



Evaluation & Management of Seizures

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Overview

- Approximately 8-10% of the population will experience a seizure at some point in their life
- Approximately 1 in 26 people will develop epilepsy
- What is a seizure?
 - ILAE (international league against epilepsy) defines it as “a transient occurrence of signs and/or symptoms due to abnormal excessive or synchronous neuronal activity in the brain”
- What is epilepsy?
 - “A disorder of the brain characterized by an *enduring predisposition to genetic epileptic seizures* and by the neurobiologic, cognitive, psychological, and social consequences of this condition”
 - 2014 “practical definition” includes any of the following: (1) At least 2 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, or (3) diagnosis of an epilepsy syndrome

Approach to diagnosis

Urgent vs non-urgent evaluation

- Urgent: patient presents with first time seizure and has ongoing mental status change, focal abnormalities on examination, signs of meningitis/encephalitis, etc
- Non-urgent: patient presents with first time seizure and returns to baseline mental status afterwards

Urgent evaluation

- Non contrast CTH – fast, identifies blood easily, ER will probably order it asap anyways
- If febrile or other meningeal signs, LP must be performed
- Labs: electrolytes, glucose, tox screen, alcohol level
- If patient female & pregnant don't forget about eclampsia
- Emergent EEG if not back to baseline to rule out non-convulsive status epilepticus

Non-urgent evaluation

- Take a good seizure history when possible: prior to, during, and after seizure
- Ask *patient* to describe event from onset, including any aura they may have experienced
- Patients will often report they are amnestic to event (typically true if epileptic, can be true if nonepileptic), so details about the seizure itself are best provided by *witnesses*. Can call family members or friends if they are not present.
- Ask about:
 - motor findings during seizure (limbs limp or stiff), types of abnormal movement (clonic vs irregular shaking/tremor), skin color changes, whether patient responded to name or touch during event
 - Postictal confusion, sleepiness, agitation/combativeness, focal weakness, or language difficulties
- Physical examination: look for evidence of lateral tongue bite, or Todd's paralysis

Seizure mimics

1. Syncope
2. Psychogenic nonepileptic events
3. Transient ischemic attack
4. Migraine with aura
5. Sleep disorders (REM sleep behavior disorder, periodic leg movements in sleep)

Mimics: Syncope

vasovagal:

- prolonged standing, dehydration, change in posture, warm environment, emotional upset (blood drawn)
- Prodrome of lightheadedness, ringing in ears, pallor, sweating.
- Loss of tone can be seen sometimes with myoclonic jerking or tonic posturing.
- Quick return to baseline

Cardiac:

- sudden LOC without prodrome, can have tonic posturing
- Often triggered by fright, exercise, surprise, and immersion in water
- Family history of cardiac arrhythmia can be present

Mimics: PNEE

- 2 main symptomatologies: (1) unresponsive periods without motor phenomena (2) motor phenomena with bizarre, irregular jerking and thrashing

Suggestive of PNEE:

- Prolonged episodes (>15-30 minutes)
- Minimal post ictal phase
- Frequent and refractory from onset
- Eyes closed during event, crying during event, side to side head/body movements, flapping movements, irregular movements, pelvic thrusting
- Can often stop and start again

*Differential includes frontal lobe epilepsy

Mimics: TIA

- Sudden onset of focal neurological symptoms that reflect loss of function (paresis, speech problems, etc) which resolve within 24 hours
- Seizures typically present with positive symptoms (example: visual would be flashing lights or shapes, somatosensory would be pain or paresthesias, motor would be clonic activity)

Mimics: migraine w/ aura

- Confusion typically arises with the visual aura
- Visual aura in migraine is typically scintillating scotoma
- Visual aura in epilepsy is typically colored shapes

Mimics: Sleep disorders

- REM sleep behavior disorder - seen in PD, violent fighting movements during sleep
- Narcolepsy/cataplexy
- Periodic limb movements of sleep

Provoked or unprovoked?

