Epilepsy Specialist Workup

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Yakima Valley Medical Conference

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OVERLAKE | MEDICAL CENTER & CLINICS

- I have no conflicts of interest to disclose. When appropriate, names of devices will be provided to help with clarity.

Objectives

1. Compare epilepsy surgery and device options
2. Diagnosis and treatment of psychogenic nonepileptic seizures (PNES) and functional neurologic disorders (FND)
3. Identify optimal treatment of seizure emergencies, including status epilepticus


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Compare epilepsy surgery and device options

What is Drug-Resistant Epilepsy? (DRE)

- International League Against Epilepsy - 2010
  - Failed to become and stay seizure free with adequate trials of two antiseizure medications (ASMs)
  - Tolerated at adequate doses and adequate adherence
  - Don’t need to be concurrent
- Probability of seizure-freedom after two ASM failures decreases exponentially
  - Less than 5% chance of seizure freedom after four failures (Guery & Rheims, 2021)
  - Patients with DRE have high probability of temporary 12-month seizure freedom
  - Do not be comforted by infrequent seizures when there is no clear trigger of breakthrough seizure
- Psychogenic non-epileptic seizures possibly lead to 20 to 25% of pseudo-resistance
  - Long-term video-EEG when the description of the ictal semiology is not clear enough to exclude the occurrence of psychogenic non-epileptic seizures
  - This is particularly relevant in patients who suffer from both epileptic and psychogenic non-epileptic seizures.
- prevalence of DRE is 30% (Guery & Rheims, 2021)
- Sudden unexpected death in epilepsy (SUDEP) incidence is 1-10 per year per 1000 epilepsy surgery candidates (Téllez-Zenteno, 2005)
  - Risk factors include frequent bilateral tonic clonic seizures, ASM polytherapy, early onset DRE

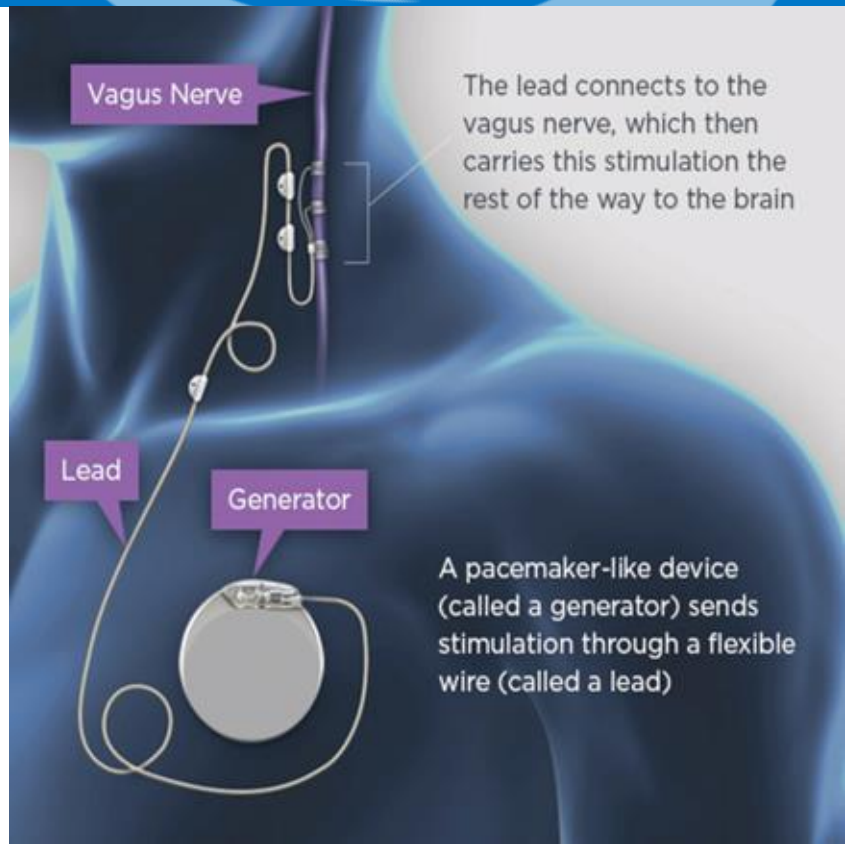
If DRE – refer to a specialist!

- UW, Swedish in downtown
- Overlake/Evergreen on Eastside – looking to grow
- Workup for most patients – EEG, MRI
- Other options:
  - 2-day ambulatory EEG – on medications
  - 4-day epilepsy monitoring unit (EMU) – will stop medications – sleep deprivation
  - 2+ days of EEG off of medications without epileptiform discharges is reassuring, suggests against epilepsy in appropriate context
  - Other diagnostic tests
- Initial question: focal epilepsy or generalized epilepsy?
  - Generalized epilepsy – GTC without aura, 10-20 second absence seizures without post-ictal state
  - Focal epilepsy – GTC +/- aura, focal impaired consciousness (30 seconds to 3 minutes), focal preserved consciousness

