

## Reoperation for recurrent temporal lobe epilepsy

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✓ The indications for and the risks and outcome of reoperation for medically refractory temporal lobe epilepsy have not been well documented. A retrospective review is presented of 40 patients who underwent reoperation on the temporal lobe for recurrent seizures. The mean patient age at the first operation was  $22 \pm 7$  years ( $\pm$  standard deviation). Electrocorticography during the first operation showed interictal epileptic abnormalities from surface electrodes in 97% of the cases and from depth electrodes in the mesiotemporal structures in 38%. The seizures recurred with the same pattern within 6 months after the first operation in 60% of patients and within 2 years in 90%. Postoperative neuroimaging studies showed residual mesiotemporal structures in all cases. The mean time between the two operations was  $5.5 \pm 5$  years and the mean patient age at the second operation was  $28 \pm 8$  years. The second operation involved focal resection of the mesiotemporal structures in 30 cases. The mean postoperative follow-up period was  $4.8 \pm 2.7$  years (range 2 to 11 years). After the second operation, 63% of the patients were seizure-free or had rare seizures (one or two per year). There were no permanent neurological complications. Patients who did not benefit from reoperation had electroencephalographic abnormalities in multiple brain areas.

Reoperation for temporal lobe epilepsy effectively controls seizures in the majority of patients, and the procedure is safe if rigorous technical rules are observed. More complete resection of mesiotemporal structures during the first operation, even in the absence of intraoperative electrographic abnormalities, could prevent the need for reoperation in defined cases.

**KEY WORDS** • epilepsy • temporal lobe • reoperation

**S**EIZURES recur after surgery for temporal lobe epilepsy in 20% to 60% of patients.<sup>3,5,8,12,20</sup> Although epilepsy surgery is practiced in an increasing number of centers, the indications for and the risks and outcome of reoperation for temporal lobe epilepsy have not been well documented. Reoperation for epilepsy was first reported in 1954 by Penfield and Jasper.<sup>15</sup> Several more recent series have demonstrated the benefit of reoperation for recurrent seizures,<sup>14</sup> including those of temporal lobe origin,<sup>3,12,20</sup> 25% to 52% of patients were seizure-free postoperatively. In most of these series, however, the postoperative follow-up time was not specified,<sup>12,20</sup> and one study included only 10 patients, who were followed for 8 to 82 months.<sup>3</sup>

In this retrospective study, we review 40 patients who underwent reoperation on the temporal lobe for recurrent temporal lobe epilepsy. In all cases, the follow-up time after the second operation was at least 2 years. The goal of the study was to assess the indications for and the risks and outcome of reoperation for temporal lobe epilepsy.

### Clinical Material and Methods

#### *Patient Population and Preoperative Workup*

The criteria for inclusion in the study were: 1) medically refractory epilepsy of temporal lobe origin after temporal lobe resection for treatment of the seizure disorder; 2) reoperation on the temporal lobe; 3) at least 2 years of follow-up evaluation after the second operation; and 4) documented therapeutic levels of antiepileptic drugs before and after both operations. Forty patients met these criteria, including 24 males and 16 females. Their mean age ( $\pm$  standard deviation) at the onset of seizures was  $19 \pm 7$  years (range 3 months to 25 years). All patients had complex partial seizures of temporal lobe origin with or without generalization.

The diagnostic workup for the first operation in all 40 cases included interictal or ictal surface electroencephalographic (EEG) recordings from surface and sphenoid electrodes. Intraparenchymal depth electrodes were used when the surface EEG data were not sufficient to determine the side or location of the sei-



FIG. 1. Intraoperative photograph of a left-sided craniotomy for recurrent temporal lobe epilepsy. To avoid damage to venous structures, the dura was opened mainly over the pseudocyst of the first temporal resection. The residual mesiotemporal structures are indicated (arrow).

zure focus. Computerized tomography scans or magnetic resonance (MR) images were obtained in 22 cases.

