Imaging the Patient with Epilepsy or Seizures

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Abstract

Neuroimaging plays an ever-increasing role in the workup of patients presenting with seizures, epilepsy, and, in particular in patients with medically refractory epilepsy. Abnormalities that may be amenable to surgery can be present in the latter group in up to 80% and thus the radiologist plays an important role in the interdisciplinary management of this patient population. In the current article, we are describing imaging protocols as well as typical pathologies and their imaging correlated to raise awareness of the spectrum of disorders typically encountered.

Keywords

Epilepsy · MRI · Hippocampal sclerosis · Malformation of cortical development

Learning Objective

- To understand the role of the radiologist in the diagnosis and management of patients with epilepsy.
- To describe the importance of a specific MR protocol in epilepsy patients, particularly if they are refractory to antiepileptic drugs.
- To describe typical pathologies and their imaging correlated to raise awareness of the spectrum of disorders typically encountered in epilepsy patients.

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It is estimated that up to 8–10% of the general population will experience a seizure during their lifetime [1]. Seizures may be defined as acute symptomatic or unprovoked. While acute symptomatic seizures occur at the time or near to a systematic insult, such cerebrovascular or traumatic brain injury, drug withdrawal, fever, sleep deprivation or metabolic insults, unprovoked seizures occurs without a precipitation factor [2]. Seizures can be focal or generalized [3]. Often, the initial imaging modality to study a patient with the first-ever seizures is an unenhanced CT head scan to exclude acute medical emergencies that can put the patient's life at risk, prior to a more extensive workup depending on clinical history and presentation. Potential epileptogenic lesions have been detected in about 30% of patients with first-ever seizures, being stroke, post-traumatic and neoplastic lesions the most common finding. Patients with epileptogenic lesions have a higher risk or seizure recurrence and therefore to develop epilepsy [4].

Approximately five millions of the general population will be diagnosed with epilepsy each year [5]. Epilepsy is defined by ILAE (International League Against Epilepsy) as at least two unprovoked (or reflex) seizures occurring >24 h apart [6], and there are several epilepsy types: focal epilepsy, generalized epilepsy, combined generalized and focal epilepsy, and also an unknown epilepsy group. The etiology of epilepsy can be classified in structural, genetic, infectious, metabolic, immune, and unknown [3]. Patients with focal epilepsy are more susceptible to have an epileptogenic lesion that irritates the brain and are more commonly present in structural etiology. This epileptogenic lesion can be identified on structural neuroimaging. Structural etiologies may be acquired such as stroke, trauma, and infection, or genetic such as many malformations of cortical development.

The vast majority of patients diagnosed with epilepsy can be treated satisfactorily with antiepileptic drugs. However, 0.4% of the general population will have recurrent and unprovoked seizures that do not respond to medication. These patients, defined as drug-resistant epilepsy patients are

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potentially treatable with surgery, and surgical intervention is an appropriate consideration for 3% of people who develop epilepsy [6].

10.1 Image Indication and Epilepsy Dedicated MR Protocol

Indication for image evaluation in patients with epilepsy can be divide in four clinical scenarios: (1) evaluation of first-ever seizure when CT head usually is the first image modality; (2) status epilepticus, that should be evaluated by CT head in the emergency department including CT perfusion if it is available. MR exam should be indicated if the etiology remains unknown or the status is not controlled. (3) in epilepsy patients, ILAE stablish that all epilepsy patient need to have a neuroimage study, however it is strongly recommended to perform an MRI exam in these situations: Onset of partial seizures at any age, onset of generalized or unclassified seizures in the first year of life or in adulthood, evidence of a fixed deficit on neurological or neuropsychological examination, difficulty obtaining seizure control with first-line antiepileptic drugs (AED) and loss of seizure control, or change in the pattern of seizure [7]. (4) Finally, the last clinical scenario is when the epilepsy patients are AED resistant. In this case, the patients should be evaluated as possible candidates for surgical treatment.

In this chapter, we will focus on neuroimaging in this epilepsy patient population, as structural imaging will find a large proportion of abnormalities reaching up to 85% of patients. Lesions that are typically involved in medication refractory epilepsy are: mesial temporal lobe sclerosis (MTS) (primary or secondary to a long-standing seizure disorder), malformations of cortical development, certain epileptogenic tumors (e.g., dysembryoplastic neuroepithelial tumors (DNET), low grade temporal lobe glioma, or ganglioglioma), temporal lobe encephaloceles, vascular malformations, trauma, remote infection, and certain phakomatoses. Imaging findings in some of these conditions will be subtle which necessitates both a dedicated imaging protocol (as compared to a standard MR) and an "expert" experience in reading these types of scans. In a landmark study of von Oertzen et al. [8], the sensitivity of "non-expert" reports of standard MRI reports for focal lesions was 39%, while sensitivity of "expert" reports of standard MRI increased to 50%. "Expert" reports of epilepsy dedicated MRI further increased the sensitivity in detecting subtle lesions to 91%. Dedicated MRI showed focal lesions in 85% of patients with "non-lesional" standard MRI. Neuropathological diagnoses were predicted correctly in 22% of "non-expert" standard MRI reports but by 89% of dedicated MRI reports. Thus, the combination of dedicated MRI protocols and specialized radiologists trained in evaluating patients with medication refractory seizures increases significantly the sensitivity of MRI in this subgroup of patients. A multidisciplinary approach that involves close communication between epilepsy neurologist, neuroradiology, EEG, nuclear medicine, neuropsychology, and neurosurgery is an important feature of modern management of the patient with seizures.

The necessity of expert MR reading with a dedicated imaging protocol is further highlighted by the fact that post-surgical seizure freedom is achieved significantly more often when a circumscribed, respectable epileptogenic lesion can be identified on MRI preoperatively compared to patients that are rated non-lesional [9]. As pointed out by Wellmer et al. in 2013 [10], the possible reasons for undetected epileptic lesions in standard outpatient MRI are insufficient clinical information from the referring clinician, routine MR protocols not optimized for the spectrum of epileptogenic lesions, and unfamiliarity with the spectrum of epileptogenic lesions. Wellmer pointed out that "because even the best focus hypothesis and most profound knowledge of epileptogenic lesions do not permit the detection of lesions when they are invisible on the MRI scan, the starting point for any improvement of outpatient MRI diagnostics should be defining an MRI protocol that is adjusted to common epileptogenic lesions."

Several recommendations for dedicated MR protocols in drug-resistant epilepsy patients have been published elsewhere, however, practices for the use of MRI are variable worldwide and may not harness the full potential of the MR to detect subtle epileptogenic lesions. In a recent consensus report from the International League Against Epilepsy Neuroimaging Task Force, Bernasconi et al. identified a set of sequences, with three-dimensional acquisitions at its core, the harmonized neuroimaging of epilepsy structural sequences—HARNESS-MRI protocol. As these sequences are available on most MR scanners, the HARNESS-MRI protocol is generalizable, regardless of the clinical setting and country [11]. Basically, the HARNESS-MRI protocol consists in these 3 core sequences: high resolution 3D T1-weighted MRI MPRAGE, with isotropic millimetric voxel resolution (voxel size, 1 × 1 × 1 mm), high resolution 3D FLAIR (named CUBE, VISTA or SPACE, depending on the MR vendor) with isotropic millimetric voxel resolution (voxel size, 1 × 1 × 1 mm), and high in plane resolution 2D coronal T2-weighted image acquired perpendicular to the long axis of the hippocampus (Fig. 10.1).

Wellmer et al. [10] reported the prevalence of epileptogenic lesions among 2740 patients and the following pathologies were found: mesial temporal lobe sclerosis (32%), tumors (including low and high grade tumors as well as malformative tumors and benign epilepsy associated tumors) in approximately 17% of patients, cortical dysplasias in 11%, glial scars (including post-traumatic, post-ischemic, post-hemorrhagic, postinfectious/abscess, ulegyria, and postsur-

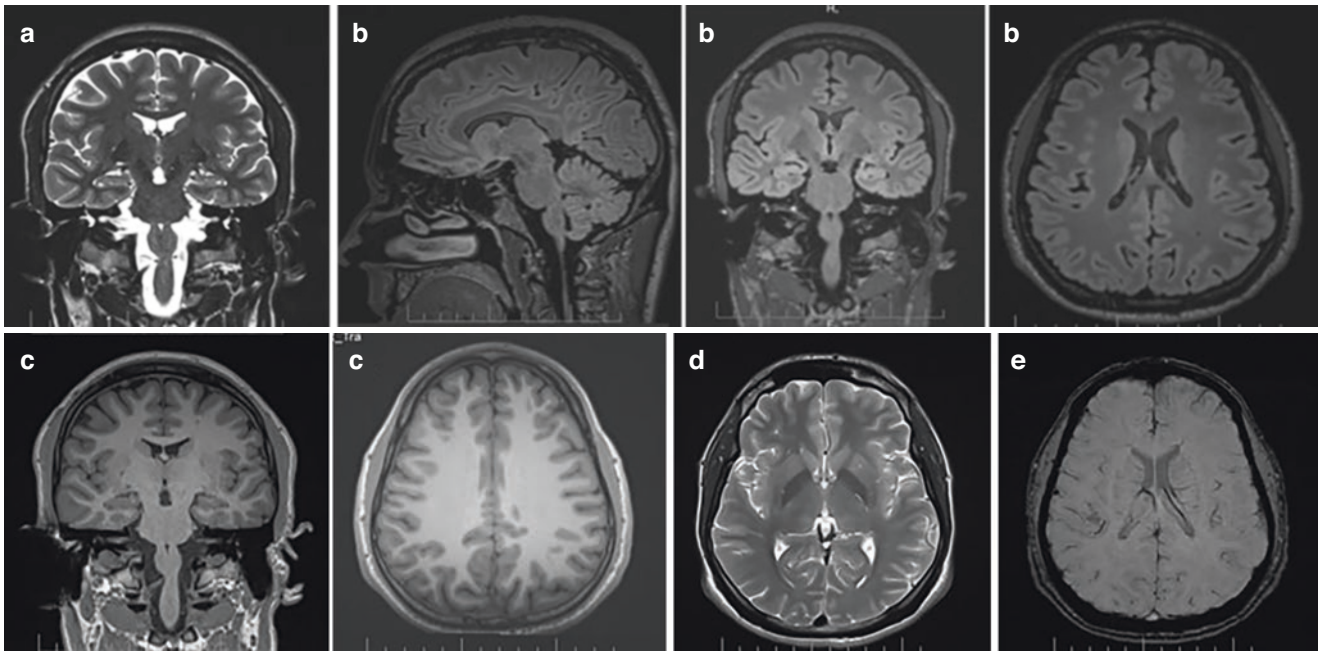

Fig. 10.1 MRI epilepsy protocol using hardness sequences: (**a**) T2 coronal perpendicular to log axis of the hippocampus with 2–3 mm of slices thickening, (**b**) 3DFLAIR acquired in sagittal (1 mm slice thickening) and posterior coronal and axial reconstruction, and (**c**) 3DMPRAGE T1 acquired in coronal (1 mm slice thickening). Other optional sequences: (**d**) T2 axial and (**e**) SWI

gical scars) in 11%, vascular diseases (cavernoma AVM, pial angiomatosis) in 5%, malformations of cortical development including nodular heterotopia, subcortical band heterotopia, polymicrogyria, lissencephaly, pachygyria, agenesis of corpus callosum, craniocephalic malformations, hemiatrophy, lobar dysgenesis, hemimegaloencephaly or hamartomas in 3%, and sequelae of encephalitis in 1% while in approximately 20% no lesion could be detected.