- Provoked: toxins, drugs, metabolic factors (hyponatremia, etc)
 - Typically, provoked seizures are generalized not focal
 - prophylactic antiseizure medications are not required
- Acute symptomatic seizures: seizures related to an acute brain process such as encephalitis, stroke, or TBI
 - Acute means within 1 week of insult
 - These patients do not necessarily go on to develop epilepsy. However, short term antiseizure medication may be needed

If unprovoked, does this person have epilepsy?

- First, double check that patient has not had a seizure before.
 - Ask about staring spells, isolated body jerks, nocturnal tongue biting or incontinence
 - Consider asking about auras (but in a very open way!)
- Estimates of recurrence rates following the first seizure have varied, but in a systematic review/meta analysis by Berg & Shinnar it was found to be 42%
- The risk increases with more seizures – 73% with 2 seizures, 76% with 3 seizures
- A diagnosis of epilepsy can be made if patient had 1 unprovoked seizure and their risk of having further seizures is high (>60%)

“Risk stratification”

- High risk features:
 - Epileptiform abnormalities on EEG
 - Remote symptomatic cause (brain tumor, malformation, stroke)
 - Abnormal neurological examination such as focal findings or intellectual disability
- Workup: MRI brain epilepsy protocol & EEG

EPILEPSY PROTOCOL – 3D MRI

T1-weighted

Sequence type: gradient echo

Voxel size (mm): 1 x 1 x 1

Best to evaluate: anatomy and morphology
(volume, thickness, sulco-gyral shape, grey-white matter interface integrity)

FLAIR

Sequence type: turbo spin echo

Voxel size (mm): 1 x 1 x 1

Best to evaluate: signal intensity

Caveat - Not sensitive in neonates and children <24 months of age due to incomplete myelination

