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Lesionectomy of MRI Detected Lesions in Children with Epilepsy

Abstract

The results of complete excision of cerebral lesions detected by MRI in 18 children presenting with epilepsy were analyzed. There were 14 boys and 4 girls with a mean age of 9.2 years. The average age of onset of seizures was 6.8 years. The mean time from onset of seizures to surgery was 2.3 years. Often, CT scans suggested that the lesions were indolent. MRI was better in differentiating neoplastic from developmental lesions. Angiography was non-contributory in this series. Interictal EEGs showed epileptiform activity correlating with imaging studies in 54% of children. The lesion was completely surgically excised in all patients. This was confirmed by intra-operative ultrasound and postoperative imaging. Electrocorticography was performed prior to and after the resection, but residual spiking did not lead to further resection. The average postoperative follow-up was 5.7 years. Five patients had low grade astrocytomas, 4 had gangliogliomas, 1 a mixed astrocytoma-oligodendroglioma, 3 had cortical dysplasia, 2 infantile desmoplastic gangliogliomas, 2 hamartomata, and 1 cavernous angioma. Sixteen patients have been seizure-free since surgery. Only 2 have partial seizures. Thus, all patients benefited from the resection, with respect to seizure control. In those with temporal lobe lesions, improvement in IQ was seen postoperatively. Early consideration of surgery in patients with epilepsy and lesions demonstrated by MRI is suggested.

Key Words

Lesionectomy
MRI
Epilepsy

Introduction

The causal relationship between brain tumours and epilepsy has been known since the beginning of modern neurology. Jackson, in 1882, reported that the seizure type may indicate the site of the lesion. More recently, with the introduction of the surgical management of epilepsy, this association was confirmed. In 1975, Rasmussen [1] indicated that seizures occurred in approximately 50% of patients with brain tumours. Further reports substantiated the epileptogenicity of intra-axial lesions, particularly if they were localized close to the centroparietal and mesiotemporal regions.

The improvement in imaging techniques, specifically the advent of MRI (now considered the standard of imaging studies), has led to regular detection of discrete lesions such as small gangliogliomas, cortical dysplasias and hamartomata. With the increase in surgical treatment of epilepsy in the pediatric population, issues such as secondary epileptogenesis and early surgical intervention have attracted more attention. Though the reduction in volume of epileptogenic tissue and interruption of the pathways of seizure propagation are goals of epilepsy surgery, there is some unwillingness among many neurosurgeons to perform extended cortical excisions, even in the so-called 'silent brain regions', in children.

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Table 1. Summary of clinical presentation and pathology in 18 patients

Patient No.	Sex	Age Sx onset years	Sx to OR	Sx number	Sx type	Pathology
1	m	12	1/12	1/week	FS+G	Ganglioglioma
2	m	6	8/12	>5/week	PC+A	Astrocytoma
3	m	9/12	3/12	>5 daily	G	Infantile desmoplastic ganglioglioma
4	f	10 6/12	1 8/12	>5/week	PC	Ganglioglioma
5	f	5 6/12	4	1/month	PC	Astrocytoma
6	m	2	7	>5 daily	PC+G	Harmatoma
7	m	11 6/12	4	1/month	FM+FS	Cavernous angioma
8	m	12	3/12	>5/week	FM+G	Astrocytoma
9	m	2	11/12	>6 daily	PC+A	Infantile desmoplastic ganglioglioma
10	f	7/12	8/12	>5 daily	G	Ganglioglioma
11	m	10	6	>5/week	G	Cortical dysplasia
12	m	5	1	1/month	PC	Astrocytoma-oligodendroglioma
13	m	1	3	>5 daily	PC+G	Cortical dysplasia
14	m	7	9	5/month	FS+G	Hamartoma
15	m	17	4/12	5/month	FM	Cortical dysplasia
16	m	13	2	1/month	FS+G	Astrocytoma
17	m	6	3/12	1/month	FM	Astrocytoma
18	f	2	3/13	>5 daily	PC+FM+G	Ganglioglioma

Sx = Seizure; OR = operation; FS = focal sensory; G = generalized; PC = partial complex; A = absence; FM = focal motor.

With these principles in mind, at The Montreal Children's Hospital, we have treated, over the last 7 years, a number of children presenting with medically refractory epilepsy, and lesions detected by CT scan or MRI. The surgical technique consisted of complete excision of the lesion. Electroconvulsography was performed in all patients but the findings obtained during recording did not alter the extent of resection. This is a report of 18 patients with a follow-up of 2 or more years.

