Nonconvulsive Status Epilepticus

Value of a Benzodiazepine Trial for Predicting Outcomes

Jennifer L. Hopp, MD, Ana Sanchez, MD, Allan Krumholz, MD, George Hart, MD, and Elizabeth Barry, MD

Objectives: Managing nonconvulsive status epilepticus (NCSE) poses many challenges that would benefit from additional early measures to predict patient outcomes. Here, we evaluate clinical and electroencephalographic responses to an acute antiepileptic drug trial as an added measure for predicting outcomes in patients presenting with suspected NCSE.

Methods: We analyzed all patients referred to our Neurology Service with suspected NCSE assessed by a standard acute intravenous (IV) benzodiazepine (BDZ) protocol. We correlated patients' clinical and electrographic (EEG) responses to the BDZ trial with their subsequent outcomes, including survival, recovery of consciousness, and functional status at hospital discharge.

Results: From 1990 to 2001, we identified 62 patients with NCSE who were initially evaluated with an acute IV BDZ protocol trial. A favorable clinical response with improvement in consciousness was observed in 22 patients (35%), whereas 40 (65%) were clinical nonresponders. All of the positive clinical responders (100%) survived, recovered consciousness, and exhibited good functional outcomes. In contrast, outcomes were significantly poorer ($P < 0.001$) for the clinical nonresponders; only 14 (35%) recovered consciousness and 22 (55%) survived, with 59% of those survivors demonstrating poor functional outcomes. EEG improvement with BDZs also predicted better outcome, but it was less robust than the clinical response, with better subsequent recovery of consciousness ($P < 0.05$), but not functional outcome or survival.

Conclusions: This study demonstrates that a clinical and, to a lesser degree, EEG response to an acute trial of IV BDZs are predictive of subsequent outcome in patients with suspected NCSE, and warrant further consideration and investigation for assessing and managing patients.

Key Words: nonconvulsive status epilepticus, status epilepticus, outcome, seizures, epilepsy

(*The Neurologist* 2011;17:325–329)

Status epilepticus (SE) is a common and serious problem. It affects an estimated 150,000 individuals annually in the United States and is associated with substantial morbidity and mortality.[1,2] The standard definition of SE requires at least 30 minutes of continuous seizure activity or repetitive seizures without full return of consciousness between seizures.[1,3,4] SE is divided into 2 major categories, convulsive SE and nonconvulsive status epilepticus (NCSE).[3,5–7] Standards for diagnosis, classification, prognosis, and aggressive early treatment of convulsive SE are well established and accepted.[4] In contrast, although etiology is an established predictor of prognosis for both convulsive and NCSE,[5,6,8,9] other predictors of prognosis and standards for the diagnosis and treatment of NCSE remain to be defined and are controversial.[6,7,10]

NCSE is SE characterized by altered or impaired mental status without convulsions and associated continuous or intermittent electrographic (EEG) seizure activity.[6,7,11] Although NCSE was previously estimated to account for approximately 20% of all SE, and had been associated with low morbidity and mortality,[5,10,11] currently its incidence is judged as substantially higher and its morbidity and mortality greater.[8] Originally, NCSE was considered principally a disorder of ambulatory individuals with modestly altered consciousness, preexisting epilepsy, and few other comorbidities, who had good outcomes and responses to treatment with antiepileptic drugs (AED).[5,7] However, the accepted spectrum for NCSE has now expanded to include deeply comatose, critically ill, and intensive care unit patients.[7–10,14,15]

Characteristically, such patients have no preexisting epilepsy, but they do have severe comorbidities and substantial morbidity and mortality.[7–9,15] The morbidity and mortality of NCSE have been directly related to and associated with these comorbidities and the cause of the status.[5,7,8] Still, standards and recommendations for diagnosing and treating NCSE vary widely, in large part, because it remains difficult to predict outcomes and potential benefits of AEDs in many such patients.[7,8,16]

Included in the originally proposed standard for diagnosing and assessing NCSE was a requirement for a prompt clinical and EEG response to an acute AED trial.[5,6,12,13] However, in recent times as the spectrum of NCSE expanded, that measure lost favor as an accepted standard and diminished in clinical importance and use.[6,9,11,16] In this study, we specifically analyze the value an acute trial of intravenous (IV) AEDs, in the form of benzodiazepines (BDZs), as a potential added predictor of outcome in a population of patients with suspected NCSE.

