



Do We Need EEGs After Temporal Lobe Epilepsy Surgery, and How Many?

Prognostic Importance of Serial Postoperative EEGs After Anterior Temporal Lobectomy.

Rathore C, Sarma SP, Radhakrishnan K. *Neurology* 2011;76(22):1925–1931.

OBJECTIVE: To assess the value of postoperative EEG in predicting seizure outcome and seizure recurrence following antiepileptic drug (AED) withdrawal in patients with mesial temporal lobe epilepsy with hippocampal sclerosis (MTLE-HS). **METHODS:** We studied 262 consecutive patients with MTLE-HS with serial EEGs at 3 months, and at 1, 2, and 3 years after anterior temporal lobectomy (ATL), and considered the presence of interictal epileptiform discharges (IED) as abnormal. We attempted AED withdrawal in all seizure-free patients. We defined favorable outcome as freedom from seizures/auras during the entire follow-up period (outcome 1) and during terminal 1-year follow-up (outcome 2). **RESULTS:** During mean follow-up period of 7.6 (range 5–12) years, 129 (49.2%) patients had favorable outcome 1 and 218 (83.2%) had favorable outcome 2. Of 225 (85.9%) patients in whom AED withdrawal was attempted, 61 (27.1%) had seizure recurrence. Compared to patients with normal EEG, those with IED on 1-year post-ATL EEG had a 3-fold increased risk for unfavorable outcome 1 and 7-fold increased risk for unfavorable outcome 2. The patients in whom all the 4 EEGs were abnormal had 9-fold odds for unfavorable outcome 1 and 26-fold odds for unfavorable outcome 2. An abnormal EEG at 1 year increased the risk of seizure recurrence following AED withdrawal by 2.6-fold. **CONCLUSIONS:** Post-ATL EEG predicts seizure outcome and seizure recurrence following AED withdrawal. Serial EEGs predict outcome better than single EEG. This information will be helpful in counseling of patients after ATL, and in making rational decisions on AED withdrawal.

Commentary

Mesial temporal lobe epilepsy with hippocampal sclerosis tends to be drug resistant but usually has excellent outcome with epilepsy surgery. Despite the excellent prognosis overall, a substantial proportion of patients are not seizure-free after surgery, and it is important to identify these patients before surgery, if possible. The few studies that have investigated outcome predictors for this specific patient group have found different predictors for short-term and long-term outcomes (1, 2). For example, secondarily generalized seizures and ictal dystonia were unfavorable predictors of outcome at 2 years, whereas longer epilepsy duration predicted surgical failure 5 years postoperatively (1). Preoperative factors are the most valuable for counseling patients so they could decide whether to proceed with surgery. However, postoperative predictors may be useful once surgery has taken place and may help guide patients with respect to actions/activities that could increase the risk of seizure recurrence, such as antiepileptic drug (AED) withdrawal. Postoperative tests that have been investigated include postoperative electrocorticography, postoperative MRI, and postoperative EEG.

In mesial temporal lobe epilepsy, postoperative electrocorticography has generally been unhelpful when recording from the lateral temporal cortex; however, there is a suggestion that recording from the stump of the hippocampus could be useful (3). The postoperative MRI is helpful for lesional epilepsy; if the lesion has been incompletely removed, there is a greater chance of seizure recurrence after surgery than if the lesion has been removed in its entirety. The postoperative test most often studied is a routine EEG, usually a single EEG recording. With a few exceptions, most studies have found the postoperative EEG to be useful in predicting outcome. In a meta-analysis of published studies (and two unpublished data sets), the presence of interictal epileptiform discharges predicted an unfavorable seizure outcome, with an odds ratio of 2.5 for the subgroup of patients who underwent temporal resection (4). The featured study of Rathore and colleagues specifically evaluated the predictive value of serial postoperative EEGs in patients with mesial temporal lobe epilepsy and hippocampal sclerosis followed for at least 5 years after surgery. The authors found that four postoperative EEGs were better than a single EEG at predicting postoperative seizure outcome in this patient group. Interestingly, postoperative EEGs were better at predicting seizure outcome for the last year of follow-up than in the entire follow-up period. Another study in patients with mesial temporal lobe epilepsy and hippocampal sclerosis found that preoperative variables were



also better at predicting seizure freedom in the last year of follow-up than for the entire follow-up period (2).

