CURRENT TOPIC

Update on surgery for epilepsy

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Surgery for epilepsy is not new, it has been performed for over 100 years. However, there has been a reluctance to consider young children for surgery other than in exceptional circumstances, owing in part to the invasive nature of the presurgical evaluation. Recent advances in investigative techniques have allowed identification of candidates early in their natural history avoiding the long term consequences of chronic epilepsy. Based on a prevalence rate of 3-6/1000 and current population figures of 60 000 children with epilepsy, about 15 000 are unresponsive to anticonvulsant medication, and of these as many as 3000 might benefit from surgery. There are currently six centres in the UK offering surgery to children. Of these, Great Ormond Street in London operates exclusively on children (30 cases/year), although for each child who comes to surgery it is likely four have been evaluated.

The case for early surgery

Most adults coming to an epilepsy surgery programme have had a history of seizures since childhood,¹ the consequences of which are severalfold. Studies of selected groups of children with ongoing seizures suggest that severe epilepsy is associated with cognitive decline² and that early cessation of seizures is associated with better developmental outcome.³ The psychological consequences of recurrent seizures through school and teenage years are also apparent, both to the individual and the community.⁴ In addition, recurrent epileptic seizures are not without risk to the individual, both with regard to self injury during a seizure and the risk of sudden death.⁵ With advances in neurosurgical and neuroanaesthetic techniques, morbidity from planned neurosurgical procedures is now low. In addition, postoperative outcome of seizure control in studies performed to date in children are similar to those in adults.⁶ There is consequently no justification in conducting a "wait and see" policy rather than referral in children with epilepsy, particularly in early onset catastrophic epilepsy, which may have a focal onset.

Candidate selection

Procedures on offer can be divided broadly into two categories: resective and functional surgery (table 1). Traditionally, consideration is given to focal resection of the seizure focus, either temporal or extratemporal. To be considered for such surgery most seizures have to been proved to arise exclusively from one

area of the brain that is functionally silent (table 2). The size of the area may be relatively small or large, partly dependent on underlying pathology and partly the area of brain involved. Complete removal or disconnection of one cerebral hemisphere (hemispherectomy) may be considered where there is a pre-existing hemiplegia associated with a structural abnormality of the contralateral hemisphere, and seizures have been proved to arise from that hemisphere. With either of these techniques, presurgical evaluation is aimed at determining whether such surgery is likely to cure or improve seizures without deterioration in function. Temporal resection is the most common operation in paediatric and adult practice, but hemispherectomy comprises up to a quarter of procedures in paediatric practice, whereas few are performed in adults. Extratemporal resection is difficult in the absence of a known structural lesion, but may be more common where invasive electroencephalography (EEG) is available.

In children there may be some difficulty in determining when seizures are drug resistant and at what point surgery should be considered. In adults, medical intractability may be considered as failure to respond to at least two anticonvulsant drugs over at least two years; these rules may not be appropriate in paediatric practice. In an infant with catastrophic onset epilepsy, seizure frequency may be such that a greater number of drugs are tried over a lesser time. There may be pressure in such cases to suppress seizures as early as possible to try and reduce the developmental morbidity

Table 1 Types of surgery for epilepsy

Focal resection—temporal or extratemporal
Hemispherectomy
Functional procedures
Corpus callosotomy
Multiple subpial transection

Table 2 Criteria for consideration for surgery for epilepsy

Focal resection
Seizures arise from a single area of the brain that is functionally silent
Drug resistant
Hemispherectomy
Structural abnormality demonstrable of one cerebral hemisphere
Seizures lateralised to that cerebral hemisphere
Pre-existing hemiplegia (in the absence of progressive disease)
Drug resistant
Corpus callosotomy
Drop attacks, whether atonic, myoclonic or tonic
Specific vocational goals to surgery

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that may occur in association with frequent seizures in early life, clinical or subclinical.

