Address correspondence to Dr John W. Miller, Harborview Medical Center, Box 359745, 325 Ninth Avenue, Seattle, WA 98104, millerjw@u.washington.edu.

Relationship Disclosure: Dr Miller receives research support from the Centers for Disease Control and Prevention, the NIH, Sunovion Pharmaceuticals, Inc, and UCB. Dr Hakimian has served as a consultant for OptumRx, Inc, and receives grants from the NIH.

Unlabeled Use of Products/Investigational Use Disclosure:

Drs Miller and Hakimian report no disclosures.
© 2013, American Academy of Neurology.

Surgical Treatment of Epilepsy

John W. Miller, MD, PhD; Shahin Hakimian, MA, MD

ABSTRACT

Purpose of Review: This article outlines indications for neurosurgical treatment of epilepsy, describes the presurgical workup, summarizes surgical approaches, and details expected risks and benefits.

Recent Findings: There is class I evidence for the efficacy of temporal lobectomy in treating intractable seizures, and accumulating documentation that successful surgical treatment reverses much of the disability, morbidity, and excess mortality of chronic epilepsy.

Summary: Chronic, uncontrolled focal epilepsy causes progressive disability and increased mortality, but these can be reversed with seizure control. Vigorous efforts to stop seizures are warranted. If two well-chosen and tolerated medication trials do not achieve seizure control, an early workup for epilepsy surgery should be arranged. If this workup definitively identifies the brain region from which the seizures arise, and this region can be removed with a low risk of disabling neurologic deficits, neurosurgery will have a much better chance of stopping seizures than further medication trials.

Continuum (Minneapolis) 2013;19(3):730–742.

REASONS FOR EPILEPSY SURGERY

About one-third of epilepsy patients have seizures that cannot be controlled with medication.^{1,2} This has severe consequences, including interference with school and work, loss of independence and social isolation, and increased risk of injury, depression, and suicide.^{3–5} Patients with uncontrolled epilepsy also have a significantly increased long-term mortality rate (1.59% per year), with sudden unexpected death in epilepsy (SUDEP) being the most common cause.⁶ Furthermore, uncontrolled temporal lobe epilepsy is associated with slowly progressive cortical atrophy and cognitive deterioration.^{7,8}

For selected patients, resection of epileptogenic brain has a far better chance of controlling drug-resistant

seizures than further medication trials. There is also class I evidence for the efficacy of temporal lobectomy⁹ and evidence that successful neurosurgical treatment reverses much of the disability and increased mortality of chronic epilepsy.^{10,11} For all of these reasons, clinicians treating chronic epilepsy must recognize which patients to refer for epilepsy surgery and what it can accomplish.

CANDIDATES

Resective surgery is a consideration in patients with drug-resistant, uncontrolled, disabling focal epilepsy if the seizures originate from a region that can be removed with minimal risk of disabling neurologic or cognitive dysfunction. Epilepsy is termed drug-resistant when two tolerated, appropriately chosen and used antiepileptic drugs (AEDs)

fail to achieve sustained seizure freedom.¹² Response to an additional medication trial ranges from 4% to 16% in different studies^{2,13} but depends on epilepsy syndrome and etiology.^{14,15} Patients with drug-resistant seizures should have an epilepsy center evaluation to confirm the diagnosis and determine the epilepsy syndrome and possible candidacy for neurosurgery. Vagus nerve stimulation is not more effective than AEDs and has a very low chance of achieving seizure freedom in drug-resistant epilepsy, so it should not be considered before resective surgery, and should be reserved for patients who are poor candidates or who refuse surgery.¹⁶

Patients with lesional epilepsy respond more poorly to AEDs than those with cryptogenic/idiopathic epilepsy but have a better chance of seizure freedom with surgery.^{14,15} Therefore, those with chronic, intractable epilepsy due to discrete lesions such as mesial temporal sclerosis (MTS), low-grade neoplasms, vascular malformations, encephalomalacia from stroke or trauma, and focal cortical dysplasias are common surgical candidates. Good surgical outcomes are also possible in patients with normal MRI if the seizures are electrographically well localized to the temporal lobe.^{17–20}

Identifying the seizure focus in patients with normal MRI and neocortical epilepsy is much more difficult. They may still be surgical candidates if electrographic seizures are clearly localized, and other tests, such as invasive video-EEG monitoring, positron emission tomography (PET), or ictal single-photon emission computed tomography (SPECT) confirm the location of the epileptic focus. Sometimes focal cortical dysplasia is documented postoperatively in such seemingly nonlesional cases. Because the chance of seizure freedom with surgery is lower in

these patients,^{21,22} and the chances of achieving seizure control with medication is somewhat higher with cryptogenic epilepsy,^{14,15} these individuals typically will receive more than two medication trials before surgery is considered.

