

Imaging in epilepsy

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Although imaging studies cannot be used to make a diagnosis of epilepsy, they are the most important means of establishing the etiology of seizures. CT can detect most large lesions, and those requiring acute treatment. But it is much less sensitive than MRI for small tumours, migration defects, and lesions such as mesial temporal sclerosis. It is important to use both t1 and t2 weighted sequences, and obtain coronal images. New sequences such as FLAIR or STIR may be helpful as well. Imaging studies are not necessary for children with simple febrile seizures, or primary generalized epilepsy. For evaluating patients with temporal lobe epilepsy being considered for surgery, FDG-PET, ictal SPECT, and MRS are useful ancillary techniques. Lesions may be more difficult to detect in patients with frontal lobe epilepsy. Newer approaches such as diffusion tensor MRI may prove eventually helpful in these cases. Functional MRI can be used for preoperative cognitive mapping. PET tracer studies, while not clinically indicated, can help elucidate the pathophysiology of epilepsy.

ORIGINALLY much less important than clinical and electroencephalographic investigations, neuroimaging has become a vital part of the evaluation of patients with epilepsy. A wide range of techniques have become available, ranging from CT scanning to positron emission tomography with benzodiazepine and serotonin receptor ligands. Computer-assisted image analysis has facilitated scan interpretation, improved our ability to detect subtle but important differences, and enhanced diagnostic accuracy by allowing comparison with groups of normal controls.

It is important to remember, however, that imaging studies cannot in themselves establish the presence of a seizure disorder. There are no CT, MR, PET or SPECT findings unique to epilepsy. Tumours, cerebral malformations, focal hypoperfusion or hypometabolism, or even mesial temporal sclerosis, can all be found in patients without clinical seizures. The diagnosis of epilepsy depends first of all on the clinical history, observation of seizures by careful historians, whether medical personnel, family members, or acquaintances, and then on supportive EEG findings. Moreover, imaging results should be interpreted in the context of the clinical and EEG data.

Once the diagnosis of a seizure disorder has been established, however, neuroimaging may become more important than any other laboratory test in assessing the patient's prognosis, course, and therapeutic options. Serial EEG, for example, is of limited utility, as fluctuations in discharges or background frequency show a poor correlation with clinical manifestations, except in the case of primary generalized epilepsy¹. Imaging studies are essential in the identification of etiology. The detection of a specific lesion, or delineation of the extent of neuronal injury underlying the epilepsy syndrome, can provide valuable prognostic data. When patients are being considered for surgery for uncontrolled seizures, imaging can provide extremely strong evidence for the localization of an epileptic focus. Recent data suggest, moreover, that imaging can be used for preoperative mapping of language and memory. Both these approaches can reduce markedly the need for invasive studies. Imaging has the potential to provide information on the effects of persistent seizures, and the 'progression' of epilepsy. Studies to help elucidate the underlying mechanisms of epilepsy can be performed as well.

Detection of seizure etiology and epileptic foci

Studies on initial presentation

X-ray CT is often the first imaging procedure performed in patients with epilepsy, particularly when MRI is not readily available. CT will detect large lesions including tumours and arteriovenous malformations, calcifications due to congenital or acquired infections, as well as lesions associated with parasites such as cysticercoids or hydrated cysts.

Single enhancing lesions on CT may be due to tumours or arteriovenous malformations, but are common in patients with cysticercosis as well, and, in endemic regions, this is the most likely cause². In a series of 247 children presenting with partial seizures without obvious cause in Southern India, 54% had had enhancing lesions or calcifications on CT³. Tuberculosis and hydatid cysts can have a similar CT appearance^{4,5}.

In a study from Washington DC, 19 of 107 children presenting with a first seizure had brain abnormalities identified on CT scan; 7 received further investigation or intervention (2 with tumours, 3 with vascular anoma-

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lies, 1 with cysticercosis, and 1 with obstructive hydrocephalus). CT scan abnormalities were more frequent in children with their first unprovoked seizure, or whose seizure onset had been focal, or who had focal abnormalities on postictal neurologic exam⁶. In a study of 203 children at the University of Washington, CT always was normal when the patient did not have an underlying high-risk condition, was older than 6 months, had a seizure of 15 minutes or less, and did not have a new-onset focal neurologic deficit⁷. CT was abnormal in only 15% of adults presenting with a first seizure in a Scottish general hospital⁸.

Thus, CT can be used to exclude most lesions requiring acute treatment, and may detect some underlying causes of epilepsy. However, MR is more sensitive, and will detect lesions missed on CT, even at first seizure presentation^{9,10}. As many as 34% of children with new onset 'cryptogenic' seizures may have an abnormal MR, providing useful prognostic information, and data on which to base further treatment should seizures persist⁹.

