epilepsy action

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CURRENT AWARENESS SERVICE

Epilepsy surgery in children: don't forget, children become adults…

The NHS England-commissioned Children's Epilepsy Surgery Service (CESS) was launched in 2014 and is now well-established. In this issue, Amitav Parida and Shakti Agrawal have written a useful review and update on CESS which has also addressed, and hopefully debunked, a couple of unfortunate and persisting myths.

It is clear that the number of children who have been and continue to be referred to a CESS for a possible surgical procedure has increased. However, the numbers do not yet seem to have reached the predicted and expected target, based on the reported epidemiology of children with epilepsy and specifically those with a drug-resistant epilepsy [Berg *et al*, 2009]. Although these data provided a baseline when designing the service specification of the four CESS centres, it must be remembered that the data were based on a US and not UK paediatric population. It would be important to triangulate, and therefore validate, the US data with those of other countries with well-established epilepsy surgery programmes in children (such as Germany, Sweden, Australia, Canada). The current criteria that determine the referral of a child with epilepsy to a CESS centre are broad, as you can read at the end of the CESS article.

As stated in their article, "The aim of epilepsy surgery is to remove a structural abnormality that is thought to be the cause of an individual's epilepsy with the explicit intention of obtaining freedom from seizures". This is the primary goal – to achieve complete seizure control or to achieve at least a very significant reduction in seizure frequency. Practically, this means that the aim is for individuals to achieve class I or IIA using the Engel classification, or class 1 or 2 using the ILAE classification (see the end of this editorial for these classifications). Clearly, these outcome scales were predominantly derived from adult data but it is generally accepted that they would be appropriate for most children who undergo a resective procedure. It would be unrealistic to expect children who undergo a palliative procedure to ever achieve Engel class I/IIA or ILAE class 1/2.

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However, seizure-freedom in isolation should not be the ultimate goal. Further efforts should continue for those individuals who do gain seizure freedom (or close to it) to try and achieve and maximise a good functional outcome. Clearly, this includes optimising educational achievements but in the longer term, it must also include professional ones. A specific focus should be on employment gains which are intimately related to the mantra of quality of life. These are important not only for the patient and their family, but also for society for health economic reasons. It has been recognised for many years that individuals with childhood-onset epilepsy show consistently lower educational attainment and rates of employment as adults compared with the general population. This is even after the exclusion of those children with early-onset developmental and epileptic encephalopathies (such as Ohtahara, West, Dravet and Lennox-Gastaut syndromes).

It has also become well-recognised that early surgical treatment of refractory epilepsy in children is associated with improved cognitive and developmental outcomes for many reasons:

- It reduces the duration of epilepsy and consequently reduces the time that the developing brain is exposed to the negative effects of ongoing seizures
- It reduces the potential adverse effects of multiple anti-epileptic drugs on attention, memory and behaviour [Helmstaedter *et al*, 2019; Braun 2020]
- It reduces the many secondary psychosocial consequences of frequent seizures, hospital attendances and emotional trauma that affect the child and their family

Clearly, other factors are associated with worse cognitive and developmental outcomes. These include younger age at epilepsy onset, the presence of malformations of cortical development, a low pre-surgical IQ and a family history of epilepsy. However, none of these factors should preclude consideration of epilepsy surgery, and many of these children may have the most to gain developmentally and cognitively from a surgical procedure. They all require an assessment by a tertiary paediatric epilepsy specialist and probable referral to a CESS centre.

Up until recently, there was very limited knowledge of employment rates after epilepsy surgery in childhood. In part, this is because it requires long follow-up periods. The participants must have reached an age at which self-sustaining employment is the norm in order for meaningful analyses to be possible. Previous reports have shown a wide range in employment rates of between 33% and 81%.

A recent study from Sweden has reported the employment outcomes of 203 patients who had undergone surgery aged less than 19 years between 1995 and 2012 [Reinholdson *et al*, 2020]. An earlier study from the same group had assessed the prospective and longitudinal long-term employment outcomes after resective epilepsy surgery in 473 adults [Edelvik *et al*, 2015]. They found that the best vocational outcomes occurred in seizure-free patients who were employed and also in those in whom surgery was undertaken at a younger age. The authors concluded that it seemed logical to suggest that early referral for surgery could contribute to better vocational outcomes in the long-term. In their most recent study [Reinholdson *et al*, 2020], the majority of the 203 patients (61%) were male and about one in three patients had a preoperative IQ of <70. Ninety-two patients (45%) underwent a resective procedure involving the temporal lobe. Predictably, most non-resective procedures were undertaken in patients with low IQ (<70). Seventy-two patients were followed up five years after surgery, 127 after 10 years, 105 after 15 years, and 42 patients 20 years after surgery.

