Epilepsy in Cerebral palsy

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진료실에서 발생하는 궁금증

- Cerebral palsy를 가진 환자 중 어떤 환자에서 epilepsy가 발생할까.
- 지금 보이는 이것이 seizure 일까.
- Epilepsy환자는 어떤 치료를 받을까. 항경련제 치료가 최종결과에는 어떤 영향을 미칠까. Seizure가 발달에 영향을 미칠까.
- Cerebral palsy환자가 seizure를 하면 재활치료를 할 수 있을까.
- 재활치료를 받고 있는 환자가 갑자기 seizure를 하면 어떻게 할까.

Epilepsy in cerebral palsy

- Epilepsy presents in 30-40% of patients with cerebral palsy. (Sellier, 2012)

- Epilepsy is related to the underlying brain lesion.
- In term children with cerebral palsy, grey matter lesions are more common.
- 35.5% of hemiplegic cerebral palsy (Tillberg, 2020)

- The first seizure appears within the first 12 months of life in almost 50% of the patients. (Zelnik, 2010)

Risk factor of Epilepsy in cerebral palsy

- Neonatal seizure is a strong predictor for epilepsy in cerebral palsy.
- Presence of brain structural lesions.

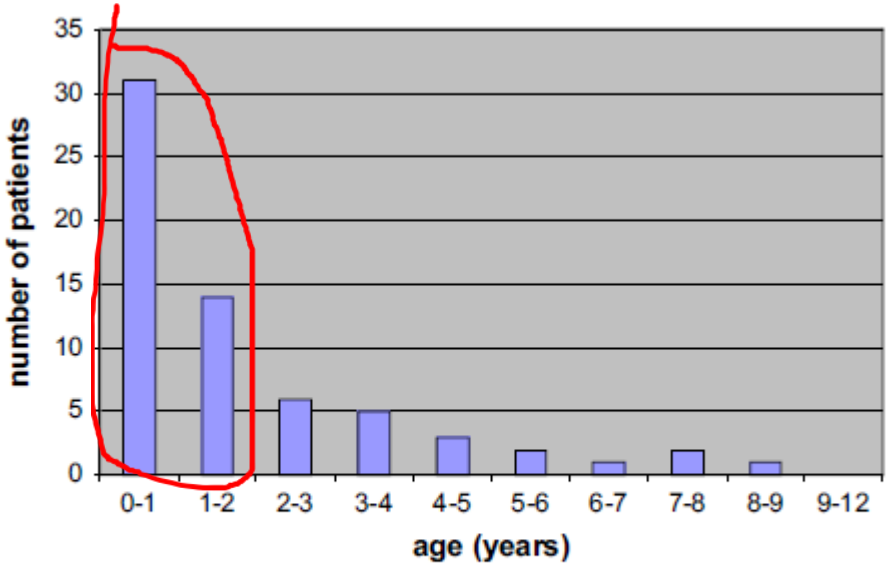

Fig. 1 – The number of patients with epilepsy onset at each age (N = 65).

Zelnik, 2010

Table 2 – The imaging findings in the epileptic and the non-epileptic children.

Imaging findings	CP Only	CP & Epilepsy	Total
Normal imaging	25 (28.7%)	10 (16.4%)	35 (23.6%)
Abnormal Imaging (all findings)	62 (71.3%)	51 (83.6%)	113 (76.4%)
Non-specific atrophy	4 (4.6 %)	11 (18.0%)	16 (10.8%)
Grey matter insult (including infarctions)	14 (16.1%)	17 (27.9%)	31 (21.0%)
White matter insult (including PVL)	16 (18.4%)	4 (11.5%)	23 (15.5%)
Cerebral malformations Dysgenesis	10 (11.5%)	7 (11.5%)	17 (11.5%)
Hydrocephalus	5 (5.7%)	5 (8.2%)	8 (5.4%)
Brain Hemorrhage (including IVH)	13 (14.9%)	7 (11.5%)	20 (13.5%)
Total	87 (100%)	61 (100%)	148 (100%)

Abbreviations: PVL – Periventricular Leukomalacia, and IVH – Intraventricular Hemorrhage.
$p < 0.003$.

