Epilepsy surgery

John S Duncan

ABSTRACT – If the first two or three antiepileptic drugs used do not control epilepsy, there is little chance that subsequent medications will be effective. In individuals with refractory focal epilepsy, neurosurgery can have a 60–70% chance of bringing long-term remission and these cases should be referred to a specialised centre for evaluation. The standard evaluation includes clinical review, brain imaging with magnetic resonance imaging, recording of seizures with prolonged scalp electroencephalography (EEG) and video, neuropsychological and psychiatric assessments. The aim is to establish converging evidence that there is a single epileptic focus and that the rest of the brain is functioning normally. In some individuals further evaluation with functional imaging and intracranial EEG recordings may be necessary. The most commonly performed resective operation is an anterior temporal lobe resection to remove a sclerotic hippocampus, followed by lesionectomies and neocortical resections. Palliative manoeuvres, to reduce seizure frequency and severity include corpus callosotomy, subpial transection and vagal nerve stimulation.

KEY WORDS: electroencephalography, epilepsy, focal seizures, magnetic resonance imaging, surgery

The context of epilepsy surgery

Epilepsy is the most common serious disorder of the brain, developing in 30,000 people per year in the UK and with a cumulative lifetime incidence of 1 in 20, and a prevalence of 450,000. Two thirds of those who develop epilepsy will have their condition controlled with currently available antiepileptic drugs (AEDs). Of those who develop epileptic seizures 47% will be controlled with the first AED prescribed, 32% with the second AED, and 9% with the third. Fourth and subsequent AEDs have at most a 5% chance of bringing remission. Given the rapidly diminishing chances of becoming seizure-free after trying three AEDs,[1] those continuing to have focal seizures should be considered for surgical treatment at an early stage. At present the median interval between onset of epilepsy and surgery is 15–20 years in the UK. Those who are potential candidates for epilepsy surgery should have this option considered much earlier, after trying two or three AEDs, which will usually be 2–3 years after the onset of the epilepsy. An estimation of the current need for epilepsy surgery in the UK is a backlog of 4,500, and a further 450 patients develop a need for a definitive resection every year.[2]

Who are candidates for epilepsy surgery?

Principally, these will be individuals who would be able to withstand neurosurgery and who have focal epileptic seizures that continue despite taking AEDs, whether as monotherapy or as a combination of agents, at doses that do not give adverse effects.

The threshold for considering surgery has come down over the last 20 years. At that time the majority of those who had surgical treatment were severely affected, with four or more complex partial seizures per month and, if an adult, were usually not in employment. Nowadays, individuals who experience one or fewer seizures per month may be considered for surgery, particularly if this level of seizure control is only attained at the cost of adverse effects from medication. It is important to remember that there is not only morbidity from seizures, but also an associated mortality (including sudden unexpected death) that may be as high as 1% per year for those patients undergoing pre-surgical assessment.

The aspiration of many of those considering surgical treatment is to be entirely seizure free, so they may drive. A consequence of the lowering of the threshold for surgical treatment to include those with less severe epilepsy is that the possible adverse effects of surgery are relatively more important, and individuals have more to lose.

Individuals need to be able to withstand neurosurgery, and serious comorbidities such as active cancer, vascular or degenerative diseases would normally be regarded as a contraindication.

In paediatric practice, multilobar resections or disconnections are carried out in the first year of life, and surgery continues throughout the paediatric age range. In adult practice, most surgery is carried out in individuals in their teens, 20s and 30s. Good results, however, can be obtained with individuals in their mid-60s, and older.[3]

Learning disability per se is not a contraindication to epilepsy surgery, but there need to be realistic expectations as to what outcome can be achieved,

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and there are important issues of consent and assent to surgery.

A history of postictal psychosis is not a contraindication to epilepsy surgery, but a persisting psychosis or affective disorder would raise concerns and mandate effective treatment before proceeding.

The evaluation

The evaluation for epilepsy surgery is complex and requires a well-functioning integrated multidisciplinary team that includes a neurologist, neurophysiologist, neuroradiologist, neuropsychologist, neuropsychiatrist, epilepsy nurse specialist and neurosurgeon. In addition, input from a counsellor and social worker may be essential to prepare the individual and their family for the outcome and recovery from surgery, and it is often useful for an individual contemplating surgery to speak with someone who has previously undergone the procedure. The complexity of the evaluation is such that this is best done by a team that evaluates at least 50–100 patients per year, in the expectation that about 50% will proceed to definitive surgical treatment. A systematic programmed approach, that involves more than one phase, is necessary. The purpose of the evaluation is to determine:

1 Is there converging evidence for a single epileptic focus?
2 Is there evidence of abnormality elsewhere in the brain?
3 What are the chances of a good outcome from surgery in terms of seizure control and improvement in quality of life?
4 What are the risks of surgery, and how do these compare with the risks of not having surgery?

