Practical Neurology 'How to do it'

Brain imaging in epilepsy

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Abstract

Brain imaging identifies structural cerebral pathology that may give rise to seizures. MRI at 3T with epilepsy protocols, reported by expert neuro-radiologists in possession of full clinical data has the greatest yield. X-ray CT has a role in assessing patients with seizures in the context of an acute neurological illness. Identifying a relevant structural lesion with MRI is fundamental in the consideration of epilepsy surgery; it is crucial to establish if a lesion is relevant to the epilepsy or not. If no lesion is identified, developmental MRI and image processing may identify a subtle abnormality. PET and SPECT may identify focal functional abnormalities that infer the location of an epileptic focus. Functional MRI is useful for localizing eloquent cortex, and tractography delineates crucial white matter tracts, so these may be avoided in epilepsy surgery. Reviewing data in 3-dimensions aids visualization of structural relationships and is helpful for surgical planning.

Reasons for brain imaging in epilepsy

Brain imaging is fundamental in the evaluation of individuals with epilepsy to identify any underlying structural brain abnormality that may be the cause of the epilepsy, and identify a treatment need such as tumour, vascular disease or infection. Those with drug–refractory focal seizures who are candidates for surgical treatment of epilepsy need particular attention.

In the acute situation when a person is admitted with onset of seizures, an X-ray CT scan is useful as it can be carried out quickly, usually in the Emergency Department, whilst the patient is being worked on, with airway being secured and placement of lines. CT will quickly reveal major acute pathologies that need treatment such as trauma, haemorrhage, large infarct, empyema.

If X-ray CT is normal or needs clarification, MRI is the next step, and would be the first step in the elective situation as it is more sensitive and specific that CT.

Indications for brain MRI are :

onset of seizures before the age of 1 year, or after the age of 20,

evidence of focal seizures on history, examination or EEG

neurological or neuropsychological focal deficit

failure of seizure control with first line AED

loss of seizure control

change in seizure pattern

status epilepticus without a clear cause such as omitting medication.

Thus, in practice, those for whom MRI is not currently indicated are those aged 1-20 years with generalized seizures only, no deficits, and control with the first AED tried. In practical terms, these individuals will frequently have MRI although the yield is low, with the exception of young children who would need a general anesthetic to have an MRI scan.

Repeat MRI is indicated if seizures continue or if a fixed deficit develops, as a lesion may have progressed and be apparent, and cortical and hippocampal atrophy may become evident. Repeat MRI is also recommended in individuals with normal MRI and refractory seizures when new scanners, with increased field strength and new sequences become available, as previously covert lesions may become evident.

Requesting imaging

Neuro-radiologists are faced with hundreds of images to report and need to be guided by detailed clinical information to the area that need particular scrutiny.

A request form that says "Ep, ?SOL" does not deserve a report that is more expansive than "NAD".
For example: "Recent onset of gelastic seizures, with subsequent development of impaired awareness and automatisms" will correctly lead to scrutiny for hypothalamic hamartoma. Onset of seizures with jerking of the left thumb and subsequent spread up the left arm puts the right primary motor cortex in the spotlight.
Seizures with a warning of fear, epigastric rising and déjà vu followed by loss of awareness, oral automatisms and formed speech in seizures in a right-handed person suggests the likely hood of a lesion in the anterior medial right temporal lobe.

MRI protocols

There are established protocols to maximize the yield of MRI.[1] It is helpful to review and discuss the protocols with the MR Unit, radiographers, clinical; scientist and radiologist so that these are optimized. The precise implementation details will vary according to the MRI scanner manufacturer and the scanner.

The mainstay of optimal MRI is a high quality 3T MRI scan. This provides better signal to noise ratio with improved spatial and contrast resolution, than 1.5T scans, and is enhanced with use of surface coils. In 65% (15/23) of cases an epileptogenic lesion could be detected following 3T scans that was not visible on 1.5T imaging.[2]
Volumetric T1-weighted gradient-recalled echo (GRE) images including sequences such as MPRAGE (magnetization prepared rapid acquisition GRE) or SPGR (spoiled gradient-recalled acquisition) provide sharp gray/white matter distinction for detection of subtle malformations of cortical development. Images should be acquired with 1-mm isotropic voxels to allow reformatting in additional planes and segmentation of the hippocampus for volumetric measurements. Gadolinium-enhancement is recommended when tumours, infection or neurocutaneous syndromes are suspected.[3]