A further issue may arise in deciding whether seizures or seizure syndromes are focal in origin and therefore treatable with surgery. Certain syndromes are catastrophic in early childhood and the question is often how hard should we look for a focal or lateralised onset. Chugani *et al* highlighted this with the use of positron emission tomography (PET) in infantile spasms, apparently increasing the number amenable to surgery⁷; 30 of 140 of children presenting with infantile spasms had focal lateralised abnormalities. It appears likely however that lateralisation may be apparent clinically or on EEG or both in patients where surgery is going to be helpful and, in many, such abnormalities may be seen on good quality magnetic resonance imaging (MRI).⁸ This does not preclude the fact that all children presenting with infantile spasms should have detailed neuroimaging in the form of optimised MRI and, where a lateralised structural abnormality is found, referred for surgical opinion even if there is initial control of seizures with anticonvulsants. This is to allow rapid intervention should seizures return or developmental progress appear compromised with continuing epileptiform activity. Other syndromes that require rigorous investigation for a localised structural abnormality are those that present with an autistic-type language disorder in association with epilepsy.⁹

Functional procedures involve modification of brain function rather than tissue removal. Corpus callosotomy—division (either two thirds or complete) of the corpus callosum—is considered in individuals having frequent “drop” attacks, whether myoclonic, atonic or tonic. Another technique recently advocated by Morrell *et al* is multiple subpial transection, used in the surgical management of Landau Kleffner syndrome (LKS).¹⁰ This procedure involves transection of transverse fibres leaving longitudinal fibres intact. For epileptic aphasia (LKS) the technique is performed over Wernicke's area on what is thought to be the leading side as determined by preoperative investigation. The technique may also be considered in individuals where the seizure focus lies within a functionally eloquent area of cortex (such as the motor cortex).

Presurgical evaluation

The primary aim of presurgical investigation is to determine whether an area of the brain responsible for seizures can be accurately defined. In addition, it has to be determined that removal of that area is not going to cause deterioration of function, whether it be control of movement, memory or language. It is highly desirable to use a non-invasive approach where possible, more recently made possible by developments in neuroimaging. There is no doubt that an epilepsy surgery programme should have ready access to expertise in neurophysiology, neuroimaging, and neuropsychology, but access to such expertise should not detract from the need for detailed clinical evaluation and interictal EEG studies.

STRUCTURAL IMAGING

Postoperative follow up studies have shown more favourable outcome with regard to seizure control where lesions are detected within the surgical specimen.¹¹ MRI has enabled the detection of such pathology preoperatively. This has included an increased detection of developmental abnormalities such as dysembryoplastic neuroepithelial tumours and focal cortical dysplasia previously undetected on computed tomography, as well as hippocampal sclerosis, the lesion most commonly responsible for temporal lobe epilepsy (TLE) in adults (fig 1).¹² There continues to be discussion as to the relevance of the hippocampus in childhood epilepsy, and whether hippocampal sclerosis is an acquired lesion.¹³ Surgical series in childhood have indicated a relatively high incidence of tumours and a low incidence of hippocampal sclerosis as the underlying responsible lesions, but recent data indicate that this may be equally common in children as in adults with TLE, and that it can be detected on MRI (as high as 60%).^{12 14}

Visual inspection of the hippocampus and temporal lobe may also be greatly enhanced, and detection of abnormalities increased by quantitative and semiquantitative techniques.^{15–17} Further detailed analysis of three dimensional datasets may also provide information, particularly in extratemporal epilepsy, not only about localised abnormalities (fig 2) but also about more widespread developmental structural abnormalities not initially apparent from visual inspection.¹⁸ This may provide some prediction of the likely outcome of surgery with regard to seizures.¹⁹ Such techniques are generally available only in centres specialising in epilepsy and epilepsy surgery, and therefore a normal routine MRI in the presence of clinical or EEG suspicion of focal epilepsy does not preclude referral. In children undergoing evaluation for hemispherectomy, MRI also plays a major role, not only in

Figure 1 Coronal section magnetic resonance image, inversion recovery sequence, perpendicular to the axis of the temporal lobes. The right hippocampus is smaller than the left, with loss of signal from within, suggestive of right hippocampal sclerosis.

