Seizures: Emergency Neuroimaging

Christopher P. Hess* and A. James Barkovich

KEYWORDS

• Seizures • Epilepsy • Peri-ictal changes
• Posttraumatic epilepsy • Mesial temporal sclerosis

The term seizure refers to an abrupt but transient interruption in normal brain function that comes about as the result of an unregulated discharge of neurons. Seizures are so common that nearly 10% of the population of the United States will have at least one seizure by age 80. New unprovoked seizures or seizures that are not rapidly controlled are viewed as a neurologic emergency, and thus in the emergent setting often undergo computed tomography (CT) scanning or less commonly, magnetic resonance (MR) imaging. Epilepsy, in contrast, is a term reserved for the chronic brain disorder characterized by recurrent and unpredictable seizures without evidence for a reversible systemic cause. The prevalence of this disorder in the United States is estimated at 0.5% to 1%. For the evaluation of patients with epilepsy, MR imaging is almost always the first-line imaging modality. Positron emission tomography (PET) with ^{18}F fluorodeoxyglucose (FDG) and magnetoencephalography (MEG) may also be used in some centers to increase diagnostic sensitivity and specificity in cases where high-quality MR imaging is negative or equivocal.

This article focuses on CT and MR imaging of unusual and potentially reversible causes for acute seizures in the emergency setting. Because many patients who develop seizures after trauma, infection, or metabolic derangements may eventually develop epilepsy, some of the chronic brain conditions that result secondarily from an acute event are also included in this review. In particular, posttraumatic epilepsy and mesial temporal sclerosis (MTS) are discussed in some detail. The interested reader is referred to several excellent articles[1–6] and texts[6–8] for a more comprehensive review of imaging in epilepsy, especially with regard to malformations of cortical development, phakomatoses, and emerging advanced MR imaging, MEG, and nuclear medicine techniques for improving localization of seizure substrates when MR imaging is unrevealing.

SEIZURE TYPES AND INDICATIONS FOR IMAGING

As a single symptom of a broad range of neurologic disorders ranging from Alzheimer to Zellweger disease, seizures have a variety of imaging manifestations. Some of these are common and some are exceedingly rare. Many findings that have been observed represent the secondary hemodynamic, metabolic, or excitotoxic effects of seizures on the brain. Others such as MTS, infarcts, tumors, or cortical dysplasia can represent the primary underlying cause of seizures. When imaging patients presenting with new or recurrent seizures, it is important that the radiologist be able to confidently distinguish between potential causes and the secondary effects of seizure activity, especially with regard to recognizing causes that may be reversible with the institution of appropriate treatment. In the emergency setting, imaging is commonly performed with CT. When CT is contraindicated or unhelpful, MR imaging may also reveal reversible causes for seizures, or may

UCSF Department of Radiology & Biomedical Imaging, 505 Parnassus Avenue, Room L-358, San Francisco, CA 94143-0628, USA
* Corresponding author.
E-mail address: christopher.hess@ucsf.edu

Neuroimag Clin N Am 20 (2010) 619–637
doi:10.1016/j.nic.2010.07.013
1052-5149/10/$ – see front matter

disclose findings that suggest the next step in the workup of seizures.

As detailed in the recently revised terminology for classification of epilepsy developed by the International League Against Epilepsy (ILAE),[9] 2 principal seizure types are recognized: focal seizures (or partial seizures), which show clinical or electroencephalographic (EEG) evidence for origin from a discrete location within the cortical or subcortical gray matter of one hemisphere, and generalized seizures, which may also arise from a single discrete location but in contrast to focal seizures rapidly propagate through both hemispheres and thus clinically do not have consistently localizing features. (Modern imaging, methods for genomic analysis, and molecular biology have significantly altered our understanding of seizures since the initial ILAE classification was published in 1960, and updated for seizures in 1981 and for epilepsy in 1989. The latest proposed revision of the ILAE classification can be found in Ref.[9]) This distinction is important, as the causes, treatment, and outcomes for these 2 types of seizures differ significantly and vary by age. Chronic generalized seizures often present in childhood and usually have normal imaging; acute generalized seizures in the adult are more ominous, as they are more likely to have significant structural lesions evident on routine CT. In contrast, both acute and chronic partial seizures are more likely to have imaging abnormalities that are occult on CT and sometimes exceedingly subtle on MR imaging. In this regard, it is important to recognize the limitations of CT. Adults with acute generalized seizures should be evaluated clinically for evidence of trauma, metabolic abnormalities, or toxic ingestion, with a low threshold for CT imaging when a significant intracranial process such as infection, tumor, or hemorrhage is suspected. In some cases, however, the evaluation should not stop when CT does not disclose any significant abnormality, but rather should include additional imaging with MR.

Multidisciplinary guidelines developed through the process of expert review have led to the development of well-defined criteria for determining whether CT and/or MR imaging are indicated in the emergency setting.[10] As a general rule, *imaging is recommended for any patient in whom a serious structural lesion is suspected based on history and physical examination, or when a clear systemic cause for seizures has not been identified*. Recommendations differ based on age and clinical presentation, with imaging strongly suggested after first-time seizures in patients older than 40, in cases of known malignancy or immune compromise, or when symptoms suggest a partial onset (all conditions that increase the likelihood of a focal brain lesion). Even in patients known to have epilepsy, repeat imaging is recommended when the seizure pattern or type changes, when seizures result in significant head trauma, or when prolonged postictal confusion or declining mental status are present. Appropriateness criteria issued by the American College of Radiology also serve as a useful resource to aid in the selection of patients for imaging.[11]

Patients with acute intracranial hemorrhage, brain tumors, infections, dural venous sinus thrombosis, traumatic brain injury (TBI), developmental abnormalities, and vascular lesions such as cavernous and arteriovenous malformations may all present with seizures. These entities are discussed in other articles in this issue.

In a cohort of 880 individuals from the city of Rochester, Minnesota, no specific cause for seizures was found in 65.5% of patients[12]; however, disorders with abnormalities that could potentially be identified by imaging were also common in this cohort. These abnormalities included cerebrovascular disease in 10.9%, congenital lesions in 8.0%, trauma in 5.5%, tumors in 4.1%, neurodegenerative disease such as Alzheimer disease in 3.5%, and infection in 2.5%. The proportion of cases with underlying brain structural abnormalities varied by age, with tumors and infarcts far more common among patients older than 65 than among those in younger age groups, where infection and trauma were more frequent. Metabolic derangements and alcohol withdrawal collectively represented common causes for seizures among the middle-aged population. In children between the ages of approximately 5 months and 6 years, many series have shown that most seizures represent simple febrile seizures. Imaging in this patient population is usually unwarranted at first presentation, especially in light of growing concerns regarding radiation exposure[13] and the availability of established clinical practice guidelines that do not routinely include CT.[14]

Logistic and cost issues aside the diagnostic yield of MR imaging is far higher than that of CT in both patients with acute seizures and patients with long-standing epilepsy. Not all MR imaging examinations are equivalent, however. The accuracy of MR imaging increases with the field strength used for acquisition, as the higher signal-to-noise and contrast-to-noise afforded by 3-T imaging allow visualization of smaller structures and more small variations in signal intensity than conventional 1.5-T imaging.[15,16] MR imaging studies performed for the evaluation of seizures should also be tailored to optimize detection of seizure foci, as routine brain protocols may miss

lesions responsible for seizures. Finally, although there is evidence that general radiologists consistently detect critical structural abnormalities, subtle abnormalities may be detected at higher rates by subspecialty-trained neuroradiologists practicing in dedicated epilepsy centers. According to one study, for example, the diagnosis of hippocampal sclerosis was missed prospectively in 86% of initial imaging reports.[17] Although controversial, this study at the very least reiterates the need for all radiologists to: (1) increase their familiarity with the MR imaging diagnosis of MTS (discussed later in this article), (2) employ dedicated high-resolution seizure protocols, and (3) incorporate clinical and EEG information regarding seizure type and localization into the process of interpretation.

Modern seizure evaluation should routinely include coronal thin-section T2-weighted images of the medial temporal lobes and a volumetric T1-weighted evaluation of the entire brain to allow critical assessment of regional sulcal anatomy, cortical thickness, and definition of gray-white boundaries.[18] In addition, it is important to include sequences sensitive to magnetic susceptibility to identify calcification and chronic blood products from prior trauma, cavernous malformations, and infections such as neurocysticercosis (one of the most important causes for seizures worldwide). New three-dimensional (3D) phase-sensitive susceptibility-weighted techniques likely have higher sensitivity in this regard than conventional gradient echo T2* sequences. Of note, high spatial resolution, formerly possible only with specialized surface coils,[19] can now be routinely obtained with most sequences on 3-T scanners using phased-array receive coils.[20] Gadolinium-enhanced images are not typically required for evaluation of chronic seizures unless a tumor is suspected. In the acute setting, however, contrast-enhanced sequences may be useful to evaluate for underlying infections, tumors, or vascular lesions (**Table 1**).

PERI-ICTAL CHANGES ON IMAGING

Independent of cause, seizures are associated with dramatic alterations in cellular metabolism, disruptions in normal cerebral autoregulation, shifts in relative compartmental water distributions, and changes in intracellular ion concentrations. The variety of pathophysiological events that take place as the direct result of seizure activity is reflected in the myriad imaging findings that have been described with ongoing or recent seizure activity. These "peri-ictal" imaging abnormalities may be reversible or irreversible, depending on the nature and duration of seizures and, like the underlying electrochemical events that cause them, may affect the brain in a focal or diffuse fashion.

Often mild or absent on unenhanced CT, peri-ictal changes commonly appear as patchy areas of high signal on T2, fluid-attenuated inversion recovery (FLAIR), or diffusion-weighted MR

Table 1
Adult epilepsy/seizure protocol

	Sequence	TR/TE/TI (ms)	FOV (mm)	Matrix	Slice/Gap (mm)
1	Axial DWI (b = 1000 s/mm^2)	10000/MIN	220 × 220	128 × 128	3 skip 0
2	Coronal T2 FSE-IR	5000/120 (ETL 16)	220 × 160	512 × 256	3 skip 0
3	Coronal 3D T1[a]	36/MIN	220 × 160	230 × 230	1.2 skip 0
4	Coronal T2 FLAIR[b]	10000/140/2200	220 × 160	256 × 192	3 skip 0
5	Axial T2 FSE	5850/100 (ETL 17)	220 × 220	384 × 384	3 skip 0
6	Coronal T2* GRE[c]	787/25	220 × 160	256 × 192	5 skip 1
7	Gad axial T1 SE	600/MIN	220 × 220	256 × 192	5 skip 1
8	Gad coronal T1 SE	600/MIN	220 × 160	256 × 192	5 skip 1

Coronal acquisitions should be acquired along the hippocampal axis.

Abbreviations: DWI, diffusion-weighted imaging; ETL, echo train length; FLAIR, fluid-attenuated inversion recovery; FOV, field of view; FSE, fast spin echo; Gad, acquired following administration of gadolinium; GRE, gradient echo; MIN, minimum possible TE; SE, spin echo; TE, echo time; TI, inversion time; TR, repetition time.