METHODS

Patients were selected from the Neurology Service at the University of Maryland Medical Center from 1990 to 2001 with suspected NCSE who were assessed with a standardized BDZ trial. All patients had impaired or altered cognition, absence of convulsions, and an epileptiform pattern on the EEG. EEGs were obtained while the patients were acutely symptomatic, and recordings were performed using standard methods. Board-certified electroencephalographers interpreted all EEGs, and abnormalities were categorized based on the major prevailing epileptiform pattern present. Epileptiform

From the Department of Neurology, University of Maryland School of Medicine, Baltimore, MD.

The authors declare no conflict of interest.

Reprints: Jennifer L. Hopp, MD, Department of Neurology: University of Maryland Medical Center; Room S12C09; 22 South Greene Street; Baltimore, MD 21201. E-mail: jhopp@som.umaryland.edu.

ISSN: 1074-7931/11/1706-0325
DOI: 10.1097/NRL.0b013e31822f688c

abnormalities considered potentially consistent with NCSE included generalized spike and wave, generalized periodic epileptiform discharges, periodic lateralized epileptiform discharges, bilateral independent periodic lateralized epileptiform discharges, and focal periodic epileptiform discharges.[11,17,18]

During the EEG recording, the IV BDZ was administered according to a prospectively defined protocol, with the goal of eliminating all epileptiform patterns on the EEG or until an intolerable adverse effect or a predetermined maximal dosage was reached. This maximal dosage was defined as the equivalent of an 80 mg diazepam dosage for adults. Patients were given the IV BDZ in increments with both the choice of the BZD and dosage determined by the evaluating physicians. The BDZ was administered acutely over a period not to exceed 30 minutes in total duration. Patients were evaluated for clinical response within 5 minutes of each incremental BDZ administration and for 1 hour after the last BDZ trial dose. Immediately after administration of the IV BDZ, patients' clinical responses and the EEG responses were assessed. Patients who demonstrated a favorable clinical response were specifically defined as showing a substantial improvement in their level of consciousness in the opinion of the evaluating neurologist, but a standardized assessment tool was not proscribed. The EEG responses were categorized as (1) no response; (2) a partial response; or (3) a complete response. A partial response was defined as a substantial improvement in the epileptiform pattern, whereas a complete EEG response was defined as the eradication of the epileptiform pattern on the EEG. After this trial, subsequent management was not standardized, with treating physicians determining optimal care and AED therapies based on individual circumstances.

Both the EEG response and the clinical response to the administration of the BDZ were correlated to survival at the time of discharge, recovery of consciousness during the hospital stay, and functional outcome of the patients alive at the time of discharge. This was performed through retrospective review of inpatient hospital charts and records. The hospital charts were analyzed for the following information: age, sex, previous history of epilepsy or seizures, recovery of consciousness during hospitalization, suspected etiology of NCSE, survival, and functional recovery at discharge.

To assess outcome, recovery was classified based on a system adapted from Levy et al.[19] The designation "good recovery" was used to define the ability to resume normal life or previous level of activity. "Moderate recovery" was defined as independent daily living but below the previous level of function. "Severe dysfunction" was used to indicate dependence on others for activities of daily living. All these states implied a return to consciousness upon discharge. "Vegetative state" implied persistent coma until discharge. Statistical significance was analyzed by contingency analysis using χ^2 test and the Fisher exact test. Results were adjusted for age, sex, and history of seizures using linear regression analysis.

