Classification of Seizures and Epilepsies, Epileptic Syndromes

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I have no financial relationships to disclose that are relative to the content of my presentation.
Self assessment questions
The diagnosis of epilepsy can be made after

A. Two unprovoked seizures >24 hours apart
B. Two unprovoked seizures <24 hours apart
C. One unprovoked seizure if there is a coexisting brain lesion
D. One provoked seizure and a second unprovoked seizure
Which of the following is not true regarding the distinction between absence seizures and complex partial seizures?

A. The absence of an aura indicates an absence seizure rather than complex partial seizure
B. An absence seizure usually lasts <15 sec, while a complex partial seizure usually lasts >30 sec.
C. The presence of an aura favors complex partial seizure over absence seizure
D. Postictal drowsiness and tiredness favor complex partial seizure
The most recent classification recommended abandoning the following terms except

A. Partial seizures
B. Generalized seizures
C. Complex partial seizure
D. Simple partial seizure
E. Secondarily generalized seizure
Which of the following is a constellation and not a syndrome in the most recent classification?

A. Rasmussen syndrome  
B. Juvenile myoclonic epilepsy (JME)  
C. Progressive myoclonus epilepsies (PME)  
D. Epilepsy with myoclonic absences
Learning objectives

- Review the evolving definition of seizure and epilepsy
- Review the most commonly used classification of seizures and epilepsies
- Review semiology terminology
- Review the new classifications of seizures and epilepsies
- Review the definition of syndromes and constellations
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 neurobiologic, cognitive, psychological, and social consequences of this condition. The definition of epilepsy requires the occurrence of at least one epileptic seizure (controversial).
New ILAE proposal- Operational (Practical) Clinical Definition of Epilepsy

Epilepsy is a disease of the brain defined by any of the following conditions:

- At least two unprovoked seizures occurring more than 24 hours apart.
- One unprovoked seizure and a probability of further seizures similar to the general recurrence risk after two unprovoked seizures (approximately 75% or more).
- At least two seizures in a setting of reflex 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 anti-seizure medicines, provided that there are no known risk factors associated with a high probability (>75%) of future seizures.
Need for classification

- Communication
- Diagnosis
- Study of drug specificity
- Appropriate treatment
- Prognosis
I. Partial (Focal, Local) Seizures
   A. Simple Partial
   B. Complex Partial
   C. Partial evolving to Generalized Tonic Clonic

II. Generalized Seizures
   A. Absence
   B. Myoclonic
   C. Clonic
   D. Tonic
   E. Tonic-Clonic
   F. Atonic

III. Unclassified Epileptic Seizures
I. PARTIAL (FOCAL, LOCAL) SEIZURES

A. Simple partial seizures (consciousness- ie awareness/ responsiveness- not impaired)

B. Complex partial seizures (with impairment of consciousness; may sometimes begin with simple symptomatology)
   1. Simple partial onset followed by impairment of consciousness
      a. with simple partial features (A.1.-A.4.) followed by impaired consciousness
      b. with automatisms
   2. With impairment of consciousness at onset
      a. with impairment of consciousness only
      b. with automatisms

C. Partial seizures evolving to secondarily generalized seizures (This may be generalized tonic-clonic, tonic, or clonic.)
   1. Simple partial seizures (A) evolving to generalized seizures
   2. Complex partial seizures (B) evolving to generalized seizures
   3. Simple partial seizures evolving to complex partial seizures evolving to generalized seizures
Simple Partial Seizures

1. With motor signs [focal motor without march, focal motor with march (Jacksonian), versive, postural, phonatory]

2. With somatosensory or special sensory symptoms (visual, auditory, olfactory, gustatory, vertiginous)

3. With autonomic symptoms / signs (epigastric sensation, pallor, sweating, flushing, piloerection, pupillary dilation)

4. With psychic symptoms (dysphasic, dysmnesic, cognitive, affective, illusions, structured hallucinations)
Revision of classification- Berg et al, 2010

- New terminology and concepts that better reflect the current understanding, while also striving for clarity and simplicity.
- Maintained the division of seizures based on generalized or focal onset but has recommended replacing “partial” with “focal”.
- Updated the definition of focal seizures as “originating within networks limited to one hemisphere,” with the possibility of the seizures being discretely localized or more widely distributed, and possibly originating in subcortical structures.
- Abandoned “simple”, “complex”, and “secondarily generalized”
Revision of classification- Berg et al, 2010

- Generalized seizures were defined as “originating at some point within, and rapidly engaging, bilaterally distributed networks,” which do not necessarily include the entire cortex.

