■ Original article

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Epileptic Disorders

Epileptiform abnormalities in the disconnected hemisphere are common in seizure-free patients after hemispherectomy

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ABSTRACT

Objective. The spectrum of EEG abnormalities in the disconnected hemisphere in seizure-free patients after hemispherectomy has not been well characterized.

Methods. Fifty consecutive patients who were seizure-free following hemispheric disconnection were identified. Data on preoperative clinical, EEG and neuroimaging findings and postoperative EEG findings and antiseizure medication status were collected.

Results. Forty-seven patients (94%) had functional hemispherectomy, and three (6%) had more extensive tissue resection of the posterior quadrant or frontal region along with hemispheric disconnection. Etiologies included: residual effects from vascular lesions including perinatal stroke in 35 patients, Rasmussen encephalitis in six, malformation of cortical development in seven, and Sturge-Weber syndrome in two. Pre-operative EEG showed focal epileptiform discharges in the affected hemisphere in 26 patients and in both hemispheres in 19. Eleven patients had diffuse bisynchronous epileptiform discharges. Postoperative EEGs at six to 12 months after surgery showed slowing and attenuation of physiological rhythms on the operated side in all patients. Thirty-four patients (68%) had epileptiform discharges exclusively from the operated hemisphere, six (12%) had bilateral independent epileptiform discharges, nine (18%) had no epileptiform discharges on either side, and one (2%) had epileptiform discharges from the contralateral hemisphere only. Lateralized periodic discharges from the operated hemisphere were noted in three patients (6%). EEG seizures from the operated hemisphere without clinical signs were noted in four patients (8%). After a median follow-up of three years, 30 patients (60%) were off all antiseizure medications, including 8/9 (89%) patients with no epileptiform discharges, 20/34 (59%) patients with postoperative epileptiform discharges from the operated hemisphere, and 2/7 (28%) patients with contralateral discharges.

Significance. The majority of patients who are seizure-free after disconnective hemispherectomy will continue to show epileptiform discharges in the operated hemisphere. The presence of such discharges should not preclude tapering, nor prompt restarting of antiseizure medication in seizure-free patients.

Key words: postoperative EEG, hemispherectomy, epilepsy surgery, pediatric epilepsy surgery, hemispheric disconnection

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Hemispheric disconnection and various forms of hemispherotomy are common and effective forms of epilepsy surgery for children with hemispheric epilepsy syndromes, with long-term postoperative seizure freedom in up to two thirds of patients [1-5]. In seizure-free patients after epilepsy surgery, discontinuation of antiseizure medications (ASM) has been correlated with better cognitive outcome [6-8]. Discontinuation of ASM is often guided by the presence or absence of epileptiform abnormalities on post-operative EEG after epilepsy surgery. The presence of interictal epileptiform abnormalities on post-operative EEG has been shown in many studies to be predictive of seizure recurrence following various types of focal resections [9-14], but to our knowledge, there is limited data on the spectrum of the postoperative EEG findings after disconnective hemispherectomy, particularly in seizure-free patients [1, 4, 5-18]. The goal of this study was to clarify the predictive implications of epileptiform discharges from the disconnected hemisphere and to inform decisions about weaning off ASM in clinically seizure-free patients.

Methods

We identified 50 consecutive patients from the Cleveland Clinic epilepsy surgery database who were operated on between 2007 and 2017 and seizure-free at the last follow-up visit after disconnective hemispherectomy. Patients who underwent total anatomic hemispherectomy were not included. Seizure outcome was determined by our internal Epilepsy Surgery Outcomes Registry. All patients had a follow-up of at least one year after the surgery. The study was approved by the Cleveland Clinic Institutional Review Board.

Medical records were reviewed for clinical presentation, seizure description, etiology, neuroimaging findings, and preoperative EEG data. Neuroimaging and histopathology were reviewed for each patient for diagnosis. Abnormalities on brain MRI in the opposite hemisphere were categorized into three groups: subcortical abnormalities only, cortical abnormality in one lobe, and cortical abnormality in two or more lobes. Most patients had functional hemispherectomy, a form of hemispheric disconnection, with resection of the temporal lobe and central regions. A few patients had more extensive tissue resection in the posterior quadrant or frontal region, along with hemispheric disconnection. All patients underwent prolonged video-EEG monitoring prior to surgery.

