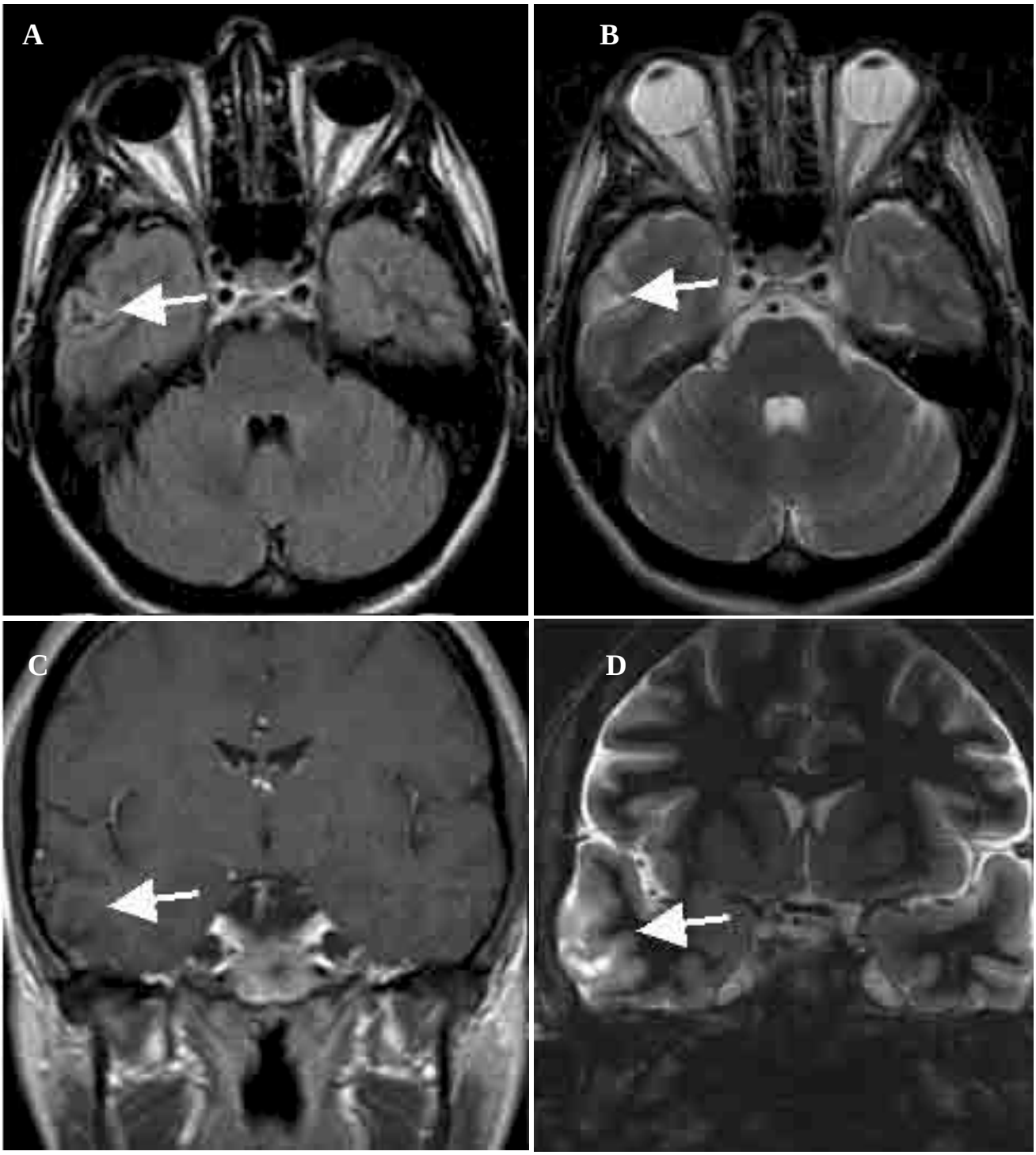

Figure 9. FLAIR axial (A), T2 FSE axial (B), post-contrast T1 coronal (C), and T2 FSE coronal (D) MR scans in a patient with ganglioglioma. The FLAIR and T2 axial images show area of signal abnormality in the lateral right temporalregion in this patient with chronic epilepsy. The T2 FSE coronal confirms the finding to be in either the middle or inferior temporal gyri. No significant mass effect or volume loss is evident. The post-contrast T1 coronal suggests slight enhancement in the inferior aspect of the lesion. Findings were judged to be most suggestive of low grade tumor.

technique, the protocol should be crafted to the needs of the individual epilepsy patient.

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