

Management of epilepsy: diagnosis and treatment



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Diagnostic algorithm

Four essential questions have to be answered:

- **Is it an epileptic seizure?**
- **If yes, is it *provoked (occasional), acute symptomatic, single not-provoked or recurrent not provoked?***
- **If epilepsy: is it an *epilepsy syndrome?***
- **Is there in the background CNS pathology that needs treatment?**

Diagnosis

I. Anamnesis, heteroanamnesis

II. Laboratory examinations

- metabolic disorders, genetics

III. Functional examinations

- EEG, video EEG, LTM EEG.....intraoperative EEG

IV. Imaging

- CT, MRI, fMRI, PET, SPECT

Anamnesis, heteroanamnesis

- **Should be detailed.**
- **Exact description of the seizure. Are there provoking factors? Home-video.**
- **Injuries- localization!**
- **Delivery, development, childhood.**
- **Diseases in the family.**

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Laboratory examinations

- **Common laboratory examinations.**
- **Special examinations in e.g. childhood epilepsy:**
e.g. serum ammonia, lactate, pyruvic acid,
neurometabolic syndromes, genetics
- **Inflammatory CNS diseases: CSF sampling**

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Electroencephalography



- **Standard EEG**

(photostimulation, hyperventilation, sleep deprivation)

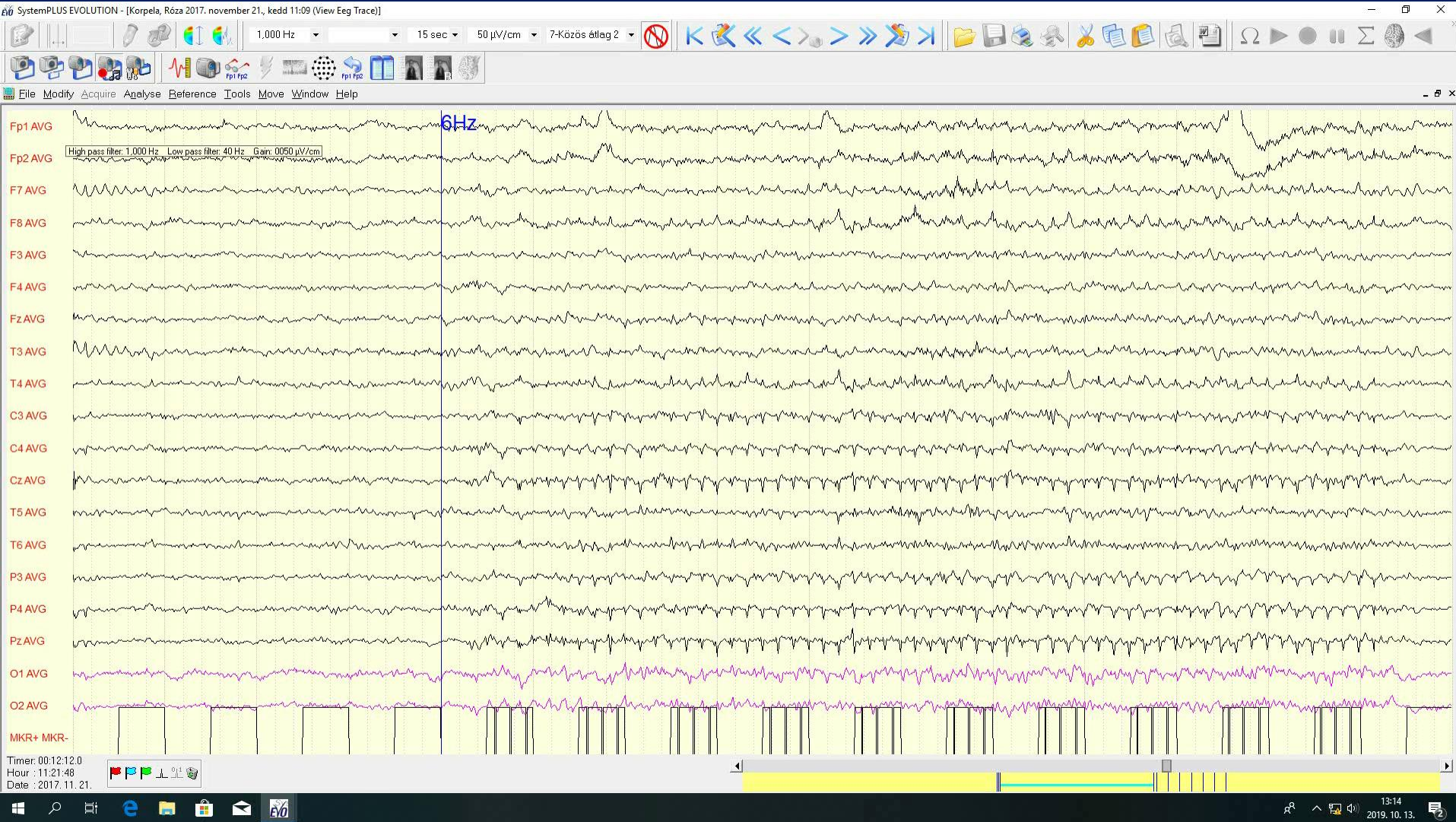
24 hours after seizure onset standard EEG increases the certainty.

Special EEG :