Fluid attenuated inversion recovery (FLAIR), T2-weighted, and susceptibility-weighted imaging T2* sequences such as GRE or SWI (susceptibility weighted images) are important to detect hemosiderin/calcification. The slice thickness for T2 and FLAIR should be the lowest the scanner can accommodate with maintaining good signal to noise ratio, and not exceed 3 mm. For T2 and FLAIR, at least two slice orientations should be taken: orthogonal to and along the axis of the hippocampus to avoid partial volume effects that make interpretation of the medial temporal lobe images difficult. The coronal sequences through the frontal and temporal cranial fossa additionally allow for detection of small encephalocoeles, which are an underestimated and surgically remediable cause of epilepsy.[4]

Interpreting MRI

The yield of relevant structural brain abnormalities in those with epilepsy is significantly higher if images are reported by a neuro-radiologist with expertise in epilepsy.[3] It is particularly beneficial for the neuro-radiologist and neurologist to review images together in an MDT to maximise the interchange of clinically relevant information and to consider the way forward. If it is possible to obtain previous MR images it is helpful to first review these with a neuro-radiologist rather than going straight to requesting another MRI scan.

Abnormalities causing epilepsy and impact on treatment.

An underlying cause of epilepsy may be revealed that mandates treatment: such as encephalitis, cysticercosis, trauma, tumours and vascular disease.

Abnormalities may be found that do not lead to specific therapy but understanding of which is important for the individual, their family and clinician to understand the cause and prognosis such as brain malformations or evidence of perinatal hypoxia-ischemia.

For those patients with focal seizures that are not fully controlled with AED at doses that do not cause adverse–effects, prompt consideration of the possibility of potentially curative neurosurgery is important. In this group, that makes up about 3% of all new incident cases of epilepsy, optimal brain imaging is of crucial importance.

Brain imaging and surgical treatment of epilepsy

Hippocampal sclerosis is the most common identified pathology in surgical series. Key imaging features are hippocampal atrophy and increased T2 signal intensity (Fig 1). Visual inspection of the hippocampus can miss subtle, focal or bilateral hippocampal sclerosis. T2 relaxometry allows for quantification of the T2 relaxation time along the length of the hippocampus. When hippocampal volume and T2 relaxometry are considered in combination this can lead to an increased rate of hippocampal sclerosis detection of up to 28% compared to expert qualitative assessment.[5] 3D T2-weighted FLAIR sequences aid the detection of focal cortical dysplasias which are often located at the bottom of a sulcus, may blur the gray-white boundary and have dyslamination extending into the white matter.

After hippocampal sclerosis and focal cortical dysplasia, common pathologies that underlie refractory focal epilepsy that may be surgically remediable are other cortical malformations, developmental and low grade tumours such as dysembryoplastic neuroepithelial tumours, gangliogliomas and gliomas, cavernomas. Diffuse lesions such as

those following perinatal hypoxia/ischaemia, closed head injury and encephalitis are less likely to present excellent surgical targets.

If a lesion has been detected, it is crucial to establish whether this is concordant with the nature of the seizure, interictal and ictal scalp video EEG. Structural lesions such as cavernomas and hippocampal sclerosis may be innocent bystanders that are not causing the epilepsy.

In 30% of potential candidates for epilepsy surgery, optimal MRI does not reveal a lesion. These patients present considerable challenges and specialized imaging methods would be used in Epilepsy Surgery Centres to try to identify focal abnormalities.

Novel MRI contrasts and processing of images after acquisition offer the possibility of identifying covert lesions. In these assessments there is the need to carefully consider sensitivity and specificity and, in particular, to avoid being misled by false-positive findings.[6-8]

Nuclear medicine

If MRI does not identify a lesion that is concordant with clinical and EEG data, functional imaging with positron emission tomography (PET) or single photon emission computer tomography (SPECT) may be useful. PET imaging in epilepsy is generally performed interictally, looking for regions of hypometabolism that infer cortical dysfunction and PET images are co-registered with MRI to give structural correlation. Interictal PET has a sensitivity of up to 90% in cases of temporal and 50% in extra-temporal lobe epilepsy.[9] The region of hypometabolism detected by ^{18}F-FDG PET is generally larger than the seizure onset zone and cannot be used to outline a surgical resection plan. The role of ^{18}F-FDG PET is to aid hemispheric lateralization and general lobar localization in cases with discordant scalp EEG and MRI. The overall positive predictive value of a good outcome following ^{18}F-FDG PET in temporal lobe epilepsy was 77.5% when MRI, EEG or both were non-concordant. An important clinical practice point is to re-review the MRI scan if focal hypometabolism is identified, as with particular focus on a restricted area, a subtle focal dysplasia may be revealed (Fig 2).

