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ILAE classification of seizure types and epilepsies 2017

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Talk overview

- **Classification of seizure types and epilepsies by ILAE 2017**

Operational classification of seizure types by the International League Against Epilepsy: Position Paper of the ILAE Commission for Classification and Terminology

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Epilepsia, **(*):1–9, 2017
doi: 10.1111/epi.13670

ILAE classification of the epilepsies: Position paper of the ILAE Commission for Classification and Terminology

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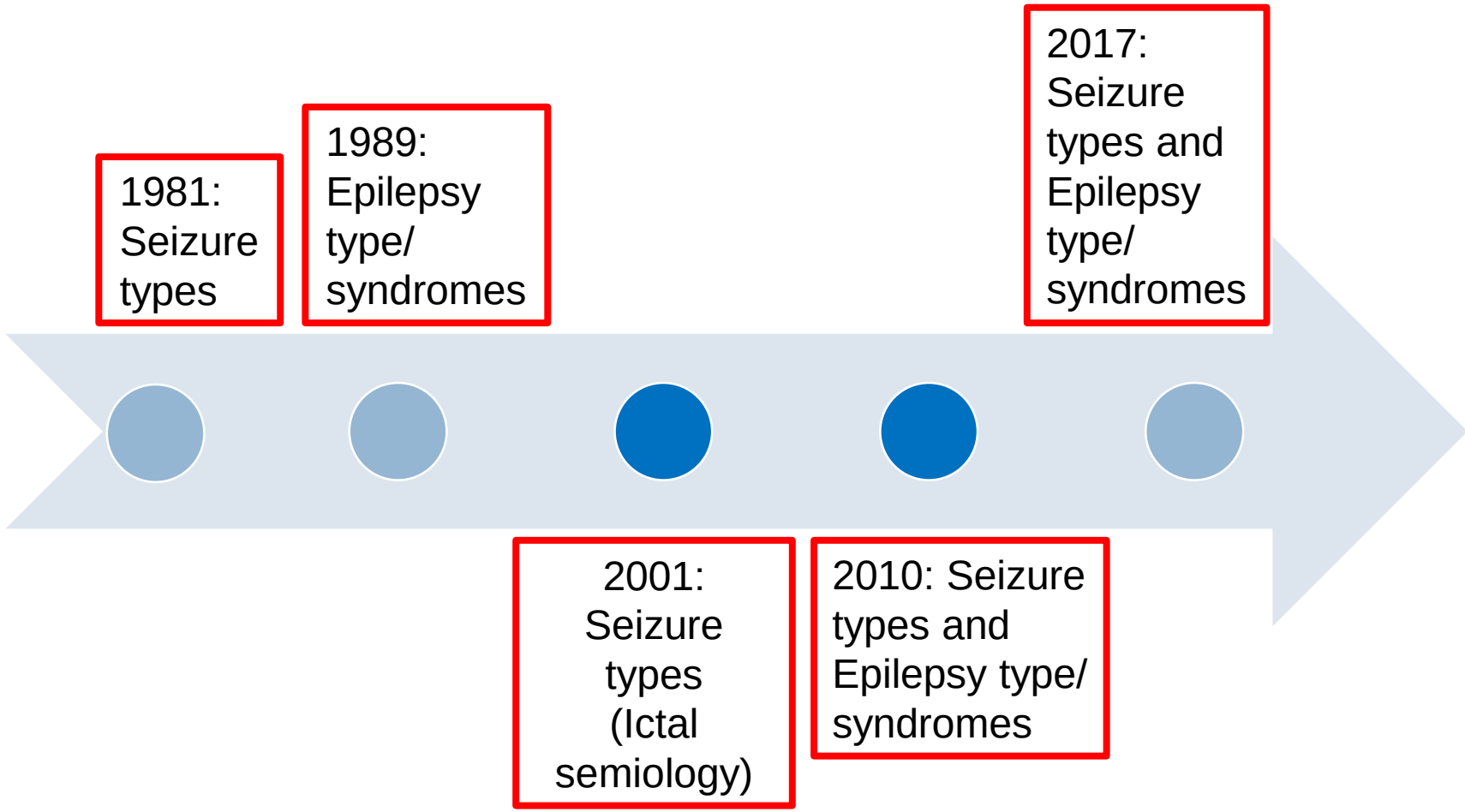
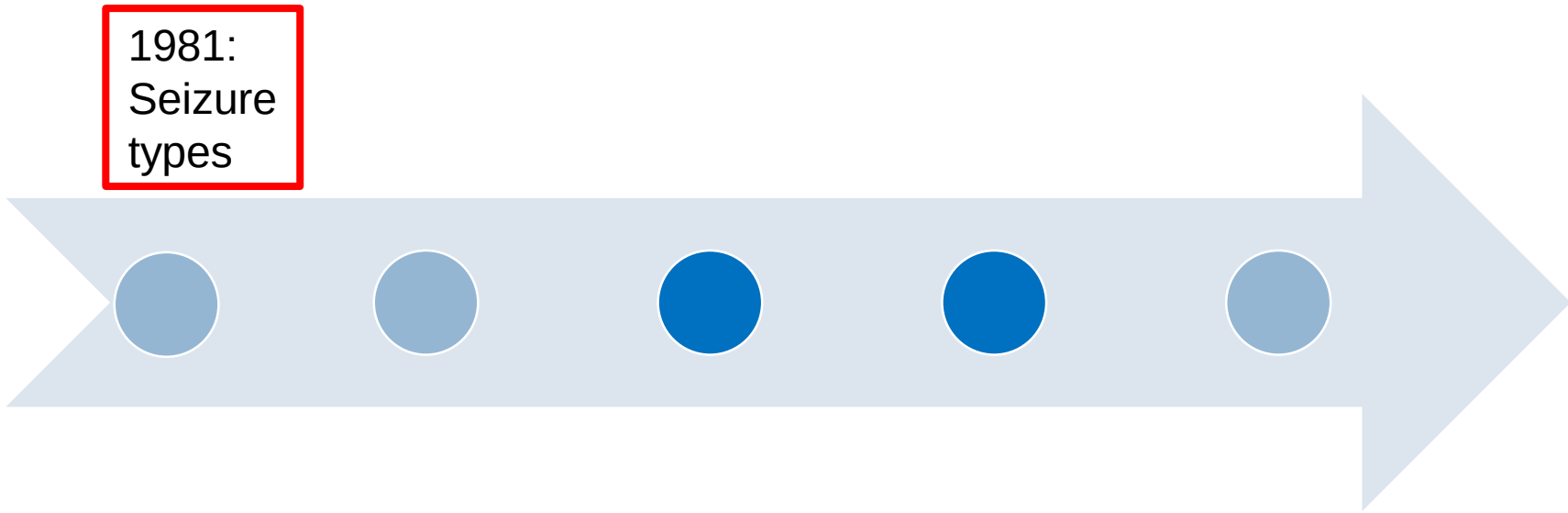
Epilepsia, **(*):1–10, 2017
doi: 10.1111/epi.13709

