Introduction

Seizures are a presenting feature of many neurosurgical disorders and can arise as a result of neurosurgical treatment or its complications. Recognition and effective management of seizures can be life-saving and will minimise long-term seizure-induced morbidity. In this Element we describe seizure diagnosis, emergency and ongoing management, and considerations in neurosurgical conditions.

What is a Seizure?

A seizure is defined as "a transient occurrence of signs and/or symptoms due to abnormal excessive or synchronous neuronal activity in the brain" (1). These bursts of synchronous electrical activity affect brain function. Seizures may present with alterations in sensory, motor, or autonomic function. There may also be altered awareness, cognition, memory, and behaviour (1)_.Seizures are temporary, with a defined start and end point (1).

Seizures can result from neurosurgical disorders, their complications, or their management. Seizures may be associated with hyponatraemia, hypoglycaemia, intracranial haemorrhage, central nervous system infection, pneumocephalus, or hydrocephalus. It can sometimes be unclear whether an event is a seizure. Clinical events that may mimic seizures or be confused with seizures include: hydrocephalic attacks, new focal neurological deficits, syncope, ischaemic events, dystonia, drug reactions or withdrawal, panic attacks, or features of pre-existing neurological disorders such as migraine aura. Pointers that an event is a seizure include:

- A discrete event with a start and end point
- Progress of symptoms and signs within seconds after onset
- Tongue biting or urinary incontinence
- Desaturation or cyanosis
- Déjà vu sensation or other aura prior to onset
- Occurrence during sleep
- Post-ictal confusion and tiredness lasting hours
- Significant injury during the event such as a vertebral fracture or shoulder dislocation

When it is not clear if events are seizures, videoing the events on a mobile phone and recording an electroencephalogram (EEG) during the events can be helpful. A neurologist should be consulted if there is doubt about whether the events are seizures.

Seizure Types

Classification and description of seizures facilitates communication between healthcare professionals, patients, their families, and carers. Seizure classification plays an important role in guiding investigations and management decisions, understanding prognosis and response to anti-seizure medication, and in teaching and research. The 2017 International League Against Epilepsy operational classification of seizures is shown in Figure 1 (2).

Seizures are described by their onset, which may be focal, generalised, or unknown. Focal onset seizures originate within one hemisphere, and may have motor, sensory, or other features (2). Generalised onset seizures imply the rapid engagement of bilateral brain networks with bilateral features (2). With focal seizures, there may or may not be impaired awareness, but generalised seizures imply a loss of awareness (2).

The ILAE definition of epilepsy is shown in Box 1. Neurosurgical patients with a structural cause for epilepsy have a high risk of further seizures following an initial seizure. Those with tumours, intracranial haemorrhage, or brain abscesses usually meet this definition of epilepsy and are treated with anti-epileptic drugs (AEDs) following their first seizure.

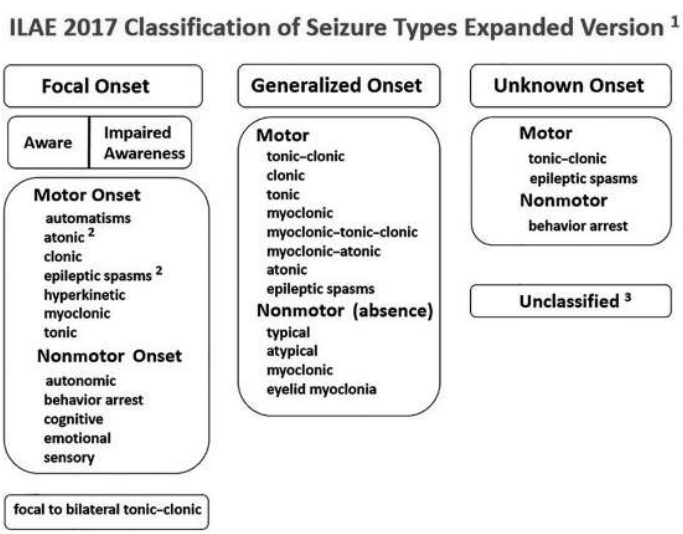

Figure 1 ILAE 2017 classification of seizure types expanded version

1. Definitions, other seizure types, and descriptors are listed in the accompanying paper and glossary of terms.
2. Degree of awareness usually is not specified.
3. Due to inadequate information or inability to place in other categories.

Box 1 ILAE 2014 definition of epilepsy

Practical clinical definition of epilepsy from the 2014 ILAE position paper (3).