Educational attainment and employment status were analysed in relation to seizure outcome. Education and employment outcomes of seizure-free patients with a preoperative IQ of ≥70 were compared to general population reference data. Unfortunately, there were some clear weaknesses in the study. There were no data on the type of employment and the fact that part and full-time employment were analysed together and not separately.

The duration of epilepsy prior to surgery was a mean of 6.5 (SD, 4.4) years and median of 6.0 (range, 0.1–17.8) years. The mean age at surgery was 13.6 years, which one could argue is rather old. This is because most resections involved the temporal lobe and the pathology of most of temporal lobe lesions is cortical dysplasia or a slow-growing tumour. This would therefore have been present for many years, and even from birth.

Two thirds (66%) had IQ scores of ≥70. Of these, most had attained at least high school education five years after surgery. Employment rates were 44%, 69%, 71%, and 77% at the five, 10, 15, and 20-year follow-ups, respectively. Seizure-free patients were significantly more likely to work full-time. Educational attainment and rates of full-time employment of seizure-free patients were similar to the general, background population. A majority of patients with IQ <70 had attended special education and were not employed. They were fully or mostly dependent on social benefits. However, it was important to note that the long-term overall employment rates were

higher compared to most previous studies that had assessed employment when surgery had been undertaken in adulthood. It was of interest that seizure-free patients with a preoperative IQ ≥70 showed rates of full-time employment that were similar to the background, reference population. Clearly, future studies should analyse the type and complexity of employment and its level of remuneration to see if there is still no difference.

Only one previous study had included comparisons with general population reference data [Puka and Smith 2016]. In this study, the authors also found that there was no difference with respect to a composite measure of employment and school attendance. However, wages earned were much lower in those who had undergone successful epilepsy surgery [Puka and Smith 2016]. Significant associations between seizure freedom and higher employment rates have been shown in two previous but relatively small studies of epilepsy surgery in childhood [Keene *et al*, 1998; Hosoyama *et al*, 2017].

Conclusion

The key take-home messages from the CESS are:

- Could this child with epilepsy benefit from surgery? If in doubt, discuss with your regional tertiary epilepsy specialist
- If this child meets the criteria for referral to CESS, refer them
- Early surgery, and particularly with a successful outcome, will improve the child's educational, psychosocial and probable employment outcomes and ultimately, their quality of life. This is very likely to improve their perceived and actual role in their community and society as a whole. It is also likely to improve the quality of life of their family, including their siblings.

Richard Appleton
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Appendix

Post-surgical outcome scales

Engel Scale [Engel *et al*, 1993]

Class I: Free of disabling seizures

IA: Completely seizure-free since surgery
IB: Non disabling simple partial seizures only since surgery
IC: Some disabling seizures after surgery, but free of disabling seizures for at least 2 years
ID: Generalized convulsions with antiepileptic drug withdrawal only

Class II: Rare disabling seizures ('almost seizure-free')

IIA: Initially free of disabling seizures but has rare seizures now
IIB: Rare disabling seizures since surgery
IIC: More than rare disabling seizures after surgery, but rare seizures for at least 2 years
IID: Nocturnal seizures only

Class III: Worthwhile improvement

IIIA: Worthwhile seizure reduction
IIIB: Prolonged seizure-free intervals amounting to greater than half the follow-up period, but not less than 2 years

Class IV: No worthwhile improvement

IVA: Significant seizure reduction
IVB: No appreciable change
IVC: Seizures worse

ILAE Scale [Wieser *et al*, 2001]

Class 1: Completely seizure free; no auras
Class 2: Only auras; no other seizures
Class 3: 1 to 3 seizure days per year; ± auras
Class 4: 4 seizure days per year to 50% reduction of baseline seizure days; ± auras
Class 5: Less than 50% reduction of baseline seizure days; ± auras
Class 6: More than 100% increase of baseline seizure days; ± auras