Lesion location—presumably related to the different epileptogenic potential in different brain regions—demonstrates preponderance for the temporal lobes (60%) followed by the frontal lobe (20%), the parietal lobe (10%) the periventricular white matter (5%) and the occipital lobe (5%).

In our own series [12]–being a tertiary epilepsy center, we recently reviewed 738 patients evaluated over a 13-year period in dedicated multidisciplinary epilepsy rounds and found mesiotemporal sclerosis in 132 (18%) of patients with 20 bilateral cases; concomitant mesiotemporal sclerosis with dual pathology in 64 (9%); encephalomalacia and gliosisin 79 (10%); focal cortical dysplasia in 47(6%); isolated enlargement of the amygdala in 40 (5%); tumors in 35 (5%) (including 18 DNET, 11 low-grade gliomas, 3 ganglioglioma, 2 pleomorphic xanthoastrocytomas, 1 choroid plexus papilloma within the choroid fissure); cavernomas is 22 (3%), polymicrogyria in 14 (2%); and periventricular nodular heterotopic gray matter in 13 (2%). Rarer pathologies included subcortical nodular heterotopic gray matter, band heterotopia, ulegyria, perinatal hypoxic gliosis; temporal lobe encephaloceles, cortical siderosis, tuberous sclerosis; Rasmussen's encephalitis; neurocysticercosis, and closed-lip schizencephaly. Exceedingly rare pathologies were pachygyria, hypothalamic hamartoma, Dandy-Walker variant, Dyke-Davidoff-Masson, diffuse axonal injury with cortical hemorrhage, hemimegalencephaly, limbic encephalitis, neurofibromatosis type I, and meningioangiomatosis.

The sensibility of the MR to detect abnormalities in temporal lobe epilepsy is about 90–97% [13]; however, this sensitivity drops in neocortical or extratemporal epilepsy, due to subtle epileptogenic abnormalities such as focal cortical dysplasia. In these cases, when the MR exam is negative, (no epileptogenic lesion detected), the use of quantitative imaging, or post-processing analysis such as voxel-based or surface-based machine-learning algorithm can increase the detection of subtle focal cortical dysplasia [14] Fig. 10.2.

In the future, the use of even higher field strengths (7 T) in clinical practice may increase the detection rate of epileptogenic substrates [15].

In presurgical evaluation, functional MRI (fMRI) can map eloquent cortex and provide information regarding language lateralization [16] Fig. 10.3, and the use of diffusion tensor imaging (DTI) and tractography may help to avoid injury to the optic radiation during temporal lobe resection [17].

Radionuclide imaging can add useful information in selected cases. Subtraction of ictal and interictal SPECT co-registered to MRI (SISCOM) can show a seizure–induced hyperperfusion (Fig. 10.4), whereas ^{18}FDG–PET and PET co-registered to MR may show hypometabolism in the seizure onset zone. This is particularly useful in lateralization of temporal lobe epilepsy in the MR negative patient [18].

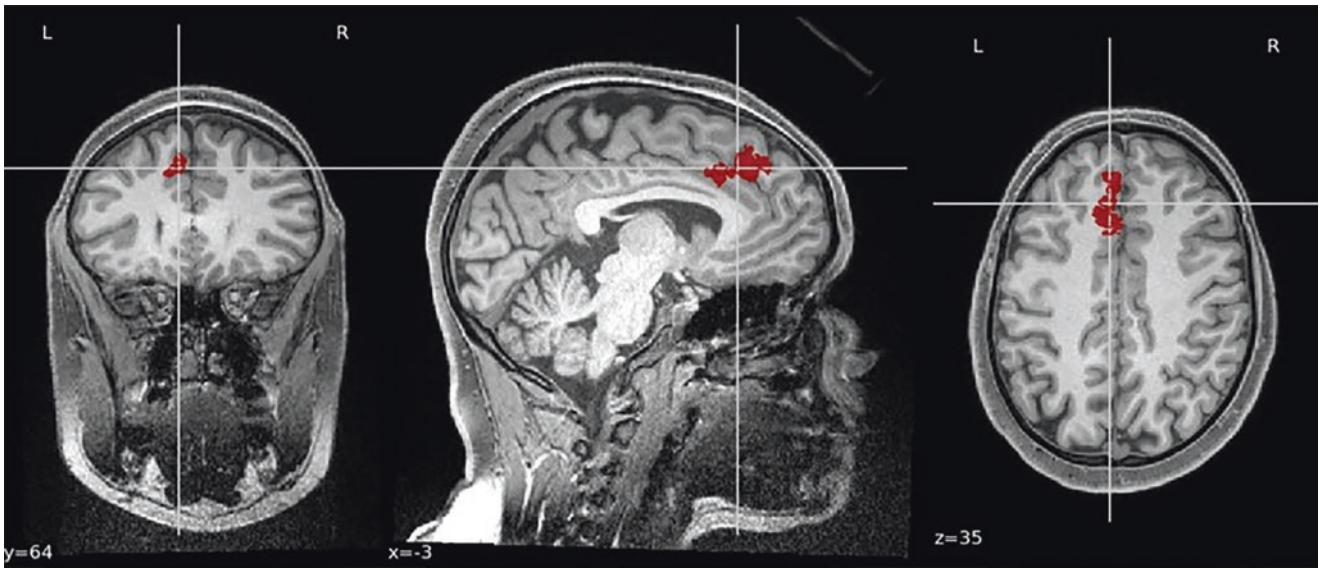

Fig. 10.2 Surface-based machine-learning algorithm (MELD-project) showing an abnormal cortical area in the left superior frontal gyrus in a patient with neocortical epilepsy and previous MR negative. https://meldproject.github.io//studies/MELD_FCD/

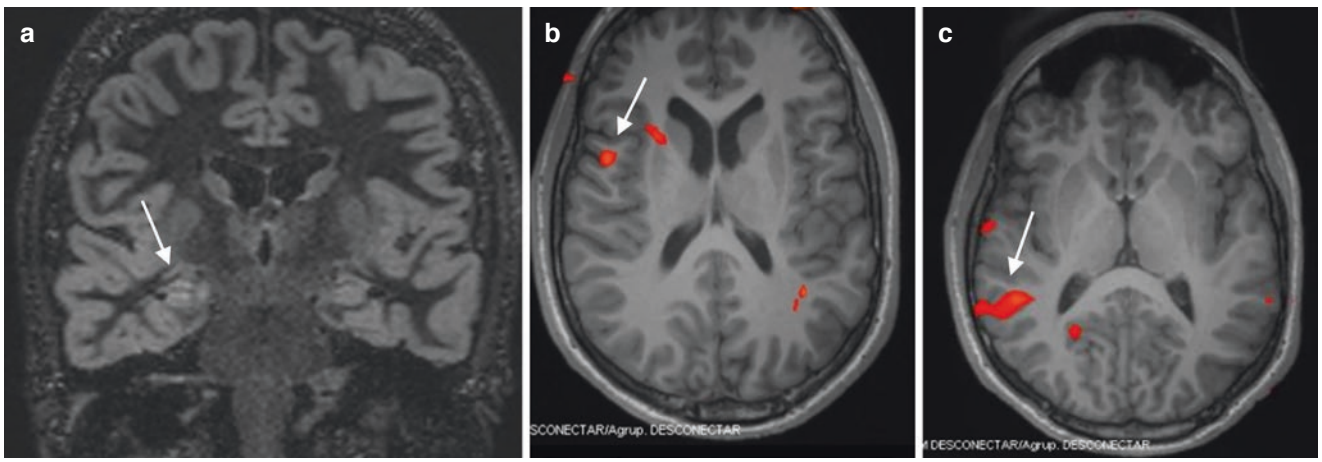

Fig. 10.3 Epilepsy patient with temporal lobe epilepsy and aphasia during the seizures. (**a**) Coronal FLAIR shows right temporal mesial sclerosis (arrow), (**b**) language fMRI with word naming paradigm demonstrates activation in the right inferior frontal gyrus (arrow). (**c**) Language MR with an auditive comprehension paradigm test demonstrating activation in the right posterior temporal gyrus (arrow). The language fMRI indicates that the language function is in the right hemisphere

Key Point

- In drug-resistant epilepsy patients, and patients with focal epilepsy, a dedicated imaging protocol with high resolution images will be necessary in order to find the epileptogenic lesion, and therefore have the potential of a surgical treatment. A variety of non-radiological adjunct tests are available that may help in the localization of the seizure focus and preferably these challenging cases are therefore discussed in multidisciplinary conferences.

In the following, we will discuss the imaging features of epileptogenic lesions highlighting imaging pearls and pitfalls.