Epilepsy is a disease of the brain defined by any of the following conditions:

1. At least two unprovoked (or reflex) seizures occurring >24 h apart
2. One unprovoked (or reflex) seizure and a probability of further seizures similar to the general recurrence risk (at least 60%) after two unprovoked seizures, occurring over the next 10 years
3. Diagnosis of an epilepsy syndrome

Epilepsy is considered to be resolved for individuals who had an age-dependent epilepsy syndrome but are now past the applicable age or those who have remained seizure free for the last 10 years, with no seizure medicines for the last 5 years.

Management of Seizures

Emergency Seizure Management

All episodes of unresponsiveness should be managed using an ABC approach to resuscitation. Emergency resuscitation and treatment should be started whilst assessing for reversible causes and prior to establishing a definitive diagnosis of seizure activity. Figure 2 shows an algorithm for the emergency management of seizures. Ambulant patients may be outside their bedspace at the time of a seizure, and their environment should be made safe to prevent injury and facilitate ongoing management.

Manual airway manoeuvres and airway adjuncts may be required. If a seizing patient is jaw clenching, a nasopharyngeal airway is easier to insert and will maintain the airway. However, a nasopharyngeal airway may be contraindicated following trauma to the nasal sinuses and skull base. Always give oxygen; seizures are associated with desaturation. The recovery position may be the safest position, but in patients with spinal trauma, this may not be possible as spinal alignment may need to be preserved and turning may require log rolling. Intravenous access should be established, and bloods sent. A full blood count, urea and electrolytes, coagulation screen, and blood transfusion sample should be sent to investigate the cause of the seizure, and in preparation for any required surgical intervention. The quickest haemoglobin and sodium levels will be available on a venous blood gas. The bedside glucose should be checked

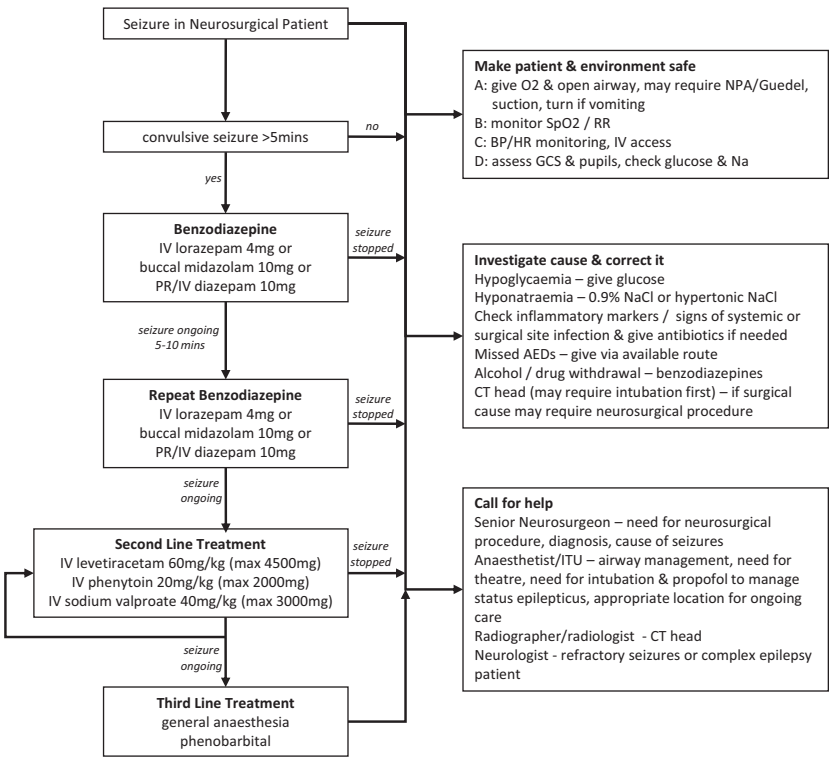

Figure 2 Seizure management in neurosurgical patients

The three boxes for making the patient safe, investigating the cause, and calling for help should be considered simultaneously. They are applicable at all stages of the treatment pathway. Doses given are for adults. Refer to the BNF and local guidelines for safety and administration considerations. (NPA, nasopharyngeal airway; RR, respiratory rate, BP, blood pressure; HR, heart rate; GCS, Glasgow Coma Scale; Na, sodium; NaCl, sodium chloride; AED, anti-epileptic drug; CT, computed tomography; IV, intravenous; PR, per rectum)

to ensure the patient is not hypoglycaemic. Hypoglycaemia is particularly a risk in those unable to eat, for example, due to being nil by mouth pre-operatively, those with post-operative nausea and vomiting, or those with a low conscious level, or brainstem or lower cranial nerve pathologies affecting swallowing. Imaging with a CT head to assess for surgically reversible causes should be considered in every neurosurgical patient with new onset seizures. This may require anaesthetic support or intubation and ventilation prior to transfer to the CT scanner.