The workup for the second operation included surface EEG recordings and neuroimaging in all cases. If the surface EEG data did not show a clear predominance of the epileptic abnormalities, EEG recordings were obtained from depth electrodes. The complete medical record was available for review in all 40 cases.

### Surgical Procedure

The first operation was performed by various surgeons at different institutions between May, 1968, and December, 1988; the senior author (A.O.) carried out the first operation in 31 of the 40 cases. Between November, 1971, and December, 1990, he performed anterior lobe resection for treatment of medically refractory epilepsy in 559 patients. All patients were referred to the Montreal Neurological Institute for the second operation, which was in all cases performed by the senior author between February, 1982, and November, 1990.

### Technical Aspects of Reoperation

Planning for surgery included a detailed review of the stereo digital cerebral angiograms; particular attention was given to the arteries and veins of the temporal region. In all cases, the second operation was performed under general anesthesia. In most patients, the dura was significantly adherent to the other meningeal layers. To avoid damage to venous channels, the dura was opened with an incision parallel to the middle fossa over the previous surgical cavity (Fig. 1); the incision was placed as anteriorly and as low as possible. Microsurgical techniques were used to resect mesiotemporal structures; an ultrasonic dissector was used at a low setting for both vibration and aspiration (20% of

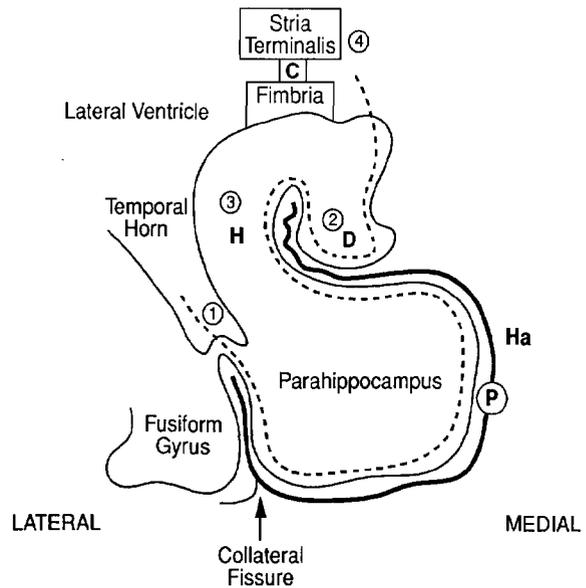


FIG. 2. Schematic diagram showing a coronal section of the left mesiotemporal structures viewed anteriorly; the numbers indicate the steps for their removal. 1: The collateral fissure is entered and the parahippocampal gyrus resected subpially with the ultrasonic aspirator. 2: After localization of the hippocampal sulcus and hippocampal artery (Ha), the dentate gyrus (D) is resected as above. 3: The hippocampus (H) is then gently lifted. 4: The hippocampus is transected posteriorly through the fimbriae at the level of the superior colliculus (C). The fimbria is identified by lifting the choroid plexus and is transected forward toward the intralimbic gyrus. The dotted line shows the extent of the final resection. P = the posterior cerebral artery in cross section.

power). After entry into the temporal horn, the hippocampus was identified. The parahippocampal gyrus was entered using the ultrasonic dissector just medial to the collateral fissure and was resected subpially (Fig. 2). The resection was extended posteriorly to the level of the superior colliculus. The hippocampal sulcus was identified by locating the hippocampal artery, and the dentate gyrus, mesial to it, was subpially resected. The hippocampus was gently lifted and posteriorly resected through the fimbriae at the level of the superior colliculus. The amygdala was then subpially resected. Because its boundaries are poorly demarcated,<sup>22</sup> the amygdala is difficult to resect radically. Therefore, a radical subpial resection of the gray matter dorsal to the head of the hippocampus was performed as far and as high anteriorly as the horizontal ( $M_1$ ) segment of the middle cerebral artery and up to the rhinal sulcus. Further details of the procedure have been reported elsewhere.<sup>11,19</sup>

### Postoperative Seizure Outcome

Seizures were classified as described by Engel:<sup>5</sup> 1 = seizure-free; 2 = rare seizures (one or two per year); 3 = worthwhile improvement ( $\geq 90\%$  reduction); and 4 = no improvement ( $< 90\%$  reduction).