Patients who are typically not surgical candidates include those with clear evidence of bilateral onset of habitual seizures (**Case 9-1**), those with severe psychiatric or medical comorbidities increasing surgical risk or compromising recovery, those with rapidly progressive CNS disease, and those with primary generalized epilepsy.

SURGICAL WORKUP

Initial Evaluation

Upon referral, the patient undergoes a detailed neurologic history and examination, neuroimaging, video-EEG monitoring, and neuropsychological testing. MRI at 3 Tesla should include coronal fine cuts of T1- and T2-weighted and fluid-attenuated inversion recovery (FLAIR) sequences to detect signal change and atrophy or loss of internal structure with hippocampal sclerosis, and detailed imaging of other regions suspected as sites of seizure origin from history or other tests.²³ Focal cortical dysplasia may be subtle; sometimes meticulous inspection will reveal mild cortical thickening or an unusually deep sulcus, but special image analysis techniques can help.²⁴

Long-term video-EEG monitoring with scalp electrodes is essential to confirm and localize focal epilepsy. If possible, several seizures should be captured to confirm a single focus. Interictal spikes also aid localization. Standard 10:10 scalp electrode placement is performed, sometimes with bilateral infratemporal electrode chains or other additional electrodes over the likely seizure-onset region. Dense array video-EEG monitoring, usually with 256 electrodes, also improves localization, especially in neocortical epilepsy (**Figure 9-2**).²⁵

KEY POINTS

- About one-third of patients with epilepsy have seizures that cannot be controlled with medication.
- Uncontrolled epilepsy causes progressive disability and increased mortality risk.
- Resective epilepsy surgery requires definite demonstration that the seizures originate from a region that can be removed with minimal risk of disabling neurologic or cognitive dysfunction.
- Epilepsy is termed drug-resistant when two appropriate, tolerated medications fail to control seizures.
- Epilepsy surgery should be considered in drug-resistant cases before the vagus nerve stimulator.
- Lesional epilepsy has a poorer response to medications than cryptogenic/idiopathic epilepsy but a better chance of seizure freedom with epilepsy surgery.

Case 9-1

A 44-year-old, right-handed man had cryptogenic epilepsy since age 18, with weekly seizures refractory to eight antiepileptic drug trials. His seizures were nocturnal (he made noises, thrashed, and wandered around), and convulsions were infrequent. Scalp EEG showed independent left and right anterior temporal epileptiform abnormalities in equal proportions, and three seizures with right anterior temporal ictal EEG changes. Repeat EEG monitoring captured three left temporal seizures and a right temporal seizure with different semiology. Single-photon emission computed tomography (SPECT) injection during a seizure with right temporal EEG changes showed right temporal hyperperfusion (Figure 9-1). The patient's MRI results were normal.

Comment. While this patient has focal onset epilepsy, there is no clear evidence all seizures are arising from a single focus (in fact, the data suggest otherwise). The normal MRI results do not provide any evidence to localize the seizures, and the EEG indicates that the seizures arise independently from the right and left temporal lobe. This patient is not a surgical candidate since only unilateral resections can be safely performed. Bilateral mesial temporal lobe resection or injury may lead to devastating global amnesia.

FIGURE 9-1 Single-photon emission computed tomography (SPECT), subtracting interictal from ictal images. Lavender patches mark area of hyperperfusion in right temporal lobe (arrow).

Neuropsychological testing establishes baseline measurements of any cognitive deficits, sometimes giving insight into the epileptic focus location.²⁶ It also allows comparison with postoperative testing to measure cognitive outcomes. Predictors of higher risk of cognitive decline after temporal lobectomy include intact baseline cognitive

ability, dominant temporal lobe resection, later age of epilepsy onset, normal MRI results, female gender, and loss of memory function during injection of amobarbital into the carotid artery on the side of planned surgery (the intracarotid amobarbital procedure [Wada test] is discussed below under “Functional Localization”).^{26,27}

FIGURE 9-2

Right temporal seizure on 256-channel scalp EEG recording. The underlying recording shows a subset of the recorded channels with the *black arrow* pointing to a cursor placed shortly after the seizure onset. Activity on all channels at the time of the cursor is displayed in the insert on upper left (anterior is superior, right hemisphere on the right), with the *orange arrow* pointing toward the right temporal ictal discharge. The insert at the bottom left shows source localization of the ictal activity at the time of the cursor to the right mesial temporal region (*white arrow*).

