Epileptiska syndrom

IVETT KÖRHEGYI

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NPH, Neurologimottagning Barn

Drottning Silvias Barnsjukhus

Utbildning, Terapigrupp Barn, Göteborg

Epilepsi

Incidens: 1 000 barn/år i Sverige
Prevalens: 10 000 barn

Oprovocerade, återkommande epileptiska anfall

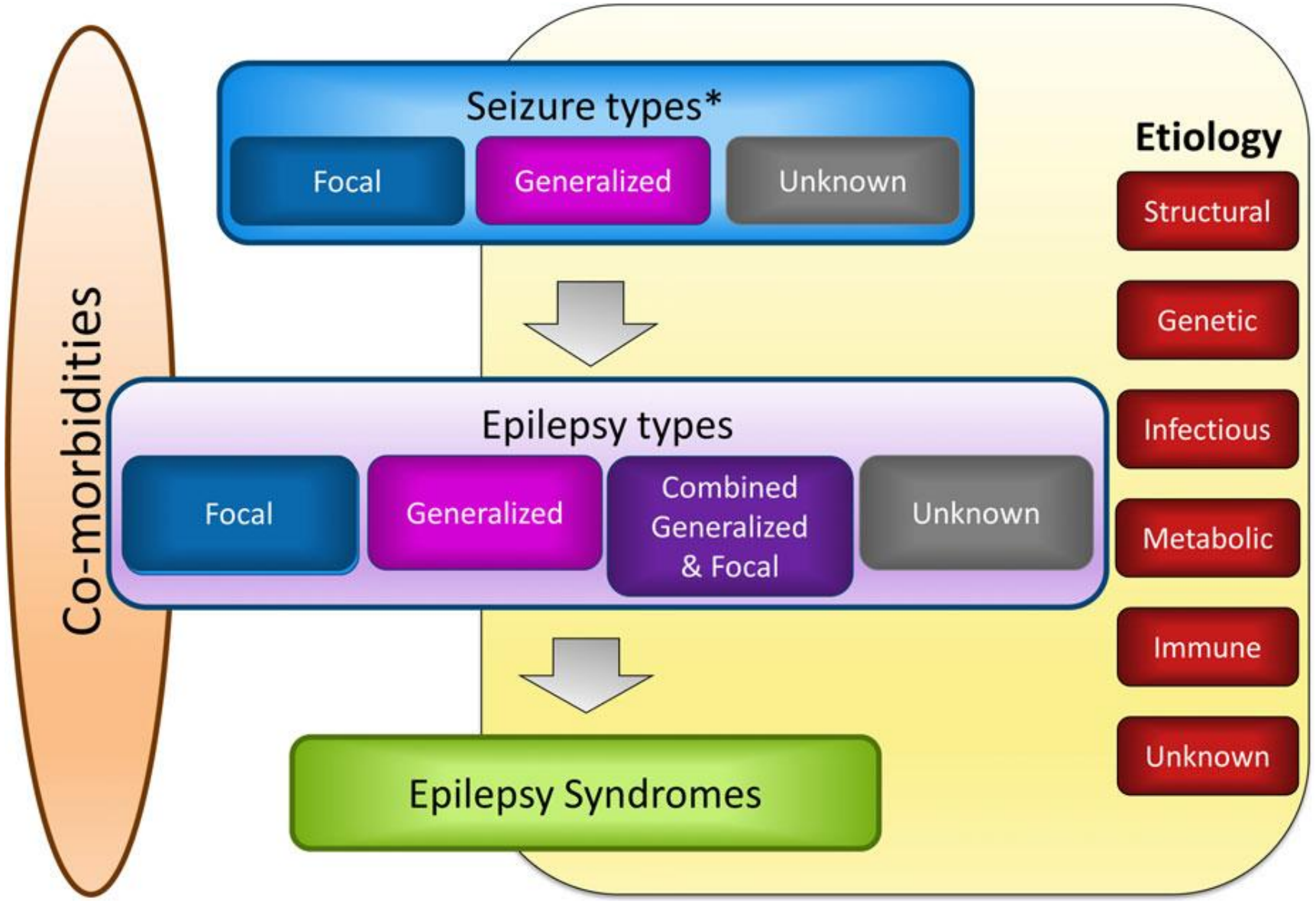
Diagnos:

- **två oprovocerade anfall** - över 70% risk för ytterligare anfall (efter första 40%)

- **ett oprovocerat anfall** + **risk för ytterligare anfall** är stor
- **Epileptiska syndrom**

Varaktig benägenhet för upprepade oprovocerade epileptiska anfall

”Ny” epilepsiklassifikation



ILAE POSITION PAPER

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

[1,2,3]Ingrid E. Scheffer, [1]Samuel Berkovic, [4]Giuseppe Capovilla, [5]Mary B. Connolly, [6]Jacqueline French, [7]Laura Guilhoto, [8,9]Edouard Hirsch, [10]Satish Jain, [11]Gary W. Mathern, [12]Solomon L. Moshé, [13]Douglas R. Nordli, [14]Emilio Perucca, [15]Torbjörn Tomson, [16]Samuel Wiebe, [17]Yue-Hua Zhang, and [18,19]Sameer M. Zuberi

Epilepsia, 58(4):512–521, 2017
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Dr. Ingrid E. Scheffer chairs the ILAE Task Force on the Classification of the Epilepsies.

SUMMARY

The International League Against Epilepsy (ILAE) Classification of the Epilepsies has been updated to reflect our gain in understanding of the epilepsies and their underlying mechanisms following the major scientific advances that have taken place since the last ratified classification in 1989. As a critical tool for the practicing clinician, epilepsy classification must be relevant and dynamic to changes in thinking, yet robust and translatable to all areas of the globe. Its primary purpose is for diagnosis of patients, but it is also critical for epilepsy research, development of antiepileptic therapies, and communication around the world. The new classification originates from a draft document submitted for public comments in 2013, which was revised to incorporate extensive feedback from the international epilepsy community over several rounds of consultation. It presents three levels, starting with *seizure type*, where it assumes that the patient is having epileptic seizures as defined by the new 2017 ILAE Seizure Classification. After diagnosis of the *seizure type*, the next step is diagnosis of *epilepsy type*, including focal epilepsy, generalized epilepsy, combined generalized, and focal epilepsy, and also an unknown epilepsy group. The third level is that of *epilepsy syndrome*, where a specific syndromic diagnosis can be made. The new classification incorporates *etiology* along each stage, emphasizing the need to consider etiology at each step of

ILAE 2017
Baserat på **genetik, etiologi, neurofysiologi**

Etiologi ska beaktas i varje klassifikationssteg

Figure 1.
Framework for classification of the epilepsies. *Denotes onset of seizure.
Epilepsia © ILAE

- **Förvärvade:** trauma, stroke, cerebral hypoxi/anoxi

- Missbildningar, kortikal dysplasi
- Tuberös skleros
- Tumör *(lokalisation)*

- **Genetisk epilepsi -** jonkanalssjukdom t.ex. Dravet-syndrom, ca 1000 gener

- CNS-infektion

- **Neurometabol sjukdom,** mitokondriell sjukdom

- Neurodegenerativ sjukdom
- Autoimmun sjukdom/encefalit

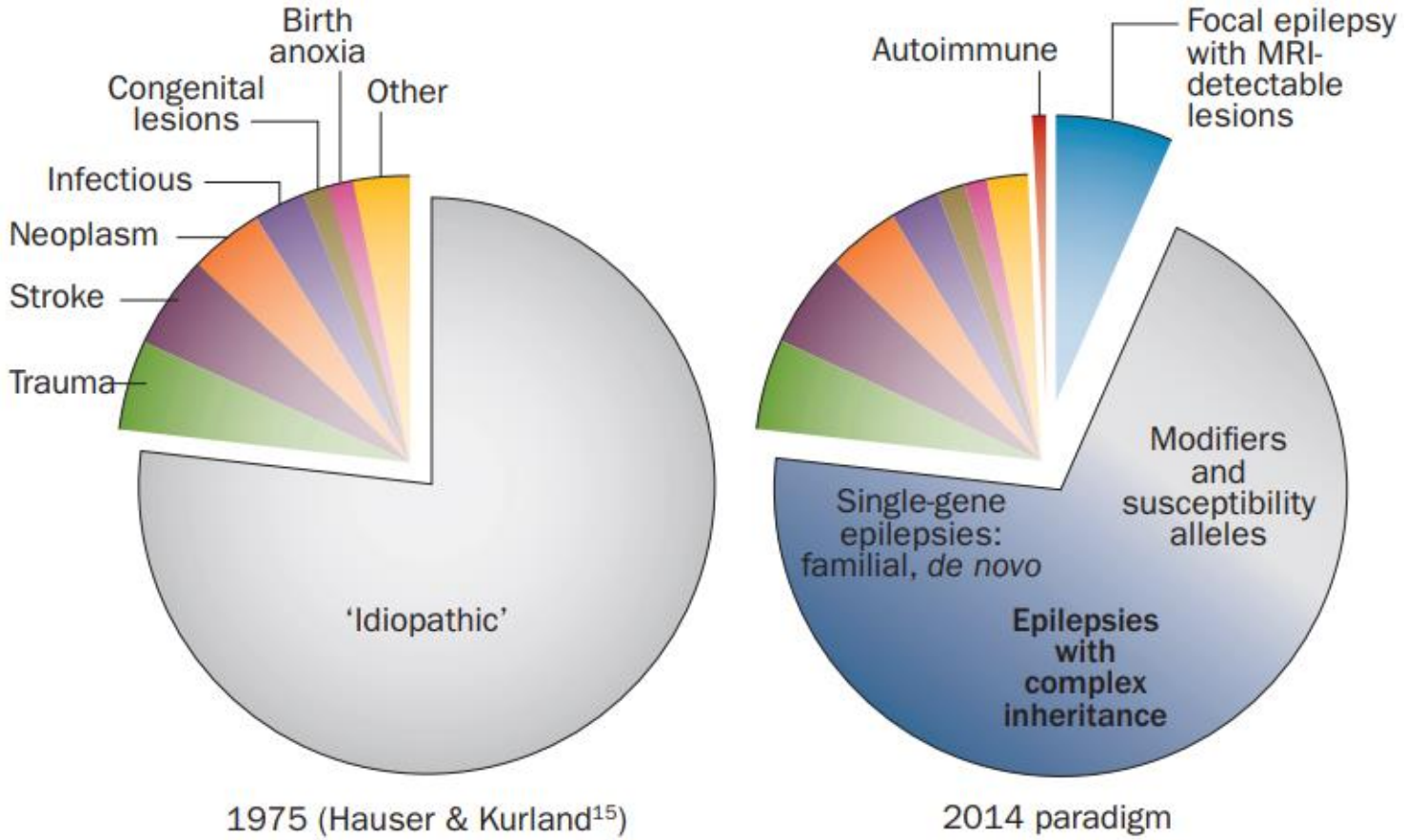


Figure 1 | Advances in understanding the causes of epilepsy. **a** | In 1975, the majority of epilepsies were characterized as 'idiopathic'. **b** | Today, epilepsy of unknown cause comprises a much smaller proportion, owing to the discovery of autoimmune epilepsies, epilepsies with lesions that are only detectable by MRI and, most importantly, the reclassification of many epilepsies previously considered idiopathic as having a genetic cause. The exact proportions of monogenic and complex or polygenic epilepsies remain uncertain. Data for part a were obtained from Hauser & Kurland.[15]

