Epilepsy and Neuroimaging

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Introduction

The radiologist plays a major role in the management of patients presenting with seizures as he has to locate and define anatomic epileptogenic lesions. These findings can influence the therapeutic decision making as to whether a surgical intervention may be indicated. Moreover, modern neuroimaging methods advance our understanding of epilepsy and are therefore paramount to evaluate causes, consequences and mechanisms responsible for epilepsy.

In this chapter we will review the different imaging methods as well as the imaging features of the most common epileptogenic lesions encountered in clinical practice.

Epilepsy

Seizures are the result of excessive and abnormal electrical discharges from the cortical neurons. Epilepsy, the condition of spontaneously recurring seizures, is quite common, affecting approximately 0.4-1% of the population. Epilepsy syndromes can be categorized into localized, partial, and generalized. Partial seizures are generated from a localized area of the brain. These can be further divided into complex partial, with loss of consciousness, and simple partial, without loss of consciousness. Partial seizures can secondarily generalize by spread from one area to another. Seizure classification has therapeutic and prognostic values that help in the care of patients with epilepsy.

The condition of epilepsy is potentially psychosocially devastating. With its associated increased incidence of sudden death, traumatic injury, and suicide, it is even a life-threatening disorder. Whereas many advances have been made in the medical therapy of epilepsy, many cases, between 15% and 30%, remain medically intractable. Medically intractable epilepsy is a social, economic, and medical burden to both the individual and the general community. Surgical therapies are appropriate for certain patients and include lesional resections, temporal lobectomies, selective amygdalohippocampectomies, callosotomies, hemispherectomies, subpial transections, and implantation of the NeuroPace Responsive Neurostimulation (RNS)©, or vagal-nerve and/or deep-brain-stimulating devices. Candidates for epilepsy surgery undergo an extensive preoperative evaluation, including surface electroencephalogram (EEG) and video EEG monitoring, neuropsychological testing, and imaging. With the increasing use of surgical management, the role of neuroimaging has increased in importance. The main purpose of neuroimaging in epileptic patients is to identify underlying structural abnormalities that require specific treatment (usually surgery) and also to aid in formulating a syndromic or etiologic diagnosis.

Multiplanar magnetic resonance imaging (MRI), particularly when performed at high field strengths (e.g., 3T) or with phased-array coils, is the primary imaging modality for this purpose, as it provides excellent spatial resolution and soft tissue contrast. These examinations may be complemented by MR perfusion imaging, MR spectroscopy (MRS), magnetization transfer imaging, functional MRI (fMRI), diffusion tensor imaging (DTI), and tractography and magnetoencephalography (MEG).

Multislice continuous arterial spin-labeled perfusion MRI has also been used to study patients with temporal lobe epilepsy. In preliminary work, Wolf et al. found interictal asymmetries in perfusion of the medial temporal lobes in these patients. The authors also reported a trend toward correlation between the magnitude of perfusional asymmetry and seizure-free outcome of surgery.

Proton MRS provides metabolic information by determining the presence and levels of select neurochemicals. In patients with suspected mesial temporal sclerosis, small regions of interest, voxels, are placed over the medial temporal lobes in these patients. The authors also reported a trend toward correlation between the magnitude of perfusional asymmetry and seizure-free outcome of surgery.

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Apparent diffusion coefficient (ADC) maps and DTI can identify abnormal diffusion at the epileptogenic foci in normal-appearing standard MRI studies. Diffusion tensor tractography can aid in depicting the relationships of epileptogenic foci and key white matter tracts. Abnormal magnetization transfer ratios in epilepsy patients with negative conventional MRI may also detect and delineate the extent of occult malformations of cortical development.

MEG is based on the principle that all electrical currents are associated with magnetic fields. Cohen developed a superconducting quantum interference device to measure magnetic fields generated by intracranial currents. Approximately 10,000-100,000 neurons must be simultaneously generating current to produce a magnetic field strong enough to be detected with present technology. Magnetic fields are minimally distorted by intervening tissue, and hence MEG may provide precise localization of the source of electrical current (e.g., seizure foci or functional cortex). Data can then be coregistered with conventional MRI.