Causes of seizures to consider in neurosurgical patients include:

- Hypoglycaemia
- Hyponatraemia
- Hypoxia
- Raised intracranial pressure
- Hydrocephalus or blocked ventriculoperitoneal shunt
- Central nervous system infection
- Cerebral oedema
- Space occupying lesion
- Intracranial haemorrhage
- Stroke or cerebral ischaemia
- Drug or toxin ingestion or withdrawal
- Missed or incorrectly prescribed or administered AEDs

Hyponatraemia is common following traumatic brain injury (TBI) and subarachnoid haemorrhage (SAH) and should be treated with slow correction of the serum sodium to avoid further seizures. Causes of seizures such as acute hydrocephalus, or post-operative haematoma or infection will require surgical treatment.

Status Epilepticus

Status epilepticus is defined as prolonged seizures lasting more than thirty minutes or recurrent seizures without a return to baseline between seizures (4). Guidelines advise treatment for anyone with convulsive seizures lasting five minutes or more (4). Intravenous lorazepam is first line in the hospital setting when intravenous access is available, but buccal midazolam or rectal diazepam may be given when intravenous access is not immediately possible. If the seizure does not stop within five to ten minutes, a further dose of benzodiazepine should be administered. If convulsive status epilepticus does not respond to two doses of a benzodiazepine, then second-line treatment with levetiracetam, phenytoin, or sodium valproate should be given. If this is not successful, one of the alternative second-line treatments can be tried. Third-line options are general anaesthesia and phenobarbital, so discussion with the senior neurosurgeon, a neurologist, an anaesthetist, and the intensive care unit should occur (4).

The Advanced Paediatric Life Support algorithm for management of paediatric seizures is shown in Figure 3. Those who are under consideration for epilepsy surgery or who have known refractory epilepsy may have individualised emergency management plans to follow in the event of refractory seizures. Guidance from a neurologist is also very helpful for those suspected to be in non-convulsive status epilepticus and those with ongoing focal seizures, clusters of seizures, or complex medication-resistant epilepsy.