The key components of the initial evaluation are:

1 A review of the history of the epilepsy and the nature of the current events, with the patient and reliable witnesses to their seizures, by a neurologist who specialises in epilepsy. This will usually require a detailed review of previous medical notes, results of investigations and responses to drug therapy. The description of the seizures may give an indication as to the likely lobe of onset, and whether there is evidence for more than one focus. For example, a history of seizures that start with an epigastric rising sensation, followed by loss of awareness, formed speech automatisms and manual automatisms involving the left limbs and dystonic posturing of the right arm is strongly suggestive of a right temporal lobe seizure.

2 A high quality MRI brain scan, to search for an underlying structural cerebral abnormality. This should be carried out using an epilepsy protocol,[4,5] including a fluid attenuated inversion recovery sequence that heightens the conspicuity of cerebral lesions. The principal pathologies being sought are hippocampal sclerosis (Fig 1), malformations of cortical development, cavernomas, dysembryoplastic neuroepithelial tumours, gliomas, arteriovenous malformations and focal cerebral damage. While the finding of a focal structural abnormality is most important, it does not necessarily follow that the demonstrated lesion is the cause of the epilepsy, and it is crucial to establish concordance with clinical and electroencephalography (EEG) data.

3 A neuropsychological assessment, to establish the overall level of functioning, and to identify evidence of focal deficits of cognitive function, whether these are concordant with the imaging, clinical and EEG data, and whether there is evidence for multifocal or generalised dysfunction. The particular issue for temporal lobe resections is to evaluate verbal and nonverbal memory and to predict the effects of resection on memory function.

4 A neuropsychiatric interview to assess personality traits, determine if there is evidence of an affective disorder, psychosis, or obsessive compulsive disorder. It is important for comorbid psychiatric conditions to be effectively treated prior to any surgery.

5 Video-EEG telemetry, to record typical seizures with simultaneous videotape and EEG recording and to obtain a prolonged recording to document the location of interictal epileptic activity. Recordings with scalp EEG electrodes would generally be carried out over several days, with consideration of reduction of AEDs by 50–75% if an

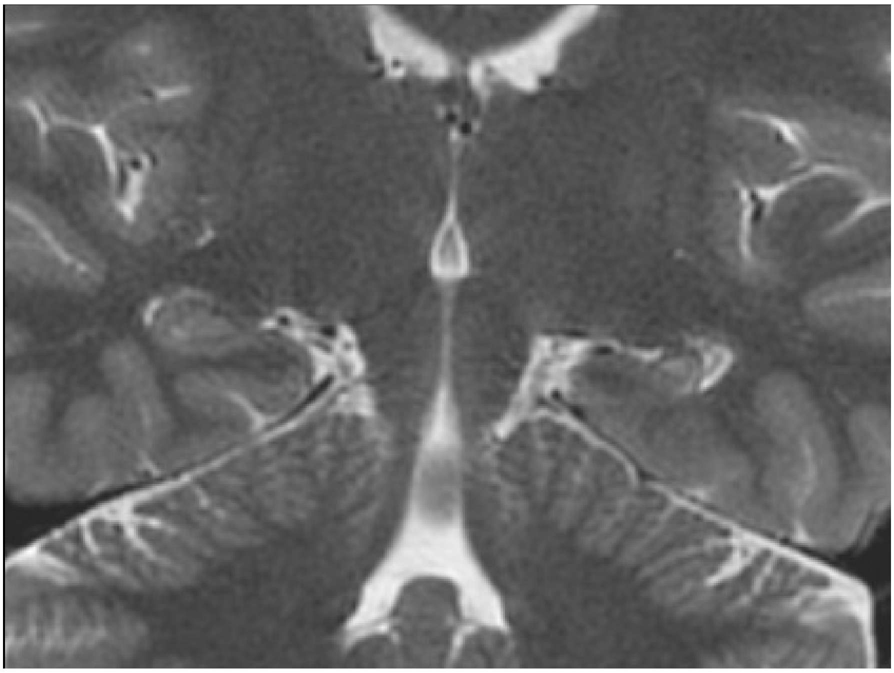


Fig 1. A coronal T2-weighted magnetic resonance imaging scan showing atrophy and increased signal in the left hippocampus (hippocampal sclerosis). Note that the left of the patient is on the right side of the image.