It is very important, when MR is performed for the evaluation of epilepsy, to obtain the proper sequences, including T_1 weighted and T_2 weighted sequences to cover the whole brain in a minimum of two orthogonal planes, with the minimum slice thickness obtainable on the scanner used. Gadolinium contrast enhancement is not necessary unless non-contrast scans detect potential lesions such as a tumour or arteriovenous malformation. Ideally, sequences should include volume acquisition with thin partition size (1.5 mm or less) to allow reformatting in any orientation and 3D reconstruction. Newer sequences such as (fluid attenuated inversion recovery (FLAIR)) may be helpful. In the first two years of life, incomplete myelination, resulting in poor white-gray contrast, may reduce MR sensitivity^{10,11}.

Imaging studies do not need to be performed in children with febrile seizures lasting less than 15 minutes, and not associated with any postictal abnormalities or persistent fever. Nor are they necessary for children with unequivocal primary generalized epilepsy associated with three-hertz spike-wave discharges and normal neurological examinations¹².

Reevaluation of persistent seizures and evaluation of patients for surgery

Patients, whose seizures do not respond to antiepileptic drugs, have increasing seizure frequency, a change in neurological examination, or who experience drug toxicity, should have additional imaging studies done even if initial CT, or even MRI, was normal. CT will miss causes of focal epilepsy such as small tumours, mesial temporal sclerosis, and focal cortical dysplasia. A normal CT does not exclude the presence of a lesion that could be removed surgically. MR may not have been

performed with the proper technique, especially for the detection of mesial temporal sclerosis (MTS), a lesion that can underlie many cases of refractory temporal lobe epilepsy.

Temporal lobe epilepsy. Modern structural MRI studies have greater than a 90% yield in patients with uncontrolled temporal lobe epilepsy being considered for surgery. Two MR approaches can be used. Increased T_2 signal identifies MTS and low-grade tumours^{10,13-15}. T_1 -weighted volumetric imaging (vMRI) can be used to detect mesial temporal atrophy^{16,17}. The two approaches have similar sensitivity and specificity for lesion detection¹⁸. Formal quantitative measurement of both signal intensity and volume is important for investigative studies, but visual analysis is sufficient for most clinical purposes.

In the relatively small number of cases where structural MR is non-revealing, functional imaging modalities, including magnetic resonance spectroscopy (MRS), positron emission tomography with fluorodeoxyglucose (FDG-PET), single-photon emission computed tomography, and most recently diffusion-weighted imaging (DWI), can be used. MRS involves measurement of the ratio of N-acetyl aspartate, a neuronal marker, to choline and creatine. Its resolution is lower than structural MRI, and it may be sensitive to parameters such as seizure frequency. Reports of MRS detection of abnormalities vary from 65 to 90% depending on the techniques used^{19,20}. In a comparative study, vMRI correctly lateralized the epileptic focus in 93% of patients and MRS in 97% of patients²¹. These results may not be obtained by all investigators.

Seventy-eight per cent of patients with temporal lobe epilepsy have unilateral interictal temporal glucose hypometabolism on FDG-PET scans²²⁻²⁴. Children with temporal lobe epilepsy who are referred for surgical evaluation for uncontrolled seizures have hypometabolism nearly as frequently as adults²⁵. Patients with bi-temporal surface EEG or non-lateralized surface ictal onset may be lateralized less frequently by FDG-PET²⁶. However, when temporal hypometabolism is present, it identifies epileptogenic cortex with a high degree of accuracy. In patients with temporal lobe EEG foci, hypometabolism may extend to ipsilateral thalamus, as well as frontal and parietal lobes²⁷⁻²⁹. Thalamic hypometabolism may be a valuable indicator of the lateralization of the epileptic focus²⁹. Cerebellar hypometabolism, frequently found, may be ipsilateral, contralateral, or bilateral^{30,31}. A study comparing FDG-PET, volumetric structural MRI, and MRS, showed that PET was slightly better than either MR study, but equivalent to both combined²⁰.

Ictal SPECT has proved to be a reliable method for localizing epileptic foci³². It is important to inject the

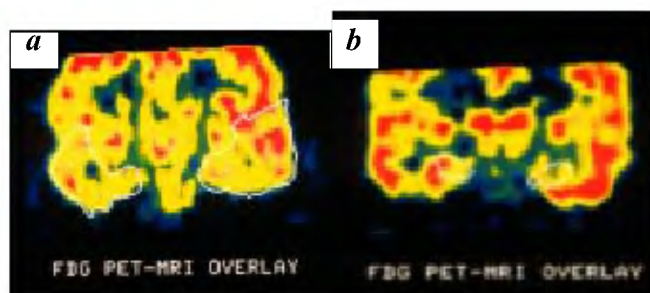


Figure 1. Two patients with mesial temporal sclerosis and hypometabolism on FDG PET. *a*, Patient has extensive hypometabolism involving both lateral and medial temporal neocortex; *b*, Patient has hypometabolism in hippocampus alone. More extensive hypometabolism may predict a poorer surgical outcome.

