

"Subtotal" hemispherectomy in children with intractable focal epilepsy

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SUMMARY



Dr. Chugani is Professor/Chief of Pediatric Neurology and Director of the PET Center at the Children's Hospital of Michigan, Wayne State University in Detroit, specializing in epilepsy, brain development, and plasticity.

Objective: Cortical resections in epilepsy surgery tend to be larger in children, compared to adults, partly due to underlying pathology. Some children show unilateral multifocal seizure onsets involving much of the hemisphere. If there were a significant hemiparesis present, hemispherectomy would be the procedure of choice. Otherwise, it is preferable to spare the primary sensorimotor cortex. We report the results of "subtotal" hemispherectomy in 23 children.

Methods: All children (ages I year and 4 months to 14 years and 2 months) were operated on between 2001 and 2013 at Children's Hospital of Michigan (Detroit). Patients were evaluated with scalp video-electroencephalography (EEG), magnetic resonance imaging (MRI), ¹⁸F-fluorodeoxyglucose-positron emission tomography (FDG-PET) scans, and neuropsychological assessments when applicable. Subsequently, each case was discussed in a multidisciplinary epilepsy surgery conference, and a consensus was reached pertaining to candidacy for surgery and optimum surgical approach. The actual extent of resection was based on the results from subdural electrocorticography (ECoG) monitoring. The surgical outcome is based on International League Against Epilepsy (ILAE) classification (class 1-6).

Results: Among the 23 patients, 11 had epileptic spasms as their major seizure type; these were associated with focal seizures in 3 children. MRI showed focal abnormalities in 12 children. FDG-PET was abnormal in all but one subject. All except two children underwent chronic subdural ECoG. Multiple subpial transections were performed over the sensorimotor cortex in three subjects. On histopathology, various malformations were seen in 9 subjects; the remainder showed gliosis alone (n = 12), porencephaly (n = 1), and gliosis with microglial activation (n = 1). Follow-up ranged from 13 to 157 months (mean = 65 months). Outcomes consisted of class 1 (n = 17, 74%), class 2 (n = 2), class 3 (n = 1), class 4 (n = 1), and class 5 (n = 2).

Significance: Extensive unilateral resections sparing only sensorimotor cortex can be performed with excellent results in seizure control. Even with the presence of widespread unilateral epileptogenicity or anatomic/functional imaging abnormalities, complete hemispherectomy can often be avoided, particularly when there is little hemiparesis.

KEY WORDS: Seizure, Pediatric, Surgery, Infantile spasms, FDG PET.

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Surgical procedures for the treatment of intractable epilepsy include focal cortical resections (including temporal lobectomy), multilobar resections, hemispherectomy (functional or anatomic), corpus callosotomy, and multiple subpial transections (MSTs).¹ In general, resections tend to be larger in children, particularly infants, compared to adults due to the underlying pathology, greater plasticity of the still-developing brain, and the goal of promoting a normal

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developmental trajectory whenever possible.^{2,3} Therefore, in children, removing "nociferous" cortex is as important as resecting cortex showing seizure onset at the time of study.^{4,5}

In addition to the conventional tools applied to evaluate children with intractable epilepsy who might be surgical candidates,⁶ the pediatric epilepsy surgery program at the Children's Hospital of Michigan in Detroit relies heavily on advanced molecular neuroimaging techniques to localize both the epileptic focus and associated nociferous cortex. Widespread extraoperative intracranial electrocorticography (ECoG) monitoring is applied not only to brain regions indicated from seizure semiology and scalp interictal/ictal electroencephalography (EEG) data, but also to cortical regions showing abnormalities on positron emission tomography (PET). However, the ultimate extent of resection is based on extraoperative ECoG data and not purely on PET data. In other words, the cortical region that appears abnormal on PET, but without accompanying intracranial ECoG epileptiform discharges, is generally not resected.

Using this approach, we have found that a number of children may show unilateral multifocal ECoG abnormalities involving the entire hemisphere, for which we concluded multilobar resections need to be performed. If there were a significant hemiparesis already present, cerebral hemispherectomy would be the procedure of choice in such cases. However, if there is no or only a mild hemiparesis, it is preferable to perform multilobar resections yet spare the primary sensory and motor cortex. We have performed such resections in 27 children (23 available for follow-up >12 months) and have used the term "subtotal" hemispherectomy to describe this operation where the entire cerebral cortex of one hemisphere is resected except for the primary sensorimotor cortex. We now describe our approach and results of this operation.