Subjects and Methods

There were 18 patients: 14 boys and 4 girls with a median age of 9.2 years. The average age of onset of seizures was 6.8 years and the average time between the onset of seizures and surgery was 2.3 years. Three patients had partial complex attacks, 2 had simple partial motor seizures. Ten had combinations of partial seizures, 7 of them went onto secondary generalization. Three of the patients presented only with generalized convulsions due to rapid spread. Six patients had more than five seizures a day. Most of these were in the younger age group, 5 had generalized attacks due to secondary generalization. Four patients had a least five seizures per week and the others had a more variable frequency of attacks (table 1).

All patients underwent CT scans and MRI, as well as multiple scalp EEGs. Among the ones with temporal lobe lesions, some had

zygomatic electrodes. The EEGs showed epileptiform activity, correlating with imaging studies in 54% of the children. Most of the patients underwent extensive neuropsychological testing, including Wechsler Intelligence Scale for Children III, VABST, BPVT-R, Denman-Memory, Wechsler, and Ray's figure. Patients with left temporal lobe lesions showed non-verbal/verbal discrepancy with lower verbal compared to performance scores. This discrepancy disappeared, or at least improved, in the postoperative period. Two of the patients show significant improvement. All patients had intra-operative cortical evoked responses. Pre-operative studies were carried out with standard scalp recorded median nerve somatosensory evoked potentials done in the laboratory.

Intra-operative evoked response recordings were carried out using ball electrode arrays. These were initially placed according to the neurosurgeon's visual estimate of the location of the motor and sensory strips. The median nerve was stimulated at the wrist by an electrical square wave pulse of 0.2 ms duration with an intensity sufficient to produce a thumb twitch at a rate of four per second.

Anteroposterior and superior to inferior electrode arrays were used. Both referential and bipolar montages helped identify the maximum amplitude of N19P22. We then attempted to locate the N19P22 phase reversal across the rolandic fissure to identify motor cortex. Two hundred and fifty-six to five hundred and twelve stimuli were administered twice, then superimposed for reproducibility.

Electrocorticography was performed with an array of eight or sixteen electrodes. Studies were obtained with a Grass EEG recorder with standard amplification. Referential and bipolar recordings were performed.

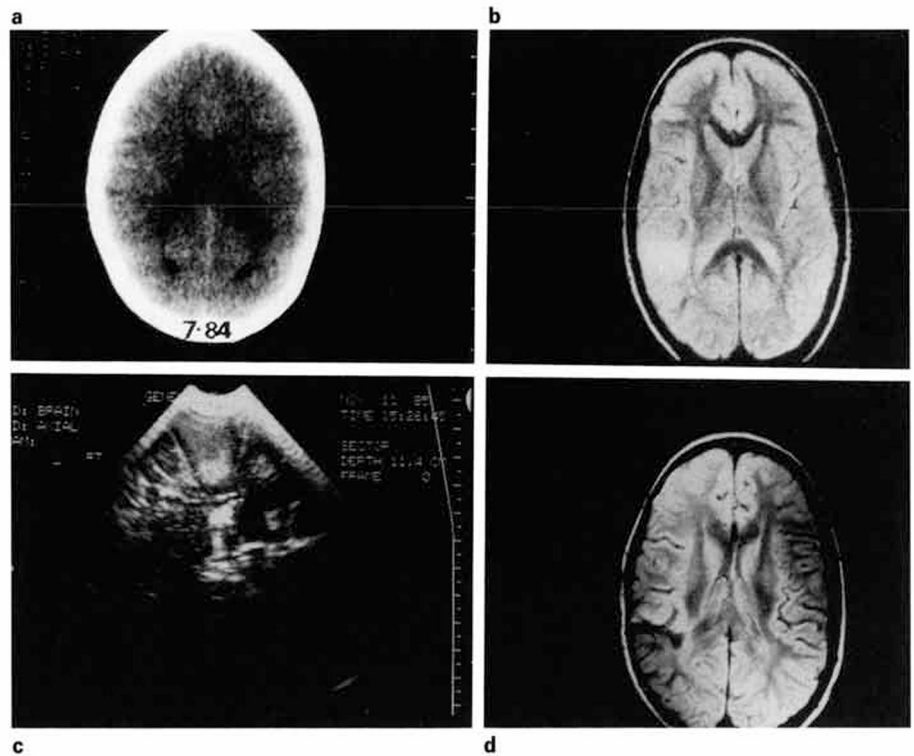


Fig. 1. a, b Pre-excision. Axial CT scan without contrast medium shows no abnormality. Axial MR image 1200/50 demonstrates focus of increased signal intensity in the region of the angular gyrus. **c** Intra-operative sonogram shows an echogenic homogeneous lesion measuring approximately 2.5 cm in diameter surrounded by a hypoechoic rim displacing the adjacent gyri. It is identified just lateral to the body of the right lateral ventricle. **d** Postexcision. Axial MR image 2200/60. There is an area of decreased signal intensity at the site of glioma resection involving the right angular gyrus.