Thomas, R. H. & Berkovic, S. F. *Nat. Rev. Neurol.* **10**, 283–292 (2014); published online 15 April 2014; doi:10.1038/nrneurol.2014.62

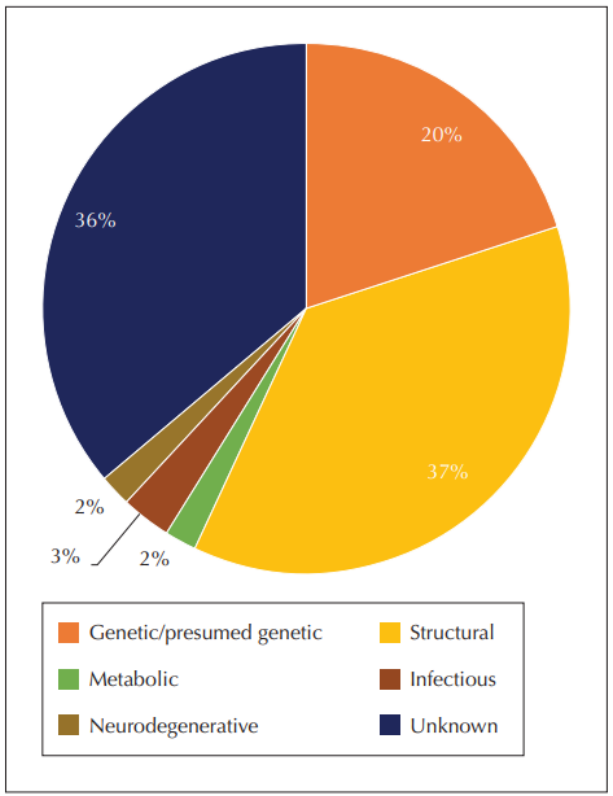
The hidden genetics of epilepsy—a clinically important new paradigm

Rhys H. Thomas and Samuel F. Berkovic

■ Seminar of Epileptology
Epileptic Disord 2021; 23 (1): 1-16
Epileptic Disorders

The aetiologies of epilepsy

Simona Balestrini [1,2], Alexis Arzimanoglou [3,4], Ingmar Blümcke [5], Ingrid E. Scheffer [6], Samuel Wiebe [7], Johan Zelano [8,9], Matthew C. Walker [1]



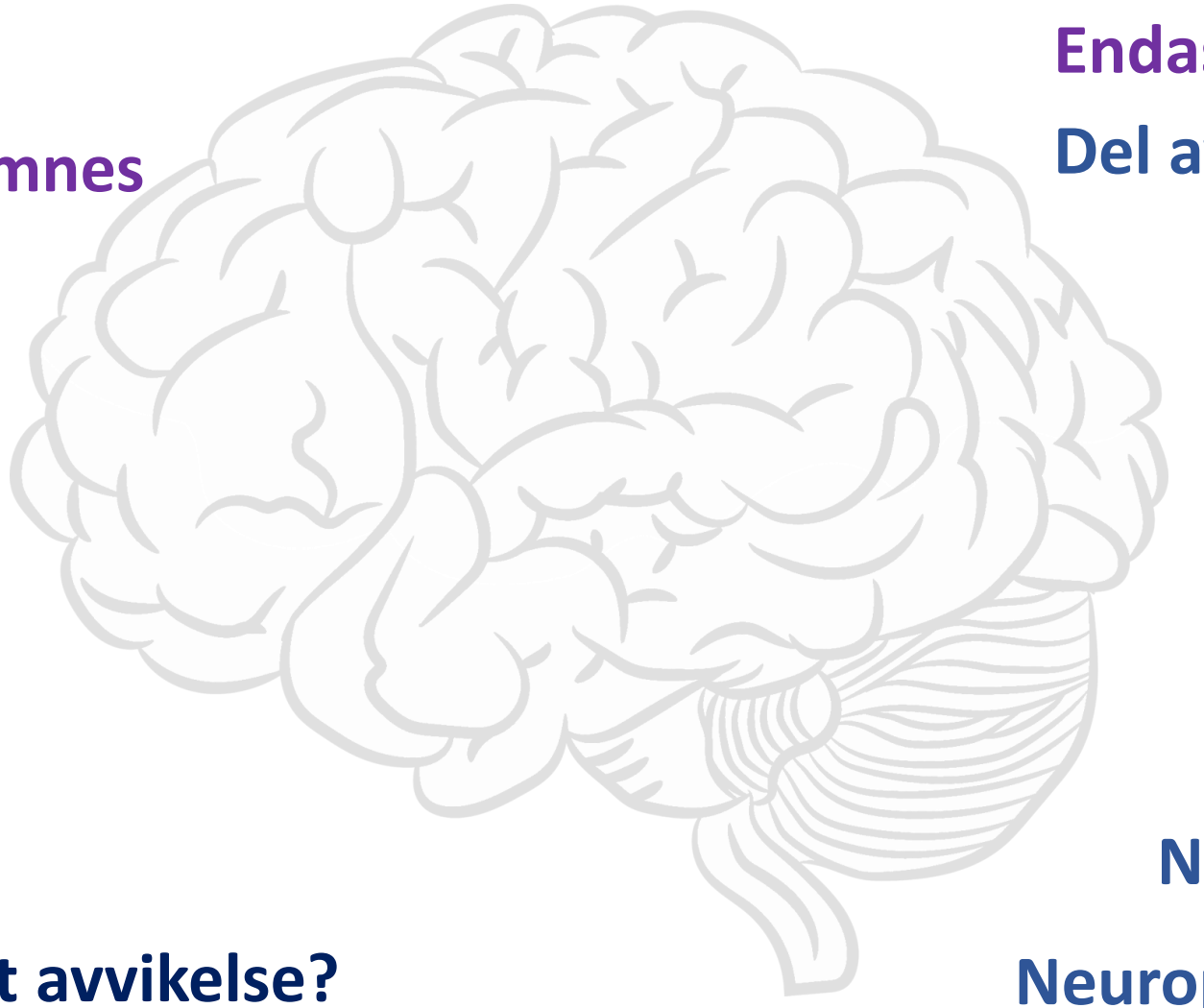
■ **Figure 1.** Aetiologies of epilepsies in a resource-rich European region (after Syvertsen *et al.* 2015).

Hereditet

Perinatal anamnes

Endast epilepsi ?

Del av syndrom ?



Anfallstyp

EEG

MR-hjärna

Samsjuklighet?

Ansiktsdysmorfi?

Avvikelse på huden ?

Neurologiskt status

Neuropsykologisk utveckling ?

Morfologiskt avvikelse?

Misstanke om neurometabol sjukdom?

Infektion? Immunologisk orsak?

Early myoclonic encephalopathy
PIGA, SETBP1, SIK1, SLC25A22

Dravet syndrome
SCN1A
GABRA1, GABRG2, HCN1, KCNA2, SCN1B, STXBP1

Epilepsy with myoclonic–atonic seizures
SLC2A1
SLC6A1
GABRA1, GABRG2, SCN1A, SCN1B

Early-onset epileptic encephalopathy
KCNQ2
AARS, CACNA2D2, NECAP1, PIGA, QARS, SCN8A

CDKL5
SCN2A
STXBP1
GNAO1
ARX, DOCK7, SLC25A22, SLC35A2, WWOX

Infantile spasms
ALG13, DNM1, FOXG1 duplications, GABRA1, GABRB3, GRIN1, GRIN2A, GRIN2B, IQSEC2, KCNT1, MAGI2, MEF2C, NEDDL4, NDP, NRXN1, PIGA, PLCB1, PTEN, SCA2,SCN1A, SCN2A, SCN8A, SETBP1, SIK1, SLC25A22, SLC35A2, SPTAN1, ST3GAL3, STXBP1, TBC1D24, TCF4

Lennox-Gastaut syndrome
ALG13, DNM1, FLNA, GABRB3, GLI3, HNRNPU, SCN1A, SCN2A, SCN8A, STXBP1

KCNQ2
KCNT1, PIGQ
Early infantile epileptic encephalopathy (Ohtahara syndrome)

Epilepsy of infancy with migrating focal seizures
KCNT1
SCN2A, SCN1A
PLCB1, QARS, SCN8A, SLC25A22, TBC1D24, SLC12A5

Epilepsy–aphasia spectrum
GRIN2A

Other predominantly myoclonic epilepsies
Onset 0–1 years: *EEF1A2, MEF2C, SCN1A, SLC2A1, SPTAN1, SYNGAP1, TBC1D24*
Onset >1 year: *CHD2, MEF2C, SYNGAP1, UBE3A*

Other predominantly focal or multifocal epilepsies
Onset 0–6 months: *ARHGEF9, DEPDC5, SCN1A, TBC1D24, PNKP, SLC2A1*
Onset 6–12 months: *ARHGEF9, DEPDC5, FOXG1 mutations, MBD5, PIGO, SLC13A5*
Onset >1 year: *ARHGEF9, DEPDC5, MBD5, PCDH19, POLG, TNK2, ZEB2*

