NÖROLOJİ YOĞUN BAKIMDA NONKONVÜLZİF STATUS EPİLEPTİKUS TEDAVİSİ

JENERALİZE KONVÜLZİF STATUS EPİLEPTİKUS TEDAVİSİNDEN FARKLILIKLARI

Dr. Özlem Kayım Yıldız

Cumhuriyet Üniversitesi Tıp Fakültesi

Nöroloji A.D.

MULTİDİSİPLİNER STATUS EPİLEPTİKUS TEDAVİ PROTOKOLÜ ÇALIŞTAYI, 08.04.2016, İSTANBUL

- *"Bir süreyi* aşan aralıksız nöbet aktivitesi veya interiktal dönemde bazal santral sinir sistemi fonksiyonları [illegible] eksizin tekrarlayıcı n[illegible]

Status epileptikus önemli morbidite ve mortalite potansiyeli taşıyan nörolojik ve medikal bir acil!!!

- Klinik çalışma[illegible]
  - 5 dk→ Jeneralize konvülzif status epileptikusun bu süreden sonra spontan sonlanması olası değil
  - 30 dk→ Eksperimental çalışmalarda 30 dk.yı aşan devamlı nöbet aktivitesinin irreversibl nöronal hasara yol açtığı gösterildi

A definition and classification of status epilepticus – Report of the ILAE Task Force on Classification of Status Epilepticus

*†‡Eugen Trinka, §Hannah Cock, ¶Dale Hesdorffer, #Andrea O. Rossetti, **Ingrid E. Scheffer, ††Shlomo Shinnar, ‡‡Simon Shorvon, and §§Daniel H. Lowenstein

Epilepsia, 56(10):1515–1523, 2015
doi: 10.1111/epi.13121

Classically SE was defined as a "a condition characterized by an epileptic seizure that is sufficiently prolonged or repeated at sufficiently brief intervals so as to produce an unvarying and enduring epileptic condition."[7,8]

The Commission on Classification and Terminology and the Commission on Epidemiology of the International League Against Epilepsy (ILAE) have charged a Task Force to revise concepts, definition, and classification of status epilepticus (SE). The proposed new definition of SE is as follows: *Status epilepticus is a condition resulting either from the failure of the mechanisms responsible for seizure termination or from the initiation of mechanisms, which lead to abnormally, prolonged seizures (after time point t_1). It is a condition, which can have long-term consequences (after time point t_2), including neuronal death, neuronal injury, and alteration of neuronal networks, depending on the type and duration of seizures.* This definition is concep-

Table 1. Operational dimensions with t_1 indicating the time that emergency treatment of SE should be started and t_2 indicating the time at which long-term consequences may be expected

Type of SE	Operational dimension 1 Time (t_1), when a seizure is likely to be prolonged leading to continuous seizure activity	Operational dimension 2 Time (t_2), when a seizure may cause long term consequences (including neuronal injury, neuronal death, alteration of neuronal networks and functional deficits)
Tonic–clonic SE	5 min	30 min
Focal SE with impaired consciousness	10 min	>60 min
Absence status epilepticus	10–15 min[a]	Unknown

[a]Evidence for the time frame is currently limited and future data may lead to modifications.

NONKONVÜLZİF STATUS EPİLEPTİKUS NEDİR?

neurocritical care society Neurocrit Care (2012) 17:3–23
DOI 10.1007/s12028-012-9695-z

REVIEW

Guidelines for the Evaluation and Management of Status Epilepticus

Gretchen M. Brophy · Rodney Bell · Jan Claassen · Brian Alldredge · Thomas P. Bleck · Tracy Glauser · Suzette M. LaRoche · James J. Riviello Jr. · Lori Shutter · Michael R. Sperling · David M. Treiman · Paul M. Vespa · Neurocritical Care Society Status Epilepticus Guideline Writing Committee

- Elektrografik nöbet aktivitesinde uzamanın (sınır genellikle 30 dk) nonkonvülzif semptomlara yol açması
- Jeneralize konvülzif status epileptikus klinik bulguları olmaksızın EEG'de izlenen nöbet aktivitesi varlığı

- Nöbetlerin semiyolojik spektrumu son derece değişken
- Negatif semptomlar; anoreksi, afazi/mutizm, amnezi, katatoni, koma, konfüzyon, letarji, staring
- Pozitif semptomlar; ajitasyon, agresyon, otomatizmalar, göz kırpma, ağlama, deliryum, sanrılar, ekolali, fasiyal twitching, gülme, bulantı-kusma, nistagmus/göz deviasyonu, perseverasyon, psikoz, huzursuzluk

J Clin Neurophysiol. 2008;25:181–6.

Table 2. Axis I: Classification of status epilepticus (SE)

(A) With prominent motor symptoms
A.1 Convulsive SE (CSE, synonym: tonic–clonic SE)
- A.1.a. Generalized convulsive
- A.1.b. Focal onset evolving into bilateral convulsive SE
- A.1.c. Unknown whether focal or generalized

A.2 Myoclonic SE (prominent epileptic myoclonic jerks)
- A.2.a. With coma
- A.2.b. Without coma

A.3 Focal motor
- A.3.a. Repeated focal motor seizures (Jacksonian)
- A.3.b. Epilepsia partialis continua (EPC)
- A.3.c. Adversive status
- A.3.d. Oculoclonic status
- A.3.e. Ictal paresis (i.e., focal inhibitory SE)

A.4 Tonic status
A.5 Hyperkinetic SE

(B) Without prominent motor symptoms (i.e., nonconvulsive SE, NCSE)
B.1 NCSE with coma (including so-called "subtle" SE)
B.2 NCSE without coma
- B.2.a. Generalized
  - B.2.a.a Typical absence status
  - B.2.a.b Atypical absence status
  - B.2.a.c Myoclonic absence status
- B.2.b. Focal
  - B.2.b.a Without impairment of consciousness (aura continua, with autonomic, sensory, visual, olfactory, gustatory, emotional/psychic/experiential, or auditory symptoms)
  - B.2.b.b Aphasic status
  - B.2.b.c With impaired consciousness
- B.2.c Unknown whether focal or generalized
  - B.2.c.a Autonomic SE

'electrographic status epilepticus in coma or status in coma'

'simple or complex partial status epilepticus'

'Convulsive'

"episodes of excessive abnormal muscle contractions, usually bilateral, which may be sustained, or interrupted"

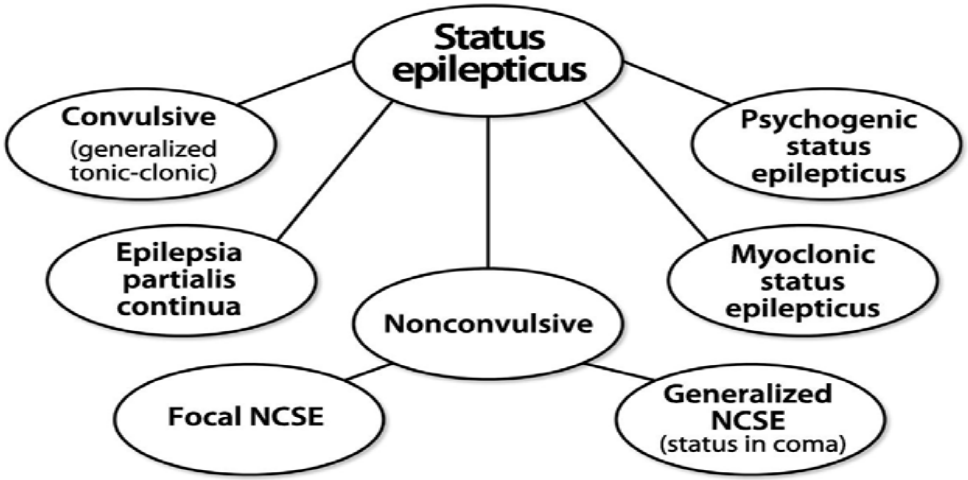

Table 3. Currently indeterminate conditions (or "boundary syndromes")

Epileptic encephalopathies
Coma with non evolving epileptiform EEG pattern[a]
Behavioral disturbance (e.g., psychosis) in patients with epilepsy
Acute confusional states, (e.g., delirium) with epileptiform EEG patterns

[a]Lateralized and generalized periodic discharges with monotonous appearance are not considered as evolving EEG patterns.[26,27]

CONTINUUM: Lifelong Learning in Neurology Issue: Volume 21(5, Neurocritical Care), 2015, 1362–83 Epilepsia 2015;56(10):1515-23.

Table 2. Axis I: Classification of status epilepticus (SE)

(A) With prominent motor symptoms

A.1 Convulsive SE (CSE, synonym: tonic–clonic SE)

A.1.a. Genera

A.1.b. Focal o

A.1.c. Unknov

A.2 Myoclonic S

A.2.a. With cc

A.2.b. Withou

A.3 Focal motor

A.3.a. Repeated focal motor seizures (Jacksonian)

A.3.b. Epilepsia partialis continua (EPC)

A.3.c. Adversive status

A.3.d. Oculoclonic status

A.3.e. Ictal paresis (i.e., focal inhibitory SE)

A.4 Tonic status

A.5 Hyperkinetic SE

(B) Without prominent motor symptoms (i.e., nonconvulsive SE, NCSE)

B.1 NCSE with coma (including so-called "subtle" SE)

B.2 NCSE without coma

B.2.a. Generalized

B.2.a.a Typical absence status

B.2.a.b Atypical absence status

B.2.a.c Myoclonic absence status

B.2.b. Focal

B.2.b.a Without impairment of consciousness (aura continua, with autonomic, sensory, visual, olfactory, gustatory, emotional/psychic/experiential, or auditory symptoms)

B.2.b.b Aphasic status

B.2.b.c With impaired consciousness

B.2.c Unknown whether focal or generalized

B.2.c.a Autonomic SE

A definition and classification of status epilepticus – Report of the ILAE Task Force on Classification of Status Epilepticus

*†‡Eugen Trinka, §Hannah Cock, ¶Dale Hesdorffer, #Andrea O. Rossetti, **Ingrid E. Scheffer, ††Shlomo Shinnar, ‡‡Simon Shorvon, and §§Daniel H. Lowenstein

Epilepsia, 56(10):1515–1523, 2015
doi: 10.1111/epi.13121

Table 1. Classification scheme for NCSE.

NCSE in the neonatal period and infancy

- Neonatal NCSE
- NCSE in neonatal and infantile epilepsy syndromes
  - West Syndrome
  - Ohtahara syndrome
  - Severe myoclonic encephalopathies of infancy
  - Benign neonatal seizures (and benign familial neonatal
  - NCSE in other early neonatal and infantile epilepsies

NCSE in childhood

- NCSE in benign focal childhood epilepsy syndromes
- NCSE (often specific forms) in severe childhood epileptic encephalopathies/syndromes
  - Electrical status epilepticus in sleep (ESES)
  - Landau Kleffner Syndrome
  - NCSE in Dravet's syndrome
  - NCSE in Ring Chromosome X
  - NCSE in myoclonic syndromes of childhood
  - NCSE in Angelman's syndrome
  - Severe myoclonic encephalopathies of childhood
  - Myoclonic-astatic epilepsy

NCSE in childhood and adult life

- NCSE in the severe epileptic encephalopathies/syndromes (atypical absence and other forms of NCSE)
  - Lennox Gastaut syndrome
  - Other childhood epileptic encephalopathies
- NCSE in acute cerebral injury
  - Acute confusional states (including acute symptomatic partial SE)
  - NCSE in coma (including myoclonic status epilepticus in coma)
- NCSE in patients with epilepsy but without encephalopathy
  - Simple partial NCSE
    EPC and non-motor forms of simple partial NCSE
  - Complex partial status epilepticus
  - Absence status epilepticus in idiopathic generalised epilepsies
    Panyotopoulos syndrome, EMA, JME
  - Myoclonic status epilepticus in idiopathic generalised epilepsy
  - NCSE in the postictal phase of tonic clonic seizures
  - NCSE inpatients without epileptic encephalopathy/acute cerebral injury, which take the form of cognitive impairment or confusion, and which do not conform to the categories of simple or complex partial SE

Status epilepticus confined to adult life

- *De novo* absence status epilepticus of late onset

Boundary syndromes

- Cases with epileptic encephalopathy in whom it is not clear to what extent electrographic seizure activity is contributing to the clinical impairment
- Cases with acute brain injury in whom it is not clear to what extent electrographic seizure activity is contributing to the clinical impairment
- Cases with behavioural disturbances/psychosis in whom it is not clear to what extent electrographic seizure activity is contributing the clinical impairment

Conference report
Epileptic Disord 2005; 7 (3): 253-96

Nonconvulsive status epilepticus: Epilepsy Research Foundation Workshop Reports

ELEKTROKLİNİK VE ETİYOLOJİK KLASİFİKASYON

- **NCSE Tipi (Elektroklinik klasifikasyon):**
  - Koma/stupor ile birlikte
  - Koma/stupor olmaksızın
    - Jeneralize başlangıçlı (absans SE: tipik, atipik, myoklonik absans)
    - Fokal başlangıçlı (bilinç bozukluğu ile birlikte veya değil, afazik NCSE)
    - Fokal veya jeneralize olduğu bilinmeyen (örneğin otonomik SE)

- **Etiyoloji:**
  - Semptomatik (bilinen)
    - Akut
    - Remote
    - Progresif
    - Yaşla ilişkili elektroklinik sendromlarda NCSE
  - Kriptojenik (bilinmeyen)

EPİDEMİYOLOJİ

Table 2. Five population-based studies of status epilepticus (convulsive and nonconvulsive)

	Richmond Virginia USA (De Lorenzo *et al.* 1995)	Rochester, Minn, USA (Hesdorffer *et al.* 1998)	French-speaking Switzerland (Coeytaux *et al.* 2000)	Hessen, Germany (Knake *et al.* 2001)	Bologna, Italy (Vignatelli *et al.* 2003)
Year	1989-1991	1965-1984	1997-1998	1997-1999	1999-2000
Population (denominator)	202,774	1,090,055+	1,735,420	743,285	336,876
Number of cases	166	199	172	150	44
Incidence of SE (per 100,000 per year)	41 (raw) 61 (adjusted)	18.3 (adjusted)	9.9 (raw) 10.3 (adjusted)	17.1	10.7
Female: male ratio of cases	1: 1.2*	1: 1.9**	1: 1.7***	1: 1.9***	1: 0.84**
History of prior epilepsy	42%	44%	32.8%	50%	39%
Exclusions	Patients one month of age or less	-	Patients with post-anoxic encephalopathy	Patients under the age of 18 years	Patients under the age of 20 years

Epileptic Disord 2005;7(3):253-96. Eur J Neurol 2004;11:800-10

- Klinik çalışmalarda tüm status epileptikus olguları içerisindeki göreceli sıklığı değişken, %5-49

TABLE 2. *Clinical factor distribution in dead and living subjects with status epilepticus*

	Subjects with SE (44)	
	Dead (17)	Living (27)
Sex		
M	52.9%	29.6%
F	47.1%	70.4%
Age		
Mean (SD)	71.2 yr (13.4)	67.1 yr (17.1)
Median	69 yr	70 yr
Range	52–95 yr	20–91 yr
Etiology		
Acute symptomatic	58.8%	18.5%
Remote symptomatic	17.6%	44.4%
Progressive symptomatic	5.9%	14.8%
Idiopathic/cryptogenic	—	11.1%
Multifactorial	17.6%	11.1%
Seizure type		
Generalized convulsive	—	14.8%
Generalized nonconvulsive	—	3.7%
Myoclonic	35.3%	3.7%
Simple partial	5.9%	11.1%
Complex partial	—	25.9%
Partial secondarily generalized	47.1%	37.0%
Unclassified	11.8%	3.7%
Duration		
<2 h	28.6%	19.2%
2–24 h	64.3%	50%
>24 h	7.1%	30.8%
NA	3 subjects	1 subject

TABLE 1. *Frequency of different types of status epilepticus classified according to the International classification of seizures (10)*

Type of status epilepticus	Frequency
Simple partial	20 (13.3%)
Complex partial	65 (43.3%)
Secondarily generalized	29 (19.3%)
Primary generalized	21 (14.0%)
Absence status	9 (6.0%)
Unknown	6 (4.0%)
Total	150 (100%)

Epilepsia, 42 (2001), pp. 714–718 Epilepsia. 2015;56(10):1515-23. Lancet 2007;6(4):329-339.

Table 4. Frequency of certain types of NCSE: comparison of literature estimates and figures from the 5 epidemiological studies

Type of NCSE	5 epidemiological studies (cases/100,00/year)	Literature estimates (cases/100,000/year)
Simple partial SE	1.1-14.1	1
Complex partial SE	1.1-14.1	15-45
Absence SE	0.2-1.2	0.2-0.5
Myoclonic SE	0.2-1.2	0.2-1.2

(Figures from the epidemiological studies extrapolated with age adjustment)

Epileptic Disord 2005;7(3):253-96.

Nonkonvülzif nöbetler ve status epileptikus YBÜ hastalarında sık

Table 1 Rates of seizures reported by hospital location

Location	Study	Study design	N[a]	% Seizures[b]	% NCS or NCSE[c]
NICU	Jordan [15]	Retrospective	124	35 %	74 %
	Young et al. [16]	Retrospective	127	38 %	46 %
	Pandian et al. [12]	Retrospective	105	68 %	27 % NCSE
	Narayanan and Murthy [5]	Prospective	210	10.50 %	10.50 %
All ICU	Privitera et al. [2][d]	Retrospective	198	37 %	100 %
	Towne et al. [1][e]	Retrospective	236	8 %	100 % NCSE
	Claassen et al. [4]	Retrospective	570	19 %	92 %
MICU	Oddo et al. [17]	Retrospective	201	10 %	67 %
Pediatric ICU	Saengpattrachai et al. [25]	Retrospective	141	16 %	100 %
	Jette et al. [13]	Retrospective	117	44 %	75 %
	Shahwan et al. [8]	Prospective	100	7 %	7 % (2 % NCS only)
	McCoy et al. [14]	Retrospective	120	32 %	90 % (72 % NCS only)
	Williams et al. [18]	Retrospective	122	38 %	83 % (49 % NCS only)
	Abend et al. [7•]	Prospective	100	46 %	100 %

cEEG continuous electroencephalography, *EEG* electroencephalography, *ICU* intensive care unit, *MICU* medical intensive care unit, *NCS* nonconvulsive seizure, *NCSE* nonconvulsive status epilepticus, *NICU* neurological intensive care unit

[a] Population size

[b] The percentage of monitored patients in which any seizure was recorded

[c] The percentage of the total seizure that were NCS or NCSE

[d] 37 % Routine EEG only

Curr Neurol Neurosci Rep 2012;12:419-28

Table 2 Rates of seizures reported by condition

Condition	Study	Study design	N[a]	% Seizures[b]	% NCS or NCSE[c]
Convulsive SE	DeLorenzo et al. [3]	Prospective	164	48 %	100 % (29 % NCSE)
TBI	Vespa et al. [19]	Retrospective	94	22 %	52 %
	Claassen [4]	Retrospective	51	18 %	100 %
SAH	Claassen et al. [4]	Retrospective	108	19 %	95 % (70 % NCSE)
	Dennis et al. [20]	Retrospective	26	8 %	100 % NCSE
Hemorrhagic stroke	Claassen et al. [23]	Retrospective	102	31 %	58 %
	Vespa et al. [22]	Prospective	63	23 %	80%[d]
Ischemic stroke	Vespa et al. [22]	Prospective	46	6 %	80%[d]
CNS infection	Carrera et al. [24]	Retrospective	42	33 %	71 %

CNS central nervous system, *NCS* nonconvulsive seizure, *NCSE* nonconvulsive status epilepticus, *SAH* subarachnoid hemorrhage, *SE* status epilepticus, *TBI* traumatic brain injury

[a] Number of patients

[b] The percentage of monitored patients in which any seizure was recorded

[c] The percentage of the total seizure that were NCS or NCSE

[d] These results were combined within one investigation

Neurology. 2004 May 25;62(10):1743-8.

Detection of electrographic seizures with continuous EEG monitoring in critically ill patients.

Claassen J[1], Mayer SA, Kowalski RG, Emerson RG, Hirsch LJ.

Author information

Abstract

OBJECTIVE: To identify patients most likely to have seizures documented on continuous EEG (cEEG) monitoring and patients who require more prolonged cEEG to record the first seizure.

METHODS: Five hundred seventy consecutive patients who underwent cEEG monitoring over a 6.5-year period were reviewed for the detection of subclinical seizures or hic, clinical, and EEG findings were recorded and a multivariate logis izure activity and 2) first seizure detected after >24 hours of mon

YBÜ HASTALARININ %19'UNDA NONKONVÜLZİF NÖBETLER VAR

RESULTS: Seizures w izures were exclusively nonconvulsive in 92% (n = 101) of these patie e time of monitoring. Electrographic seizures were associated with coma (odds ratio [OR] 7.7, 95% CI 4.2 to 14.2), age <18 years (OR 6.7, 95% CI 2.8 to 16.2), a history of epilepsy (OR 2.7, 95% CI 1.3 to 5.5), and convulsive seizures during the current illness prior to monitoring (OR 2.4, 95% CI 1.4 to 4.3). Seizures were detected within the first 24 hours of cEEG monitoring in 88% of all patients who would eventually have seizures detected by cEEG. In another 5% (n = 6), the first seizure was recorded on monitoring day 2, and in 7% (n = 8), the first seizure was detected after 48 hours of monitoring. Comatose patients were more likely to have their first seizure recorded after >24 hours of monitoring (20% vs 5% of noncomatose patients; OR 4.5, p = 0.018).

CONCLUSIONS: CEEG monitoring detected seizure activity in 19% of patients, and the seizures were almost always nonconvulsive. Coma, age <18 years, a history of epilepsy, and convulsive seizures prior to monitoring were risk factors for electrographic seizures. Comatose patients frequently required >24 hours of monitoring to detect the first electrographic seizure.

neurocritical care society Neurocrit Care (2012) 16:114–122
DOI 10.1007/s12028-011-9565-0

ORIGINAL ARTICLE

Frequency and Timing of Nonconvulsive Status Epilepticus in Comatose Post-Cardiac Arrest Subjects Treated with Hypothermia

Jon C. Rittenberger · Alexandra Popescu · Richard P. Brenner · Francis X. Guyette · Clifton W. Callaway

Abstract

Background Therapeutic hypothermia (TH) improves outcomes in comatose patients resuscitated from cardiac arrest. However, nonconvulsive status epilepticus (NCSE) may ng of NCS *Meti* th TH and tween 8/1/ l, and func Each cEE lefine NCS non- parametric statistics.

POSTKARDİYAK ARREST TERAPÖTİK HİPOTERMİ UYGULANAN KOMADAKİ HASTALARIN %12'SİNDE NCSE VAR

Results Mean age of the 101 subjects was 57 years (SD 15) with most subjects being male ($N = 55$, 54%) and experiencing out-of-hospital cardiac arrest ($N = 78$; 77%). Ventricular fibrillation was the initial cardiac rhythm in 39 (38%). All subjects received TH. Thirty subjects (30%) awoke at a median of 41 h (IQR 30, 61) after cardiac arrest. A total of 29/30 (97%) subjects surviving to hospital discharge were awake. Median interval from arrest to placement of cEEG was 9 h (IQR 6, 12), at which time the mean temperature was 33.9°C. NCSE occurred in 12 (12%) subjects. In 3/12 (25%) subjects, NCSE was present when the cEEG recording began. In 4 subjects, NCSE occurred

Prevalence of nonconvulsive status epilepticus in comatose patients

A.R. Towne, MD, E.J. Waterhouse, MD, J.G. Boggs, MD, L.K. Garnett, RN, MS, A.J. Brown, R EEG T, J.R. Smith Jr., BSEE and R.J. DeLorenzo, MD, PhD, MPH

Background: Nonconvulsive status epilepticus (NCSE) is a form of status epilepticus (SE) that is an often unrecognized cause of coma.

KOMADAKİ HASTALARDA NCSE %8

that we identify over 95% of all SE cases at the Medical College of Virginia Hospitals. Only cases that were found to have no clinical signs of SE were included in this study.

Results: EEG demonstrated that 8% of these patients met the criteria for the diagnosis of NCSE. The study included an age range from 1 month to 87 years.

Conclusions: This large-scale EEG evaluation of comatose patients without clinical signs of seizure activity found that NCSE is an under-recognized cause of coma, occurring in 8% of all comatose patients without signs of seizure activity. EEG should be included in the routine evaluation of comatose patients even if clinical seizure activity is not apparent.

Epilepsy Research

Volume 18, Issue 2, June 1994, Pages 155–166

Research report

EEG detection of nontonic-clonic status epilepticus in patients with altered consciousness

Michael Privitera [a], Michael Hoffman[a], J.Layne Moore[a, †], Debra Jester[b]

Abstract

Subtypes of status epilepticus (SE) without tonic-clonic convulsions (nontonic-clonic SE) present as alter
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where physicians ordered EEG to evaluate altered consciousness or possible SE. Out of 198 cases with altered consciousness but no clinical convulsions, 74 (37%) showed EEG and clinical evidence of definite or probable nontonic-clonic SE. Forty-two episodes (57%) were probable or definite complex partial SE, 29 (39%) were probable or definite subtle generalized SE, and three (4%) were myoclonic SE. In 23 SE cases altered consciousness was the only clinical sign at the time of diagnosis; subtle motor activity was present in 36 others. Neither clinical signs nor prior history predicted which patients showed SE on EEG. Nontonic-clonic SE followed a cerebral infarction in 16 cases. Contrary to other reports, we found no relationship between duration of SE and EEG pattern. Subtle generalized SE occurred most commonly in the setting of a diffuse brain injury rather than evolving from convulsive SE. This study demonstrates that nontonic-clonic SE is a common finding in patients with unexplained altered consciousness and EEG is necessary in the evaluation of these patients .

BİLİNÇ DEĞİŞİKLİĞİ OLAN HASTALARDA NCSE %10,5-37

Epilepsia, 48(5):900–906, 2007
Blackwell Publishing, Inc.

Nonconvulsive Status Epilepticus in a Neurological Intensive Care Unit: Profile in a Developing Country

Jaishree T. Narayanan and Jagarlapudi M. K. Murthy

Material and Methods: Prospectively 210 consecutive patients with altered mental status admitted to neurological intensive care unit (NICU) of a tertiary care center in south India were studied for the frequency of NCSE. All patients were evaluated initially with 60-min emergent EEG (EmEEG) and subsequently by continuous EEG (cEEG) monitoring.

Results: Of the 210 with altered mental status admitted to NICU, the diagnosis of NCSE was established in 22 (10.5%) patients, in 12 (55%) patients with 60-min EmEEG and in 10 (45%) after cEEG monitoring for 12 to 48 hours.

Of the 22 patients with NCSE, 32% had subtle motor phenomena, these were not an initial presenting features, but were apparent during cEEG recording. Acute medical or neurologic etiology was the risk factor in 68% of patients. Central nervous system (CNS) infections and cortical sino-venous thrombosis

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19 patients
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NCSE, 4 (18%) had poor prognosis (3 deaths and one persistent vegetative state). The etiological risk factors in the 9 (41%) patients with excellent outcome included epilepsy (3), remote symptomatic (2), cryptogenic (1), and metabolic and drugs (3).

Conclusions: The frequency of NCSE in the current study was comparable with those in prior reports from developed countries. CNS infections accounted for about a fifth of the etiology. Outcome was excellent in patients with nonacute symptomatic NCSE. Initial 60-min EmEEG may be performed in establishing the diagnosis of NCSE, but almost half of patients with NCSE will be missed with this approach. **Key Words:** Nonconvulsive status epilepticus—Emergent EEG—Continuous EEG monitoring—Central nervous system infections—Midazolam.

J Neurosurg. 1999 November ; 91(5): 750–760. doi:10.3171/jns.1999.91.5.0750.

Increased incidence and impact of nonconvulsive and convulsive seizures after traumatic brain injury as detected by continuous electroencephalographic monitoring

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Division of Neurosurgery and Department of Neurology, University of California at Los Angeles School of Medicine, Los Angeles, California; and Department of Neurosurgery, Uppsala Un

KAFA TRAVMASI OLAN HASTALARIN %21'İNDE NÖBET, %52'Sİ NONKONVÜLZİF

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incidence of convulsive and nonconvulsive seizures by using continuous EEG monitoring in patients in the ICU during the initial 14 days post-injury.

Methods—Ninety-four patients with moderate-to-severe brain injuries underwent continuous EEG monitoring beginning at admission to the ICU (mean delay 9.6 ± 5.4 hours) and extending up to 14 days postinjury. Convulsive and non-convulsive seizures occurred in 21 (22%) of the 94 patients, with six of them displaying status epilepticus. In more than half of the patients (52%) the seizures were nonconvulsive and were diagnosed on the basis of EEG studies alone. All six patients with status epilepticus died, compared with a mortality rate of 24% (18 of 73) in the nonseizure group ($p < 0.001$). The patients with status epilepticus had a shorter mean length of stay (9.14 ± 5.9 days compared with 14 ± 9 days [t-test, $p < 0.03$]). Seizures occurred despite initiation of prophylactic phenytoin on admission to the emergency room, with maintenance at mean levels of 16.6 ± 2.8 mg/dl. No differences in key prognostic factors (such as the Glasgow Coma Scale score, early hypoxemia, early hypotension, or 1-month Glasgow Outcome Scale score) were found between the patients with seizures and those without.

Conclusions—Seizures occur in more than one in five patients during the 1st week after moderate-to-severe brain injury and may play a role in the pathobiological conditions associated with brain injury.

Nonconvulsive Status Epilepticus after Subarachnoid Hemorrhage

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SAK HASTALARINDA NCSE %8

OBJECTIVE: Although in-hospital seizures have been reported for 3 to 24% of patients with aneurysmal subarachnoid hemorrhage (SAH), nonconvulsive status epilepticus (NCSE) has not been previously described. We sought to determine the frequency and clinical features of NCSE among comatose patients with SAH.

METHODS: Between November 1997 and February 2000, we performed continuous electroencephalographic (cEEG) monitoring for at least 24 hours for all patients with aneurysmal SAH who were treated in our neurological intensive care unit and exhib- ited unexplained coma or neurological deterioration. NCSE was diagnosed when cEEG eding 1 nticon-

zation, nty-six having s were coma- d overt tonicoclonic activity. A worst Hunt and Hess grade of IV or V, older age, ventricular drainage, and cerebral edema on computed tomographic scans were identified as risk factors for NCSE (all $P < 0.01$). NCSE was successfully terminated for five patients (63%), but only one experienced clinical improvement, which was transient; all eight patients eventually died after a period of prolonged coma.

CONCLUSION: cEEG monitoring detected NCSE for 8% of patients with SAH and otherwise unexplained coma or neurological deterioration. The seizures were highly refractory to therapy, and the prognosis for these patients was extremely poor. Routine postoperative cEEG monitoring of patients with SAH who are at high risk for NCSE, allowing earlier diagnosis and treatment, offers the best chance of improving the outcomes for patients with this disorder.

KEY WORDS: Coma, Electroencephalography, Neurological Intensive care, Nonconvulsive status epilepticus, Subarachnoid hemorrhage

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Lippincott-Raven Publishers, Philadelphia
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Persistent Nonconvulsive Status Epilepticus After the Control of Convulsive Status Epilepticus

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KONVÜLZİF STATUS EPİLEPTİKUS SONRASINDA
NONKONVÜLZİF NÖBET: % 48, STATUS: % 14

Summary: *Purpose:* Convulsive status epilepticus (CSE) is a major medical and neurological emergency that is associated with significant morbidity and mortality. Despite this high morbidity and mortality, most acute care facilities in the United States cannot evaluate patients with EEG monitoring during or immediately after SE. The present study was initiated to determine whether control of CSE by standard treatment protocols was sufficient to terminate electrographic seizures.

Methods: One hundred sixty-four prospective patients were evaluated at the Medical College of Virginia/VCU Status Epilepticus Program. Continuous EEG monitoring was performed for a minimum of 24 h after clinical control of CSE. SE and seizure types were defined as described previously. A standardized data form entry system was compiled for each patient and used to evaluate the data collected.

