Diagnostic investigation

Electrocardiogram (ECG)

All patients attending the first seizure clinic or the epilepsy clinic should have at least one ECG. Some studies would suggest that 20% of patients with refractory epilepsy may have a contribution from cardiac problems. Also, cardiac problems such as QT prolongation may be a serious but treatable cause of collapse.

EEG - role in classification

It is a myth long-held by both the medical profession and the general public that electro-encephalography is a useful diagnostic test for epilepsy. In fact, there are few things more likely to cloud an uncertain diagnostic picture than an unwarranted EEG.

Many patients with epilepsy will have a completely normal EEG in between attacks - even those with a recognised generalised syndrome such as juvenile myoclonic epilepsy will only exhibit generalised discharges in around 50% of cases. Conversely, the EEG will be abnormal in a sizeable minority of those who do not have epilepsy, so false positive results will confuse the management of those who have had a routine EEG for diagnostic reasons. In this section we will discuss the EEG, its benefits and potential failings, and ways to enhance its usefulness.

Electro-encephalography is a method of studying cortical electrical activity by application of a number of leads to the scalp. These electrodes are spaced out over the skull, allowing an assessment of where in the brain any activity is greatest. Initially, the patient will have recording done while sitting rested and allowed to become drowsy.

Some activation procedures are carried out whereby the patient is asked to hyperventilate, reducing CO_2 levels and enhancing the tendency for both focal and generalised discharges to appear (Figures 1 and 2).

Photic stimulation will often be carried out, where the patient is asked to look at a stroboscopic light at varying frequencies with eyes open and closed. This will have no effect on focal discharges, but will enhance generalised epileptiform discharges.

As can be seen in Table 3, the EEG is neither a sensitive test, nor a specific one. The role of the routine EEG is in classifying epilepsy, i.e. determining if it is of generalised or partial origin. Since anyone with generalised epilepsy will present at a relatively young age, routine EEG should only be requested in a patient with definite seizures beginning at less than 35 years of age.

Anyone who doubts this should see the confusion and uncertainty caused when a routine EEG throws up some non-specific slow wave

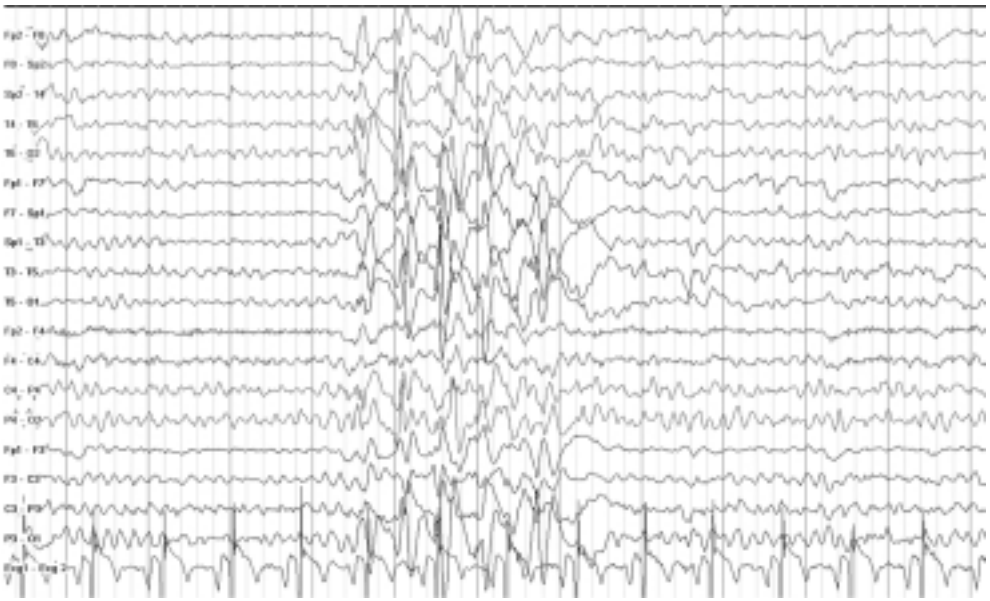

Figure 1 EEG showing generalised epileptic discharges.