[a] Volumetric spoiled gradient echo (SPGR) or magnetization-prepared rapid acquisition gradient echo (MPRAGE) sequences are recommended to optimize gray-white contrast with high spatial resolution. Images should be reformatted and reviewed in 3 planes.

[b] Volumetric FLAIR sequences are also useful when available, as they facilitate review in 3 planes at high spatial resolution.

[c] 3D susceptibility-sensitive sequences may be substituted for conventional T2* gradient echo imaging.

imaging (**Fig. 1**).[21–26] Typically involving gray matter, either within the cerebral cortex or in the deep gray nuclei, these abnormalities are frequently bilateral and may be migratory on serial imaging. Peri-ictal changes may arise within a localized epileptogenic region of the brain or remotely within areas of the brain distant from the actual seizure focus. Changes in the region of seizure onset are thought to be the direct result of localized metabolic and vascular changes associated with abnormal neuronal discharge[27]; the precise cause for remote changes is more difficult to understand. Frequent involvement of limbic structures, especially the hippocampus, suggests that seizures preferentially involve neuronal populations with a lower intrinsic seizure threshold. Alternatively, as suggested by signal changes in the thalamus or cerebellum, seizures may propagate secondarily through distributed networks in the brain.

The signal abnormalities related to seizures on MR imaging are commonly associated with mild mass effect, causing subtle sulcal effacement within involved areas. Occasionally, seizures may be associated with more pronounced mass effect. In these cases, imaging may erroneously lead to the diagnosis of a mass lesion[28] or, in patients with known tumors, be mistaken for tumor progression.[29] The transient and migratory nature of these changes on serial imaging and associated clinical picture may provide the only clues that the abnormalities are related to seizures. Other reported, but less common, findings include transient sulcal hyperintensity on FLAIR sequences, leptomeningeal enhancement, cross-cerebellar diaschisis, and asymmetric enlargement of arterial branches on MR angiography. These less common findings may confound the diagnosis of postictal changes; follow-up imaging can be useful in assessing the degree to which abnormalities are reversible and in differentiating postictal changes from other disorders that may have similar imaging features, such as encephalitis and infarction. Short-term follow-up imaging and/or lumbar puncture may be warranted to differentiate among these different possibilities.

The observation of peri-ictal changes on MR imaging depends on the duration of seizures and the time between the cessation of seizure activity and imaging. Transient partial seizures are infrequently associated with peri-ictal changes whereas prolonged, refractory seizures or status epilepticus are more likely to exhibit these abnormalities. The exact timing and duration of seizure activity is often difficult to establish with certainty because whereas generalized tonic-clonic seizures are dramatic and more readily documented, partial or nonconvulsive seizures may be clinically occult. In the authors' experience, patients with underlying comorbid diseases such as lupus, immunocompromised patients, solid organ transplant patients, and patients on chemotherapy agents are also more likely to show peri-ictal changes on MR imaging.

Peri-ictal changes may be transient and reversible, or they may progress to permanent cell death and gliosis. The extent of brain injury may be evident clinically. However, longitudinal follow-up

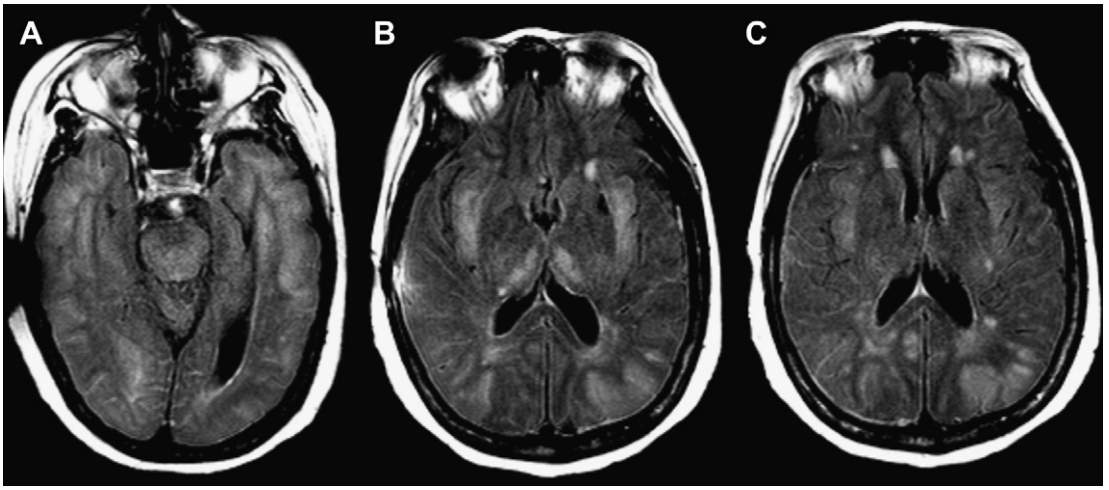

Fig. 1. Peri-ictal changes. Axial T2-weighted FLAIR images show multifocal bilateral frontal, temporal, and occipital abnormal hyperintensity in a patient presenting with medically refractory status epilepticus 2 days before MR imaging. Note widespread involvement of both cortex and white matter. Involvement of the brainstem (*A*), thalami (*B*), and insulae (*B, C*) is characteristic of severe seizure-related changes.

in some cases after prolonged seizures can provide supplementary evidence for permanent brain injury, usually manifest as focal or global cerebral atrophy or cortical injury, including laminar necrosis on T1-weighted images (**Fig. 2**). Cytotoxic edema, as implied by the presence of reduced diffusion, is a more ominous finding, but does not necessarily imply irreversible injury.[30–32] One interesting location for high T2 signal and reduced diffusion that is typically reversible is the splenium of the corpus callosum (**Fig. 3**), in which a rare circumscribed lesion has been variably ascribed to certain antiepileptic medications such as vigabatrin or to seizures themselves.[33–35] The reversibility of this finding suggests that reduced diffusion in this lesion does not reflect cytotoxic edema; a transient disturbance in energy metabolism and ionic transport that results in reversible myelin vacuolization or intramyelinic edema has been proposed.[35]

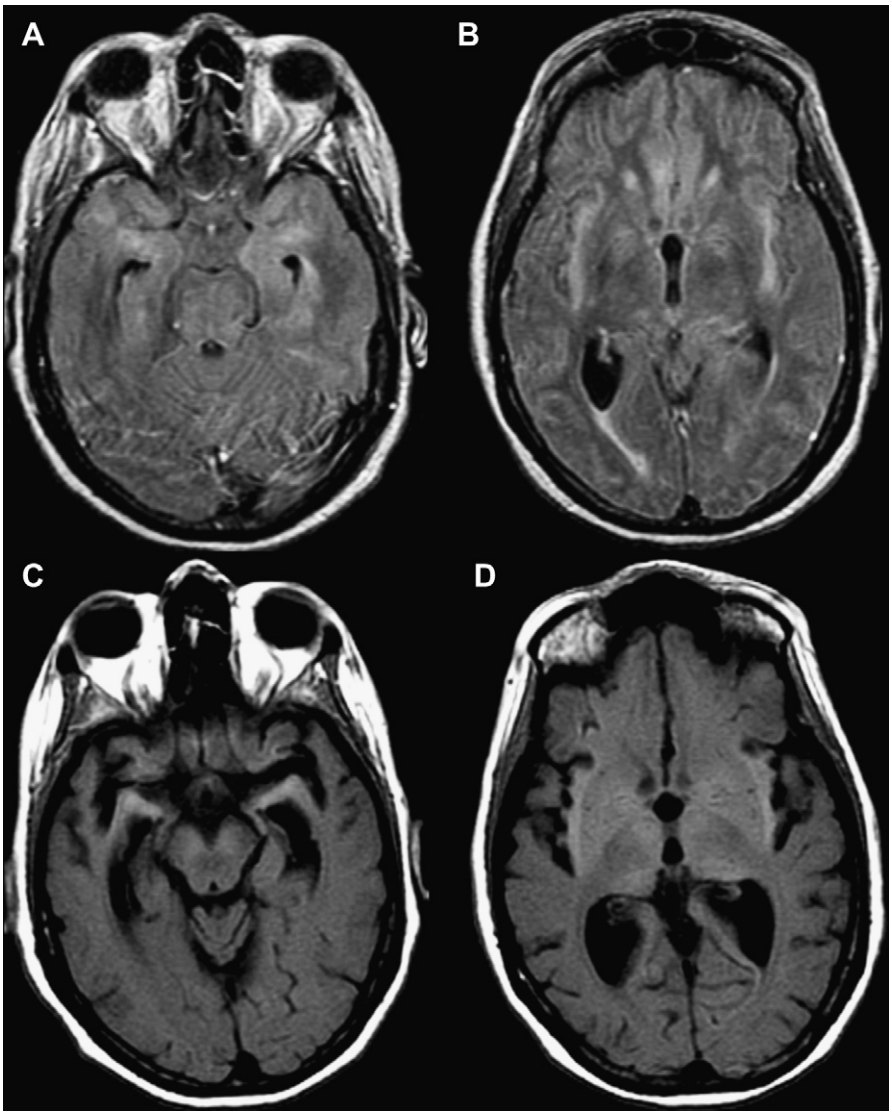

Fig. 2. Permanent injury after prolonged status epilepticus following orthotopic liver transplant. Initial axial FLAIR images obtained shortly following transplant during nonconvulsive status epilepticus (*A, B*) show abnormal hyperintensity of the medial temporal lobes, medial frontal cortex, thalami, and insulae bilaterally. Noncontrast T1-weighted images obtained several months later (*C, D*) illustrate interval development of bilateral cerebral atrophy, especially within the medial temporal lobes, as well as intrinsic T1 shortening in the anterior temporal lobes, insulae, and thalami.

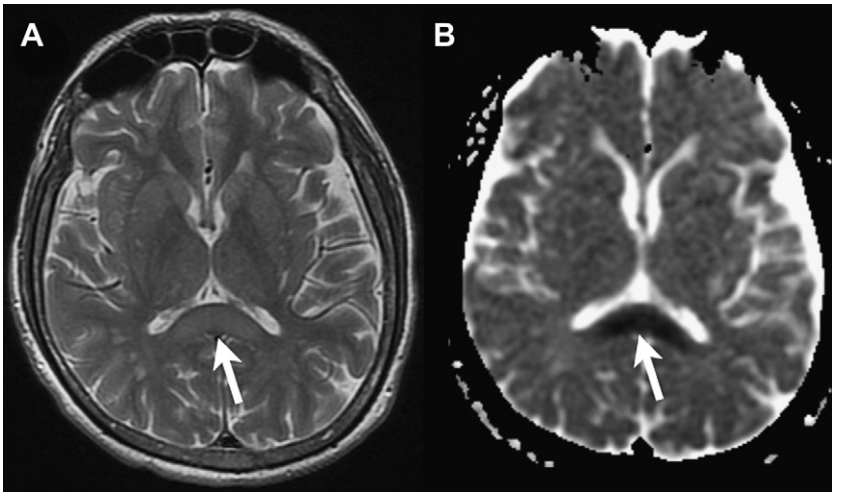

Fig. 3. Signal abnormalities in the splenium of the corpus callosum. Axial T2-weighted (*A*) and apparent diffusivity coefficient (*B*) images show subtle high T2 signal and reduced diffusion within the splenium of the corpus callosum (*arrows*). This reversible signal abnormality has been described both in the setting of recent seizure activity and in patients on certain antiepileptic medications with well-controlled seizures. The finding is not specific to seizures, however, and has also been described in infectious and inflammatory encephalitis.

