Seizures and Epilepsy: Structural Brain Imaging in Chronic Epilepsies

Contributor and Editor:
Thomas R. Henry, MD
Professor of Neurology, Director, Comprehensive Epilepsy Center, University of Minnesota Medical School, Minneapolis, MN

Contributor:
Alexander M. McKinney, IV, MD
Associate Professor of Radiology, University of Minnesota Medical School, Minneapolis, MN

Table of Contents

Introduction ........................................1
Anatomical Basis of the Analysis of Seizures and Epilepsy ..................1
Anatomical Pathology in Seizures and Epilepsy ..............................2
Structural Imaging Findings Interictally in Evaluation of Chronic Epilepsy ............5
Board Review Questions .........................25
References .......................................25
INTRODUCTION

Structural brain imaging is essential in the diagnosis of seizures and epilepsy, and is complementary to laboratory diagnosis with electroencephalography (EEG). Magnetic resonance imaging (MRI) is the technique of choice for initial epilepsy diagnosis and for epilepsy re-evaluations, including planning of epilepsy surgery. When exposure to high-frequency magnetic flux is contraindicated by the presence of a cardiac pacemaker or for other reasons, brain X-ray computed tomography (CT) substitutes for MRI. While brain CT has lower spatial resolution and more limited tissue contrast than MRI, CT scanners are less expensive and more widely available. The physics of magnetic resonance (MR) signals and the technology of image acquisition and reconstruction are complex disciplines that are critical to high-quality imaging; fortunately, they are practiced by experts with whom epileptologists collaborate on a daily basis. Epileptologists who participate in clinical imaging research would benefit by greater knowledge of the physics and technology of MR imaging, which has been reviewed in several books.1–5 This article briefly reviews the cerebral anatomy and the anatomical pathology that determine imaging abnormalities in patients with seizures and epilepsy, and provides a more detailed review of structural imaging abnormalities in chronic epilepsies. (See Table 1 for a list of radiology and diagnostic imaging terms used throughout this article.)

ANATOMICAL BASIS OF THE ANALYSIS OF SEIZURES AND EPILEPSY

Clinical imaging is used to create anatomical maps of brain structure and function. Used only for specialized applications, these images most often are displayed tomographically as surface-rendered cortical maps. Seizure semiology of neocortical epileptic syndromes is defined by the initial ictal signs and symptoms, which are conceptualized with regard to cortical surface anatomy (Figure 1). Cortical surface anatomy is visible at craniotomy, and functional mapping with direct cortical electrical stimulation is performed on the cortical surface. Human brain atlases display brain slices parallel to or perpendicular to the
Structural Brain Imaging in Chronic Epilepsies

anterior-posterior commissure (AC-PC) line, which connects the centers of the anterior commissure and posterior commissure on the midline sagittal slice line. When the patient’s head is positioned asymmetrically in the scanner or the MRI technologist has intentionally acquired images off the AC-PC line, the patient’s MRI tomographic slices will deviate from the standard atlases. Clinicians must be able to mentally translate cortical surface anatomy (Figure 1), which is most commonly used to define functional areas, into tomographic correlates. Deep gray matter structures of complex morphology are particularly difficult to mentally visualize for tomographic correlation. For example, the hippocampus is a complex structure in surface representation and internal anatomy. Most epileptologists recognize coronal sections of the body of the hippocampus on brain MRI (Figure 2), although epileptogenic lesions can be located in the morphologically more complex head of the hippocampus. Human brain anatomy has been reviewed in several books that specifically address the anatomical substrates of the epilepsies.

Table 1. Radiology and Diagnostic Imaging Terms

<table>
<thead>
<tr>
<th>Term</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>AC-PC</td>
<td>anterior-posterior commissure</td>
</tr>
<tr>
<td>ADC</td>
<td>apparent diffusion coefficient</td>
</tr>
<tr>
<td>DWI</td>
<td>diffusion-weighted imaging</td>
</tr>
<tr>
<td>FDG-PET</td>
<td>18F-fluorodeoxyglucose positron emission tomography</td>
</tr>
<tr>
<td>FLAIR</td>
<td>fluid-attenuated inversion recovery</td>
</tr>
<tr>
<td>MR</td>
<td>magnetic resonance</td>
</tr>
<tr>
<td>MRA</td>
<td>magnetic resonance angiography</td>
</tr>
<tr>
<td>MRI</td>
<td>magnetic resonance imaging</td>
</tr>
<tr>
<td>MRP</td>
<td>magnetic resonance perfusion</td>
</tr>
<tr>
<td>MRS</td>
<td>magnetic resonance spectroscopy</td>
</tr>
<tr>
<td>MRV</td>
<td>magnetic resonance venography</td>
</tr>
<tr>
<td>SWI</td>
<td>susceptibility-weighted imaging</td>
</tr>
<tr>
<td>T1WI</td>
<td>T1-weighted imaging</td>
</tr>
<tr>
<td>T2WI</td>
<td>T2-weighted imaging</td>
</tr>
</tbody>
</table>

Brain imaging is critical in comprehensive epilepsy diagnosis and for planning epilepsy surgery, but it also is important when a seizure is the initial manifestation of a tumor or other lesion which in itself requires resection. Histopathologi-
Structural Brain Imaging in Chronic Epilepsies

Cal studies of tissue resected at epilepsy surgery and of postmortem tissue have established etiological relationships between particular lesions and specific epilepsy syndromes. Many neoplastic and other gray matter lesions are more variably related to clinical epilepsies, however. Some lesions, such as small venous angiomas, have little association with epilepsy. Anatomical location and lesion characteristics are important variables in diagnosis with structural imaging as they are in histopathological analysis. The pathology of temporal lobe epilepsy has been reviewed by Bruton.