- **12-24 EEG monitoring**
- **seizure provocation EEG**
- **Video-EEG**

Provocation tests

Photostimulation: photic driving



Photoparoxizmal response, intermittent photic stimulation



Juvenile myoclonus epilepsy

Hyperventilation: rapid, 4-6 Hz spike and wave, multiple spikes

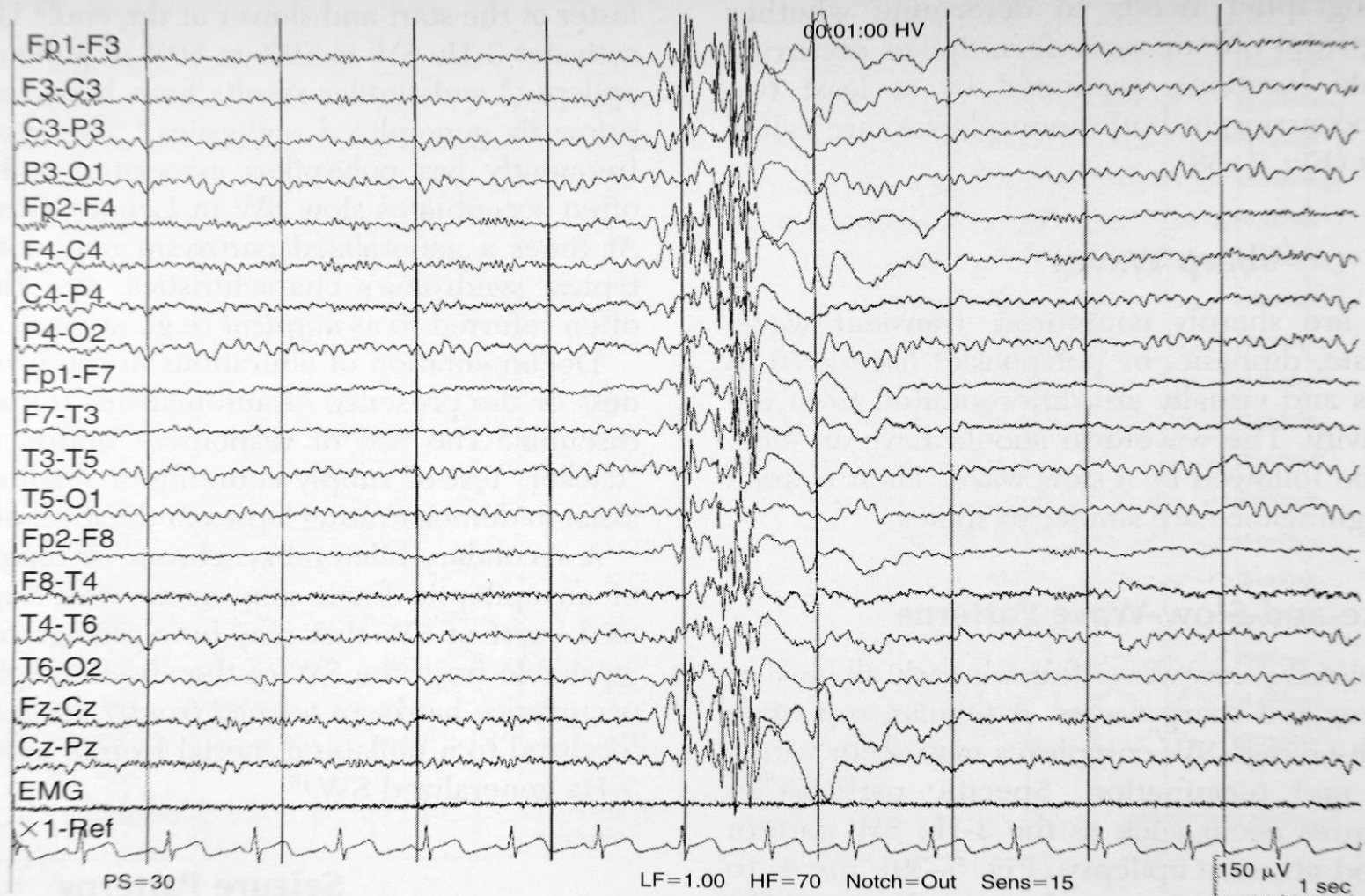
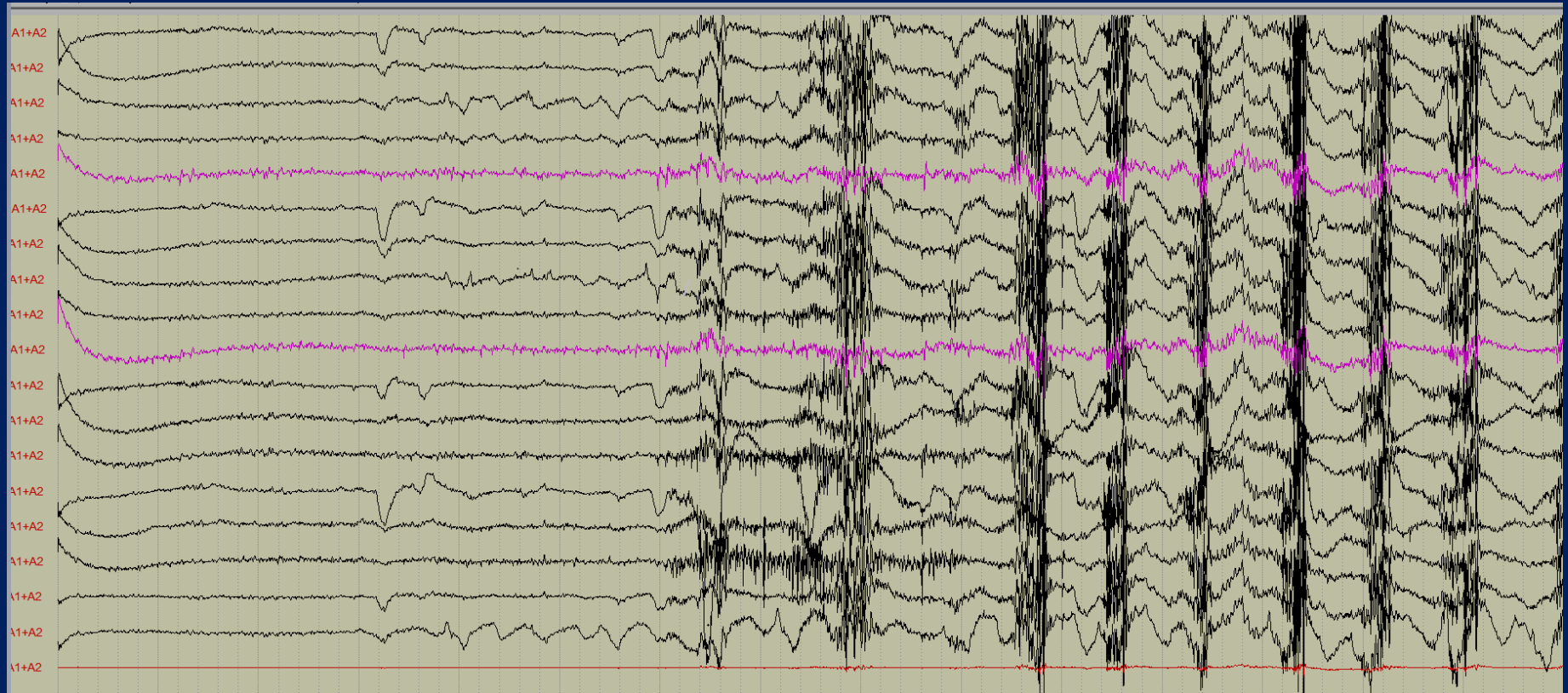
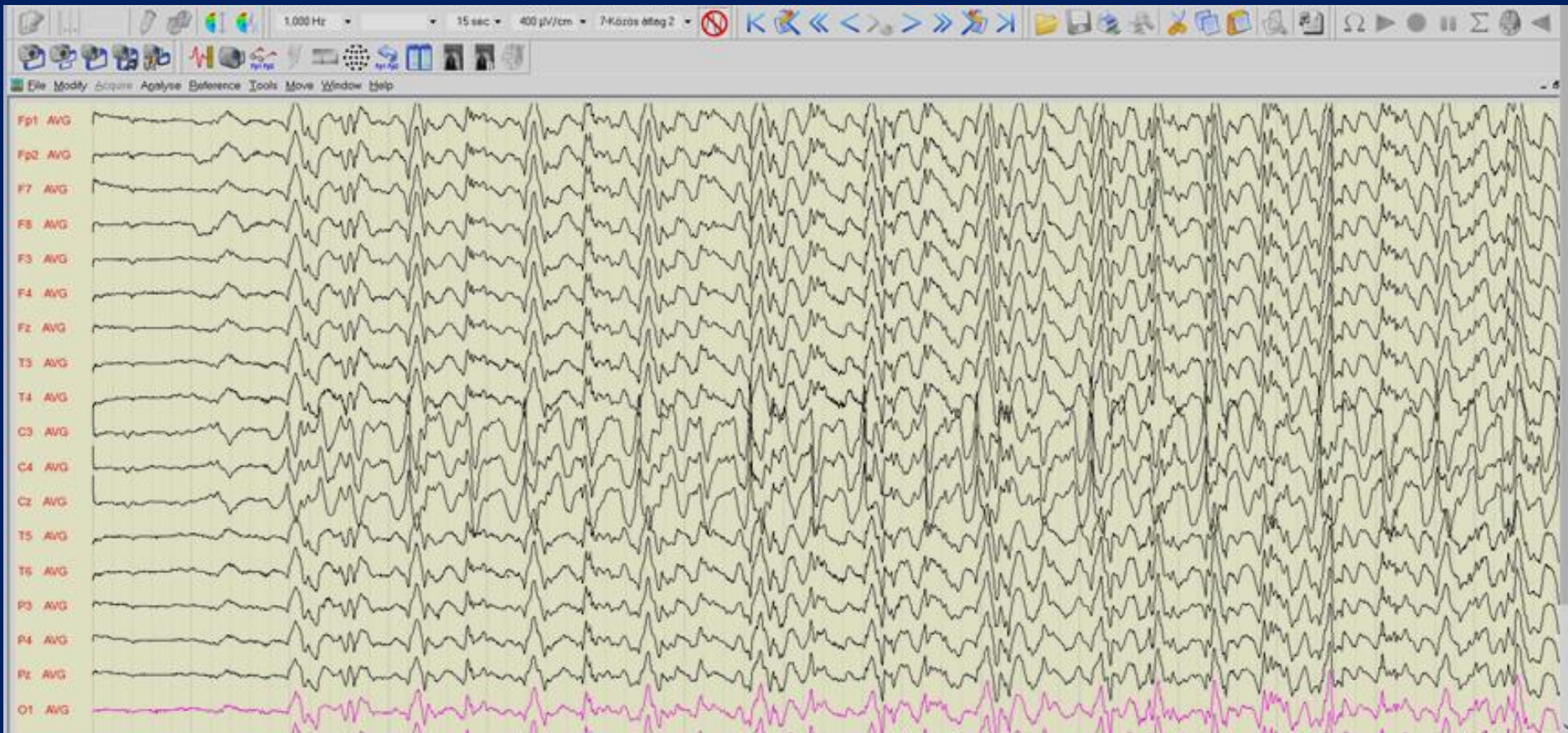


FIGURE 5-40

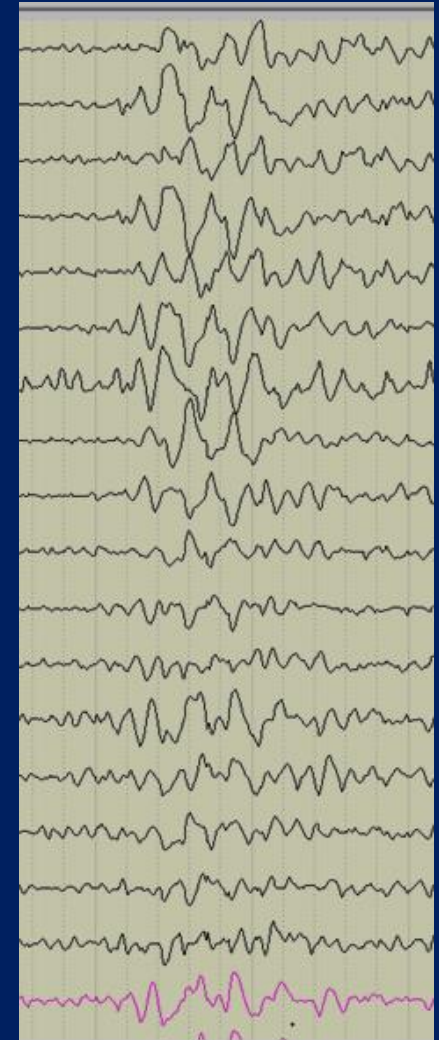
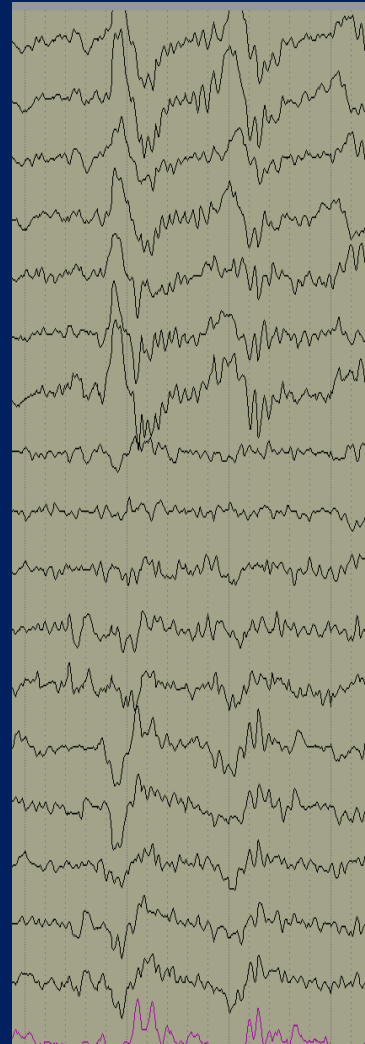
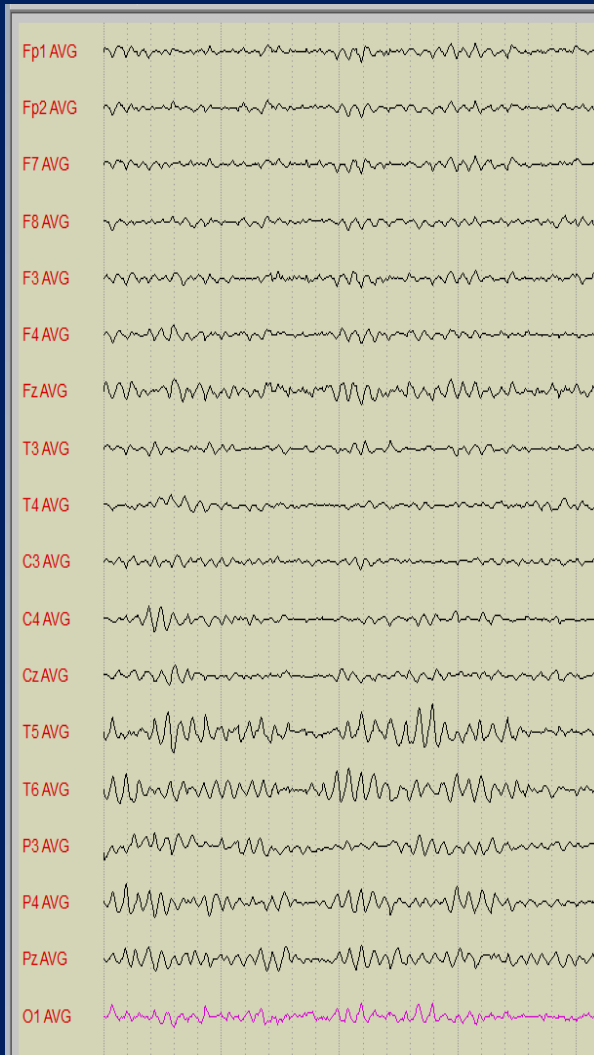
Long-term EEG