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- Keeping your child safe
- The impact of epilepsy on family life
- Your child's wellbeing
- Learning and behaviour
- Growing up and independence
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Children's Epilepsy Surgery: a concise review

New advances and fundamental concepts for the paediatrician

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Introduction

The Children's Epilepsy Surgery Service (CESS) in England is designed to develop a clinical approach that recognises the neurobiology of the developing brain and offer surgical options for pharmaco-resistant epilepsy in a timeous manner. The goal of surgery is to reduce epilepsy-induced cognitive disabilities by stopping seizures as soon as possible. Data from clinical seizure semiology, neuroimaging and neurophysiology are correlated by a multidisciplinary team (MDT), with the aim of developing a 'surgical hypothesis'. If the abnormalities from different modalities are concordant, then a proposal for epilepsy surgery can be made [Cross, 2002].

The pathologies and types of surgery are often varied in paediatric epilepsy surgery patients. In the University of California, Los Angeles (UCLA) series, for example, the most common aetiologies in children who had an operation by the age of 20 years of age were extratemporal (70%). In the extratemporal group, the most common causes of seizures were cortical dysplasias (50%), infarct or ischemic lesions (17%), and Rasmussen encephalitis (12%). This is consistent with an international paediatric epilepsy surgery survey [Harvey *et al*, 2008]. By comparison, in surgically treated temporal lobe epilepsy patients under the age of 20 years, the most common aetiology was hippocampal sclerosis (45%). The second most common were lesions, which mostly consisted of tumours such as dysembryoplastic neuroepithelial tumours and gangliogliomas (27%).

The aim of this brief review is to highlight the importance of epilepsy surgery and the probable reasons for the low rates of epilepsy surgery in the United Kingdom. It will also present recent advances in the field, which are likely to expand the spectrum of children that may be suitable for epilepsy surgery. We aim to cover the important considerations and information needed in epilepsy surgery assessment.

Importance of epilepsy surgery referral

Due to the challenges of classifying epilepsy, epidemiological studies do not give a precise idea of what proportion of children with epilepsy have a structural focal aetiology. This is because around 50% of children have no known cause of their epilepsy [Camfield and Camfield, 2007; Camfield and Camfield, 2015]. Long-term neuro-epidemiological studies have shown that the presence of ongoing seizures is a strong predictor of adverse outcomes in adult life [Camfield and Camfield, 2007]. This is in terms of risk of death, psychiatric comorbidity, unemployment and lack of independent living. These findings highlight the importance of trying to achieve seizure freedom, not just seizure reduction, in as many children as possible with epilepsy.

Of children with a diagnosis of epilepsy, 25% will go on to develop drug-resistant seizures [Kwan *et al*, 2011]. This is defined as ongoing epileptic seizures despite treatment with two appropriately selected anti-epileptic drugs (AEDs) for an adequate period of time.

It is fundamental that non-drug options are explored early in children with drug-refractory epilepsy. Nonetheless, it must be stated that the ketogenic diet and vagus nerve stimulation are 'palliative' treatment solutions where the aim is to reduce frequency of seizures rather than achieve complete seizure freedom [Benifla *et al*, 2006; Mackay *et al*, 2005].

In suitable cases, epilepsy surgery is the single most effective treatment for drug-refractory seizures. In the UK, seizure freedom rates across all epilepsy surgery procedures done with curative intention are around 70% for temporal lobe epilepsy [Agrawal *et al*, 2016]. Thus, it stands to reason that the possibility of resective epilepsy surgery must be considered in all children with drug-refractory epilepsy so that the best life prospects and opportunities are afforded to them.

The CESS is the nationally commissioned service for England. Wales and Northern Ireland are included within this service and their children are evaluated within one of its four centres. Scotland is excluded as it has its own paediatric epilepsy surgery service. The intention of the CESS is to centralise expertise, enhance access to epilepsy surgery assessment and improve outcomes for children who may be suitable candidates for epilepsy surgery. It is evident from the data that although the number of children being referred for epilepsy surgery in England, Wales and Northern Ireland has increased significantly since the inception of CESS, the treatment gap still exists.

