Intraoperative Electrocorticography in Children with Medically Intractable Epilepsy

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Abstract

Intraoperative electrocorticography (ECoG) was performed to localize epileptic foci in 20 children undergoing temporal and extratemporal surgery for intractable epilepsy under modified neuroleptanalgesia. Nitrous oxide gas was discontinued at least 15 minutes before and during preresection ECoG recording, which lasted for 30 minutes. Seventeen patients showed epileptiform discharges on preresection ECoG. Hyperventilation loading, monitored by electroencephalography or ECoG in all patients, induced enhanced or induced epileptiform activities in 17 patients and provoked electroencephalographic seizures in 10 patients. All foci in non-eloquent areas were resected. Fifteen patients have been seizure-free with reduced medication, and two patients have achieved worthwhile improvement. Habitual seizures have remained in three patients. Two of these patients had foci in eloquent areas which could not be resected. Intraoperative ECoG can improve the outcome of surgery for intractable epilepsy by localizing epileptic foci for resection.

Key words: epilepsy surgery, children, long-term monitoring, electroencephalography, electrocorticography, neuroleptanalgesia

Introduction

Early epilepsy surgery is mainly performed in adults and less in children because of difficulties in the assessment of presurgical evaluations and/or reluctance to resect the developing brain. Especially in Japan, neuropsychologists and pediatric neurologists hesitate to consider epilepsy surgery for children. However, recent studies have emphasized the importance of early surgery to treat medically intractable epilepsy in children, as a reduction in seizures can result in remarkable improvements in verbal, intelligence, and social outcomes.^{5,9,11,13)} The importance of intraoperative electrocorticography (ECoG) for the confirmation of precise focus localizations has been recognized.^{3,14-17)}

We describe our series of pediatric patients who underwent epilepsy surgery using intraoperative ECoG with neuroleptanalgesia to detect localizations of epileptic foci, and analyze the postoperative courses.

Materials and Methods

This retrospective study included 20 patients below 18 years old who underwent epilepsy surgery for intractable epilepsy at the Department of Neurosurgery, Asahikawa Medical College over a 5-year period (Table 1). There were nine girls and 11 boys aged from 10 months to 18 years (mean 10.2 years).

All 20 patients underwent preoperative assessments according to the presurgical evaluation protocols of Asahikawa Medical College Hospital,¹⁸⁾ including long-term video-electroencephalography (EEG) monitoring (non-invasive, although sphenoidal electrodes were used in older children with temporal lobe epilepsy), neuroimaging including thin slice magnetic resonance (MR) imaging (1.5 Tesla), computed tomography, single photon emission computed tomography (SPECT) with technetium-99m-hexamethylpropyleneamine oxime (^{99m}Tc-HMPAO) during the interictal period and the ictal period in recent patients, and angiography including the Wada test when possible.¹⁸⁾ Video-EEG monitoring (SYNAFIT; NEC-Sanei, Tokyo) was conducted (usually over 24 hours) until three habitual seizures

Table 1 Results of temporal lobe surgery and extratemporal surgery

Case No.	Age/ Sex	Seizure type	Seizure frequency	EEG focus	Spike focus on pre- resection ECoG	Spontaneous seizure on posthyper- ventilation EEG	Operation/ Hippocampus resection	Post- resection ECoG (grade*)	Diagnosis	Outcome (class**)
Temporal lobe surgery:										
1	9/F	CPS	2-3/wk	rt mT	+	+	rt ATL/2.0 cm	A	porencephalic cyst	1
2	10/M	CPS, GS	3-4/wk	rt aT, rt mT, rt F	+	+	rt ATL/3.0 cm	C	MTS	4
3	18/M	CPS, GS	2/wk	lt aT, rt F	+	-	lt ATL/1.5 cm	C	MTS	4
4	6/F	Lennox, CPS	2/mo	rt aT, rt mT	-	-	rt ATL/-	A	pilocytic astrocytoma	1
5	18/F	CPS, GS	5/wk	rt aT, rt mT	+	+	rt ATL/3.0 cm	A	DNT	1
6	7/F	CPS, GS	5/day	rt aT	-	-	rt ATL/-	A	cavernoma	1
7	4/M	CPS, GS	3/day	rt aT, rt mT	+	+	rt ATL/2.5 cm	A	DNT	1
8	17/M	CPS, GS	1/wk	lt aT, lt mT	+	+	lt ATL/-	A	DNT	1
9	10/M	CPS, GS	2/wk	rt aT	+	-	rt ATL/-	A	DNT	1
Extratemporal surgery:										
10	5/M	PS, SGS	1/day	lt C, lt P	+	-	lesionectomy	A	ganglioglioma	1
11	3/M	PS, SGS	1-2/wk	rt F	+	+	lesionectomy, focus resection	A	PNET	1
12	13/F	PS, SGS	2-3/wk	lt P	+	-	lesionectomy, focus resection	B	cerebral fungus	1
13	16/M	PS, SGS	2/day	rt O	+	+	lesionectomy, focus resection	A	cortical dysplasia	1
14	6/F	SGS	1-2/wk	lt F	-	-	lesionectomy	A	hamartoma	1
15	17/M	SGS	4-5/day	lt FP	-	-	lesionectomy, MST	C	ectopic gray matter	2
16	14/F	SGS	3-4/mo	rt O	+	+	lesionectomy, focus resection	C	hamartoma	3
17	17/F	PS, SGS	5-6/day	rt FP	+	+	lesionectomy, focus resection, MST	B	cortical tuberous sclerosis	1
18	2/M	West	4-6/day	lt F	+	+	lesionectomy, focus resection	C	cortical tuberous sclerosis	4
19	11/F	PS, SGS	4-5/day	rt P	+	-	lesionectomy, focus resection	A	DNT	1
20	10 mos/ M	West	1-2/day	rt TO	+	-	lesionectomy, focus resection	A	mixed glioma	1

