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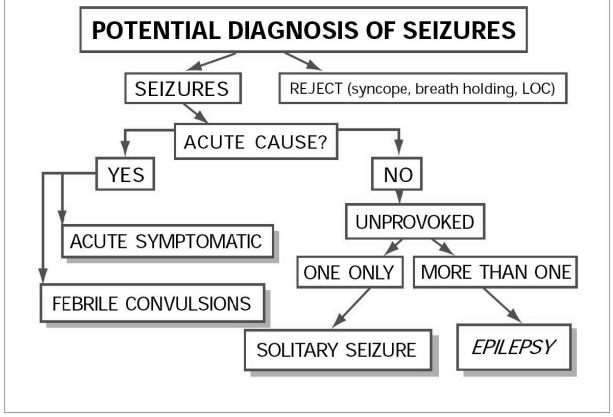
일년차가 알아야 할 Seizure Disorders

2016. 03. 05.

신경과 전공의 입문교육, 천안

이 상암
서울아산병원 신경과

EPILEPSY
SEIZURE
CONVULSION



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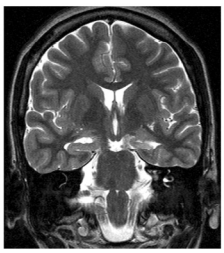
Seizure Disorders

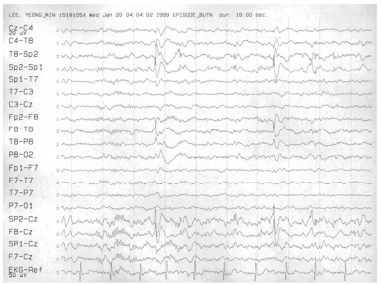
- Seizures Classification
- Epilepsy
- Seizures' Differential Diagnosis
- Acute symptomatic seizures
- Status epilepticus

International Classification of Epileptic Seizures (1981)

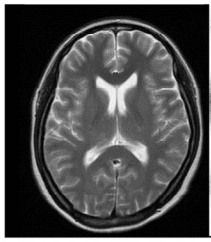
- Partial seizures
  1. Simple partial
  2. Complex partial
  3. Partial Sz evolving to secondary GTC
- Generalized seizures
  1. Tonic-Clonic
  2. Absence
  3. Myoclonic
  4. Tonic
  5. Atonic
  6. Clonic
- Unclassified Seizures

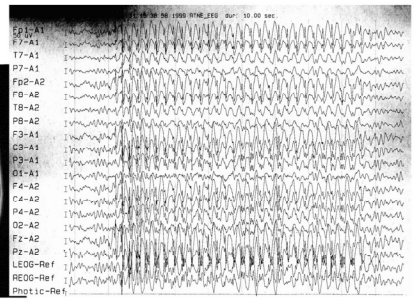
Partial





Generalized





International Classification of Epileptic Seizures (1981)

- **Partial seizures**
  1. **Simple partial** 1, 2, 3
  2. **Complex partial** 1, 2, 3
  3. **Partial Sz evolving to secondary GTC** 2 GTC
- **Generalized seizures**
  1. Tonic-Clonic
  2. Absence
  3. Myoclonic
  4. Tonic
  5. Atonic
  6. **Clonic**
- **Reflex Seizures** 1, 2

Seizure Disorders

- Seizures Classification
- Epilepsy
- Seizures' Differential Diagnosis
- Acute symptomatic seizures
- Nonconvulsive status epilepticus

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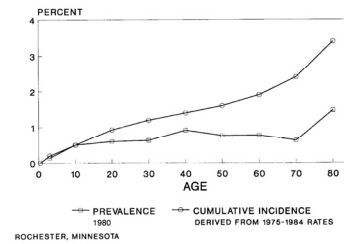
The 1989 Classification of Epilepsies, Epileptic Syndromes, and Related Seizure Disorders