- Revised concepts acknowledge that generalized seizures can be asymmetrical and that individual seizures may appear to have a localized onset, but the location and laterality of that onset will vary from seizure to seizure.
Revised classification of seizures -
Berg et al, 2010

- Generalized seizures
  - Tonic–clonic (in any combination)
  - Absence
    - Typical
    - Atypical
    - Absence with special features
      - Myoclonic absence
      - Eyelid myoclonia
  - Myoclonic
    - Myoclonic
    - Myoclonic atonic
    - Myoclonic tonic
  - Clonic
  - Tonic
  - Atonic

- Focal seizures
  - Unknown
    - Epileptic spasms
Revised classification of seizures- Berg et al, 2010

For focal seizures, the distinction between the different types (e.g., complex partial and simple partial) is eliminated. It is important, however, to recognize that impairment of consciousness/awareness or other dyscognitive features, localization, and progression of ictal events can be of primary importance in the evaluation of individual
Descriptors of focal seizures according to degree of impairment during seizure

- Without impairment of consciousness or awareness
  - With observable motor or autonomic components. This roughly corresponds to the concept of “simple partial seizure. “Focal motor” and “autonomic” are terms that may adequately convey this concept depending on the seizure manifestations).
  - Involving subjective sensory or psychic phenomena only. This corresponds to the concept of an aura, a term endorsed in the 2001 Glossary.

- With impairment of consciousness or awareness. This roughly corresponds to the concept of complex partial seizure.
  - “Dyscognitive” is a term that has been proposed for this concept (Blume et al., 2001).

- Evolving to a bilateral, convulsive seizure (involving tonic, clonic, or tonic and clonic components). This expression replaces the term “secondarily generalized seizure.”
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   A. Simple Partial
   B. Complex Partial
   C. Partial evolving to Generalized Tonic Clonic

II. Generalized Seizures
   A. Absence
   B. Myoclonic
   C. Clonic
   D. Tonic
   E. Tonic-Clonic
   F. Atonic

III. Unclassified Epileptic Seizures
Absence seizures versus Complex partial seizures

<table>
<thead>
<tr>
<th></th>
<th>Absence</th>
<th>Complex partial</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aura</td>
<td>No</td>
<td>May occur</td>
</tr>
<tr>
<td>Onset</td>
<td>Sudden</td>
<td>May be gradual</td>
</tr>
<tr>
<td>Duration</td>
<td>Usually &lt;15 sec</td>
<td>Usually &gt;30 sec</td>
</tr>
<tr>
<td>Termination</td>
<td>Sudden</td>
<td>May be gradual</td>
</tr>
<tr>
<td>Postictal State</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>HV activation</td>
<td>Yes</td>
<td>Usually no</td>
</tr>
</tbody>
</table>
GENERALIZED ABSENCE SEIZURES

- TYPICAL
  - **Simple**: impaired consciousness only
  - **Complex**:
    - mild clonic components
    - atonic components
    - tonic components
    - automatisms
    - autonomic phenomena
    - combinations of the above

- ATYPICAL
Epidemiology by Seizure Type
(from Hauser et al, Epilepsia 1992)
Epilepsy: Classification/Diagnosis Steps

Classify Seizure Type(s) → Classify Epileptic Syndrome → Identify Etiology
ILAE 2001 Diagnostic Scheme

Axes

- **Axis 1**: Ictal phenomenology - can be used to describe ictal events with any degree of detail needed.

- **Axis 2**: Seizure type - (from the List of Epileptic Seizures). Localization within the brain and precipitating stimuli for reflex seizures should be specified when appropriate.

- **Axis 3**: Syndrome - (from the List of Epilepsy Syndromes), with the understanding that a syndromic diagnosis may not always be possible.

- **Axis 4**: Etiology - from a Classification of Diseases Frequently Associated with Epileptic Seizures or Epilepsy Syndromes when possible, genetic defects, or specific pathologic substrates (for symptomatic focal epilepsies).

- **Axis 5**: Impairment - optional, but often useful, additional diagnostic parameter (can be derived from an impairment classification adapted from the WHO ICIDH-2).
Glossary of Seizure Terminology and Other Definitions

- *Ictal semiology:* signs and symptoms associated with seizures.

- *Motor manifestations:* involvement of the musculature, usually with an increase in muscle contraction that produces a movement.
  
  - can also be negative, associated with a decrease in muscle contraction.
  