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TABLE 1  
*Neuroimaging findings before the first temporal surgery in 22 patients*

Finding	No. of Cases
atrophy	
generalized	2
localized	11
cyst	2
normal	7

### Statistical Analysis

The statistical significance of differences in seizure outcome according to patient age, seizure-free interval, time between operations, and duration of follow-up monitoring was determined by analysis of variance, using Bonferroni's correction when necessary ( $p < 0.05$  was considered significant). Values are given as means  $\pm$  standard deviations.

## Results

### First Operation

The preoperative diagnostic workup for the first surgery in all 40 cases included interictal and/or ictal surface EEG recording with sphenoid electrodes. Depth electrodes were placed in six patients in whom surface EEG tracings were inconclusive. The results of preoperative neuroimaging studies in 22 patients are shown in Table 1. The age of the patients at the time of first operation and the side and type of that procedure are reported in Table 2. Intraoperative electrocorticography showed surface spikes in 31 (97%) of the 32 patients in whom it was used. Intraoperative depth electrodes showed spikes originating from the deep mesiotemporal structures in nine (38%) of 24 cases. The histopathological findings at the first operation are summarized in Table 3. The seizures recurred within 6 months after surgery in 60% of patients and within 2 years in 90% (Fig. 3). There were no surgical complications in 39 cases. One patient whose operation was performed elsewhere suffered a contralateral hemiparesis that improved over time.

### Second Operation

**Preoperative Workup.** Neuroimaging studies showed residual mesiotemporal structures in all 40 cases (Fig. 4). The surface EEG recording revealed clear evidence of electrographic abnormalities in the residual ipsilateral temporal lobe in 31 cases. In five cases, EEG abnormalities were found in multiple areas, but they were predominantly in the ipsilateral temporal lobe. In three of four cases in which the surface EEG tracing did not show a clear predominance of the epileptic abnormalities, depth electrodes showed EEG abnormalities in multiple areas; in one case, the abnormalities were localized to the ipsilateral temporal lobe.

**Surgery and Seizure Outcome.** The mean interval between the two operations was  $5.5 \pm 5$  years (range 1 to 27 years). Clinical data for the second operation are

TABLE 2  
*Clinical details for the first operation for temporal lobe epilepsy in 40 patients*

Variable	No. of Cases
side	
left	16
right	24
patient age (yrs)	
mean $\pm$ standard deviation	$22 \pm 7$
range	11-39
surgical procedure	
anterior temporal resection	37
selective amygdalohippocampectomy	2
resection of arachnoid cyst	1

TABLE 3  
*Histopathological findings in 40 patients*

Findings	No. of Cases
minimal changes	33
mesiotemporal sclerosis	3
other*	4

\* Encephalitis, low-grade astrocytoma, cyst, and unknown.

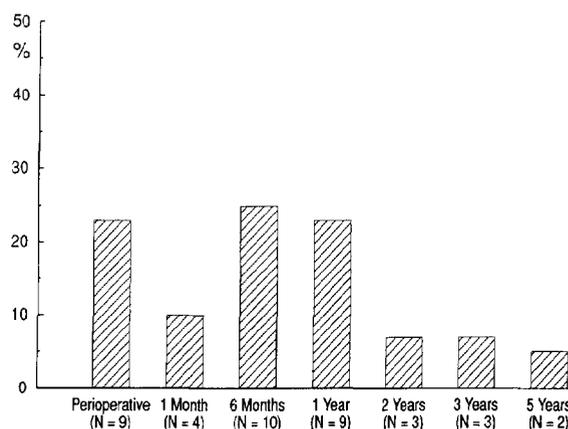


FIG. 3. Bar graph showing the seizure-free interval after the first operation in 40 patients. Seizures recurred within 2 years in 90% of the patients and within 5 years in 100%. N = number of patients.