Results: After CSE was controlled, continuous EEG monitoring demonstrated that 52% of the patients had no after-SE ictal discharges (ASIDS) and manifested EEG patterns of generalized slowing, attenuation, periodic lateralizing epileptiform discharges (PLEDS), focal slowing, and/or burst suppression. The remaining 48% demonstrated persistent electrographic seizures. More than 14% of the patients manifested nonconvulsive SE (NCSE) predominantly of the complex partial NCSE seizure (CPS) type (2). These patients were comatose and showed no overt clinical signs of convulsive activity. Clinical detection of NCSE in these patients would not have been possible with routine neurological evaluations without use of EEG monitoring. The clinical presentation, mortality, morbidity, and demographic information on this population are reported.

Conclusions: Our results demonstrate that EEG monitoring after treatment of CSE is essential to recognition of persistent electrographic seizures and NCSE unresponsive to routine therapeutic management of CSE. These findings also suggest that EEG monitoring immediately after control of CSE is an important diagnostic test to guide treatment plans and to evaluate prognosis in the management of SE. **Key Words:** Epilepsy—Status epilepticus—Nonconvulsive status epilepticus—Electroencephalographic monitoring.

Nonconvulsive seizures are common in critically ill children

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PEDİATRİK YBÜ HASTALARINDA
ELEKTROGRAFİK NÖBET: % 46, STATUS: % 19

EEG monitoring if they met institutional clinical practice criteria. Study enrollment and data collection were prospective. Logistic regression analysis was utilized to identify risk factors for seizure occurrence.

Results: One hundred children were evaluated. Electrographic seizures occurred in 46 and electrographic status epilepticus occurred in 19. Seizures were exclusively nonconvulsive in 32. The only clinical risk factor for seizure occurrence was younger age ($p = 0.03$). Of patients with seizures, only 52% had seizures detected in the first hour of monitoring, while 87% were detected within 24 hours.

Conclusions: Seizures were common in critically ill children with acute encephalopathy. Most were nonconvulsive. Clinical features had little predictive value for seizure occurrence. Further study is needed to confirm these data in independent high-risk populations, to clarify which children are at highest risk for seizures so limited monitoring resources can be allocated optimally, and to determine whether seizure detection and management improves outcome.

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Neurology®
2011;76:1071-1077

Neurology. 2003 May 13;60(9):1441-6.

Acute seizures after intracerebral hemorrhage: a factor in progressive midline shift and outcome.

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Author information

Abstract

OBJECTIVE: To determine whether early seizures that occur frequently after intracerebral hemorrhage (ICH) lead to increased brain edema as manifested by increased midline shift.

METH ...uous EEG monitc ...ed at admiss ...harge was asses...

RESULTS: Electrographic seizures occurred in 18 of 63 (28%) patients with ICH, compared with 3 of 46 (6%) patients with ischemic stroke (OR = 5.7, 95% CI 1.4 to 26.5, p < 0.004) during the initial 72 hours after admission. Seizures were most often focal with secondary generalization. Seizures were more common in lobar hemorrhages but occurred in 21% of subcortical hemorrhages. Posthemorrhagic seizures were associated with neurologic worsening on the NIH Stroke Scale (14.8 vs 18.6, p < 0.05) and with an increase in midline shift (+ 2.7 mm vs -2.4 mm, p < 0.03). There was a trend toward increased poor outcome (p < 0.06) in patients with posthemorrhagic seizures. On multivariate analysis, age and initial NIH Stroke Scale score were independent predictors of outcome.

CONCLUSION: Seizures occur commonly after ICH and may be nonconvulsive. Seizures are independently associated with increased midline shift after intraparenchymal hemorrhage.

ICH HASTALARININ %28'İNDE İSKEMİK İNME HASTALARININ %6'SINDA ELEKTROGRAFİK NÖBETLER VAR

Arch Neurol. 2008 Dec;65(12):1612-8. doi: 10.1001/archneur.65.12.1612.

Continuous electroencephalographic monitoring in critically ill patients with central nervous system infections.

Carrera E[1], Claassen J, Oddo M, Emerson RG, Mayer SA, Hirsch LJ.

Author information

Abstract

OBJECTIVES: To determine the prevalence, predictors, and clinical significance of electrographic seizures (ESz) and other continuous electroencephalographic monitoring findings in critically ill patients with central nervous system infections.

DESIGN

SETTIN

PATIEN ...atients [18%]; and fung ...d February 28, 2007.

MAIN OUTCOME MEASURES: Presence of ESz or periodic epileptiform discharges (PEDs).

RESULTS: Electrographic seizures were recorded in 14 patients (33%), and PEDs were recorded in 17 patients (40%). Twenty patients (48%) had either PEDs or ESz. Of the 14 patients with ESz, only 5 (36%) had a clinical correlate. Periodic epileptiform discharges (odds ratio=13.4; P=.001) and viral cause (odds ratio=13.0; P=.02) were independently associated with ESz. Both ESz (odds ratio=5.9; P=.02) and PEDs (odds ratio=6.1; P=.01) were independently associated with poor outcome at discharge (severe disability, vegetative state, or death).

CONCLUSIONS: In patients with central nervous system infections undergoing continuous electroencephalographic monitoring, ESz and/or PEDs were frequent, occurring in 48% of our cohort. More than half of the ESz had no clinical correlate. Both ESz and PEDs were independently associated with poor outcome. Additional studies are needed to determine whether prevention or treatment of these electrographic findings improves outcome.

SSS ENFEKSİYONLARI OLAN HASTALARIN %33'ÜNDE ELEKTROGRAFİK NÖBETLER VAR

Yoğun bakım hastalarının önemli bir kısmında nonkonvülzif nöbetler/status epileptikus var!!!

Tanı için yüksek klinik kuşku ve devamlı EEG monitorizasyonu gerekli!!!

Nonkonvülzif status epileptikus YBÜ'de şu şekillerde prezente olabilir

1. Akut medikal ve nörolojik hastalık, ilaç maruziyeti veya yoksunluğu hallerinde gelişen stupor/koma ve jeneralize elektrografik epileptik aktivite

2. Sekonder jeneralizasyon gösteren fokal nonkonvülzif status epileptikus, stupor veya komaya progrese olan konfüzyon ve jeneralize elektrografik epileptik aktivite

3. Klonik hareketlerin seyrekleşerek sonunda kaybolduğu jeneralize tonik klonik status epileptikus ile birlikte persistan elektrografik epileptik aktivite; 'end-stage' veya 'subtle status epileptikus'

CONTINUUM: Lifelong Learning in Neurology 2015;21(5):1362–1383

Şu durumlarda nonkonvülzif status epileptikus tanısı akla gelmeli

1. Akut beyin hasarı (genellikle intraserebral lober hemoraji, enfeksiyon, şiddetli travma, subaraknoid kanama veya cerrahi)
2. Akut beyin hasarı ile orantısız bilinç bozukluğu
3. Eski semptomatik beyin lezyonu
4. Epilepsi öyküsü
5. Tonik klonik nöbet/konvülzif status epileptikus sonrası persistan bilinç bozukluğu
6. Açıklanamayan fokal nörolojik defisit
7. Bilinç bozukluğu düzelmeyen/çok yavaş düzelen sepsis hastaları
8. Subtle motor fenomenler, nistagmus, klonus, opsoklonus

CONTINUUM: Lifelong Learning in Neurology 2015;21(5):1362–1383

Nonconvulsive status epilepticus

Factors associated with poor outcome after NCSE:

For patients diagnosed within 30 min of seizure onset, mortality was 36 % compared with 75 % for those patients diagnosed ≥24 h after seizure onset seizures [51]

Patients with NCSE treated and resolved within 10 h had 10 % mortality vs. 85 % mortality if seizures continued longer than 20 h [51]

- EEG monitorizasyonu yapılmaması NCSE tanısını geciktirir
- Tanıda gecikme refrakter status epileptikus gelişimi ve mortalite riskinde artış ile ilişkili

Indication	Rationale	Neurocritical Care Society Guidelines 2012[b]
Suspected seizures in patients with unexplained coma or altered mental status	Exclude nonconvulsive status epilepticus	Class I, Level B
Otherwise unexplained focal neurologic deficits (eg, aphasia or focal weakness)	Exclude nonconvulsive status epilepticus	No recommendation
Recent clinical seizure activity or status epilepticus without return to baseline within 10 minutes	Exclude nonconvulsive status epilepticus; titrate anesthetic agent to cessation of electrographic seizures; monitor for breakthrough subclinical seizures	Class I, Level B
Clinical seizure activity is of a start-stop-start quality	Confirm status epilepticus; exclude nonepileptic (psychogenic) status epilepticus	No recommendation

Table 10 Indications for cEEG in SE

Indication	Rationale	Grade
Recent clinical seizure or SE without return to baseline >10 min	Ongoing non-convulsive status despite cessation of motor activity 18–50 %	Class I, level B
Coma, including post-cardiac arrest	Frequent non-convulsive seizures, 20–60 %	Class I, level B
Epileptiform activity or periodic discharges on initial 30 min EEG	Risk of non-convulsive seizures, 40–60 %	Class I, level B
Intracranial hemorrhage including TBI, SAH, ICH	Frequent non-convulsive seizures, 20–35 %	Class I, level B
Suspected non-convulsive seizures in patients with altered mental status	Frequent non-convulsive seizures, 10–30 %	Class I, level B

Klinik kuşku varlığında en az bir rutin EEG çekilerek elektrografik nöbet dışlanmalı

Epileptiform aktivite saptanırsa devamlı EEG monitorizasyonu yapılmalı

CONTINUUM: Lifelong Learning in Neurology 2015;21(5):1362–1383

Table 2 GRADE recommendations for the indications for EEG in the ICU

GRADE recommendations			Patient description		Objective
Direction	Strength	Level of evidence	Underlying etiology	Scenario	
Pro	Strong (1)	Low quality (C)	Generalized convulsive status epilepticus	No return to functional baseline after initial antiepileptic therapy	Detect nonconvulsive seizures
Pro	Strong (1)	Low quality (C)	Refractory status epilepticus	Concern for ongoing seizure activity	Detect nonconvulsive seizures
Pro	Strong (1)	Low quality (C)	Traumatic brain injury	Unexplained alteration in consciousness[a]	Detect nonconvulsive seizures
Pro	Strong (1)	Low quality (C)	Subarachnoid hemorrhage	Unexplained alteration in consciousness[a]	Detect nonconvulsive seizures
Pro	Strong (1)	Low quality (C)	Intracerebral hemorrhage	Unexplained alteration in consciousness[a]	Detect nonconvulsive seizures
Pro	Strong (1)	Low quality (C)	Cardiac arrest	Persistent coma	Detect nonconvulsive seizures
Pro	Strong (1)	Low quality (C)	Encephalitis	Unexplained alteration in consciousness[a]	Detect nonconvulsive seizures
Pro	Strong (1)	Low quality (B)	Comatose patients without primary brain injury	Unexplained alteration in consciousness[a]	Detect nonconvulsive seizures
Pro	Weak (2)	Low quality (C)	Severe traumatic brain injury	Concern for ongoing seizure activity in high-risk patients (large cortical hemorrhagic contusion/hematoma)	Detect nonconvulsive seizures
Pro	Weak (2)	Very low quality (D)	Acute ischemic stroke	Unexplained alteration in consciousness[a]	Detect nonconvulsive seizures
Pro	Weak (2)	Low quality (C)	Subarachnoid hemorrhage	Patients in whom clinical examination is unreliable	Detect ischemia
Pro	Weak (2)				Prognostication
Pro	Weak (2)				Prognostication
Pro	Weak (2)				Prognostication

[a] Unexplained alte…rders (sodium, calcium, glucose, ammoniu…ain lesions on imaging (cerebral CT scan)

Intensive Care Med (2013) 39:1337–1351
DOI 10.1007/s00134-013-2938-4

SYSTEMATIC REVIEW

Jan Claassen
Fabio S. Taccone
Peter Horn
Martin Holtkamp
Nino Stocchetti
Mauro Oddo

Recommendations on the use of EEG monitoring in critically ill patients: consensus statement from the neurointensive care section of the ESICM

Recommendations for patients with TBI

1. We recommend EEG in all TBI patients with unexplained and persistent altered consciousness (strong recommendation, low quality of evidence—grade 1C).
2. We suggest EEG to rule out NCSz in patients with TBI and GCS $\leq$8, particularly in those with large cortical contusion/hematoma, depressed skull fracture or penetrating injury (weak recommendation, low quality of evidence—grade 2C).

Recommendations for patients with SAH

1. We recommend EEG to rule out NCSz in all SAH patients with unexplained and persistent altered consciousness (strong recommendation, low quality of evidence—grade 1C).

Recommendations for patients with ICH

1. We recommend EEG to ru
patients with unexplained a
sciousness (strong recomm
evidence—grade 1C).

Recommendations for comatose ICU patients without acute primary brain injury

1. We suggest EEG in comatose ICU patients without an acute primary brain condition and with unexplained impairment of mental status or unexplained neurological deficits to rule out NCSz, particularly in those with severe sepsis or renal/hepatic failure (weak recommendation, low quality of evidence—grade 2C).

Recommendations for patients with AIS

1. We suggest EEG to rule out NCSz in all AIS patients with unexplained and/or persistently altered consciousness (weak recommendation, very low quality of evidence—grade 2D).

Recommendations for comatose patients after CA

1. We recommend EEG during TH and within 24 h after rewarming to rule out NCSz in all comatose patients after CA (strong recommendation, low quality of evidence—grade 1C).

Recommendations for patients with infectious and non-infectious encephalitis

patients with encephalitis that
nexplained neurological deficits
g recommendation, low quality
).

Table 1. Working clinical criteria for nonconvulsive status epilepticus

Patients without known epileptic encephalopathy
- EDs > 2.5 Hz, *or*
- EDs ≤ 2.5 Hz or rhythmic delta/theta activity (>0.5 Hz) AND one of the following:
  - EEG and clinical improvement after IV AED[a], *or*
  - Subtle clinical ictal phenomena during the EEG patterns mentioned above, *or*
  - Typical spatiotemporal evolution[b]

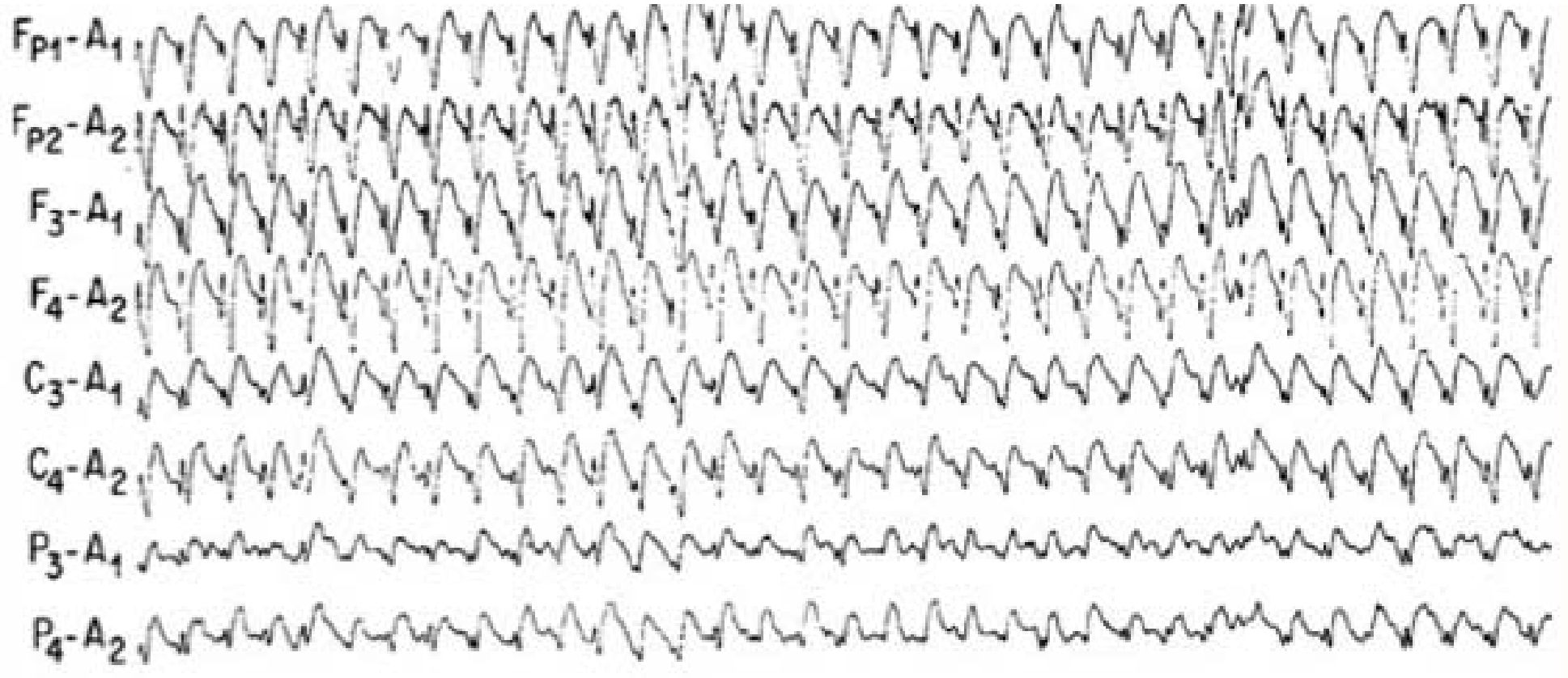
Patients with known epileptic encephalopathy
- Increase in prominence or frequency of the features mentioned above, when compared to baseline **with** observable change in clinical state
- Improvement of clinical and EEG[a] features with IV AEDs

Modified from Kaplan (2007).
EDs, epileptiform discharges (spikes, poly spikes, sharp-waves, sharp-and-slow-wave complexes); IV AEDs: intravenous antiepileptic drugs.
[a]If EEG improvement occurs without clinical improvement, or if fluctuation without definite evolution, this should be considered possible NCSE.
[b]Incrementing onset (increase in voltage and change in frequency), or evolution in pattern (change in frequency >1 Hz or change in location), or decrementing termination (voltage or frequency).

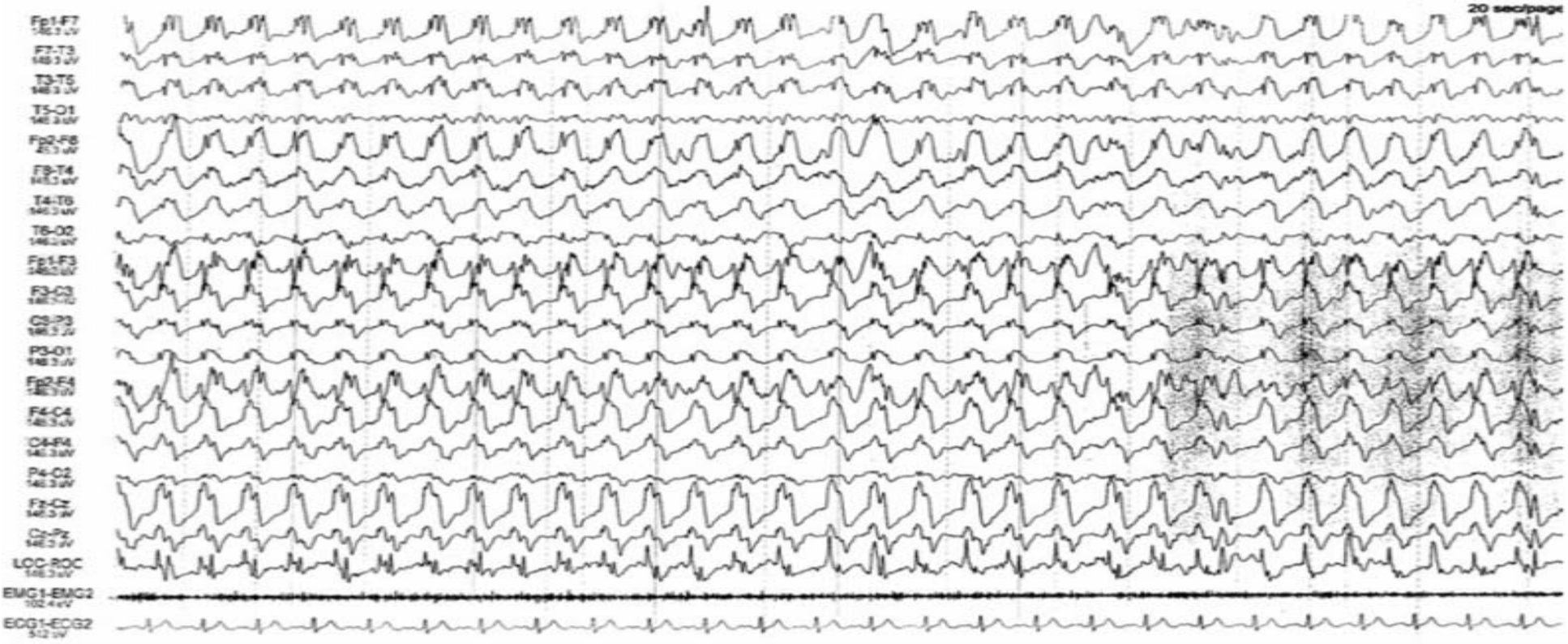
- Tercih edilen yanıt: hastanın klinik durumunda ve EEG'de düzelme olması
- Yalnızca EEG'de düzelme, deşarjların sonlanması, bazal EEG paternlerinin ortaya çıkması
- IV AEİ ile klinik düzelmenin olmaması olayın epileptik doğasını dışlatmaz, yanıt gecikmiş olabilir veya özellikle koma ile birlikte gelişen NCSE olgularında olmak üzere hiç alınamayabilir

Epilepsia. 2013 Sep;54 Suppl 6:28-9.

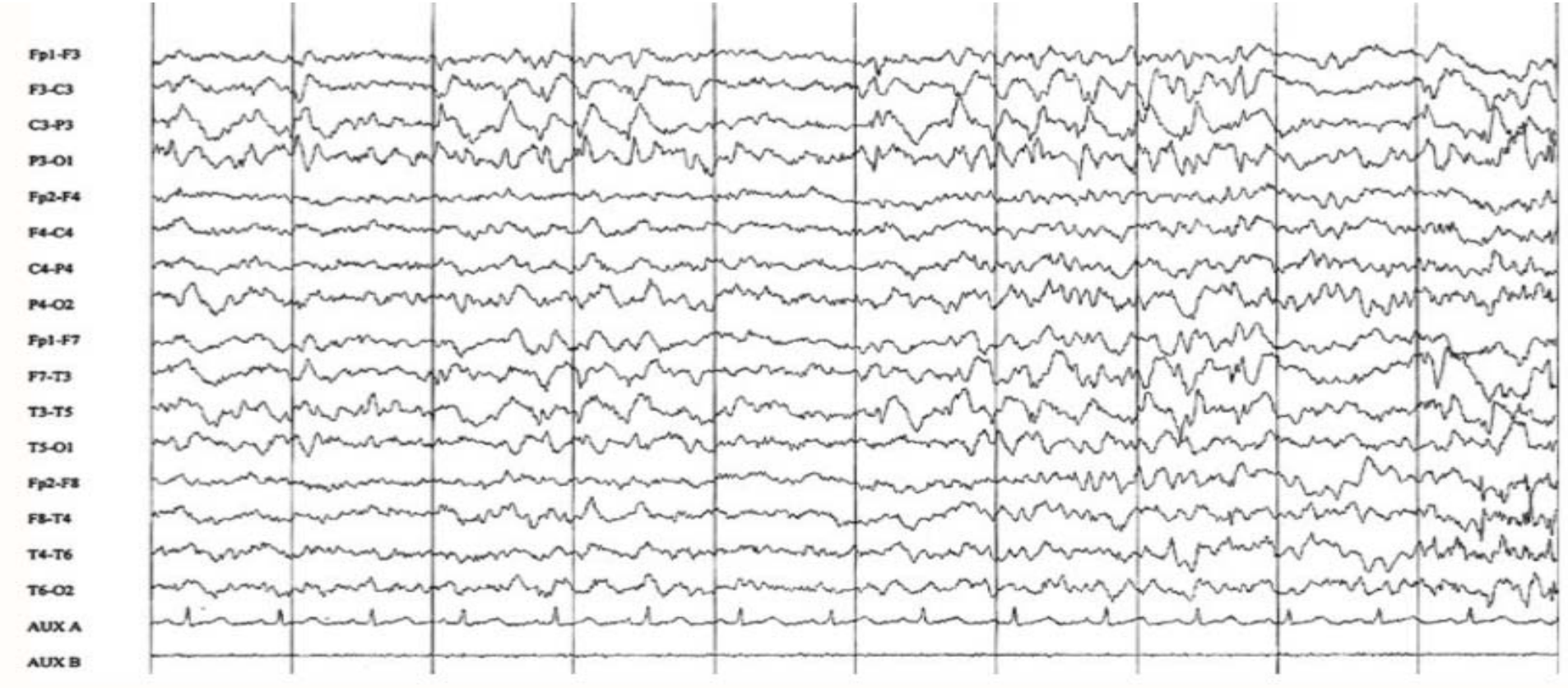
Tipik absans statusu



De novo, geç başlangıçlı absans statusu



Limbik status epileptikus



Nonlimbik kompleks parsiyel status epileptikus

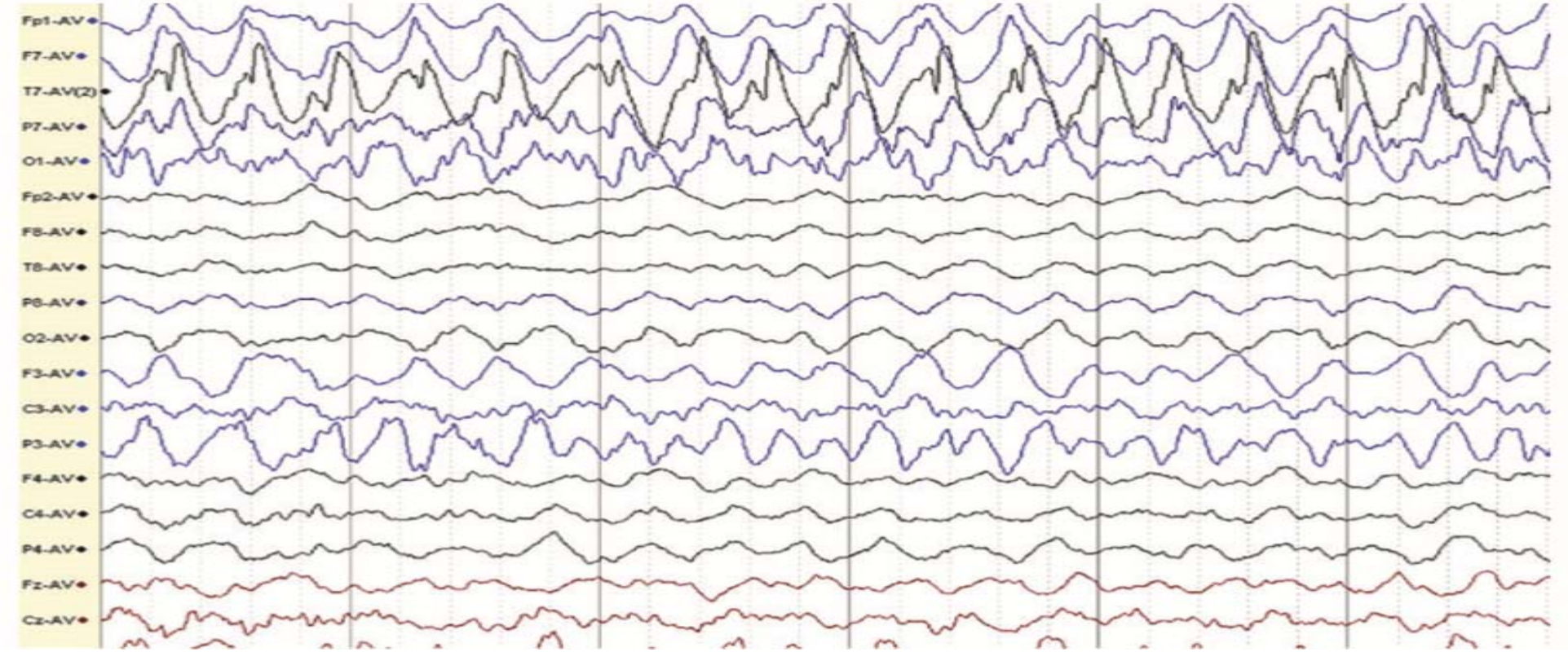


Table 1. Etiologic factors and EEG pattern in generalized and lateralized comatose NCSE

	Etiology	EEG pattern
coma-GED	Diffuse primary or secondary brain disturbances (anoxic, toxic, metabolic, infectious, degenerative)	Continuous generalized spiking Periodic spiking Burst suppression pattern in different variations
	Space-occupying lesions with brainstem compression (direct or due to tentorial herniation)[a]	Other generalized periodic abnormalities Bilateral triphasic waves
	Known epilepsies?	
coma-LED	Focal brain lesions (in most cases acutely acquired)	Continuous focal spiking PLEDs Bi-PLEDS
	In rare cases diffuse abnormalities (aminophylline intoxication, some forms of diabetic coma)	Unilateral burst suppression pattern Unilateral triphasic waves
	Known epilepsies?	

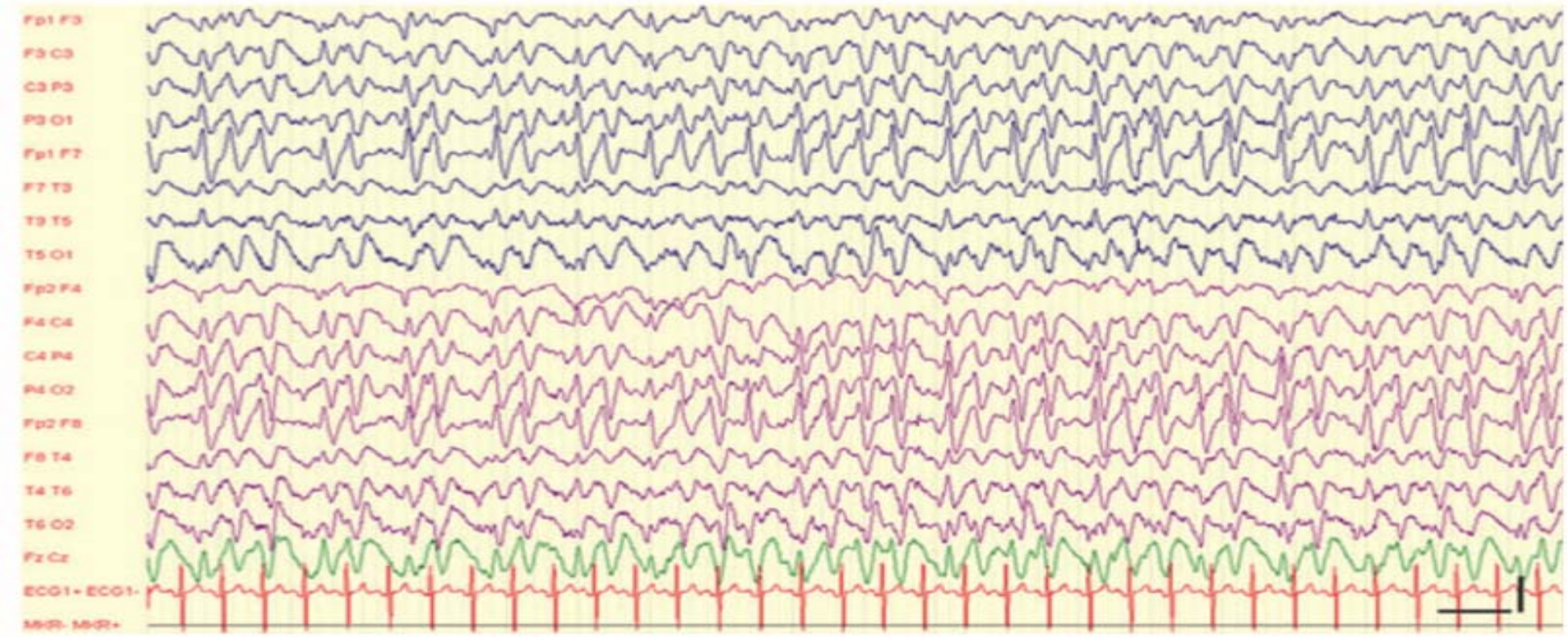
[a]Might also present as coma-LED.