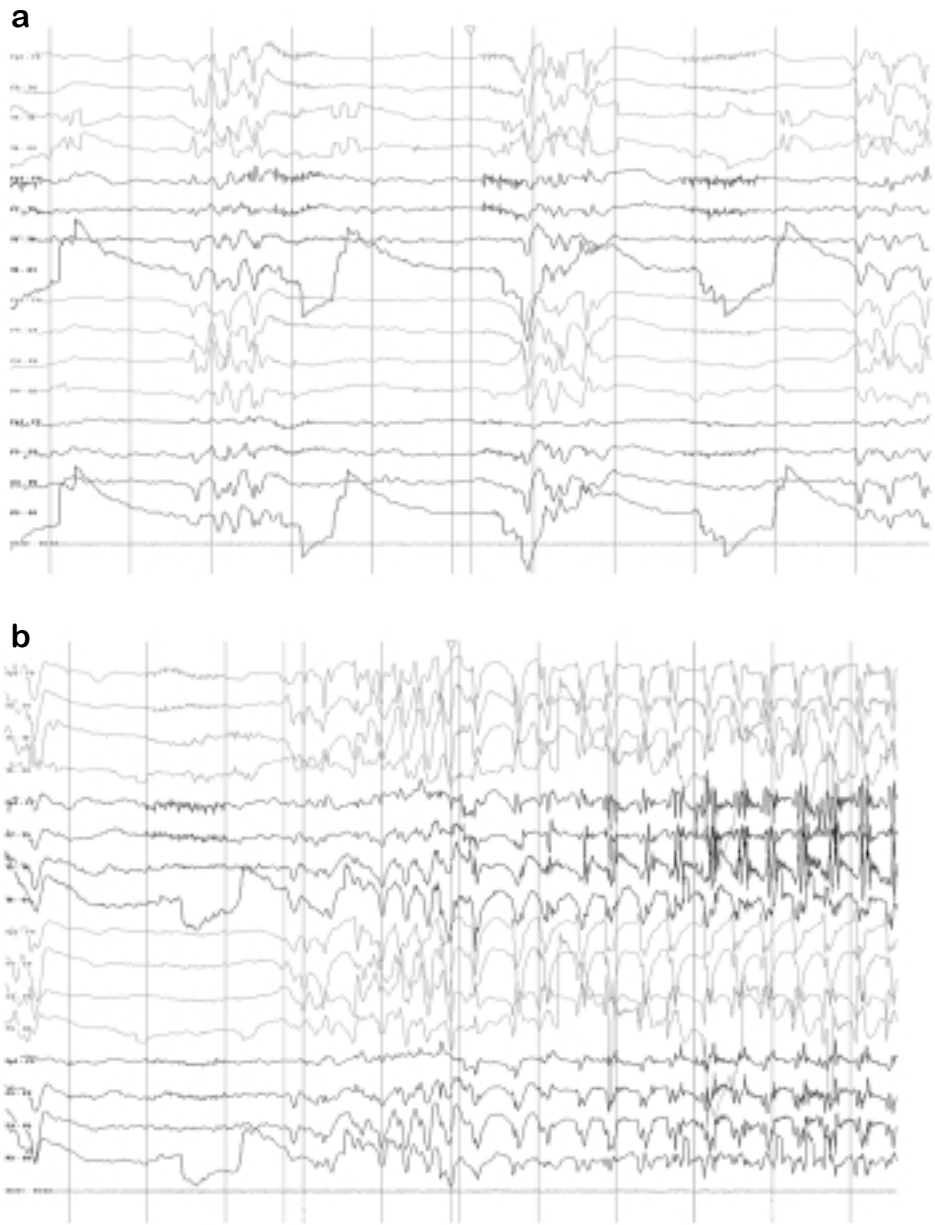

Figure 2 a) EEG showing right-sided focal epileptiform discharges (seen on even numbered leads); b) The same patient as in the top tracing: showing a build up of EEG discharges evolving into a seizure.