POSTERIOR REVERSIBLE ENCEPHALOPATHY SYNDROME

Peri-ictal changes may overlap with the so-called posterior reversible encephalopathy syndrome (PRES), a controversial entity that may also be associated with seizures. Several conditions have been associated with this disorder, including hypertension, eclampsia, certain medications, infection, autoimmune diseases, hypercalcemia, hemolytic uremic syndrome, and renal failure.[36–38] Seizures in PRES clinically may initially show focal onset, though frequently generalize and often recur. The pathogenesis of PRES is poorly understood and controversial. One popular hypothesis is that the disorder results from loss of normal cerebral autoregulation with consequent hyperperfusion. Another suggests vasoconstriction with hypoperfusion, and yet another implicating endothelial cell dysfunction.

Following the brain watershed zones,[39] signal abnormalities in cases in PRES are most often bilateral and symmetric. As implied by the acronym, typical findings are reversible focal or patchy areas of T2/FLAIR hyperintensity in the subcortical white matter, especially within the parietal and occipital lobes. The imaging manifestations are broader than the moniker implies, however, and include irreversible cytotoxic injury, abnormalities in both gray and white matter, and involvement of not only the parietal and occipital lobes but also the frontal lobes, the inferior temporo-occipital junction, thalami and basal ganglia, brainstem, and cerebellum. Cross-sectional and catheter angiographic studies may show vasospasm, vasodilation, and/or beading. Hemorrhage occurs in 15% to 20% of cases. These less common imaging findings may be mistaken for other disorders such as infarct or tumor, especially when reduced diffusion, marked asymmetry, mass effect, and/or enhancement is present (**Fig. 4**).[39–41]

METABOLIC ABNORMALITIES

Because laboratory analysis in the emergency setting routinely includes a metabolic panel, metabolic derangements that lead to seizures are usually diagnosed clinically. Occasionally, however, imaging may provide the first clue as to the initial severity of a corrected metabolic abnormality, or alternatively may show findings related to a known metabolic abnormality that are mistaken for another process.

Metabolic derangements may occur spontaneously or may be precipitated by organ failure, diet, medications, hormonally active tumors, or systemic stress. Most of these abnormalities result in generalized seizures. The underlying physiologic mechanisms for seizure induction depend on the specific metabolite in question and its role in the brain. For example, because of its critical role in the regulation of water distribution and serum osmolarity, rapid changes in serum sodium can be associated with changes in brain volume that result in acute seizures. With hyponatremia, movement of water from the interstitial space into cells results in cellular swelling. When hyponatremia

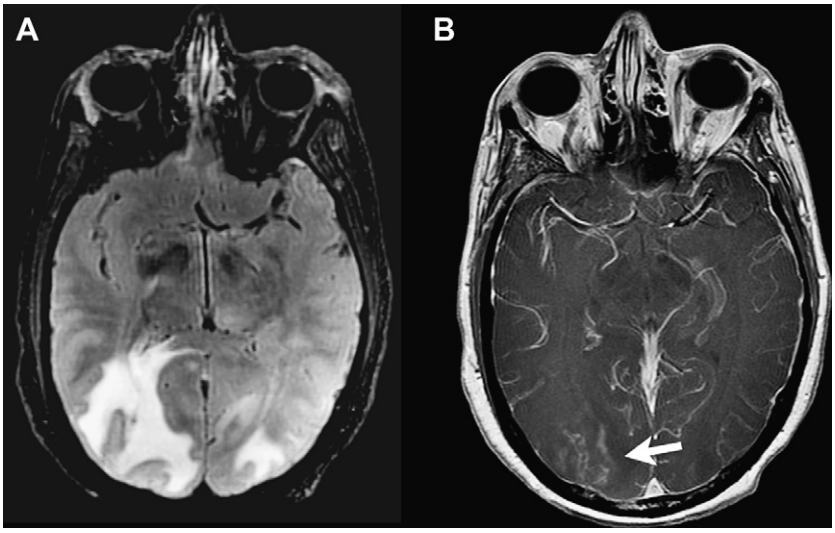

Fig. 4. Atypical PRES in a patient presenting with altered mental status and acute-onset seizures. Axial FLAIR image (*A*) shows hyperintensity within both occipital lobes. Note the asymmetric involvement and additional high signal intensity within the left thalamus. T1-weighted image obtained following administration of gadolinium contrast (*B*) shows patchy areas of enhancement (*arrow*), which can be observed in between 30% and 40% of cases.

develops slowly, this is typically compensated and does not result in cerebral edema, and as a result has no imaging correlate. However, in severe cases with rapid development of low serum sodium, this phenomenon results in an overall increase in brain volume and elevated intracranial pressure. However, as the changes in parenchymal volume observed with hyponatremic brain edema are usually mild, comparison with prior studies may provide the only clue that a change in brain volume has occurred. Subtlety notwithstanding, an assessment of overall brain parenchymal volume, ventricular size, and cisternal spaces should be included in all cases of acute seizures with low serum sodium (**Fig. 5**). Rapid correction of hyponatremia resulting in pontine or extrapontine myelinolysis may also cause seizures.

The most common cause of hypoglycemic seizures is overzealous use of parenteral or oral hypoglycemic treatments for diabetes mellitus, but low serum glucose can also be caused by other medications, hepatic failure, or insulin-secreting tumors. Imaging abnormalities related to hypoglycemia are uncommon, but have a relatively unique appearance on MR imaging. Within the first several days after a severe hypoglycemia episode, symmetric high T2 signal and reduced diffusion may appear within the corona radiata, corpus callosum, and internal capsules (**Fig. 6**).[42,43] Other cases may show high T2 signal within the hippocampi and cortical gray matter. Reduced diffusion can be reversible in many cases.[44,45] Involvement of the basal ganglia tends to appear in the days to weeks following the initial insult, and may portend a less favorable outcome.[43,46] The thalami and cerebellum are typically spared. The appearance and time course of hypoglycemic injury differ between adults and neonates; neonatal hypoglycemia results in extensive edema and infarcts that affect the parietal and occipital lobes most severely, reflecting regional hypoperfusion and cell-specific excitotoxic injury. As in adults, the most severe cases of hypoglycemia in neonates also show abnormalities within the basal ganglia.

Although rare as a presenting symptom of hyperglycemia, seizures may also occur with high serum glucose. It is speculated that elevated blood sugar lowers γ-aminobutyric acid levels, thus diminishing the seizure threshold.[47] Because ketosis and intracellular acidosis actually increase the seizure threshold,[48] seizures are more frequently seen in nonketotic hyperglycemia than in diabetic ketoacidosis. An interesting constellation of MR imaging findings that have been ascribed to hyperglycemia includes T1 hyperintensity, T2 hypointensity, and reduced diffusion within the putamen but sparing other structures. Involvement of the putamen in this case is hypothesized to reflect selective metabolic vulnerability of neurons within this structure, and subsequent deposition of tissue manganese and reactive astrocytosis and/or ischemic injury.[49,50] The clinical

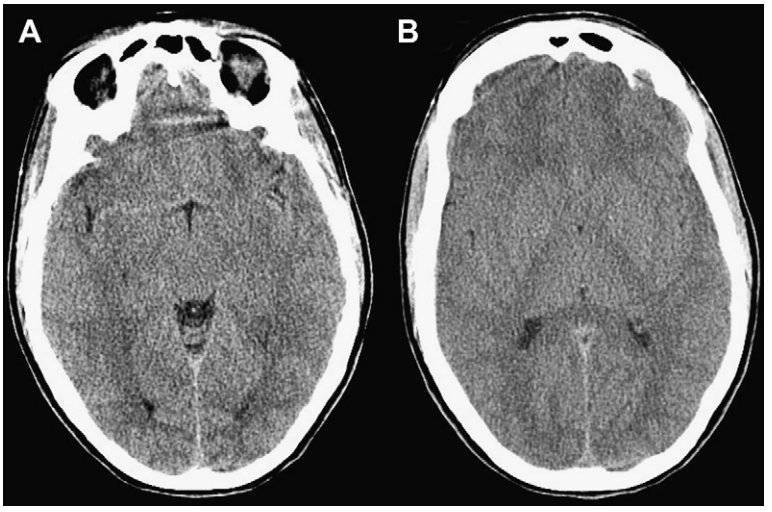

Fig. 5. **Hyponatremic cerebral edema.** Noncontrast axial CT images at the level of the midbrain (*A*) and thalami (*B*) in a marathon runner presenting with seizures and altered mental status. The patient consumed large quantities of water and was found to be hyponatremic (serum sodium 119). The images show poor visualization of sulci and effaced Sylvian fissures.

presentation in reported cases with these imaging findings is usually hemiballism rather than seizures, however.

STROKE

It is not uncommon that patients with acute seizures present with symptoms that can be confused clinically for acute infarcts. For example, in epileptic hemiplegia or so-called Todd paralysis, transient hemiparesis follows an episode of seizure activity. Especially in patients who also have postictal aphasia and sensory deficits, the disorder may masquerade as a dominant hemisphere middle cerebral artery infarct. Conventional CT and MR imaging are typically unrevealing in this clinical scenario, but may occasionally show subtle asymmetries in sulcal morphology (Fig. 7). Regional abnormal sulcal FLAIR hyperintensity has also been described. Postictal hypoperfusion and hyperfusion have been described on CT perfusion imaging, both distinguished from ischemia by their atypical vascular distribution and the absence of associated arterial occlusion

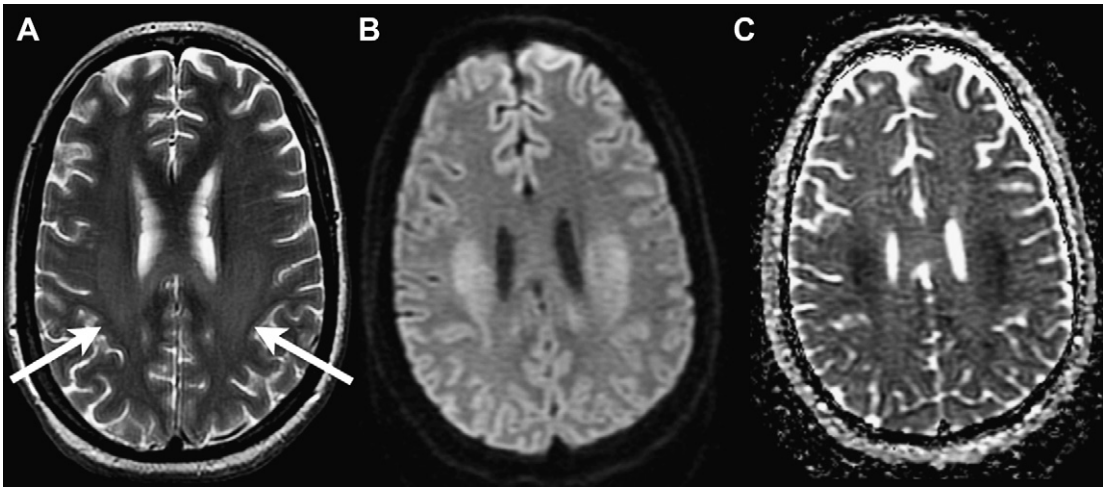

Fig. 6. **Hypoglycemic encephalopathy.** Axial T2-weighted (*A*), diffusion trace (*B*), and apparent diffusion (*C*) images obtained in a patient with hepatic abscess and severe hypoglycemic event. Note the subtle symmetric hyperintensity (*arrows*) on T2-weighted imaging (*A*) involving the posterior body of the corpus callosum and corona radiata with high signal on diffusion trace and reduced diffusion on apparent diffusion images.

