DEFINITION AND CLASSIFICATION OF EPILEPSY

KAMORNWAN KATANYUWONG MD.

4th epilepsy camp 2013 : Ayutthaya

OUTLINE

- Definition of epilepsy
  Definition of seizure
- Epilepsy classification
- Test your recent memory….

DEFINITION OF EPILEPSY

SEIZURE

- **Greek** : meaning ***to take hold***
- **Modern** : sudden and severe event
- **Seizure = epileptic seizure**
- *Cardiology : heart seizure*

Glossary of Descriptive Terminology for Ictal Semiology:
Report of the ILAE Task Force on Classification and Terminology

Warren T. Blume—Chair, Hans O. Lüders, Eli Mizrahi, Carlo Tassinari, Walter van Emde Boas, and Jerome Engel, Jr., Ex-officio

Epilepsia 2001

Special Article

Epileptic Seizures and Epilepsy: Definitions Proposed by the International League Against Epilepsy (ILAE) and the International Bureau for Epilepsy (IBE)

Epilepsia 2005

An Operational Clinical Definition of Epilepsy

Fisher RS[1], Acevedo C[2], Arzimanoglou A[3], Bogacz A[4], Cross JH[5], Elger C[6], Engel JJ, Jr[7], French JA[8], Glynn M[9], Hesdorffer DC[10], Lee B-I[11], Mathern G[12], Moshé SL[13], Perucca E[14], Scheffer IE[15], Tomson T[16], Watanabe M[17], Wiebe S[18]

ILAE website 2013

2001

I GENERAL TERMS

1.0 SEMIOLOGY
That branch of linguistics concerned with signs and symptoms.

2.0 EPILEPTIC SEIZURE
Manifestation(s) of epileptic (excessive and/or hypersynchronous), usually self-limited activity of neurons in the brain.

3.0 ICTUS
A sudden neurologic occurrence such as a stroke or an epileptic seizure.

4.0 EPILEPSY

a) Epileptic Disorder: A chronic neurologic condition characterized by recurrent epileptic seizures.
b) Epilepsies: Those conditions involving chronic recurrent epileptic seizures that can be considered epileptic disorders.

2005: EPILEPSY

- A disorder of the brain characterized by enduring predisposition to generate epileptic seizure
- Usually practically applied as having 2 unprovoked seizures more than 24 hours apart

2013: EPILEPSY

A **disease** of the brain defined by any of the following conditions

1. At least 2 unprovoked seizures occurring more than 24 hours apart
2. One unprovoked seizure and a probability of further seizures similar to the general recurrence risk after two unprovoked seizures (approx 75% or more)

No longer present ≠ cure

2013: EPILEPSY

Epilepsy is considered **to be no longer present** for

- individuals who had an age-dependent epilepsy syndrome but are now past the applicable age or
- those who have remained seizure-free for at least 10 years off AEDs
- No known risk factors associated with a high probability (≥ 75%) of future seizure

2013

- Cure = disappearance
- Remission = abeyance of a disease
- " no longer present" = the person no longer has epilepsy, although it does not guarantee that it will not return

2005

Table 1: Conceptual Definition of Seizure and Epilepsy – 2005 Report

An **epileptic seizure** is a transient occurrence of signs and/or symptoms due to abnormal excessive or synchronous neuronal activity in the brain.

Epilepsy is a disorder of the brain characterized by an enduring predisposition to generate epileptic seizures, and by the neurobiological, cognitive, psychological, and social consequences of this condition. The definition of epilepsy requires the occurrence of at least one epileptic seizure.

2005: ELEMENTS OF A DEFINITION OF EPILEPSY

- History of at least one seizure
- Enduring alteration in the brain that increase the likelihood of future seizures
- Associated neurobiologic, cognitive, psychological and social disturbances

2013

- Epilepsy presents after 2 unprovoked seizures occurring at least 24 hours apart (Hauser et al 1991)
- After 2 unprovoked non-febrile seizure, the chance of having another is 73% (Hauser et al 1998) at 4 years
- After a single unprovoked seizure, the chance of having another is 40-52% (Berg&Shinnar 1991)

2013

Q: Why 24 hours apart ?