Methods

Subjects

The patient population consisted of 27 infants and children with medically refractory epilepsy who underwent surgery between April 2001 and March 2013 (Table 1). Four of the 27 patients were lost to follow-up. The remaining 23 patients form the subject of this report. Age at the time of surgery in these 23 children ranged between 1 year 4 months and 14 years 2 months (mean age 5 years 8 months). Patients were evaluated with scalp interictal and ictal video-EEG, magnetic resonance imaging (MRI), and glucose metabolism PET scans, and neuropsychological assessments when applicable. Some children also received PET scans with ¹¹C-flumazenil (FMZ)⁷ or ¹¹C-alphamethyl-L-tryptophan (AMT)⁸ under research protocols. Subsequently, the patients were discussed in a weekly held multidisciplinary epilepsy surgery conference, and a consensus was reached pertaining to candidacy for surgery and

optimum surgical approach, with the understanding that the actual extent of resection would be based on results from subdural ECoG monitoring.

Subdural electrode placement and extraoperative ECoG recording

A craniotomy was made over the frontal-parietotemporal region of the presumed epileptogenic hemisphere. A combination of platinum grid and strip electrodes (interelectrode distance 1 cm) were placed over the region suspected to be epileptogenic based on the results of presurgical assessment.9 Electrodes were placed on the precentral and postcentral gyri as well as the medial temporal regions in all cases. The medial and inferior surfaces of the frontal lobe were also sampled when suggested by any of the noninvasive diagnostic tools. All electrode plates were stitched to adjacent plates or the edge of the dura mater to avoid movement of subdural electrodes after placement; in addition, the leads were tunneled about an inch from the main wound to minimize the risk of infection. In all patients, intraoperative photographs were taken with a digital camera before dural closure. The dura was closed in a semiwatertight fashion, and the bone flap was replaced but not secured. A subgaleal drain was placed to minimize postoperative scalp swelling. All electrodes were subsequently displayed on the threedimensional brain surface reconstructed from high-resolution MRI.¹⁰

Extraoperative video-ECoG recordings were obtained for 2-5 days. The seizure-onset zones responsible for habitual seizures were determined as described previously.9 The extent of resection generally included the seizure-onset zones and the regions showing frequent interictal epileptiform bursts that could not be explained by propagation from the seizure-onset zone. We also generally intended to remove the region showing anatomic/functional imaging abnormalities proximal to that showing the aforementioned ECoG abnormalities. Electrical stimulation mapping was employed to localize the eloquent areas, including the primary sensorimotor area.¹¹ Prior to the resective surgery, the team and the family of the patient had extensive discussions regarding the pros and cons of "subtotal' hemispherectomy," "subtotal' hemispherectomy plus MSTs on the sensorimotor cortex," and "hemispherectomy."

Resection procedure

At the second stage of surgery, grids and strips were again photographed and sequentially removed. The anterior and posterior resection margins were defined. Under microscope, the Sylvian fissure was widely opened and through the circular sulcus the temporal-parietooccipital lobe was disconnected from the rest of the brain along the posterior resection margin. The bridging veins from the temporal and the parietal lobes were coagulated and cut, and the entire temporal-parietooccipital lobe including hippocampus was removed in one piece. The subiculum and medial part of the

