Review

Neuroimaging in refractory epilepsy. Current practice and evolving trends

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Identification of the epileptogenic zone is of paramount importance in refractory epilepsy as the success of surgical treatment depends on complete resection of the epileptogenic zone. Imaging plays an important role in the locating and defining anatomic epileptogenic abnormalities in patients with medically refractory epilepsy. The aim of this article is to present an overview of the current MRI sequences used in epilepsy imaging with special emphasis of lesion seen in our practices. Optimisation of epilepsy imaging protocols are addressed and current trends in functional MRI sequences including MR spectroscopy, diffusion tensor imaging and fusion MR with PET and SPECT are discussed.

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1. Introduction

About a 15–30% of patients with epilepsy are refractory to medical therapy, and surgery is the most effective method for controlling seizures in this group of individuals [1–3]. Pre-surgical evaluation aims to delineate the epileptogenic zone, which is a theoretical concept of a cortical area that is indispensable for the generation of epileptic seizure [4]. The extent of epileptogenic zone cannot be measured directly but the hypothesis of the localisation of the epileptogenic zone can be generated by localisation of other cortical zones including ictal onset zone, irritative zone (the area occupied by interictal discharges in EEG), epileptogenic lesion, symptomatic, and functional deficit zone. Neuroimaging is essential and mandatory in the pre-surgical work-up of the localisation and lateralisation of epileptogenic zone. CT scan of the head has the advantages of easier access, quicker scanning time, and lower cost. It is thus particularly useful in acute symptomatic seizures and status epilepticus, and when MRI is less accessible. CT is also able to better demonstrate bone pathology, calcification and haemorrhage. During epilepsy pre-surgical evaluation, CT is also useful to coregister invasive electrodes with the magnetic resonance imaging (MRI).

Surgery has become an invaluable treatment modality of refractory epilepsy. The role of neuroimaging is in particular to delineate discrete lesions amenable to surgical resection, such as mesial temporal sclerosis, focal cortical dysplasia, or hypothalamic hamartoma. MRI has become the method of choice due to its superior soft tissue contrast, multiplanar imaging capability and lack of beam hardening artifacts. MRI of the brain should be the investigation of choice in children and adults with epilepsy to screen for structural abnormalities as recommended by the National Institute of Health and Clinical Excellence (NICE) guidelines [5]. In particular, MRI is indicated in those individuals who develop epilepsy before the age of 2 years or in adulthood, suggestion of focal onset based on history, examination or EEG (unless clear evidence of benign focal epilepsy) and refractory to anti-epileptic medications.

In this article, we first review the applications of MRI in refractory epilepsy with use of conventional imaging protocols with regards to the common cortical abnormalities associated with refractory epilepsies that are surgically remediable. The second part of this review focuses on the role of EEG and integrated MRI and EEG. The final part looks at other neuroimaging modalities including CT and nuclear imaging techniques.

2. Conventional MRI imaging protocols in epilepsy

The recommended epilepsy protocol MRI at 1.5T or 3.0T includes the entire brain from nasion to inion, T1-weighted magnetisation prepared rapid gradient echo (MPRAGE), or spoiled gradient recalled (FSPGR) Images 1.5-mm slice thickness with no
intervening gap obtained in the coronal oblique plane (if TLE is suspected), coronal, and axial FLAIR sequences with 2–3-mm slice thickness and 0–1-mm interslice gap. These images are acquired as a 3D volume, thereby allowing post-processing to correct for head misalignment and for reformatting images into multiple planes to confirm a subtle malformation of cortical development [6–9]. It has been reported that the overall specificity for finding of focal lesion in standard MRI was 22%, if re-assessed by experts 40%, and of dedicated MRI epilepsy protocol is 89%. The use of standard MRI in epilepsy should be limited to exclusion of abnormalities, which have to be treated irrespective of seizure considerations at the onset of the disorder like stroke or malignant brain tumours [10]. In order to optimise a dedicated epilepsy MRI imaging protocol; increasing field strength, hard ware and sequences contributions are required.