Intra-axial and extra-axial mass lesions cause acute symptomatic seizures as well as epileptogenesis, resulting in chronic epilepsy. Among the intracerebral neoplasia, those with acute or chronic hemorrhage tend to be more highly epileptogenic, and increased concentrations of the tumor marker Ki-67 are associated with a higher rate of seizure recurrence following glioma resection. Most types of benign and malignant primary brain tumors frequently manifest with neurologic deficits independently of or together with seizures. Exceptions are gangliogliomas and gangliocytomas, which rarely if ever present with neurologic deficits; these lesions are unlikely to present with any signs other than seizures. Their histopathology has features that overlap with cortical dysplasias.

Arteriovenous malformations (AVMs) may be epileptogenic based on mass effect, dependent ischemia, surrounding hemorrhage or chronic hemosiderin deposition, and presence of superficial draining veins. Cavernous malformations were once known as “occult AVMs” due to the difficulty in diagnosing them with contrast catheter angiography. Cavernomas now are highly recognizable on MRI by their typical rim of hemosiderin staining, which pathophysiologically also accounts for their highly epileptogenic nature. Only the larger and more complex venous angiomas are likely to be associated with epilepsy, and capillary tel-

Figure 2. Human hippocampal anatomy. These coronal sections through the body of the hippocampus were obtained from a cadaver donor without known brain disease using (A) 8-T MRI of a tissue section and (B) subsequent Bielschowski-stained photomicrography. (Adapted with permission from Chakeres DW, Whitaker CD, Dashner RA, et al. High-resolution 8 Tesla imaging of the formalin-fixed normal human hippocampus. Clin Anat 2005;18:88–91.)
angiectasias are said to never be causative of epilepsy.

Ablative lesions often cause acute symptomatic seizures, particularly lobar hemorrhages (which expose cortex to blood), encephalitides (which expose cortex to inflammatory injuries; Figure 4), and acute hydrocephalus (which injures cortex as a rapidly expanding lesion). Recent studies of epileptogenic encephalitides have revealed specific antibody-mediated inflammation directed variously at N-methyl-D-aspartate receptors (NMDARs), voltage-gated potassium channel complexes (VGKCs), glutamic acid decarboxylase (GAD), and numerous other neurochemicals. In many cases these autoimmune encephalitides may present as a monophasic inflammation that results in chronic epilepsy, although some are chronic inflammation with ongoing injury and seizures. In general any type of ablative lesion may also cause both acute symptomatic seizures and development of chronic epilepsy. Some lesions such as hippocampal sclerosis rarely are associated with a specific etiologic hippocampal insult. Presumably, ablative lesions and injurious alien tissue lesions (tumors and vascular malformations) evoke reparative mechanisms which cause local reorganization with enhanced epileptic excitability. In the case of hippocampal sclerosis, considerable evidence supports mossy fiber sprouting as an example of local reorganization causing enhanced epileptic excitability (Figure 5), but no single specific type of hippocampal injury is known to account for this lesion.

Malformations of cortical development (MCD) have variable and often very close associations
Structural Brain Imaging in Chronic Epilepsies

The classification of MCDs (Table 2) continues to evolve rapidly, with ongoing advancements in neurogenetics, neuroimaging, and neuropathology. Many MCDs are associated with profoundly disabling cognitive-behavioral and sensorimotor deficits, and seizure control is elusive in many of these patients. Other MCDs, such as small focal cortical dysplasias (FCDs), cause epilepsy without other significant disabilities. Small FCDs are often difficult to detect even with the best available clinical 3-Tesla (T) MRI scanners, but detection of these FCDs (Figure 6) can lead to efficacious resection in refractory epilepsies.

The phakomatoses are a heterogeneous collection of congenital genetic and nongenetic syndromes with neurocutaneous manifestations. Cerebral tumors, vascular malformations, and MCDs are the epilepsy-associated lesions in tuberous sclerosis, neurofibromatosis, and encephalotrigeminal angiomatosis. Other congenital genetic and nongenetic syndromes lack cutaneous manifestations but, as with the phakomatoses, are readily identified by clinical presentation, EEG manifestations, brain MRI abnormalities, and increasingly by genetic markers.

Figure 5. Hippocampal sclerosis. (A) Cadaver tissue without premortem brain disease. (B) Normal hippocampal structure in patient with extrahippocampal tumor. (C) Severe hippocampal sclerosis, with major reduction of hilar (H) and CA1 and A3 neurons. (D) End folium sclerosis, with severe reduction of hilar neurons, sparing other hippocampal populations. (Magnification x10.) (Reprinted with permission from Sloviter RS. The functional organization of the hippocampal dentate gyrus and its relevance to the pathogenesis of temporal lobe epilepsy. Ann Neurol 1994;35:640–54.)

NEOPLASTIC LESIONS

Primary cerebral neoplasms and cerebral metastases are in general highly epileptogenic, with perhaps two-thirds of low-grade glial neoplasms presenting initially with seizures, and are usually recognized as neoplasms based on MRI findings. Primary cerebral neoplasms often can be suspected on the initial CT, based on edema that causes either more pronounced gray-white differentiation (as opposed to infarction, in which the gray-white is obscured), or based on the extent of white matter edema that can cross the midline (such as the corpus callosum in astrocytomas). Metastatic lesions typically cause more focal edema, but can be innumerable and diffuse. Such regions of parenchymal edema are best visualized on fluid-attenuated inversion recovery (FLAIR) MRI. Postcontrast T1-weighted MRI (T1WI) is more sensitive than CT and variably demonstrates enhancement depending on the extent, grade, and type (primary versus metastatic) of neoplasm. For example, nearly all metastatic lesions are considered high grade, and as expected these lesions enhance after administration of intravenous contrast. Lower-grade primary brain tumors may variably enhance to a mild degree, but there should be no “necrosis” (ie, no peripheral en-
Table 2. Classification of Malformations of Cortical Development

