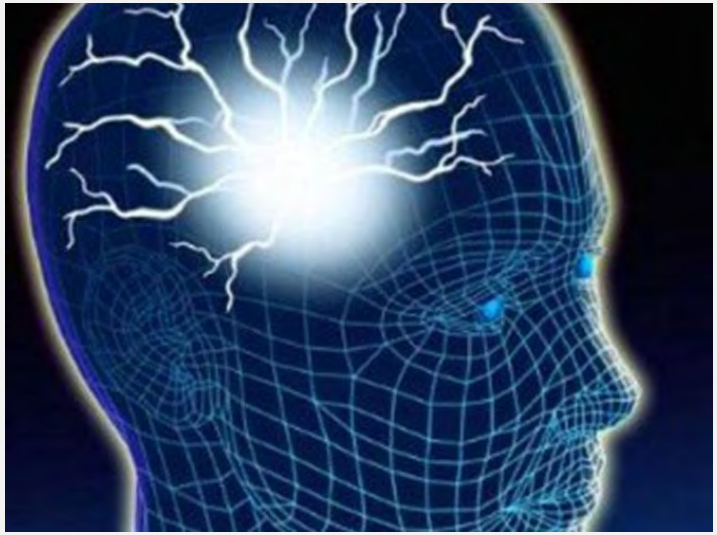
EPILEPSY 2019



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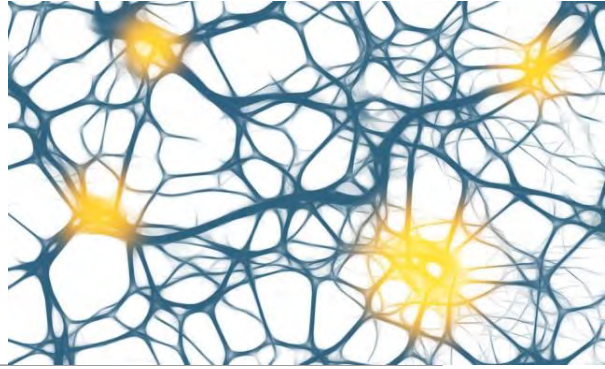
What is epilepsy?



An epileptic seizure is a transient occurrence of signs and/or symptoms due to abnormal excessive or synchronous neuronal activity in the brain.

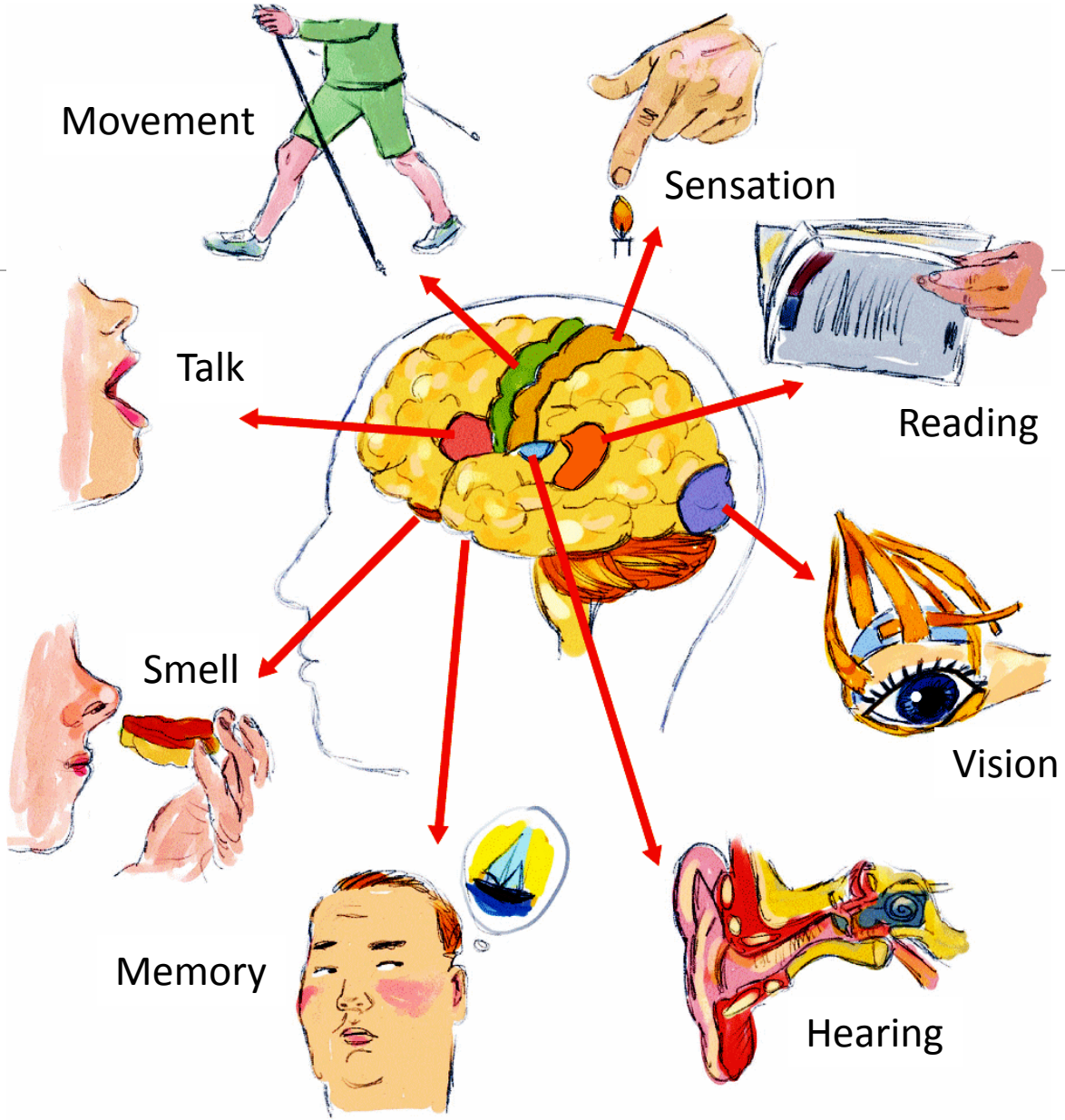
Epilepsy is a disorder of the brain characterized by an enduring predisposition to generate epileptic seizures, and by the neurobiologic, cognitive, psychological, and social consequences of this condition. The definition of epilepsy requires the occurrence of at least one epileptic seizure.

MOST COMMON SYMPTOMS

- Total or partial blurring of the consciousness (impared awareness)
- Involuntary motor symptom, e.g. rhytmic jerks, stiffness, single muscle jerks, flaccid/limp muscles
- Automatisms ie. swallowing or twiddling
- Sensations without a stimulus, e.g. visual / auditory / sensory / taste / smell
- Emotional sensations, e.g. fear or panic
- Inability to act, e.g. inability to talk or to maintain the position of the limb

Tonic-clonic seizure

https://www.youtube.com/watch?v=gWZGMABBfYo


Movement
Sensation
Talk
Reading
Smell
Vision
Memory
Hearing

Examinations

Imaging: MRI / CT (contrast enhanced)

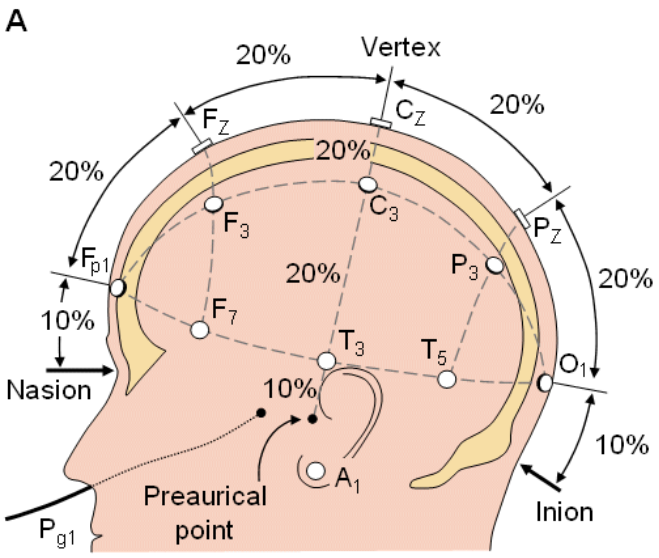
- As a rule: MRI when epilepsy started in adulthood, or in suspicion of partial epilepsy

