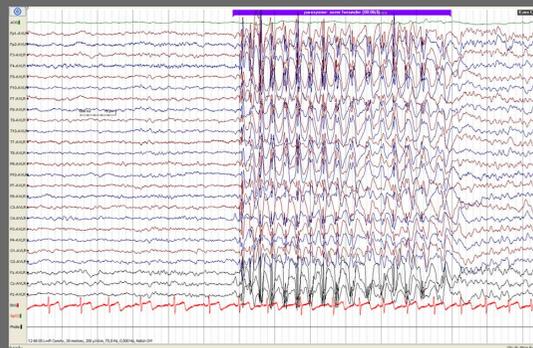




Challenges in idiopathic/ genetic epilepsy syndromes

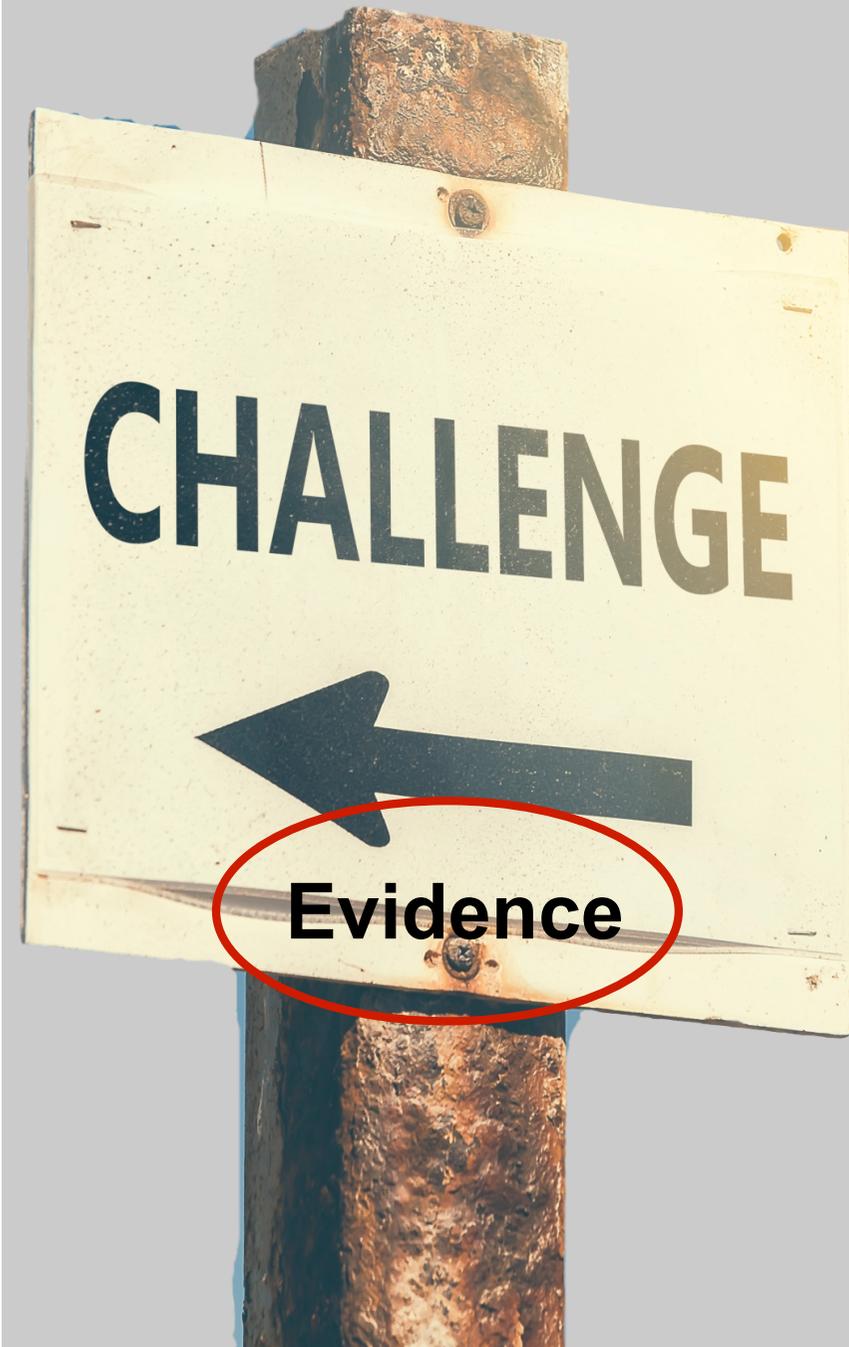


Maria J. Miranda, MD Ph.D., Department of Pediatrics,
Herlev University hospital



Which challenges do we face when treating and following children with Childhood absence epilepsy (CAE) and Epilepsy with Centro-Temporal Spikes (ECTS)?





Childhood
Absence
Epilepsy (CAE)

Epilepsy with
Centro-
Temporal
Spikes (ECTS)

Questions

- Treat or not to treat
- Which antiepileptic drug (AED)?
- Consequences?
- Risks?
- School?
- Future?