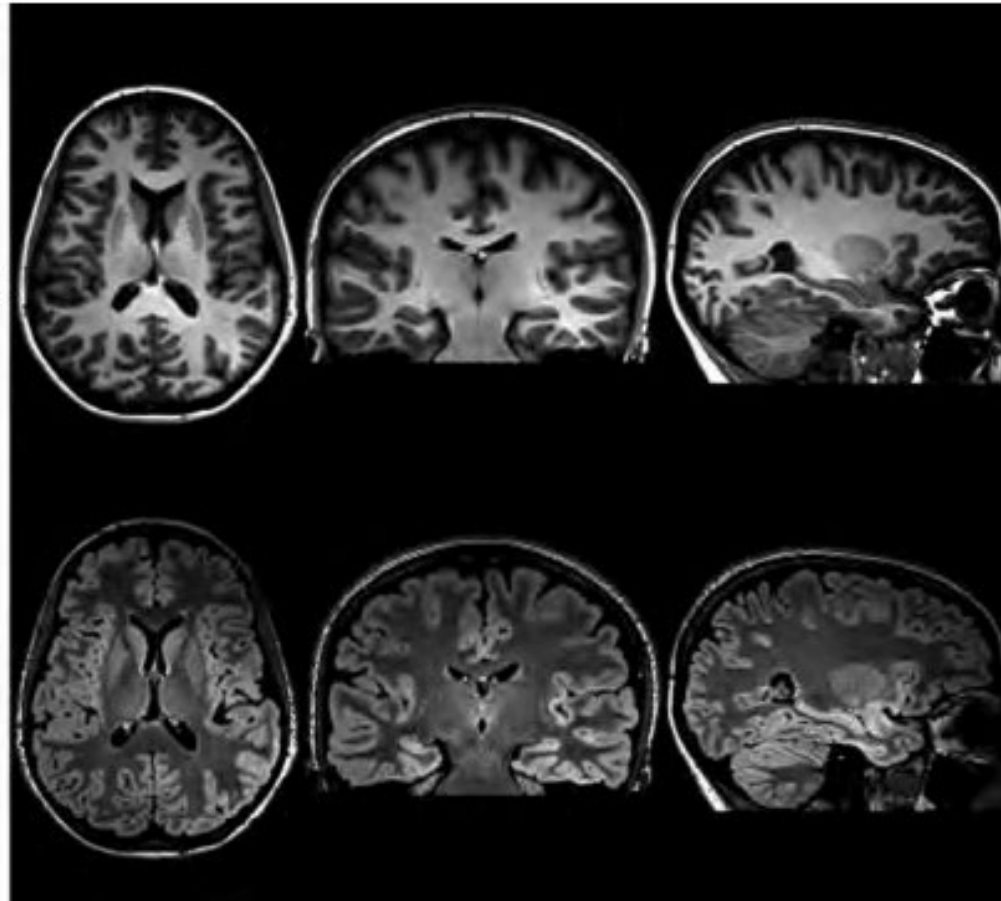


FIGURE 1 HARNESS-MRI (Harmonized Neuroimaging of Epilepsy Structural Sequences) three-dimensional (3D) protocol at 3 T. T1-weighted and fluid-attenuated inversion recovery (FLAIR) images are shown, with representative axial, coronal, and sagittal cuts with millimetric resolution

EPILEPSY PROTOCOL – 2D MRI

Coronal T2-weighted

Acquired perpendicular to hippocampal long axis

Sequence type: turbo spin echo

Voxel size (mm): 0.4 x 0.4 x 2; no inter-slice gap

Best to evaluate: Hippocampal internal structure (distinction of CA subfields, dentate gyrus), amygdala, and parahippocampal cortices

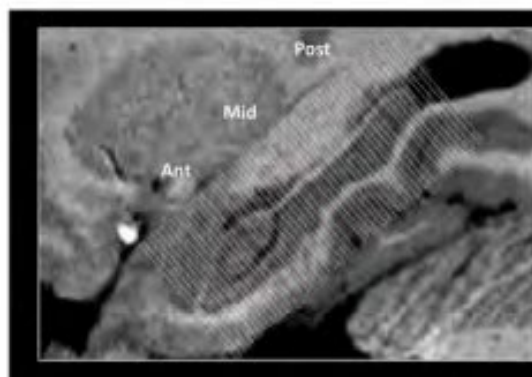
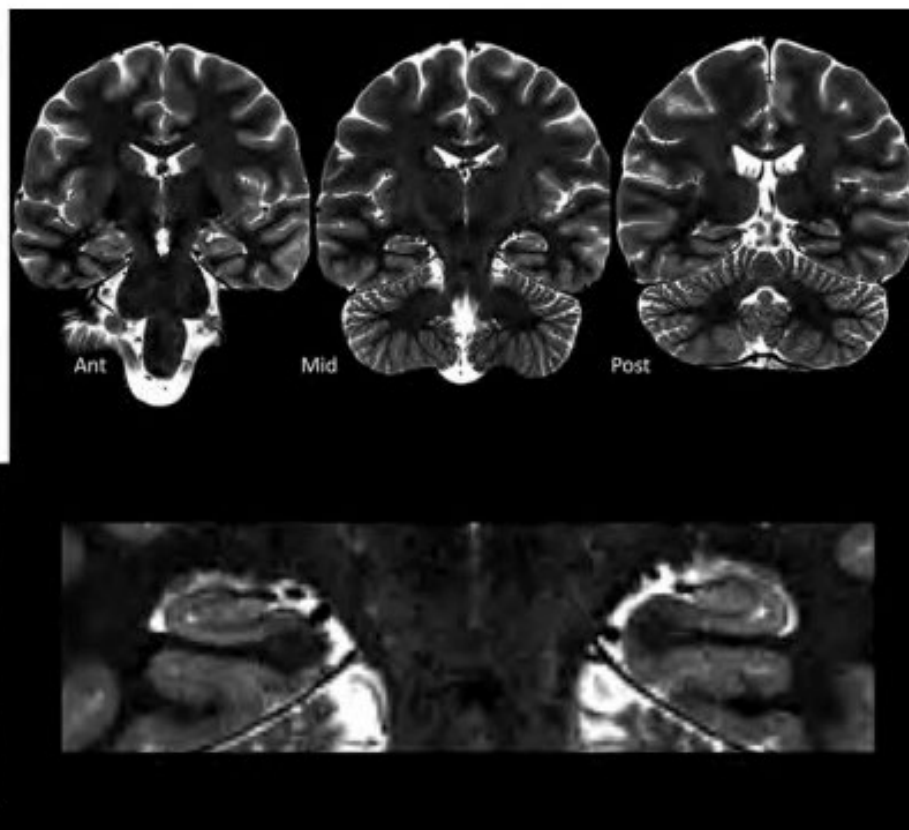


