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일년차가 알아야 할 Seizure Disorders

2016. 03. 04.

신경과 전공의 입문교육, 천안

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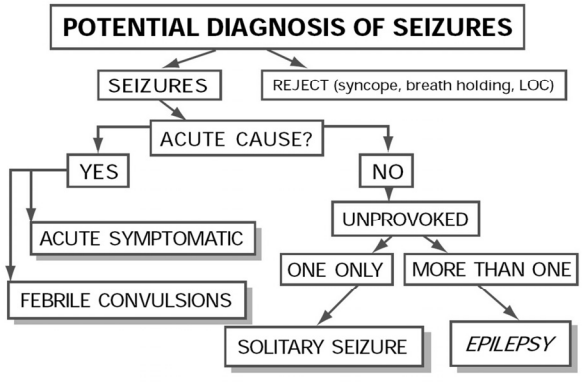
서울아산병원 신경과

EPILEPSY
SEIZURE
CONVULSION



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Seizure Disorders

- Seizures & Epilepsy Classification
- 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

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**

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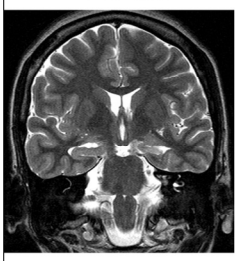
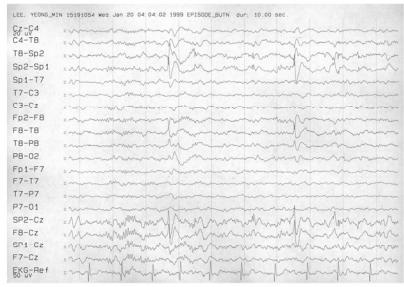
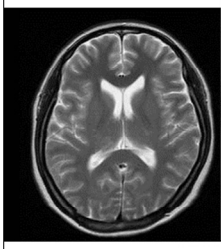
Partial





Generalized



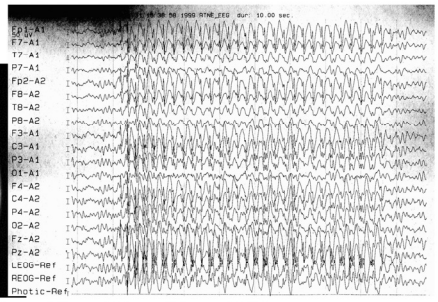


TABLE 1-4 Seizure Types and Terminology Used in the 1981 Classification of Seizures and Recommended in the 2010 Report[a,b]

Mode of Onset	1981 Seizure Types[c]	2010 Seizure Descriptions[d]
Focal	Simple partial With motor signs With sensory symptoms With autonomic symptoms With psychic symptoms (but no impaired consciousness)	Without impairment of consciousness or awareness: With observable motor or autonomic components Involving subjective sensory or psychic phenomena only, corresponding to the concept of an aura
	Complex partial Consciousness impaired at onset Simple partial onset followed by impairment of consciousness	With impairment of consciousness or awareness. *Dyscognitive* is a term that has been proposed for this concept.[21]
	Partial evolving to secondarily generalized seizure (tonic, clonic, or tonic-clonic) Simple evolving to generalized tonic-clonic Complex evolving to generalized tonic-clonic (including those with simple partial onset)	Evolving to a bilateral, convulsive seizure (involving tonic, clonic, or tonic and clonic components).

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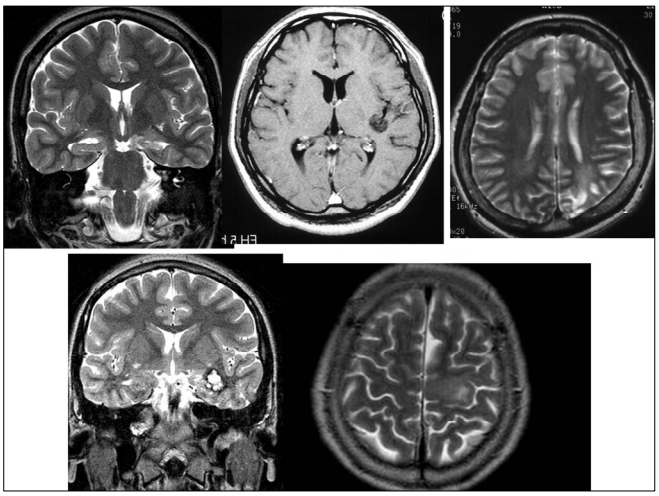
Generalized onset	Tonic-clonic	Tonic-clonic (in any combination)
	Myoclonic	Myoclonic Myoclonic Myoclonic-atonic Myoclonic-tonic
	Absence With various accompanying manifestations Atypical	Absence Typical absence Atypical absence With special features Eyelid myoclonia[e] Myoclonic absence
	Clonic	Clonic
	Tonic	Tonic
	Atonic (astatic)	Atonic
Not clear	Anything that does not fit in above, eg, rhythmic eye movements, chewing, swimming movements	Epileptic spasms