Further Noninvasive Assessment

Localization of the epileptic focus requires that different tests give congruent information. 18F-fluorodeoxyglucose (FDG) PET, which measures interictal cerebral glucose, is particularly useful for additional confirmation (**Figure 9-3**). Unilateral temporal lobe hypometabolism on 18F-FDG-PET strongly predicts seizure freedom with resection of that temporal lobe, independent of MRI findings.²⁸ Another approach is ictal SPECT, which images cerebral blood flow with a radioactive tracer (usually ^{99m}Tc–hexamethylpropylene amine oxime [HMPAO]). This tracer is injected intravenously as early as possible during a seizure and is taken up by tissue on its first pass through the brain, producing a “snapshot” of ictal blood flow. Imaging is enhanced by digital subtraction of a second image taken after an interictal injection; this subtracted image can be coregistered

with MRI.²⁹ SPECT is a powerful method for confirming localization of both mesial temporal and cortical seizures.³⁰ Other imaging modalities include PET with other tracers, including agents binding to opioid, benzodiazepine, dopamine, or serotonin receptors, and magnetic resonance spectroscopy that can detect decreased *N*-acetylaspartate (NAA) concentration in mesial temporal epilepsy. Magnetoencephalography can better localize interictal spikes in three dimensions, but is not suitable for recording and localizing actual seizures.^{31,32}

Invasive Video-EEG Monitoring

This is performed when noninvasive testing suggests a resectable epileptic focus with some uncertainty. Invasive video-EEG can also more precisely delineate the extent of a neocortical epileptogenic zone and its relationship to areas of eloquent functional cortex. Arrays of disk electrodes embedded in sheets or strips of silastic are usually subdurally implanted. Depth electrodes can also be inserted into the brain, typically to record from deeper structures, although some centers also use these for cortical recordings. Monitoring occurs in the patient's room over several days to localize typical seizures.

Functional Localization

Defining speech and language dominance for temporal and some frontal resections is necessary. In addition, eloquent cortices essential for language, motor, or sensory functions must often be delineated so resection can be tailored to avoid causing deficits.

The intracarotid amobarbital procedure is the best validated method of determining the speech dominant hemisphere and can also assess risk of postoperative memory deterioration after temporal lobectomy.^{26,27} Amobarbital or another anesthetic is

FIGURE 9-3

Positron emission tomography (PET) of a woman with prior resection of a right temporal oligodendroglioma and bitemporal seizures, showing right lateral temporal hypometabolism (dark orange area marked by white arrow) and left mesial temporal hypometabolism (dark orange area marked by blue arrow).

injected into the internal carotid artery, temporarily disrupting function on that side, while language and memory tests are performed. In addition, functional MRI and magnetoencephalography are being developed as alternatives for lateralizing or localizing temporal language function.^{33,34}

Although functional MRI can be used to locate functional neocortex and associated connections, the standard approach in epilepsy surgery is mapping by electrical cortical stimulation. This can be carried out intraoperatively (during brief period of wakefulness during the operation) or at bedside with the same subdural electrodes used for invasive EEG monitoring. Mapping of temporal language cortex then is done with the patient naming objects displayed on a computer screen while the physician systematically maps cortex by stimulating various brain regions.

COMMON SURGICALLY TREATABLE EPILEPSY SYNDROMES

Mesial Temporal Lobe Epilepsy

Mesial temporal lobe epilepsy is the most common surgically treated epilepsy, with efficacy of lobectomy demonstrated in a randomized controlled trial.⁹ Seizures often begin with rising epigastric sensations, smells, fear, déjà vu or jamais vu, and progress to loss of responsiveness, often with behavioral arrest, orofacial automatisms, ipsilateral hand movements, and contralateral arm posturing. The most common associated pathology is MTS (Case 9-2), which may be associated with a history of early-life febrile seizures or neurologic insult, and is pathologically characterized by hippocampal neuronal loss in CA1 and CA3 as well as the dentate granule cell layer.³⁵ Identical seizures can result from mesial temporal tumors, vascular malformations, and dysplasia. A few MTS pa-

tients have a second, ipsilateral cortical focus (ie, “dual pathology”), with better surgical outcome if the second focus can also be resected.³⁶