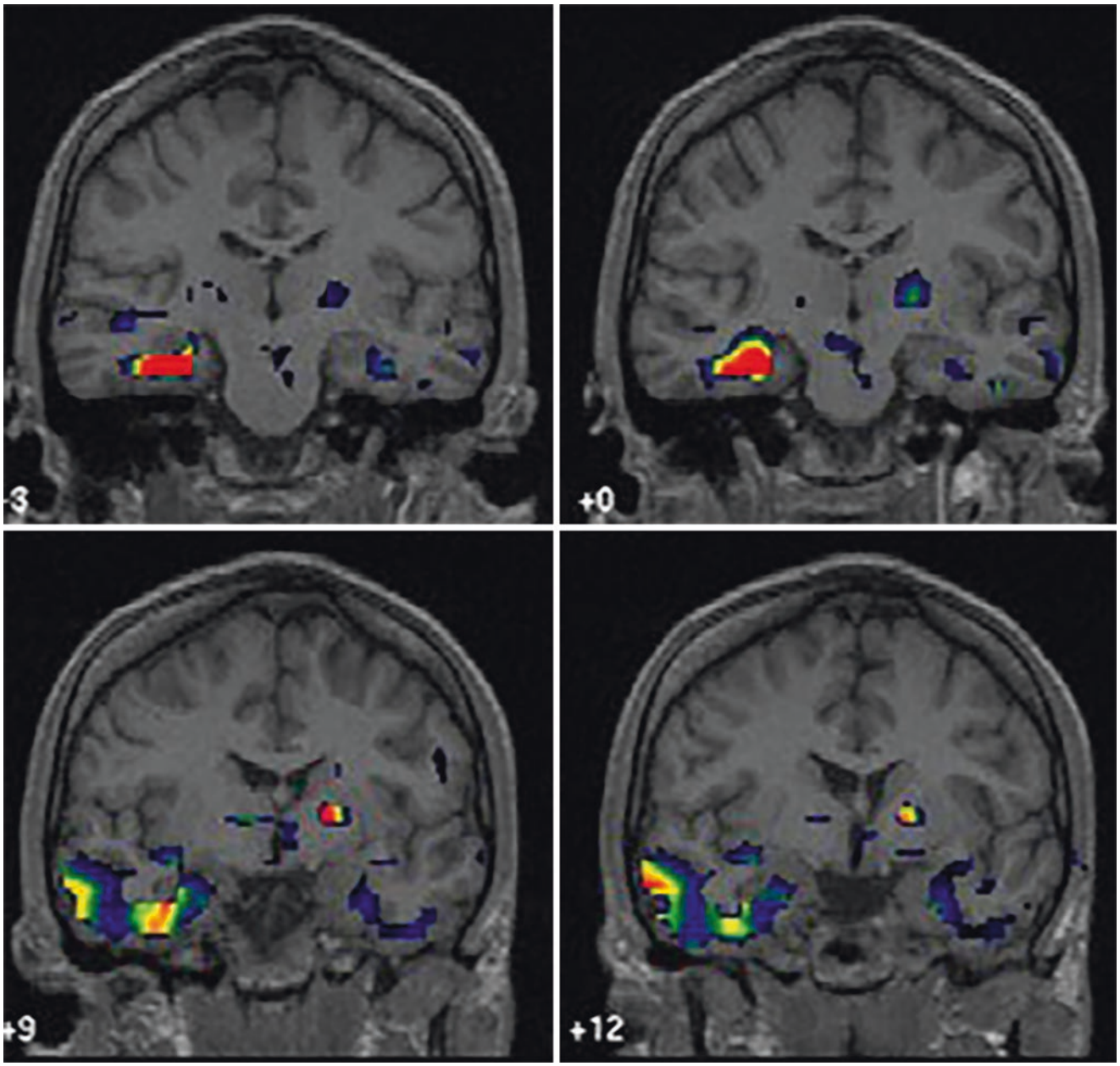

Fig. 10.4 SISCOM (subtracted ictal and interictal SPECT co-registered with MR) in an epilepsy patient with temporal lobe epilepsy demonstrates that there is hyperperfusion in the right hippocampus and anterior temporal lobe during the seizures, indicating the ictal onset zone

10.2 Mesial Temporal Lobe/Hippocampal Sclerosis

Most patients with mesial temporal sclerosis (MTS) present with complex partial seizures. These are characterized by seizure semiology that comprises déjà vu sensations, epigastric auras, lip smacking, or other oral automatisms and often have in their past medical history febrile seizures as a child with progressive worsening of seizure frequency and severity over time. MTS is characterized by sclerosis and volume loss in the hippocampus that often starting with loss of tissue in the stratum pyramidale in CA1 region [19]. The affected hippocampus will appear hyperintense on T2/FLAIR sequences due to the gliosis/sclerosis. The atrophy will lead to loss of the interdigitations of the head of the hippocampus, widening of the temporal horn, and atrophy of the white matter of the temporal lobe (Fig. 10.5). As a consequence of Wallerian degeneration, there may be atrophy of the projecting pathways of the hippocampus, including the Papez circuit, with atrophy of the ipsilateral fornix and the mammillary body. Importantly to

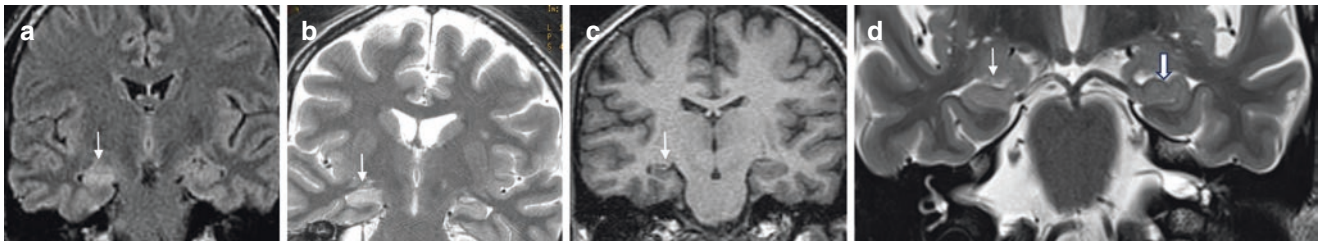

Fig. 10.5 Typical radiological findings in hippocampal sclerosis: (**a**) Coronal FLAIR, (**b**) coronal T2 demonstrates hyperintensity in the right hippocampus (white arrows), (**c**) coronal 3DMPRAGE shows better than T2 and FLAIR the atrophy in the right hippocampus (white arrow), (**d**) coronal T2 centered on the hippocampus shows loss of the interdigitation in the head of the right hippocampus (white arrow) with normal appearances in the left hippocampus (thick white arrow)

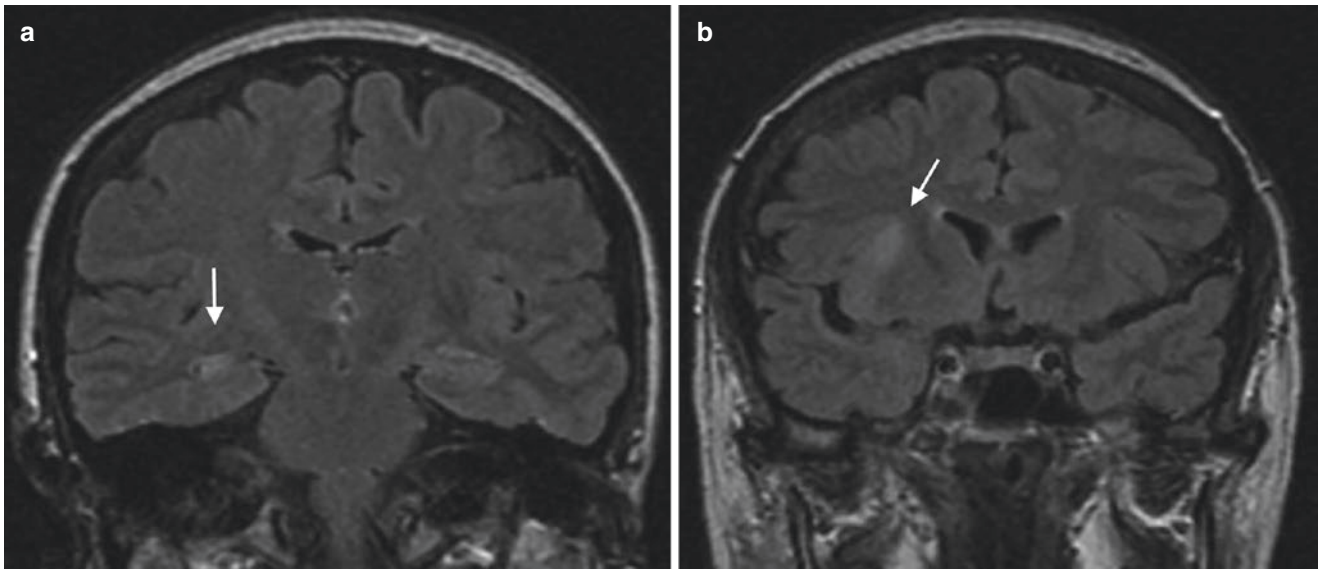

Fig. 10.6 Example of dual pathology in a patient with right hippocampal sclerosis and focal cortical dysplasia in the right inferior frontal gyrus. (**a**) Coronal FLAIR at the level of the hippocampi demonstrates the typical findings of HS with atrophy and hyperintensity within the right hippocampus (white arrow), (**b**) coronal FLAIR at the level of the frontal and anterior temporal lobes, showing blurring between gray and white matter in the right inferior frontal gyrus, consisting in focal cortical dysplasia (white arrow)

note, in nearly 20% of patients with MTS dual pathology is present with a second epileptogenic focus (Fig. 10.6). It is believed that in these cases, the other epileptogenic lesions triggered the mesial temporal lobe sclerosis (similar to febrile seizures as a child can trigger or "kindle" a mesial temporal lobe sclerosis). Dual pathology may also consist also of bilateral mesiotemporal lobe sclerosis as one hemisphere may trigger the other hippocampus to become sclerotic, thus constituting bilateral abnormalities. As the internal reference (i.e., the contralateral hippocampus) is similarly affected, comparison of the signal with other regions of 3-layered cortex, i.e., limbic structures can identify whether a mesial temporal lobe sclerosis is present bilaterally. Thus, if the T2/FLAIR signal of the hippocampus is bilateral symmetrical but higher as compared to the cingulum or insula one may consider bilateral mesial temporal lobe sclerosis (Fig. 10.7).

Key Point

- Mesial temporal lobe sclerosis is the most commonly seen cause for medication refractory epilepsy in temporal lobe epilepsy and is characterized by an indistinct gray–white matter differentiation, abnormal high signal on T2/FLAIR sequences, and atrophy. In up to 15–20% of cases, additional epileptogenic pathology is found in patients with mesial temporal lobe sclerosis.

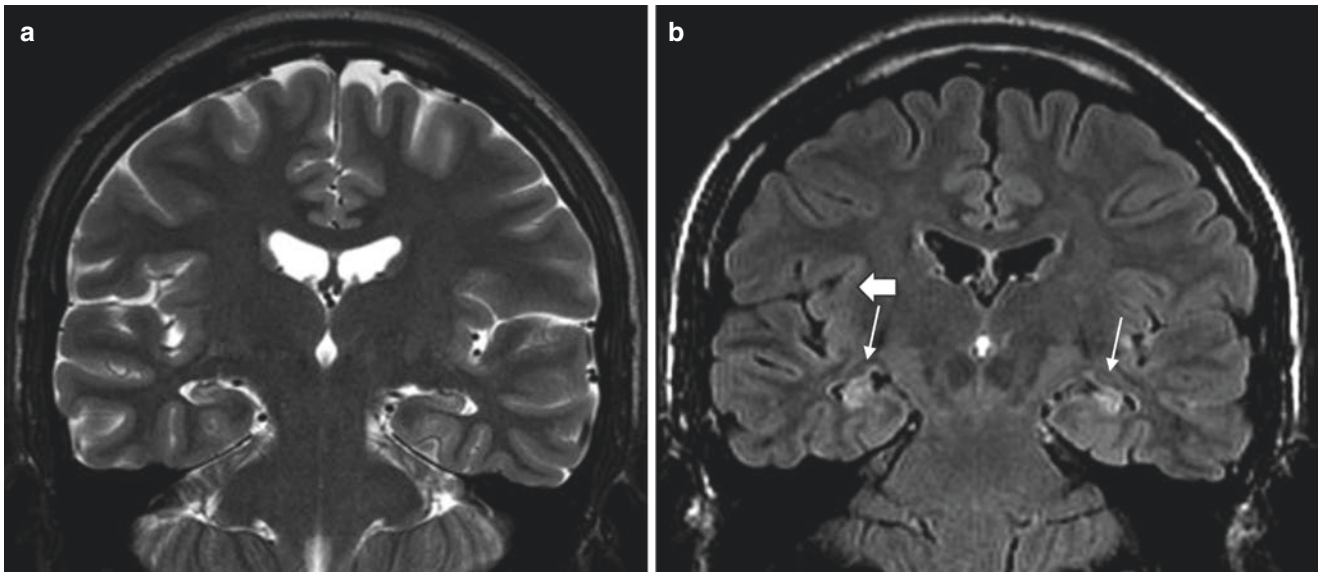

Fig. 10.7 Patient with bilateral hippocampi sclerosis. (**a**) Coronal T2 at the level of the body of the hippocampi demonstrates atrophy of both hippocampi, being difficult to distinguish abnormal signal because both are affected, (**b**) coronal FLAIR at the same level that T2 shows that both hippocampi are hyperintense (white arrows) in comparison with the insula (white thick arrow)