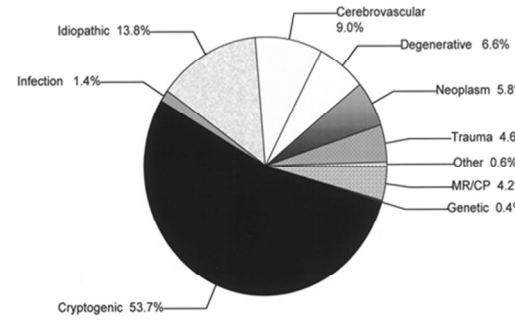
- **Idiopathic Generalized Epilepsy**
  - Childhood absence epilepsy
  - Juvenile absence epilepsy
  - Juvenile myoclonic epilepsy
  - Epilepsy with GTCS on awakening
- **Symptomatic (or Cryptogenic) Generalized Epilepsy**
  - Lennox-Gastaut Syndrome
- **Idiopathic Localization-related Epilepsy**
  - Benign partial epilepsies of childhood (Rolandic epilepsy)
- **Symptomatic (or Cryptogenic) Localization-related Epilepsy**
  - Temporal lobe epilepsy
  - Frontal lobe epilepsy
  - Occipital lobe epilepsy
  - Parietal lobe epilepsy

- **Etiology:**
  - **Idiopathic**
  - **Symptomatic**
  - **Cryptogenic**
- **Epileptogenic mechanism:**
  - **Generalized**
  - **Partial**
  - **Undetermined**

Epilepsy: Prevalence and Cumulative Incidence

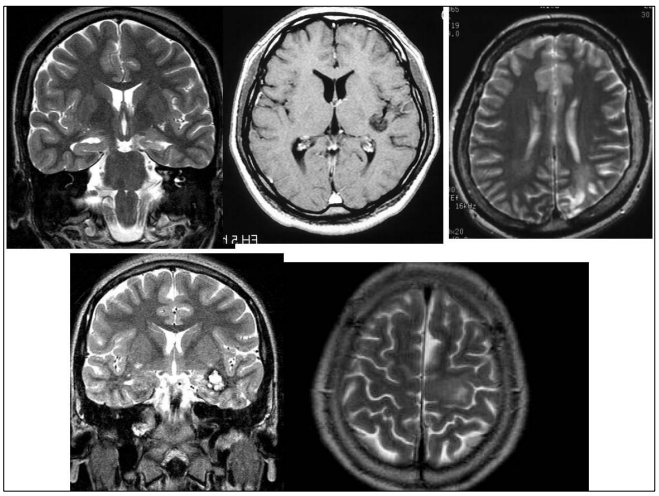


- Epilepsy is one of the most common disorders of the brain.
- One of every 10 people will have at least one epileptic seizure during a normal lifespan, and a third of these will develop epilepsy.
- According to WHO survey, epilepsy accounts for 1% of the global burden of disease, a figure equivalent to breast cancer in women and lung cancer in men.



Iceland 1995–1999

Figure. Classic risk factors.



Epilepsy Is More Than Seizures

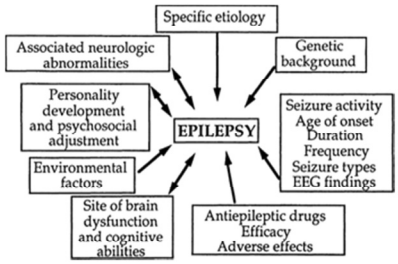
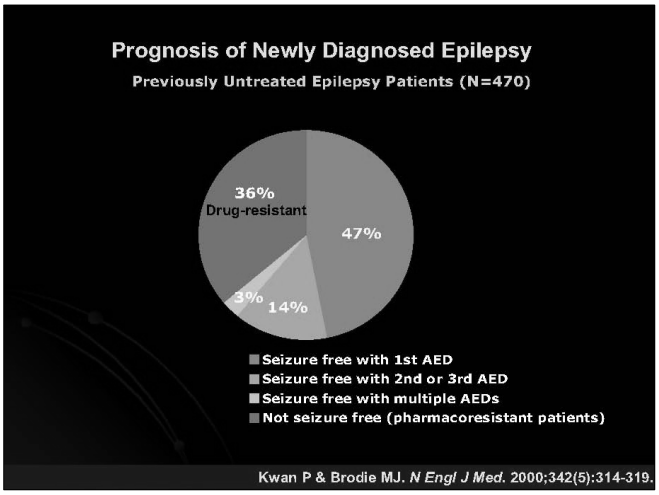


FIGURE 1. The multiple, interacting factors that contribute to the totality of epilepsy for an individual patient.