Findings on preoperative EEG were categorized as ipsilateral epileptiform discharges without generalization, ipsilateral epileptiform discharges with generalization, multiregional epileptiform discharges, generalized/diffuse bisynchronous epileptiform discharges and no epileptiform discharges. Features of epileptic encephalopathy such as hypsarrhythmia, pervasive slow-spike-wave complexes and electrical status epilepticus in sleep were noted when present. Seizures were noted as focal or generalized or both, epilepsia partialis continua was noted if present, and ictal EEG findings were assessed as concordant or discordant with the hemisphere that was planned for surgery. All EEGs were interpreted by board-certified epileptologists at the Cleveland Clinic.

Acute post-operative seizures that occurred in the first week after surgery were noted. By design of the study, patients who had seizures after the first week were not included in the study. All patients had a minimum of one year of follow-up. ASM status at the last follow-up visit was documented regarding the number of medications.

All patients had postoperative EEG at six months or one year after surgery. Postoperative interictal epileptiform findings were categorized based on distribution. Lateralized periodic discharges and subclinical electrographic seizures were also noted. Abnormalities in the contralateral unoperated hemisphere were also documented.

Results

Fifty seizure-free patients were identified with a median follow-up of three years (mean: 3.8 years; range: 1-14 years). Twenty-six were males (52%). Forty-seven patients (94%) had functional hemispherectomy, and three (6%) had more extensive tissue resection in the posterior quadrant or frontal region along with hemispheric disconnection. Right hemispherectomy was performed in 23 (46%) patients. Two patients had acute post-operative seizures within the first week of hemispherectomy, with no further seizures afterwards.

Age at time of surgery ranged from eight months to 21 years (mean: 7.5 years; median: 6 years). Age at seizure onset ranged from one day after birth to 11 years of age. A single seizure type was reported in 30 patients (60%), and others (40%) had more than one seizure type. Gliosis and residual effects from vascular lesions, including perinatal stroke, were the most common etiologies in 35 (70%) patients. Other etiologies included malformation of cortical development in seven patients, Rasmussen encephalitis in six patients, and Sturge-Weber syndrome in two patients. Brain MRI showed some abnormalities in the unoperated hemisphere in 16 patients. These included subcortical white matter abnormalities in six patients and cortical abnormality in one or more lobes in 10

▼ **Table 1.** Preoperative EEG findings in 50 patients.

Interictal epileptiform EEG findings	
Ipsilateral epileptiform discharges without generalization	22 (44%)
Ipsilateral epileptiform discharges with generalization	4 (8%)
Bilateral independent discharges without generalization	16 (32%)
Bilateral independent discharges with generalization	3 (6%)
Diffuse bisynchronous/ generalized epileptiform discharges only	4 (8%)
No epileptiform discharges	1 (2%)
Epileptic encephalopathy in 12 patients	
Hypsarrhythmia	5 (10%)
Slow spike-and-wave complexes	4 (8%)
Continuous spike-waves during sleep	3 (6%)
Seizure types	
Focal seizures only	29 (58%)
Generalized seizures only	11 (22%)
Focal and generalized seizures	7 (14%)
No seizures recorded during video-EEG	3 (6%)
Semiology assessed on video-EEG	
Focal seizure with concordant / lateralizing sign(s)	33 (66%)
Focal seizure without concordant / lateralizing sign	4 (8%)
Generalized seizures only- spasms, tonic, myoclonic	10 (20%)
No seizures	3 (6%)
Epileptia partialis continua	4 (8%)
Ictal EEG findings	
Concordant ipsilateral hemisphere	36 (72%)
Generalized/non-localized	11 (22%)
No seizures recorded	3 (6%)

patients. FDG-PET was performed in 27 patients and showed unilateral abnormalities in the operated hemisphere in 17 patients; 10 patients had bilateral PET abnormalities, typically worse on the side of surgery.

Preoperative EEG findings are summarized in *table 1* table 1. Post-operative EEGs were performed at six months or one year after the surgery. Thirty-nine patients underwent outpatient EEG lasting for more than one hour, four had a 20-minute outpatient EEG, and seven underwent EEG recording for 24 hours or longer. Thirty-five of 50 patients slept during the EEG recording. Postoperative EEG findings are summarized in *table 2* table 2.