The most common surgical procedure for mesial temporal epilepsy is the anterior temporal lobectomy, in which the temporal pole is removed to allow resection of the hippocampus and part of the amygdala. The anterior temporal resection may be measured (4.0 to 4.5 cm from the temporal tip on the dominant side, and 5.0 to 5.5 cm on the nondominant side).³⁷ Cortical resection can also be tailored based on language mapping (because temporal language cortex location is variable)³⁸ and intraoperative electrocorticography, and the extent of hippocampal resection may be determined by the presence of interictal epileptiform discharges along its length.³⁹ Alternate techniques to amygdalohippocampectomy include approaches through the superior temporal gyrus, the middle temporal gyrus, the basal temporal cortex, or parahippocampal gyrus.^{40–42} Radiosurgery and MRI-guided laser ablation of the hippocampus are also being investigated as alternative approaches to treat hippocampal epilepsy while reducing injury to other nearby temporal structures.⁴³

Neocortical Epilepsy

The clinical manifestations of neocortical epilepsy depend on the region involved.⁴⁴ Lateral temporal lobe seizures are more likely to have experiential auras and less likely to have epigastric auras and contralateral dystonia. Frontal lobe seizures tend to be shorter and more frequent than temporal lobe seizures, with manifestations varying from motionless staring to violent automatisms, and often may be confined to sleep. Parietal and occipital seizures often have complex sensory symptoms such as visual hallucinations

KEY POINT

- The effectiveness of temporal lobectomy for mesial temporal epilepsy has been demonstrated in a randomized controlled trial.

Case 9-2

A 34-year-old, right-handed woman presented with a history of status epilepticus of unknown cause at age 3, and subsequent complex partial seizures with orofacial automatisms and postictal aphasia that were refractory to five antiepileptic drugs. EEG showed interictal left anterior temporal sharp waves and left temporal seizures, and MRI demonstrated left mesial temporal sclerosis (**Figure 9-4**). The patient became seizure free after a left temporal lobectomy.

Comment. Mesial temporal epilepsy is a highly surgically remediable epilepsy syndrome, with anterior temporal lobectomy often offering an excellent chance for seizure freedom.

FIGURE 9-4

MRI showing left mesial temporal sclerosis (arrow) with a smaller hippocampus with increased signal and loss of internal architecture.

FIGURE 9-5

Right inferior frontal ganglioglioma (arrow) in a 29-year-old man with lifelong intractable epilepsy that was later successfully treated with surgery.

of objects or scenes. Convulsive seizures are more common with neocortical epilepsy. With neocortical foci, invasive monitoring is usually required for adequate localization and tailoring of the resection to spare eloquent cortex. Surgical procedures range from topectomy (ie, removal of cortex while sparing underlying white matter), to lesionectomy with removal of adjacent epileptogenic cortex, to lobar and multilobar resections.

Epilepsy Due to Tumors

Benign or low-grade neoplasms such as meningiomas, gangliogliomas (**Figure 9-5**), dysplastic neuroepithelial tumors, astrocytomas, and oligodendrogliomas may cause chronic but surgically remediable epilepsy. The goal is to completely remove the lesion and the surrounding epileptogenic brain, if possible. Sometimes invasive monitoring

with mapping of the seizure-onset region and of brain function is needed.

Epilepsy Due to Developmental Abnormalities

Type I focal cortical dysplasia is characterized by delamination in the temporal lobe, but only some patients develop drug-resistant epilepsy.⁴⁵ On the other hand, type II (Taylor type) dysplasia contains dysmorphic neurons and is characterized by medically refractory extratemporal epilepsy.⁴⁵ If the entire dysplastic area visible on MRI can be completely removed at surgery, good seizure outcome is possible (Case 9-3, Figure 9-6).⁴⁶

Tuberous sclerosis complex may result in medically intractable focal epilepsy, and resection of an epileptogenic tuber may sometimes palliate seizures.⁴⁷ In patients with Sturge-Weber syndrome, seizures may be controlled with medication in about 50% of cases, or spontaneously remit. Resection of brain affected by the leptomeningeal venous angioma may control seizures. After partial resection of venous angiomas, however, intractable epilepsy often recurs. The most effective treatment is hemispherectomy in those who have developed severe hemiparesis.⁴⁸

Hypothalamic hamartomas are rare developmental lesions attached to the tuber cinereum or the mammillary bodies, sometimes resulting in intractable epilepsy with gelastic (laughing) seizures. Complete microdissection by an endoscopic technique, or radiosurgery, can be effective.⁴⁹

Epilepsy Due to Vascular Malformations

Arteriovenous malformations may cause intractable epilepsy. Treatment is with embolization, radiosurgery, or microsurgery. These last two approaches have been shown to have a good chance of seizure control.^{50,51}

Symptomatic cavernous hemangiomas most commonly present with seizures. They can be resected when they cause drug-resistant epilepsy or, less frequently, clinically significant hemorrhages. Surgery consists of lesionectomy plus resection of surrounding epileptogenic cortex,⁵² often guided by invasive monitoring or intraoperative electrocorticography.