0 months | 3 months | 6 months | 1 year | 2 years | 4 years

Figure 1: **Genetic causes of epilepsy syndromes**

The genetic landscape of the epileptic encephalopathies of infancy and childhood

Amy McTague, Katherine B Howell*, J Helen Cross, Manju A Kurian, Ingrid E Scheffer*

Lancet Neurol 2016; 15: 304–16
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*Authors contributed equally
Molecular Neurosciences (A McTague MBChB, M A Kurian PhD) **and Clinical Neurosciences** (Prof J H Cross PhD), **Developmental Neurosciences Programme, UCL Institute of Child Health, London, UK; Department of Neurology, Great Ormond Street Hospital for Children NHS Foundation Trust, London, UK** (A McTague, Prof J H Cross, M A Kurian); **Department of Neurology,**

Epileptic encephalopathies of infancy and childhood comprise a large, heterogeneous group of severe epilepsies characterised by several seizure types, frequent epileptiform activity on EEG, and developmental slowing or regression. The encephalopathies include many age-related electroclinical syndromes with specific seizure types and EEG features. With the molecular revolution, the number of known monogenic determinants underlying the epileptic encephalopathies has grown rapidly. De-novo dominant mutations are frequently identified; somatic mosaicism and recessive disorders are also seen. Several genes can cause one electroclinical syndrome, and, conversely, one gene might be associated with phenotypic pleiotropy. Diverse genetic causes and molecular pathways have been implicated, involving ion channels, and proteins needed for synaptic, regulatory, and developmental functions. Gene discovery provides the basis for neurobiological insights, often showing convergence of mechanistic pathways. These findings underpin the development of targeted therapies, which are essential to improve the outcome of these devastating disorders.

Introduction

Severe epilepsies of infancy and childhood are a group of devastating disorders characterised by frequent epileptic seizures associated with developmental delay or regression. These conditions encompass a large group of with an incidence of 25–42 per 100 000 per year,[1] and Dravet syndrome, with an incidence of one per 22 000.[2,3]

In this Review, we explore the genetic landscape of the epileptic encephalopathies by focusing on how growth in gene discovery has radically changed our understanding

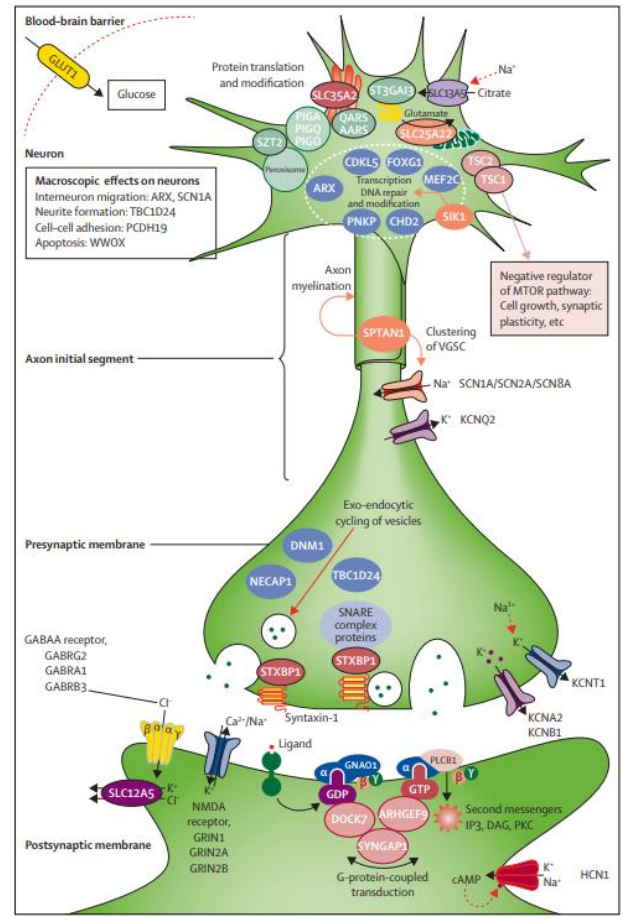


Figure 2: **Disease mechanisms in childhood epileptic encephalopathies**
Neuron, axon, presynaptic, and post-synaptic compartments. Many areas of abnormal neuronal function, including DNA repair, transcriptional regulation, axon myelination, metabolite and ion transport, and peroxisomal function, in addition to channelopathies and synaptic dysfunction, are implicated in childhood epileptic encephalopathies.

EEG

MR

Neurometabolisk utredning (< 2 år)

Genanalys (Epilepsi/EE Genpanel)

Anfallstyp

Klinisk bild

Debutålder

< 2 år
Tonårsålder

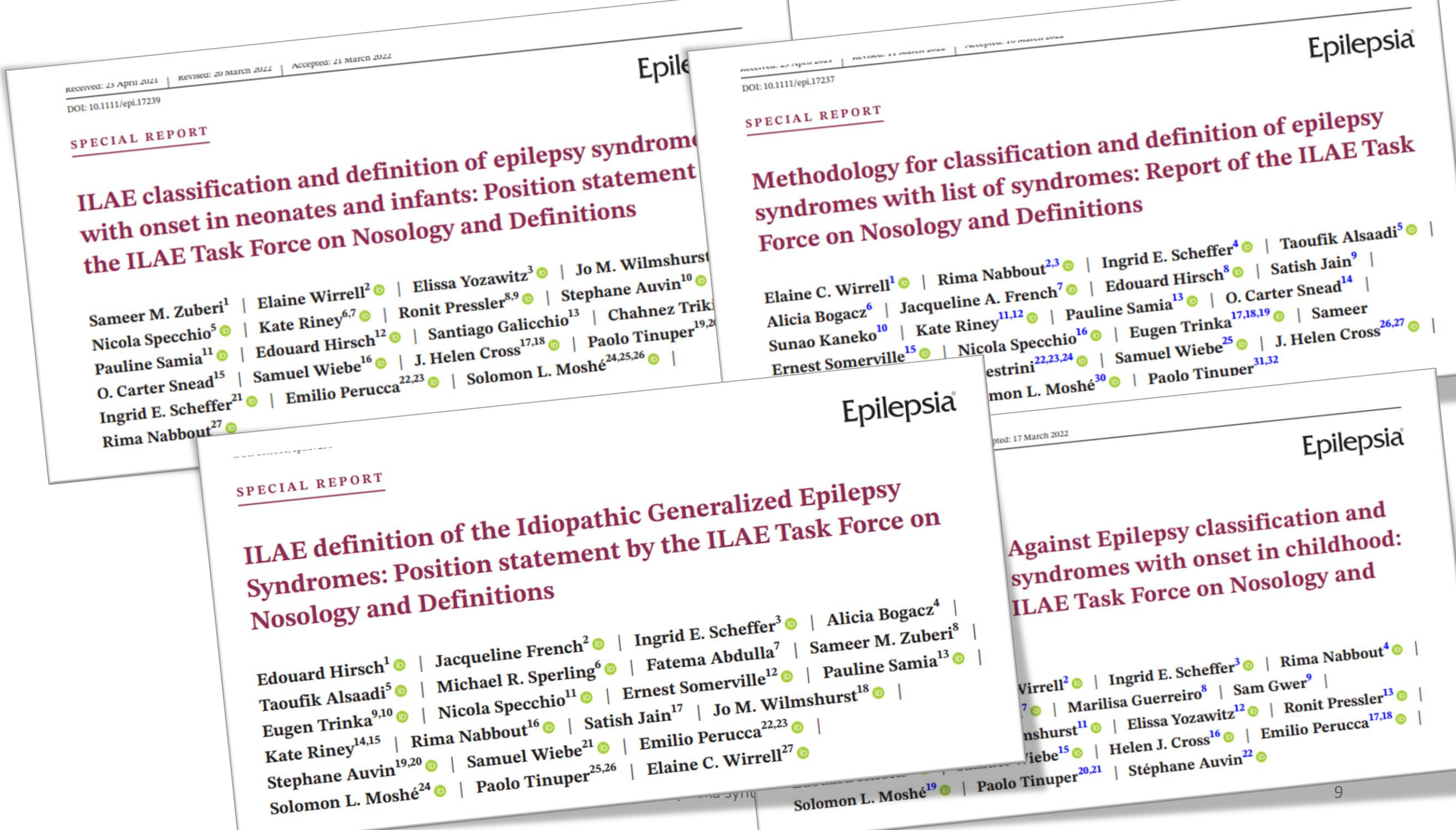
Epileptiskt syndrom

Etiologi

Morfologisk avvikelse
Neurometabolisk orsak
Genetisk
Immunologisk, infektiös orsak

Komorbiditet

”Genetiskt” syndrom?
ADHD, autism, utvecklingsstörning



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SPECIAL REPORT

ILAE classification and definition of epilepsy syndrome with onset in neonates and infants: Position statement the ILAE Task Force on Nosology and Definitions

Sameer M. Zuberi[1] | Elaine Wirrell[2] | Elissa Yozawitz[3] | Jo M. Wilmshurst
Nicola Specchio[5] | Kate Riney[6,7] | Ronit Pressler[8,9] | Stephane Auvin[10]
Pauline Samia[11] | Edouard Hirsch[12] | Santiago Galicchio[13] | Chahnez Triki
O. Carter Snead[15] | Samuel Wiebe[16] | J. Helen Cross[17,18] | Paolo Tinuper[19,2
Ingrid E. Scheffer[21] | Emilio Perucca[22,23] | Solomon L. Moshé[24,25,26] |
Rima Nabbout[27]

Epilepsia

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Methodology for classification and definition of epilepsy syndromes with list of syndromes: Report of the ILAE Task Force on Nosology and Definitions

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estrini[22,23,24] | Samuel Wiebe[25] | J. Helen Cross[26,27] |
mon L. Moshé[30] | Paolo Tinuper[31,32]

Epilepsia

SPECIAL REPORT

ILAE definition of the Idiopathic Generalized Epilepsy Syndromes: Position statement by the ILAE Task Force on Nosology and Definitions