Forty patients (80%) had epileptiform discharges from the operated hemisphere, as shown in *figures 1-3*. These discharges were frequently abundant and repetitive. The detection of spikes in the operated hemisphere was not affected by the duration of recording. Of 10 patients who did not have spikes in the operated hemisphere, eight patients had outpatient EEG lasting for more than one hour, one had 24-hour ambulatory EEG, and another had a 20-minute EEG. Of 15 patients with no sleep recording, 12 had spikes in the operated hemisphere; conversely, of 35 patients with sleep recording, 28 had spikes in the operated hemisphere. The presence or absence of sleep during the recording and the duration of the recording had not effect on the yield of epileptiform discharges in the disconnected hemisphere. Among the 40 patients who had persistent epileptiform abnormalities in the operated hemisphere, the average age at surgery was 7.05 years (SD = 5.34). Among the 10 patients with no epileptiform abnormalities, the

▼ **Table 2.** Post-operative EEG findings in 50 patients.

Background slowing and attenuated sleep structures- on the operated side	50
Epileptiform discharges	
Present	41 (82%)
Operated hemisphere only	34 (68%)
Both hemispheres	6 (12%)
Unoperated opposite hemisphere only	1 (2%)
No epileptiform discharges on either side	9 (18%)
Location of ipsilateral epileptiform discharges	
Frontal/fronto-polar only	7 (14%)
Centro-temporo-parietal only	8 (16%)
Fronto-temporal only	3 (6%)
Occipital only	2 (4%)
Combination of the above discharges	20 (40%)
No epileptiform discharges	10 (20%)
Vertex/ midline epileptiform discharges	
Midline with maximum on the ipsilateral side	12 (24%)
Midline with maximum on the contralateral side	2 (4%)
Lateralized periodic discharges (LPDs)	3 (6%)
EEG seizures from the operated side without clinical signs	4 (8%)
Location of contralateral epileptiform discharges	
Lateralized to the hemisphere	2 (4%)
Frontal or fronto-temporal	3 (6%)
Centro-parietal	2 (4%)

average age at surgery was 9.46 years (SD = 3.91). A two-sample t-test indicated no significant difference in age between these two groups (p=0.124).

Seven patients had epileptiform discharges noted in the contralateral hemisphere. These were sporadic and infrequent in every case. Only one of the seven patients with epileptiform discharges in the contralateral hemisphere had structural abnormalities on that side based on brain MRI. The other 15 patients with structural abnormalities in the contralateral hemisphere had no epileptiform discharges in that hemisphere. Generalized/diffuse bisynchronous epileptiform discharges were not recorded postoperatively in any patient, including the 11 who had generalized interictal epileptiform discharges on preoperative EEG. Postoperative EEG in all 12 patients with features of epileptic encephalopathy showed resolution of these findings. Two of these patients had sporadic rare epileptiform discharges in the opposite hemisphere.

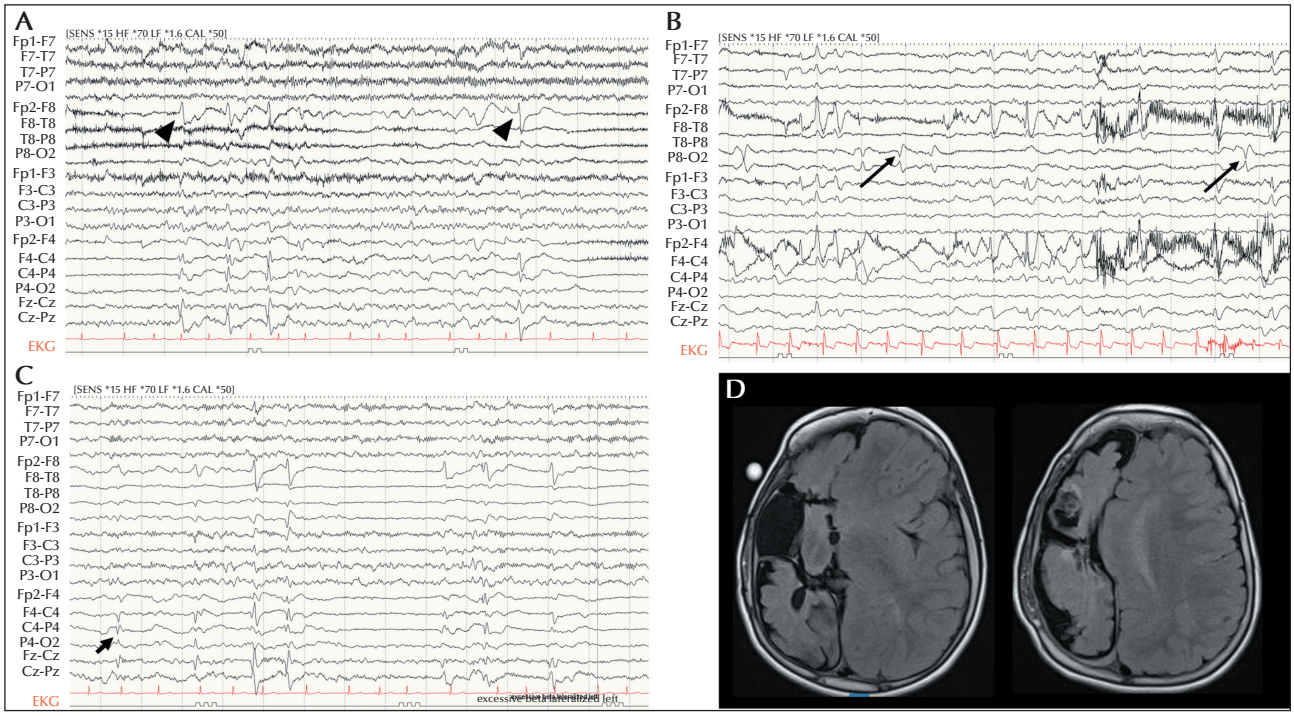
Of the nine patients with no epileptiform discharges in either hemisphere, two had prenatal/brain malformation, six had residual effects secondary to ischemic injury, and one had Rasmussen encephalitis. There was no correlation between the nature of etiology and the presence or absence of spikes on the postoperative EEG.