Old term	New term	Rationale
Idiopathic	Genetic	idiopathic – not clear genetic, self-limited, excellent prognosis, no major associated disability
Symptomatic	Structural / metabolic	All epilepsies are caused by something (symptomatic)
Cryptogenic	Unknown	Many of the formerly cryptogenic epilepsies have been show to have a genetic basis

	1981 / 1989	2010
Generalized seizures	The first clinical changes indicate initial involvement of both hemisphere	Originating at some point within, and rapidly engaging, bilaterally distributed networks (including cortical and subcortical structures)
Generalized epilepsy		abandoned
Focal seizures	The first clinical and EEG changes indicate initial EEG activation of a system of neurons limited to a part of one hemisphere	Originating within networks limited to one hemisphere (either discretely localized or more widely distributed)
Focal epilepsy		abandoned

TABLE 1-7 Organization of the Epilepsies Proposed in 2010 According to Specificity of Epilepsy Diagnosis and Age at Onset *(continued)*

Level of Epilepsy Diagnosis	Epilepsy Diagnosis[a]
Electroclinical syndromes arranged by typical age at onset	**Adolescence to Adult**
	Juvenile absence epilepsy [2.1]
	Juvenile myoclonic epilepsy [2.1]
	Epilepsy with generalized tonic–clonic seizures alone[2.1d]
	Progressive myoclonus epilepsies[2.3]
	Autosomal dominant epilepsy with auditory features**
	Other familial temporal lobe epilepsies**
	Less specific age relationship
	Familial focal epilepsy with variable foci (childhood to adult)**
	Reflex epilepsies[1.1, 1.2, 2.1]
Surgical syndromes[1.2]	Mesial temporal lobe epilepsy with hippocampal sclerosis[1.2]
	Rasmussen syndrome[1.2]
	Gelastic seizures with hypothalamic hamartoma[1.2]
Epilepsy with structural-metabolic causes[1.2, 3.1, 3.2]	Malformations of cortical development (hemimeganencephaly, heterotopias, etc)
	Neurocutaneous syndromes (tuberous sclerosis complex, Sturge-Weber syndrome, etc)
	Tumor
	Infection
	Autoimmune/inflammation
	Trauma
	Angioma
	Perinatal insults
	Hypoxic ischemic encephalopathy/intraventricular hemorrhage
	Stroke
	Neurometabolic conditions
	Neurodegenerative conditions
	Etc



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

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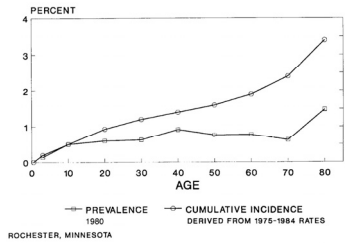
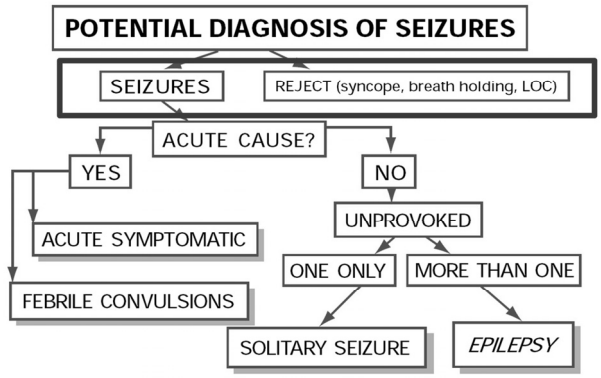
Epilepsy: Prevalence and Cumulative Incidence



- 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.