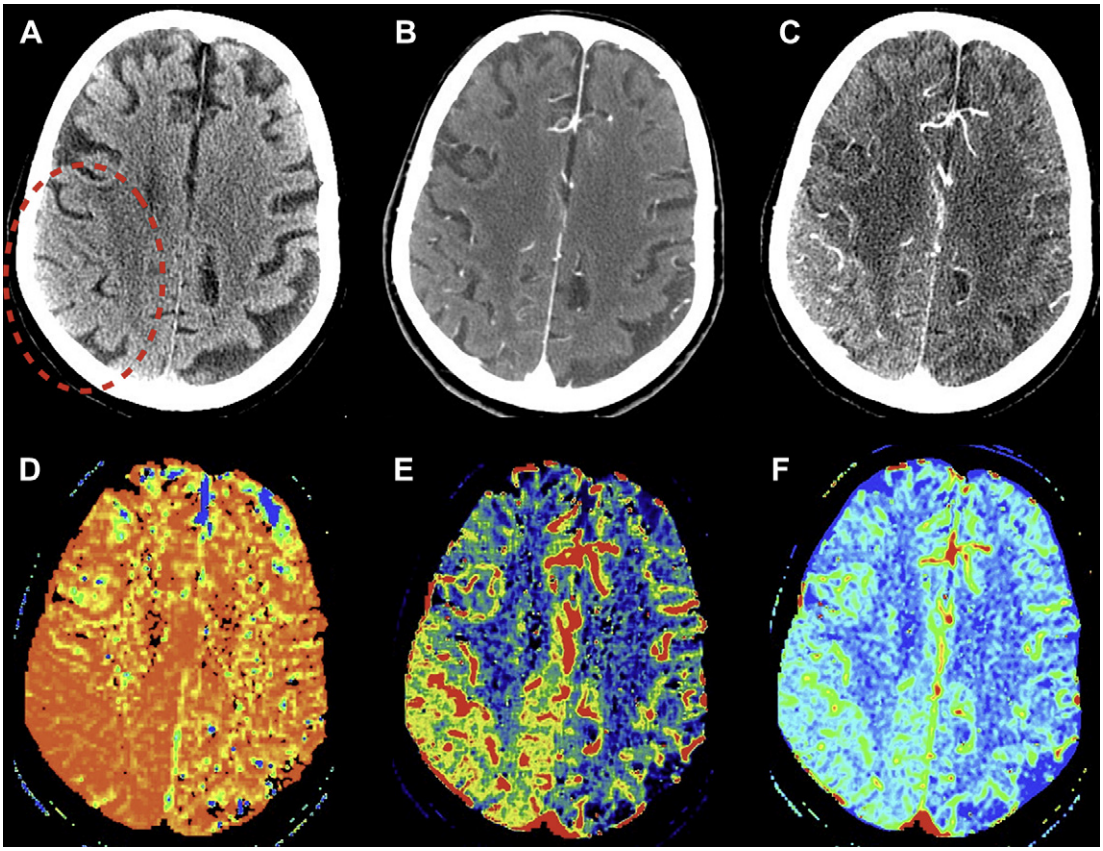

Fig. 7. Postictal Todd's paralysis. Noncontrast (*A*) and postcontrast (*B*) axial CT images at the level of the centrum semiovale show relative effacement of right parietal and posterior frontal sulci (*circle*) and subtle prominence of vessels in this region in a patient presenting with left hemiparesis. CT perfusion image (*C*) from at a single time point during bolus injection of contrast reveals hyperemia in the same region. Processed perfusion maps show reduced mean transit time (*D*), increased cerebral blood flow (*E*), and increased cerebral blood volume (*F*) relative to the remainder of the brain.

or narrowing on accompanying bolus CT angiography.[51–53] As is the case for other reversible postictal abnormalities on imaging, perfusion is less likely to be abnormal as the time between the cessation of seizures and imaging increases, during the usual period of clinical recovery from symptoms.

Although neonates with infarcts commonly present with seizures, seizures are rare as the initial presenting symptom of acute infarct in adults. However, the likelihood of seizures increases shortly after the onset of stroke symptoms, and in the days to years that follow. The multicenter Seizures After Stroke Study Group found an overall incidence of seizures of 8.9% following stroke, although only 2.5% of patients went on to develop epilepsy.[54] Because of the focal nature of most infarcts, postinfarct seizures commonly have a focal onset, although secondary generalization is common. In clinical terms, seizures after stroke are arbitrarily divided at a time point of 2 weeks into those of early or late onset.[55] Almost half of the patients with the early-onset subset of seizures have their first seizure within the first 24 hours after presenting with stroke, although few of these patients will ultimately develop chronic seizures. Late-onset seizures, by contrast, are less common overall, but are associated with a considerably higher incidence of epilepsy. Seizures in both cases are more likely to be associated with larger infarcts, with cortical as opposed to subcortical injury, and in cases where significant hemorrhage has occurred. Infarcts involving the hippocampus and posterior insula, and venous infarcts are also reported to be associated with a higher incidence of developing seizures.

Global anoxic injury is one of the most common causes for status epilepticus and recurrent seizures, especially following respiratory or cardiac arrest. Roughly one-third of patients will have seizures or myoclonus (uncontrolled muscle

contractions elicited by movement or sensory stimuli) after resuscitation. Imaging in this scenario may prove useful in documenting that significant injury has taken place. The spectrum of brain injury seen depends on both the partial pressure of blood oxygen and the degree to which normal cerebral autoregulation was disrupted. Pure hypoxic injury, in which adequate cerebral perfusion pressure is maintained but the oxygen concentration in the blood is either insufficient or inadequately extracted by tissue, selectively affects areas of the brain with the highest metabolism. Gray matter structures, particularly the globus pallidus, caudate nuclei, thalami, and dentate nuclei of the cerebellum, are more vulnerable to this type of injury than white matter. Typical causes for hypoxic injury include carbon monoxide poisoning, anemia, and primary lung disease such as severe pneumonia and acute respiratory distress syndrome. By contrast, ischemic injury, in which blood flow to the brain is reduced but blood oxygen concentration is preserved disproportionately, involves areas of the brain for which the blood supply is most tenuous. These "watershed" areas of the brain include both gray and white matter located at the boundary zones between primary arterial territories. The deep white matter, supplied by small-caliber, perfusion-pressure sensitive penetrating arteries, is a boundary zone that is particularly vulnerable to this type of injury. On imaging, hypoperfusion injury may show changes at the boundaries between major vascular territories or in the deep white matter, the latter frequently seen as an anteroposteriorly oriented "string of pearls" (**Fig. 8**). In the majority of cases, both hypoperfusion and hypoxic injury are present together. The extent of injury depends on the duration and magnitude of hypoxia and circulatory collapse. The most severe cases show diffuse cerebral swelling, poor gray-white differentiation, "pseudo-subarachnoid hemorrhage," and in the worst cases, reversal of normal gray and white matter signal.

AUTOIMMUNE AND PARANEOPLASTIC ENCEPHALITIS

In a patient with known systemic malignancy, the most common underlying cause for a first-time seizure includes metastasis and associated hemorrhage or mass effect. However, even in the absence of intracranial metastatic disease, patients with cancer remain at higher risk for developing seizures. During the course of chemotherapy, many antineoplastic agents and adjuvant medications, including alkylating agents, high-dose methotrexate, cytarabine, and ondansetron, are known to decrease the seizure threshold and may precipitate seizures. Certain malignancies have also been associated with immunologically mediated seizures.[56–58] The immune system in these cases mounts a cell-mediated response to remove tumor cells that express certain cell surface proteins. When these cells coincidentally also target normal, non-neoplastic neurons that express antigenically similar surface proteins, the brain may be the unanticipated target of the response. The regions of the brain affected in these disorders vary, and any region of the brain may be affected.[59] The limbic system, however, is most frequently affected.

Paraneoplastic limbic encephalitis (PLE) is characterized by the clinical triad of seizures, anterograde memory loss, and psychiatric symptoms (usually depression, psychosis, or personality changes). As with other autoimmune disorders, females are disproportionately affected. The most common tumors associated with PLE are small-cell lung carcinoma, testicular and ovarian cancer, thymoma, and breast cancer. Many patients exhibit symptoms in the face of a normal MRI. In others, unilateral or bilateral T2 signal abnormalities may be found within the mesial temporal lobes (**Fig. 9**). Atrophy of the same structures may be present in patients with long-standing disease. Because clinical symptoms of PLE usually precede the diagnosis of underlying cancer, whole-body FDG PET or CT may be indicated for the evaluation of patients with unexplained limbic signal abnormalities. Several autoantibody markers have been developed to assist in the diagnosis, though many of these are not widely available in the community and up to a third of patients with pathologically confirmed paraneoplastic encephalitis have negative antibody studies.