Bi-PLED, bilateral periodic epileptiform discharges; GEDs, generalized epileptiform discharges; LED, lateralized epileptiform discharges; PLED, periodic epileptiform discharges.

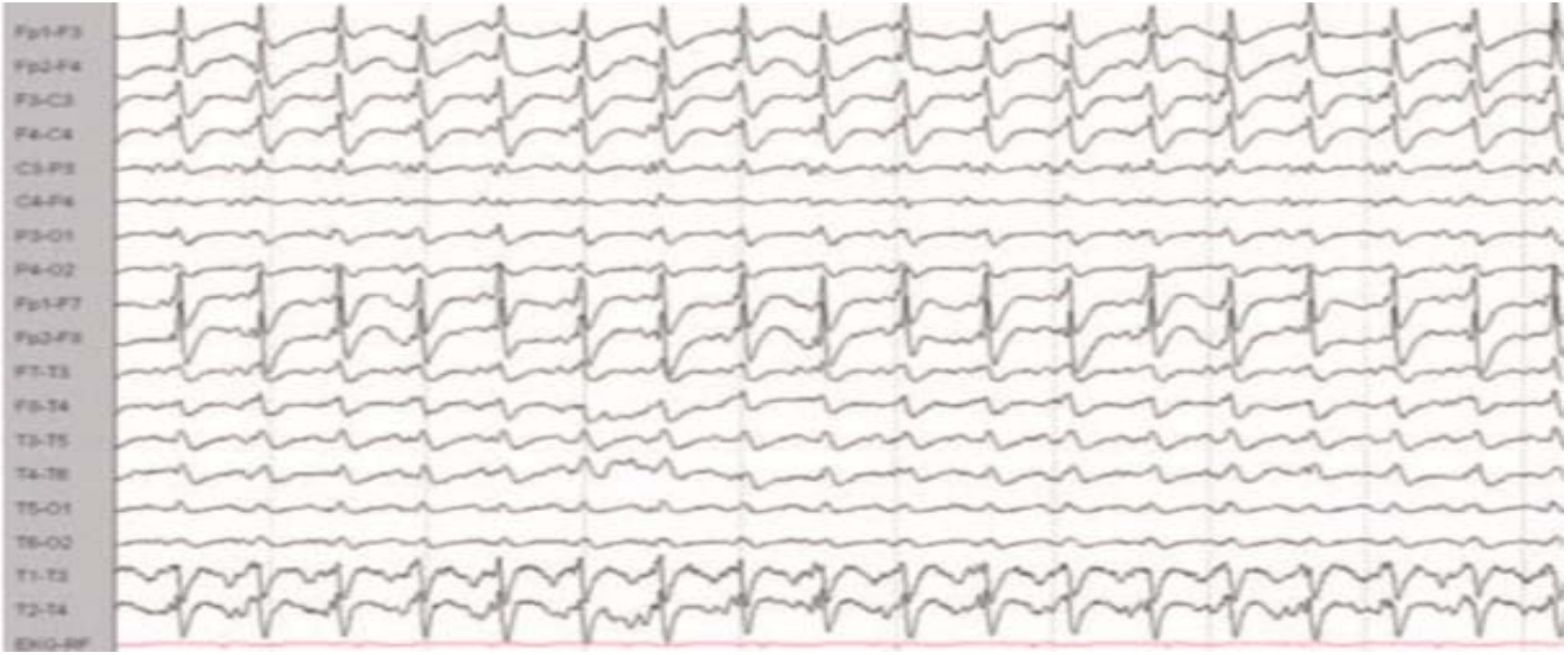
Komadaki nonkonvülzif status epileptikus hastalarında EEG bulguları etiyoloji ile ilişkili

Epilepsia 2010;51(2):177-90

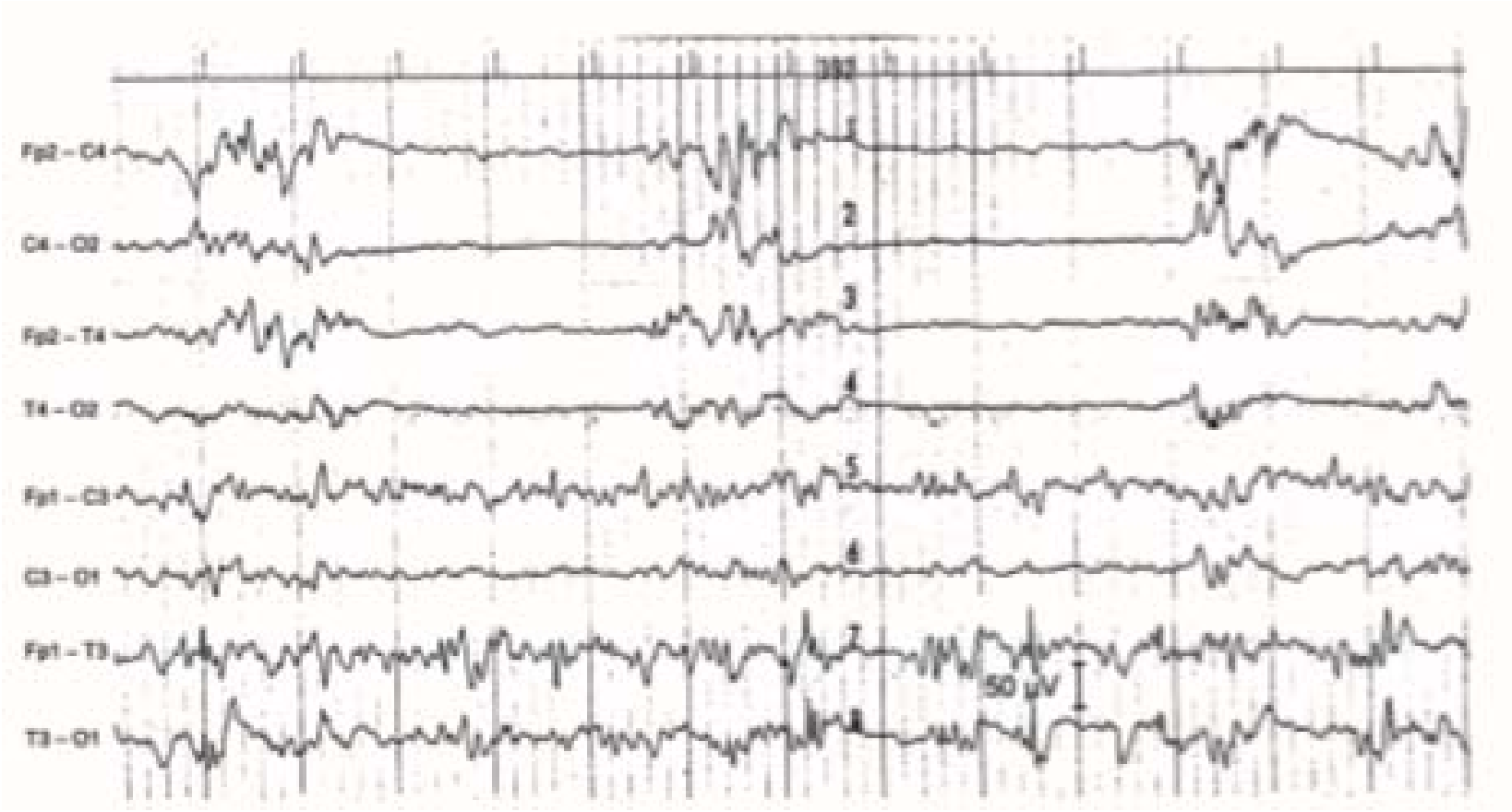
Komada NCSE


Fp1 F3
F3 C3
C3 P3
P3 O1
Fp1 F7
F7 T3
T3 T5
T5 O1
Fp2 F4
F4 C4
C4 P4
P4 O2
Fp2 F8
F8 T4
T4 T6
T6 O2
Fz Cz
ECG1- ECG1-
MKR- MKR+

Komada NCSE, hipoksik ensefalopati



Komada NCSE, BİPLED, sağ kraniotomi



Aynı zamanda video kayıtlama yapılmalı mı?

EEG'nin yorumlanmasını ve iktal EEG'ye eşlik eden klinik bulguların saptanmasını kolaylaştırabilir
Ancak video kayıtlamalarının etkinliğini gösteren prospektif çalışma yok

Monitorizasyona hızla başlanmalı

(tüm hastalarda bir saat içerisinde)

Tanıda gecikme olumsuz prognozla ilişkili!!!

Nonconvulsive status epilepticus

Factors associated with poor outcome after NCSE:

For patients diagnosed within 30 min of seizure onset, mortality was 36 % compared with 75 % for those patients diagnosed ≥24 h after seizure onset seizures [51]

Patients with NCSE treated and resolved within 10 h had 10 % mortality vs. 85 % mortality if seizures continued longer than 20 h [51]

Yorumlayıcılar devamlı EEG monitorizasyonu konusunda eğitimli ve deneyimli olmalı, raw ve kantitatif EEG

Elektriksel gürültü
Hareket artefaktları
Ventilatörle ilişkili artefaktlar (periyodik deşarjları taklit edebilir)
Göğüs perküsyonları (iktal aktiviteyi taklit edebilir)
Teknik artefaktlar
Elektrot diskonneksiyonu (zemin aktivitesinde yavaşlama ve baskılanmayı taklit edebilir)
Stimülasyonla ortaya çıkan periyodik veya iktal görünümlü paternler

Current Neurology and Neuroscience Reports 2002, 2:534–540

Devamlı EEG monitorizasyonunda hedef/süre?

HEDEF?

Table 11 Continuous EEG treatment endpoints

EEG defined endpoint	Rationale	Grade
Cessation of non-convulsive seizures	Recurrent non-co[illegible] seizures result in ongoing brain injury a[illegible] worsen mortality	Class I, level B
Diffuse beta activity	Verifies effect of anesth[illegible]ic agents	Class IIb, level C
Burst suppression 8–20 s intervals	Interruption of synap[illegible]c transmission of electrical activity	Class IIb, level C
Complete suppression of EEG	Interruption of synaptic transmission	Class IIb, level C

?

SÜRE?

- Komadaki hastalarda akut beyin hasarı sonrası en az 48 saat
- Elektrografik nöbetler sonlandıktan sonra en az 24 saat
- Antiepileptiklerin weaning'i süresince

Neurocrit Care 2012;17:3-23

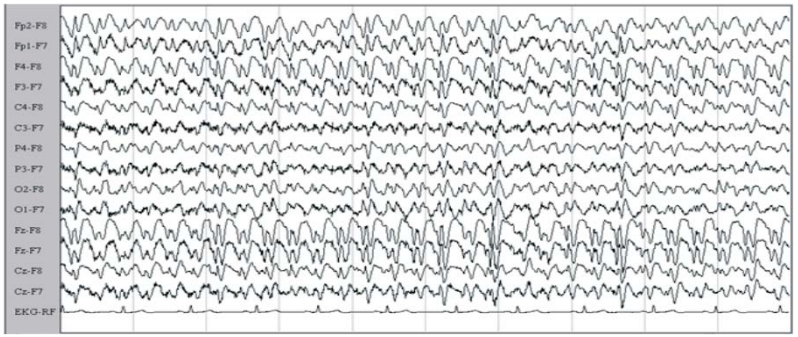
Konvülzif status epileptikus ciddi morbidite ve mortalite ile ilişkili, medikal bir acil olarak kabul ediliyor

Nonkonvülzif status epileptikusun acil tanı ve tedavisine konvülzif status epileptikus kadar vurgu yapılmıyor

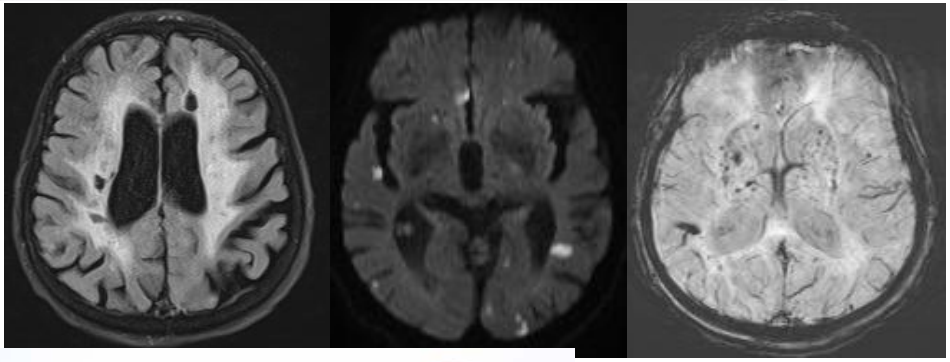
Peki gerçekten nonkonvülzif status epileptikus benign bir antite mi?

Nonkonvülzif status epileptikus sonrası prognozun belirlenmesindeki temel güçlük şudur: Olası olumsuz prognoz şunlardan hangisi ile ilişkili?

1. Devam eden nöbet aktivitesi ile ilişkili?



2. Altta yatan neden ile ilişkili?



3. Tedavi komplikasyonları ile ilişkili?

SECTION EDITOR: VLADIMIR HACHINSKI, MD, FRCPC, DSCMED

Do Nonconvulsive Seizures Damage the Brain?—Yes

G. Bryan Young, MD; Kenneth G. Jordan, MD

NONCONVULSIVE seizures (NCSs) are heterogeneous and include absence, complex partial, and simple partial seizures without convulsive activity.[1] Although typical absence seizures do not damage the brain, other nonconvulsive seizures, usually complex partial status epilepticus (CPSE), can cause enduring cerebral dysfunction, affecting memory and other functions. Epileptic brain damage has been documented in humans and animals and includes cognitive impairment, recurring seizures, and neuronal death.[2,3]

ANIMAL MODELS

In animal studies, prolonged NCSs can cause behavioral deficits.[4-7] Repeated NCSs and induced nonconvulsive status epilepticus (NCSE) have produced epilepsy in some animals.[8-11] The classic studies of Meldrum and Brierley[12] and Nevander et al[13] demonstrated that, even without attendant hypoxemia, acidosis, hyperthermia, and hypoglycemia, ongoing seizures in primates and rats can cause neuronal death. Epileptic brain damage is likely caused by excitotoxic effects produced by glutamate or aspartate-activating *N*-methyl-D-asparate and other receptors with contributions by increased free-radical production and activation of apoptotic mechanisms.[14-17] Spontaneous NCSE is preceded by a reduction of γ-aminobutyric acid–mediated inhibition, related to the death of neurons that normally excite inhibitory neurons.[18-20] Neuronal death, following limbic status epilepticus, occurs at sites remote from regional brain injections and in the hippocampus after the systemic injection of kainic acid, cholinergic drugs (with or without lithium), bicuculine, folic acid, or dipiperidinoethane.[21-25] Histopathological changes occur that are identical to hippocampal sclerosis in humans.[26-29] In addition, partial kindling, insufficient to produce convulsive seizures, can produce long-lasting spatial memory disruption, increased paired-pulse facilitation, and enhanced long-term potentiation of population spikes after stimulation of the medial perforant path.[30-33]

While animal models cannot be uncritically applied to patients, humans and animals demonstrate similar behavioral and electroencephalographic (EEG) changes in the evolution of status epilepticus, both convulsive and nonconvulsive.[34]

CLINICAL EVIDENCE

It has been difficult to confirm that NCSE causes brain damage in patients, because its underlying causes by themselves often injure the brain. Also, some patients may be neurologically abnormal before they experience NCSE.[35,36] Proof is also hampered by the definitional need for EEG confirmation of the diagnosis, because NCSs and NCSE are mimicked by numerous conditions. Continuous EEG monitoring is necessary to establish seizure onset, duration, and termination.[36,37] However, from a clinical point of view, we believe that it is artificial to try to separate the relative injurious effects of acute brain injuries (ABIs) and seizures, as the 2 probably act synergistically to produce brain damage, by augmenting the release of excitatory neurotransmitters, among other mechanisms.[38] Among a variety of patients admitted to a neurology intensive care unit with ABIs, more than twice as many with NCSs and NCSE died or subsequently required custodial care than patients without seizures.[39]

Acute seizures occur in 20% of cases of ABIs that are fatal, but they are less common in nonfatal injuries.[40] Mortality is significantly higher among patients with stroke who have seizures than among those who do not; seizure activity is secondary only to impaired consciousness as a predictor of mortality.[41,42] When strokes and seizures are separated by time, it is clear that seizures can cause additional deficits. Bogousslavsky et al[43] studied 48 patients with focal seizures that occurred an average of 7 months after strokes. Ten had persistent worsening of neurological deficits after partial seizures; two had only epileptic aphasia. None had additional strokes to account for the worsening. Seizure duration was the only significant factor that differentiated those with additional deficits from the 38 who recovered.

Even without coinciding ABI, NCSE has been documented to produce neuronal damage. Among 8 patients with NCSE, the mean value of the serum neuron-specific enolase concentration, a marker for acute neuronal injury, was significantly elevated compared with that in controls with epilepsy.[44] Three of the 8 patients had abnormal outcomes (Glasgow Outcome Score <5). In another study, an increase in neuron-specific enolase concentration occurred in 2 patients with NCSE who did not have preceding or coexistent cerebral injury.[45] In addition, the neuron-specific enolase concentration was elevated in both serum and cerebrospinal fluid during NCSs induced by methohexital.[46,47]

In the absence of preexisting neurological damage, patients with NCSs may suffer significant cognitive morbidity.[48,49] Patients with complex partial seizures may develop enduring neurological deficits, including cognitive dysfunction.[50,51] Wasterlain et al[52] reported neuronal loss in the hippocampus and other brain regions after NCSE in 3 patients who did not have preexisting seizures or systemic abnormalities. Engel et al[53] described a patient with recurrent

From the University of Western Ontario, London, Ontario (Dr Young), and Jordan Neuroscience, San Bernardino, Calif (Dr Jordan).

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Do Nonconvulsive Seizures Damage the Brain?—No

Michael J. Aminoff, MD, FRCP

WHEN attempting to determine whether nonconvulsive seizures cause brain damage, it is appropriate to examine initially whether nonconvulsive status epilepticus produces such damage. If it does, the aggressive treatment of this form of status epilepticus may be justified despite the potential morbidity of certain therapeutic approaches. If it does not, it may reasonably be concluded that isolated nonconvulsive seizures also fail to produce brain damage. To my knowledge, there is no information to indicate whether isolated nonconvulsive seizures recurring over many years are harmful, although it is pertinent that a benign course and an excellent prognosis for remission without evidence of cerebral damage are associated with certain hereditary, childhood-onset, nonconvulsive seizure disorders.

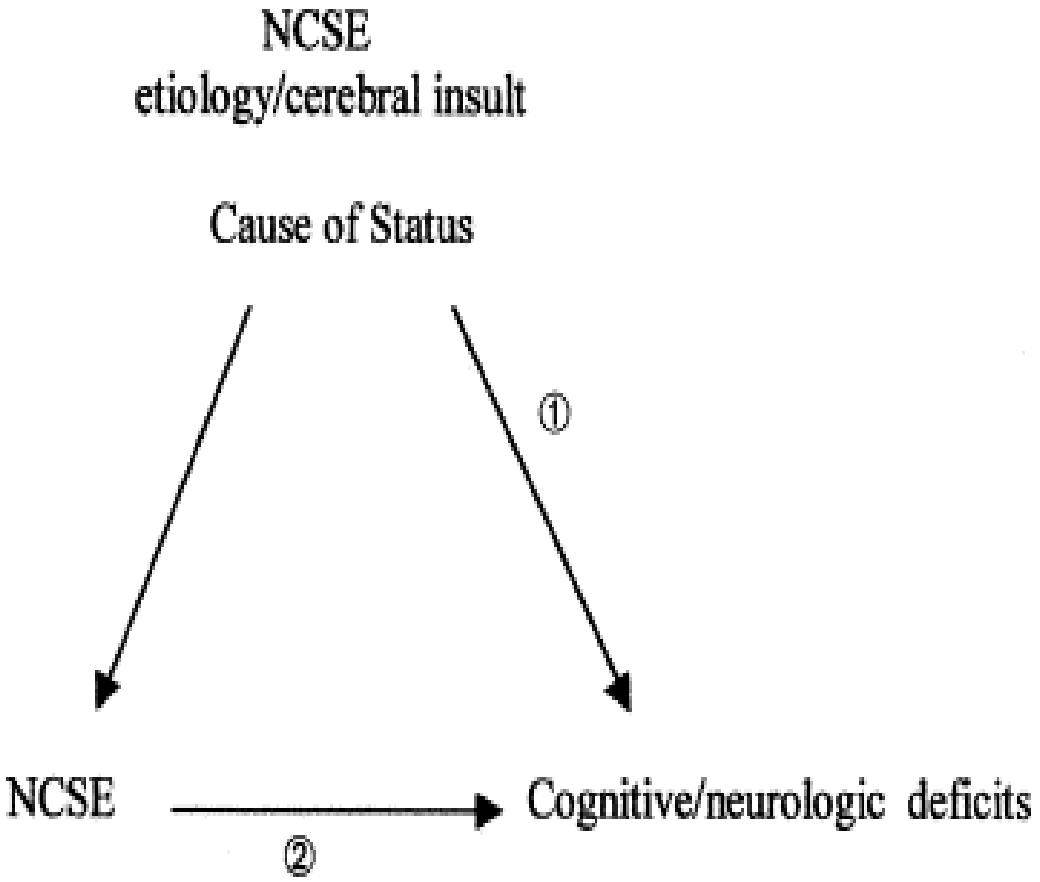
Nonconvulsive status epilepticus may be difficult to identify. Some patients with Lennox-Gastaut syndrome, for example, show near-continuous atypical spike-wave activity in the electroencephalogram and a variable state of mental dullness, but it is not clear that this properly represents an ictal phenomenon. Nonconvulsive status epilepticus has been divided into absence status (generalized status or spike-wave stupor) and complex partial status. It may be difficult, however, to distinguish between them, because in some patients the electroencephalogram shows transitional features.[1,2]

Nonconvulsive status epilepticus has not been convincingly associated with severe morbidity or death. Ballenger et al[3] described 8 patients with complex partial status epilepticus due to either continuous or recurrent seizures. These patients ictally had reduced responsiveness or automatisms, sometimes accompanied by more conspicuous motor activity, and they showed a gradual return to baseline cognitive function on cessation of their seizures. A patient with a prolonged memory deficit after complex partial status epilepticus has been described, but full recovery occurred eventually.[4] Two other patients with memory deficits after complex partial status epilepticus have been described, but detailed long-term follow-up information was not provided.[5] Krumholz et al[6] described 10 patients with persistent neurological deficits or death after well-documented nonconvulsive status epilepticus of the complex partial variety. However, in 5 of their patients (4 with vascular disease or encephalitis and 1 with a metabolic disturbance and human immunodeficiency virus encephalopathy), morbidity was probably due to the underlying disease rather than to the status epilepticus per se. Three other patients had convulsive seizures shortly before the onset of the status epilepticus, which may have been responsible for complications, and the remaining 2 patients died of general medical complications without evidence of any direct harmful effect of the seizures on brain function.[6] Finally, Cockerell et al[7] recently described 20 patients with complex partial status epilepticus that was recurrent in 17. They found no decline in performance on serial psychometric studies, when these were performed, and no "marked clinical evidence" of cognitive or neurological decline in the other patients.

With regard to nonconvulsive generalized status epilepticus, Guberman et al[1] studied 13 episodes in 10 adults and found no evidence of long-term cognitive, memory, or behavioral changes. Recurrences of status epilepticus occurred in some instances, but there was no reason to attribute this to the initial episode. Others have also noted that absence status epilepticus is not associated with clinically significant postictal abnormality.[8]

From the Department of Neurology, School of Medicine, University of California, San Francisco.

NCSE kalıcı nörolojik sekele yol açar mı yoksa sadece altta yatan beyin hastalığının şiddetinin göstergesi mi?



Neurophysiol Clin 2000 ; 30 : 377-82

Nonkonvülzif status epileptikus etiyoloji/prognoz ve tedavisi homojen bir antite mi?

YBÜ hastalarında

UNDERDIAGNOSIS?

İdyopatik jeneralize epilepsilerde prognoz?

TEDAVİ HANGİ HASTA GRUBUNDA NASIL OLMALI?

NE KADAR AGRESİF OLUNMALI?

Komad

ognoz?

'epiphenomenon'

Akut nörolojik hasarı olanlarda risk altındaki beyin bölgelerinde iktal aktivite ile ilişkili artmış metabolik yük?

Agresif tedavinin prognoz üzerine etkisi?

HAYVAN MODELLERİNDE NCSE NÖRONAL KAYIP İLE İLİŞKİLİ

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Experimental Neurology 183 (2003) 87–99

Experimental Neurology
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An animal model of generalized nonconvulsive status epilepticus: immediate characteristics and long-term effects

Michael Wong,[a,d,*] David F. Wozniak,[b] and Kelvin A. Yamada[a]

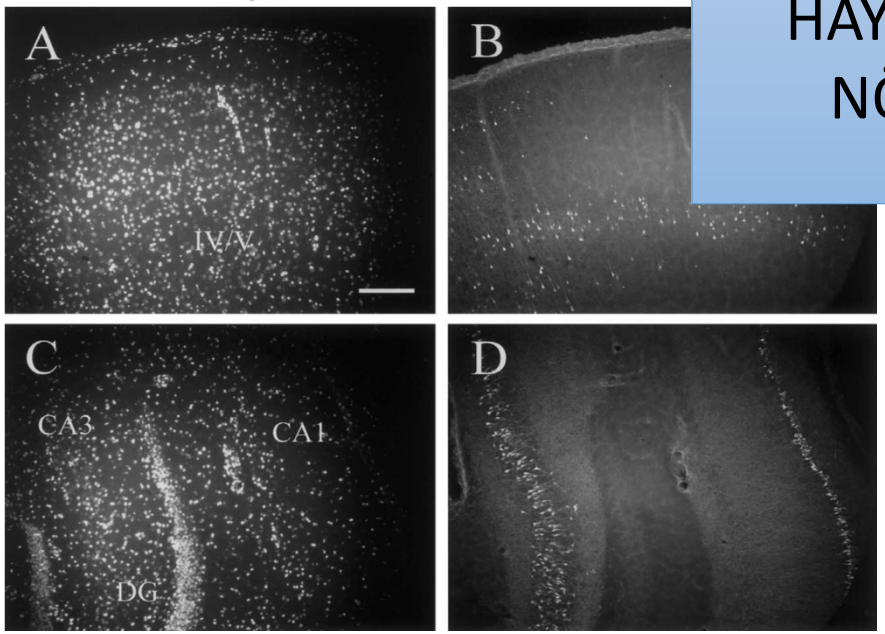

Fig. 5. DAPI and Fluoro-Jade B staining in a rat 1 week after kainic acid-induced status epilepticus. In addition to viable DAPI-positive cells in neocortex (A) and hippocampus (C), abundant Fluoro-Jade B-positive cells in specific neocortical layers (B), dentate hilus, CA3, and CA1 cell layers (D) occur, indicating kainate-induced status epilepticus results in cell death in specific cell populations. IV/V, neocortical layers IV/V; CA1, CA1 pyramidal cell layer of hippocampus; CA3, CA3 pyramidal cell layer of hippocampus; DG, granule cell layer of dentate gyrus. Calibration bar = 200 μm applies to all photomicrographs.

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Long-term behavioral and morphological consequences of nonconvulsive status epilepticus in rats

Pavel Kršek, Anna Mikulecká, Rastislav Druga, Hana Kubová, Zdeněk Hliňák, Lucie Suchomelová, and Pavel Mareš*

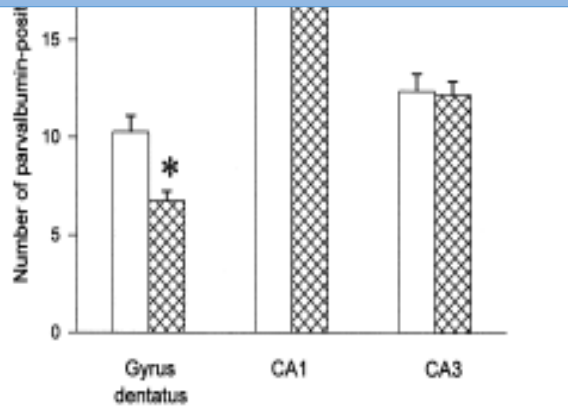

Fig. 6. Average number of parvalbumin-positive neurons in the dentate gyrus (counted in the whole extent of both blades) and in the CA1 and CA3 hippocampal fields (counted in a square of 0.3 × 0.3 mm). Open bars: control group ($n = 5$); crosshatched bars: pilocarpine group ($n = 11$). Data are expressed as mean + SEM. Statistical significance, $P < 0.05$ (two-tailed): *Pilocarpine group versus control group.

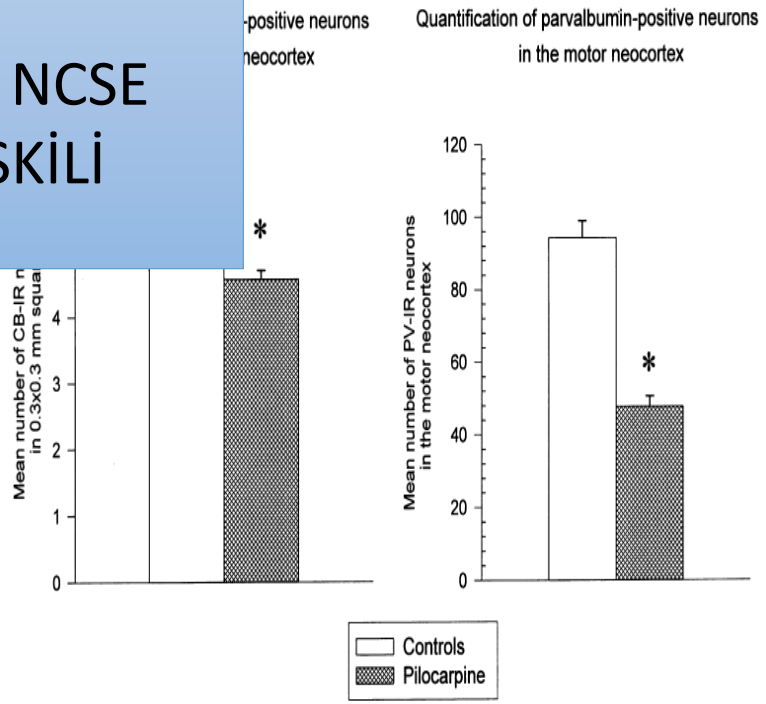

Fig. 5. Average number of calbindin-positive neurons counted in the square of 0.3 × 0.3 mm localized randomly in layers V and VI of the motor neocortex (left); average number of parvalbumin-positive neurons counted in the whole range of layers V and VI of the motor neocortical fields Fr 1–3 of both hemispheres (right). Open bars: control group ($n = 5$); crosshatched bars: pilocarpine group ($n = 11$). Data are expressed as means + SEM. Statistical significance, $P < 0.05$ (two-tailed): *pilocarpine versus control group.

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Long-term behavioral and morphological consequences of nonconvulsive status epilepticus in rats

Pavel Kršek, Anna Mikulecká, Rastislav Druga, Hana Kubová, Zdeněk Hliňák, Lucie Suchomelová, and Pavel Mareš*

The aims of the present study were to ascertain whether nonconvulsive status epilepticus (NCSE) could give rise to long-term behavioral deficits and permanent brain damage. Two months after NCSE was elicited with pilocarpine (15 mg/kg ip) in LiCl-pretreated adult male rats, animals were assigned to either behavioral (spontaneous behavior, social interaction, elevated plus-maze, rotorod, and bar-holding tests) or EEG studies. Another group of animals was sacrificed and their brains were processed for Nissl and Timm staining as well as for parvalbumin and calbindin immunohistochemistry. Behavioral analysis revealed motor deficits (shorter latencies to fall from rotorod as well as from bar) and disturbances in the social behavior of experimental animals (decreased interest in juvenile conspecific). EEGs showed no apparent abnormalities. Quantification of immunohistochemically stained sections revealed decreased amounts of parvalbumin- and calbindin-immunoreactive neurons in the motor cortex and of parvalbumin-positive neurons in the dentate gyrus. Despite relatively inconspicuous manifestations, NCSE may represent a risk for long-term deficits.