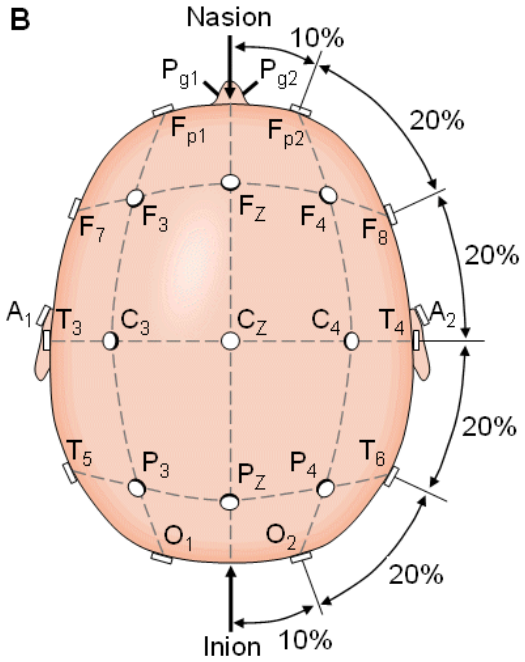
EEG

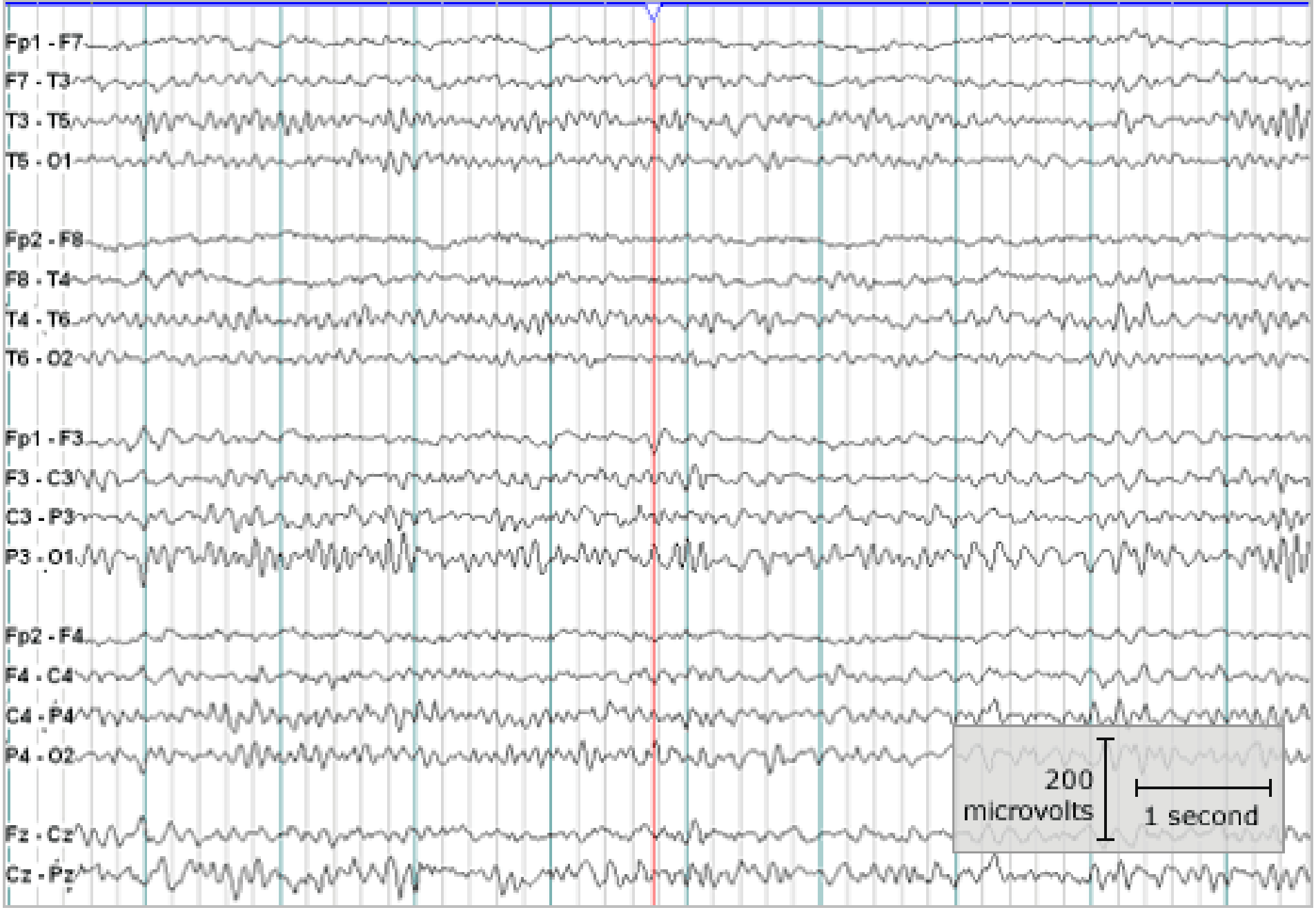
- EEG-abnormalities increase the probability of reoccurrence of the seizure
- EEG is needed to classify epilepsy, e.g. classification of the epilepsy to generalized epilepsy cannot be done without a specific EEG-finding
- Avoid EEG if the symptoms are vague or obscure, because unspecific abnormalities can be found in more than 10% of people, and epileptic paroxysmal activity without seizures has been reported in 1% of people
- Normal EEG does NOT exclude epilepsy

EEG

EEG (electroencephalogram) measures the electrical activity of the brain.






Fp1 - F7
F7 - T3
T3 - T5
T5 - O1
Fp2 - F8
F8 - T4
T4 - T6
T6 - O2
Fp1 - F3
F3 - C3
C3 - P3
P3 - O1
Fp2 - F4
F4 - C4
C4 - P4
P4 - O2
Fz - Cz
Cz - Pz
200 microvolts
1 second

Normal EEG

The prevalence of epilepsy in Finland

- 10 % of population → epileptic seizure
- Prevalence **0.6%** of the population
- 52000 patients in Finland has reimbursement for medication
- 36000 patients buy the prescribed medication
- 9000 patients has epilepsy that is hard to treat
- Incidence among adults is approx 40-70/100000
- The prevalence of fainting in people older than 45 years is approx **19%**
- The incidence of fainting among healthy people is approx 27%

Prevalence and incidence of epilepsy

A systematic review and meta-analysis of international studies

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Samuel Wiebe, MD, MSc
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Churl-Su Kwon, MD
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ABSTRACT

Objective: To review population-based studies of the prevalence and incidence of epilepsy worldwide and use meta-analytic techniques to explore factors that may explain heterogeneity between estimates.

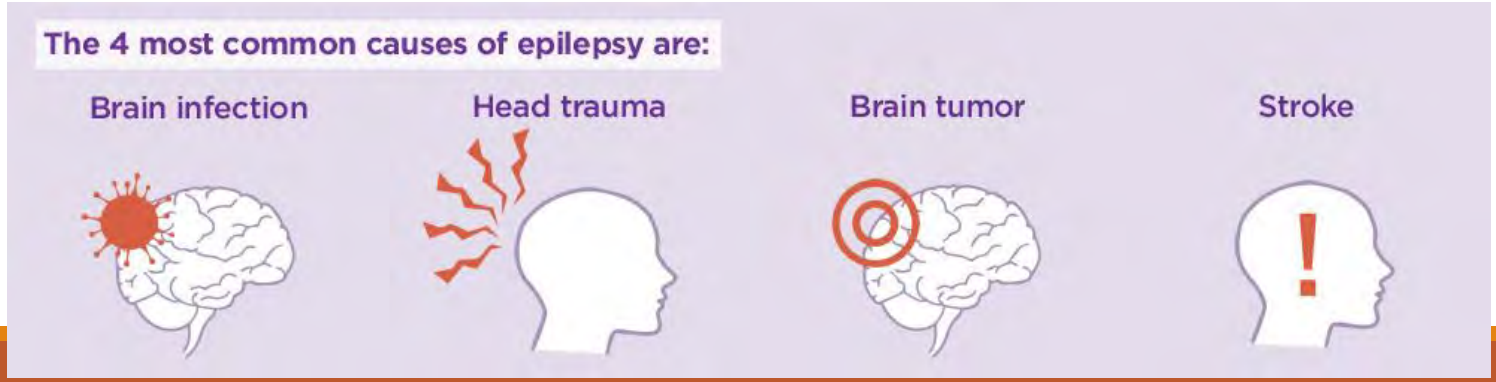
Methods: The Preferred Reporting Items for Systematic Reviews and Meta-Analyses standards were followed. We searched MEDLINE and EMBASE for articles published on the prevalence or incidence of epilepsy since 1985. Abstract, full-text review, and data abstraction were conducted in duplicate. Meta-analyses and meta-regressions were used to explore the association between prevalence or incidence, age group, sex, country level income, and study quality.

Results: A total of 222 studies were included (197 on prevalence, 48 on incidence). The point prevalence of active epilepsy was 6.38 per 1,000 persons (95% confidence interval [95% CI] 5.57–7.30), while the lifetime prevalence was 7.60 per 1,000 persons (95% CI 6.17–9.38). The annual cumulative incidence of epilepsy was 67.77 per 100,000 persons (95% CI 56.69–81.03) while the incidence rate was 61.44 per 100,000 person-years (95% CI 50.75–74.38). The prevalence of epilepsy did not differ by age group, sex, or study quality. The active annual period prevalence, lifetime prevalence, and incidence rate of epilepsy were higher in low to middle income countries. Epilepsies of unknown etiology and those with generalized seizures had the highest prevalence.