Clinical history and lumbar puncture may be necessary to differentiate PLE from infectious encephalitis, particularly herpes encephalitis, which also has a predilection for the limbic system and frequently present with seizures. Although the hippocampus, amygdala, insula, and sometimes the cingulate gyrus may be involved in both disorders, PLE tends to be more symmetric than herpes encephalitis in cases with bilateral temporal lobe involvement. Signal abnormalities also tend to be less dramatic in PLE than herpes encephalitis on MR imaging. Finally, although enhancement is present in up to 30% of cases,[60] hemorrhage and reduced diffusion, typical findings in herpes, have not been described in PLE. Other types of non-paraneoplastic autoimmune encephalitis, in particular that caused by antibodies to neuronal

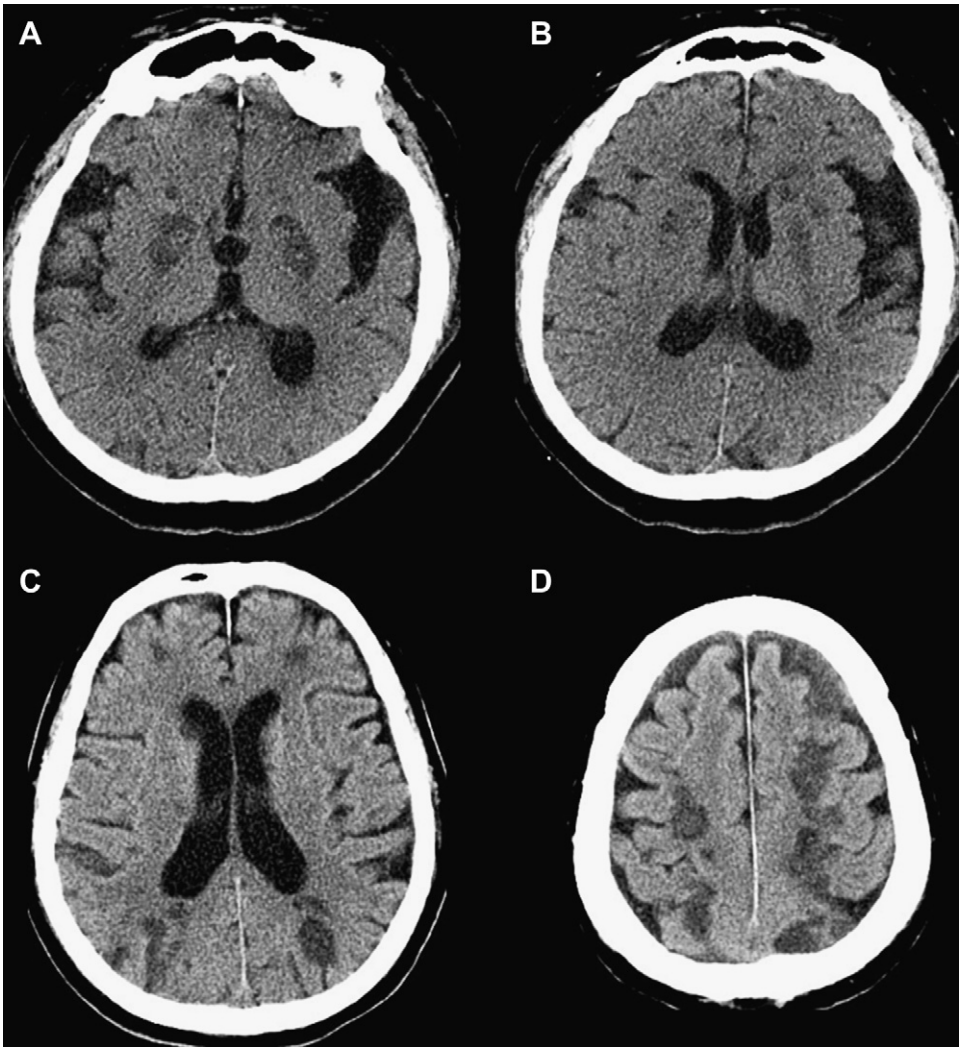

Fig. 8. Hypoxic and hypoperfusion injury. Noncontrast axial CT images (*A, B*) in a patient with respiratory arrest whose circulation was maintained by cardiopulmonary resuscitation show low density primarily confined to the globi pallidi and caudate nuclei, typical sites of hypoxic injury. In a different patient with cardiac arrest and ventricular fibrillation, low blood flow to the brain resulted in bilateral anterior cerebral artery/middle cerebral artery and middle cerebral artery/posterior cerebral artery watershed infarction on noncontrast CT (*C, D*).

voltage-gated potassium channels (VGKC antibodies), can also overlap clinically and radiologically with PLE. VGKC autoantibodies, however, are more likely to occur in males and are frequently associated with hyponatremia. Furthermore, the disorder is more frequently responsive to high-dose corticosteroids than PLE.

MALFORMATIONS OF CORTICAL DEVELOPMENT

Most malformations of cortical development (MCD) are identified in childhood when patients present with recurrent seizures together with developmental delay or congenital hemiparesis. However, the clinical phenotype of MCD is broad, and other patients have occult MCD that is found only incidentally or manifests later in life, when the seizure threshold is lowered for other reasons. Although a full discussion of the imaging appearance of MCD is beyond the scope of this article, it is important to recognize that CT may be the initial modality obtained when these patients present with a first-time seizure or when patients with otherwise quiescent MCD experience seizures. As a result, review of CT scans in patients with seizures should routinely include a careful inspection of the appearance of gray and white

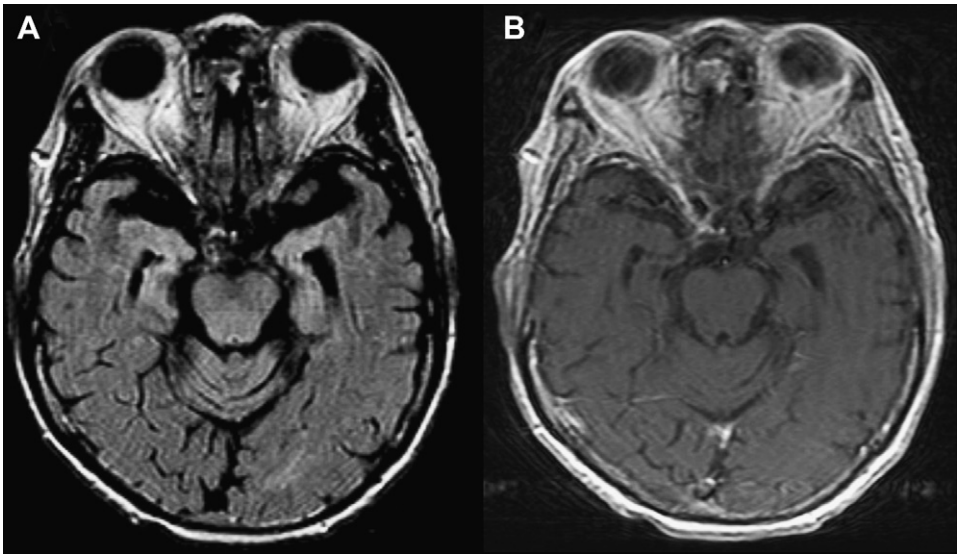

Fig. 9. **Paraneoplastic limbic encephalitis.** 67-year-old woman with a thymoma. Axial T2 FLAIR (*A*) and gadolinium-enhanced T1-weighted (*B*) images show symmetric high T2 signal and atrophy of the medial temporal lobes without enhancement.

matter, particularly along the cortical surface and the margins of the ventricular system. Subtle abnormalities in sulcation or gyral contour may provide the only clue on noncontrast CT that MCD may be present (**Fig. 10**). When seizures are attributed to systemic causes such as hypertension, alcohol withdrawal, or metabolic abnormality, these abnormalities may be easily overlooked. It is incumbent on the radiologist to remind referring physicians that MR imaging is more sensitive in detecting an underlying substrate for seizures, especially when recurrent, as CT misses significant abnormalities in more than 30% of affected patients.[61]

POSTTRAUMATIC EPILEPSY

Posttraumatic epilepsy (PTE) accounts for 4% of focal epilepsy, and is the leading cause of epilepsy with onset in young adulthood. Seizure onset may be shortly after injury or after a latent period of months or years. The disorder is classified clinically into early and late types, depending on the timing of initial seizure onset. Early posttraumatic seizures, which are further divided into immediate (within the first 24 hours) and delayed (within the first week) subtypes, are usually attributable to the direct effects of brain injury. Chronic PTE, by contrast, first occurs 1 week or later after TBI and often is associated with a developing meningocerebral cicatrix as the underlying epileptogenic substrate. Most early-onset seizures are of the generalized tonic-clonic type, whereas late PTE has a more variable clinical presentation. Although an initial early seizure does not correlate with the development of late recurrent seizures, patients with a single late seizure have between a 65% and 90% chance of progressing to recurrent seizures. Unfortunately, both early and late PTE are less likely to be controlled with medical therapy than other causes of chronic seizures.

First described by Jennet and Lewin[62] in a landmark study on military head injuries, several of the risk factors for the development of PTE have been enumerated.[63–65] Penetrating injury is associated with a higher risk of developing seizures (50% cumulative incidence) than nonpenetrating injury (30%). Other risk factors for PTE include depressed skull fracture, intracranial hematoma, prolonged unconsciousness, prolonged antegrade amnesia, and low Glasgow Coma Scale score. Other factors include genetic influences and age at the time of trauma; patients with ApoE4 and haptoglobin 2-2 alleles appear to be more vulnerable to developing epilepsy after trauma, and injuries later in life appear less likely to be associated with the development of PTE than childhood trauma.

Although direct injury to the hippocampus is rare after TBI, several surgical series implicate trauma, especially trauma during early childhood, as a significant risk factor for the development of MTS. In a series of 259 patients undergoing temporal lobectomy for treatment of medically refractory seizures, Mathern and colleagues[66] found that 10% had prior traumatic injury as the

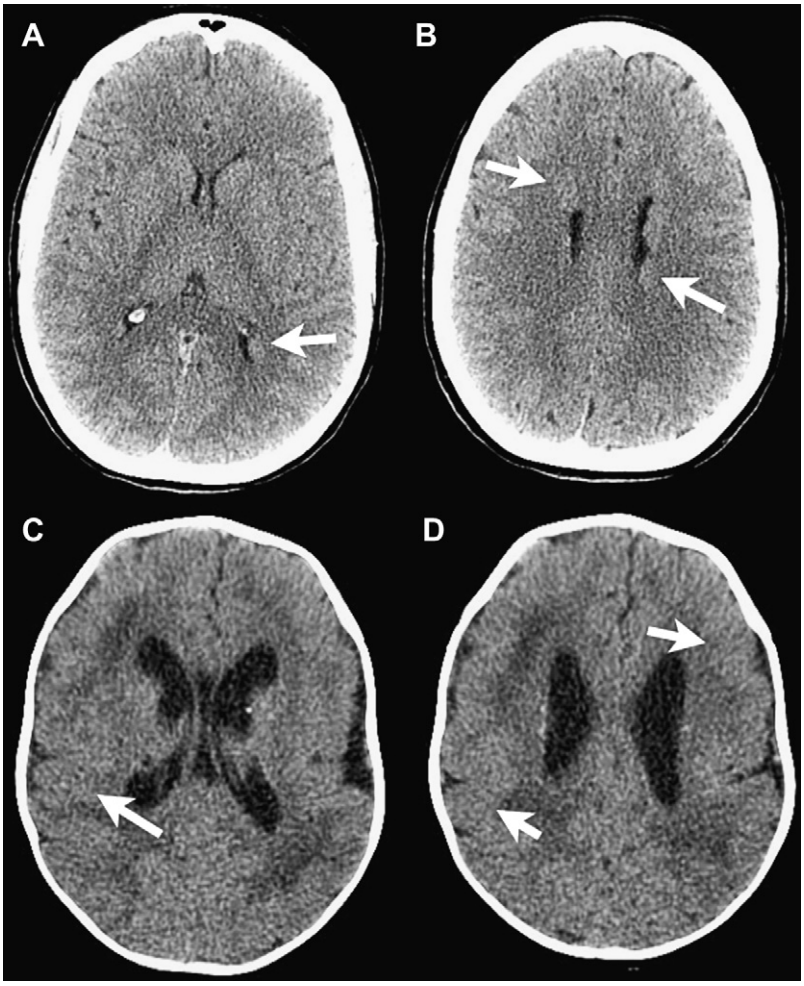

Fig. 10. Malformations of cortical development on unenhanced CT. Images from a postpartum woman (*A, B*) and an infant (*C, D*) presenting with first-time seizures. CT was performed in the first patient to evaluate for PRES, but showed multiple lesions (*arrows*) along the surface of both ventricles with the same density as cortical gray matter, consistent with periventricular nodular heterotopia. The second patient was initially thought to have venous sinus thrombosis clinically, but was later found to have thickened areas of cortex bilaterally (*arrows*) consistent with bilateral perisylvian polymicrogyria.