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Common misconceptions about epilepsy surgery

Low rates of referral for epilepsy surgery have been postulated to result from a number of misconceptions from clinicians regarding the risks of epilepsy surgery in children. The purpose of referral is to evaluate children to be sure they have an accurate diagnosis of epilepsy and to consider optional therapies, including surgery, in an attempt to stop refractory epilepsy. Thus, not all children referred to a paediatric epilepsy centre will be surgical candidates. In our experience, changes in medical management, after a thorough diagnostic evaluation, can often control seizures, and children are returned to their local paediatric services in about 20% to 30% of cases [Wu *et al*, 2006; Widjaja *et al*, 2011]. Around 50% of children referred for epilepsy surgery assessment do not go on to have a resective epilepsy surgery. This is either because a surgical hypothesis is not identified, or the clinical team or family come to the conclusion that the risks of surgery outweigh the potential benefits. Sometimes, an alternative diagnosis, for example a genetic aetiology, is established after evaluation, which may preclude surgical intervention.

The concept of surgery being seen as a 'last resort' due to the high risk of morbidity and mortality has been debunked by transparent outcome reporting from all epilepsy surgery centres. This reporting has shown no mortality and extremely low rates of unexpected morbidity since the conception of the nationally commissioned CESS. Similarly, the idea that epilepsy surgery is best deferred until adolescence or adulthood due to the perception of lower risk of surgery in older age groups can also be challenged by these outcome data.

There is emerging data to support the concept that early epilepsy surgery may, in some children, improve developmental and intellectual outcome [Boshuisen *et al*, 2015; D'Argenzio *et al*, 2011]. This may be particularly applicable to children under two years of age, when a structural lesion is driving a developmental and epileptic encephalopathy.

In these children, the epilepsy itself is altering the brain's overall functioning. For instance, an infant with drug-resistant epileptic spasms caused by a structural abnormality, where the background EEG shows a persistent encephalopathic/ hysparrythmic pattern, may have developmental regression or stagnation as a result. Similarly, epilepsy surgery should also be considered where a unilateral structural lesion is causing Continuous Spikes and Waves in Sleep (CSWS) resulting in cognitive decline [Veggiotti *et al*, 2012]. This is if medical treatment (for instance with corticosteroids or benzodiazepines) has been ineffective. In addition, there are intuitive benefits to operating early on children before hemispheric dominance has been fully established. That way, lateralised functions, such as speech and language, have time to 'cross over' to the unaffected hemisphere [Helmstaedter, 2004].

The absence of an obvious epileptogenic focus on neuroimaging is not a contra-indication for referral for epilepsy surgery assessment [So and Lee, 2014]. Similarly, a normal interictal EEG, or the absence of lateralising focal epileptiform activity on interictal EEG, are not contra-indications for referral either.

In children with small areas of focal cortical dysplasias, the interictal EEG can often be normal. Furthermore, if the epileptogenic zone is located in a 'deep seated' area, such as the inferior frontal lobe, obvious ictal changes may not even be seen during captured seizures. In these challenging cases the diagnosis is made based on the clinical semiology of events, with further evaluation with invasive Stereo-EEG required before a surgical hypothesis can be proposed [Cossu *et al*, 2006].

The presence of bilateral epileptiform paroxysms or transients should not necessarily preclude epilepsy surgery referral. In children with a parasagittal or midline epileptogenic focus, bilateral EEG changes may be seen on scalp EEG. Rapid ictal spread from one hemisphere to another may give the appearance of a generalised seizure disorder on EEG. In these cases, the semiology at the onset of captured seizures on videotelemetry is critical in determining whether the seizure is focal or generalised. Similarly, frontal and thalamic structural lesions can sometimes produce interictal EEG changes that mimic a generalised epilepsy [Pizarro *et al*, 2019].

Evolving role of imaging in epilepsy surgery assessment

The National Institute for Health and Care Excellence (NICE) guidelines suggest neuroimaging, preferably with an MRI brain scan, in all children with epilepsy aged less than two years. This is also recommended in all children where seizures are not controlled after trial of one AED [Appleton *et al*, 2012]. Imaging may also be normal in children suitable for epilepsy surgery.

Subtle areas of focal cortical dysplasia may not be appreciated, particularly with a 1.5 Tesla magnet [Mellerio *et al*, 2014]. Subtle abnormalities may be missed if there is movement artefact or if dedicated epilepsy imaging sequences (including coronal, axial and sagittal sequences as well as dedicated imaging of the temporal lobes) have not been undertaken.