Conclusions: This study provides a comprehensive synthesis of the prevalence and incidence of epilepsy from published international studies and offers insight into factors that contribute to heterogeneity between estimates. Significant gaps (e.g., lack of incidence studies, stratification by age groups) were identified. Standardized reporting of future epidemiologic studies of epilepsy is needed. *Neurology*® 2017;88:296–303

ETIOLOGIES

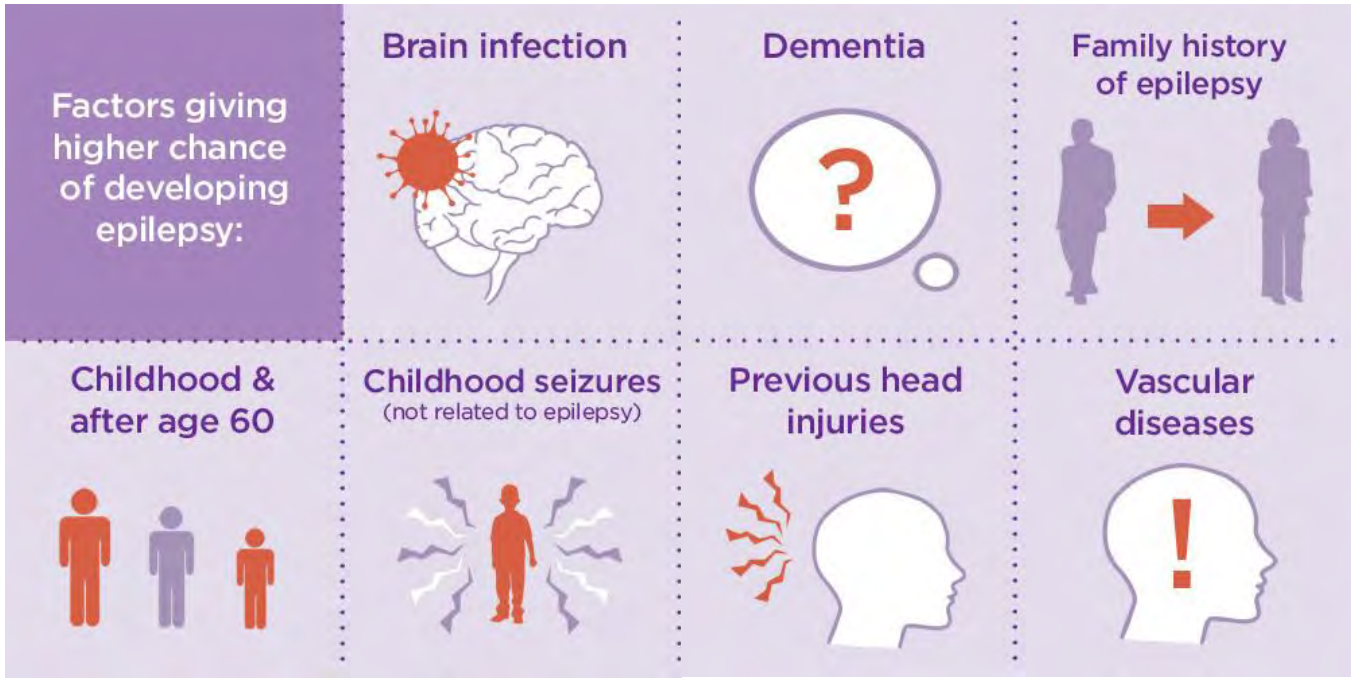
STRUCTURAL	GENETIC
Brain injury	Absence epilepsy
Stroke	Juvenile myoclonus epilepsy
Encephalitis	Severe myoclonus epilepsy starting at infancy
Degenerative process	Neuronal ceroid lipofuscinosis
Hippocampal sclerosis	Unverricht-Lundborg disease
Tumors	Tuberous sclerosis
Developmental anomalities of the brain	
Anomalities of the brain blood vessels	

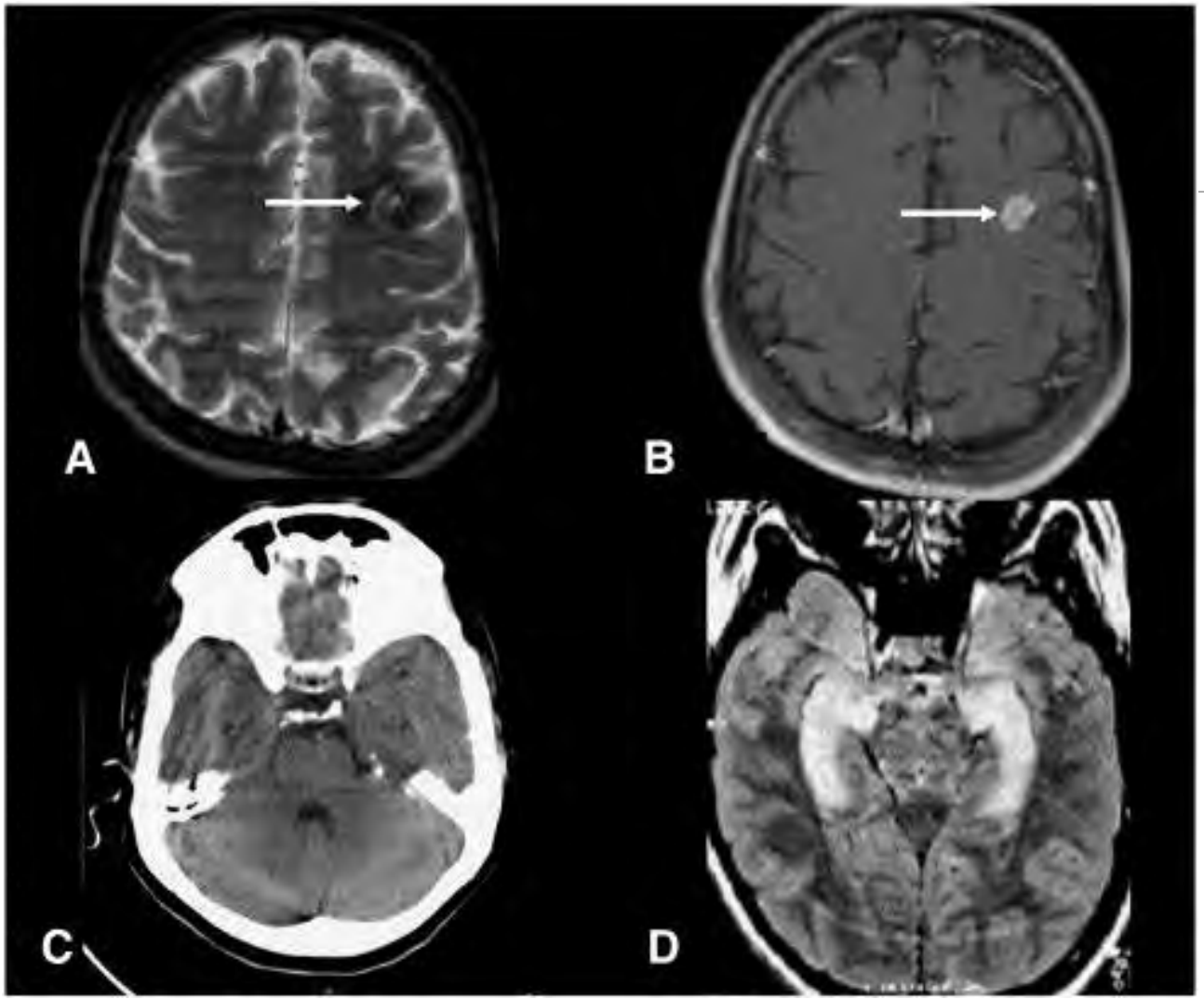


ETIOLOGIES IN FINLAND

ETIOLOGY	%
Brain injury	10
Brain injury during birth	10
Post-stroke	6
Post encephalitis	5
Brain tumors	3
Other brain diseases	5
Unknown	61

