Idiopathic epileptic syndromes

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Definition

Idiopathic

- Meaning of unknown origin
- Primary disorder with an independent etiology, pathogenesis, and pathology, not caused or occasioned by, or secondary to another disorder

"Genetic defect"

Definition

Epileptic seizure : a transient occurrence of signs and/or symptoms due to abnormal excessive or synchronous neuronal activity in the brain*

*Fisher et al. *Epilepsia* 2005;46:470-2.

Epileptic seizure

1. Mode of onset – 'transient', demarcated in time, with a clear start and finish
2. Clinical manifestations – sensory, motor, and autonomic function; consciousness; emotional state; memory; cognition; and behavior
3. Ictogenesis - abnormal enhanced synchrony of neurones

Definition

Epilepsy : 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*

*Fisher et al. *Epilepsia* 2005;46:470-2.

Definition

Epileptic syndrome

- Group of clinical and EEG features common to patients with similar
- Not necessarily identical etiologies
- Helps determine the appropriate therapy and the prognosis

ILAE Classification 1989

syndromes were organized primarily according to

- Mode of expression (localization-related versus generalized)
- Underlying cause (idiopathic, symptomatic, and cryptogenic)

ILAE Classification 1989

Idiopathic localization-related (focal, local, partial) epilepsy (ILRE)

1. Benign childhood epilepsy with centrotemporal spikes (benign Rolandic epilepsy)
2. Childhood epilepsy with occipital paroxysms
3. Primary reading epilepsy

ILAE Classification 1989

Idiopathic generalized epilepsy (IGE)

1. Benign neonatal familial convulsions
2. Benign neonatal convulsions
3. Benign myoclonic epilepsy in infancy
4. Childhood absence epilepsy (pyknolepsy) : CAE
5. Juvenile absence epilepsy : JAE

ILAE Classification 1989

Idiopathic generalized epilepsy (IGE)

6. Juvenile myoclonic epilepsy (impulsive petit mal) : JME
7. Epilepsy with grand mal seizures (GTCs) on awakening
8. Other generalized idiopathic epilepsies
9. Epilepsies with seizures precipitated by specific modes of activation

Epileptic syndrome

- “benign” refers to prognosis
- “idiopathic” refers to etiology, some patients with IGE are difficult to control
- “generalized” : generalized seizure types and bilateral EEG abnormalities, some patients have focal seizure clinical and EEG*

*** Panayiotopoulos CP et al.*Epilepsia* 1991;32:672-6.**

Epileptic syndrome

- Value in children greater than adults
- Some syndromes have specific pathology, aetiology
- Some specific pathologies result in a variety of syndromes
- Knowledge advances, syndromes reclassified, and distinction from disease becomes blurred – eg. molecular genetics

The 2006 ILAE report

Epilepsy Syndromes by Age of Onset and Related Conditions

Neonatal period
- Benign familial neonatal seizures (BFNS)
- Early myoclonic encephalopathy (EME)
- Ohtahara syndrome

Infancy
- Migrating partial seizures of infancy
- West syndrome
- Myoclonic epilepsy in infancy (MEI)
- Benign infantile seizures
- Dravet syndrome
- Myoclonic encephalopathy in nonprogressive disorders

The 2006 ILAE report

Epilepsy Syndromes by Age of Onset and Related Conditions

Childhood
- Early onset benign childhood occipital epilepsy (Panayiotopoulos type)
- Epilepsy with myoclonic astatic seizures
- Benign childhood epilepsy with centrotemporal spikes (BCECTS)
- Late-onset childhood occipital epilepsy (Gastaut type)
- Epilepsy with myoclonic absences
- Lennox-Gastaut syndrome
- Epileptic encephalopathy with continuous spike-and-wave during sleep (CSWS) including:
  - Landau-Kleffner syndrome (LKS)
  - Childhood absence epilepsy (CAE)

The 2006 ILAE report

Epilepsy Syndromes by Age of Onset and Related Conditions

Adolescence
- Juvenile absence epilepsy (JAE)
- Juvenile myoclonic epilepsy (JME)
- Progressive myoclonus epilepsies (PME)

Less-specific age relationship
- Autosomal-dominant nocturnal frontal lobe epilepsy (ADNFLE)
- Familial temporal lobe epilepsies
- Mesial temporal lobe epilepsy with hippocampal sclerosis (MTLE with HS)
- Rasmussen syndrome
- Gelastic seizures with hypothalamic hamartoma