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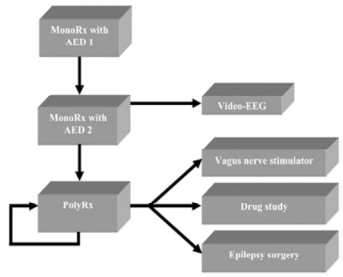
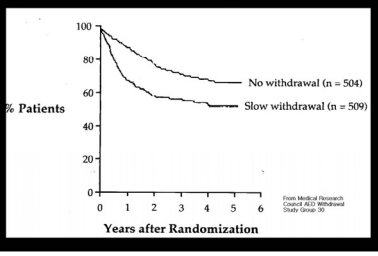


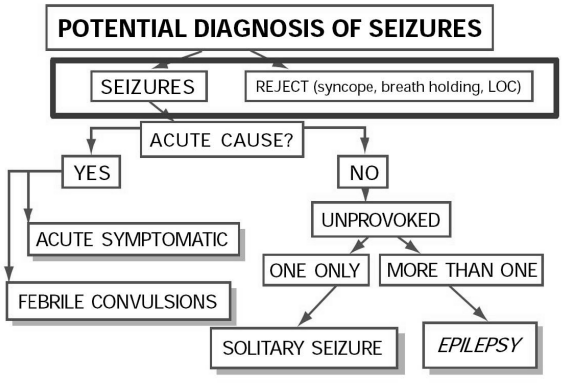
Fig. (1). Therapeutic Triage in Epilepsy Care. Newly diagnosed epilepsy patients are most appropriately treated with AED monotherapy. Following failure of a second monotherapy, clinicians should implement courses of sequential chronic maintenance polytherapy and intensive evaluation to ensure correct epilepsy syndrome diagnosis and exclusion of nonepileptic spells.

Prognosis of Epilepsy after Treatment Withdrawal

- Population-base study[1]: 61% 5-year terminal remission of epilepsy
- Critical review of relapse after discontinuation of drug treatment[2]
  - overall, 12% to 66% relapse rates
  - the cumulative probability of remaining seizure free
    in children, 66% to 96% at 1 year and 61% to 91% at 2 years
    in adults, 39% to 74% at 1 year and 35% to 57% at 2 years
  - relapse rate was highest in the first 12 months (esp in the first 6 mo)
- Only randomized trial[3] on the effects of AED withdrawal



[1]*Annegers JF, et al. Epilepsia.* 1979;20(6):729–737.
[2]*Specchio LM, Beghi E. CNS Drugs.* 2004;18(4):201–212.
[3]*MRC AED Withdrawal Study Group. Lancet.* 1991;337(8751):1175–1180.



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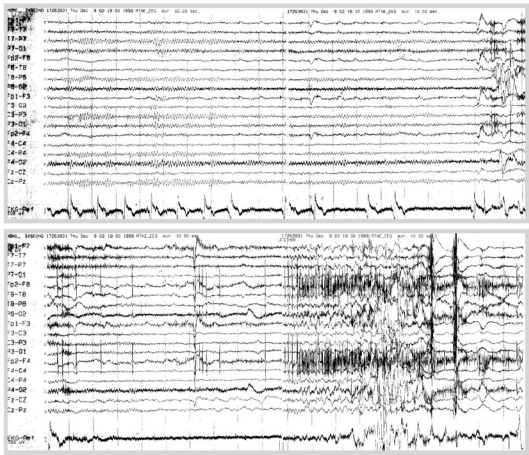
Differential diagnosis of acute seizures

