

Temporal lobe resection for intractable epilepsy: review of 11 cases

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Objective. To review the management of medically intractable epilepsy by performing temporal lobe resection.

Design. Retrospective study.

Setting. University teaching hospital, Hong Kong.

Patients. Eleven patients: seven women and four men (mean age, 28 years; range, 19-49 years) who underwent temporal lobe resection for intractable epilepsy from 1994 through 1998.

Main outcome measures. Preoperative and operative aspects of treatment, postoperative complications, mortality, and seizure control before and after surgery.

Results. All but one patient had long-standing medically intractable temporal lobe epilepsy; the duration between the onset of seizure and surgery ranged from 12 to 27 years (mean, 17.2 years). A total of 12 resections were performed without any mortalities or major postoperative complications. After surgery, two patients became seizure-free without the need for antiepileptic medication; six patients were seizure-free but required medication; and two patients showed >90% of improvement in seizure control, whereas one patient showed between 50% and 90% of improvement. Nine (81%) of the 11 patients reported significant improvement in their social life and performance of daily activities. Two (18%) patients, including one with improved seizure control, reported no improvement in their performance of daily functions.

Conclusions. Temporal lobe resection can produce significant improvements in patients who have medically intractable epilepsy. The risks of surgery are relatively small and justifiable.

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Key words: Brain diseases; Epilepsy/surgery; Epilepsy, temporal lobe; Temporal lobe/surgery; Treatment outcome

Introduction

Epilepsy affects approximately 1% of the general population.¹ Despite modern anticonvulsant therapy and serum drug level monitoring techniques, between 20% and 30% of patients with epilepsy are refractory to all forms of medical treatment.² Chronically intractable epilepsy is not only psychosocially disabling, but also biologically damaging. Uncontrolled seizures may result in ongoing neuronal damage, neuropsychological deficits, and increased risks of injury or sudden death.³

Although epidemiological data on epilepsy in Hong Kong are not available, the proportion of epileptic patients in Hong Kong whose seizure control is considered unsatisfactory has been estimated to be 27%⁴ and 40%⁵ in two studies. For this group of patients with medically intractable epilepsy, surgery may improve the quality of life by achieving complete or maximal seizure control without causing added neurological deficit.

A large number of surgical procedures have been described, including cortical resection (eg temporal lobe resection),⁶ lesionectomy (eg tumour resection),⁷ hemispherectomy,⁸ and disconnection procedures such as multiple subpial transections⁹ and corpus callosotomy.¹⁰ Examples of other methods are chronic electrical stimulation of the vagus nerve,¹¹ chronic cerebellar stimulation,¹² and stereotactic thalamic stimulation.¹³ The choice of surgical procedure depends on the precise localisation of the focus of epilepsy.

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Complex partial seizure is the type of epilepsy that is most frequently refractory to medical therapy.¹⁴ The majority of cases involve the temporal region of the brain (temporal lobe seizure or temporal lobe epilepsy); other cases may arise from the frontal, parietal, or occipital lobes (extra-temporal lobe epilepsy). As a result, temporal lobe resection (ie cortical resection) is the most widely and most effective method used. The most common pathological findings in patients who undergo temporal lobe surgery is mesial temporal sclerosis or hippocampal sclerosis, which is characterised by atrophy and gliotic changes of the structures of the medial temporal lobe.¹⁵ Patients with intractable temporal lobe epilepsy that is associated with hippocampal sclerosis respond particularly well to surgery and constitute the largest group of epileptic patients who benefit from surgical treatment.

The Epilepsy Surgery Programme at the Queen Mary Hospital (QMH) was initiated in 1993, and is a multidisciplinary venture involving the departments of medicine, neurosurgery, paediatrics, psychiatry, nuclear medicine, and diagnostic radiology. In this review, we report on our early experience with patients who underwent temporal lobe resections for medically intractable epilepsy.