					Table	I. Clinical, ra	Table 1. Clinical, radiologic, and treatment profile	reatment prof	ile				
		Age (vear)	Seizure	Scalp EEG		Imaging abnormalities	nalities			Surgerv		Follow-up	Outcome
Pt #	Sex		type	Interictal spikes	lctal onset	MRI	FDG-PET	FMZ-PET	AMT-PET	stage	Histopathology	(months)	class
_	ш	l y4 m	IS	R-FC; R-T; R-TPO	Diffuse but leading	Normal	R FPT decrease			2	Mild MCD; diosis	67	_
2	щ	ly5m	IS	R-TPO; R-TCP; L-TCP;	Diffuse	R PT (atrophy)	RP,medT decrease;			_	Gliosis,	40	_
'n	Σ	8 6 -	<u>v</u>	L-1PO; (+) Hypsarrhythmia R_T·R_F·1_T	Diffuse but leading	R F (FCD)	R DO decrease		R FPT increase	ç	porencephaly Gliosis mild	<u>~</u>	
)	:		2		on R)			ı	MCD	2	-
4	ш	I y 10 m	IS	L-F; Diffuse	Diffuse but leading in 1_F	Normal	L FP, thalamus decrease	L F, thalamus decrease	L FP Increase	2	Mild gliosis	157	_
2	Σ	2 y 5 m	IS	R-TPO; B-F; L-T; (+)	Diffuse but greater	R post (WM	R PT decrease			2	Gliosis	24	_
9	Σ	2 y 6 m	SI	Hypsarrhythmia L-TCP; R-TCP; (+)	R involvement Diffuse	atrophy) L F (grey-white	L FPT decrease			2	Gliosis, WM	55	m
				Hypsarrhythmia		blurring)					heterotopia		
~	Σ	2 y 8 m	CP, GTC	L-TPO; Diffuse	L-TPO; Diffuse but leading on L	Normal	L OTP decrease			2	Gliosis	68	_
œ	Σ	3 y 2 m	SI	L-OTP; L-F; R-C; R-T	Diffuse but leading in L-OT	Normal	L FPT decrease	L T decrease		2	Gliosis	86	_
6	ш	3 y 6 m	IS, CTC	L-T; R-T; Diffuse; (+)	Diffuse	Normal	L TPO decrease		L FPO decrease	2	Gliosis	29	4
0	ш	4 v	פור וצי	пурsarrnyunma R-F; R-TPO	Diffuse but greater	R T, insula	R T decrease			2	Gliosis.	4	_
			GTC		Rinvolvement	(atrophy)					chronic inflammation		
Ξ	ш	4 y	IS	L-T; L-O; R-T-C· Diffuse	Diffuse but leading	TSC lesions	Multifocal		L PO increase	2	TSC	71	2
12	ш	4 y 6 m	IS, CP	L-T; L-Hemispheric	L-Hemispheric but leading in L-T	Normal	L FPTO decrease	L InfF, postP,T decrease		2	PMG (F); gliosis (TPO)	87	_
13	Σ	6 y 4 m	G	L-TCP; L-Hemispheric	L-Hemispheric but greater involvement in L-T	Normal	Normal			7	FCD 2B	77	2
4	Σ	7 y 5 m	CP, GTC	L-FTC	L-FTC	Normal	L FPTO decrease	L FPTO decrease		_	FCD 2B	46	5
15	Σ	7 y 6 m	CP D	L-CPT; Diffuse	Diffuse but greater involvement in L	LF,TO (arachnoid	L FPTO decrease			2	Gliosis, microglia	30	_
16	щ	7 y 9 m	CP, GTC	R-T; L-T; Diffuse	Diffuse	cysts) Normal	R T decrease	R T decrease		2	activation Gliosis	132	_
17	ш	7 y I1 m	GTC GTC	L-TOPC	L-TOP	Normal	L FPTO decrease			2	Gliosis	75	_
8	Σ	8 y 8 m	GTC GTC	L-TPO; Diffuse	Diffuse but greater involvement in L	LT (FCD)	L T increase (ictal)		L TO increase	2	Gliosis, heterotopia	139	_
61	Σ	8 y 9 m	IS then	L-OTPC; L-T	L-OTPC; L-T	TSC	L TPO decrease		L parahippocampal,O	5	TSC	81	_
20	Σ	8 y 10 m	IS then CP	R-TO; Diffuse	Diffuse	R T (FCD)	R PTO decrease	R PT,latO decrease		7	Gliosis	60	_
													Continued