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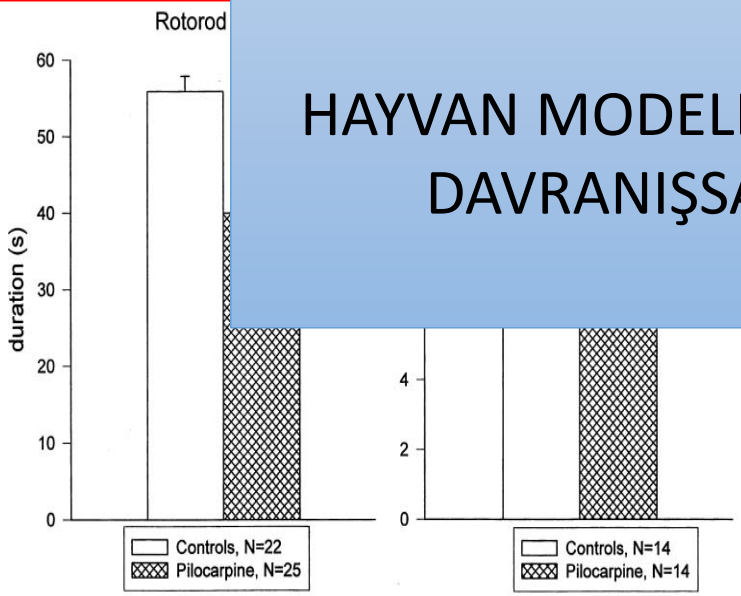


Fig. 3. Motor performance in the rotorod test (left, expressed as the time spent on the rod without falling down) and the bar-holding test (right, expressed as the time of grasping). Data are expressed as means + SEM. Open bars: control group ($n = 22$ and 14, respectively); crosshatched bars: pilocarpine group ($n = 25$ and 14, respectively). Statistical significance, $P < 0.05$ (two-tailed): *Pilocarpine versus control group.

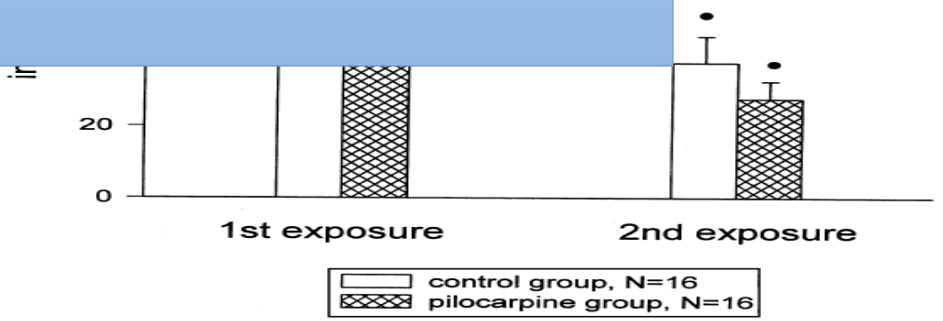


Fig. 2. Total time spent by adult males in investigation of juveniles in the social interaction test (means + SEM). The second exposure to the same juveniles was performed 30 minutes after the first one. Open bars: control group ($n = 16$); crosshatched bars: pilocarpine group ($n = 16$). Statistical significance, $P < 0.05$ (two tailed): *Pilocarpine versus control group, ● second session versus first session.

Epilepsia. 1996 Jul;37(7):606-9.

Neuron-specific enolase, a marker of acute neuronal injury, is increased in complex partial status epilepticus.

DeGiorgio CM[1], Gott PS, Rabinowicz AL, Heck CN, Smith TD, Correale JD.

Author information

Abstract

PURPOSE: To determine whether complex partial
an accepted marker of acute brain injury, and incre
epilepticus. s-NSE levels in CPSE are unknown. In
and would help confirm that CPSE is a medical em

METHODS: This was a pilot prospective study of s
neurologic deficit were identified prospectively. Re
at hospital discharge or at 7 days with the Glasgow

RESULTS: The mean peak s-NSE was 21.81 ng/m
s-NSE = 5.36 SD = 1.66, p = 0.0003) and epileptic

CONCLUSION: The increase in s-NSE provides new evidence that CPSE causes brain injury in humans.

İNSANLARDA NCSE NÖRON-SPESİFİK ENOLAZ DÜZEYLERİNDE ARTIŞ İLE İLİŞKİLİ

Epilepsia. 1995 May;36(5):475-9.

Neuron-specific enolase is increased after nonconvulsive status epilepticus.

Rabinowicz AL[1], Correale JD, Bracht KA, Smith TD, DeGiorgio CM.

Author information

Abstract

Serum neuron-specific enolase (s-NSE), a marker of brain injury and acute seizures, was increased in 2 patients with nonconvulsive SE. Neither patient had an acute neurologic insult other than nonconvulsive SE (NCSE) accounting for s-NSE changes. Increase in s-NSE provides further in vivo evidence of transient brain injury after NCSE.

European Journal of Paediatric Neurology 1998; **2**: 193–197

ORIGINAL ARTICLE

ejpn

Serum neuron specific enolase: A marker for neuronal dysfunction in children with continuous

Children, Edinburgh, UK

plication of the childhood epileptic encephalopathies. An epilepticus is a continuous epileptiform activity on the a possible long-term sequel of non-convulsive status Neuron specific enolase is a marker of neuronal damage. E) has been measured in 17 children with continuous lepsy but without a continuous dysrhythmia. There was a the two groups.

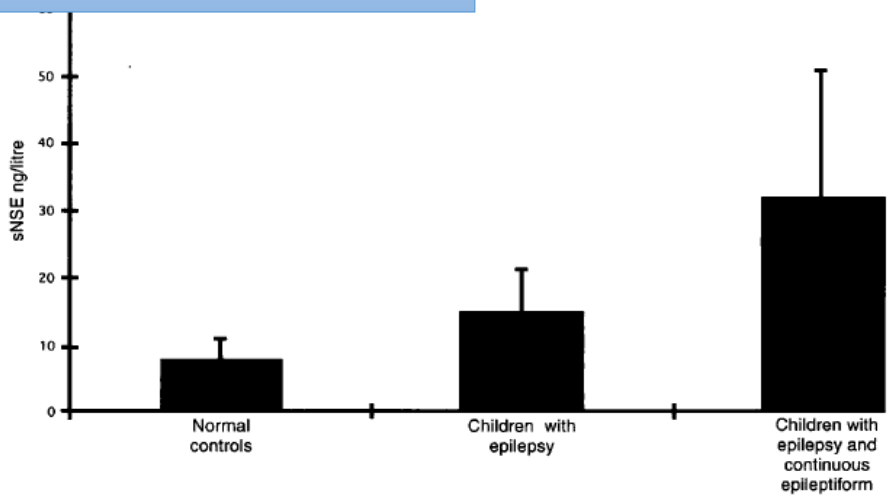


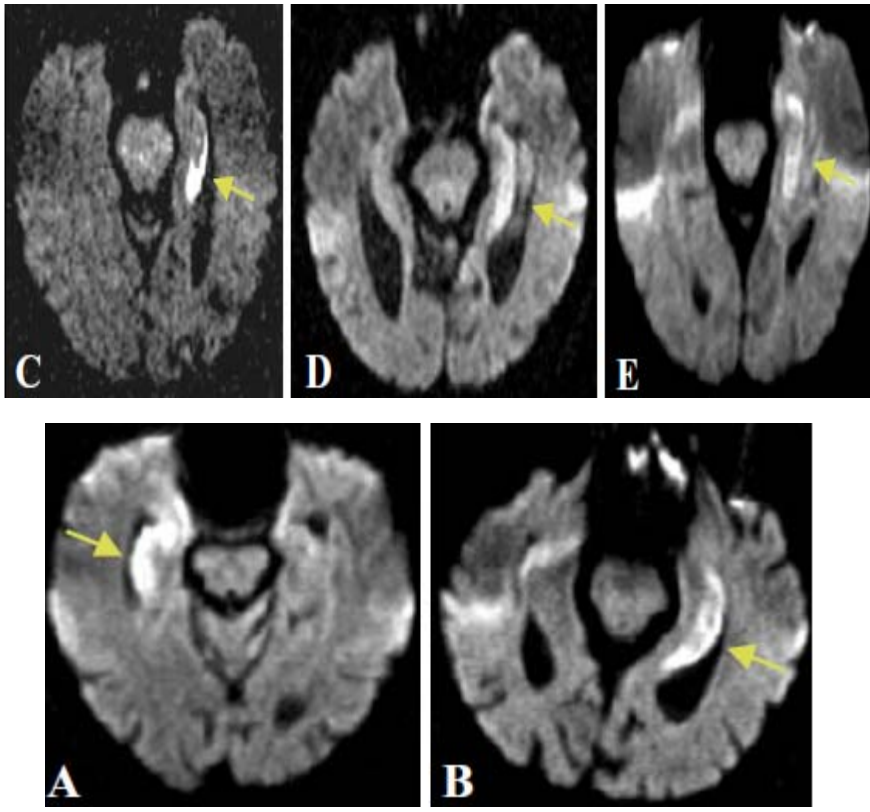
Fig. 1. Mean sNSE (ng/litre) +2SD in children with and without epilepsy.

Nonkonvülzif status epileptikus nöronal eksitotoksisite sonunucu sitotoksik beyin ödemine yol açabilir

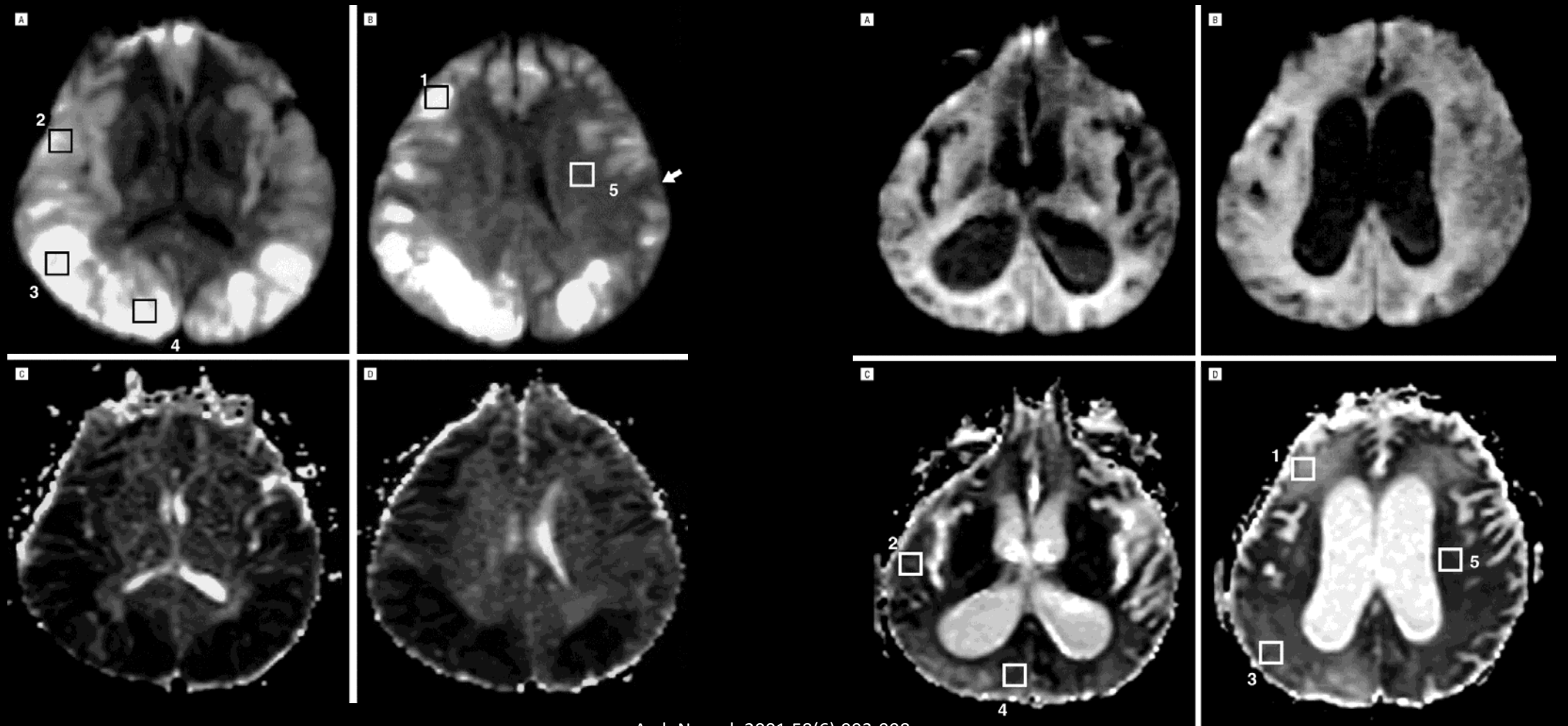
Table 2 *MRI findings*

Patient	Acute ictal/peri-ictal signal abnormality		Follow-up	
	DWI/T2/PWI/MRA	Location and size of DWI hyperintensity	DWI/T2/PWI follow-up	Conventional MRI findings
1	DWI ↑; ADC ↓ (−35%); T2 →; PWI ↑ (+SPECT)	Right parieto-occipital cortex and right pulvinar; 12 ml	Complete resolution of PWI (day 2), DWI (day 13), T2 (month 1) abnormalities	Previous small haemorrhage after cortical vein thrombosis
2	DWI ↑, ADC ↓ (−37%); T2 ↑; PWI ↑ (+SPECT)	Right hippocampal formation, right pulvinar and right parieto-occipital cortex; 5.2 ml	Complete resolution of DWI/T2/PWI abnormalities (month 4)	Chronic right occipital intracranial haemorrhage in cerebral vasculitis
3	DWI ↑, ADC ↓ (−28%); T2 ↑; PWI ↑	Right hippocampal formation and right pulvinar; 1.5 ml	Resolution of PWI, partial resolution of DWI/T2 signal change (day 7)	Right hippocampal sclerosis
4	DWI ↑; ADC ↓ (−22%); T2 ↑; PWI ↑, PCA ↑	Left hippocampal formation and left pulvinar; 1.9 ml	Complete resolution of DWI/T2/PWI abnormalities (day 14)	Chronic white matter lesions; occlusion of left ICA with hypoperfusion of left MCA territory
5	DWI ↑; ADC ↓ (−11%); T2 ↑; PWI ↑	Left hippocampal formation and left pulvinar; 1.6 ml	Lost to follow-up	Left frontopolar post-traumatic lesion
6	DWI ↑, ADC ↓ (−25%); T2 ↑; PWI ↑, PCA ↑	Left hippocampal formation and left pulvinar; 1.5 ml	Resolution of PWI, partial resolution of DWI/T2 signal change (day 2)	Chronic left temporoparietal MCA stroke; MCA stenosis and hypoperfusion
7	DWI ↑, ADC ↓ (−25%); T2 ↑; PWI ↑	Left hippocampal formation and left pulvinar; 1.9 ml	Complete resolution of DWI/T2/PWI abnormalities (month 3)	Acute and chronic left temporoparietal MCA stroke; MCA stenosis and hypoperfusion
8	DWI ↑, ADC ↓ (−13%); T2 ↑; PWI ↑, PCA ↑	Left hippocampal formation; 1.4 ml	Resolution of PWI, partial resolution of DWI/T2 signal change (day 7)	Chronic right MCA and PCA stroke
9	DWI ↑, ADC ↓ (−22%); T2 ↑; PWI ↑, PCA ↑	Left hippocampal formation and left pulvinar; 1.7 ml	Complete resolution of DWI/T2/PWI abnormalities (month 5)	Cortical atrophy, chronic white matter lesions
10	DWI ↑; ADC ↓ (−34%); T2 →; PWI ↑	Extensive right temporal and parietal cortical involvement; right pulvinar; 10 ml	Resolution of PWI, partial resolution of DWI/T2 signal change (day 7)	Right parietal glioblastoma

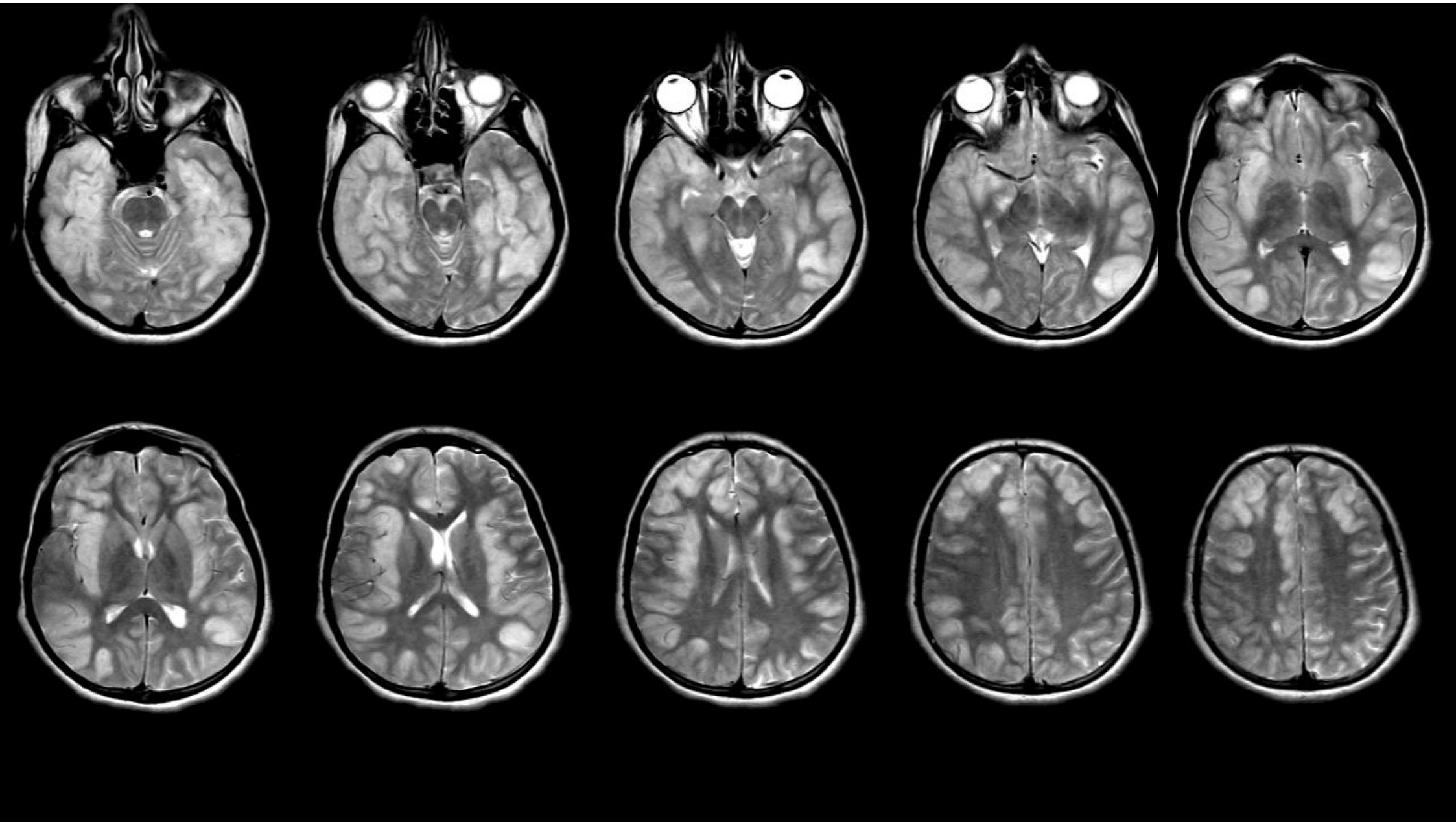
DWI ↑ = hyperintensity; ADC ↓ = reduction (%); PWI ↑ = signs of hyperperfusion; PCA ↑ = increased flow signal in the PCA; MCA = middle cerebral artery; PCA = posterior cerebral artery; ICA = internal carotid artery.



Nonkonvülzif status epileptikus serebral atrofiye yol açabilir



Arch Neurol. 2001;58(6):993-998.



Assessment of acute morbidity and mortality in nonconvulsive status epilepticus

Bassel F. Shneker, MD and Nathan B. Fountain, MD

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doi: http://dx.doi.org/10.1212/01.WNL.0000082653.40257.0B
Neurology October 28, 2003 vol. 61 no. 8 1066-1073

ABSTRACT

Objectives: The natural history of nonconvulsive status epilepticus (NCSE) is not well defined, especially mortality and morbidity. The authors hypothesized that the mortality of NCSE is higher when NCSE is due to acute medical causes (systemic or neurologic) or associated with severe impairment of mental status or with acute complications, and lower when associated with generalized spike-wave (SW) discharges on EEG.

Methods: The authors retrospectively identified 100 consecutive patients with NCSE from an EEG database. Data were collected from systematic review of medical records and actual EEG tracings. Specific etiologies were divided into three groups: acute medical, epilepsy, and cryptogenic.

Results: Of the 100 patients, 18 died. Fourteen of 52 patients in the acute medical group died, 1 of 31 in the epilepsy group died, and 3 of 17 in the cryptogenic group died. Mental status impairment was severe in 33, complications occurred in 39, and generalized SW discharges occurred in 36. Mortality rates were higher in patients 1) in the acute medical group (27%) vs the epilepsy (3%) and the cryptogenic (18%) groups ($p < 0.02$), 2) with severe mental status impairment (39%) compared to those with mild impairment (7%, $p < 0.001$), and 3) with acute complications (36%) when compared with those without complications (7%, $p < 0.0002$). The presence of generalized SW discharges on EEG did not correlate with mortality. Mental status impairment and etiology were independently associated with mortality ($p < 0.001$).

Conclusion: NCSE is associated with substantial mortality. Mortality is associated with an acute medical cause as the underlying etiology, severe mental status impairment, and development of acute complications, but not the type of EEG discharge.

Journal of Neurology, Neurosurgery, and Psychiatry 1996;61:93–95

SHORT REPORT

Non-convulsive status epilepticus: causes, treatment, and outcome in 65 patients

Frans B Scholtes, Willy O Renier, Harry Meinardi

ÖNCEDEN EPİLEPTİK OLAN HASTALARDA PROGNOZ DAHA İYİ, AKUT SEMPTOMATİK OLGULARDA PROGNOZ ALTTA YATAN NEDENLE İLİŞKİLİ

The incidence of non-convulsive status epilepticus (NCSE) in The Netherlands is not known. Files of admissions in the years 1980–7 were studied from 40 adult patients (older than 15 years) with complex partial status epilepticus (CPSE) and 25 with absence status epilepticus (ASE). The clinical presentation sometimes made distinction between CPSE and ASE possible. Focal clinical signs were more frequent in CPSE; a fluctuating level of consciousness was more often present in ASE. All patients, but one, with ASE and most patients with CPSE (28) were known to have had previous epilepsy. Outcome in ASE was good in all. Outcome in CPSE depended on the underlying cause and quality of treatment. In three patients inadequate treatment probably contributed to morbidity.

Distribution of age and sex in patients with CPSE and ASE

	Age 15–30		Age 30–50		Age > 50	
	Male	Female	Male	Female	Male	Female
CPSE:						
Previous epilepsy (28)	9	3	5	3	5	3
No previous epilepsy (12)	0	1	1	2	3	5
ASE:						
Previous epilepsy (24)	5	4	0	1	4	10
No previous epilepsy (1)	1	0	0	0	0	0

In patients with previous epilepsy, problems with treatment such as non-compliance were the most frequent precipitating factor (12 patients). On two occasions systemic infection, on one occasion a stroke, and on another stress triggered the CPSE. In 12 patients the cause remained unknown. In patients without previous epilepsy various acute symptomatic causes were present: stroke (two), brain tumour (two), pneumococcal meningo-encephalitis (one), carcinomatous meningitis and lung cancer (one), digoxin intoxication (one), pneumococcal pneumonia (one), and a case without a clear cause. Three patients had remote causes of epilepsy—multiple sclerosis, global cerebral atrophy and chronic dialysis with aluminium encephalopathy. Outcome in patients with previous epilepsy was good in all but one, a 78 year old man who had successful treatment stopping his CPSE but died later because of aspiration pneumonia, acquired during the status epilepticus.

In patients without previous epilepsy six had sequelae after CPSE: paresis because of underlying cause (two), persistent cognitive disturbances because of underlying (one) and unknown cause (one), and persistent impaired consciousness of unknown cause (one). The CPSE itself caused morbidity in a 74 year old woman who developed CPSE lasting 24 hours after digoxin intoxication; she was confused with jerking of the right arm, alternating with short periods of staring. After recovery from CPSE this patient exhibited word finding problems and a memory deficit. Patients with morbidity were, except for one (38 years), older than 60. In patients without previous epilepsy one patient of 67 died because of the underlying cause (lung cancer and carcinomatous meningitis).

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Nonconvulsive Status Epilepticus in the Critically Ill Elderly

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YBÜ HASTALARINDA NCSE SAPTANDIĞINDA GENELLİKLE ALTTA YATAN AKUT MEDİKAL HASTALIKLARLA İLİŞKİLİ VE PROGNOZ KÖTÜ

Summary: *Purpose:* To describe the electrographic and clinical features of nonconvulsive status epilepticus (NCSE) in the critically ill elderly and to identify potential predictors of outcome.

Methods: We prospectively identified 25 episodes of altered mentation and NCSE in 24 critically ill elderly patients associated with generalized, focal, or bihemispheric epileptiform EEG patterns. Patients with anoxic encephalopathy were excluded.

Results: Of 25 hospitalizations, 13 (52%) resulted in death, and 12 (48%) patients survived to discharge. Death was associated with the number of acute, life-threatening medical problems on presentation (survivors, 1.8; fatalities, 2.8; p = 0.013) and with generalized EEG pattern (p = 0.017). Higher doses or greater number of antiepileptic drugs (AEDs) did not improve outcome. Treatment with intravenous benzodiazepines was associated with increased risk of death (p = 0.033). Ten patients with advance directives were managed outside the intensive care unit (ICU). Mean hospitalization was 39 days in the ICU group and 22 for those with advance directives (p = 0.017).

Conclusions: Severity of illness correlates with mortality in critically ill elderly patients with NCSE. Treatment with intravenous benzodiazepines may increase their risk of death. Aggressive ICU management may prolong hospitalization at considerable cost, without improving outcome. It is unclear whether NCSE affects outcome in the critically ill elderly or is merely a marker for severity of disease in predisposed patients. The benefits of aggressive therapy are unclear. Carefully controlled, prospective trials will be necessary to determine the best therapies for NCSE in the critically ill elderly and the appropriate role of the ICU in their management. **Key Words:** Critical illness—Elderly—Nonconvulsive status epilepticus—Electroencephalography—Outcome.

TABLE 1. *Acute, life-threatening medical problems occurring in study patients*

Renal	Acute renal failure, acute exacerbation of chronic renal failure
Cardiac	Congestive failure, acute life-threatening arrhythmia, myocardial infarction
Pulmonary	Respiratory failure due to pneumonia, neoplasm, pulmonary embolism, exacerbation of lung disease
CNS	Subarachnoid hemorrhage, acute stroke, acute complication from brain neoplasm, meningitis
	Sepsis
	Shock, severe dehydration
	Nonketotic hyperosmolar coma
	Acute gastrointestinal bleeding, bowel necrosis requiring surgery, hepatic failure, acute colitis
	Acute long-bone fracture (e.g., femur)
	Acute coagulopathy, acute complication from advanced multiple myeloma
	Acute toxic encephalopathy (lithium, phenobarbital, alcohol), severe hyponatremia, hypocalcemia, delirium tremens

TABLE 3. *Comparison of patients by outcome*

	Died	Survived
No. episodes of NCSE	13	12
Mean age (yr)	78.9	75.1
Mean no. AEDs	2.36	2.69
No. acute problems[a]	**2.77**	**1.73**
Mean no. hospital days	32.1	33.5
i.v. Benzodiazepines[b]	**11**	**5**
Focal EEG pattern	1	3
Generalized EEG pattern[c]	**6**	**0**
Convulsive seizure	1	2
Bihemispheric EEG pattern	6	9
Treated in ICU	10	5
Mean no. hours to control	80.5	68.7

Patterns, patterns of nonconvulsive status epilepticus (NCSE) on EEG; acute problems, acute life-threatening problems on presentation; hospital days, days from presentation until death or discharge from hospital; mean hours to control, number of hours required to control NCSE from diagnosis by EEG until documented absence of NCSE on EEG; bold, statistically significant results.
[a] p = 0.015.
[b] p = 0.033.
[c] p = 0.010.

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Electrographic Status Epilepticus is Associated with Mortality and Worse Short-Term Outcome in Critically Ill Children

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Main Results—Two hundred children underwent cEEG. Eighty-four (42%) had seizures which were categorized as ES in 41 (20.5%) and ESE in 43 (21.5%). Thirty-six subjects (18%) died and 88 subjects (44%) had PCPC worsening. In multivariable analysis ESE was associated with an increased risk of mortality (OR 5.1; 95%CI 1.4, 18, p=0.01) and PCPC worsening (OR 17.3; 95%CI 3.7, 80, p<0.001) while ES was not associated with an increased risk of mortality (OR 1.3; 95%CI 0.3, 5.1; p=0.74) or PCPC worsening (OR 1.2; 95%CI 0.4, 3.9; p=0.77).

Adjusted outcomes for seizures categories.

Variable	Mortality OR (95% CI)	p-value	Worsened PCPC OR (95% CI)	p-value
Seizure Category				
No Seizures	Ref	Ref	Ref	Ref
Electrographic Seizures	1.3 (0.3, 5.1)	0.74	1.2 (0.4, 3.9)	0.77
Electrographic Status Epilepticus	5.1 (1.4, 18)	0.01	17.3 (3.7, 80)	<0.001
Age	1 (0.9, 1)	0.8	1 (0.99, 1.01)	0.61
Sex				
Male	ref	ref	Ref	Ref
			1.7 (0.7, 4)	0.24
			Ref	Ref
			12 (2, 72)	0.006
			0 (5.2, 304)	<0.001
			5 (3.1,197)	0.002
			7 (0.5, 430)	0.16
Sepsis	10.6 (0.8, 137)	0.07	6.6 (0.5, 88)	0.15
Posterior Reversible Leukoencephalopathy Syndrome	-	-	2.5 (0.14, 43)	0.5
Neurosurgical Procedure	2 (0.2, 22)	0.56	4.6 (0.6, 33)	0.13
Provoked Seizure	2.2 (0.12, 38)	0.6	0.4 (0.03, 6)	0.5
Systemic/Metabolic	1.5 (0.1, 21)	0.77	7.4 (0.95, 52)	0.06
Prior Neurodevelopment				
Abnormal	Ref	Ref	Ref	Ref
Normal	2.2 (0.74, 6.6)	0.16	10.5 (3.6, 31)	<0.001

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FULL-LENGTH ORIGINAL RESEARCH

Mortality and recovery from refractory status epilepticus in the intensive care unit: A 7-year observational study

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Table 1. Baseline characteristics

	Mean	SD
Demographics		
Age		
Years		
Gender		
Male		
Female		
Clinical characteristics		
Presumed etiologies of RSE		
Hypoxic encephalopathy	25	23
Brain tumor	15	14
Uncontrolled epilepsy	11	10
Ischemic st		
Meningitis/		
Traumatic		
Intracereb		
Metabolic		
Alcohol withdrawal	3	3
Neurodegenerative	3	3
Others	11	10
Not known	10	9
Level of consciousness at SE onset		
Awake or somnolent	27	24
Stuporous or comatose	84	76
Worst seizure type at SE onset		
Simple partial/complex partial/absence	29	26
Generalized convulsive	10	9
NCSE in coma	72	65

RSE, refractory status epilepticus; SE, status epilepticus; NCSE, nonconvulsive status epilepticus.