<table>
<thead>
<tr>
<th>Type</th>
<th>Subtype</th>
<th>Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>I. Malformations secondary to abnormal neuronal and glial proliferation or apoptosis</td>
<td>I. Malformations secondary to abnormal neuronal and glial proliferation or apoptosis</td>
<td>Seckel syndrome with specific mutations or unknown cause</td>
</tr>
<tr>
<td></td>
<td>IB. Megalencephaly</td>
<td>Sotos syndrome</td>
</tr>
<tr>
<td></td>
<td>IC. Cortical dysgenesis with abnormal cell proliferation but without neoplasia</td>
<td>Tuberous sclerosis with cortical hamartomas and mutations of TSC1 or TSC2</td>
</tr>
<tr>
<td></td>
<td>ID. Cortical dysplasias with abnormal cell proliferation and neoplasia</td>
<td>Dysembryoplastic neuroepithelial tumor (DNET)</td>
</tr>
<tr>
<td>II. Malformations due to abnormal neuronal migration</td>
<td>IIA. Malformations with neuroependymal abnormalities: periventricular heterotopia</td>
<td>Diffuse periventricular nodular heterotopia with frontonasal dysplasia</td>
</tr>
<tr>
<td></td>
<td>IIB. Malformations due to generalized abnormal transmantle migration</td>
<td>Miller-Dieker syndrome (with lissencephaly)</td>
</tr>
<tr>
<td></td>
<td>IIC. Malformations presumably due to localized abnormal transmantle migration</td>
<td>Curvilinear transmantle heterotopia</td>
</tr>
<tr>
<td></td>
<td>IID. Malformations due to abnormal terminal migration and defects in pial limiting membrane</td>
<td>Walker-Warburg syndrome</td>
</tr>
<tr>
<td>III. Malformations due to abnormal postmigrational development</td>
<td>IIIA. Malformations with polymicrogyria or cortical malformations resembling polymicrogyria</td>
<td>Bilateral perisylvian polymicrogyria</td>
</tr>
<tr>
<td></td>
<td>IIIB. Cortical dysgenesis secondary to inborn errors of metabolism</td>
<td>Zellweger syndrome</td>
</tr>
<tr>
<td></td>
<td>IIC. Focal cortical dysplasias (without dysmorphic neurons) due to late developmental disturbances</td>
<td>Abnormal radial cortical lamination</td>
</tr>
<tr>
<td></td>
<td>IIID. Postmigrational developmental microcephaly</td>
<td>Progressive encephalopathy, hypsarrhythmia, and optic atrophy (PEHO) syndrome</td>
</tr>
</tbody>
</table>


Enhancement with central fluid density/signal intensity (Figure 7 and Figure 8). Higher-grade primary brain tumors typically exhibit 3 major characteristics on 3 routine imaging sequences: (1) peripheral contrast enhancement with central necrosis (fluid signal intensity) on postcontrast MRI, (2) reduced diffusion on diffusion-weighted imaging (DWI; bright on DWI, dark on apparent diffusion coefficient [ADC] map) around the periphery of the lesion in a distribution similar to what is avidly enhancing, and (3) dark foci on susceptibility-weighted imaging (SWI) greater than 3 to 4 mm in size, the larger of which are more concerning for higher-grade tumor (Figure 9 and Figure 10). Of note, MR spectroscopy (MRS) identifies an elevated choline-to-N-acetylaspartate ratio in primary brain tumors (nearly double), but cannot differentiate high- from low-grade primary brain tumor. Positron emission tomography (PET) scanning with 18F-fluorodeoxyglucose (18F-FDG) can discriminate high- from low-grade primary brain tumor but cannot reliably differentiate one type of high-grade tumor from another (eg, astrocytoma from oligodendroglioma, or even glioma from metastasis). Finally, magnetic resonance perfusion
(MRP) has shown utility in aiding tumor grading, particularly when combined with the 3 above-mentioned criteria, as higher-grade primary brain tumors (grades 3 and 4) demonstrate an elevated cerebral blood volume (along with other parameters) in the regions of contrast enhancement relative to more normal contralateral white matter parenchyma.

Dysembryoplastic neuroepithelial tumors (DNETs, Figure 11) are typically low density on CT, while on MRI they can be quite bright on T2-weighted imaging (T2WI), possibly more so than cerebrospinal fluid (CSF) in some instances. On FLAIR, the signal internally can vary, possibly being bright, or even can suppress (become dark) similar to CSF. Typically there is not associated contrast enhancement. DNETs also are typically located peripherally near the cortex relative to the ventricles.

Primitive neuroectodermal tumors (PNETs) (Figure 12) are most common in the posterior fossa (medulloblastoma), but the signal characteristics on CT and MRI are similar regardless of location. On CT, these vary depending on the amount of surrounding edema, and the enhancing lesions may appear isodense or even slightly hyperdense to cerebral parenchyma prior to contrast administration. On MRI, a typical finding that can distinguish PNET from other tumors is bright signal (reduced) on DWI that is dark on ADC maps, particularly in the posterior fossa, where ependymomas and juvenile pilocytic astrocytoma (JPA) are a consideration in pediatric patients. These tumors typically enhance avidly.

Ependymomas have been likened to “caulk streaming from a caulk gun,” wherein the enhancing lesion on postcontrast CT or MRI typically follows the ventricular system along its path. This characteristic, along with the lack of reduced diffusion on DWI and ADC maps, may distinguish ependymoma in the posterior fossa from PNET/medulloblastoma and juvenile pilocytic astrocytoma.

Gangliogliomas and gangliocytomas (Figure 13) usually occur in the temporal lobes. The enhancement pattern on postcontrast imaging is variable, and FLAIR demonstrates bright signal, as occurs with other primary brain tumors. DWI and SWI are typically unremarkable. The other considerations of nonenhancing tumors in this location are DNET, pleomorphic xanthoastrocytomas, and other low-grade gliomas.

Lymphomas can be classified as primary or secondary. Primary lymphoma typically has more diffuse white matter involvement, but both forms typically demonstrate avid contrast enhancement and have
a degree of reduced diffusion along the periphery, which can make them difficult to distinguish from high-grade gliomas when diffuse. Additionally, one interesting feature is that focal lesions or the edge of larger lesions are most commonly hyperdense relative to the remainder of the cerebral parenchyma on CT. Also, 18F-FDG-PET may demonstrate these well.