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					Tab	Table I. Continued.	ed.					
	Age (year) Seizure	Seizure	Scalp EEG		Imaging abnormalities	malities			Surgery		Follow-up	Follow-up Outcome
Pt# S	Pt# Sex (at surgery) type) type	Interictal spikes	lctal onset	MRI	FDG-PET	FMZ-PET	AMT-PET	stage	Histopathology (months)	(months)	class
21 F	F 10 y 6 m	СР	R-F; R-TOP; L-T;	Diffuse but greater	R thalamus	R FPT, thalamus	R T,latO	RT decrease;	2	Gliosis,	93	2
			Diffuse but greater	involvement in R	(infarct)	decrease	decrease	R thalamus		hippocampal		
			involvement in R					decrease		sclerosis		
22 F	11 y 2 m	Ð	R-T; R-Hemisphere	R-T; R-F	Normal	R FPT decrease			2	Mild MCD	43	_
		GTC										
23 M	M 14 y 2 m	Ð	R-FCT; Diffuse	R-FCT	R hemisphere	R FPO decrease			2	Gliosis,	67	_
		GTC			(atrophy)					nodular		
										heterotopia		
FDG	fluorodeoxy gluc	cose; FMZ,	FDG, fluorodeoxy glucose; FMZ, ¹¹ C-flumazenil; AMT, ¹¹ C-alpha-methyl-L-tryptophan; F, female; M, male; y, year(s); m, month(s); IS, infantile spasms; CP, complex partial seizures; GTC, generalized tonic-clonic sei-	C-alpha-methyl-L-trypt	tophan; F, female.	; M, male; y, year(s);	m, month(s); IS, inf	antile spasms; CP, con	nplex partial	seizures; GTC, gen	ieralized tonic	-clonic sei-
zures; K	, right; L, left; Inf, i	Interior; Po	zures; K, right; L, left; Inf, Inferior; Posterior; med, medial; lat, lateral; P, parietal; I, temporal; F, frontal; O, occipital; F.CD, focal cortical dysplasia; WM, white matter; ISC, tuberous sclerosis complex; MCD, malfor-	al; lat, lateral; P, parieta	ıl; I, temporal; F,	frontal; O, occipital;	; FCD, focal cortica.	l dysplasia; WM, white	matter; ISC	, tuberous sclerosi:	s complex; M	CD, malfor-
mation	of cortical develo	pment; PMC	mation of cortical development; אישר, polymicrogyria.									
Surg	ical outcome base	ed on 2001	^d Surgical outcome based on 2001 International League Against Epilepsy classification.	ainst Epilepsy classificat	tion.							

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uncus was then removed using gentle suction. Corticectomy was performed along the course of the anterior cerebral artery, dividing the branches to the frontal lobe along its course up to the anterior resection margin. Then the corticectomy was carried to the superior sagittal sinus along the anterior resection margin, disconnecting the frontal lobe from the rest of the brain. The frontal lobe was removed after cutting the bridging veins and the olfactory tract. The cavity was irrigated with Lactated Ringer's solution and hemostasis was secured. ECoG was obtained from the residual cortex (i.e., sensorimotor cortex) to confirm adequate resection and the potential need for MSTs. An external ventricular drain was left in the cavity and closure was performed.

Histopathology

All surgical specimens were subjected to detailed histologic examination, including staining with hematoxylin and eosin, cresyl-violet, Luxol fast-blue, and glial fibrillary acidic protein (GFAP) antibody. Further stains (such as periodic-acid Schiff, Bielschowsky, Bodian, Congo red, or various immunostains) were applied as indicated to clarify the nature of pathology.

Outcome analysis

Follow-up ranged from 13 to 157 months (mean 65 months). The surgical outcome was reported according to the International League Against Epilepsy (ILAE) classification¹² at last clinical follow-up or by telephone interview:

Class 1: completely seizure-free; no auras.

Class 2: only auras; no other seizures.

Class 3: one to three seizure days per year; with or without auras.

Class 4: four seizure days per year to 50% reduction of baseline seizure days; with or without auras.

Class 5: less than 50% reduction of baseline seizure days to 100% increase of baseline seizure days; with or without auras.

Class 6: more than 100% increase of baseline seizure days; with or without auras.

RESULTS

Among the 23 patients, 11 had infantile or epileptic spasms as their major seizure type; the spasms occurred as the *only* seizure type in 8 patients, or were associated with complex partial epilepsy with (n = 2) or without (n = 1) secondary generalization (see Table 1). Of the 12 patients without spasms, 12 had complex partial epilepsy with (n = 8) or without (n = 4) secondary generalization; 2 of the latter had a history of spasms. Two patients had tuberous sclerosis complex (TSC; patients 11 and 19) and one (patient 10) had a history of herpes meningitis in early infancy.