Methods

Patient selection

Records of all the patients who had undergone temporal lobe resections for medically intractable epilepsy in the Department of Surgery at the QMH from 1994 through 1998 were reviewed. Medically intractable epilepsy is defined as epilepsy that remains persistent despite using an adequate therapeutic trial of

Box 1. Selection criteria for epilepsy surgery

- Functionally incapacitating seizures
- Refractory to medical treatment
- Chronic seizure (>2 years duration)
- Intelligent patient (IQ >70)
- No major contra-indications to surgery
- Patient can cooperate with preoperative studies
- Age is not a contra-indication but 15-50 years is optimum
- No history of habitual non-compliance or chronic drug abuse

phenytoin and carbamazepine—both alone or in combination—such that appropriate serum drug levels are reached, and despite using a regimen of several second-line antiepileptics for a duration of more than 2 years. Only patients who had evidence of hippocampal sclerosis or non-specific temporal lobe pathology were included. Patients who had received other treatment modalities or who had undergone temporal lobe resection for other pathologies such as tumours or vascular malformations (ie lesionectomy) were not included, even if epilepsy was the primary indication for surgery.

Box 1 shows the initial selection criteria for patients entering the Epilepsy Surgery Programme. The degree of functional capacity due to intractable seizure was mainly based on clinical history and neuropsychological assessment; specific references were made to employment, education, social, and psychological well-being. Patients who fulfilled these criteria were subjected to a series of preoperative assessments (Table 1). The aim of the preoperative evaluation was to define precisely the epileptic focus in each patient and the extent of resection that would produce the maximum reduction in seizure and the minimum functional deficit. Suitable candidates needed to have

Table 1. Results of preoperative assessment

Patient	Sex/age (years)	EEG*	MRI†	SPECT‡	Language§	Memory ^{xx}	Focus¶
1	F/49	Right	Right HS**	Normal	Left	Left	Right
2	F/33	Left	Normal	Bilateral	Bilateral	Right	Left
3	M/19	Right	Right cyst	Right	Left	Bilateral	Right
4	M/28	Bilateral	Right HS	Right	Left	Left	Right
5	F/27	Right	Right HS	Bilateral	Left	Bilateral	Right
6	F/21	Left	Left HS	Left	Left	Right	Left
7	F/35	Bilateral	Right HS	Right	Left	Left	Right
8	F/21	Left	Left HS	Bilateral	Left	Right	Left
9	M/27	Right	Right HS	Right	Bilateral	Left	Right
10	F/27	Right	Right HS	Right	Left	Left	Right
11	M/25	Right	Right HS	Right	Left	Left	Right

* Temporal lobe with primary epileptic focus on inter-ictal or ictal video-electroencephalography
 † Temporal lobe abnormality on magnetic resonance image
 ‡ Temporal lobe that shows hypoperfusion on inter-ictal single-positron emission computed tomography scan
 § Cerebral hemisphere supporting language function (from the Wada test)
^{xx} Cerebral hemisphere supporting memory function (from the Wada test)
 ¶ Temporal lobe concluded to be containing the primary focus
 ** HS hippocampal sclerosis

an identifiable unilateral epileptic focus over the anterior temporal lobe area after complete evaluation. In addition, resection of this area should not result in any unacceptable neurological deficit such as aphasia or memory impairment. Informed consent was obtained from each patient and the next of kin after a formal interview was conducted.

Preoperative assessment

History and clinical examination

The adequacy of medication trials previously used was assessed to ensure that the patient was truly refractory to medical therapy. Detailed information on the types, frequency, severity, and duration of seizure was obtained to help localise the focus of epilepsy. The extent of disability (including psychiatric morbidity) due to uncontrolled seizure, general physical fitness, and the past medical history or other intracranial pathology were assessed. Focal neurological or cognitive abnormalities that became evident during the clinical examination also provided important information.

Non-invasive electroencephalography

Although consistent and lateralised epileptiform discharges (eg spikes and slow-wave complexes) on inter-ictal scalp electroencephalograms may theoretically provide adequate focus identification, video-electroencephalography (EEG) recording was performed for all patients who were being assessed. Ictal EEG facilitated the localisation of the primary epileptic focus by recording the electrical events at the scalp at the onset of spontaneous seizure. The method identified patients who had pseudoseizure or multifocal seizure, both of which would constitute contra-indications to surgery. The procedure was carried out on an inpatient basis and the administration of antiepileptics was tapered to increase the probability of recording a seizure. With the use of synchronous 24-hour video and scalp-electrode monitoring systems, EEG changes can be directly correlated with clinical events. An ideal candidate should demonstrate a unilateral primary focus at the anterior temporal lobe during the onset of a 'typical' seizure.