FIGURE 2 HARNESS-MRI (Harmonized Neuroimaging of Epilepsy Structural Sequences) two-dimensional (2D) protocol at 3 T. Coronal T2-weighted images at submillimetric in-plane resolution cover the entire extent of the temporal lobes and hippocampi. Representative cuts at the level of the hippocampal head (Ant), body (Mid), and tail (Post) are shown. Slices are acquired perpendicular to the long axis of the hippocampus as shown in the sagittal view to optimize the evaluation of the hippocampal internal structure. In the magnified panel, one can appreciate the densely myelinated molecular layer of the Cornu Ammonis (CA) and dentate gyrus fused across the hippocampal sulcus appearing as a dark ribbon, which allows discriminating these compartments

EEG

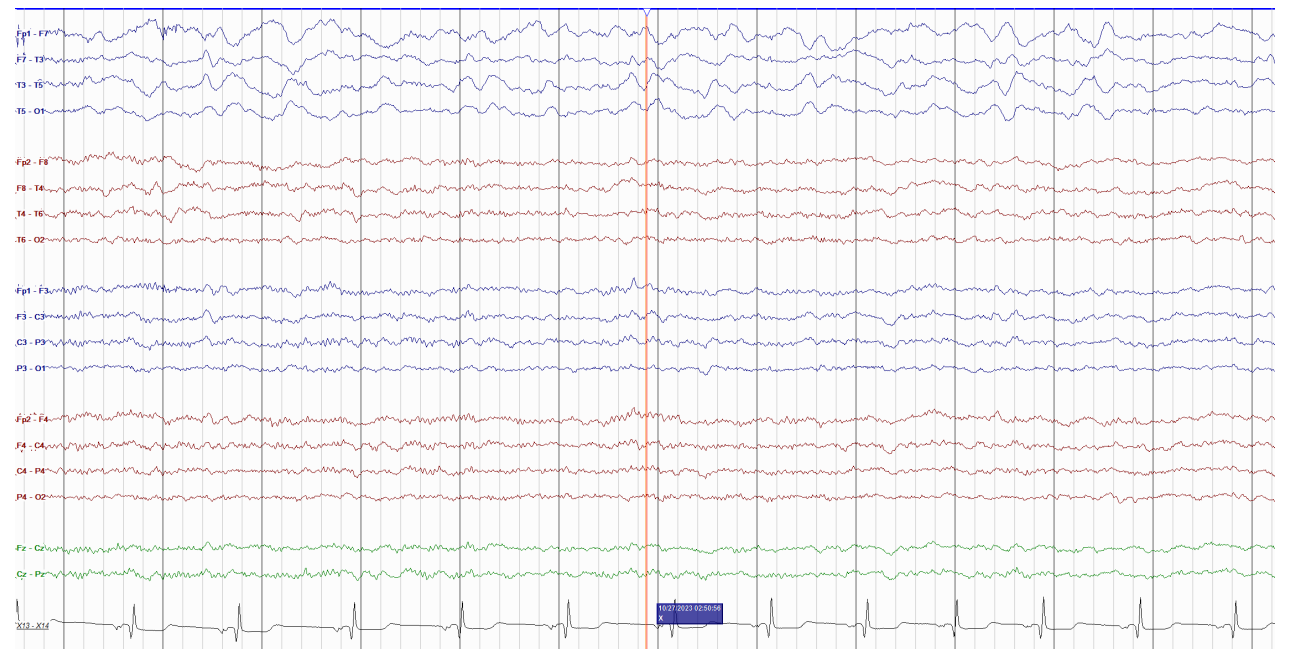
Who needs an EEG?