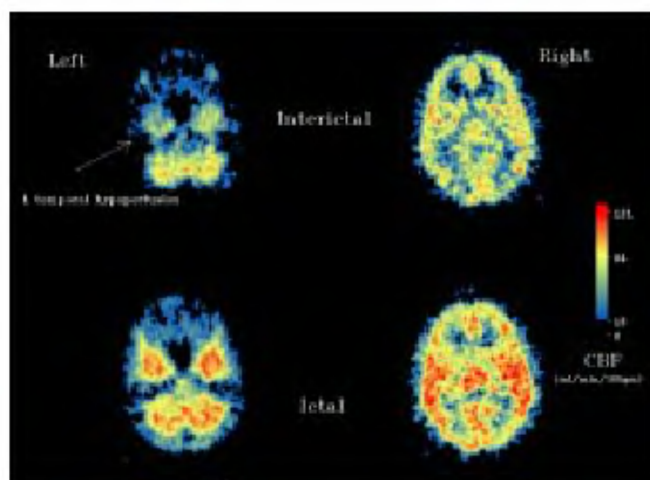


Figure 2. Ictal and interictal cerebral blood flow scans showing that there is a diffuse increase in blood flow even during complex partial seizures.

tracer as soon as possible after seizure onset, while patients are being monitored with Video-EEG. Initially (in patient with mesial temporal foci), relative hyperperfusion of both mesial and lateral temporal cortex (30–35% compared to the opposite side) is seen, followed by persistent mesial hyper- and lateral hypoperfusion^{32,33}. Recent studies suggest that temporal lobe foci may be localized in up to 90% of patients, and false positives are rare. However, if the injection is delayed, only hypoperfusion will be found, leading to potential errors³³. Ictal SPECT may also be reliable for detection of extratemporal foci as well, particularly in frontal and parietal regions. Ictal hyperperfusion was found in 90% of patients, but postictal hypoperfusion in only 40–45% (ref. 34). SPECT has lower resolution than PET, making it more difficult to detect activation in subcortical regions, and quantitative data cannot be obtained. Interictal SPECT by itself is not reliable for detecting epileptic foci. Subtraction of the interictal SPECT data from the ictal SPECT facilitates localization of the epileptic focus, especially if the result is co-registered with the patient's structural MR scan^{35,36}.

DWI is a new MR imaging approach that measures changes in the apparent diffusion coefficient of water in brain regions. A preliminary study showed increased diffusion in hippocampus ipsilateral to epileptic foci³⁷. Transient decreases, possibly due to cytotoxic edema, may occur after focal seizures, and particularly if they are prolonged³⁸. The value of this technique for clinical use is uncertain.

The sensitivity of CT is much lower than any of these newer imaging modalities, and there is no reason to repeat a CT scan at this point in a patient's evaluation³⁹. MR, FDG-PET, and ictal SPECT all correlate well with outcome after temporal lobectomy^{10,40–43}. If a patient has a well-localized EEG focus, and a confirmatory imaging study, depth or subdural electrode implantation is not necessary to perform surgery. For all the imaging studies, false lateralization, compared with depth EEG and eventual surgical outcome, has been reported to occur in a small percentage of patients. Disagreement between the results of surface EEG, clinical evaluation and imaging is an indication for invasive neurophysiological studies.

In addition to FDG-PET, receptor studies, primarily to measure benzodiazepine binding with the antagonist flumazenil, have been performed. Benzodiazepine receptor binding is reduced ipsilateral to temporal (as well as frontal) epileptic foci^{43–45}. Benzodiazepine abnormalities may be confined to mesial temporal regions even when hypometabolism is widespread, and have as much localizing value as FDG scans^{46,47}. However, these studies are unlikely to be necessary for seizure focus localization except in rare circumstances.

Extra-temporal focal epilepsy. MR is the most important imaging modality for patients with extra-temporal lesional epilepsy, detecting most of the substrates of this syndrome, such as tumours, structural malformation, and focal cortical dysgenesis¹⁰. Structural MR is usually very sensitive for detection of such lesions^{48,49}. The absence of a lesion on MRI may predict poor surgical outcome after extratemporal surgery^{10,50–52}. It is uncertain if this is related to the difficulty of detecting a focus when MRI is negative, or a difference in the underlying pathology. For patients suspected of having cortical dysplasia, a coronal T_1 weighted high-resolution volume acquisition, with thin section high resolution T_2 and flair sequences should be obtained.