major risk factor, at a mean age of 6.3 years. Among this subgroup, 50% had hippocampal sclerosis on pathologic analysis of surgical specimens. A smaller series by Marks and colleagues[67] found that among 21 patients undergoing surgery for treatment of PTE, 6 patients with pathologically confirmed MTS had excellent outcomes, in contrast to 8 patients without MTS on pathology in whom seizures continued after surgery. There is a controversial relationship between the age at the time of TBI and MTS, with some investigators suggesting that MTS is more likely to develop in younger patients after TBI.

From an imaging standpoint, MTS is also one of the most common abnormalities observed in patients with PTE. Other imaging findings that have a reported association with seizures in this setting include hemorrhagic contusions and reactive astrogliosis (**Fig. 11**). Angeleri and colleagues[63] studied MR imaging scans from 104 patients with TBI 1 year following initial trauma to identify risk factors for PTE. In this cohort, a significant association was identified between cortical or subcortical T2 hyperintense lesions and development of PTE. It is interesting that hemosiderin deposition, by contrast, was not by itself associated with an increased risk of late seizures in this study. Other modalities may also be useful in assessing the risk of PTE following TBI. In a study of 143 patients with TBI, 27 of whom ultimately developed PTE after a mean follow-up of

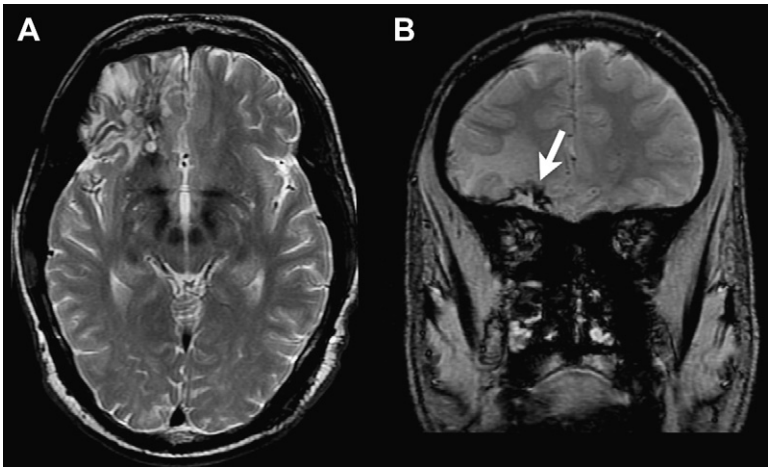

Fig. 11. Late-onset posttraumatic epilepsy. Axial T2 (*A*) and coronal T2*-weighted gradient echo (*B*) images in a patient who initially had traumatic injury resulting in hemorrhagic contusions and then developed medically refractory seizures several months later. Images show right frontal encephalomalacia with subcortical T2 hyperintensity and overlying hemosiderin staining (*arrow*). The patient was free of seizures after local resection.

11.9 months, Mazzini and colleagues[68] found that patients with temporal lobe hypoperfusion on ^{99m}Tc-hexamethylpropylene amine oxime single-photon emission CT (SPECT) developed PTE at a higher rate than patients with normal SPECT scans.

MESIAL TEMPORAL SCLEROSIS

A frequent cause of seizures after TBI, MTS is also the most common overall substrate for epilepsy with onset after childhood. Clinical presentation is heterogeneous, but most affected patients present during or after the adolescent period. Specific symptoms range from abnormal sensations to automatisms and autonomic nervous system dysfunction. All patients have partial seizures, though many ultimately develop secondary generalized tonic-clonic seizures. Partial seizures related to MTS are controlled by antiepileptic medications in most cases. However, approximately 25% of patients with MTS suffer from medically refractory seizures. Up to 80% of patients in this subgroup become seizure free following temporal lobectomy. MR imaging plays a critical role in the selection of patients for temporal lobectomy, with the highest postresection seizure-free rates occurring in patients with positive MR imaging and concordant EEG and clinical localization of seizure onset.

An understanding of normal hippocampal and surrounding temporal lobe anatomy is critical to the MR imaging diagnosis of MTS.[69,70] The 2 primary structures of interest in this regard are the hippocampus and amygdala, both found along the medial surface of the temporal lobe (**Fig. 12**). The amygdala, the smaller of the two structures, is an almond-shaped group of nuclei anterior to the hippocampus and immediately lateral to the uncus of the temporal lobe. The amygdala lies along the anterior and superior aspect of the temporal horn of the lateral ventricle and, as part of the limbic system, plays a role in the processing of memory and emotion. Other useful landmarks for localization are best seen on coronal images. The gyrus immediately below the hippocampus is the parahippocampal gyrus. As this gyrus wraps around the posterior aspect of the lateral ventricles, it is continuous with the cingulate gyrus, the gyrus immediately above the corpus callosum. Within the medial temporal lobe, the parahippocampal gyrus is separated from the more inferior fusiform gyrus by the collateral sulcus. This gyrus is lateral to the lateral temporal gyri (superior, middle, and inferior temporal gyri).

The hippocampal formation, responsible for the formation of new memories and spatial navigation, is a complex, 3-dimensional structure that is anatomically divided into 3 segments. From anterior to posterior, these are the head (or pes), body, and tail. (For reference, the red nuclei within the midbrain are located at the approximate level of the mid-hippocampal body.) The most anterior portion, the hippocampal head, lies posterior to the amygdala and exhibits undulating "digitations" along its superior surface that form a series of ridges along the floor of the anterior temporal horn. Posterior to the hippocampal pes, the body and tail of the hippocampus have a smooth superior contour along the inferomedial ventricular

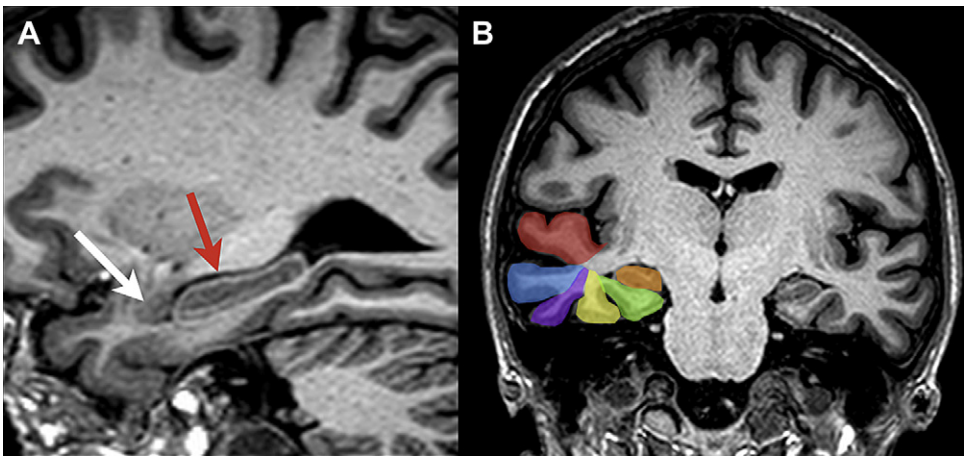

Fig. 12. Normal medial temporal lobe anatomy (Images from a volumetric gradient echo T1 sequence). Sagittal image (*A*) shows the normal hippocampus located along the floor of the temporal horn of the lateral ventricle (*red arrow*), as well as the amygdala along the anterosuperior surface of the temporal horn (*white arrow*). Coronal imaging (*B*) best shows the gyral anatomy of the temporal lobe. The superior temporal (*red*), middle temporal (*blue*), inferior temporal (*purple*), fusiform (*yellow*), and parahippocampal (*green*) gyri of the right temporal lobe are labeled. The body of the right hippocampus (*orange*) is located directly above the parahippocampal gyrus.

surface. On coronal images at the level of the hippocampal body and tail, the inner portion of the hippocampus, the dentate gyrus, is continuous with and encircled by the gray matter of the cornu Ammonis (Ammon's horn) (Fig. 13). Ammon's horn is comprised histologically of 4 sectors (CA1 through CA4), and continues medially and inferiorly along the medial surface of the temporal lobe as the subiculum, presubiculum, parasubiculum, and entorhinal cortex (the cortex of the parahippocampal gyrus). A vestigial sulcus, the hippocampal sulcus, separates the dentate gyrus superiorly from the CA1 sector of Ammon's horn and subiculum inferiorly. Tiny cystic foci of T2 hyperintensity are occasionally seen incidentally within this sulcus and have no association with seizures.