Milestones of ILAE classification



Milestones of ILAE classification of seizure types



Epileptic Seizures in Accordance with the ILAE Classification of 1981

- **Partial seizures**
  - simple partial seizure (**without** impairment of consciousness)
  - complex partial seizure (**with** impairment of consciousness)
  - focal seizure evolving to secondarily generalized seizures

- **Generalized seizures**

(tonic, clonic or tonic-clonic, myoclonic and typical or atypical absences)

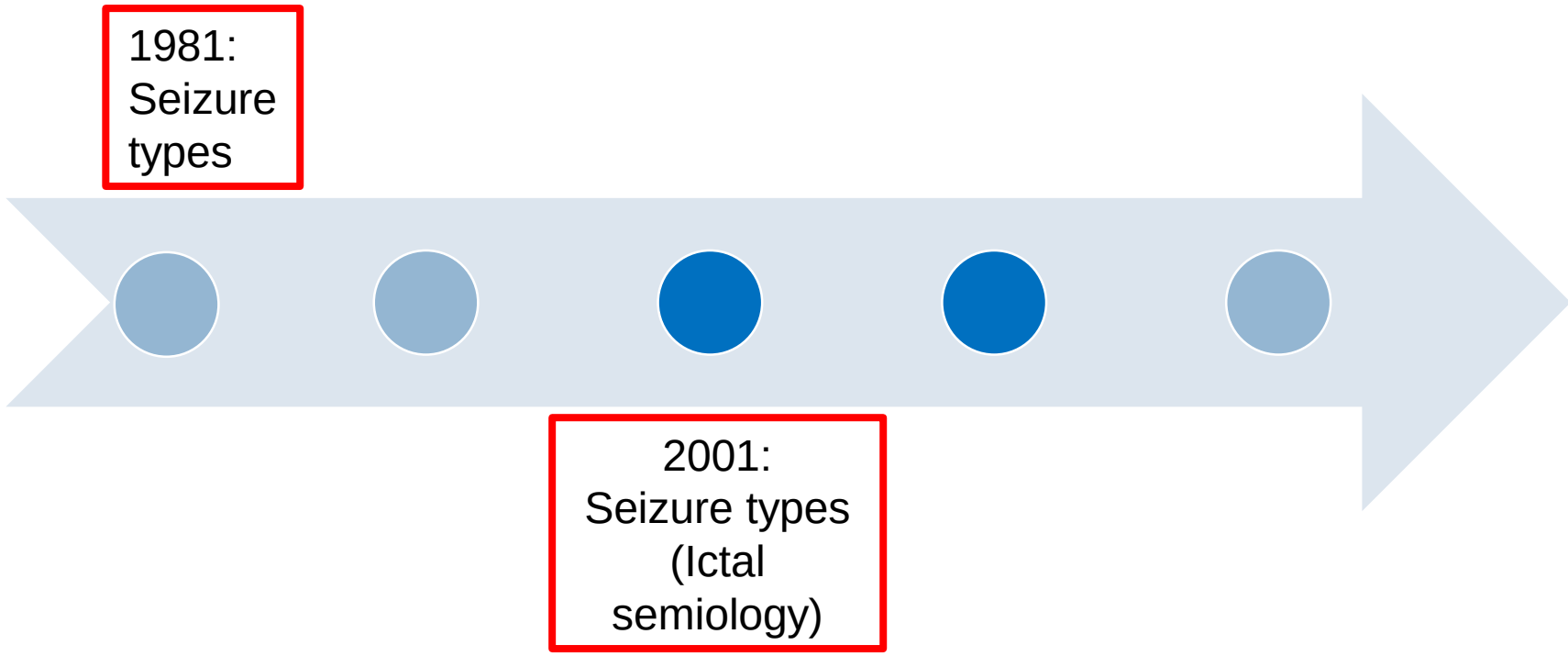
- **Unclassified epileptic seizures**
- **Prolonged or repetitive seizures (status epilepticus)**

Commission of Classification and Terminology of the International League Against Epilepsy; Epilepsia 1981

International Classification of Epileptic Seizures (ICES) 1981

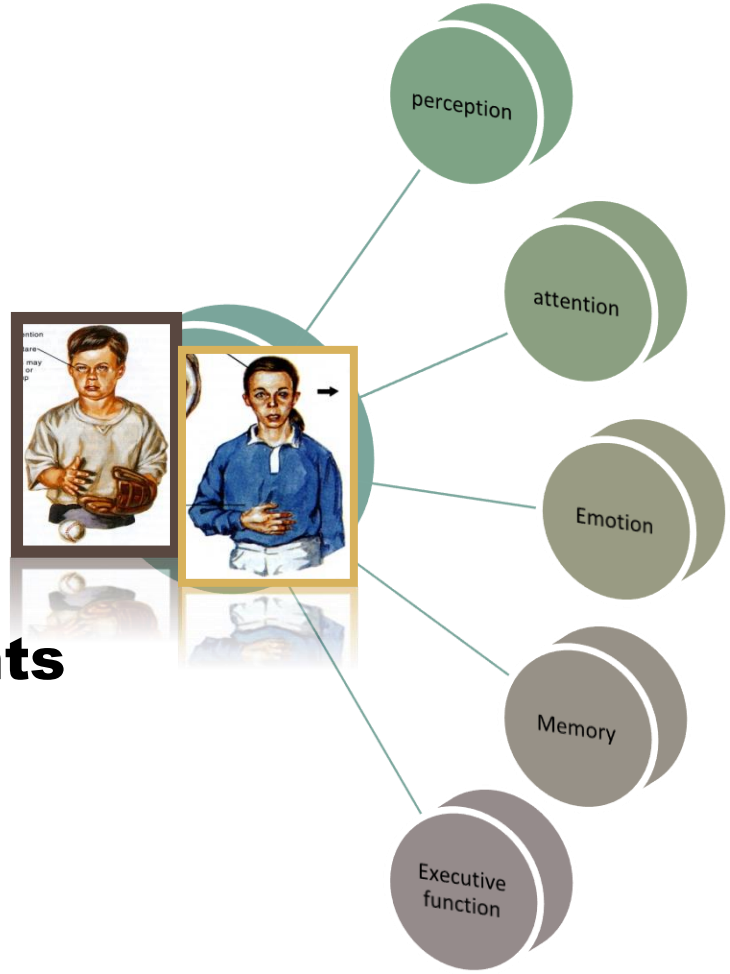
- Electroclinical approach
- Focusing on the presence/ absence of altered consciousness
  - Simple partial seizures
  - Complex partial seizures

