Magnetic Resonance Imaging in Temporal Lobe Epilepsy: Usefulness for the Etiological Diagnosis of Temporal Lobe Epilepsy

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Abstract

With improvement in magnetic resonance (MR) imaging techniques, the ability to identify lesions responsible for temporal lobe epilepsy has increased. MR imaging has also enabled the *in vivo* diagnosis of hippocampal sclerosis. Brain tumors are responsible for 2–4% of epilepsies in adult population and 10–20% of medically intractable epilepsy. The sensitivity of MR imaging in the diagnosis of tumors and other lesions of the temporal lobe (vascular malformations, etc.) is around 90%. Both hippocampal sclerosis and other temporal lobe lesions are amenable to surgical therapy with excellent postsurgical seizure outcome. In this article, we characterize and underline distinguishing features of the different pathological entities. We also suggest an approach to reviewing the MR images of an epileptic patient.

Key words: temporal lobe epilepsy, magnetic resonance imaging, lesional epilepsy, surgery, hippocampal sclerosis

Introduction

Historically, the paradigm of abnormal structure and/or abnormal function at one time or another has been the cornerstone of research and treatment in epilepsy. In particular, abnormalities in brain structure have been increasingly used in guiding treatment with epilepsy surgery. This is based on the assumption of a cause-and-effect relationship between brain lesions and seizures. It is presumed that seizures arise from neurons adjacent to the lesion with a reduced threshold for spontaneous coherent discharges.

The advent of magnetic resonance (MR) imaging and its continual technical improvement has enabled epileptologists to make *in vivo* diagnoses not possible previously, redefining many presumed “non-lesional” cases using this technique’s higher sensitivity. As a tool, MR imaging has also allowed better planning of invasive neurophysiological studies, and the correlation of these findings with structure. Other MR imaging techniques such as functional MR imaging, MR spectroscopy, and

diffusion-weighted imaging have provided additional functional correlates of epileptogenic tissue together with the structural information.

MR Techniques

The MR acquisition sequences used are paramount in the detection and characterization of lesions. Although modifications may be needed in individual cases, a standardized approach to the epileptic patient will be desirable in many cases. T₁-weighted images (T₁WI) are excellent for differentiating gray and white matter, allowing assessment of the cortical ribbon and deeper gray matter structures. A volume-acquired image (that with 0 gap) and thin slices (1–3 mm depending on signal-to-noise ratios) are highly recommended to allow qualitative and quantitative assessment of volumes of various structures (hippocampus and cortical ribbon) and allowing comprehension of a three-dimensional object from a two-dimensional representation. This is particularly relevant when assessing the cortical ribbon for areas of thickening and discounting

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changes due to partial volume averaging or tangential cuts through normal cortex. T₂-weighted images (T2WI) are sensitive to signal changes due to gliosis, edema, and/or abnormal structure that may be subtle or absent in the T1WI.

Long repetition time (TR) sequences with suppression of water signal, especially fluid-attenuated inversion recovery (FLAIR), provide better contrast between abnormally increased signal and cerebrospinal fluid (CSF) and can increase the yield of MR imaging examinations by 30%.^{4,20,24)} This is especially helpful in structures like the hippocampus that is engulfed in CSF. Another advantage of this technique is the detection of blurring of the gray-white junction in areas of abnormal cortex where there may be little to see on T1WI. In a pediatric series of patients with temporal lobe epilepsy due to hippocampal sclerosis, blurring of the gray-white junction in the adjacent temporal neocortex on

FLAIR images correlated with the presence of microscopic cortical dysplasia.^{33,38)}

The use of contrast agents such as gadolinium does not improve sensitivity but may provide additional information about the histopathological identity of the lesion seen on other sequences.

Approach to Reading the MR Images of an Epileptic Patient

A systematic approach to reading these sequences is crucial for the detection of subtle epileptogenic lesions (Fig. 1). Other authors have suggested algorithms⁷⁾ and neurosurgeons should adopt an approach that is applied routinely when reviewing MR images. We suggest starting with the FLAIR sequences, as signal changes are easy to identify, and may guide attention to areas of interest. It is important to note any signal asymmetries in the hip-

Fig. 1 Approach to reading the magnetic resonance images of an epileptic patient. exTLE: extra-temporal lobe epilepsy, FLAIR: fluid-attenuated inversion recovery, MCD: malformation of cortical development, TLE: temporal lobe epilepsy, T1WI: T₁-weighted image, T2WI: T₂-weighted image.

pocampi and temporal neocortex, together with areas of blurring of the gray-white junction that may be associated with underlying areas of malformations of cortical development (MCDs). Next, looking at T1WI, it is important to assess the degree of rotation or tilt of the subject in the scanner. This may give the false impression of volume asymmetries or cortical thickening. The degree of rotation of the subject can be assessed anteriorly by comparing the orbits, or the internal auditory canals⁹⁾ or caudate bodies and the crus of the fornix more posteriorly. Using the atria of the ventricles may be misleading as these are frequently asymmetrical. Asymmetry of lateral ventricles occurs in 32–72% of subjects across radiological and pathological series, often with the left side being larger.⁸⁾ With this information in hand, the hippocampi should be assessed for atrophy or volume asymmetry, unusual morphology, and signal changes. Next, the periventricular areas should be examined for the presence of ectopic gray matter, especially in the parieto-occipital areas. Any subtle gray matter tracts may also be traced to reveal areas with neuronal migrational cortical abnormalities. The inferior temporal lobes should be examined for the presence of encephalocele. Focal or diffuse areas of cortical thickening may be detected by tracing the cortical ribbon systematically and identifying major gyri in each slice. Finally, any diffuse or focal atrophy of cerebral structures should be noted and the underlying brain should be examined for lesions or MCDs.