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Neuroimaging with MRI showed normal findings in 11 of the 23 patients. The MRI abnormalities in the remaining 12 patients included focal/lateralized cortical atrophy (n = 4), suggestion of cortical dysplasia (n = 4), tuberous sclerosis (n = 2), unilateral thalamic infarct (n = 1), and cystic abnormality (n = 1). By comparison, glucose metabolism PET scan was normal in only one subject (patient 13, with class 5 outcome). PET abnormalities almost always included lateralized/localized hypometabolism, but also hypermetabolism (n = 2: patients 2 and 18) (Fig. 1). The two patients with tuberous sclerosis both had AMT PET scans, and these showed increased tracer uptake in the epileptogenic tubers. AMT PET was performed in five more patients and showed lateralized/localized abnormalities in all of them. FMZ PET scans were performed in seven patients and showed lateralizing/localizing abnormalities in all of them (see Table 1).

All patients had a two-stage epilepsy surgery except two (patients 2 and 14). In these two patients, the resection margin was determined using intraoperative ECoG and neuroimaging findings. Three (patients 1, 6, and 22) of the 23 had

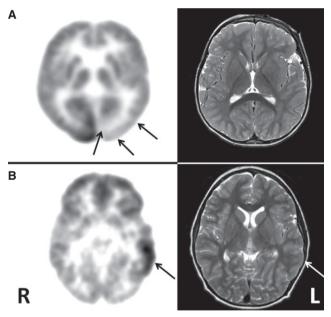


Figure 1.

FDG-PET showing (**A**) decreased glucose metabolism in the left temporooccipital regions (arrows) in a 3-year-old child with intractable complex partial and generalized tonic–clonic seizures and normal fluid-attenuated inversion recovery (FLAIR) MRI, and (**B**) increased glucose metabolism in the left temporal cortex (arrow) in a 9-year-old child with intractable complex partial and generalized tonic–clonic seizures, with T-2 weighted MRI showing some cortical thinning and loss of gray–white matter differentiation in the same region (arrow). Postsurgical histopathologic evaluation revealed gliosis in the first and gliosis and some heterotopia in the second child. Both children were seizure free at 6 and 12 years after the surgery, respectively. *Epilepsia* © ILAE

MSTs on the sensorimotor cortex following "subtotal" hemispherectomy because postresection ECoG showed persistent frequent spiking on the sensorimotor cortex. Patient 14 had the motor face area resected in addition to the "subtotal" hemispherectomy. Thirteen of the 23 children had a left hemispheric resection. One patient (patient 17) developed postoperative hydrocephalus requiring a ventriculoperitoneal shunt.

On histopathologic evaluation, various malformations were seen in nine subjects (including two with tuberous sclerosis); the remainder showed gliosis alone (n = 12), porencephaly (n = 1), and gliosis with microglial activation (n = 1) (see Table 1).

Follow-up ranged from 13 to 157 months (mean 65 months). Outcome consisted of class 1 (n = 17, 74%), class 2 (n = 2), class 3 (n = 1), class 4 (n = 1), and class 5 (n = 2). None of the patients developed hemiparesis/hemiplegia or worsening of an existing mild hemiparesis.

Patient 13 rated as class 5 had habitual seizures characterized by brief hypermotor semiology accompanied by an asymmetric tonic posture with right upper extremity extension. Both PET and MRI were normal. Chronic ECoG recording showed frequent spike-wave bursts arising from the left frontal and temporal regions immediately prior to habitual seizures (Fig. 2). We initially performed resection of the left frontotemporal lobes. Postoperative ECoG showed episodes of electrographic seizures arising from the remaining parietoccipital region; therefore, we immediately added parietoccipital resection before dural closure. Histopathology report suggested the presence of cortical dysplasia with balloon cells involving all four lobes, with the frontal and temporal regions most severely affected. He achieved seizure freedom for a period of 6 months, but developed recurrent hypermotor seizures. Two years after the first surgery, we completed the "subtotal" hemispherectomy plus resection of the primary sensorimotor area; he continues to have habitual hypermotor events without discernible changes in scalp EEG signals. We interpreted such hypermotor events as residual seizures arising from a deep focus (such as insular cortex), which was not completely removed.