5.5 million inhabitants

~ 1,3% have epilepsy by age 15

~ 12.000 children have epilepsy in DK

15-25% = ECTS

~ 10% = CAE



New ILAE epilepsy classification: V. Etiology

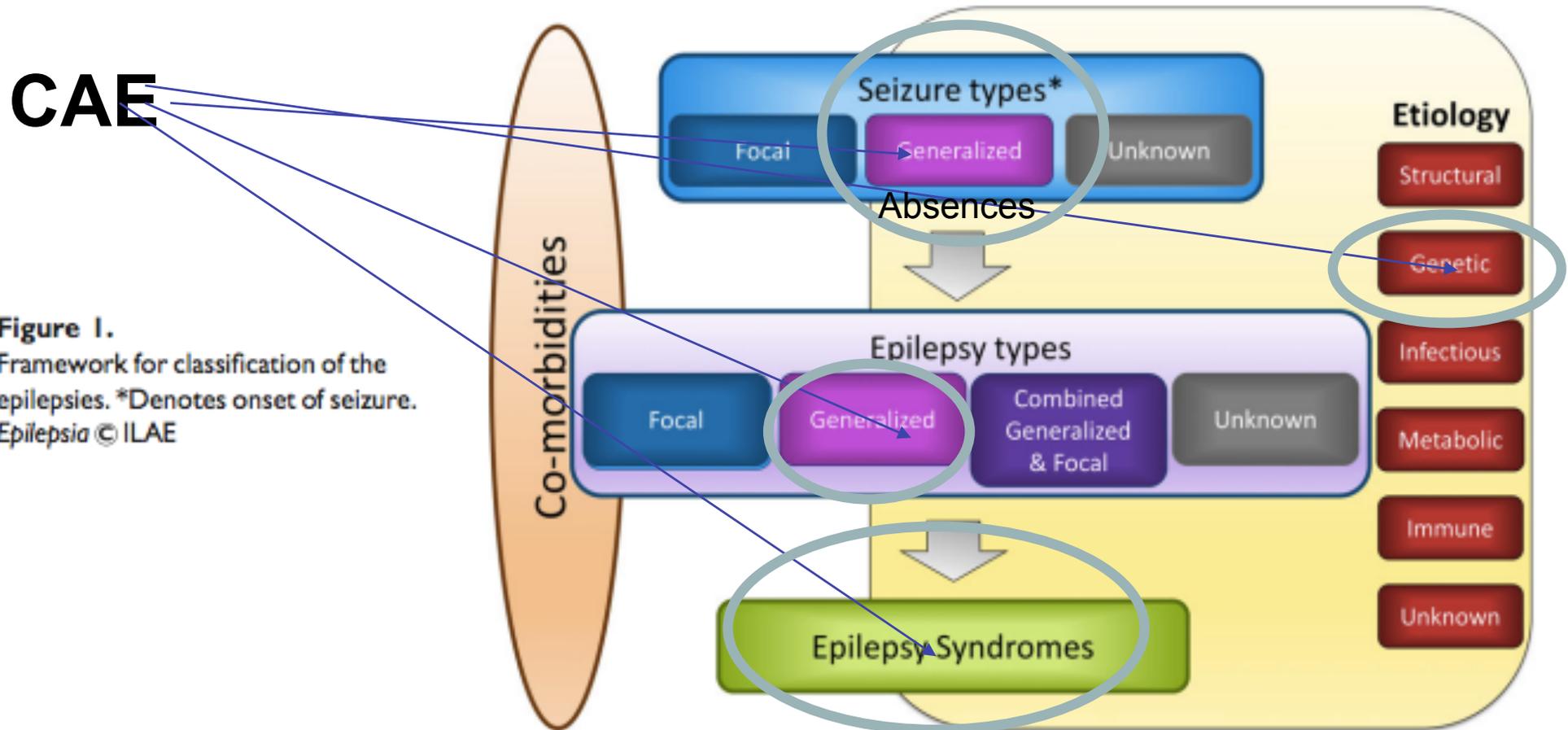


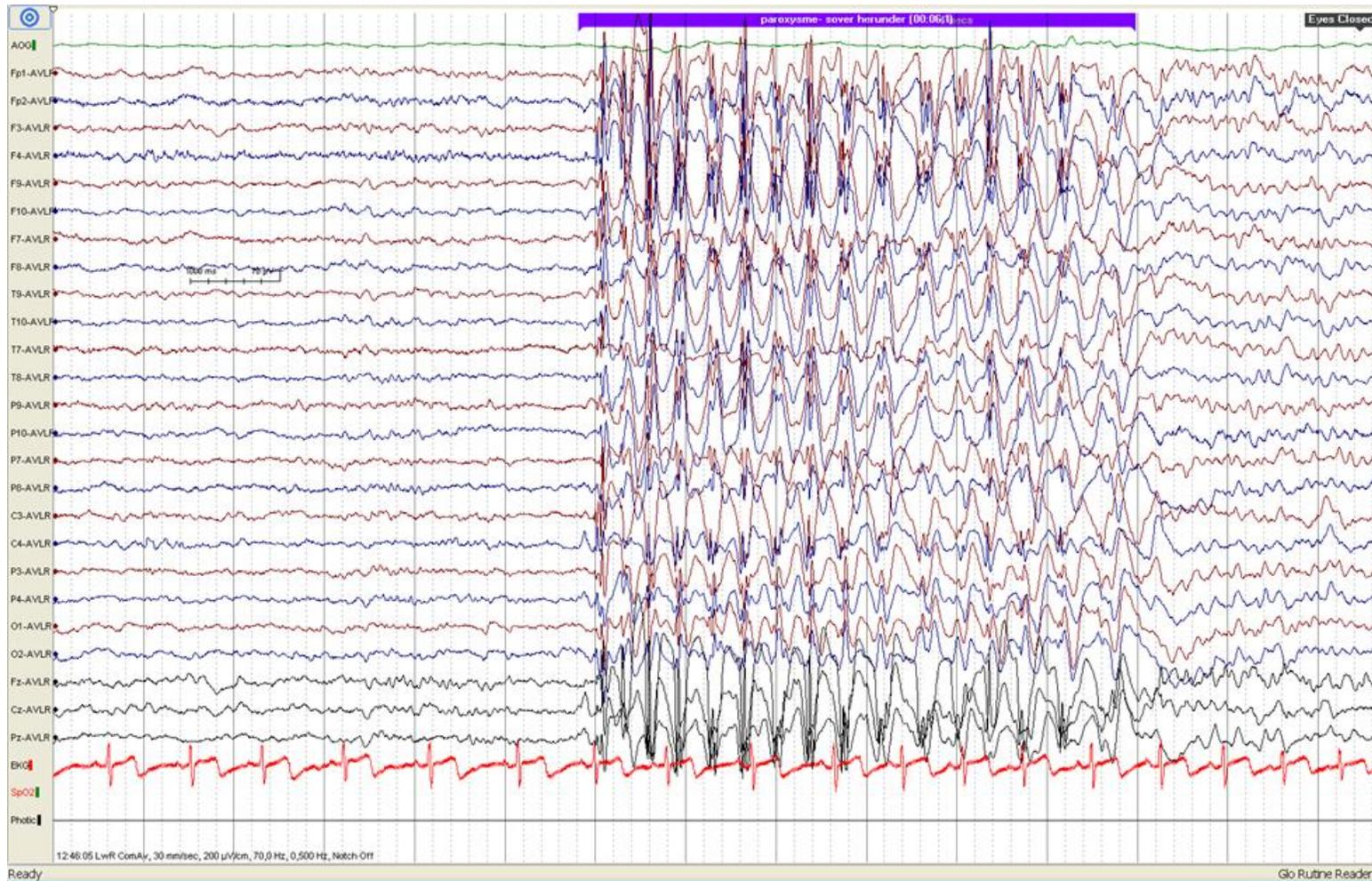
Figure 1.
Framework for classification of the epilepsies. *Denotes onset of seizure.
Epilepsia © ILAE