In four patients with EEG seizures in the operated hemisphere, patients had no clinical signs during these seizures and the EEG seizures remained in the affected hemisphere without spread to the opposite side (*figure 4*). Each seizure lasted for 1-3 minutes, and often occurred every 10-20 minutes. Two of these patients had Rasmussen encephalitis, and two had residual effects secondary to ischemic injury.

At the last follow-up visit, 30 patients (60%) were off all ASM, including 8/9 (89%) patients with no epileptiform discharges, 20/34 (59%) patients with postoperative epileptiform discharges from the operated hemisphere, and 2/7 (28%) patients with contralateral discharges (differences were not significant). Among the 20 patients still taking ASM at the last follow-up visit, 15 were on one medication, four were on two medications, and one was on three medications.

Discussion

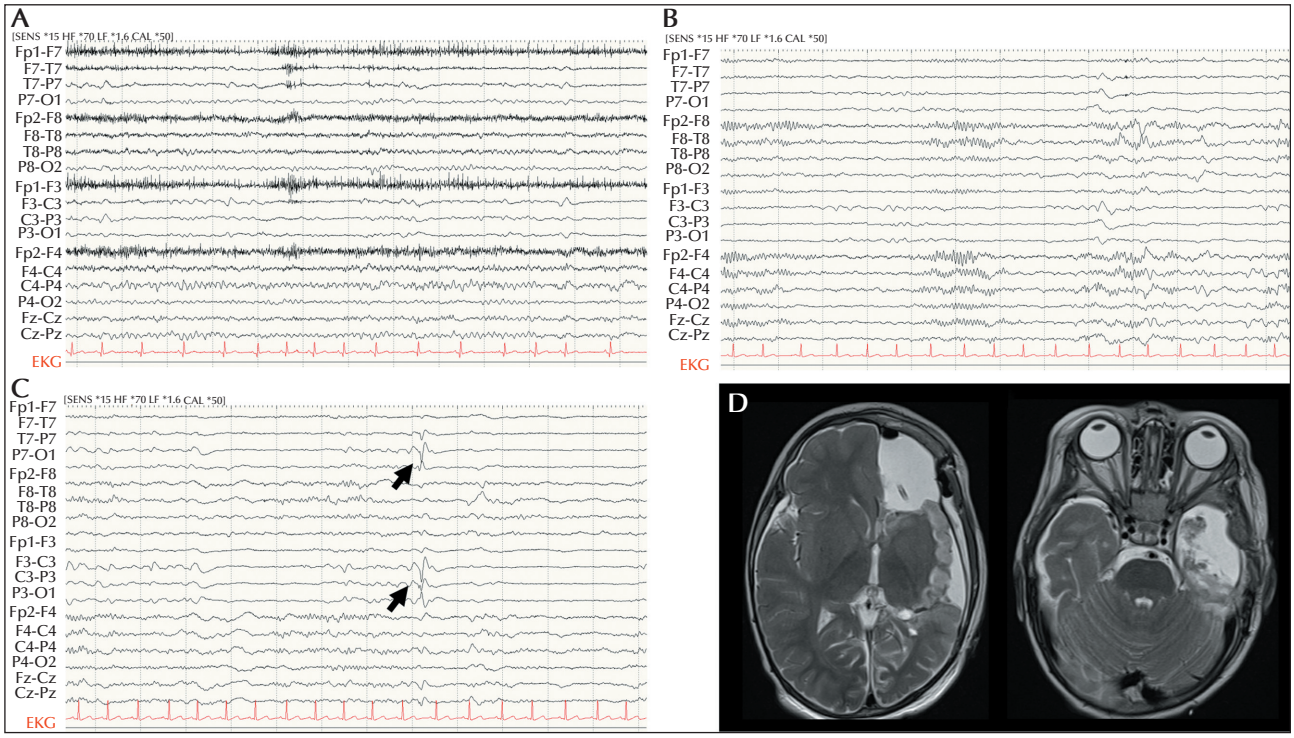
This study highlights the common interictal EEG findings after hemispheric disconnection in seizure-free patients after surgery. The majority of these