  - positive motor can be used to specifically indicate an increase in muscle contraction.
**Elementary motor**

- Contraction of muscle or group of muscles that is usually stereotyped and does not include multiple phases.
  - Tonic- sustained increase in muscle contraction lasting up to minutes.
  - Epileptic spasms: sudden flexion and/or extension which is more sustained than a myoclonic jerk but yet very short in duration, affecting predominantly proximal or truncal muscles.
  - Postural manifestation: tonic activity that results in a posture. This will usually involve contraction of more than one muscle.
Elementary motor

- Versive: sustained/forced deviation of eyes or head to one side. May be associated with a truncal rotation.

- Dystonic posturing: sustained contraction resulting in an abnormal posture with a rotator or twisting motion.

- Myoclonic jerk or myoclonus: very brief involuntary contraction usually lasting <100 msec.
  - Negative myoclonus: interruption of tonic muscle activity for less than 500 msec without prior positive contraction. Negative myoclonus may produce a jerk-like motion in association with a transitory loss of posture of that body part. Negative myoclonus would not be visible if the affected body part were resting.
Elementary motor

- Clonic activity: regularly repetitive jerking that is prolonged.
  - without a march: confined to the same body part from beginning to end.
  - Jacksonian march: spreads through contiguous body parts on the same side, reflecting horizontal spread of seizure activity over the motor strip.

- Tonic-clonic activity: sequence of initial tonic posturing that evolves to a clonic phase.

- Atonic activity: sudden decrease or loss of muscle tone usually lasting more than 1 second. This can affect the head, trunk, or limbs, usually bilaterally. Focal atonic activity can also occur.

- Astatic: loss of erect posture; an astatic seizure is synonymous with a drop attack.
Automatisms

- Repetitive motor activities that are more or less coordinated and resemble a voluntary movement but are not purposeful.
- Usually occur in association with altered sensorium, and the individual is usually amnestic to their occurrence.
- Perseverative automatisms: inappropriate continuation of previously ongoing activity.
- De novo automatisms: start after seizure onset.
- Reactive- ex. fumbling with an object that was present or newly placed in the patient’s hand.
Automatisms

- Can be described by affected body part
  - Oroalimentary automatisms- lip smacking, chewing, swallowing, ictal spitting and ictal drinking.
  - Manual or pedal- affect distal extremities. Can be bilateral or unilateral. Manual automatisms can be manipulative (involving picking and fumbling motions, typically reflecting interaction with the environment) or non-manipulative (rhythmic, with no interaction with the environment), mainly RINCH (rhythmic ictal nonclonic hand) movements.
  - Gestural automatisms include extremity movements such as those used to enhance speech.
  - Hyperkinetic automatisms: inappropriately rapid sequence of movements that predominantly involve axial and proximal limb muscles. The resulting motion can be thrashing, rocking, pelvic thrusting, kicking, or bicycling motions.
Automatisms

- Mimetic: facial expressions indicating emotion
- Ambulatory: walking or running (cursive epilepsy), usually avoiding obstacles
- Sexual: include pelvic thrusting and masturbation.
- Verbal: verbal output usually of stereotyped simple phrases such as "Help me", "Don’t let me die", etc..
- Gelastic: abrupt inappropriate laughter or giggling.
- Dacrystic: abrupt inappropriate crying
Sensory phenomena

- Elementary if they involve a single primary sensory modality with unformed phenomena
- Applied predominantly to visual (flickering or flashing lights and other simple patterns such as spots, scotomata, or visual loss) or auditory hallucination (buzzing, ringing, or humming sounds or single tones, but may also be negative, with loss of hearing).
Somatosensory phenomena

- Tingling and other paresthesias; shock-like sensations; numbness; pain; sense of movement or a desire to move a body part.

- Can remain confined to the same body part or could also have a Jacksonian march, reflecting spread of the seizure discharge in the sensory cortex.
Other sensory phenomena

- Olfactory hallucinations most often disagreeable and usually difficult to characterize.
- Variety of gustatory hallucinations can occur, particularly with a metallic taste.
- Cephalic sensation: sensation in the head that can be described as tingling, fullness, pressure, or lightheadedness.
Experiential phenomena

- Affective experiences such as fear, sadness, elation
- Dysmnesic phenomena such as feelings of familiarity (déjà vu) or unfamiliarity (jamais vu)
- Complex hallucination (such as seeing people or hearing music)
- Illusions (alterations of perception)
Dyscognitive

