Surgical Treatment of Children with Medically Intractable Epilepsy —Outcome of Various Surgical Procedures—

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Abstract

Outcome after temporal lobe resection, extratemporal resection, and corpus callosotomy was studied in 33 children aged 15 years or less with medically intractable epilepsy. Seizure-free control was achieved in 67% (6/9) of pediatric patients *versus* 67% (60/90) of adult patients receiving temporal lobe resection and in 33% (4/12) of pediatric patients *versus* 25% (7/28) of adult patients receiving extratemporal resection. Among patients suffering from drop attacks and generalized convulsive seizures, 42% (5/12) of pediatric patients *versus* 25% (6/24) of adult patients receiving corpus callosotomy became seizure-free. The most prominent histological diagnoses in temporal lobe resections were three cases of mesial temporal sclerosis, four of ganglioglioma, and two of neuronal migration disorders. Neuronal migration disorders were the main histology in extratemporal resections. Four of five patients with behavioral problems treated by corpus callosotomy exhibited improved hyperactivity and/or attention deficits. There was no surgical morbidity or mortality. The outcome of pediatric patients was at least as favorable as that of adult patients, and improvement of behavioral disturbances could be expected after surgery. Surgical treatment is an effective and safe procedure for children with medically intractable epilepsy.

Key words: children, epilepsy, temporal lobe resection, extratemporal resection, corpus callosotomy

Introduction

Surgical treatment of children with medically intractable epilepsy has recently become an important subject. It is widely admitted that epilepsy in children during critical periods of development should be controlled as early as possible to avoid possible brain damage and even psychosocial problems.^{12,17)} Surgery has a beneficial effect in children with medication-resistant epilepsy, especially temporal lobe resection.^{2,10)} However, surgery tends to be avoided in the treatment of pediatric epilepsy because of the hope for spontaneous resolution,¹²⁾ fear of surgical complications, and doubts regarding surgical outcome. The

latter two problems are partly related to the application of different surgical procedures to different types of epilepsy. Since surgical outcome and complications vary according to surgical procedure,⁹⁾ the selection of surgical procedure is as important as the selection of surgical candidates. Moreover, surgical outcome in children should be compared to those in adults to assess the surgical effect on pediatric patients.

We investigated the surgical outcome in patients 15 years or less of age undergoing temporal lobe resection, extratemporal resection, or corpus callosotomy for comparison with the outcome in adult patients to assess the efficacy and safety of surgical treatment for medically intractable epilepsy.

Clinical Materials and Methods

Forty-three children with medically intractable epilepsy, excluding seizures possibly caused by tumor (except ganglioglioma), underwent surgical treatment at the Tokyo Metropolitan Neurological Hospital between 1983 and 1994. Twenty-nine of the 43 patients were treated during the last 3 years (1992–1994). Patients were aged 8 months to 15 years at the time of operation. Thirty-three patients were aged under 12.

All children were first treated medically by pediatricians and then referred to us. Preoperative evaluation included repeat electroencephalography (EEG), computed tomography, and/or magnetic resonance (MR) imaging. In addition, some patients underwent neuropsychological examinations, single photon emission computed tomography and/or positron emission tomography (PET), and 24-hour video evaluation and/or intracranial electrocorticographic recording.

Selection of surgical procedures to treat medication-resistant epilepsy was as follows. Resective surgery was performed on children with partial seizures, in whom seizure type, localized EEG abnormality, or localized neuroradiological abnormality was confirmed in the resectable region. Corpus callosotomy was applied to children with drop attacks and/or generalized convulsive seizures without localized foci. Drop attacks included both atonic and tonic seizures causing falls.^{13,15} Most patients demonstrated status epilepticus after generalized convulsive seizures. (We considered drop attacks and generalized convulsive seizures as disabling seizures.) Functional hemispherectomy was performed on children with whole hemispheric lesions. The initial surgical treatment was selected based on seizure type, distribution of epileptic foci, and abnormal neuroradiological findings.

Temporal lobe resections were performed on nine patients aged 7–13 years (mean 9.2 yrs). All patients had complex partial seizures of typical mesial temporal lobe epilepsy.¹⁸ Extratemporal resections were performed on 16 patients aged 8 months to 15 years (mean 8.4 yrs). The main focus was demonstrated in the frontal lobe in 11 of the 16 patients. Corpus callosotomies were performed on 16 patients aged 5–15 years (mean 9.9 yrs). Two of the 16 patients underwent anterior 2/3 resection, eight anterior 4/5 resection, and six total resection. Functional hemispherectomies were performed on two patients (a 1-year-old boy with hemimegalencephaly and a 13-year-old boy with vascular occlusive hemispheric lesion). No mortality nor morbidity occurred after the surgical treat-

ment.