Edouard Hirsch[1] | Jacqueline French[2] | Ingrid E. Scheffer[3] | Alicia Bogacz[4] |
Taoufik Alsaadi[5] | Michael R. Sperling[6] | Fatema Abdulla[7] | Sameer M. Zuberi[8] |
Eugen Trinka[9,10] | Nicola Specchio[11] | Ernest Somerville[12] | Pauline Samia[13] |
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Stephane Auvin[19,20] | Samuel Wiebe[21] | Emilio Perucca[22,23] |
Solomon L. Moshé[24] | Paolo Tinuper[25,26] | Elaine C. Wirrell[27]

pted: 17 March 2022

Epilepsia

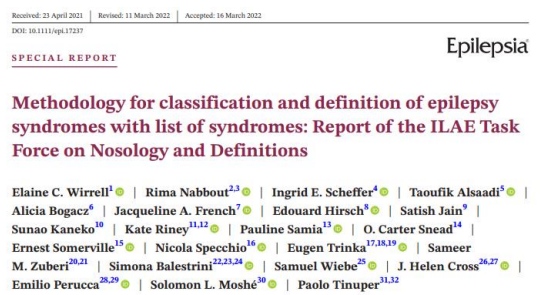
Against Epilepsy classification and syndromes with onset in childhood: ILAE Task Force on Nosology and

Virrell[2] | Ingrid E. Scheffer[3] | Rima Nabbout[4] |
[7] | Marilisa Guerreiro[8] | Sam Gwer[9] |
nshurst[11] | Elissa Yozawitz[12] | Ronit Pressler[13] |
iebe[15] | Helen J. Cross[16] | Emilio Perucca[17,18] |
Solomon L. Moshé[19] | Paolo Tinuper[20,21] | Stéphane Auvin[22]

Klassifikation

Key Points

- An epilepsy syndrome is a characteristic cluster of clinical and EEG features, often supported by specific etiological findings
- The diagnosis of a syndrome in an individual with epilepsy frequently carries prognostic and treatment implications
- Syndromes can be subdivided into those with (1) generalized onset seizures, (2) focal onset seizures, (3) generalized and focal onset seizures, and (4) developmental and/or epileptic encephalopathy or progressive neurological deterioration
- Syndromes are also divided based on age at onset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- **Typisk ålder för symtomdebut**
  - Neonatal och spädbarnsålder (< 2 år)
  - Under barndomen
  - Variabel åldersdebut (≤ 18 år eller ≥ 19 år)

  - *Idiopatisk generaliserad epilepsi (IGE)*

- **Anfallstyp, epilepsityp** (fokal, generaliserad, fokal-generaliserad)

- ***Developmental* Epileptisk encefalopati** eller progressivt neurologiskt tillstånd

Klassifikation - Kriterier

- **Mandatory**
  - Obligatorisk
  - Om det saknas kan syndromet inte fastställas
- **Exclusionary**
  - Exklusion
  - Om det saknas kan syndromet fastställas
- **Alerts**
  - Brukar saknas, men kan ses ibland
  - Kan inte utesluta syndromet själv – men tänk om!

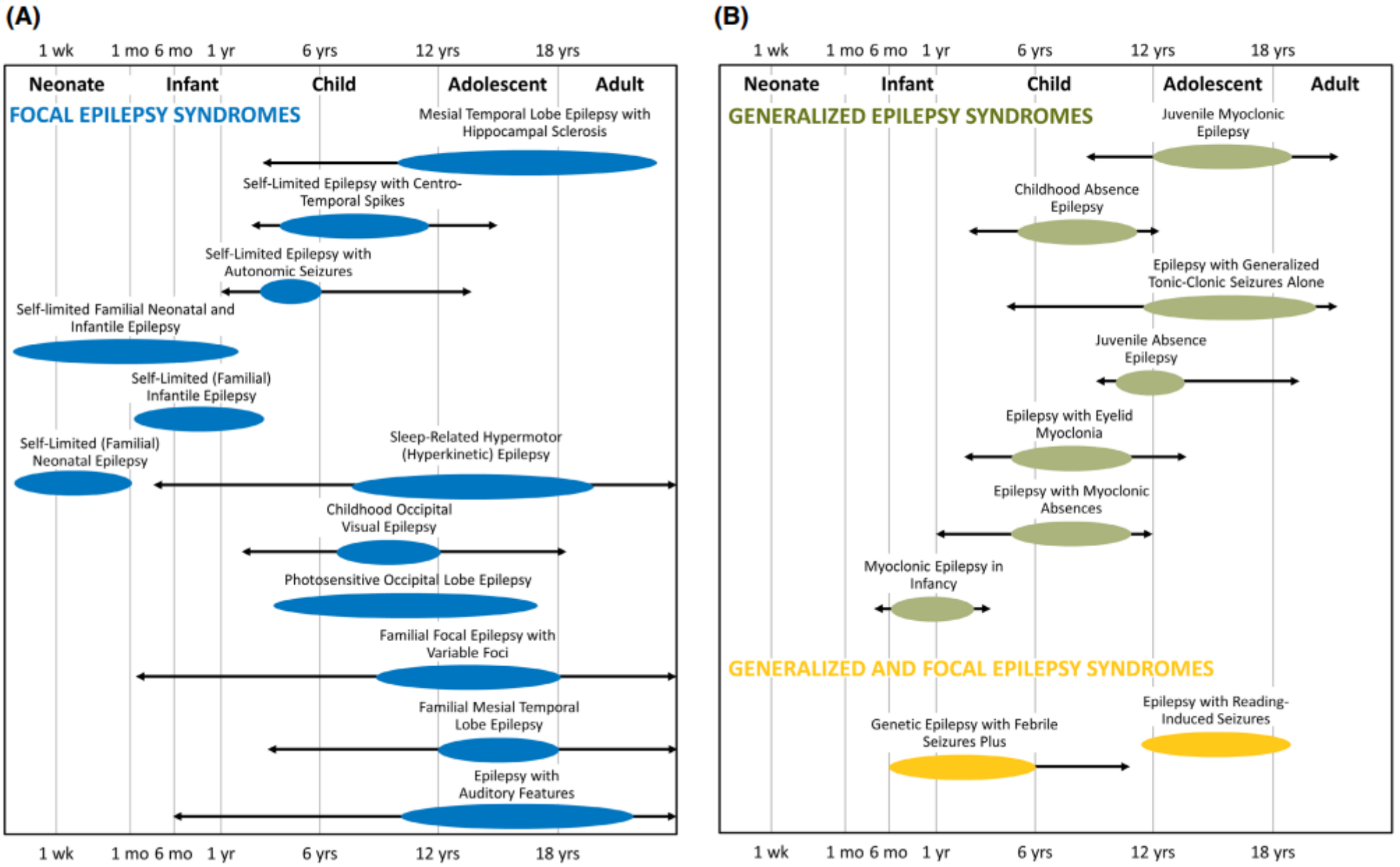

(A)
1 wk
1 mo
6 mo
1 yr
6 yrs
12 yrs
18 yrs
Neonate
Infant
Child
Adolescent
Adult
FOCAL EPILEPSY SYNDROMES
Mesial Temporal Lobe Epilepsy with Hippocampal Sclerosis
Self-Limited Epilepsy with Centro-Temporal Spikes
Self-Limited Epilepsy with Autonomic Seizures
Self-limited Familial Neonatal and Infantile Epilepsy
Self-Limited (Familial) Infantile Epilepsy
Self-Limited (Familial) Neonatal Epilepsy
Sleep-Related Hypermotor (Hyperkinetic) Epilepsy
Childhood Occipital Visual Epilepsy
Photosensitive Occipital Lobe Epilepsy
Familial Focal Epilepsy with Variable Foci
Familial Mesial Temporal Lobe Epilepsy
Epilepsy with Auditory Features
(B)
GENERALIZED EPILEPSY SYNDROMES
Juvenile Myoclonic Epilepsy
Childhood Absence Epilepsy
Epilepsy with Generalized Tonic-Clonic Seizures Alone
Juvenile Absence Epilepsy
Epilepsy with Eyelid Myoclonia
Epilepsy with Myoclonic Absences
Myoclonic Epilepsy in Infancy
GENERALIZED AND FOCAL EPILEPSY SYNDROMES
Genetic Epilepsy with Febrile Seizures Plus
Epilepsy with Reading-Induced Seizures

TABLE 1 Epilepsy syndromes included in specific position papers

Position paper	Type of epilepsy: Focal	Focal and/or generalized	Generalized	Syndromes with DEE or with progressive neurological deterioration

Epilepsy syndromes with onset in neonates and infants[22]	• Self-limited (familial) neonatal epilepsy
	• Self-limited (familial) infantile epilepsy
	• Self-limited familial neonatal-infantile epilepsy
		• Genetic epilepsy with febrile seizures plus	• Myoclonic epilepsy in infancy	• Early infantile DEE Ohtahara
				• Epilepsy of infancy with migrating focal seizures
				• Infantile epileptic spasms syndrome
				• Dravet syndrome
				• Etiology-specific DEEs
				  • *KCNQ2*-DEE
				  • Pyridoxine-dependent and pyridox(am)ine 5′ phosphate deficiency DEE
				  • *CDKL5*-DEE
				  • *PCDH19* clustering epilepsy
				  • GLUT1DS-DEE
				  • Sturge–Weber syndrome
				  • Gelastic seizures with HH

Epilepsy Syndromes with onset in childhood[23]	Self-limited focal epilepsies • Self-limited epilepsy with centrotemporal spikes • Self-limited epilepsy with autonomic seizures • Childhood occipital visual epilepsy • Photosensitive occipital lobe epilepsy		• Epilepsy with myoclonic absences • Epilepsy with eyelid myoclonia	• Epilepsy with myoclonic–atonic seizures • Lennox–Gastaut syndrome • DEE or EE with spike-and-wave activation in sleep • Febrile infection-related epilepsy syndrome • Hemiconvulsion–hemiplegia–epilepsy
Epilepsy syndromes with onset at a variable age[24]	• Mesial temporal lobe epilepsy with hippocampal sclerosis • Familial mesial temporal lobe epilepsy • Sleep-related hypermotor (hyperkinetic) epilepsy • Familial focal epilepsy with variable foci • Epilepsy with auditory features	Epilepsy with reading-induced seizures		Rasmussen syndrome Progressive myoclonus epilepsies
Idiopathic generalized epilepsies[21]			• Childhood absence epilepsy • Juvenile absence epilepsy • Juvenile myoclonic epilepsy • Epilepsy with generalized tonic–clonic seizures alone	

Abbreviations: DEE, developmental and/or epileptic encephalopathy; EE, epileptic encephalopathy; GLUT1DS, glucose transporter 1 deficiency syndrome; HH, hypothalamic hamartoma.