RESULTS

Characteristics of the Study Group

A total of 62 patients were included in this study. The age of the patients ranged from 6 months to 82 years (mean 51.6 y). Fifty-eight of the 62 patients (94%) were adults. Twenty-six patients were male (42%). The etiology of the suspected NCSE was presumed to be secondary to preexisting epilepsy in 7 patients (11%). All the presumed etiologies for patients' NCSE are listed together in Table 1. The overall mortality rate was 29%. The predominant epileptiform abnormality on EEGs was categorized as generalized in 38 patients (61%) and localization-related in the remaining 24 patients (39%) (Table 1).[11,17,18,20] For analysis, the actual doses of IV BDZ delivered in the individual trials were converted to an equivalent reference dose of diazepam, with the administered dose ranging from 0.6 mg to a predetermined maximum of 80 mg (mean 7.8 mg) equivalent dose of diazepam (Table 1).

TABLE 1. Characteristics of the Study Group (62 patients)

Demographics	
Age	6 mo-82 y (mean 51.6 y)
Sex	26 (42%) male 36 (58%) female
Etiology of NCSE	
Epilepsy	7 (11%)
Cerebral anoxia	18 (30%)
Stroke (ischemic and hemorrhagic)	8 (13%)
Toxic/metabolic	7 (11%)
Other	15 (24%)
Unknown	7 (11%)
Epileptiform abnormalities	
Generalized	38 (61%)
Focal	24 (39%)
Dosage of intravenous benzodiazepine	0.6-80 mg diazepam equivalents

Clinical Response: Correlated to Recovery of Consciousness and Survival

Twenty-two patients (35%) were classified as favorable clinical responders and 40 patients (65%) were classified as clinical nonresponders to BDZ (Table 2). All of the clinical responders recovered consciousness during their hospitalization and were alive at the time of hospital discharge. In contrast, of the 40 clinical nonresponders, 14 (35%) recovered consciousness during hospitalization and 22 (55%) were alive at the time of hospital discharge. The patients with substantial improvement in their level of consciousness immediately after the IV BDZ trial were significantly more likely to subsequently recover consciousness during their hospitalization and to be alive at the time of hospital discharge than the clinical nonresponders ($P < 0.001$).

Clinical Response: Correlated to Functional Outcome at Hospital Discharge

Of the 22 patients who were clinical responders, 18 (82%) had a good recovery and 4 (18%) had a moderate recovery. None of the 22 with a favorable clinical response to an IV BDZ were left with severe dysfunction or remained in a persistent vegetative state. In comparison, of the 22 patients who were clinical nonresponders and were alive at the time of hospital

TABLE 2. Clinical and EEG Response to IV BDZ

	Nonresponder	Responder
Clinical	No substantial improvement in level of consciousness 40 patients (65%)	Substantial improvement in level of consciousness 22 patients (35%)
EEG	No response	Partial or complete response
	No substantial change in EEG	Substantial improvement or eradication of patterns on EEG
	9 patients (15%)	53 patients (85%)

BDZ indicates benzodiazepine; EEG, electrography; IV, intravenous.

discharge, 7 (32%) had a good recovery, 2 (9%) had a moderate recovery, 9 (41%) were left with severe dysfunction, and 4 (18%) remained in a persistent vegetative state. Clinical responders experienced a better overall functional recovery at the time of hospital discharge than clinical nonresponders ($P < 0.001$). This relationship remained statistically significant when adjusted for age, sex, and the presence of a history of a seizure disorder ($P < 0.001$).

EEG Response: Correlated to Recovery of Consciousness and Survival

Fifty-three patients (85%) were classified as partial or complete EEG responders and 9 (15%) were classified as EEG nonresponders (Table 2). Of the 53 EEG responders, 35 (66%) recovered consciousness during their hospitalization and 40 (76%) were alive at the time of hospital discharge. Of the 9 EEG nonresponders, 1 (11%) recovered consciousness during their hospitalization and 4 (44%) were alive at the time of hospital discharge. Compared with the EEG nonresponders, the EEG responders were significantly more likely to recover consciousness during the hospitalization ($P < 0.05$), but survival at hospital discharge was not significantly better.