DISCUSSION

When focal onset (or localization-related) seizures cannot be controlled with medication, surgical resection of the epileptic focus may be considered. The most important aspect of presurgical evaluation is to identify a discrete epileptogenic region that can be resected without causing an unacceptable loss of neurologic function, and which will lead to complete cessation of seizures. Furthermore, in treating children with intractable epilepsy, it is important to consider both seizure control and allowing for normal cognitive development. To achieve these goals, the epilepsy surgery team integrates localization data obtained from seizure

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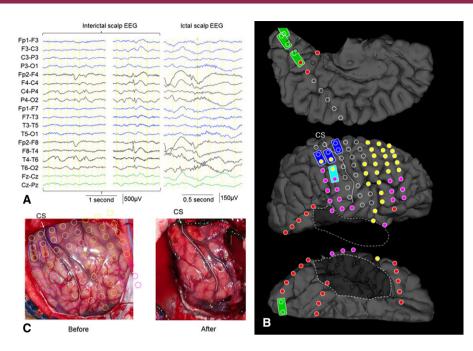


Figure 2.

(A) Interictal scalp EEG showed frequent spike discharges independently originating from the right posterior and anterior head regions. Ictal EEG showed widespread low-amplitude fast oscillations superimposed on delta waves with greater involvement in the right hemisphere. Low-frequency filter: 0.53 Hz. High-frequency filter: 70 Hz. (B) Subdural ECoG and stimulation data are presented on her threedimensional surface image. MRI showed an encephalomalacic cyst in the right temporal lobe (broken white line). CS: Central sulcus defined by an anatomic landmark.¹¹ White circles: electrodes free from artifacts. Black circles: electrodes affected by artifacts and excluded from analysis. Circles filled in red: seizure-onset zones. Circles filled in pink: nonseizure onset sites showing frequent interictal spike discharges. Circles filled in yellow: nonseizure onset sites with occasional involvement in the field of interictal spike discharges. Unfilled circles: nonseizure onset sites not affected by interictal spike discharges. Blue squares: hand jerking induced by stimulation. Light blue square: mouth movement induced by stimulation. Green squares: forced eye deviation to the left side induced by stimulation. (C) Intraoperative photographs before and after surgery. The seizure-onset zones cannot be directly visualized in these photographs. *Epilepsia* © ILAE

semiology, ictal and interictal EEG, anatomic and functional neuroimaging, and neuropsychological assessment. The most dramatic surgical treatment for intractable epilepsy is cerebral hemispherectomy,¹³ which leaves the patient with a contralateral hemiplegia and hemianopsia. If these deficits are already present preoperatively (such as in many children with intrauterine unilateral middle cerebral artery infarcts), the surgical procedure is well accepted by the patient and family. Hemispherectomy is associated with seizure freedom in 90% of those operated at an early age,¹⁴ with a range of 63% to 85% from various centers.^{15–17}

The most difficult challenge is when the epileptogenic zone is perceived to diffusely involve the hemisphere but the child does *not* exhibit hemiparesis or hemianopsia. Although a hemianopsia induced by resection is generally accepted and tolerated well, hemiplegia caused by surgery in a child with reasonable hand function prior to surgery is less acceptable, and parents are usually reluctant to subject their child to this acute dramatic loss of function. A possible exception is in the case of Rasmussen encephalitis, for which there is often a dilemma and it may be futile to perform a lesser operation than hemispherectomy because of the progressive nature of the disorder.¹⁸ The present series did not include any patients with Rasmussen encephalitis.

In some children with mild to moderate hemiparesis associated with very early injury or unilateral malformations, a hemispherectomy that includes resection of sensorimotor cortex actually may not lead to any worsening of the hemiparesis if there already has been reorganization of motor tracts. We routinely use diffusion tensor imaging (DTI) with tractography to document motor tracts of these children preoperatively. For example, we have previously described the preoperative DTI tractography findings in an 8-year-old girl showing near-complete absence of the left corticospinal tract and a more robust than normal corticospinal tract in the right hemisphere, suggesting that her right motor function had reorganized to the right hemisphere and the ipsilateral corticospinal tract. This was confirmed by the observation that there was no change in right hemiparesis following left hemispherectomy.¹⁹

Multilobar resections are often performed in children with intractable epilepsy, particularly when the condition is caused by cortical dysplasia.²⁰ In one large series of multilo-