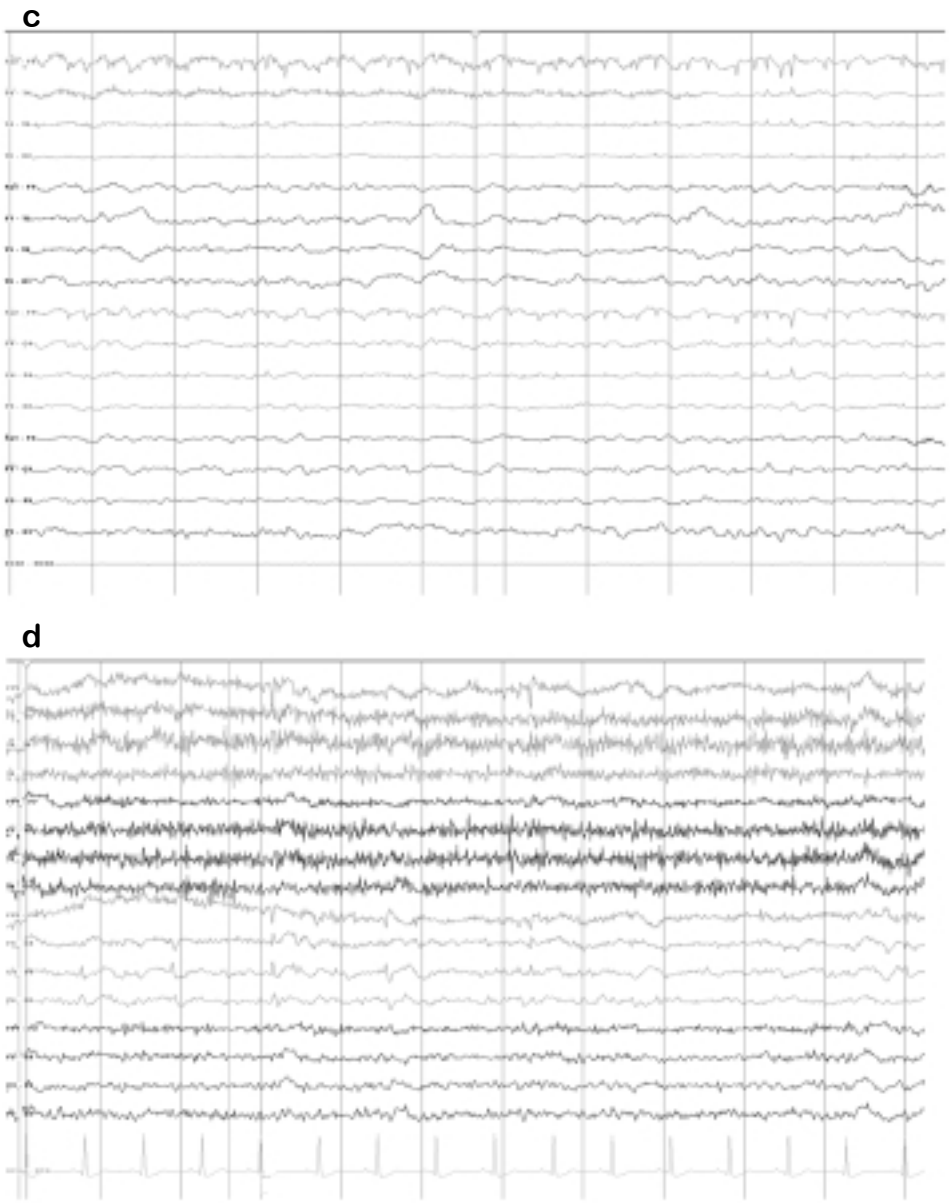

Figure 2 ***continued*** c) The patient showing some right-sided phase reversals (a sign of focal epileptiform activity); d) Spike and slow waves are seen over the right frontal region (the same patient as in the top tracing).