Neurocardiogenic syncope	**vasovagal syncope**
	carotid sinus syncope
	cough and micturition syncope
Orthostatic syncope	**autonomic failure**
	age-related autonomic dysfunction
	medications, especially vasodilator
Cardiogenic syncope	tachyarrhythmia
	bradyarrhythmia
	structural cardiac disease
Cerebral syncope	ictal bradycardic syncope (seizure with bradycardia)
	migraine (esp. hemiplegic and basilar artery migraine)
	brainstem TIA
Psychogenic	**panic disorder**
	dissociative non-epileptic attack (‘**pseudo seizures**’)
Sleep disorders	**parasomnia**
Acute vertigo	acute labyrinthitis, Ménière’s disease
Paroxysmal movement disorders	familial kinesigenic dystonia

69 female:
Recurrent transient episodes since 1 week ago
Usually during night (2-3 times/night)



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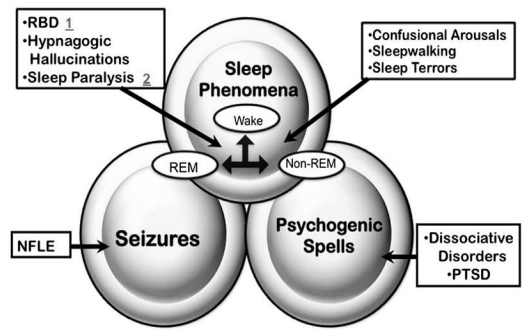
Clinical distinction between seizures, syncope and pseudoseizures

	Seizure	Syncope	Pseudoseizure
Trigger	rare (unless photosensitive)	common (upright, bathroom, blood)	common (stress)
Prodrome	common (*déjà vu*, epigastric), often brief	almost always (vision, nausea, hot), 2–10 min	common (anxiety symptoms), often prolonged
Duration	2–5 min	30 sec–2 min	1–60 min
Jerking	common (1–2 min)	common (secs)	common (prolonged, erratic, variable)
Eyes	open	open, elevated	closed, resists eye contact
Colour	pale (partial seizure), red/blue (tonic-clonic seizure)	very pale	normal, red, occasionally blue
Breathing	apnoea in expiration	apnoea in expiration	hyperventilation, coughing, apnoea in inspiration
Incontinence	common	uncommon	uncommon
Injury	common (can be severe)	uncommon (can be severe)	common (trivial)
Tongue biting	common (side)	rare	occasional (tip tongue, cheek, lip)
Afterwards	confused (wakes in ambulance)	rapidly orientated (wakes on floor)	orientated, often tearful

Nocturnal Spells: overlapping states



Malhotra & Avidan. Neurol Clin 2012

Table 1
Key similarities and differentiating features between NREM and REM parasomnias as well as nocturnal seizures

	Confusional Arousals	Sleep Terrors	Sleepwalking	Nightmares	RBD	Nocturnal Seizures
Time	Early	Early	Early-Mid	Late	Late	Any
Sleep stage	SWA	SWA	SWA	REM	REM	Any
EEG discharges	–	–	–	–	–	+
Scream	–	++++	–	++	+	+
CNS activation	+	++++	+	+	+	+
Motor activity	–	+	+++	+	++++	++++
Awakens	–	–	–	+	+	+
Duration (min)	0.5–10	1–10	2–30	3–20	1–10	5–15
Postevent confusion	+	+	+	–	–	+
Age	Child	Child	Child	Child-adult	Older adult	Young adult
Genetics	+	+	+	–	–	±
Organic CNS lesion	–	–	–	–	++	++++

Avidan AY & Kaplish N. Clin Chest Med 2010;31(2)

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Psychogenic "Pseudo-seizure"

- **Hypermotor** 1, 2
- **Hypomotor** 1

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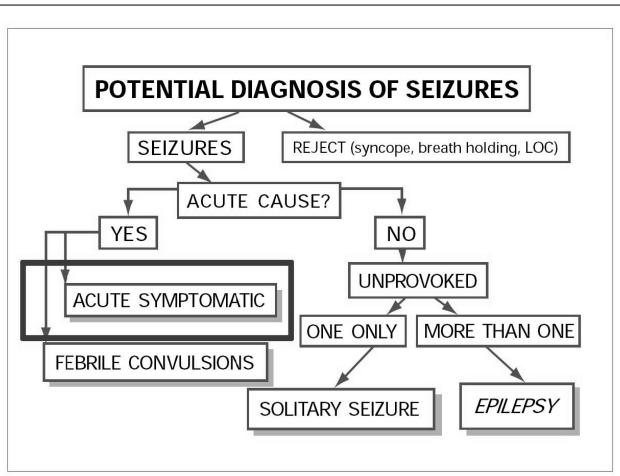

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Table 1. Common causes of acute symptomatic seizures in adults.