Subklassifikation
Self-limited
DEE
Etiology specific

Self-limited neonatal epilepsy (SeLNE)

- Debut: vid 2-7 dagars ålder
- **Fokala toniska anfall**
- Sekventiella anfall: toniskt, kloniskt, myokloniskt och/eller autonoma symtom, apné, cyanos

- **EEG:** normal bakgrund, normalt interiktalt
- Iktalt: centro-fronto-temporala repetitiva spikes
- Normal utveckling
- **Etiologi**: AD, vanligast *KCNQ2, KCNQ3, (SCN2A)*

- **Prognos:** bra, anfallsregression tills 6 månaders ålder (6 veckor)

Early-infantile developmental and epileptic encephalopathy (EIDEE)

- *Ohtahara syndrom (samt Early Myoclonic Encephalopathy)*
- **Debut: < 3 månader, terapiresistent, frekventa anfall**

- Många olika bakomliggande orsaker: genetisk, metabolisk, morfologisk avvikelse
- Gener: **KCNQ2-DEE, SCN2A-DEE, SCN8A-DEE, STXBP1-DEE, CDKL5-DEE, KCNT1-DEE**
- Neurologisk avvikelse, medel/svår utvecklingspåverkan

EEG: interiktalt: burst-suppression, multifokal spike-waves aktivitet, långsam aktivitet

Obligatorisk anfallstyp - en eller fler av dessa

- 1. **Toniska anfall** – 10-20 kluster/dag
- 2. Myokloni – fokal eller multifokal myokloni, ”oregelbundna”
- 3. Epileptiska spasmer
- 4. Sekventiella anfall: toniskt, kloniskt och/eller autonom symtom, automatismer

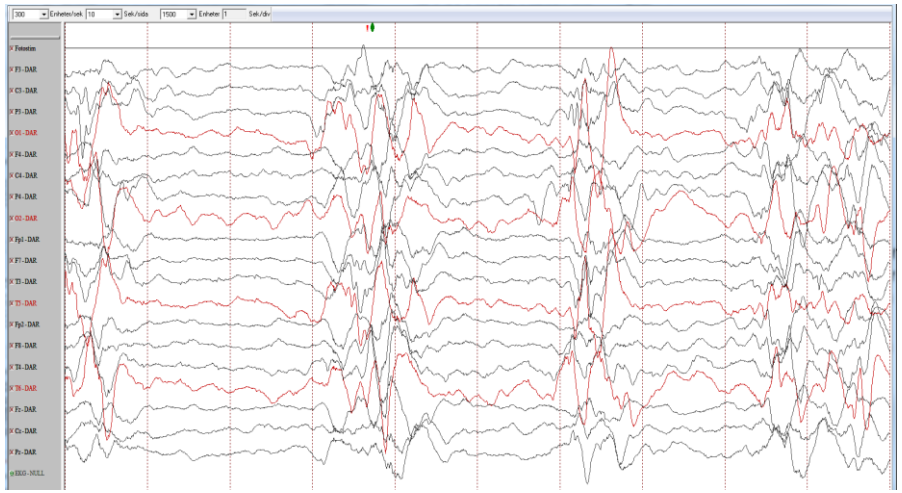
Infantile *epileptic* spasms *syndrome*
IESS

- **Debut**: 3-12 månader (1-24 månader)
- Epileptiska spasmer
- **EEG** interiktalt: **hypsarytmi**, multifokal epileptiform aktivitet

- **Morfologisk avvikelse 50-60 %**
- Tuberös skleros
- 40%: trisomi 21, ARX, CDKL5, STXBP1, IQSEC2, **TSC1, TSC2**

Infantile spasms

ALG13, DNM1, FOXG1 duplications, GABRA1, GABRB3, GRIN1, GRIN2A, GRIN2B, IQSEC2, KCNT1, MAGI2, MEF2C, NEDDL4, NDP, NRXN1, PIGA, PLCB1, PTEN, SCA2,SCN1A, SCN2A, SCN8A, SETBP1, SIK1, SLC25A22, SLC35A2, SPTAN1, ST3GAL3, STXBP1, TBC1D24, TCF4



West syndrom: triad av

- Anfall: **Infantila epileptiska spasmer**
- EEG: **Hypsarytmi**
- **Utvecklingsstagnation, regression**

DRAVETS syndrom

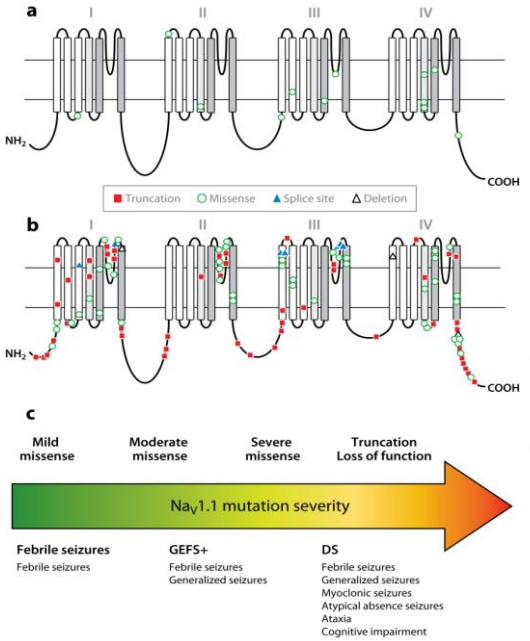
- **SCN1A mutation** (80-85%)**– voltage-gated Na-kanal, terapiresistent epilepsi**
- (*GABRA1, GABRG2, SCN1B, STXBP1*)
- Debut: 3-9 månader

Första levnadsåret: feberutlösta anfall

– ⏩ fokalt kloniskt (hemikloniskt), generaliserat kloniskt anfall

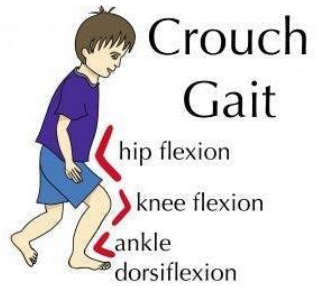
1.5-5 år:

- Myokloni
- Fokalt anfall med medvetandepåverkan
- Fokalt till bilateralt tonisk-kloniskt anfall
- Atypisk absens
- Atoniskt anfall
- NSE
- Toniskt och tonisk-kloniskt anfall i sömn, i kluster



Catterall WA. 2014.
Annu. Rev. Pharmacol. Toxicol. 54:317–38

Trigger:
Feber
Infektion
Värme
Kraftigt ljus
Fysisk aktivitet

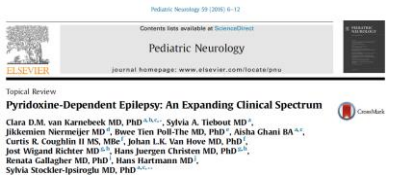


DRAVETS syndrom

- **1. fasen**: första levnadsåret: feberutlösta anfall –⏩ fokalt kloniskt (hemikloniskt), generaliserat kloniskt
- **2. fasen**: 1-4 år: oftare, mer långdragna anfall, myokloni, atypisk absens, status epilepticus, atoniska anfall
- **3. fasen**: 4-5 år: bättre anfallskontroll

- Kognitiv-, beteende-, språk- påverkan, ”crouch gait”
- **EEG**: fokal, multifokal generaliserad epileptiform aktivitet

- **Anfall blir färre med åldern, minskad risk för SE**
- **Tonåringar/Vuxna: tonisk-kloniskt anfall**


Pediatric Neurology

Topical Review

Pyridoxine-Dependent Epilepsy: An Expanding Clinical Spectrum

Vitamin B_6-beroende epilepsi

Pyridoxinberoende epilepsi (PDE):

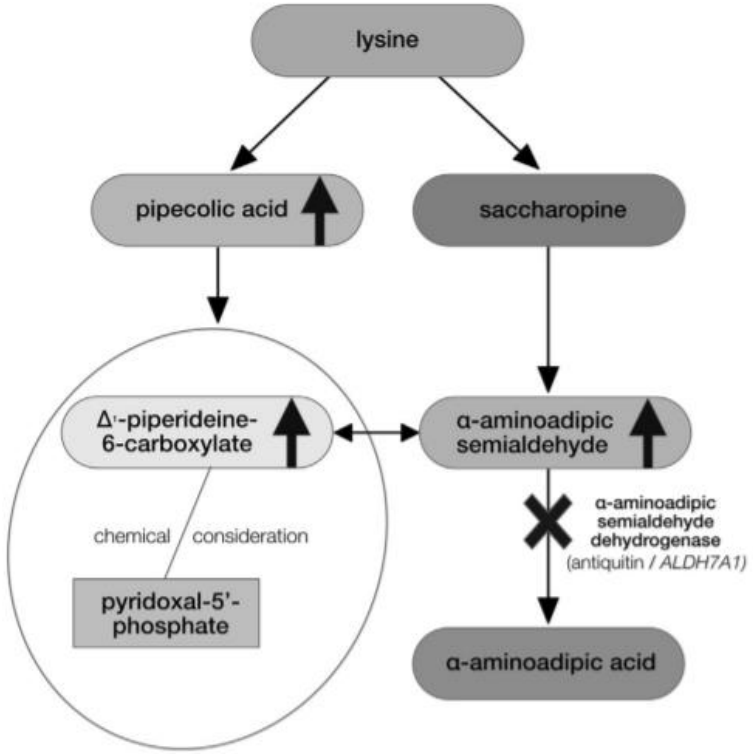


FIGURE 1.
Role of antiquitin (ALDH7A1) in the catabolic pathway of lysine.