Magnetic resonance imaging

Magnetic resonance imaging (MRI) identified structurally abnormal areas and hence probable epileptic foci, which may not be identifiable on conventional computed tomography scans. All patients who underwent temporal lobe resections received an MRI examination preoperatively. Hippocampal sclerosis was seen as asymmetrical atrophy of the hippocampus over the medial temporal lobe and was characteristically hyperintense on T2-weighted images

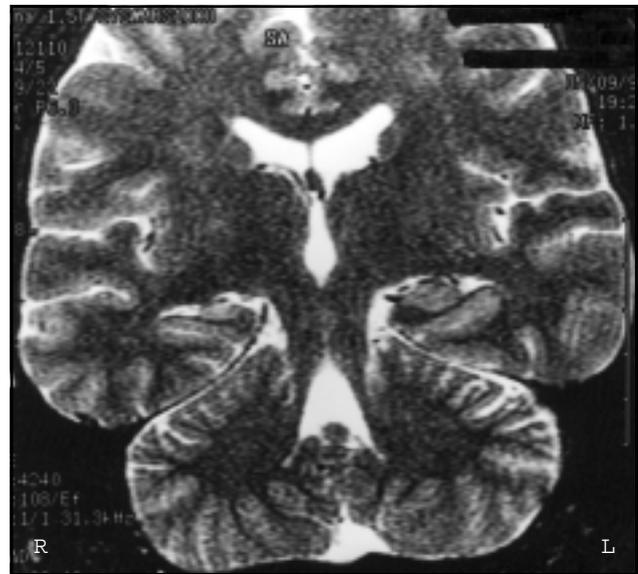


Fig 1. T2-weighted coronal section magnetic resonance image showing right hippocampal sclerosis. Note the atrophy of the hippocampus over the right medial temporal lobe.

(Fig 1). Patients who were found to have pathology other than hippocampal sclerosis on the MRI scan (eg ganglioglioma or arteriovenous malformation) were treated accordingly and were excluded from this study. Normal findings on the MRI scan did not exclude the patients from further assessment.

Single-photon emission computed tomography

Single-photon emission computed tomography (SPECT) was used to demonstrate characteristic changes in local blood flow in epileptogenic areas of the brain. The radioactively labelled compound hexamethylpropylene-amino oxime passes the blood-brain barrier and is retained by brain cells. Because its uptake is a function of both regional cerebral blood flow and the characteristics of the perfused tissue, SPECT allows the regional cerebral blood flow to be studied in different tissues in various physiological and pathological states. The local perfusion is often reduced between seizure attacks, and the blood flow markedly increases during or soon after seizures. Typical findings from SPECT studies provided supportive information on focus localisation. Equivocal results, however, did not preclude surgery.

The Wada (Amytal) test

The intracarotid injection of amobarbital 75 to 125 mg (amylobarbitone [Amytal; Flynn, Harrow, United Kingdom]), by using selective digital subtraction angiography and selective catheterisation techniques, produced selective hemispheric inactivation and was used to define hemispheric language and memory functions. Each carotid artery was catheterised under

radiological guidance and injected with amobarbital, during which both language and memory functions, now only supported by the contralateral 'active' cerebral hemisphere, were assessed with standardised tests. A memory retention score above 60% was considered adequate to support the memory function after the operation. If the proposed resection area was found to be in the language-dominant hemisphere or if the contralateral hemisphere could not alone support memory, resection was either contra-indicated or modified.

Neuropsychological assessment

Preoperative psychological assessment offered insight into the patients' perception of the disease and understanding of the potential implications of surgical treatment. Cognitive changes after unilateral temporal resection can be predicted and used to guide postoperative rehabilitation. Neuropsychological functions, such as verbal and non-verbal memory, and attention and cognitive processing speed, were assessed using the revised Wechsler adult intelligence scale and the revised Wechsler memory scale. Only patients whose performances were within or above the normal range were selected for surgical resection. Understanding the patients' psychological make-up and expectations enabled us to offer the appropriate preoperative counselling.

Operative procedures

The operation was performed under general anaesthesia with the use of standard microsurgical techniques. A curvilinear scalp incision was made behind the hairline to achieve the best cosmetic results. A temporal craniotomy was performed to gain access to the anterior temporal lobe. The extent of resection was tailored for each patient based on preoperative assessment findings. In general, the anterior tip of the temporal lobe, the mesial structures (eg amygdala, hippocampus) and a variable amount of the lateral temporal cortex were resected. Resections of the 'non-dominant' hemisphere with regards to language and memory functions would include a greater amount of the lateral cortex to achieve better seizure control whereas resection of the 'dominant' hemisphere would be more conservative to minimise the chance of incurring postoperative dysfunctions (Fig 2). After the operation, the patients resumed their preoperative antiepileptic drug therapy.

