IDIOPATHIC EPILEPSY SYNDROME

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Outline

- Operational definition of epilepsy
- Idiopathic epilepsy syndrome
- Idiopathic generalize epilepsy
- Idiopathic focal epilepsy

Operational (Practical) Clinical Definition of Epilepsy

1. At least two unprovoked (or reflex) seizures occurring more than 24 hours apart.

2. One unprovoked (or reflex) seizure and a probability of further seizures similar to the general recurrence risk (at least 60%) after two unprovoked seizures, occurring over the next 10 years.

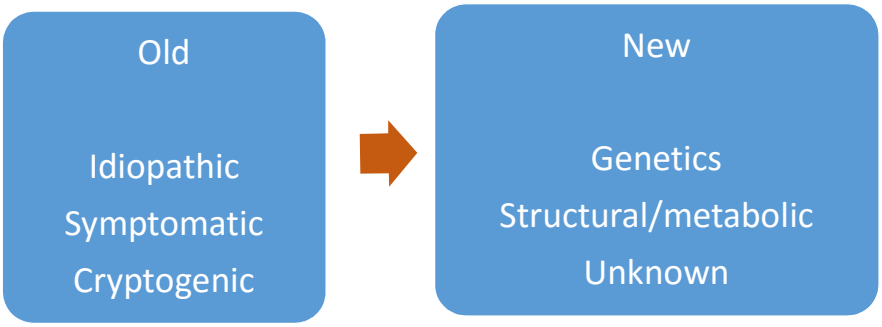
3. **Diagnosis of an epilepsy syndrome.**

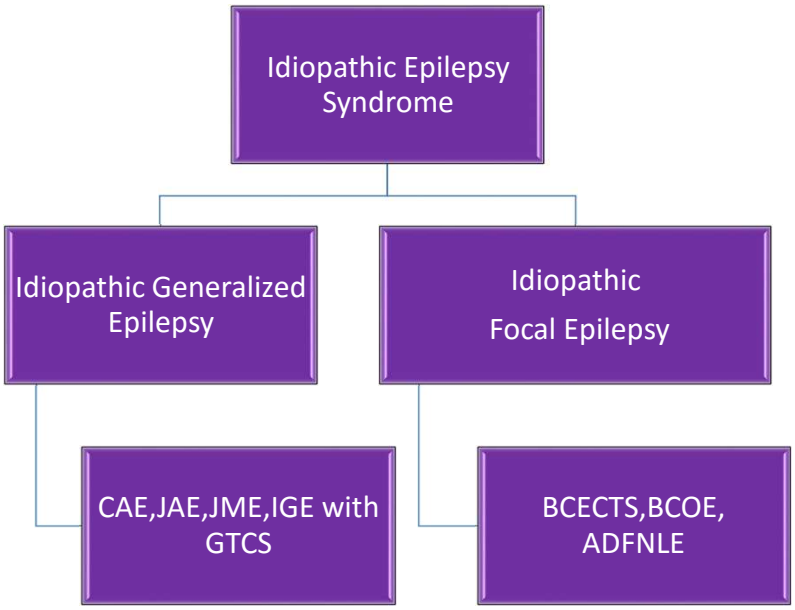
Epilepsia The Journal of the International League Against Epilepsy

Fisher et al., 2014, DOI: 10.1111/epi.12550

ILAE

Type of Epilepsy





IGE

15-30% of all patients with epilepsy

Characteristics

- Seizure types
  - Absence seizures (AS)
  - Generalized tonic clonic seizures (GTCS)
  - Bilateral myoclonic seizures (BMS)
- Age dependent seizure onset
- Typical pathological EEG pattern
- Lack of apparent MRI abnormalities

Characteristics

- Interictal EEG showed generalized epileptiform discharge.
- Neurological exam and intelligence were normal
- Highly response to appropriate AED.

Overview: idiopathic generalized epilepsies.
Mattson RH.
Epilepsia. 2003;44 Suppl 2:2-6. Review.