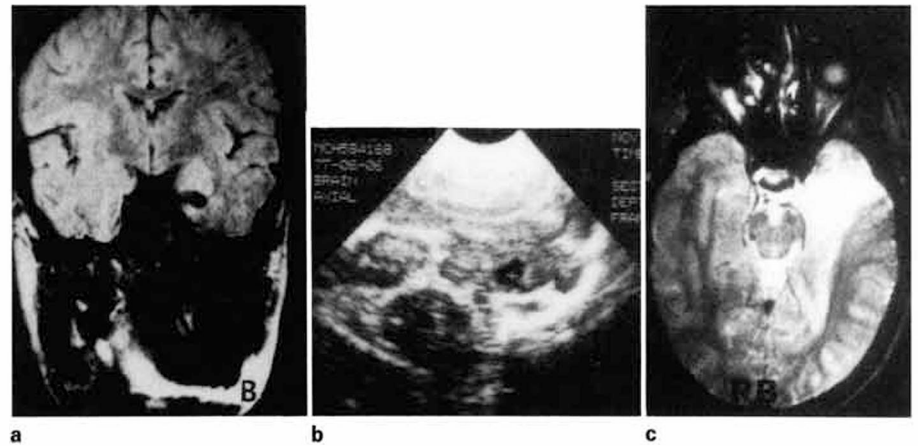


Fig. 2. a Pre-excision MR. Coronal SE, 1800/30. A well-circumscribed round focus of low intensity is identified in the medial temporal lobe surrounded by a slightly increased signal. **b** Intra-operative sonogram. Cursor is identified in a 1-cm irregularly shaped anechoic lesion imaged in the antero-medial temporal lobe. **c** Postexcision. Axial T2 image demonstrates increased signal intensity in the region of the operative site following resection of the focus of cortical dysplasia.

Real time ultrasound was used for identification of the lesion, because a number of them were not obvious on the brain surface either visually or by palpation. We verified the completeness of the lesionectomy with ultrasound and when possible, usually in the cases of a neoplasm, histologically with frozen sections. Postoperative imaging confirmed in all cases the completeness of the excision.

Illustrative Patients

Patient 1 (fig. 1). A 16-year-old girl developed partial complex seizures characterized by staring and lip smacking at age 5 years. The initial CT scan showed a hypodense lesion in the right parietal lobe which was thought to be due to a vascular accident. Repeat CT scans

over the next 2 years showed regression of the lesion and 3 years later the scan was normal. The patient continued to have partial complex seizures despite optimal anticonvulsant treatment and had persistent focal EEG abnormalities. An MRI performed 4 years after the onset of seizures showed changes compatible with a low grade astrocytoma. The tumor localized in the supramarginal gyrus was resected. The pathology confirmed a grade I astrocytoma. No morbidity was associated with the surgical procedure. Seven years later she was seizure-free and not taking anti-epileptic medications.

Patient 2 (fig. 2). A 14-year-old boy began having partial complex seizures with secondary generalization at 2 years of age. Postictally, he was confused and dysphasic. One year prior to surgery, he had

between five and ten seizures a day despite triple anticonvulsant therapy. A CT scan showed a small cyst in the left mesial temporal region.

An MRI showed increased signal intensity around the cystic lesion in the mesial temporal structures. At age 9, he underwent a craniotomy with radical removal of the lesion. There was no neurosurgical morbidity. The histopathological diagnosis was cortical dysplasia. Psychological testing showed disappearance of the verbal performance discrepancy with marked improvement in verbal skills and fluency as well as auditory verbal and visual motor functions. He is now 7 years postsurgery. Six months after surgery, he had a partial seizure which lasted 15 s, and was different from the seizures he had preoperatively. He has been seizure-free for 6.5 years, and for the last 2 off medication.