summarized in Table 4. Postoperatively, 25 (63%) of the patients were seizure-free or had rare seizures (one or two per year) (Fig. 5). The mean postoperative follow-up period was  $4.8 \pm 2.7$  years (range 2 to 11 years). There were no neurological complications in 39 patients; one patient had transient worsening of a pre-existing visual field deficit. One patient required reoperation to remove a subgaleal fluid collection. In another case, the operation was aborted because of venous bleeding after opening of the dura; the same patient later underwent reoperation without complications.

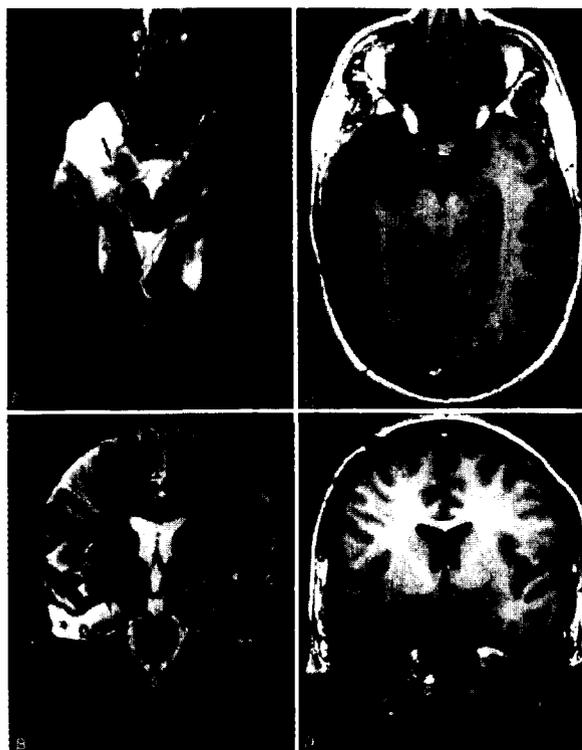


FIG. 4. Neuroimaging in a patient who underwent anterior temporal lobectomy without improvement of his seizure disorder. A and B: Axial (A) and coronal (B) magnetic resonance images (TR 2100 msec, TE 30 msec). The residual amygdala is best seen in A (arrow), and the residual hippocampus is best seen in B. C and D: Axial (C) and coronal (D) magnetic resonance images (TR 523 msec, TE 19 msec) after reoperation showing resection of the above structures. The patient is seizure-free after reoperation.

#### Seizure Recurrence After Reoperation

Fifteen patients had seizure outcome scores of 3 or 4 after the second operation; factors associated with this poor outcome are listed in Table 5. Eight of the 15 patients had multifocal electrographic abnormalities before reoperation. Their age at seizure onset, age at first operation, age at second operation, interval between operations, and follow-up time did not significantly influence seizure outcome.

Three patients underwent a third operation. In one patient from the pre-MR imaging era, the lack of MR images before the second surgery precluded the diagnosis of a cryptic vascular malformation. With the advent of MR imaging, the lesion was identified and excised. In another patient, stereotactic aspiration of a temporal cyst during the second surgery did not reduce the seizure frequency. Open excision of the cyst and further temporal neocortical resection were performed at the third operation. In the third patient, the second operation consisted of removing temporal neocortex only. Postoperative EEG recording from intracranial depth electrodes suggested that the origin of the seizures was from residual mesiotemporal structures, which were removed during the third operation. These

TABLE 4

Clinical details for the second operation for temporal lobe epilepsy in 40 patients\*

Variable	No. of Cases
side	
ipsilateral to first op	40
patient age (yrs)	
mean $\pm$ standard deviation	28 $\pm$ 8
range	15-47
surgical procedure	
resection of MT structures	30
resection of MT structures + neocortex	8
stereotactic aspiration of cyst	1
temporal lobe lesionectomy	1†

\* In 16 (70%) of 21 patients who were seizure-free after reoperation, only the residual mesiotemporal (MT) structures were resected.