Surgical outcome according to Engel's classification⁶ was evaluated in the patients receiving temporal lobe or extratemporal resection at least 6 months after the surgery. If the child suffered from residual seizures at least 6 months after the initial surgery, we investigated additional surgery. The surgical outcome of the disabling seizures was evaluated in the same way in the patients undergoing corpus callosotomy. Thus, we evaluated the surgical outcome in nine temporal lobe resections, 12 extratemporal resections, and 12 corpus callosotomies, but not after functional hemispherectomy. The histology of the surgical specimens from the temporal lobe and extratemporal resections was studied.

To compare the efficacy of surgical treatment in children with intractable epilepsy, the surgical outcome in the pediatric (≤ 15 yrs) patients was compared with that in 142 adult (≥ 16 yrs) patients, who were treated between 1982 and 1994. Adult patients with tumors were excluded from this series (except ganglioglioma).

The statistical significance of differences in surgical outcome between pediatric and adult temporal lobe and extratemporal resections and corpus callosotomies was analyzed in the numbers of seizure-free patients using Fisher's exact probability test.

Results

I. Temporal lobe and extratemporal resections

Six of nine patients receiving temporal lobe resection became seizure-free and the other three were significantly improved (Table 1). All the nine patients became free from the complex partial seizures of typical mesial temporal lobe epilepsy, but three of them continued to suffer from other types of seizures. These three patients underwent additional surgical treatment at least 6 months after the initial temporal lobectomy, and all are seizure-free at the present

Table 1 Outcome in children receiving temporal lobe or extratemporal resection

Seizure outcome	Temporal lobe resection	Extratemporal resection
Free	6	4
Rare	0	1
Worthwhile improvement	3	4
No worthwhile improvement	0	3
Total	9	12

Table 2 Histological findings in children receiving temporal lobe or extratemporal resection

Histological diagnosis	Temporal lobe resection	Extratemporal resection
Mesial temporal sclerosis	3	0
Ganglioglioma	4	0
NMDs	2	9
Gliosis	0	2
Normal	0	3
Hamartoma	0	1
Ulegryic change	0	1
Total	9	16

time. In contrast, only four of the 12 patients undergoing extratemporal resection became seizure-free. Nine patients including these four showed some improvement after the surgical treatment, but three patients were unchanged. Two of these three patients underwent additional surgical treatment at least 6 months after the initial extratemporal resection. Although temporal lobe resections tended to have more favorable outcomes than extratemporal resections, there was no significant difference ($p = 0.14$).

The most common histological diagnoses in temporal lobe resections were: three cases of mesial temporal sclerosis, four of ganglioglioma, and two of neuronal migration disorders (NMDs)⁽¹⁴⁾ (Table 2). In contrast, NMDs were the main histology in extratemporal resections.

II. Corpus callosotomy

Most patients had acute disconnection syndrome represented as akinetic states which disappeared within 1 or 2 weeks. Although some patients showed transient neurological deficits such as dysarthria or motor dysfunction, these disappeared within a few months and no deficits persisted. Five of 12 patients undergoing corpus callosotomy became completely free from disabling seizures, and all but one showed some improvement in disabling seizures after surgery (Table 3). In addition, four of five patients with behavioral problems, namely hyperactivity and attention deficits, exhibited improvement. The one patient with no improvement in behavioral problems also showed no improvement in disabling seizures.

III. Surgical outcomes in pediatric and adult patients

Seizure-free control was achieved in 67% of pediatric patients *versus* 67% of adult patients receiving temporal lobe resection, and in 33% of pediatric

Table 3 Outcome in children receiving corpus callosotomy

Seizure outcome	Corpus callosotomy	Improvement in behavioral problems
Free	5	0
Rare	1	1/1
Worthwhile improvement	5	3/3
No worthwhile improvement	1	0/1
Total	12	4/5

Table 4 Seizure-free outcome after surgical procedures in pediatric and adult patients

Surgical procedure	Pediatric	Adult
Temporal lobe resection	6/9 (67%)	60/90 (67%)
Extratemporal resection	4/12 (33%)	7/28 (25%)
Corpus callosotomy	5/12 (42%)	6/24 (25%)

patients *versus* 25% of adult patients receiving extratemporal resection (Table 4). Among patients suffering from disabling seizures, 42% of pediatric patients *versus* 25% of adult patients receiving corpus callosotomy became seizure-free. Although pediatric patients tended to have a more favorable outcome, there was no significant difference between the two age groups ($p = 0.82$ for extratemporal resections and $p = 0.92$ for corpus callosotomies).