SPECT imaging utilizes technetium-99m-labelled ligands to measure regional cerebral blood flow. Due to the very short brain uptake time the tracer can be administered at the time of seizure onset and will be distributed in the brain as a reflection of the relative cerebral blood flow (rCBF) at the time of injection. The ictal studies need to be carried out in a video-EEG telemetry Unit, with dedicated staff poised to give the intravenous tracer

at the onset of a seizure. Tracer administration as early into the seizure onset as possible is crucial to identify hyperperfusion associated with the seizure onset zone. Delayed administration will result in visualisation of areas that show hyperperfusion due to seizure propagation. Studies comparing ictal SPECT to interictal ^{18}F-FDG PET showed a sensitivity of 70.3% and 77.7% respectively.[10]

Functional MRI to identify eloquent cortex

Functional MRI (fMRI) is based on the detection of increased blood flow and brain tissue oxygenation in specific regions during specially designed cerebral tasks. This is referred to as the blood oxygen level dependent (BOLD) signal. Commonly used fMRI language paradigms, verbal fluency and verb generation, are used to lateralize, rather than precisely localize, language functions. The sensitivity and specificity of fMRI for language lateralization is between 80-90% and has replaced Wada testing (intracarotid sodium amobarbital procedure) in nearly all cases.[11] If planned resection margins are close to eloquent cortex, functional mapping techniques such as language and motor functional MRI (fMRI) may help to delineate the boundaries of a safe resection.

Tractography

Tractography is derived from diffusion-weighted MRI sequences in which the anisotropic movement of water molecules within a voxel provides information regarding the most likely direction of white matter tracts between user specified regions of interest.[12] Tractography is used to localize major white matter tracts such as the cortical spinal tract, optic radiation and arcuate fasciculus, and cam help to avoid causing surgical damage. Preventing damage to the major white matter tracts is more important than cortical grey matter as unlike the cortex, white matter tracts do not exhibit plasticity and therefore functional recovery following damage is not possible. Tractography may be derived using a variety of methods, and results are operator dependent so need to be carried out with skilled image processing specialists (Fig x).

The anterior extent of Meyer's loop ranges from 20 – 50mm from the temporal pole.[13,14] Presentation of the tractographic representation of the optic radiation into the surgical microscope eyepiece during temporal lobe resection successfully averted visual field defects.[15] Tractography of the corticospinal tract may be of particular benefit in the pediatric population where both fMRI and awake neurosurgical resection with functional mapping is not possible.

3D-visualisation

The integration of multimodal imaging into common space and 3-dimensional visualization enables the correlation and understanding of the spatial relationships of normal and abnormal structures and function in the brain. This is beneficial when evaluating patients for resection, or for intracranial EEG electrode placement (Fig 3).[16]

Key points

1. X-ray CT is useful for the immediate assessment of individuals who present with seizures in the context of an acute neurological illness.
2. MRI should be acquired using an Epilepsy protocol, and detailed clinical information needs to be given on the request.
3. MRI should be reported by a neuro-radiologist with expertise in epilepsy, ideally with the neurologist.
4. A structural lesion does not necessarily cause the epilepsy.
5. If MRI is normal, developmental methods, PET and SPECT may identify a surgically relevant abnormality

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Legend

Figure 1
MRI of Common pathologies underlying focal epilepsy, amenable to surgical treatment (With thanks to Mr Vejay Vakharia, Neurosurgeon)**.**
Coronal T1 MPRAGE and corresponding T2 FLAIR images of:
A) Right temporal cavernous malformation within the parahippocampal gyrus. Characteristically described as 'popcorn' lesions due to the hypointense haemosiderin ring and mixed signal intensity within the lesion due to the presence of blood at different stages of evolution.
B) 'Bottom of the sulcus' type 2 focal cortical dysplasia (FCD) deep to the left superior frontal sulcus. Imaging features include blurring of the grey-white matter junction and hyperintense signal on FLAIR imaging. Often the hyperintense signal can be seen extending from the underlying ventricle to the cortex (Transmantle sign).
C) A left temporal dysembryoplastic neuroepithelial tumour (DNET) within the fusiform gyrus. Features include a well-demarcated cortically-based ovoid cystic or multi-cystic lesion with a predilection for the temporal lobe.
D) Right hippocampal sclerosis with atrophy and loss of the normal internal architecture. FLAIR image reveals increased signal intensity.
E) Bilateral temporal encephaloceles. A subtle and often overlooked cause of drug-resistant focal epilepsy with the extension of brain tissue through a defect in the floor of the middle cranial fossa.
F) Left frontal low-grade glioma (diffuse astrocytoma) with gyral expansion, homogenous hypointense signal on T1 and hyperintense signal on FLAIR. No contrast-enhancement seen on the post-gadolinium image (not shown).