RISK FACTORS FOR EPILEPSY



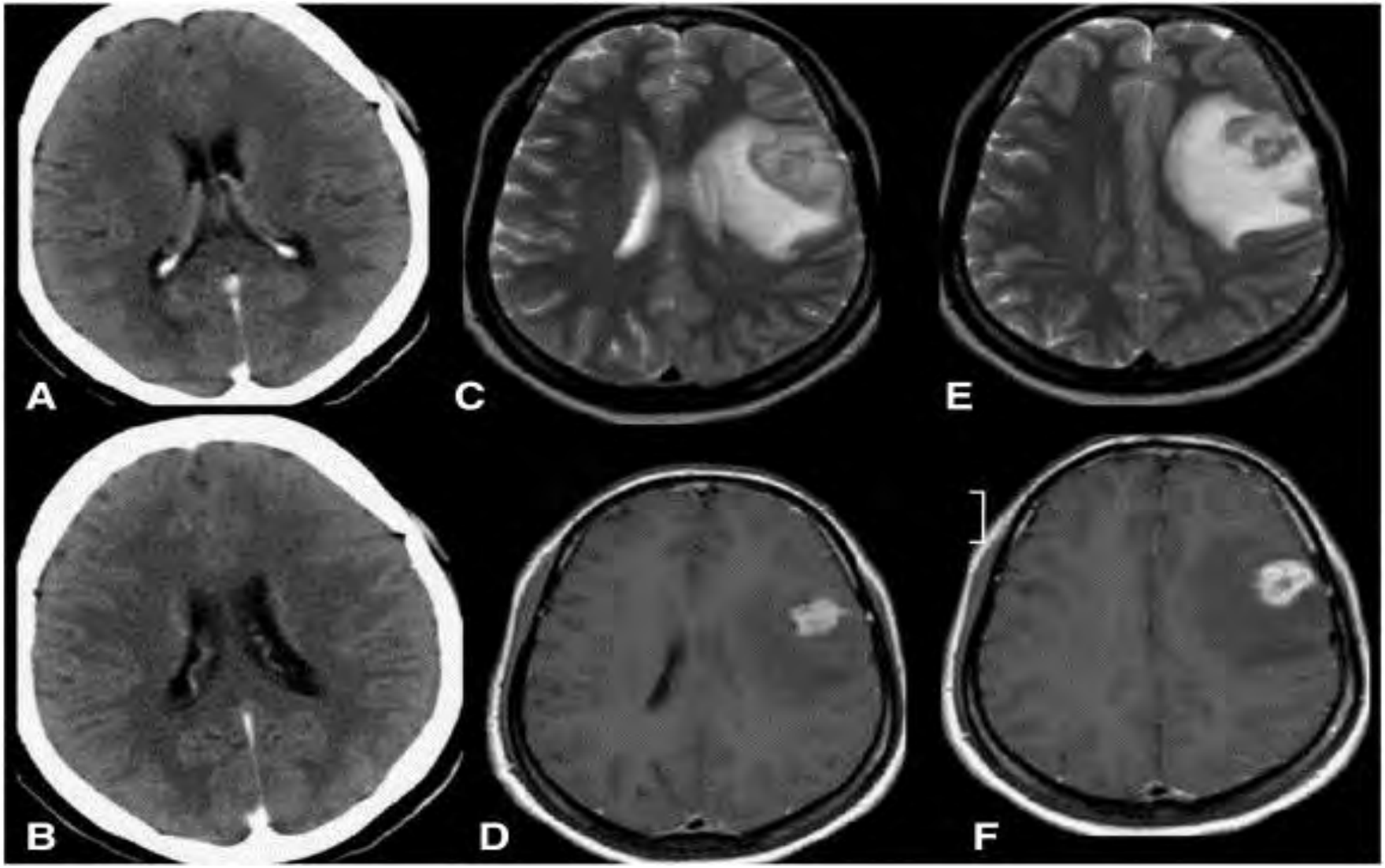


A, B:
Cavernoma/
Cavernous
hemangioma

C:
Acute imaging:
normal CT →

D:
MRI: bilat.temp.
hyperintensity/
Herpes simplex-
enkephalicitis

Tuberculoma



Diagnosis of epilepsy

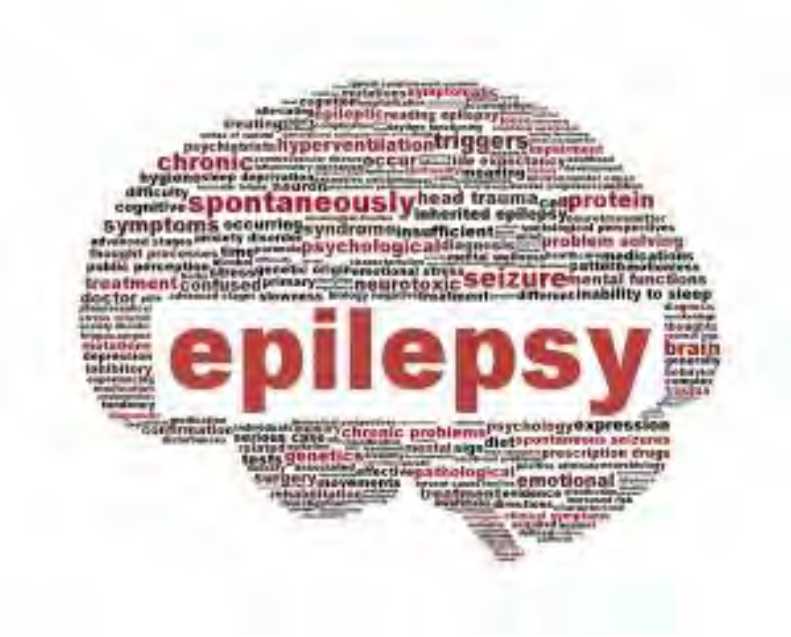
At least two unprovoked seizures on separate days, occurring during 1-2 years of time (=*clinical diagnosis*)

OR

After one epileptic seizure if the probability of further seizures is high:

- Epileptic seizure due to previous brain infarct, brain injury, dementia in an elderly person, other reliable etiological factor
- Juvenile myoclonus epilepsy or other syndrome, if the diagnosis is verified by the anamnesis and EEG-finding.
- The first seizure is prolonged or complicated

Diagnosis



Description of the seizure

- Preferably eyewitness

Imaging (CT or MRI)

EEG

- Classifying/ type of epilepsy
- Differential diagnosis
- If EEG is normal, it does not exclude epilepsy!

Classification of the Epilepsies

1) Seizure type
2) Epilepsy type
3) Epilepsy syndrome

www.ilae.org

The classification is based on the generalization and etiology.

Classification of the Epilepsies

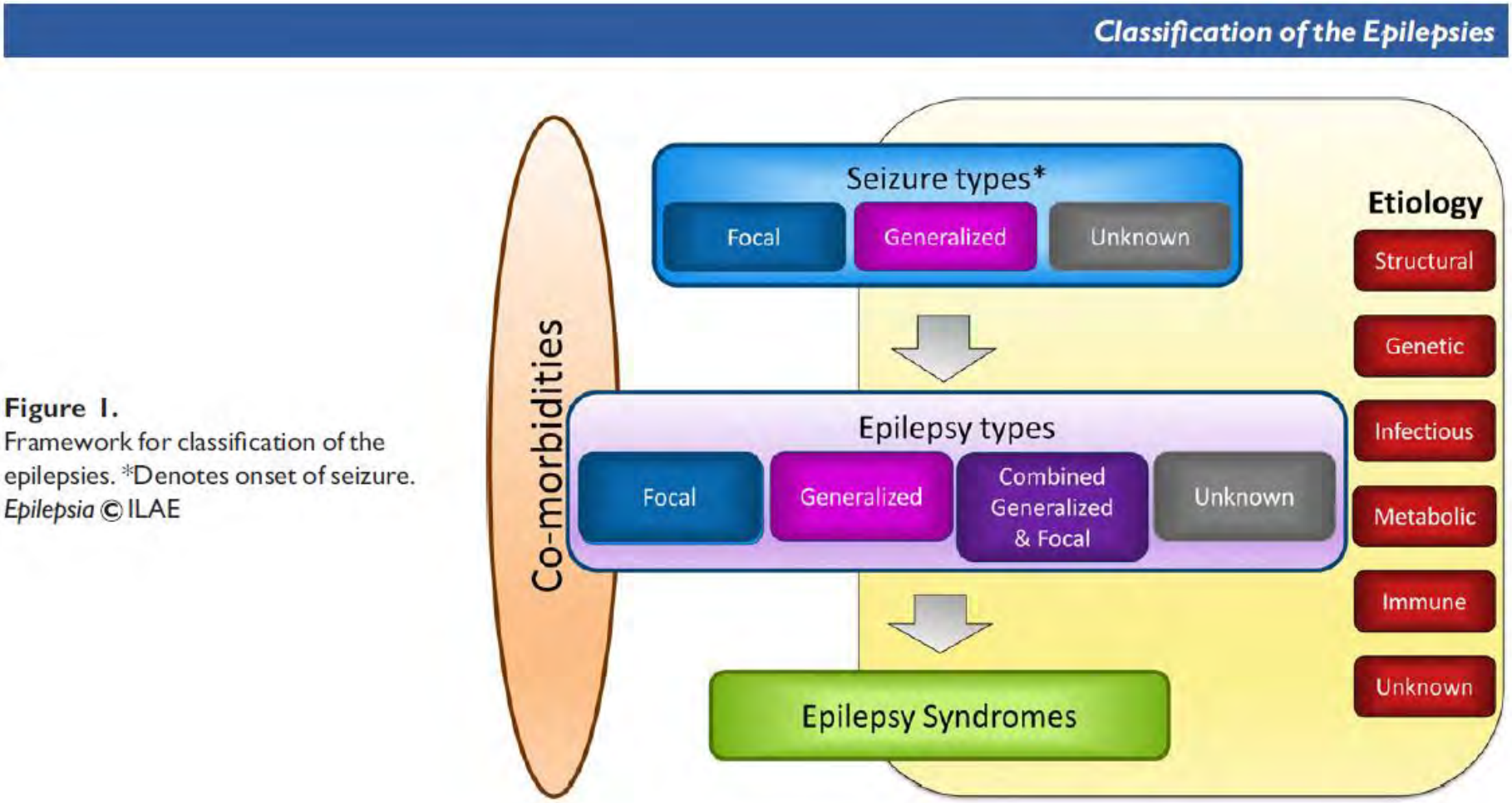
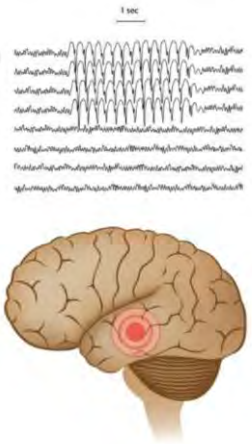