Infective	meningitis/encephalitis	
	cerebral abscess	
Trauma:	Head injury (especially penetrating)	immediate (concussive) early (<24 hours) post-traumatic
	Neurosurgery	craniotomy
Vascular:	stroke (especially haemorrhagic)	
	cerebral venous thrombosis	
	hypertensive encephalopathy	
	eclampsia	
Hypoxia:	cardiac arrest	
Toxic	alcohol and medication withdrawal	
	poisoning and overdose	
	medication toxicity	
	illicit drugs	
Neoplastic	leukaemia	
	lymphoma	
	metastatic cancer	
Metabolic / Endocrine	porphyria	
	hypoglycaemia, hypocalcaemia, hyponatraemia	
Immune	acute demyelination	
	cerebral vasculitis	

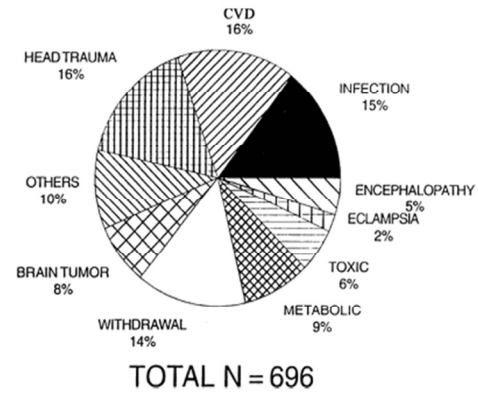

Figure. Acute symptomatic seizure precipitating causes

Drugs to Precipitate Seizures

- Anticholinesterase
- Antihistamines
- Aqueous iodinated contrast agents
- Baclofen
- Beta blockers
- Cephalosporins
- Chlorambucil
- Cycloserine
- Cyclosporine
- Ergonovine
- Folic acid
- Foscarnet
- Imipenem
- Isoniazid
- Lindane
- Local anesthetics
- Mefenamic acid
- Methotrexate
- Metronidazole
- Misonidazole
- Nalidixic acid
- Narcotic analgesic
- Oxytocin
- Penicillins
- Sympathomimetics

Metabolic Disorder

Electrolyte disturbances
Hyponatremia < 115 mEq/L

Glucose
Nonketotic hyperglycemia
focal motor seizures: 20% of patients
Hypoglycemia

Hypocalcemia	< 6 mg/dL	DDx: Tetany
Hypomagnesemia	< 0.8 mEq/L	
Hypophosphatemia	< 1 mg/dL	

Hypoparathyroidism: usually with hypocalcemia
Thyroid: Myxedema, Thyrotoxicosis

Drugs used for acute symptomatic seizure

- Benzodiazepines
  - Lorazepam 4 mg bolus, repeated after 10 min if necessary.
  - Rectal diazepam and buccal midazolam are alternatives.
  - Short course of oral clobazam useful in patients with recurrent seizures that do not develop into status epilepticus.
  - Main side-effects are sedation and respiratory depression
- Phenytoin
  - Intravenous loading (15 mg/kg over 20 min) effective in terminating tonic-clonic and partial status epilepticus.
  - Cardiac monitoring required (risks of arrhythmias).
  - Long term side-effects, complex drug interactions and PKs make this a less attractive maintenance agent.
  - Fosphenytoin is considerably more expensive, but has the advantages of fewer injection sites and cardiovascular side effects, and can be given intramuscularly.