Anatomy of the Hippocampus and Temporal Lobe

Familiarity with the anatomy and borders of the hippocampus is crucial in identifying pathology in this region. The hippocampus is a tadpole-shaped structure, nested in the most medial aspect of the temporal lobe. It is best assessed in the coronal plane. For a detailed description of the hippocampal anatomy, the reader is referred to the description by Watson et al.⁴⁸⁾ Briefly, the hippocampus anteriorly appears inferior to the amygdala and is separated from the same by the uncus recess of the inferior horn of the lateral ventricle. The temporal horn is lateral and superior to the body of the hippocampus. Inferiorly, the margin is defined by the subicular complex and parahippocampal gyrus. The lateral border is defined by the white matter of the temporal stem.

The hippocampus has three segments that are defined by morphology and relationship to the brainstem. The head, which constitutes most of its volume, is recognized by its digitations and lies an-

terior to the brainstem. The body is a flattened ovoid or cylindrical structure and lies next to the brainstem.⁶⁾ The tail wraps around the brainstem and rapidly narrows in diameter. Bronen and Cheung⁷⁾ identified structures on coronal MR imaging that allows the demarcation of the three segments. The head of the hippocampus spans from the coronal slice containing the inferior horn of the lateral ventricle to the slice containing the interpeduncular cistern. The body then extends to the slice that contains the superior colliculi and the remainder being the tail.

Hippocampal Sclerosis

This is a specific pattern of neuronal loss in the hippocampus, principally of the CA1, CA3, and CA4 pyramidal cells and granular cells of the dentate gyrus. This is not necessarily associated with epilepsy. It is thought that the epileptogenicity arises out of excitable aberrant axonal sprouting, and loss of lateral inhibition from the loss of basket cells, and an alteration of secondary messenger systems.^{3,41)} There is often a history of febrile seizures, and a seizure-free interval of years, followed by onset of partial seizures of temporal origin. It is the commonest cause of intractable temporal lobe epilepsy, which in selected populations may have a 90% cure rate with surgery.

Fig. 2 Coronal T₁-weighted image showing right hippocampal volume loss.

Fig. 3 upper row: Coronal T₁-weighted, T₂-weighted, and fluid-attenuated inversion recovery (FLAIR) images of a 17-year-old boy who presented with staring episodes and generalized motor seizures, showing a dilated right ventricular horn. Note there is no increased signal intensity on FLAIR image. Volumetric measurements of the hippocampi were normal. lower row: Video-electroencephalography monitoring revealing nocturnal myoclonic jerks, and staring episodes associated with generalized spike wave complexes. The patient was diagnosed as having generalized epilepsy.

Volume loss and signal changes are the MR hallmarks of this disease (Fig. 2). Although visual inspection alone by an experienced observer is 80–90% sensitive,³¹⁾ the studies regarding the added value of quantitative analysis are disparate.^{9,15,48)} Quantitative hippocampal volume measurements have been linked to amount of atrophy, and degree

of cell loss in resected specimens,^{34,36,47)} a history of febrile convulsion,^{9,31)} postoperative neuropsychological memory loss,¹⁴⁾ and seizure outcome.^{9,25)} Signal changes with long TR sequences have been seen in 70–100% of cases.

There are other associated features of hippocampal sclerosis on MR imaging that should be used

with caution as they may reduce the specificity of the observation. The most frequent pitfall is that of a dilated temporal horn that is not always associated with atrophy (Fig. 3). Bronen and Cheung⁶⁾ found asymmetry of temporal horns in 68% of normal volunteers. The presence of temporal lobe atrophy or white matter changes ipsilateral to the dilated horn are inconsistent findings. In fact, normal subjects not infrequently have mild enlargement of the right temporal lobe on visual inspection.⁸⁾ Other interesting findings that are usually present in clear cases of hippocampal atrophy include atrophy of the ipsilateral fornix, of the white matter bundle in the parahippocampal gyrus, and of the mamillary bodies.

Hippocampal sclerosis occurs bilaterally in 20–80% of cases based on autopsy and imaging studies.^{2,27,37,40)} In the majority of these, one side is more affected than the other. True bilateral symmetrical hippocampal sclerosis occurs only in approximately 10% of patients with mesial temporal epilepsy. In this latter group, epilepsy surgery has a less favorable outcome.

It is important to note that hippocampal atrophy and signal changes occur also in asymptomatic subjects, extrahippocampal pathology, Alzheimer's disease, aging, and schizophrenia. Therefore, the MR imaging findings have to be interpreted in the light of other neurophysiological and clinical findings. This pertains particularly to dual pathology, where hippocampal sclerosis coexists with some other potentially epileptogenic pathology.

Space-occupying Lesions in the Temporal Lobe

A number of other space-occupying lesions may cause temporal lobe epilepsy and constitute 10–20% of cases of temporal lobe epilepsy. Although most of these lesions have a predisposition for the temporal lobe, they may present with epilepsy in other regions of the brain with exactly the same imaging characteristics. Thus, the following description also applies to epileptogenic lesions outside the temporal lobe. Surgical treatment of most of these lesions is associated with good outcome of up to 80–90% seizure freedom.^{1,5,22,32,42,44)} The sensitivity of MR imaging in detecting these lesions approaches 100% with a specificity of 87% in surgical series.^{11,26)} The ability of experienced observers to accurately predict pathological category approaches 88% in ideal circumstances.¹¹⁾ As seizures are a presenting symptom, by necessity these lesions are in or adjacent to the cortex.