C.D.M. van Karnebeek et al. / Pediatric Neurology xxx (2016) 1e7

- *autosomal recessiv epileptisk encefalopati*
- antiquitin (ALDH7A1) deficiency – påverkan på lysin katabolismen
- ackumulering av **pipekolsyra** ⬆
- Pyridoxin substitution - ⬆ pyridoxal 5-fosfat – kompenserar påverkan

- **Debut**: under första levnadsdagarna, intrauterin (25% <3 år)
- Svår encefalopati
- Fokala, multifokala anfall, toniska, epileptiska spasmer

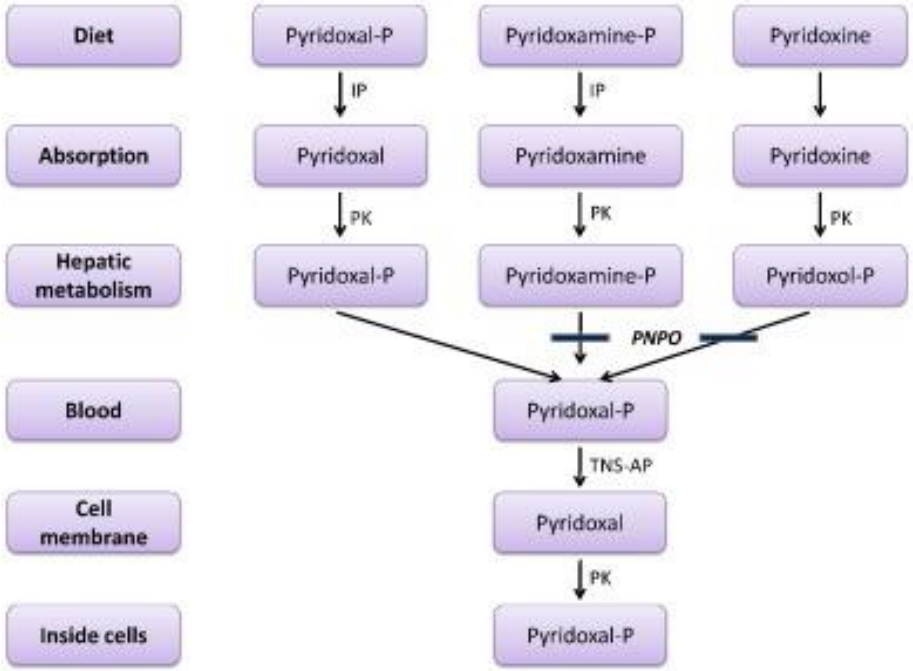
Pyridox(am)in 5´-phosfate oxidase deficiency PNPO

- **PNPO deficiency** (pyridoxamine 5`-phosphate oxidase deficiency) påverkad PLP-syntes och återupptag
- **PLP - Pyridoxal 5`-phosphate:** viktig roll i **GABA syntes**

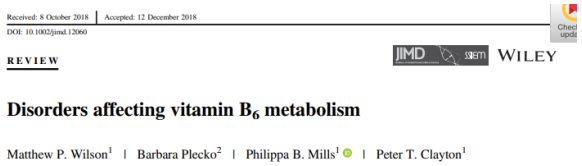
- Prematurfödda, tidig encefalopati, laktat acidos, hypoglykemi
- **Grimarsering, oregelbundna ögonrörelser, automatismer**

- **Diagnostik:**
  - **finns ingen specifik biomarkör**
  - **PNPO genanalys**

- **Behandling:** Pyridoxal 5- fosfat 30-50 mg/kg/dag p.o. fördelat på 4-6 doser
  - Pyridoxin kan också ge terapeutisk effekt ibland – vid vissa mutationer
  - OBS! apnérisk!



B. Jaeger et al. / Molecular Genetics and Metabolism Reports 6 (2016) 60–63


Received: 8 October 2018 | Accepted: 12 December 2018
DOI: 10.1002/jimd.12060
REVIEW
JIMD SSIEM WILEY
Disorders affecting vitamin B_6 metabolism
Matthew P. Wilson[1] | Barbara Plecko[2] | Philippa B. Mills[1] | Peter T. Clayton[1]

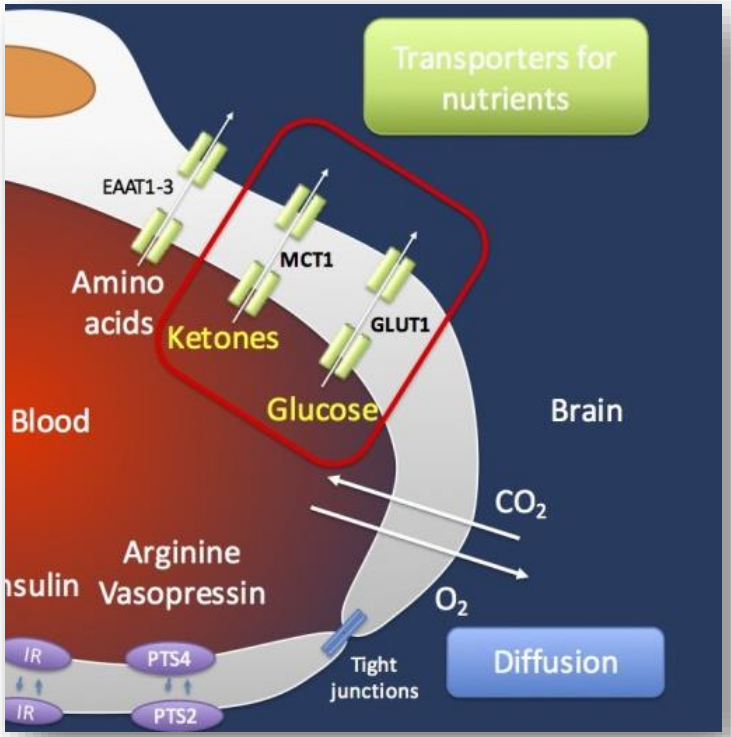
Glukostransportprotein typ 1-brist – GLUT1-brist syndrom

- Varierande svårighetsgrad, terapiresistent epilepsi
- **Typisk åldersdebut av ”klassisk form” < 2 år - under första 6 månaderna**
- (senare debut 2-10 år), det finns en ”non-classical” form med kognitiv påverkan, movement disorder, utan epilepsi)
- Cyanotisk attack, ”konstiga” ögonrörelser i början, eye-head gaze saccades
- Generaliserade anfall: myokloni, myoklon-atoniska, atypiska absenser (<4 år)

- EEG: interiktalt normal, iktalt fokal epileptiform aktivitet. Skillnad mellan pre- och postprandial EEG-bild

- **CSF glukos < 2.5 mmol/L, CSF/plasma glukos: < 0.5**
- **SLC2A1- mutation (80%)**
- **Behandling: ketogen kost**

Blood-brain-barrier



Source: epilepsigenetics.net
Figure inspired by Zlokovic, Nature Reviews Neuroscience 12, 723-738 (December 2011).

GLUT1 – membranbundet transportprotein för glukos genom blod-hjärnbarriären

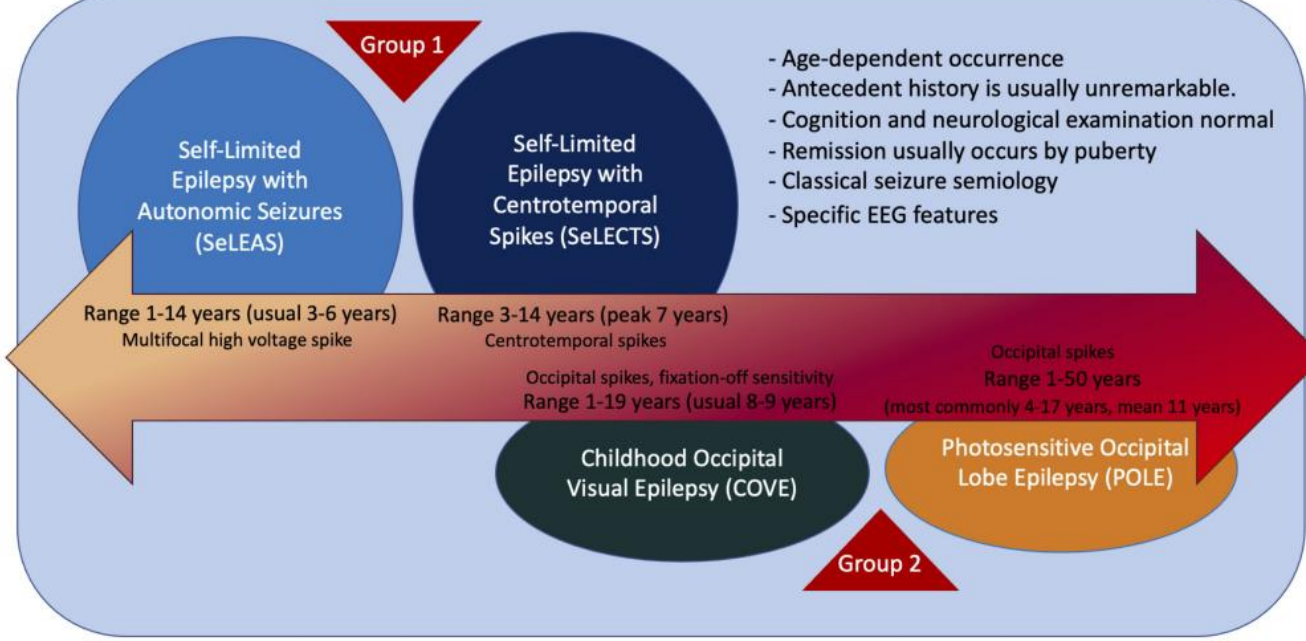
Gelastiska anfall med hypotalamushamartom

- **Debut:** under första levnadsåret (85%)
- Kongenital, non-neoplastisk lesion
- **Terapiresistent**
- **Neurokirurgisk åtgärd**: LITT, endoskopisk diskonnektion