Long-term prognosis

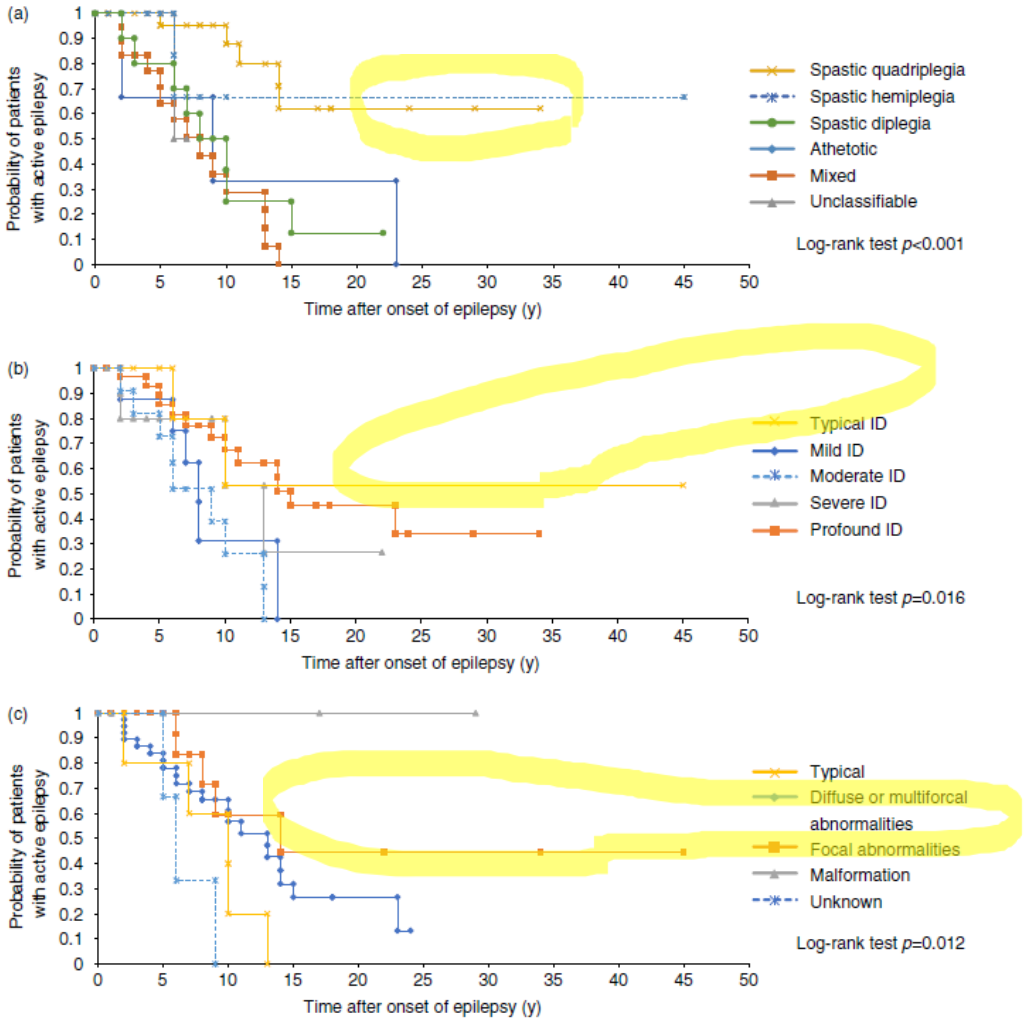

Figure 1: Kaplan–Meier plots showing the proportion of patients with active epilepsy after onset. Each panel demonstrates curves for subgroups of (a) different types of cerebral palsy, (b) cognitive levels, and (c) findings on neuroimaging. ID, intellectual disability. [Colour figure can be viewed at wileyonlinelibrary.com].

Tsibouchi, 2019

Brain imaging

- Publication review from 1995-2012, meta-analysis, review article

- Brain abnormalities were observed in 86% of scans
  - observed least often in children with ataxia (24–57%).

- White matter injury was the most common imaging pattern (19–45%).
- Grey matter injury was in 21% of the patients
- Focal vascular insults (10%), malformations (11%), and miscellaneous findings (4–22%).

Reid, 2013

Brain imaging

- **Cerebral lesion; cerebral cortex, pyramidal tract, extrapyramidal systems, cerebellum**

- **Epileptogenesis is usually associated with cerebral cortex and interaction between cortex and deep cortex**

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BMC Pediatrics

RESEARCH ARTICLE Open Access

Hemiplegic (unilateral) cerebral palsy in northern Stockholm: clinical assessment, brain imaging, EEG, epilepsy and aetiologic background factors

Elsa Tillberg[1*], Bengt Isberg[2] and Jonas K. E. Persson[3]

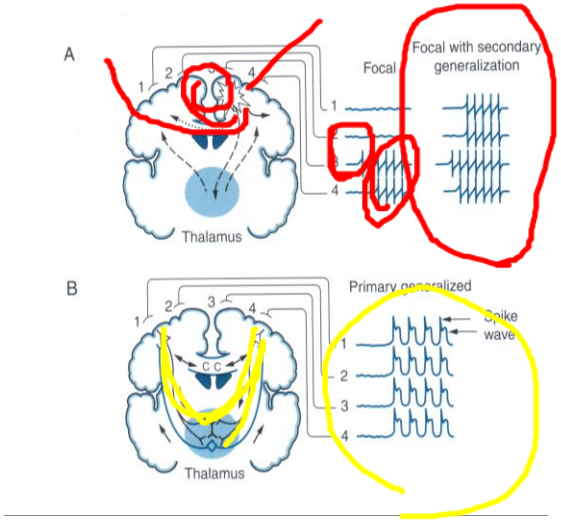


Fig. 1 White matter lesion. Sequelae after periventricular leucomalacia in left parietal lobe, but also in right cerebral hemisphere. Coronal image

Fig. 3 Cortical malformation, polymicrogyri, in right frontal lobe. In addition dilated ventricles. Coronal image