Discussion

MR imaging has enabled better identification of morphological abnormalities of the brain structure in children with intractable epilepsy.^{14,19)} As a result, the number of children referred for resective surgery has increased markedly recently. In addition to resective surgery, corpus callosotomy is also widely performed on children with disabling generalized seizures.¹⁾ The present study demonstrated that surgical treatment using resective surgery and corpus callosotomy is both effective and safe for children with medically intractable epilepsy.

Temporal lobe resection is the most established surgical treatment for medication-resistant temporal lobe epilepsy. Recent surgical series indicate that temporal lobe resection has advantages in the treatment of pediatric patients.^{5,7,11,19)} In our series, six of nine pediatric patients became seizure-free after receiving temporal lobe resection, *i.e.* the same success rate as that achieved for adults. A fairly large proportion of

pediatric patients became seizure-free after temporal lobe resection, and the outcome of the temporal lobectomy for children is at least successful as that for adults.⁶⁾ Moreover, patients in our series became seizure-free if they suffered from no other seizure types caused by extratemporal lesion. A favorable outcome can be expected for children undergoing temporal lobe resection who had no extratemporal epilepsy.⁷⁾ The histology of temporal lobe resections was mostly mesial temporal sclerosis, ganglioglioma, and NMDs. Mass lesion is often found in children with temporal lobe epilepsy, but the same successful outcome can be obtained by initiating a combined treatment of lesionectomy and temporal lobectomy.³⁾ Moreover, Dreifuss⁴⁾ stressed that symptomatic epilepsies including those due to neoplasms and NMDs had a less satisfactory response to anti-epileptic drugs. Therefore, surgical treatment is effective in children with medication-resistant temporal lobe epilepsy.

In contrast, only four of 12 pediatric patients undergoing extratemporal resection became seizure-free, which is a success rate slightly better than that achieved for adults in our series (not significant). Nine of the 12 patients with medication-resistant extratemporal epilepsy benefited from surgery. Almost the same success of outcome was seen in the adult⁶⁾ and pediatric groups. However, the surgical outcome was poor when compared with temporal lobe resections. Fish *et al.*⁷⁾ reported that the temporal lobe resection had a better surgical outcome than frontal lobe resection, and that an excellent outcome only occurred in patients with defined resectable lesions. In our series, NMDs and gliosis were the common histological changes in the extratemporal resections. The surgical outcome for patients with NMDs is not satisfactory.¹⁴⁾ Modern neurological imaging methods such as MR imaging and PET are very important in identifying the abnormal cerebral lesion in patients with epilepsy. However, epileptogenic areas in extratemporal regions are often more extensive than lesions demonstrated by neuroimaging techniques, especially in NMDs. Accurate localization of epileptogenic areas and the extent of effective resection avoiding eloquent areas are still difficult to define. More effective techniques should be considered for treating extratemporal epilepsy in the future, although most patients achieved some seizure control⁶⁾ in our series.

Corpus callosotomy was effective for patients with severe secondary generalized seizures without discrete epileptic foci. The procedure is believed to diminish the bilateral synchrony of epileptiform discharges through the corpus callosum, resulting in greater control of the frequency and severity of dis-

abling seizures.¹⁶⁾ Five of 12 pediatric patients became seizure-free in this series, which is slightly better than the rate achieved for adults (not significant). Moreover, behavioral problems improved in all children except one who also showed no improvement in disabling seizures. The beneficial effect of corpus callosotomy on disabling seizures such as drop attacks and generalized seizures has been noted in both the pediatric¹⁾ and other age groups.^{8,9,13,15)} Improvement of behavioral disturbances is the most important factor in increasing the quality of life for both patients and parents.¹⁾ Contrary to these favorable effects, several surgical complications may occur after corpus callosotomy, such as decreased speech output, dysarthria, and gait apraxia¹⁾ after total callosotomy, as well as disturbance of dichotic listening and tachistoscopic presentation.¹⁶⁾ In our series, akinetic states, motor dysfunction, and dysarthria occurred transiently, but these deficits disappeared within a few months and did not interfere with daily life. Permanent neurological deficits caused by trauma or vascular disturbances have become extremely rare since the introduction of microsurgical techniques, so that corpus callosotomy has become an acceptable surgical treatment.¹⁶⁾ Corpus callosotomy is an effective and safe treatment for pediatric patients with medication-resistant disabling seizures for whom no other surgical treatment is considered suitable.