A: if seizures clustering within 24 hours
⇨risk factor for later seizures = risk after a single seizure

2013

- Stroke, CNS infection and trauma is important
- If the patient has a single unprovoked seizure after a remote brain insult ⇨ risk of a second unprovoked seizure = risk for further seizures after two unprovoked seizures

2013

- Some patient with a single unprovoked seizure in a circumstance of an epilepsy syndrome
  - ⇨ high risk of recurrence
  - ⇨ epilepsy

NEW DEFINITION

- ? Affect prevalence of epilepsy
- Making the clinicians more comfortable in initiating treatment after some unprovoked seizures
- Required specialized diagnostic and interpretative skills- esp in ***assessing recurrence risks*** or in ***diagnosing syndromes***

CLASSIFICATION

WHY CLASSIFICATION IS NEEDED ?

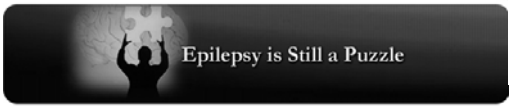
- A universal vocabulary that facilitated communication among clinicians
- Also established a taxonomy foundation for the research on epilepsy

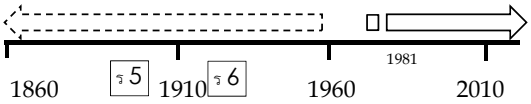
In general

TYPES OF CLASSIFICATION

- Biology:
- Etiology: 1^0 (idiopathic) or 2^0 (symptomatic)
- Pathology: Cancer
- Imaging: Cortical dysplasia
- Clinical criteria e.g. age onset, disease course, distribution of symptoms: HA
- Mixed:

OVER THE PAST 150 YEARS





COMMISSION ON CLASSIFICATION AND TERMINOLOGY OF ILAE

- Classification of Epileptic Seizures in 1981
- Classification of Epilepsies and Epileptic syndromes in 1989
- A proposed diagnostic scheme for people with epileptic seizures and with epilepsy : Report of the ILAE Task Force on Classification and Terminology in 2001
- ….2006,……2010

2010…2013…WINNER

ILAE CLASSIFICATION WORKING GROUP

2005-2009

Epilepsia, 51(4):676–685, 2010
doi: 10.1111/j.1528-1167.2010.02522.x

SPECIAL REPORT

Revised terminology and concepts for organization of seizures and epilepsies: Report of the ILAE Commission on Classification and Terminology, 2005–2009

*†Anne T. Berg, ‡Samuel F. Berkovic, §Martin J. Brodie, ¶Jeffrey Buchhalter, #**J. Helen Cross, ††Walter van Emde Boas, ‡‡Jerome Engel, §§Jacqueline French, ¶¶Tracy A. Glauser, ##Gary W. Mathern, ***Solomon L. Moshé, †Douglas Nordli, †††Perrine Plouin, and ‡Ingrid E. Scheffer

THE CLASSIFICATION CRITERIA OF

Epilepsies (Merlis 1970)	Epileptic seizures (Gastuat 1970)
• Clinical criteria Seizures Neurologic status Age of onset Etiology • EEG criteria Interictal EEG Ictal EEG	• Clinical seizure type • EEG seizure type • EEG interictal expression • Anatomical substrate • Etiology • Age

ILAE 1981

Clinical seizure type | EEG sz type | EEG interictal expression

1. Partial (focal, local) seizures
- Simple partial sz
  - with motor signs
  - with somatosensory symptoms
  - with autonomic symptoms and signs
  - with psychic symptoms
- Complex partial sz
  - start with SPS followed by impairment of consciousness
  - with impairment of consciousness at onset
- Partial sz evolving to 2^0 gen sz
  - SPS → GTC
  - CPS → GTC
  - SPS → CPS → GTC