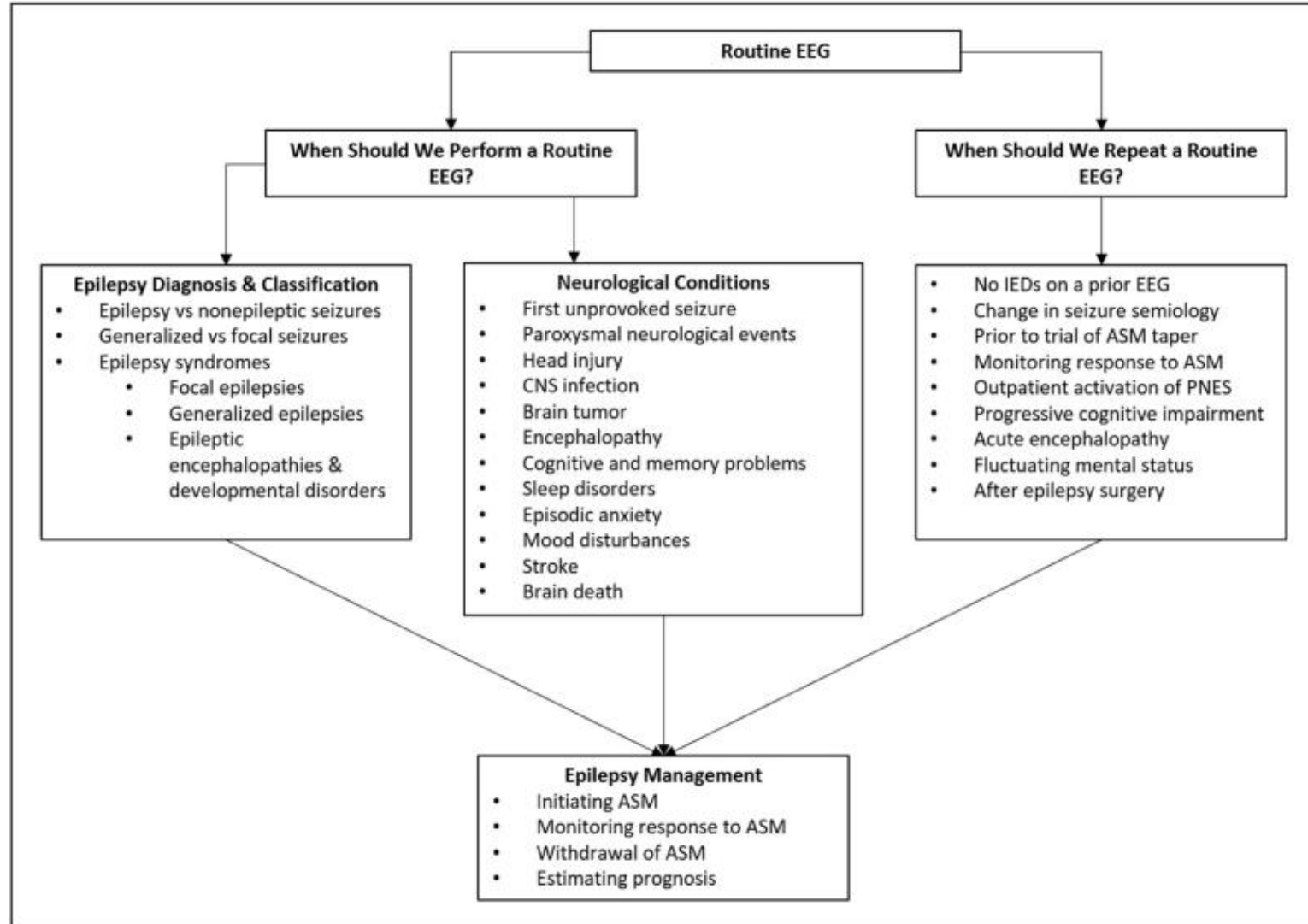
Stat studies are indicated when:

- Acute seizures and not returning to baseline
- Mental status change with no underlying etiology identified, especially if subtle motor activity

Not needed when:

- Clinical seizure which was treated and patient slowly improving
- Patient awaiting discharge (can be done as outpatient)





Yield of routine EEG

- Normal EEGs are often seen even in patients with epilepsy
- Slightly higher yield of recording IEDs when study contains sleep, is sleep deprived, or extended to 60 minutes
- IED (interictal epileptiform discharges) are associated with a 2-3x higher risk for seizure recurrence than a normal EEG