The 2006 ILAE report

Epilepsy Syndromes by Age of Onset and Related Conditions

Special epilepsy conditions
- Symptomatic focal epilepsies not otherwise specified
- Epilepsy with generalized tonic-clonic seizures only
- Reflex epilepsies
- Febrile seizures plus (FS+)
- Familial focal epilepsy with variable foci

Conditions with epileptic seizures that do not require a diagnosis of epilepsy
- Benign neonatal seizures (BNS)
- Febrile seizures (FS)

IPE

- 1/5 of all epilepsies in children and adolescents
- Differ from lesional focal epilepsy syndromes

1. Genetically determined focal disturbances of cerebral activity w/o apparent structural abnormality on MRI
2. Most IPEs remit by adolescence

IPE

- Age-dependent occurrence-onset generally after 18 months
- Normal neurological status, most children intellectually intact and w/o prior neurologic insult
- Favorable long-term outcome

IPE

- Specific semiology – simple partial motor or sensory, nocturnal occurrence is common
- Rapid response to AEDs
- Specific EEG features, epileptiform discharges often activated by sleep

IGE

- 15-20% of all epilepsies
- Classical age of onset in the first and second decades
- Normal neurological status, intellectual intact
- Electro-clinical correlation eases the diagnosis

IGE

Seizure types

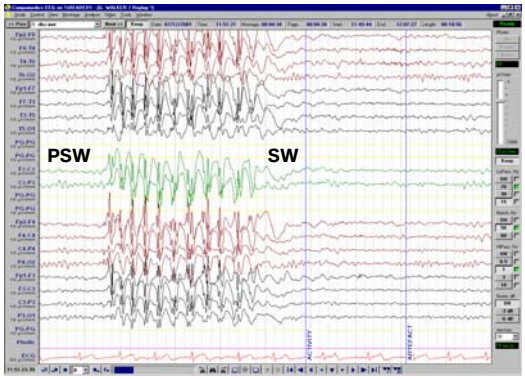
1. Absence
2. Myoclonic seizure
3. Tonic-clonic seizures

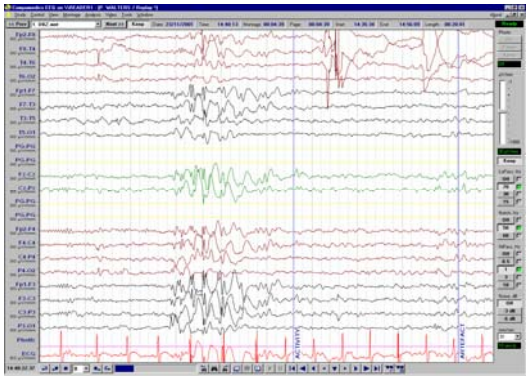
- CAE, JME and EGTCA are most common

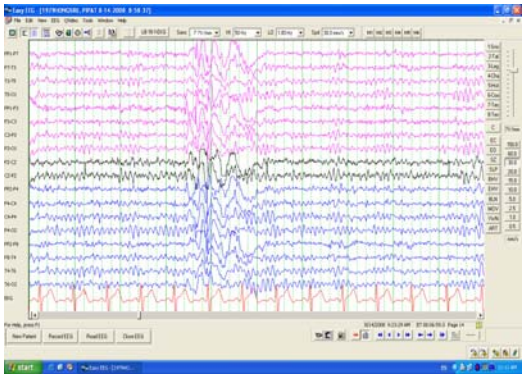
IGE

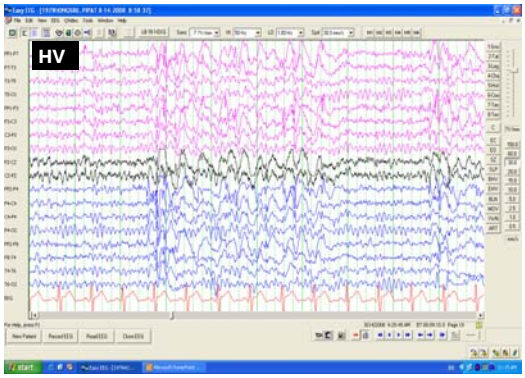
EEG

- Hallmark: GSW, GPSW
- Fast generalization secondary to a symptomatic focus can mimic IGE
- Focal ictal semeiology in IGEs may reflect regional ictal discharges of varying duration









IGE

EEG

- Typical absences : 3Hz or faster GSW, GPSW
- Myoclonic seizures : brief (1-4 s) and fast GSW, GPSW with anterior maximum and varying intradischarge frequency
- GSW influenced by circardian rhythm and provocation*

*Sadleir LG et al.*Epilepsia* 2009;50(6):1572-8.