IGE Syndrome

- Childhood Absence Epilepsy (CAE)
- Juvenile Absence Epilepsy (JAE)
- Juvenile Myoclonic Epilepsy (JME)
- IGE with GTCS on awakening

Differential diagnosis

	Absence	CPS	Day dreaming
Frequency	Multiple/day	1-2 times/day	Not frequent
Situation	Any	Any	Boring
Onset	Abrupt	Abrupt	Gradual
Interrupted	No	No	Yes
Duration	Rarely >20 sec	Up to several minute	Until something interesting
Automatism	May occur	Common	None
Post episode	Alert	Confused	Alert

Childhood Absence Epilepsy

- 10% to 17% of epilepsy Dx in school-aged.
- Girls > Boys (11.4% vs. 2.5%).
- Begins between 4 and 10 years with a peak at 5-7 years.

Clinical Presentation

- Key : striking impairment of consciousness
- Other associated ictal clinical features in CAE consisted of
  - Staring
  - 3-Hz regular eyelid movement
  - Eye opening that usually occur in an inconsistent manner during seizure.

Clinical presentation

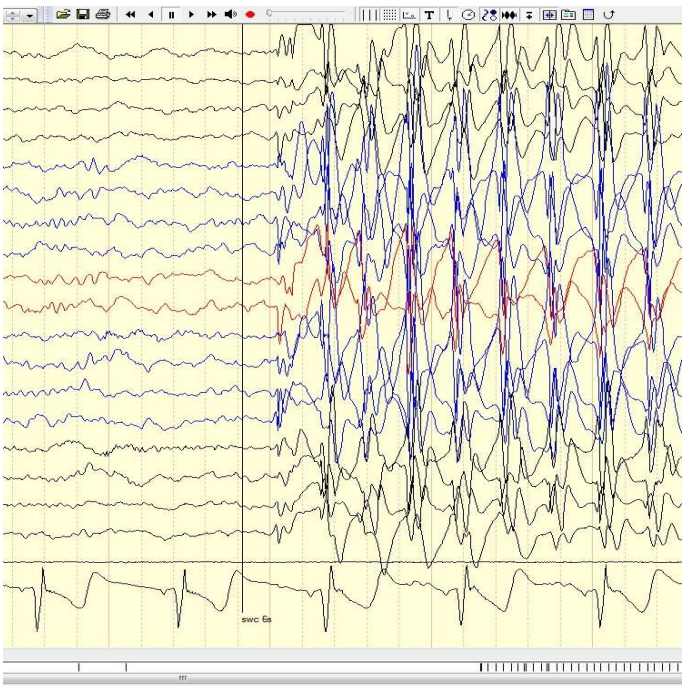
- Automatisms occur frequently in CAE
  - during longer seizures
  - during hyperventilation
- Mild clonic or tonic movements often occur during the first seconds of the absence seizure.
- Atonic falls never occur.

Seizure Duration

- Seizure duration is influenced by factors
  - provocation (hyperventilation and intermittent photic stimulation)
  - state of arousal
  - sleep deprivation
  - medication
  - individual factors.
- Seizure duration of less than 4 seconds or more than 30 seconds is not typical of CAE.

Exclusion Criteria

- The presence of seizures other than typical absence seizure before or during the active stage of absences.
- Eyelid and perioral myoclonia and single violent jerks .