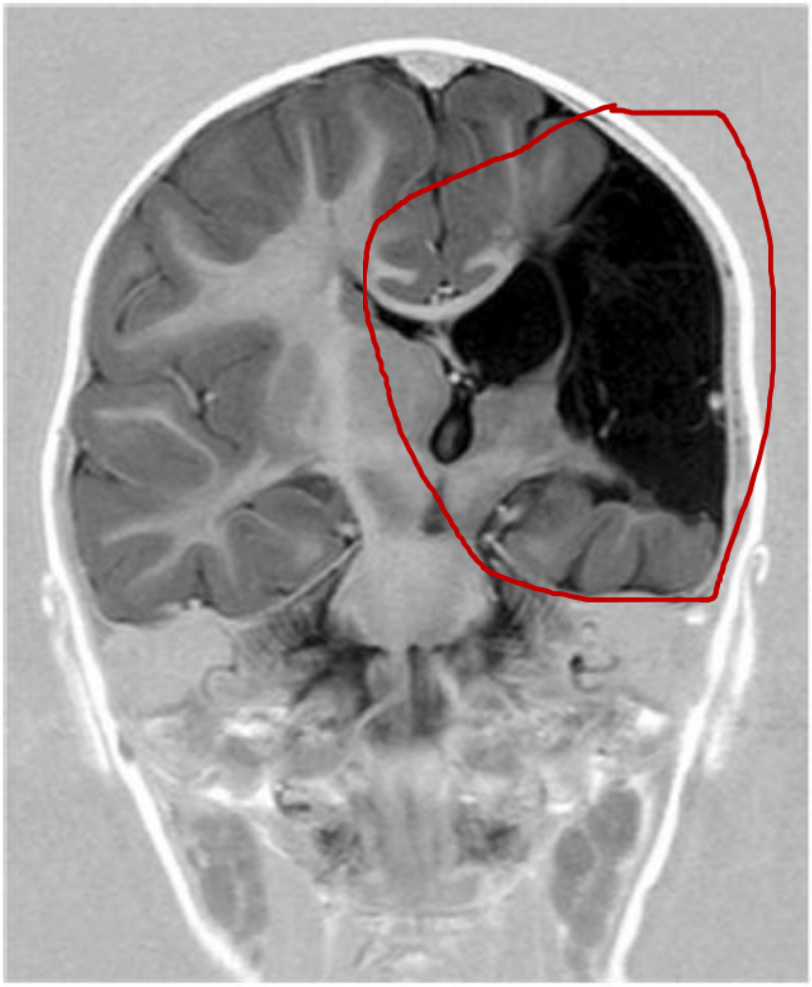


Fig. 2 Sequelae after vascular insult of left middle cerebral artery with major volume loss. Coronal image