10.3 Malformations of Cortical Development

To understand the different types of malformations of cortical development (MCD), it is important to be aware of the embryology of cortical development: While during the seventh week of gestation neuronal proliferation in the subependymal germinal matrix occurs, at the eighth week of gestation, these cells migrate outward in multiple waves of radial outward migration aided by chemotaxis, i.e., radial glial cell guidance. In the last part of the cortical development, the lamination, cells are organized within different cortical layers in a process that is orchestrated by the subplate in the lowest layer of cortex. Chromosomal mutations, destructive events, or toxins may inhibit either of these three processes (proliferation, chemotaxis, or cortical organization) which will lead to abnormalities in stem cell development, migration, or lamination [20, 21].

Malformations related to abnormal stem cell development include focal or transmantle cortical dysplasias (balloon ell or type II FCDs) and the hemimegalencephalies.

Type II FCD is characterized by dysmorphic neurons with or without balloon cells in addition to cortical dyslamination and is identical to cortical hamartomas in tuberous sclerosis. The transmantle sign is a specific radiologic feature of FCD type II, which is more frequently detected in patients with FCD type IIb than FCD type IIa. Histologically, the transmantle sign reflects abnormal cells extending from the ventricle to the cortex manifesting as a linear T2-weighted or FLAIR hyperintensity from ventricle toward the cortex (the radial band or foot) can be seen in association with a subcortical FLAIR hyperintensity [14] (Fig.10.8).

There are MCD that predominantly or exclusively involve complete or substantial portion of one cerebral hemishere. There are disorders of neuronal proliferation and neuronal migration. It can occur as an isolated anomaly or in association with various neurocutaneous syndromes. There are two categories of hemispheric MCD: hemimegalencephaly and sublobar MCD, depending on the severity of the hemiphere involvement. In hemimegalencephaly, a diffuse hamartomatous overgrowth as a result of abnormal stem cell proliferation is present resulting in broad gyri, shallow sulci, and a blurred gray–white matter junction. The ipsilateral ventricle is often enlarged and demonstrates an abnormal straight course of the frontal horn. In sublobar MCD, the affected hemisphere usually is not enlarged and the malformation may partially spare anterior or posterior regions of the affected hemisphere (Fig. 10.9). Clinically, patients present with macrocephaly, hemiplegia, developmental delay, and seizures. The affected hemisphere is non-functional, thus hemispherectomy can be proposed to these patients, if the contralateral hemisphere has no other epileptogenic lesions. Thus, pre-operative detailed clinical and radiologic assessments are required to determine if there are co-existing abnormalities in the contralateral hemisphere [22].

Lissencephalies, the agyria-pachygyria complex and heterotopia are malformations related to abnormal migration .

In the lissencephalies, there has been a global halt in the migration . An impaired last phase of neural migration will lead to paucity of the gyral and sulcal development with a

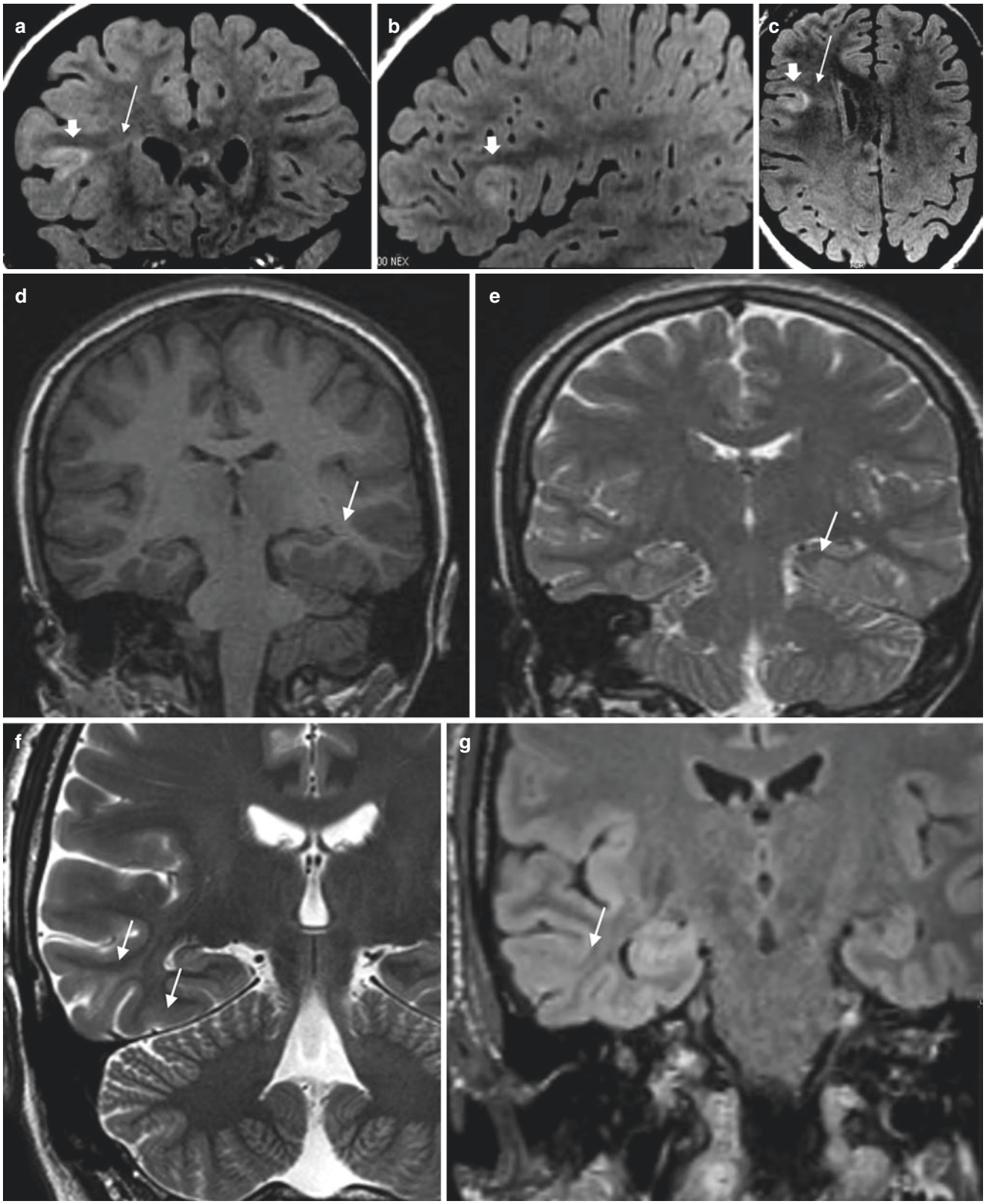

Fig. 10.8 Three cases of FCD type II. (**a**, **b**, **c**) patient 1; (**a**) 3DFLAIR with (**a**) coronal, (**b**) sagittal, and (**c**) axial, showing the typical signs of FCD type II, blurring between white and gray matter, juxtacortical (thick arrow), white matter hyperintensity, and the transmantle signs (arrow). (**d**, **e**) patient 2; (**d**) coronal 3DT1 (**e**) and coronal T2 show thickened cortex, blurring between gray and white matter in the left fusiform gyrus without transmantle sign (arrows) (**e**, **f**) patient 3, (**f**) coronal T2, and (**g**) coronal FLAIR shows juxtacortical white matter hyperintensity in the right inferior temporal gyrus and incomplete transmantle sign (arrow). The right hippocampus shows high signal on FLAIR indicating HS (dual pathology)