Figure 1.
Framework for classification of the epilepsies. *Denotes onset of seizure.
Epilepsia © ILAE

https://www.ilae.org/files/ilaeGuideline/ClassificationOfEpilepsies_Scheffer_et_al-2017-Epilepsia.pdf

Classification of the epilepsies According to seizure type

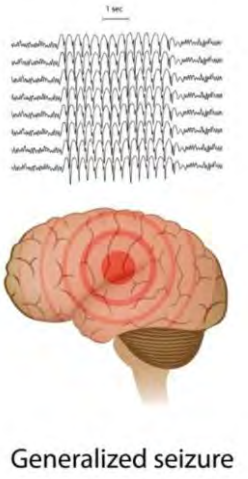


Partial (focal) epilepsy 60%

- Most common in adults
- Local injury in the brain → abnormal neuronal irritation → epilepsy

Generalized (thalamocortical) epilepsy 10%

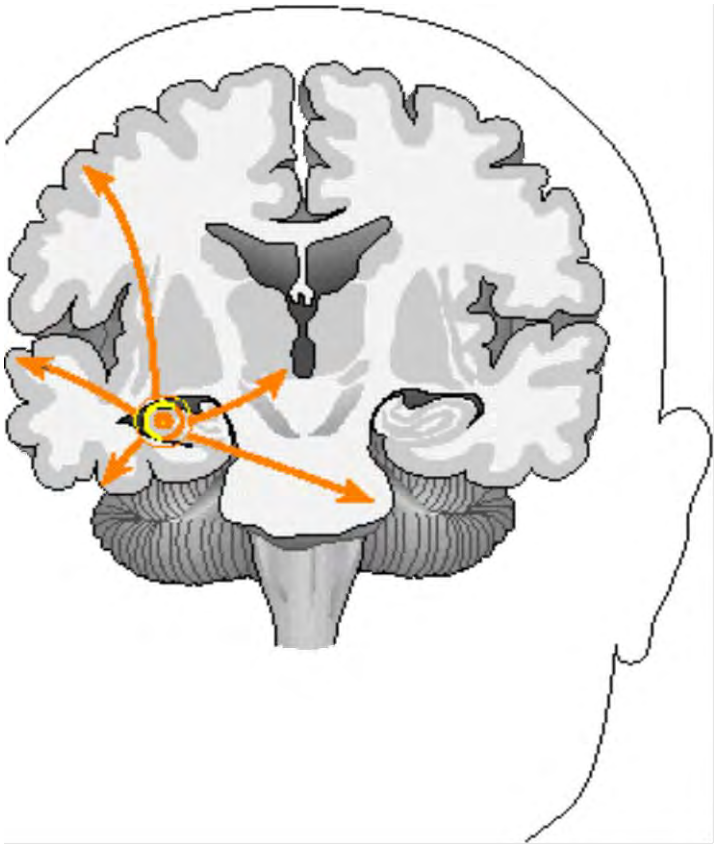
- Begins usually in childhood or in adolescence
- Abnormal neuronal irritation of the normal neural network



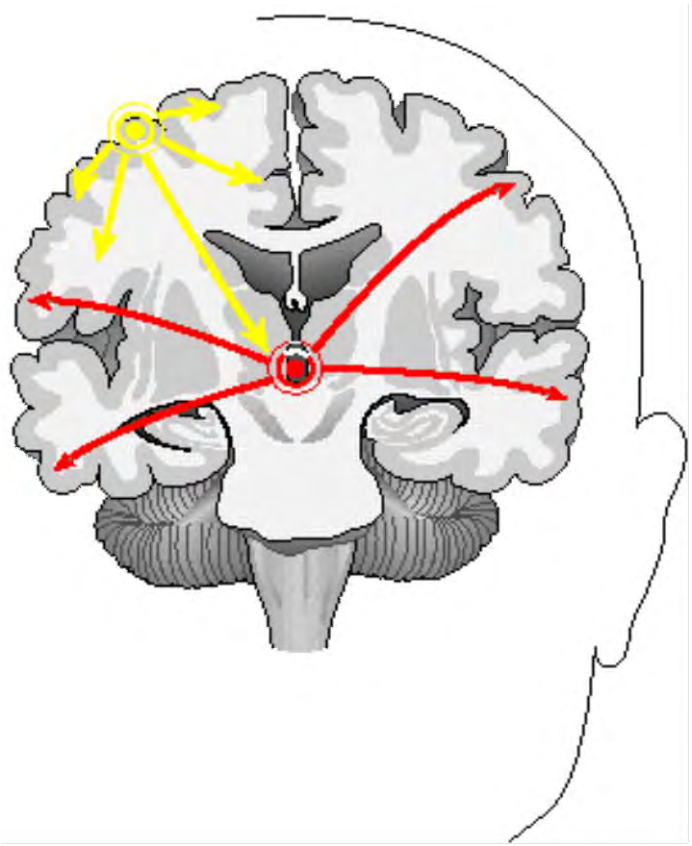
Unclassified 30%

www.ilae.org

Focal seizure



Generalized focal seizure



Focal seizures (partial onset)