RSE hastalarının önemli bir kısmı komada NCSE olan hastalar

RSE süresinde uzama ve NCSE ölümcül sonlanımla ilişkili

Table 2. Demographics and clinical characteristics of surviving and nonsurviving patients after refractory status epilepticus

	Total cohort					After exclusion of patients with hypoxic encephalopathy				
	Survivors (n = 69)		Nonsurvivors (n = 42)			Survivors (n = 61)		Nonsurvivors (n = 25)		
Age	Mean	SD	Mean	SD	p-Value	Mean	SD	Mean	SD	p-Value
Years	60.5	±16.6	65.0	±15.8	0.162	61.2	±16.7	65.3	±15.0	0.272
	n	%	n	%		n	%	n	%	
Gender										
Male	34	49.3	26	61.9	0.195	29	48	16	64	0.235
Female	35	50.7	16	38.1		32	52	9	36	
Presumed etiology of RSE										
Hypoxic encephalopathy	8	12	17	41	**<0.0001**	–	–	–	–	–
Brain tumor	5	7	10	24	**0.021**	5	8	10	40	**0.001**
Uncontrolled epilepsy	8	12	3	7	0.529	8	13	3	12	1.000
Ischemic stroke	7	10	2	5	0.470	7	11	2	8	1.000
Meningitis/encephalitis	7	10	1	2	0.255	7	11	1	4	0.428
Traumatic brain injury	4	6	3	7	1.000	4	7	3	12	0.409
Intracerebral hemorrhage	5	7	1	2	0.406	5	8	1	4	0.667
Other or unknown etiologies	25	36	6	14		25	40	6	24	
Level of consciousness at SE onset										
Awake or somnolent	23	33	4	10	**0.006**	23	38	4	16	0.072
Stuporous or comatose	46	67	38	90		38	62	21	84	
Worst seizure type at SE onset										
Simple partial/complex partial/absence	26	38	3	7	**0.001**	26	43	3	12	**0.010**
Generalized convulsive	4	6	6	14		4	7	1	4	
NCSE in coma	39	57	33	79		31	51	21	84	
	Mean	SD	Mean	SD		Mean	SD	Mean	SD	
Duration of RSE (hours)	88.9	±158.1	120.3	±164.1	**0.002***	89.4	±160	159.2	±201	**0.001***
Number of AEDs	4.4	±1.4	4.4	±1.3	1.000*	4.9	±1.1	4.4	±1.6	0.100*
	n	%	n	%		n	%	n	%	
Anesthetic drugs										
Barbiturates	8	12	6	14	0.771	8	13	4	16	0.739
Propofol	17	25	15	36	0.280	16	26	9	36	0.435
Critical interventions (before or during RSE)										
Mechanical ventilation	54	78	37	88	0.191	47	77	21	84	0.569
CPR	3	4	14	33	**<0.0001**	0	0	0	0	–
Complications										
Infections during SE	28	41	18	43	0.813	24	39	13	52	0.282
Severe hypotension (requiring vasopressors)	3	4	4	10	0.423	2	3	1	4	1.000

RSE, refractory status epilepticus; AEDs, antiepileptic drugs; NCSE, nonconvulsive status epilepticus; CPR, cardiopulmonary resuscitation; SE, status epilepticus.
Bold p-values are considered statistically significant.
Continuous variables were analyzed with the Student's *t*-test if normally distributed or the Mann-Whitney *U*-test if nonnormally distributed (*). For comparisons of proportions chi-square and Fisher's exact test were applied where appropriate.

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Mortality and recovery from refractory status epilepticus in the intensive care unit: A 7-year observational study

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Table 3. Univariable and multivariable analysis for death in patients with refractory status epilepticus

	Crude			Adjusted[a]		
	RR	95% CI	p-Value	RR	95% CI	p-Value
Total cohort (n = 111)						
Death						
Age					0.99–1.03	0.109
Worst seizure type at SE						
Simple partial/complex						
Generalized convulsive					1.59–13.97	**0.005**
NCSE in coma					1.34–9.77	**0.011**
Brain tumors					1.59–4.96	**<0.0001**
Hypoxic encephalopathy					1.40–4.12	**0.001**
RSE duration (per hour)					1.00–1.002	**0.005**

				Adjusted[b]		
					95% CI	p-Value
After exclusion of patients wit						
Death						
Age	1.012	0.99–1.03	0.285	1.009	0.99–1.03	0.393
Worst seizure type at SE onset						
Simple partial/complex partial/absence	Ref.			Ref.		
Generalized convulsive	1.933	0.25–15.27	0.532	2.206	0.28–17.50	0.454
NCSE in coma	3.904	1.26–12.06	**0.018**	3.881	1.41–10.67	**0.009**
Brain tumors	3.156	1.77–5.62	**<0.0001**	2.875	1.66–4.97	**<0.0001**
RSE duration (per hour)	1.001	1.00–1.002	**0.047**	1.001	1.00–1.002	**<0.0001**

SE, status epilepticus; RSE, refractory status epilepticus; NCSE, nonconvulsive status epilepticus.
Bold p-values are considered statistically significant.
[a]Adjusted for age, RSE duration, brain tumors, worst seizure type, and hypoxic encephalopathy.
[b]Adjusted for age, RSE duration, brain tumors, worst seizure type, and exclusion of hypoxic encephalopathy.

YBÜ HASTALARINDA NCSE HİPOKSİK ENSEFALOPATİ HASTALARI DIŞLANDIĞINDA BİLE ARTMIŞ MORTALİTE İÇİN BAĞIMSIZ BİR FAKTÖR

- Absans status epileptikusunun morbidite veya mortalite oluşturmadığı kabul edilir
- Semptomatik NCSE yüksek mortalite oranları ile ilişkili (%70)
- Hastanede kalış süreleri uzun, sağ kalanlarda fonksiyonel bozulma sık, %20 bazal duruma dönüş
- NCSE'un morbidite ve morta disfonksiyonundan bağımsız
- Tanıda gecikme morbidite ve
  - >30 dk→ %3
  - 30-60 dk→ %19
  - 1-6 saat→%32
- Serebral mikrodiyaliz çalışmaları serebral glutamat, gliserol ve laktat-pirüvat oranında artış gösterdi
- Nonkonvülzif nöbetler KİBAS, orta hat şiftinde artış, ipsilateral hipokampal ve neokortikal atrofi riskinde artışla ilişkili

İnme, SAK, travmatik beyin injurisi hastalarında konvülzif ve nonkonvülzif status epileptikus akut beyin patolojisi ile birlikte sinerjistik hareket ederek prognozu kötüleştirir

Table 4 Prognosis

Convulsive status epilepticus	*Nonconvulsive status epilepticus*
Mortality	Mortality
At hospital discharge: 9–21 % [19, 36–38]	At hospital discharge: 18–52 % [51–53]
At 30 days: 19–27 % [30, 39, 40]	At 30 days: 65 % [30]
At 90 days: 19 % [41]	Factors associated with poor outcome after NCSE:
Standardized 10-year mortality ratio: 2.8 in general population [42]	Underlying etiology, severe mental status impairment, longer seizure duration [28, 51, 53, 54]
In children, the mortality ranges from 3 to 11 % in retrospective series [43]. In a prospective study, the mortality was 3 % [34]	For patients diagnosed within 30 min of seizure onset, mortality was 36 % compared with 75 % for those patients diagnosed ≥24 h after seizure onset seizures [51]
Morbidity	Patients with NCSE treated and resolved within 10 h had 10 % mortality vs. 85 % mortality if seizures continued longer than 20 h [51]
Severe neurological or cognitive sequelae: 11–16 % [19, 44–46]	Mortality at hospital discharge in NCSE was 27 % vs. 3 % comparing patients with vs. without known acute medical cause [53]
Deterioration in functional status 23–26 % [19, 36, 38]	
At 90 days after SE, 39 % had marked functional impairment (glasgow outcome scale score 2–4) and 43 % had good recovery (glasgow outcome scale score 5) [41]	
Factors associated with poor outcome after GCSE	
Underlying etiology, de novo development of SE in hospitalized patients, old at onset focal neurological signs, and the presence of medical complicatio	
Mortality rate is higher (61 %) when SE develops de novo in hospitalized pa	
In patients with adequate therapy, the mortality rate may be as low as 8 % whil (insufficient dose given, wrong route of administration, unnecessary delay complications, or lack of EEG monitoring to guide treatment) [47]. Adheren control and shorter ICU and hospital length of stay [50]	

NONKONVÜLZİF STATUS EPİLEPTİKUS EN AZ KONVÜLZİF STATUS EPİLEPTİKUS KADAR OLUMSUZ PROGNOZLA İLİŞKİLİ

Yoğun bakım ünitesinde nonkonvülzif status epileptikus etkin bir biçimde tedavi edilmesi gereken bir durum!!!

Yoğun bakım ünitesinde nonkonvülzif status epileptikus yönetimi

- Status epileptikus değerlendirme ve tedavisi eşzamanlı yapılmalı
- HEDEF: KLİNİK VE ELEKTROGRAFİK NÖBET AKTİVİTESİNİN BİR AN ÖNCE SONLANDIRILMASI!!!
- İlk değerlendirmenin amaçları:

1. *Stabilizasyon ve sekonder nöronal injuriden korunma*
2. *Status epileptikusu presipite eden ya da gelişimine katkıda bulunan akut beyin hasarı ya da metabolik bozuklukların tanınması*
3. *Sistemik injuri belirteçlerinin taranması*

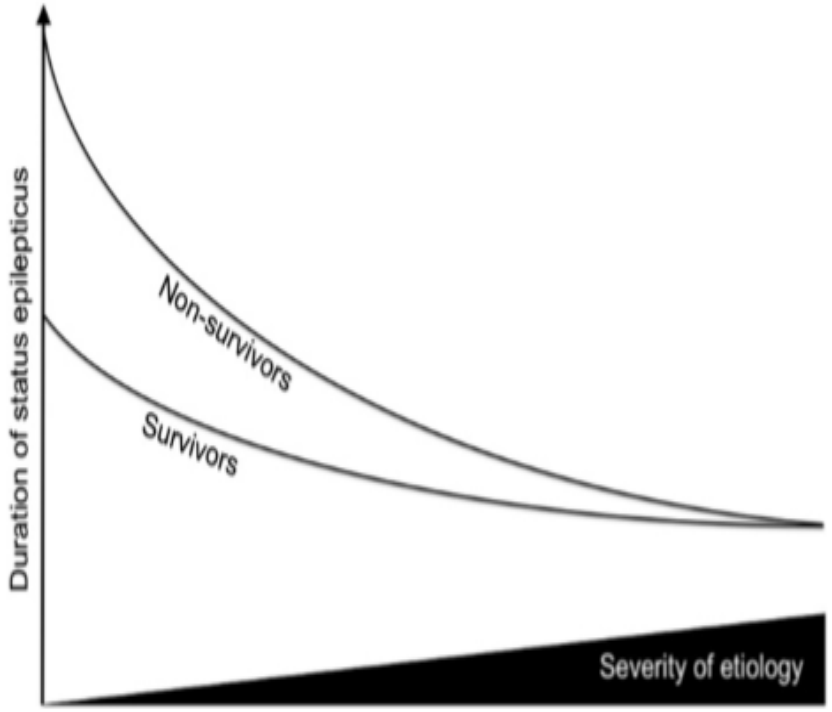

Fig. 1. The duration of status epilepticus in survivors and nonsurvivors dependent of the severity of etiology (based on the results from the original study [20]). Seizure duration is longer in non-survivors as compared to survivors. This relation is less distinct in patients with more severe underlying etiology of status epilepticus (e.g., patients with brain tumors, or patients with hypoxic-ischemic brain injury).

Epilepsy and Behavior 2015;49:294-7

Yoğun bakım ünitesinde nonkonvülzif status epileptikus yönetimi

- İlk adım tüm medikal ve nörolojik acillerde olduğu gibi *A, B, C*
- Havayolunun korunması, yeterli oksijenasyon ve ventilasyonun ve hemodinamik stabilitenin sağlanması
- IV giriş, O2, noninvaziv/IV anestetik ajanlar kullanılacaksa invaziv hava yolu
- Öncelikle kan şekeri bakılmalı ve düşükse önce tiamin sonra glukoz verilmeli
- Ateş varsa asetaminofen, soğutucu battaniyeler, aksilla ve kasıklara buz paketleri
- Sekonder nöronal injuri gelişimini engellemek için hipoksemi, hipotansiyon, hipoglisemi ve ateşten kaçınılmalı/tedavi edilmeli

Etiyolojik araştırma

neurocritical care society Neurocrit Care (2012) 17:3–23
DOI 10.1007/s12028-012-9695-z

REVIEW

Guidelines for the Evaluation and Management of Status Epilepticus

Gretchen M. Brophy · Rodney Bell · Jan Claassen · Brian Alldredge · Thomas P. Bleck · Tracy Glauser · Suzette M. LaRoche · James J. Riviello Jr. · Lori Shutter · Michael R. Sperling · David M. Treiman · Paul M. Vespa · Neurocritical Care Society Status Epilepticus Guideline Writing Committee

Table 3 Suggested diagnostic work-up [21]

The steps included in the diagnostic work-up should be completed as soon as possible and occur simultaneously and in parallel with treatment.

All patients

1. Fingerstick glucose
2. Monitor vital signs.
3. Head computed tomography (CT) scan (appropriate for most cases)
4. Order laboratory test: blood glucose, complete blood count, basic metabolic panel, calcium (total and ionized), magnesium, AED levels.
5. Continuous electroencephalograph (EEG) monitoring

Consider based on clinical presentation

1. Brain magnetic resonance imaging (MRI)
2. Lumbar puncture (LP)
3. Comprehensive toxicology panel including toxins that frequently cause seizures (i.e. isoniazid, tricyclic antidepressants, theophylline, cocaine, sympathomimetics, alcohol, organophosphates, and cyclosporine)
4. Other laboratory tests: liver function tests, serial troponins, type and hold, coagulation studies, arterial blood gas, AED levels, toxicology screen (urine and blood), and inborn errors of metabolism

▶ **Etiologic Investigation**

- Glucose
- Antiepileptic drug levels
- Acid-base disturbances
- Arterial blood gas
- Basic metabolic panel
- Lactic acid
- Acute organ failure
- Creatinine
- Blood urea nitrogen
- Transaminases (aspartate and alanine aminotransferase)
- Ammonia
- Electrolyte imbalances
- Calcium
- Magnesium
- Phosphorus
- Intoxications
- Alcohol level
- Adulterant survey

▶ **Systemic Injury Screening**

- Creatine kinase
- Troponin

▶ **CSF (As Indicated)**

- Cell count
- Glucose
- Protein
- Gram stain and bacterial culture
- Herpes simplex virus PCR[a]

CSF = cerebrospinal fluid; PCR = polymerase chain reaction.
[a] Testing for other infectious agents may be indicated depending on the clinical scenario.

CONTINUUM: Lifelong Learning in Neurology Issue: Volume 21(5, Neurocritical Care), October 2015, p 1362–1383

Etiyolojik araştırma

- Öykü
- Fizik muayene
- Kontrastsız BBT
- Temel laboratuvar tetkikleri
- Epileptik olduğu bilinen olgularda serum AEİ düzeyleri, non-kompliyans???
- Toksikoloji analizleri
- Epilepsi öyküsü olmayan hastalarda ve epileptik olmasına karşın seyrek nöbetleri olan ve ilk değerlendirmelerle status epileptikusa yol açan faktörün belirlenemediği hastalarda LP düşünülmeli
- Yakın zamanda geçirilmiş enfeksiyon semptomları olan, lisan bozuklukları olan, ateş veya hipotermisi olan ve immünkompromize olan hastalarda LP ile SSS enfeksiyonu dışlanmalı

- Etiyoloji belirlendikten sonra acilen düzeltilmeli
- Ancak seçilecek tedavinin nöbet eşiğini düşürmemesine, nöbet veya status epileptikusu presipite etmemesine dikkat edilmeli (florokinolon grubu antibiyotikler, sefepim, karbapenemler,…)
- İlaç yoksunluğu ile ilişkili status epileptikus olgularında mümkünse parenteral yolla olmak üzere ilaç hemen uygulanmalı
- KİBAS saptanan/kuşku duyulan hastalarda uygun yönetim

CONTINUUM: Lifelong Learning in Neurology Issue: Volume 21(5, Neurocritical Care), October 2015, p 1362–1383

Etiyolojik araştırma

- İlk incelemeler ile etiyoloji belirlenemediyse;
- *'New-onset refractory status epilepticus', NORSE*

Epilepsy & Behavior Case Reports 3 (2015) 33–35

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Case Report

'The great imitator': Neurosyphilis and new-onset refractory status epilepticus (NORSE) syndrome

Sonia Kumari *, Tom Hayton, Pauline Jumaa, Dougall McCorry

Unusual presentation of more common disease/injury

CASE REPORT

New onset refractory status epilepticus (NORSE) as the heralding manifestation of herpes simplex encephalitis

Rajesh Verma,[1] Tushar Premraj Raut,[1] Prithvi Giri,[1] Heramba Narayan Praharaj[2]

Clinical commentary

Epileptic Disord 2014; 16 (4): 486-93

Treatment responsive GABA(B)-receptor limbic encephalitis presenting as new-onset super-refractory status epilepticus (NORSE) in a deployed U.S. soldier

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Five cases of new onset refractory status epilepticus (NORSE) syndrome: Outcomes with early immunotherapy

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CONTINUUM: Lifelong Learning in Neurology Issue: Volume 21(5, Neurocritical Care), October 2015, p 1362–1383

Diagnostic Test	Consider In
Imaging	
Brain MRI	Patients in whom an etiology is not established after history, basic laboratory evaluation, brain CT scan, and lumbar puncture (LP)
Chest/abdomen/pelvis CT	Patients in whom an etiology is not established after history, basic laboratory evaluation, brain CT scan, LP, and brain MRI
Ovarian or testicular ultrasound	Patients in whom an etiology is not established after history, basic laboratory evaluation, head CT scan, LP, brain MRI, and chest/abdomen/pelvis CT
CSF[33]	Patients in whom an etiology is not established after history, basic laboratory evaluation, CT scan, LP, and MRI AND Patients in whom history of present illness, demographics, exposure history, comorbidities, and family history are potentially suggestive of the diagnosis under consideration
Cell count, glucose, protein, Gram stain	
Cytology and flow cytometry	
Microbiologic serologies, PCRs, Gram stain and cultures: herpes simplex virus types 1 and 2, varicella-zoster virus, Epstein-Barr virus, cytomegalovirus, human herpes virus 6, enterovirus, influenza, adenovirus, JC virus, measles, HIV, hepatitis C virus, West Nile virus, Japanese encephalitis virus, St Louis encephalitis viru… encephalomyelitis virus, encephalomyelitis virus, Valley virus, *Mycoplasma tuberculosis*, *Chlamydia* … cryptococcal antigen, sy… toxoplasmosis, malaria,	
CSF exclusive oligoclona… and synthesis	
Radioimmunoprecipitat… antibody, VGKC antibo…	
Immunofluorescence assay (tissue immunofluorescence): ANNA-1, ANNA-2, ANNA-3, PCA-1, PCA-2, PCA-Tr, amphiphysin antibody, CRMP-5-IgG, AGNA-1	
Immunofluorescence assay (cell-binding immunofluorescence): NMDA receptor antibody, AMPA receptor antibody, GABA-B receptor antibody	
Neuromyelitis optica (aquaporin-4 IgG) cell-binding assay	
Anti-Ma 1 and Anti-Ma 2/Ta antibody	
14-3-3 protein	
Serum[33]	Patients in whom an etiology is not established after history, basic laboratory evaluation, CT scan, LP, and MRI AND Patients in whom history of present illness, demographics, exposure history, comorbidities, and family history are potentially suggestive of the diagnosis under consideration
Microbiologic serologies, PCRs, and cultures: herpes simplex virus types 1 and 2, varicella-zoster virus, Epstein-Barr virus, cytomegalovirus, influenza, adenovirus, JC virus, measles, HIV, hepatitis C virus, West Nile virus, Japanese encephalitis virus, St Louis encephalitis virus, eastern equine encephalomyelitis virus, western equine encephalomyelitis virus, *Mycoplasma pneumoniae*, *Chlamydia* species, *Bartonella henselae*, cryptococcal antigen, syphilis (rapid plasma reagin), toxoplasmosis, malaria, Lyme	
Nonparaneoplastic autoantibodies: ANA, double-stranded DNA, lupus anticoagulant, antiphospholipid, rheumatoid factor, SSA, SSB, ANCA, thyroid peroxidase, thyroglobulin, transglutaminase, antigliadin, endomysium	
Angiotensin-converting enzyme	
Paraneoplastic antibody panel: AchR binding, Anti-Hu (ANNA-1), Anti-Ri (ANNA-2), striated muscle, AchR ganglionic, P/Q-type voltage-gated calcium channel antibodies, N-type voltage-gated calcium channel antibody, Anti-Yo (ANNA-3), AGNA-1, PCA-1, PCA-2, PCA-Tr, amphiphysin, CRMP-5/CV2, VGKC, NMDA	
Radioimmunoprecipitation assay: P/Q-type calcium channel antibody, N-type calcium channel antibody, muscle AchR binding antibody, ganglionic AchR antibody, VGKC antibody, GAD65 antibody	
Immunofluorescence assay (tissue immunofluorescence):	
	…in whom the above evaluation is nondiagnostic
	…s in whom brain MRI, CSF analysis, and/or …boratory evaluation are suggestive of vasculitis
Brain SPECT or FDG-PET	Patients in whom a thorough evaluation is nondiagnostic AND Imaging does not reveal a potential biopsy site
Brain and/or meningeal biopsy	Patients in whom a thorough evaluation is nondiagnostic AND Any ill-defined lesion is present on MRI (T1 postcontrast, T2 FLAIR) in a superficial cortical or meningeal location

AchR = acetylcholine receptor; AGNA = antiglial nuclear antibody; AMPA = α-amino-3-hydroxy-5-methylisoxazole-4-propionic acid; ANA = antinuclear antibody; ANCA = antineutrophil cytoplasmic antibody; ANNA = antineuronal nuclear antibody; CRMP-5 = collapsin response mediator protein-5; CSF = cerebrospinal fluid; CT = computed tomography; DNA = deoxyribonucleic acid; FDG-PET = fluorodeoxyglucose positron emission tomography; FLAIR = fluid-attenuated inversion recovery; GABA-B = γ-aminobutyric acid type B; GAD65 = glutamic acid decarboxylase 65; HIV = human immunodeficiency virus; IgG = immunoglobulin G; MRI = magnetic resonance imaging; NMDA = *N*-Methyl-D-aspartate; PCA = Purkinje cell antibody; PCR = polymerase chain reaction; PET = positron emission tomography; SPECT = single-photon emission computed tomography; SSA = Sjögren syndrome A; SSB = Sjögren syndrome B; VGKC = voltage-gated potassium channel.

Her tetkik her hasta için gerekli değil
Seçilecek etiyolojik tetkikler öykü ve fizik muayene bulgularına göre belirlenmeli

İleri inceleme ile hastaların önemli bir kısmında altta yatan neden belirlenebilir

Yoğun bakım ünitesinde nonkonvülzif status epileptikus tedavisi

- Status epileptikus 60 dk içerisinde kontrol altına alınmış olmalı
- Nöbet aktivitesi kontrol altına alınmış olsa bile tüm hastalara *'emergent initial AED therapy (ilk sıra)'* ve 'urgent control AED therapy (ikinci sıra)' ve idame AEİ tedavisi uygulanmalı
- Neden metabolik bir bozukluksa düzeltilmeli, bu hastalarda idame AEİ tedavisi gerekli olmayabilir
- İlk iki AEİ başarısız olduğunda refrakter status epileptikus tedavisi (3. ve 4. sıra) uygulanmalı

Table 5 Critical care treatment outline for convulsive and non-convulsive SE that should be completed prior or upon arrival to the intensive care unit (Note: timing is merely a guide as all interventions should be done as soon as possible.)

Critical care treatment	Timing (minutes post seizure onset)	Goals	Rationale/references
Non-invasive airway protection and gas exchange with head positioning	Immediate (0–2 min)	Maintain airway patency, avoid snoring, administer O_2	[40, 76–79]
Intubation (if airway/gas exchange compromised or elevated ICP suspected)	Immediate (0–10 min)	Establish secure oxygenation and ventilation	Expert opinion
Vital signs: O_2 saturation, BP, HR	Immediate (0–2 min)	Establish and support baseline vital signs	[80–81]
Vasopressor support of BP if SBP <90 mmHg or MAP <70	Immediate (5–15 min)	Support CPP	Expert opinion
Finger stick blood glucose	Immediate (0–2 min)	Diagnose hypoglycemia	
Peripheral IV access	Immediate (0–5 min)	Establish medication route	[80–82]
1. Emergent initial AED therapy (i.e. benzodiazepine)		1. Stop seizure	
2. Fluid resuscitation		2. Establish euvolemia	
3. Nutrient resuscitation (thiamine given before dextrose; dextrose)		3. Reverse thiamine deficiency, treat hypoglycemia	
Urgent SE control therapy with AED	Immediate after initial AED given (5–10 min)	Stop seizure	[80–82]
Neurologic exam	Urgent (5–10 min)	Evaluate for mass lesion, acute intracranial process	Expert opinion
Triage lab test panel (see Table 2)	Immediate (5 min)	Diagnose life threatening metabolic condition	Expert opinion
Refractory SE treatment	Urgent (20–60 min after 2nd AED)	Stop seizures; treatment strategies based on individual patient response and AED concentrations (if applicable)	Expert opinion
Urinary catheter	Urgent (0–60 min)	Evaluate systemic circulation	Expert opinion
Continuous EEG	Urgent (15–60 min)	Evaluate for NCSE if not waking up after clinically obvious seizures cease	[50, 73, 75]
Diagnostic testing (selection depends on clinical presentation)	Urgent (0–60 min)	Evaluate for mass lesions, meningitis, encephalitis	Expert opinion
CT			
LP			
MRI			
Intracranial pressure monitoring (depending on clinical presentation)	Urgent (0–60 min of imaging diagnosis)	Measure and control ICP	Expert opinion

AED antiepileptic drug; *BP* blood pressure; *CPP* cerebral perfusion pressure; *CT* computed tomography; *EEG* electroencephalogram; *HR* heart rate; *ICP* intracranial pressure; *LP* lumbar puncture; *MAP* mean arterial pressure; *MRI* magnetic resonance imaging; *SBP* systolic blood pressure

Tedavi evreler halinde belirtilse de ‘continuum’ ve her bir evrede nöbet aktivitesinin bir an önce sonlandırılması hedef

Table 6 Treatment recommendations for SE

Treatment	Class/level of evidence
Emergent treatment	
Lorazepam	Class I, level A
Midazolam	Class I, level A
Diazepam	Class IIa, level A
Phenytoin/fosphenytoin	Class IIb, level A
Phenobarbital	Class IIb, level A
Valproate sodium	Class IIb, level A
Levetiracetam	Class IIb, level C
Urgent treatment	
Valproate sodium	Class IIa, level A
Phenytoin/fosphenytoin	Class IIa, level B
Midazolam (continuous infusion)	Class IIb, level B
Phenobarbital	Class IIb, level C
Levetiracetam	Class IIb, level C
Refractory treatment	
Midazolam	Class IIa, level B
Propofol	Class IIb, level B
Pentobarbital/thiopental	Class IIb, level B
Valproate sodium	Class IIa, level B
Levetiracetam	Class IIb, level C
Phenytoin/fosphenytoin	Class IIb, level C
Lacosamide	Class IIb, level C
Topiramate	Class IIb, level C
Phenobarbital	Class IIb, level C

Neurocrit Care 2012;17:3-23

'Emergent Initial Therapy' – Acil İlk Tedavi – 1. sıra AEİ

- **Benzodiazepinler**
- IV yol tercih edilir
- Mümkün değilse IM, rektal, nazal, bukkal
- IV: lorazepam
- IM: midazolam (nazal veya bukkal yolla da uygulanabilir)
- Rektal: diazepam
- Entübe olmayan hastalarda IV BDZ uygulanırken solunum depresyonu riskine dikkat!
- Hızlı uygulama solunum depresyonu ve hipotansiyona yol açabilir!!!

Table 6 Treatment recommendations for SE

Treatment	Class/level of evidence
Emergent treatment	
Lorazepam	Class I, level A
Midazolam	Class I, level A
Diazepam	Class IIa, level A
Phenytoin/fosphenytoin	Class IIb, level A
Phenobarbital	Class IIb, level A
Valproate sodium	Class IIb, level A
Levetiracetam	Class IIb, level C

'Emergent Initial Therapy' – Acil İlk Tedavi – 1. sıra AEİ

- Status epileptikus tedavisinde kullanılan ilaçların optimal doz aralıklarını belirlemek için yapılmış kontrollü klinik çalışmalar yok
- Bu nedenle dozlar gözlem verileri ve uzman görüşü ile belirlenmiştir
- Klinik uygulamada kullanılan dozlar daha yüksek olabilir, klinik ve EEG bulgularına göre titre edilmeli
- Fenitoin/fosfenitoin infüzyonları sırasında kardiyak monitorizasyon yapılmalı, QT uzaması ve aritmi riskleri!!!