Cerebral metastases typically demonstrate avid enhancement, and the number of enhancing lesions varies immensely. Also, the appearance on other imaging sequences varies with the tumor type. For example, many adenomatous tumors may exhibit reduced diffusion on DWI (bright), while many squamous lesions often do not have reduced diffusion relative to gray matter. Additionally, on SWI, lesions with propensity to hemorrhage have dark signal from “susceptibility” artifact caused by the hemorrhage (which may lead to a presentation with seizures). A mnemonic often used to describe the tumors that have a high propensity for hemorrhage and cause this finding is MRCT: melanoma, renal cell, choriocarcinoma, and thyroid cancers; breast cancer should be added due to its high incidence.

Extra-axial, intracranial lesions also frequently present with seizures. The list of such lesions is extensive, but most are rare. The most common extra-axial epileptogenic lesions are meningiomas, followed in epilepsy-associated prevalence by various histopathological types of dural and bony metastases with cortical mass effect. Notably, meningiomas can be quite large at the time of diagnosis and can exhibit a large amount of surrounding and adjacent edema, which can simulate a high-grade primary brain tumor. However, a few imaging characteristics can distinguish meningioma and confirm that it is extra-axial, such as a “CSF cleft” (on T2WI), a dural tail (on postcontrast T1WI), and the presence of either adjacent bony erosions or hyperostosis as a reaction to this dural-based tumor. Rarely, tumors narrow the internal carotid artery at the skull base, resulting in epileptogenic cerebral ischemia-infarction, and meningioma is most commonly causative in this pathophysiological mechanism.

**VASCULAR LESIONS**

Cavernomas (Figure 14) are the most commonly epileptogenic among vascular malformations, and may be considered underdiagnosed. Given their high prevalence in the general population (thought to be in the region of 5%), cavernomas are incidentally noted in some fraction
of patients who undergo CT or MRI evaluation for other reasons, and their varying appearance can cause some confusion. On CT, these most commonly present as a focal hyperdense lesion related to prior hemorrhage, when there is a lack of surrounding edema. Some patients present with acute lobar hemorrhage, which has a greater degree of surrounding edema. More chronic lesions may calcify, but this occurs in a minority. On MRI, calcified lesions often have been described as “popcorn-like” on routine T1WI, having variably bright and dark rim; their appearance is uniformly dark on T2WI in larger lesions. T2*-weighted images and SWI may depict smaller lesions, and larger lesions may demonstrate quite large regions of dark susceptibility artifact. Notably, these usually do not exhibit much enhancement on postcontrast T1WI. There is debate as to whether the minority, majority, or all of these lesions are associated with developmental venous anomalies (DVAs, or venous angiomas), as the recent imple-
mentation of SWI is depicting more and more cavernomas having underlying DVAs.

AVMs may be the most common cause of nontraumatic intracranial hemorrhage in juveniles, adolescents, and young adults, and are thus not an uncommon cause of seizure. These can grow quite large prior to diagnosis; hence, their size and degree of vascular recruitment varies widely. On routine MR sequences, enlarged flow voids are noted, particularly on T2WI, whereas on postcontrast images an enlarged arterial supply, venous varices, and the enhancing nidus are usually well-demonstrated (Figure 15). However, noncontrast CT may only depict larger AVMs, whereas small or occult AVMs without hemorrhage, enlarged arteries, or atrophy (resulting from “steal” away from normal parenchyma) may be relatively invisible. Although catheter angiography is considered the diagnostic test of choice for AVMs, MR angiography (MRA) and MR venography (MRV) may also depict the enlarged arterial supply and venous drainage, respectively. Higher resolution postcontrast MRA can be quite helpful in detecting intranidal aneurysms as well. Newer time-resolved (so-called 4D) MRA and MRV have shown promising results in

Figure 10. Glioblastoma multiforme. A 33-year-old male presenting with seizures had a peripherally enhancing lesion (arrows) within the left medial temporal lobe, as demonstrated on (A) postcontrast T1WI. There was (B) moderate surrounding edema on FLAIR, with (C) intratumoral dark hemorrhage on SWI. (D) Dynamic MR perfusion demonstrated an elevated cerebral blood volume and leakage (dashed circle), consistent with a high-grade primary brain tumor.

Figure 11. Dysembryoplastic neuroepithelial tumor (DNET). A 39-year-old male presenting with seizures had a large left frontal mass that was quite bright on (A) T2-weighted images, which suppressed somewhat (ie, exhibited dark signal) on (B) FLAIR, and did not demonstrate reduced diffusivity on (C) diffusion images or have contrast enhancement on (D) T1-weighted images. These findings suggested a benign tumor, and the subsequent biopsy confirmed a frontal DNET.
the noninvasive work-up of AVMs and in presurgical planning. Finally, SWI can be utilized to visualize both the abnormal vasculature and the internal hemorrhage that may be associated with an AVM.

Venous angiomas (Figure 16) have also been termed DVAs, a name that has been gaining greater acceptance within the literature. The anomaly consists of an enlarged draining vein passing through and draining normal cerebral parenchyma, which usually is asymptomatic unless thrombosed. These are not typically considered epileptogenic in and of themselves; as a matter of fact, they do not seem to be associated with any particular clinical presentation. However, cavernomas can be present in 20% to 30% of patients with DVAs, and this number has yet to be revised and likely will be higher when reassessed with SWI. On MRI, DVAs are typically invisible on routine T1WI and T2WI, and become quite evident on postcontrast T1WI, with a “caput medusa” appearance of drainage. They are also usually quite

Figure 12. Primitive neuroectodermal tumor (PNET), supratentorial. A 6-month-old female with seizures underwent 1.5-T MRI, which demonstrated a (A) medial temporal lobe hyperintense lesion on T2-weighted images, along with avid contrast enhancement on (B) postcontrast axial and (C) coronal T1-weighted images (red arrows). This was later found to be a PNET, although a ganglioglioma could have a similar appearance.