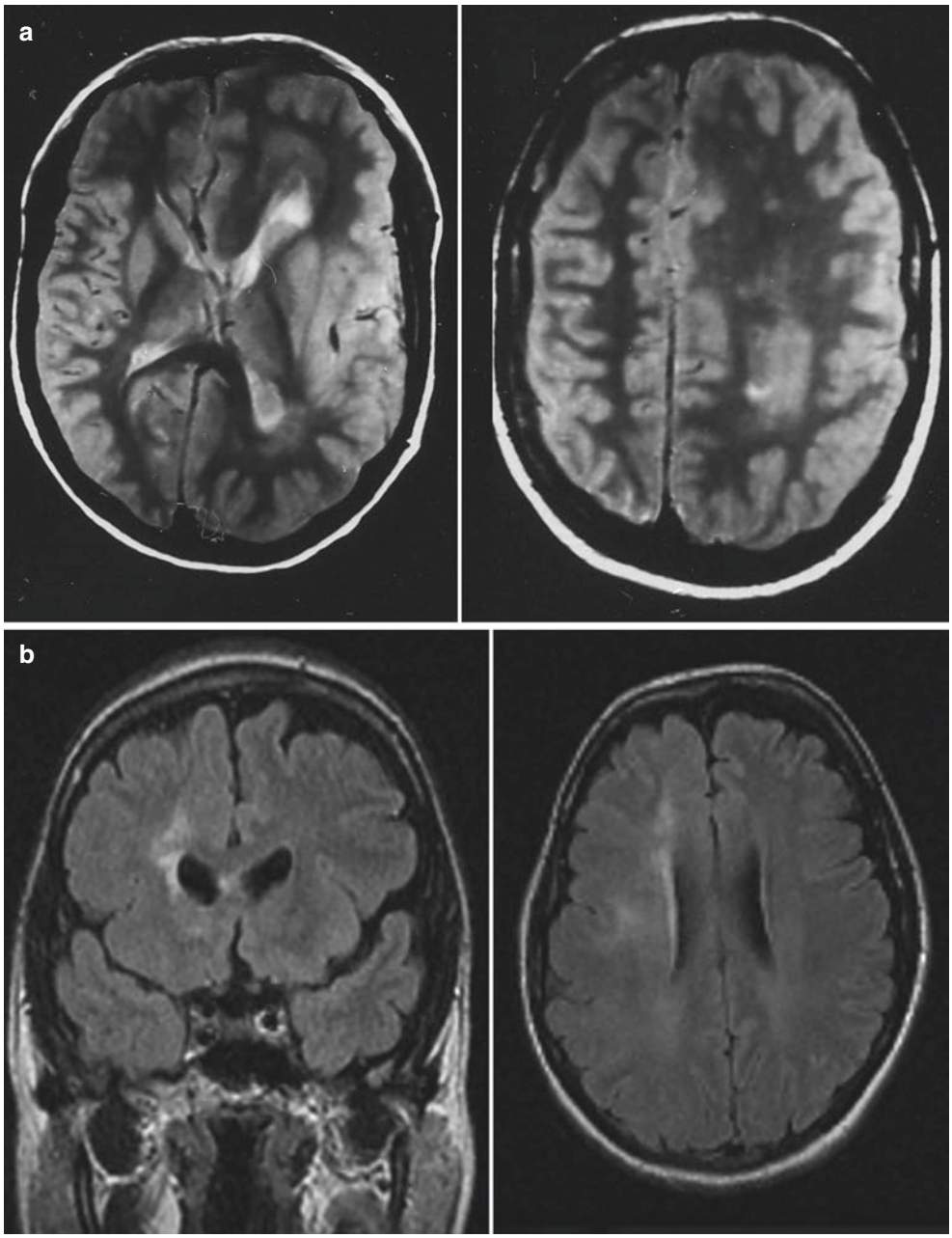

Fig. 10.9 Two cases of hemispheric malformation of cortical development. (**a**) Patient with hemimegalencephaly. Axial and coronal FLAIR showing the typical findings of enlargement of the affected hemisphere, diffuse thickening of the cortex with shallow sulci, blurred gray and white matter interface, heterotopic gray matter in the subcortical region, white matter increased volume with signal abnormalities, enlargement and abnormal configuration of the lateral ventricle, and dysplasia of subcortical gray matter structures. (**b**) Patient with sublobar FCD, coronal, and axial FLAIR showing similar findings than hemimegalencephaly but the abnormal hemisphere and the lateral ventricle are not enlarged, and the malformation spares the posterior region of the affected hemisphere

smooth brain surface and diminished white matter. Patients present with global developmental delay and seizures. Two different types of lissencephaly can be distinguished: the posterior agyria (related to an alteration on Chromosome 17) (Fig. 10.10) and the anterior agyria which is an X-linked disease.

Female carriers of the affected X-chromosome present with band heterotopias that is more present in the frontal lobes compared to the parietal lobes. Thus, if females present with band heterotopias, genetic counseling may be indicated. The band may be thin or thick depending on the amount of arrested migration. Patients with a thick band have less normal cortex (that can be thinned) and present with a more severe developmental delay.

In addition to the "band heterotopia," focal subcortical heterotopia can be present, On imaging, swirling, curvilinear bands of gray matter as well as thinned cortex, and paucity of the white matter are seen. The ipsilateral ventricle may be distorted, and there can be an associated callosal hypogenesis.

The third type of heterotopia is coined periventricular nodular heterotopia. On imaging an exophytic smooth ovoid mass in the residual germinal matrix, i.e., along the ventricular surface is seen. The periventricular nodular heterotopia may exhibit quite mild symptoms with normal development

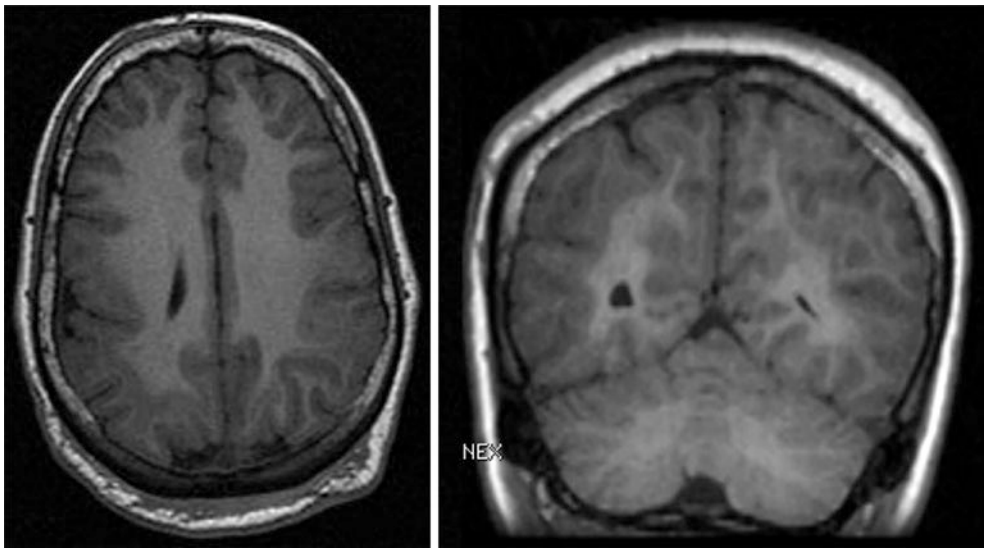

Fig. 10.10 Patient with posterior lissencephaly. Axial 3DMPRAGE shows diffuse blurring between gray and white matter, cortical thickening, and abnormal gyral pattern in the posterior part of the brain

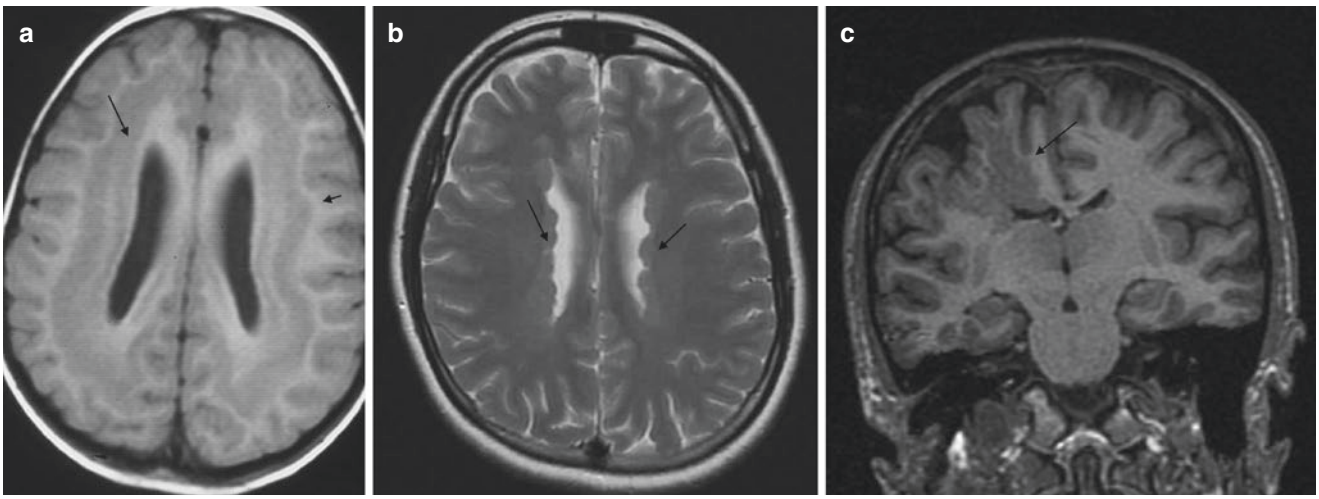

Fig. 10.11 Three examples of malformations related to abnormal migration: (**a**) T1 axial demonstrates typical band heterotopia (arrow), (**b**) T2 axial shows periventricular heterotopias involving both lateral ventricles (arrows), and (**c**) coronal T1 shows subcortical heterotopias extending from the subcortical white matter of the right lateral ventricle (arrow) and associated with abnormal gyral pattern and focal subarachnoid space enlargement

and late onset of seizures, if the amount of abnormal tissue is small. If the periventricular heterotopia completely lines the walls of both ventricles, a familiar form has to be considered, and in these cases developmental delay and seizure activity are typically more pronounced (Fig. 10.11).

Malformations related to abnormal cortical organization can be subdifferntiated into polymicrogyria, schizencephaly, and FCD type I (non-balloon cell). In polymicrogyria, neurons reach the cortex but distribute abnormally, thus multiple small gyri are formed. Polymicrogyria is most found around the posterior sylvian fissures when bilateral present in the perisylvian region patients who can present with pseudobulbar palsy (Fig. 10.12).

In open-lip schizencephaly, a cleft that is lined by gray matter reaches from the periphery to the ventricle while in the closed-lip schizencephaly, gray matter is reaching from the periphery to the ventricle and a dimple is seen in the ventricular wall. Schizencephaly can be multifocal and bilateral. The cortex lining the defect is polymicrogyria with ill-defined margins to the white matter. Disorders of lamination can be very subtle, and only mild focal blurring of the gray–white matter junction may be present.

Key Point

- Malformations of cortical development are commonly seen in pediatric patients with medication refractory epilepsy and usually are neocortical epilepsy. There malformations of cortical development depend on the embryological stage that they occur and can be very diffuse or very subtle.

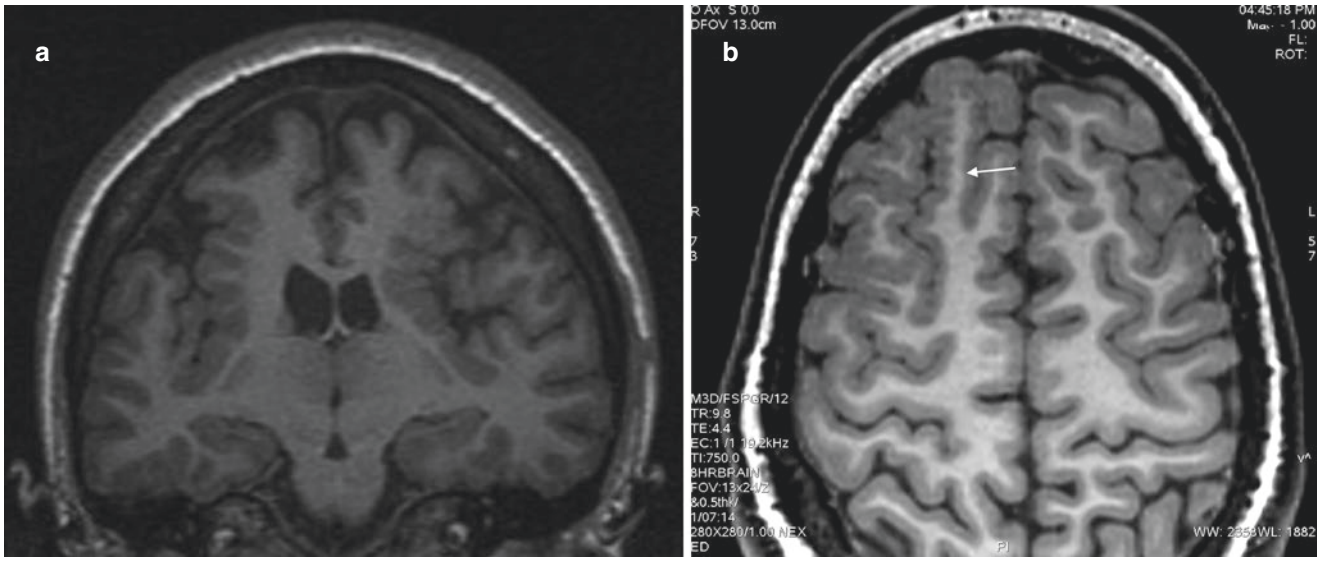

Fig. 10.12 Two patients with malformation of abnormal cortical organization. (**a**) coronal 3DMPRAGE demonstrates bilateral perirolandic bilateral polymicrogyria and abnormal and deep sulci. No dimple is seen in the lateral ventricles. (**b**) Axial 3DMPRAGE shows polymicrogyria in the right superior and middle frontal gyrus (arrow)