■ **Figure 1.** EEG of a seven-year-old boy after right functional hemispherectomy for epilepsy due to right hemispheric malformation. (A, B, C) Interictal EEG showing continuous slowing and attenuation of physiological rhythms in the disconnected right hemisphere and multiregional epileptiform discharges in right frontal (A); arrow heads), right temporoparietal (B); long arrow), and right centro-parietal (C); short arrow) areas. The right frontal discharges were widely expressed in the parasagittal vertex regions (A). (D) Axial FLAIR images of brain MRI demonstrate changes after right functional hemispherectomy. The child has been seizure-free since surgery, after one year of follow-up.

patients, 80%, continued to show epileptiform discharges from the operated hemisphere. These discharges were often abundant, at times seen in the form of periodic lateralized epileptiform discharges or subclinical EEG seizures, and yet clinical seizures did not recur in any of the 20 such patients who had discontinuation of all ASMs. These results indicate that the presence of interictal epileptiform discharges and EEG seizures should not preclude the discontinuation of ASM in patients who are clinically seizure-free after disconnective hemispherectomy. Our results suggest that in children with MRI and EEG features limited to the operated hemisphere, weaning off ASM after disconnective hemispherectomy is an appropriate option.

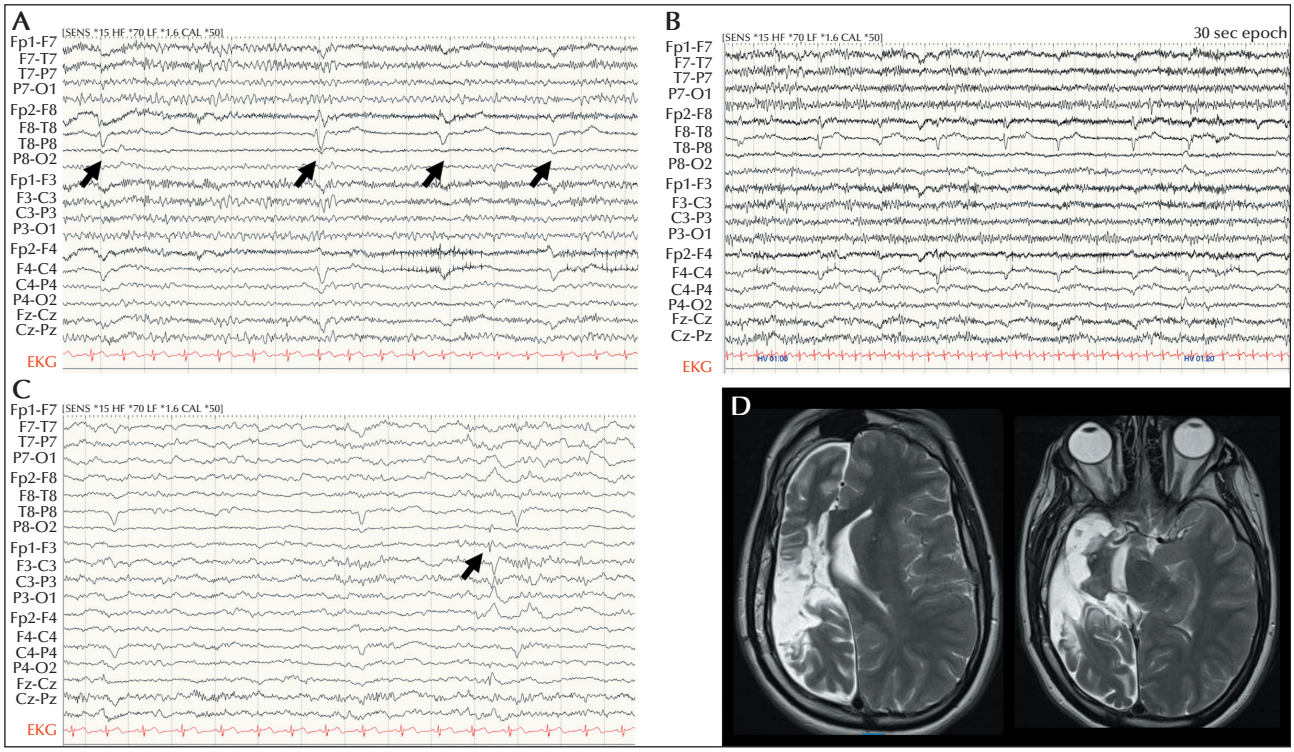
Limited previous data are available on the postoperative EEG findings after disconnective hemispherectomy [1, 2, 4, 15-16]. In a study of postoperative EEG findings after disconnective hemispherectomy in 24 patients, 12 had no epileptiform discharges, eight had epileptiform discharges exclusively in the disconnected frontal and/or occipital regions, and four had epileptiform discharges in the non-operated hemisphere [17]. Epileptiform discharges were reported to be in isolation and not in runs, and subclinical EEG seizures were not seen. Seizure recurrence occurred in all four with contralateral epileptiform discharges, and one with no epileptiform discharges. In another series of 14 patients, 10 had "no further epileptiform abnormalities", two had rare non-rhythmic spikes over the frontal region on the operated side, and two patients had epileptiform discharges over the unoperated side [18]. Findings were similar in nine of the 14 patients who had late postoperative EEG in this series [18]. None of the studies on large series with hemispherectomy reported findings from postoperative EEG [1, 2, 4, 15-16]. In our report, consisting exclusively of seizure-free patients, we noted a higher frequency of epileptiform discharges from the operated hemisphere. We also noted lateralized periodic discharges and subclinical EEG seizures, not previously reported.