- Describes events in which the predominant feature is alteration of cognition including perception, attention, memory, or executive function.
Autonomic phenomena

- Very common in seizures
- May be subjective, including an epigastric sensation, a feeling of palpitation, or a feeling of flushing
- Can be objective, including pupillary dilation, piloerection, pallor or flushing, nausea, vomiting, flatulence.
Semiological classification of seizures by Lüders et al

- Seizures classified purely by semiology, independent of EEG, MRI
- Spheres affected during seizures
  - Cognitive sphere → aura
  - Autonomic sphere → autonomic seizure
  - Consciousness sphere → dialeptic seizure
  - Motor sphere → motor seizure
Semiologic seizure classification

- Auras
- Autonomic seizures
- Dialeptic seizures
- Motor seizures
- Special seizures
Motor seizures

Simple motor seizures
- Myoclonic
- Tonic
- Epileptic spasms
- Clonic seizures
- Tonic-clonic seizures
- Versive seizures

Complex motor seizures
- Hypermotor seizures
- Automotor seizures
- Gelastic seizures
Special seizures

- Astatic seizures - epileptic falls
- Atonic seizures - cause a loss of postural tone
- Akinetic seizures - Conscious but unable to move
- Negative myoclonic seizures
- Aphasic seizures
- Hypomotor seizures - Immobility or marked decrease in motion
Seizure evolution in semiological classification of seizures

- Evolution is indicated by considering each component of a seizure, listed in order of appearance and linked by arrows. Limit is 4 components- examples:
  - L visual aura → L hand clonic seizure → GTC seizure
  - L visual aura → B asymmetric tonic seizure → L arm clonic seizure
  - Abdominal aura → L hemispheric automotor seizure
  - Olfactory aura → automotor seizure → left versive seizure → generalized tonic-clonic seizure
  - Generalized myoclonic seizure → generalized tonic-clonic seizure
  - Typical dialeptic seizure → generalized tonic-clonic seizure
Definition of Key Terms
ILAE 2001 classification scheme new concepts

- **Epileptic seizure type:** An ictal event believed to represent a unique pathophysiologic mechanism and anatomic substrate. This is a diagnostic entity with etiologic, therapeutic, and prognostic implications.

- **Epilepsy syndrome:** A complex of signs and symptoms that define a unique epilepsy condition. This must involve more than just the seizure type.

- **Epileptic disease:** A pathologic condition with a single specific, well-defined etiology. Thus progressive myoclonus epilepsy is a syndrome, but Unverricht–Lundborg is a disease.
**Definition of Syndrome Categories**

**ILAE 2001 classification scheme**

- **Idiopathic epilepsy syndrome:** A syndrome that is only epilepsy, with no underlying structural brain lesion or other neurologic signs or symptoms. These are presumed to be genetic and are usually age dependent.

- **Symptomatic epilepsy syndrome:** A syndrome in which the epileptic seizures are the result of one or more identifiable structural lesions of the brain.

- **Probably symptomatic epilepsy syndrome:** Synonymous with, but preferred to, the term cryptogenic, used to define syndromes that are believed to be symptomatic, but no etiology has been identified.
Criteria for syndromes

- Epileptic seizure type(s), including
  - Types must occur to diagnose a syndrome
  - Types that may occur but are not necessary for diagnosis
  - Types that would preclude a diagnosis of this syndrome

- Interictal EEG findings that
  - must be observed in order to diagnose the syndrome,
  - may be observed in some cases
  - preclude diagnosis of the syndrome if observed

- Age of onset
  - distinctive range for age of onset
  - How strictly it should be applied for diagnostic purposes
Progressive nature (i.e., epileptic encephalopathy)

Associated interictal signs and symptoms (particularly neurological and neuropsychological status and deficits).

- It is important to distinguish between deficits that are due to the cause of the epilepsy, those that are due to pharmacotherapy, and those that are due to the epilepsy itself (can be difficult).