Self-limited idiopathic/
genetic generalised
epilepsy syndrome

Case S, 3,5 years old

- Girl S, born as twin A, GA 36+1, Apgar score 8/1 10/5
- Normal development
- Febrile seizures from 17 month old, x 7-8, last 2½ years old, uncomplicated
- Since the age of 3 y. 4 mo. many daily episodes lasting 5-10 seconds where she suddenly stares, stops activity, non-reacting, sometimes chewing loud

EEG



- EEG: Spike-wave 3 Hz paroxysms

Cont. case S

- EEG: 3 Hz generalised spike-wave paroxysms and several absences
- Starts Valproic acid (VPA), on 30 mg/ kg
- Starts ethosuximide (ETX) 5 weeks later, 25 mg/kg, VPA unchanged
- 2nd EEG ½ year later: normalised
- 2 year later (2016): medicine-free, absence-free and normal EEG
- Normal development, starts school

CAE history



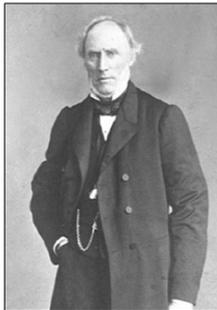
A



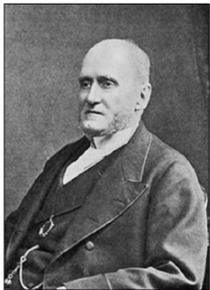
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C



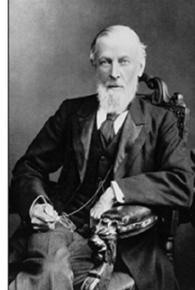
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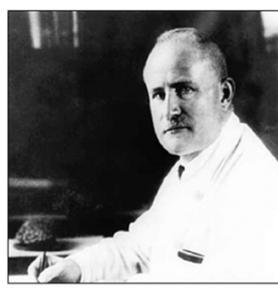
E



F



G



H

g. 1. A. Simon-Auguste Tissot (1728–1797); B. Louis-Florentin Calmeil (1798–1895); C. Jean-Étienne Dominique Esquirol (1772–1840); D. Louis Jean François Delasiauve (1804–1893); John Russell Reynolds (1828–1896); F. Otto Binswanger (1852–1929); G. William Richard Gowers (1845–1915); H. Hans Berger (1873–1941).

- First described in 1705 by Poupart and Tissot in 1770
- 1924: hyperventilation and absences
- 1930: EEG