2. Generalized sz (convulsive and non-convulsive)
Absence, Myoclonic, Clonic, Tonic, Tonic-clonic, Atonic

3. Unclassified epileptic sz

4. Prolonged or repetitive seizure (status epilepticus)

ILAE 1989

1. Localization-related epilepsies and syndromes

1.1 Idiopathic
- benign childhood epilepsy with centro-temporal spike
- childhood epilepsy with occipital paroxysms
- primary reading epilepsy

1.2 Symptomatic e.g. TLE, FLE, PLE, OLE

1.3 Cryptogenic

ILAE 1989

2. Generalized epilepsies and syndromes

2.1 Idiopathic (with age-related onset, listed in order to age)
- Benign neonatal familial convulsions
- Benign neonatal convulsions
- Benign myoclonic epilepsy of infancy
- Childhood absence epilepsy (pyknolepsy)
- Juvenile absence epilepsy
- Juvenile myoclonic epilepsy
- Epilepsy w grand mal (GTCS) sz on awakening
- etc.

2.2 Cryptogenic or symptomatic (in order to age)
- West syndrome
- Lennox-Gastaut syndrome
- Epilepsy w myoclonic-astatic sz
- Epilepsy w myoclonic absences

ILAE 1989

2. Generalized epilepsies and syndromes

2.3 Symptomatic

2.3.1 Non specific etiology
- EME
- EIEE w supression burst
- other symptomatic generalised epilepsies not defined above

2.3.2 Specific syndromes/etiologies
- Cerebral malformation
- IBEM

3. Epilepsies and syndromes undetermined whether focal or generalized e.g. SMEI, LKS, CSWS, neonatal sz

4. Special syndromes e.g. FC, reflex epilepsy, isolated sz

TWO DICHOTOMIES, A 4-PART CLASSIFICATION

Cryptogenic
Special syndromes

	Localization-related	Generalized
Idiopathic	Localization-related Idiopathic **IPE**	Generalized Idiopathic **IGE**
Symptomatic	Localization-related Symptomatic **SPE**	Generalized Symptomatic **SGE**

ILAE 1989

1. **Localization-related epilepsies and syndromes**
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TWO DICHOTOMIES, A 4-PART CLASSIFICATION

Cryptogenic
Special syndromes

	Localization-related	Generalized
Idiopathic	Localization-related idiopathic IPE	Generalized idiopathic IGE
Symptomatic	Localization-related Symptomatic SPE	Generalized Symptomatic SGE

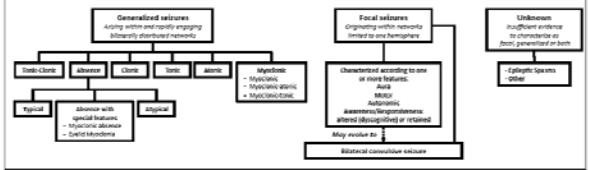
2001

Axis 1: ictal phenomenology
Axis 2: Seizure type
Axis 3: Epileptic syndromes
Axis 4: Etiology
Axis 5: Impairment

I

ILAE Proposal for Revised Terminology for Organization of Seizures and Epilepsies 2010

Classification of Seizures



Changes in terminology and concepts

New Term and Concept	Examples	Old Term and Concept
Etiology		
Genetic: genetic defect directly contributes to the epilepsy and seizures are the core symptom of the disorder	Channelopathies, Glut1 deficiency, etc.	**Idiopathic:** presumed genetic
Structural-metabolic: caused by a structural or metabolic disorder of the brain	Tuberous sclerosis, cortical malformations, etc.	**Symptomatic:** secondary to a known or presumed disorder of the brain
Unknown: the cause is unknown and might be genetic, structural or metabolic		**Cryptogenic:** presumed symptomatic
Terminology	Terms no longer recommended	
Self-limited: tendency to resolve spontaneously with time **Pharmacoresponsive:** highly likely to be controlled with medication		**Benign** **Catastrophic**
Focal seizures: seizure semiology described according to specific subjective (auras), motor, autonomic, and dyscognitive features		**Complex partial** **Simple partial**
Evolving to a bilateral convulsive seizure: eg, tonic, clonic, tonic-clonic		**Secondarily generalized**

old

New

Table 1. Comparison of major changes between the 1989 and 1981 Classification and Terminology and the newly proposed Terminology and Concepts (Commission 1981, 1989; Berg et al., 2010)