Figure 13. Ganglioglioma. An 18-year-old male with a lesion (arrows) centered between the right temporal lobe and basal ganglia, which is bright on (A) T2-weighted and (B) FLAIR images, and enhances on (C) postcontrast T1-weighted images.
visible on SWI, given the ability of SWI to image deoxygenated hemoglobin.

Capillary telangiectasias are asymptomatic and are not typically associated with DVAs or cavernomas, although they occasionally occur concomitantly with both of the aforementioned vascular lesions. They are usually invisible on routine T1WI, T2WI, and FLAIR, while exhibiting mild, “brush-like” enhancement on postcontrast T1WI. SWI demonstrates a brush-like appearance of deoxygenated blood as well. These lesions are most commonly located within the pons, although occasionally they can be mistaken for malignant lesions such as metastases when occurring in the supratentorial parenchyma or basal ganglia.

**ABLATIVE LESIONS**

Hippocampal sclerosis (HS) may occur with or without atrophy (Figure 17 and Figure 18), possibly related to the age and acuity of the lesion. Also, sclerosis or atrophy may occur within the hippocampus even if another cerebral parenchymal lesion is the

---

**Figure 14.** Cavernomas in 2 patients. A 58-year-old female presenting with seizures and motor deficits had a hemorrhagic lesion within the left precentral gyrus on (A) noncontrast CT, with a moderate amount of surrounding edema (B) on FLAIR; a hemorrhage was confirmed on (C) SWI. This lesion was later confirmed to be a cavernoma at biopsy. In a 40-year-old female, (D) subarachnoid hemorrhage (white arrows) was noted on noncontrast CT, which arose from a left frontal cavernoma; the cavernoma was not visible on the CT, but was focally dark on (E) SWI (black arrow). The cavernoma was associated with a draining developmental venous anomaly (DVA; ie, a venous angioma). The DVA that drained centrally from the cavernoma was visualized as a linear structure perpendicular to the lateral ventricular margins on both (E) SWI and (F) postcontrast T1-weighted images (red arrows).
Structural Brain Imaging in Chronic Epilepsies

Focal source of seizures. This lesion is best appreciated on coronal FLAIR or T2WI in the oblique coronal plane, perpendicular to the length of the hippocampus. There is typically no associated contrast enhancement. The principal features of HS are variable degrees of atrophy, T2-signal increase, T1-signal decrease, and obscuration of internal architecture.\(^9,^{34–45}\) The latter feature has been appreciated on 3-T MRI as partial loss of the hippocampal striation.\(^{46}\) Numerous small features of hippocampal abnormality can be discerned in HS, including paucity of digitations of the hippocampal head.\(^{9,47,48}\) Additional features of HS, including relatively greater atrophy of Ammon’s horn than of the dentate gyrus, can be observed with ultra-high-field MRI.\(^9\) Atrophy of perihippocampal white matter, and to a lesser extent of the entire temporal lobe of the sclerotic hippocampus, is typical, as are ipsilateral fornix and mammillary body atrophy (Figure 19). Minor malformations of the hippocampus and adjacent cortex are occasionally observed in mesial temporal lobe epilepsy (TLE), with or without HS.\(^{49,50}\) The common variant of a “verticalized” (incompletely inverted) hippocampus should not be mistaken as a MCD.\(^{51}\) Abnormalities of cerebral water content

Figure 15. Arteriovenous malformation (AVM). A 27-year-old female with seizures was found to have a large AVM involving most of the left temporal lobe and extending into the occipital region, as shown on (A) axial and (B, C) coronal T2-weighted images. The AVM’s nidus (white arrows) is rather large, and multiple enlarged feeding arteries (red arrows) are shown, which arise from the middle cerebral artery. (D) Gradient echo sagittal T1-weighted images demonstrate the multiple bright vascular flow voids associated with the AVM.

Figure 16. Developmental venous anomaly (DVA, venous angioma). A healthy 78-year-old female suffered a seizure, following which (A) noncontrast CT was normal. On 3.0-T MRI, (B) FLAIR and (C) T2-weighted images were nearly normal, but SWI (D) revealed a relatively large right frontal DVA (arrow). The dark signal on SWI is thought to be due to draining deoxygenated blood.
and diffusivity on DWI and of white matter tracts on diffusion tensor imaging are often bilateral but more severe on the side of unilateral TLE.52–54

Chronic infarcts appear as T2-bright and T1-dark, and are dark on DWI. There may be underlying hemorrhage (hemosiderin) within the region of encephalomalacia, which can be visualized on T2*WI or SWI (Figure 20). The epileptogenicity of hemosiderin in contact with neurons of the cortex is well established, and these MRI findings assist in decision making with regard to continuation of antiseizure medication following sustained control of seizures. Although typically present in the late subacute phase, smaller degrees of contrast enhancement can be visualized even in the chronic phase.

Traumatic brain injury (TBI) sequelae depend on the type of initial injury. Parenchymal injuries such as cortical contusions and shear injury (diffuse axonal injury) have hemorrhage in nearly all cases on histopathologic exam, and the majority of such

Figure 17. Hippocampal sclerosis with atrophy. (A) A 3.0-T MRI in a 3-year-old male showed enlargement of the right temporal horn and choroidal fissure (red arrows) on T2WI. The hippocampus (white arrows) had corresponding abnormal signal and atrophy on (B) coronal FLAIR and (C) T1WI. Note the normal hippocampal thickness and signal (black arrows) on the opposite side.