Table 3 The EEG in different clinical situations.

	Generalised epilepsy	Partial epilepsy	Not epilepsy
Routine EEG	Generalised discharges at approx 3Hz, often with frontal predominance	Focal changes with spikes having most diagnostic usefulness	Usually normal, occasional short-lived focal slow wave changes
	Often normal (circa 50%)	Often normal (circa 70%)	Usually normal (circa 95%)
Sleep-deprived EEG	Enhanced yield of generalised discharges, especially during wakening	Enhanced yield of focal spiking	Usually normal, but some focal sleep-related changes may appear
24-hour EEG	Enhanced yield of generalised discharges, especially during wakening	Longer recordings yielding more abnormalities	Usually normal, but still recognised incidence of asymmetry

changes (or even so-called 'epileptiform abnormalities'!) in a young girl who has clearly fainted. The clinician has, with good intentions, requested an EEG "just to be sure". The return visit then entails a lot of head scratching followed in the worst case by use of an anti-epileptic drug and erroneous application of lifestyle changes. In countries where the health care system means there may be a financial gain for the doctor to request and report the EEG, it can be seen that this incentive may increase use of the EEG.

Increasing the usefulness of the EEG

Where classification or diagnosis of epilepsy is difficult or elusive, the EEG can be helpful. With modification, the EEG's utility can be enhanced by recording an attack. This approach can help distinguish epilepsy from non-epilepsy and also help clarify the exact area of onset, which may be

vital information if surgery is to be planned. The following four EEG methods should be considered in these circumstances.

Short video EEG

Differentiation of pseudoseizures from epilepsy can be made easier if a typical attack can be recorded. Suggestion techniques can be used by the supervising doctor or technician to elicit typical clinical features. Use of video recording will allow the patient and eye witness ways to try and record an attack, and can be helpful in demonstrating that throughout this provoked event there are no epileptiform discharges noted.

24-hour EEG

Ambulatory EEG can record continuous EEG activity over 1-2 days at a time. The patient may keep diary accounts of any seizure activity to allow correlation of clinical and electrical events. The period immediately on awakening will be the most likely to produce generalised epileptiform discharges.

Video telemetry

For some patients undergoing consideration of surgery, or for those where they may be unable to keep a reliable diary of their events, admission for video monitoring is justified. These purpose-built suites have camera facilities and the patient remains in the room for the duration of their stay, having the EEG correlated with the clinical status.

Intracranial monitoring

Where there is doubt about the origin of attacks, and where imaging shows either no lesion or multiple lesions, the certainty of origin can be enhanced with placement of intracranial electrodes either in grid form lying across the cortical surface, or depth electrodes with insertion of long tubes into cortical tissue. Obviously, this involves anaesthesia and a small operative risk, so this will only be considered where seizures are frequent enough and severe enough to justify epilepsy surgery, should the results prove conclusive.

Neuro-imaging in epilepsy

Neuro-imaging is central to the evaluation of patients with epilepsy and as advances in imaging techniques are made, we gain more knowledge about the underlying pathology and potential operative options.

The clinical use of X-ray technologies such as computed tomography (CT) has diminished greatly due to the increased superior sensitivity and specificity of magnetic resonance imaging (MRI). The detection of possible epileptic lesions on neuro-imaging can greatly influence and shape the therapeutic strategies chosen by clinicians. Other advances in nuclear medicine, such as positron emission tomography (PET), MR spectroscopy, and single photon emission tomography (SPECT), have some merit as adjunctive imaging modalitites, adding clinically useful information, especially in those with no lesion seen in MRI. Thanks to progress in neuro-imaging, the number of patients deemed to have a cryptogenic epilepsy (as defined earlier) will dwindle and the true prevalence of other pathologies will become more evident.

