Epilepsy surgery in children and adults

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Epilepsy surgery is the most effective way to control seizures in patients with drug-resistant focal epilepsy, often leading to improvements in cognition, behaviour, and quality of life. Risks of serious adverse events and deterioration of clinical status can be minimised in carefully selected patients. Accordingly, guidelines recommend earlier and more systematic assessment of patients' eligibility for surgery than is seen at present. The effectiveness of surgical treatment depends on epilepsy type, underlying pathology, and accurate localisation of the epileptogenic brain region by various clinical, neuroimaging, and neurophysiological investigations. Substantial progress has been made in the methods of presurgical assessment, particularly in patients with normal features on MRI, but evidence is scarce for the indication and effect of most presurgical investigations, with no biomarker precisely delineating the epileptogenic zone. A priority for the development of epilepsy surgery is the generation of high-level evidence to promote the harmonisation and dissemination of best practices.

Introduction

Epilepsy surgery is now accepted for the management of drug-resistant focal epilepsy. Seizure freedom is achieved in a variable proportion of patients according to epilepsy type, underlying pathology, duration of follow-up, and series reported. In specific situations in which a surgical cure is not possible, palliative epilepsy surgery might be offered with the main aim of minimising the frequency and severity of seizures. Cognition, behaviour, and quality of life can improve substantially after epilepsy surgery, particularly in children. The risks of serious adverse events and deterioration of clinical status should not be neglected, but can be minimised in carefully selected patients in whom surgical treatment offers a favourable risk–benefit balance. Epilepsy surgery has consistently proved to be a cost-effective strategy in both adults and children.[1–3]

The location and volume of brain tissue to be surgically targeted is identified during presurgical assessment, and ranges from a few millimetres (eg, hypothalamic hamartoma) to an entire hemisphere (eg, hemimegalencephaly; figure 1). Delineation of the so-called epileptogenic zone (ie, the brain region for which resection or destruction or disconnection is both necessary and sufficient to ensure a surgical cure) is complicated by the absence of a gold-standard biomarker and paucity of evidence for the indications, methods of acquisition, and data analysis for most presurgical investigations.

In this Review, we focus on present indications for epilepsy surgery, state-of-the-art presurgical investigations, outcomes of epilepsy surgery, and postoperative management of antiepileptic drugs.

Indications and referral for epilepsy surgery

Current guidelines and recommendations

The first practice parameters for epilepsy surgery in adults were published by the American Academy of Neurology (AAN) in 2003 and have not since been revised.[4] These parameters were developed on the basis of a single class I randomised controlled trial for temporal lobe surgery and a further 24 class IV studies. For localised neocortical resections, eight class IV studies were considered. The panel concluded that "Patients with disabling complex partial seizures, with or without secondarily generalized seizures, who have failed appropriate trials of first-line antiepileptic drugs should be considered for referral to an epilepsy surgery centre (level A)". Although they outlined evidence available to recommend temporal lobe resection in individuals who met established criteria, it was accepted that there was "insufficient evidence at [that] time to make a definitive recommendation as to whether patients with a localized neocortical epileptogenic region will benefit or not benefit from surgical resection (level U)". The panel acknowledged limited applicability to children since paediatric series were excluded from the analysis of evidence. This restricted applicability was addressed by the International League Against Epilepsy (ILAE) Subcommission for Paediatric Epilepsy Surgery, who declined to recommend practice guidelines because of the absence of class I evidence in this age group, but did produce consensus recommendations.[5] Specifically, the ILAE recognised that the diversity of childhood epilepsy syndromes and the effect of uncontrolled seizures on cognitive and behavioural development should prompt timely assessment of children with drug-resistant epilepsy by paediatric specialty centers.[5]

Current trends in indications and referral patterns

Since the 2003 guidelines were published,[4] efforts have been made to promote and monitor increased and earlier access to epilepsy surgery. One important move forward has been the proposal of a working definition of drug resistance by the ILAE as "failure of adequate trials of two tolerated, appropriately chosen and used antiepileptic drug schedules (whether as monotherapies or in combination) to achieve sustained seizure freedom".[6]

The Early Randomized Surgical Epilepsy Trial[7] compared early surgical with continued medical treatment in patients with mesial temporal lobe epilepsy, hippocampal sclerosis, and disabling drug-resistant seizures for less than 2 consecutive years. Despite a much lower enrolment rate than initially planned, the benefits of early surgery were shown: none of the 23 patients in the medical group and