2.1. The role of MRI field strength in epilepsy imaging

High field 3 T when compared to the 1.5 T is found to increase detection of new lesions, providing additional relevant clinical information and detection of lesion in 65% of cases referred with a normal routine epilepsy 1.5 T MRI studies [11]. The high field 3 T with the presence of strong gradients allows the use of 3D sequences of greater signal-to-noise ratio than on the 1.5 T MRI, which are very useful for small lesions with an advantage of reduced acquisition time. A recent study on focal epilepsy found that 3 T scans offer better performance than 1.5 T scans in terms of better characterisation of atrophy and gliosis. Focal cortical dysplasia (FCD) was detected in 11% of patients using 3 T, majority of whom were tested to be negative on 1.5 T MR [12]. A study on the detection of transmantine sign in type 2 focal cortical dysplasia (FCD2) showed that 3 T MRI allowed a high spatial resolution in a given acquisition time with isotropic millimetric voxels. The authors stated that the detection and characterisation of FCD2 was better at 3 T than at 1.5 T with similar head coils and acquisition time, owing to greater ability at 3 T to detect the transmantine sign [13].

2.2. Hardware requirement in epilepsy imaging

The hard ware required, is a phased array (PA) surface coil instead of a quadrature head-coil to increase signal to noise ratio (SNR) dependence, PA improves SNR up to fivefold in the cortex which turn results in an increased lesion detection and diagnosis in 64% of patients with focal epilepsy [14]. PA imaging at 3 T significantly improves image quality compared with that in routine 1.5 T head coil studies that will also significantly increase lesion detection in patients with focal epilepsy. In previous study on children with intractable epilepsy, high-resolution MRI identified lesions not detected by standard MRI in more than half the children (56%). Technical advances such as four-coil phased surface array MRI can help identify and better delineate lesions, improving the diagnosis of patients who are candidates for surgical treatment of refractory epilepsy [15].

Increasing the number of channels within the coil has the effect to provide improved signal-to-noise ratio (SNR) in the periphery field of view as well as providing accelerated imaging. For example, 64-channel array provides similar SNR in the brain centre as the 32-channel array but a 1.3-fold more SNR in the brain cortex [16]. This plays an important role in optimizing grey and white matter differentiation on epilepsy imaging.

High resolution MRI including thin coronal slices, in addition to a “dynamic” analysis in a workstation with MPR allows a significative improvement in lesion detection compared to the traditional analysis with radiographic films (94% versus 80%). Patients with focal epilepsy and “normal” MRI need to be investigated further with thin slices and post-processing techniques such as volume acquisitions that allow adequate multi-planar re-slicing [17]. Semi-automated image-analysis techniques have the potential to improve lesion detection, assess lesion burden more accurately, characterise cortical abnormalities, and determine the location and extent of associated cortical and deep grey nuclei involvement. [11]

2.3. Sequence contribution

At our institute routine scanning protocol for a patient with epilepsy includes: T1 Volumetric 3D spoiled gradient echo sequence, T2 W Axial fast spin echo (FSE), Coronal white matter inversion recovery (WMIR), Coronal T2 fluid attenuation inversion recovery (FLAIR), Coronal gradient echo (GE) and high resolution T2 W FSE (Table 1) 2-plane post-contrast images and spectroscopy are required when there is a need to evaluate for suspected conditions such as neoplastic, inflammatory or infectious process. These sequences are used with three main aims: (1) to optimise grey and white matter differentiation, (2) delineate detail of small structures and volumetric assessment, and (3) enhance lesion conspicuity. The total scan time for routine epilepsy protocol is approximately 30–35 min (Table 1)

2.3.1. Optimisation of grey and white matter differentiation

Optimisation in the grey and white matter differentiation assists in localisation and identification of the various types of grey matter heterotopia, delineation of malformation of cortical development [6] and mesial temporal sclerosis (MTS) [18]. MCD has been increasingly recognised as a cause for uncontrolled epilepsy, with the improvement and utilisation of high-resolution MRI techniques. MCD contributes to 25–45% of medically refractory childhood epilepsy [19]. The sequence for optimisation of grey and white matter differentiation is high resolution fast inversion T2-weighted sequence, which is done in near coronal oblique with slice thickness of 3 mm, slice interval of 0.5 mm and scan time of approximately 6 min 9 s. This sequence utilises T2-based sequence with modification of inversion time that will increase the contrast between grey and white matter (Figs 1 and 2). T2W Images are then inverted at the review console to appear like a T1WI. It is also referred to as white matter inversion recovery (WMIR). There is improved sensitivity of high-resolution protocols compared to standard MRI as a result of improved signal to noise ratio and superior anatomical detail [20]. New high-resolution sequence such as 3D double inversion recovery (DIR) has been shown to be more sensitive than FLAIR and T2WI in the detection of seizure laterality in temporal lobe epilepsy [21]. Overall, the largest consecutive analysis investigating 2000 patients referred for MRI after a seizure reported epilepsy related abnormalities in roughly 20% of the cases. In patients with refractory epilepsy, structural lesions can be depicted in up to 82–86% of imaging studies by visual inspection [22].