10.4 Epileptogenic Tumors

Nearly all brain tumors are epileptogenic, however, given their location, there are certain tumors that have a very high propensity of eliciting medication refractory seizures. Most of these are benign and just by means of location (i.e., within the cortical-white matter interface and with temporal lobe predilection) cause the seizures, these are often considered good candidates for surgery. As a general discussion of all tumors is beyond the scope of this chapter, we will focus only on three tumors that are commonly associated with epilepsy., Usually are slow growing tumors that appear during childhood or early adulthood and are defined as long-term epilepsy associated tumors (LEAT) [23]., The most common are (1) gangliogliomas, (2) DNETs, and (3) tuber cinereum hamartomas.

1. Gangliogliomas are cortically based, partly cystic tumors that may calcify and often harbor an enhancing nodule. Gangliogliomas occur in young adults and older children, when present under the age of 10, they are often larger with more cystic components. They are mainly located in the temporal lobes but can also occur in parietal and frontal lobes (Fig. 10.13).
2. DNETs are well demarcated, bubbly, intracortical masses that also are most common in the temporal, parietal, and frontal lobes. They may calcify but enhancement is very rare and if present should lead to more intensive follow-up as the enhancing portion of a DNET may recur following surgery (Fig. 10.14).
3. Tuber cinereum hamartoma present with the combination of gelastic seizures and precocious puberty. They are located at the floor of the third ventricle (i.e., the tuber cinereum) do not enhance and are isointense to cortex. They are non-neoplastic tumors with disorganized collection of neurons and glia (Fig. 10.15).

Key Point

- Long-term associated epilepsy tumors are usually low-grade tumors and usually appear in the infancy or early adulthood. Usually they involve the gray matter, and most commonly are located in the temporal and frontal lobes.

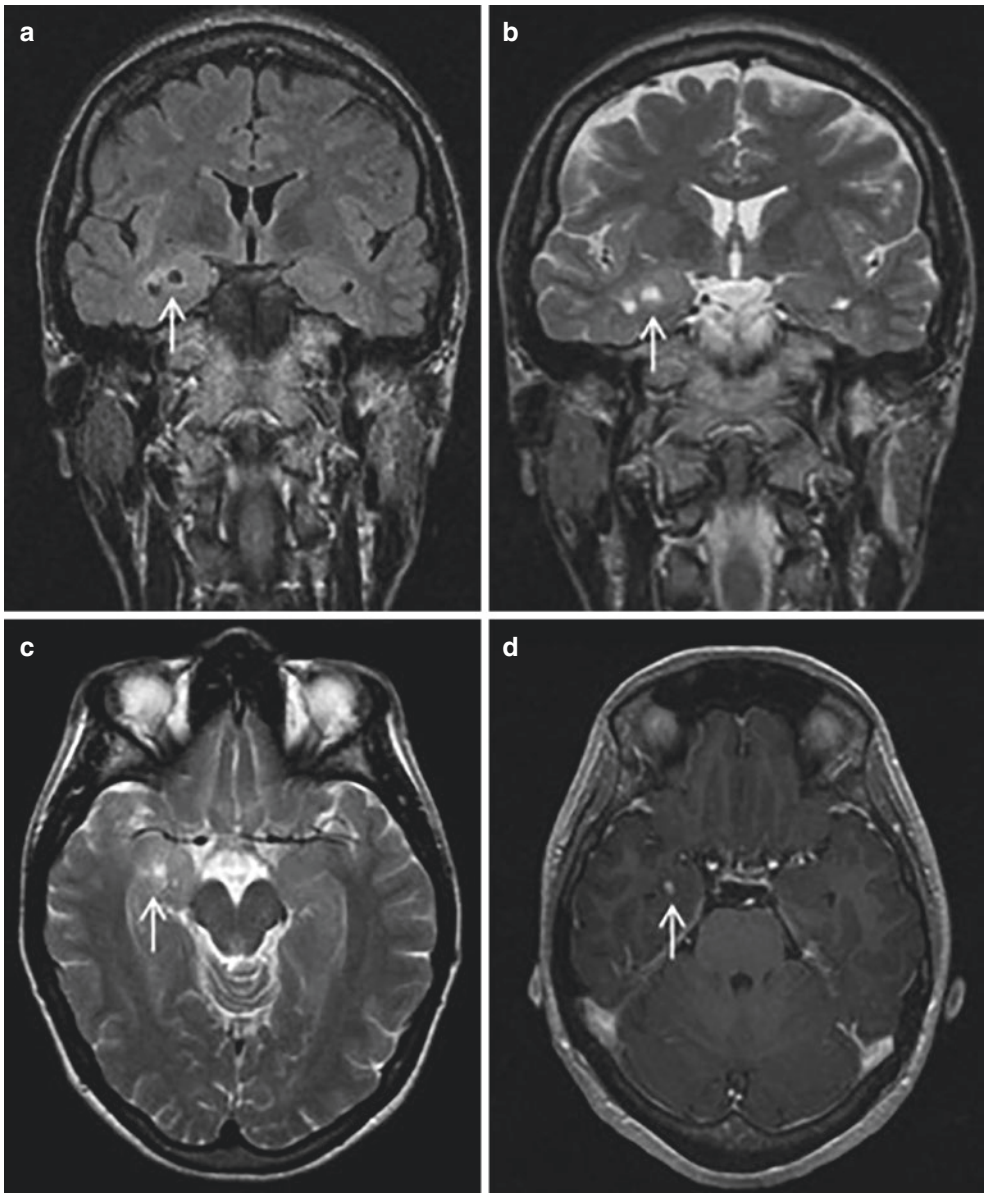

Fig. 10.13 Patient with temporal lobe epilepsy and ganglioglioma: (**a**) coronal FLAIR, (**b**) coronal T2, and (**c**) axial T2 demonstrate a heterogenous lesion in the right amygdala with a small cyst (arrow). (**d**) Post-contrast T1 shows a small enhancing nodule (arrow)

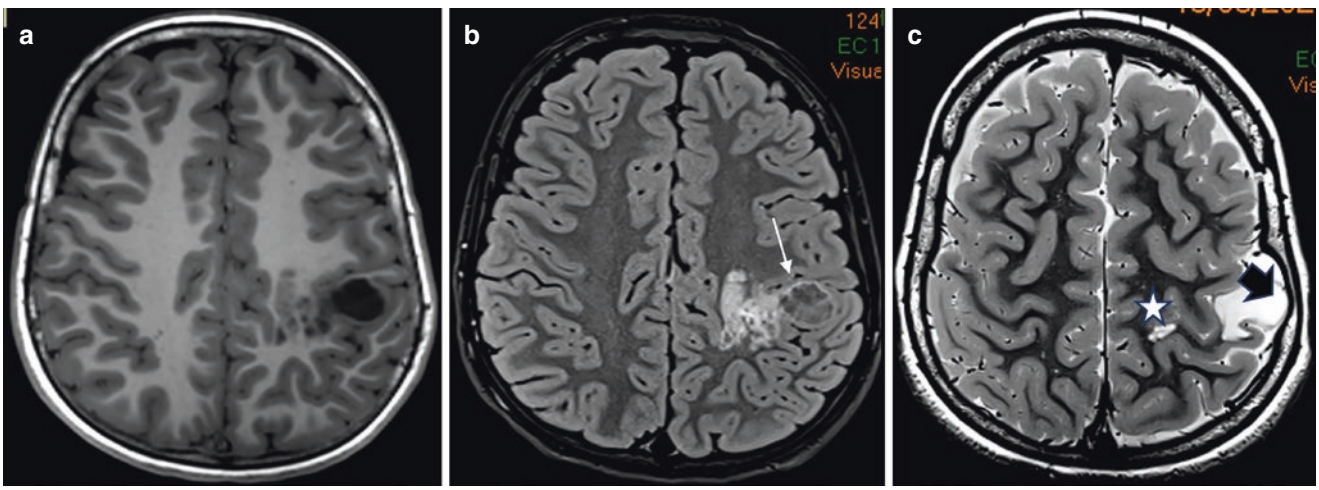

Fig. 10.14 DNET. (**a**) Axial 3DMPRAGE, (**b**) axial FLAIR, and (**c**) axial T2 showing a superficially multicystic lesion in the left parietal lobe with mixed signal of FLAIR (arrow), satellite cyst (star), and remodelling of the calvarium (thick black arrow)