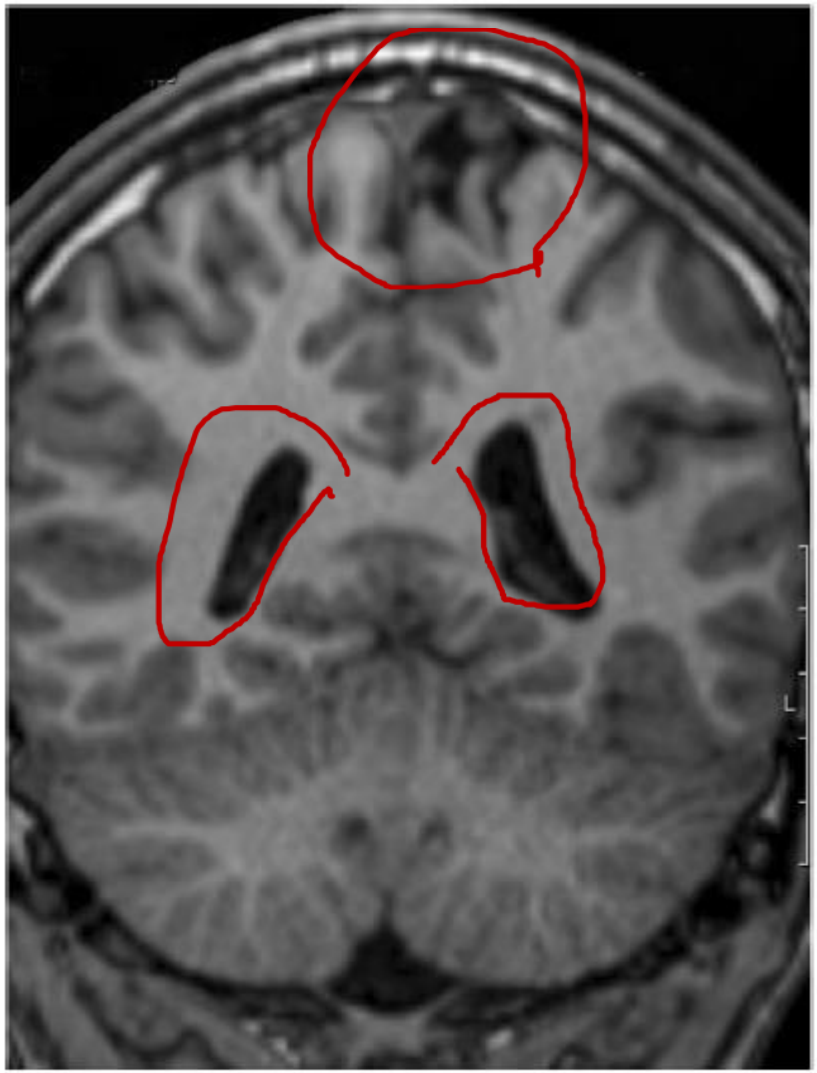


Fig. 4 Combined lesion in white matter and cortex. Coronal image

SEIZURE와 EPILEPSY 개요

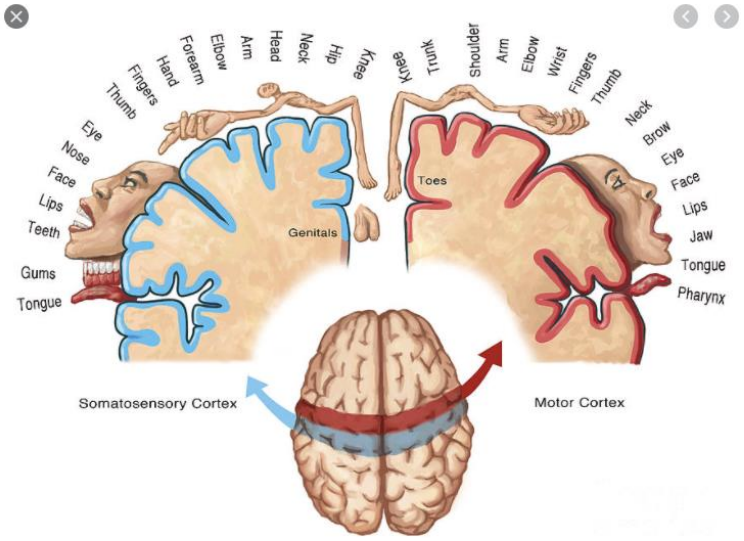
Definitions

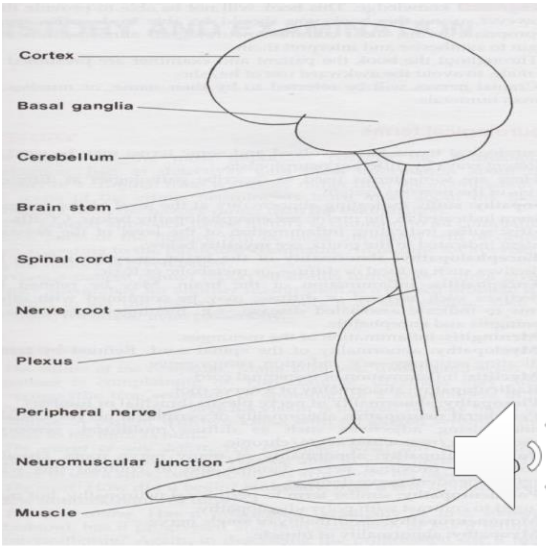
- **Seizure; 발작**

  “ Excessive and disorderly discharges of the cerebral nervous tissue (cortical neuron)”

→ loss of consciousness, alteration of perception or impairment of psychic function, convulsive movements, disturbance of sensation, or some combination

cf. convulsion





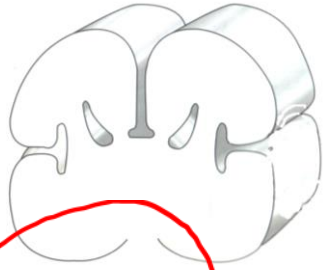
Definitions

- **Epilepsy**, 간질, 뇌전증
  - Diagnosed after two or more unprovoked seizures

Unprovoked

No closely associated concurrent illness, fever, or acute brain injury

cf. **Reflex seizure, stresses related to personal activity**



Classification of Seizures

Partial Seizures

Simple partial seizures
- With motor signs
- With somatosensory or special sensory hallucinations
- With autonomic symptoms
- With psychic symptoms

Complex partial seizures
- Simple partial followed by impairment of consciousness
- With impaired consciousness at onset

Partial seizures evolving to secondary generalized seizures
- Simple partial seizures evolving to generalized
- Complex partial seizures evolving to generalized
- Simple partial seizures evolving to complex partial seizures

Generalized Seizures

Absence seizures
- Atypical absence seizures

Myoclonic seizures

Clonic seizures

Tonic seizures

Tonic-clonic seizures

Atonic seizures

Unclassifiable Epileptic Seizures

Adapted from the Commission on Classification and Terminology of the International League against Epilepsy. Proposal for revised clinical and electroencephalographic classification of epileptic seizures. Epilepsia 1981;22:489.

ILAE 2017 Classification of Seizure Types Expanded Version[1]

Focal Onset

Aware | Impaired Awareness

Motor Onset

- automatisms
- atonic[2]
- clonic
- epileptic spasms[2]
- hyperkinetic
- myoclonic
- tonic

Non-Motor Onset

- autonomic
- behavior arrest
- cognitive
- emotional
- sensory

focal to bilateral tonic-clonic

Generalized Onset

Motor

- tonic-clonic
- clonic
- tonic
- myoclonic
- myoclonic-tonic-clonic
- myoclonic-atonic
- atonic
- epileptic spasms[2]

Non-Motor (absence)