Figure 18. Hippocampal sclerosis without definite atrophy. A 7-year-old male has hyperintensity within the left hippocampal formation (white arrows) on 3.0-T MRI (A) T2-weighted and (B) FLAIR images, without associated enlargement of the choroidal fissure (red arrows). Note the normal hippocampal signal within the right hippocampus (black arrows), which normally can be slightly bright on FLAIR, particularly at 3.0 T.
Lesions contain microhemorrhage, best depicted on SWI. FLAIR MRI demonstrates more than 50% of lesions acutely, and DWI a smaller number (thought to represent focal cytotoxic edema), some of which do not progress to encephalomalacia. In the chronic phase, FLAIR images may depict bright foci with focal atrophy from encephalomalacia, while SWI demonstrates the remote hemorrhage. Subarachnoid hemorrhage may lead to siderosis of the CNS, which appears as dark signal along the pia (sulci and surrounding the brainstem) on T2*WI and SWI. Thus, FLAIR, DWI, and SWI are crucial in the acute work-up of TBI, while FLAIR and SWI are necessary in evaluating patients with a remote history of TBI.

Other causes of encephalomalacia include chronic sequela of infection (whether meningitis, cerebritis, or encephalitis) or inflammation (eg, vasculitides, granulomatous disorders, demyelinating diseases).

Atrophy in such cases appears similar to the encephalomalacia seen as a sequela of stroke. Rasmussen's encephalitis is a rare cause of epilepsy in children with intractable seizures, usually epilepsy partial continua, in which the imaging findings can strongly suggest the diagnosis. Neuroimaging in the early stages of onset demonstrates nearly hemispheric reduction of diffusion (bright on DWI and dark on ADC map), later progressing to diffuse enhancement of the affected hemisphere and eventually hemispheric scarring/atrophy (Figure 21). Typically, the posterior fossa is unremarkable.

MALFORMATIONS OF CORTICAL DEVELOPMENT

Gray matter heterotopias have been morphologically described to be periventricular (most common), subcortical (less common), or band (rare). Periventricular nodular heterotopias (PVNH) may be singular or numerous, and are similar to the gray matter of the cerebral cortex on all imaging sequences (Figure 22). These may be noted incidentally in patients without seizures. Subcortical heterotopias (SCH)
may appear either nodular or curvilinear; both appear conglomerated, mass-like, and rather disorganized (Figure 23) relative to focal PVNH lesions. Band heterotopia (Figure 24) is considered to be part of the pachgyria-lissencephaly spectrum, being less clinically severe than pachgyria but usually more symptomatic than PVNH and SCH. Diffuse band and smaller curvilinear subcortical heterotopias, sometimes termed “double cortex” malformations, may be activated during language and sensorimotor processing, as well as during seizures.

Focal cortical dysplasia is often associated with subcortical neuronal heterotopia. Most often the thickened cortex of the small dysplasia occurs at the base of a sulcus as a “dimple,” which typically lies above a radially oriented, linear cluster of heterotopic neurons in the subcortical white matter (Figure 25).

Hemimegalencephaly (Figure 26) is a rare and severe malformation that consists of largely dysfunctional and disorganized hamartomatous tissue. The disorder can be diffuse, involving nearly the entire hemisphere, or focal. On CT there may
be calcifications, while the density of the malformation is slightly greater than normal (given the internal composition of the tissue, which consists of a larger degree of gray matter, perhaps with interspersed calcium). The hemisphere is generally overgrown and most or all of the affected hemisphere may appear mass-like. This can be mistaken for a higher-grade tumor. However, on FLAIR images, a key characteristic is the lack of surrounding bright edema and contrast enhancement, which are usually noted within higher-grade primary brain tumors.

Lissencephaly is considered the severe end of the spectrum of the band heterotopia-pachygyria-lissencephaly complex, and it occurs in varying degrees (Figure 27). The entity of lissencephaly (previously termed type I) can be subdivided into simple (usually autosomal recessive or X-linked, with microcephaly) or complex (associated with another malformation and syndromic). The simple form can be further subdivided into microlissencephaly (microcephaly plus lissencephaly, ie, complete lissencephaly) and microcephaly with a simplified gyral pattern (short, shallow gyri, ie, partial/incomplete lissencephaly). Cobblestone lissencephaly (previously also termed type II) is discussed separately below. Pachygyria is considered on the spectrum of lissencephaly and is typically diffuse; although a “focal” form exists, it is not really focal, but rather is symmetric and limited to a particular lobe.

Cobblestone malformations (also termed cobblestone lissencephaly, or type II lissencephaly) are rare cerebral anomalies that usually occur with congenital muscular dystrophies.

The 3 syndromes that characterize the mildest, intermediate, and most severe degrees of this spectrum are Fukuyama’s syndrome, muscle-eye-brain disease, and Walker-Warburg syndrome, respectively. In each, there is a variable degree of abnormal sulation, polymicrogyria, cerebellar cysts, and hypomyelination of the white matter. There may also be associated malformations or hypoplasia of the cerebellum, brainstem, globes, and corpus callosum, occasionally associated with hydrocephalus.

Schizencephaly consists of a transmantle cleft of gray matter or polymicrogyria extending between the ventricular system to the external surface of the cerebral convexity (Figure 28). These may
be characterized further as “close-lipped” (closely apposed edges of the cleft) or “open-lipped” (the cleft edges are widely patent). Schizencephaly may be associated with any of a number of other congenital malformations such as callosal dysgenesis, polymicrogyria, and gray matter heterotopia. Notably, this should not be confused with porencephaly or a porencephalic cyst, which occurs from the lack of the brain’s ability to mount a gliotic response to a cerebral insult (occurring in insults prior to the third trimester); with porencephaly the cleft is lined by white matter and gliotic tissue.

Polymicrogyria is generally considered to have the morphologic appearance of an overfolded cortex, with an abnormal sulcal pattern and depth (Figure 29). Subtypes include: (1) a focal form, which is an idiopathic form that is either due to a post-intrauterine insult or is familial; (2) a diffuse form often resulting from a TORCH intrauterine infection; less commonly, it is bilateral and symmetrical in the genetic form; (3) a perisylvian form that may be unilateral or bilateral surrounding the sylvian fissures in the frontal and/or parietal lobes, or surrounding the central sulcus.\textsuperscript{74–76} Polymicrogyria is usually distinguished radiologically by an irregular gray-white matter margin on thin (1–2 mm thickness) T1-weighted or T2-weighted images and by the cortical inrolling. However, caution should be exercised as bilateral forms can mimic “focal” pachygyria (discussed under lissencephaly), as the overfolded sulci may be difficult to discern on thicker images.