Magnetic resonance imaging (MRI)

Of those patients newly diagnosed with epilepsy, 12-14% will have an identifiable causative lesion on MRI. In contrast, however, 80% of patients with recurrent seizures have structural abnormalities evident on MRI. There are five reasons for doing MRI in patients with epilepsy:

- clinically focal onset of seizures;
- onset of generalized or unclassified seizures in the first year of life, or in adulthood;
- focal deficit on neurological or neuropsychological examination;
- failure to obtain seizure control after adequate trial on first line anti-epileptic drugs;
- loss of seizure control or change in seizure pattern.

An optimal routine MRI protocol should include T1- and T2-weighted, proton density and fluid attenuated inversion recovery (FLAIR) sequences. These contrasts should be acquired in at least two orthogonal planes, using the thinnest slice thickness possible. A coronal plane gives the best

definition of the mesial temporal structures and allows the clearest outline of hippocampal sclerosis.

T1-weighted images (Figure 3) show the grey-white matter junction most clearly and allow the cerebral anatomy to be defined most easily. T2-weighted images are highly sensitive to showing pathological lesions within the cortex. FLAIR imaging (Figure 4) enhances anatomical detail near CSF.

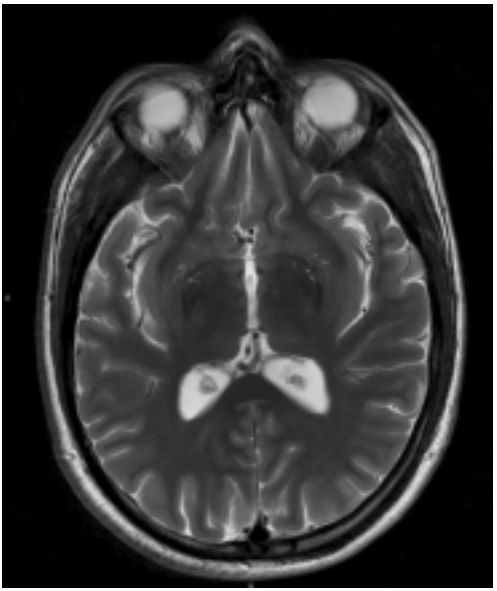

Figure 3 Normal T1 axial image.

Approximately 80% of patients with partial epilepsy have seizures originating in the temporal lobe, the majority arising from the mesial structures of the temporal lobe. The pathological hallmark of mesial temporal lobe epilepsy (TLE) is hippocampal sclerosis which has particular characteristics on MRI. Hippocampal atrophy is best seen on T1-weighted images, while T2-weighted images will show the high signal change. Hippocampal sclerosis will cause other MRI abnormalities such as atrophy of the white and grey matter of the temporal lobe, dilatation of