- typical
- atypical
- myoclonic
- eyelid myoclonia

Unknown Onset

Motor

- tonic-clonic
- epileptic spasms

Non-Motor

- behavior arrest

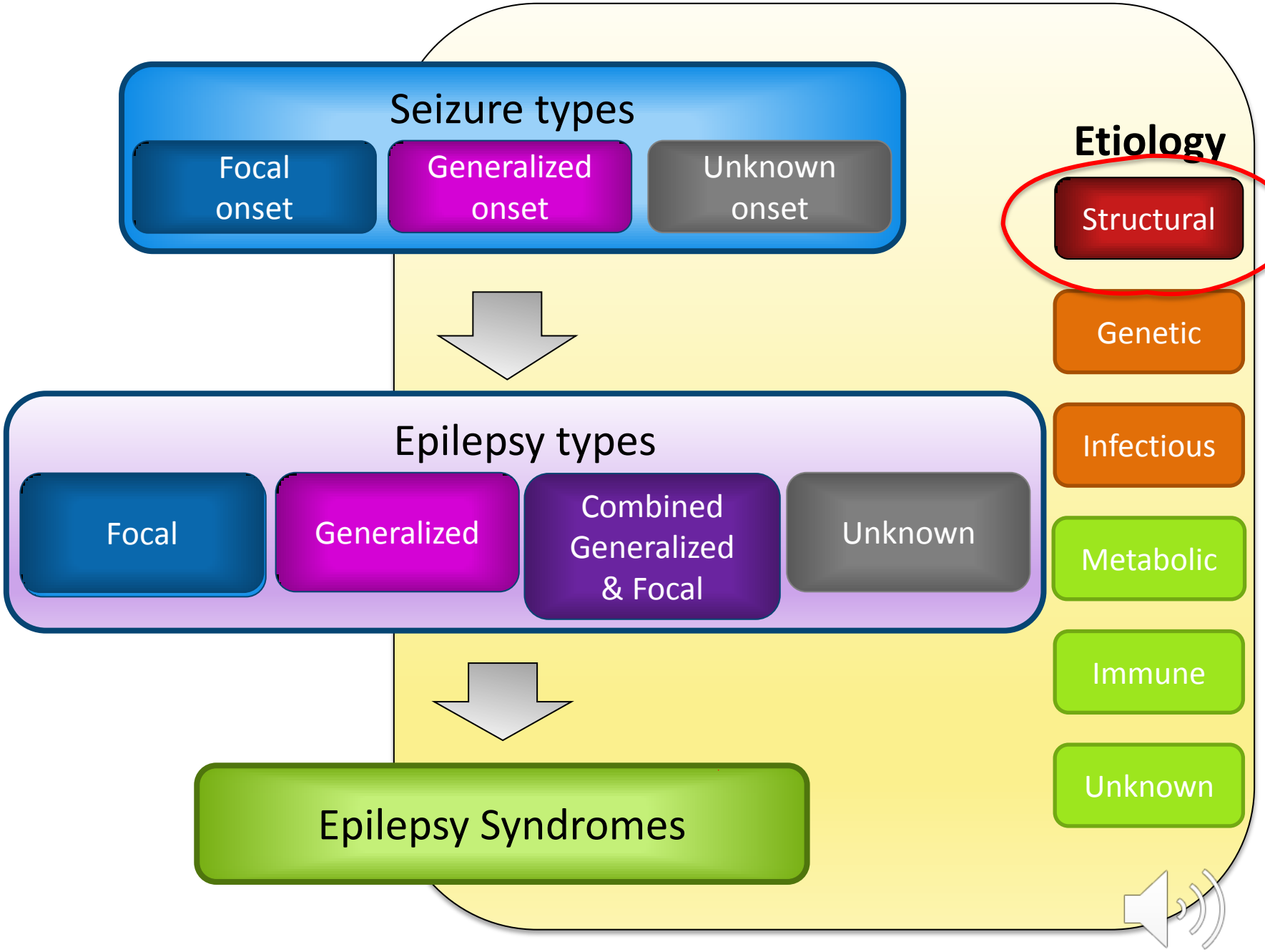
Unclassified[3]

1 Definitions, other seizure types and descriptors are listed in the accompanying paper and glossary of terms.

2 These could be focal or generalized, with or without alteration of awareness

3 Due to inadequate information or inability to place in other categories

From *Fisher et al. Instruction manual for the ILAE 2017 operational classification of seizure types. Epilepsia doi: 10.1111/epi.13671*


Seizure types
Focal onset
Generalized onset
Unknown onset
Epilepsy types
Focal
Generalized
Combined Generalized & Focal
Unknown
Epilepsy Syndromes
Etiology
Structural
Genetic
Infectious
Metabolic
Immune
Unknown

어떤 것이 seizure일까

- Tonus
- Clonus
- Tonic clonic seizure
- Myoclonus
- Atonus
- Spasm –flexor, extensor, tonic

어떤 것이 seizure일까

- 눈을 뜨고 한다.; 눈동자가 같은 리듬으로 움직인다.
- 눈을 감고하면 seizur가 아니다?

- 지속시간이 길다.
- Stereotypic movement
- Tonus → clonus
- Jacksonian march
- Todd paralysis

- 구별하기 어려운 증상
  - Involuntary movement
  - Dystonia

뇌파검사는 무엇에 사용되는가

- Diagnosis of epilepsy
  - Differential diagnosis of paroxysmal neurological events
  - Distinction between a focal and generalized seizure disorder
  - Identification of syndrome specific changes
  - Recognition of photosensitivity

Sensitivity and specificity routine EEG

- **Epileptiform activity**
  - Specific, not sensitive for the diagnosis of epilepsy
  - Sensitivity ranging between 25-56%
  - Specificity ranging at 78-98%

  - 뇌전증파 (epileptiform discharges): associated with seizure disorders at a sufficiently high rate to be of clinical use

  - Abnormalities of background cerebral rhythms, focal slow activity or regional attenuation

    → much less specific than epileptiform activity

EEG - Epilepsy

- Normal EEG does *not exclude* epilepsy
  - Around 10% of patients with epilepsy never show epileptiform discharges.

EEG - Epilepsy

- An abnormal EEG demonstrating interictal epileptiform discharges (IEDs)