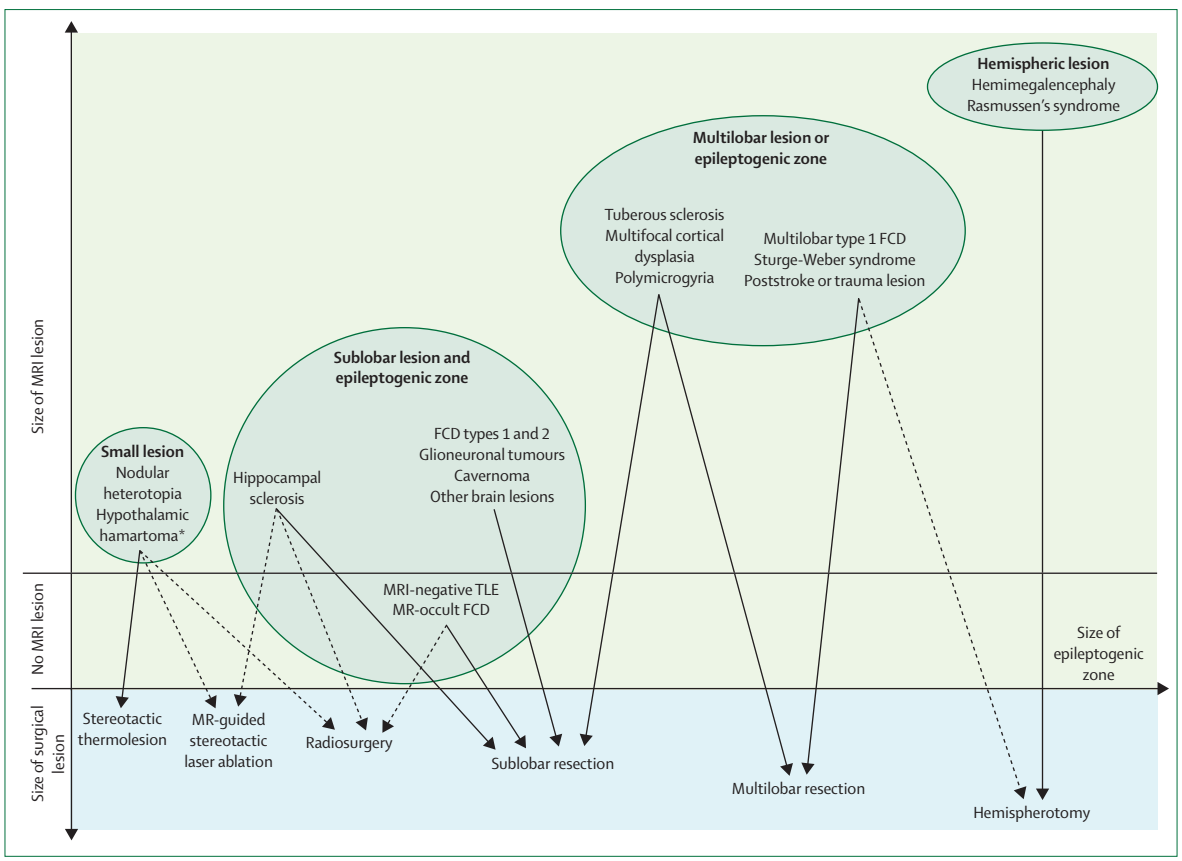

Figure 1: **Indications for the various forms of epilepsy surgery**
Indications are shown according to the cause of epilepsy, size of the MRI lesion, and size of the epileptogenic zone. Dotted arrows represent surgical indications that remain exceptions compared with those delineated by solid arrows. FCD=focal cortical dysplasia. MR=magnetic resonance. TLE=temporal lobe epilepsy, FCD=focal cortical dysplasia. *Can additionally be treated with surgical disconnection or resection, with or without an intraventricular endoscopic approach.

11 of the 15 in the surgical group were seizure free during the 2 years of follow-up (odds ratio ∞, 95% CI 11·8 to ∞, p<0·001). Greater improvement in quality of life was also seen in operated patients. In terms of serious adverse events, surgery caused a verbal memory decrease in 36% of operated patients and transient neurological deficit due to postoperative stroke for one patient, whereas three patients from the medical group had status epilepticus.

The difficulty in recruitment of individuals to this study echoes the fact that the duration from diagnosis of epilepsy to referral for surgery remains steadily high. At Columbia University (New York, NY, USA), this duration was a mean of 22·6 (SD 12·7) years from 1996 to 1999 and 21·1 (14·2) years from 2004 to 2007,[8] which are the respective periods before and after the publication of the 2003 AAN practice parameters on epilepsy surgery.[4] Similarly, at the University of California, Los Angeles (CA, USA), the mean duration was 17·1 (SD 10·0) years from 1995 to 1998 and 18·6 (12·6) from 2005 to 2008.[9] However, this apparent stability might mask dual changes that associate earlier referral of straightforward temporal lobe epilepsy together with more delayed assessment of complex cases previously deemed to be non-operable.[9] In the paediatric population, an international survey of epilepsy surgery centres[10] showed that only a third of children had proceeded to surgery within 2 years of epilepsy onset, despite this onset having occurred at less than 2 years of age in 60% of the children.

These findings do not seem to be because of restricted access to epilepsy centres. On the contrary, findings from a survey of the Nationwide Inpatient Sample of non-federal US hospitals[11] showed that admissions for medically refractory focal epilepsy doubled between 1990 and 2008, although admissions at the highest-volume epilepsy centres have decreased by 50% during the same period. Furthermore, the overall number of surgical procedures remained stable, possibly because of the fact that low-volume and less experienced centres are less inclined to proceed to surgery after presurgical assessment.[11]

Other data even suggest that what might be regarded as classic epilepsy surgery disorders are less common, particularly mesial temporal lobe epilepsy. The Rochester Epidemiology Project[12] based in Olmsted County (MN, USA) reported that referral for anterior temporal lobectomy decreased from 1·9 to 0·7 per 100 000 person-years between 1993–2000 and 2001–09. Similarly, nationwide