Functional imaging studies have been less useful in extra temporal than in temporal lobe epilepsy. Well-localized hypometabolism may be less frequent in association with extratemporal than temporal EEG foci unless a structural lesion is present⁵³. Reported correlation with EEG is less precise than for patients with temporal lobe foci. In contrast to the general agreement of results in patients with TLE, there have been marked differences in reports of the sensitivity of FDG-PET in

non-lesional FLE, ranging from 20% to 80%. For example, we found that only 4 of 15 patients without structural lesions had focal hypometabolism⁵⁴. Even when present, hypometabolism may be bilateral or widespread in a majority of patients^{55–58}.

However, some investigators have had better results, finding quantitative analysis was much more accurate than visual interpretation, detecting hypometabolism congruent with the results of depth electrode studies and surgical outcome in 75% of patients with FLE, including nonlesional cases⁵⁹. Patients with either focal hypometabolism, or normal PET scans, were more likely to have a good surgical outcome than those with diffuse or multifocal hypometabolism, which could suggest poor localization of the epileptic focus⁶⁰. Some authors have suggested that mild degrees of cortical dysgenesis may be detected by FDG-PET but not MRI⁶¹. In a study of 117 patients with neocortical foci, 77 of whom had cortical dysplasia, MR detected 60%, FDG-PET 77%, and ictal; SPECT 70% of lesions; however, concordance was only about 40% (ref. 62). FMZ-PET has also been used to try to detect neocortical foci. In most studies the results have been less clear than for temporal lobe foci (neither FDG nor FMZ-PET proved valuable in MR + frontal lobe epilepsy⁶³). FMZ-PET was superior to FDG-PET in patients with MR negative frontal lobe epilepsy who had unilateral EEG discharges, but neither was useful when MR was negative and EEG was bifrontal⁶⁴. In a small study, carbon-11 methionine PET showed promise for localizing cortical dysplasia when other modalities were unrevealing⁶⁵.

SPECT may be more reliable than PET for detection of extratemporal foci, particularly in frontal and parietal regions. Ictal hyperperfusion was found in 90% of patients, but postictal hypoperfusion in only 40–45% (refs 66–69). SPECT has lower resolution than PET, making it more difficult to detect activation in subcortical regions, and quantitative data cannot be obtained. It is also very important to inject the tracer as soon as possible after seizure onset, and to correlate the results with video-EEG monitoring. One potential pitfall, for example, would be to image an event that was not one of the patient's habitual seizures.

Several studies using 'functional' magnetic resonance imaging (fMRI) with EPI-BOLD detected signal alterations during focal seizures and the seizure focus localization matched EEG and ictal SPECT^{70,71}. It is possible to record EEG during fMRI using cable telemetry equipment, if special steps are used to eliminate interference⁷². Two patients with subclinical seizures and generalized spike-wave bursts had fMRI signal acquisition triggered by EEG. Focal (but bilateral) regions of increased signal were seen in both cases⁷³.

Extra-temporal epilepsy is a more complex problem than temporal lobe epilepsy. Multiple imaging modalities may be necessary to identify lesions, and close cor-

relation with EEG and clinical data is crucial to obtain good surgical results.

Surgery for infantile spasms and other secondary generalized epilepsies. Some children with diffuse epileptic encephalopathies (such as LGS following infantile spasms) have hypometabolic regions even if MRI is normal^{74,75}. Patients with cortical dysplasia may have regions of decreased and increased CMRglc, which generally correspond to the pattern of structural defects, but may extend beyond their limit⁷⁶. FDG-PET but not structural imaging might detect small heterotopic regions, although this will become increasingly less common with improvements in MR technology⁷⁷. Children with cryptogenic infantile spasms may have posterior quadrant hypometabolism, associated with underlying cortical dysplasia, even if structural imaging studies are normal; most have focal or lateralized EEG abnormalities, rather than consistent generalized hypsarrhythmia, at some point in their course⁷⁸. FDG-PET abnormalities have been used to plan surgery in these patients, with apparently good success⁷⁹. PET in children with Sturge-Weber syndrome tended to show diffuse abnormalities with little localizing value⁸⁰. When hypometabolism contralateral to the side of the anatomic lesion is present in children with hemimegalencephaly, surgical outcome is worse⁸¹. In infants and children with this spectrum of disorders, concordance between functional imaging and EEG localization should encourage, and discordance discourage, consideration of surgery⁸².