Patient 3. An 8-year-old boy developed generalized convulsions at 1 year of age. Seizures were difficult to control despite multiple anticonvulsant therapy and good therapeutic levels. He had a CT scan soon after onset which was reported as normal. His neurological examination was normal, but his developmental skills began to lag. Verbal skills were most involved. Over the next few months he developed partial complex seizures with secondary generalization. A repeat CT scan, 7 months later, showed a cystic lesion in the right temporal lobe including an enhancing nodule. The lesion was resected and, postoperatively, his examination has remained normal. The pathological diagnosis was infantile desmoplastic ganglioglioma. He has been seizure-free for 6 years, he is not taking medication, and his development has returned to normal.

Results

Of the eighteen lesions, eight were temporal and ten extratemporal. Six temporal lesions were in the mesial structures and two in the temporal neocortex. Of the extratemporal lesions, the large majority were located around the central region, including one in the cingulate gyrus just in front of the motor cortex. Five of the patients had astrocytomas (all low grade), 4 had gangliogliomas, 1 a mixed astrocytoma-oligodendroglioma, 3 cortical dysplasias, 2 infantile desmoplastic gangliogliomas, 2 hamartomas, and 1 cavernous angioma.

We have identified three types of electrocorticographic changes. The first group showed diffuse changes, with alterations in rhythm and generalized epileptic discharges (fig. 3). The second group presented with a depression of electrical activity at the site of the lesion and epileptic discharges in the surrounding brain. The distance from the lesion to the periphery of the electrical spiking was variable but, in the majority of cases, it was between 1 and 2 cm. A third group presented with epileptic discharges localized to the lesion. Postoperatively, 2 of the patients with central lesions exhibited significant weakness. One in the face and upper extremity, and the other in the upper extremity only. The first patient recovered com-

pletely, and exhibits only clumsiness when fatigued. The second patient, with a very large astrocytoma, had an excellent recovery including individual finger movements, but one hand remains clumsier than the other. No other postoperative complications were observed. No speech disturbances detectable by psychological or speech assessments have been encountered.

The average postoperative follow-up in this series is 5.7 years; 16 patients have been seizure-free. Two have had residual auras or partial simple seizures. One of them had a single atypical episode 6 months after surgery and the other, who had a cavernous angioma located in the motor strip, had two partial simple seizures.

Discussion

Lesionectomy for the treatment of children with difficult to control epilepsy seems preferable to large cortical excisions. Excision of low grade tumours, without resection of additional epileptogenic cortex has been associated with good therapeutic outcome [2]. In 1989, Hirsch et al. [3] reported that tumour resection in 42 children led to cessation of seizures in 81% of those who had seizures pre-operatively. Resection of the lesion, even when seizures are controlled by anti-epileptic medication, offers advantages. It permits accurate diagnosis of the nature of the process and, in many children, allows reduction or cessation of anti-epileptic medication with resultant cognitive benefit.

Different mechanisms have been invoked to explain the relationship between structural lesions and epilepsy. Local neuronal injury, vascular compromise, interstitial oedema, and neurotransmitter release may explain epileptogenesis in the region of the lesion [4]. The congruity or incongruity of lesion epileptogenicity versus focus, as electrographically defined, has been increasingly debated in recent years; the most frequent conclusion is that the single most important factor for good outcome is the complete excision of the lesion [5, 6; Clarke et al., pers. commun.]. In patients with neuronal migration defects, the most important factor correlative with good outcome is removal of all, or most, of the visible structural abnormalities [7].

Patients with vascular lesions raise specific questions in the surgical management of their epilepsy. MRI and intra-operative ultrasound of cavernous angiomas show that the vascular lesion is surrounded by an area of increased signal which histologically represents an area of gliosis and hemosiderin deposition. Whether lesionecto-