*According to Jay *et al.*¹²⁾: A, no residual epileptiform activity; B, mild residual activity; C, moderate residual activity; D, unchanged from preresection ECoG; and E, undetermined due to drug effect. **According to Engel *et al.*⁸⁾: 1, free of disabling seizures; 2, rare disabling seizures; 3, worthwhile improvement; and 4, no worthwhile improvement.

aT: anterior temporal, ATL: anterior temporal lobectomy, C: central, CPS: complex partial seizure, DNT: dysembryoplastic neuroepithelial tumor, F: frontal, GS: generalized seizure, Lennox: Lennox-Gastaut syndrome, MST: multiple subpial transection, mT: middle temporal, MTS: mesial temporal lobe sclerosis, O: occipital, P: parietal, PNET: primary neuroectodermal tumor, PS: partial seizure, SGS: secondarily generalized seizure, West: West syndrome.

were recorded. All recordings were analyzed off-line in earlier patients and on-line in recent patients by computer (Stellate System; Nihon-Kohden, Tokyo). A Wada test was performed in children over 6 years of age. Preoperative and postoperative neuropsychological assessments were carried out by a neu-

ropediatrician for younger children and by a neuropsychiatrist for older children. Surgery was not scheduled in patients in whom independent seizures were recorded from the bilateral temporal lobes. Patients with medically intractable seizures with a possibility of spontaneous remission such as age-de-

pendent, benign partial seizures were also excluded from this study.

Anterior temporal lobectomy was performed in nine patients with complex partial seizures, seven of whom had both complex partial seizures and secondarily generalized seizures (Cases 1–9). Extratemporal surgery was performed in 11 patients, six with partial seizures and secondarily generalized seizures, three with immediate bilateral synchrony after seizure onset, and two with symptomatic West syndrome and frequent tonic spasms (Cases 10–20). The mean time from the onset to surgery was 5.8 years (range 0.3–15.0 years).

All anticonvulsant medication was discontinued from 1 to 3 days prior to surgery to allow recording of spontaneous electroencephalographic seizures during intraoperative ECoG monitoring. Benzodiazepine was not used as a premedication for anesthesia because of its strong suppressive effect on cortical activity. Surgery was performed under modified neuroleptanalgesia consisting of fentanyl and pancuronium bromide. At least 15 minutes prior to and during the ECoG recordings, nitrous oxide was discontinued and artificial respiration was maintained with oxygen. Concurrently, scalp electrodes were placed in O₁ and O₂ and the level of anesthesia was continuously monitored and evaluated by occipital EEG. About 10–15 minutes after discontinuation of the nitrous oxide, the scalp EEG began to demonstrate rapid theta waves (6–7 Hz) or slow alpha rhythms. ECoG recordings were performed after the confirmation of these rapid EEG rhythms in the occipital leads. All patients underwent intraoperative pre- and postresection ECoG with strip²⁰⁾ or grid electrodes (Ad-Tech Corporation, Nihon-Kohden, Tokyo) or an ECoG recording system developed in Asahikawa Medical College to monitor deeply situated structures after anterior temporal lobectomy, such as the hippocampal surface, amygdala, or parahippocampal gyrus. Preresection ECoG monitoring lasted for 30 minutes. During the operation, the frequency of respiration was maintained according to the age of the child. The oxygen partial pressure (PO₂) and carbon dioxide partial pressure (PCO₂) during ECoG recording were 100–200 mmHg and 35–40 mmHg, respectively. Hyperventilation was then loaded for 3 minutes. This procedure resulted in an elevation of PO₂ (150–250 mmHg) and a reduction of PCO₂ (25–30 mmHg). Under these hypocapnic conditions, the cerebral vessels were constricted, causing a decrease in the cerebral blood volume and a fall in the intracranial pressure.⁶⁾