In patients with medically refractory epilepsy, the sensitivity of MR in identifying epileptogenic substrates has been reported as being between 82% and 86%. In patients with idiopathic generalized epilepsy, however, MRI has not been shown to be useful. The major utility of computed tomography (CT) scanning is in the initial imaging modality for evaluating seizures, particularly in a trauma or emergent setting or when associated with focal neurologic signs or fever.

In surgical candidates, MRI plays a crucial role not only in identifying the anatomic location of a substrate but also in demonstrating the relationship of the lesion to the eloquent regions of the brain. Correlation and concordance of MRI-identified substrate with clinical and electrophysiologic findings is essential to avoid false positive localization of the epileptogenic substrate. In some instances, when MR findings and noninvasive electrophysiologic data are concordant, invasive EEG evaluation can be avoided.

The diagnostic potential of MRI depends on the population being imaged. Published guidelines indicate that nonemergent MRI should always be performed in patients with epilepsy, with the exception of primary idiopathic generalized epilepsy. Patients with febrile seizures and those with primary idiopathic generalized epilepsy do not routinely require imaging unless there are complicating factors. One should also keep in mind that the sensitivity of MR is high for patients with intractable partial epilepsy and relatively low for those with new onset of seizures. Additionally, common causes of seizure disorders in the neonate (anoxia, infarction, infection, metabolic disorders) and the elderly (metastatic disease, cerebral ischemia) differ significantly from those entities typically producing seizures in young and middle-aged adults (hippocampal sclerosis, malformations of cortical development, gliosis). As such, imaging protocols must be tailored to the population being studied, with gadolinium-enhanced sequences being of greater utility in adults with new-onset seizures and with higher resolution and coronal imaging being of greater value in patients with longer-standing, medically intractable epilepsy. MRI can also prognosticate the postoperative seizure control of epileptogenic substrates. Postoperative seizure control depends on identifying the substrate by MRI and the characteristics of the MR abnormality. Lastly, in the postoperative setting, MRI can identify surgical complications as well as causes for failure of surgical treatment, such as recurrent or residual lesion.

Imaging evaluation of the surgical candidate also frequently includes positron emission tomography (PET), ictal single-photon-emission CT (SPECT) [or computer-aided subtraction ictal SPECT coregistered to MRI (SISCOM), and, in some cases, angiography.

Nuclear medicine studies, PET and SPECT, provide physiologic information about the epileptogenic brain. PET studies use the radioisotope fludeoxyglucose [18F]-FDG to measure glucose metabolism in neurons. Intercitially, the temporal lobe ipsilateral to the seizure focus is hypometabolic. The sensitivity of FDG-PET for identifying the abnormal temporal lobe in patients with partial epilepsy has been reported to be 70-91%. The sensitivity of this study for localizing the seizure focus is reduced in extratemporal epilepsy, however. SPECT is performed with the radiotracer technetium-99m hexamethyl propyleneamine oxime (Tc99m HMPAO), which is distributed in the brain in proportion to regional blood flow. Intercially, SPECT sensitivity is much lower than that of PET. However, when the isotope is injected during a seizure, increased blood flow typically results in increased uptake of the radiotracer, and sensitivity of the study for lateralizing the seizure focus has been reported to exceed 95%; however, it may be technically difficult to obtain an injection during seizure and requires dedicated resources in terms of audiovisual EEG monitoring and personnel to obtain such high sensitivity. Researchers from the Mayo Clinic reported that SISCOM improves the sensitivity and specificity of SPECT in localization of seizure foci and that concordance between SISCOM localization and surgery site is predictive of postoperative improvement in seizure outcome.

Many candidates for epilepsy surgery undergo preoperative Wada testing (cerebral angiography and intracarotid injections of amobarbital followed by neuropsychological testing) in an effort to lateralize memory and language function and thereby minimize postoperative deficits. However, noninvasive tests have increasingly been used to replace the Wada test in the presurgical evaluation of patients with intractable epilepsy. A review of practices in European centers revealed a decrease in performance of the Wada test in presurgical patients from 56% in 2000 to 35% in 2005. In one US center, only 14.4% of patients scheduled for temporal lobectomy in 2007 underwent Wada testing, as opposed to 81% in 1997. Functional MRI has the advantages of being less time consuming (typically requiring 30-60 min), of posing minimal risk to the patient, and of being significantly less effective in identifying the eloquent cortex.