■ **Figure 2.** EEG of an eight-year-old child after modified anatomic left hemispherectomy for epilepsy due to left hemispheric Sturge-Weber syndrome. (A-C) Interictal EEG shows continuous slowing (A) and absence of sleep spindles (B, C) in the operated hemisphere; sporadic sharp waves are noted in the left centro-parieto-temporal region (C); arrows). (D) Resection of the left frontal region and temporal lobe. The child has remained seizure-free since surgery after six years of follow-up.

Early "anatomic" hemispherectomy surgeries involved complete resection of the abnormal hemisphere [19-21]. In such instances, marked attenuation of the EEG on the affected side was the expected finding [21]. With complete removal, no epileptiform abnormalities were expected to be present over the side of anatomic hemispherectomy. Subsequently, several variations in hemispheric disconnection were practiced in centers worldwide to minimize the risk of hydrocephalus and other delayed complications [3, 16, 22-23]. The amount of hemispheric tissue resected varied depending on the type of hemispheric disconnection. With these hemispheric disconnection procedures, much of the abnormal hemisphere was left *in situ* with an intact blood supply. In such settings, the residual disconnected cortex with intact blood supply may continue to show electrical activity including epileptiform discharges, in addition to attenuated background rhythms and sleep structures, and excessive slowing [17].

In our study of seizure-free patients who had disconnective hemispherectomy, we found that epileptiform discharges on postoperative EEG were the norm rather than the exception. Epileptiform discharges may also occur as periodic lateralized discharges, often with regional localization. Some patients, 8% in our series, may also have subclinical seizures, a finding not reported previously. These EEG seizures were frequently repetitive, occurring several times in an hour. With appropriate effective hemispheric disconnection, these EEG seizures do not produce clinical seizures and do not spread to the opposite hemisphere. Hence, these epileptiform discharges and EEG seizures without clinical signs in the disconnected hemisphere have no clinical relevance in a patient who is clinically seizure-free. Generalized epileptiform discharges were not recorded in any patients postoperatively, including the 11 who had generalized interictal epileptiform discharges on their preoperative EEG. This supports the view that these apparent generalized discharges were a result of "secondary bilateral synchrony", and these generalized discharges should not preclude surgery in this setting [24].