https://seizelifesmoments.com/48-hour-eeg-tests/

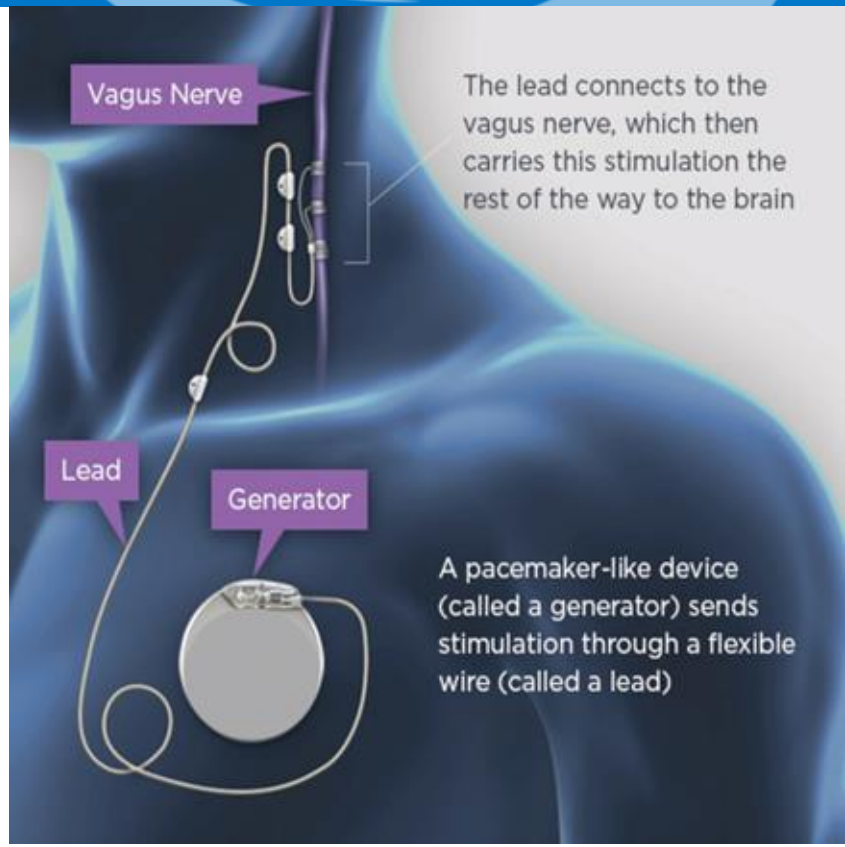
VNS – good option for generalized epilepsy

- Vagus nerve stimulator – VNS
  - EEG with generalized discharges
  - video confirming GTC rather than other behaviors
- Effects thought to be produced by modulating nodes of the Vagus Afferent Network
  - Brainstem, subcortical, cortical structures
  - Reduce ictal spread and synchronization (Afra et al., 2021)
  - FDA approved for DRE 1997
  - FDA approved for treatment-resistant depression 2005
  - Expand to official pediatric approval (age 4+) 2017
- Patient/family has a magnet, can swipe to activate stimulation during a seizure
  - This is not the main way the device works, stimulates every 1-3 minutes



VNS

- Not a curative therapy, reduction in seizure frequency/severity
- All devices have improved efficacy over time
- Englot et al 2016 meta-analysis
    - 5554 patients in the VNS Patient Outcome Registry - Two to 4 years after implantation, approximately **8%** of patients achieved complete **seizure freedom**, while approximately **60%** of patients had responded to treatment, showing **≥50% decrease in seizure frequency**.
- Unpublished data: CORE-VNS - livanova.com - 51% of patients had >80% reduction in focal seizure frequency (super-responders)
- Reduction in hospital admissions and ER visits
- 50% report mood improvements, improved seizure worry, 40-60% report cognitive improvements - memory, verbal skills, alertness (livanova.com)
- 125,000 patients implanted as of 2021 (mostly for epilepsy)



VNS Logistics

- One day surgery - neck and chest incisions
- Stimulator turned on at low settings, increased every 2 weeks – takes 2-3 months to get to target milliamps (current) settings
- Most common AE is voice change or tingling in neck
  - if this is the case, decrease current, goes away
  - Many patients notice this, lasts for 30 seconds, happens every 1-3 minutes, they get used to it, is not bothersome
  - If bad AEs, can completely turn off device, more difficult to remove the lead wrapped around the vagus nerve, but generally this does not cause problems
- Good for all seizure types – generalized or focal, but more options for focal...