Preoperative functional mapping

Functional mapping is an important part of presurgical evaluation for patients with uncontrolled epilepsy. Due to the disadvantages of standard approaches such as intraoperative mapping and the intracarotid amytal procedure (IAP), imaging offers an attractive alternative. Either fMRI or PET can be used. The environment of the PET scanner is somewhat more comfortable, and patients who are claustrophobic or who have a medical contraindication to scanning such as braces or metal dental devices (but not fillings) cardiac pacemakers or surgical clips, cannot undergo fMRI studies. PET offers better subject access and monitoring. FMRI is more sensitive to movement artifact. PET, however, requires an onsite cyclotron, due to the short half-life (2 min) 15O-tracer. As PET involves radiation exposure it cannot be repeated as often, or used to obtain normal data for pediatric populations. FMRI uses the same equipment, although different software, as structural studies.

There have been extensive 15O-PET and fMRI activation studies in normal volunteers, and a wide range of cognitive processes have been mapped. Group studies

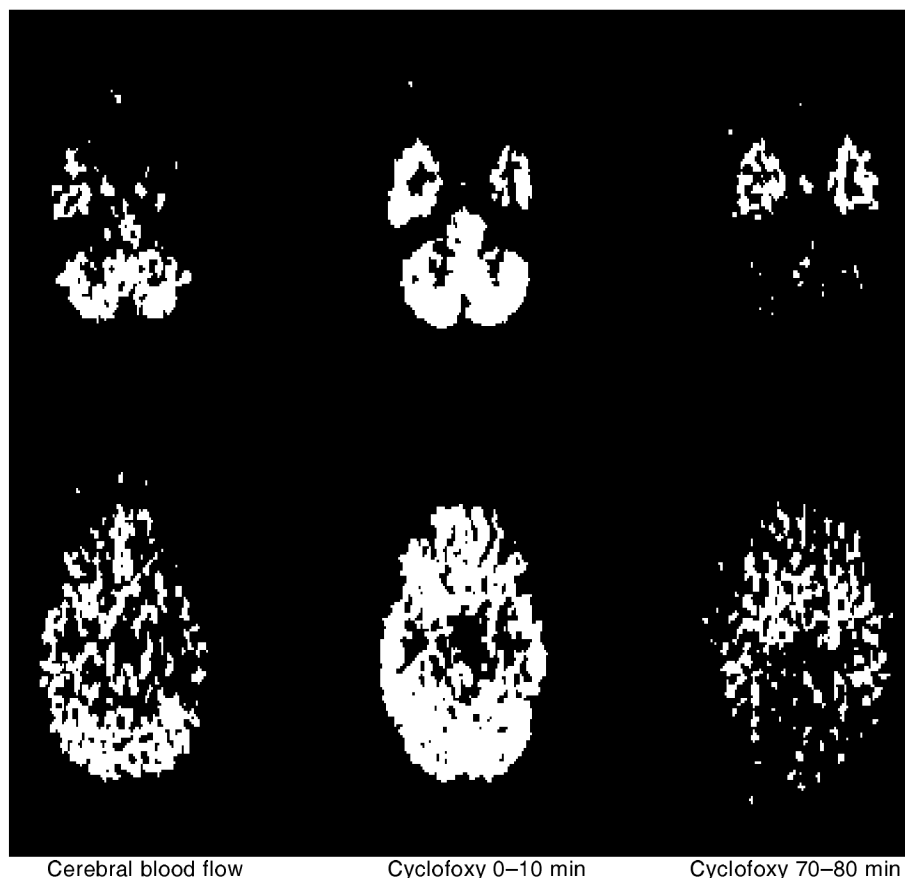


Figure 3. An opiate receptor scan using the kappa ligand ^{18}F -cyclofoxy shows increased specific binding in mesial temporal cortex ipsilateral to the epileptic focus. The earlier cyclofoxy uptake image shows decreased non-specific binding, while the scan with ^{15}O -water shows decreased blood flow. Complex partial seizures, right temporal EEG focus increased right temporal opiate receptor activity.

of normative data provide expected normal activation patterns against which patient data may be compared. However, individual normal data is important to be able to understand what is a normal variant and what a pathological variant. 'Language laterality' is a relative, rather than an absolute measure; normal right-handers for example, show some degree of right as well as left cerebral activation during language-related tasks^{83,84}. Patients with epilepsy tend to have more variability in lateralization, reinforcing the need for individual preoperative mapping.