Old terminology and concepts	Recommended new terminology and concepts
Focal and generalized	
For seizures	
Focal (previously "partial"): the first clinical and electroencephalographic changes indicate initial activation of a system of neurons limited to a part of one cerebral hemisphere	Focal seizures are conceptualized as originating at some point within networks limited to one hemisphere
Generalized: the first clinical changes indicate initial involvement of both hemispheres	Generalized seizures are conceptualized as originating at some point within and rapidly engaging bilaterally distributed networks
For epilepsies	
Localization-related (focal, partial): epilepsies with focal seizures	These terms were abandoned as overarching categories for classifying epilepsies per se, as many syndromes include both seizure types; they may still apply in some but not all instances
Generalized: epilepsies with generalized seizures	

- The use of generalized and partial (focal) to refer to the underlying was abandoned
- But the terms were retained in reference to mode of seizure initiation and presentation

focal seizure should be described according to their manifestation

I

ILAE Proposal for Revised Terminology for Organization of Seizures and Epilepsies 2010

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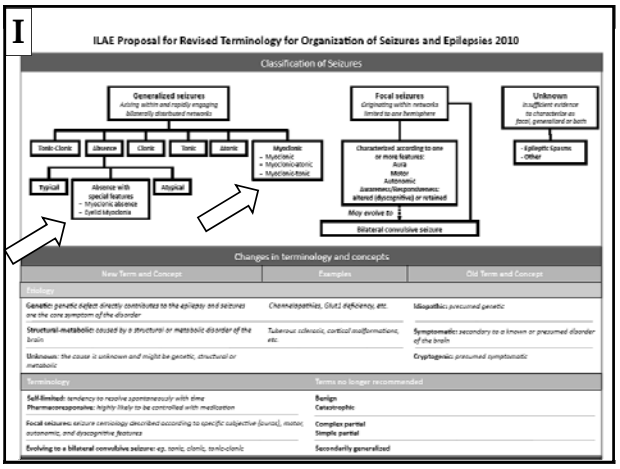
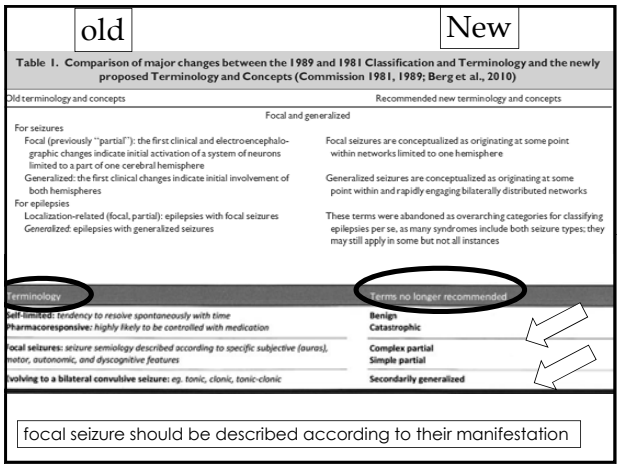