Milestones of ILAE classification of seizure types



Glossary of descriptive terminology for ictal semiology; 2001

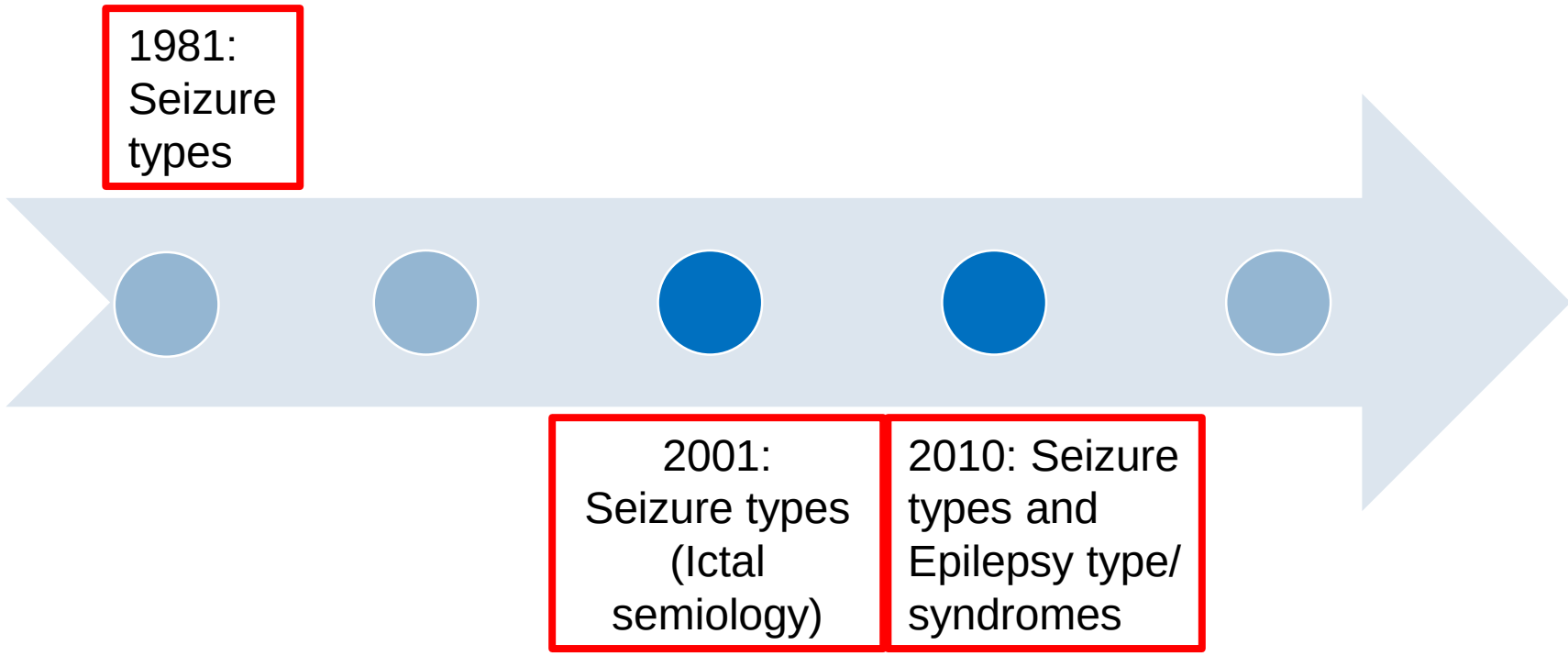
- **Motor**
  - elementary
  - automatism
- **Non-motor**
  - aura
  - sensory
  - **dyscognitive**
- **Autonomic events**
  - autonomic aura
  - autonomic seizure



Describe seizure with unbundling from EEG, MRI or other data

Report of the ILAE Task Force on Classification and terminology; Epilepsia 2001; Blume WT et al

Milestones of ILAE classification of seizure types



Revised terminology and concepts for organization of seizures and epilepsies 2010

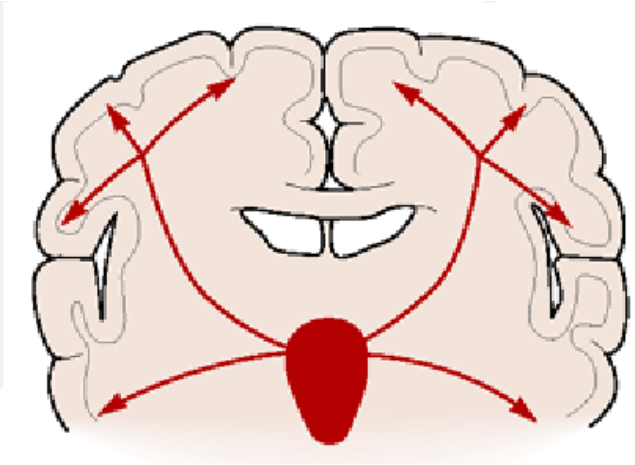
Concept of mode of seizure onset

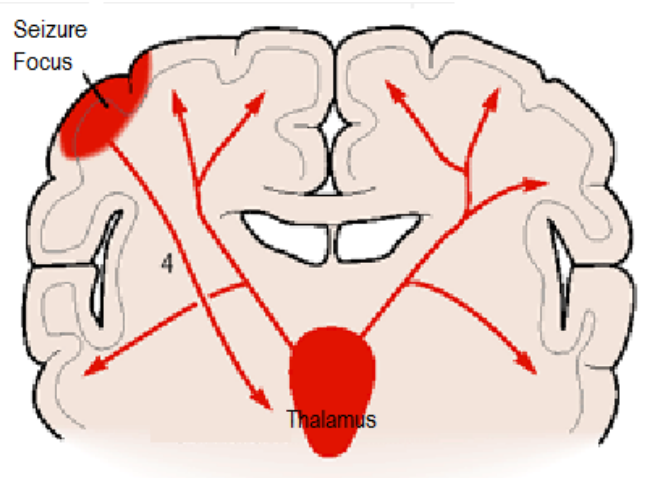
Generalized seizures: originating at some point within, and rapidly engaging, bilaterally distributed networks

✓ Although individual seizure onsets can appear localized, the location and lateralization are not consistent from one seizure to another.

Focal seizures: originating within networks limited to one hemisphere

✓ Ictal onset is consistent from one seizure to another





Berg AT; Epilepsia 2010

The distinction between **simple and complex partial seizures** is **eliminated**

Descriptors of seizure type: suggested to consult ILAE 2001

Table 1. Classification of seizures[a]