IGE

MRI

- Usually normal MRI findings
- A study of 134 MRIs of IGE evaluated*
  - 24% showed abnormalities
  - Most of which (88%) were nonspecific

*Betting LE et al.*Neurology* 2006;67:848-52.

IGE

- 8 main abnormalities:

1. arachnoid cyst
2. diffuse cortical atrophy
3. BG abnormality
4. ventricular abnormality
5. WM abnormality
6. reduced hippocampal volume
7. focal gyral abnormality
8. area of gliosis in the frontal lobe

Betting LE et al.*Neurology* 2006;67:848-52.

IGE

- First-line drug :VPA
- Second-line drugs : BDZ, LTG, LEV, TPM,ZNS
- Some AEDs cause “pseudo-intractability” in absence and myoclonic seizures : CBZ, OXC,PHT, GBP, TGB
- In general, good response to treatment and about 80-90% becoming fully controlled
- Not increased standard mortality ratio (SMR)*

*Sillanpaa M et al. *NEJM* 1998;338:1715-22.

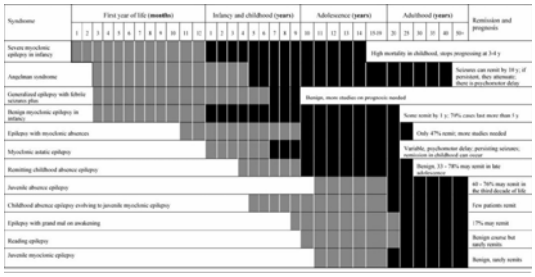
Epileptic syndrome

IGE syndromes not recognized by ILAE*

- IGE with absences of early childhood
- Perioral myoclonia with absences (PMA)
- IGE with phantom absences
- Jeavon syndromes (eyelid myoclonia with absences)
- Monogenic IGE syndromes
- …..

*Panayiotopoulos CP. Oxford: Bladon Medical Publishing,2005: 271-348.

Temporal profile of generalized seizures with absences and myoclonias showing their age dependency



Duron RM. Et al.*Epilepsia* 2005;46(suppl.9):34-47.

Epileptic syndrome

IGE syndromes not recognized by ILAE*

Adult-onset IGE

- Onset beyond the third decade
- Increasing evidence for the existence of syndromes
- EEG and sleep-deprived EEGs within 24 hrs. may improved the detection*

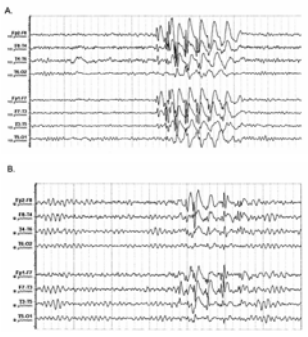
*Marini C et al. *JNNP* 2003;74:192-6.

Adult-onset IGE

EEG in adult-onset IGE*

- 87 EEGs (56 adolescent-onset, 31 adult-onset)
- Background was normal in all patients
- No differences in EEG morphology, amplitude, duration, frequency, occurrence, or activation of GSW

*Yenjun S et al. *Epilepsia* 2003;44(2):252-6.



Adolescence-onset IGE

Adult-onset IGE

Yenjun S et al. *Epilepsia* 2003;44(2):252-6.

Adult-onset IGE

- Similar incidence of FH of epilepsy, EEG findings, and remission rates to classic-onset IGE but low incidence of FC#
- High incidence of absence status and only infrequent tonic-clonic seizures*
- Many reports of families with adult-onset IGE, “genetic epilepsy”

Nicolson A et al.*JNNP* 2004;75:72-74.
* Panayiotopoulos CP et al.*JNNP* 1997;63:622-7.

Epileptic syndrome

Debate !

- “Lumpers”
- “Splitters”

? Different and separate syndromes or different facets of a broader neurobiological spectrum of epilepsy