



## The Role of EEG After Cardiac Arrest and Hypothermia

### Continuous EEG in Therapeutic Hypothermia After Cardiac Arrest: Prognostic and Clinical Value.

Crepeau AZ, Rabinstein AA, Fugate JE, Mandrekar J, Wijdicks EF, White RD, Britton JW. *Neurology* 2013;80:339–344.

**OBJECTIVES:** To determine the prognostic value of an EEG grading scale and clinical outcome of treated seizures detected with continuous EEG (cEEG) during therapeutic hypothermia (TH) and rewarming post cardiac arrest (CA). **METHODS:** Our cohort study retrospectively reviewed the electronic medical records and cEEGs of all patients undergoing TH after CA under protocol over 2 years. cEEG was initiated during TH and continued until restoration of normothermia (NT). EEGs were graded 1–3 (3 = most severe) using a departmentally developed EEG severity grading scale by 2 authors blinded to clinical outcome. Outcome was measured using the Cerebral Performance Category scale; grades 1–2 were considered a “good” outcome, “3–5” poor. **RESULTS:** Fifty-four patients were included; 51 remained on cEEG through NT. Nineteen died. EEG severity grading during both TH and NT statistically correlated with outcome (grade 1 = good, grade 3 = poor). Other EEG features correlating with poor outcome included seizures, nonreactive background, and epileptiform discharges. Changes in EEG grade during monitoring did not statistically correlate with outcome. Five patients had seizures; all occurred in patients with grade 3 EEG backgrounds and all had a poor outcome. **CONCLUSION:** Grades 1 and 3 on our EEG severity grading scale during TH and NT correlated with outcome. Treating seizures did not improve outcome in our cohort.

### Commentary

Despite decades of research, the exact role of EEG in predicting and improving outcomes in survivors of cardiac arrest (CA) remains a hot topic of discussion. *Here are the facts:* Since the 1960s, EEG has become an integral part of prognostication after CA (1). In 2002, two randomized clinical trials documented the benefits of mild therapeutic hypothermia (TH) in comatose survivors of CA, improving neurologic outcomes and survival (2). In 2005, the American Heart Association recommended TH as a standard of care (3), and in 2006, the American Academy of Neurology (AAN) formalized outcome prediction in comatose survivors, after cardiopulmonary resuscitation, through practice guidelines (4). So, on the surface, we have an effective treatment and “officially endorsed” guidelines for using various tools, including EEG, in prognostication. *Here is the catch:* despite TH, almost half of patients still do poorly after CA, and all the data driving the AAN guidelines were generated *before* the routine implementation of TH. Yet, many prognostication criteria are potentially affected by TH. A recent prospective study showed a higher rate of false positive rate (FPR) mortality predictions using incomplete recovery of brainstem reflexes (4% FPR), myoclonus (3% FPR), and absent motor response to pain (24% FPR) in the TH population compared with CA survivors from the pre-TH era (0% FPR for all these variables)

(5). The door then remains open for work like the study by Crepeau et al., chosen for this commentary, to evaluate the current role of EEG.

### Where Do We Stand Now?

#### *First, EEG Findings Remain Highly Predictive of Neurologic Outcome After the Routine Implementation of TH.*

The study at hand classifies the “traditional malignant” EEG findings of burst suppression, low-voltage output pattern, alpha/theta coma, focal or generalized seizures, generalized periodic epileptiform discharges, status epilepticus, and background unreactivity into a “grade 3” or “severe” abnormality. Eighty-nine percent of patients with grade 3 abnormality during TH and all those who had it during subsequent normothermia had a poor neurologic outcome (high specificity). Conversely, 76% of patients with a poor outcome had a grade 3 abnormality (high sensitivity). All the patients with mild (grade 1) abnormalities as defined by excessive beta, theta slowing, or anesthetic pattern during TH or normothermia recovered with no to moderate disability. This and other grading systems (1, 6) offer reasonable accuracy but require the clinician to remember the individual classification. An alternate practical approach focuses on the prognostic significance of one critical EEG finding: the extent of background reactivity. In several recent studies (5, 7–9), a nonreactive EEG background was incompatible with good neurologic recovery (100% specificity), regardless of whether it was seen within 12, 24, or 72 hours after CA. The sensitivity of this EEG finding varies from 40% (8) to 81% (5), with an accuracy of 81% (5). Overall, it seems then that—short of applying a comprehensive grading scale—as-



sessing background EEG reactivity is a very useful and valid prognostication tool, regardless of core temperature and sedation levels. Work to quantify and characterize the value of using EEG severity grading scales as opposed to relying on individual findings (such as EEG reactivity) would be helpful.

### **Second, EEG Alone Is Insufficient to Adequately Predict Neurologic Outcome.**

In Crepeau et al., as shown previously (5, 7–10), an unacceptably high number of survivors would be missed if EEG classification were used as the sole prognostic tool. Incorporating additional clinical and electrophysiological indicators improves the accuracy of assessment (4). In a recent prospective study (5), the best prediction of poor long-term neurologic outcome in survivors of CA treated with TH (100% specificity, 100% positive predictive value) was accomplished with the presence of any two of the following four independent outcome predictors: 1) nonreactive EEG background, 2) incomplete recovery of brainstem reflexes, 3) bilaterally absent Somatosensory Evoked Potentials (SSEP)s, and 4) myoclonus. For this sick patient population, a multidisciplinary and conservative approach seems justifiable.