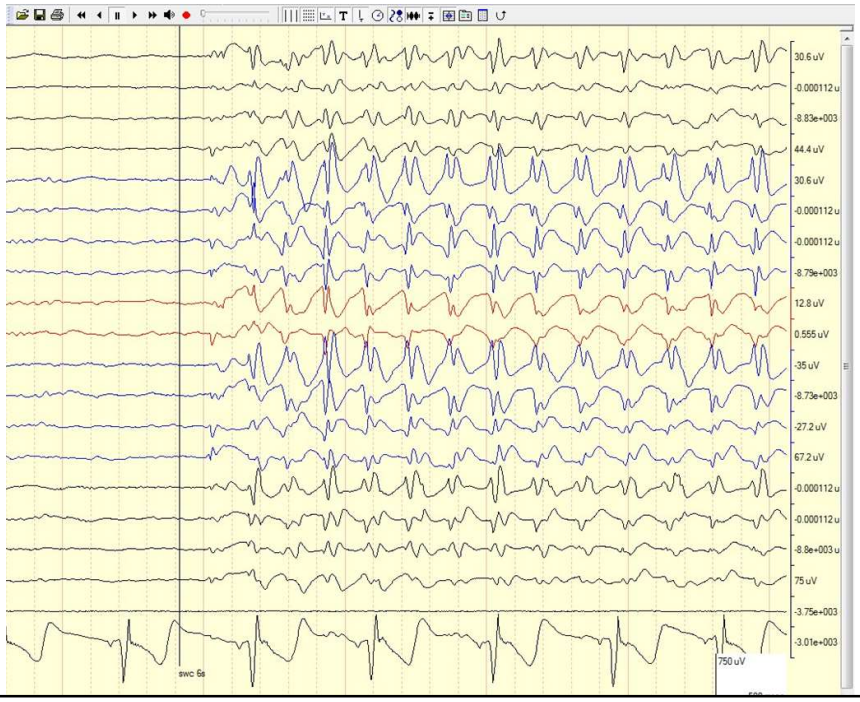


Ictal EEG

Hyperventilation induce 83%

Photic induce

21 %

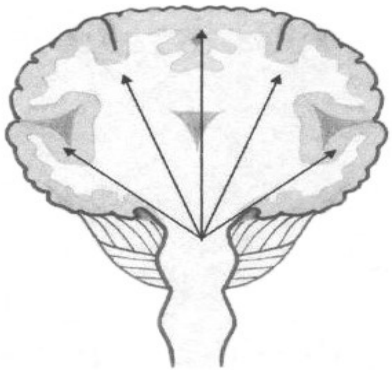


Neuropsychological/cognitive aspects

- cognitive and linguistic impairment as well as behavioral disorders
- Cognitive difficulty
  - The attentional domain
  - The executive functions
  - Verbal memory
  - Visuospatial memory
- Language and reading disabilities
- ADHD,Depression, Anxiety disorder.

Pathophysiology

- An intact thalamocortical circuitry is required for the generation of typical spike-wave discharges.



www.epilepsyaustralia.net

Evolution and Prognosis

- Excellent prognosis
- Remission rate range from 56-84%
- total duration of epilepsy 3.9 years
- mean age at final remission 9.5 years
- 7% still have seizures after 12-17 years of follow-up

Prognostic factor

- **Poor**
  - Absence status
  - Late onset of absence seizures (more than 8 years)
  - An abnormal background activity on EEG
  - Multiple spikes
  - Focal abnormalities
- **Good**
  - Prompt seizure control after introduction of an appropriate AED treatment.

Treatment

- Ethosuximide
- Valproate
- Ethosuximide and valproate
- Lamotrigine
  - Two double-blind, RCT comparing ESM, VPA, and LTG in children with newly diagnosed CAE
    - VPA and ESM were more effective than LTG
    - ESM was associated with fewer cognitive side effects.
    - These studies indicate that ESM is the optimal initial empiric monotherapy for CAE

Contraindicated AEDs

- Phenytoin,Phenobarbital
- CBZ,Oxcarbamazepine
- Gabapentin,Vigabatrin, Tiagabine

GLUT1 Deficiency

- Glucose Transporter Type I Deficiency syndrome
- Early onset absence seizures
- Refractory absence seizures
- Low CSF glucose
- Treatment: Ketogenic diet

Juvenile Absence Epilepsy

- 10 -16 yrs. (average 13)
- Strong genetic component.
- JAE clinical absence the same with CAE but :
  - Less frequent
  - Less severe impairment of consciousness.
  - Longer duration .

Juvenile Absence Epilepsy

- The prognosis of this syndrome is good; although seizures tend to persist for many years.
- Patients have a good response to antiepileptic drugs.

Juvenile Myoclonic Epilepsy

- 5–10% of all epilepsies.
- 12–18 years with an average of 15 years.
- Hallmarks : Single or arrhythmical bilateral myoclonic jerks with retained consciousness.

Juvenile Myoclonic Epilepsy

- Often have GTCS.
- Absence seizures : 1/3 of the cases.
- Precipitated by sleep deprivation or alcohol.
- Reflex seizures in this syndrome include
  - Photosensitivity (up to 50%)
  - Praxis (≥30%)
  - Perioral reflex myoclonias (~ 25%)
  - Eye-closure sensitivity (3–4%).

Ictal EEG

- Characterized by polyspike and waves ≥3 Hz.