PET. ^{15}O water PET can be used for both lateralization and localization of language. Two studies comparing PET with ICA language lateralization suggested that imaging might be slightly less sensitive but more specific^{85,86}. Several studies have investigated the effects of the presence of an epileptic focus or lesion on activation patterns. During visual confrontation naming, the left fusiform gyrus was activated in nine healthy subjects, but only in two of 13 patients with left TLE⁸⁷. Tumours in the vicinity of language-related regions however did

not alter activation responses⁸⁸. Patients with early onset of 'lesional' epilepsy may have reduced leftward activation asymmetry in the prefrontal, inferior frontal, and inferior parietal regions for expressive language, suggesting enhanced postlesional plasticity in childhood⁸⁹.

In order to assess the value of O15 activation PET for more detailed cortical localization in six patients with epilepsy being considered for surgery, we compared it to direct cortical stimulation via chronic subdural electrodes using visual and auditory responsive naming tests⁹⁰. Cortical regions showing increased cerebral blood flow during both visual and auditory naming tasks were located in the same regions as subdural electrodes, which disrupted language during electrical stimulation. Cortical regions underlying electrodes that did not disrupt language showed no consistent changes in regional cerebral blood flow during PET activation. ^{15}O -water PET activation also agreed with intraoperative electrical stimulation mapping of motor, visual and language tasks, although overlap was not complete⁹¹. During resection of structural lesions, intraoperative

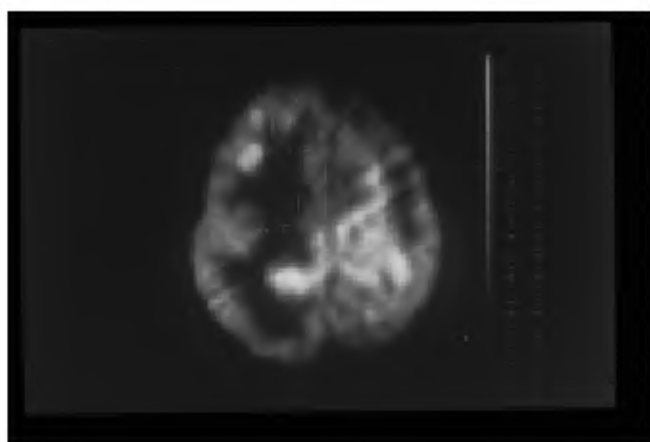
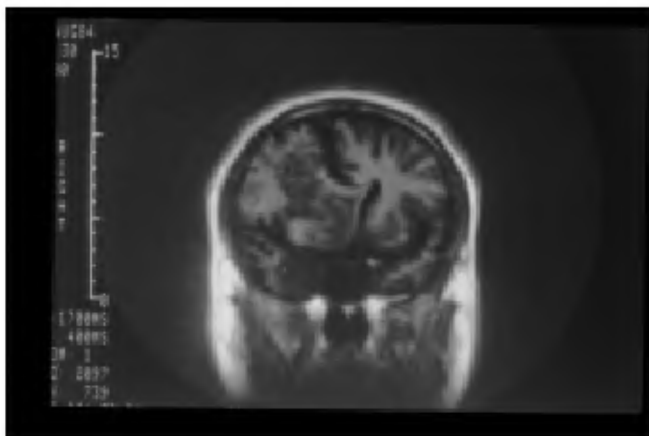


Figure 4. A patient with agenesis of the corpus callosum and a large heterotopia. The FDG-PET scan shows increased activity in the centrum semiovale. FDG PET : Heterotopia, Callosal Agenesis.

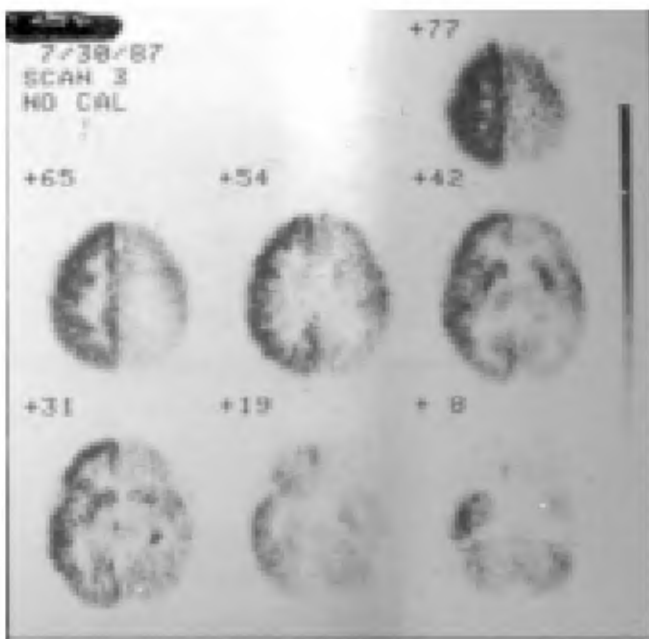


Figure 5. Rasmussen's encephalitis. Hypometabolism on FDG-PET ipsilateral to the abnormal hemisphere.