A hypothalamic hamartoma is gray-matter–like hamartomatous tissue in an abnormal location (Figure 30). In this case, the location is the hypothalamus, which may be displaced or expanded to varying degrees. Hypothalamic hamartomas have gray matter signal on all MR sequences and do not enhance after intravenous contrast administration.\textsuperscript{77,78}

Agenesis of the corpus callosum occurs in several epileptic conditions and is often not a complete lesion (Figure 31). Until recently, callosal dysgenesis was thought to occur bidirectionally in severity; the mildest cases have been described to consist of solely rostral or splenial dysgenesis,
with more severe cases involving the entire corpus callosum or sparing only the genu. However, recent evidence suggests that the dysgenesis may occur in a multifocal pattern. In the setting of agenesis, there is a typical “steer horn” appearance of the lateral ventricles on coronal images, with a “race car” (colpocephaly of the posterior horns of the lateral ventricles simulating the “wheel wells” of the race car) appearance of the lateral ventricles on axial images. There is often malrotation/malformation of the hippocampi in such severe cases of dysgenesis/agenesis, and various other congenital malformations may occur in the setting of callosal agenesis (eg, Chiari malformations, PVNH, Dandy-Walker syndrome, cerebellar dysplasias, schizencephaly). Milder forms of callosal dysgenesis can involve solely the rostrum or splenium, and may necessitate acquiring thin, sagittal images to detect them. Of note, callosal agenesis/dysgenesis should not be confused with callosal atrophy or encephalomalacia, which may occur from chronic hydrocephalus with multiple shunt placements, trauma, or other remote callosal injury.

**PHAKOMATOSES**

Phakomatoses feature cerebral malformations and intracranial neoplasia in association with cutaneous lesions and often lesions of other organ systems. Tuberous sclerosis, neurofibromatosis type I, and encephalotrigeminal angiomatosis all are important causes of partial and generalized epilepsies.\(^{79}\)

Tuberous sclerosis may consist of various cerebral anomalies that can be detected on CT or MRI (Figure 32). Cortical tubers may be similar to gray matter in density (hyperdense to white matter) on CT or may be partially calcified, while on MRI their signal intensity is hyperintense relative to the remainder of the parenchyma on FLAIR or T2WI; they may variably enhance after contrast administration.\(^{80}\) There may be associated centripetal-periventricular hyperintensity on FLAIR and T2WI radiating between the lateral ventricle ependymal surface and these cortical lesions, reflecting the underlying neuronal migration anomaly; detection of this anomaly can be enhanced with DWI.\(^{81}\) Other nonspecific T2-hyperintensities may exist
within the deep white matter. Additionally, subependymal giant cell astrocytomas (SEGAs) may be located near the foramen of Monro, which typically enhance; if an enhancing lesion in that location causes hydrocephalus in a patient known to have tuberous sclerosis, then the obstructing lesion should be considered a SEGA.

Neurofibromatosis may consist of skin, orbital, bony, cerebral, cerebellar, brainstem, or basal ganglial lesions on CT and MRI. The most common abnormality is nonspecific T2-hyperintense foci within the optic pathways, basal ganglia, and cerebellum, which are considered optic gliomas (histopathologically juvenile pilocytic astrocytomas) when enlarged and enhancing. One-third of these gliomas enlarge, one-third decrease in size, and one-third stay the same size if followed for years. Sphenoid wing dysplasia of the orbit may occur, causing buphthalmos and other orbital anomalies. Vascular intimal injury may occur chronically, in the worst case causing progressive occlusion of the anterior circulation major vessels such as the internal carotid artery (Moyamoya syndrome). Additionally, plexiform neurofibromas may be noted.

Figure 29. Polymicrogyria: perisylvian bilateral variant. A 16-year-old male with seizures has bilateral blurring of the gray-white matter junction (arrows) on axial (A) T2-weighted images, (B) T1-weighted images, and (C) sagittal T1-weighted images of the right side.

Figure 30. Hypothalamic hamartoma. A 27-year-old male with gelastic seizures underwent a 1.5-T MRI scan, which showed (A) a small (<1.0 cm) lesion (arrows) along the inferior aspect of the hypothalamus, being similar in signal intensity to gray matter on a sagittal T1-weighted image. The lesion did not enhance on (B) postcontrast T1-weighted images, and was bright on T2-weighted images and (C) FLAIR images; note the normal, slightly bright pituitary infundibulum just anterior to the lesion on axial FLAIR (C, red arrow).
throughout the soft tissues of any part of the body. Neurofibromas may involve the skull base and sites of cranial nerve exit, as well as neural foramina throughout the spine, which can simulate schwannomas given their extra-axial appearance and enhancement.

Encephalotrigeminal angiomatosis (Sturge-Weber syndrome, or SWS) is a phakomatosis that consists of a large and often hemispheric pial malformation, which typically has diffuse calcification along the pia and sulci on CT, variably being bilateral.\(^{62,63}\) The associated hemisphere may be atrophied. On MRI, the pial enhancement is quite avid related to the malformation, and is best visualized on postcontrast FLAIR or T1WI (Figure 33). Dyke-Davidoff-Masson syndrome is a complex of findings ipsilateral to an area of severe cerebral atrophy of early onset, in which the ipsilateral paranasal sinuses and mastoid
air cells appear enlarged as if to replace the volume lost due to the cerebral atrophy.