- 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

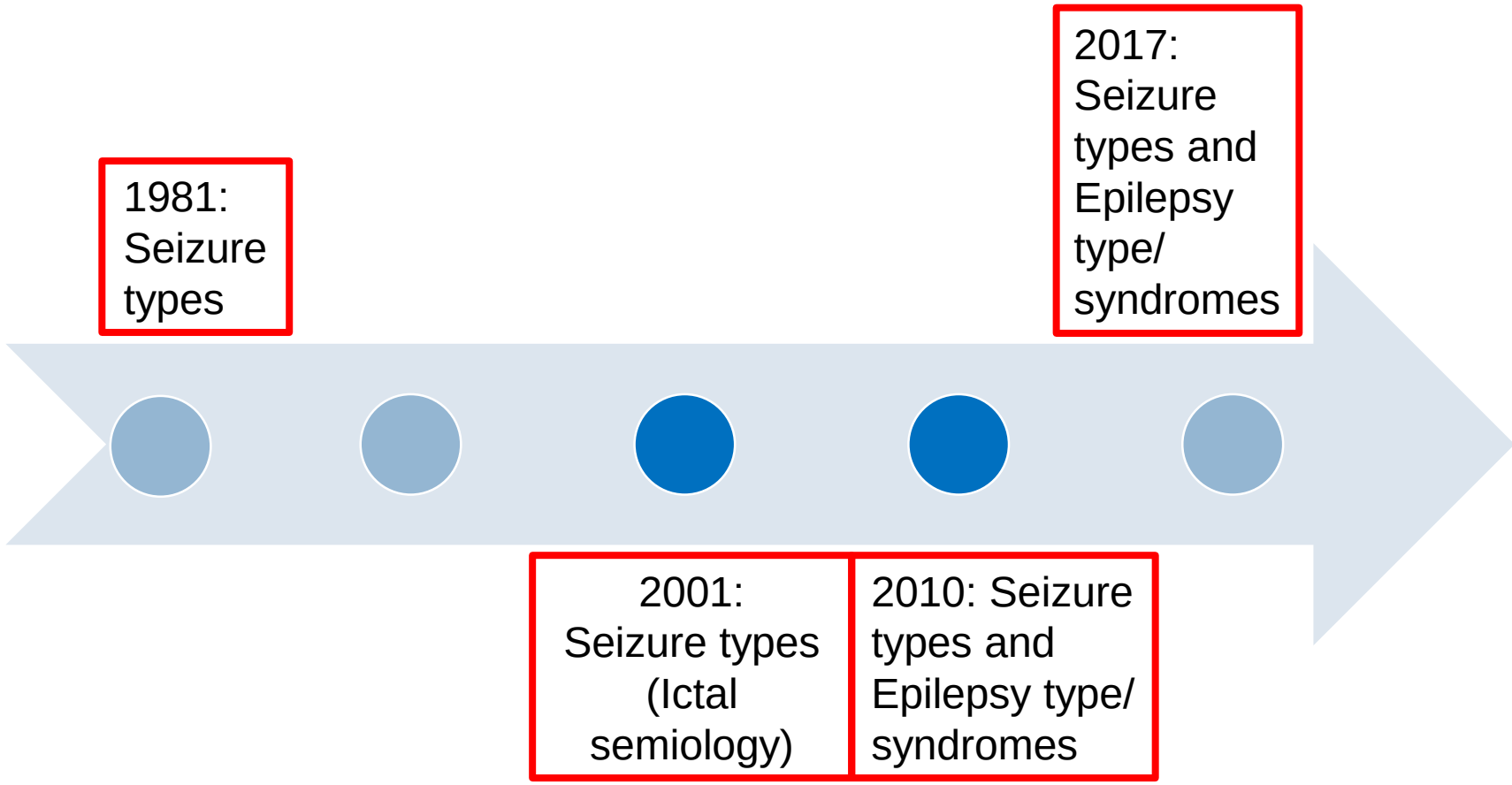
[a]Seizure that cannot be clearly diagnosed into one of the preceding categories should be considered unclassified until further information allows their accurate diagnosis. This is not considered a classification category, however.

Absence with special features (Myoclonic absence, Eyelid myoclonia) → Recognized and added

Myoclonic atonic → Recognized and added (previously called myoclonic astatic)

Epileptic spasms → Recognized and added (inadequate knowledge to make a firm decision regarding whether spasms should be classified as focal, generalized, or both)

Milestones of ILAE classification of seizure types



Fisher RS et.al., Epilepsia 2017

Table 1. Changes in seizure type classification from 1981 to 2017

1. Change of "partial" to "focal"
2. Certain seizure types can be either of focal, generalized, or unknown onset
3. Seizures of unknown onset may have features that can still be classified
4. Awareness is used as a classifier of focal seizures
5. The terms dyscognitive, simple partial, complex partial, psychic, and secondarily generalized were eliminated
6. New focal seizure types include automatisms, autonomic, behavior arrest, cognitive, emotional, hyperkinetic, sensory, and focal to bilateral tonic–clonic seizures. Atonic, clonic, epileptic spasms, myoclonic, and tonic seizures can be either focal or generalized
7. New generalized seizure types include absence with eyelid myoclonia, myoclonic absence, myoclonic–tonic–clonic, myoclonic–atonic, and epileptic spasms

Atonic, **clonic**, **epileptic spasms**, **myoclonic**, and **tonic** seizures can be of either focal or generalized onset

Dyscognitive, **simple partial**, **complex partial**, **psychic**, and **secondarily generalized** seizure are eliminated

New seizure types

- **Focal**: automatisms, autonomic, behavior arrest, cognitive, emotional, hyperkinetic, sensory, focal to bilateral tonic-clonic seizures
- **Generalized**: eyelid myoclonia, myoclonic absence, myoclonic-tonic-clonic, myoclonic atonic, epileptic spasm