† This posterior temporal lesion was not removed at the first surgery as the electroencephalographic abnormalities were located anteriorly.

TABLE 5

Factors possibly influencing poor seizure outcome after reoperation in 15 patients

Factor	No. of Cases
multiple foci with depth electrodes	3
multiple foci with surface electrodes	5
"missed lesion"	1*
lack of "optimal surgery"	2*
history of encephalitis	1
unknown	3

\* Underwent a third surgery and became seizure-free.

three patients were seizure-free at evaluation 10, 7.3, and 10 years, respectively, after the third operation.

#### Discussion

##### Causes of Seizure Recurrence After Surgery

The cause of recurrent seizures after surgery for temporal lobe epilepsy is probably multifactorial. Possible contributing factors may include genetic predisposition<sup>1</sup> and scar at the site of resection.<sup>3</sup> In some patients, however, seizures recur because the surgical procedure was inadequate,<sup>12,19,20</sup> owing to inaccurate localization of the epileptogenic area, insufficient excision of the epileptogenic brain, or an undetected structural lesion.<sup>3,20</sup>

It has been suggested that intracranial EEG monitoring improves seizure outcome by decreasing mislocalization of the epileptogenic focus.<sup>12,15,17,21</sup> Wyler, *et al.*,<sup>21</sup> showed that a seizure-free outcome was more common in patients operated on after invasive monitoring than after scalp monitoring (77% vs. 59%). Postoperative recurrence of seizures might, therefore, result from imprecise preoperative localization of the seizure focus. These authors reported two cases in which scalp EEG recordings led to a callosotomy, but subsequent intracranial EEG recordings showed that the seizure focus was in the neocortex.<sup>20</sup> Awad, *et al.*,<sup>3</sup> reported

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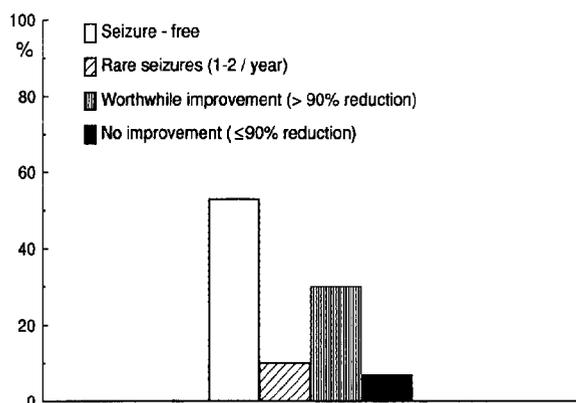


FIG. 5. Bar graph showing seizure outcome after reoperation in 40 patients.

three cases in which the seizure focus was located outside the resected area. This could represent recurrent epileptogenicity outside the area of the previous resection or mislocalization at the first surgery. Our findings cannot clarify this issue, as all of the operations were on the temporal lobe only.

Recent advances in neuroimaging allow the preoperative diagnosis of cryptic vascular malformations, small glial tumors, and neuronal migration disorders,<sup>2,4,7</sup> which often cause epilepsy. Preoperative diagnosis of such lesions makes it possible to plan appropriate surgical resections. Retrospective studies of temporal lobe reoperation may include patients who were not studied preoperatively with MR imaging. Awad, *et al.*,<sup>3</sup> reported that two of 10 patients who underwent reoperation on the temporal lobe had a structural lesion that was not resected at the first surgery. In the series of Wyler, *et al.*,<sup>20</sup> seven of 37 patients who underwent reoperation for temporal or extratemporal epilepsy had structural lesions that were not removed during the first operation. In our study, we found only one such case. These findings confirm that preoperative MR imaging is mandatory for patients being evaluated for epilepsy surgery.