Table 7 Intermittent drug dosing in SE

Drug	Initial dosing	Administration rates and alternative dosing recommendations	Serious adverse effects	Considerations
Diazepam	0.15 mg/kg IV up to 10 mg per dose, may repeat in 5 min	Up to 5 mg/min (IVP) Peds: 2–5 years, 0.5 mg/kg (PR); 6–11 years, 0.3 mg/kg (PR); greater than 12 years, 0.2 mg/kg (PR)	Hypotension Respiratory depression	Rapid redistribution (short duration), active metabolite, IV contains propylene glycol
Lorazepam	0.1 mg/kg IV up to 4 mg per dose, may repeat in 5–10 min	Up to 2 mg/min (IVP)	Hypotension Respiratory depression	Dilute 1:1 with saline IV contains propylene glycol
Midazolam	0.2 mg/kg IM up to maximum of 10 mg	Peds: 10 mg IM (>40 kg); 5 mg IM (13–40 kg); 0.2 mg/kg (intranasal); 0.5 mg/kg (buccal)	Respiratory depression Hypotension	Active metabolite, renal elimination, rapid redistribution (short duration)
Fosphenytoin	20 mg PE/kg IV, may give additional 5 mg/kg	Up to 150 mg PE/min; may give additional dose 10 min after loading infusion Peds: up to 3 mg/kg/min	Hypotension Arrhythmias	Compatible in saline, dextrose, and lactated ringers solutions
Lacosamide	200–400 mg IV	200 mg IV over 15 min No pediatric dosing established	PR prolongation Hypotension	Minimal drug interactions Limited experience in treatment of SE
Levetiracetam	1,000–3,000 mg IV Peds: 20–60 mg/kg IV	2–5 mg/kg/min IV		Minimal drug interactions Not hepatically metabolized
Phenobarbital	20 mg/kg IV, may give an additional 5–10 mg/kg	50–100 mg/min IV, may give additional dose 10 min after loading infusion	Hypotension Respiratory depression	IV contains propylene glycol
Phenytoin	20 mg/kg IV, may give an additional 5–10 mg/kg	Up to 50 mg/min IV; may give additional dose 10 min after loading infusion Peds: up to 1 mg/kg/min	Arrhythmias Hypotension Purple glove syndrome	Only compatible in saline IV contains propylene glycol
Topiramate	200–400 mg NG/PO	300–1,600 mg/day orally (divided 2–4 times daily) No pediatric dosing established	Metabolic acidosis	No IV formulation available
Valproate sodium	20–40 mg/kg IV, may give an additional 20 mg/kg	3–6 mg/kg/min, may give additional dose 10 min after loading infusion Peds: 1.5–3 mg/kg/min	Hyperammonemia Pancreatitis Thrombocytopenia Hepatotoxicity	Use with caution in patients with traumatic head injury; may be a preferred agent in patients with glioblastoma multiforme

IM intramuscular; *IV* intravenous; *IVP* intravenous push; *min* minute; *NG* nasogastric; *PE* phenytoin equivalents; *PEDs* pediatric; *PO* by mouth; *PR* rectal administration; *PRIS* propofol related infusion syndrome

'Urgent Control Therapy' – Hızlı Kontrol Tedavisi – 2. sıra AEİ

- Nedenin bilindiği ve düzeltildiği (örneğin hipoglisemi) durumlar hariç tüm hastalarda gerekli
- Hedefler:

1. İlk sıra tedaviye yanıt veren ve statusun sonlandığı hastalarda idame AEİ'ların terapötik düzeyine hızla ulaşmak
2. Yanıtsız hastalarda statusun sonlandırılması

- Bu aşamada hangi ilacın en etkili olduğu tartışmalı, seçim bireyselleştirilmeli
- Primer jeneralize epilepsi öyküsü olanlarda valproat, diğer hastalarda fenitoin ilk tercih olabilir
- Terapötik düzeye hızla ulaşılması için IV yol tercih edilmeli
- Epileptik olan ve AEİ kullanım öyküsü olan hastalarda varsa bu AEİ'ın IV bolusunu uygulamak daha doğru
- Nöbet aktivitesinin sonlanması için normal hedef konsantrasyonları aşmak üzere ek bolus uygulamalar yapılabilir

Table 6 Treatment recommendations for SE

Treatment	Class/level of evidence
Urgent treatment	
Valproate sodium	Class IIa, level A
Phenytoin/fosphenytoin	Class IIa, level B
Midazolam (continuous infusion)	Class IIb, level B
Phenobarbital	Class IIb, level C
Levetiracetam	Class IIb, level C

'Refrakter status epileptikus tedavisi' – 3. ve 4. sıra AEİ

- 1. ve 2. sıra tedavilere karşın devamlı EEG monitorizasyonu ve/veya klinik değerlendirme ile statusun devam ettiğinin belirlendiği hastalar
- Güvenli olduğu belirlenmiş bir gözlem periyodu yok
- Bu nedenle agresif tedaviye devam
- Kullanılan AEİ tekrar bolusu?
- Ek ajan?
- Bolus intermittan tedavilere yanıtsızlık halinde devamlı AEİ infüzyonuna geçilmeli
- Hemodinamik olarak stabil, entübasyon gerektirmeyen NCSE hastalarında daha önce uygulanmadıysa intermittan bolus halinde valproat sodyum, levetirasetam, fenitoin
- Devamlı infüzyonla birlikte gerektiği hallerde aynı ilacın bolus dozları uygulanabilir
- İlk ajanla başarısızlık halinde farklı bir ajanın devamlı infüzyonuna geçilebilir

Table 6 Treatment recommendations for SE

Treatment	Class/level of evidence
Refractory treatment	
Midazolam	Class IIa, level B
Propofol	Class IIb, level B
Pentobarbital/thiopental	Class IIb, level B
Valproate sodium	Class IIa, level B
Levetiracetam	Class IIb, level C
Phenytoin/fosphenytoin	Class IIb, level C
Lacosamide	Class IIb, level C
Topiramate	Class IIb, level C
Phenobarbital	Class IIb, level C

'Refrakter status epileptikus tedavisi' – 3. ve 4. sıra AEİ

Table 8 RSE dosing recommendations

Drug	Initial dose	Continuous infusion dosing recommendations-titrated to EEG	Serious adverse effects	Considerations
Midazolam	0.2 mg/kg; administer at an infusion rate of 2 mg/min	0.05–2 mg/kg/hr CI Breakthrough SE: 0.1–0.2 mg/kg bolus, increase CI rate by 0.05–0.1 mg/kg/hr every 3–4 h	Respiratory depression Hypotension	Tachyphylaxis occurs after prolonged use Active metabolite, renally eliminated, rapid redistribution (short duration), does NOT contain propylene glycol
Pentobarbital	5–15 mg/kg, may give additional 5–10 mg/kg; administer at an infusion rate ≤50 mg/min	0.5–5 mg/kg/h CI Breakthrough SE: 5 mg/kg bolus, increase CI rate by 0.5–1 mg/kg/h every 12 h	Hypotension Respiratory depression Cardiac depression Paralytic ileus At high doses, complete loss of neurological function	Requires mechanical ventilation IV contains propylene glycol
Propofol	Start at 20 mcg/kg/min, with 1–2 mg/kg loading dose	30–200 mcg/kg/min CI Use caution when administering high doses (>80 mcg/kg/min) for extended periods of time (i.e., >48 h) Peds: Use caution with doses >65 mcg/kg/min; contraindicated in young children Breakthrough SE: Increase CI rate by 5–10 mcg/kg/min every 5 min or 1 mg/kg bolus plus CI titration	Hypotension (especially with loading dose in critically ill patients) Respiratory depression Cardiac failure Rhabdomyolysis Metabolic acidosis Renal failure (PRIS)	Requires mechanical ventilation Must adjust daily caloric intake (1.1 kcal/ml)
Thiopental	2–7 mg/kg, administer at an infusion rate ≤50 mg/min	0.5–5 mg/kg/h CI Breakthrough SE: 1–2 mg/kg bolus, increase CI rate by 0.5–1 mg/kg/h every 12 h	Hypotension Respiratory depression Cardiac depression	Requires mechanical ventilation Metabolized to pentobarbital

CI continuous infusion; *EEG* electroencephalogram; *h* hour; *IM* intramuscular; *IV* intravenous; *IVP* intravenous push; *min* minute; *PRIS* propofol related infusion syndrome

- Devamlı infüzyonla verilmesi önerilen ajanlar: midazolam, propofol, pentobarbital, thiopental
- Hangisinin tercih edilmesi gerektiğine ilişkin veri yok
- Propofol infüzyon sendromu!!!
- Midazolam daha az hipotansiyona yol açar
- Pentobarbital > midazolam, ancak yan etki daha fazla
- Tümüyle asiste ventilasyon ve kardiyovasküler monitorizasyon gerekli
- Vazopressör ajanlar gerekebilir

Refrakter status epileptikus tedavisinin intensite ve süresi

- Kanıta dayalı veri yok
- Tedavi intensitesi devamlı EEG monitorizasyonu bulgularına göre belirlenir
- Hedef: elektrografik nöbet aktivitesinin sonlanması veya burst süpresyon
- Serum ilaç düzeyleri yönlendirici olmamalı
- Tedavi süresi?
- Geleneksel uygulama elektrografik nöbet kontrolünün 24-48 saat sürdürülmesi, sonrasında AEİ'ların yavaş doz azaltımı
- Rekürren refrakter status halinde devamlı infüzyonun önceki dozuna veya daha yüksek bir doza çıkılmalı/yeni ilaç eklenmeli
- Haftalar-aylar süren refrakter status tedavisinden sonra olumlu prognoz mümkün

Devamlı infüzyon tedavisinden idame AEİ tedavisine geçiş

- Kanıta dayalı veri yok
- Devamlı infüzyon uygulaması ve weaningi süresince terapötik konsantrasyonları sağlayacak idame AEİ tedavisi verilmeli
- Terapötik konsantrasyonlar bir çok AEİ için yayımlanmış hedef konsantrasyonları aşabilir, dozlar etkinliği sağlamak ve yan etkileri minimize etmek üzere bireyselleştirilmeli
- İdame tedavinin başarısını belirleyen faktörler: klinik özellikler, EEG paterni, altta yatan neden, eşlik eden sistemik hastalık, ilaç-ilaç etkileşimleri
- Uzun süre pentobarbital infüzyonu uygulanan hastalarda çekilme nöbetleri olabilir

Refrakter status epileptikus için alternatif tedaviler

- Özellikle şu hastalarda agresif tedaviye devam edilmeli:
  - Premorbid sağlıklı olan, genç hastalar
  - Kendi kendini sınırlayan hastalık süreci
  - Olumsuz prognozla ilişkili intrakranial lezyonu olmayan hastalar
- Alternatif tedaviler kanıta dayalı değil
- Anekdotal olgu bildirimleri

Refrakter status epileptikus için alternatif tedaviler, farmakolojik

Table 1 Summary table for pharmacological options in SRSE treatment

Pharmacologic agent	Studied doses	Adverse effects	Clinical pearls and considerations
Ketamine	Bolus: 0.5–3 mg/kg Infusion: 1–10 mg/kg/h	Tachycardia, acute elevation in blood pressure, ICP elevation, and theoretical neurotoxic effects when used for prolonged periods	Caution if the patient has an etiology that might increase ICP (e.g., severe brain edema from anoxic brain injury). Early use of ketamine may provide better and faster control of seizures. Consider in hypotensive patients
Isoflurane	Concentration: 1–5 % Infusion: titrate to burst suppression on EEG	Hypotension requiring IV vasopressors support, infection, paralytic ileus, deep vein thrombosis, and cognitive dysfunction with prolonged use	Likely to stop seizures but not a sustained effect. Consider as last-line therapy
IVIG	1–2 g/kg divided over 3–5 days	Injection site and hypersensitivity reactions, renal dysfunction with concentrated solutions and high infusion rates, transfusion related acute lung injury, and thromboembolic events	Consider for patients with no history of seizures, a presence of other acute psychiatric behavioral or dementia-like changes, an underlying malignancy, or presence of other autonomic dysfunction
Corticosteroids Methylprednisolone Prednisone	 1 g/day for 3–5 days 60 mg daily	Glucose intolerance, psychiatric disturbances, impaired immunological function, and adrenal suppression	Similar to IVIG.

Curr Neurol Neurosci Rep 2015;15:66

Refrakter status epileptikus için alternatif tedaviler, non-farmakolojik

Table 2 Summary table for non-pharmacological options in SRSE treatment

Intervention	Studied doses	Adverse effects	Clinical pearls and considerations
Ketogenic diet	4:1 (the ratio of fat to carbohydrates and protein)	Hyperlipidemia, weight loss. Contraindicated in pyruvate carboxylase and beta-oxidation deficiency	Unlikely compliance with long-term use of the diet due to social and dietary restrictions, cost, and the complexity involved. Lack of well-designed trials
Hypothermia	Goal temperature of 32–35 °C×24 h with rewarming of no more than 0.5 °C per hour	Coagulation disorders, venous thrombosis, cardiac arrhythmia, electrolyte abnormalities, infections, pharmacokinetic and pharmacodynamics changes, and acute intestinal ischemia/necrosis	Hypothermia can potentially be used as an alternative to two or more unsuccessful EEG burst suppression trials. Goal temperature aimed at appropriate burst suppression pattern on EEG
Electroconvulsive therapy	Protocols vary	Can induce convulsive and non-convulsive status epilepticus after treatment, cognitive impairment, amnesia, and headache	EEG monitoring required Routine use not well established, further studies are needed
Transcranial magnetic stimulation	Can be performed in the ICU setting	Rare seizures, headache, dizziness, and other neurological side effects	Considered a very safe intervention and does not require surgery or device implantation. Still investigational therapy
Vagal nerve stimulator	Surgical implantation	Voice hoarseness, infection risk at the implantation site, and rare bradycardia	No strong evidence to support its use in the acute settings

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FULL-LENGTH ORIGINAL RESEARCH

Intravenous ketamine for the treatment of refractory status epilepticus: A retrospective multicenter study

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IV ketamin fokal ve jeneralize NCSE tedavisinde yararlı olabilir

Table 1. Demographics and clinical data (N = 60 episodes of RSE)

Age; median (range)	24 y (7 m–74 y)
Children (<18 y) (%)	12 (20)
Female gender (%)	30 (50)
Etiology (%)	
Unknown	34 (57)
Acute symptomatic	20 (33)
Nonanoxic brain injury[a]	11 (18)
Postanoxic encephalopathy	7 (12)
Systemic etiology[a]	2 (3)
Remote symptomatic	6 (10)
Prior history of epilepsy (%)	9 (15)
Duration of SE (days); median (range)	26.5 d (1 h–10 m)
CEEG (%)	59 (98)
Time from onset of SE to CEEG (median, range)	<24 h (0–17 d)
Classification of SE (%)	
Generalized convulsive	14 (23)
Tonic–clonic	5 (8)
Myoclonic	6 (10)
Tonic	3 (5)
Generalized nonconvulsive	3 (5)
Focal convulsive	4 (7)
Epilepsia partialis continua	2 (3)
Hemiconvulsive	2 (3)
Focal nonconvulsive	38 (63)
Status epilepticus of infantile spasms	1 (2)

Data presented as N (row percentage) unless stated otherwise. h, hours; d, days; m, months; y, years; CEEG, continuous EEG monitoring; SE, status epilepticus.
[a]Causes of nonanoxic brain injury and systemic etiologies included proven infectious (N = 4) or autoimmune (N = 2; both anti-NMDA) meningoencephalitis, subarachnoid hemorrhage (N = 2), ischemic stroke (N = 2), traumatic brain injury (N = 1), sepsis-associated encephalopathy (N = 1), and posterior reversible encephalopathy syndrome (N = 1).

Table 2. Determinants of ketamine efficacy (N = 60 episodes)

	Likely response (N = 7)	Possible response (N = 12)	Likely or possible response (N = 19)	No response (N = 41)	p-Value (univ.)[$]	p-Value (multiv.)
Latency to ketamine; median (range)	12 h (6 h–7 d)	5 d (18 h–30 d)	4.5 d (6 h–30 d)	10 d (12 h–122 d)	0.0053	NS
Number of previously failed drugs; median (range)	4 (3–7)	6 (3–11)	6 (3–11)	8 (3–16)	0.0012	<0.01
Etiology						
Unknown (N = 34)	1	7	8	26	<0.001	NS
Anoxic (N = 7)	4	0	4	3		
Acute nonanoxic (N = 13)	2	2	4	9		
Remote (N = 6)	0	3	3	3		
SE classification						
Generalized convulsive (N = 14)	2	4	6	8	NS	–
Generalized nonconvulsive (N = 3)	0	1	1	2		
Focal convulsive (N = 4)	0	2	2	2		
Focal nonconvulsive (N = 38)	5	5	10	28		
Infantile spasms (N = 1)	0	0	0	1		
Maximum infusion rate (mg/kg/h); median (range)[a]	7 (0.9–10)	1.8 (0.6–7)	2 (0.6–10)	3 (0.05–10)	NS	–
Loading dose administered[b]	6/6 (100%)	5/8 (63%)	11/14 (79%)	23/32 (72%)	NS	–
Duration of administration	1 (0–2)	3 (0–10)	2 (0–10)	5 (0–27)	<0.001	NS
Number of concurrent drugs	3 (1–5)	5 (1–11)	4 (1–11)	6 (1–10)	<0.001	NS
Number of concurrent anesthetic drugs[c]	1 (0–1)	1 (1–3)	1 (0–3)	2 (1–3)	<0.001	NS

h, hours; d, days; m, months; univ., univariate analysis; multiv., multivariate analysis.
[$]p-value refers to analysis using likely, possible, and no response as three separate categories.
[a]Information available in 54 of 60 cases.
[b]Information available in 46 of 60 cases.
[c]Anesthetic drugs included pentobarbital, thiopental, midazolam, and propofol.

Treatment of Refractory Status Epilepticus With Inhalational Anesthetic Agents Isoflurane and Desflurane

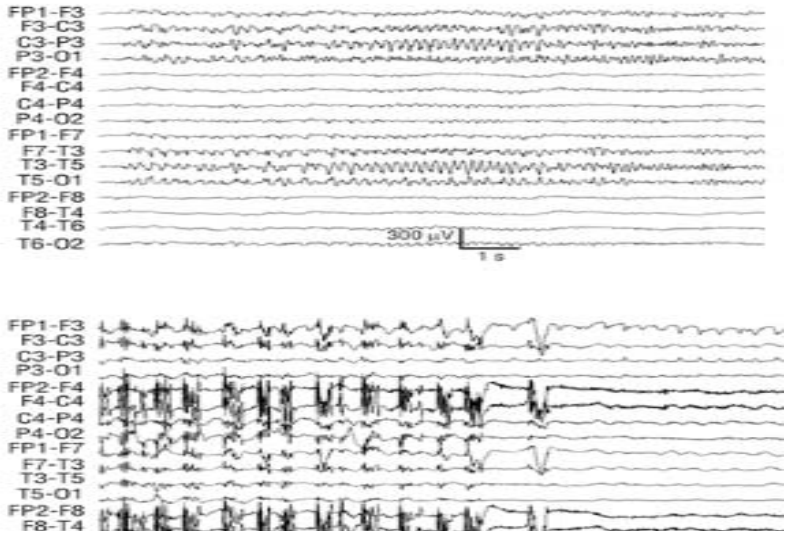
Seyed M. Mirsattari, MD; Michael D. Sharpe, MD; G. Bryan Young, MD, FRCPC

Arch Neurol. 2004;61(8):1254-1259. doi:10.1001/archneur.61.8.1254.

Table 1. Clinical Profile of Patients With Refractory Status Epilepticus (RSE)

Patient/Age, y/Sex	History of Seizures	Etiology of RSE	Seizure Type During RSE
1/19/F	Cryptogenic RSE with multiple seizure types (GTC, CPS, atypical absences, drop attacks); onset at age 1 y	Cryptogenic, preceded by increased frequency of seizures (especially drop attacks), precipitated by corpus callosotomy and right frontal resection	NCSE (generalized, maximum left hemisphere)
2/51/M	Cryptogenic epilepsy with GTC for 3 y	Poor compliance with AEDs (serum PHT level <0.5 g/mL)	GCS and NCSE
3/51/M	Symptomatic epilepsy with partial motor (rolandic) seizures due to a low-grade oligodendroglioma of left frontal lobe for 3 y	Oligodendroglioma (left frontal)	Partial motor (rolandic) and secondary generalized convulsive status epilepticus and NCSE
4/71/M	None	Silver toxicity	Multifocal and general myoclonus;
5/17/F			
6/56/F			
7/32/M			

Abbreviations
seizure; NCSE, n
SI conversion

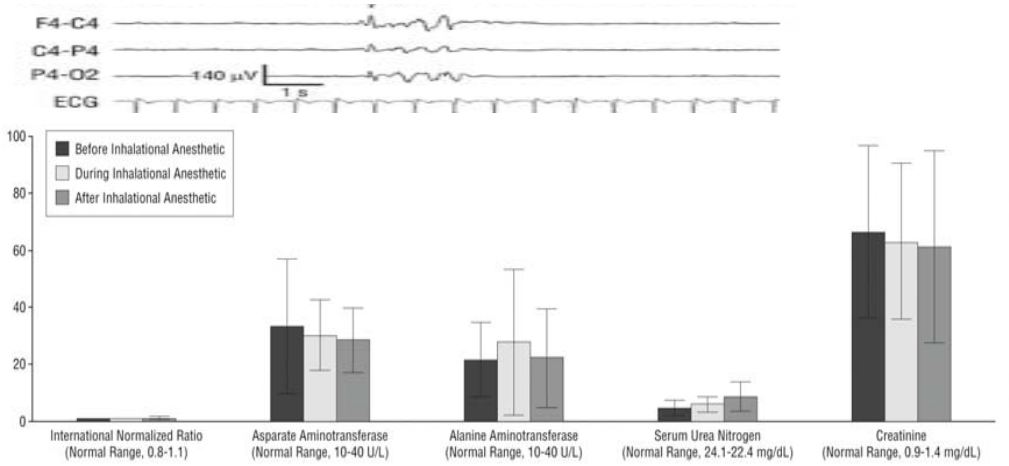


The IAs, isoflurane and desflurane, effectively stopped seizures in all 7 cases of RSE. Adequately sustained burst-suppression EEG patterns were obtained in all patients within minutes of initiation of IA therapy in a dose-dependent manner during administration of IA.

Table 3. Course of Therapy for Patients With Refractory Status Epilepticus (RSE)

Patient	Hospital Stay, d	ICU Stay, d	Ventilatory Support, d	MAC-Hours of Isoflurane (d)	RSE Prior to Isoflurane, d	Other AEDs Tried During RSE
1	53	30	27	33.8 (2)	3	LZP, diazepam, MDL, PHT, PB, TS, PRO, VPA, LMT
2	15	12	11	43.9 (3)	4	LZP, diazepam, MDL, PHT, PB, TS, PRO
3	49	27	18	151.4 (6)	1	LZP, diazepam, clonazepam, MDL, PRO, CBZ, VPA, GBP, TPM
4	84	58	56	276.9 (26)*	Isoflurane, 19 d; desflurane, 7 d	LZP, diazepam, clonazepam, MDL, PHT, PB, PTB, TS, PRO, CBZ, VPA
5	67	67	57	11.6 (19)	103	LZP, diazepam, MDL, PHT, PB, primidone, PTB, TS, PRO, CBZ, VPA, clobazem, LMT, VGB, TPM, paraldehyde
6	9	9	9	248.2 (8)	2	LZP, MDL, PHT, PB, CBZ, VPA, LMT, fentanyl citrate
7	18	17	17	444.3 (13)	2	LZP, diazepam, MDL, PHT PB, PRO, CBZ

Abbreviations: AED, antiepileptic drug; CBZ, carbamazepine; GBP, gabapentin; ICU, intensive care unit; LMT, lamotrigine; LZP, lorazepam; MAC, minimal alveolar concentration; MDL, midazolam; PB, phenobarbital; PTB, pentobarbital; PHT, phenytoin ; PRO, propofol; TPM, topiramate; TS, thiopental sodium; VGB, vigabatrin; VPA, valproic acid.
*237.9 MAC-hours (19 days) of desflurane and 39 MAC-hours (7 days) of isoflurane.



Vagus sinir stimülasyonu refrakter status epileptikusta yararlı olabilir

Refractory Status Epilepticus Treated With Vagal Nerve Stimulation: Case Report

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James Valeriano, MD‡
Andrea Synowiec, DO‡
Daniel Thielmann, MD‡
Carole Lane, MA‡
Jack Wilberger, MD§

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BACKGROUND AND IMPORTANCE: Status epilepticus (SE) refractory to medical treatment has a high mortality rate and few effective treatments.

CLINICAL PRESENTATION: We describe the implantation of a vagal nerve stimulator to help terminate a case of refractory SE. A 23-year-old man was in SE for 3 weeks without being able to be weaned from intravenous anesthetic agents. After implantation of a vagal nerve stimulator, SE soon terminated, and the patient could be weaned from sedative agents and made a full recovery.

CONCLUSION: Vagal nerve stimulator should be considered in cases of refractory SE.

KEY WORDS: Anesthetic agents, Status epilepticus, Vagal nerve stimulator

Neurosurgery 69:E1172–E1175, 2011 DOI: 10.1227/NEU.0b013e318223b979 www.neurosurgery-online.com

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Surgical Neurology 64 (2005) 170–173

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Epilepsy

Control of refractory status epilepticus precipitated by anticonvulsant withdrawal using left vagal nerve stimulation: a case report

Ravish V. Patwardhan, MD[a], John Dellabadia Jr., MD[b], Mahmoud Rashidi, MD[a], Laurie Grier, MD[c], Anil Nanda, MD, FACS[a,*]

Clinical commentary

Epileptic Disord 2010; 12 (2): 155-8

Malignant autosomal dominant frontal lobe epilepsy with repeated episodes of status epilepticus: successful treatment with vagal nerve stimulation

EUROPEAN JOURNAL OF PAEDIATRIC NEUROLOGY 13 (2009) 286–289

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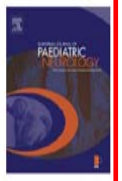
Official Journal of the European Paediatric Neurology Society



Case study

Vagus nerve stimulation for refractory status epilepticus

Veerle De Herdt[a,], Liesbeth Waterschoot[a], Kristl Vonck[a], Bart Dermaut[a], Helene Verhelst[b], Rudy Van Coster[b], Annick De Jaeger[c], Dirk Van Roost[d], Paul Boon[a]*

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Case Report

VNS terminating refractory nonconvulsive SE secondary to anti-NMDA encephalitis: A case report

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[b] Department of Medicine, Sheikh Khalifa Medical City (SKMC), Abu Dhabi, United Arab Emirates

Vagus sinir stimülasyonu nonkonvülzif status epileptikusta da yararlı olabilir

Table 2 Previous reports on SE treated with VNS.

Author	No. of cases	Type of SE	Sex/mean age (years)	Duration of SE before VNS	VNS parameters	Follow up	Outcome
Winston et al. (2001)	1	Convulsive SE	M;13	15 days	I: 0.25 mA F: 30 Hz PW: 500 μs on/off: 7 s/120 s	18 months	No SE; reduction of seizures frequency
Zimmerman et al. (2002)	3	Non convulsive SE	2 M, 1 F; 55 (20–82)	1 week-5 weeks	I: 3 mA F: 30 Hz PW: 500 μs on/off: 60 s/60 s	12 months	No SE
Malik and Hernandez (2004)	3	Not specified	Not specified	Not specified	Pt A: I: 1.0 mA on/off: 30 s/1.1 min Pt B: I: 1.75 mA on/off: 7 s/0.2 min Pt C: I: 2.5 mA on/off: 7 s/0.2 min	2 months	No SE; reduction of seizures frequency in 2 cases
Patwardhan et al. (2005)	1	Convulsive SE	M;30	12 days	I: 0.25 mA F: 20 Hz 30 on/off: 30 s/5 min PW 250 μs	42 days	No SE; seizure free
De Herdt et al. (2009)	1	Non convulsive SE	F;6	11 days	I: 1.25 mA F: 30 Hz on/off: 30 s/5 min PW 500 μs	15 months	No SE; seizure free
O'Neill et al. (2011)	1	Convulsive SE	M;23	> 21 days	I: 1 mA F:25 Hz PW: 250 μs on/off: 30 s/1.1 min	2 months	No SE; reduction of seizures frequency
Sierra-Marcos et al. (2012)	8	Convulsive (6); non-convulsive (2) SE	5 M,3 F;21 (7–39)	> 21 days	I:0.25 mA F: 30 Hz PW: 500 μs on/off: 30 s/5 min	Not specified	SE free: 5; reduction: 1; same frequency: 2

Abbreviations: SE: *status epilepticus*; I: intensity; F: frequency; PW: pulse width.

Epilepsy Research 2013;107:163-171

The Journal of ECT
17(3):210–215 © 2001 Lippincott Williams & Wilkins, Inc., Philadelphia

Case Report

ECT in the Treatment of Status Epilepticus

*†Sarah H. Lisanby, M.D., ‡Carl W. Bazil, M.D., Ph.D., ‡Stanley R. Resor, M.D., *†Mitchell S. Nobler, M.D., §Donald A. Finck, M.D., and *†‖Harold A. Sackeim, Ph.D.

*Department of Biological Psychiatry, New York State Psychiatric Institute, New York; and Departments of †Psychiatry, ‡Neurology, §Anesthesiology, and ‖Radiology, College of Physicians and Surgeons of Columbia University, New York, New York, U.S.A.

Introduction: Owing to its potent anticonvulsant actions, electroconvulsive therapy (ECT) has been proposed as an intervention for treatment-resistant seizure disorders. *Method:* We review the literature on the use of ECT in treatment-resistant epilepsy and status epilepticus (SE) and present a case of a patient who was in nonconvulsive SE for 26 days and then treated with ECT after all standard pharmacol
skull defects, a nov
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comitant anticonvul
cal dosage was ne
Status was terminat
However, the long
poor. *Discussion:* T
SE is discussed.

neurocritical care society Neurocrit Care (2010) 12:204–210
DOI 10.1007/s12028-009-9288-7

ORIGINAL ARTICLE

Electroconvulsive Therapy for Refractory Status Epilepticus: A Case Series

Hooman Kamel · Susannah Brock Cornes · Manu Hegde · Stephen E. Hall · S. Andrew Josephson

Table 4 Summary of published case reports describing the use of electroconvulsive therapy (ECT) for status epilepticus or frequent seizures

	Clinical features	Therapies prior to ECT	Timing of ECT	Dose of ECT	Outcome
Viparelli and Viparelli [9]	A 19-year-old woman with epilepsy presented with over 40 seizures per day, without overt status epilepticus	Phenytoin and diazepam	Not reported	Two sessions over 3 days	Seizures stopped and patient returned to baseline
Carrasco Gonzalez et al. [10]	A 25-year-old man with a history of traumatic brain injury presented with status epilepticus	Phenytoin, carbamazepine, diazepam, phenobarbital, pentobarbital	40 days after onset of seizures	Six sessions over 2 weeks	Seizures stopped and patient returned to baseline
				Four sessions over 9 days	Mild improvement in seizure frequency and severity
				Three daily sessions	Termination of status epilepticus, with significant decrease in seizure frequency over following month
	presented with frequent seizures	valproate, felbamate, and gabapentin		Six sessions over 2 weeks	Temporary decrease in seizure frequency
Lisanby et al. [12]	A 36-year-old man with epilepsy presented with status epilepticus	Phenytoin, nitrazepam, phenobarbital, vigabatrin, pentobarbital, propofol, midazolam	26 days after onset of seizures	Five daily sessions	Seizures stopped but patient remained comatose
Cline and Roos [13]	A 39-year-old previously healthy man presented with herpes simplex encephalitis and status epilepticus	Fosphenytoin, valproate, pentobarbital, levetiracetam, oxcarbazepine, topiramate, lorazepam, felbamate	103 days after onset of seizures	Three daily sessions	Termination of status epilepticus, continued episodic seizures, and significant residual neurological deficits

Elektrokonvülzif tedavinin hem konvülzif hem de nonkonvülzif status epileptikusta yararlı olabileceğine ilişkin olgu bildirimleri var

Table 3
Oxford and GRADE level of evidence.

Reference	Study type	Oxford[28] Level of Evidence	GRADE[29–34] Level of Evidence
Carrasco et al.[9]	Retrospective Case report	4	D
Cline et al.[10]	Retrospective Case Report	4	D
Fernandez-Torre et al.[11]	Retrospective case Report	4	D
Griesemer et al.[12]	Retrospective Case Series	4	D
Kamel et al.[13]	Retrospective Case Series	4	D
Koong et al.[14]	Retrospective Case Report	4	D
Lisanby et al.[15]	Retrospective Case Report	4	D
Moddel et al.[16]	Retrospective Case Series	4	D
Morales et al.[17]	Retrospective Case Report	4	D
Regenold et al.[18]	Retrospective Case Report	4	D
Savard et al.[19]	Retrospective Case Report	4	D
Shin et al.[20]	Retrospective Case Report	4	D
Viparelli et al.[21]	Retrospective Case Report	4	D
Wusthoff et al.[22]	Retrospective Case Report	4	D
Shin et al.[23]	Retrospective Case Report	4	D

* Shin et al.[23] is a meeting abstract which contains the same patient data as Shin et al.[20]. Patient data from Shin et al[23] was not included in the final data analysis in order to avoid duplication of data.

Oxford level 4, GRADE D evidence exists to suggest an improvement in seizure control with ECT application for RSE. Routine use of ECT cannot be recommended at this time. Further prospective study of this therapy is required in order to determine its efficacy in this setting.

Seizure 2016;35:23-32

2 haftalık süre boyunca 3 farklı AEİ tedasine yanıtsızlık halinde cerrahi yöntemler düşünülebilir

- Kortikal rezeksiyondan en çok fayda gören hastalar semiyoloji, MRI, PET, SPECT ve EEG ile tek epileptojenik zon saptanan ve altta yatan nedenin fokal kortikal displazi olduğu hastalar
- Multifokal veya lokalize edilemeyen dirençli SE halinde korpus kallozotomi

Epilepsia, 54(Suppl. 6):68–71, 2013
doi: 10.1111/epi.12282

STATUS EPILEPTICUS 2013

Surgical treatment of status epilepticus: A palliative approach

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SUMMARY

Although status epilepticus (SE) does not resemble a domain for neurosurgical indications in single occasions, a microneurosurgical procedure in patients with catastrophic epilepsy and status epilepticus should be considered as an ultimate ratio-choice in these patients. From a personal series of >600 epilepsy surgery procedures in a period from August 1, 1993 until March 13, 2013, 22 patients were identified with catastrophic epilepsy and all of them with at least one episode of status epilepticus. Five of the patients had surgery under ongoing status epilepticus. Twelve patients became seizure-free, two patients had >90% seizure reduction, seven patients >50% seizure reduction, and one patient was unchanged. No surgery-related complications in terms of permanent morbidity were ascertained in the presented series. In the subgroup of the five patients operated in the acute phase of SE one patient became seizure-free (Engel class. I), one showed Engel class II, two Engel class III, and one Engel class IV with no worthwhile improvement. Patients with catastrophic epilepsy including status epilepticus can benefit from resective epilepsy surgery, even with incomplete resection of the epileptogenic lesion.