New ILAE epilepsy classification: V. Etiology

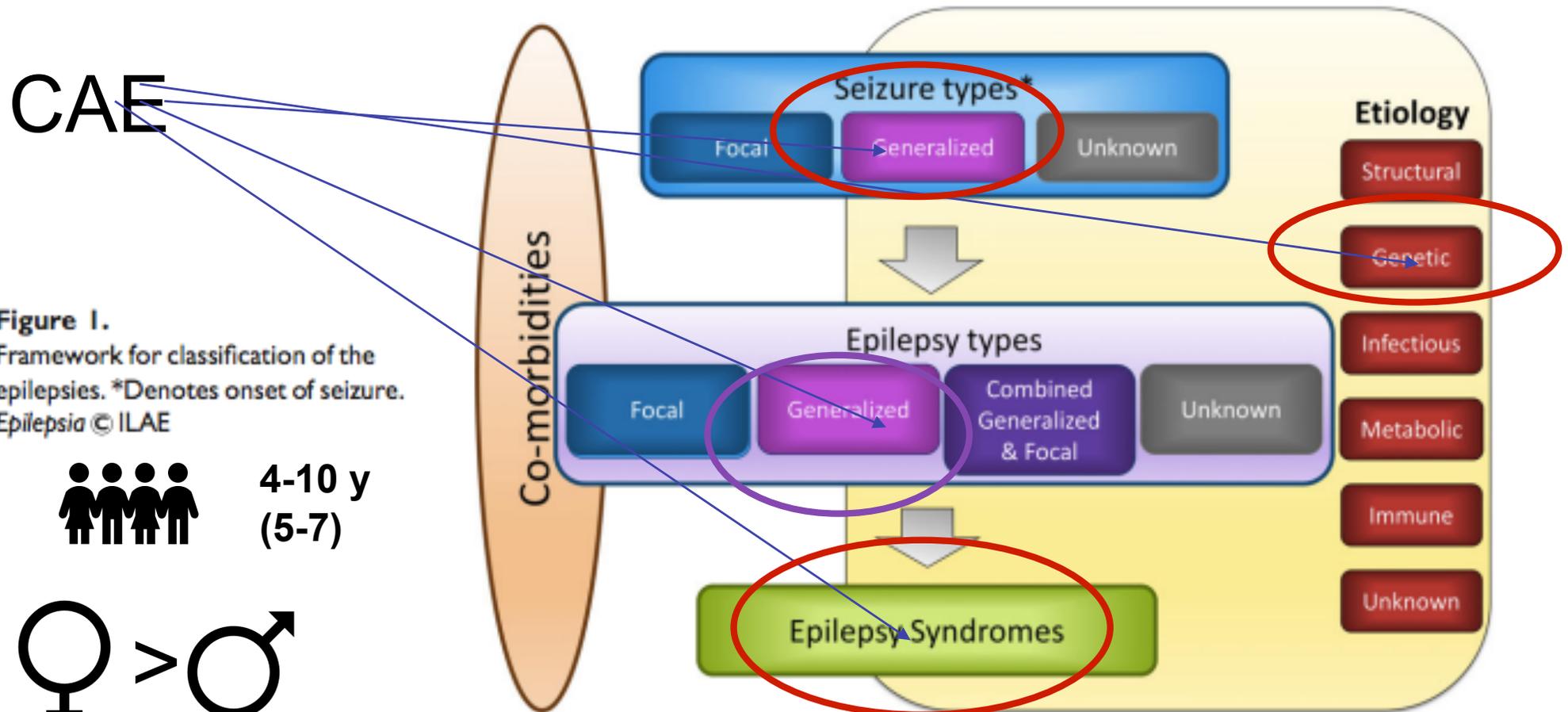


Figure 1.
Framework for classification of the epilepsies. *Denotes onset of seizure.
Epilepsia © ILAE

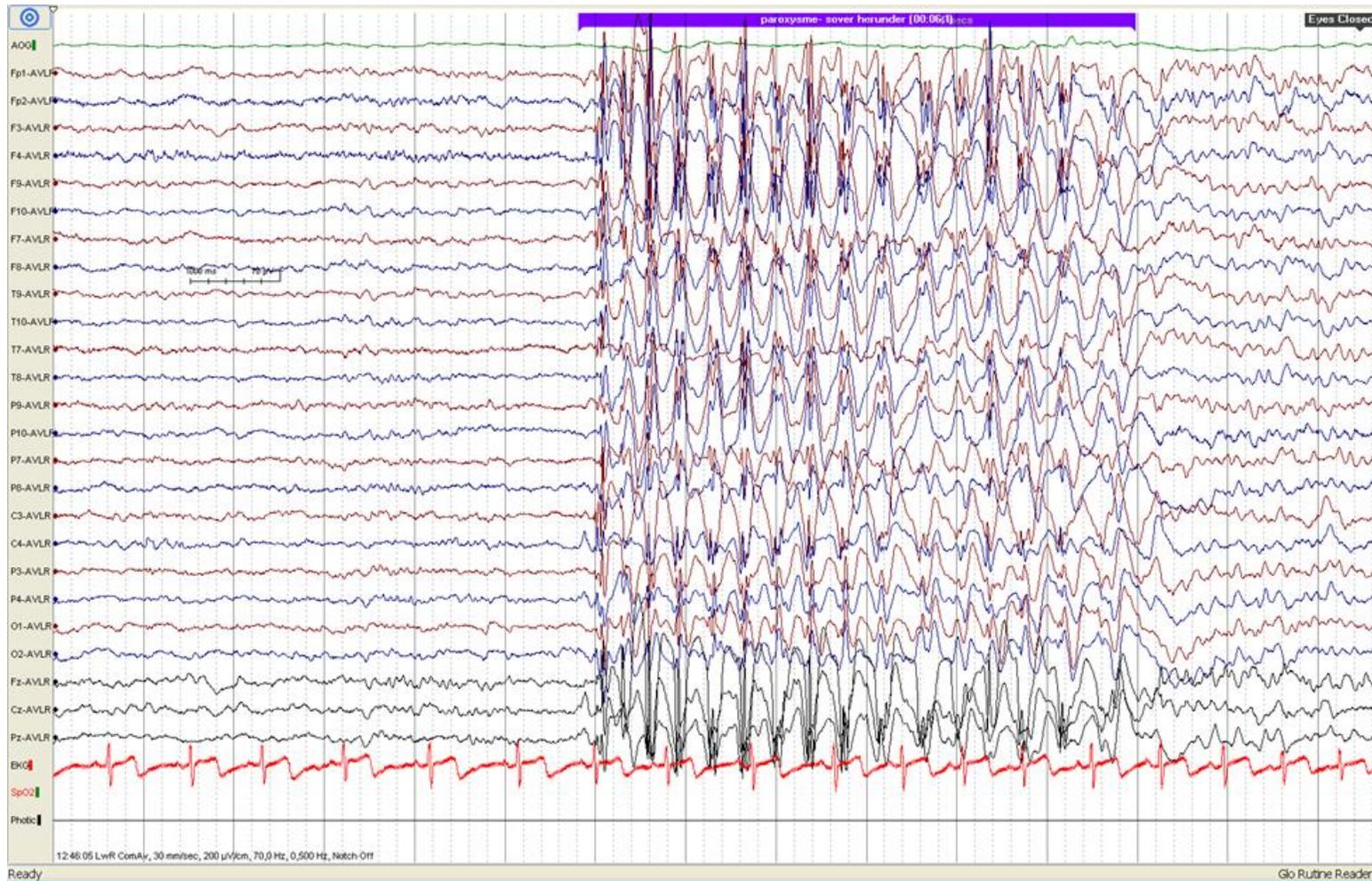
4-10 y
(5-7)