Epilepsy Due to Atrophic Lesions

Stroke is a significant cause of epilepsy, which is sometimes drug resistant. In the setting of remote congenital or early childhood middle cerebral artery infarctions, patients often have residual hemiplegia, and the imaging may show porencephalic cysts. Hemispherectomy or multilobar resection in such cases offers an excellent chance of seizure control.⁵³ Posttraumatic epilepsy may be intractable as well. Some posttraumatic epilepsy has widespread or multifocal injury, making these patients

FIGURE 9-6 Right occipital heterotopia (arrow) in a 19-year-old man with intractable simple and complex partial seizures who became seizure free after resection with a modest left visual scotoma.

poor surgical candidates. However, many have MTS or localized cortical encephalomalacia and may achieve good seizure control with resection.⁵⁴

Hemispheric Syndromes

In addition to Sturge-Weber syndrome and large congenital hemiplegic strokes, hemispherectomy is considered for hemimegalencephaly (ie, hemispheric dysplastic malformation and overgrowth), other forms of extensive unilateral cortical dysplasia with severe hemiparesis, and Rasmussen syndrome. In Rasmussen syndrome, a progressive

hemispheric condition, hemispherectomy has a high chance of controlling seizures and improving cognition.⁵⁵ The usual procedure is the functional hemispherectomy, in which the central region and temporal lobe are removed and the frontal and occipital lobes are disconnected.⁵⁶ This eliminates the superficial cerebral hemosiderosis that complicated the original anatomical hemispherectomy procedure.

Corpus Callosotomy

Corpus callosotomy is most often performed for palliation of atonic seizures

Case 9-3

A 21-year-old, right-handed man experienced daily clusters of seizures with right arm elevation and head turning to the left since age 2. The patient's seizures were refractory to four antiepileptic drugs and the ketogenic diet. Scalp EEG showed left frontal interictal epileptiform discharges and ictal fast activity, MRI showed subtle left frontal cortical thickening (**Figure 9-7**), single-photon emission computed tomography (SPECT) demonstrated increased ictal blood flow in the left frontal pole, and positron emission tomography (PET) showed subtle left frontal hypometabolism (**Figure 9-8**). Invasive EEG demonstrated left frontopolar seizure onset (**Figure 9-9**), and the patient's frontal dysplastic cortex was resected.

FIGURE 9-7 MRI showing left lateral frontal cortical thickening (*arrow*) consistent with cortical dysplasia.

FIGURE 9-8 Positron emission tomography (PET) showing left frontal decreased metabolism (*arrow*). The lateral cortical surface is orange, signifying hypometabolism, whereas the lateral cortical surface on the opposite side is bright yellow.

Continued on page 739

Continued from page 738

FIGURE 9-9 Invasive monitoring in Case 9-3 showing low- and high-frequency EEG changes over left frontal pole during a typical seizure.

Comment. Detection of subtle cortical abnormalities is crucial to successful epilepsy surgery for cortical dysplasia.

TABLE 9-1 Ongoing and Future Trends

- ▶ Earlier consideration of epilepsy surgery
- ▶ Continued expansion of use of epilepsy surgery in children
- ▶ Wider geographic distribution of medical and surgical epilepsy centers
- ▶ Continuing efforts to improve MRI detection of occult cortical dysplasia
- ▶ Development of EEG signal analysis methods to better define the seizure-onset zone with scalp and invasive EEG monitoring
- ▶ Increased use of functional MRI for functional localization
- ▶ Continued development of less invasive methods of resection, such as stereotaxic surgery, laser ablation, and radiosurgery
- ▶ Development of devices to focally suppress seizures without resection

KEY POINT

■ Current evidence and practice guidelines indicate that epilepsy surgery should be considered more often and earlier in the course of chronic uncontrolled epilepsy.

in patients with Lennox-Gastaut syndrome. The anterior two-thirds portion of the corpus callosum is sectioned; if this procedure is ineffective, the remaining posterior portion may be divided later.⁵⁷

OUTCOMES

The goal of resective epilepsy surgery is long-term seizure freedom. The best outcomes are for temporal lobectomy for MTS, lesional resections, and hemispherectomy. Seizure-free rates are lower in patients with nonlesional neocortical resections. Reported outcomes depend primarily on case selection and on the accurate and complete evaluation of postoperative seizures over a sufficient time. A multicenter study of 339 patients followed for at least 2 years found that 68% of patients with mesial temporal resections and 50% of patients with neocortical resections were seizure free except for possible auras.⁵⁸ This difference was not significant, and with multivariate analysis, only absence of convulsive seizures and presence of hippocampal atrophy in the mesial temporal group were independently associated with remission. While some patients are able to discontinue AEDs and remain seizure free, there are no randomized studies allowing prediction of the risk of seizure recurrence with drug withdrawal.⁵⁹