Figure 2.
Centre: Fluorodeoxyglucose PET scan showing hypometabolism in left frontal lobe in individual with refectory frontal lobe epilepsy and apparently normal MRI (arrow).
Left. Reevaluation of MRI reveals subtle focal cortical dysplasia in left frontal lobe (arrow).
Right. 3D surface rendering showing the left frontal hypometabolism on the FDG uptake image (top) and statistical comparison with normative data (bottom)

Figure 3.
Utility of 3D imaging and integration of EEG data with tractography (With thanks to Ms Anna Miserocchi, Consultant Neurosurgeon)

(A) Top left panel shows surface representation of right cortico-spinal tract (green), lesion (pink) and stereotactically placed EEG electrodes withcontacts involved in seizure onset (pink). Other panels show the outline of the cortical spinal tract.
(B) Surface reconstruction of the right cerebral hemisphere with the planned resection volume (green) and relation to cortical surface veins.

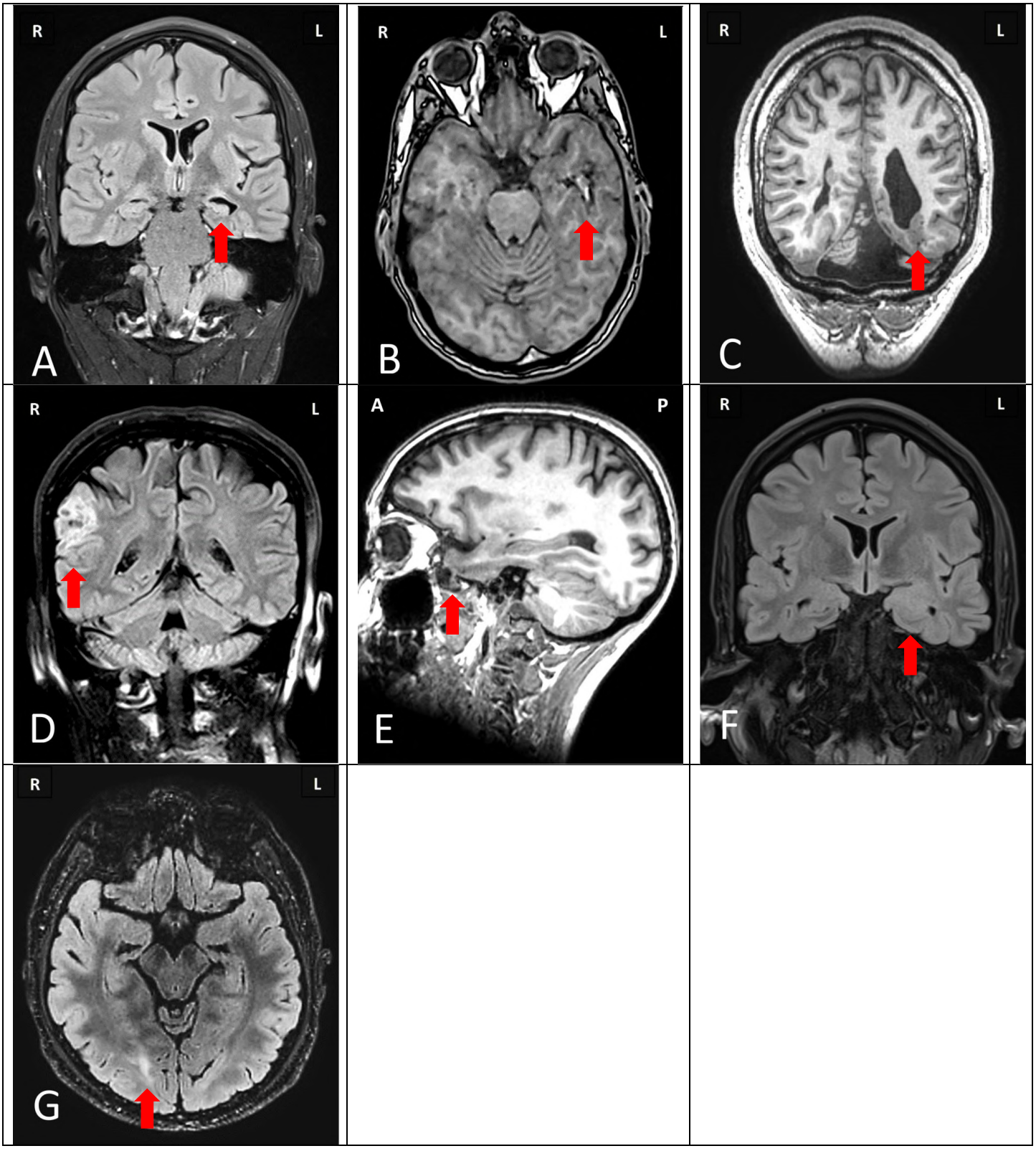

Figure 1