Table 1

<table>
<thead>
<tr>
<th>Sequence</th>
<th>TR/TE</th>
<th>Plane</th>
<th>Time (min)</th>
<th>Slice thickness (mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>T1 FSPGR</td>
<td>6.7/1.8</td>
<td>Coronal</td>
<td>3.5</td>
<td>1.2 (0.6 overlap)</td>
</tr>
<tr>
<td>or BRAVO(\text{iso-tunable})</td>
<td>7.4/2.9</td>
<td>Coronal</td>
<td>4.0</td>
<td>0.8–1.0</td>
</tr>
<tr>
<td>FLAIR</td>
<td>8000/120</td>
<td>TL Coronal</td>
<td>7.0</td>
<td>3.0</td>
</tr>
<tr>
<td>T2 FSE</td>
<td>3760/102</td>
<td>Axial</td>
<td>2.2</td>
<td>5.0</td>
</tr>
<tr>
<td>T2 FRFSE</td>
<td>7400/102</td>
<td>TL Coronal</td>
<td>3.2</td>
<td>3.0</td>
</tr>
<tr>
<td>FSEIR</td>
<td>8000/50</td>
<td>TL Coronal</td>
<td>6.0</td>
<td>3.0</td>
</tr>
<tr>
<td>GE</td>
<td>655/20</td>
<td>Coronal</td>
<td>2.19</td>
<td>5.0</td>
</tr>
</tbody>
</table>

FSPGR, Fast Spoiled Gradient Echo; BRAVO, brain volume 3D isotropic FSPGR; FLAIR, fluid-attenuated inversion recovery; FSEIR, fast spin echo inversion recovery GE, gradient echo; TL, temporal lobe angulation.

Volumetric 3D spoiled gradient echo sequence (SPGR) or Fast Spoiled Gradient Echo (FSPGR) should be performed using
continuous coronal isotropic acquisition of 1.0–1.2 mm slice thickness, without slice interval and perpendicular to the corpus callosum. It provides excellent T1-weighted contrast between grey and white matter and helps to detect subtle cortical dysplasia and internal structure of hippocampus in patients with mesial temporal sclerosis (MTS) [14, 23, 24]. Scan time is approximately 3–4 min. FSPGR allows visualisation of subtle abnormalities that are not demonstrated on T2-weighted sequence and hence is also capable of demonstrating abnormality like cortical dysplasia (Fig. 3). This acquisition also utilises the parameters that will augment the grey-white matter differentiation that in turn improves the anatomical details [25–28]. Another sequence newly available is the brain volume 3D T1 Bravo sequence (GE Healthcare), which is an enhanced version of FSPGR. Bravo deploys a 3D IR-prepared FSPGR acquisition to produce isotropic T1W volumes that is compatible with parallel imaging, generates images with improved signal to noise characteristics and showing less susceptibility artifacts (Fig. 4).

2.3.2. Optimizing detail of small structures and volumetric assessment

The sequence to look at the detail of small structures such as the hippocampal formations is high resolution near coronal T2-weighted FSE acquisition. This sequence is useful in MTS, which is characterised by selective neuronal loss and gliosis of the hippocampus with resultant architectural abnormality of the neuronal pathway involving the amygdala, fornix and mammillary body.

Fig. 1. Complex partial seizures in an 18-year-old. Coronal MRI in (a) high resolution fast inversion recovery, (b) FSPGR, (c) and T2-weighted FSE showing multiple periventricular and subependymal nodules (arrow) at the right lateral ventricle, isointense to cortical grey matter on all sequences consistent with periventricular nodular heterotopia.

Fig. 2. Coronal high-resolution fast inversion recovery (a) T1W and (b) Axial T2W showing subependymal heterotopia (short arrows) and pachygyria (asterisks).

Fig. 3. MRI in coronal high resolution 3D FSPGR (Fast Spoiled Gradient Echo) reveals cortical grey matter thickening associated with indistinct grey white matter margination at the peri-Sylvian right insular cortex (arrow head) compatible with Type 2 focal cortical dysplasia.