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

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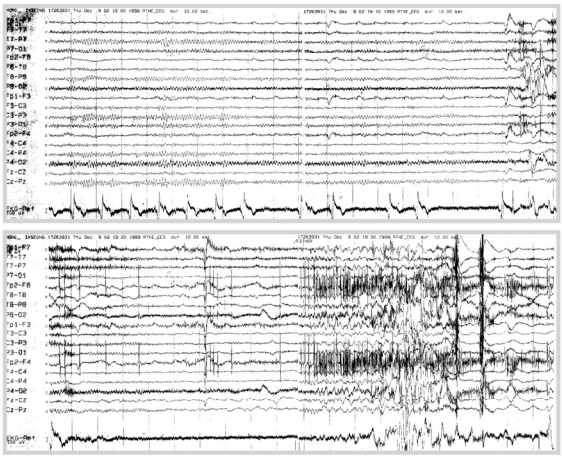
69 female:
Recurrent transient episodes since 1 week ago
Usually during night (2-3 times/night)



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

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Look The Semiology in This Patient

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

Clinical distinction between seizures, syncope and pseudoseizures

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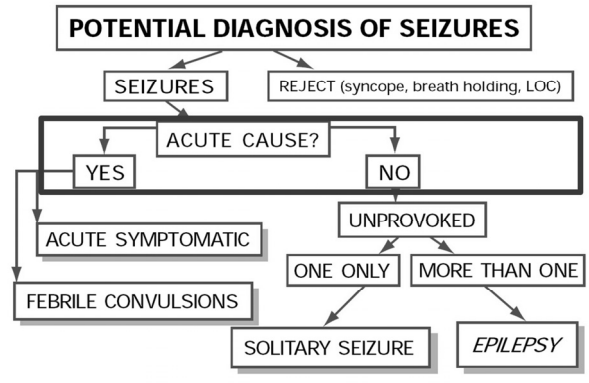

TABLE 6-1 Causes of Acute Symptomatic Seizures

- ▶ **Neurologic**
  - Head trauma (including brain surgery)
  - CNS infection
  - CNS tumor
  - Cerebrovascular disease (eg, stroke, hemorrhage)
  - Cerebral hypoxia/ischemia (eg, cardiovascular or respiratory compromise)
- ▶ **Medications**
  - Toxicity/overdose
  - Withdrawal
- ▶ **Drugs and Alcohol**
  - Acute use of cocaine, methaqualone, and stimulants
  - Withdrawal from alcohol and benzodiazepines
- ▶ **Metabolic and Electrolyte Imbalances**
  - Sodium
  - Calcium
  - Magnesium
  - Glucose
  - Urea nitrogen
- ▶ **Posterior Reversible Encephalopathy Syndrome**

CNS = central nervous system.

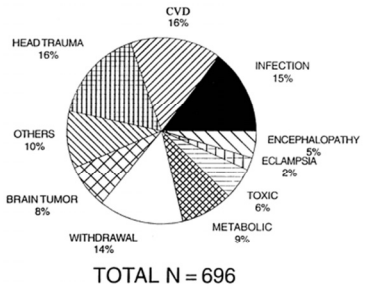

TABLE 6-2 Electrolyte Abnormalities and Acute Symptomatic Seizures

Electrolyte	Normal Values	"Cutoff" Value Most Likely to Be Associated with Acute Symptomatic Seizures
Sodium	135–145 mEq/L	<115–120 mg/dL (hyponatremia) >145 mmol/L (hypernatremia)
Calcium	8.5–10.2 mg/dL	<5.0 mg/dL
Magnesium	1.5–2.5 mEq/L	<0.8 mg/dL (hypomagnesemia)
Glucose	70–100 mg/dL (fasting) <125 mg/dL (nonfasting)	<36–40 mg/dL >~400 mg/dL

Continuum (Minneap Minn) 2014;20(3):614–623

Drugs to Precipitate Seizures

- Medications related to a moderate risk of seizures
  chlorpromazine, clozapine, maprotiline, clomipramine, bupropion, meperidine, and flumazenil
- A particularly high risk of seizures
  overdose of cyclic antidepressants (up to 20% of patients) (especially amoxapine and maprotiline), theophylline, isoniazid, alkylating antineoplastic agents, and cyclosporine
- An intermediate risk of seizures
  - penicillin
    prevents GABA from binding to the $GABA_A$ receptor.
  - cephalosporins, imipenem, and fluoroquinolones
    antagonize $GABA_A$ receptors.
  - isoniazid
    competes with pyridoxine, which is usually transformed into pyridoxal phosphate, a cofactor for GABA synthesis, thus leading to a decrease in GABA levels.

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Seizure Disorders

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

A definition and classification of status epilepticus (ILAE)

SE 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 t1). It is a condition that can have long-term consequences (after time point t2), including neuronal death, neuronal injury, and alteration of neuronal networks, depending on the type and duration of seizures.