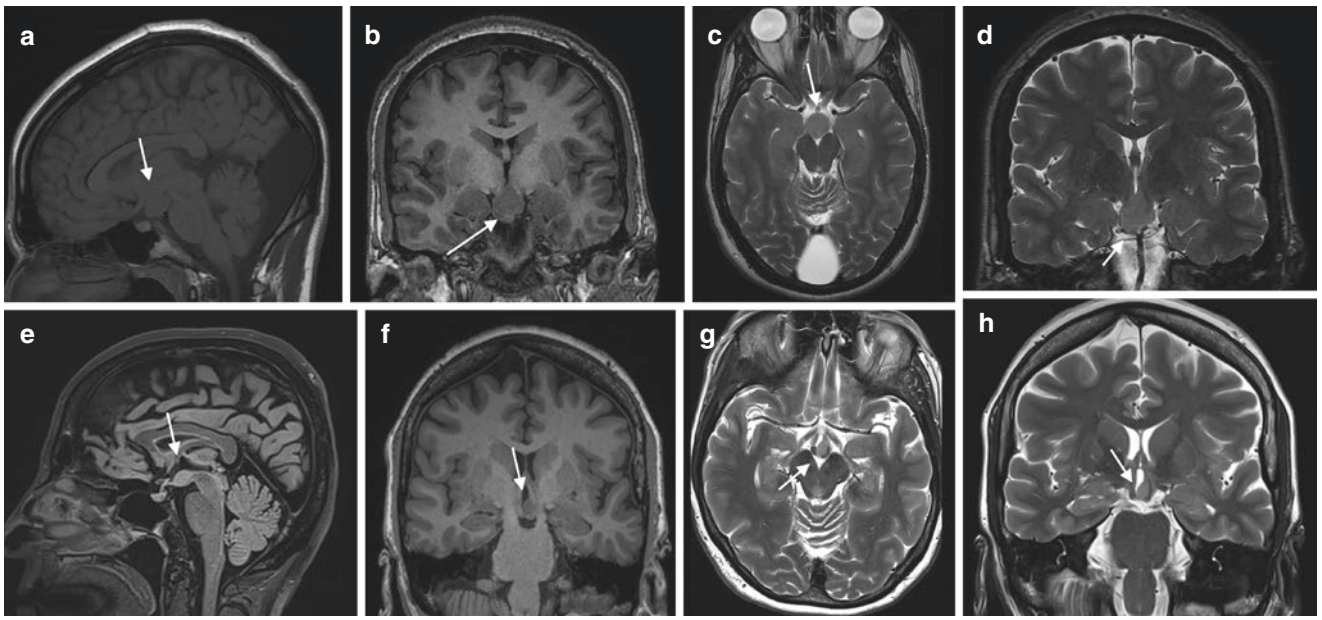

Fig. 10.15 Two epileptic patients with hamartomas of the tuber cinereum. The upper row shows a large tumor in the floor of the 3° ventricle extending into the suprasellar region with a similar signal to the hippocampus on T1 (**a**, **b**) and T2 sequences (**c**, **d**) (arrows). The patient has a retrocerebellar cyst. The lower row shows a small hamartoma inside the 3°ventricle with the same signal as the gray matter on sagittal FLAIR (**e**), coronal T1MPRAGE (**f**), and axial and coronal T2 (**g** and **h**) (arrows)

10.5 Other Causes of Focal Epilepsy

Many other pathologies can cause seizure. Similar to the previous paragraph, it is beyond the scope to in detail describe imaging features of vascular malformations, infections, or trauma that can go along with seizures, and most of the entities are described in other chapters of this syllabus. We therefore only want to highlight few epilepsy-relevant facts and features of these conditions.

Vascular malformations can cause seizures due to previous hemorrhage and scarring, hemosiderin deposition (especially when close to the cortex), or gliosis. AVMs in the temporal lobe have a higher likelihood of producing seizure due to interference of the normal blood supply and drainage of potentially epileptogenic structures such as the hippocampus.

Cavernous malformations that are cortically located and have hemosiderin staining reaching the cortex, and in particular the mesial temporal lobe structures, are very often associated with seizures as the hemosiderin stain is believed to have a strong irritative potential for neurons. They are best visualized on T2 gradient echo or SWI sequences where they demonstrate with the classical blooming artifact (Fig. 10.16).

Patients with previous trauma can experience post-traumatic seizure disorder, especially after having sustained contusional hemorrhages of their temporal lobes as gliosis and hemosiderin staining can cause irritation of the surrounding cortex.

Neonatal anoxic ischemia or hypoxemia can cause ulegyria—i.e., a scar/defect of the cerebral cortex that mainly involves the cortex in the depth of the sulcus, whereas the cortical crowns remain relatively unaffected [24].

If the perinatal ischemia has only involved one hemisphere (perinatal stroke), a Dyke-Davidoff-Masson syndrome will ensue where stable hemiatrophy is present with hypertrophy of the skull and the sinuses, paucity of white matter, ventricular enlargement, and mild gliosis (Fig. 10.17).

Virtually any infection (bacterial, fungal, parasitic) can produce epileptogenic lesions, and worldwide infections are the leading cause of epilepsy (Fig. 10.18). A typical example is neurocysticercosis which is a very common cause of focal epilepsy in the developing world.

Antero-basal temporal lobe encephaloceles are lesions that are either related to a congenital defect of the bone or to previous trauma. Brain tissue can extend into the pterygopalatine fossa through the bony defect at the base of the greater sphenoid wing in the region of the foramen rotundum and pterygoid process. The herniated brain demonstrates high T2/FLAIR signal and is believed to be the epileptogenic focus (Fig. 10.19). Following resection of the abnormal brain tissue seizure freedom can be obtained in a very large proportion of cases.

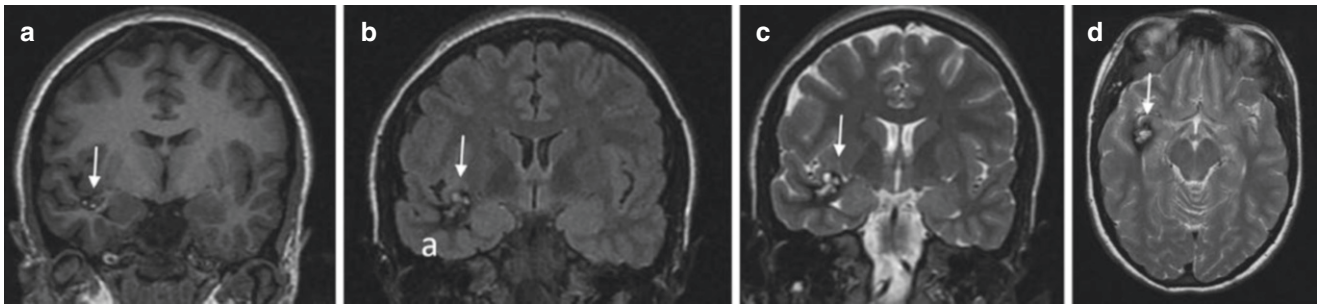

Fig. 10.16 Patient with temporal lobe epilepsy, showing a typical cavernoma finding with (**a**) popcorn appearances on T1 coronal, and surrounded by hemosiderin in the white matter seen on (**b**) coronal FLAIR, (**c**) coronal T1, and (**d**) axial T2 sequences. Note that the right amygdala and hippocampus are normal

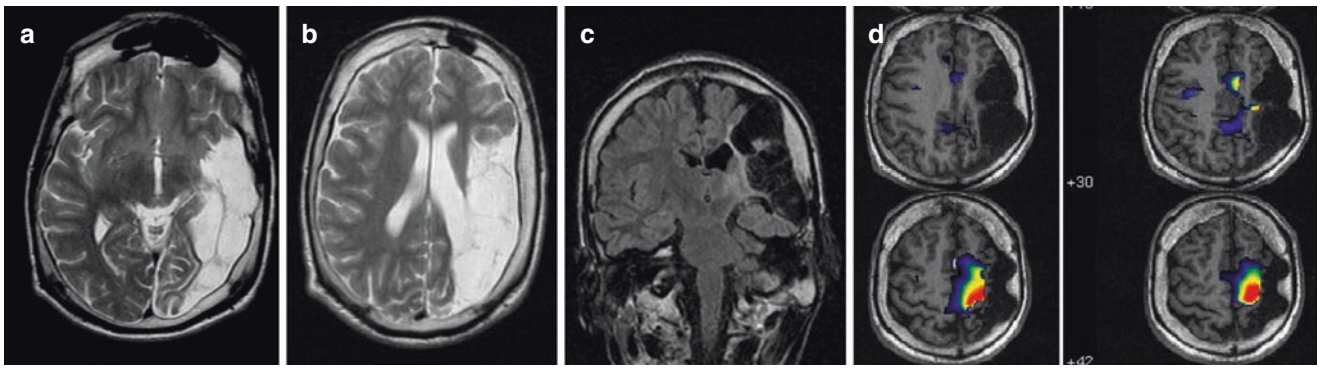

Fig. 10.17 A 16-year-old boy with perinatal vascular injury and epilepsy and right hemiparesis. A large porencephalic cyst that involves the part of the left middle cerebral artery territory. The cyst shows some septa and contacts with the ependyma of the left lateral ventricle. There is an abnormal signal in white matter indicating gliosis and Wallerian degeneration. Note the hypertrophy of the left side of the skull and asymmetric enlargement of the frontal sinus (**a**, **b**) axial T2WI; (**c**) coronal FLAIR. (**d**) SISCOM indicates that the seizure onset zone is in the midsagittal cortex near the porencephalic cyst

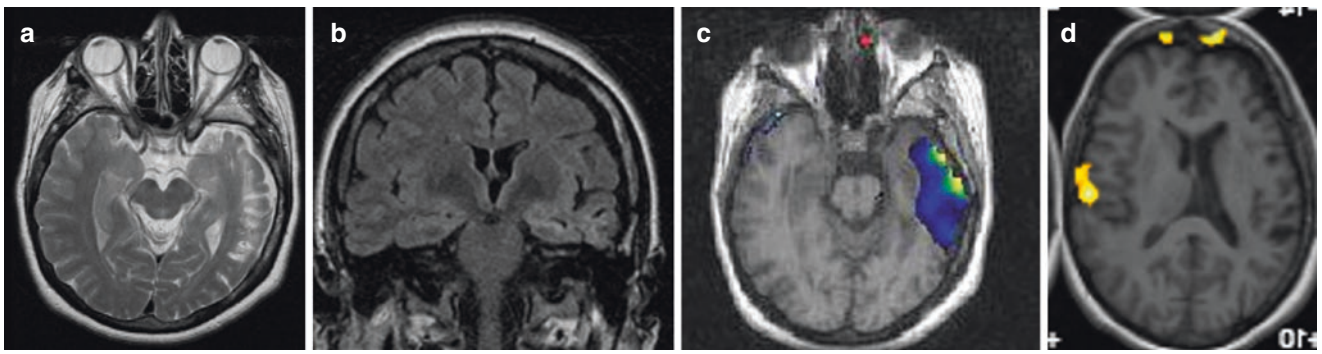

Fig. 10.18 A 35-year-old female with a previous history of meningitis and epilepsy. MRI (**a**) axial T2WI (**b**) coronal FLAIR shows atrophy of the left temporal lobe with white matter hyperintensity associated with left HS (arrow). (**c**) SISCOM images indicate that the ictal onset zone initiates in the left neocortical temporal lobe. (**d**) Language fMRI demonstrates activation of the right hemisphere during an auditive comprehension paradigm, indicating that the language function has been transferred to the other hemisphere

Rasmussen's encephalitis is a presumably autoimmune-mediated chronic inflammation of the brain that presents with progressive gliosis and volume loss. Patients experience seizures and a progressive hemiparesis (Fig. 10.20).

Key Point

- Many other pathologies including vascular malformations, phakomatoses, or remote infections or trauma can cause medication refractory epilepsy, particularly if they involve the gray matter.