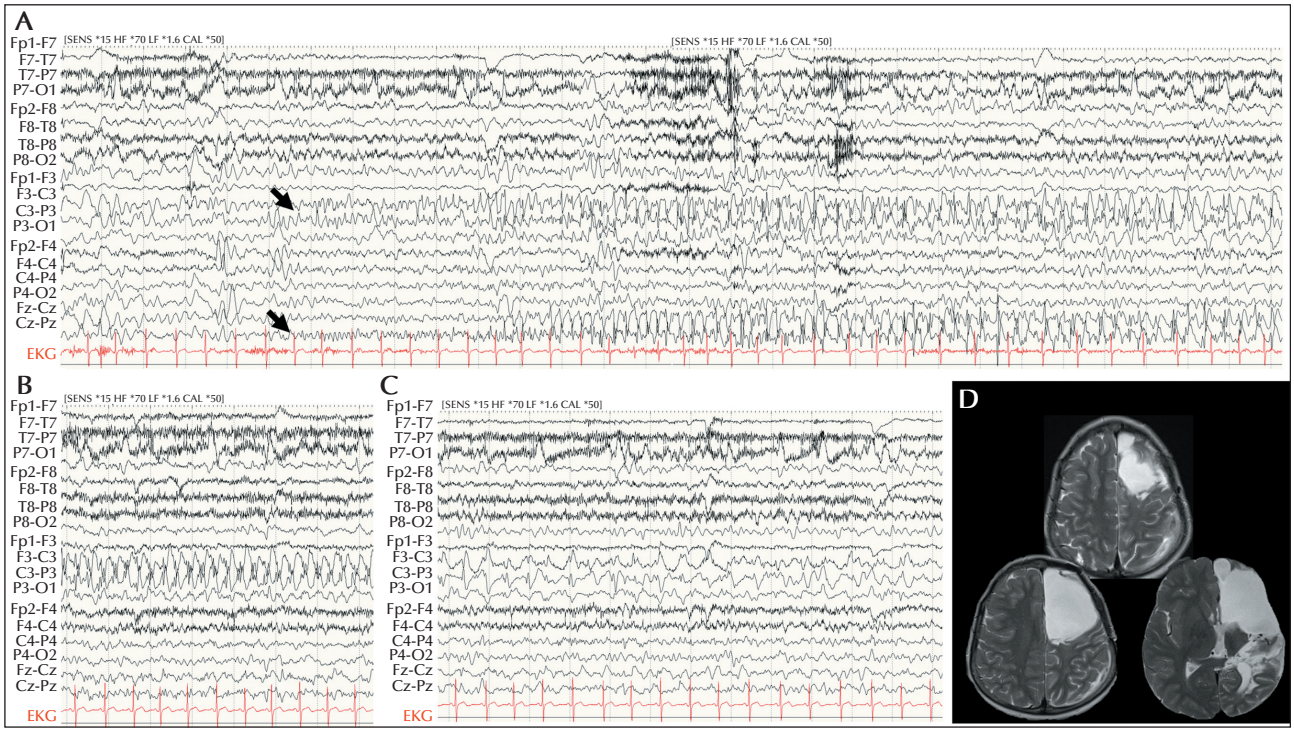


■ **Figure 3.** EEG of an 18-year-old patient after right functional hemispherectomy for epilepsy due to remote hemispheric infarct. (A-C) Interictal EEG shows attenuation of background rhythms in the right hemisphere and lateralized periodic discharges over the right frontal region (arrows). (B) A 30-sec epoch shows the repetitive periodic nature of the discharges. (D) Resection of the temporal and central regions. The patient has been seizure-free since surgery after five years of follow-up.

The decision to wean off ASM in seizure-free patients after epilepsy surgery is often guided by postoperative EEG at six months or a year after surgery. After hemispheric disconnection, interictal epileptiform discharges from the operated hemisphere should be considered as typical and expected, and should not impact the decision to wean off medication. This is in contrast to lobectomy and lesionectomy, for which the weaning decisions may be influenced by the presence or absence of epileptiform discharges on the side of surgery [9, 10]. The purpose of performing postoperative EEG in seizure-free patients after disconnective hemispherectomy would be to assess their potential for seizures arising from the opposite hemisphere.

Prior studies on hemispherectomy have reported epileptiform abnormalities from the contralateral hemisphere on postoperative EEG to be predictive of seizure recurrence [2, 25]. In seizure-free patients, even in the presence of contralateral epileptiform abnormalities, the decision to wean off ASM should be individualized and one may elect to minimize the medication burden if a patient is on multiple medications. In our experience, the epileptiform discharges from the contralateral hemisphere in seizure-free patients were sparse and infrequent, and two of the seven patients with such discharges were successfully weaned off ASM in this study. A similar observation has been made by others [26].