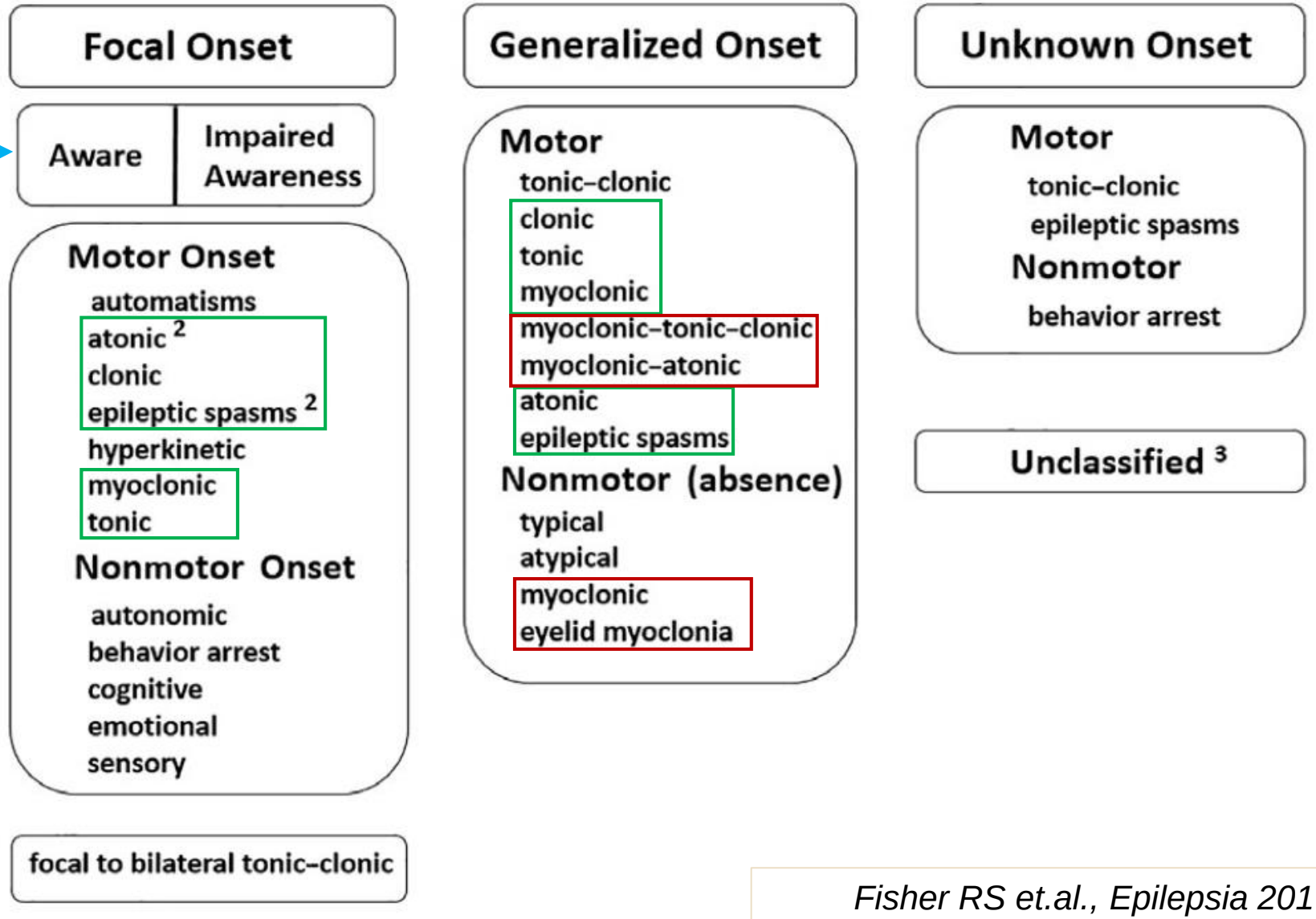
Focal onset

Awareness is initially used for classifying focal seizures

Motor activity

If further develop bilateral tonic-clonic seizure

ILAE 2017 Classification of Seizure Types Expanded Version [1]



Fisher RS et.al., Epilepsia 2017

Optional further descriptions

- **Focal aware or impaired awareness** seizures optionally may be further characterized by one of the listed motor onset or nonmotor onset symptoms, reflecting **the first prominent sign or symptom in the seizure**, for example, **focal impaired awareness automatism seizure**

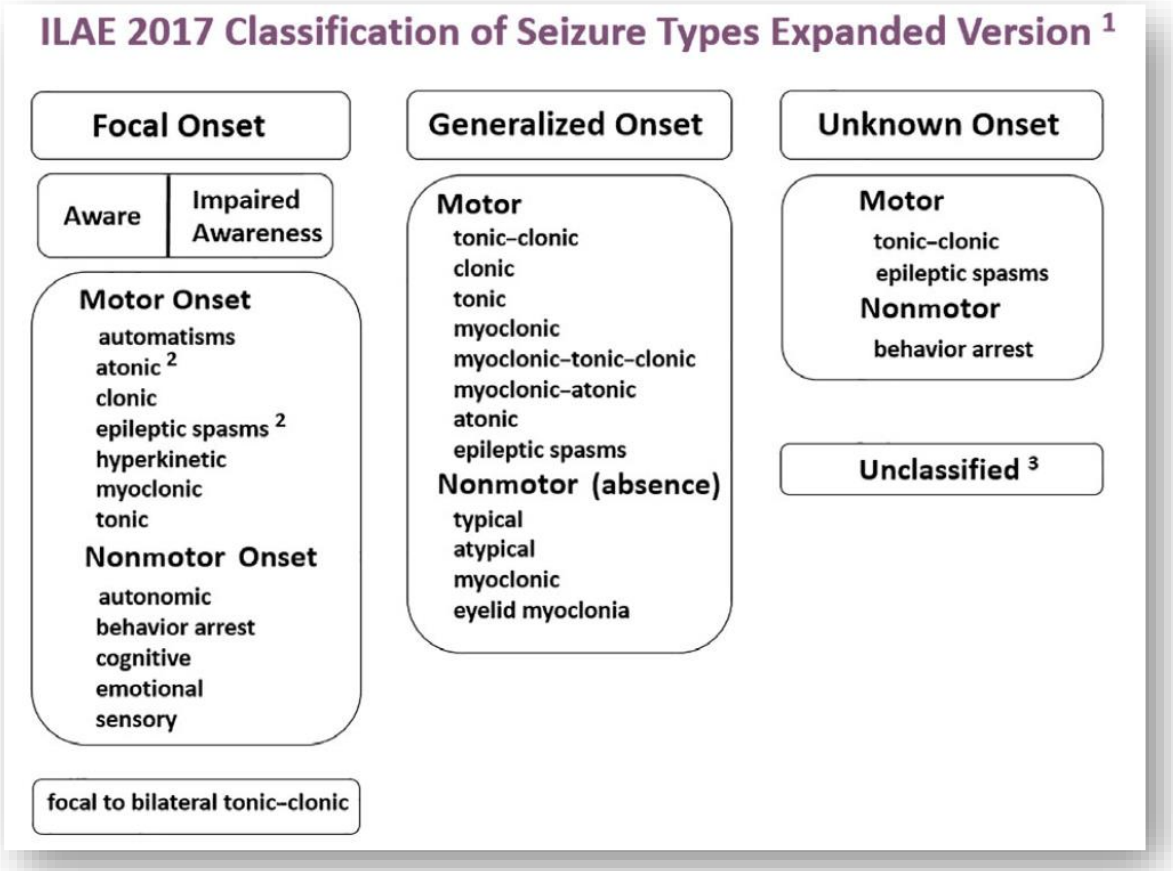
- A focal seizure name **can omit mention of awareness** when awareness is not applicable or unknown, thereby classifying the seizure directly by motor onset or nonmotor onset characteristics

Level 1

Level 2
(only focal)

Level 3

Level 4



- The classification of an individual seizure **can stop at any level**: a "**focal onset**" or "**generalized onset**" seizure, with no other elaboration, or a "**focal sensory seizure**," "**focal motor seizure**," "**focal tonic seizure**," or "**focal automatism seizure**," and so on

- The Task Force recommends classifying a seizure as having focal or generalized onset only when there is a **high degree of confidence** (e.g., ≥80% arbitrarily chosen to parallel the usual allowable beta error) in the accuracy of the determination