Drugs used for acute symptomatic seizure

- Sodium valproate
  - Increasingly favoured over phenytoin in the acute situation, with few side-effects when given rapidly at high doses (25 mg/kg over 10 min)
  - Effective for other seizure types (absence, myoclonic).- Should be avoided in patients with liver impairment.
  - Risk of congenital malformations limits use in women of child-bearing age.
- Levetiracetam
  - Efficacy of intravenous loading in status epilepticus and in critically ill patients with acute symptomatic seizures
  - Usually well tolerated and therapeutic oral dose (1000 mg daily) achievable over several days or quicker.
  - Can be started orally alongside more aggressive treatment, allowing the withdrawal of phenytoin more safely.
  - Useful when trying to avoid drug interactions (eg, patients on warfarin, HIV patients).

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Seizure Disorders

- Seizures Classification
- Epilepsy
- Seizures' Differential Diagnosis
- Acute symptomatic seizures
- Nonconvulsive status epilepticus

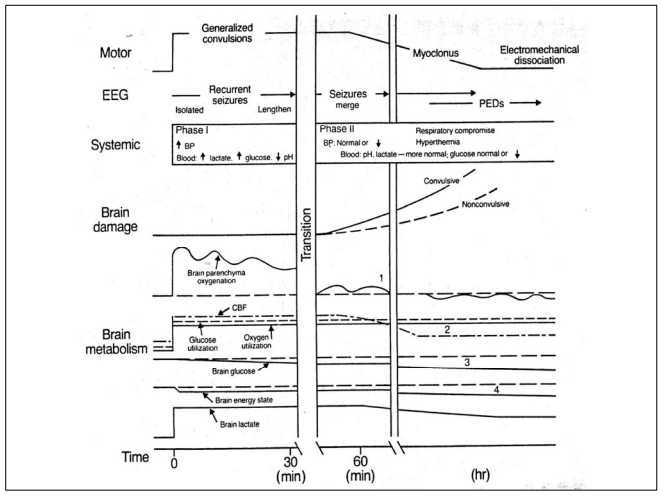
Definition of Status Epilepticus

- International League against Epilepsy (1981):
  "a seizure that persists for a sufficient length of time or is repeated frequently enough that recovery between attacks does not occur"
- More recent publications:
  defined SE as seizures that persist for 20-30 minutes

Status Epilepticus and its Equivalents

1. Thirty minutes of continuous seizures or lack of recovery between discrete seizure for focal, complex partial, absence, and other forms of nonconvulsive status epilepticus
2. Five minutes of continuous convulsive seizures
3. Three discrete convulsions within an hour

(Roth & Drislane. Neurologic Clinics 1998;16:257-84)



Principles of Drug Treatment

Without Delay

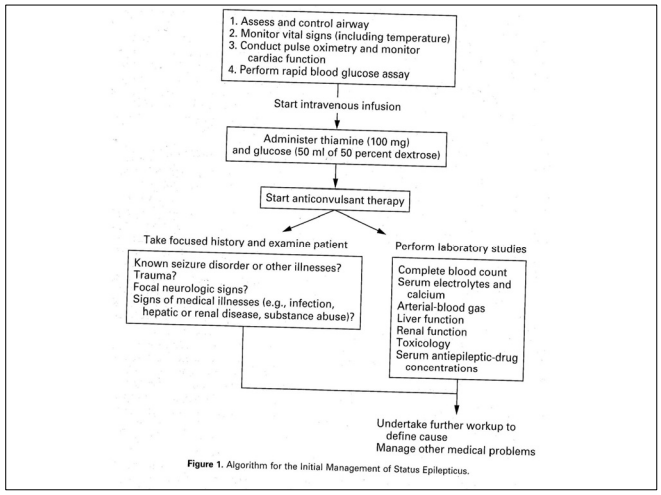


Figure 1. Algorithm for the Initial Management of Status Epilepticus.