In population-based studies, the yield for epileptiform abnormalities in people with epilepsy was 53% after the first routine EEG and 72% after the third. Patients with a single unprovoked seizure had a yield of 29% after the first routine EEG and 68% after the third. As a result, the sensitivity in detecting IEDs increases when ≥ 3 serial EEGs are performed

Ambulatory EEG

Ambulatory EEG – outpatient prolonged EEG without video

- less expensive than inpatient monitoring (EMU)
- Can do 24, 48, 72 hours
- Provides typical environment and level of stress in which episodes normally occur
- Limitations: no camera, lots of artifact, cannot decrease or stop medications

Epilepsy monitoring unit

Inpatient prolonged EEG with video

- Gold standard for diagnosing epileptic vs non epileptic events
- Characterize generalized vs focal
- Controlled environment with ability to safely reduce/stop antiseizure medications

Treatment

So many AEDs!

Broad spectrum is safest if you don't know whether the patient has focal or generalized epilepsy

Narrow spectrum -> for treatment of focal onset seizures or secondary generalized seizures

- carbamazepine, eslicarbazepine, gabapentin, lacosamide, oxcarbazepine, phenobarbital, phenytoin, pregabalin, cenobamate, stiripentol, tigabine, vigabatrin

- **Broad spectrum:** levetiracetam, brivaracetam, clobazam, felbamate, lamotrigine, topiramate, valproate, zonisamide, perampanel, rufinamide

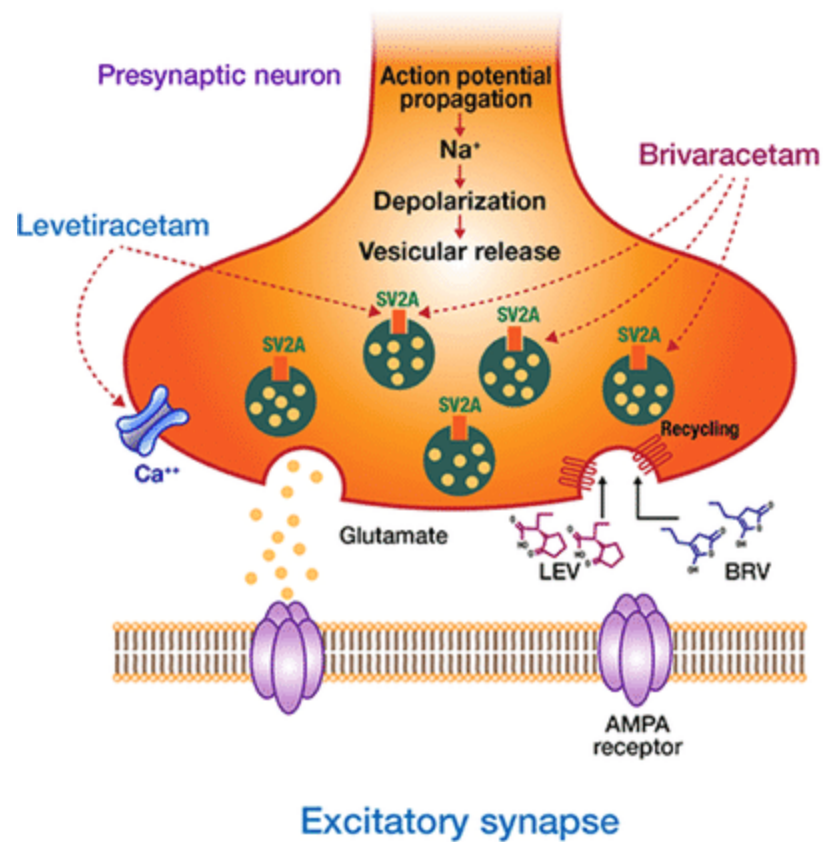
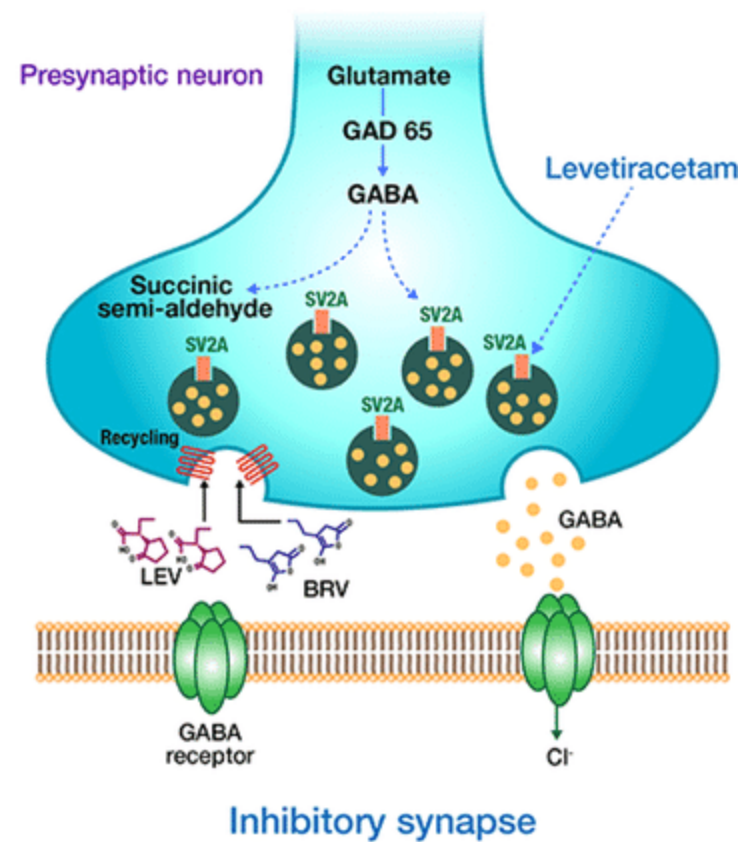
Bottom line – just ask neurology