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MTS classically demonstrates T2-weighted and FLAIR hyperintensity. Using 3 T MRI, the T2-weighted fast spin echo (FSE) sequence with 512 × 384 matrixes and 3–4 mm section thickness done in near coronal plane oblique and scan time of approximately 3 min and 36 s provides exquisite details of the hippocampal high signal changes (Fig. 5).

Optimisation in the visualisation of the detailed structures or anatomy of small structures is performed with the use of thin slices. This is again performed using the FSPGR/BRAVO sequences, which allows multi-planar reconstructions when acquired in isotropic voxel. It provides better anatomical localisation and the 3D acquisition datasets can be used for volumetric measurements of the hippocampal formations (Fig. 6). Hippocampal volume loss or atrophy can be determined by subjective visual estimation or by means of objective volume measurement through manual, semi-automated or automated MRI computer segmentation methods. Quantitative hippocampal volumetric measurement is known to be more sensitive and reliable than visual inspection alone in determining the size affected in various neurological disorders [29]. Despite the time consuming post processing technique involved in delineating the hippocampal borders for manual or semiautomatic methods of measurement, the objective yield is very useful in the setting of less than experienced interpreting reader conditions as well as in presence of bilateral hippocampal atrophy. Furthermore the measurement is reproducible and reliable for interventional purposes and future reference. The most important pitfall in quantitative volumetric and structural neuroimaging is the presence of partial volume effects (PVE). Thus, PVE has to be taken into account not only during the quantification, but also during possible pre-processing steps of data like fMRI, DTI, or perfusion images [30].

2.3.3. Optimising lesion conspicuity

The FLAIR sequence is helpful to enhance lesion conspicuity especially those located in the subcortical and subependymal region. Abnormal sulcation and associated abnormal white matter signal alteration usually occurs in type II focal cortical dysplasia (FCD) that may be apparent as transmantle sign on FLAIR and T2 weighted images (Fig. 7) [31]. The FLAIR sequence done in near coronal plane oblique is performed orthogonal to the long axis of the hippocampus (so called “temporal lobe oblique*) with slice thickness of 3–5 mm, slice interval of 0.5 mm and a scan time of approximately 3 min. The two common neoplastic developmental entities are dysembryoplastic neuroepithelial tumor (DNET) and ganglioglioma (Fig. 8). Sequences of susceptibility artifacts such as gradient echo (GRE)/T2* or susceptibility weighted imaging [29] are particularly useful in cases of trauma or vascular malformations, SWI has been used in the further assessment studies of arterial venous malformations, occult venous disease, multiple sclerosis, trauma, tumors and functional brain imaging. This sequence is helpful when searching for haemoglobin breakdown products or to look for calcifications in tuberous sclerosis, or Sturge-Weber [32,33].

3. Integration of EEG with imaging

Electroencephalography (EEG) is the most useful diagnostic procedure for epilepsy, and despite the advent of more sophisticated methods of imaging structural damage, epilepsy remains as one of the clinical problems routinely requiring EEG evaluation. EEG plays an important role in the diagnosis and classification of epilepsy [34]. In EEG, irritative zone is the area in the brain where spikes are generated during the interictal phase. Ictal onset zone determined by EEG is usually but not necessary a subset of the irritative zone. Ictal onset zone is the region of the brain that is able to generate spontaneous after discharges which is adequate to induce a seizure. Although it provides excellent temporal resolution, the EEG has limited spatial resolution. By the time the seizure focus is detected on the EEG monitor it may be some distance away from the actual seizure focus. Intracranial EEG monitoring improves temporal and spatial resolution, however for such an invasive procedure it

Fig. 4. Comparison between a) BRAVO and b) FSPGR with similar slice thickness of 1 mm. This case of lissencephaly demonstrated with symmetrical loss of sulcation of all the cerebral lobes. The abnormal cortical laminations are displayed in greater clarity in the BRAVO sequence.

Fig. 5. Left mesial temporal sclerosis with volume loss of the parahippocampal gyrus (arrow) as well as the sclerosis of the cornu amonis (*) depicted on high resolution T2-weighted coronal view.
suffers from the small field of view. An invasive EEG derivation may already show a seizure pattern while the surface EEG seems still undisturbed.