CONCLUSIONS

This review details the severe progressive consequences of uncontrolled epilepsy, the criteria determining epilepsy surgery candidacy, and the evidence for surgical efficacy. Despite these factors, the number of surgical lobectomies in the United States is less than 500 per year, with no significant change over almost 2 decades—far lower than expected from estimates of the prevalence of surgically remediable epilepsies.⁶⁰ In addition, the average delay from on-

set of habitual seizures to referral for surgical treatment is 17 to 18 years (Table 9-1).⁶¹ Chronic, uncontrolled epilepsy can be a malignant condition, and timely, systematic intervention to attain seizure freedom, including early consideration of epilepsy surgery, is the standard for neurologic practice.⁶²

REFERENCES

1. Sillanpää M, Schmidt D. Natural history of treated childhood-onset epilepsy: prospective, long-term population-based study. *Brain* 2006;129(pt 3):617–624.
2. Kwan P, Brodie MJ. Early identification of refractory epilepsy. *N Engl J Med* 2000;342(5):314–319.
3. Baca CB, Vickrey BG, Caplan R, et al. Psychiatric and medical comorbidity and quality of life outcomes in childhood-onset epilepsy. *Pediatrics* 2011;128(6):e1532–e1543.
4. Luoni C, Bisulli F, Canevini MP, et al. Determinants of health-related quality of life in pharmacoresistant epilepsy: results from a large multicenter study of consecutively enrolled patients using validated quantitative assessments. *Epilepsia* 2011;52(12):2181–2191.
5. Barry JJ, Ettinger AB, Friel P, et al. Consensus statement: the evaluation and treatment of people with epilepsy and affective disorders. *Epilepsy Behav* 2008;13(suppl 1):S1–S29.
6. Sillanpää M, Shinnar S. Long-term mortality in childhood-onset epilepsy. *N Engl J Med* 2010;363(26):2522–2529.
7. Bernhardt BC, Bernasconi N, Concha L, et al. Cortical thickness analysis in temporal lobe epilepsy: reproducibility and relation to outcome. *Neurology* 2010;74(22):1776–1784.
8. Bell B, Lin JJ, Seidenberg M, Hermann B. The neurobiology of cognitive disorders in temporal lobe epilepsy. *Nat Rev Neurol* 2011;7(3):154–164.
9. Wiebe S, Blume WT, Girvin JP, et al. A randomized, controlled trial of surgery for temporal-lobe epilepsy. *N Engl J Med* 2001;345(5):311–318.
10. Sperling MR, Feldman H, Kinman J, et al. Seizure control and mortality in epilepsy. *Ann Neurol* 1999;46(1):45–50.
11. Mohammed HS, Kaufman CB, Limbrick DD, et al. Impact of epilepsy surgery on seizure control and quality of life: a 26-year follow-up study. *Epilepsia* 2012;53(4):712–720.