  → Not in itself indicate an individual having a seizure disorder

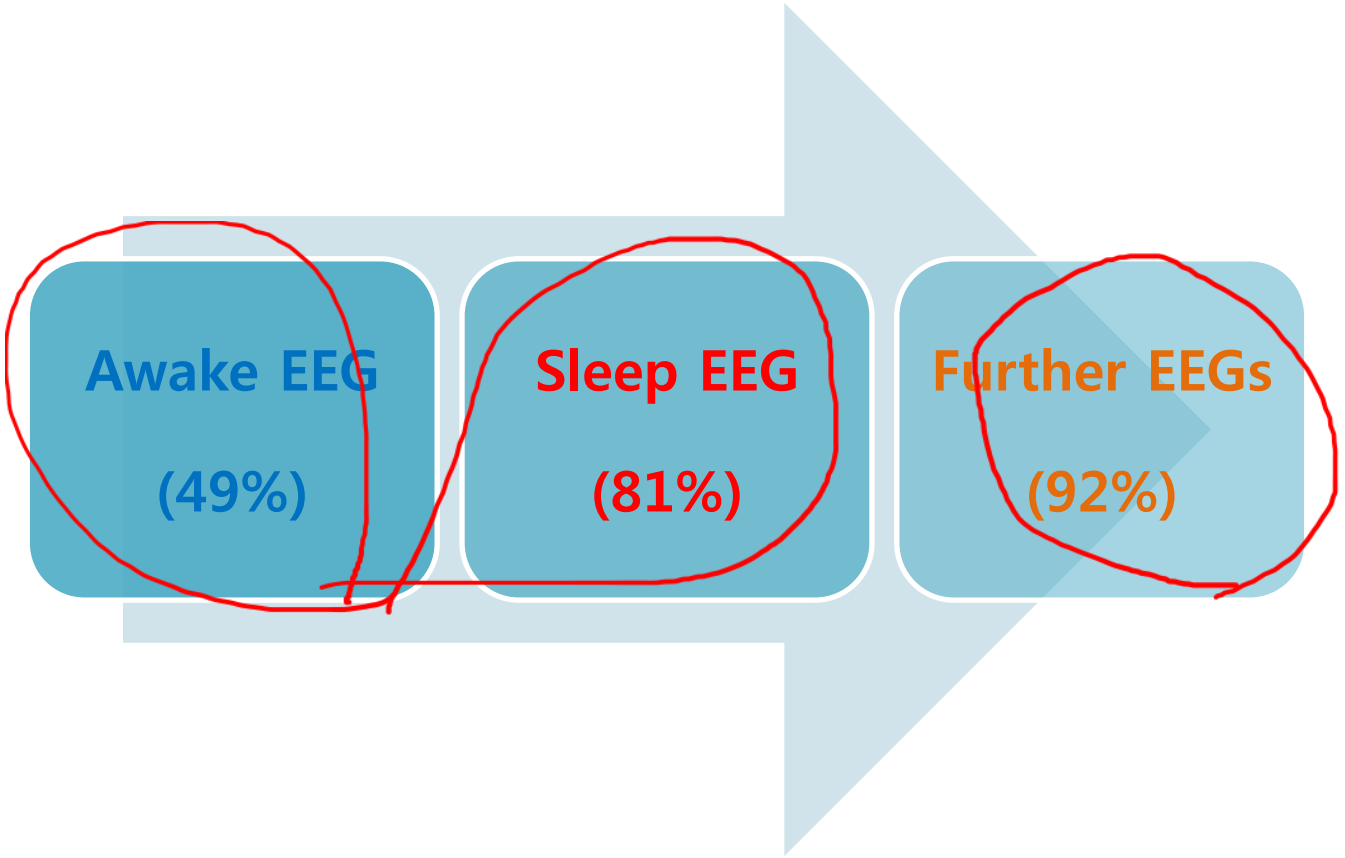
  - IED seen in a small percentage of normal subjects who never develop epilepsy

  - IED found in patients with neurological disorders which are not complicated by epilepsy

EEG - Epilepsy

- IED in non-epileptic subjects
  - Incidence of epileptiform discharges in routine EEG: 0.5%
  - Healthy children/non-epileptic pts. referred to hospital: 2-4%
  - Cerebral pathology such as tumor, prior head injury, cranial surgery, or congenital brain injury: 10-30%

Improving yield



3000 patients with epilepsy, Binnie, 1994

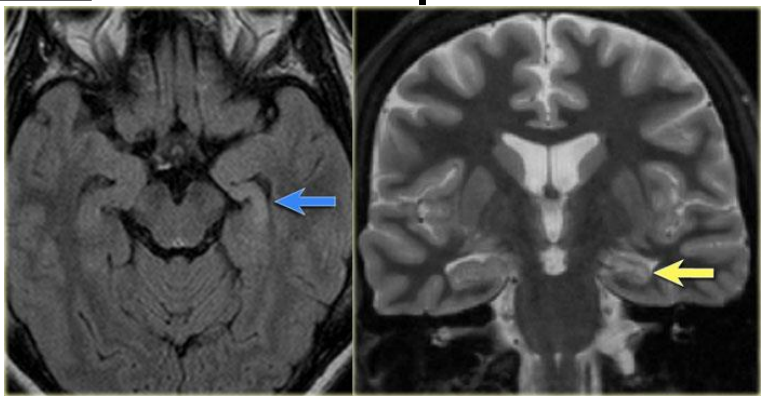
비디오 뇌파검사

- 유용성
  - 긴 시간의 발작간기 뇌파를 얻을 수 있다.
  - 환자가 보이는 다양한 증상이 있을 때 당시의 뇌파를 확인하여 발작여부를 알 수 있다.
  - Focal seizure/generalized seizure의 구분이 가능하다.
  - Area of seizure onset을 확인할 수 있다.
  - 약제의 반응에 대한 정보를 알 수 있다.

- 단점
  - 증상이 없으면 발작간기 뇌파를 확인하는 것에 그친다.
  - 과잉행동 등으로 검사가 어려울 수 있다.