old New



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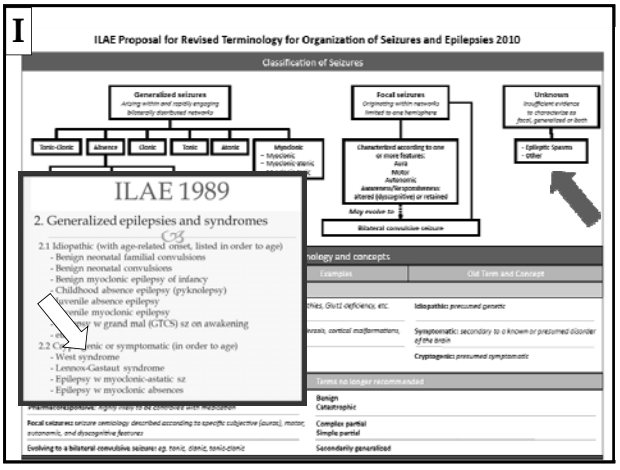
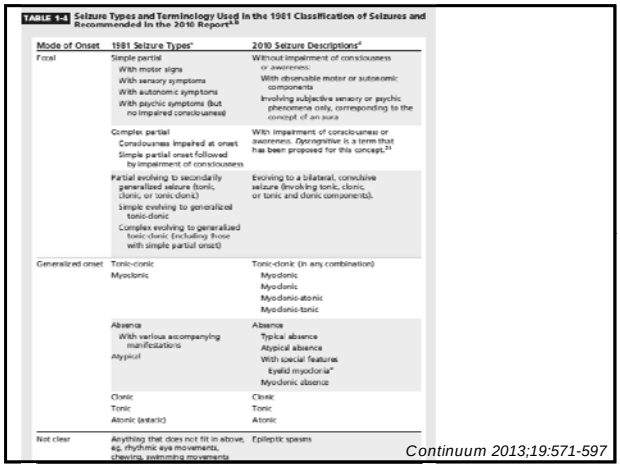
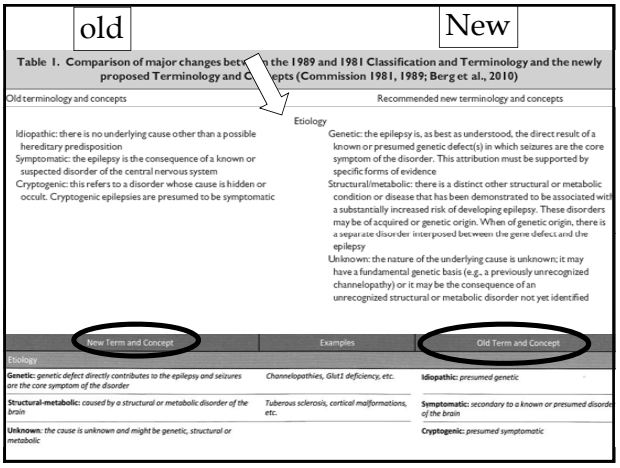




Continuum 2013;19:571-597

old New



old New

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Old terminology and concepts	Recommended new terminology and concepts
Etiology	
Idiopathic: there is no underlying cause other than a possible hereditary predisposition	Genetic: the epilepsy is, as best as understood, the direct result of a known or presumed genetic defect(s) in which seizures are the core symptom of the disorder. This attribution must be supported by specific forms of evidence
Symptomatic: the epilepsy is the consequence of a known or suspected disorder of the central nervous system	
Cryptogenic: this refers to a disorder whose cause is hidden or	Structural/metabolic: there is a distinct other structural or metabolic

Structural/metabolic: proven to be associated with and increased risk of developing epilepsy, include stroke, trauma, infection or may be genetic origin (TSC)

unrecognized structural or metabolic disorder not yet identified

New Term and Concept	Examples	Old Term and Concept
Etiology		
Genetic: *genetic defect directly contributes to the epilepsy and seizures are the core symptom of the disorder*	*Channelopathies, Glut1 deficiency, etc.*	**Idiopathic:** *presumed genetic*
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Symptomatic: the epilepsy is the consequence of a known or suspected disorder of the central nervous system	
Cryptogenic: this refers to a disorder whose cause is hidden or occult. Cryptogenic epilepsies are presumed to be symptomatic	Structural/metabolic: there is a distinct other structural or metabolic condition or disease that has been demonstrated to be associated with a substantially increased risk of developing epilepsy. These disorders may be of acquired or genetic origin. When of genetic origin, there is a separate disorder interposed between the gene defect and the epilepsy
	Unknown: the nature of the underlying cause is unknown; it may have a fundamental genetic basis (e.g., a previously unrecognized channelopathy) or it may be the consequence of an unrecognized structural or metabolic disorder not yet identified

Unknown ?