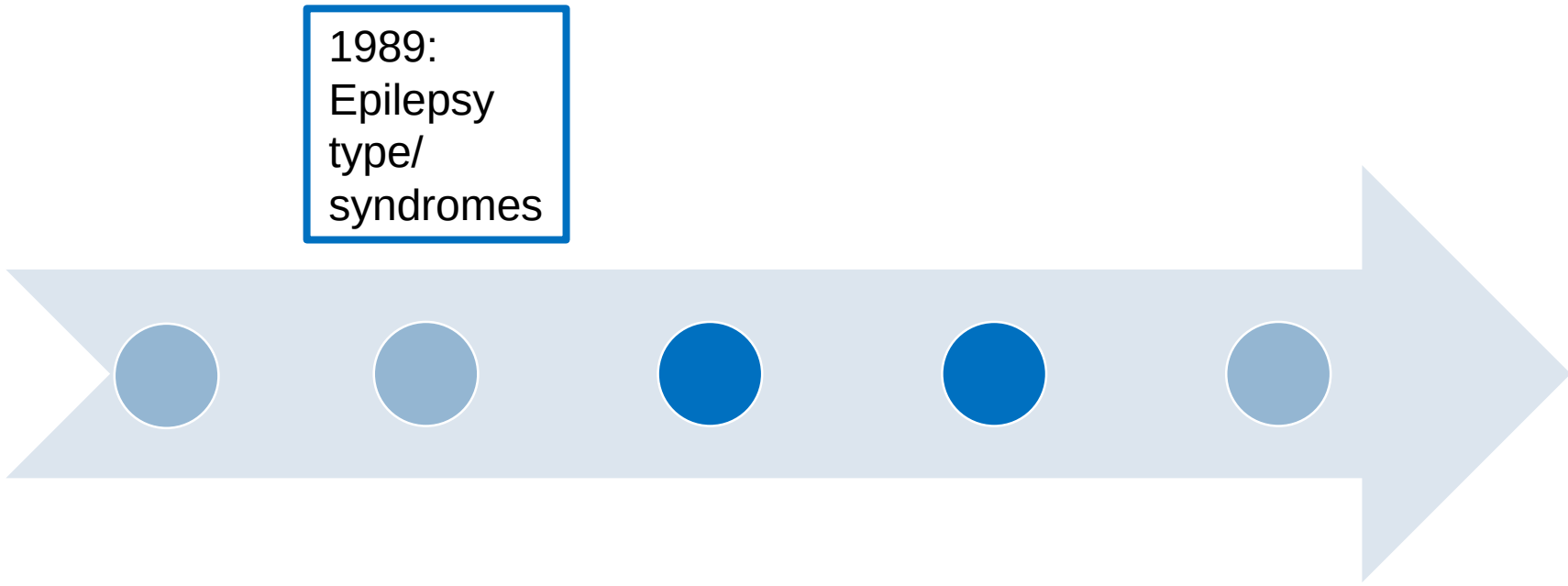
Example

- A seizure beginning with **sudden inability to understand language** followed by **impaired awareness and clonic left arm jerks** would be classified as a

"**Focal impaired awareness (nonmotor onset) cognitive seizure**" (progressing to clonic left arm jerks)

- The terms in parentheses are optional

Milestones of ILAE classification of epilepsy type, epilepsy syndromes and epilepsy etiology



Epileptic Syndromes in Accordance with Currently Valid ILAE Classification of 1989

- **Localization-related (focal, local and partial) epilepsies and syndromes**

  idiopathic, symptomatic, cryptogenic

- **Generalized epilepsies and syndromes**

  idiopathic, cryptogenic or symptomatic,

  symptomatic (EIEE, EMA)

- **Epilepsies and syndromes undetermined as to whether they are focal or generalized**
- **Special syndromes**

  FS, isolated seizure, acute symptomatic seizure

Etiology

- **Idiopathic (primary) epileptic syndrome**

  - no underlying structural brain lesion or other neurological signs or symptoms

  - presumed to be genetic and are usually age-dependent

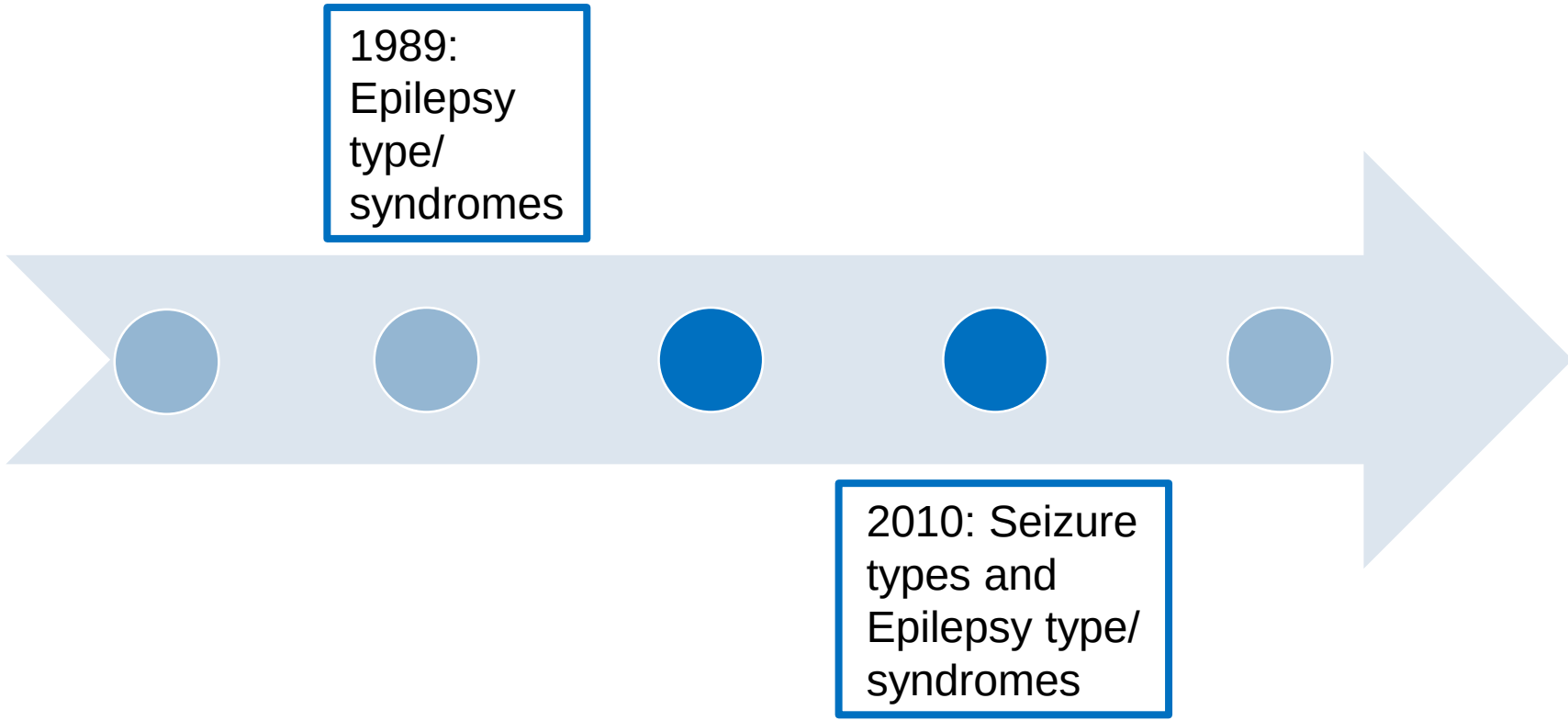
- **Symptomatic**

  - result of one or more identifiable structural lesions of the brain

- **Cryptogenic (Probably symptomatic)**

  - believed to be symptomatic, but no etiology has been identified e.g. Lennox-Gastaut syndrome, West syndrome