Treatment and Prognosis

- Excellent response to adequate AED .
- Even if the patient has been free of seizures for many years, there is a high risk of relapse if the antiepileptic medication is stopped.
- Valproate : first line treatment
- Alternative : Lamotrigine, Levetiracetam

Syndrome	Age at onset (years)	Predominant seizure types	EEG	Response to AED,Prognosis
CAE	4 – 10	Typical absence seizures Rare GTC seizures	3-Hz spike and wave	Good; most remit by adolescence
JAE	10-17	Typical absence seizures Infrequent myoclonus Infrequent GTC seizures	3 – 4-Hz spike and wave	Good; easy to control but tend to persist through life
JME	10-16	Myoclonus, GTC, absence seizures in ~ 1/3 of patients	3.5 – 4-Hz spike and polyspikes	Good; easy to control but usually persist through life

Beydoun A1, D'Souza J.
Treatment of idiopathic generalized epilepsy - a review of the evidence.
Expert Opin Pharmacother. 2012 Jun;13(9):1283-98.

IGE with GTCS on awakening

- Later age than JAE and JME.
- 6 - 28 years, with a peak at 17 years.
- GTCS occur predominantly within 1–2 h after awakening; the second seizure peak is during the evening.
- 81% have, in addition, absences or myoclonic jerks (or both).

IGE with GTCS on awakening

- A genetic predisposition is frequent.
- There are nonspecific bilateral epileptiform patterns in the EEG.
- In this syndrome, a response to adequate antiepileptic medication is good.

Beghi M1, Beghi E, Cornaggia CM, Gobbi G.
Idiopathic generalized epilepsies of adolescence.
Epilepsia. 2006;47 Suppl 2:107-10.

Syndromes of Idiopathic Generalized Epilepsies Not Recognized by the International League Against Epilepsy

- IGE with absences of early childhood
- IGE with phantom absences
- Perioral myoclonia with absences
- Eyelid myoclonia with absences

Panayiotopoulos CP.
Syndromes of idiopathic generalized epilepsies not recognized by the International League Against Epilepsy. Epilepsia. 2005;46 Suppl 9:57-66.

IGE with absences of early childhood

- An epileptic condition characterized by absences with onset in early childhood, before the age of 4.
- Absence of neurologic and cognitive deficits.
- Possible occurrence of GTCS, myoclonic jerks, and myoclonic–astatic seizures (in about 40% of children)

IGE with absences of early childhood

- Ictal EEG showing irregular 3–4 Hz spike-and-wave complexes that end progressively in a sequence of slow waves
- A family history of IGE and generalized spike-wave abnormalities in the EEG of unaffected members.
- This condition bears a worse prognosis than CAE.

Perioral myoclonia with absences

- The symptom of perioral myoclonia may rarely occur in absence seizures of other IGEs.
- GTCS that often start early prior to or together with the absences
- Frequent occurrence of absence status epilepticus (ASE)
- Resistance to treatment
- Persistence in adult life.
- No photosensitivity

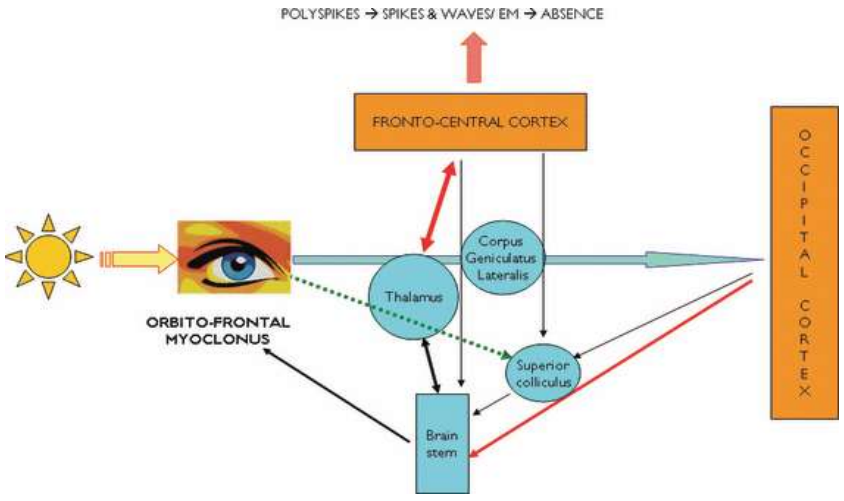
Eyelid myoclonia with absences (Jeavons syndrome)

- Eyelid myoclonia (EM) with or without absences
- Eye closure-induced electroencephalography (EEG) paroxysms
- Photosensitivity
- In addition, rare tonic–clonic seizures may also occur.