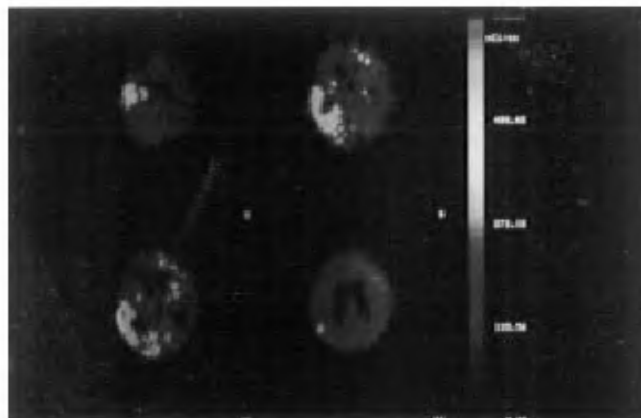


Figure 6. Infantile spasms. During seizures, there is marked hypermetabolism in the left posterior quadrant.

stimulation was continued in the subcortical pathways, and some patients had positive responses on areas not identified by the functional PET. PET blood flow studies (as well as fMRI) may identify areas involved in, but not essential for, language processing, and important language areas may be missed because they do not exceed the statistical activation threshold for the paradigm used.

fMRI. Several studies have shown that fMRI can probably lateralize language as accurately as the IAP^{83,84,92}. In addition, there is good but not complete agreement between fMRI and electrocortical stimulation mapping studies^{93,94}. Patients with epilepsy and early age of brain injury or seizure onset are more likely to have 'atypical' language dominance⁸³.

Some patients perform less well on some tasks, and it is important to use multiple test paradigms, such as a verbal fluency task (letters or categories, depending upon the patient's age), read response naming, and auditory response naming, and when possible, reading and listening to a story⁹⁵. MRI language lateralization should be consistent across all paradigms used, when clinical decisions are being made⁹⁶.

fMRI is particularly useful for children, since there is no radiation exposure, and it is easy to repeat if the test is inconclusive. We have had a few studies where patients fell asleep in the scanner, and no activation was found. Failed studies have occurred in patients who have been significantly cognitively impaired and who would not enter the scanner (and for obvious reasons sedation cannot be used). Rare patients are unable to perform the tasks, for example those with severe reading disabilities. Reading paradigms failed in patients who could not see the stimuli without their visual aids. Contact lenses and plastic visual devices are MRI compatible. In these instances, auditory stimuli have been more reliable. Although IAP may be more reliable in cognitively impaired and inattentive children, we have

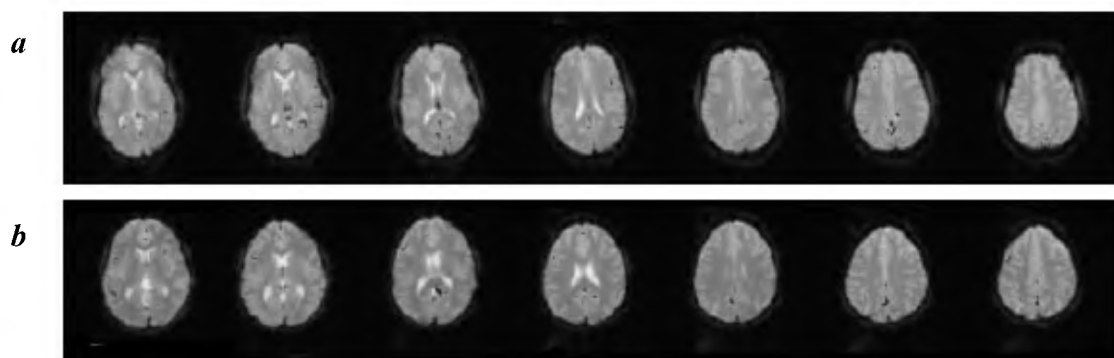


Figure 7. Functional MRI during a language task. *a*, The patient who had early onset seizures in the left temporal lobe has shifted cerebral dominance; *b*, The normal volunteer has left temporal activation.

had some children who had successful fMRI and who were unable to complete the IAP. fMRI can be more readily repeated for failed studies, often with success, more readily than IAP, or intra-operative cortical mapping⁹⁷.