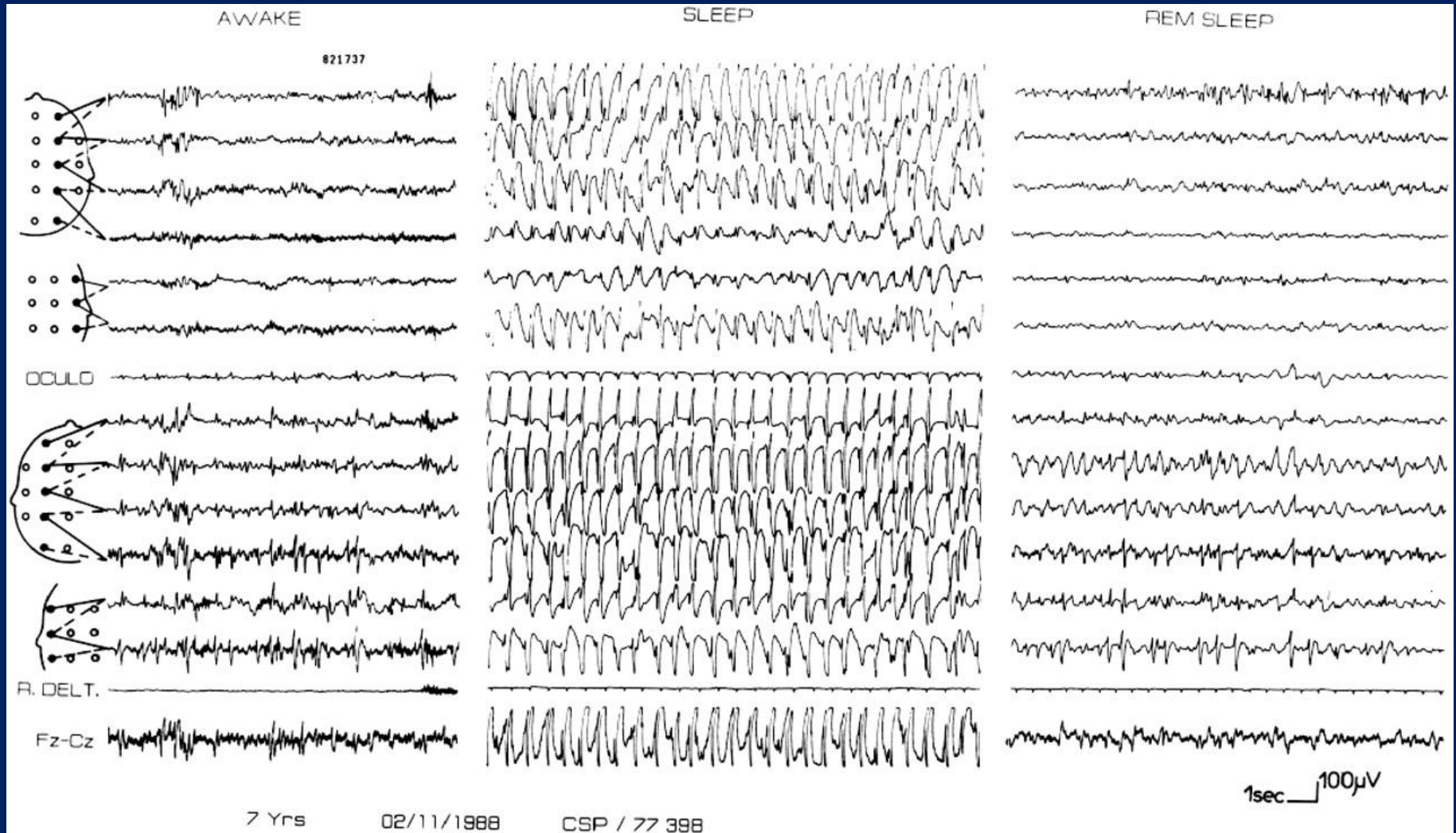
Long-term EEG



Sleep deprivation EEG



Electric Status Epilepticus Syndrome

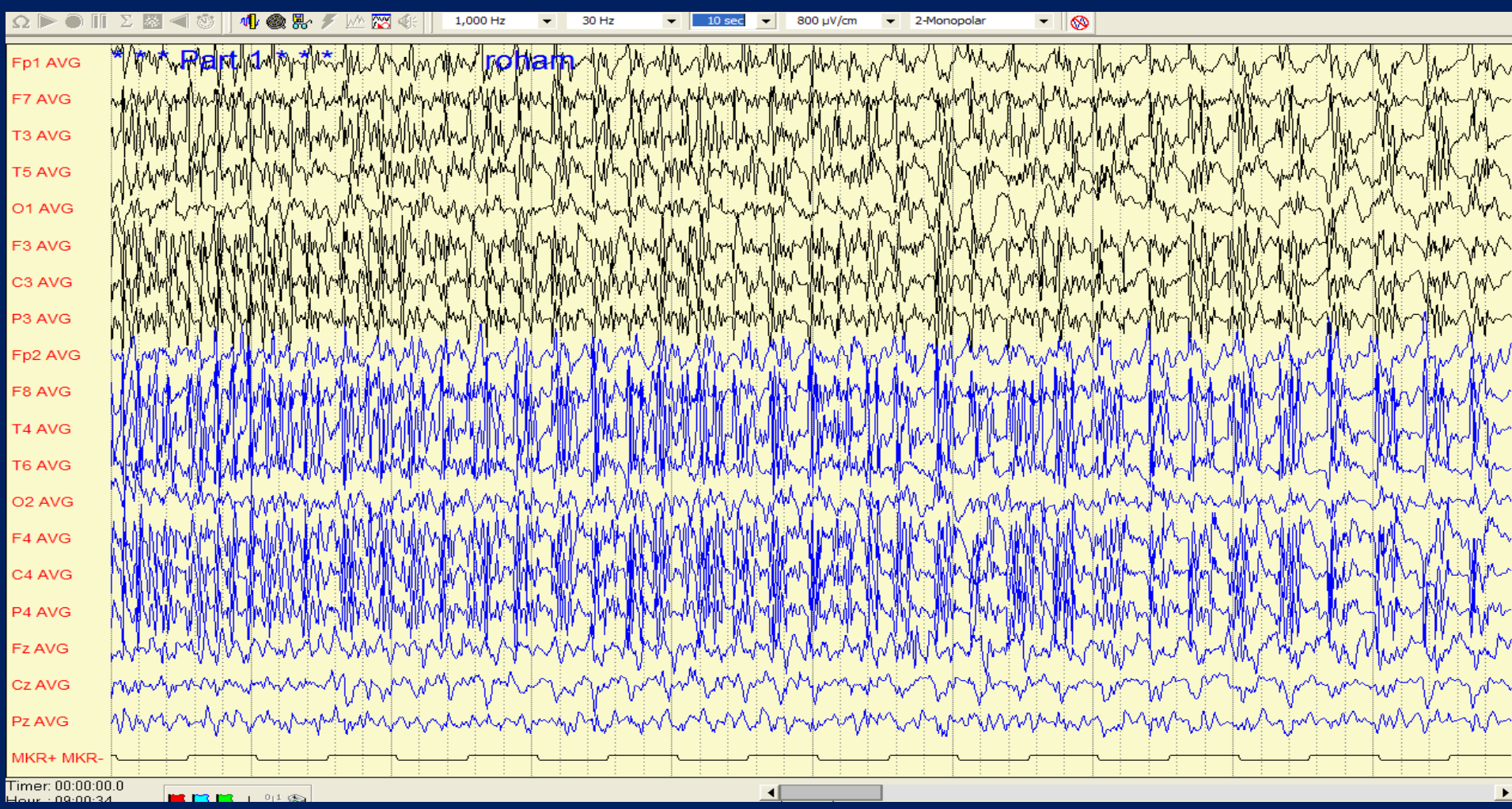


R. Guerrini, P. Genton, M. Bureau, A. Parmeggiani, X. Salas-Puig, M. Santucci, P. Bonanni, G. Ambrosetto, C. Dravet F
Multilobar polymicrogyria, intractable drop attack seizures, and sleep-related electrical status epilepticus