- **Gelastiska anfall (skratt-episoder)**
- *Dacrystic seizure (crying)*

SeLFE syndromes

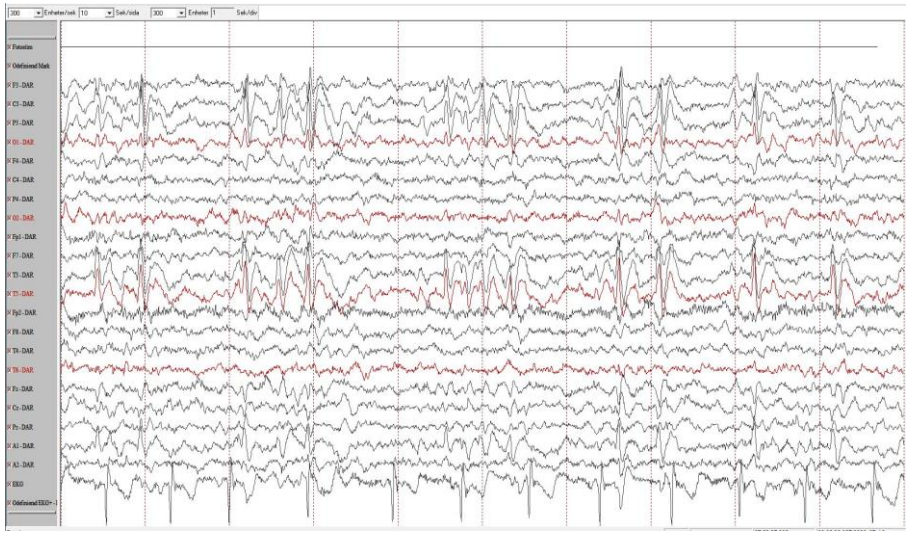
- Okänd orsak
- Karakteristisk elektro-klinisk presentation
- 25% av barnepilepsi



- **2 subgrupp**: I. SeLECTs , SeLEAS II. COVE, POLE
- Åldersspecifik debut
- Ingen signifikant strukturell avvikelse i hjärnan
- Normal kognition och normalt neurologiskt status
- Regression vid puberteten
- Svarar på behandling
- Genetisk predisposition för EEG-bild
- Typisk anfallssemiologi
- Specifik EEG-avvikelse: karakteristisk epileptiform aktivitet, lokalisation

Self-limited epilepsy with centrotemporal spikes SeLECTS

- *BECTs, Rolandisk epilepsi*
- Debut: 4-10 år (90%) peek 7 år
- **Self-limited – tills pubertet, 18 års ålder**
- **80%-90% under sömn** Sömn-associerad, vid uppvakning
- **20% under vakenhet**



- **Fokala anfall** med karakteristisk frontoparietal opercular ursprung semiologi och/eller nattliga bilaterala toniska-kloniska anfall
- Somatosensoriska symtom, orofaciala motoriska symtom, dysarthri, sialorrhea
- **EEG:** centrotemporal sharp-and slow-wave komplex – under dåsighet och sömn **mandatory**

Self-limited epilepsy with autonomic seizures SeLEAS

- *Panayiotopoulos syndrom*
- Debut: 3-6 år (70%) (1-14 år)

- Fokala långa autonoma anfall – utan/med medvetandepåverkan (-30 min)
- Låg anfallsfrekvens
- **Autonoma symtom**: illamående, kräkningar (75%), buksmärta, flush
  (liknande akut gastroenterit/migrän)
- Ögon-/huvud-deviation, generaliserad hypotoni, fokalt kloniskt (hemikloniskt) eller fokalt till bilateralt tonisk-kloniskt anfall
- Sömn-association: 70%
- EEG: multifokal, high-voltage sharp waves/spike-and-wave kompex över posterior regionen

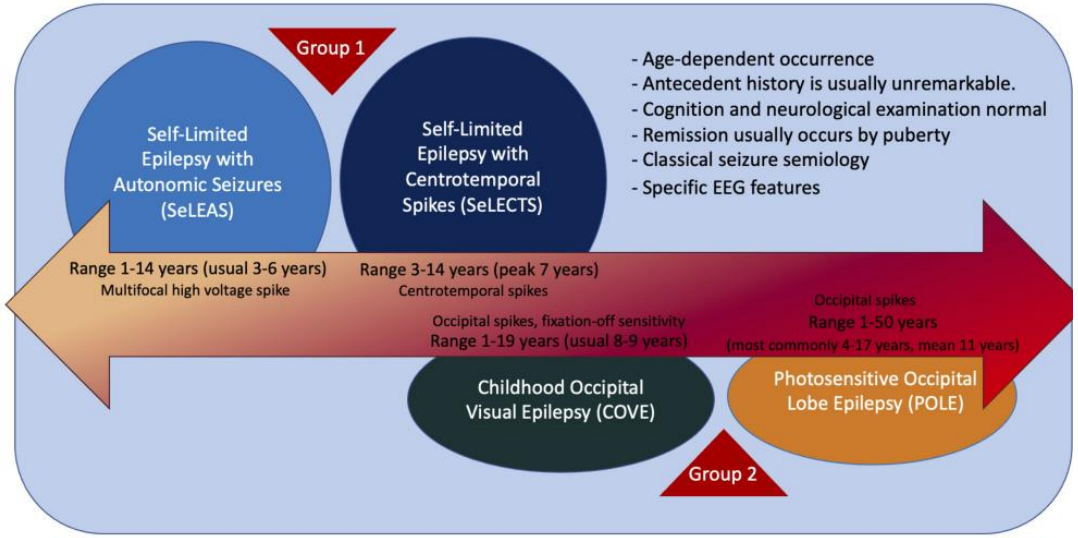
SeLFE syndromes Grupp 2

COVE : Childhood occipital visual epilepsy

Gastaut

TABLE 4 Childhood onset visual epilepsy

	Mandatory	Alerts	Exclusionary
Seizures	Focal sensory visual seizures with elementary visual phenomena (multicolored circles), with or without impaired awareness, and with or without motor signs (deviation of the eyes or turning of the head) Seizures arise predominantly or exclusively from wakefulness	Prolonged seizure lasting >15 min GTCS during wakefulness	Drop (tonic or atonic) seizures Atypical absences Progressive myoclonus
EEG	Occipital spikes or spikes-and-wave abnormalities (awake or sleep)	Sustained focal slowing not limited to the postictal phase	
Age at onset		<6 years >14 years	<1 year or >19 years
Development at onset		Intellectual disability	Neurocognitive regression
Neurological exam		Any significant neurological examination abnormality	Persistent visual field deficit
Imaging			Causal lesion on brain MRI Cerebral occipital lobe calcifications
Course of illness			Neurocognitive regression Development of myoclonic seizures, ataxia, spasticity
An MRI is required for diagnosis to exclude a causal lesion. An ictal EEG is not required for diagnosis.			
Syndrome without laboratory confirmation: In resource-limited regions, at a minimum, an interictal EEG and MRI are required to confidently diagnose this syndrome.			



DEE

Epilepsy with myoclonic atonic seizures EMAtS

- *Doose syndrome*
- ”stormy” plötslig debut med GTKA, myoklonier
- Debut: 2-6 år
- 25-83%: hereditet för epilepsi, feberkramp

- **Mandatory**:
- **Myoklon-atoniska anfall**:
- kort myokloni i proximala muskler + vokalisering +
- kort atoniskt anfall (nickning, eller större)

- **EEG:** generalized polyspike or spike –
- high-voltage slow wave

- Andra typer av anfall: myokloni, absens, GTKA, NSE

Epilepsy with eyelid myoclonia (EEM)

- *Jeavons syndrome*

- **Triad:**
- Frekventa ögonlocksmyoklonier – med/utan absens, utlöses av ögonstängning och fotostimulation
- Debut: 2-14 år, peak 6-8 år
- 25-83%: hereditet för epilepsi
- **Mandatory**: Ögonlocksmyoklonier + ögondeviation uppåt + extension av huvud/nacke

- **EEG**: 3-6 Hz irregular generalized polyspike-and –wave complex
- GTKA: förekommer, låg anfallsfrekvens, sömnbrist, alkohol, fotostimulation provocerar

Lennox-Gastaut syndrom

- *DEE*
- Olika bakomliggande etiologi
- Debut: 18 månader – 8 år (peak 3-5 år)
- Utvecklingsstörning, regression

Mandatory:

1. **TONISKA ANFALL (under sömn)** + annan typ av anfall
2. **EEG**: diffuse slow spike-and-wave (<2.5 Hz)and generalized paroxysmal fast activity in sleep
3. Kognitiv och beteendepåverkan

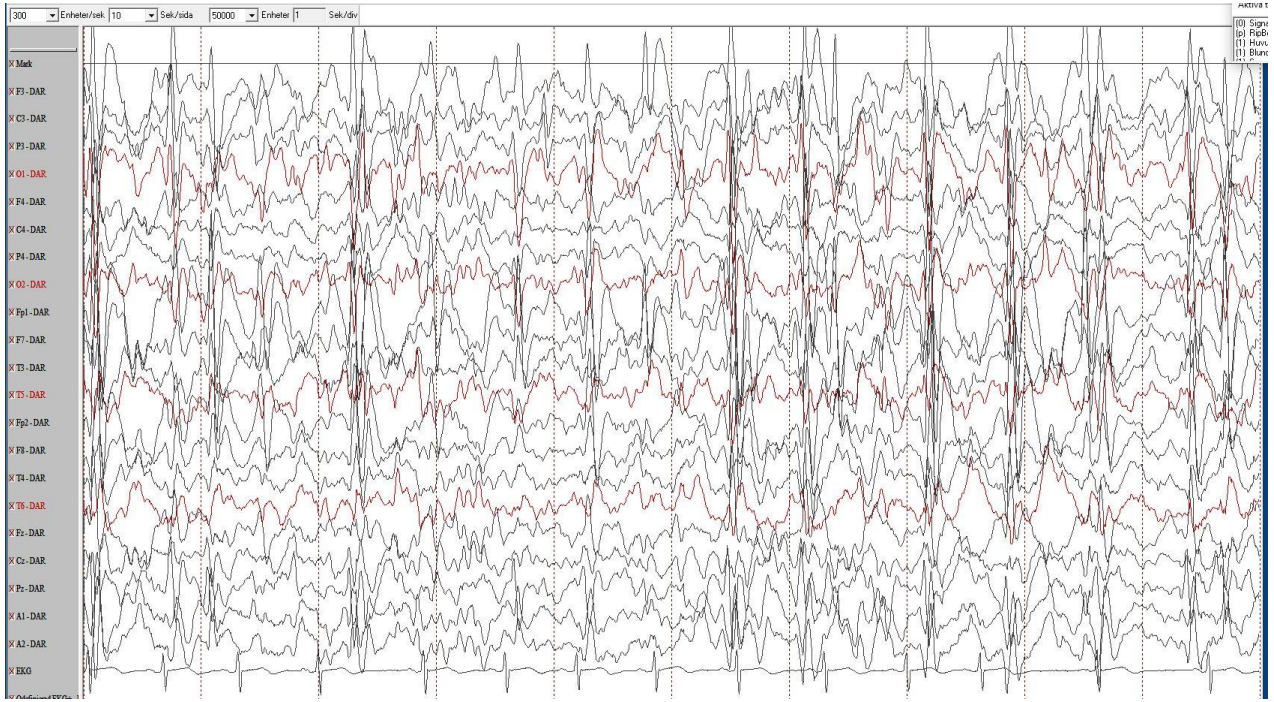
1. **Atypiska absenser**
2. **Atoniska anfall**
3. **Myokloni**
4. **Fokalt anfall med medvetandepåverkan**
5. **GTKA**
6. **Non-konvulsivt status epilepticus**
7. **Epileptiska spasmer**