1. SIMPLE PARTIAL SEIZURES

- **Motor symptoms**

  Limb jerks, sounds/cessation of talking, turning of gaze/head

- **Symptoms from sense**

  Visual or auditory sensation, dizziness, smell, taste

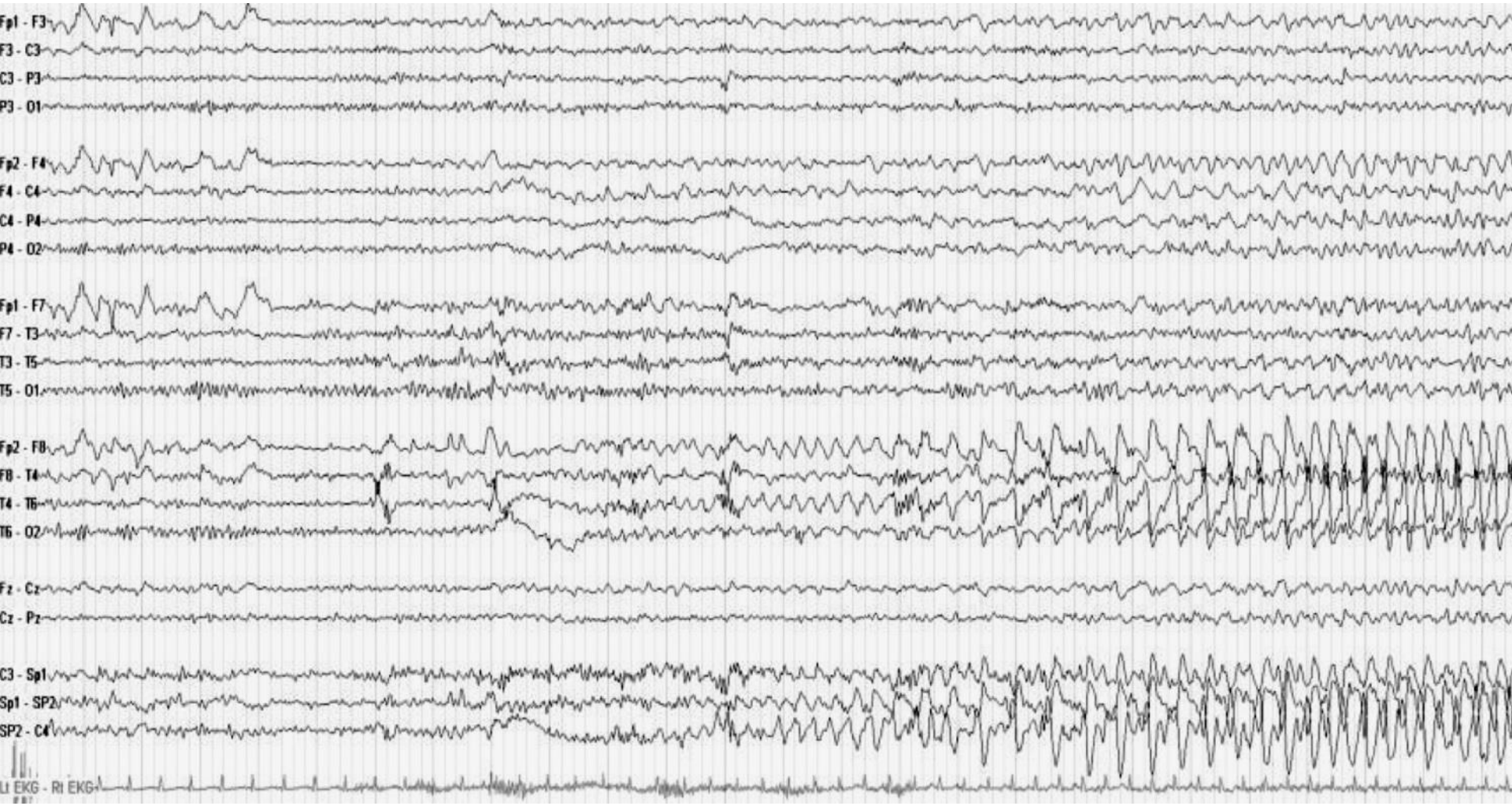
- **Autonomic symptoms**

  Gastric symptoms, palpitation, swetting, salivation, blushing

- **Mental symptoms**

  Memory disorder, Déjà-vu sensation, fear, anxiety, delusions, disorder of understanding

Focal seizure



Focal seizures (partial onset)

2. COMPLEX PARTIAL SEIZURES

Same symptoms as previously + impaired awareness

3. (SECONDARILY) GENERALIZED SEIZURES

Tonic-clonic seizure

https://www.youtube.com/watch?v=Nds2U4CzvC4

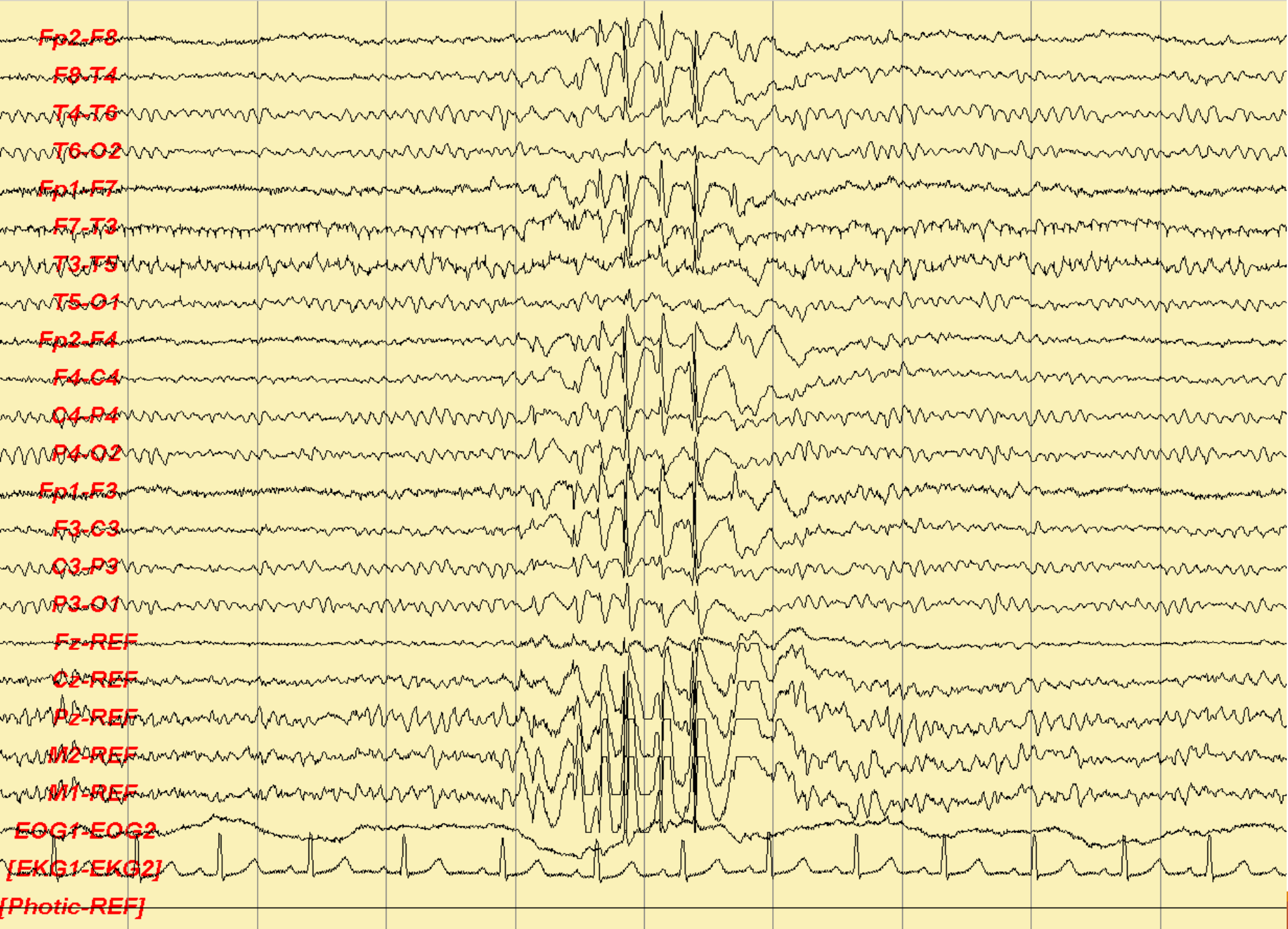
Primary generalized seizures

Loss of consciousness without warning

(Clinically it is not usually possible to differentiate between primary generalized and secondarily generalized focal seizures!)

Primary generalized tonic-clonic

- Tonic-clonic cramps, tonic, clonic, atonic myoclonies
- Cramps 30 s - 2 min
- Biting of tongue
- Incontinence
- Postictal desorientation and fatigue (15-30min - hours)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Fp2-F4
F4-C4
C4-P4
P4-O2
Fp1-F3
F3-C3
C3-P3
P3-O1
Fz-REF
O2-REF
P2-REF
M2-REF
M1-REF
EOG1-EOG2
[EKG1-EKG2]
[Photic-REF]
PRIMARY GENERALIZED SEIZURE
100µV

Primary generalized seizures

Absence seizures

- Juvenile absence epilepsy
- Couple of seconds

Figure 3. Typical Absence with Tonic Upgaze.

These results are in accordance with recent studies using *f*MRI, showing that seizure-related BOLD (blood oxygen level dependent) changes, time-locked to the occurrence of SWD induced profound negative changes in all brain areas with the exception of the thalamus (Salek-Haddadi *et al.*, 2003, Labate *et al.*, 2005).

Generalized seizure provoked by hyperventilation

https://youtu.be/obbg1BFt26Q

Primary generalized seizures

Juvenile myoclonus epilepsy

- Myoclonic jerks usually in the mornings
- 3y → Generalized tonic-clonic seizures (80-95 %) often in the morning when waking up or during the night
- May start with myoclonic jerks
- Absence seizures 15-30 %
- 8-**12-18**-24y starting age
- EEG diagnostic

DIFFERENTIAL DIAGNOSIS OF A SEIZURE

Syncope

Functional

Cerebrovascular symptom

Hemonynamic etiologies

Meningitis / encephalitis

Increased ICP (pressure)

Migraine

TGA

Delirium related to dementia

Hypoglycemia

Hyponatremia

Hypocalsemia

Intoxication

Delirium

REM-sleep disturbance

Desorientation related to waking-up

Nocturnal limb movement disturbance

Narcolepsy

Dystonia

DIFFERENTIAL DIAGNOSIS
Syncope

Syncope usually when standing

- Fear, pain, coughing, urinating and defacating may trigger

Etiology: vasovagal / hemodynamic / orthostatic

Quick preliminary symptoms (not always): blurring of vision, dizziness, nausea, swetting, yawning, restlessness, paleness

Symptoms during the attack: loss of muscle tone

- Clonic jerks may be seen
- In cardiac / hemodynamic fainting, the hypoxia may last so long, that the patient has an epileptic seizure

Post symptoms: rarely biting of the tongue, sometimes incontinence, usually consciousness is quickly recovered without desorientation

DIFFERENTIAL DIAGNOSIS
Syncope

https://www.youtube.com/watch?v=SOsNeUg1iGA

DIFFERENTIAL DIAGNOSTICS
Functional seizure

5-20% of the patients having epilepsy, may also have pseudoepileptic seizures ie. functional seizures. The same patient may have various seizure types.