Patient follow-up

Patients were followed up at the Epilepsy Surgery Clinic, which is conducted jointly by the neurosurgeons and neurologists of the QMH. The mean duration of follow-up was 21.5 months (range, 6-47 months). The

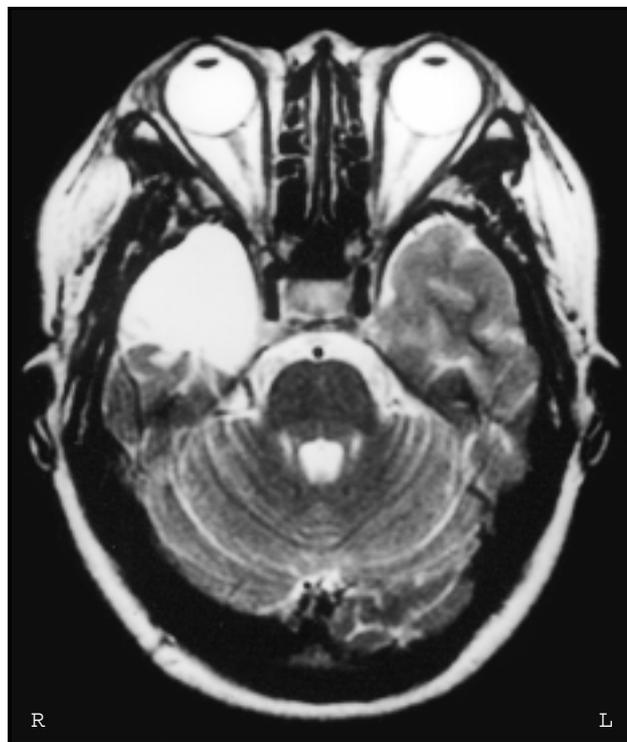


Fig 2 . Postoperative T2-weighted axial magnetic resonance image after a right-sided temporal lobe resection

extent of seizure control was evaluated by using a modified version of Engel's criteria (Box 2).¹⁶ Patients who were seizure-free would have their medication gradually reduced. Those who experienced persistent seizure or recurrence after a seizure-free interval would have their regimens modified based on individual assessment.

Results

Eleven patients (seven women and four men) fulfilled the study selection criteria (Table 1). Their mean age at surgery was 28 years (range, 19-49 years). All but one patient (patient 3) had long-standing medically intractable temporal lobe epilepsy; patient 3 had long-standing petit mal and hyperkinetic seizure. The duration between the onset of seizure and surgery ranged from 12 to 27 years (mean, 17.2 years). A total of 12 resections (eight right-sided and four left-sided) were performed; one patient required a second operation on the same side 2 years after the initial resection (patient 8).

Seizure control

The results of seizure control after surgery are shown in Table 2. Seizure control was assessed at fixed intervals of 6 months (three patients), 1 year (three patients) or 2 years (five patients) after the operation. Two (18%) patients were seizure-free without needing

Box 2. Seizure outcome evaluation¹⁶

Group Ia	Seizure-free without medication
Group Ib	Seizure-free with medication
Group II	≥90% reduction of seizure
Group III	<90% but >50 % reduction of seizure
Group IV	No change from baseline
Group V	Deterioration

medication (group Ia). One of them (patient 8) had undergone a left-sided resection 2 years previously but with unsatisfactory outcome (group III); only the anterior portion of the medial temporal structures and a small amount of the lateral cortex had been resected in the first operation. Marked improvement was seen in this patient after the second ipsilateral temporal lobe resection, in which a temporal lobectomy was performed to a posterior margin of 5 cm from the temporal pole. Six (55%) patients were seizure-free while remaining on the preoperative or reduced regimen of antiepileptics (group Ib). Two (18%) patients experienced greater than 90% of improvement in their seizure control (group II). One (9%) patient had less than 90% but greater than 50% of improvement (group III). This patient (patient 3) had a history of psychiatric illness and psychosocial adjustment disorder. Postoperative EEG studies, however, did not demonstrate any clear correlation between cortical activities and the persistent 'seizures'. Pseudoseizure was diagnosed and this patient's response to surgery thus could not be reliably assessed. No patients were classified as belonging to group IV or V. Nine (81%) patients experienced either significant or noticeable improvement in their overall function and performance of daily activities. Two (18%) patients reported no improvement or worsening after surgery: one of them (patient 3) had poor seizure control (group III) and the other (patient 4) had experienced deterioration in memory function postoperatively.