### **Where Do We Go From Here?**

The first obvious question is: Do we really need continuous video-EEG (c-EEG) for prognostication in *all* CA survivors treated with TH, or can this practice be tailored to particular patient populations, at particular times? Even though EEG patterns changed in up to 25% of patients in Crepeau et al., this change would have had a prognostic implication (into or out of a grade 1 or 3 severity degree) in only 16%. In continuous EEG studies of TH patients, prognostication was related to the presence or absence of specific EEG characteristics at specific time points, rather than findings throughout the entirety of the record: for example, outcome was good in all patients with a continuous EEG pattern 12 hours post resuscitation, and poor in all patients with iso-electric or low-voltage EEG 24 hours post resuscitation (8). Most studies do in fact concur that even when EEG changes occur in this patient population, the evolution is over several hours to days, so the question of whether continuous recording is necessary naturally poses itself. Could the same clinical information be derived from periodic EEG recordings? In an evolving landscape of health-care delivery, proving the superiority of a more-expensive and labor-intensive technique falls upon us. In this context, superiority would be defined as “added value” and “advanced performance” in improving patient outcomes, and not simply a higher rate of detecting findings of questionable clinical implications on patient care.

The second question is tightly linked to the above c-EEG discussion and relates to the significance of seizures in CA survivors treated with TH. In Crepeau et al., all patients with seizures died, although seizures were successfully controlled in more than 80% of the cases. Similarly, seven out of eight TH patients with seizures died in another study (9). The two common features that unite these seizure-related mortalities are that 1) seizures started *during* the hypothermia phase, and 2) seizures emerged out of a nonreactive EEG background. In fact, survivors of postanoxic seizures typically have their first

seizures during the rewarming or late phases of hypothermia (7) and have preserved background reactivity. Considering that hypothermia itself carries some neuroprotective effects (2, 3, 5, 7, 9), one could hypothesize that seizures *during* TH are simply a reflection of the severity of the underlying insult, better reflected by the background EEG activity; so detecting these seizures—and possibly even treating them—does not necessarily alter prognosis. For patients then with a nonreactive background or seizures during the TH phase, the exact role of further prolonging cEEG remains unclear. Later seizures, starting during or after rewarming, especially when arising from a reactive EEG background, represent a different category where treatment may actually make a difference. Confirming the distinction between these two “seizure categories,” clarifying the role of c-EEG in this setting (to detect subclinical seizures), and documenting the outcome implications of treating seizures are all questions needing further research.

by Lara E. Jehi, MD

### **References**

1. Hockaday JM, Potts F, Epstein E, Bonazzi A, Schwab RS. Electroencephalographic changes in acute cerebral anoxia from cardiac or respiratory arrest. *Electroencephalogr Clin Neurophysiol* 1965;18:575–586.
2. Hypothermia after Cardiac Arrest Study Group. Mild therapeutic hypothermia to improve the neurologic outcome after cardiac arrest. *N Engl J Med* 2002;346:549–556.
3. ECC Committee, Subcommittees and Task Forces of the American Heart Association. 2005 American Heart Association Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care. *Circulation* 2005;112(suppl):IV1–203.
4. Wijdicks EF, Hijdra A, Young GB, Bassetti CL, Wiebe S; Quality Standards Subcommittee of the American Academy of Neurology. Practice parameter: Prediction of outcome in comatose survivors after cardiopulmonary resuscitation (an evidence-based review). Report of the Quality Standards Subcommittee of the American Academy of Neurology. *Neurology* 2006;67:203–210.
5. Rossetti AO, Oddo M, Logroscino G, Kaplan PW. Prognostication after cardiac arrest and hypothermia: A prospective study. *Ann Neurol* 2010;67:301–307.
6. Synek VM. Value of a revised EEG coma scale for prognosis after cerebral anoxia and diffuse head injury. *Clin Electroencephalogr* 1990;21:25–30.
7. Rossetti AO, Oddo M, Liaudet L, Kaplan PW. Predictors of awakening from postanoxic status epilepticus after therapeutic hypothermia. *Neurology* 2009;72:744–749.
8. Cloostermans MC, van Meulen FB, Eertman CJ, Hom HW, van Putten MJ. Continuous electroencephalography monitoring for early prediction of neurological outcome in postanoxic patients after cardiac arrest: A prospective cohort study. *Crit Care Med* 2012;40:2867–2875.
9. Rossetti AO, Urbano LA, Delodder F, Kaplan PW, Oddo M. Prognostic value of continuous EEG monitoring during therapeutic hypothermia after cardiac arrest. *Crit Care* 2010;14:R173.
10. Wennervirta JE, Ermes MJ, Tiainen SM, Salmi TK, Hynninen MS, Sarkela MO, Hynninen MJ, Stenman UH, Viertio-oja HE, Saastamoinen KP, Pettila VY, Vakkuri AP. Hypothermia-treated cardiac arrest patients with good neurological outcome differ early in quantitative variables of EEG suppression and epileptiform activity. *Crit Care Med* 2009;37:2427–2435.



# 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: 06/13/12
2. First Name Lara Last Name Jehi Degree MD
3. Are you the Main Assigned Author?  Yes  No

If no, enter your name as co-author:

4. Manuscript/Article Title: The role of EEG after cardiac arrest and hypothermia AND Medication Management after Epilepsy Surgery: Opinions versus Facts.
5. Journal Issue you are submitting for: 13.4

#### 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 checked="" type="checkbox"/>				
3. Employment	<input checked="" type="checkbox"/>				
4. Expert testimony	<input checked="" type="checkbox"/>				
5. Grants/grants pending	<input checked="" type="checkbox"/>				
6. Payment for lectures including service on speakers bureaus	<input checked="" type="checkbox"/>				
7. Payment for manuscript preparation.	<input checked="" type="checkbox"/>				
8. Patents (planned, pending or issued)	<input checked="" type="checkbox"/>				
9. Royalties	<input checked="" type="checkbox"/>				
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 activities listed.**	<input checked="" type="checkbox"/>				
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:

Thank you for your assistance.  
*Epilepsy Currents* Editorial Board