MRI is useful to identify the epileptogenic lesion in epilepsy, whereas interictal EEG is useful for assessing the irritative zone and ictal EEG for ictal onset zone. The variations and limitations of each investigation in localizing the epileptogenic zone need to be recognised. If a potential epileptogenic lesion identified by MRI, it is essential to have a congruent EEG finding to prove the epileptogenicity of the lesion. Not all lesions evidenced by MRI in epileptic patients are epileptogenic. Thus, further investigations including ictal single photon emission computed tomography (SPECT), interictal Positron emission tomography (PET) or intracranial EEG monitoring might be necessary.

According to early studies, MRI was reported to be able to demonstrate structural pathology in about 70% of all patients with focal epilepsy [35,36]. However, the MRI imaging was interpreted in relative to other investigations, in which a subtle MRI abnormality might become more apparent when interpreted with the additional localizing information from other investigations such as EEG. Many studies had reported that a conventional MRI had 90% sensitivity and 85% specificity in the diagnosis of patients with hippocampal sclerosis of epilepsy undergoing temporal lobectomy [23–25,37]. However, most published surgical outcomes depend on concordance of imaging with ictal and interictal EEG [26,28], 92% of those with more than 90% lateralisation of the interictal epileptiform discharges (IEDs) had a good surgical outcome as compared to 50% with less than 90% lateralisation [27]. Similarly, seizure outcome is also determined by ictal EEG. Satisfactory surgical outcome is more likely seen in those with ictal EEG recordings localised to the lesion (83%), as compared to those with non-lateralised seizures (63%) or seizures that propagate contralaterally (46%) [38].

Lesion negative refractory focal epilepsy is a major challenge in the epilepsy surgery. Normal MRI has been correlated with poor surgical outcomes [18,28]. However, subtle dysplasia could result in “imaging negative” focal epilepsy [39]. In patients with an apparently normal MRI, identifying the irritative or ictal onset zone in EEG might guide further exploration of epileptogenic lesion in the MRI.

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Here the role of higher strength MRI such as 3T and other imaging modalities such as PET or SPECT fused with MRI images may increase lesion detection.

4. Nuclear medicine imaging in epilepsy

FDG-PET has a role in the pre-surgical evaluation of patients with intractable focal epilepsy [40]. PET has been used to detect the functional deficit zone rather than the epileptogenic zone. Ictal SPECT is able to demonstrate the ictal neuronal activation and is a non-invasive marker of ictal onset zone. Both are particularly useful in cases with negative MRI [41]. Interictal PET and ictal SPECT may provide additional information in some patients that aids clinical decision-making. PET and SPECT are usually not indicated for the majority of patients with epilepsy but play an important role in the surgical candidates. The epileptogenic focus will typically

![Fig. 7. (a–d) Axial T1W FSPGR, T2W, Coronal FLAIR and IR T1W images depicting a focal cortical dysplasia at the right parietal lobe with transmantle sign.](image)

Her seizures persisted despite resection of the tumour.

![Fig. 8. Axial T2W FSE, FSPGR and post contrast FSPGR of dysembryoplastic neuroepithelial tumour (DNET) in the right posterior temporal lobe showing a well defined cortical cystic lesion which demonstrate nodular peripheral enhancement. The patient's EEG however showed discordant left anterior temporal sharp-and-slow-waves complex.](image)
manifest as an area of hyperperfusion if radiotracer was injected during the ictal stage or hypoperfusion if it was injected interictally. It has been reported that the correct localisation rate of MRI, interictal PET and ictal SPECT in temporal lobe epilepsy were 64%, 87% and 81%, respectively; and corresponding rates in non- temporal lobe epilepsy were 57%, 71%, and 64%, respectively [42]. Although the diagnostic accuracy is limited to some extent, PET and SPECT and its co-registration with MRI is especially helpful in improving lesion localisation [43–45]. Ictal SPECT and interictal FDG-PET as non-invasive functional tools can provide important information in addition to MRI and video-EEG. The presence of concordance between ictal SPECT and PET predicted a better long-term post-surgical outcome for extratemporal epilepsies, compared with temporal epilepsies [46,47].