Limitations of EEG

- Incomplete spatial sampling
  - Particularly in basal and mesial areas of the hemispheres
  - Limited temporal sampling



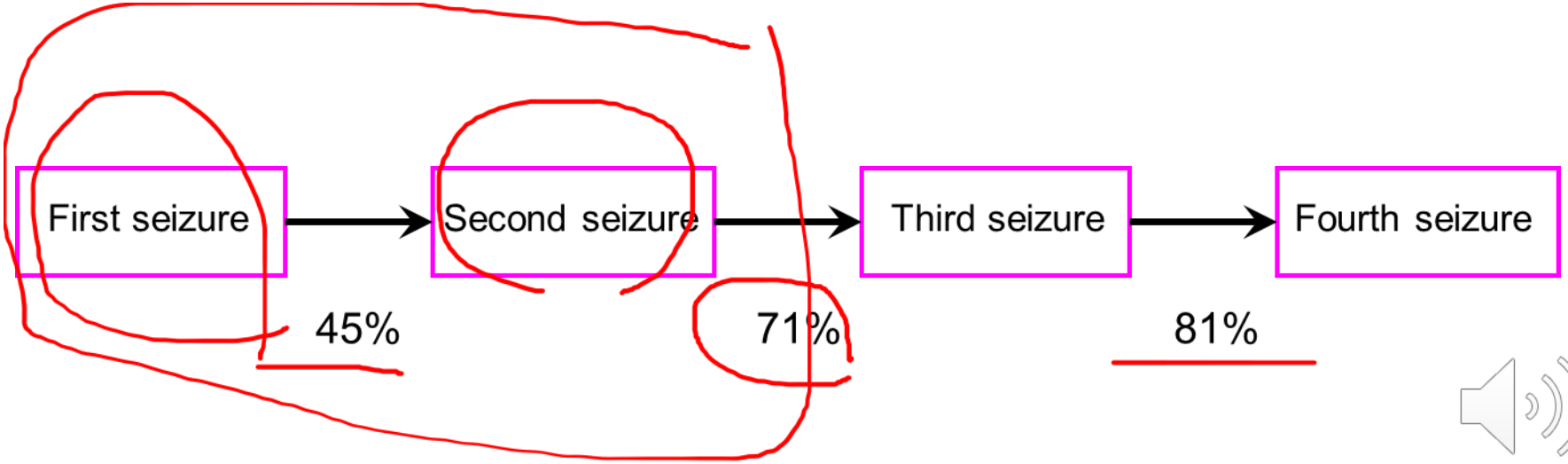
- Relatively short duration of routine interictal EEG
- Not single neuron
- Summation of excitatory and inhibitory postsynaptic potentials in apical dendrites of pyramidal neurons in the more superficial layers of the cortex
- Require activation of large areas of cortex

  (> a few cm^3)

뇌전증의 일반적인 예후는

General prognosis of pediatric epilepsy

- **The majority of childhood epilepsy patients have a good prognosis both in terms of the likelihood of seizure recurrence and of obtaining remission**
- **Some children with epilepsy continue to have seizures into adult life**
- **Once one recurrent seizure, further seizures become likely.** ***(Shinnar S et al., Ann Neurol 2000)***



Risk factors for recurrence

Shinnar study (*Ann Neurol*, 2000)

- **Prospective study including 407 children**
- **Follow-up for mean of 9.6 years**
- **Factors associated with increased risk of recurrence**
  - **Remote onset symptomatic etiology (*RR*=1.7)**
  - **Occurrence of second seizure within 6 months (*RR*=1.7)**

Cerebral palsy

Risk factors for intractability

Berg AT study (Epilepsia, 1996)

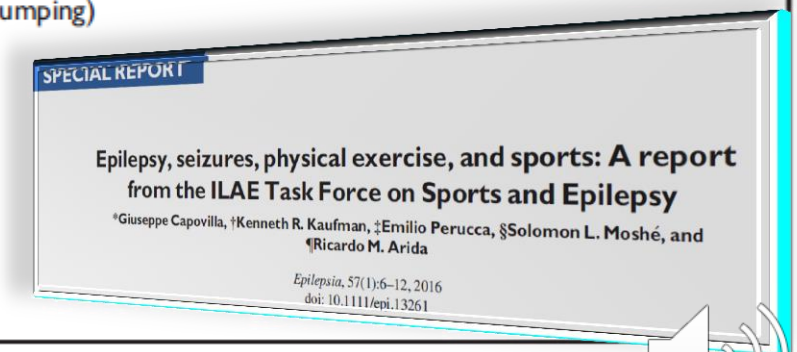
- **Factors predicting intractable epilepsy at the time of initial diagnosis.**
  - **Univariate analysis**
    - **Infantile spasms**
    - **Remote symptomatic epilepsy**
    - **History of status epilepticus before the diagnosis of epilepsy**
    - **Neonatal seizures**
    - **Microcephaly**
    - **Younger age at onset.**

발작이 있는데 재활치료를 할 수 있을까

Physical activity in people with epilepsy

Table 1. Categorization of sports by level of risk of injury or death for PWEs, or for bystanders, should a seizure occur during the event

Group 1 sports (no significant additional risk)	Group 2 sports (moderate risks to the PWEs but not to bystanders)	Group 3 sports (high risk for PWEs, and, for some sports, also for bystanders)
Athletics (except for sports listed under group 2)	Alpine skiing	Aviation
Bowling	Archery	Climbing
Most collective contact sports (judo, wrestling, etc.)	Athletics (pole vault)	Diving (platform, springboard)
Collective sports on the ground (baseball, basketball, cricket, field hockey, football, rugby, volleyball, etc.)	Biathlon, triathlon, modern pentathlon	Horse racing (competitive)
Cross-country skiing	Canoeing	Motor sports
Curling	Collective contact sports involving potentially serious injury (e.g., boxing, karate, etc)	Parachuting (and similar sports)
Dancing	Cycling	Rodeo
Golf	Fencing	Scuba diving
Racquet sports (squash, table tennis, tennis, etc.)	Gymnastics	Ski jumping
	Horse riding (e.g., Olympic equestrian events—dressage, eventing, show jumping)	Solitary sailing
	Ice hockey	Surfing, wind-surfing
	Shooting	
	Skateboarding	
	Skating	
	Snowboarding	
	Swimming	
	Water skiing	
	Weightlifting	