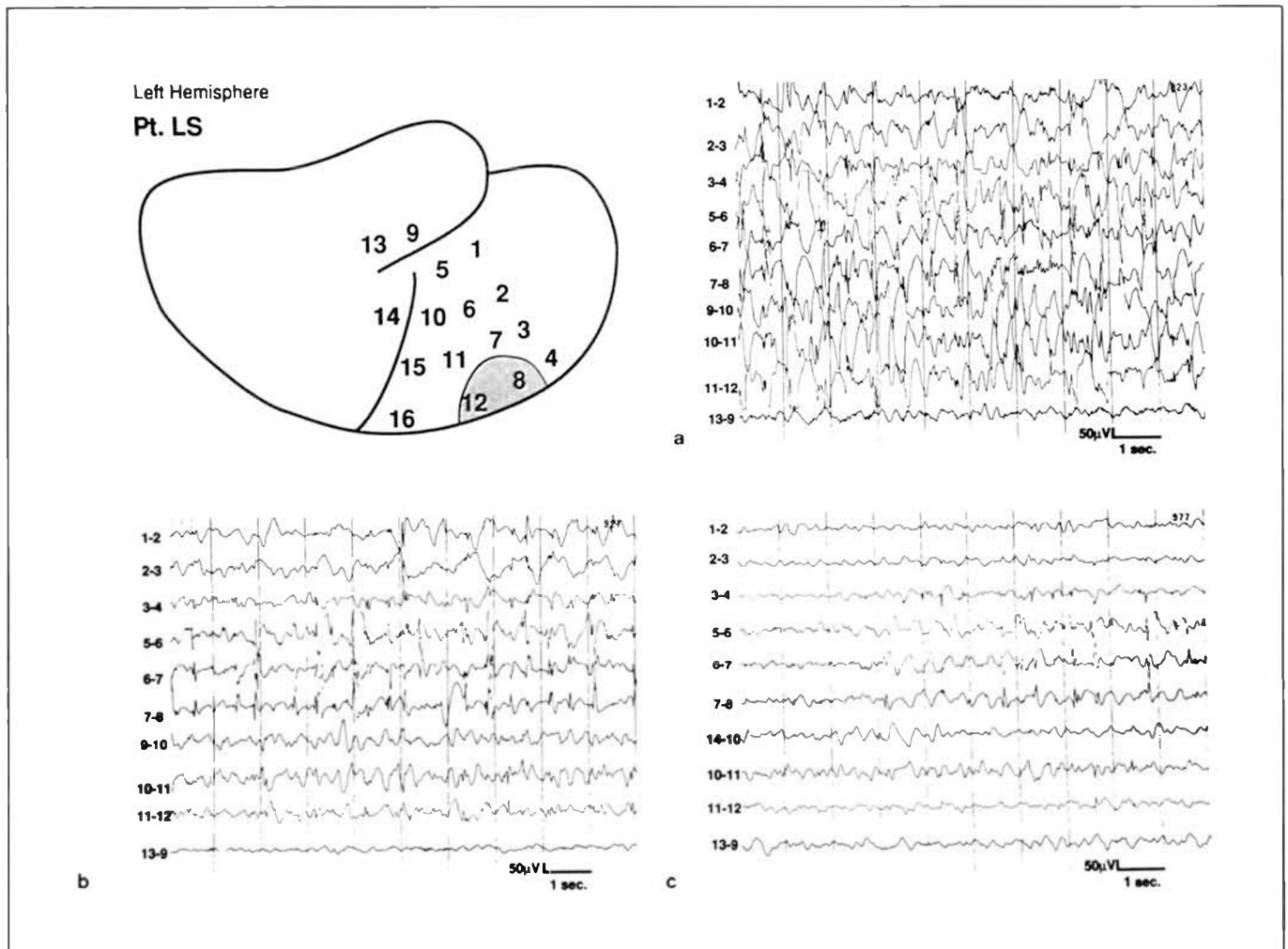


Fig. 3. **a, b** Pre-excision electrocorticography. In addition to generalized epileptiform discharges seen pre-resection, active focal discharges were noted to occur surrounding the lesion. **c** Post-resection electrocorticography. Persistent epileptiform activity can be seen at electrode sites 6 and 7.

my in these patients should include the area of gliosis, which usually is not extensive, is still debatable. One of our 2 patients with residual auras had a cavernous angioma and the surrounding gliotic tissue was not removed. In this series, no attempt was made to remove any of the surrounding or remote brain, even in cases where corticography showed evidence of residual epileptic activity. The presence of epileptogenic abnormalities remote from the structural lesion, compatible with secondary epileptogenesis, has been well established [8–10]. The pre-operative duration of seizures in these reports was significantly longer than in our series. With the current improvements in imaging and neurophysiological techniques, and given the increased awareness of the benefits of surgery in the

management of epilepsy, the interval between diagnosis of the lesion and surgical treatment is becoming shorter, particularly in children. Shortening the duration of intractable epilepsy may reduce the incidence of development of secondary epileptogenesis.