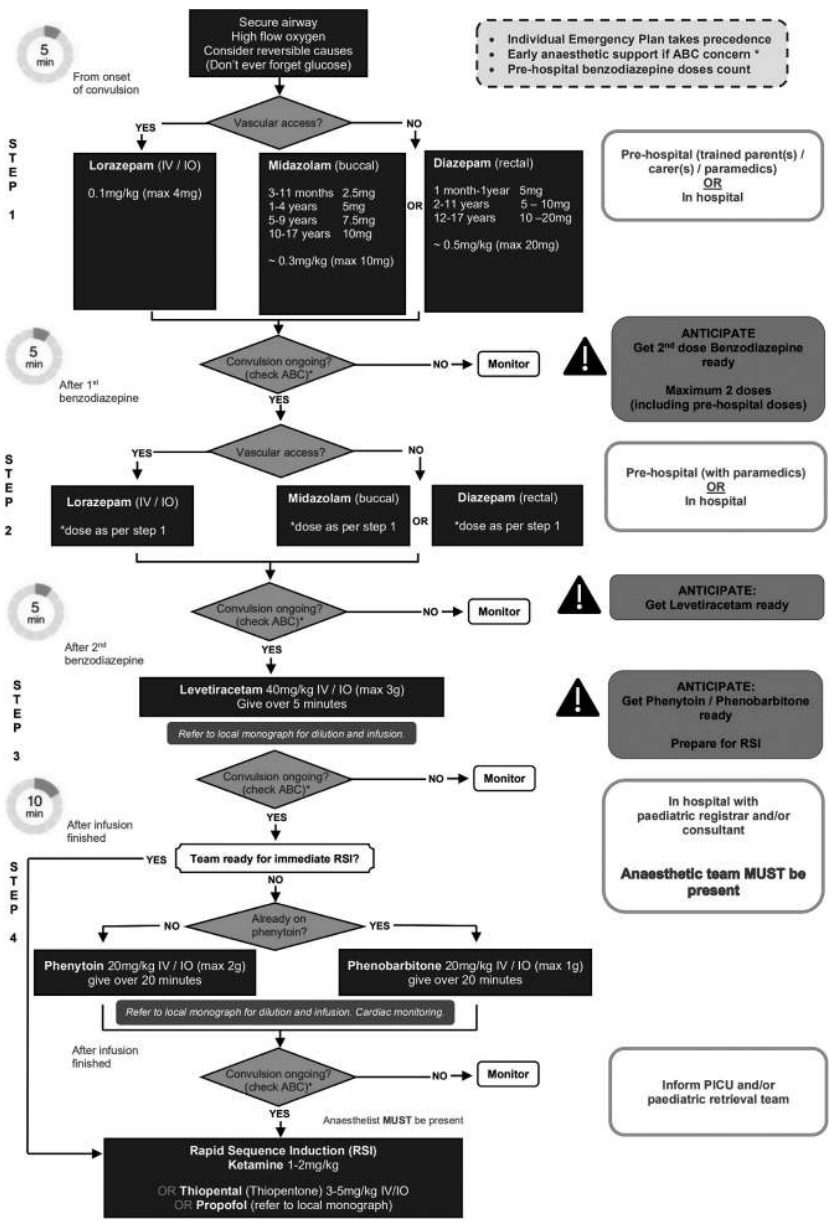

Figure 3 APLS 2021 Algorithm for management of the convulsing child

Anti-epileptic Drugs

Recommended treatment options for generalised tonic clonic seizures are levetiracetam or lamotrigine in women who can bear children and sodium valproate in men, girls under the age of ten, girls who are unlikely to need sodium valproate

after they reach childbearing age, and women who cannot bear children (4). For focal seizures, lamotrigine or levetiracetam is the first-line monotherapy, with carbamazepine, oxcarbazepine, and zonisamide as second-line treatments (4). Levetiracetam and phenytoin are often used for seizures with a neurosurgical cause. Commonly used anti-epileptics and considerations for prescribing in neurosurgical patients are shown in Table 1. Sodium valproate is not given to women of childbearing age because up to four in ten babies are at risk of developmental disorders and approximately one in ten are at risk of birth defects if valproate is used in pregnancy (5).

Seizures and Neurosurgical Conditions

Traumatic Brain Injury and Seizures

Seizures occur in up to 15 per cent of people following a TBI, and may be associated with a poorer prognosis or complications (6). Seizures following TBI are classified as immediate (within twenty-four hours of injury), early (within one week of injury), and late (more than one week following injury) (6, 7). Meta-analyses suggest anticonvulsants reduce the rate of early, but not late, post-traumatic seizures (6, 7). Brain Trauma Foundation Guidelines recommend prophylactic AED treatment to decrease the incidence of early post-traumatic seizures when the overall benefit is felt to outweigh the complications associated with treatment (8). Although levetiracetam may be theoretically favoured over phenytoin due to its better side effect profile and lack of need for blood monitoring, systematic reviews do not show an advantage in side effect frequency (9), and Brain Trauma Foundation Guidelines state that there is insufficient evidence to recommend levetiracetam over phenytoin (8). When AEDs are given for post-traumatic seizure prophylaxis, a one- or two-week course at full dose is usually given without weaning the dose up or down.

Tumour Surgery and Seizures

Up to 60 per cent of those with a brain tumour will have a seizure at some time (10). Low-grade lesions tend to be more epileptogenic, and complete resection of a low-grade lesion can give seizure freedom rates up to 85 per cent in epilepsy surgery programmes (10). There is no compelling evidence that treatment with AEDs prevents the development of seizures, and guidelines recommend that in the absence of seizures, there is no role for prophylactic AEDs, even for those undergoing neurosurgical procedures (11, 12). There is no robust evidence that the use of levetiracetam or sodium valproate prolongs survival in those with gliomas (11, 12). However, seizure control can affect quality of life, and in those