Brain tumors are responsible for 2–4% of epilep-

sies in adult population and 10–20% of medically intractable epilepsy. Seizures are the presenting symptom in 60–76% of patients with tumors. In a study at the Montreal Neurological Institute, seizures occurred in 92% of oligodendrogliomas. Five percent of all epilepsies are caused by arteriovenous malformations (AVMs) and MR imaging is a sensitive technique in detecting these lesions even when compared to angiography. In a group of 50 patients with epilepsy and space-occupying lesions, Boon et al.⁵⁾ found 70% were neoplastic. Of these 54% were in the temporal lobe, consistent with previous reports of the predilection of these lesions for the temporal lobe.^{10,19,44)} The majority of the space-occupying lesions were low grade gliomas (74–85%),^{5,42)} followed by vascular malformations (14–20%), hamartomas (8%), gangliogliomas (5–6%), oligodendrogliomas (2–4%), and granulomas.⁵⁾

Differential Diagnosis

The differentiation of malignant tumors from the remainder of the group is usually easy due to associated edema and contrast enhancement (Table 1).¹⁸⁾ In contrast, low grade gliomas, gangliogliomas, dysembryoplastic neuroepithelial tumors (DNETs), and some vascular malformations have many shared characteristics, making an accurate histological diagnosis from MR imaging more difficult. These include absence or mild associated tissue edema and mass effect, well-circumscribed margins, the presence of calcification and breakdown products of hemoglobin, and the low signal intensity on T1WI and high signal intensity on T2WI. Despite this, certain constellations of characteristics may suggest a histological diagnosis. It is important to emphasize that there is a significant amount of overlap in appearance between different histological entities and that an accurate histological diagnosis based on MR appearance may not be always possible.

The differentiation of vascular malformations from neoplasms, hamartomas, and MCDs is usually possible due to the presence of serpiginous or curvilinear signal flow voids on T1WI and T2WI in high flow lesions such as AVMs. This is usually interspersed with heterogeneous signal from calcium, hemorrhage, and gliosis. Cavernous angiomas have a characteristic reticulated hyperintense central focus with a rim of signal void (due to paramagnetic hemosiderin) on T1WI, distinguishing them from other lesions. There is usually little edema associated with these lesions.¹⁰⁾ A caveat to this description is that partially thrombosed AVMs or hemorrhagic metastases⁴⁵⁾ may occasionally have a similar ap-

Table 1 Differential diagnosis of low grade tumors and dysembryoplastic neuroepithelial tumors (DNET)

	MR imaging						CT		Age	Sex	Position
	T1WI	T2WI	Edema	Gadolinium	Cyst	Calcification	Hemorrhage	Other features	Non-contrast	Contrast enhancement	
Oligodendrogliomas	hypo/iso-intense to gray matter	hyper-intense	+	+	+	+(20%)	+(40-60%)	may have subarachnoid seeding	hypo/iso-dense	minor in 75%	septal FL/TL/ cerebellum
Gangliogliomas	iso/hyper/hypo-intense if cystic, poor margins	hyper-intense	0/+	+	+	+(38-50%)	0/+	avascular, cyst higher signal than CSF on PDWI	hypo/iso-dense	minor, correlated with prognosis	TL/FL/ cerebellum/ anterior third ventricle
Low grade gliomas	iso/hypo-intense	hyper-intense	0/+	little or none		0/+	0	poorly circumscribed deep white matter	hypo/iso-dense	none/little	any age supratentorial
DNET	hypo/mixed intense (30%), lobular tumor margins (80%)	hyper-intense	0	mild (20%)	none	+(23%)	none	gyral or nodular configuration, blurring of gray-white junction, extends from gray matter	hypodense, some calcification in 23-30%	none/little, focal contrast enhancement in 18%	F = M TL/FL/PL

CSF: cerebrospinal fluid, CT: computed tomography, FL: frontal lobe, MR: magnetic resonance, PDWI: proton density-weighted images, PL: parietal lobe, TL: temporal lobe, T1WI: T₁-weighted images, T2WI: T₂-weighted images. 0/+ : minimal/rare, + : mild/occasional, ++ : moderate or common.

pearance.

The differentiation of low grade astrocytomas, DNETs, oligodendrogliomas, and gangliogliomas is more difficult but certain clues may be useful (Table 1). DNETs and gangliogliomas occur predominantly in the first two decades of life, whereas oligodendrogliomas have a peak incidence in the fifth decade. There is male preponderance for oligodendrogliomas and female preponderance for gangliogliomas. Gangliogliomas may have poorly defined margins. It is not uncommon for oligodendrogliomas and gangliogliomas to have patchy enhancement with gadolinium, or mild amounts of associated tissue edema. DNETs are the least likely to have associated edema or enhancement. Cystic components are most commonly seen in gangliogliomas and less frequently oligodendrogliomas. Calcification is more frequently seen in oligodendrogliomas, closely followed by gangliogliomas. Together with hemorrhage, this gives oligodendrogliomas a very heterogeneous MR signal profile. Gangliogliomas may have a higher signal intensity than water on proton diffusion-weighted images. Low grade astrocytomas are usually positioned deeper and are infiltrative. A gyral or nodular configuration associated with blurring of the gray-white matter junction is said to be characteristic of DNETs.²⁹ Other characteristics that may help distinguish DNETs from gliomas include entirely intracortical location, frequent association with adjacent areas of cortical dysplasia,^{17,29} and clear demarcation on T2WI without associated edema.²⁹

Tumors

Astrocytomas (Fig. 4): Low grade astrocytomas are usually more epileptogenic than high grade ones (61% of gliomas that present with seizures are low grade).²¹ In epilepsy surgery series, these have a predilection for the temporal lobes (63%).²¹ They have an indolent course (median duration of symptoms 17 yrs).²¹ These tumors tend to be poorly circumscribed with little mass effect, edema, or contrast enhancement. Calcification may be seen in 20% on computed tomography and less commonly with MR imaging. Astrocytomas have low signal intensity in comparison to gray matter on T1WI. In about 25% of cases, there is hemosiderin staining (very low signal on T1WI).²¹ There is usually little mass effect, vasogenic edema, or inhomogeneity.