KEY WORDS: Status epilepticus, Microneurosurgery, Epilepsy surgery – catastrophic epilepsy.

Table 1. Treatment in patients with status epilepticus (SE) = 22[a]

8	Palliative primary incomplete resections
13	Unilateral resections of bilateral lesions
1	Bilateral resection

[a]Five of them were operated on with ongoing status epilepticus.

Table 2. Results

12	Seizure-free
2	>90% seizure reduction
7	>50% seizure reduction
1	Unchanged

No surgery-related complications in terms of permanent morbidity were ascertained in the presented series.

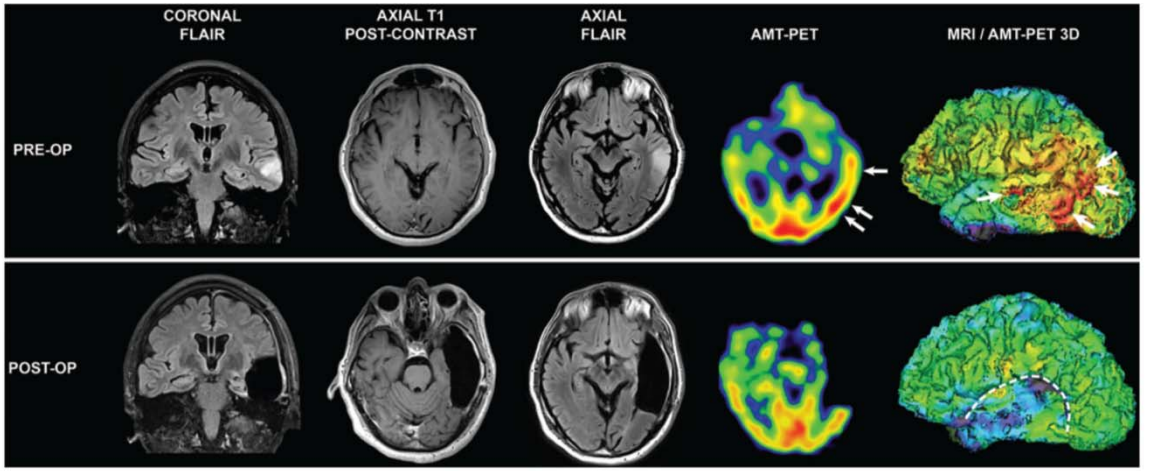
Table 4. Surgical treatment of status epilepticus—published cases

Procedure(s)	Total number
Resections of epileptogenic focus	44 ± 1
Tumor resection	1
Multilobar resection	1
Callosotomy	1
Multiple subpial transsection	2
Vagus nerve stimulation	7
Deep brain stimulation	0
Alternative methods, e.g., trigeminal stimulation	1
	∑57 ± 1

Table 3. Patients operated in acute phase of SE

Patients number	Outcome
1	Engel class I
1	Engel class II
2	Engel class III
1	Engel class IV

Refrakter nonkonvülzif status epileptikus tedavisinde cerrahi yöntemler uygulanabilir



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Successful surgical treatment of an inflammatory lesion associated with new-onset refractory status epilepticus

Csaba Juhász, M.D., Ph.D.[1,2,6,7], **Amy Buth, M.S.**[3,7], **Diane C. Chugani, Ph.D.**[1,4,6], **William J. Kupsky, M.D.**[5,7], **Harry T. Chugani, M.D.**[1,2,4,6], **Aashit K. Shah, M.D.**[2], and **Sandeep Mittal, M.D., F.R.C.S.C.**[3,7]

A 56-year-old right-handed man with a history of high blood pressure presented with sudden-onset progressive headache, followed by new-onset complex partial seizures 3 days later. There was no history of fever. On admission, general and neurological examinations were normal, except for fluctuating fluent dysphasia. Cranial MRI showed a nonenhancing lesion in the left temporal lobe, hyperintense on T2-weighted and FLAIR sequences, suspicious for a low-grade glioma (Fig. 1). One week later, he had a generalized seizure and, despite aggressive treatment, developed nonconvulsive partial status epilepticus nonresponsive to maximal doses of 4 antiepileptic drugs and intermittent intravenous benzodiazepines to treat breakthrough seizures. Initial CSF analysis showed 0 WBC/mm^3, 1 RBC/mm^3, normal protein and glucose levels, and negative polymerase chain reaction for herpes simplex virus 1 and 2. Upon arrival to our institution, continuous video-EEG monitoring showed periodic epileptiform discharges from the left temporal region with frequent electroclinical seizures resulting in episodic fluent aphasia. AMT-PET imaging was performed after obtaining informed consent and showed a relatively large cortical region of increased uptake within and adjacent (mostly posterior) to the MRI-defined lesion (Fig. 1).

CLINICAL REPORT

Focal Cortical Resection for Complex Partial Status Epilepticus Due to a Paraneoplastic Encephalitis

Fadi Nahab, MD, Adam Heller, MD, and Suzette M. LaRoche, MD

Abstract: We report a 57-year-old female who presented with epilepsia partialis continua and rapidly progressed to refractory complex partial status epilepticus (CPSE) with brain magnetic resonance imaging revealing a focal cortical lesion on T2 sequences corresponding to the seizure focus on ictal electroencephalographic recordings. The patient underwent focal cortical resection of the seizure focus. Though clinical and electrographic seizure activity ceased, the patient remained unresponsive with repeat neuroimaging showing diffuse limbic and brainstem involvement. Serological tests revealed anti-Hu antibodies suggesting a paraneoplastic encephalitis. Chest computed tomography showed a 5-mm pulmonary nodule and resection of the pulmonary nodule confirmed the diagnosis of small cell lung cancer. Plasmapheresis was performed without clinical improvement. Focal resection can be effective in terminating refractory CPSE but evaluation for a paraneoplastic syndrome must be considered early in the diagnosis of epilepsia partialis continua and CPSE as these patients have a poor prognosis.

Key Words: epilepsia partialis continua, paraneoplastic encephalitis, anti-Hu antibodies, complex partial status epilepticus, focal resection

(*The Neurologist* 2008;14: 56–59)

CASE PRESENTATION

A 57-year-old female was evaluated for a 2 month history of refractory simple partial seizures. Her first seizure consisted of right upper extremity clonic movements that progressed to a generalized tonic-clonic seizure. These developed into frequent episodes of clonic right face, arm, and occasionally leg movements without alteration of awareness. She had no significant medical history other than an 80 pack-year smoking history. Despite trials of phenytoin, valproic acid, and levetiracetam titrated to toxic doses, she continued to have these persistent movements. Our clinical diagnosis was EPC of unclear etiology. Previous evaluation had included 2 normal brain magnetic resonance imaging (MRIs) and an ambulatory electroencephalograph (EEG) that demonstrated frequent epileptiform discharges over the left fronto-central region correlating with clinical seizure activity (Fig. 1). Inpatient admission for further evaluation was declined by the patient and topiramate was added to her AED regimen of phenytoin, valproic acid, and levetiracetam.

Four days later the patient was brought to the hospital by family after they noticed some speech difficulty. Examination was notable for expressive aphasia with persistent clonic movements of the right face and arm. The patient was

Absans statusu

- Status epileptikus olgularında <10%; daha çok çocuklarda

Tipik absans statusu

- EEG: >2.5 Hz diken veya multipl diken-yavaş jeneralize dalgalar
- Genellikle idyopatik jeneralize epilepsilerde uygun olmayan AEİ kullanımı ile ilişkili

Atipik absans statusu

- EEG: <2.5 Hz jeneralize epileptiform deşarjlar
- Genellikle çocukluk çağının semptomatik ve kriptojenik jeneralize epilepsilerinde (Lennox-Gastaut syndrome)

Akut semptomatik absans statusu

- Önceden epileptik olmayan hastalarda bir takım faktörlerle ortaya çıkar

Acute symptomatic absence status	Hypocalcemia[133] Infections (HIV,[134] neurosyphilis[135] Medications (tiagabine, benzodiazepines abrupt withdrawal, antidepressants, neuroleptics, lithium, cephalosporins, cyclosporine, ifosfamide, cyclophosphamide, chemotherapy of urothelial cancer)[136–143] Electroconvulsive therapy[144]

	Typical absence SE	Atypical absence SE
Context—type of epilepsy syndrome	Idiopathic generalized epilepsy	Cryptogenic and secondarily generalized epilepsy (e.g., Lennox–Gastaut syndrome)
Associated clinical signs	Photosensitivity (in some cases), no other neurologic abnormalities	Learning disability, neurologic handicaps (in some cases)
Clinical features	Episodes shorter than in atypical absence SE, onset and offset clear cut, often terminated by tonic–clonic seizure, myoclonus common	Prodromal phase, frequent episodes, onset and offset ill-defined, no myoclonus, intercurrent tonic or minor motor seizures
EEG	3 Hz spike-wave discharges, normal background interictal EEG	2–3 Hz spike-wave discharges, ictally and interictally, background activity slow
Response to IV benzodiazepine treatment	Rapid and complete response	Often no response or partial response only, IV benzodiazepines may precipitate tonic seizures

J Clin Neurophysiol. 1995;12:316–325. Epilepsia. 2005;46(suppl 9):73–79. Epilepsia. 2001;42:714–718.

TABLE 3. *Frequency of typical absence status epilepticus (SE) in different IGE subtypes*

Classification of idiopathic generalized epilepsy (IGE)	Proportion of patients with a history of typical absence SE
Perioral myoclonus with absences (n = 7)	57.1%
Phantom absence and generalized tonic-closure seizures (n = 13)	46.2%
IGE with specific modes of precipitation (n = 4)	25%
Juvenile absence epilepsy (n = 10)	20%
Eyelid myoclonia with absences (n = 11)	18.2%
Unclassified IGE (n = 11)	12.8%
Juvenile myoclonic epilepsy (n = 30)	6.7%

Series of 86 adult patients with absence seizures and IGE, of whom 21 had documented episodes of typical absence SE, published by Agathonikou et al. 1998 (7).

doi:10.1093/brain/awl047 *Brain* (2006), **129**, 1281–1292

Absence and myoclonic status epilepticus precipitated by antiepileptic drugs in idiopathic generaliz

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Aggravation of idiopathic generalized ep is increasingly recognized as a serious ar propriate medication has rarely been reported. We retrospectively studied all adult patients with IGE taking at least one potentially aggravating AED, who developed video-EEG documented SE over 8 years, and whose long-term outcome was favourable after adjustment of medication. We identified 14 patients (seven male patients) aged 15–46 years with a mean duration of epilepsy of 16.4 years. Video-EEG demonstrated typical absence SE (ASE) in five, atypical ASE in five, atypical myoclonic SE (MSE) in three and typical MSE in one. Epilepsy had been misclassified as cryptogenic partial in eight cases and cryptogenic generalized in four. The correct diagnosis proved to be juvenile absence epilepsy (JAE) in six patients, juvenile myoclonic epilepsy (JME) in four, epilepsy with grand mal on awakening (EGMA) in two and childhood absence epilepsy (CAE) in two. All patients had been treated with carbamazepine (CBZ) and had experienced seizure aggravation or new seizure types before referral. Seven patients had polytherapy with phenytoin (PHT), vigabatrin (VGB) or gabapentin (GBP). Potential precipitating factors included dose increase of CBZ or of CBZ and PHT; initiation of CBZ, VGB or GBP; and decrease of phenobarbital. Withdrawal of the aggravating agents and adjustment of medication resulted in full seizure control. This series shows that severe pharmacodynamic aggravation of seizures in IGE may result in ASE or MSE, often with atypical features.

pilepsia, 41(7):887–894, 2000
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Clinical Research

Refractory Idiopathic Absence Status Epilepticus: A Probable Paradoxical Effect of Phenytoin and Carbamazepine

Jill N. Peltzer

*Kansas City, Kansas, U.S.A.; and *Department of Cleveland, Ohio, U.S.A.*

d proved intractable to treatment with valproic acid or azepines, compared with a cohort of subjects also with ic generalized epilepsies, but naive to, or receiving sub- tic or therapeutic doses of other agents.
usions: Our observations strongly suggest that thera- oncentrations of phenytoin and carbamazepine exacer- opathic generalized epilepsies. Subjects in whom ab- one of the seizure types seem at a particularly high risk onding paradoxically. These findings underscore the accurate classification of seizures and particularly the syndromic approach to diagnosis and point to the potential for iatrogenic complications with indiscriminate use of antiseizure drugs. **Key Words:** Idiopathic generalized epilepsies—Absence status epilepticus—Refractoriness—Paradoxical effects—Phenytoin- –Carbamazepine.

mazepine or phenytoin before and after discontinuation of these compounds, and interindividually to subjects without treatment or receiving other drugs.
Results: Bouts of absence or tonic-clonic status epilepticus and seizures in subjects treated with phenytoin or carbamaze- pine at therapeutic concentrations were considerably more fre-

Seizure 1999; **8**: 314–317
Article No. seiz.1999.0303, available online at http://www.idealibrary.com on IDEAL

CASE REPORT

Tiagabine-induced absence status in idiopathic generalized epilepsy

S. KNAKE, H. M. HAMER, U. SCHOMBURG, W. H. OERTEL & F. ROSENOW

İDYOPATİK JENERALİZE EPİLEPSİLERDE UYGUNSUZ AEİ KULLANIMI ABSANS STATUS EPİLEPTİKUSUNA YOL AÇABİLİR

'*De novo*' absans statusu, akut semptomatik absans statusu, ileri yaş başlangıçlı absans statusu

- İleri yaşta gelişir
- Ani başlangıçlı konfüzyon
- Saatler-günler sürer
- Akut demans veya SVH ile karışabilir
- EEG ile tanınabilir
- Çoğu olguda neden psikotrop kullanımı veya yoksunluğu (özellikle benzodiazepin)
- Metabolik nedenlerle gelişebilir
- IV BDZ'e hızlı yanıtlı
- Rekürrens beklenmez
- Uzun süreli AEİ kullanımı gerekmez

Seizure 1999; 8: 364–366
Article No. seiz.1999.0309, available online at http://www.idealibrary.com on IDEAL

CASE REPORT

Ictal catatonia as a manifestation of *de novo* absence status epilepticus following benzodiazepine withdrawal

KOUSUKE KANEMOTO*, TOSHIO MIYAMOTO & RYUJI ABE

Seizure 2001; **10**: 433–437
doi:10.1053/seiz.2000.0510, available online at http://www.idealibrary.com on IDEAL®

CASE REPORT

De novo absence status of late onset following withdrawal of lorazepam: a case report

J. L. FERNÁNDEZ-TORRE

Neurology. 1992 Jan;42(1):104-10.

'De novo' absence status of late onset: report of 11 cases.

Thomas P[1], Beaumanoir A, Genton P, Dolisi C, Chatel M.

Author information

Abstract

Absence status (AS) is a heterogenous epileptic syndrome that can occur at any age, usually in a context of prior epilepsy. Eleven cases of AS occurring in middle-aged patients who had no history of epilepsy were retrospectively collected over a 10-year period (10 women and one man; mean age, 58.6 years). Eight patients were receiving high doses of psychotropic drugs. Clinical and EEG presentation was similar to AS occurring in patients with prior epilepsy. Evaluation of precipitating factors revealed that AS coincided with benzodiazepine withdrawal in eight cases. Cofactors included excessive use of other psychotropic drugs, nonpsychotropic treatment, hypocalcemia, hyponatremia, and chronic alcoholism. CT demonstrated mild cerebral atrophy in six cases. There was no recurrence, even without chronic antiepileptic treatment. These data indicate that (1) most cases of "de novo" AS of middle age or late onset result from the addition of various epileptogenic factors; (2) AS can be considered a new and uncommon complication of benzodiazepine withdrawal, and (3) long-term administration of anticonvulsant medication may not be required.

Absans statusu - Tedavi

- Benzodiazepinlere duyarlı
- IV diazepam ile %93 nöbet kontrolü
- Benzodiazepinlere yanıtsız hastalar 20 to 40 mg/kg IV valproik asit eklenmesinden yarar görürler, %80 başarı
- Levetirasetamın etkinliğine ilişkin veri yok
- Atipik absans statusunun tedavisi tipik absans statusuna benzer
- Absans statusunun nöronal hasar oluşturabileceğine ilişkin veri yok bu nedenle agresif tedavi şart değil

	Etiology	Treatment	Prognosis
Typical absence status	Use of inapropriate AED (eg, carbamazepine) in idiopathic generalized epilepsy[129]	Diazepam IV effective in 93% of cases[130] Add-on VPA (20-40 mg/kg) IV[114]	There is no evidence that absence status induces neuronal damage[131]
Atypical absence status	Symptomatic and cryptogenic generalized epilepsies mainly of childhood (eg, Lennox-Gastaut syndrome)	Treatment of atypical AS is similar to that of typical AS[14]	Usually poorly responsive to benzodiaze-pines IV, which should, in any case, be given cautiously, as they can induce tonic status epilepticus[132]
Acute symptom-atic absence status	Hypocalcemia[133] Infections (HIV,[134] neurosyphilis[135] Medications (tiagabine, benzodiazepines abrupt withdrawal, antidepressants, neuroleptics, lithium, cephalosporins, cyclosporine, ifosfamide, cyclophosphamide, chemotherapy of urothelial cancer)[136–143] Electroconvulsive therapy[144]	Removal of the precipitat-ing factor may suffice[145]	The overall prognosis is excellent, with little risk of recurrence[145]

AED indicates antiepileptic drugs; AS, absence status; IV, intravenous; VPA, valproic acid.

Neurology. 2000;54:2188–2189, Epilepsia. 1973;14:277–310. Adv Neurol. 1983; 34:61–67.

Pratikte nonkonvülzif status epileptikus

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Use of EEG Monitoring and Management of Non-Convulsive Seizures in Critically Ill Patients: A Survey of Neurologists

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Abstract

Background—Continuous EEG monitoring (cEEG) of critically ill patients is frequently utilized to detect non-convulsive seizures (NCS) and status epilepticus (NCSE). The indications for cEEG, as well as when and how to treat NCS, remain unclear. We aimed to describe the current practice of cEEG in critically ill patients to define areas of uncertainty that could aid in designing future research.

Methods—We conducted an international survey of neurologists focused on cEEG utilization and NCS management.

Results—Three-hundred and thirty physicians completed the survey. 83% use cEEG at least once per month and 86% manage NCS at least five times per year. The use of cEEG in patients with altered mental status was common (69%), with higher use if the patient had a prior convulsion (89%) or abnormal eye movements (85%). Most respondents would continue cEEG for 24 h. If NCS or NCSE is identified, the most common anticonvulsants administered were phenytoin/fosphenytoin, lorazepam, or levetiracetam, with slightly more use of levetiracetam for NCS than NCSE.

Conclusions—Continuous EEG monitoring (cEEG) is commonly employed in critically ill patients to detect NCS and NCSE. However, there is substantial variability in current practice related to cEEG indications and duration and to management of NCS and NCSE. The fact that such variability exists in the management of this common clinical problem suggests that further prospective study is needed. Multiple points of uncertainty are identified that require investigation.

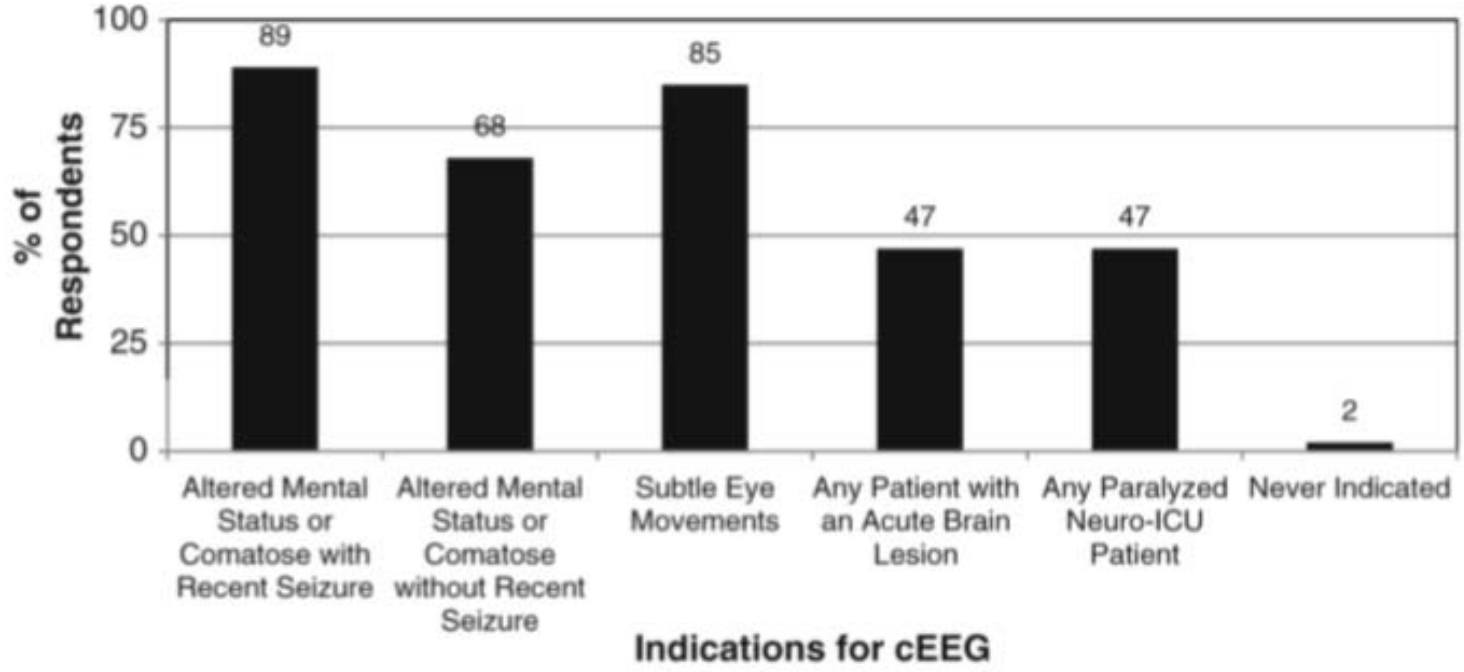

Fig. 1.
Which indications lead you to order cEEG to detect non-convulsive seizures or non-convulsive status epilepticus? (296 respondents)

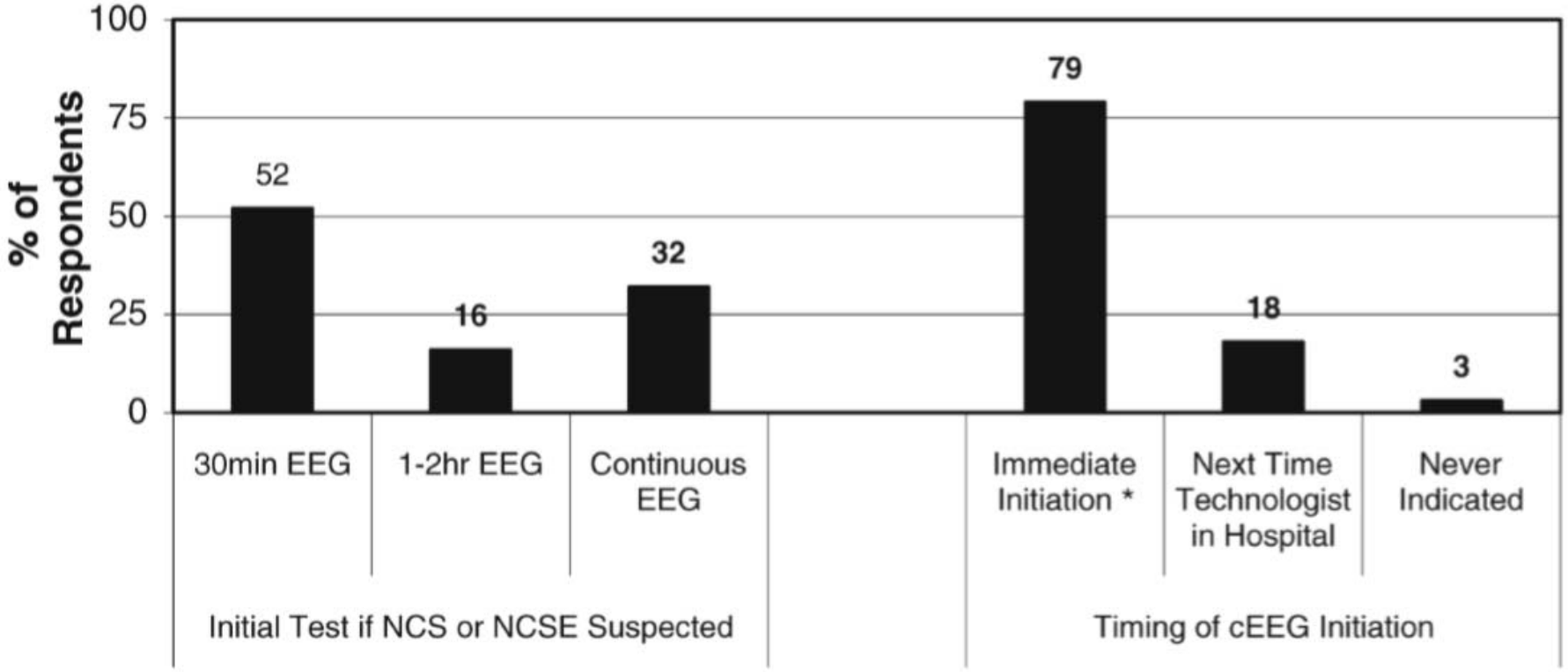

Fig. 2.
If NCS (non-convulsive seizures) or NCSE (non-convulsive status epilepticus) is suspected then what type of EEG do you obtain and how urgently do you obtain the EEG? (294 respondents). * Including initiation by a 24/7 in-hospital EEG technologist or calling in an on-call technologist

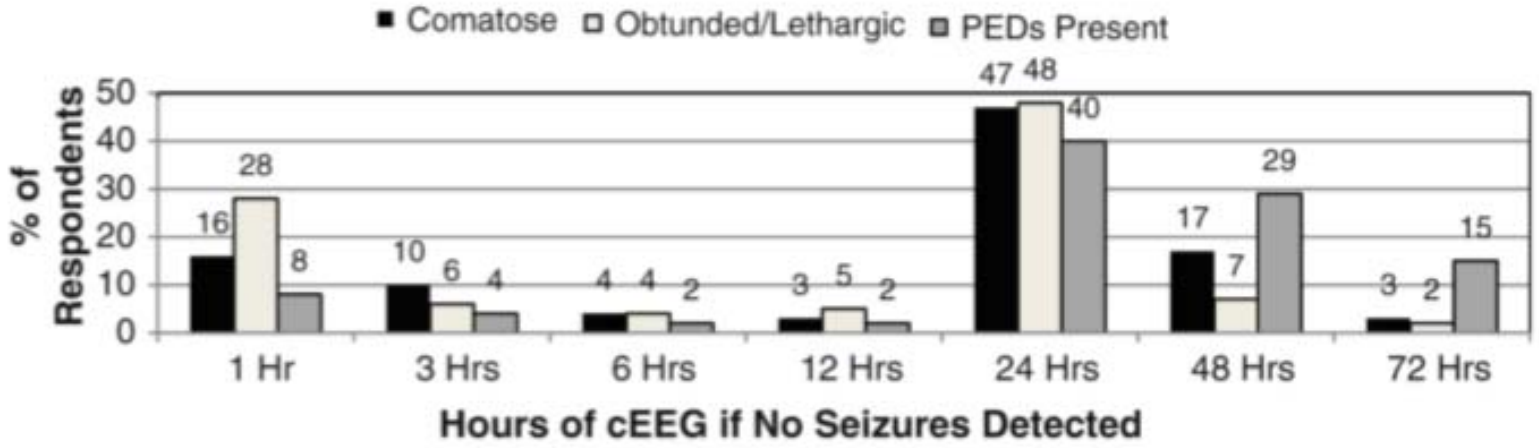

Fig. 3.
How long do you continue cEEG if no seizures are detected in a patient who is comatose (292 respondents), obtunded/lethargic (291 respondents), or if PEDs (periodic epileptiform discharges) were detected (289 respondents)?