Ictal EEG: generalized epilepsy



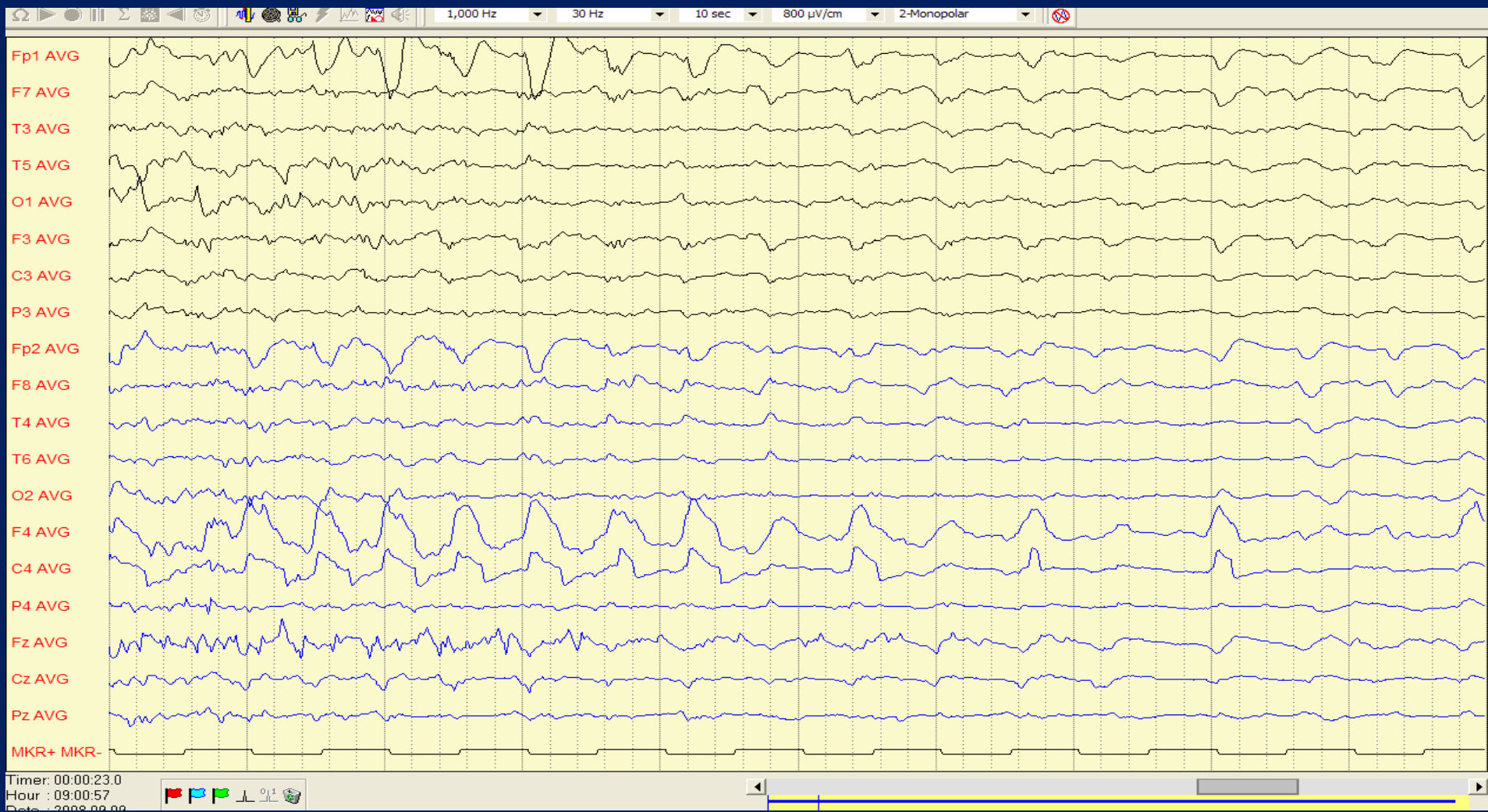
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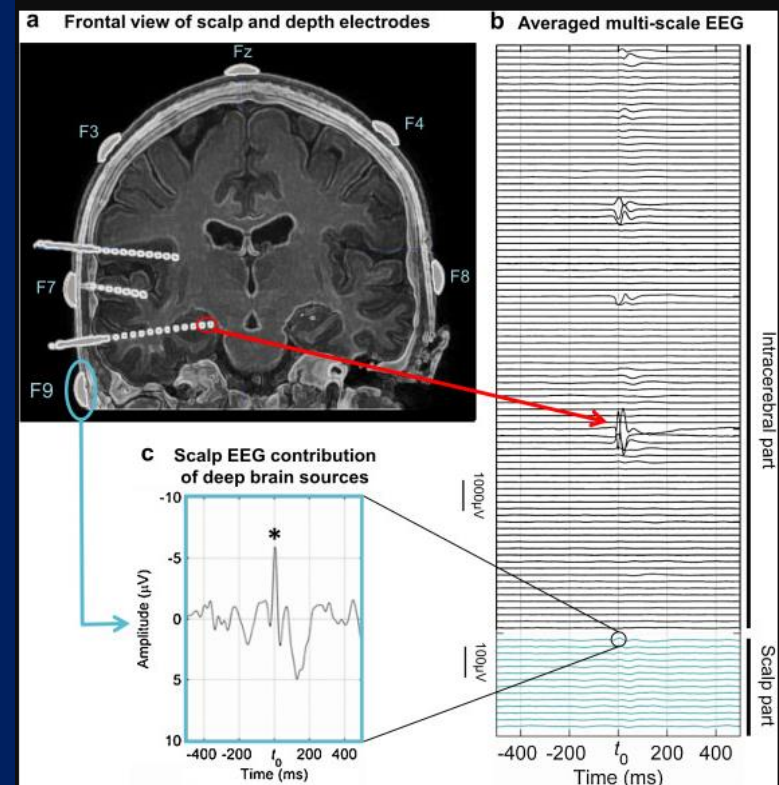
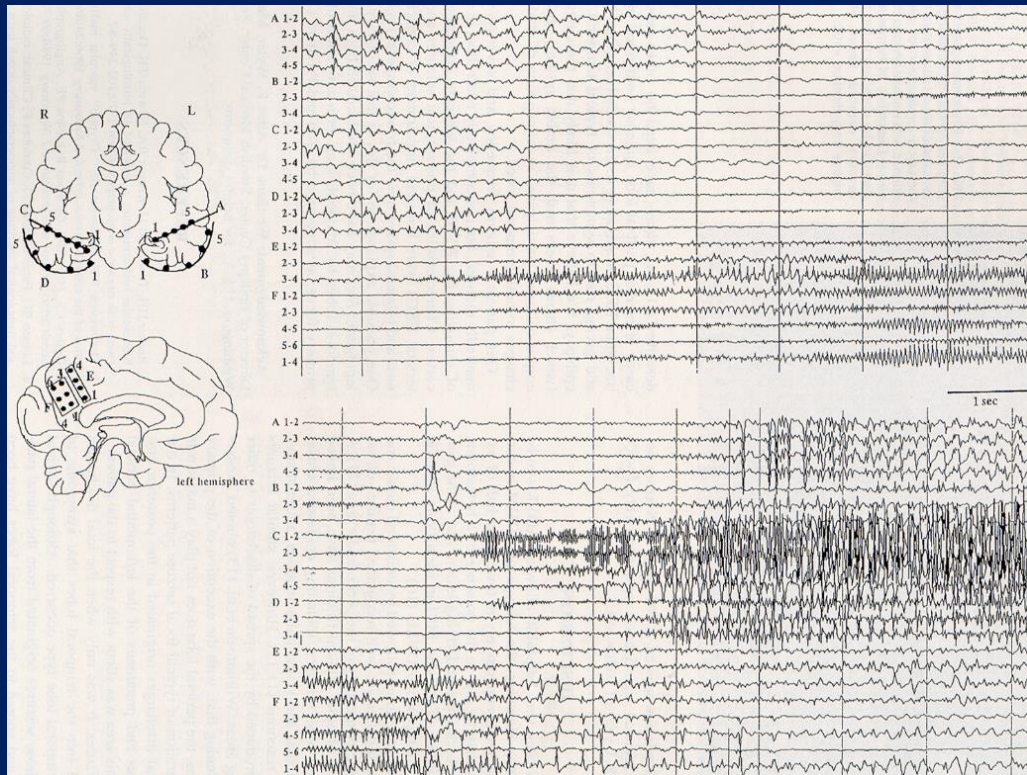
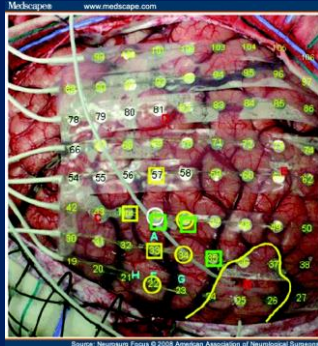
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Examinations before epilepsy surgery: subdural and intracerebral EEG



Caution needed...

- **Epilepsy is one of the most stigmatizing diseases.**
- **EEG is one of the most common misinterpreted examinations („overinterpretation”).**
- **EEG has to be interpreted only together with the clinical findings.**

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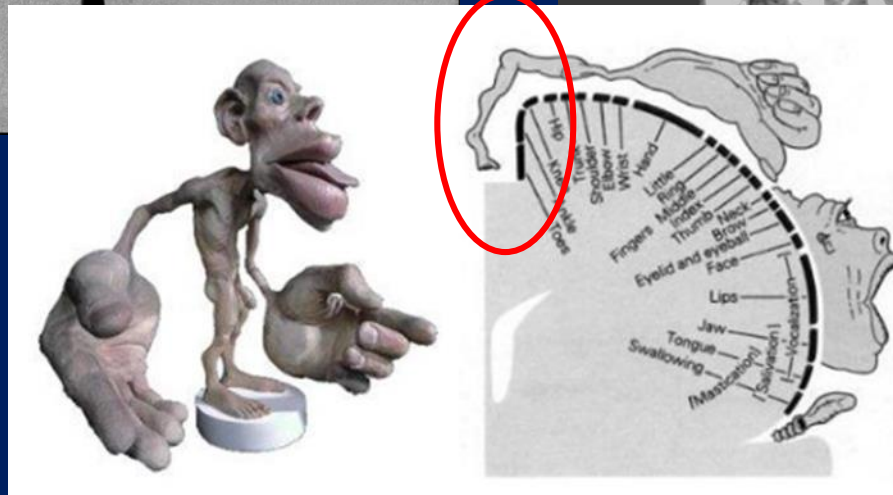
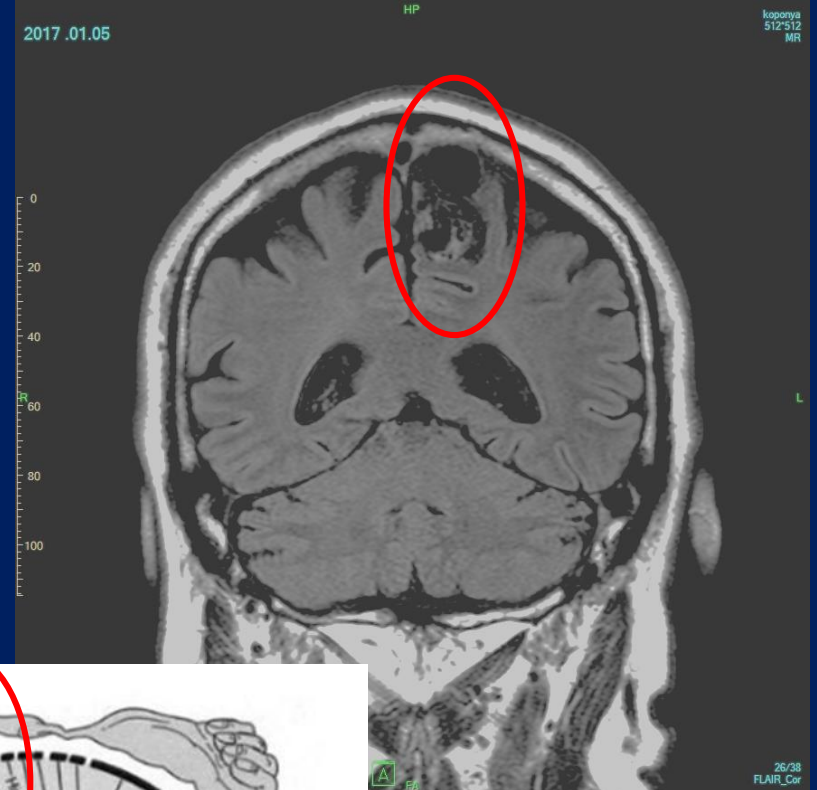
Imaging

Goal:

to find the cerebral structural lesions, epileptogen lesion.