Pilocytic astrocytomas are a special variant and are as common as low grade diffuse astrocytomas in epilepsy surgery series. These are benign tumors that do not infiltrate adjacent tissue, are sharply demarcated, and may calcify and form cysts. En-

Fig. 4 Solid smoothly margined low grade glioma in the left insular region on T₁-weighted image (T1WI) (left), with increased signal intensity on fluid-attenuated inversion recovery image (center) and circumscribed area of contrast enhancement on sagittal T1WI with gadolinium (right).

Fig. 5 Oligodendroglioma appearing as a coarsely heterogeneous signal intensity on T₁-weighted (T1WI) (upper left) and fluid-attenuated inversion recovery (lower left) images with cyst formation, and calcification (the less hypointense signal region) on coronal (upper left) and sagittal (lower right) T1WI. Ring-like contrast enhancement is seen with gadolinium (upper right).

hancement is a common feature of this tumor. They usually occur in the diencephalon, optic nerve, and cerebellar hemispheres where they do not produce seizures.

Pleomorphic xanthoastrocytomas are low grade cystic benign tumors that have a predilection for the temporal lobes. These are superficially or peripherally located, partially cystic masses, being isointense to gray matter on T1WI, and mildly hyperintense on T2WI. Enhancement of the solid portions may occur with gadolinium. Calcification is infrequent.

Oligodendrogliomas (Fig. 5): Oligodendrogliomas, although comprising 4–7% of intracranial tumors, are disproportionately represented in epilepsy surgical series. They are frequently calcified (40–60%).²³⁾ Oligodendrogliomas are not uncommonly mixed tumors containing astrocytic components. As with all gliomas, these tumors are hypo/isointense on T1WI and hyperintense on T2WI. They are often heterogeneous in appearance due to the presence of calcification, hemorrhage, or a cystic component (less common). Therefore, there may be patchy enhancement with gadolinium in half of cases. Edema is rare. A tumor blush on angiography is linked to aggression of the tumor.³⁹⁾

Gangliogliomas (Fig. 6): These most commonly occur in children (60–80% in <30 yrs²³⁾). Gangliogliomas have a predilection for the temporal lobes,¹³⁾ and although infrequent in the general population, they are not an uncommon cause for seizures. These are hypo/iso/hyperintense on T1WI (depending on degree of cyst formation) and hyperintense on T2WI. They are cystic lesions in 38–50% of cases,^{13,23)} which may be heterogeneous

Fig. 6 Cystic ganglioglioma with isointense margin on T₁-weighted image (T1WI) (upper left) and increased signal intensity in the cyst on T₂-weighted image (T2WI) (upper right). There is some hemorrhage at the lower margin seen with increased signal intensity on T1WI (upper left, lower right) and hypointensity on T2WI (upper right) and fluid-attenuated inversion recovery (lower left) image.

in signal changes. When solid they may have contrast enhancement and calcification. They have an excellent post-surgical seizure prognosis.

DNETs (Fig. 7): These account for 5–8% of resections in epilepsy surgery series.²⁸⁾ Histologically these lesions have both astrocytic and oligodendroglial components and are often associated with areas of cortical dysplasia. DNETs have a predilection for the temporal lobes.^{17,28)} These patients are neurologically normal, have a long history of seizures, and present in childhood. Imaging characteristics are similar to oligodendrogliomas and gangliogliomas with hypointensity on T1WI and hyperintense on T2WI, and variable signal changes on proton density. They are often multicystic in appearance and may have areas of calcification or enhancement. They may be locally multifocal.¹⁷⁾

Other tumors: Metastases comprise the most common supratentorial masses in the adult and are relatively easily distinguished from less aggressive

Fig. 7 Dysembryoplastic neuroepithelial tumor as a superficial lesion on T₁-weighted image (left) associated with gyriform thickening and increased signal intensity on fluid-attenuated inversion recovery image (right).

Fig. 8 Glioblastoma multiforme on T₂-weighted (upper left), fluid-attenuated inversion recovery (upper right), and T₁-weighted (lower right) images. There is a large amount of edema and mass effect, and enhancement with gadolinium (lower left).

space-occupying lesions due to a short history, older age group of patients, and MR characteristics.

Metastases may be solitary in 30–50% of cases²³⁾ and should be differentiated from a glioma. The characteristics include a relatively well-defined mass with moderate edema, and contrast enhancement. Metastases follow blood flow dynamics and usually lodge at the gray-white matter junction due to the small caliber of vessels in this area and thus their predisposition in causing seizures.

Cortical metastases which are most epileptogenic are often associated with minimal edema and hence the necessity of contrast for identification. A difficult differential diagnosis may be from occult vascular malformations.⁴⁵⁾ Multiplicity of lesions and associated edema may be distinguishing features.

Occasionally, meningiomas, neurofibromas, high grade gliomas (Fig. 8), and multiple gliomas (related neurofibromatosis I and II) may give rise to seizures.