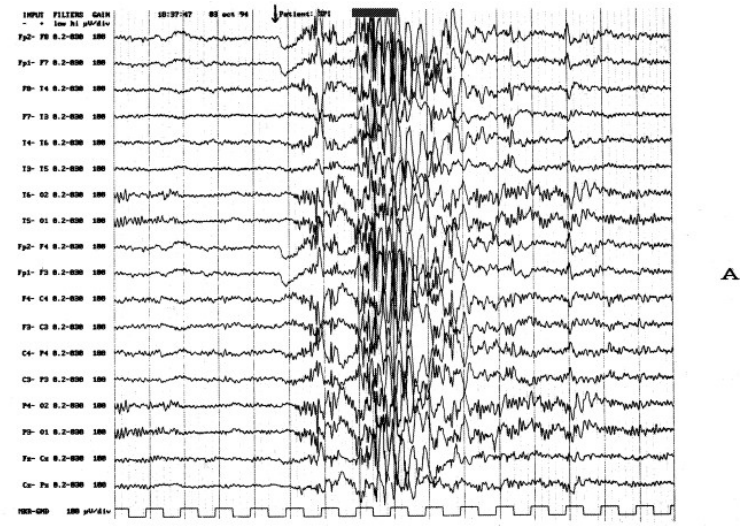
Charateristics

- EMA onset is typically in childhood, with a peak at 6–8 years.
- Eyelid jerks are frequently misinterpreted as tics or mannerisms, and absences may be overlooked.
- Treatment : Levetiracetam, Zonisamide
- Some patient: poor response to treatment

Eyelid myoclonia with absences (Jeavons syndrome)



Epilepsia
pages 15-19, 4 MAY 2009 DOI: 10.1111/j.1528-1167.2009.02114.x
http://onlinelibrary.wiley.com/doi/10.1111/j.1528-1167.2009.02114.x/full#f1



Eyelid myoclonia with absences: an overlooked epileptic syndrome?
Neurophysiologie Clinique/Clinical Neurophysiology, Volume 32, Issue 5, 2002, 287 - 296

Idiopathic focal epilepsy

No structural lesion. Functional mechanism

Idiopathic Focal Epilepsy

- Benign rolandic epilepsy (BRE) or Benign epilepsy with centrotemporal spikes (BECTS)
- Childhood idiopathic occipital epilepsy
  - Late-onset (Gastaut type)
  - Early-onset (Panayiotopoulos type)
  - idiopathic photosensitive occipital lobe epilepsy

Benign epilepsy with centrotemporal spikes

- 15% of all children with epilepsy
- Onset 3-13 years old and resolved by age 15-17 years old.
- Sleep related
- Simple partial, involving the face and tongue→ secondary GTCS

P. Camfield, C. Camfield
Epileptic syndromes in childhood: clinical features, outcomes, and treatment
Epilepsia, 43 (Suppl. 3) (2002

Diagnosis

- Clinical
- Normal neurological examination
- A typical EEG with broad, centrotemporal spikes that show an anterior–posterior dipole on monopolar recording
- Cognitive and behavioral problems in BECTS are well-documented.
- General intellectual function is normal in BECTS, but deficits are in specific cognitive domains.
- More frequent centrotemporal spikes during sleep in BECTS may be associated with poorer outcomes.

Vannest J, Tenney JR, et al. Cognitive and behavioral outcomes in benign childhood epilepsy with centrotemporal spikes. Epilepsy Behav. 2015 Apr;45:85-91