Surgical complications

There were no mortalities or major postoperative complications in this series of patients. One (9%) patient

had transient vocal cord palsy and hoarseness, which was most probably related to endotracheal intubation during induction of general anaesthesia (patient 11). The patient recovered fully after receiving conservative treatment. One (9%) patient had asymptomatic upper quadrantanopia contralateral to the side of resection, as detected by postoperative visual field testing (patient 5). Two (18%) patients had symptomatic permanent deficits: one of them had persistent paralysis of the frontalis muscle ipsilateral to the resected side, which was caused by inadvertent injury to the frontal branch of the facial nerve during the operation (patient 8). The second patient, who had undergone a right-sided resection, experienced postoperative deterioration in memory function (patient 4), which occurred despite the fact that the results from the preoperative Wada test indicated left-hemisphere language dominance and 100% memory retention on right-hemisphere inactivation. No other patients had functionally significant memory or language deficits.

Discussion

Patient selection is one of the most important factors in determining the success of surgery for epilepsy. During the early phase of the Epilepsy Surgery Programme, we deliberately selected patients who had a more predictable response to surgery—namely, those who had intractable complex partial seizure of temporal lobe origin. Surgical results are most promising for patients with temporal lobe epilepsy; the success rate is 81%, compared with 50% for patients with frontal lobe seizure.¹⁴

All but two of the patients in this series had preoperative evidence of hippocampal sclerosis, which is a strong predictor of excellent postoperative seizure control.^{17,18} The characteristic features of hippocampal sclerosis are local atrophy and gliosis of the mesial temporal structures—namely, the uncus, amygdala, anterior hippocampus, and hippocampal gyrus. It has

Table 2. Surgical outcome: seizure control and postoperative complications

Patient	Operation date	Resection	Postoperative assessment	Seizure-control group	Complications
1	Aug 1994	Right	2 years	Ib	None
2	Jan 1995	Left	2 years	Ib	None
3	Jul 1995	Right	2 years	III	None
4	Apr 1996	Right	2 years	Ib	Memory decline
5	Dec 1996	Right	2 years	II	Visual field defect
6	May 1997	Left	1 year	Ia	None
7	Jul 1997	Right	1 year	Ib	None
8	Oct 1995, Nov 1997	Left	1 year	Ia	Frontalis paralysis
9	Feb 1998	Right	6 months	Ib	None
10	Apr 1998	Right	6 months	II	None
11	May 1998	Right	6 months	Ib	Vocal cord palsy

been suggested that during head moulding at birth, herniation of the medial temporal gyri through the incisura of the tentorium cerebelli results in ischaemic damage.¹⁹ It has also been suggested that the neuronal damage associated with hippocampal sclerosis is the result of consumptive hypoxia due to severe febrile convulsion in infancy.²⁰ The subsequent cell loss might stimulate the synaptic reorganisation of the remaining neurones, which could give rise to abnormal discharges that eventually propagate sufficiently to produce clinical seizure.²¹ Surgical resection of the damaged areas of the brain affected by hippocampal sclerosis—the anterior and medial temporal lobe—is effective in eradicating seizure.²² In addition, the presence of hippocampal sclerosis and mesial temporal damage may result in the abnormal displacement of memory function to the contralateral hippocampus, which may then help protect against postoperative memory deterioration.²² Conversely, resection of an intact temporal lobe can be associated with significant memory decline.²³

Comparing the results of surgery for epilepsy in different hospitals is difficult because patient selection, operative approaches, and criteria for outcome assessment vary widely. Engel et al¹⁶ reviewed 3579 patients from 100 epilepsy centres and found significant clinical improvement in 92% of the patients. The proportion of patients who remain seizure-free after temporal lobe resection is approximately 70%.^{6,24,25} In our series, 73% (8/11) of the patients were seizure-free with or without the need for medication (patients in groups Ia and Ib) and significant improvement was found in 91% (10/11) of patients (groups I and II). The majority (5/6) of the patients who became seizure-free by taking reduced dosages of their preoperative antiepileptics (group Ib), reported that being able to control their seizure with drug therapy has made a tremendous impact on their overall physical and psychological functioning. These results are encouraging, but the fact that these patients were a highly selected group compared with those in larger series has to be considered. Furthermore, our follow-up duration was relatively short (mean, 21.5 months). In general, follow-up of at least 6 months to 1 year is required before the outcome of surgery for epilepsy can be reliably assessed.³ Seizure control in the second postoperative year should predict the 5-year outcome.²⁵