- Cranial CT and cranial ultrasound (children), only as an emergency measure.
- **Cranial MR: with epilepsy protocol.**

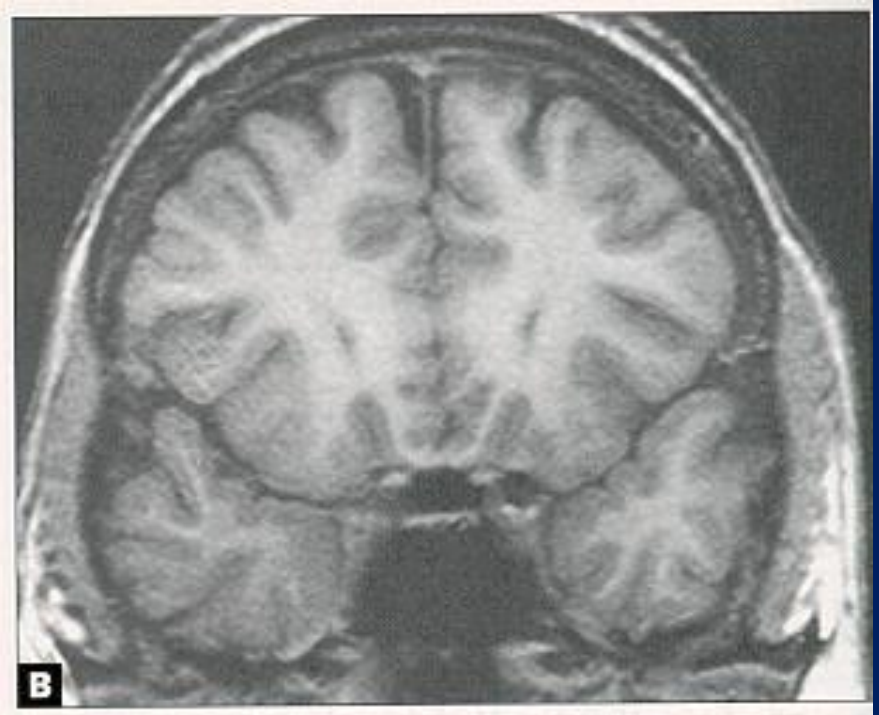
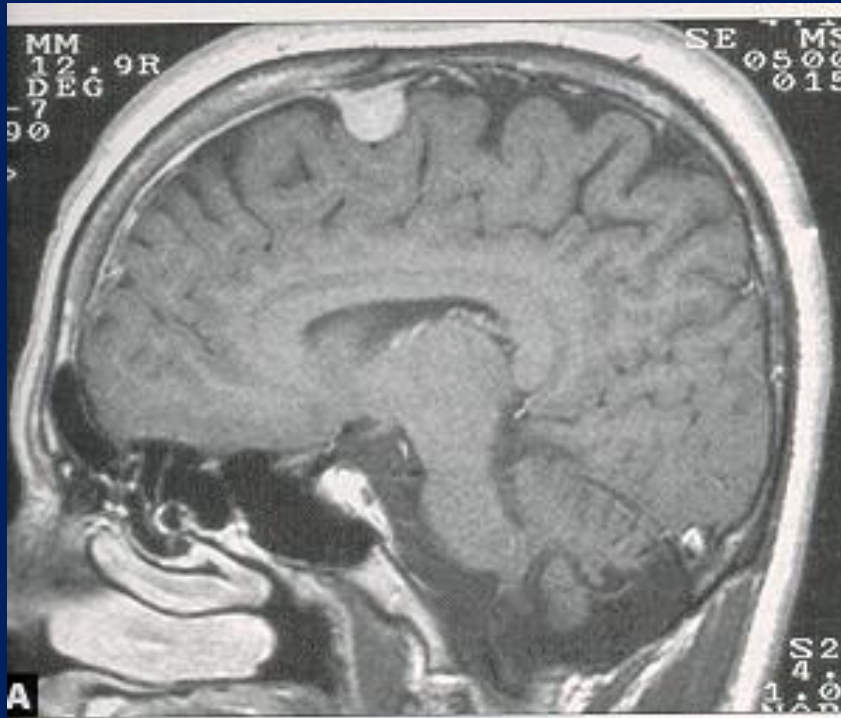
Arteriovenous malformation (right lower limb clonisation)



Sturge-Weber-syndrom



BUT! The abnormality has to be in concordance with the detailed seizure description (EEG: temporal lobe seizure - MRI)



Parasagittalis meningeoma

Temporal lobe lesion

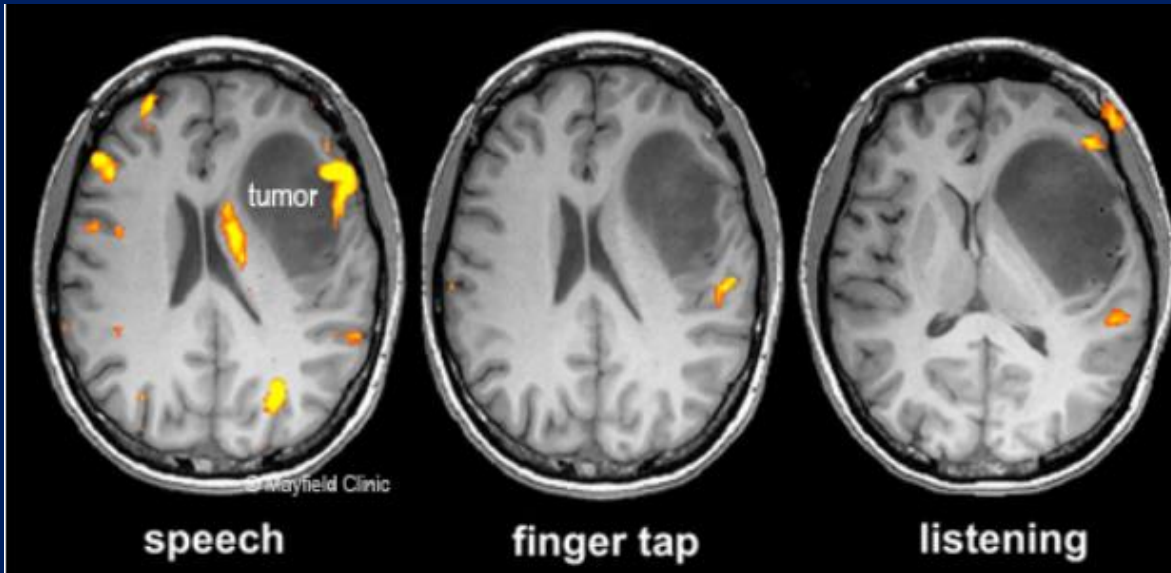
Special examinations

Before epilepsy surgery.

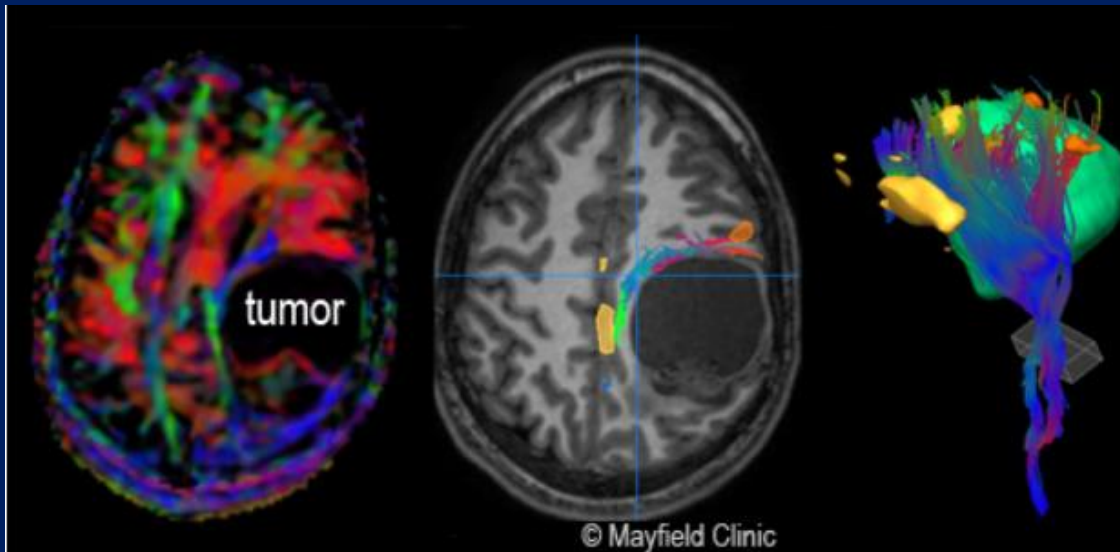
Individually chosen special examinations:

- Diffusion tensor imaging (DTI) and tractography,
- functional MR, MR perfusion, MR spectroscopy,
- brain SPECT and PET,
- cerebral angiography (DSA).