Milestones of ILAE classification



Revised terminology and concepts for organization of seizures and epilepsies 2010

- The dichotomy of focal versus generalized is abandoned

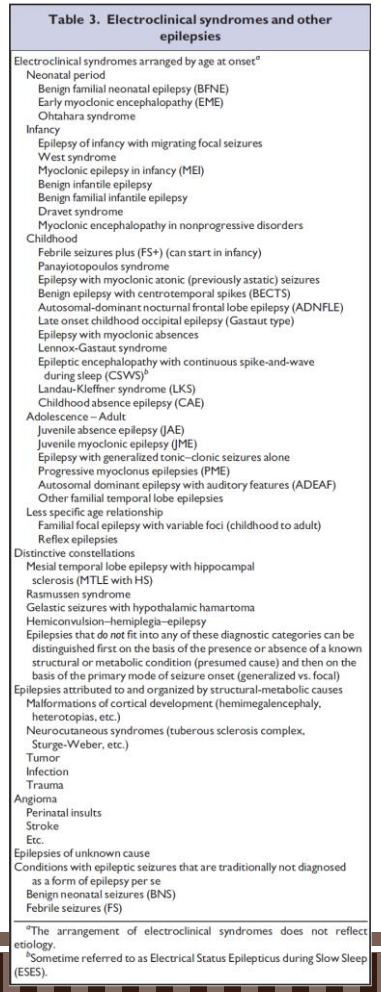


Table 3. Electroclinical syndromes and other epilepsies

Electroclinical syndromes arranged by age at onset[a]
- 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)[b]
  - 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 that *do not* fit into any of these diagnostic categories can be distinguished first on the basis of the presence or absence of a known structural or metabolic condition (presumed cause) and then on the basis of the primary mode of seizure onset (generalized vs. focal)

Epilepsies attributed to and organized by structural-metabolic causes
- Malformations of cortical development (hemimegalencephaly, heterotopias, etc.)
- Neurocutaneous syndromes (tuberous sclerosis complex, Sturge-Weber, etc.)
- Tumor
- Infection
- Trauma
- Angioma
- Perinatal insults
- Stroke
- Etc.

Epilepsies of unknown cause

Conditions with epileptic seizures that are traditionally not diagnosed as a form of epilepsy per se
- Benign neonatal seizures (BNS)
- Febrile seizures (FS)

[a]The arrangement of electroclinical syndromes does not reflect etiology.
[b]Sometime referred to as Electrical Status Epilepticus during Slow Sleep (ESES).