Vascular Malformations

Cavernous angiomas (Fig. 9): Cavernous angiomas have an incidence of 0.5% in autopsy studies and may be multiple in 10–40% of cases. They are almost always familial when multiple. MR imaging is very sensitive for detecting these lesions, although it is often difficult to distinguish them from partially thrombosed AVMs. Hemorrhagic metastases may have a similar appearance.⁴⁵⁾ Cavernous angiomas appear as reticulated lesions with an hyperintense central focus of subacute or chronic hemorrhage, with a hypointense rim of hemosiderin (gradient echo and T2WI). Although patients usually have

easily controlled epilepsy, the risk of a clinically significant bleeding is 0.25%¹⁶⁾ to 0.7%⁴³⁾ annually, and is an additional consideration with choice of treatment.

AVMs: AVMs are a collection of arterial to venous shunts without intervening capillaries. Seizures are presumed to occur from a steal phenomenon and ischemia of neighboring cortex or hemorrhage and hemosiderin deposition. Seizures quickly follow hemorrhage as the commonest presenting event. The risk of epilepsy with AVMs is 10–20% and size, a frontal or temporal lobe location, and its proximity to cortex are all risk factors. The MR imaging characteristics include serpiginous flow voids on T1WI and T2WI, a dilated arterial supply, and large draining veins. They have a heterogeneous signal with calcification, hemorrhage, and gliosis.

Occult vascular malformations are not visualized on conventional arteriography and include cavernous hemangiomas, capillary telangiectasia, and thrombosed AVMs. These all have a similar MR appearance with large abnormal vascular spaces surrounded by a gliotic hemosiderin-laden rim, which appears as a dark ring on T2WI. Blood products and gliosis at the center of the nidus are responsible for the high signal seen on T1WI and T2WI.

Venous angiomas, which are considered a normal variant and not usually epileptogenic, are found along ependymal surfaces draining a network of veins which converge into a single large draining vein.

Sturge-Weber syndrome (Fig. 10) is associated with leptomeningeal angiomas. MR imaging shows

Fig. 9 Cavernous angioma with a central hyperintense region with a hypointense ring of hemosiderin on T₁-weighted (left) and fluid-attenuated inversion recovery (center) images. There is no enhancement with gadolinium (right).

Fig. 10 Sturge-Weber syndrome affecting the left hemisphere with atrophy of the underlying cortex on axial (upper left) and sagittal (lower right) T₁-weighted images, and T₂-weighted image (upper right). There is pial enhancement with gadolinium (lower left).

subtle enhancement of the angioma, atrophy of the underlying cortex, and a characteristic tram-track of low signal intensity along the cortical ribbon due to

calcification. There may be enhancement and enlargement of the choroid plexus ipsilaterally. The malformations are classically parieto-occipital and unilateral.

MCDs

MCDs are a wide spectrum of disorders ranging from gross structural disturbances such as tuberous sclerosis and lissencephaly, to microscopic abnormalities such as microdysgenesis. The normal development of the cerebral cortex involves proliferation, differentiation, and migration of cells, and finally cortical organization. Ninety percent of neurons migrate radially from the surface along glial process to the subpial surface. Disorders of neuronal migration occur when this complex process is interrupted (between the seventh and sixteenth weeks of gestation) and is frequently associated with epilepsy. The incidence of developmental abnormalities in the temporal lobe has been quoted between 5.2–7.2%.³⁵⁾

Tuberous sclerosis: Cortical tubers have been classified as tumors and at other times as MCDs. Pathologically, radially oriented columns of dysplastic cells span focal subependymal and subcortical cell deposits. The MR appearance is that of a well-circumscribed area of increased T2WI and decreased T1WI signal intensity located immediately beneath the cortical gray mantle. Frequently, there may be a ray-like projection of increased signal from the tuber to the ventricular surface. Older,

Fig. 11 Polymicrogyria with multiple secondary gyri and areas of right parieto-occipital cortical thickening on axial T₁-weighted (left), axial T₂-weighted (center), and coronal T₁-weighted (right) images.

Fig. 12 Periventricular focal nodular heterotopia on the right on T₁-weighted (left) and fluid-attenuated inversion recovery (center) images, with no enhancement with gadolinium (right).

densely calcified tubers are seen as very low density signal on T1WI.

Focal cortical dysplasia: This term was first used by Taylor and colleagues⁴⁶⁾ as a pathological description of areas of cortex that have lost normal laminar organization and contain giant balloon cells. More commonly though, the cortical dysplasia of Taylor, forme fruste of tuberous sclerosis, and polymicrogyria are considered together as focal cortical dysplasia. The MR appearance varies according to the pathological extent. There may be a subtle area of cortical thickening or a large abnormal cortical cleft lined with polymicrogyric cortex. There may be increased signal of subjacent white matter on T2WI, at times extending to the ventricular surface. There may be increased signal or blurring of the gray-white junction on FLAIR images.

Polymicrogyria (Fig. 11): In polymicrogyria, there is a microscopic and macroscopic surplus of small gyri. These may be separated by sulci or virtually fused. MR imaging shows thickened cortex with blurring of the gray-white junction.

Schizencephaly: Schizencephaly denotes an abnormal cleft extending from the subpial to ependymal surface, usually in the perisylvian region. It is considered with MCDs, as this cleft is frequently lined by dysplastic and polymicrogyric cortex. The syndrome of bilateral perisylvian polymicrogyria described by Kuzniecky and Andermann³⁰⁾ is a variation on this theme, with abnormal clefts of varying

Fig. 13 Double cortex (best seen in the left fronto-central region) on coronal T₁-weighted image.

size continuous with the sylvian fissure, lined by polymicrogyric cortex.