Insufficient excision of epileptogenic brain has been cited as a cause of recurrent seizures after operation for temporal lobe epilepsy,<sup>3,12</sup> and large neocortical excision has been advocated.<sup>9</sup> However, a larger resection does not necessarily result in a better postoperative seizure outcome. Recent data suggest that temporal lobe epilepsy can be well controlled by selective resection of mesiotemporal structures.<sup>6,16,22</sup> In some cases, failure of surgery for temporal lobe epilepsy could be related to inadequate resection of the hippocampus.<sup>10,18</sup> In our study, 16 (70%) of 21 patients who were seizure-free after reoperation underwent resection of residual mesiotemporal structures only. These results support the concept that, in selected cases, temporal lobe epilepsy can be optimally controlled by radical removal of the mesiotemporal structures. A more complete resection of the mesiotemporal structures during the first operation, even in the absence of intraoperative elec-

trographic abnormalities, could prevent the need for reoperation in some cases.

### Preoperative Evaluation

There is no consensus about the "ideal" preoperative workup for patients with temporal lobe epilepsy, and data on preoperative evaluation for reoperation for recurrent temporal lobe seizures are scarce. To reduce the chance of missing an epileptogenic lesion or residual mesiotemporal structures, MR imaging is required. Awad, *et al.*,<sup>3</sup> found subdural electrodes helpful in selected cases. We believe that when MR images show residual mesiotemporal structures or a lesion, intracranial EEG recording is necessary only when the surface EEG recording with sphenoid electrodes is equivocal.

### Indications for Reoperation

The indications for reoperation should include criteria similar to those used for the first operation: 1) epilepsy refractory to documented therapeutic levels of antiepileptic drugs; 2) surface or intracranial EEG recordings showing epileptic activity in the residual temporal lobe; and 3) a residual lesion. In our retrospective study, a short seizure-free interval (< 1 month) after the first operation and surface or intracranial EEG recordings showing multifocal abnormalities were both associated with a poor postoperative seizure outcome. Further studies are needed to investigate whether these two factors are also seen in patients who were successfully treated at the first operation.

### Seizure Outcome and Morbidity After Reoperation

Patients who are seizure-free may more likely be lost to follow-up review. Despite the potential bias, it has been well documented that the postoperative recurrence of seizures increases over time.<sup>5</sup> Engel<sup>5</sup> showed that 81% of 27 patients who were seizure-free at 2 years remained seizure-free at 5 years. In our study, 90% of patients who required reoperation had recurrent seizures within 2 years after the first operation. Thus, a 2-year follow-up period gives a good indication of the surgical success rate.

Our series is the first in which the follow-up period after reoperation is at least 2 years in all cases. Awad, *et al.*,<sup>3</sup> reported that 60% of 10 patients were seizure-free 8 to 82 months (mean 18 months) postoperatively. Wyler, *et al.*,<sup>20</sup> reported that 52% of 23 patients became seizure-free after reoperation for temporal lobe epilepsy, but the postoperative follow-up time was not reported. Fifty-three percent of our patients are seizure-free 2 to 11 years (mean  $4.8 \pm 2.7$  years) postoperatively. These findings demonstrate that reoperation for medically refractory temporal lobe epilepsy effectively controls seizures in selected patients.

Despite reports of increased neurological deficit after reoperation,<sup>8</sup> 39 of the 40 patients in our series had no neurological complications; one patient had temporary worsening of a pre-existing visual field deficit. We strongly believe that the low incidence of complications in our patients reflects rigorous observation of

the technical details described in the Clinical Material and Methods section.

### Conclusions

This study shows that reoperation for recurrent temporal lobe epilepsy provides good seizure control in selected patients. The preoperative workup for reoperation must include MR images to identify residual mesiotemporal structures or lesions. Multifocal EEG abnormalities after the first operation seem to be associated with a poor seizure outcome after reoperation. More complete resection of the mesiotemporal structures during the first operation, even in the absence of intraoperative electrographic abnormalities, could prevent the need for reoperation in defined cases.

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