Features related to functional seizures

- No pupil reactions
- Patient actively closes his/her eyes
- Possible to have a reaction to a stimulus (patients responds by talking or other way)
- Seizures are very variable
- Seizures are very complex
- Response to medical therapy is not good

Clinically the differentiation may be difficult since some frontal lobe seizures may consist of very peculiar behavior and strong motor symptoms without alteration of consciusness.

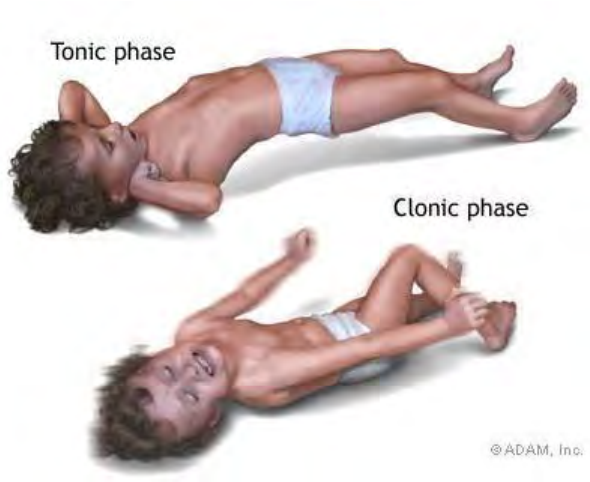
TREATMENT – Part I: Emergency room

TREATMENT IN THE EMERGENCY ROOM

- OBJECTIVE OF TREATMENT IS TO STOP THE SEIZURE
- Vitals (Airway, Breathing, Circulation)
- Glucose?
- I.v. bentsodiazepin
  - ✓Lorazepam 2- 4 mg i.v. Every 5 minutes when needed, ad 8 mg, lasting about 12-24 h
  - ✓Diazepam 10 mg i.v. every 5 minutes when needed ad x 3 (-5), lasting 15-30 minutes
- Vitamin B1: 250 mg i.v.
- Laboratory tests (also the concentrations of antiepileptics)

DESCRIPTION OF THE SEIZURE

- Pupils? Reaction to light? Dilated?
- Symmetric or asymmetric seizure?
- Upper or lower limbs or both were shaking?
- How did it evolve?
- Head turning/version? To witch side?
- Devation of gaze?
- Reaction when addressed?



IMPORTANT INFORMATION OF SEIZURE

- Prodromal symptoms? Sensations before seizure?
- Automatisms before/during seizure?
- Duration of the seizure? Incontinence? Biting of the tongue? Other injuries?
- Postictal symptoms? Desorientation? Aphasia?
- Postictal paresis (Todd's paresis)? On which side?

TREATMENT IN ER

Medical treatment in three phases:

- 1. Bentsodiazepins
- 2. Loading with antiepileptics
- 3. General anesthesia

TREATMENT IN ER – 2

Indications to load with antiepileptics:

- Seizure is not finished after treatment with 1. phase medication
- First aid brings the patient in sedation (Propofol) due to imminent status epilepticus
- Serial seizure (3 seizures during the same day, even if patients recovers awareness in between)

STATUS EPILEPTICUS

ILAE: Classically SE was defined as a "a condition characterized by an epileptic seizure that is sufficiently prolonged or repeated at sufficiently brief intervals so as to produce an unvarying and enduring epileptic condition."

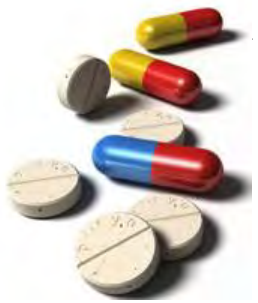
A seizure lasting more than 5 min is an imminent SE.

If a seizures lasts 30 min or more, or the seizures are repeated so often that the patient doesn't recover in between, the state is considered a status epilepticus.

SE requires intensive care

Different types: Convulsive, non-convulsive, absence, myoclonic, focal..

STATUS EPILEPTICUS Treatment



Objectives of the treatment:

- Secure vital functions
- Terminating the abnormal electrical activity of the brain as quick as possible
- Prevention of new seizures
- Detecting and treatment of systemic complications
- Finding out etiologic factors and treating them
- Minimizing functional impairment and mortality

First epileptic seizure in ER

Anamnesis, seizure description, status

Laboratory tests:

- CBC, liver, kidney, CRP, Na, K, Ca-ion, Gluk, CK
- EKG
- (CSF, EEG)

Imaging of the brain

Monitoring 6 h

Driving ban minimum 3 months (Finland)

TREATMENT – Part II:
After a new epilepsy diagnosis

INDICATIONS FOR ANTIEPILEPTIC MEDICAL THERAPY

Medical therapy is started immediately after diagnosing epilepsy ➡

At least two unprovoked seizures on separate days, occurring during 1-2 years of time (=*clinical diagnosis*)

OR

After one epileptic seizure if the probability of further seizures is high:

- Epileptic seizure due to previous brain infarct, brain injury, dementia in an elderly person, other reliable etiological factor
- Juvenile myoclonus epilepsy or other syndrome, if the diagnosis is verified by the anamnesis and EEG-finding.
- The first seizure is prolonged or complicated

Principles of medical therapy

Only one medication at the beginning, and if necessary, the dose in increased

As simple medical therapy as possible

- There is very little evidence of the advantange of polytherapy

Principal mechanisms of action of antiepileptic drugs

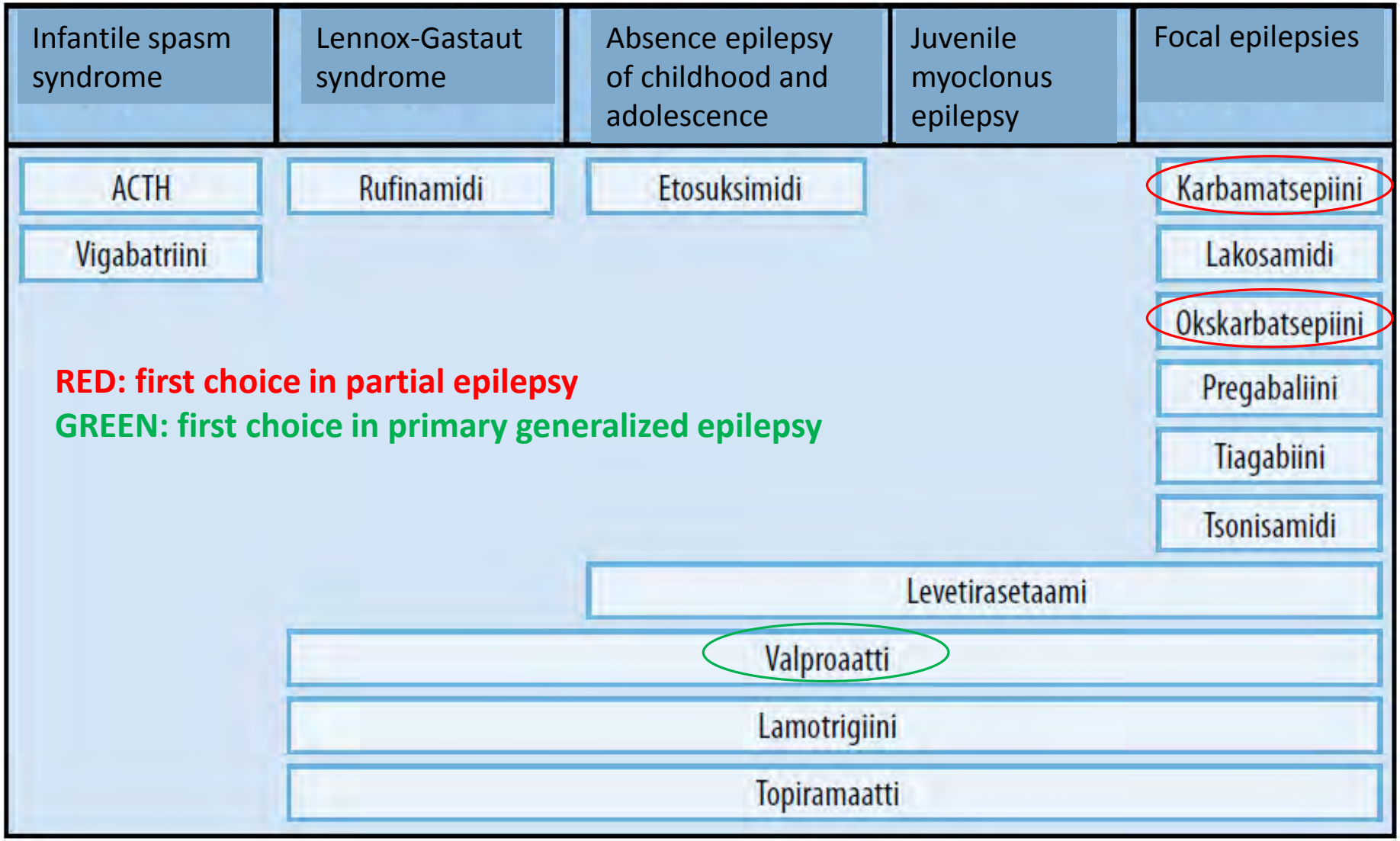
Antiepileptics effect by inhibiting Na- or Ca-channels, by opening K-channels, by strenghtening GABAergic inhibition, by inhibiting glutamatergic exitatory activity or by modifying cellular signaling pathways in the brain cells.