One potential reason for the different short-term and long-term predictors may be the withdrawal of AEDs, which is usually a more important factor in long-term follow-up. AEDs are typically withdrawn starting 1 to 2 years after epilepsy surgery; the timing of AED withdrawal is based on experience from medically treated patients rather than evidence from operated patients. AED withdrawal is usually initiated after discussion of risk-benefit ratio with the patient. It is not known how important AED withdrawal is as a factor in late seizure recurrence. Retrospective analyses of surgical case series have not found AED withdrawal to be associated with seizure recurrence (5, 6). This counterintuitive finding may be related to selection bias; that is, it is possible that AED withdrawal was attempted preferentially in patients thought to have lower risk for seizure recurrence. Only a prospective randomized study can definitively evaluate the role of AED withdrawal in postoperative seizure recurrence. A prospective multicenter randomized study of continued AED treatment versus slow withdrawal in nonsurgical seizure-free patients reported a 41 percent seizure relapse rate in the withdrawal group as compared with 22 percent in patients who continued treatment (7).

Rathore and colleagues withdrew AEDs in all patients who were free of seizures impairing consciousness, including patients who became seizure-free after having early postoperative seizure recurrence and patients with persistent isolated auras. They started a slow AED withdrawal as early as 3 months after surgery in those taking two or more AEDs, and 1 year after surgery in those taking one AED. Their study thus evaluated surgical outcome after AED withdrawal and unequivocally demonstrated that serial abnormal EEGs predicted seizure recurrence. However, the study cannot answer the question of whether patients who had seizure recurrence after AED withdrawal would have been seizure free if AEDs were maintained. In a previous publication, the same authors evaluated safety of AED withdrawal in 258 patients with mesial temporal lobe epilepsy, most of whom had hippocampal sclerosis. Seizures recurred during the process of AED withdrawal in 15 percent and after complete discontinuation in 10 percent of patients (8). More than 80 percent of seizure recurrences that occurred during AED tapering occurred within 2 months of the last change, the temporal proximity suggesting a cause-and-effect relationship. Conversely, the timing of recurrence was highly variable for those in whom seizure recurrence occurred after complete AED discontinuation. A long latency between AED discontinuation and seizure recurrence (sometimes more than 4 years after discontinuation) reduces the chance of cause-and-effect relationship.

The most important practical purpose for predicting outcome will be to counsel patients regarding AED withdrawal. The study of Rathore and colleagues suggests that serial EEGs are better than a single EEG for predicting seizure recurrence after AED withdrawal. It is remarkable that the authors were able to secure compliance in obtaining four EEGs after epilepsy surgery in every patient. This would be difficult to arrange in most other centers. Could a smaller number of EEGs provide an almost equivalent predictive power? In the

subset of 225 patients in whom withdrawal was attempted, the EEGs at 3 months and 1 year were almost as predictive as all four EEGs combined. Although all four EEGs combined had a greater sensitivity (48% as compared with 36%), the combination of EEGs at 3 months and 1 year had a greater specificity (78% vs 68%), and equal positive predictive value (38% vs 36%) and negative predictive value (77% vs 78%). For practical purposes, EEGs at 3 months and 1 year postoperatively may be sufficient to counsel patients regarding AED withdrawal.

The decision to withdraw AEDs will not be based on EEG alone, but will also have to take into consideration other predictors, individual factors, and patient preference. Other factors that have been found to predict seizure recurrence include early postoperative seizures, longer duration of epilepsy, and older age at surgery (8). Interestingly, the success rate of AED withdrawal seems greater in pediatric studies, supporting that older age at surgery is unfavorable. One important concern in relation to AED withdrawal is whether seizure control can be easily regained after seizure recurrence. In medically treated patients, about 19 percent of patients with seizure recurrence could no longer achieve seizure control (9). Rathore and colleagues reported recurrence of seizures in 23 percent of patients in whom AED withdrawal was attempted. In a population with mesial temporal lobe epilepsy, most with hippocampal sclerosis, Rathore and colleagues reported that 87.5 percent of patients with seizure recurrence regained seizure freedom with medication adjustment. These numbers are much better than noted in patients with neocortical epilepsy, who had an alarming recurrence rate of 53 percent upon attempted AED withdrawal, with only 46 percent of these patients regaining seizure control after AED reinstitution (10).

