The role of the neurosurgeon in the treatment of epilepsy

Epilepsy is a common condition with significant associated patient morbidity. While many patients are managed exclusively by physicians, as many as one third of patients with epilepsy will develop seizures that are refractory to medical treatment.

Neurosurgery is able to offer multiple, evidence-based treatment options for patients with refractory epilepsy, but knowledge of the available surgical therapies, their indications and their evidence base is not well taught as part of basic medical training. This article highlights the role that the neurosurgeon has in the management of patients with epilepsy and outlines the key surgical options available.

Introduction

Epilepsy is the second most common neurological condition in the world (Prilipko and Saxena, 2004) and can cause substantial patient morbidity. In addition to seizures themselves, those with epilepsy are more likely to suffer problems with physical and mental health as well as with educational development and economic status (de Boer et al, 2008). Traditionally, epilepsy is the domain of neurologists and most patients will be managed medically. Despite a multitude of available pharmacological options, as many as one third of patients will develop epilepsy that is refractory to medical treatment (Schuele and Lüders, 2008).

The International League Against Epilepsy has defined drug-resistant epilepsy as 'Failure of adequate trials of two tolerated and appropriately chosen and used AED [anti-epileptic drug] schedules (whether as monotherapies or in combination) to achieve sustained seizure freedom' (Kwan et al, 2010).

Neurosurgical treatment strategies for the management of epilepsy may be broadly categorised into three groups: resection surgery, ablative surgery and neuromodulation. This article discusses these surgical options, their potential indications and outcomes.

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Preoperative workup

In the UK, National Institute for Health and Care Excellence (2012) guidelines state that potential surgical cases are to be worked up in a tertiary centre. The multidisciplinary epilepsy team should include those with experience in managing complex epilepsy with representation from psychology, psychiatry, social work, occupational therapy, counselling, neuroradiology, clinical nurse specialists, neurophysiology, neurology, neurosurgery and neuroanaesthesia.

Teams should have magnetic resonance imaging and video telemetry facilities available to them. The neurosurgeon in the multidisciplinary team should have specialist experience of and/or training in epilepsy surgery and have access to invasive electroencephalogram recording facilities.

The task of the multidisciplinary team is essentially to establish three things:

1. That the patient (or the parent(s), in the case of children) understands (and is willing to engage in) the assessment process and would be agreeable to surgery
2. That the patient suffers from refractory epilepsy
3. That the electroencephalogram and/or imaging data suggest a suitable surgical target (Ryvlin and Rheims, 2008).

Invasive electroencephalography

While conventional scalp electroencephalography is well recognized in the workup of many epilepsies, in cases where the target is less clearly defined (such as extratemporal epilepsy or even non-lesional temporal lobe epilepsy) more invasive recording may be undertaken, from electrodes on the surface of the brain (known as subdural 'grid' or 'strip' electrodes) or even from within the parenchyma itself (known as depth electrodes). The decision of which electrodes (if any) to use is case-specific, but in broad terms, subdural electrodes provide excellent mapping of the cortex but are limited by the fact that they can only record at the surface of the brain and that they frequently require a craniotomy for insertion (which may explain their higher complication rate). Conversely, depth electrodes can be used to monitor deeper brain structures and could be considered less invasive, since they can be placed through a burr hole with the aid of neuronavigation in theatre (Shah and Mittal, 2014).

Surgical resection

Surgical resections are the most commonly performed operations for epilepsy and have some of the strongest clinical evidence (Jette et al, 2014). The surgery itself may be targeted at removing a specific epileptogenic focus or may offer a broader disconnection of abnormal pathways between the cortical hemispheres.

Temporal lobectomy and selective amygdalohippocampectomy

Temporal lobectomy and selective amygdalohippocampectomy are usually considered for cases of focal epilepsy that are refractory to medical treatment. There is randomized trial evidence that temporal lobectomy offers patients significantly improved seizure control and quality of life at 1 year as compared with medical therapy alone (Wiebe et al, 2001).

Preoperative evaluation plays a large role in determining the odds of surgical success. Potential patients will undergo preoperative video electroencephalography and will typically be found to suffer complex partial seizures although secondary generalization is also possible as a feature of temporal lobe epilepsy. Most patients will also have magnetic resonance imaging scans performed to assess the temporal architecture for evidence of either a specific lesion or of mesial temporal sclerosis (*Figure 1*).

Traditionally, resections aimed to remove as much tissue as possible, the assumption being that a larger resection would be more likely to result in seizure freedom, but more selective resections are now being performed in order to try to preserve normal brain function. There is evidence that rates of seizure control (patients who are either seizure free or have a worthwhile improvement in seizure pattern) are comparable with either technique and are in the region of 90–95% in appropriately selected patients (Engel, 1996; Sagher et al, 2012).