Pathophysiologic mechanisms, anatomical substrates, and etiological categories

Genetic basis
1. Localization related (Partial, Focal, Local) Epilepsies and Syndromes
   1.1 Idiopathic (with age related onset)
   1.2 Symptomatic
   1.3 Cryptogenic (probably symptomatic)

2. Generalized Epilepsies and Syndromes
   2.1 Idiopathic
   2.2 Cryptogenic or Symptomatic
   2.3 Symptomatic (probably symptomatic)

3. Epilepsies and syndromes undetermined as to whether they are focal or generalized

4. Special syndromes
International Classification of Epilepsies and Epileptic Syndromes  

1. Localization related (Partial, Focal, Local) Epilepsies and Syndromes

1.2 Symptomatic

**Temporal:** Amygdalo-hippocampal
**Frontal:** Supplementary motor
  - Anterior frontopolar
  - Dorsolateral
  - Motor Cortex

1.3 Cryptogenic

**Lateral Temporal**
**Cingulate**
**Orbitofrontal**
**Opercular**
Revised classification - Berg et al, 2010

- Abandoned Localization-related vs generalized. Syndromes were arranged by age at onset.
- Instead of the terms idiopathic, symptomatic, and cryptogenic, the following three terms were recommended:
  - 1. 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.
  - 2. “Structural/metabolic”
  - 3. “Unknown cause”
Syndromes

Electroclinical syndromes: “syndrome” will be restricted to a group of clinical entities that are reliably identified by a cluster of electroclinical characteristics. Patients whose epilepsy does not fit the criteria for a specific electroclinical syndrome can be described with respect to a variety of clinically relevant factors (e.g., known etiology and seizure types). This does not, however, provide a precise (syndromic) diagnosis of their epilepsy.
In addition to the electroclinical syndromes with strong developmental and genetic components to them, there are a number of entities that are not exactly electroclinical syndromes in the same sense but which represent clinically distinctive constellations on the basis of specific lesions or other causes. These are diagnostically meaningful forms of epilepsy and may have implications for clinical treatment, particularly surgery. These include mesial temporal lobe epilepsy (with hippocampal sclerosis), hypothalamic hamartoma with gelastic seizures, epilepsy with hemiconvulsion and hemiplegia, and Rasmussen “syndrome.” Age at presentation is not a defining feature in these disorders, as we understand them; however, they are sufficiently distinctive to be recognized as relatively specific diagnostic entities.
Electroclinical Syndromes and other Epilepsies (Berg et al., 2010)

- Electroclinical syndromes arranged by age at onset (Neonatal period; Infancy; Childhood; Adolescence – Adult; Less specific age relationship)

- Distinctive constellations

- Epilepsies attributed to and organized by structural-metabolic causes

- Epilepsies of unknown cause

- Conditions with epileptic seizures that are traditionally not diagnosed as a form of epilepsy
Neonatal period

- Benign familial neonatal epilepsy (BFNE)
- Early myoclonic encephalopathy (EME)
- Ohtahara syndrome
Infancy

- Epilepsy of infancy with migrating focal seizures
- West syndrome
- Myoclonic epilepsy in infancy (MEI)
- Benign infantile epilepsy
- Benign familial infantile epilepsy
- Dravet syndrome
- Myoclonic encephalopathy in nonprogressive disorders
Childhood

- Febrile seizures plus (FS+) (can start in infancy)
- Panayiotopoulos syndrome
- Epilepsy with myoclonic atonic (previously astatic) seizures
- Benign epilepsy with centrotemporal spikes (BECTS)
- Autosomal-dominant nocturnal frontal lobe epilepsy (ADNFLE)
- Late onset childhood occipital epilepsy (Gastaut type)
- Epilepsy with myoclonic absences
- Lennox-Gastaut syndrome
- Epileptic encephalopathy with continuous spike-and-wave during sleep (CSWS)
- Landau-Kleffner syndrome (LKS)
- Childhood absence epilepsy (CAE)
Adolescence – Adult

- Juvenile absence epilepsy (JAE)
- Juvenile myoclonic epilepsy (JME)
- Epilepsy with generalized tonic–clonic seizures alone
- Progressive myoclonus epilepsies (PME)
- Autosomal dominant epilepsy with auditory features (ADEAF)
- Other familial temporal lobe epilepsies
Less specific age relationship

- Familial focal epilepsy with variable foci (childhood to adult)
- Reflex epilepsies
Distinctive constellations

- Mesial temporal lobe epilepsy with hippocampal sclerosis (MTLE with HS)
- Rasmussen syndrome
- Gelastic seizures with hypothalamic hamartoma
- Hemiconvulsion–hemiplegia–epilepsy
Epilepsies attributed to and organized by structural-metabolic causes

- Malformations of cortical development
- Neurocutaneous syndromes
- Tumor
- Infection
- Trauma
- Angioma
- Perinatal insults
- Stroke
Conditions with epileptic seizures that are traditionally not diagnosed as a form of epilepsy

- Benign neonatal seizures
- Febrile seizures
Self assessment questions
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