On high-resolution T2-weighted MR imaging, the normal hippocampus consistently exhibits a well-defined laminar architecture comprising concentric layers of gray and white matter. At a minimum, 3 layers should be seen. The

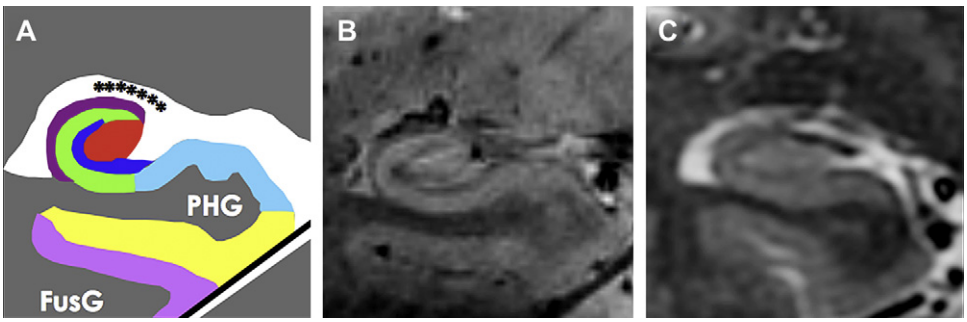

Fig. 13. Normal hippocampal anatomy. (*A*) Coronal schematic of the medial right temporal lobe at the level of the hippocampal body. The hippocampus at this level is appreciated as a curvilinear structure bordered by cerebrospinal fluid within the temporal horn laterally and the choroidal fissure superiorly (*asterisks*). Although the internal architecture of the hippocampus is better visualized at 7 T (*B*) than at 3 T (*C*), several layers can be discerned on both images. These layers include the dentate gyrus (*red*) and Ammon's horn (*green*), which are separated by several internal layers (*dark blue*). The superficial aspect of Ammon's horn is invested with a thin white matter layer called the alveus (*dark purple*). The gray matter of Ammon's horn is continuous with the subiculum (*light blue*), which continues around the medial surface of the temporal lobe as the entorhinal cortex (*yellow*); these comprise the cortex of the parahippocampal gyrus (PHG). The fusiform gyrus (FusG) lies below the PHG, separated by the collateral sulcus.

outermost white matter layer, the alveus, is darker on T2 than the adjacent dentate gyrus and cornu Ammonis, and appears isointense to white matter elsewhere in the brain. This outer layer extends along the subependymal surface of the inferomedial temporal horn, and continues posteriorly as the ipsilateral fornix. Deep to the alveus, the gray matter of the cornu Ammonis appears brighter on T2, with a similar signal to gray matter elsewhere in the brain. The innermost white matter layer between the dentate gyrus and Ammon's horn and subiculum consists of several internal hippocampal white matter layers with darker T2 signal. These layers, which consist primarily of the stratum radiatum, stratum lacunosum, and stratum moleculare, are not visualized separately on in vivo clinical 3-T MR imaging but together can be seen as a single layer of white matter on high-quality images.

Corresponding to the neuropathological abnormalities described on surgical specimens with confirmed mesial sclerosis,[71–73] several imaging features of MTS have been described on high-resolution T1-, T2-, and FLAIR images of the medial temporal lobes. The triad of (1) hippocampal atrophy, (2) loss of normal internal laminar architecture, and (3) high T2 signal intensity on MR imaging can be used to make this diagnosis. Thin-section T2-weighted images best demonstrate the derangement of the normal internal hippocampal architecture and may show asymmetric T2 hyperintensity (**Fig. 14**). FLAIR sequences are often more sensitive to subtle asymmetries in T2 signal and high resolution, however, and volumetric T1-weighted images may best show the degree of associated hippocampal atrophy. Atrophy of the hippocampus may also been seen as loss of the digitations of the hippocampal head and enlargement of the ipsilateral temporal horn and choroidal fissure. In addition to the characteristic T2 signal abnormality within the hippocampus, high T2 signal and atrophy may also be evident within the amygdala. Correlative pathology studies have shown that T2 signal in MTS is directly related to the presence of astrogliosis, whereas volume loss is a feature of hippocampal cell loss.

Secondary findings that have been described with hippocampal sclerosis mirror the propagation of seizures along ipsilateral networks that project from the medial temporal lobe. Like the hippocampus, the ipsilateral fornix may also appear atrophic, as may the ipsilateral mammillary body to which the fornix ultimately projects. Similarly, as a major hub for connections between the limbic system and the remainder of the cortex, the ipsilateral thalamus may appear atrophic. Ipsilateral atrophy of the entire temporal lobe has also been described as a feature of MTS, typically seen in more advanced cases. Unfortunately, there is considerable variability in volume of the fornices, mammillary bodies, and temporal lobes across the hemispheres, and these imaging findings are not useful for diagnosis in the absence of other features of MTS.

Although the finding of MTS increases the overall likelihood of surgical success, is important to critically assess MR imaging sequences for additional seizure substrates. Between 5% and 30% of cases of MTS are accompanied by "dual pathology," defined by the presence of a second extrahippocampal area of epileptogenic cortex.[74] Prospective identification of dual pathology is important for surgical planning and patient counseling, as it significantly lowers the success rate of temporal lobectomy, and in some cases may obviate surgery entirely. MCD, contusion, cavernous malformation, glial or glioneuronal tumor, or contralateral hippocampal sclerosis all

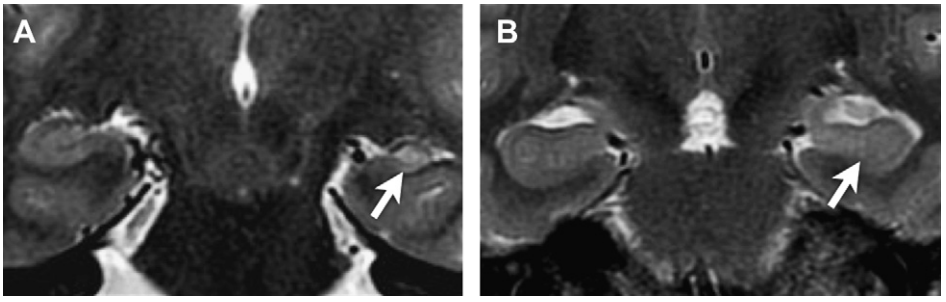

Fig. 14. Hippocampal sclerosis. High-resolution coronal T2-weighted images illustrate severe (*A*) and mild (*B*) findings of left MTS (*arrows*). In *A*, the sclerotic left hippocampus is tiny and shows abnormal T2 hyperintensity and poor visualization of internal layers. In *B*, mild volume loss is appreciated by asymmetric increase in size of the choroidal fissure and temporal horn, along with effacement of the normal internal architecture and mild increase in T2 signal.

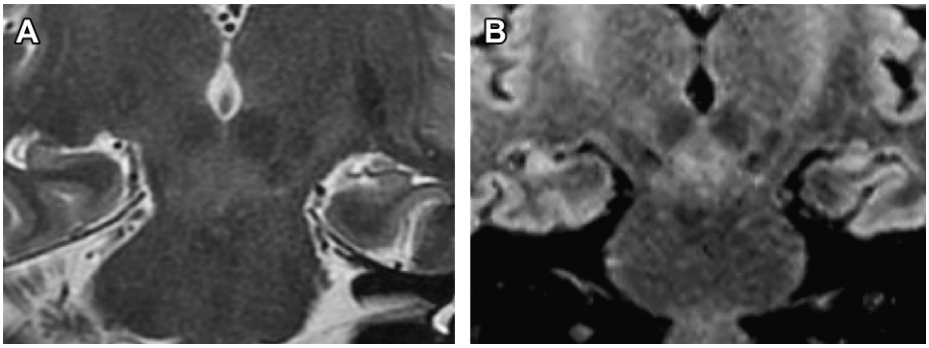

Fig. 15. Bilateral MTS. Coronal T2 (*A*) and FLAIR (*B*) images obtained in a woman presenting with chronic seizures after a prolonged episode of status epilepticus. Decreased volume and abnormal T2 hyperintensity of the hippocampus are more pronounced on the left, and only subtle derangement of the normal hippocampal laminar architecture is evident on the right.

represent important causes for dual pathology. Bilateral hippocampal sclerosis, also implicated as a cause for recurrent seizures after temporal lobectomy, may be overlooked because of the apparent visual symmetry between the sclerotic hippocampi (Fig. 15).

CT AND MR IMAGING FOR SEIZURES

As the clinical end point of a variety of acute and chronic neurologic insults, seizures are a common symptom that may or may not require imaging. When imaging is obtained in the acute setting, CT is useful to exclude that require emergent surgical intervention, and may in some cases suggest a cause for seizures. However, because CT may miss important sources of seizures and epilepsy, MR imaging remains the diagnostic modality of choice. For both CT and MR imaging, images should be interpreted together with the knowledge of the seizure type and onset, and in cases with partial onset, particular attention should be given to available clinical and EEG-localizing information. Even in patients presenting acutely with first-time seizures, it is important to exclude epileptogenic structural lesions such as mesial sclerosis, the most common cause for seizures after childhood and a frequent cause for seizures following TBI.

REFERENCES

1. Bronen RA, Fulbright RK, Kim JH, et al. A systematic approach for interpreting MR images of the seizure patient. AJR Am J Roentgenol 1997;169:241–7.
2. Duncan JS. Imaging and epilepsy. Brain 1997; 120(pt 2):339–77.
3. Bronen RA, Knowlton R, Garwood M, et al. High-resolution imaging in epilepsy. Epilepsia 2002;43(S1): 11–8.
4. Vattipally VR, Bronen RA. MR imaging of epilepsy: strategies for successful interpretation. Neuroimaging Clin N Am 2004;14(3):349–72.
5. Wieshmann UC. Clinical application of neuroimaging in epilepsy. J Neurol Neurosurg Psychiatry 2003;74(4):466–70.
6. Gupta V, Bronen RA. Epilepsy. In: Atlas SW, editor. Magnetic resonance imaging of the brain and spine. 4th edition. Philadelphia: Lippincott Williams & Wilkins; 2009. p. 307–42.
7. Kuzniecky RI, Jackson GD, editors. Magnetic resonance in epilepsy: neuroimaging techniques. 2nd edition. Burlington (MA): Elsevier Academic Press; 2004.
8. Duncan JS, editor. Epilepsy. Neuroimag Clin N Am 2004;14(3).
9. Berg AT, Berkovic SF, Brodie MJ, et al. Revised terminology and concepts for organization of seizures and epilepsies: report of the ILAE Commission on Classification and Terminology, 2005–2009. Epilepsia 2010;51(4):676–85.
10. American College of Emergency Physicians, American Academy of Neurology, American Association of Neurological Surgeons, et al. Practice parameter: neuroimaging in the emergency patient presenting with seizure (summary statement). Ann Emerg Med 1996;28(1):114–8.
11. Karis JP, Seidenwurm DJ, Davis PC, et al. Expert panel on neurologic imaging Epilepsy. [online publication]. Reston (VA): American College of Radiology (ACR); 2006.
12. Hauser WA, Annegers JF, Kurland LT. Incidence of epilepsy and unprovoked seizures in Rochester, Minnesota: 1935-1984. Epilepsia 1993;34(3): 453–68.
13. Brenner DJ, Hall EJ. Computed tomography—an increasing source of radiation exposure. N Engl J Med 2007;357(22):2277–84.
14. Practice parameter: the neurodiagnostic evaluation of the child with a first simple febrile seizure.