Keppra

- 1st line due to effective, no need for close monitoring, relatively well tolerated
- MOA: targets Sv2A receptors and prohibits neurotransmitter (GABA) release
- Usual starting dose is 500 mg BID, may do 250 mg BID for elderly patients with low BMI
- “Max dose” is 2000 mg BID
- Cleared through kidneys so dose adjustment is needed in patients with CKD or HD
- Limited to no interactions with other medications
- Adverse reactions: drowsiness, irritability
- Safe in pregnancy

Briviact

- Newer AED that also targets SV2A receptor with higher affinity



Lamotrigine

Broad spectrum (although some evidence may worsen myoclonic seizures)

Mood stabilizer

MOA: Na channel blocker

Adverse reactions: nausea, dizziness, hematologic abnormalities, SJS and hypersensitivity reactions

Safe in pregnancy

Lacosamide

- Focal onset to secondary generalized seizures
- MOA: Na channel blocker
- Dosing 100 mg BID
- Adverse reactions: dizziness, nausea, drowsiness, PR interval prolongation

Depakote

Broad spectrum, also used as mood stabilizer, migraine prevention

MOA: multiple including inhibition of Na channels, inhibition of GABA transaminase, modulation of calcium channels

Adverse effects: weight gain, tremor, hair loss, hepatotoxicity, SIADH/hyponatremia, pancreatitis, SJS, teratogen

[1] Syed Rizvi, Lady Diana Ladino, Lizbeth Hernandez-Ronquillo, José F. Téllez-Zenteno, Epidemiology of early stages of epilepsy: Risk of seizure recurrence after a first seizure, <https://doi.org/10.1016/j.seizure.2017.02.006>.

(<https://www.sciencedirect.com/science/article/pii/S1059131117301188>)

[2] Hasan TF, Tatum WO. When should we obtain a routine EEG while managing people with epilepsy? Epilepsy Behav Rep. 2021 May 3;16:100454. doi: 10.1016/j.ebr.2021.100454. PMID: 34041475; PMCID: PMC8141667.

[3] Baldin E., Hauser W.A., Buchhalter J.R., Hesdorffer D.C., Ottman R. Yield of epileptiform electroencephalogram abnormalities in incident unprovoked seizures: a population-based study. Epilepsia. 2014;55:1389–1398.