Nodular heterotopia (Fig. 12): This is a collection of gray matter in an abnormal position, commonly subependymally (but also found subcortically),

Fig. 14 Hemimegalencephaly of the right hemisphere with thickened cortex on axial (upper left) and sagittal (lower right) T₁-weighted, axial T₂-weighted (upper right), and spin echo density (lower left) images.

unilateral or bilateral, singular or multiple, or in bands lining the ependymal surface. The subcortical heterotopia extend from the ventricular surface into the white matter, usually with a ray-like projection from the ependymal surface to the base of the heterotopia. The overlying cortex may be abnormal with pachygyria or polymicrogyria. These lesions are usually close in signal intensity to gray matter and do not produce any mass effect or edema, and there is no contrast enhancement.¹²⁾

Laminar heterotopia (Fig. 13): The synonyms of this syndrome include double cortex and band heterotopia. It consists of a zone of laminar heterotopic cortex bound by white matter on either side. The overlying cortex is usually abnormal and pachygyric. It is a relatively uncommon abnormality that is usually fatal in the male. This abnormality may be more appropriately classified as a subset of lissencephalies.

Lissencephaly: This spectrum of abnormalities encompasses deficient formation of gyri and sulci. This spans a severe form known as agyria to pachygyria where densely packed gyri appear broad and flat. In some forms the sylvian fissures are oriented vertically, and their poor formation leads to

a figure-of-eight appearance. The ventricular atria may be dilated and the corpus callosum hypoplastic.

Unilateral hemimegalencephaly (Fig. 14): In these cases, there is unilateral enlargement of a hemisphere with concomitant increase in ventricular size and white matter, with abnormalities in the cortex of pachygyria, polymicrogyria, nodular heterotopic gray, and gliosis. The cortex in the contralateral hemisphere may also be abnormal but to a lesser extent.

Neocortical Sclerosis Secondary to Brain Injury

A variety of insults can result in neocortical sclerosis, which is a uniform response of the brain to injury. Cell death and necrosis from trauma, infection, infarction, and inflammation lead to a typical appearance on MR imaging of atrophy and increased signal consistent with increased tissue water. Hemosiderin deposits may also be seen. Post-traumatic epilepsy is usually associated with penetrating skull injuries and may occur up to a 25-year latent period from the time of injury. Cerebral infarction or hypoxia, although more common in the elderly, can lead to seizures in any age group. Encephalitis leading to neocortical or mesial temporal sclerosis, and parasitic infections such as cysticercosis and tuberculosis are leading causes of seizures worldwide. Cerebritis causes increased signal intensity on proton diffusion-weighted images and T2WI in the subcortical white matter at the gray-white junction, with parenchymal and adjacent meningeal contrast enhancement.

Encephalitis: The etiologies causing encephalitis can be divided into infectious causes, both viral and nonviral (bacterial, mycobacterial, fungal, rickettsial), and noninfectious causes (post-infectious encephalitis, encephalomyelitis, Behçet's disease, vasculitis). Viruses account for approximately 90% of encephalitis cases, and are the major etiologic agents. Herpes simplex virus encephalitis is associated with seizures due to its predisposition for the temporal lobes. The MR imaging evolution of herpes simplex encephalitis includes lesions that may appear as early as 24 hours after symptom onset. These lesions are hyperintense on T2WI and mildly hypointense on T1WI. The appearance of hemorrhage or petechiae would alter this appearance as the hemoglobin is degraded. As with other forms of cerebritis, gyriform, and leptomeningeal and intravascular enhancement are seen in the subacute stage. Chronic lesions are characterized by atrophy and encephalomalacia, with or without calcifications.

Fig. 15 Rasmussen's encephalitis showing atrophy of the left hemisphere predominantly in the frontocentral region on sagittal (upper left) and coronal T₁-weighted (lower right), axial T₂-weighted (upper right), and fluid-attenuated inversion recovery (lower left) images.

Rasmussen's encephalitis: In 1958, Rasmussen described a syndrome of progressive and slowly spreading cortical atrophy, progressive and severe neurologic and intellectual impairment, and seizures (often *epilepsia partialis continua*) in childhood. MR imaging shows progressive unilateral (or bilateral) cortical atrophy and ventriculomegaly and increased white matter signal changes in the chronic stages (Fig. 15). In the acute stage, there may be transient and migratory hyperintense signal foci on long TR images.

Tuberculosis: Cerebritis, as a result of meningeal or hematogenous dissemination, results in parenchymal damage that leads to seizures. Damage to the cortex may be as a result of cerebritis, abscess formation, or tuberculomas. Tuberculomas are isointense on T1WI and of variable signal intensity on T2WI. A hyperintense ring on T1WI, which is hypointense in T2WI together with ring enhancement following contrast administration, is the usual finding.

Neurocysticercosis: Parenchymal cysts are usually associated with seizures and they appear

hypointense or mildly hyperintense on T1WI and iso/hyperintense on T2WI at the gray-white junction or within the cortex. Hyperintensity on T1WI at the center of the cyst is the scolex. There may be surrounding edema with variable contrast enhancement, with the cyst wall hyperintense on T1WI and hypointense on T2WI.

Conclusion

With the advances in characterization of the molecular basis of some genetically inherited epilepsies and with a better understanding of the changes in neurotransmitters and secondary messenger systems that are related to increased epileptogenicity, we may be able to finally combine the paradigms of abnormal structure and function. Development of neuroimaging techniques that allows the study of changes in molecular composition in relation to different brain structures offers not only exciting prospects for diagnosis but also for tailored treatments for different epilepsies. Already glimpses of this future are apparent with MR spectroscopy and new positron emission tomography ligands.