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bar epilepsy surgery, a favorable outcome was achieved in only 41% of patients at 10 years of follow-up, with the greatest predictors of seizure recurrence being incomplete resection and persistent epileptiform discharges on scalp EEG following surgery.²¹ These two predictors of surgical failure can be addressed when there are preoperative functional neuroimaging data to suggest a larger area of possible nociferous cortex than can be predicted by seizure semiology, MRI, and scalp interictal/ictal EEG data, thus guiding a wider area of intracranial electrode coverage. In such instances, as in the 23 children of the present study, the inevitable conclusion is reached that seizure onset and/or nociferous cortex involves much of the hemisphere. The decision then has to be made as to whether a complete or "subtotal" hemispherectomy should be performed. All 23 patients in the present series had good use of the limbs contralateral to the affected hemisphere, although mild hemiparesis was present in some. It should be noted that mild hemiparesis in children with very frequent seizures occasionally may be caused by a postictal effect. In these children, parents often report that there is no hemiparesis on seizure-free days.

After discussion with the parents, we chose to perform a "subtotal" hemispherectomy in these 23 children (Fig. 3). The presence of rare or occasional interictal epileptiform discharges from the primary sensorimotor cortex during ECoG was insufficient to warrant resection, since we could offer MSTs over this region. In contrast, ictal onset or frequent independent epileptiform discharges from sensorimotor cortex generally resulted in resection of this region, that is, a standard hemispherectomy, and exclusion from the present study.

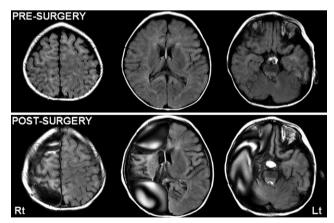


Figure 3.

Presurgical (upper row) and postsurgical (lower row) FLAIR images showing the results of right-sided "subtotal" hemispherectomy in a child with intractable seizures. Presurgical MRI was read as essentially normal. The child had only a mild left hemiparesis prior to surgery, which did not worsen after the surgery, and is seizure free.

Epilepsia © ILAE

Chronic subdural EEG recording was recommended for the patients in the present study and was performed to determine the extent of epileptogenic zone, when noninvasive assessment failed to confidently presume the boundary between the epileptogenic zone and eloquent cortices. All patients in this cohort showed widespread seizure-onset zones and/or frequent interictal spike-wave discharges in widespread regions. The present study, however, excluded patients who underwent cortical resection other than "subtotal" hemispherectomy. Most of the patients whose subdural EEG recording revealed the seizure-onset zone involving the sensorimotor cortex for the hand were recommended for anatomic hemispherectomy, and excluded from this series. Similarly, patients, whose interictal spikes in the frontal lobe were all explained/considered as those propagating from the temporal-parietooccipital regions, were generally recommended for temporal-parietooccipital resection sparing the frontal lobe and sensorimotor cortex, and also excluded from this series. Therefore, subdural recordings contributed to the final surgical decision.

In the present series, 3 (patients 1, 6, and 22) of the 23 children had MSTs over the sensorimotor cortex in addition to the "subtotal" hemispherectomy. We relied on several criteria in deciding whether to perform MSTs on the sensory/motor cortex rather than a complete hemispherectomy, including: (1) degree of interictal epileptiform activity in this region during extraoperative ECoG, (2) no or only mild hemiparesis, (3) presence of a strong corticospinal tract in the affected hemisphere as shown on MRI DTI tractography, and (4) parental discussion. Although the "subtotal" hemispherectomy procedure spares motor function but introduces a hemianopsia if not already present preoperatively, parents were always willing to accept this visual deficit.

Neuroimaging with MRI, in general, provided less localizing/lateralizing information than functional imaging with PET. In some cases, MRI abnormalities were appreciated only after studying the PET findings. Furthermore, the use of AMT and FMZ PET scans provided additional lateralizing and localizing information in some patients. FMZ and AMT abnormalities were usually more circumscribed than FDG abnormalities. The abnormalities revealed by AMT (increases) and FMZ PET (decreases) were always unilateral, and either concordant with FDG data or revealed some additional foci of abnormalities concordant with EEG changes, thus providing complementary information and increasing the confidence for surgical decision-making in these very difficult cases.