Table 1 AEDs in neurosurgical practice

AED	Usage notes	Side effects
Lorazepam	First-line IV to terminate seizure	Respiratory depression, drowsiness, agitation
Diazepam (Diazemuls-emulsion for injection)	PR or IV to terminate seizure Oral tablets used to manage alcohol withdrawal, anxiety, etc. (e.g. facilitate MRI scanning)	Respiratory depression, drowsiness, agitation
Midazolam (Buccolam/Epistatus)	Buccal oral gel to terminate seizure	Respiratory depression, drowsiness, agitation, vomiting
Levetiracetam (Keppra)	Loading dose (60 mg/kg IV, up to 4.5 g) for status epilepticus, then maintenance dose	Anxiety, mood/behaviour alteration – "Keppra rage," decreased appetite, skin reactions, vertigo, vomiting
Phenytoin (Dilantin/Epanutin)	Loading dose (20 mg/kg, up to 2 g) for status epilepticus, then maintenance dose Oral and IV doses may not be equivalent Requires IV filter on giving set, cardiac monitoring, blood level monitoring, avoid in pregnancy	Cardiovascular instability and arrhythmias (do not give in heart block), rash and skin reactions, extravasation and injection necrosis, respiratory disorders, seizures, abnormal blood counts, gingival hyperplasia, lip swelling, nephritis, paraesthesia, vomiting Phenytoin toxicity: nystagmus, diplopia, slurred speech, ataxia, confusion, hyperglycaemia

Sodium valproate/ valproic acid (Epilim/Depakote/ Depakin/Dyzantil/ Epival/Episenta)	Long acting forms not equivalent to short acting forms Do not give to women or girls able to have children unless pregnancy prevention programme in place May be discontinued prior to neurosurgical procedures due to risk of bleeding with platelet dysfunction	Platelet dysfunction, thrombocytopaenia, dizziness, alopecia, anaemia, abnormal behaviour/concentration, deafness, hyponatraemia, nail disorders, nausea, abdominal pain, weight gain, teratogenic
Lamotrigine (Lamictal)	Avoid abrupt withdrawal	Suicidal thoughts, aggression, agitation, diarrhoea, rash, nausea and vomiting, sleep disorders, skin reactions
Carbamazepine (Tegretol)	Used for focal seizures Used for trigeminal neuralgia	Hyponatraemia, dizziness, drowsiness, dry mouth, fatigue, vomiting, weight gain, abdominal pain, headache, oedema, skin reactions, blurred vision
Clobazam (Frisium Perizam/Tapclob/ Zacco)	Add-on drug, used in medication-resistant epilepsy when neurosurgery may provoke seizures	Drowsiness, aggression, respiratory depression, dysarthria, nystagmus, headache, hypotension, muscle weakness, nausea, tremor, withdrawal

Generic names are given with brand or other names are in brackets. Only common or neurosurgically relevant side effects are shown. For a full list of side effects and dosing information, consult the British National Formulary.
(AED, anti-epileptic drug; IV, intravenous)

with seizures and a brain tumour, AEDs should be started, and are usually prescribed following a single seizure (12).

Intracranial Infection and Seizures

One-third of those with a brain abscess will develop epilepsy (13). Although some authors recommend three to six months of treatment with AEDs for those with brain abscesses, there is little evidence to support this strategy (13). Post-operative cranial infectious complications may also cause seizures, and both AEDs and antimicrobials should be given in this scenario (14).

Vascular Disorders and Seizures

In SAH, seizures may occur at onset or be associated with complications such as hyponatraemia, hydrocephalus, re-bleeding, or delayed ischaemic neurological deficit (15). There are no randomised controlled trials of primary or secondary prevention of seizures following SAH (16), and the use of seizure prophylaxis varies worldwide (15). When seizures occur after the time of ictus, they are usually treated with AEDs, but any associated complications such as hydrocephalus or hyponatraemia should also be managed to prevent further seizures.

Following intracranial haemorrhage, seizures occur in up to 30 per cent (17), and 90 per cent of those who have had one seizure will have a further seizure (18). Haemorrhagic stroke guidelines do not recommend prophylactic treatment with AEDs, but AEDs should be started if seizures occur, although they do not reduce the risk of late seizures (19, 20).

Epilepsy Surgery

Patients with medication-resistant epilepsy may be admitted to neurosurgery and neurology wards for investigation and surgical management of their epilepsy. Video EEG using scalp electrodes or implantable depth or subdural electrodes, ictal SPECT, vagal nerve stimulator insertion or battery changes, or disconnective or resective surgical procedures may all be carried out. Patients are usually taking at least two AEDs and may take significantly more. It is important to ensure that patients with epilepsy have their AEDs prescribed and given at the correct times via the correct routes, or alternative dose and route adjustments are made peri-operatively. Those with medication-resistant epilepsy may have personalised seizure plans and these should be easily available, consulted, and followed if seizures occur. Personal plans may