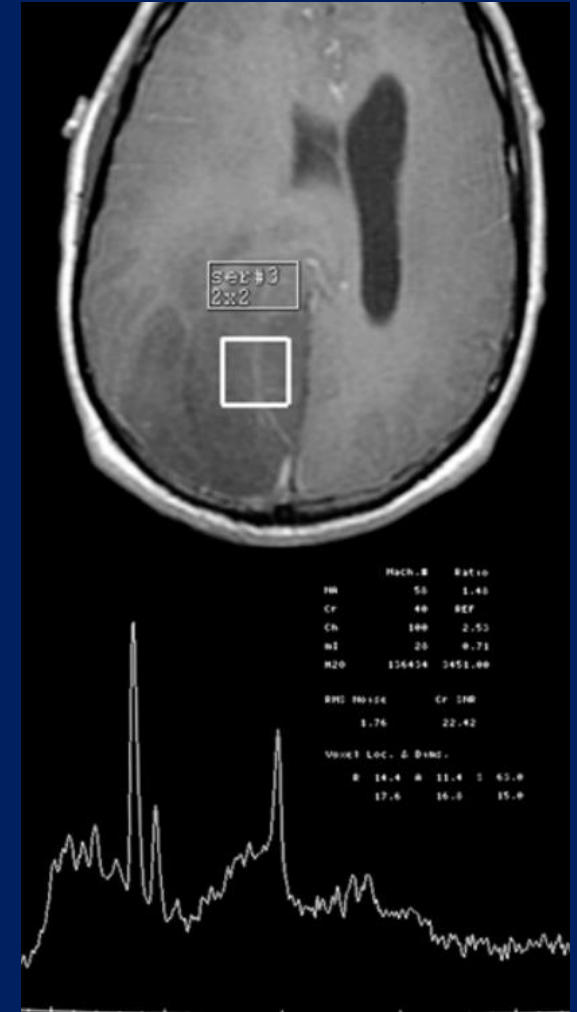
Functional MRI



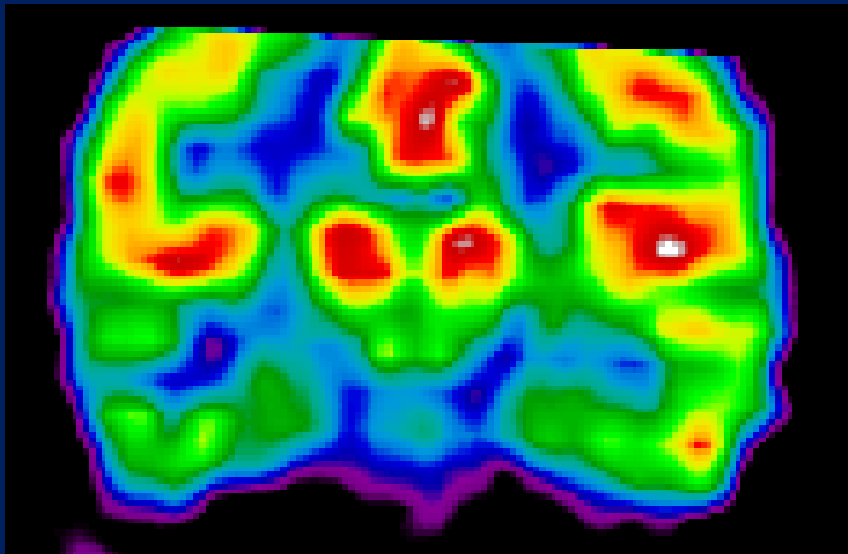
MR tractography



MR spectroscopy

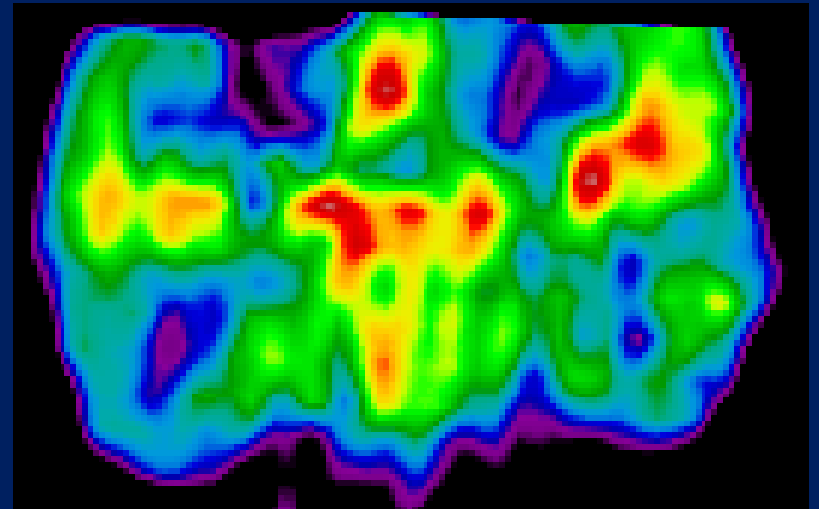


Left sided temporal lobe epilepsy patient coronal FDG and butanol PET images



hypometabolism

^{18}F FDG



^{15}O Butanol

Differential diagnostics

Cardiovascular reasons

Syncope

Arrhythmias (*even drug induced*)

Orthostatic hypotension

Migraine with aura

Movement disorders

- Tic, Tourette disease,
- myoclonus, chorea and choreoathetosis
- Parkinson syndrome collapse

Sleep disorders

- narcolepsy
- periodic leg movement

Differential diagnostics

Metabolic-toxic disturbance

medications, drugs, intoxications

Gastrointestinal diseases

gastric dyscomfort, vomitus, diarrhoea (electrolytes)

Psychiatric diseases

- psychogenic seizure
- panic disorder (Dd. autonom seizure)
- intermittant explosive diseases

Treatment options

- **Wait and see? Oligoepilepsy?**
- **Antiepileptics**
- **Ketogen diet**
- **Surgery, VNS, DBS**
- **Other (IVIg, behaviour therapy...)**

What to do in case of an epileptic seizure?

First steps

- **Avoid injuries and aspiration.**
- **Ambulance, transportation to hospital, pt should not be left alone.**
- **In case of seizure-clusters 10 mg diazepam or 1 mg clonazepam i.v. slowly. MONITOR BREATHING!**
- **In children in case of febrile convulsion decrease temperature!**

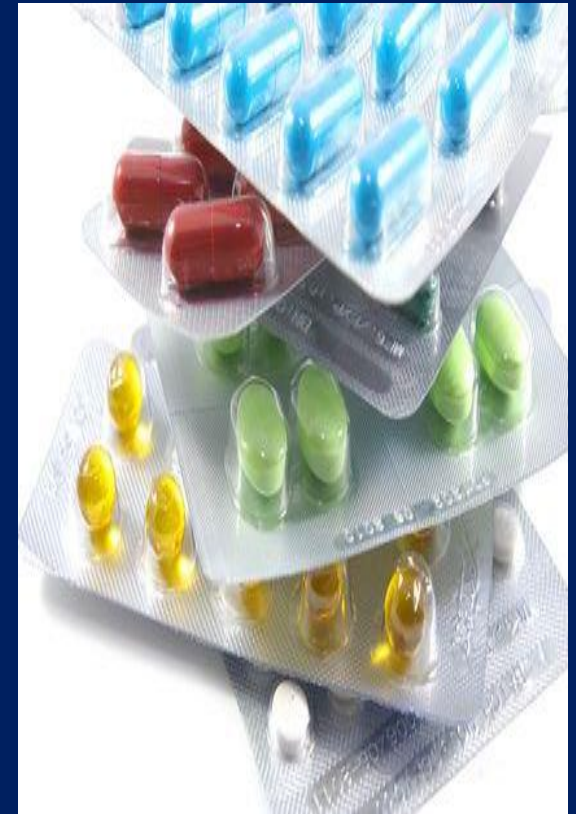
Antiepileptic medication



Phytoterapy



Therapy refracter patients?



New antiepileptic drugs

„Old” and „new” antiepileptics

„Old AE”

Phenobarbital
Primidon
Phenytoin
Diazepam
Ethosuximide
Carbamazepine
Sultiam
Clonazepam
Clobazam
Sodium –valproate
Steroid, ACTH
Acetazolamide

„New AE”

Oxcarbazepine
Vigabatrin
Lamotrigin
Gabapentin
Felbamat
Topiramate
Zonisamid
Tiagabine
Levetiracetam
Rufinamid
Lacosamide
Eslicarbazepin
Retigabin
Brivaracetam
Perampanel