Tidigare CSWS, ESES

DEE-SWAS och EE-SWAS

Developmental and epileptic encephalopathy with spike-and-wave activation in sleep

Kombination av **kognitiv, språk, beteende och motorisk regression** kliniskt med **spike-and-wave activation** under sömn på EEG



- Debut: 2-12 år (peak 4-5 år)
- Ingen ”obligatorisk” anfallstyp
- Subtyp: Landau-Kleffner syndrom

Sömnrelaterad hypermotor epilepsi - SHE

Tidigare: Autosomal dominant nocturnal frontal lobe epilepsy ADNFLE

- **Sleep-related hypermotor (hyperkinetic) epilepsy - SHE**
- Debut: 11-14 år
- Motoriska anfall i kluster, < 2 min, stereotypiskt hyperkinetiskt toniskt anfall/ asymmetrisk dystoni, autonoma symtom (takypne, takykardi), vokalisation

- **EEG:** interiktalt: epileptiform aktivitet frontalt (50%), iktalt anfallsktivitet insulo-operculo-temporalt, parietalt

- **Etiologi:** genetisk, genetisk-strukturell
- AD: GATOR1 komplex gener (DEPDC5, NPRL2, NPRL3, CHRNA4, CHRNB2, CHRNA2, KCNT1)
- **Differentialdiagnos:** parasomnier (längre duration > 10 min)

Idiopatisk generaliserad epilepsi (IGE) = Epilepsisyndrom (4)

Gemensamma karaktäristika:

- Polygen etiologi, åldersberoende
- Normal utveckling
- **Anfallstyp**: absens, myokloni, tonisk-kloniskt, myoklonisk-tonisk-kloniskt anfall
- Bra prognos för anfallskontroll
- Ingen risk för utveckling av epileptisk encefalopati
- Liknande EEG bild: 2.5-5.5 Hz spike-wave, triggas av hyperventilation eller fotostimulation

1. **Absensepilepsi i barndomen** (Childhood Absence Epilepsy, CAE)
2. **Juvenil absensepilepsi** (JAE)
3. **Juvenil myoklon epilepsi** (JME)
4. **Generaliserad epilepsi med enbart tonisk-kloniska anfall**

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DOI: 10.1111/epi.17237
SPECIAL REPORT
Epilepsia

Methodology for classification and definition of epilepsy syndromes with list of syndromes: Report of the ILAE Task Force on Nosology and Definitions

Elaine C. Wirrell[1] | Rima Nabbout[2,3] | Ingrid E. Scheffer[4] | Taoufik Alsaadi[5] | Alicia Bogacz[6] | Jacqueline A. French[7] | Edouard Hirsch[8] | Satish Jain[9] | Sunao Kaneko[10] | Kate Riney[11,12] | Pauline Samia[13] | O. Carter Snead[14] | Ernest Somerville[15] | Nicola Specchio[16] | Eugen Trinka[17,18,19] | Sameer M. Zuberi[20,21] | Simona Balestrini[22,23,24] | Samuel Wiebe[25] | J. Helen Cross[26,27] | Emilio Perucca[28,29] | Solomon L. Moshé[30] | Paolo Tinuper[31,32]

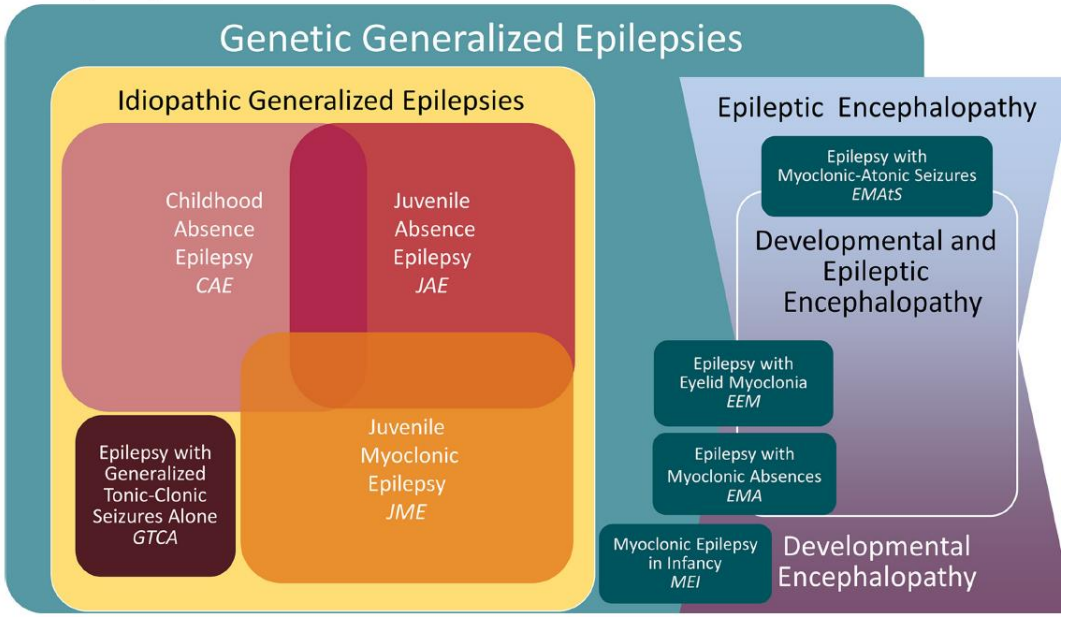
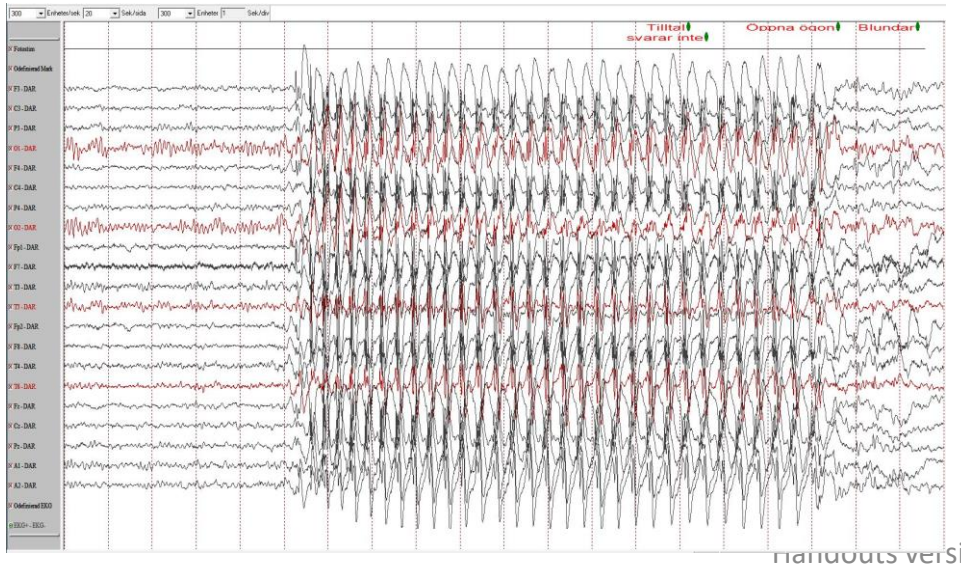


FIGURE 2 Concept of genetic generalized epilepsy (GGE) versus idiopathic generalized epilepsy (IGE). The IGEs are a subgroup of GGEs, comprised of the following four syndromes: childhood absence epilepsy, juvenile absence epilepsy, juvenile myoclonic epilepsy, and epilepsy with generalized tonic-clonic seizures alone. These four syndromes may show some degree of overlap. In addition to the

Absensepilepsi i barndomen CAE

- Debut: 4-10 år (2-13 år)
- *Anfallsfrekvens*: daglig, flera/dag
- Absens 3-20 sek (10 sek)
- **EEG**: 3 Hz (2.5-4 Hz) spike-wave, OIRDA



Juvenil absensepilepsi JAE

- Debut: 9-13 år (8-20 år)
- *Anfallsfrekvens*: färre
- Absens 5-30 sek, GTKA (>90%)
- **EEG**: 3-4 Hz (3-5.5 Hz) gen spike-wave

Juvenil myoklon epilepsi JME

- Debut: 10-24 år (8-40 år)

- **Obligatorisk anfallstyp**: myokloni
- Myokloni: unilateral, bilateral, övre extremiteter
- Inom 1 timme efter uppvakning, vid **sömndeprivation**
- GTKA (>90%) vid uppvakning, vid sömndeprivation
- Absens (30%)

- **EEG**: 3-5.5 Hz irregular generalizerad spike-wave, polyspike-wave under vakenhet och sömn
- Fotosensitivitet vanligt
- 5-15% utvecklas från CAE

Epileptiska syndrom

1. Karakteristisk klinisk bild/anfallstyp(er)
2. Karakteristiskt EEG
3. Debutålder
4. **Specifik etiologi - DEE** *(Epilepsigener!)*
5. Behandling
6. Prognos