CEREBRAL WHITE MATTER LESIONS

Peroxisomal disorders and metabolic disorders compose a wide spectrum of disorders with myriad imaging appearances. However, some entities (particularly the peroxisomal disorders) have characteristic findings that may alert the clinicians to the diagnosis. For example, X-linked adrenoleukodystrophy typically presents in the juvenile age-group (most commonly aged 5–10 years), is centered in the deep white matter, and typically involves the splenium of the corpus callosum even in the earliest stages, progressing outwards. Metachromatic leukodystrophies may present in an older age-group but typically have pronounced deep white matter findings surrounding the ventricles that are confluent. With many of these disorders, white matter is often affected in a confluent and symmetric fashion. In other disorders, such as the mitochondrial diseases, there may be predominately gray matter involvement, such as bilateral basal ganglial or cortical involvement, in a symmetric fashion. Further information on this subject can be obtained in the text by Barkovich.84

Multiple sclerosis and other demyelinating disorders have various imaging appearances, but in general the lesions follow a characteristic temporal sequence. In the acute phase of inflammation and presentation, there is mildly-moderately bright signal on FLAIR and T2WI, with mildly reduced diffusivity (bright signal) on DWI and mild enhancement. In the subacute phase (roughly after 1–2 weeks), the enhancement becomes more avid, while the reduced diffusion recedes; notably, the contrast enhancement around the periphery of such lesions often does not form a complete ring (C-type of contrast enhancement). In the chronic phase, the lesions’ enhancement fades, occasionally progressing to being near CSF signal intensity of dark signal and suppressing on FLAIR as the lesions “burn out,” becoming akin to “black holes” at the end stage. A relatively common finding in multiple sclerosis at any stage is periventricular lesions on FLAIR that are oriented perpendicular to the lateral ventricles on thinner images (subcallosal striations, only seen if 1–2 mm thickness or less), which may eventually become “Dawson’s fingers” if they continue to enlarge.85

OTHER PATHOLOGY

Neurocysticercosis is a common cause of chronic epilepsy in endemic regions, but also is frequently associated with acute symptomatic seizures. Neurocysticercosis may have several appearances (Figure 34), based on the CT and MRI evolution of the lesions through 4 recognized stages.86–88 In the vesicular stage, the viable cysticercus has no inflammation and appears as CSF-like cystic density on CT (hypodense with CSF) and MRI (bright on T2WI and mostly dark on FLAIR); a “dot” of bright signal on DWI may be present centrally.
from the scolex in about 30% of cases). Next, in the colloidal vesicular stage, the cyst’s scolex has degenerated with subsequent inflammation that is represented by perilesional edema (bright on FLAIR/T2WI surrounding the lesion; DWI has reduced diffusivity with bright signal within the cyst in about 20% of cases). There may be minimal surrounding enhancement, although typically there is little enhancement associated with this stage of neurocysticercosis. By the granular nodular stage, the parasite has died and the lesion retracts and begins to mineralize (represented as T1-bright with decreasing perilesional edema on FLAIR and T2WI; lesions in this stage typically have no bright signal on DWI). However, postcontrast images in this stage typically demonstrate ring-like peripheral enhancement in the previous region of perilesional edema. Finally, in the nodular calcified stage, the lesion becomes completely mineralized, having no surrounding edema (the calcium appears hyperdense on CT and dark on T2*WI/SWI, with no surrounding signal on FLAIR/T2WI; DWI appears normal). Occasionally, the racemose (grape-like cluster) form may occur, which can cause multiple cysts within the subarachnoid space and/or ventricles that can be diffuse and expand the ventricular system, or can be focal and surround vital structures such as major intracranial arteries. It is not uncommon to encounter patients with imaging following a seizure wherein re-infection occurs, and to note lesions of differing stages: calcified chronic lesions (calcified nodular stage) with superimposed perilesional edema in more acute/subacute lesions (colloidal vesicular or granular nodular stage).

Chronic hydrocephalus may resemble atrophy, but a few distinguishing characteristics may delineate this entity from atrophy. In atrophy, the ventricles enlarge proportionally to the sulci; in hydrocephalus, the ventricles are disproportionately larger. Also, in hydrocephalus the anterior portions of the temporal horns and the anterior-inferior recesses of the third ventricle (the optic and infundibular recesses) enlarge and no longer have

Figure 34. Neurocysticercosis (2 patients). In a 29-year-old male with seizures, a cysticercus (arrows) is noted on coronal (A) T1WI and (B) T2WI, with (C) surrounding perilesional edema on FLAIR and a (D) thin rim of contrast enhancement on coronal T1WI; note the small scolex (thin arrows) of this lesion within the colloidal vesicular phase. In a 33-year-old female with a lesion in the same phase, (E) a thin rim of enhancement is noted on postcontrast axial T1WI (arrow), with (F) a small scolex centrally (small arrows), seen as a “dot” on DWI.
acute angles, while these angles remain acute in atrophy.

Chronic subdural hygromas are in most cases sites of prior hemorrhage filled with proteinaceous fluid; they often are associated with subacute or chronic seizures. Cystic hygromas are generally hypodense on CT and hyperintense (possibly even greater than CSF) on T2WI; on FLAIR images, these may or may not suppress (become dark) with CSF (Figure 35). Occasionally, these may contain internal hemorrhage if superimposed trauma occurs.

Figure 35. Chronic subdural hygroma. A 79-year-old male had (A) bilateral hypodense fluid collections on noncontrast CT, being nearly the same density as cerebrospinal fluid (CSF). On DWI (B), these are not bright, excluding subacute subdural hematomas or abscesses. On (C) T2WI, (D) FLAIR, (E) SWI, and (F) postcontrast T1WI, the cortical veins and distal arteries (both represented by arrows) are displaced inwards, confirming that these are actually fluid collections and not prominent subarachnoid spaces from cerebral volume loss. Additionally, the suppression of these collections with CSF on FLAIR (ie, bright on T2WI, but dark on FLAIR) and the lack of internal hemorrhage on SWI confirms a subdural hygroma.

REFERENCES


78. Kuzniecky R, Guthrie B, Mountz J, et al. Intrinsic epilepto-