12. Kwan P, Azimanoglou A, Berg AT, et al. Definition of drug resistant epilepsy: consensus proposal by the ad hoc task force of the ILAE Commission on Therapeutic Strategies. *Epilepsia* 2010;51(6):1069–1077.
13. Luciano AL, Shorvon SD. Results of treatment changes in patients with apparently drug-resistant chronic epilepsy. *Ann Neurol* 2007;62(4):375–381.
14. Sillanpää M, Schmidt D. Is incident drug-resistance of childhood-onset epilepsy reversible? A long-term follow-up study. *Brain* 2012;135(pt 7):2256–2262.
15. Spooner CG, Berkovic SF, Mitchell LA, et al. New-onset temporal lobe epilepsy in children: lesion on MRI predicts poor seizure outcome. *Neurology* 2006;12(67):2147–2153.
16. Salinsky MC. Vagus nerve stimulation as treatment for epileptic seizures. *Curr Treat Options Neurol* 2003;5(2):111–120.
17. Holmes MD, Born DE, Kutsy RL, et al. Outcome after surgery in patients with refractory temporal lobe epilepsy and normal MRI. *Seizure* 2000;9(6):407–411.
18. Tatum WO IV, Benbadis SR, Hussain A, et al. Ictal EEG remains the prominent predictor of seizure-free outcome after temporal lobectomy in epileptic patients with normal brain MRI. *Seizure* 2008;17(7):631–636.
19. Cukiert A, Burattini JA, Mariani PP, et al. Outcome after cortico-amygdalohippocampectomy in patients with temporal lobe epilepsy and normal MRI. *Seizure* 2010;19:319–323.
20. Sylaja PN, Radhakrishnan K, Kesavada C, Sarma PS. Seizure outcome after anterior temporal lobectomy and its predictors in patients with apparent temporal lobe epilepsy and normal MRI. *Epilepsia* 2004;45(7):803–808.
21. Jeha LE, Najm I, Bingaman W, et al. Surgical outcome and prognostic factors of frontal lobe epilepsy surgery. *Brain* 2007;130(pt 2):574–584.
22. Mosewich RK, So EL, O'Brien TJ, et al. Factors predictive of the outcome of frontal lobe epilepsy surgery. *Epilepsia* 2000;41(7):843–849.
23. Jackson GD, Badawy RA. Selecting patients for epilepsy surgery: identifying a structural lesion. *Epilepsy Behav* 2011;20(2):182–189.
24. Besson P, Andermann F, Dubeau F, Bernasconi A. Small focal cortical dysplasia lesions are located at the bottom of a deep sulcus. *Brain* 2008;131(pt 12):3246–3255.
25. Holmes MD, Tucker DM, Quiring JM, et al. Comparing noninvasive dense array and intracranial electroencephalography for localization of seizures. *Neurosurgery* 2010;66(2):354–362.
26. Rausch R. Integrative neuropsychology in the preoperative workup of the epilepsy surgery patient. In Miller JW, Silbergeld DL, eds. *Epilepsy surgery: principles and controversies*. New York, NY: Taylor and Francis, 2006:183–199.
27. Loring DW, Meador KJ. The Wada test is a useful predictor of memory outcome. In Miller JW, Silbergeld DL, eds. *Epilepsy surgery: principles and controversies*. New York, NY: Taylor and Francis, 2006:229–232.
28. Theodore WH, Sato S, Kufta C, et al. Temporal lobectomy for uncontrolled seizures: the role of positron emission tomography. *Ann Neurol* 1992;32(6):789–794.
29. O'Brien TJ, So EL, Mullan BP, et al. Subtraction ictal SPECT co-registered to MRI improves clinical usefulness of SPECT in localizing the surgical seizure focus. *Neurology* 1998;50(2):445–454.
30. Knowlton RC, Elgavish RA, Bartolucci A, et al. Functional imaging: II. Prediction of epilepsy surgery outcome. *Ann Neurol* 2008;64(1):35–41.
31. Stefan H, Rampp S, Knowlton RC. Magnetoencephalography adds to the surgical evaluation process. *Epilepsy Behav* 2011;20(2):172–177.
32. Lau M, Yam D, Burneo JG. A systematic review on MEG and its use in the presurgical evaluation of localization-related epilepsy. *Epilepsy Res* 2008;79(2–3):97–104.
33. Binder JR, Gross WL, Allendorfer JB, et al. Mapping anterior temporal lobe language areas with fMRI: a multicenter normative study. *Neuroimage* 2011;54(2):1465–1475.
34. Findlay AM, Ambrose JB, Cahn-Weiner DA, et al. Dynamics of hemispheric dominance for language assessed by magnetoencephalographic imaging. *Ann Neurol* 2012;71(5):668–686.
35. Margerison JH, Corsellis JA. Epilepsy and the temporal lobes. A clinical, electroencephalographic and neuropathological study of the brain in epilepsy, with particular reference to the temporal lobes. *Brain* 1966;89(3):499–530.
36. Li LM, Cendes F, Watson C, et al. Surgical treatment of patients with single and dual pathology: relevance of lesion and of hippocampal atrophy to seizure outcome. *Neurology* 1997;48(2):437–444.
37. Falconer MA, Meyer A, Hill D, et al. Treatment of temporal-lobe epilepsy by