- ❑ **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 per se**

Epilepsy etiology

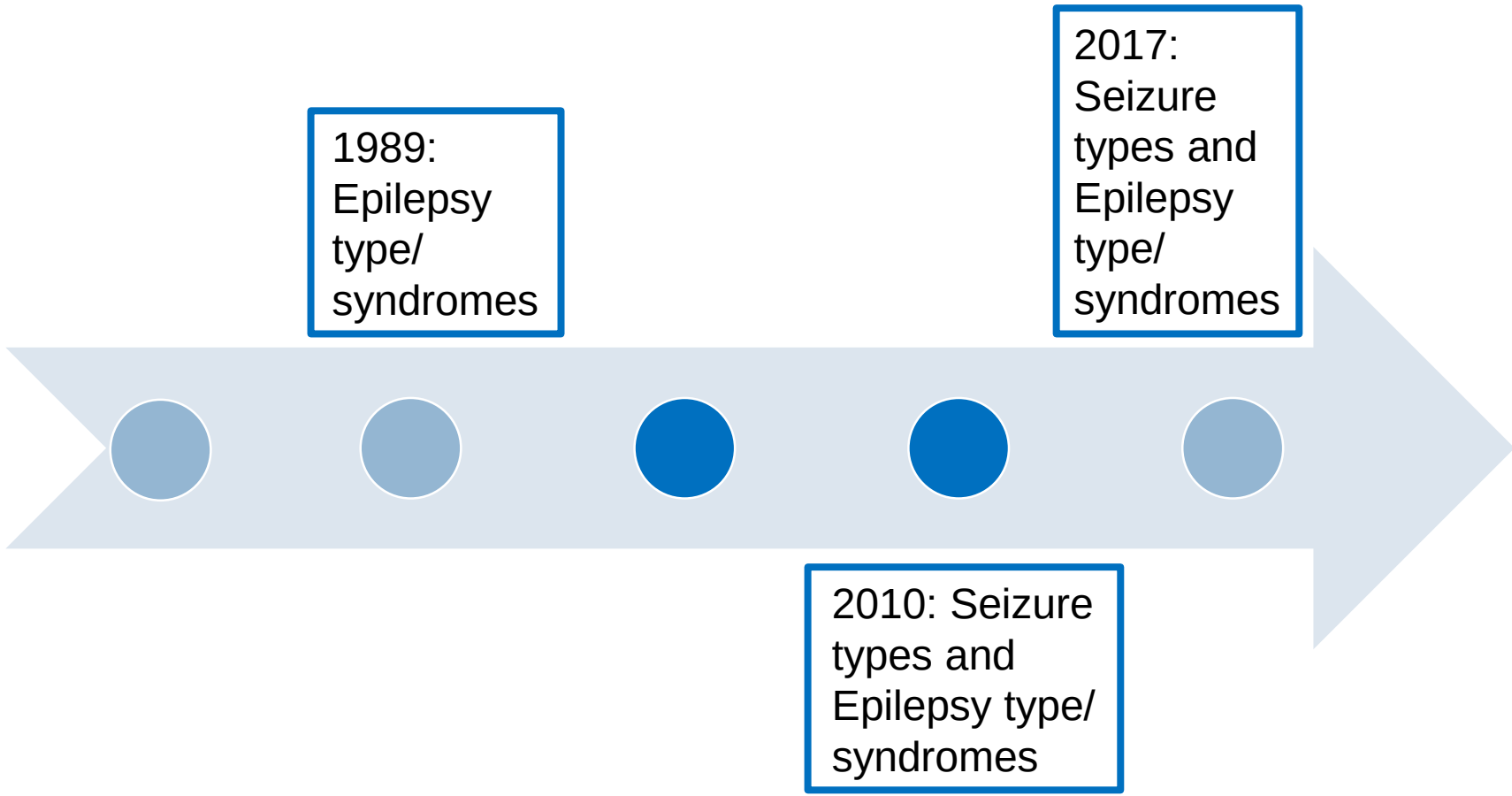
1989

- Idiopathic
- Symptomatic
- Cryptogenic

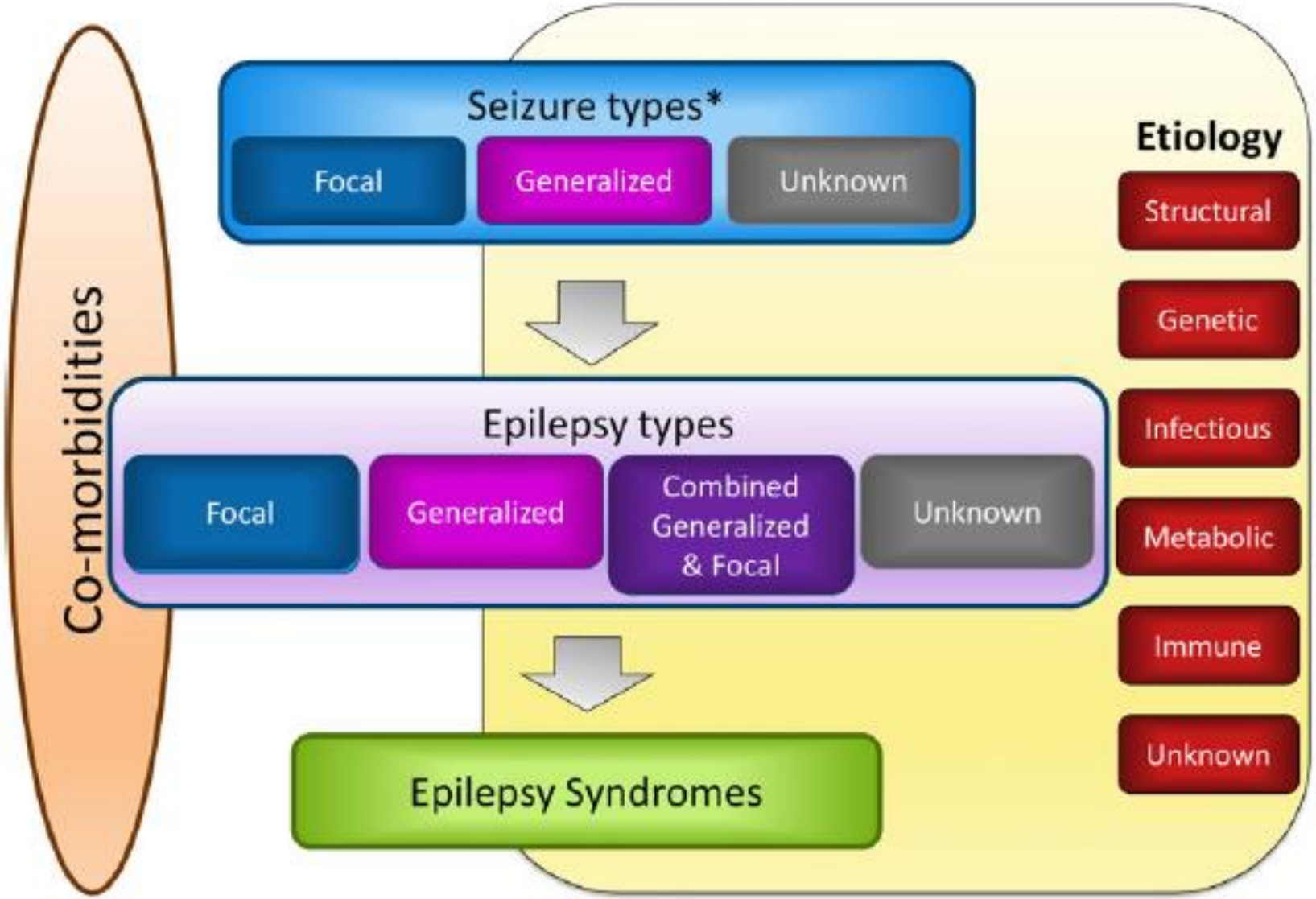
2010

- Genetic
- Structural-metabolic
- Unknown

Milestones of ILAE classification



Scheffer IE et.al., Epilepsia 2017



Epilepsy types

The diagnosis is made on clinical grounds (seizure types), supported by EEG findings

Combined generalized & Focal: both types of seizures occur e.g. Dravet syndrome and Lennox-Gastaut syndrome

Unknown: the clinician is unable to determine if the Epilepsy Type is focal or generalized because there is insufficient information available

The Epilepsy type may also be the final level of diagnosis achievable where the clinician is unable to make an Epilepsy Syndrome diagnosis

Epilepsy etiology

- **1989**
  - Idiopathic
  - Symptomatic
  - Cryptogenic
- **2010**
  - Genetic
  - Structural-metabolic
  - Unknown
- **2017**
  - Genetic
  - Structural
  - Infectious
  - Metabolic
  - Immune
  - Unknown

Genetic etiology

- **Diagnosis of genetic etiology** based on
  - solely on a **family history of an autosomal dominant** disorder
  - may be suggested by **clinical research in populations (familial aggregation studies)** with the same syndrome such as Childhood Absence Epilepsy or Juvenile Myoclonic Epilepsy
  - a **molecular basis** may have been identified and may implicate a single gene or copy number variant of major effect e.g. Dravet's syndrome in which >80% of patients have a pathogenic variant of SCN1A

Epilepsy syndromes

- Epilepsy syndrome refers to a cluster of features incorporating seizure types, EEG, and imaging features that tend to occur together

- Retain the term "**Idiopathic generalized epilepsy (IGE)**"
  - Childhood Absence Epilepsy (CAE)
  - Juvenile Absence Epilepsy (JAE)
  - Juvenile Myoclonic Epilepsy (JME)
  - Generalized Tonic–Clonic Seizures Alone

Developmental and Epileptic encephalopathies

- The concept of the **epileptic encephalopathy** may be **applicable to epilepsies at all ages** and should be utilized more widely than just for the severe epilepsies with onset in infancy and childhood
- A key component of the concept is that **amelioration of the epileptiform activity may have the potential to improve the developmental consequences** of the disorder

Developmental and Epileptic encephalopathies (cont.)

"symptomatic generalized epilepsies" will no longer be used as it was applied to a highly heterogeneous group of patients

- **Developmental encephalopathy**: where there is just developmental impairment without frequent epileptic activity associated with regression or further slowing of development
- **Epileptic encephalopathy**: where there is no preexisting developmental delay and the genetic mutation is not thought to cause slowing in its own right
- **Developmental and epileptic encephalopathy**: where both factors play a role e.g. SCN1A causes Dravet's syndrome

Self-limited and pharmacoresponsive

- "**Benign**" as a descriptor for epilepsy, is replaced by both "self-limited" and "pharmacoresponsive"
- "**Self-limited**" refers to the likely spontaneous resolution of a syndrome
- "**Pharmacoresponsive**" means that the epilepsy syndrome will be likely to be controlled with appropriate antiepileptic therapy

Thank you for your attention