Patients with cerebral cortical lesions underwent lesionectomy with epileptic focus resection. Patients

with temporal lobe epilepsy underwent lateral temporal lobe resection en bloc, basically 5.0 cm along the base and 4.0 cm along the sylvian fissure from the temporal pole in the dominant hemisphere, and 5.5 and 4.5 cm, respectively, in the non-dominant hemisphere, according to Olivier.¹⁴⁾ The vein of Labbé was always left intact. After anterior temporal lobectomy, nitrous oxide was discontinued and ECoG was again recorded using strip electrodes from the hippocampal surface, cut edges of the amygdala and parahippocampal gyrus. If the hippocampal EEG demonstrated no epileptiform activity, the mesial temporal structures were left intact. If EEG or ECoG detected focal seizures or focal spikes in the mesial structures, the anterior part of the hippocampus (hippocampal head) was resected.¹⁷⁾ The resected hippocampus was immediately sent for histological examination. The parahippocampal gyrus and amygdala were also resected subpially by CUSA or suction. Postresection ECoG was performed in all patients and any residual epileptiform foci were resected with subpial suction when possible. Focus resection and multiple subpial transection were performed in Cases 15 and 17 of the extratemporal group due to extent of the epileptic focus over the eloquent cortex. Postresection ECoG was graded according to Jay *et al.*¹²⁾

All resected materials were processed for conventional histological study and, when necessary, immunohistochemical staining for glial fibrillary acidic protein and neuron-specific enolase. The frozen hippocampal specimen was further processed for Timm's staining in recent cases of temporal lobectomy.

Every patient was assessed at 1 month, 6 months, and 1 year postoperatively by neurological evaluation and EEG studies. Subsequently, assessments were made yearly. Follow-up MR imaging was scheduled for 1 month and 1 year postoperatively. The postoperative seizure outcomes were graded according to Engel *et al.*⁸⁾: class 1 (free of disabling seizures), class 2 (rare disabling seizures), class 3 (worthwhile improvement), and class 4 (no worthwhile improvement). The clinical follow-up period ranged from 1.1 to 5.0 years (mean 2.8 years).

Results

The clinical findings for the 20 patients are summarized in Table 1. MR imaging demonstrated organic lesions in 18 patients and unilateral hippocampal atrophy in two patients. EEG revealed unilateral epilepsy focus in all patients. Cases 2 and 3 had the major spike focus in the temporal lobe and minor

spike focus in the frontal lobe. Interictal SPECT revealed unilateral focal abnormalities in seven of 11 patients. Ictal SPECT detected focal abnormalities in five of six patients.

Preresection ECoG showed 17 patients had epileptiform discharges. Hyperventilation loading was carried out in all patients, showing a further spike focus on EEG or ECoG in 17 patients and spontaneous electroencephalographic seizure in 10 patients. Reduction of the anesthetic agents or repetition of the hyperventilation loading were also carried out in Cases 4 and 6 of the temporal group and Case 14 of the extratemporal group, but no seizure focus was detected. Only lesionectomy was performed in these patients.

Postresection ECoG showed that 13 patients were grade A (no residual epileptiform activity), two grade B (mild residual activity), and five grade C (moderate residual activity). There were no patients in grade D (unchanged from preresection ECoG) or grade E (undetermined due to drug effect).

Postoperatively, 15 patients became seizure-free with reduced medications (class 1), one patient was class 2, and one patient class 3. The three patients who received only lesionectomy were among the patients who became seizure-free (class 1). Three patients (Cases 2 and 3 of the temporal group and Case 18 of the extratemporal group) still had habitual seizures without improvement (class 4). Intraoperative ECoG of Cases 2 and 3 had revealed that the spike foci were not confirmed to the temporal lobe, but were also present over the lateral

frontal cortex, which may be why residual seizures persisted after surgery. One patient (Case 18 of the extratemporal group) required cranioplasty due to infected bone flap.