- temporal lobectomy; a survey of findings and results. *Lancet* 1955;268(6869):827–835.
38. Ojemann G, Ojemann J, Lettich E, Berger M. Cortical language localization in left, dominant hemisphere. An electrical stimulation mapping investigation in 117 patients. 1989. *J Neurosurg* 1989;71(3):316–326.
39. Silbergeld DL, Ojemann GA. The tailored temporal lobectomy. *Neurosurg Clin N Am* 1993;4(2):273–281.
40. Wieser HG, Yaşargil MG. Selective amygdalohippocampectomy as a surgical treatment of mesiobasal limbic epilepsy. *Surg Neurol* 1982;17(6):445–457.
41. Olivier A. Transcortical selective amygdalohippocampectomy in temporal lobe epilepsy. *Can J Neurol Sci* 2000;27(suppl 1):S68–S76.
42. Robinson S, Park TS, Blackburn LB, et al. Transparahippocampal selective amygdalohippocampectomy in children and adolescents: efficacy of the procedure and cognitive morbidity in patients. *J Neurosurg* 2000;93(3):402–409.
43. Barbaro NM, Quigg M, Broshek DK, et al. A multicenter, prospective pilot study of gamma knife radiosurgery for mesial temporal lobe epilepsy: seizure response, adverse events, and verbal memory. *Ann Neurol* 2009;65(2):167–175.
44. Simon EA, Doherty MJ, Miller JW. Surgically treatable epilepsy syndrome in adults. In Miller JW, Silbergeld DL, ed. *Epilepsy surgery: principles and controversies*. New York, NY: Taylor and Francis, 2006:45–70.
45. Palmini A, Majm I, Avanzini G, et al. Terminology and classification of the cortical dysplasias. *Neurology* 2004;62(6 suppl 3):S2–S8.
46. Lerner JT, Salamon N, Hauptman JS, et al. Assessment and surgical outcomes for mild type I and severe type II cortical dysplasia: a critical review and the UCLA experience. *Epilepsia* 2009;50(6):1310–1335.
47. Guerreiro MM, Andermann F, Andermann E, et al. Surgical treatment of epilepsy in tuberous sclerosis: strategies and results in 18 patients. *Neurology* 1998;51(5):1263–1269.
48. Arzimanoglou AA, Andermann F, Aicardi J, et al. Sturge-Weber syndrome: indications and results of surgery in 20 patients. *Neurology* 2000;55(10):1472–1479.
49. Berkovic SF, Arzimanoglou A, Kuzniecky R, et al. Hypothalamic hamartoma and seizures: a treatable epileptic encephalopathy. *Epilepsia* 2003;44(7):969–973.
50. Piepgras DG, Sundt TM Jr, Ragoowansi AT, Stevens L. Seizure outcome in patients with surgically treated cerebral arteriovenous malformations. *J Neurosurg* 1993;78(1):5–11.
51. Kurita H, Kawamoto S, Suzuki I, et al. Control of epilepsy associated with cerebral arteriovenous malformations after radiosurgery. *J Neurol Neurosurg Psychiatry* 1998;65(5):648–655.
52. Cosgrove GR. Occult vascular malformations and seizures. *Neurosurg Clin N Am* 1999;10(3):527–535.
53. Devlin AM, Cross JH, Harkness W, et al. Clinical outcomes of hemispherectomy for epilepsy in childhood and adolescence. *Brain* 2003;126(pt 3):556–566.
54. Hakimian S, Kershenovich A, Miller JW, et al. Long-term outcome of extratemporal resection in posttraumatic epilepsy. *Neurosurg Focus* 2012;32(3):E10.
55. Kossoff EH, Vining EP, Pillas DJ, et al. Hemispherectomy for intractable unihemispheric epilepsy etiology vs outcome. *Neurology* 2003;61(7):887–890.
56. Rasmussen T. Hemispherectomy for seizures revisited. *Can J Neurol Sci* 1983;10(2):71–78.
57. Lucas TH, West GA. Corpus callosotomy: indications, surgical procedures, and outcomes. In Miller JW, Silbergeld DL, eds. *Epilepsy surgery: principles and controversies*. New York, NY: Taylor and Francis, 2006: 541–551.
58. Spencer SS, Berg AT, Vickrey BG, et al. Predicting long-term seizure outcome after resective epilepsy surgery: the multicenter study. *Neurology* 2005;65(6):912–918.
59. Berg AT, Langfitt JT, Spencer SS, Vickrey BG. Stopping antiepileptic drugs after epilepsy surgery: a survey of U.S. epilepsy center neurologists. *Epilepsy Behav* 2007;10(2): 219–222.
60. Englot DJ, Ouyang D, Garcia PA, et al. Epilepsy surgery trends in the United States, 1990–2008. *Neurology* 2012;78(16):1200–1206.
61. Haneef Z, Stern J, Dewar S, Engel J Jr. Referral pattern for epilepsy surgery after evidence-based recommendations: a retrospective study. *Neurology* 2010;75(8): 699–704.
62. Engel J Jr, Wiebe S, French J, et al. Practice parameter: temporal lobe and localized neocortical resections for epilepsy: report of the Quality Standards Subcommittee of the American Academy of Neurology, in association with the American Epilepsy Society and the American Association of Neurological Surgeons. *Neurology* 2003;60(4):538–547.