On further analysis of the EEG data from the 53 patients with some EEG response to IV BDZ administration, 24 (45%) had a complete response, whereas 22 (55%) had a partial response. Twenty of the 24 patients (83%) with a complete EEG response were alive at the time of hospital discharge, and 18 of the 24 patients (75%) with a complete EEG response recovered consciousness during the hospitalization. In comparison, 21 of the 29 patients (72%) with a partial EEG response were alive at the time of hospital discharge and 16 of the 29 (55%) of patients with a partial EEG response recovered consciousness during the hospitalization. Using odds ratio (OR) analysis, there was a trend toward a better chance of survival for those patients with a complete EEG response compared with those patients with a partial EEG response (OR = 6.25 for complete EEG response vs. 2.77 for partial EEG response). This relationship was also true for recovery of consciousness during hospitalization (OR = 24.00 for complete EEG response vs. 11.33 for partial EEG response). However, neither of these trends was statistically significant using the χ^2 analysis.

EEG Response: Correlated to Functional Outcome at Hospital Discharge

Of the 40 EEG responders who were alive at the time of hospital discharge, 24 (60%) patients had a good recovery, 6 (15%) had a moderate recovery, 8 (20%) were left with severe dysfunction, and 2 (5%) remained in a persistent vegetative state. Of the 4 EEG nonresponders who were alive at the time of hospital discharge, 1 (25%) had a good recovery, 1 (25%) suffered severe dysfunction, and 2 (50%) remained in a persistent vegetative state. EEG responders experienced an overall better functional recovery than EEG nonresponders ($P < 0.05$). However, this difference is not as robust as that observed with the clinical response to BDZ because the association does not remain statistically significant when adjusted for age, sex, and history of a seizure disorder.

Of the 20 patients with a complete EEG response who were alive at the time of hospital discharge, 14 (70%) had a good recovery, 2 (10%) had a moderate recovery, 3 (15%) were left with severe dysfunction, and 1 (5%) remained in a persistent vegetative state. Of the 21 patients with a partial EEG response who were alive at the time of hospital discharge, 10 (48%) had a good recovery, 4 (19%) have a moderate recovery, 5 (24%) were left with severe dysfunction, and 2 (9%) remained in a persistent vegetative state. Functional recovery was not statistically different in patients with a complete EEG response compared with patients with a partial EEG response. These results fail to demonstrate a significantly better functional recovery for a complete as compared with a partial EEG response.

DISCUSSION

NCSE is a major and important form of SE accounting for over 20% of all patients presenting with SE and associated with substantial morbidity and mortality.[6–8] The 2 original and main categories of NCSE are generalized NCSE and complex partial SE (CPSE), but other subtypes and classifications have also been proposed.[3,6,7,10] Initial reports and reviews of NCSE did not emphasize rapid diagnosis or aggressive treatment as the causes, associated comorbidities and potential consequences of NCSE were considered relatively benign.[5,6,12,13,21] Currently, although only 1 type of generalized NCSE, absence SE, is still acknowledged as having an excellent prognosis for recovery,[8,21] most other forms of NCSE, particularly CPSE and NCSE in comatose patients, are recognized as having substantial morbidity and mortality.[5,6,8] The morbidity and mortality in NCSE are associated with the causes and comorbidities of the SE,[5,6,8,9] but as in convulsive SE, the seizures in NCSE have also been proposed to contribute to brain injury or prevent full recovery.[5,6,8,22,23] Therefore, prompt diagnosis and aggressive treatment of NCSE, particularly in patients with coma or with CPSE, are increasingly emphasized.[6,15,16] For the individual patient with suspected NCSE, determining exactly when epileptiform EEG abnormalities are clinically relevant and merit aggressive treatment can be difficult. This is a critical issue because aggressive AED treatment poses it own risks and substantial costs.[16,24] IV AEDs and prolonged drug-induced coma as used for standard therapy in convulsive SE are cautioned against for some patients with NCSE because of concern that this type of treatment may be more dangerous than the disorder being treated, as it remains unclear whether the seizures of NCSE actually damage brain.[16,25] The decision as to how quickly and aggressively to treat patients with suspected NCSE is therefore a difficult one for many clinicians.