♀ > ♂

3 / 1

Self-limited idiopathic/
genetic generalised
epilepsy syndrome

CAE EEG



- EEG: Spike-wave 3 Hz paroxysms

Challenges



Treatment



Developmental
consequences



Treatment of CAE

VPA

Valproic acid

ETX

Ethosuximide

LTG

Lamotrigine

CAE treatment study



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Ethosuximide, Valproic Acid, and Lamotrigine in Childhood Absence Epilepsy

Tracy A. Glauser, M.D., Avital Cnaan, Ph.D., Shlomo Shinnar, M.D., Ph.D., Deborah G. Hirtz, M.D., Dennis Dlugos, M.D., David Masur, Ph.D., Peggy O. Clark, M.S.N., Edmund V. Capparelli, Pharm.D., and Peter C. Adamson, M.D. [on behalf of for the Childhood Absence Epilepsy Study Group]*

A double-blind RCT comparing efficacy, tolerability and neuropsychological effects of ETX, VPA and LTG in children with CAE.

CAE study

- **ETX and VPA were similar in efficacy**
- **LTG less efficacy**

- **ETX better cognitive profile**
- **ETX less relapse**

- Patients with no response to ETX: Higher risk of GTCs and progression to JME
- ETX: disease-modifying effect?

Treatment protocol

- **ETX:**
 - Start 10 mg/ kg, increase every 5th day to 20-40 mg/kg
 - Side effects: gastrointestinal, tiredness

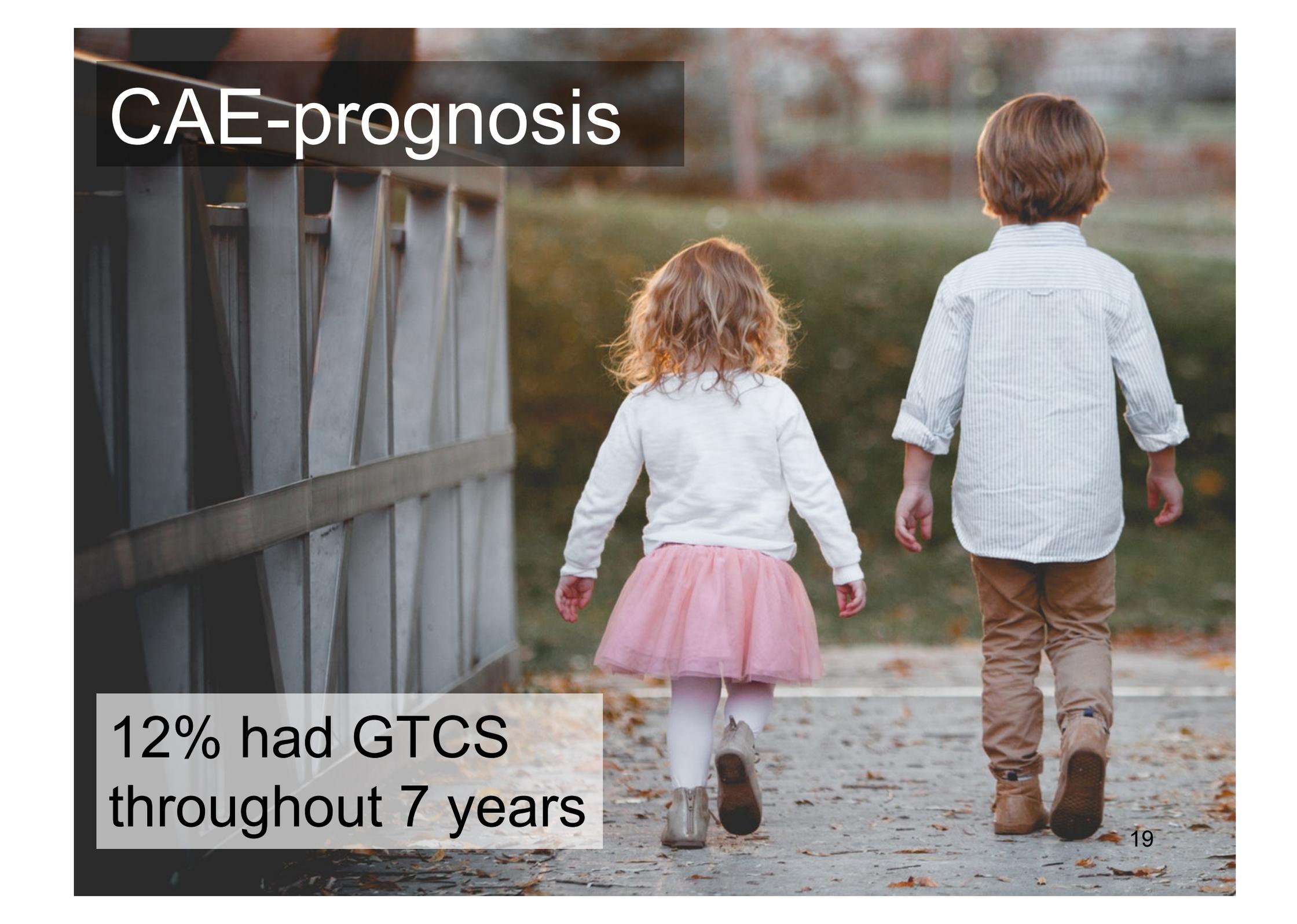


Ethosuximide: Zarondan® syrup or Petnidan® capsules (in DK requires special application to Danish Medicines Agency)