Referral for epilepsy surgery assessment permits review of a child's neuroimaging by a highly specialised paediatric radiologist or neuroradiologist with specific expertise and high-volume practice in paediatric epilepsy imaging. It could be argued that all children with drug-resistant epilepsy (DRE) should have access to a 3 Tesla epilepsy protocol

MRI brain scan (with general anaesthesia if needed). The use of 7 and 11.7 Tesla MRI is currently limited to the research setting but is likely to come into clinical use over the next few years [Veersema *et al*, 2017]. The extra resolution may again help identify subtle cortical dysplasias not seen on lower resolution imaging.

Referral for epilepsy surgery assessment will give children access to advanced imaging modalities such as fluorodeoxyglucose positron emission tomography (FDG-PET), single-photon emission computerized tomography (SPECT) and magnetoencephalography (MEG) [Pardoe and Kuzniecky, 2014]. Of course, more recently, Stereo EEG (SEEG) has become one of the more commonly used investigations in lesion negative epilepsies. These sophisticated investigations have proven to be invaluable in helping to determine an epileptogenic focus where no definite focus can be identified on conventional MRI imaging. Functional imaging such as fMRI will also help with determining memory, speech and language lateralisation. This can give important information on risks of surgery, particularly if the lesion is thought to be in the dominant hemisphere. Similarly, diffusion tensor imaging (DTI) can be used in surgical planning to map white matter tracts [Chen *et al*, 2009].

Evolving role of neurophysiology in epilepsy surgery assessment

The gold standard neurophysiological modality required in almost all cases referred for epilepsy surgery is videotelemetry. The aim of videotelemetry is to capture typical seizures with a video from multiple angles at the same time as a scalp EEG. This usually involves an inpatient stay(Pressler *et al*., 2017). Measures to 'provoke' seizures, such as medication reduction may be needed if seizure frequency is not high enough. Assessment of the seizure semiology in association with EEG changes during a captured seizure is critical in determining the localisation and lateralisation of the epileptogenic focus.

Dense array EEG is starting to be used in the clinical setting with the aim of giving more precise localisation and lateralisation data [Groppa *et al*, 2019]. Dense array EEG uses up to 256 electrodes including on the face and the neck. This has the intention of sampling 'deep seated' brain regions (such as the inferior frontal and basal temporal areas) as well as the convexity of cerebrum. It helps to detect epileptic activity that may not be readily appreciable with standard EEG scalp montages.

The increasing use of invasive SEEG has markedly increased the number of cases that are suitable for epilepsy surgery. This is particularly in those case where no epileptogenic focus has been identified on conventional MRI imaging [Isnard *et al*, 2018]. Preparing for SEEG insertion involves a complex multidisciplinary planning process.

The ability to fuse multiple imaging modalities, such as PET and MRI, using computer software, can also help planning of the location of SEEG electrode insertion. Extremely precise placement of SEEG electrodes can be facilitated by use of robotic technology. The ability to stimulate specific SEEG electrodes to provoke seizures may give additional information to identify an epileptogenic focus. SEEG electrodes may also be used for mapping motor and speech areas of the brain to help with surgical planning [Trebuchon *et al*, 2021].

Intraoperative electrocorticography may also help the surgeon determine the extent of the 'epileptogenic zone' which may extend beyond the limits suggested on imaging or even SEEG [Kuruvilla and Flink, 2003]. Electrocorticography can also be used to map eloquent areas which must be avoided during operations.

Specific conditions which may be amenable to epilepsy surgery

Clinicians should have an extremely low threshold to refer children with specific genetic conditions which are associated with structural pathologies that may be amenable to epilepsy surgery.

In tuberous sclerosis (TS) and familial epilepsy with multiple variable foci (associated with DEPDC5 pathogenic variants) multiple tubers are seen, which are, in fact, areas of focal cortical dysplasia. Seizures are often drug-refractory in these conditions. In some children, it may be shown that all or most seizures are arising from one or two areas of focal cortical dysplasia which could be targets for surgical resection [Jansen *et al*, 2007]. NICE guidelines suggest that all children with TS and intractable seizures should have their cases discussed at an epilepsy surgery MDT before consideration of mTOR inhibitors such as everolimus [Mizuguchi *et al*, 2019; Amin *et al*, 2019].