Figure 2 Coronal section magnetic resonance image, reconstructed from a three dimensional magnetisation prepared rapid acquisition gradient echo (MP-RAGE) dataset, showing an area of thickened cortex suggestive of cortical dysplasia in the right frontal region.

detailing the extent and nature of the hemispheric abnormality, but also excluding the presence of any abnormality on the contralateral side, which may also have an influence on outcome.

FUNCTIONAL IMAGING

Although there is a high detection rate of focal brain abnormality in children with partial epilepsy, such abnormalities may only be assumed to be related to seizure onset. Video-EEG monitoring is imperative for documentation of clinical symptomology and where possible electrical seizure onset. However, both may be misleading in the young child, particularly infants. Where such is helpful and correlates with a focal structural abnormality, the decision about whether to offer surgery may be relatively easy to make. In children with less helpful investigative data, non-invasive functional imaging in the form of ictal and interictal single photon emission computed tomography (SPECT) or interictal PET may enhance this information.

Functional imaging in the form of ictal SPECT can provide information about seizure onset; an area of hyperperfusion seen after injection of a radioisotope during a seizure is highly suggestive of the seizure focus.^{20–21} Such scans however give optimal yield only if injection of the isotope is truly during a seizure with concomitant EEG monitoring, particularly in extratemporal epilepsy, and if examined in the context of an interictal scan (to determine a change in perfusion), and other investigations. Interictal SPECT (showing hypoperfusion) and fluorodeoxyglucose (FDG) PET (showing hypometabolism), are more likely to demonstrate abnormalities relating to structural defects. PET may be particularly useful in infants where incomplete myelination may restrict the structural information provided by MRI.⁸

NEUROPSYCHOLOGY

The role of neuropsychology testing in the determination of verbal and non-verbal function in older children cannot be underplayed. There is also a role in the determination of cerebral dominance, and Wada (sodium amytal) testing may be required in older children to lateralise language function. However, early onset localisation related epilepsy, particularly that associated with a structural abnormality, is likely to lead to some relocation of function. Functional imaging techniques (MRI or PET) are increasingly being used to localise language function and may preclude the need for Wada testing in the future.²²

INVASIVE MONITORING

Traditionally, invasive EEG techniques were the only definitive way to determine accurately the area of seizure onset. These involved depth electrodes and were associated with relatively high morbidity. The current use of subdural electrode grids by experienced centres has been shown to be well tolerated, even in young children, and allows not only accurate localisation of seizure onset, but also localisation of function,²³ which may be particularly important in children with extratemporal epilepsy, either with normal structural imaging (with highly concordant functional data) or with a structural abnormality close to functionally useful cortex.

Outcome

The clinical spectrum of children coming to epilepsy surgery is wide. Although freedom from seizures is important in determining success, it may not be the primary goal in all children undergoing evaluation. For example, compare the teenager in a normal school aiming for freedom from seizures from a temporal lobectomy with the infant with hemimegalencephaly striving to avoid status epilepticus and optimise developmental outcome. In addition, outcome may depend on a wide range of factors including the type and extent of the responsible lesions, and extent and type of surgery, which can be determined preoperatively to a certain degree. Consequently it is important to obtain as much information as possible about the nature of the epilepsy and the procedure planned, with distinct outcome aims clarified with the family. A system has been proposed that attempts to correlate all such information, and clarify the likely outcome with the family.²⁴ Information to date suggests that seizure outcome is similar in children and adults; 60–70% seizure free from temporal and extratemporal resection.²⁵ However, the results may not be as good in children with developmental lesions compared with acquired lesions, probably due to the presence of more widespread lesions that cannot be seen with current imaging techniques.²⁶ This does not preclude considering surgery for these patients, providing the aims of surgery are realistic and clearly identified.

Conclusions

Advances in neuroimaging, neurosurgery, and neuroanaesthesia mean that surgery for children with epilepsy is a real consideration. There is no reason to delay surgery; whether an infant presents with catastrophic epilepsy, or an older child is reviewed with ongoing intermittent seizures with little response to medication. In view of the high morbidity associated with chronic epilepsy, children should be referred early for surgical consideration. Nothing is lost from evaluation without surgery; there is much to be lost by the patient experiencing 20 years of seizures that could have been resolved in childhood.

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