Developmental consequences CAE

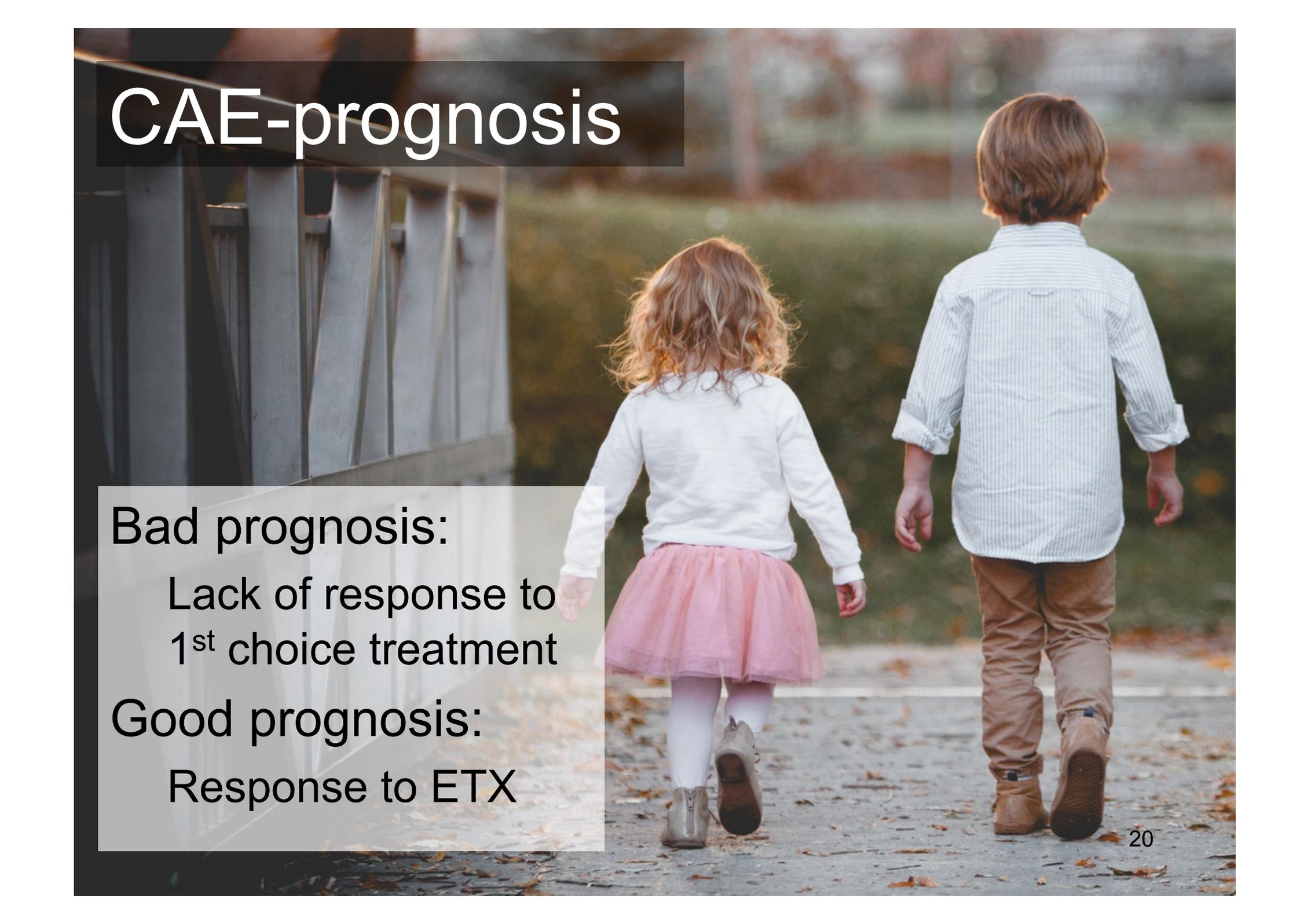
- 36% have attention deficits before treatment start (x 4 background population)
- IQ: normal
- Attention deficits similar in seizure-free and non-seizure free
- **Important to pay attention to school achievements and children's well-being**

CAE-prognosis



12% had GTCS
throughout 7 years

CAE-prognosis



Bad prognosis:

Lack of response to
1st choice treatment

Good prognosis:

Response to ETX

ECTS- Epilepsy with Centro-temporal spikes or Rolandic Epilepsy

- Self-limited idiopathic/ genetic focal epilepsy syndrome
- 25% of epilepsies in children under 16 years
- 2/3 of self-limited focal epilepsy syndromes
- Peak of onset 5-8 years (2-14 years)