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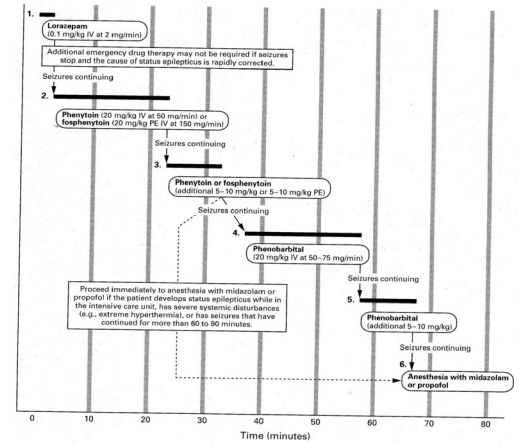

Figure 2. Antiepileptic-Drug Therapy for Status Epilepticus.
IV denotes intravenous, and PE phenytoin equivalents. The horizontal bars indicate the approximate duration of drug infusions.

Clinical patterns of GCSE

Overt GCSE

A gradual
electroclinical disassociation
over time

Subtle GCSE

Generalized Convulsive Status Epilepticus:
Etiology in adults*

ACUTE
- Brain hypoxia
- Cerebrovascular accident
- Brain neoplasm
- Head trauma
- Metabolic encephalopathy
- Central nervous system infection

CHRONIC OR REMOTE
- Pre-existing epilepsy
- Subtherapeutic antiepileptic drug levels
- Alcohol or drug abuse
- Drug withdrawal (benzodiazepines)
- Previous brain surgery
- Previous cardiovascular accident
- Head trauma

*In children, infections, central nervous system infections, and metabolic conditions are the primary etiologies.

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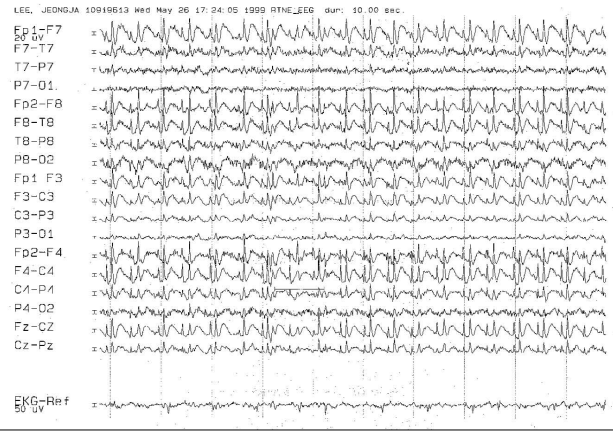
Table 1. Definition of nonconvulsive status epilepticus (NCSE)

Nonconvulsive status epilepticus (NCSE) is a term used to denote a range of conditions in which electrographic seizure activity is prolonged and results in nonconvulsive clinical symptoms.

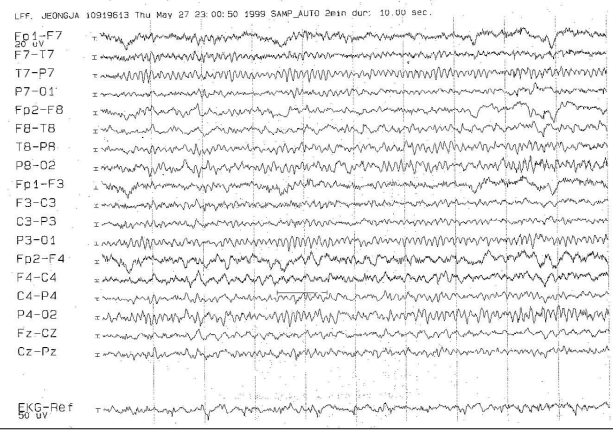
Note:

1. NCSE can be most usefully viewed as a form of cerebral response, which is dependant largely on the level of cerebral development of the individual (age and cerebral integrity/development/maturity), epilepsy syndrome, and the anatomical location of the epileptic activity.
2. The electrographic activity can take various forms.

Ictal EEG-3 (May-26 17:24)



Interictal EEG (Valium/Dilantin loading)



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Seizures in Specific Situations

Acute Symptomatic Seizures
Identify the Causes

Generalized Convulsive Status Epilepticus
Aggressive IV Treatment without Delay

Nonconvulsive Status Epilepticus
Early Detection: Suspicion & EEG