Surgery is performed via a frontotemporal craniotomy to gain access, followed by ultrasonic aspiration of the affected tissue, working at the anterior portion of the temporal lobe and gradually working medially to reach the hippocampus. When a selective amygdalohippocampectomy is to be performed, there are three main surgical corridors that can provide access: transsylvian, transcortical and subtemporal (*Figure 2*). In addition to the usual risks of cranial neurosurgery, temporal lobectomy carries a risk of visual field defect (quadrantanopia) as a result of damage to Meyer's loop (temporal optic radiation) or problems with verbal memory function. A decline in verbal memory function will be present in two thirds of cases, but this may not always be functionally significant (Meador, 2006). The risk of visual problems is in the region of 1% (Fisch, 2011).

Lesionectomy

The specifics of surgery will vary from case to case, depending on lesion size, type and location but the goal is to excise the lesion, thereby removing the epileptogenic focus. The workup is similar to that for temporal lobectomy; patients will have electroencephalography performed to localize the lesion and a magnetic resonance imaging scan will highlight its location and potentially be used for intraoperative navigation purposes also. The most commonly encountered lesions are cavernoma, focal cortical dysplasia and tumours (such as dysembryoplastic neuroepithelial tumours).

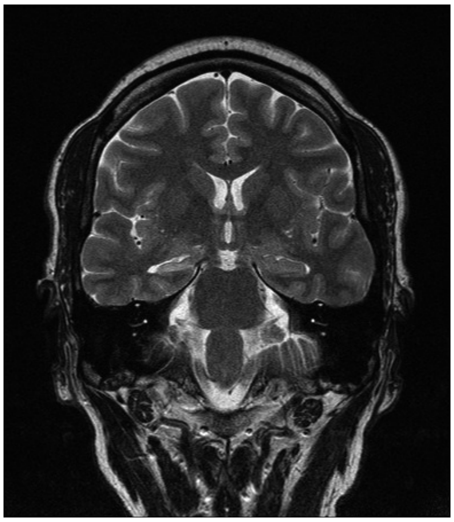

Figure 1. Coronal, T2-weighted magnetic resonance imaging scan showing a patient with right-sided mesial temporal sclerosis.

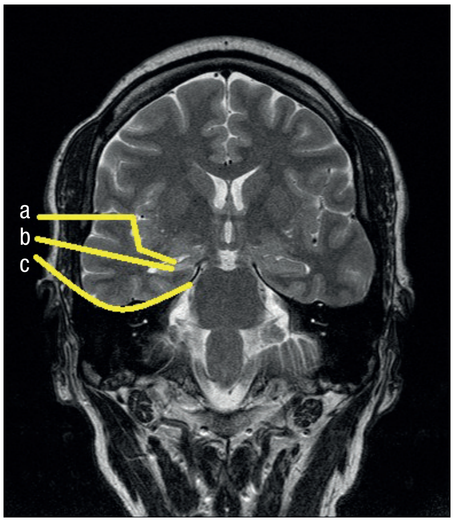

Figure 2. The same image as in *Figure 1* but illustrating the three main surgical corridors used to perform selective amygdalohippocampectomy: **(a)** transsylvian, **(b)** transcortical and **(c)** subtemporal.

Hemispherectomy (disconnection)

Hemispherectomy represents the most destructive surgical option for epilepsy and is reserved for patients with intractable seizures of diffuse origin (such as may occur secondary to perinatal haemorrhage or infarction, cortical dysplasia, hemimegalencephaly or Sturge–Weber syndrome). In recent decades, surgical techniques have developed such that anatomical hemispherectomy (where the surgeon would remove the entire cerebral cortex of one hemisphere) is becoming a thing of the past, being replaced by functional hemispherectomy (or disconnection).

Functional hemispherectomy is a technique whereby the surgeon performs a temporal lobectomy and additionally divides a portion of the corpus callosum in order to disconnect the abnormal cortex of the affected hemisphere from the opposite hemisphere and deeper structures (Griessenauer et al, 2015). The main advantage of functional hemispherectomy over anatomical hemispherectomy is that the risks of complications (including hydrocephalus, haemosiderosis and intraoperative blood loss) are decreased (Devlin et al, 2003; Samandouras, 2010). Two thirds of patients will be seizure free following hemispherectomy (Engel, 1996).

Surgical ablation

Ablation procedures provide a minimally invasive means to destroy epileptogenic brain tissue (Patil et al, 1995). Ablation can be performed using radiofrequency electrodes, placed under stereotactic navigation. Patients require a focal epileptogenic area to target (includes mesial temporal sclerosis) which will have been identified on magnetic resonance imaging before surgery. Magnetic resonance imaging will also be used to navigate the radiofrequency needle intraoperatively so that only a burr hole is required for access. The results of ablative procedures appear variable; rates of significant seizure reduction appear to be in the order of 40–50%, but very few patients are seizure-free post-ablation (Malikova et al, 2012; Nowell et al, 2014). There are also concerns that the high temperatures caused by the radiofrequency needle may, in fact, cause destruction to surrounding tissue. Despite its lower success rates than those quoted for larger operations, the role for ablation remains; surgery offers the potential to treat epilepsy without large scale disruption or removal of surrounding normal cortical tissue. It may also be considered as palliative surgery for patients who are deemed unsuitable for larger operations.