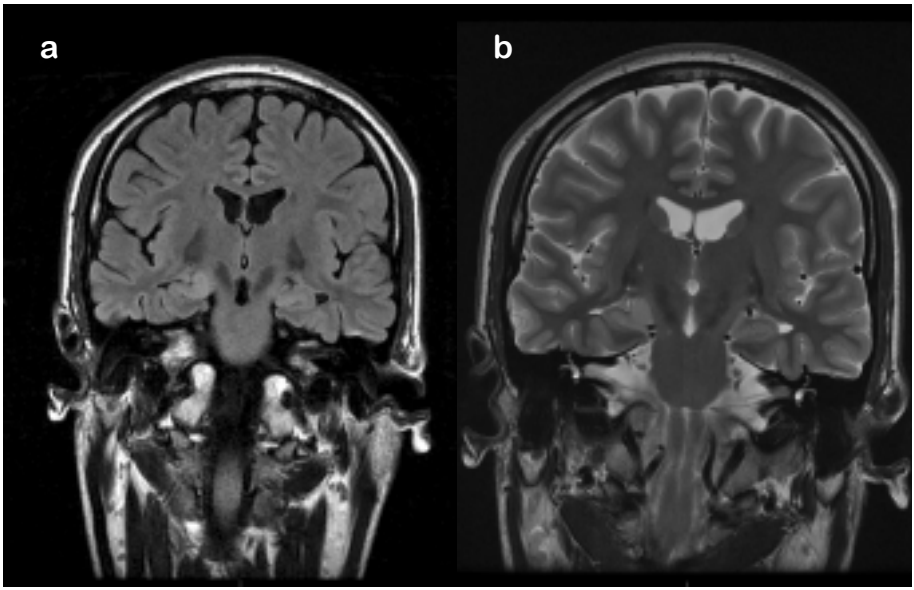

Figure 4 a) Coronal flair MRI. b) Coronal T2 MRI showing a right hippocampal signal change.

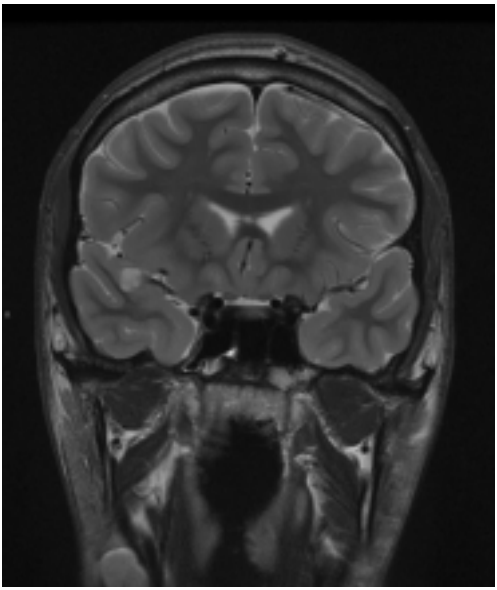

Figure 5 Right temporal lobe lesion on a T1 axial MRI.

the temporal horn and blurring of the grey-white border in the temporal neocortex.

Patients with low-grade primary brain neoplasms often present with focal seizures. The most common pathologies include dysembryoplastic neuroepithelial tumours (DNET), ganglioglioma, gangliocytoma, and piliocytic and fibrillary astrocytoma. In general such lesions are associated with a low signal on T1- and a high signal on T2-weighted images with an absence of vasogenic oedema (Figure 5).

Vascular malformations are another source of focal seizures that can be easily identified by MR imaging. Arteriovenous malformations (AVMs) have demonstrated high blood flow with a nidus, with feeding arteries and draining veins being identified (Figure 6). Cavernous angiomas are small

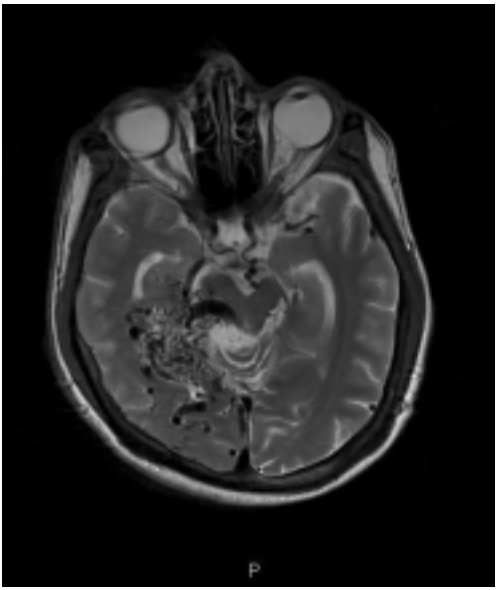

Figure 6 Left posterior temporal AVM. The numerous small flow voids demonstrate a nidus and the larger flow voids are abnormally dilated draining veins. The brainstem is distorted.

dilated veins which have a distinctive appearance on MRI, being circumscribed by a ring of haemosiderin that appears dark on T2-weighted imaging. The central part contains areas of high signal on both T1- and T2-weighted studies (Figure 7).