Our current selection criteria may have excluded some patients who could have otherwise undergone and benefitted from surgery. In the past, performing surgery to manage epilepsy was largely limited to lesionectomy (eg excision of post-traumatic scarring

or tumour). The development of MRI and modern EEG techniques has greatly increased the number of patients who may benefit from surgery. The current gold standard of focus localisation that would predict a favourable outcome involves the demonstration of regional activation on inter-ictal and ictal EEG scans and focal abnormalities, especially hippocampal sclerosis, on MRI scans.¹⁸ Some patients may not demonstrate these features on initial evaluation but they are by no means excluded from further consideration for surgical treatment. The use of multimodality investigations allows the better identification of any isolated epileptic foci by providing valuable supportive information. For instance, in our series, all but two patients showed unilateral temporal foci according to the results of EEG telemetry. The remaining two patients (patients 4 and 7) had bilateral temporal discharges on inter-ictal and ictal EEG scans. There were, however, unequivocal findings of right-sided hippocampal sclerosis on MRI, and right-sided inter-ictal hypoperfusion on SPECT. Both patients had good outcome after right-sided resection (group 1b). In other centres, more invasive techniques such as direct brain recording using subdural grid electrodes or multicontact depth electrodes are used.^{26,27} Although these procedures are associated with increased surgical risks, they have enhanced the selection of patients with genuinely localised foci who are amenable to surgical treatment.

Recurrent or persistent seizure constitutes surgical failure and the most important cause is insufficient resection (and hence, for example, retained mesial structures).²⁸ Other causes of treatment failure include localisation error (eg bitemporal or extratemporal foci), and the development or activation of a separate focus.²⁹ Results of reoperation are good,²⁸ as demonstrated by one of the patients in this series, who had a poor outcome after the first, more 'conservative' resection, which was most likely due to retained epileptogenic structures. More extensive resection including more of the lateral cortex and mesial temporal structures in the second operation had resulted in much improved outcome.

Complications of cortical resection to manage epilepsy are not common. The incidence ranges from 1%³⁰ to 16%.³¹ One of the patients in this series had mild bilateral upper quadrantanopia postoperatively; this is a well-recognised complication of temporal lobectomy and is caused by damage to the Meyer's loop of optic radiation in the temporal lobe. Other major complications that are specific to temporal lobe resection are postoperative memory and language

dysfunction. One of the main objectives of preoperative assessment is to ascertain whether the proposed area of resection is dispensable with respect to memory and language functions. Although the Wada test is a widely used technique, concern has been raised regarding its reliability.³² The reason for the significant postoperative memory dysfunction experienced by one of the patients in this series is unclear. The results of this patient's preoperative Wada test showed that the hemisphere contralateral to the resection side was able to fully support memory. And the results of the postoperative memory test actually contradicted the patient's subjective complaints, thus suggesting that a significant part of his 'memory decline' was psychogenic. This patient had had intractable epilepsy for 13 years and became seizure-free (group Ib) after surgery. The sudden removal of a 'sick role' may have resulted in certain difficulties in psychosocial adjustment. This case shows that surgery for epilepsy can alter only the control and frequency of seizure but not other dysfunctions that result from a prolonged period of uncontrolled seizure. Surgical treatment should be considered at an early stage of the disease, before these dysfunctions are permanently established. For complex partial seizure, an adequate medical trial involves the use of phenytoin and carbamazepine, both alone or in combination at dosages to attain appropriate serum levels; second-line antiepileptics can then be added for 1 to 2 years.³ Most patients who respond favourably to drug treatment would have done so by the first year of treatment. If not, the possibility of medical intractability should be entertained and surgical treatment seriously considered. In our series of patients, the duration between the onset of seizure and surgery was prolonged, because the Epilepsy Surgery Programme at the QMH commenced only in 1993.

In conclusion, surgery can produce significant improvement in patients who have medically intractable epilepsy. The associated risks are relatively small and justifiable in view of the benefit of treatment and harmful consequences of long-term uncontrolled seizure. By adopting more advanced techniques such as direct brain-recording, we hope to be able to broaden the selection criteria provide successful treatment to more patients in the future.

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