It is, in large part, based on whether the observed EEG seizure discharges are judged to be damaging brain or impairing function, and whether if they are abolished the patient is likely to improve clinically.[5,7,8,15,16] Determining this is difficult and controversial.[5,16,24,26,27] There are, however, some controlled and prospective studies indicating that in some conditions, particularly head injury,[23] and possibly subarachnoid hemorrhage,[22] the seizures of NCSE may sometimes damage brain leading to poorer outcomes. More reliable early measures to help predict responses to AED therapy and outcomes would be helpful in clarifying such issues and potentially better guiding therapy for patients with NCSE.

Although the etiology of NCSE is the best established predictor of both outcome and survival,[5,8,9] in our study, we found that a favorable clinical response to an acute IV trial of a BDZ was also predictive of survival, recovery of consciousness before hospital discharge, and better functional recovery at discharge. In addition, we observed that an EEG response to this acute IV BDZ trial was predictive of recovery of consciousness before discharge. On the basis of such findings, both the clinical and EEG response to an acute BDZ trial may aid in predicting outcomes and stratifying those individuals

with NCSE more likely to benefit from aggressive treatment. Ideally, such information should be combined with other reported predictors or measures of outcome in NCSE, particularly etiology, but also with others potential predictors such as severe impairment of mental status and the development of acute complications,[9] to form an optimal individual management strategy.

On the basis of the findings in our study, the clinical response to an acute IV BDZ in patients with NCSE is a stronger predictor of outcome than the EEG response. In our study, we determined the clinical response at up to 1 hour after the last IV BZD dose, but it remains to be determined whether a longer time range would be better for concluding assessment of a clinical response as some deeply sedated or patients in coma with related comorbidities may have delayed responses. Although we found that the EEG response to an acute IV trial of BDZ is predictive of recovery of consciousness during the hospitalization, it is not predictive for survival and functional recovery. Furthermore, although our findings indicate a trend showing that a complete EEG response may be more predictive than a partial response, this did not prove statistically significant.

This pilot study has several limitations. In particular, it was not a prospective, randomized, controlled study, so the results of the BDZ trial may have influenced subsequent therapy and outcome. However, this protocol was used as a diagnostic aid in suspected NCSE,[5,7,12,13] and the findings were not promoted to direct or influence subsequent treatment. Indeed, treating physicians were specifically advised to individualize their patient's optimal therapy based on their best judgment of the clinical situation because this type of acute BDZ trial was not an established or proven predictor of outcome. Another limitation of this study is that the initial degree of impairment of consciousness and the clinical response after IV BDZs were not rigorously quantified. Quantified and standardized measures of conscious impairment and recovery would be preferable.[28] Also, only initial improvement in cognitive function was analyzed, but in some patients, particularly those in deep coma, it has been proposed that such clinical improvement may lag EEG improvement and also warrants consideration.[7]