Not all lesions lead to intractable epilepsy. When the lesion does not require a surgical approach for its own sake and when the seizures can be fully controlled by medication, surgical treatment may not be necessary. The disadvantages of long-term use of anti-epileptic drugs have attracted attention recently. At present, surgical treatment, devised merely to avoid the use of anti-epileptic drugs, is not generally accepted. This approach, however, may be considered in the future. In this series 8 of the

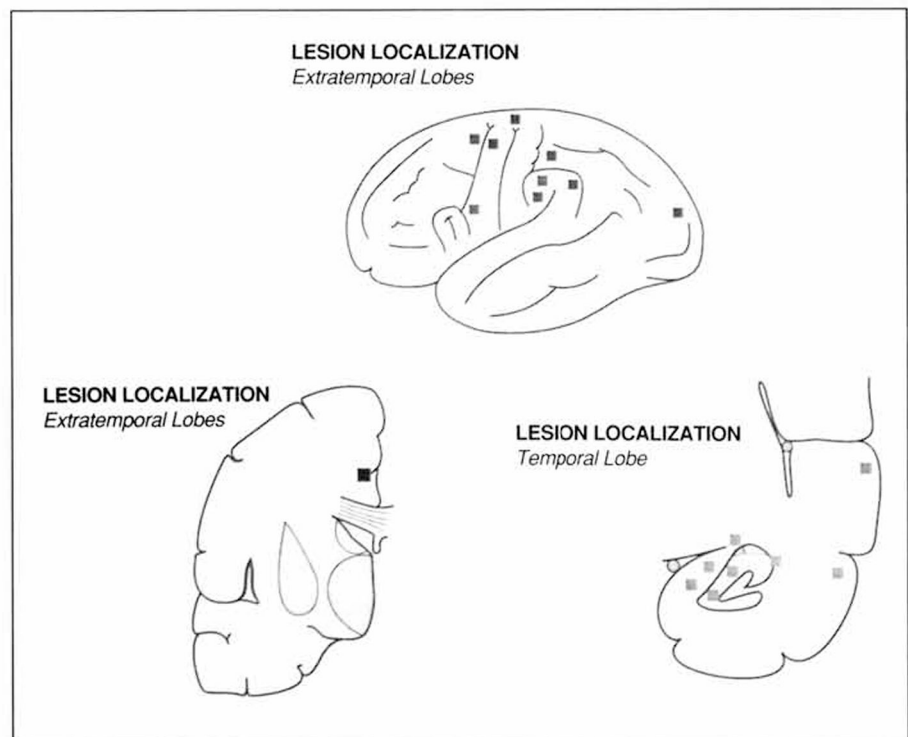


Fig. 4. The localization of the different lesions is shown. Most of the frontoparietal lesions were located around the central region. In the temporal lobe six lesions were mesiotemporal and two in the neocortex.

children had a relatively small number of seizures and the time from initial seizure to surgery was comparatively short. They may, in this sense, not be fully representative of patients with a long history of intractable epilepsy and our better results compared to those of Cascino [4] may reflect this. Of these 8 patients, however, 5 had tumours, 4 low grade gliomas, and 1 the mixed oligodendroglioma.

Early surgery may represent an important positive factor accounting for the good results obtained with lesionectomy in children. However, in a number of patients, particularly children with cortical dysplasias or tuberous sclerosis, the need for electroclinical correlation is paramount; lesions distant to the ones recognized, but invisible to current imaging techniques, may mimic secondary epileptogenesis.

It is still not certain whether lesionectomy is equally effective depending on the location of the lesion: temporal versus extratemporal, or temporal, neocortical versus inferomesial. Our results show that children with temporal and extratemporal lesions do equally well with respect to seizure control after radical excision. In the temporal lobe, six lesions were located in mesial structures and two in the neocortex (fig. 4). One of the patients with mesial temporal lesionectomy had an atypical single seizure 6

months after surgery and both patients with neocortical lesions have remained seizure-free, even though their epilepsy was particularly intractable pre-operatively. Nonetheless, the numbers are too small to allow definitive conclusions.

Conclusion

All 18 patients benefited from surgical treatment with respect to seizure control. In addition, radical excision of low grade tumours may improve the long-term prognosis of these patients from an oncological point of view. More extended follow-up is needed to confirm this. In the group with temporal lobe lesions, improvement between verbal and performance discrepancy was observed.

Lesionectomy allows for excision and pathological identification of low grade tumours, cortical dysplasias, and vascular malformation. It controls seizure activity in most children with difficult to control epilepsy, minimizes morbidity and the potential deleterious effects of more extensive brain volume excisions.

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