In children with hemimegalencephaly syndromes, where there is overgrowth or significant structural abnormality limited to one hemisphere, a hemispherotomy (a functional disconnection operation) should be considered early [Di Rocco *et al*, 2006]. Similarly, in Sturge-Weber syndrome, hemispherotomy should be considered if pial angioma are limited to one hemisphere and all seizures arise from that hemisphere [Bourgeois *et al*, 2007].

Rasmussen's encephalitis is a T-cell mediated neuroinflammatory condition. It typically presents with a subacute onset of drug-refractory focal seizures with progression to unilateral hemiparesis and sometimes epilepsia partialis continua (persistent focal motor seizures) over time. Response to immune suppression is often only transient or limited. Therefore, hemispherotomy should be considered as an option early in children with Rasmussen's encephalitis and intractable seizures [Varadkar *et al*, 2014].

Children who have suffered a unilateral (often antenatal) stroke can often be good candidates for hemispherotomy,

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where seizures are drug-refractory [Maehara *et al*, 2002]. Hemispherotomy will result in a unilateral functional motor deficit, as well as a homonymous hemianopia. However, in many children a motor or visual deficit may already be present pre-operatively, due to their underlying condition. The vast majority of pre-operatively ambulant children will regain the ability to walk post hemispherotomy but will have limited upper limb and hand function on the affected side. The rehabilitation journey in younger children and in those with pre-operative motor deficits is often much shorter than in older children with no previous weakness.

Palliative epilepsy surgery procedures

The majority of children undergoing epilepsy surgery undergo a resective surgery with the intention of achieving seizure freedom, but important palliative treatments exist. Vagus nerve stimulation (VNS) is the most common palliative surgical intervention. VNS involves insertion of a pacemaker-like generator implanted in the chest wall that is connected to the vagus nerve via a lead. Regular electrical impulses are sent to the vagus nerve which then propagate to the brain. A hand-held magnet can be swept over the device to send more impulses to the brain with the aim of aborting a seizure that has already started [Wheless *et al*, 2018]. Similarly, new VNS models can detect rises in heart rate which may be associated with seizures and thus automatically send extra impulses to help abort a seizure [Fisher *et al*, 2016].

VNS has been shown to reduce seizure frequency by half in 40-50% of children [Benifla *et al*, 2006]. Traditionally, VNS insertion is only considered after a resective hypothesis has been considered and excluded as an option. Nonetheless, with special precautions, children with pre-existing VNS devices can still undergo MRI scans as part of assessment for possible resective epilepsy surgery if needed [Sayed *et al*, 2020].

Corpus callosotomy is still frequently performed in children with drug resistant seizures, particularly drop seizures associated with Lennox-Gastaut syndrome. In this operation the white matter tract between the cerebral hemispheres (corpus callosum) is cut with the aim of preventing spread of seizures between both hemispheres [Asadi-Pooya *et al*, 2008]. In one systematic review corpus callosotomy was shown to be superior to VNS in reducing the frequency of drop attacks [You *et al*, 2008].

The technique of multiple subpial transection, used in the past as surgical treatment for Landau-Kleffner syndrome, has fallen out of favour. This came after a Cochrane review demonstrated a lack of evidence for the efficacy and safety of this procedure [Krishnaiah *et al*, 2018]. The use of hemispherotomy as a palliative procedure, where seizures are emanating from both hemispheres, is generally not recommended. Nonetheless, in specific cases where the vast majority of seizures come from one hemisphere and there is a significant seizure burden, it can be considered after detailed multidisciplinary discussion in expert centres [Ciliberto *et al*, 2012].

New surgical developments

Intracranial Magnetic Resonance guided laser-induced thermal therapy (LiTT) combines a laser applicator with image guidance to ablate brain targets including those that may be difficult to access with a conventional approach. No craniotomy is required and damage to cortical areas is reduced. LiTT may be particularly beneficial where eloquent brain areas or important structures or vessels may be damaged using a standard approach [Tovar-Spinoza *et al*, 2013]. LiTT has been used extensively in clinical practice in North America and its use is likely to increase in UK neurosurgical practice.