In addition to the radiofrequency technique, ablation may also be delivered using magnetic resonance imaging-guided ultrasound and magnetic resonance imaging-guided laser interstitial thermal energy, the principles being largely similar to those of radiofrequency ablation (Nowell et al, 2014).

Even more recently, stereotactic radiosurgery has been used such that 'surgery' can be performed without the need to perform a burr hole at all (Régis et al, 2006). Stereotactic lesioning can be performed with magnetic resonance imaging-guided accuracy and has proven success in tumour treatment. The main pitfalls of stereotactic radiosurgery are a delay from treatment to clinical effect (in the region of 1 year) and the potential for post-procedural swelling at the site of surgery.

Neuromodulation

Neuromodulation (stimulation of neurological pathways) has been used with some success in other neurological conditions including movement disorders and has evidence for use in the management of epilepsy. The three most frequently used types of neuromodulation are vagal nerve stimulation, deep brain stimulation and responsive neurostimulation (closed loop stimulation).

Vagal nerve stimulation

Vagal nerve stimulation insertion is the most frequently undertaken neuromodulation surgery. The procedure is typically offered for patients with medically-refractory partial seizures or Lennox–Gastaut syndrome. The mechanism of action remains debatable although there is evidence that it alters cerebral blood flow in the medulla, thalamus, posterior temporal cortex, putamen and inferior cerebellum. Vagal nerve stimulation devices may also affect the amino acid composition of the CSF (Anderson and Marks, 2013).

The surgery itself requires implantation of a generator box in the pectoral region and tunnelling of a lead that runs subcutaneously from the generator box to a second incision in the antero-lateral aspect of the neck, where the lead's electrodes are then wrapped around the vagus nerve fibres within the carotid sheath. While efficacy is likely to be comparable if surgery were to be performed on the right or on the left, the left vagus is favoured since the right side is thought to provide the innervation to the sinoatrial node, therefore stimulation may induce bradyarrhythmia (Rolston et al, 2012).

Following insertion of a vagal nerve stimulator, 35% of patients will have a seizure reduction at 1 year, rising to 44% at 3 years postopeartion (Morris and Mueller, 1999). Given the relatively low success rates of vagal nerve stimulation in comparison with resection surgery, stimulators are generally considered as palliative procedures for patients who are not candidates for resection surgery. It is worth noting that vagal nerve stimulation generators will need replacing approximately 5 years post-insertion, depending on model and usage.

Deep brain stimulation and responsive neurostimulation

Deep brain stimulation is a technique whereby electrodes are placed into the brain under stereotactic guidance. These electrodes are thought to work by interrupting the electrical propagation of a seizure within the circuit of Papez. There are many possible target locations, including the thalamus, hippocampus and cerebellum (Wu and Sharan, 2013). The evidence for deep brain stimulation remains weak and potential side effects of long-term stimulation may include psychiatric disturbance, depression and tolerance (Nowell et al, 2014).

Responsive neurostimulation has evolved from deep brain stimulation – rather than continuous stimulation, responsive neurostimulation devices will detect the initiation of epileptiform activity within the brain and then stimulate to flood this site with activity, thereby preventing seizure propagation before the seizure manifests itself clinically (Rolston et al, 2012). Early results (Morrell, 2011) suggest that the responsive neurostimulation device implantation results in a decrease in patient-reported seizure frequency of ≥50% in 29% of patients at 3 months postoperation, rising to 46% at 2 years (patients were unblinded after the 3-month follow-up).

Conclusions

Despite the fact that many patients with epilepsy will never need neurosurgical input, there is a community of patients for whom medical treatment proves insufficient. For patients whose epilepsy is refractory to medical management, neurosurgery may be able to offer a good chance of seizure control or cure.

There are a wide variety of neurosurgical options in the treatment of epilepsy. Epilepsy surgery represents an evolving and developing area of neurosurgery with new technologies arriving on the market year on year. While traditional epilepsy operations were large and destructive procedures, there is a trend towards less invasive options, as understanding of the condition improves. **BJHM**

KEY POINTS

- Open neurosurgical procedures, such as temporal lobectomy, selective amygdalohippocampectomy, lesionectomy and functional hemispherectomy offer a high cure rate for patients with medically intractable epilepsy.
- For patients who are not suitable for open resection, either as a result of comorbidity or epilepsy type, there are a range of palliative operations that offer a good chance of significant reduction in seizure burden.
- Appropriate patient selection and preoperative counselling are vital components of epilepsy surgery.
- Decisions regarding appropriateness of neurosurgical intervention for patients with epilepsy need to me made on a case-by-case basis, with the neurosurgeon forming part of a wider multidisciplinary epilepsy team.

Conflict of interest: none.

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