References

- 1) Awad IA, Rosenfeld J, Ahl J, Hahn JF, Lüders H: Intractable epilepsy and structural lesions of the brain: mapping, resection strategies, and seizure outcome. *Epilepsia* 32: 179-186, 1991
- 2) Babb TL, Brown WJ: Pathological findings in epilepsy, in Engel J Jr (ed): *Surgical Treatment of Epilepsies*. New York, Raven Press, 1987, pp 511-539
- 3) Babb TL, Ying Z, Hadam J, Penrod C: Glutamate receptor mechanisms in human epileptic dysplastic cortex. *Epilepsy Res* 32: 24-33, 1998
- 4) Bergin PS, Fish DR, Shorvon SD, Oatridge A, de Souza NM, Bydder GM: Magnetic resonance imaging in partial epilepsy: additional abnormalities shown with the fluid attenuated inversion recovery (FLAIR) pulse sequence. *J Neurol Neurosurg Psychiatry* 58: 439-443, 1995
- 5) Boon PA, Williamson PD, Fried I, Spencer DD, Novelly RA, Spencer SS, Mattson RH: Intracranial, intraaxial, space-occupying lesions in patients with intractable partial seizures: an anatomoclinical, neuropsychological, and surgical correlation. *Epilepsia* 32: 467-476, 1991
- 6) Bronen RA, Cheung G: MRI of the normal hippocampus. *Magn Reson Imaging* 9: 497-500, 1991
- 7) Bronen RA, Cheung G: Relationship of hippocampus and amygdala to coronal MRI landmarks. *Magn Reson Imaging* 9: 449-457, 1991
- 8) Bronen RA, Cheung G: MRI of the temporal lobe: normal variations, with special reference toward

- epilepsy. *Magn Reson Imaging* 9: 501-507, 1991
- 9) Bronen RA, Fulbright RK, King D, Kim JH, Spencer SS, Spencer DD, Lange RC: Qualitative MR imaging of refractory temporal lobe epilepsy requiring surgery: correlation with pathology and seizure outcome after surgery. *AJR Am J Roentgenol* 169: 875-882, 1997
 - 10) Bronen RA, Fulbright RK, Spencer DD, Spencer SS, Kim JH, Lange RC: MR characteristics of neoplasms and vascular malformations associated with epilepsy. *Magn Reson Imaging* 13: 1153-1162, 1995
 - 11) Bronen RA, Fulbright RK, Spencer DD, Spencer SS, Kim JH, Lange RC, Sutilla C: Refractory epilepsy: comparison of MR imaging, CT, and histopathologic findings in 117 patients. *Radiology* 201: 97-105, 1996
 - 12) Bronen RA, Vives KP, Kim JH, Fulbright RK, Spencer SS, Spencer DD: Focal cortical dysplasia of Taylor, balloon cell subtype: MR differentiation from low-grade tumors. *AJNR Am J Neuroradiol* 18: 1141-1151, 1997
 - 13) Castillo M, Davis PC, Yoshii T, Hoffman JC: Intracranial ganglioglioma: MR, CT, and clinical findings in 18 patients. *AJNR Am J Neuroradiol* 11: 109-114, 1990
 - 14) Chelune GJ, Comair YG, Najm IM, Ruggieri P, Lüders HO: MRI volumetrics and memory function in patients with intractable temporal lobe epilepsy. *Epilepsia* 36: 147, 1995
 - 15) Cheon JE, Chang KH, Kim HD, Han MH, Hong SH, Seong SO, Kim IO, Lee SG, Hwang YS, Kim HJ: MR of hippocampal sclerosis: comparison of qualitative and quantitative assessments. *AJNR Am J Neuroradiol* 19: 465-468, 1998
 - 16) Curling OD, Kelly DL, Elster AD, Craven TE: An analysis of the natural history of cavernous angiomas. *J Neurosurg* 75: 702-708, 1991
 - 17) Dumas-Duport C, Scheithauer BW, Chodkiewicz JP, Laws ER Jr, Vedrenne C: Dysembryoplastic neuroepithelial tumor: a surgically curable tumor of young patients with intractable partial seizures. Report of thirty-nine cases. *Neurosurgery* 23: 545-556, 1988
 - 18) Destian S, Sze G, Krol G, Zimmerman RD, Deck MD: MR imaging of hemorrhagic intracranial neoplasms. *AJR Am J Roentgenol* 152: 137-144, 1989
 - 19) Falconer M, Cavanagh J: Clinicopathological considerations of temporal lobe epilepsy due to small focal lesions. *Brain* 87: 483-504, 1959
 - 20) Ferone E, Pierallini A, Bonamini M, Bozzao A, Prosperi D, Giallonardo AT, Fantozzi LM: [Assessment with magnetic resonance with Turbo-FLAIR sequences and volumetric analysis of the hippocampal region in drug-resistant temporal epilepsy]. *Radiol Med (Torino)* 95: 456-460, 1998 (Ital, with Eng abstract)
 - 21) Fried I, Kim JH, Spencer DD: Limbic and neocortical gliomas associated with intractable seizures: a distinct clinicopathological group. *Neurosurgery* 34: 815-823; discussion 823-824, 1994
 - 22) Goldring S: Pediatric epilepsy surgery. *Epilepsia* 28 (Suppl 1): S82-102, 1987 (review)
 - 23) Grossman CB: Neoplasms of the brain, in: *Magnetic Resonance Imaging and Computed Tomography of Head and Spine*. Baltimore, Williams & Wilkins, 1996, pp 67-103
 - 24) Jack CR Jr, Rydberg CH, Krecke KN, Trenerry MR, Parisi JE, Rydberg JN, Cascino GD, Riederer SJ: Medial temporal sclerosis: diagnosis with fluid-attenuated inversion-recovery versus spin-echo MR imaging. *Radiology* 199: 367-373, 1996
 - 25) Jack CR Jr, Sharbrough FW, Cascino GD, Hirschorn KA, O'Brien PC, Marsh WR: Magnetic resonance image-based hippocampal volumetry: correlation with outcome after temporal lobectomy. *Ann Neurol* 31: 138-146, 1992
 - 26) Jackson GD: New techniques in magnetic resonance and epilepsy. *Epilepsia* 35 (Suppl 6): 2-13, 1994
 - 27) King D, Spencer SS, McCarthy G, Luby M, Spencer DD: Bilateral hippocampal atrophy in medial temporal lobe epilepsy. *Epilepsia* 36: 905-910, 1995
 - 28) Kuroiwa T, Bergey GK, Rothman MI, Zoarski GH, Wolf A, Zagardo MT, Kristt DA, Hudson LP, Krumholz A, Barry E: Radiologic appearance of the dysembryoplastic neuroepithelial tumor. *Radiology* 197: 233-238, 1995
 - 29) Kuroiwa T, Kishikawa T, Kato A, Ueno M, Kudo S, Tabuchi K: Dysembryoplastic neuroepithelial tumors: MR findings. *J Comput Assist Tomogr* 18: 352-356, 1994
 - 30) Kuzniecky R, Andermann F: The congenital bilateral perisylvian syndrome: imaging findings in a multicenter study. CBPS Study Group. *AJNR Am J Neuroradiol* 15: 139-144, 1994
 - 31) Kuzniecky R, Burgard S, Faught E, Morawetz R, Bartolucci A: Predictive value of magnetic resonance imaging in temporal lobe epilepsy surgery. *Arch Neurol* 50: 65-69, 1993
 - 32) Laws ER Jr, Taylor WF, Clifton MB, Okazaki H: Neurosurgical management of low-grade astrocytoma of the cerebral hemispheres. *J Neurosurg* 61: 665-673, 1984
 - 33) Lee BC, Schmidt RE, Hatfield GA, Bourgeois B, Park TS: MRI of focal cortical dysplasia. *Neuroradiology* 40: 675-683, 1998
 - 34) Lee N, Tien RD, Lewis DV, Friedman AH, Felsberg GJ, Crain B, Hulette C, Osumi AK, Smith JS, Van Landingham KE: Fast spin-echo, magnetic resonance imaging-measured hippocampal volume: correlation with neuronal density in anterior temporal lobectomy patients. *Epilepsia* 36: 899-904, 1995
 - 35) Lehericy S, Dormont D, Semah F, Clemenceau S, Granat O, Marsault C, Baulac M: Developmental abnormalities of the medial temporal lobe in patients with temporal lobe epilepsy. *AJNR Am J Neuroradiol* 16: 617-626, 1995
 - 36) Lencz T, McCarthy G, Bronen RA, Scott TM, Insigni JA, Sass KJ, Novelty RA, Kim JH, Spencer DD: Quantitative magnetic resonance imaging in temporal lobe epilepsy: relationship to neuropathology and neuropsychological function. *Ann Neurol* 31:

- 629-637, 1992
- 37) Margerison JH, Corsellis JAN: Epilepsy and the temporal lobes. *Brain* 89: 499-530, 1966
 - 38) Mohamed A, Wyllie E, Najm I, Ruggieri P, Kotagal P, Bingaman W: The semiological features and EEG characteristics of children and adolescents with mesial temporal sclerosis (MTS) and temporal lobe epilepsy (TLE) due to MTS. *Neurology* 52: A106-A107, 1999
 - 39) Mork SJ, Lindegaard KF, Halvorsen TB, Lehmann EH, Solgaard T, Hatlevoll R, Harvei S, Ganz J: Oligodendroglioma: incidence and biological behavior in a defined population. *J Neurosurg* 63: 881-889, 1985
 - 40) Mouritzen-Dam A: Hippocampal neuronal loss in epilepsy and after experimental seizures. *Acta Neurol Scand* 66: 601-642, 1982
 - 41) Najm IM, Ying Z, Mohamed A, La Presto E, Wyllie E, Kotagal P, Bingaman W, Foldvary N, Morris HH, Lüders HO: NMDA receptor 2A/B subtype differential expression in human cortical dysplasia: Correlation with in situ epileptogenicity. *Epilepsia* 39 (Suppl 6): 24, 1998
 - 42) Rich KM, Goldring S, Gado M: Computed tomography in chronic seizure disorder caused by glioma. *Arch Neurol* 42: 26-27, 1985
 - 43) Robinson JR, Awad I, Little JR: Natural history of cavernous angioma. *J Neurosurg* 75: 709-714, 1991
 - 44) Spencer DD, Spencer SS, Mattson RH, Williamson PD: Intracerebral masses in patients with intractable partial epilepsy. *Neurology* 34: 432-436, 1984
 - 45) Sze G, Krol G, Olsen WL, Harper PS, Galicich JH, Heier LA, Zimmerman RD, Deck MD: Hemorrhagic neoplasms: MR mimics of occult vascular malformations. *AJR Am J Roentgenol* 149: 1223-1230, 1987
 - 46) Taylor DC, Falconer MA, Bruton CJ, Corsellis JA: Focal dysplasia of the cerebral cortex in epilepsy. *J Neurol Neurosurg Psychiatry* 34: 369-387, 1971
 - 47) Van Paesschen W, Revesz T, Duncan JS, King MD, Connelly A: Quantitative neuropathology and quantitative magnetic resonance imaging of the hippocampus in temporal lobe epilepsy. *Ann Neurol* 42: 756-766, 1997
 - 48) Watson C, Jack CR Jr, Cendes F: Volumetric magnetic resonance imaging. Clinical applications and contributions to the understanding of temporal lobe epilepsy. *Arch Neurol* 54: 1521-1531, 1997 (review)

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