LiTT has gained particular attention for its role in the treatment of hypothalamic harmatomas. However, it has also been used to treat mesial temporal lobe sclerosis, deep seated focal cortical dysplasia, cavernomas and nodular periventricular heterotopias [Patel *et al*, 2016].

Deep brain stimulation as a palliative treatment for children with DRE has also shown some promising early results in one case series. However, it is not currently used in clinical practice in the UK. It remains unclear which targets to stimulate in the context of epilepsy. Stimulation targets including the centromedian nucleus of the thalamus, anterior thalamic nuclei, hippocampi and hypothalamus have been attempted [Zangiabadi *et al*, 2019].

Life after epilepsy surgery

If seizure remission after epilepsy surgery is achieved, then withdrawal of AEDs should take place. Withdrawal of AEDs brings the benefits of reducing medication side-effects which may include mood and cognitive difficulties [Boshuisen *et al*, 2015].

Traditionally, AEDs were withdrawn after one year of post-operative seizure freedom. A recent study has suggested there was no adverse consequences of AED withdrawal at six months [Boshuisen *et al*, 2012]. Earlier withdrawal of AEDs may help to unmask inadequate surgical resection and thus prompt re-evaluation and consideration of further surgical intervention.

Long-term seizure freedom rates have been shown to be higher in temporal lobe versus extra-temporal surgery and in cases where a clear abnormality is seen on MRI versus MRI 'negative' cases [D'Argenzio *et al*, 2012]. Recurrence of seizures after epilepsy surgery, even after complete removal of an epileptogenic lesion as demonstrated on post-operative imaging, has sparked interest. It has led to

the concept of the 'epileptogenic zone' which extends beyond an epileptogenic lesion [Kahane *et al*, 2006]. The epileptogenic zone may be defined as the area of cortex necessary and sufficient to initiate seizures and the removal of which is needed for complete seizure abolition. Further evaluation of a child with recurrence of seizures after epilepsy surgery, which may include the use of SEEG and electrocorticography, should be always considered [Muthaffar *et al*, 2017; Reed *et al*, 2017].

Conclusions, current referral criteria and perspectives for the future

Given the poor long-term outcomes of children with DRE, the possibility of a resective surgical hypothesis to achieve complete seizure remission must be considered in all children with DRE. This should include cases where imaging and neurophysiological data may not obviously point towards a structural focal aetiology.

At the moment the criteria for referral for epilepsy surgery are:

1. All children under 24 months with evidence of focality to seizure onset, with or without an MRI lesion
2. Children of any age with evident focal epilepsy or lateralised seizures associated with congenital hemiplegia resistant to two appropriate AEDs
3. Children associated with a lateralised abnormality seen on a brain scan
4. Children with Sturge-Weber syndrome, benign tumours associated with ongoing seizures or developmental issues
5. Children with Rasmussen's encephalitis
6. Children with TS with epilepsy resistant to two appropriate AEDs
7. Children with drop attacks as part of a complex epilepsy
8. Children with hypothalamic harmatomas

A recent randomised control trial, which demonstrated the superiority of epilepsy surgery over conventional AED therapy as a first line treatment for structural focal epilepsy, has sparked much interest and debate [Dwivedi *et al*, 2017]. At the moment, in majority of the cases epilepsy surgery is only considered if medical management has failed, but this may change in the future. Given the expanding range of diagnostic and interventional tools available, the number of children suitable for epilepsy surgery is likely to continue to rise which will have ongoing implications for provision of CESS in the UK.

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The mobile friendly website is a helping hand for 16-25 year olds to live their best life with epilepsy

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- Feel less alone
- Increase their confidence
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There's lots of epilepsy facts, tips and stories from young people sharing their experience.

The content is short and interactive. It's not all reading, there's video and young people can share their own quotes, stories and videos too.

It's been created with young people and reviewed by epilepsy nurses.

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Leaflets about The Epilepsy Space to give to young people can be requested by emailing:
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Recently published papers

This section highlights recently published papers. Hopefully this will be very useful to all, helping to keep everyone up to date with the latest developments. It will certainly save you research and reading time, not having to search so many journals.

There are many (often over 300) epilepsy papers published every three months, so what follows has been edited. All animal papers have been excluded and as many review papers as possible have been included. We hope you find the papers of interest in your pursuit to keep abreast of the very latest knowledge.

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