The histological results are summarized in Table 2. The histological types of the tumors were well correlated with the imaging studies, as previously reported.¹⁾ The postoperative course of patients with mesial temporal sclerosis was not favorable despite excision of the anterior temporal lobe and mesial temporal structures, probably due to the extent of the spike focus. ECoG revealed spike foci in the temporal lobe and ipsilateral frontal lobe in Case 2 and the temporal lobe and contralateral frontal lobe in Case 3.

Illustrative Cases

Case 13: A 16-year-old right-handed boy had an 8-year history of intractable simple partial seizures with secondary generalizations. T₂-weighted MR imaging revealed a localized high intensity area in the right occipital lobe (Fig. 1). Interictal scalp EEG revealed continuous right parieto-occipital spikes (Fig. 2). Interictal SPECT with ^{99m}Tc-HMPAO showed a hypoperfusion area in the right parieto-occipital region. Cortical dysplasia with cortical epileptic foci was suspected. Intraoperative ECoG monitoring with light neuroleptanalgesia disclosed scattered and sporadic spikes around the cortical dysplasia. Hyperventilation was loaded for 3 minutes and the PCO₂ decreased to 27 mmHg from 33

Table 2 Result of histological examination

Histological diagnosis	Seizure-free rate (No. of cases)
Temporal surgery:	
MTS	0/2
DNT*	4/4
Cavernoma	1/1
Pilocytic astrocytoma	1/1
Porencephalic cyst	1/1
Extratemporal surgery:	
Cortical tuberous sclerosis	1/2
Hamartoma	1/2
Ectopic gray matter	0/1
Ganglioglioma	1/1
Cortical dysplasia	1/1
DNT*	1/1
PNET	1/1
Mixed glioma	1/1
Cerebral fungus	1/1

*Histology of DNT, see Daumas-Duport *et al.*⁴⁾

Fig. 1 Case 13. Undergoing extratemporal surgery. T₂-weighted MR image showing a high intensity area in the right parieto-occipital region (arrowhead).

Fig. 2 Case 13. Preoperative conventional EEG demonstrating continuous spike discharges in the parieto-occipital region.

Fig. 4 Case 13. Postoperative conventional EEG demonstrating no abnormal epileptiform activity.

Fig. 3 Case 13. Intraoperative preresection ECoG and concurrent scalp EEG showing focal seizures induced by hyperventilation loading (*upper*). Schematic drawing demonstrates the right parieto-occipital craniotomy (posteroanterior view). The dotted circle shows the area of cortical dysplasia and the superior sagittal sinus running along the left margin (*upper left*). Note the spike foci are circumscribed and remote from the cortical dysplasia. Scalp EEG demonstrates no propagation of this seizure. The alpha rhythms in the O₁ lead are due to light neuroleptanalgesia. Intraoperative postresection ECoG demonstrating no epileptiform activity (*lower*). Dotted circle demonstrates the area of cortical resection (*lower left*).

mmHg. Concurrent ECoG demonstrated focal seizures in electrodes 2 and 3 (Fig. 3 *upper*). After focus resection and lesionectomy, ECoG showed no spike or abnormal epileptic paroxysms (Fig. 3 *lower*). The histological diagnosis was cortical dysplasia. Postoperative EEG showed no spike activity in the right parieto-occipital region (Fig. 4). No visual field defect was detected. Postoperatively, he has been seizure-free for 3 years, with reduced medication.

Case 18: A 2-year-old boy had bifrontal cortical tuberous sclerosis. The left cortical tuber was a large mass (3 × 3 cm) and the right cortical tuber was a small mass (1 × 1 cm). Interictal SPECT with ^{99m}Tc-HMPAO revealed a low perfusion area at the left cortical tuber (Fig. 5 *upper*), and ictal SPECT demonstrated an abnormal hyperperfusion area at the left cortical tuber (Fig. 5 *lower*). Preoperative EEG demonstrated hypersarrhythmia during his infantile spasms and an additional spike focus in the left frontal lobe. Surgery was chosen based on the EEG spike focus and SPECT study. Intraoperative ECoG demonstrated widespread cortical spike foci around the cortical tuber in the left frontal lobe. Lesionectomy and spike focus resection were performed. However, the spike focus over Broca's area was not resected. The postoperative course was excellent and tonic spasms disappeared completely for a month. However, tonic spasms occurred again 2 months postoperatively, and continued subsequently. Follow-up EEG again demonstrated the hypersarrhythmic pattern.