The categorization was done by consensus, taking into account the most common conditions that are likely to apply when PWEs practice these sports. We recognize that some sports fall in a gray zone, and that there are specific individual characteristics or circumstances for which a different categorization would be indicated, based on the judgment of the physician.

Table 2. Suggestions of physical activities/sports participation for PWEs or with othe

	One or more symptomatic seizures	Single unprovoked seizure	Seizure-free (12 months or longer)	Sleep-related seizures only	Seizures without impaired awareness	Seizures with impaired awareness
Group 1 sports	Permitted	Permitted	Permitted	Permitted	Permitted	Permitted at neurologist's discretion applies when seizures are precipitated by specific activities
Group 2 sports	Permitted at neurologist's discretion, with restrictions (see text)	Permitted after 12 months of seizure freedom[a]	Permitted	Permitted at neurologist's discretion, with restrictions (see text)	Permitted at neurologist's discretion, with restrictions (see text)	Permitted at neurologist's discretion, with restrictions (see text)	Permitted	Permitted after appropriate periods following AED cessation (see text)[a]
Group 3 sports	Permitted at neurologist's discretion, with restrictions (see text)	Permitted after 12 months of seizure freedom[a]	Permitted	Generally barred, but may be considered, with restrictions, at neurologist's discretion, for sports posing no risk to bystanders (see text)	Generally barred, but may be considered, with restrictions, at neurologist's discretion, for sports posing no risk to bystanders (see text)	Generally barred, but may be considered, with restrictions, at neurologist's discretion for sports posing no risk to bystanders (see text)	Permitted	Permitted after appropriate periods following AED cessation (see text)[a]

발작이 있는데 재활치료를 할 수 있을까

- 넘어질 우려가 없는 발작을 가진 환자는 대부분의 재활운동이 가능할 것으로 판단됩니다.

- Seizure with impaired awareness의 경우,
  일반적으로 2일 이후에는 증상이 재발하지 않으나,
  발작의 빈도에 따라 다릅니다.
- 환자의 발작 양상과 빈도에 따른 개별화된 발작위험도를 판단하는 것이 필요합니다.

- 운동이 발작을 유발한다는 근거는 없습니다.

- 발작의 주된 유발요인은
  - 항경련제의 중단
  - 수면부족 및 수면주기의 변화
  - 발열

발작이 발생하면 대처하는 방법

『발작의 응급처치는 어떻게 하나요?』

주변 에서 발작하는 환자를 목격하게 되면 일단 환자가 숨을 쉬고 있는지 확인하고 발작이 멈출 때까지 환자가 다치지 않도록 안전하게 유지하는 것이 중요합니다. 환자의 안전을 위하여 다음의 사항들을 유의하여 침착하게 대처해야 합니다.

- 주변에 뾰족하거나 단단해서 환자를 다치게 할 수 있는 것들을 치워야 합니다.
- 발작 중인 환자를 누르거나 팔다리를 억지로 붙잡지 않도록 합니다.
- 숨쉬기 편하도록 목 주위의 넥타이나 단추를 풉니다. 허리띠를 느슨하게 해줍니다.
- 환자의 몸을 모로 눕게 하여 환자를 옆으로 눕혀 혀가 기도를 막지 않고 숨쉬기 편하게 해야 합니다.
- 손가락을 입안에 넣어 억지로 입을 벌리려 하지 말아야 합니다.
- 손가락을 바늘로 찌르거나 복합 따거나 해서는 안됩니다.
- 발작이 끝날 때까지 옆에서 대기하여 예기치 못한 일에 대비해야 합니다.
- 상비약 등을 입으로 투여하면 흡인성 폐렴이나 기도폐색을 일으킬 수 있으므로 절대 하시면 안됩니다.

뇌전증을 앓고 있는 환자에서 발작이 발생했을 때 곧장 응급실에 가야 하는 것은 아닙니다.
대부분 몇 분이 경과하면 자연적으로 회복되기 때문입니다. 그러나 하루에도 수회이상 발작이 계속 반복되거나 의식의 회복 없이 30분 이상 지속되면 뇌전증지속증이라는 매우 위급한 상황이므로 즉시 응급실로 가서 적절한 치료를 받아야 합니다.

- 발작은 대부분 3-5분 이내에 멈춥니다.
- 입안의 분비물이 환자의 기도를 막지 않도록 옆으로 눕히거나 고개를 돌리세요.

요약

- Epilepsy presents in 30-40% of patients with cerebral palsy.
- The first seizure appears within the first 12 months of life in almost 50% of the patients.
- Neonatal seizure is a strong predictor for epilepsy in cerebral palsy. Presence of brain structural lesions (esp. grey matter lesion) is associated with epilepsy.
- More than 50% of the patients have continued epilepsy over 3 years and the relapse rate is about 15-27.1% per 100 persons-years.
- Most of the rehabilitation treatment could be provided, the indication can be discussed based on the basal frequency and type of seizure.