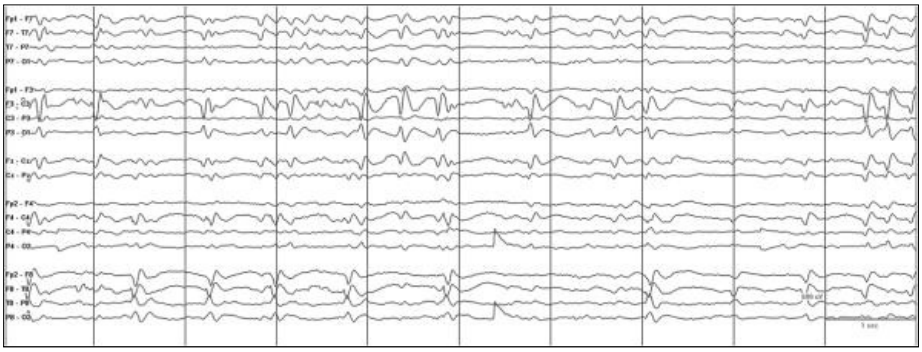


FIG. 4 . Interictal epileptiform activity in patients with benign epilepsy of childhood with centrotemporal spikes. Diphasic spikes and sharp waves occur in the left centro-temporo-parietal regions.

Pediatric Focal Epilepsy Syndromes.
Sanchez Fernandez, Ivan; Loddenkemper, Tobias

Journal of Clinical Neurophysiology. 29(5):425-440, October 2012.
DOI: 10.1097/WNP.0b013e31826bd943

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Treatment

- Debate “treat” VS “not to treat”
- Treat all
- Selective treatment in
  - early onset
  - multiple seizures at onset, or large numbers of seizures, especially GTCSs
  - Symptoms related to the discharges include transient change of awareness, transient cognitive impairment, language disorders, and different neuropsychological disorders.

Drug of Choice

- Valproate : European expert recommended
  - Reduce seizure frequency , cause fewer EEG abnormalities
  - Reduce epileptic negative myoclonus
- Carbamazepine, Oxcarbamazepine : American Epileptologist recommended
  - Major problem : induction of epileptic negative myoclonus, atypical absence or Electrical status epilepticus in sleep.
- Benzodiazepine
- Levetiracetam

Hughes J. Benign epilepsy of childhood with centrotemporal spikes (BECTS): To treat or not to treat,that is the question.

Idiopathic childhood occipital epilepsy of Gastaut

- Seizures are occipital
- primarily manifest with elementary visual hallucinations, blindness or both
- Consciousness is intact during the visual symptoms (simple focal seizures)
- Visual seizures are usually brief;1-3 minutes.

Panayiotopoulos type

- Early and mid-childhood.
- Hallmark of PS is ictal autonomic aberrations.
- Mainly emesis (70–80% of seizures).
- Consciousness and speech, as a rule, are preserved.

idiopathic photosensitive occipital lobe epilepsy

- A syndrome of reflex epilepsy with age-related onset
- Reflex occipital seizures induced by television, video games and intermittent photic stimulation (IPS)
- Manifest with similar semiology as the spontaneous visual seizures

Panayiotopoulos CP, Michael M, Sanders S,et al. Benign childhood focal epilepsies: assessment of established and newly recognized syndromes. Brain. 2008 Sep;131(Pt 9):2264-86.

Element of visual hallucination	Occipital	Migraine
Speed of development from onset to full image	Fast in seconds	Slow in minutes
Speed and direction of movement	Fast in seconds and usually towards the centre of the visual field and contalateral to the side of onset	Slow in minutes and usually towards the periphery of the visual field and ipsilateral to the side of onset
Quality	Usually with bright colours and circular shapes	Usually achromatic or black and white linear zigzag patterns
Duration	Usually 1–3 min	Usually over 15 min
Progression to transient neurological symptoms	Eye deviation, eyelid closures and sometimes convulsions	Scotoma, hemianopia, hemi-anaesthesia or hemi-paresis and for basilar migraine, vertigo, ataxia, bilateral weakness and dysaesthesiae

Autosomal –dominant nocturnal frontal lobe epilepsy (ADNFLE)

- began during sleep ;seizure peaks in early morning.
  - Three characteristic manifestation of NFLE

	Paroxysmal Arousal s	**Nocturnal paroxysmal dystonia**	**Episodic Nocturnal Wandering**
Onset	Abrupt, recurring arousals form NREM	Begins as PA ;then complex movements	Starts as PA
Description	Vocalization with sterotyped movement	Kicking ,bicycling,trunk rocking ,tonic or clonic asymmetric, dystonic or ballistic movements	Patient jump out of bed,ambulate, appear agitate
% of recorded seizure	75%	23%	2%