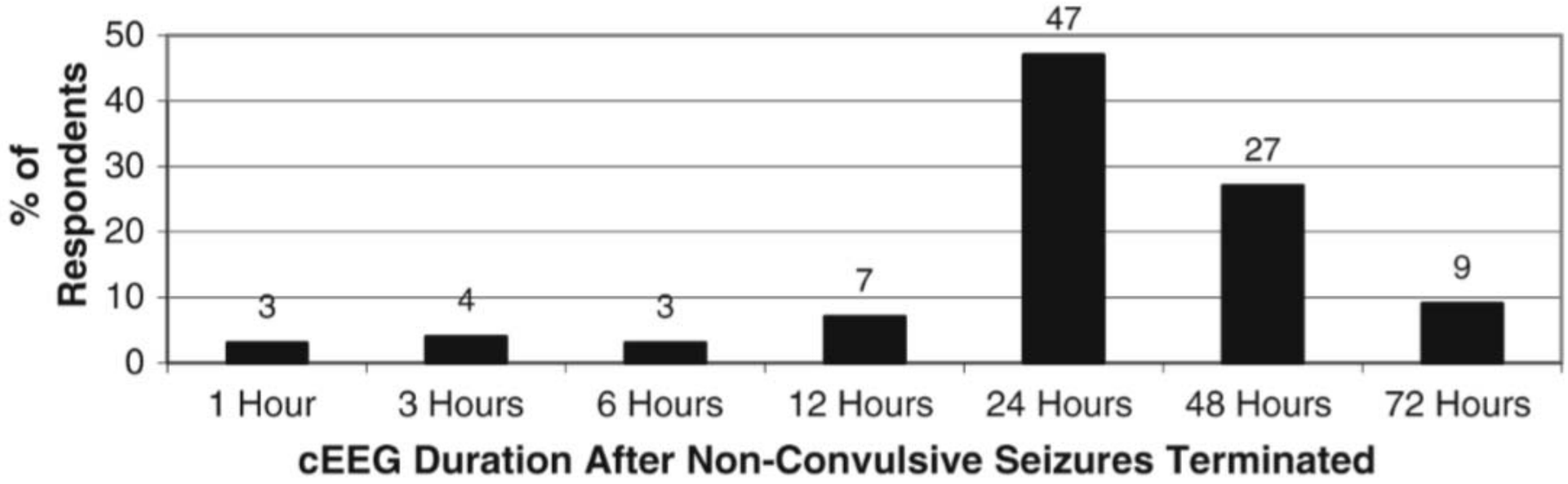

Fig. 4.
How long do you continue cEEG after non-convulsive seizures terminated? (288 respondents)

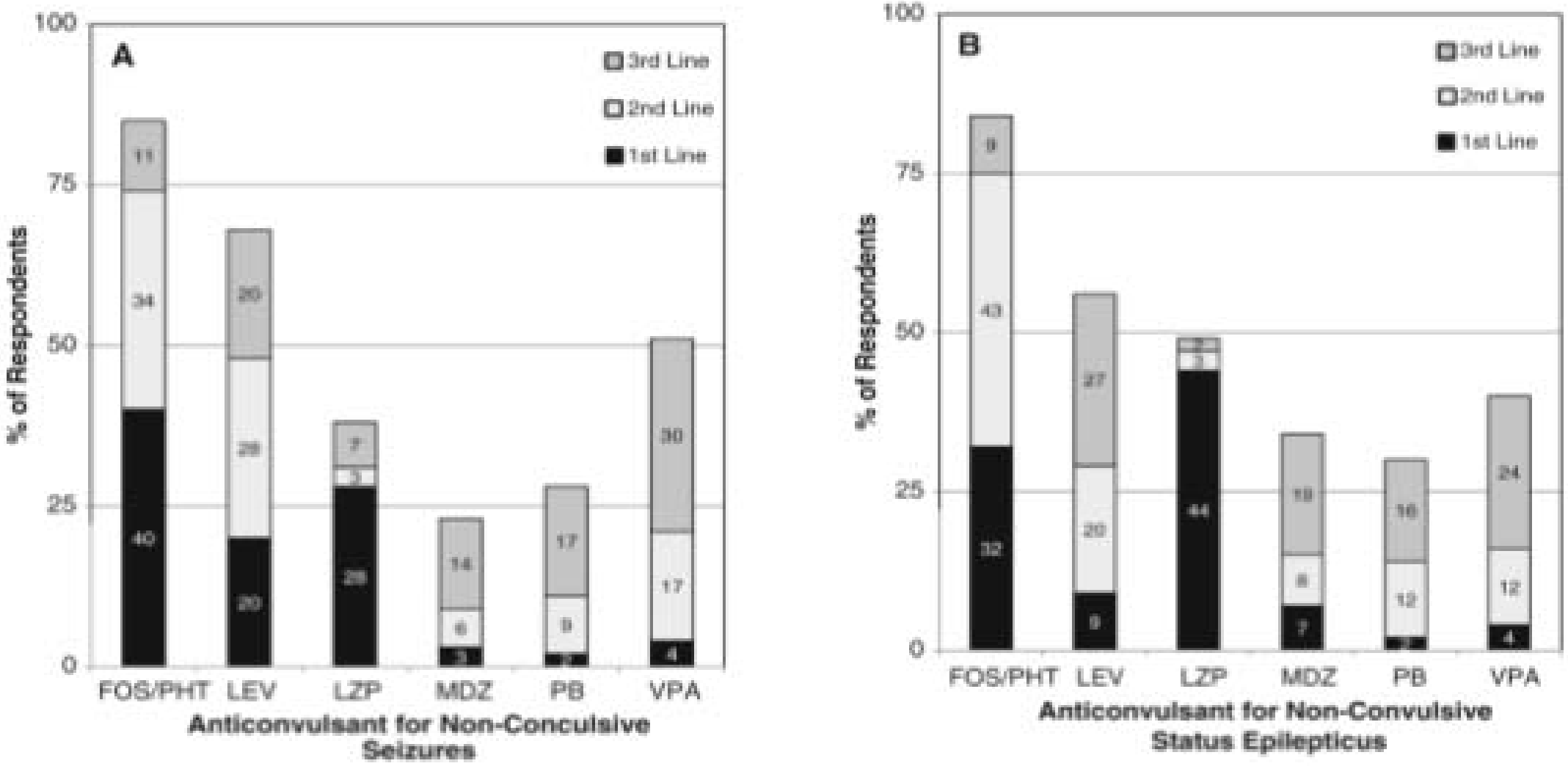

Fig. 5.
What anticonvulsant do you administer as a first, second, and third line medication of (**a**) non-convulsive seizures (271 respondents) or (**b**) non-convulsive status epilepticus? (268 respondents). *FOS* fosphenytoin, *LEV* levetiracetam, *LZP* lorazepam, *MDZ* midazolam, *PB* phenobarbital, *PHT* phenytoin, *VPA* valproic acid

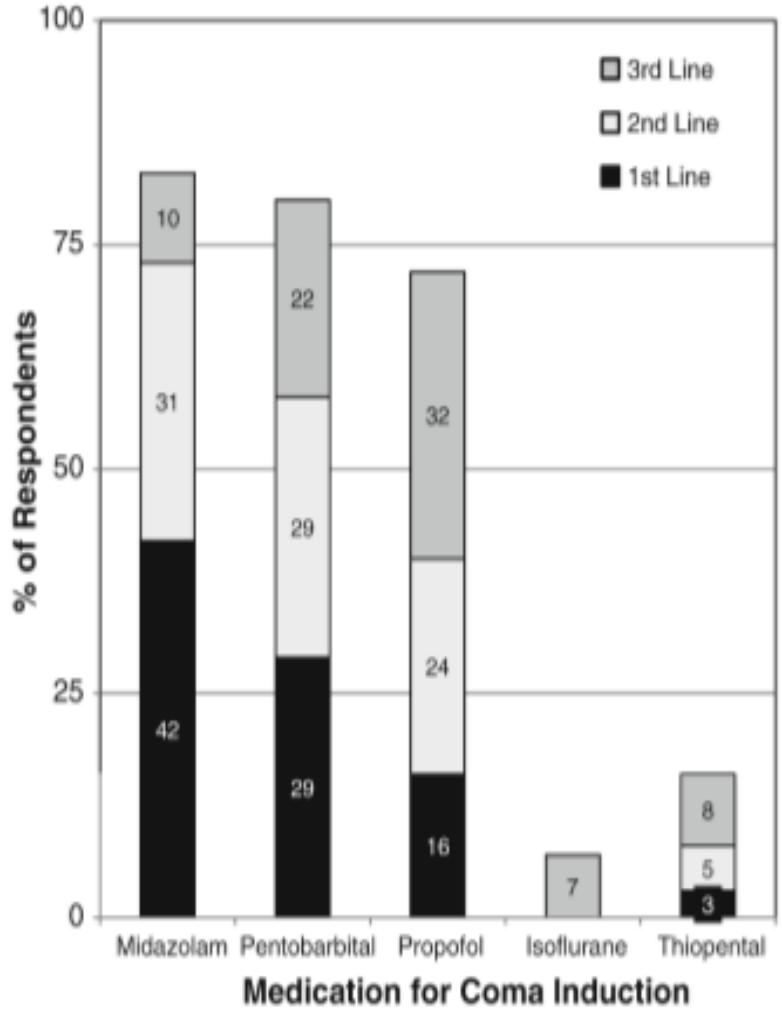

Fig. 6.
If non-convulsive seizures or status epilepticus persist despite initial anticonvulsants and you want to initiate coma, which medications do you use as first, second, and third line choices? (267 respondents)

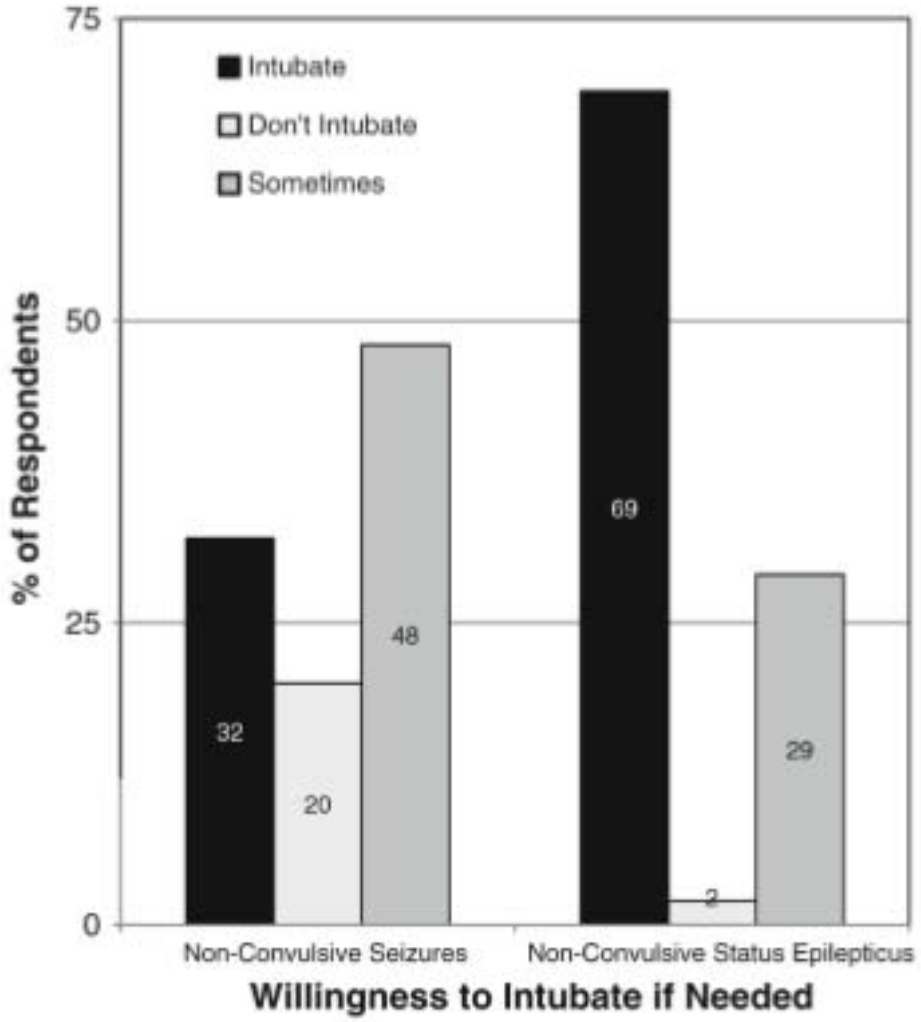

Fig. 7.
If non-convulsive seizures or non-convulsive status epilepticus is present, are you willing to intubate the patient to escalate treatment? (273 respondents)

Tedavi hastalığın kendisinden daha mı zararlı?

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Intravenous anesthesia in treatment of nonconvulsive status epilepticus: Characteristics and outcomes

Utku Uysal[a,*], Mark Quigg[b], Brennen Bittel[c], Nancy Hammond[a], Theresa I. Shireman[d]

ABSTRACT

Objective: To determine factors associated with continuous anesthetic drug (IVAD) use in nonconvulsive status epilepticus (NCSE).

Methods: Retrospective cohort study of patients who met clinical and EEG criteria of NCSE from 2009 to 2014 at a tertiary academic medical center. Patients were categorized according to IVAD use. Outcome variables were response to treatment and in-hospital death. We used descriptive analyses for baseline characteristics and outcome variable differences among patients who did and did not receive IVAD.

Results: Forty-three patients had a total of 45 NCSE episodes. IVAD was used in 69% of the episodes. Patients treated with IVAD were younger (53.1 ± 14.1 vs 64.1 ± 13.3, $p = 0.019$). The episodes treated with IVAD occurred more frequently in patients with an acute neurologic pathology (58% vs 21%, $p = 0.024$) and those presenting in a coma (39% vs 7%, $p = 0.030$). NCSE resolved in 74% of the patients who received IVAD. Duration of NCSE did not differ significantly by treatment group. There were total 13 in-hospital deaths: ten in IVAD users vs three in the no-IVAD group ($p > 0.05$). Only one in-hospital death appeared to be a direct consequence of IVAD use. Mortality was more common among episodes that were not treated according to the published status epilepticus treatment guidelines compared to the episodes where guidelines were followed.

Conclusion: Our findings showed that factors such as younger age, acute neurologic pathology and coma at presentation were associated with IVAD use in patients with NCSE. These factors should be controlled in the future outcome and effectiveness studies to determine the effect of IVAD use on outcome of NCSE.

Demographics and clinical characteristics.

	Whole group	NonIVAD	IVAD	*p*-Value
Number of patients	43	14	29	
Age	56.7 ± 14.7	64.1 ± 13.3	53.1 ± 14.1	0.019*
Sex-Male	20 (46.5%)	6 (42.9%)	14 (48.3%)	NS
Number of NCSE episodes	45	14	31	
Symptom at onset				
AMS only	12 (26.7%)	5 (35.7%)	7 (22.6%)	NS
AMS with subtle motor findings	20 (44.4%)	5 (35.7%)	15 (48.4%)	NS
AMS following GTCS	9 (20.0%)	3 (21.4%)	6 (19.3%)	NS
AMS with subtle motor finding following GTCS	4 (8.9%)	1 (7.1%)	3 (9.7%)	NS
Epilepsy	17 (37.8%)	6 (42.9%)	11 (35.5%)	NS
Acute Medical Pathology	26 (57.8%)	8 (57.1%)	18 (58.1%)	NS
Acute Neurologic Pathology	21 (46.7%)	3 (21.4%)	18 (58.1%)	0.024*
STESS ≥3 (Status severity score)	23 (51.1%)	6 (42.9%)	17 (54.8%)	NS
Coma	8 (17.8%)	0 (0%)	8 (25.8%)	0.036*
Already intubated before NCSE	13 (28.9%)	1 (7.1%)	12 (38.7%)	0.030*

IVAD = iv anesthetic drug, AMS = Altered mental status, GTCS = generalized tonic–clonic seizure, STESS = Status Epilepticus Severity Score, NS = Not significant.

* Statistically significant at level $p < 0.05$.

Etiology and EEG findings of the patients who died in the hospital.

Patient	Reason for death	Etiology of NCSE	EEG finding at the time of death
IVAD			
1	Multi organ dysfunction	Meningoencephalitis	NCSE-BS-NCSE
2	Meningoencephalitis	Meningoencephalitis	Diffuse slowing
3	NCSE	Meningoencephalitis	NCSE-BS-NCSE
4	Sepsis	Stroke	BS
5	Sepsis	Sepsis	BS
6	Stroke	Ruptured thoracic aortic aneurysm	Diffuse slowing
7	Sepsis	Epilepsy/Urinary tract infection	BS
8	Sepsis	Sepsis	NCSE
9	Intracranial hemorrhage/ischemic stroke	Intracranial hemorrhage	Diffuse slow
10	Propofol infusion syndrome/sepsis	Epilepsy	BS
No IVAD			
11	Sepsis, NCSE (family denied further care)	Sepsis	NCSE
12	Non Hodgkin Lymphoma/Leptomeningeal involvement	Non Hodgkin Lymphoma/Leptomeningeal involvement	Diffuse slowing
13	Pneumonia/Progressive multifocal leukoencephalopathy, graft versus host disease	Infection	Diffuse slowing/GPD

Death = In-hospital death, NCSE = nonconvulsive status epilepticus, BS = burst-suppression, GPD = generalized periodic discharges.

Status Epilepticus: Impact of Therapeutic Coma on Outcome*

Nicola A. Marchi, BM[1]; Jan Novy, MD[1]; Mohamed Faouzi, PhD[2]; Christine Stähli, RN[1]; Bernard Burnand, MD, MPH[2]; Andrea O. Rossetti, MD[1]

Objectives: Therapeutic coma is advocated in guidelines for management of refractory status epilepticus; this is, however, based on weak evidence. We here address the specific impact of therapeutic coma on status epilepticus outcome.

Design: Retrospective assessment of a prospectively collected

between potential predictors and clinical outcome were analyzed using multinomial logistic regressions. Of 467 patients with incident status epilepticus, 238 returned to baseline (51.1%), 162 had new disability (34.6%), and 67 died (14.3%); 50 subjects (10.7%) were managed with therapeutic coma. Therapeutic coma

Terapötik koma özellikle kompleks parsiyel status epileptikus olmak üzere tüm hastalarda kötü prognozla ilişkili

managed with therapeutic coma.

Conclusions: This study provides class III evidence that therapeutic coma is associated with poorer outcome after status epilepticus; furthermore, it portends higher infection rates and longer hospitalizations. These data suggest caution in the straightforward use of this approach, especially in patients with complex partial status epilepticus. (*Crit Care Med* 2015; 43:1003–1009)

Key Words: hospital stay; infections; mortality; prognosis; semiology; treatment

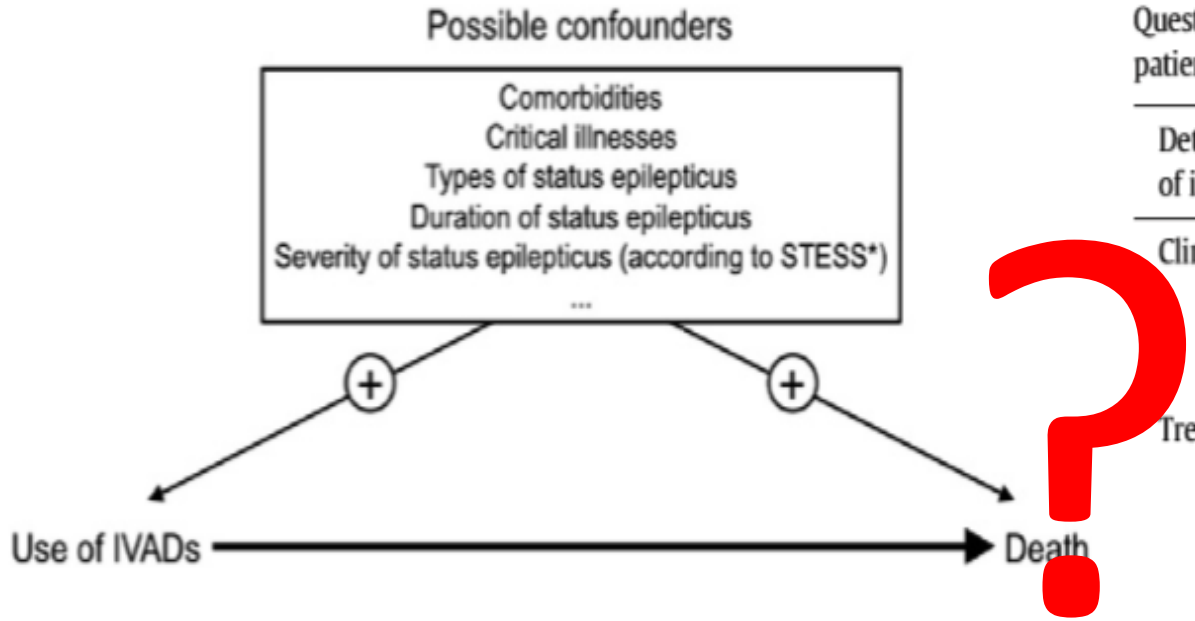

Fig. 2. Possible confounders for the association between continuously administered intravenous anesthetic drugs and death in patients with treatment-refractory status epilepticus. IVADs = intravenous anesthetic drugs; STESS = Status Epilepticus Severity Score. *STESS includes age, level of consciousness, worst seizure type, and seizure history [27,42].

Table 1
Questions regarding the use of continuously administered intravenous anesthetic drugs in patients with status epilepticus.

Determinants of interest	Questions
Clinical conditions	Are patients with specific status epilepticus types at higher risk for IVADs-related adverse effects?
	Are patients with specific status epilepticus etiologies at higher risk for IVADs-related adverse effects?
Treatment strategy	May early use of IVADs (i.e., before status epilepticus becomes treatment-refractory) be less critical?
	Can early administration of new generations of broad-spectrum antiepileptic drugs reduce the use of IVADs?
	Does the increased mortality caused by IVADs outweigh the mortality resulting from treatment-refractory status epilepticus?
	Should we favor prolonged status epilepticus over the use of IVADs in patients with certain risk profiles?

IVADs = intravenous administered anesthetic drugs.

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Calculating the Risk Benefit Equation for Aggressive Treatment of Non-convulsive Status Epilepticus

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Abstract

Objective—To address the question: does non-convulsive status epilepticus warrant the same aggressive treatment as convulsive status epilepticus?

Method—We used a decision model to evaluate the risks and benefits of treating non-convulsive status epilepticus with intravenous anesthetics and ICU-level aggressive care. We investigated how the decision to use aggressive versus non-aggressive management for non-convulsive status epilepticus impacts expected patient outcome for four etiologies: absence epilepsy, discontinued antiepileptic drugs, intraparenchymal hemorrhage, and hypoxic ischemic encephalopathy. Each etiology was defined by distinct values for five key parameters: baseline mortality rate of the inciting etiology; efficacy of non-aggressive treatment in gaining control of seizures; the relative contribution of seizures to overall mortality; the degree of excess disability expected in the case of delayed seizure control; and the mortality risk of aggressive treatment.

Results—Non-aggressive treatment was favored for etiologies with low morbidity and mortality such as absence epilepsy and discontinued antiepileptic drugs. The risk of aggressive treatment was only warranted in etiologies where there was significant risk of seizure-induced neurologic damage. In the case of post-anoxic status epilepticus, expected outcomes were poor regardless of the treatment chosen. The favored strategy in each case was determined by strong interactions of all five model parameters.

Conclusions—Determination of the optimal management approach to non-convulsive status epilepticus is complex and is ultimately determined by the inciting etiology.

The model considers two treatment strategies for NCSE: (1) aggressive treatment, including admission to an intensive care unit (ICU), endotracheal intubation (if not already performed), and induction of pharmacological coma with close clinical and physiologic monitoring; and (2) non-aggressive treatment, limited to non-sedating anticonvulsants without specified admission to an ICU and without intubation or ventilation for the express purpose of achieving anesthetic levels that facilitate electrographic burst suppression. Aggressive treatment is assumed to immediately suppress seizure activity, whereas non-aggressive treatment incurs a longer duration of NCSE. Conceptually, the decision between aggressive and non-aggressive treatment occurs after 30 min of attempting to control NCSE with first-line non-sedating antiepileptic drugs (AEDs). Outcomes are expressed in terms of quality of life (QOL) based on long-term neurologic disability (see below). With the hypothesis that the marginal benefit of aggressive management would vary in a disease-specific manner, we separately considered four different etiologies for NCSE with distinct clinical characteristics: hypoxic-ischemic encephalopathy (HIE), IPH, discontinuation of antiepileptic drugs (dAED), and absence epilepsy. 3-month functional outcomes are presumed, a sufficient duration to permit stable rates of mortality and functional outcome to emerge.

We considered five variables to incorporate in our model of NCSE management: (1) baseline mortality rate for specific etiologies of NCSE, (2) efficacy of non-aggressive treatment, (3) impact of etiology on outcome, (4) excess disability attributable to delayed seizure control, and (5) mortality risk of aggressive treatment.

Table 1
Data required in the analysis: probabilities, significance weights, and QOL

Etiology	Absence epilepsy	Discontinuation of anti-seizure medication	Intraparenchymal hemorrhage	Hypoxic ischemic encephalopathy
Model parameters				
%Baseline mortality	1	10	30	90
Weighting of etiology vs NCSE	1:10	1:10	5:1	10:1
%Mortality of aggressive treatment	20	20	20	20
%With disability incurred by delay	1	20	20	20
%Efficacy of non-aggressive treatment	99	70	25	10
Survivor baseline outcome distribution (%)				
Mild/No disability	100	100	44	16
Moderate disability	0	0	30	42
Severe disability	0	0	26	42

Table 2

Results for base-case analyses

Etiology	Absence epilepsy	Discontinuation of anti-seizure medication	Intraparenchymal hemorrhage	Hypoxic ischemic encephalopathy
Preferred management	Non-aggressive	Non-aggressive	Aggressive	Aggressive
QOL difference between strategies (%)	20 (100 vs 80)	9 (88 vs 79)	5 (36 vs 41)	<1 (4.7 vs 5.1)
Crossover points				
%Baseline mortality	–	40	–	73
Weighting of etiology vs NCSE	–	–	–	–
%Mortality of aggressive treatment	–	–	–	49
%With disability incurred by delay	36	33	21	–
%Efficacy of non-aggressive treatment	–	11	30	26

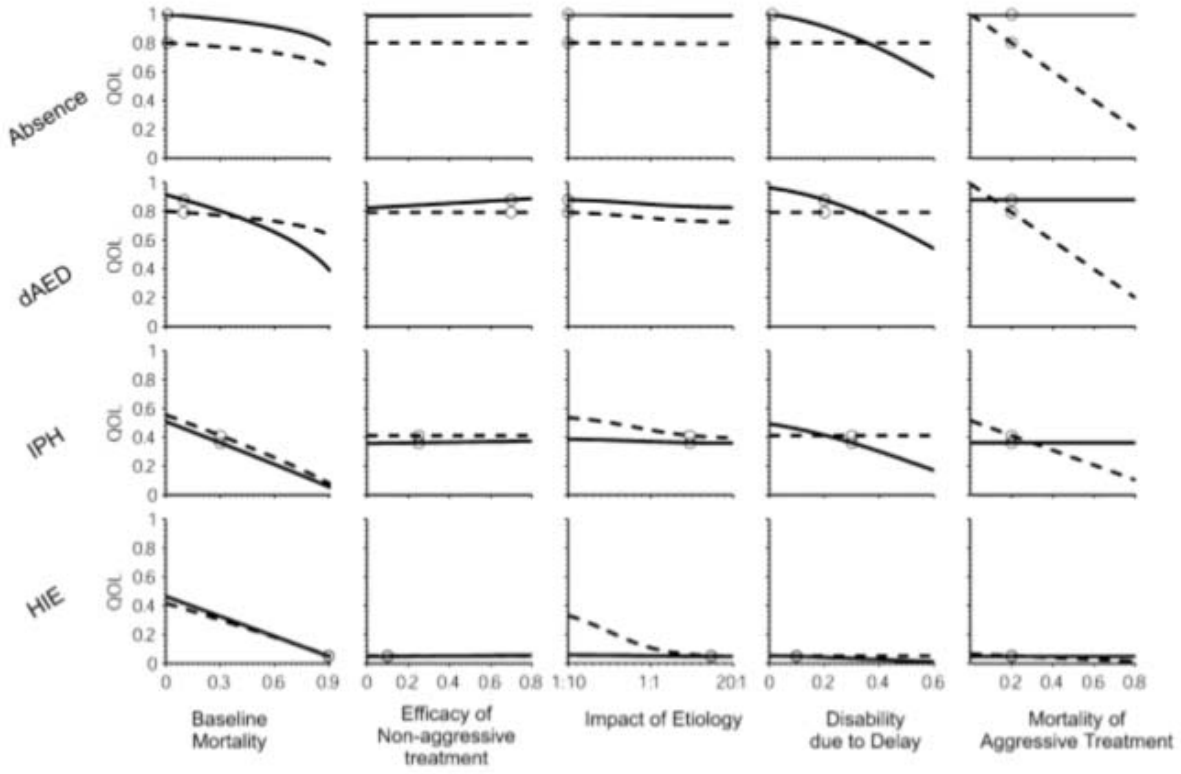

Fig. 2.
One-way sensitivity analysis. From *top* to *bottom*, the etiology progresses from least to most severe: absence epilepsy (*Absence*), discontinued antiepileptic drugs (*dEAD*), intraparenchymal hemorrhage (*IPH*), and hypoxic ischemic encephalopathy (*HIE*). Across the columns, the parameter which is varied changes, from left to right: baseline mortality, efficacy of non-aggressive treatment, impact of etiology, disability due to delay and mortality of aggressive treatment. The solid line represents non-aggressive treatment and the *dotted line* represents aggressive treatment. The *y axis* shows the expected QOL. The circles represent our base-case values

Results—Non-aggressive treatment was favored for etiologies with low morbidity and mortality such as absence epilepsy and discontinued antiepileptic drugs. The risk of aggressive treatment was only warranted in etiologies where there was significant risk of seizure-induced neurologic damage. In the case of post-anoxic status epilepticus, expected outcomes were poor regardless of the treatment chosen. The favored strategy in each case was determined by strong interactions of all five model parameters.

Conclusions—Determination of the optimal management approach to non-convulsive status epilepticus is complex and is ultimately determined by the inciting etiology.

- Entübe olmayan nonkonvülzif status epileptikus hastaları hızla entübe edilmeli ve yüksek doz anesteziklerle tedavi edilmeli mi?
- Yoksa nöbet kontrolü süresini uzatmayı göze alarak daha az güçlü ilaçlarla mı tedavi edilmeli?
- Bu sorunun yanıtı oldukça kompleks
- Tek, basit bir algoritma yok
- Optimal risk-yarar dengesi gözetilerek bu karar bireyselleştirilmeli

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EDITORIAL

What is Specialized Care in Status Epilepticus and in Which ICU?

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What is the place and expected benefits of a specialized unit to manage SE?

(1) Dispatching SE to NICU or MICU can be based on the type and severity of the status.

In the majority of cases, SE stops after the first dose of benzodiazepines and invasive intensive care is not required [9, 10].

In the case of refractory SE, namely when seizures did not respond to two antiepileptic drugs, most patients will have been placed under general anesthetic and mechanical ventilation. The anesthetic weaning is often easy, without any recurrence of the status, and its management may not significantly benefit from a neurological team.

Patients with several organ dysfunctions, furthermore if they are possible candidates for specific techniques, e.g., renal replacement therapy, extracorporeal life support, should be admitted in a MICU.

Management of partial SE by a neurointensivist with antiepileptic drugs could avoid general anesthesia as suggested by Varelas et al. who found that fewer patients were intubated in the NICU.

Few cases of SE are superrefractory, with persistence or recurrence of status, whether clinical or based on EEG evidence. The management of anesthetic and antiepileptic drugs of these superrefractory SEs requires a multidisciplinary team of neurointensivists, neurologists, electrophysiologists, neuroradiologists, and specialist nurses.

(2) We pointed some expected benefits of the management of SE in a NICU.

NICU is associated to better chart documentation, and seizures description appears as being fundamental to both interpret EEG findings but also choose the best antiepileptic drug.

The management of general anesthesia is poorly defined, and the clinician has to balance the risk of a recurrence of seizures with the potential complications associated with prolonging sedation and mechanical ventilation [11, 12, 13]. In NICU, the use and duration of anesthesia may be limited, notably to treat partial seizures.

During the withdrawal of anesthetic agents, isolated epileptic seizures may occur, especially if the SE lasted for a long period; it is important to deal with these short seizures appropriately, moving from the management of SE to the management of epilepsy, which requires a different approach. This step requires the experience of neurointensivists, neurologists, and epileptologists used to dealing with forms of epilepsy other than SE.

Continuous EEG monitoring allows early detection of seizures recurrence, and real-time anesthetic medication adjustment. This type of monitoring is principally available in NICU, where the medical and paramedical staff is experienced in its use. This also involves a close collaboration with the neurophysiological staff. However, data on the usefulness of cEEG are still lacking in SE [14].

In comatose patients, the EEG can be difficult to interpret and diagnostic errors are common. EEG recordings in the case of severe encephalopathies or brain injuries show grapho-elements (PLEDs, triphasic potentials) that can be wrongly interpreted as resulting from SE, leading to an unwarranted increase of sedation. We therefore reported the observation of 10 patients referred to our NICU as refractory nonconvulsive status, whose final diagnosis was sporadic Creutzfeldt–Jakob disease with EEG features mimicking a status [15]. In particular, the test using intravenous injection of a benzodiazepine is suggestive of an epileptic origin only if both clinical and EEG symptoms improve. The combined expertise of a clinical neurologist trained in epileptology and an electrophysiologist trained in intensive care recordings is essential to establish the correct diagnosis.

Less common etiologies of SE can be difficult to diagnose and may pose therapeutic problems. SE can be a complication in many congenital epileptic diseases, like Dravet syndrome; the clinical semiology, EEG and treatment are very different, and epileptologist's expertise is crucial [16]. It is important to be aware not to use aggressive treatment in the form of general anesthesia for myoclonic SEs, which may have a spontaneously favorable course, and to suspect a mitochondrial disease, which would contraindicate the use of sodium valproate [17]. Similarly, tonic SE, as observed in the Lennox–Gastaut syndrome can be worsened by benzodiazepine. SE is a classic complication of infectious or inflammatory encephalitis. Early etiological diagnosis is difficult in some rare cases and requires a specialized team, aware of the newly described syndromes related to antibodies against neuropils [18]. The ability to distinguish clonic movements of epileptic origin from other abnormal involuntary movements of brainstem or basal ganglia origin, such as those seen in anti-NMDAr encephalitis, is of paramount importance for the therapeutic management [19]. The rapid introduction of corticosteroid or immunomodulatory drugs, without waiting for confirmation of the etiology, requires experience of these pathologies.

- Nonkonvülzif status epileptikus heterojen bir antite
- Klinik, EEG ve görüntüleme bulguları temelinde sendromik klasifikasyon yapılmalı
- Yönetim bireyselleştirilmeli
- Agresif tedavinin gerekli olduğu alt tipler belirlenmeli
- Tanı ve yönetimi mutlaka nöroloji uzmanı/nöroyoğun bakım uzmanı yürütmeli