Challenging our findings is a previous report of a similar study that conflicts with our results.[9] That study identified several significant predictors of outcome in NCSE including etiology of the SE, severity of impairment of mental status, and development of acute complications, but it did not find the BDZ test significant.[9] It is unclear why the results of that study differ from ours. In some ways, the BDZ test populations were comparable in the 2 studies, with, for example, similar mortality rates, but there were also potentially relevant differences. In the previous report, there was a higher percentage (48%) of individuals whose SE was attributed to the preexisting epilepsy,[9] as compared with only 11% in our study. Methodologies also varied, with the previous study focusing on a large number of variables other than the BDZ test but with less detail regarding the BDZ protocols employed.[9] Although both studies retrospectively studied the BDZ test, only our study prospectively established a BDZ protocol. Also, the criteria for defining a "clinical response" varied between the studies with our study using a higher standard focusing more on cognitive improvement. This may, in part, account for why only 35% of the individuals in our study were clinical responders as compared with 61% in the other report.[9] The better predictive value of a BDZ trial for outcome in our study may reflect these higher criteria for cognitive improvement, because severity of mental status impairment has been described as a predictor of outcome.[9] Still, both the previous report and this study were retrospective and uncontrolled, so it is difficult to determine the exact reasons for the observed differences and disparity in the conclusions.

We propose that this issue warrants further consideration and investigation. We recommend future large, prospective, randomized, controlled studies to better define the potential predictive value of a BDZ trial, and other proposed variables,[9] particularly including etiology and associated comorbidities, in patients with suspected NCSE. Also, to properly study outcomes in NCSE and the risks and benefits of early and aggressive AED therapy on outcomes, interventions should be well standardized and controlled. Such future studies should be designed to incorporate strict, standardized criteria to measure both the clinical[7,9,28] and EEG[7,9,11,17] responses to acute IV BDZs, or other AEDs. In addition, terminology describing the epileptiform patterns associated in NCSE should incorporate recently proposed standardized guidelines.[17]

Our study concludes that a favorable clinical response to an acute IV dose of BDZ in patients with suspected NCSE is predictive of survival, recovery of consciousness before hospital discharge, and better functional recovery at discharge. An EEG response to a BDZ is also predictive of recovery of consciousness before discharge. Although we do not propose that the clinical and EEG responses to acute AED administration should be reinstituted as requirements for diagnosing NCSE, as originally proposed by some authors,[12,13] we conclude that they merit inclusion, along with other important factors, particularly etiology and associated comorbidities,[9] for the study and assessment of prognosis and outcome in NCSE. Acute AED trials, with agents like a BZD, warrant further consideration and investigation to determine if they may aid in the characterization, classification, stratification, and optimal management of patients with suspected NCSE.

REFERENCES

1. DeLorenzo RJ, Hauser WA, Towne AR, et al. A prospective, population-based epidemiologic study of status epilepticus in Richmond, Virginia. *Neurology*. 1996;46:1029–1035.
2. Logroscino G, Hesdorffer DC, Cascino G, et al. Short term mortality after a first episode of status epilepticus. *Epilepsia*. 1997; 38:1344–1349.
3. Gastaut H. Classification of status epilepticus. In: Delgado-Escueta AV, Wasterlain CG, Treiman DM, et al, eds. *Status Epilepticus (Advances in Neurology; vol 34)*. New York: Raven Press; 1983:15–34.
4. Dodson WE, DeLorenzo RF, Pedley TA, et al. Treatment of convulsive status epilepticus: recommendations of the Epilepsy Foundation of America's Working Group on the Treatment of Status Epilepticus. *JAMA*. 1993;270:854–859.
5. Krumholz A, Sung GY, Fisher RS, et al. Complex partial status epilepticus accompanied by serious morbidity and mortality. *Neurology*. 1995;45:1499–1504.
6. Krumholz A. Epidemiology and evidence for morbidity of nonconvulsive status epilepticus. *J Clin Neurophysiol*. 1999;16: 314–322.
7. Kaplan PW. The clinical features, diagnosis, and prognosis of nonconvulsive status epilepticus. *Neurologist*. 2005;6:348–361.
8. Waterhouse EJ. The epidemiology of nonconvulsive status epilepticus. In: Kaplan PW, Drislane FW, eds. *Nonconvulsive Status Epilepticus*. New York: Demos Medical; 2009:23–29.
9. Shneker BF, Fountain NB. Assessement of acute morbidity and mortality in nonconvulsive status epilepticus. *Neurology*. 2003; 61:1066–1073.
10. Shorvon S. What is nonconvulsive status epilepticus, and what are its subtypes? *Epilepsia*. 2007;48(suppl 8):35–38.