The authors acknowledged that they failed to evaluate sleep versus waking EEG, as not all patients slept during their EEGs. The authors also were not able to determine if it was the number of EEGs or the length of the recording that improves the prediction of seizure recurrence. The findings of Rathore and colleagues apply specifically to patients with mesial temporal lobe epilepsy with hippocampal sclerosis who underwent standard temporal lobectomy. It is not known whether the results would also apply after selective amygdalohippocampectomy or neocortical temporal or extratemporal lobe resections. Nevertheless, mesial temporal lobe epilepsy with hippocampal sclerosis is the most common form of epilepsy presenting for surgical therapy and is most surgically remediable; standard temporal lobectomy also remains the most common surgical modality. Hence, the current study has implications for the majority of excellent surgical candidates.

by Bassel W. Abou-Khalil, MD

References

1. Janszky J, Janszky I, Schulz R, Hoppe M, Behne F, Pannek HW, Ebner A. Temporal lobe epilepsy with hippocampal sclerosis: predictors for long-term surgical outcome. *Brain* 2005;128:395–404.
2. Aull-Watschinger S, Pataria E, Czech T, Baumgartner C. Outcome predictors for surgical treatment of temporal lobe epilepsy with hippocampal sclerosis. *Epilepsia* 2008;49:1308–1316.



3. McKhann GM, 2nd, Schoenfeld-McNeill J, Born DE, Haglund MM, Ojemann GA. Intraoperative hippocampal electrocorticography to predict the extent of hippocampal resection in temporal lobe epilepsy surgery. *J Neurosurg* 2000;93:44–52.
4. Rathore C, Radhakrishnan K. Prognostic significance of interictal epileptiform discharges after epilepsy surgery. *J Clin Neurophysiol* 2010;27:255–262.
5. Berg AT, Vickrey BG, Langfitt JT, Sperling MR, Shinnar S, Bazil C, Walczak T, Spencer SS. Reduction of AEDs in postsurgical patients who attain remission. *Epilepsia* 2006;47:64–71.
6. McIntosh AM, Kalnins RM, Mitchell LA, Fabinyi GC, Briellmann RS, Berkovic SF. Temporal lobectomy: Long-term seizure outcome, late recurrence and risks for seizure recurrence. *Brain* 2004;127:2018–2030.
7. Medical Research Council Antiepileptic Drug Withdrawal Study Group. Randomised study of antiepileptic drug withdrawal in patients in remission. Medical Research Council Antiepileptic Drug Withdrawal Study Group. *Lancet* 1991;337:1175–1180.
8. Rathore C, Panda S, Sarma PS, Radhakrishnan K. How safe is it to withdraw antiepileptic drugs following successful surgery for mesial temporal lobe epilepsy? *Epilepsia* 2011;52:627–635.
9. Schmidt D, Loscher W. Uncontrolled epilepsy following discontinuation of antiepileptic drugs in seizure-free patients: A review of current clinical experience. *Acta Neurol Scand* 2005;111:291–300.
10. Park KI, Lee SK, Chu K, Jung KH, Bae EK, Kim JS, Lee JJ, Lee SY, Chung CK. Withdrawal of antiepileptic drugs after neocortical epilepsy surgery. *Ann Neurol* 2010;67:230–238.



American Epilepsy Society

Epilepsy Currents Journal

Disclosure of Potential Conflicts of Interest

Instructions

The purpose of this form is to provide readers of your manuscript with information about your other interests that could influence how they receive and understand your work. Each author should submit a separate form and is responsible for the accuracy and completeness of the submitted information. The form is in four parts.

1. Identifying information.

Enter your full name. If you are NOT the main contributing author, please check the box “no” and enter the name of the main contributing author in the space that appears. Provide the requested manuscript information.

2. The work under consideration for publication.

This section asks for information about the work that you have submitted for publication. The time frame for this reporting is that of the work itself, from the initial conception and planning to the present. The requested information is about resources that you received, either directly or indirectly (via your institution), to enable you to complete the work. Checking “No” means that you did the work without receiving any financial support from any third party – that is, the work was supported by funds from the same institution that pays your salary and that institution did not receive third-party funds with which to pay you. If you or your institution received funds from a third party to support the work, such as a government granting agency, charitable foundation or commercial sponsor, check “Yes”. Then complete the appropriate boxes to indicate the type of support and whether the payment went to you, or to your institution, or both.

3. Relevant financial activities outside the submitted work.

This section asks about your financial relationships with entities in the bio-medical arena that could be perceived to influence, or that give the appearance of potentially influencing, what you wrote in the submitted work. For example, if your article is about testing an epidermal growth factor receptor (EGFR) antagonist in lung cancer, you should report all associations with entities pursuing diagnostic or therapeutic strategies in cancer in general, not just in the area of EGFR or lung cancer.

Report all sources of revenue paid (or promised to be paid) directly to you or your institution on your behalf over the 36 months prior to submission of the work. This should include all monies from sources with relevance to the submitted work, not just monies from the entity that sponsored the research. Please note that your interactions with the work’s sponsor that are outside the submitted work should also be listed here. If there is any question, it is usually better to disclose a relationship than not to do so.