New Term and Concept	Examples	Old Term and Concept
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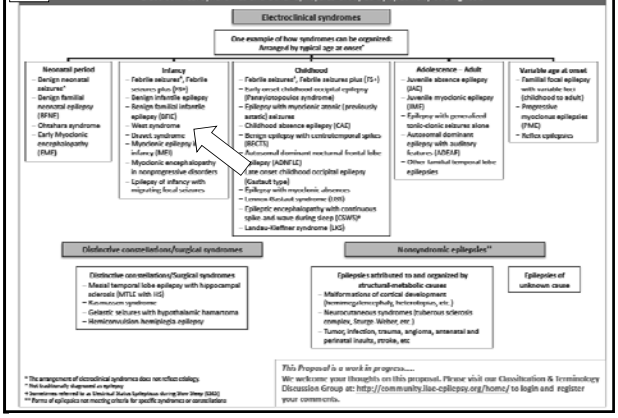
II

ILAE Proposal for Revised Terminology for Organization of Seizures and Epilepsies 2010

Electroclinical Syndromes and Other Epilepsies Grouped by Specificity of Diagnosis



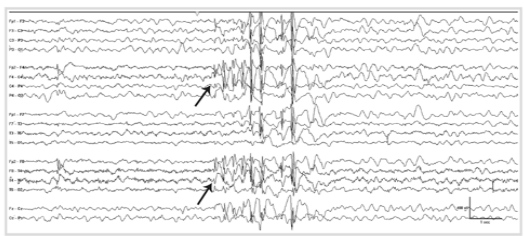
2010

- Classification system versus diagnosis
- 2010 entail little or no change in what health care providers do in daily practice
  (diagnose and treat individual patients)

- CAE : IGE (old)
  : generalized epilepsy, absence, genetic cause (new)

Case 1-1

A 3-year-old boy presented with persistent monthly seizures. Seizure onset was at 4 months old with recurrent hemiclonic seizures and status epilepticus, at times triggered by fever. Initial interictal EEG was significant for rare focal sharp-wave discharges in the right frontal region, and the original



Causes of Epilepsy	Examples of Epilepsy Syndromes or Diseases
Genetic (single gene)*	
Channelopathies (*SCN1A, SCN1B, SCN2A, GABRG1, GABRG2, KCNQ2, KCNQ3, CHRNA4, CHRNB2, CHRNA2, KCNA1, CACNA1A*)	Dravet syndrome; generalized epilepsy with febrile seizures plus; benign familial neonatal convulsions; early myoclonic epilepsy; Ohtahara syndrome; autosomal dominant nocturnal frontal lobe epilepsy; juvenile myoclonic epilepsy; episodic ataxia types 1 and 2
Progressive myoclonic epilepsies (*CLN3, CLN5, CLN6, CLN8, CSTB, CTSD, EPM2A, MERosR, NHLRC1, PPT1, PRICKLE1, TPP1, NEU1, DHPLA*)	Unverricht disease; neuronal ceroid lipofuscinoses; Lafora body disease; sialidosis; dentatorubral pallidoluysian atrophy
Infantile developmental/genetic encephalopathies (*ALDH7A1, ARX, ATP1A2, CDKL5, PCDH19, PNPO, SCN1A, SLC2A1, SLC25A22, SPTAN1, STXBP1, TSC1, TSC2, UBE3A, CNTNAP2, SCL8A6, NRXN1, TCF4, SYN1, PMR1, TTR2, PNKP*)	Early myoclonic epilepsy; Ohtahara syndrome; West syndrome; pyridoxine-dependent epilepsy; glucose transporter type 1 deficiency syndrome; tuberous sclerosis complex; lissencephaly; early-onset absence epilepsy
Malformations of cortical development[†] (hamartomas, lissencephaly, periventricular nodular heterotopias, schizencephaly, double cortex, heterotopias, cobblestone malformation, holoprosencephaly, polymicrogyria, etc.)	Generally associated with nonspecific epilepsy presentation as well as with West and Lennox-Gastaut syndromes. Specific neurologic syndromes are associated with these malformations, eg, Walker-Warburg syndrome, Fukuyama congenital dystrophy
Neurometabolic/mitochondrial (*POLG, SURF1, ADSL*; mitochondrial DNA mutations; *GAMT, PSAP, MMACHC, OTC, PDHA1, PDHB, GALC*)	Generally associated with a nonspecific epilepsy presentation but cause specific neurologic syndromes or conditions, eg, Alper syndrome, Leigh syndrome; adenylosuccinate lyase deficiency; myoclonic epilepsy with ragged red fibers; mitochondrial encephalomyopathy, lactic acidosis, and strokelike episodes; creatine deficiency syndrome; Gaucher disease; cobalamin C deficiency; ornithine transcarbamylase deficiency; pyruvate dehydrogenase deficiency; Krabbe disease
Other genetic (*IGF*; trisomy 21)	Autosomal dominant epilepsy with auditory features (also known as autosomal dominant lateral temporal lobe epilepsy; Down syndrome; Ring chromosome 20
Neoplasms with known or suspected genetic contributions	Dysembryoplastic neuroepithelial tumor; hypothalamic hamartoma; glioma; ganglioglioma; meningioma