New ILAE epilepsy classification: V. Etiology

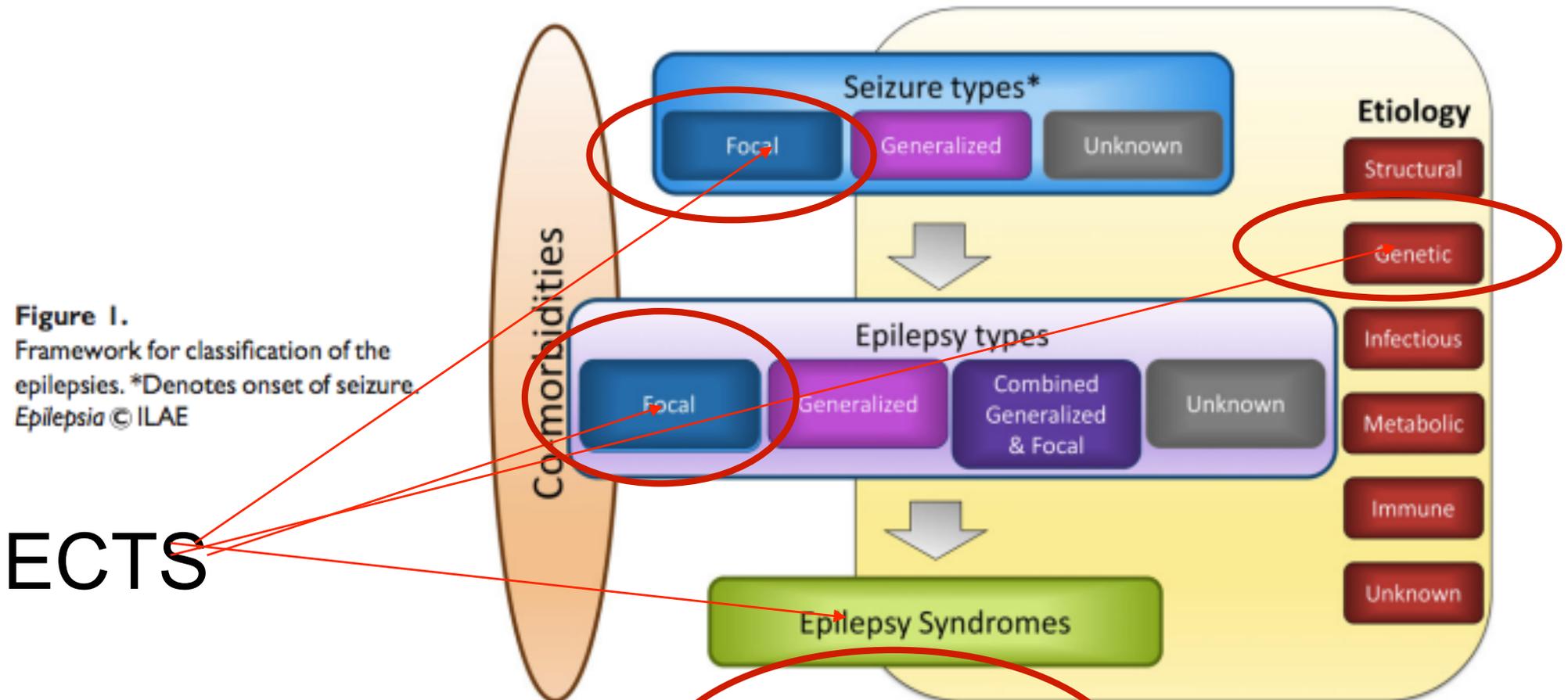
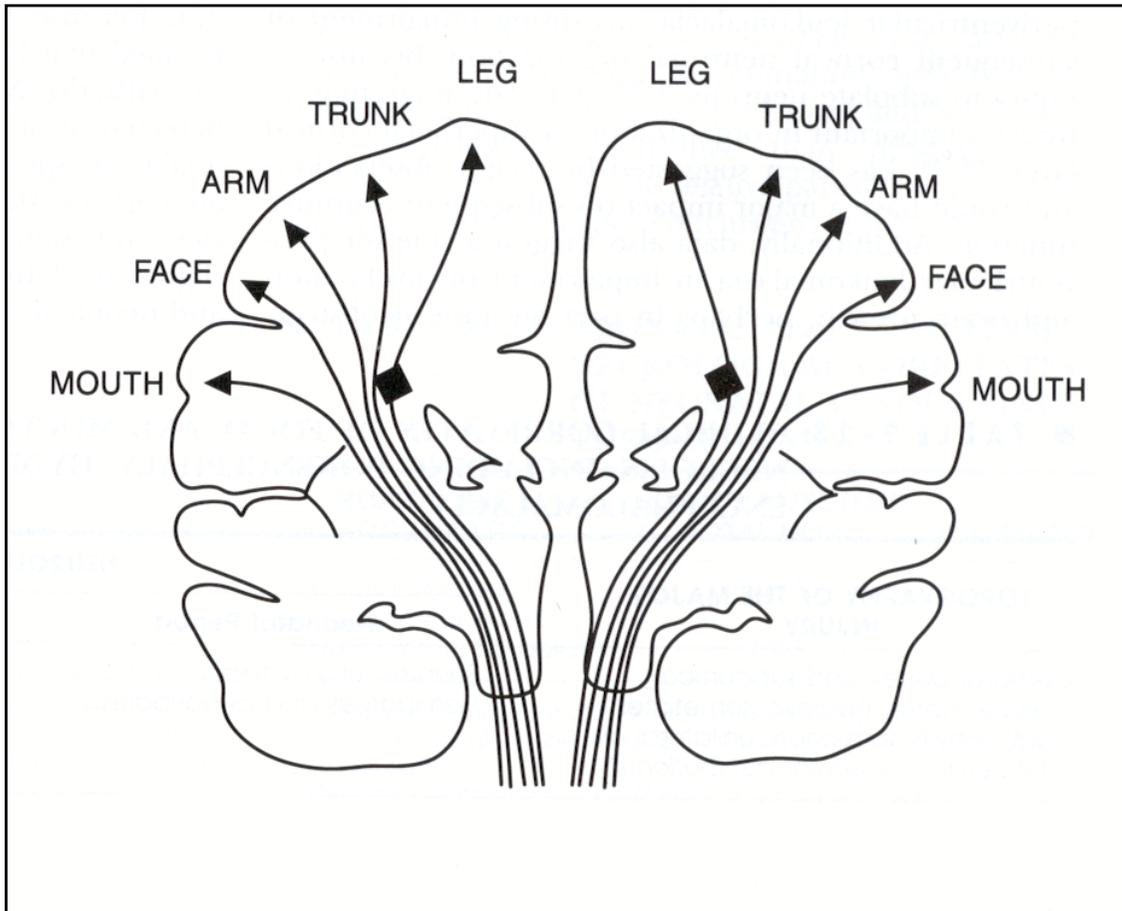


Figure 1. Framework for classification of the epilepsies. *Denotes onset of seizure. *Epilepsia* © ILAE