American Academy of Pediatrics. Provisional Committee on Quality Improvement, Subcommittee on Febrile Seizures. Pediatrics 1996;97(5):769–72.
15. Briellmann RS, Pell GS, Wellard RM, et al. MR imaging of epilepsy: state of the art at 1.5 T and potential of 3 T. Epileptic Disord 2003;5(1):3–20.
16. Phal PM, Usmanov A, Nesbit GM, et al. Qualitative comparison of 3-T and 1.5-T MRI in the evaluation of epilepsy. AJR Am J Roentgenol 2008;191(3): 890–5.
17. Von Oertzen J, Urbach H, Jungbluth S, et al. Standard magnetic resonance imaging is inadequate for patients with refractory focal epilepsy. J Neurol Neurosurg Psychiatry 2002;73(6):643–7.
18. Barkovich AJ, Rowley HA, Andermann F. MR in partial epilepsy: value of high-resolution volumetric techniques. AJNR Am J Neuroradiol 1995;16(2): 339–43.
19. Grant PE, Barkovich AJ, Wald LL, et al. High-resolution surface-coil MR of cortical lesions in medically refractory epilepsy: a prospective study. AJNR Am J Neuroradiol 1997;18(2):291–301.
20. Knake S, Triantafyllou C, Wald LL, et al. 3T phased array MRI improves the presurgical evaluation in focal epilepsies: a prospective study. Neurology 2005;65(7):1026–31.
21. Yaffe K, Ferriero D, Barkovich AJ, et al. Reversible MRI abnormalities following seizures. Neurology 1995;45:104–8.
22. Chan S, Chin SS, Kartha K, et al. Reversible signal abnormalities in the hippocampus and neocortex after prolonged seizures. AJNR Am J Neuroradiol 1996;17:1725–31.
23. Silverstein AM, Alexander JA. Acute postictal cerebral imaging. AJNR Am J Neuroradiol 1998;19: 1485–8.
24. Briellmann RS, Wellard RM, Jackson GD. Seizure-associated abnormalities in epilepsy: evidence from MR imaging. Epilepsia 2005;46:760–6.
25. Huang YC, Weng HH, Tsai YT, et al. Periictal magnetic resonance imaging in status epilepticus. Epilepsy Res 2009;86(1):72–81.
26. Goyal MK, Sinha S, Ravishankar S, et al. Peri-ictal signal changes in seven patients with status epilepticus: interesting MRI observations. Neuroradiology 2009;51:151–61.
27. Cole AJ. Status epilepticus and periictal imaging. Epilepsia 2004;45(Suppl 4):72–7.
28. Hicdonmez T, Utku U, Turgut N, et al. Reversible postictal MRI change mimicking structural lesion. Clin Neurol Neurosurg 2003;105(4):288–90.
29. Finn MA, Blumenthal DT, Salzman KL, et al. Transient postictal MRI changes in patients with brain tumors may mimic disease progression. Surg Neurol 2007; 67(3):246–50.
30. Kim JA, Chung JI, Yoon PH, et al. Transient MR signal changes in patients with generalized tonic-clonic seizure or status epilepticus: peri-ictal diffusion-weighted imaging. AJNR Am J Neuroradiol 2001;22:1149–60.
31. Moritani T, Smoker WRK, Sato Y, et al. Diffusion-weighted imaging of acute excitotoxic brain injury. AJNR Am J Neuroradiol 2005;26:216–28.
32. Katramados AM, Burdette D, Patel SC, et al. Peri-ictal diffusion abnormalities of the thalamus in partial status epilepticus. Epilepsia 2009;50(2): 265–75.
33. Kim SS, Chang KH, Kim ST, et al. Focal lesion in the splenium of the corpus callosum in epileptic patients: antiepileptic drug toxicity? AJNR Am J Neuroradiol 1999;20:125–9.
34. Polster T, Hoppe M, Ebner A. Transient lesion in the splenium of the corpus callosum: three further cases in epileptic patients and a pathophysiological hypothesis. J Neurol Neurosurg Psychiatry 2001; 70:459–63.
35. Oster J, Doherty C, Grant PE, et al. Diffusion-weighted imaging abnormalities in the splenium after seizures. Epilepsia 2003;44(6):1–3.
36. Hinchey J, Chaves C, Appignani B, et al. A reversible posterior leukoencephalopathy syndrome. N Engl J Med 1996;334:494–500.
37. Casey SO, Sampaio RC, Michel E, et al. Posterior reversible encephalopathy syndrome: Utility of fluid-attenuated inversion recovery MR imaging in the detection of cortical and subcortical lesions. AJNR Am J Neuroradiol 2000;21:1199–206.
38. Lee VH, Wijdicks EF, Manno EM, et al. Clinical spectrum of reversible posterior leukoencephalopathy syndrome. Arch Neurol 2008;65(2):205–10.
39. Covarrubias DJ, Luetmer PH, Campeau NG. Posterior reversible encephalopathy syndrome: prognostic utility of quantitative diffusion-weighted MR images. AJNR Am J Neuroradiol 2002;23(6): 1038–48.
40. Bartynski WS, Boardman JF. Distinct imaging patterns and lesion distribution in posterior reversible encephalopathy syndrome. AJNR Am J Neuroradiol 2007;28(7):1320–7.
41. McKinney AM, Short J, Truwit CL, et al. Posterior reversible encephalopathy syndrome: incidence of atypical regions of involvement and imaging findings. AJR Am J Roentgenol 2007;189:904.
42. Hasegawa Y, Formato JE, Latour LL, et al. Severe transient hypoglycemia causes reversible change in the apparent diffusion coefficient of water. Stroke 1996;27:1648–55.
43. Fujioka M, Okuchi K, Hiramatsu KI, et al. Specific changes in human brain after hypoglycemic injury. Stroke 1997;28:584–7.
44. Finelli PF. Diffusion-weighted MR in hypoglycemic coma. Neurology 2001;57:933–5.
45. Bottcher J, Kunze A, Kurrat C, et al. Localized reversible reduction of apparent diffusion coefficient

in transient hypoglycemia-induced hemiparesis. Stroke 2005;36:20–2.
46. Maekawa S, Aibiki M, Kikuchi K, et al. Time-related changes in reversible MRI findings after prolonged hypoglycemia. Clin Neurol Neurosurg 2006;108: 511–3.
47. Hennis A, Corbin D, Fraser H. Focal seizures and non-ketotic hyperglycaemia. J Neurol Neurosurg Psychiatry 1992;55:195–7.
48. Singh BM, Strobos RJ. Epilepsia partialis continua associated with nonketotic hyperglycemia: clinical and biochemical profile of 21 patients. Ann Neurol 1980;8:155–60.
49. Shan DE, Ho DM, Chang C, et al. Hemichorea-hemiballism: an explanation for MR signal changes. AJNR Am J Neuroradiol 1998;19:863–70.
50. Wintermark M, Fischbein NJ, Mukherjee P, et al. Unilateral putaminal CT, MR, and diffusion abnormalities secondary to nonketotic hyperglycemia in the setting of acute neurologic symptoms mimicking stroke. AJNR Am J Neuroradiol 2004; 25(6):975–6.
51. Mathews MS, Smith WS, Wintermark M, et al. Local cortical hypoperfusion imaged with CT perfusion during postictal Todd's paresis. Neuroradiology 2008;50(5):397–401.
52. Royter V, Paletz L, Waters MF. Stroke vs. status epilepticus: a case report utilizing CT perfusion. J Neurol Sci 2008;266:174–7.
53. Gelfand JM, Wintermark M, Josephson SA. Cerebral perfusion-CT patterns following seizure. Eur J Neurol 2010;17(4):594–601.
54. Bladin C, Alexandrov A, Bellavance A, et al. Seizures after stroke: a prospective multicenter study. Arch Neurol 2000;57:1617–22.
55. Silverman IE, Restrepo L, Mathews GC. Poststroke seizures. Arch Neurol 2002 Feb;59(2):195–201.
56. Gultekin SH, Rosenfeld MR, Voltz R, et al. Paraneoplastic limbic encephalitis: neurological symptoms, immunological findings and tumour association in 50 patients. Brain 2000;123(Pt 7):1481–94.
57. Ances BM, Vitaliani R, Taylor RA, et al. Treatment-responsive limbic encephalitis identified by neuropil antibodies: MRI and PET correlates. Brain 2005; 128(8):1764–77.
58. Vernino S, Geschwind M, Boeve B. Autoimmune encephalopathies. Neurologist 2007;13(3):140–7.
59. McKeon A, Ahlskog JE, Britton JA, et al. Reversible extralimbic paraneoplastic encephalopathies with large abnormalities on magnetic resonance images. Arch Neurol 2009;66(2):268–71.
60. Bien CG, Urbach H, Schramm J, et al. Limbic encephalitis as a precipitating event in adult-onset temporal lobe epilepsy. Neurology 2007;69:1236–44.
61. Raymond AA, Fish DR, Sisodaya SM, et al. Abnormalities of gyration, heterotopias, tuberous sclerosis, focal cortical dysplasia, microdysgenesis, dysembryoplastic neuroepithelial tumour and dysgenesis of the archicortex in epilepsy. Clinical, EEG and neuroimaging features in 100 adult patients. Brain 1995;118:629–60.
62. Jennett WB, Lewin W. Traumatic epilepsy after closed head injuries. J Neurol Neurosurg Psychiatry 1960;23:295–301.
63. Angeleri F, Majkowski J, Cacchib G, et al. Posttraumatic epilepsy risk factors: one-year prospective study after head injury. Epilepsia 1999;40(9): 1222–30.
64. Diaz-Arrastia R, Agostini MA, Frol AB, et al. Neurophysiologic and neuroradiologic features of intractable epilepsy after traumatic brain injury in adults. Arch Neurol 2000;57(11):1611–6.
65. Messori A, Polonara G, Carle F, et al. Predicting posttraumatic epilepsy with MRI: prospective longitudinal morphologic study in adults. Epilepsia 2005;46(9):1472–81.
66. Mathern GW, Babb TL, Vickrey BG, et al. Traumatic compared to non-traumatic clinical-pathologic associations in temporal lobe epilepsy. Epilepsy Res 1994;19:129–13927.
67. Marks DA, Kim J, Spencer DD, et al. Seizure localization and pathology following head injury in patients with uncontrolled epilepsy. Neurology 1995;45:2051–7.
68. Mazzini L, Cossa FM, Angelino E, et al. Posttraumatic epilepsy: neuroradiologic and neuropsychological assessment of long-term outcome. Epilepsia 2003;44(4):569–74.
69. Naidich TP, Daniels DL, Haughton VM, et al. Hippocampal formation and related structures of the limbic lobe: anatomic-MR correlation. Part I. Surface features and coronal sections. Radiology 1987;162(3): 747–54.
70. Naidich TP, Daniels DL, Haughton VM, et al. Hippocampal formation and related structures of the limbic lobe: anatomic-MR correlation. Part II. Sagittal sections. Radiology 1987;162(3):755–61.
71. Jackson GD, Berkovic SF, Tree BM, et al. Hippocampal sclerosis can be reliably detected by magnetic resonance imaging. Neurology 1990;40: 1869–75.
72. Meiners LC, van Gils A, Jansen GH, et al. Temporal lobe epilepsy: the various MR appearances of histologically proven mesial temporal sclerosis. AJNR Am J Neuroradiol 1994;15(8):1547–55.
73. Lee DH, Gao FQ, Rogers JM, et al. MR in temporal lobe epilepsy: analysis with pathologic confirmation. AJNR Am J Neuroradiol 1998;19(1): 19–27.
74. Li LM, Cendes F, Andermann F, et al. Surgical outcome in patients with epilepsy and dual pathology. Brain 1999;122:799–805.