TABLE 1-8 Examples of Specific Genes First Associated With One Epilepsy Syndrome and Then Found to be Associated With Very Different Epilepsy Syndromes[a]

Gene (Protein Function)	Associated Electroclinical Syndromes	Brief Description of Syndrome
SCN1A (α-1 subunit of the neuronal voltage-gated sodium channel)	Dravet syndrome[27,28]	Onset <1 y old; multiple seizure types, often prolonged hemiconvulsions; progressive cognitive impairment; EEG evolves from normal to background slowing with admixed multifocal polyspike-wave discharges
	Epilepsy in females with mental retardation[29]	Onset <1 y old (often <6 mo old); focal seizures with prominent autonomic features (apnea, flushing, cyanosis); progressive cognitive impairment; EEG background slowing with admixed multifocal spike-wave discharges
	Generalized epilepsy with febrile seizures plus[30]	Onset in early childhood; may have febrile seizures initially, but continue to have fever-triggered seizures of all types after 6 y old; development may be normal, variable; EEG is normal or abnormal (generalized or multifocal)
SLC2A1 (glucose-transport protein 1)	Severe glucose transporter type 1 (*GLUT1*) deficiency syndrome[31]	Onset in infancy; epileptic encephalopathy with multiple seizure types; progressive cognitive decline; movement disorder; acquired microcephaly; EEG shows background slowing with generalized or multifocal spike-wave discharges
	Early-onset absence[32]	Onset <4 y old; refractory absence seizures; initially normal development, but may decline; EEG shows generalized spike-wave discharges
	Doose syndrome[33,34]	Onset in early childhood; multiple seizure types, but predominantly myoclonic and atonic seizures; development may be normal, variable; EEG background may evolve from normal to diffuse background slowing; generalized polyspike-wave discharges
	Nonsyndromic focal[35]	Epilepsies with predominantly focal electrographic and semiologic manifestations. the features of which do not correspond to any well-delineated electroclinical syndrome; such epilepsies are occasionally found in association with genetic errors that themselves are typically associated with very distinct electroclinical syndromes
KCNQ2 (neuronal potassium channel)	Benign familial neonatal epilepsy[36]	Onset at birth; multiple seizures types; development normal; interictal EEG normal
	KCNQ2 encephalopathy[37]	Onset at birth to first weeks/months; myoclonus or brief tonic seizures as an infant, but seizures usually well controlled by 3 y old; poor neurodevelopmental outcome; EEG background severely abnormal with suppression-burst during infancy and gradually evolves toward normal after several years