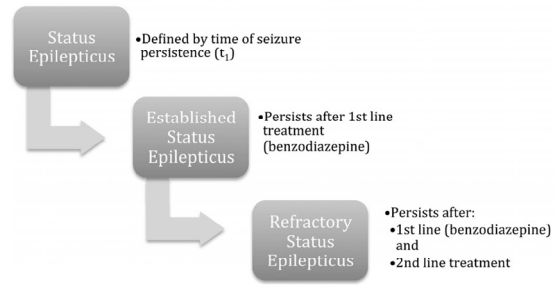
Table 1. Operational dimensions with t_1 indicating the time that emergency treatment of SE should be started and t_2 indicating the time at which long-term consequences may be expected

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.

Trinka et al. Epilepsia, 56(10):1515–1523, 2015

Timeline of the progression of status epilepticus.



Falco-Walter JJ & Bleck T.
J Clin Med 2016

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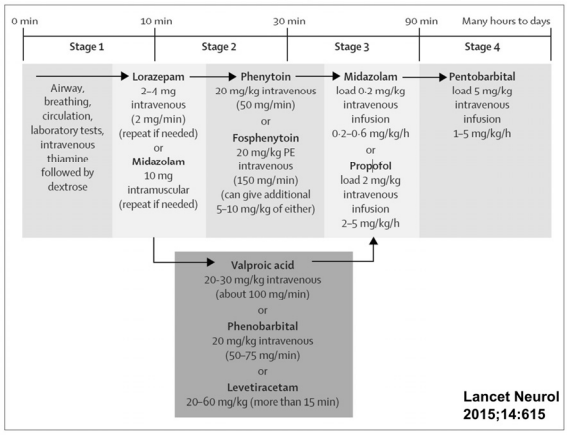
Generalized convulsive status epilepticus treatment algorithm.



Lancet Neurol 2015;14:615

Table 1. Drug dosing and features in treatment of status epilepticus

Drug	Initial dosing	Administration rates or continuous infusion dosing	Mechanisms	Serious adverse effects
Lorazepam	0.1 mg/kg IV up to 4 mg per dose, may repeat after 10 min	Rate up to 2 mg/min	GABA receptor agonist	Respiratory depression, hypotension, sedation
Diazepam	0.15 mg/kg IV up to 10 mg per dose, may repeat after 5 min	Rate up to 5 mg/min	GABA receptor agonist	Respiratory depression, hypotension, sedation
Phenytoin	15-20 mg/kg IV, may give an additional 5-10 mg/kg 10 min after loading	Rate up to 50 mg/min	Sodium channel blocker	Arrhythmia, hypotension
Valproic acid	20-40 mg/kg IV, may give an additional 20 mg/kg 10 min after loading infusion	Rate of 3-6 mg/kg/min	Unknown	Hyperammonemia, pancreatitis, hepatotoxicity, thrombocytopenia
Levetiracetam	1000-3000 mg IV	Rate of 2-5 mg/kg/min	Unknown	Somnolence, pancytopenia
Midazolam	0.2 mg/kg IV	0.05-0.4 mg/kg/hr continuous infusion	GABA receptor agonist	Respiratory depression, hypotension
Propofol	2-3 mg/kg IV	2-10 mg/kg/hr continuous infusion	Modulation of GABA receptor	Propofol infusion syndrome

Table 1: The frequency and mortality associated with acute and chronic causes of status epilepticus in adults

	Frequency (%)	Mortality (%)
Acute		
Stroke	22%	33%
Metabolic abnormalities	15%	30%
Hypoxia	13%	53%
Systemic infection	7%	10%
Anoxia	5%	71%
Trauma	3%	25%
Drug overdose	3%	25%
CNS infection	3%	0%
CNS haemorrhage	1%	0%
Chronic		
Low concentration of anti-epileptic drugs	34%	4%
Remote symptomatic (eg, tumour, stroke, trauma)	25%	14%
Alcohol misuse	13%	20%
Tumour	7%	30%
Idiopathic	3%	25%

Lancet Neurol 2015

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

(A) With prominent motor symptoms
A. I Convulsive SE (CSE, synonym: tonic–clonic SE)
A. I.a. Generalized convulsive
A. I.b. Focal onset evolving into bilateral convulsive SE
A. I.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. I 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

Trinka et al. Epilepsia, 56(10):1515–1523, 2015

Clinical patterns of GCSE

Overt GCSE

A gradual electroclinical disassociation over time

Subtle GCSE

Thank You