Seizure progression. Several lines of evidence can be used to try to answer the question of whether epilepsy is a progressive disease, and whether persistent seizures, or the underlying process itself, cause neuronal injury. The results of clinical studies have been inconclusive. Neuroimaging studies offer a quantitative approach. In patients with temporal lobe epilepsy, structural magnetic resonance imaging (MRI) has shown volume reductions ipsilateral to the epileptic focus in hippocampal and extrahippocampal regions; the former, in cross-sectional studies, increase with increasing epilepsy duration^{98–101}. Other factors associated with increasing hippocampal atrophy include a history of complex or prolonged febrile seizures, and generalized tonic-clonic seizure number. Positron emission tomography (PET) has shown supporting results. However, these studies have been cross-sectional rather than longitudinal. Preliminary results from prospective imaging studies using fluorodeoxyglucose PET and volumetric MRI show that patients with more recent seizure onset are less likely to have hypometabolism or volume loss than those with a long history of epilepsy^{102,103}. Preliminary studies suggest that hippocampal sclerosis may develop after status epilepticus^{104,105}. Alternate interpretations of these data include a possible progressive effect of epilepsy, or a tendency for patients with structural or functional findings at seizure onset to be more likely to develop uncontrolled epilepsy. In addition to the human studies that have been performed, parallel investigations in animal models using some of the same imaging techniques may help to unravel the factors associated with neuronal injury due to seizures, and aid in interpreting results of clinical studies.

Studying the underlying mechanisms of epilepsy

FDG- and receptor PET have been used to study the pathophysiology of epilepsy and the mechanisms of action of antiepileptic drugs (AEDs). There is disagreement on how well reduced glucose metabolism correlates with MR evidence of hippocampal atrophy on volumetric MRI, as well as cell loss measured in resected specimens^{27,106–110}. PET hypometabolism usually is more extensive than overt structural or pathologic abnormalities^{22,24,28,111,112}. Patients with mesial temporal sclerosis, for example, usually have lateral as well as mesial temporal hypometabolism. Lateral temporal hypometabolism in patients with mesial temporal foci may be due to decreased metabolism in projection fields of dysfunctional or absent neurons, from hippocampus or other structures such as the thalamus or amygdala²⁷. These findings parallel the subtle but widespread cerebral dysfunction that may occur even in focal epilepsy.

In addition to reduced benzodiazepine receptor binding, increased mu and delta, and possibly reduced kappa, opiate receptor binding have been reported^{113–116}. Reduced benzodiazepine receptor binding might suggest reduced inhibitory neurotransmission in epileptic foci, but might be related to non-specific cell loss. Increased opiate receptor binding might help to explain lateral temporal hypometabolism in patients with mesial temporal epileptic foci, and could possibly be related to an endogenous antiepileptic response. The *N*-methyl-D-aspartate (NMDA) receptor ligand 11C-labeled (*S*)-[*N*-methyl]ketamine, showed a 9–34% reduction of tracer radioactivity in the temporal lobes of ictal onset. This may reflect reduced NMDA-receptor density, reduced perfusion, focal atrophy, or other factors¹¹⁷. Recently, reduced 5HT1A serotonin receptor binding was reported as well¹¹⁸. In most animal models, 5HT1A activation inhibits neuronal firing.

Ictal FDG studies show increased cerebral glucose metabolism at the site of the interictal hypometabolism^{24,119,120}. Activation varies widely, from 30% to

300%, depending on clinical as well as technical factors. In a study using bolus $^{15}\text{O}\text{-H}_2\text{O}$, flow increases ranged from 70% to 80% for CPS, and 60% to 133% for GTCS¹²¹. FDG-PET may be less accurate for ictal than interictal glucose metabolism measurements since seizures may alter the 'lumped constant', which describes the relation between tracer (fluorodeoxyglucose) and physiologic substrate (glucose) use. Both complex partial and generalized tonic-clonic seizures are usually much shorter than the 30 to 40 min FDG uptake period, and an 'ictal' scan may include interictal, ictal, and postictal metabolic phases, depending on when the seizure occurs in relation to isotope injection. Combinations of hypermetabolic and hypometabolic regions may be found. If the seizure occurs late in the uptake period, and is 'mild,' there may be little change from the interictal scan. Moreover, relative changes in glucose metabolism may persist for a prolonged postictal period¹²².

Conclusions

Imaging studies are an important part of the evaluation of all patients with epilepsy. A comprehensive MR scan, tailored to the particular epilepsy syndrome, should be obtained. CT can be used for initial screening if MR is not available, but MR should be performed for all patients with negative CT and focal or localization-related epilepsy. Other studies such as PET or ictal SPECT are only needed if surgery is considered and MR has not identified a lesion consistent with EEG localization.

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