In our series, 40% of patients remained on one or more ASMs despite being seizure-free at the last follow-up visit, due to family or physician preference. It is possible that with longer follow-up, more patients may be weaned off their ASM. In hemispherectomy series, medication-free status in seizure-free patients ranged from 54% to 76% [2, 4, 27]. In a study with longitudinal follow-up, 58% of 71 patients were seizure-free at five years, whereas only 38% were no longer taking ASM at five years [1]. In another study of 47 adults who had hemispherectomy, at a mean follow-up of 5.4 years, only 15% of seizure-free patients were medication-free [25]. In our study, all



■ **Figure 4.** A routine outpatient EEG of a six-year-old child with Rasmussen encephalitis, after modified left anatomic hemispherectomy. The EEG shows a subclinical electrographic seizure arising from the left centro-parietal and vertex region (A); arrows), evolving and ending in the same region (B, C). The seizure lasted approximately four minutes, and recurred multiple times an hour. There was no spread to the other hemisphere. (D) Resection of the left frontal region. The child has been seizure-free since surgery after 18 months of follow-up.

except one (of nine patients) with no epileptiform discharges on either side had been weaned off their ASM, but about 41% of patients with ipsilateral epileptiform discharges remained on medications. Our study was not designed to determine if the decision to remain on medications was influenced by family or physician, but our results suggest that in patients with ipsilateral epileptiform discharges, this may have been an influencing factor. Successful weaning off ASM in 59% of those with persistent epileptiform discharges in the operated hemisphere suggests that ASM could be safely tapered in such patients.

Epileptologists familiar with post-hemispherectomy EEG are less likely to be perturbed by the findings of epileptiform discharges or subclinical seizures in the operated hemisphere. However, any decision to wean off ASM after successful epilepsy surgery is influenced by the patients' and their families' preferences and risk averseness. Appropriate pre-operative counseling about the likely possibility of persistent epileptiform abnormalities on postoperative EEGs would alleviate the patients' and caregivers' concerns of seizure recurrence with weaning off medications. This counseling should be reinforced at the time of weaning off medications in order to avoid overzealous interpretation of expected benign findings if a patient were to undergo EEG testing later in life for other reasons.

Conclusion

Persistent epileptiform abnormalities and even subclinical EEG seizures on the side of surgery are a common finding after hemispheric disconnection. Such abnormalities are not clinically relevant in seizure-free patients. ASMs may be safely weaned off and stopped in clinically seizure-free patients despite epileptiform discharges in the operated hemisphere. Similarly, the presence of such findings should not prompt restarting ASM later in life in seizure-free patients whose drugs have been withdrawn. ■

Key points

- The majority of patients who are seizure-free after disconnective hemispherectomy will continue to show epileptiform discharges in the operated hemisphere.
- EEG seizures in the operated hemisphere may also occur in 8% of seizure-free patients, with no clinical signs.
- The disconnected hemisphere may continue to show epileptiform discharges but will not cause clinical seizures after effective hemispheric disconnection.
- Epileptiform abnormalities on EEG on the operated side should not preclude tapering, nor prompt restarting of antiseizure medication in seizure-free patients.

Supplementary material.
Summary slides accompanying the manuscript are available at www.epilepticdisorders.com.

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TEST YOURSELF

(1) A six-year-old boy with daily multiple seizures due to right hemispheric Rasmussen encephalitis had right disconnective hemispherectomy. He was seizure-free after surgery, and remained on two medications at therapeutic doses. After one year of follow-up, a 75-minute EEG showed four subclinical seizures from the right hemisphere. He had no clinical symptoms during the EEG seizures and the seizure did not spread to the left hemisphere. The next appropriate step is:

A. Admit for long-term inpatient monitoring for further study
B. Add another antiseizure medication for better control of these seizures
C. Perform brain MRI to look for any incomplete disconnection
D. In clinically seizure-free patients, these subclinical EEG seizures limited to the disconnected hemisphere are not a cause for concern

(2) Which of the following is NOT an expected finding on post-operative EEG in seizure-free patients after successful disconnective hemispherectomy?

A. Focal sharp waves in the operated hemisphere
B. Frequent multi-regional sharp waves in the operated hemisphere
C. Frequent generalized epileptiform discharges
D. Lateralized periodic discharges in the operated hemisphere

(3) According to this study, what percentage of seizure-free patients after disconnective hemispherectomy will continue to show epileptiform discharges in the operated hemisphere?

A. 80%
B. 40%
C. 50%
D. 20%

Note: Reading the manuscript provides an answer to all questions. Correct answers may be accessed on the website, www.epilepticdisorders.com.