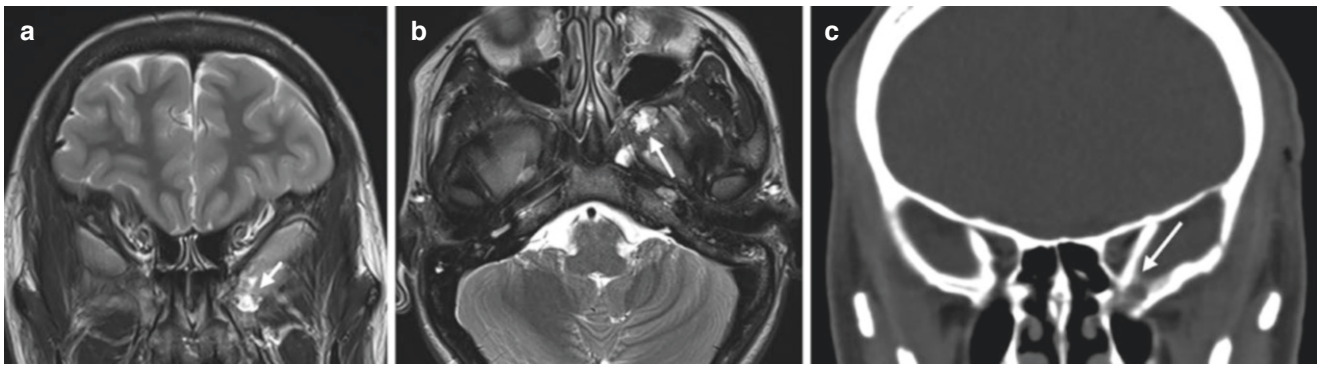

Fig. 10.19 Patient with temporal lobe epilepsy. MRI exam (**a**) T2 coronal and (**b**) axial T2MRI show the left temporal pole extending into the pterygopalatine fossa throughout a small defect of the left greater sphenoid wing seen on (**c**) coronal CT (arrows)

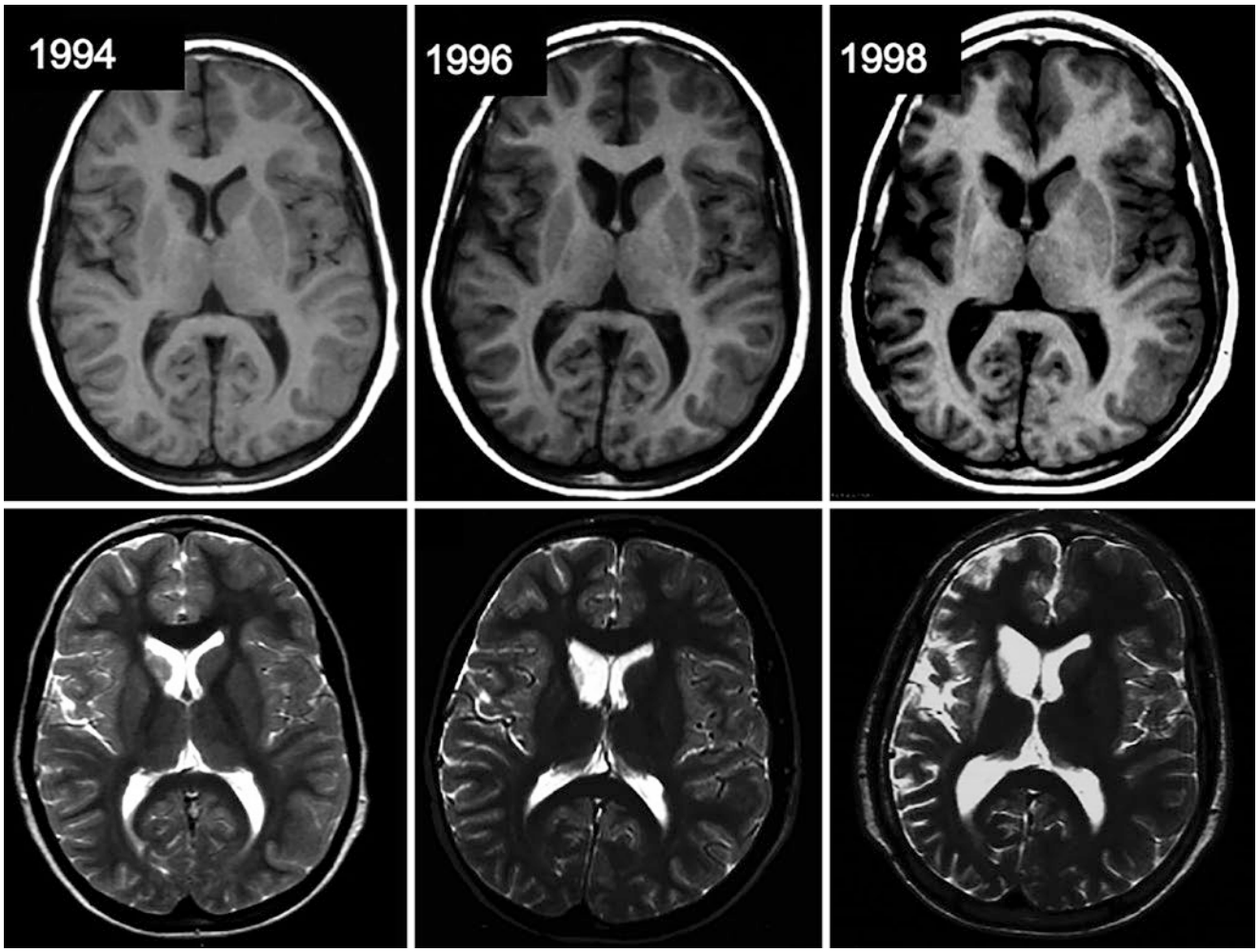

Fig. 10.20 A 9-year-old patient with continuous partial seizures arising from the right hemisphere, progressive cognitive deterioration, and left hemiparesis. MRI studies over time show progressive atrophy of the right lentiform and caudate nuclei with progressive right hemisphere atrophy. (Axial 3DT1 upper row, axial T2 lower row)

10.6 Concluding Remarks

Neuroimaging in patients with medication refractory epilepsy should identify clinically relevant abnormalities in a high percentage of cases and therefore the radiologist plays a crucial role in the identification of epileptogenic lesions and their possible surgical removal. A dedicated epilepsy protocol is necessary to identify these lesions, and the MR should be interpreted and multidisciplinary rounds with radiological input are paramount to manage these challenging patients.

Take-Home Messages

- When evaluating a dedicated seizure protocol MR, a structured approach is helpful that includes a detailed assessment of (a) the hippocampus and mesial temporal lobe structures, (b) the ventricular outline, and (c) the gyral and the sulcal anatomy.
- Particular emphasis should be paid upon the T2/FLAIR signal within the cortex and hippocampus, its similarity to other regions of neo- and archicortex, the internal architecture of the hippocampus, the indentations of the head of the hippocampi, the fornix and mammillary bodies, and the gray–white matter interface of the neocortex (blurring, gray matter thinning, or thickening).
- The malformations of cortical development can be differentiated into disorders of neuronal proliferation, migration, and cortical organization and can be diffuse or very subtle. There are slow growing tumors, usually neuroglial lineage that are associated with chronic epilepsy.

References

1. Gavvala JR, Schuele SU. New-onset seizure in adults and adolescents: a review. JAMA. 2016;316(24):2657–68.
2. Hauser WA, Beghi E. First seizure definitions and worldwide incidence and mortality. Epilepsia. 2008;49(Suppl 1):8–12.
3. Scheffer IE, et al. ILAE classification of the epilepsies: position paper of the ILAE Commission for Classification and Terminology. Epilepsia. 2017;58(4):512–21.
4. Ho K, et al. Neuroimaging of first-ever seizure: contribution of MRI if CT is normal. Neurol Clin Pract. 2013;3(5):398–403.
5. Organization, W.H. Epilepsy: a public health imperative. Geneva: CC BY-NC-SA 3.0 IGO; 2019.
6. Fisher RS, et al. ILAE official report: a practical clinical definition of epilepsy. Epilepsia. 2014;55(4):475–82.
7. Epilepsy, C.o.N.o.t.I.L.A. Recommendations for neuroimaging of patients with epilepsy. Commission on Neuroimaging of the International League Against Epilepsy. Epilepsia. 1997;38(11):1255–6.
8. Von Oertzen J, et al. Standard magnetic resonance imaging is inadequate for patients with refractory focal epilepsy. J Neurol Neurosurg Psychiatry. 2002;73(6):643–7.
9. Téllez-Zenteno JF, et al. Surgical outcomes in lesional and nonlesional epilepsy: a systematic review and meta-analysis. Epilepsy Res. 2010;89(2–3):310–8.
10. Wellmer J, et al. Proposal for a magnetic resonance imaging protocol for the detection of epileptogenic lesions at early outpatient stages. Epilepsia. 2013;54(11):1977–87.
11. Bernasconi A, et al. Recommendations for the use of structural magnetic resonance imaging in the care of patients with epilepsy: a consensus report from the International League Against Epilepsy Neuroimaging Task Force. Epilepsia. 2019;60(6):1054–68.
12. Hainc N, et al. Imaging in medically refractory epilepsy at 3 tesla: a 13-year tertiary adult epilepsy center experience. Insights Imaging. 2022;13(1):99.
13. Lee DH, et al. MR in temporal lobe epilepsy: analysis with pathologic confirmation. AJNR Am J Neuroradiol. 1998;19(1):19–27.
14. Urbach H, et al. MRI of focal cortical dysplasia. Neuroradiology. 2022;64(3):443–52.
15. van Lanen RHGJ, et al. Ultra-high field magnetic resonance imaging in human epilepsy: a systematic review. NeuroImage Clin. 2021;30:102602.
16. Bauer PR, et al. Can fMRI safely replace the Wada test for preoperative assessment of language lateralisation? A meta-analysis and systematic review. J Neurol Neurosurg Psychiatry. 2014;85(5):581–8.
17. Piper RJ, et al. Application of diffusion tensor imaging and tractography of the optic radiation in anterior temporal lobe resection for epilepsy: a systematic review. Clin Neurol Neurosurg. 2014;124:59–65.
18. von Oertzen TJ, et al. SPECT and PET in nonlesional epilepsy. Clin Epileptol. 2023;36(2):104–10.
19. Howe KL, et al. Histologically confirmed hippocampal structural features revealed by 3T MR imaging: potential to increase diagnostic specificity of mesial temporal sclerosis. AJNR Am J Neuroradiol. 2010;31(9):1682–9.
20. Barkovich AJ, et al. A developmental and genetic classification for malformations of cortical development: update 2012. Brain. 2012;135(Pt 5):1348–69.
21. Severino M, et al. Definitions and classification of malformations of cortical development: practical guidelines. Brain. 2020;143(10):2874–94.
22. Sato N, et al. Aberrant midsagittal fiber tracts in patients with hemimegalencephaly. AJNR Am J Neuroradiol. 2008;29(4):823–7.
23. Urbach H. Long-term epilepsy-associated tumors. In: Barkhof F, et al., editors. Clinical neuroradiology: the ESNR textbook. Cham: Springer International Publishing; 2019. p. 951–63.
24. Colombo N, Bargalló N, Redaelli D. Neuroimaging evaluation in neocortical epilepsies. In: Barkhof F, et al., editors. Clinical neuroradiology: the ESNR textbook. Cham: Springer International Publishing; 2018. p. 1–35.