11. Brenner RP. EEG in convulsive and nonconvulsive status epilepticus. *J Clin Neurophysiol*. 2004;21:319–331.
12. Porter RJ, Penry JK. Petit mal status. In: Delgado-Escueta AV, Wasterlain CG, Treiman DM, et al, eds. *Status Epilepticus (Advances in Neurology; vol 34)*. New York: Raven Press; 1983:61–67.
13. Treiman DM, Delgado-Escueta AV. Complex partial status epilepticus. *Adv Neurol*. 1983;34:69–81.
14. Towne AR, Waterhouse EJ, Boggs JG, et al. Prevalence of nonconvulsive status epilepticus in comatose patients. *Neurology*. 2000;54:340–345.
15. Drislane FW, Lopez MR, Blum AS, et al. Detection and treatment of refractory status epilepticus in the intensive care unit. *J Clin Neurophysiol*. 2008;25:181–186.
16. Jordan KG, Hirsch LJ. In nonconvulsive status epilepticus (NCSE), treat to burst suppression: pro and con. *Epilepsia*. 2006;47(suppl 1):41–45.
17. Hirsch LJ, Benner RP, Drislane FW, et al. American Clinical Neurophysiology Society Subcommittee on Research Terminology for Continuous EEG Monitoring: proposed standardized terminology for rhythmic and periodic patterns encountered in critically ill patients. *J Clin Neurophysiol*. 2005;22:122–135.
18. Granner MA, Lee SI. Nonconvulsive status epilepticus: EEG analysis in a large series. *Epilepsia*. 1994;35:42–47.
19. Levy DE, Bates D, Caronna JJ, et al. Prognosis in nontraumatic coma. *Ann Intern Med*. 1981;94:293–3.
20. Privitera M, Hoffman M, Moore JL, et al. EEG detection of nontonic-clonic status epilepticus in patients with altered consciousness. *Epilepsy Res*. 1994;18:155–166.
21. Guberman A, Cantu-Reyna G, Stuss D, et al. Nonconvulsive generalized status epilepticus: clinical features, neuropsychological testing, and long-term follow-up. *Neurology*. 1986;36:1284–1291.
22. Claassen J, Hirsch LJ, Frontera JA, et al. Prognostic significance of continuous EEG monitoring in patients with poor-grade subarachnoid hemorrhage. *Neurocrit Care*. 2006;4:103–112.
23. Vespa PM, McArthur DL, Xu Y, et al. Nonconvulsive seizures after traumatic brain injury are associated with hippocampal atrophy. *Neurology*. 2010;75:792–798.
24. Thomas P. How urgent is the treatment of nonconvulsive status epilepticus? *Epilepsia*. 2007;48(Suppl 8):44–45.
25. Kaplan PW. Assessing the outcomes in patients with nonconvulsive status epilepticus: nonconvulsive status epilepticus is underdiagnosed, potentially overtreated, and confounded by comorbidity. *J Clin Neurophysiol*. 1999;16:341–352.
26. Terzano MG, Parrino L, Mazzucchi A, et al. Confusional state with periodic lateralized epileptiform discharges (PLEDs): a peculiar epileptic syndrome in the elderly. *Epilepsia*. 1986;27:446–457.
27. Treiman DM, Walton NY, Kendrick C. Progressive sequence of electroencephalographic changes during generalized convulsive status epilepticus. *Epilepsy Res*. 1990;5:49–60.
28. Kirby D, Fountain N, Quigg M. Technical tips: standardized mental status testing for nonconvulsive status epilepticus. *Am J Electroneurodiagnositic Technol*. 2004;44:199.