individual may have seizure-free intervals that are longer than the duration of the planned recording. The video tape of any seizures is then analysed and events characterised as to the likely site of onset. The prolonged interictal EEG and ictal EEG are reviewed for evidence of focal epileptic activity that concords with the other data (Fig 2). EEG data are usually more clear in temporal lobe epilepsy and may be less clear-cut, or not identifiable in extra-temporal seizures.

If there is concordance between data, these may be the only required investigations. The emphasis then is on preparing the individual and their family for surgery and for the possible outcomes in terms of seizure control, likely effects on memory and other functions, possible effects on mood, and longer-term prospects.

Further evaluations may be needed if there is not a clear conclusion from the initial series of investigations. These may include functional magnetic resonance imaging (fMRI) to lateralise language function,[6] and to localise primary sensory and motor cortex if the planned surgery is close to the eloquent cortex.[7]

The intracarotid sodium amytal test used to be carried out prior to all anterior temporal lobe resections, and resection close to the language cortex. This test involves angiography and injection of a short-acting barbiturate into the internal carotid artery, to temporarily simulate the effects of temporal lobe surgery on language and memory. The usage of this test has waned in recent years, as the data acquired may be largely obtained from high-resolution structural imaging with MRI, neuropsychological evaluation and fMRI. It is over two years since an amytal test was carried out at the National Hospital for Neurology and Neurosurgery, Queen Square.

If optimal structural MRI does not reveal a discrete cerebral lesion that is concordant with the other data, functional imaging with 18F-fluorodeoxyglucose positron emission tomography looking for an area of hypometabolism, and an ictal single-photon emission computed tomography scan using a blood flow tracer, to search for an area of ictal blood flow increase and interictal area of blood flow decrease, may be useful to help pinpoint the area of seizure onset.[8,9]

If scalp interictal and ictal EEG do not adequately localise the area of seizure onset, it may be necessary to undertake intracranial EEG recordings, with intracerebral depth electrodes and/or subdural strips and grids of electrodes (Fig 3). These are a major undertaking with a risk of significant morbidity. Electrodes may be used both for recording and for stimulation, allowing assessment of the relationship between the epileptogenic lesion and eloquent cortex. While intracranial recordings can give accurate localisation, they only sample from the immediately surrounding cortex and so placement has to be considered and carried out very carefully to test specific hypotheses about the area of seizure onset. There is no place for extensive, blind intracranial implantations of electrodes.[10]

The range of surgical procedures

Epilepsy surgery falls into two major categories: resective and functional. The aim of resective surgery is to remove the epileptogenic zone that gives rise to seizures, and render the patient seizure free. The presurgical evaluation leads to an estimation of the risks and benefits of surgery that the patient and their family can consider.

Peroperative image guidance assists with precise localisation of the area to be resected while accurate tissue removal is facilitated by high-quality operating microscopes and the use of the ultrasonic aspirator that permits removal of gliotic, tumour and dysplastic tissues while preserving the pia mater.