Surgical treatment is an effective and safe procedure for children with medically intractable epilepsy. Pediatric patients treated by temporal lobe resection, extratemporal resection, and corpus callosotomy have surgical outcomes at least as favorable as those of adults. Moreover, corpus callosotomy is effective in improving behavioral disturbances.

References

- 1) Cendes F, Ragazzo PC, de Costa V, Martins LF: Corpus callosotomy in treatment of medically resistant epilepsy: Preliminary results in a pediatric population. *Epilepsia* 34: 910-917, 1993
- 2) Davidson S, Falconer MA: Outcome of surgery in 40 children with temporal lobe epilepsy. *Lancet* 1: 1260-1273, 1975
- 3) Drake J, Hoffman HJ, Kobayashi J, Hwang P, Becker LE: Surgical management of children with temporal lobe epilepsy and mass lesions. *Neurosurgery* 21: 792-797, 1987
- 4) Dreifuss FE: Prognosis of childhood seizure disorders: Present and future. *Epilepsia* 35 [Suppl 2]: S30-S34, 1994
- 5) Duchowny M, Levin B, Jayakar P, Resnick T, Alvarez L, Morrison G, Dean P: Temporal lobectomy in early childhood. *Epilepsia* 33: 298-303,

- 1992
- 6) Engel J Jr, Van Ness PC, Rasmussen TB, Ojemann LM: Outcome with respect to epileptic seizures, in Engel J Jr (ed): *Surgical Treatment of the Epilepsies*, ed 2. New York, Raven Press, 1993, pp 609-623
 - 7) Fish DR, Smith SJ, Quesney LF, Andermann F, Rasmussen T: Surgical treatment of children with medically intractable frontal or temporal lobe epilepsy: Results and highlights of 40 year's experience. *Epilepsia* 34: 244-247, 1993
 - 8) Fuiks KS, Wyler AR, Hermann BP, Somes G: Seizure outcome from anterior and complete corpus callosotomy. *J Neurosurg* 74: 573-578, 1991
 - 9) Gates JR, Leppik IE, Yap J, Gumnit RJ: Corpus callosotomy: Clinical and electroencephalographic effects. *Epilepsia* 25: 308-316, 1984
 - 10) Goldring S: Surgical management of epilepsy in children, in Engel J Jr (ed): *Surgical Treatment of the Epilepsies*. New York, Raven Press, 1987, pp 445-464
 - 11) Goldvog B, Løyning Y, Hauglie-Hanssen E, Flood S, Bjørnæs H: Surgical treatment for partial epilepsy among Norwegian children and adolescents. *Epilepsia* 35: 554-565, 1994
 - 12) Lindsay J, Ounsted C, Richards P: Long-term outcome in children with temporal lobe seizures. V. Indications and contra-indications for neurosurgery. *Dev Med Child Neurol* 26: 25-32, 1984
 - 13) Oguni H, Olivier A, Andermann F, Comair J: Anterior callosotomy in the treatment of medically intractable epilepsies: A study of 43 patients with a mean follow-up of 39 months. *Ann Neurol* 30: 357-364, 1991
 - 14) Palmini A, Andermann F, Olivier A, Tampieri D, Robitaille Y, Andermann E, Wright G: Focal neuronal migration disorders and intractable partial epilepsy: A study of 30 patients. *Ann Neurol* 30: 741-749, 1991
 - 15) Reutens DC, Bye AM, Hopkins IJ, Danks A, Somerville E, Walsh J, Bleasel A, Ouvrier R, MacKenzie RA, Manson JI, Bladin PF, Berkovic SF: Corpus callosotomy for intractable epilepsy: Seizure outcome and prognostic factors. *Epilepsia* 34: 904-909, 1993
 - 16) Spencer SS, Gates JR, Reeves AR, Spencer DD, Maxwell RE, Roberts D: Corpus callosum section, in Engel J Jr (ed): *Surgical Treatment of the Epilepsies*. New York, Raven Press, 1987, pp 425-444
 - 17) Wheless J: Evaluation of children for epilepsy surgery. *Pediatr Ann* 20: 41-49, 1991
 - 18) Wieser HG, Engel JJ, Williamson PD, Babb TL, Gloor P: Surgically remediable temporal lobe syndromes, in Engel J Jr (ed): *Surgical Treatment of the Epilepsies*, ed 2. New York, Raven Press, 1993, pp 49-63
 - 19) Wyllie E, Chee M, Granström M-L, DelGiudice E, Estes M, Comair Y, Pizzi M, Kotagal P, Bourgeois B, Lüders H: Temporal lobe epilepsy in early childhood. *Epilepsia* 34: 859-868, 1993

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