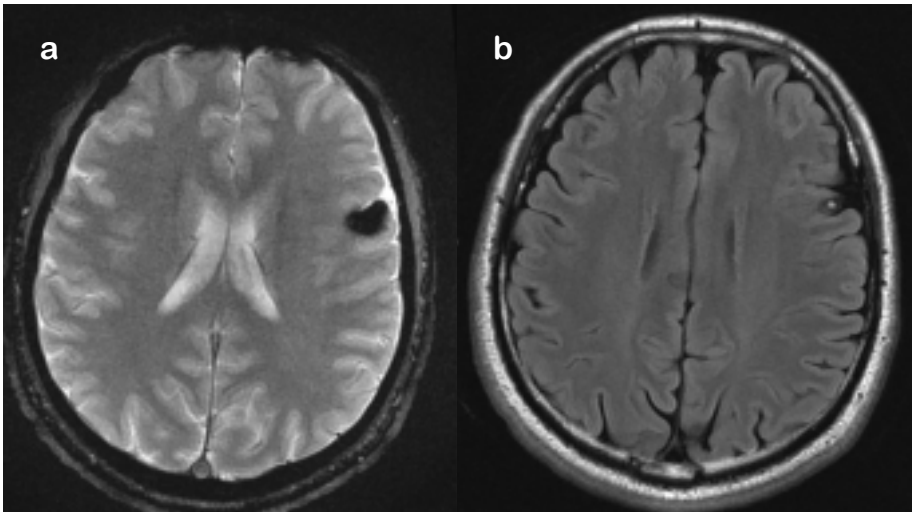

Figure 7 a) Axial T1 and b) axial T2 images showing a cavernous angioma.

Malformations of cortical development pose more difficulties. The important MRI findings of focal cortical dysplasia are focal cortical thickening, simplified gyration, blurring of the grey-white matter junction and T2 prolongation in the underlying white matter, that often forms a cone tapering towards the lateral ventricle.

Single photon emission computed tomography

Single photon emission computed tomography (SPECT) is a useful nuclear medicine technique that measures the regional cerebral blood flow changes in areas affected by epileptic activity. Radioligands are injected intravenously which enter neurones with regional distribution proportionate to the volume of blood flow. Once becoming intracellular, their stabilised

forms remain stable *in vitro* for several hours, giving up to 6 hours to acquire imaging. These scans can then be used to assess blood flow during and between seizures. Correct localization of complex partial seizures may be achieved in over 90% of TLE and extratemporal epilepsy patients. The use of subtraction ictal SPECT coregistered to MRI (SISCOM) improves the rate of localization, in particular in cases of malformations of cortical development. SPECT is utilized as a complimentary method for localization of the seizure focus in surgical candidates with intractable epilepsy. It is often of greatest use in patients who have no lesion seen on MRI.

Positron emission tomography

Positron emission tomography (PET) has more technical difficulty than SPECT and is only offered by tertiary care centres. It is another complimentary method that may be used to help confirm or create a hypothesis about the region of seizure onset. Using isotopes attached to glucose and water, PET outlines glucose metabolism in cerebral regions. Cortex responsible for the seizure onset usually shows reduced glucose metabolism and blood flow interictally on PET scans with spatial resolution of ^{18}FDG-PET superior to SPECT.

As MRI evolves with improving sensitivity and resolution, the need for ^{18}FDG-PET may decrease in the coming years.

Conclusions

History taking is an important skill to learn. It forms the basis of the diagnostic process and is less expensive than investigation. Routine EEG should be used with caution. It should only be used for classification in patients with epilepsy, or for prognostication following a single seizure. Specialised methods (ambulatory, video EEG, or EEG with provocation) can help capture an attack and may be more useful in cases of diagnostic doubt or pre-surgical work-up. Imaging is progressing constantly and is usually best with MRI. It continues to be of help in classifying epilepsy, giving patients information about the root cause of their epilepsy, and in pre-surgical work-up.