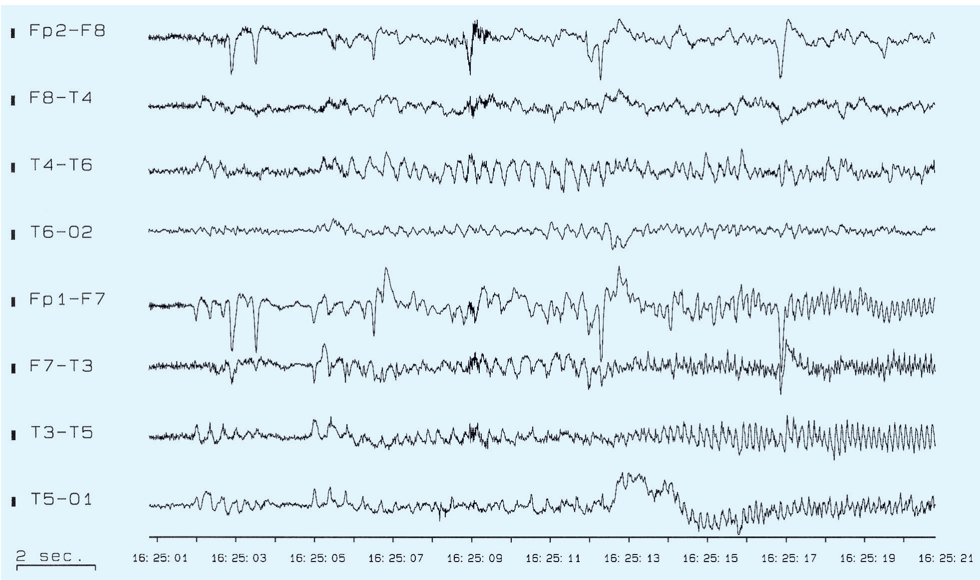


Fig 2. Scalp electroencephalogram showing interictal epileptic discharges and ictal onset over the left anterior temporal lobe (electrodes T3–T5).

Anterior temporal lobe resection

This procedure makes up 70–80% of resections in epilepsy surgery programmes, and the rate of complete seizure freedom is 60–70% if there is hippocampal sclerosis and concordant other data.[11,12] Seizure control is associated with a marked improvement in quality of life.[13]

The resection of a large amount of temporal neocortex has the disadvantage of producing significant neuropsychological deficits as well as a superior quadrantanopia that will prevent driving. For this reason there have been moves to reduce the size of the neocortical resection, either by carrying out a selective amygdalohippocampectomy or a limited resection of the anterior temporal lobe that allows access to the hippocampus. Resections of the speech dominant temporal lobe are associated with a reduction in verbal memory, that is most evident in patients who have well-preserved memory preoperatively.[14] A homonymous quadrantanopia occurs in approximately 10% of patients and in 5% this is severe enough to prevent driving.

Lesionectomy

Resection of small epileptogenic lesions such as cavernomas, focal cortical dysplasia, and indolent tumours such as dysembryoplastic neuroepithelial tumours, are associated with a 40–50% rate of freedom from seizures. Success depends on complete resection of the epileptogenic zone, which may be more extensive than the visible lesion and require invasive EEG recordings to delineate. Lesionectomies in the temporal lobe carry less chance of seizure freedom than do anterior temporal lobe resections that also remove the anterior hippocampus. The latter, however, carry a higher risk of resulting in an impairment of memory, so careful consideration of the risks and benefits of the alternatives for each individual patient is necessary.

Neocortical resections

These comprise single and multi-lobar resections. Chronic invasive EEG recording may be needed to determine the extent of resection. Depending on the underlying lesion, large resections may be necessary to remove the epileptogenic zone and careful consideration must be given to the possible effect on eloquent functions, particularly motor, somato-sensory, language, vision and memory.