Practical issues do arise with performing ictal injection of radiopharmaceuticals as needed in SPECT. The Tc-99m HMPOA must be drawn and ready for rapid injection on seizure onset. The timing accepted as ictal SPECT is injection of the radiopharmaceuticals within 30s of the seizure onset. In a non-specialised epilepsy unit this would be near impossible and most studies will be likely per- ictal demonstrating areas involved in seizure propagation rather than the seizure focus itself. Coregistered PET or SPECT with MRI represents another promising technique for presurgical evaluation of epilepsy, since this procedure offers a potential improvement in epileptogenic zone localisation with very little additional workload or time required. In patients undergoing epilepsy surgery with nonlesional MRI or discordant multimodal investigations, further evaluation can be done by subtraction ictal single photon emission computed tomography (SPECT) coregistered to MRI (SISCOM). Oertzen et al. prospectively evaluated a cohort of patients undergoing presurgical evaluation with SISCOM and found it to be a highly valuable diagnostic tool to localise the seizure-onset zone in non-lesional MRI and extratemporal epilepsies as well as to generate hypotheses for site of surgery or intracranial electrode implantation [48].

Fig. 9 illustrates the congruity of multimodal findings between epileptogenic lesion on MRI and epileptogenic zone on the ictal SPECT/CT in a case of intractable temporal lobe epilepsy. Video EEG telemetry showed electrical spikes originating in the left temporal lobe. The MRI was initially reported as normal. Following the result of intense tracer uptake in the left lateral temporal lobe on ictal SPECT/CT, a second look MRI was prompted which led to the finding of subtle cortical dysplasia in the left temporal lobe.

In recent years, integrated PET/MRI technique has been increasingly used at tertiary centres in the diagnostic work-up of patients with refractory epilepsy [42,44,49,50]. In their cohort of paediatric patients with non-lesional refractory epilepsy, Rubi et al. reported that PET/MRI was as accurate as PET alone in detecting the epileptogenic zones and in addition it was very useful in the guidance of a repeat MRI scan [51]. They found that PET/MRI detected 43% of cases with subtle-lesions on repeated MRI scans. Salamon et al. used FDG PET/MRI to identify cortical dysplasia in patients with therapy-resistant epilepsy [52]. Their protocol added value for the 33% of patients with nonconcordant EEG and neuroimaging findings who otherwise would have required other tests, such as intracranial electrodes, to identify the focus. Another advantage of PET/MRI is to provide more precise presurgical planning as the borders of the cortical lesions can be more clearly identified. Thus,
further advances in the surgical treatment of patients with refractory epilepsy lie in the development and validation of newer imaging techniques and incorporation of these tools into the multimodality presurgical evaluation. The newer simultaneous hybrid PET-MRI acquisition system has been found to minimise patient discomfort while maximise clinical information and optimise registration of both modalities. Dose reduction when compared to PET/CT is also an advantage in the hybrid MRI/PET system [45,53].

5. Evolving trends

In patients with epilepsy, functions including sensory and motor, language and memory have been studied with advanced MRI techniques. Advanced imaging techniques include proton spectroscopy (MR spectroscopy), diffusion tensor imaging (DTI), MR perfusion, arterial spin labelling (ASL) and fMRI with blood oxygen level-dependent [54] activation. These techniques detect dynamic changes in the brain associated with brain functions and seizure focus [55,44].

MR spectroscopy although lacking in spatial resolution, has proven to be a sensitive measure to detect metabolic dysfunction in patients with temporal lobe epilepsy, particularly MTS involving hippocampus. In particular reduction of NAA has assisted in localisation of MTS in 65–96% of cases [56,57]. Reduction in NAA is hypothesised to reflect neuronal loss and dysfunction that occurs in the hippocampus region (Fig. 10). The 2 main techniques in MR spectroscopy are single voxel spectroscopy (SVS) or multi-voxel spectroscopy (MVS). SVS permits interrogation of brain metabolites in a single location selected by the operator. The typical imaging times are 2–8 min, depending on voxel dimensions. SVS is a rapid method for characterising the metabolic information in a 4–8 cm3 region of interest; however it is hampered by poor spatial resolution and does not address the problem of lesion heterogeneity. On the other hand, the multi-voxel spectroscopy (MVS) covers a large volume of interest (VOI) in a single measurement. MVS requires longer acquisition, precisely shimmed MRI equipment and processing time, which leads to potential artifacts but provides metabolic data from multiple areas within the region of interest, tumor and surrounding tissue [58]. Although MVS is technically more demanding, it provides wider anatomical coverage and better spatial resolution, taken into account lesion heterogeneity [59].