ECTS

Syndrome: self-limited idiopathic/ genetic focal epilepsy syndrome

Seizures in ECTS

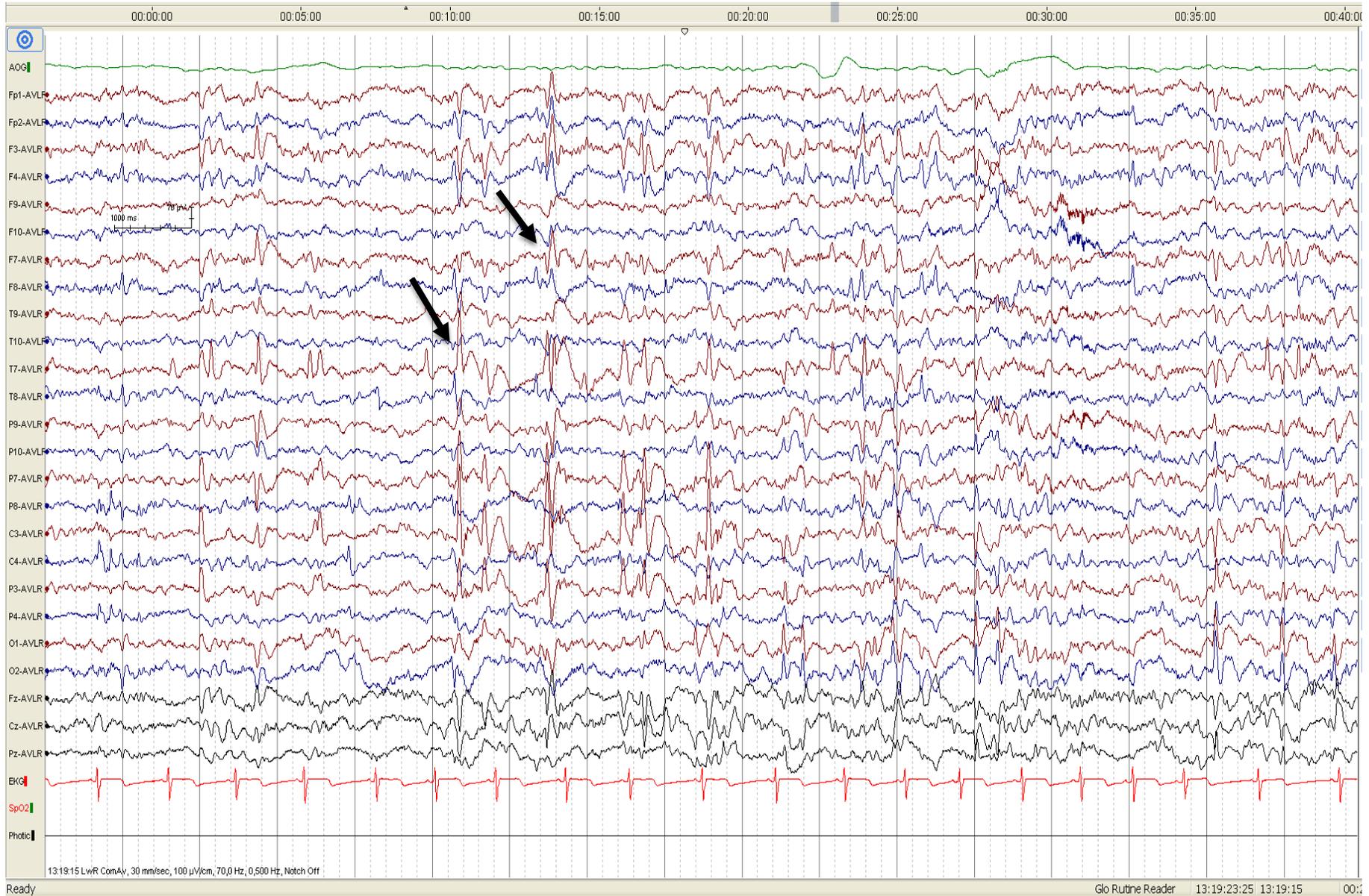


- Only 20% have frequent seizures
- Brief seizures, 1-2 min.
- 70% in sleep (may occur during wakefulness, far less common)

ECTS- EEG awake



ECTS- EEG sleep



Prognosis ECTS



- For seizure remission good
- Self-limited in most children by 15-16 years
- And usually within 2-4 years of onset



ECTS-comorbidity

Neuro-cognitive and behavioural:

increasing evidence of significant difficulties



ECTS- comorbidity



- 12-30% difficulties in:
 - Language
 - Memory
 - Behaviour
 - Attention
 - Anxiety
 - Depression
 - Cognition...

ECTS- evolution

- ECTS
- CSWS/ ESES (electric status epilepticus in slow sleep)
- Landau-Kleffners syndrome (acquired aphasia)
- ECTS with frequent refractory seizures



ECTS- treatment challenges

- Treat or not to treat
 - individual decision
 - seizure frequency
 - parents/ child
 - Cost/ benefit
- Which AED?
 - No clear scientific evidence
 - Levetiracetam
 - Others: Valproic acid, Sulthiam



Questions and challenges regarding ECTS



- AED reduces seizures: YES
- EEG SW activity in sleep correlates with comorbidities??
- AED ameliorates EEG SW activity in sleep??
- AED reduces comorbidity??
- AED may prevent (or worsen) development to atypical evolution of ECTS?

Treatment with AED- challenges (cont.)

- Will AED reduce SW-frequency under sleep?
 - Some evidence
- Reducing SW in sleep by treating with AED, will we ameliorate cognitive and behavioural issues?
 - No clear scientific evidence



Take home messages

TREATMENT:

CAE: 1. choice ETX

ECTS: Individual (start LEV?)

DEVELOPMENTAL CHALLENGES:

CAE: YES

ECTS: YES

FUTURE: SELF-LIMITED

CAE: YES

ECTS: YES

BUT....



Take home messages

- Treat right from the beginning
- Be aware of children's school difficulties, behaviour and psychiatric symptoms
- Be aware of changes