In conclusion, the present study demonstrates that extensive unilateral resections sparing only sensorimotor cortex can be performed with excellent results in seizure control. Even with the presence of widespread unilateral epileptogenicity or anatomic/functional imaging abnormalities, complete hemispherectomy can often be avoided, particularly when there is little or no hemiparesis.

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DISCLOSURE

None of the authors have any conflict of interest to disclose. We confirm that we have read the Journal's position on issues involved in ethical publication and affirm that this report is consistent with those guidelines.

REFERENCES

- 1. Dunkley C, Kung J, Scott RC, et al. Epilepsy surgery in children under 3 years. *Epilepsy Res* 2011;93:96–106.
- Otsuki T, Honda R, Takahashi A, et al. Surgical management of cortical dysplasia in infancy and early childhood. *Brain Dev* 2013;35:802–809.
- Wiebe S, Berg AT. Big epilepsy surgery for little people: what's the full story on hemispherectomy? *Neurology* 2013;80:232–233.
- Devinsky O, Romanelli P, Orbach D, et al. Surgical treatment of multifocal epilepsy involving eloquent cortex. *Epilepsia* 2003;44:718– 723.
- 5. Penfield W, Jasper H. *Epilepsy and the functional anatomy of the human brain*. Boston: Little Brown and Company; 1954.
- Jayakar P, Gaillard WD, Tripathi M, et al. Diagnostic test utilization in evaluation for resective epilepsy surgery in children. *Epilepsia* 2014;55:507–518.
- Juhasz C, Chugani DC, Muzik O, et al. Relationship of flumazenil and glucose PET abnormalities to neocortical epilepsy surgery outcome. *Neurology* 2001;56:1650–1658.
- Kumar A, Asano E, Chugani HT. alpha-[(1)(1)C]-methyl-Ltryptophan PET for tracer localization of epileptogenic brain regions: clinical studies. *Biomark Med* 2011;5:577–584.
- Asano E, Juhasz C, Shah A, et al. Role of subdural electrocorticography in prediction of long-term seizure outcome in epilepsy surgery. *Brain* 2009;132:1038–1047.

- Alkonyi B, Juhasz C, Muzik O, et al. Quantitative brain surface mapping of an electrophysiologic/metabolic mismatch in human neocortical epilepsy. *Epilepsy Res* 2009;87:77–87.
- 11. Haseeb A, Asano E, Juhasz C, et al. Young patients with focal seizures may have the primary motor area for the hand in the postcentral gyrus. *Epilepsy Res* 2007;76:131–139.
- Wieser HG, Blume WT, Fish D, et al. ILAE Commission Report. Proposal for a new classification of outcome with respect to epileptic seizures following epilepsy surgery. *Epilepsia* 2001;42:282–286.
- Sood S, Asano E, Chugani HT. Role of external ventriculostomy in the management of fever after hemispherectomy. J Neurosurg Pediatr 2008;2:427–429.
- Althausen A, Gleissner U, Hoppe C, et al. Long-term outcome of hemispheric surgery at different ages in 61 epilepsy patients. *J Neurol Neurosurg Psychiatry* 2013;84:529–536.
- Jonas R, Nguyen S, Hu B, et al. Cerebral hemispherectomy: hospital course, seizure, developmental, language, and motor outcomes. *Neurology* 2004;62:1712–1721.
- Moosa AN, Gupta A, Jehi L, et al. Longitudinal seizure outcome and prognostic predictors after hemispherectomy in 170 children. *Neurology* 2013;80:253–260.
- Ramantani G, Kadish NE, Brandt A, et al. Seizure control and developmental trajectories after hemispherotomy for refractory epilepsy in childhood and adolescence. *Epilepsia* 2013;54:1046–1055.
- Bien CG, Schramm J. Treatment of Rasmussen encephalitis half a century after its initial description: promising prospects and a dilemma. *Epilepsy Res* 2009;86:101–112.
- Govindan RM, Chugani HT, Luat AF, et al. Presurgical prediction of motor functional loss using tractography. *Pediatr Neurol* 2010;43:70– 72.
- Hauptman JS, Mathern GW. Surgical treatment of epilepsy associated with cortical dysplasia: 2012 update. *Epilepsia* 2012;53(Suppl. 4):98– 104.
- Sarkis RA, Jehi L, Najm IM, et al. Seizure outcomes following multilobar epilepsy surgery. *Epilepsia* 2012;53:44–50.