Effect of antiepileptics

1. A. Na⁺-channel

↓ frequency of action potential

B. Ca⁺⁺ -channel

T-type

↓ thalamocortical current

L-type

↓ neuronal excitation

N-type

↓ neurotransmitter clearance

2. GABA transmission

Increase GABA_A receptor activity

↑ inhibition

Increased GABA synthesis/ release

↑ inhibition

Block GABA reuptake

↑ inhibition

Inverse GABA uptake

↑ inhibition

Effect on serotonin release

↑ inhibition

3. Glutamate transmission

Glutamate receptor inhibition

↓ excitation

4. Glutamate synthesis and inhibition of release

↓ excitation

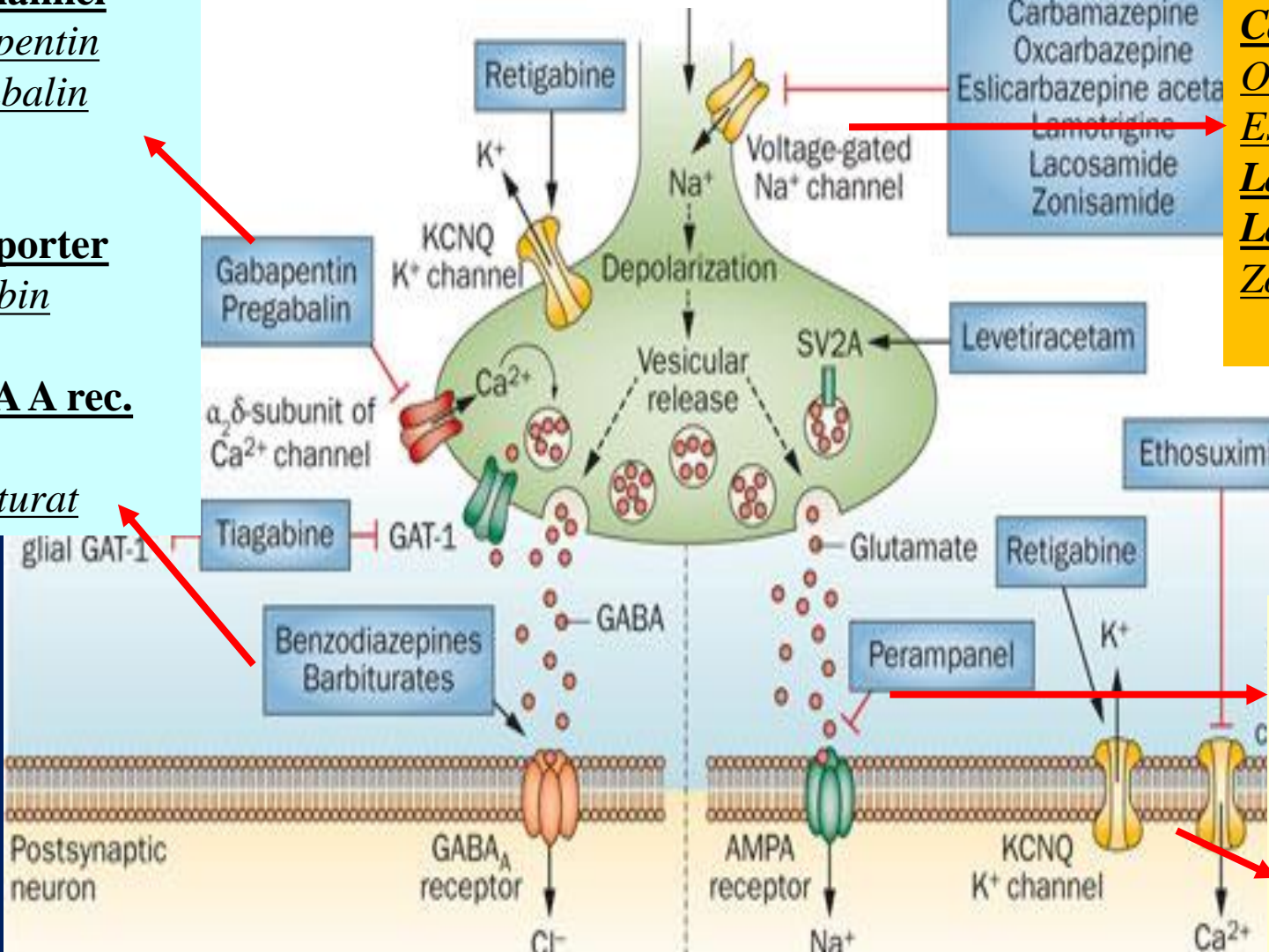
Action potential

Ca-channel
Gabapentin
Pregabalin

Glu transporter
Tiagabin

GABA A rec.
BDZ
Barbiturat

Sodium channel
Phenytoin
Carbamazepine
Oxcarbazepine
Eslicarbazepine
Lacosamide
Lamotrigine
Zonisamide



Retigabine
 K⁺
 KCNQ K⁺ channel
 Depolarization
 Na⁺
 Voltage-gated Na⁺ channel
 Phenytoin
 Carbamazepine
 Oxcarbazepine
 Eslicarbazepine aceta
 Lamotrigine
 Lacosamide
 Zonisamide

Gabapentin
 Pregabalin
 Ca²⁺
 Vesicular release
 SV2A
 Levetiracetam

α₂δ-subunit of Ca²⁺ channel
 glial GAT-1
 Tiagabine
 GAT-1
 Ethosuximide
 Retigabine
 Glutamate
 Perampanel

Benzodiazepines
 Barbiturates
 GABA
 GABA_A receptor
 Cl⁻
 AMPA receptor
 Na⁺
 KCNQ K⁺ channel
 K⁺
 T-type Ca channel
 Ca²⁺
 Ethosuximid

Inhibitory **Excitatory**

Goal and chances of the therapy

- **Goal: constant (total) seizure freedom**
- **With the appropriate AE the 70-75% of the patients become seizure free.**
- **Idiopathic generalized epilepsy: $\geq 90\%$ seizure free with appropriate AE.**
- **By therapy refracter (combination of 2 appropriate AE does not bring seizure freedom) patients: 30-40% surgery.
The chance for seizure freedom : 50-70 %
(better outcome in e.g.: dysgenesis, temporal lobe epilepsy /HS/).**

How to build up AE therapy?

1. monotherapy (start low dose, gradually increase)