DTI is a novel MR technique, which has evolved from diffusion-weighted imaging by adding diffusion weighting gradients in different directions. DTI provides the means to fully categorise the degree of anisotropy in the scanned volume using multiple diffusion-weighted images. It has been shown to be useful in localisation of epileptogenic focus, in which increased mean diffusivity and decreased fractional anisotropy were observed at the seizure focus [60,61]. Visualisation of white matter tracts done with DTI, enable the surgeon to accurately plan and preserve vital tracts while maximizing resected affected lesion [62,63].

fMRI using the BOLD technique has been regarded as a method of non-invasive mapping of the eloquent cortex and used for assessing memory function in temporal lobe [64]. It can help determine the language dominant hemisphere in both epilepsy and non-epilepsy populations and can also act as a predictor of deficits after temporal lobe resection [43,64]. Emerging new sequence such as the arterial spin labelling (ASL) perfusion has been shown to be highly accurate in detecting the laterality of a lesion. In particular, asymmetry of ASL perfusion is strongly correlated with lateralised clinical symptoms in stroke, CBF asymmetries in stenotic-occlusive disease; haemodynamic asymmetries produced by lateralised brain tumors and lateralised temporal lobe epilepsy. Using continuous ASL, one study found abnormal asymmetries of medial temporal lobe flow in patients with intractable temporal lobe epilepsy [65]. Given that ASL offers visualisation of flow values and not metabolism, it may represent a better means of visualising interictal hypoperfusion in patients with epilepsy. In addition, ASL does not require the use of intravenous contrast agents, which is an advantage in young patients and/or in those with renal impairment. It is also an advantage for patients in whom standards ictal perfusion imaging cannot be performed, and in those cases where interictal examinations may have to be repeated often. This study believes that adding brain perfusion investigations to the MRI protocol in patients with intractable epilepsy may have a number of advantages [66]. Pulsed ASL may be a promising approach to detecting interictal hypoperfusion in TLE. This method has potential as a clinical alternative to H215O PET due to noninvasiveness and easy accessibility [67].

EEG-correlated functional MRI (EEG-fMRI) is a functional MRI technique studying the hemodynamic effect corresponding to interictal epileptiform activity [68]. This technique has been used to understand the epileptic network in certain epilepsy syndrome such as absence seizures, reflex epilepsy and genetic generalised epilepsies [69–71]. In epilepsy surgery, EEG-fMRI was used to understand the network of focal epilepsy, the reason for treatment failure, and to guide invasive monitoring [72–74].

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researchers started to study to role of EEG-fMRI in detecting the ictal onset zone [75].

Sundram et al., studied patients with temporal lobe epilepsy, using voxel-based morphometry (VBM) that were applied to grey and white matter anatomy. They demonstrated that participants with temporal lobe epilepsy and psychosis have marked cortical, subcortical and extratemporal grey and white matter deficits compared with those with temporal lobe epilepsy alone and thus provide support for the psychosis literature that also shows this pattern of change [76]. Voxel-based morphometry revealed that GM pathology in TLE extends beyond the hippocampus involving other limbic areas such as the cingulum and the thalamus, as well as extralimbic areas, particularly the frontal lobe. White matter reduction was found only ipsilateral to the seizure focus, including the temporopolar, entorhinal, and perirhinal areas. This pattern of structural changes is suggestive of disconnection involving preferentially frontolimbic pathways in patients with pharmacologically intractable TLE [77].

6. Conclusions

Neuroimaging is mandatory and crucial in the diagnostic work up of patients with medically refractory epilepsy as well as for therapeutic assessment in search for potential surgical cure. MRI is considered to be the most important neuroradiological investigation tool given its robust capability to demonstrate precise anatomical brain structure with high-resolution detail. The current trend as seen from this review, is that focal lesions influence brain areas beyond the epileptogenic lesion, across assemblies of functionally and anatomically connected brain areas. This has led to the hypothesis that epilepsy represents fundamentally a disease of neural networks. Recent technical advances in high performance MRI have greatly enhanced the ability to illustrate neuroanatomy, neural networks, clarify metabolic information and elucidate funcitons of the brain. In addition to EEG, which characterizes epilepsy syndromes and nuclear medicine, that characterise metabolic activity, the fusion of all these information allow greater understanding of the effects of epilepsy on the neuronal networks.

Conflict of interest

None.

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