Discussion

The seizure-free rate of previous studies varied from

Fig. 5 Case 18. Undergoing extratemporal surgery. Interictal SPECT scan demonstrating a focal low perfusion area in the left frontal lobe over the left cortical tuber (*upper*). Ictal SPECT scan demonstrating a focal increase of cerebral blood flow in the left frontal lobe (*lower*).

60% to 80% in children with medically intractable temporal lobe epilepsy,^{7,9,10,12)} with less favorable results for extratemporal focal resection.^{2,10,19)} The results of extratemporal surgery are clearly not as good as for temporal surgery. Van Ness *et al.*¹⁹⁾ reported that only six of 37 patients (16%) became seizure-free, and 22 patients (59%) had a notable reduction in seizures. They concluded that factors associated with seizure control require further study to establish better patient selection criteria. During temporal or extratemporal surgery, we repeatedly tested for residual cortical spikes after cortical focus resection or lesionectomy, and as many of the residual foci as possible were resected when located in the non-eloquent cortex. However, foci in the eloquent cortex were left in place. Consequently, the seizures in Cases 2 and 3 of the temporal group were not improved even after surgery. In our series, 8/11 patients (73%) undergoing extratemporal surgery and 7/9 (78%) undergoing temporal surgery became seizure-free (class 1) after surgery. Overall, 17/20

patients (85%) benefited from surgery. Unfortunately, three patients showed no improvements following surgery (class 4).

Analysis of postresection ECoG in these three patients is another important result of the present study. Postresection ECoGs were all grade C, suggesting that presurgical evaluations, including evaluation of the craniotomy area, may have been incorrect. Further examinations or surgical procedures are required when postresection ECoG shows persistent epileptiform activities. This study showed that postresection ECoG examination is one of the most important predictors for postoperative seizure outcome.

This study suggests the following points should be considered when using intraoperative EEG/ECoG monitoring and analysis during epilepsy surgery. Anticonvulsant medication should be stopped 1–3 days before surgery depending on the frequency of intractable seizures. General anesthesia with neurolept-analgesia but without benzodiazepine is favorable. Local anesthesia may result in sudden panic in pediatric surgery. EEG began to show rapid theta waves or slow alpha rhythms in the occipital leads within 15 minutes following the disconnection of nitrous oxide. Initial EEG/ECoG monitoring should be continued for at least 30 minutes. Loading of artificial hyperventilation for 3 minutes resulted in the detection of new spike foci in 17 of 20 patients (85%) by ECoG and spontaneous electrocorticographic seizures or spontaneous hippocampal seizures in 10 patients (50%) by EEG. These procedures are not so hazardous during epilepsy surgery, so intraoperative ECoG monitorings should be considered to improve the detection of seizure foci during surgery. For this reason, we never used short-acting barbiturate to elicit epileptiform activities.

Further improvement in ECoG recording methods and conditions during intraoperative monitoring are required to obtain better results in pediatric epilepsy surgery. Improvements in these intraoperative ECoG procedures could be applied to adult epilepsy patients to eliminate invasive preoperative monitoring.

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Commentary

This article is another valuable contribution to the scarce literature on epilepsy surgery in children. The authors should be commended for the excellent results they were able to obtain in this series. Excluding the two cases with mesial temporal sclerosis, they reported that 83% of the neocortical epilepsies had an Engel class I outcome. This is one of the best if not the best outcome of epilepsy surgery for neocortical epilepsy reported in the literature. The most probable explanation for the excellent results is the careful case selection applied in this study. All the cases (except the two cases with mesial temporal sclerosis) had clearly defined lesions on the MRI which were removed during surgery. This is in clear contrast with most of the series reported in the literature which predate the availability of high resolution MRI and, therefore, usually include a high percentage of patients with no lesions visible on neuroimaging. On the other hand, it is surprising to see that both cases with mesial temporal sclerosis did not profit from surgery. These are the cases in which usually epilepsy surgery is most effective.

There is still great debate in the literature if surgery guided by acute ECoG actually improves the results of epilepsy surgery. I do not feel that this paper answers that question either. It is usually accepted that a lesionectomy with extensive resection of the margins around the lesion has a very high chance of success. This is particularly true for tumors or tumor-like lesions which include the majority of the cases in this report. The only way to answer this question would be to design a study with appropriate controls (surgery guided by ECoG vs. surgery performed without ECoG). Such a study has still not been performed.

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