Not effective

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graph TD; A[1. monotherapy (start low dose, gradually increase)] --> B[Not effective]; B --> C[2. alternative monotherapy]; B --> D[bitherapy]; C --> D;
```

2. alternative monotherapy → bitherapy

- examination toward **SURGERY** parallelly!
- The changing, tapering of the AE should be done gradually because of the risk of *withdrawal seizure*.

Recommendation for AE treatment

A./ First choice of AE:

- **carbamazepine** (focal),
- **lamotrigin** (focal, generalized),
- **levetiracetam** (focal, generalized),
- **valproate** (generalized or not specified epilepsy)
- ***Fertile women: lamotrigin or levetiracetam (valproate should be avoided).***

Recommendation for AE treatment

**B. / For patients who cannot be treated as given in group „A”
(non-responder, side effects):**

- valproate, lamotrigin,
- levetiracetam, carbamazepine,
- oxcarbazepine, topiramate,
- clobazam, phenytoin,
- zonisamide
- phenobarbital

Recommendation for AE treatment

Special cases

- *In elderly (> 60 years), polymorbid patients, drug interactions, inherited metabolic diseases:* lamotrigin, levetiracetam, gabapentin, valproate
- *West syndrome:* vigabatrin, ACTH
- *Absence epilepsy:* succinimide or adults valproate
- *Myoclonus epilepsy:* levetiracetam, clonazepam

Special subgroups that need emphasized attention, individual treatment

- ***Teenagers:*** trigger, adherence to the treatment
- ***Fertile age:*** male and female sex hormones
- ***Pregnancy, delivery, breast feeding*** (serum level monitoring, delivery per vias naturales)
- ***Elderly:*** (interactions, low sodium level, osteoporosis, adherence)

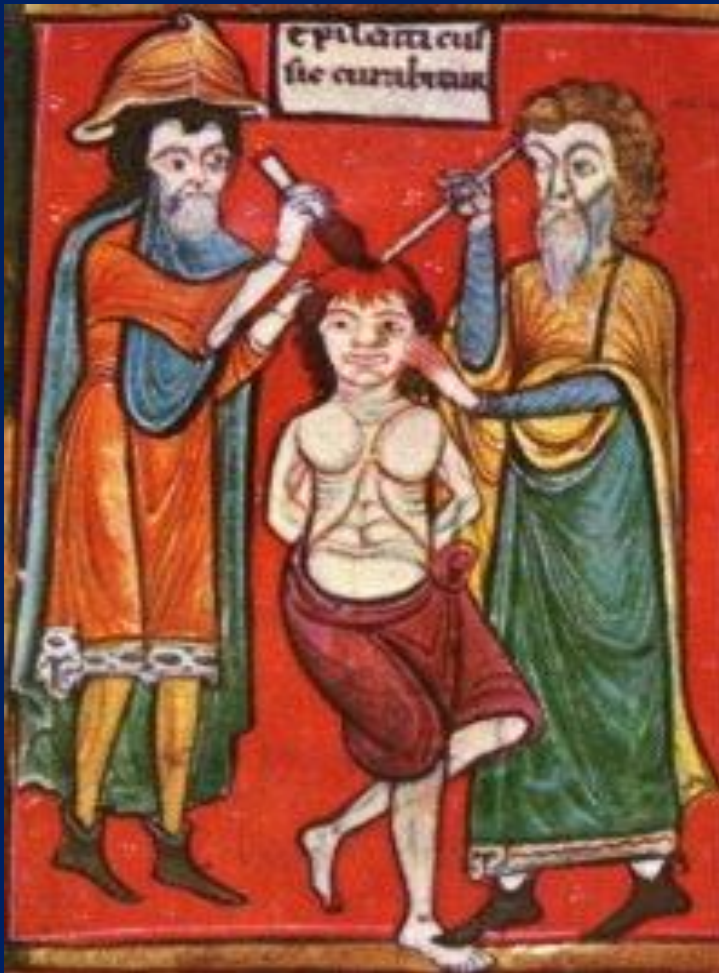
Treatment after the first seizure, rather start if...

- **Malignant epilepsy syndrome.**
- **Epileptogen lesion (e.g. hippocampal sclerosis).**
- **Active interictal epileptic activity with involvement of more loci on EEG.**

BUT treat the patient not the EEG!

- **Long lasting severe seizure.**
- **Dangerous life or work circumstances -patients individual attitude.**
- **Febrile seizure in the past.**

Epilepsy surgery



Epilepsy surgery

If the patient does not respond to the first 2 appropriate AE, surgery has to be considered.

From all patients with epilepsy 15-20 %-may need surgical treatment.

Surgery

- **Lesionectomy** (dysplasia, ganglioma, vascular anomaly, posttraumatic scar, migration disturbance)
- **Local resection** (amygdalo-hippocampectomy in mesial-temporal sclerosis)
- **Lobectomy** (anterior temporal, multilobular resection)

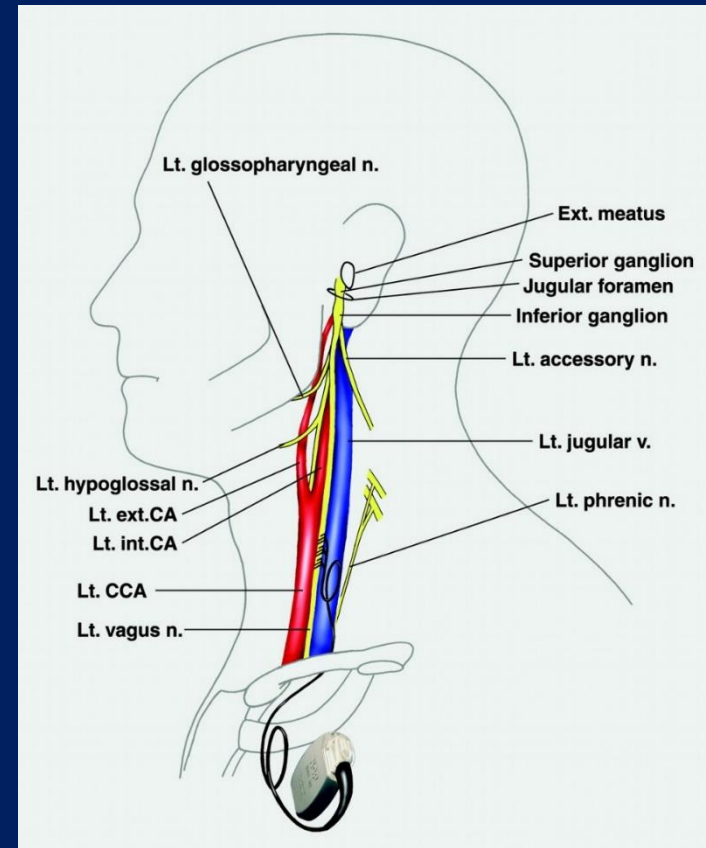
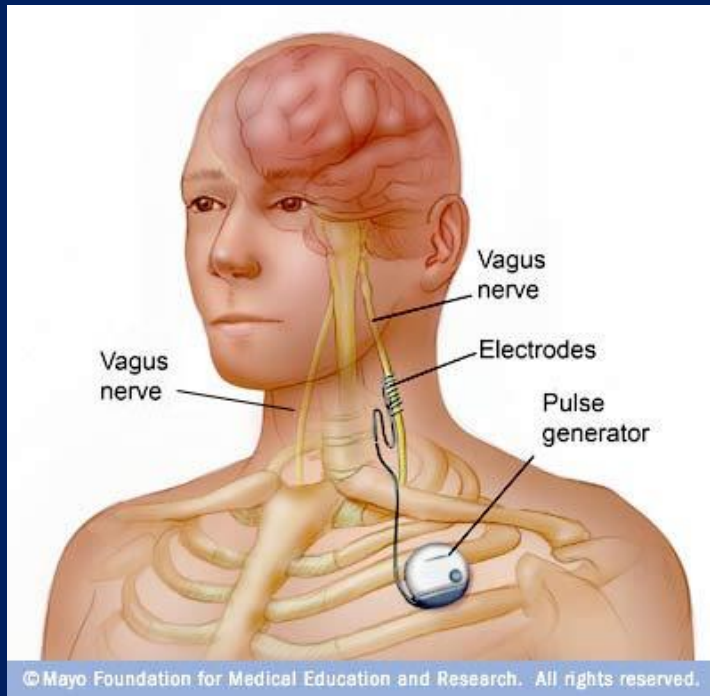
Surgery

- **Hemispherectomy, hemispherotomia**
- **Callosotomy (anterior 2/3 or total)**
- **Multiple subpial transection (cortico-cortical incision)-usually combined with other methods**

Surgery

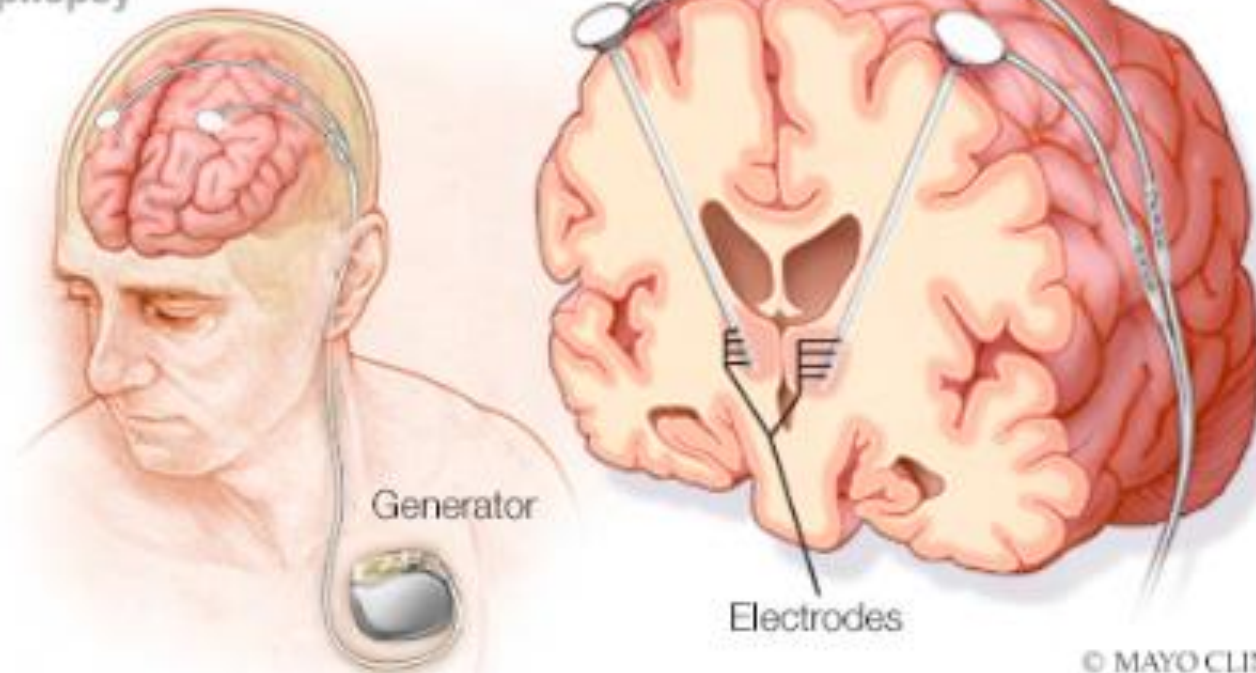
- **Hemispherectomy, hemisphaerotomy**
- **Callosotomy (anterior 2/3 or total)**
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Vagal nerve stimulation



Deep brain stimulation

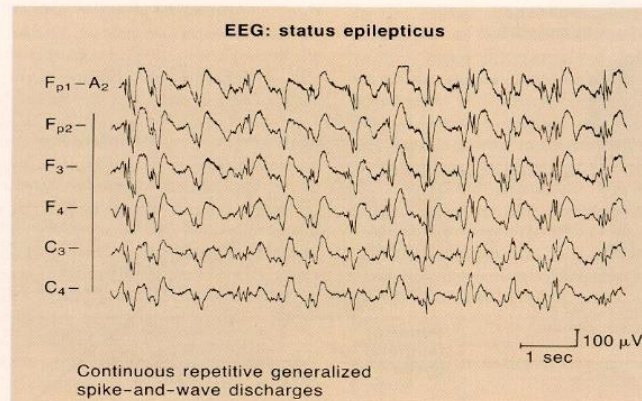
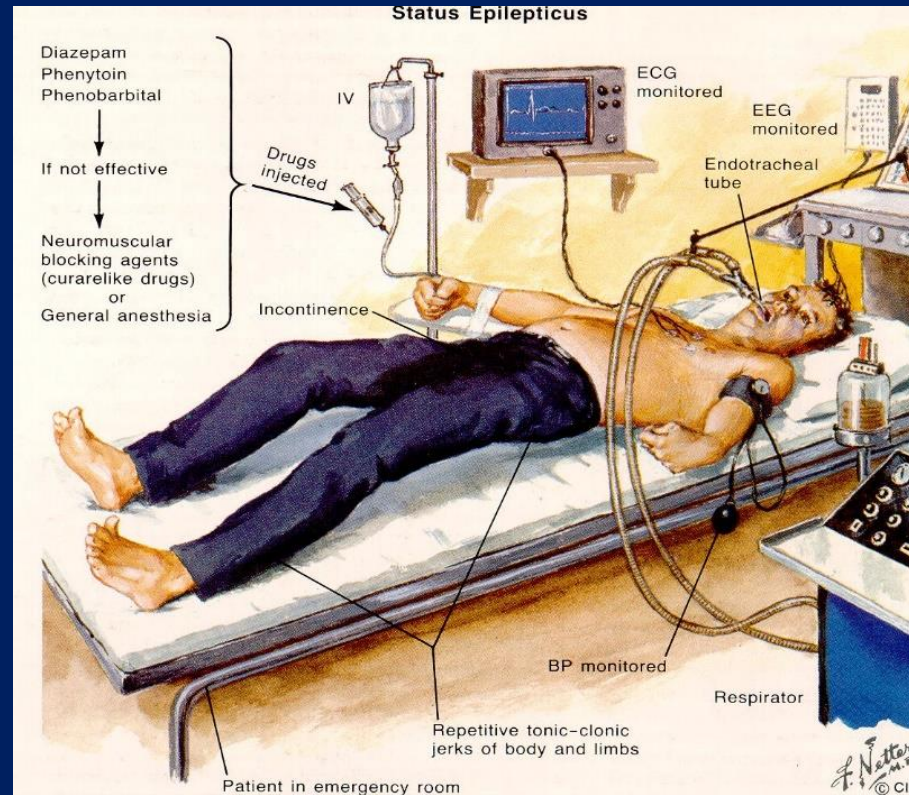
DEEP BRAIN STIMULATION for epilepsy



Status epilepticus



Therapy of status epilepticus



Therapy of status epilepticus

First line thx: benzodiazepin:

diazepam, clonazepam (lorazepam)

Second line thx:

*i.v. phenytoin, valproate, levetiracetam, diphedan,
lacosamide*

Third line thx: propofol, midazolam

Special questions in epileptic outpatient department

- depression
- suicidium
- Sudden death (SUDEP)

Make your **HOME SAFER** **MANAGING EPILEPSY & SEIZURES**

 <p>Cook with a partner</p>	 <p>Use non-breakable dishes</p>	 <p>Take a shower instead of a bath</p>	 <p>Consider using a seizure alert monitor or sharing a room so others can hear if a seizure happens</p>
 <p>Use the microwave for most cooking</p>	 <p>Install a rubber mat or non-skid strips on the tub or shower floor</p>	 <p>Move your bed away from walls, night tables and other sharp or hard objects</p>	 <p>Use caution with hot foods and liquids</p>



© Facebook/Shannon Locke | Disability Assistance@Dogs

Shannon Locke's dog Poppy's sixth sense alerted her owner that she was about to have an epileptic fit. Shannon, 23, had enough time to set up a camera and capture the scene on film, which sees Poppy bringing Shannon out of a seizure by ensuring her airways are clear

+5

Take home message

- **Epilepsy needs professional epileptic care, maybe lifelong.**
- **Diagnostic examinations must be started as soon as possible.**
- **The antiepileptic treatment has to be tailored to the individual need of the patient according to the guidelines.**

Thank you for your attention!