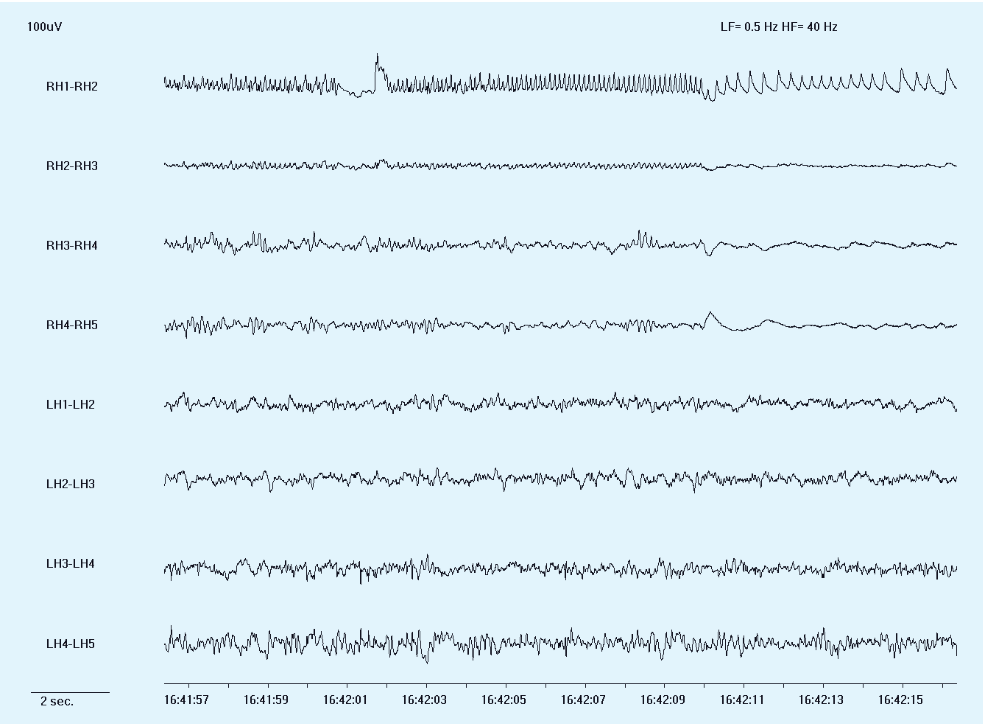
Hemispherectomy

A functional hemispherectomy comprises resection of the temporal lobe and central cortex followed by disconnection of frontal and occipital neocortex from the subcortical structures and corpus callosum. This operation is carried out mainly in paediatric practice and has a place when the function from the hemisphere to be resected is already very limited, and the patient has an established hemiparesis, for example as a result of a malformation, middle cerebral infarct, or chronic Rasmussen's encephalitis.

Functional procedures

Functional procedures are palliative rather than curative, and should only be considered once resective surgery has been deemed inappropriate.

Fig 3. Depth electroencephalogram recording showing onset of seizure in right hippocampus (RH1–RH2).



Corpus callosotomy

Corpus callosotomy is only rarely carried out in adult practice. The primary indication for corpus callosotomy are atonic drop attacks. The callosotomy should be carried out in two stages in order to minimise the risk of a disconnection syndrome, with the anterior two-thirds being divided at the first operation and the posterior third divided if and when the callosal section is completed.

Multiple subpial transection

Multiple subpial transection, comprising vertical incisions in the grey matter at 4 mm intervals, has been advocated for the palliation of seizure generation and propagation within eloquent cortex, with the objective of maintaining anatomical function while reducing seizure generation. It is commonly used in combination with resections which makes assessment of outcome difficult. In children with Landau-Kleffner syndrome, multiple subpial transection may result in improvement in language and behaviour.

Stimulation

Vagal nerve stimulation is a palliative procedure in patients for whom surgical resections are not suitable. The pulse generator is usually placed subcutaneously in the left praecordium and connected to the left vagal nerve. Thirty per cent of patients have a 50% reduction of seizures, and seizure freedom is rare. Common adverse effects include hoarseness and coughing during stimulation and discomfort in the neck. There are suggestions that efficacy of seizure suppression, mood and quality of life improve over time.[15,16]

Deep brain stimulation is being evaluated for refractory epilepsy, and at present there is no consensus regarding utility.[16] Given the heterogeneity of structural and functional networks that may sustain epilepsy, the likelihood of achieving more than palliation, through an effect on a final common pathway, does not seem probable.

Potential adverse effects

In general, the risk of severe long-lasting new morbidity, such as a hemiparesis or aphasia as a result of epilepsy surgery, is less than 1%. In addition there may be predictable deficits for individual patients, such as impairment of verbal memory after a left anterior temporal lobe resection, weakness of an upper limb after resection close to the primary motor cortex, and a visual field loss as a result of an occipital resection, or interruption of the optic radiation in the temporal lobe.

Postoperative emotional lability is common but usually self-limiting. Depression or disturbed thoughts occur in about 10% following temporal lobe resection[17] and is more common in patients with a previous history of psychiatric problems.

Consideration of the risks of epilepsy surgery needs to be in the context of the risk of not having surgical treatment. As a rule of thumb, for most individuals having epilepsy surgery, the risks of the procedure are equivalent to the risks engendered by 1–2 years of their epilepsy.

Outcome and follow-up

There needs to be easy access to the team in the postoperative period. This is best organised by an epilepsy nurse specialist, who knows the patient well, being the point of contact. In addition, it is good practice to have neurological, psychiatric and surgical follow-up at 2–3 months after surgery, and again at one year, followed by annual review in the neurology clinic. Neuropsychological evaluation at three and 12 months and MRI at three months are useful to establish the consequences of surgery. If an individual is seizure free following surgery, it would be usual to start to reduce antiepileptic medication after 12 months, with the aim to be on a single agent at two years postoperation. At that stage, if the individual is seizure free, the risk of relapse in the next 2–3 years is 10% if they remain on an AED, increasing to 30% if AEDs are withdrawn. In the longer term, 24% of those who are seizure free following epilepsy surgery discontinue AEDs, with a greater proportion of men than women choosing to continue medication, reflecting women's concern about the teratogenic effects of AEDs.[18]

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