For grants you have received for work outside the submitted work, you should disclose support ONLY from entities that could be perceived to be affected financially by the published work, such as drug companies, or foundations supported by entities that could be perceived to have a financial stake in the outcome. Public funding sources, such as government agencies, charitable foundations or academic institutions, need not be disclosed. For example, if a government agency sponsored a study in which you have been involved and drugs were provided by a pharmaceutical company, you need only list the pharmaceutical company.

4. Other relationships

Use this section to report other relationships or activities that readers could perceive to have influenced, or that give the appearance of potentially influencing, what you wrote in the submitted work.



American Epilepsy Society

Epilepsy Currents Journal

Disclosure of Potential Conflicts of Interest

Section #1 Identifying Information

1. Today's Date: 12/15/2011
2. First Name Bassel Last Name Abou-Khalil Degree M.D.
3. Are you the Main Assigned Author? Yes No
If no, enter your name as co-author:
4. Manuscript/Article Title: Do We Need EEGs After Temporal Lobe Epilepsy Surgery, and How Many?
5. Journal Issue you are submitting for: 12.1

Section #2 The Work Under Consideration for Publication

Did you or your institution at any time receive payment or services from a third party for any aspect of the submitted work (including but not limited to grants, data monitoring board, study design, manuscript preparation, statistical analysis, etc.)?

Complete each row by checking "No" or providing the requested information. If you have more than one relationship just add rows to this table.

Type	No	Money Paid to You	Money to Your Institution*	Name of Entity	Comments**
1. Grant	<input checked="" type="checkbox"/>				
2. Consulting fee or honorarium	<input checked="" type="checkbox"/>				
3. Support for travel to meetings for the study or other purposes	<input checked="" type="checkbox"/>				
4. Fees for participating in review activities such as data monitoring boards, statistical analysis, end point committees, and the like	<input checked="" type="checkbox"/>				
5. Payment for writing or reviewing the manuscript	<input checked="" type="checkbox"/>				
6. Provision of writing assistance, medicines, equipment, or administrative support.	<input checked="" type="checkbox"/>				
7. Other	<input checked="" type="checkbox"/>				

* This means money that your institution received for your efforts on this study.

** Use this section to provide any needed explanation.

Section #3 Relevant financial activities outside the submitted work.

Place a check in the appropriate boxes in the table to indicate whether you have financial relationships (regardless of amount of compensation) with entities as described in the instructions. Use one line for each entity; add as many lines as you need by clicking the “Add” box. You should report relationships that were present during the 36 months prior to submission.

Complete each row by checking “No” or providing the requested information. If you have more than one relationship just add rows to this table.

Type of relationship (in alphabetical order)	No	Money Paid to You	Money to Your Institution*	Name of Entity	Comments**
1. Board membership	<input checked="" type="checkbox"/>				
2. Consultancy	<input type="checkbox"/>	X		UCB	This was >2 years ago, single consultation related to research data analysis
3. Employment	<input checked="" type="checkbox"/>				
4. Expert testimony	<input checked="" type="checkbox"/>				
5. Grants/grants pending	<input type="checkbox"/>		X	NIH UCB Shwarz Glaxo Valeant J&J King Marinus Pfizer Supernus, Sepracor/Sunovion, Icagen, Abbott, Cyberonics, Upsher Smith, Neuronex	
6. Payment for lectures including service on speakers bureaus	<input type="checkbox"/>	X		UCB	No relationship x2.5 years
7. Payment for manuscript preparation.	<input checked="" type="checkbox"/>				
8. Patents (planned, pending or issued)	<input checked="" type="checkbox"/>				
9. Royalties	<input type="checkbox"/>	X		Elsevier	Atlas of EEG and Seizure Semiology
10. Payment for development of educational presentations	<input checked="" type="checkbox"/>				
11. Stock/stock options	<input checked="" type="checkbox"/>				
12. Travel/accommodations/meeting expenses unrelated to	<input checked="" type="checkbox"/>				

activities listed.**					
13. Other (err on the side of full disclosure)	<input checked="" type="checkbox"/>				

* This means money that your institution received for your efforts.

** For example, if you report a consultancy above there is no need to report travel related to that consultancy on this line.

Section #4 Other relationships

Are there other relationships or activities that readers could perceive to have influenced, or that give the appearance of potentially influencing, what you wrote in the submitted work?

No other relationships/conditions/circumstances that present a potential conflict of interest.

Yes, the following relationships/conditions/circumstances are present:

Bassel Abou-Khalil, M.D.

Thank you for your assistance.

Epilepsy Currents Editorial Board