MECHANISMS OF ACTION OF ANTIEPILEPTIC DRUGS

AED	Na+	Ca2+	SV2A	Glutamaatti	GABA	KCNQ	CA inh
Fenytoiini (PHT)	++						
Karbamatsepiini/Okskarba(CBZ/OXCBZ)	++						
Valproaatti (VPA)	?	?		?	+		
Etosuksimidi (ESM)		++					
Phenobarbitaali (PB)		?		?	++		
Bentsodiatsepiinit (CLN/CLB)					++		
Eslikarbatsepiini (ESL)	++						
Lakosamidi (LCM)	++ (slow)						
Lamotrigiini (LTG)	++	+					
Tsonisamidi (ZON)	++	+			+		+
Topiramaatti (TMP)	+	+		++ (KA)	+		+
Perampaneeli (PMP)				++ AMPA			
Gabapentiini/Pregabaliini (GBP/PGB)		++					
Levetirasetaami (LEV)/brivarasetaami		+	++		+		
Vigabatriini (VGB)					++		
Tiagabiini (TGB)					++		
retigabiini					?	++	

How to select the medication?

PATIENT	EPILEPSY	MEDICATION
Age	Syndrome	Effect
Sex	Epilepsy type	Modes of action
Plans for pregnancy	New diagnosis	Adverse effect
Other diseases of the pt.	Difficulty	Forms to use
Motivation		Pharmacokinetics
Medical history		Combined effects
Personal views		Indications
		How quickly can be started
		Price



Keränen et Holopainen, Duodecim 2009

Side effects of antiepileptic drugs

Fatigue

Tremor

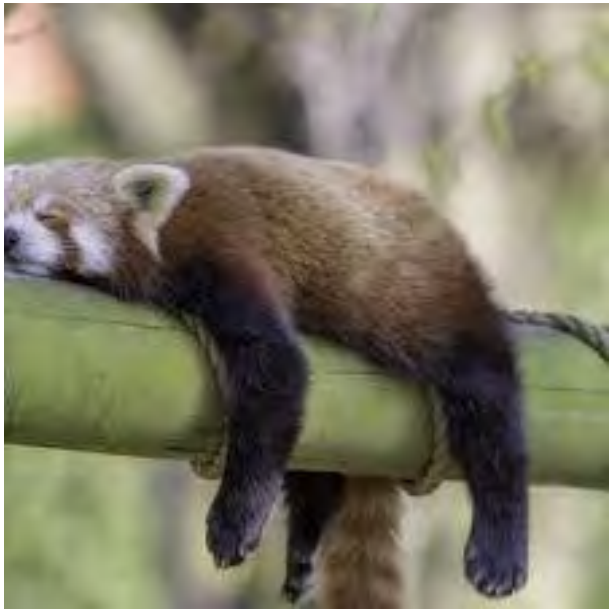
Dizziness

Gait disturbance

Diplopia

Cognitive disturbance

Etc.



Important information related to medication

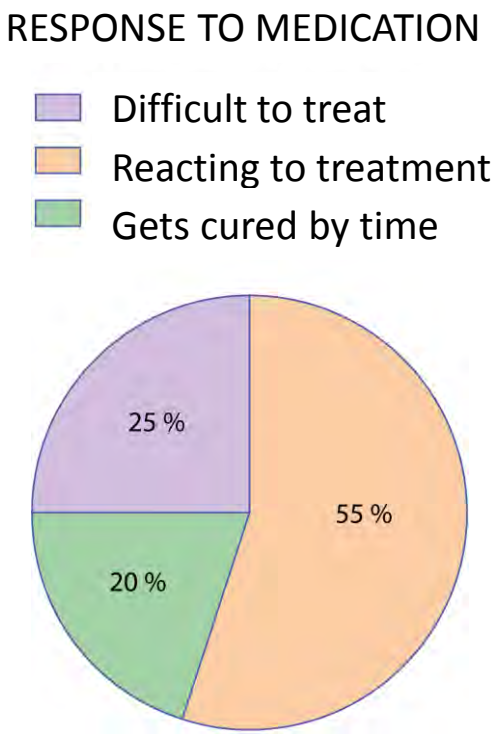
- Often combined effects with other medications, take into consideration
- Other drugs may be even proconvulsive (e.g. Clotsapine)
- Don’t stop antiepileptics too quickly

RESPONSE TO MEDICAL THERAPY

≈ 70% get seizure-free with monotherapy

≈ 30% need 2 or more antiepileptic drugs

There is rarely advantage of using 3 or more antiepileptic drugs (consider other treatment options)



PROGNOSIS

Epilepsy is cured when the patient has passed the critical age for a specific epilepsy syndrome OR

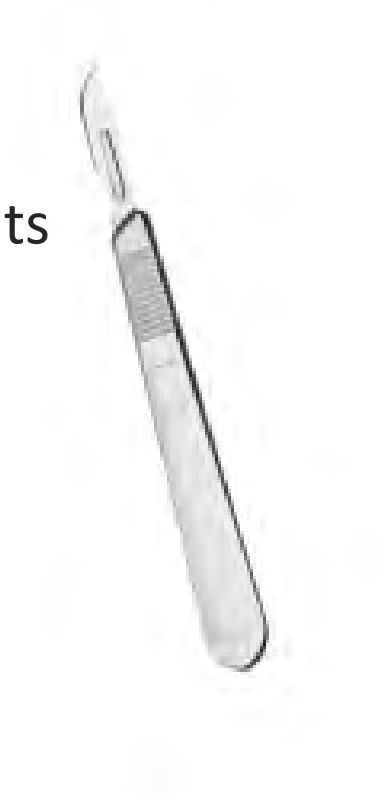
The patients hasn’t had any seizures in 10 yearsor more and has been without medication for more than 5 years

In half of the epilepsies started in childhood, the medication can be stopped after at least 3-5 years of seizure-free period

Other treatment options – Surgery

The surgical removal of the epileptogenic area in the brain

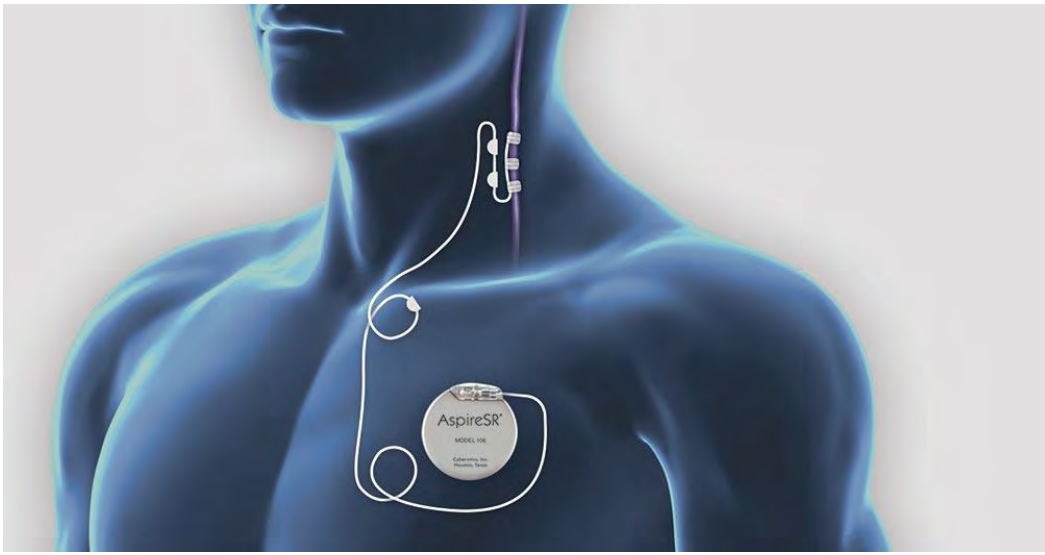
* Only to carefully selected group of patients



VAGUS NERVE STIMULATION (VNS)

Seizures ↓ - effective in approx 50%

Battery change in 5-7 years



DEEP BRAIN STIMULATION (DBS)

Bilateral electrodes in the anterior thalamic nuclei

EPILEPSY AND WOMEN

- Pregnancies usually go well
- Risk for fetal developmental disorders is 2x higher compared to healthy mothers
- Don’t use valproate, the risk for developmental disorders is substantially high!
- Folic acid substitution (min 0.4mg/day) preferably when planning the pregnancy and lasting until the end of breast-feeding
- Monitoring during the pregnancy is important (neurology and prenatal clinic)
- Some antiepileptic drugs may increase the metabolism of contraceptives, consult of gynecologist

THANK YOU!