Focal epilepsy

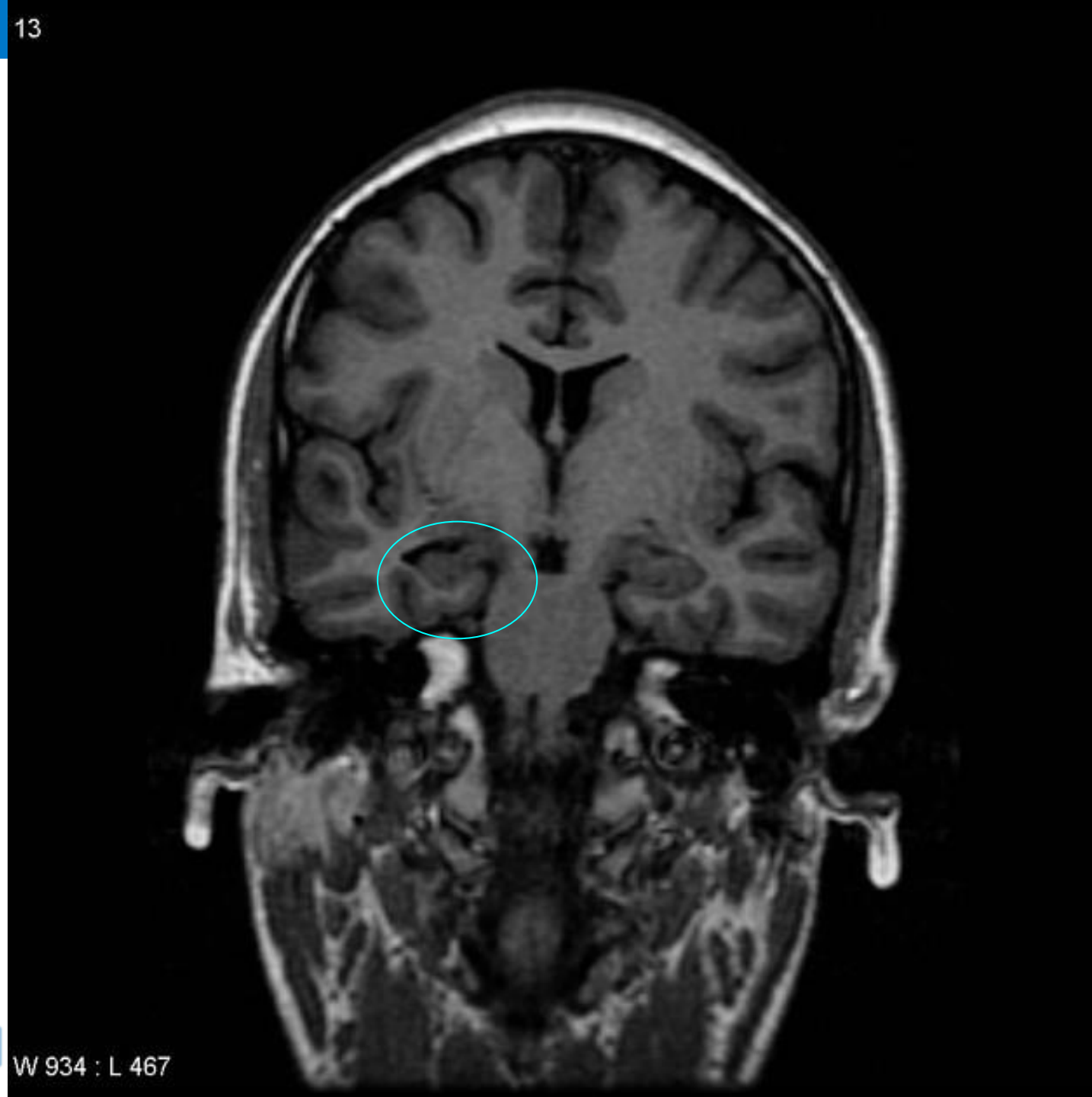
- Most common lobe for focal epilepsy – temporal
- Aware/perserved consciousness - Rising epigastric sensation, nausea, and olfactory and/or gustatory hallucination
- Psychic sensations can occur, such as depersonalization (out-of-body feeling), **déjà vu** (a feeling of familiarity)
- Often, the patients find the aura **hard to describe.**
- **Impaired awareness/consciousness -** Behavioral arrest, blank staring, **oroalimentary automatisms** such as lip-smacking, chewing, or swallowing
- **Ipsilateral** gestural automatisms such as repetitive hand movements, picking and/or fidgeting behavior, disrobing
  - The better functioning side of the brain is trying to still do things
- 2nd most common – frontal
  - Weird seizures – often nocturnal, patient suddenly starts yelling or having bicycling movements of legs, back arching – often mistaken for psychogenic nonepileptic spells (PNES)

Fig 1. A cat with a typical temporal lobe seizure: orofacial automatism with head turning upwards, salivation, facial twitching, mastication, and licking.

Figure 1. Video EEG screenshots of sleep-related hypermotor epilepsy patient. **(A)** Bilateral hand raising, leg flexion, and moaning. **(B)** Yelling and abrupt up. **(C)** Forceful lay back and bilateral pedal kicking. (Tchopev et al, 2018)

MRI

- If you see a lesion (not just white matter disease) and patient has failed 2 medications
  - Refer to epilepsy center!
- Hippocampus = mesial temporal lobe
- Mesial temporal sclerosis on R in this image
- reduced volume
- increased T2 signal – hyperintense/bright
- abnormal morphology: loss of internal architecture (interdigitations of hippocampus)
- Other findings
  - dilation of temporal horn of lateral ventricle
- Mesial temporal sclerosis is often not seen on MRI, but found on pathology
- Present in up to 75% of temporal lobe epilepsy resections
- Trimodal pattern of epilepsy manifestation - 5.5 years, 15.3 years, 26.7 years
  - Lots of kids, but also 20-somethings!

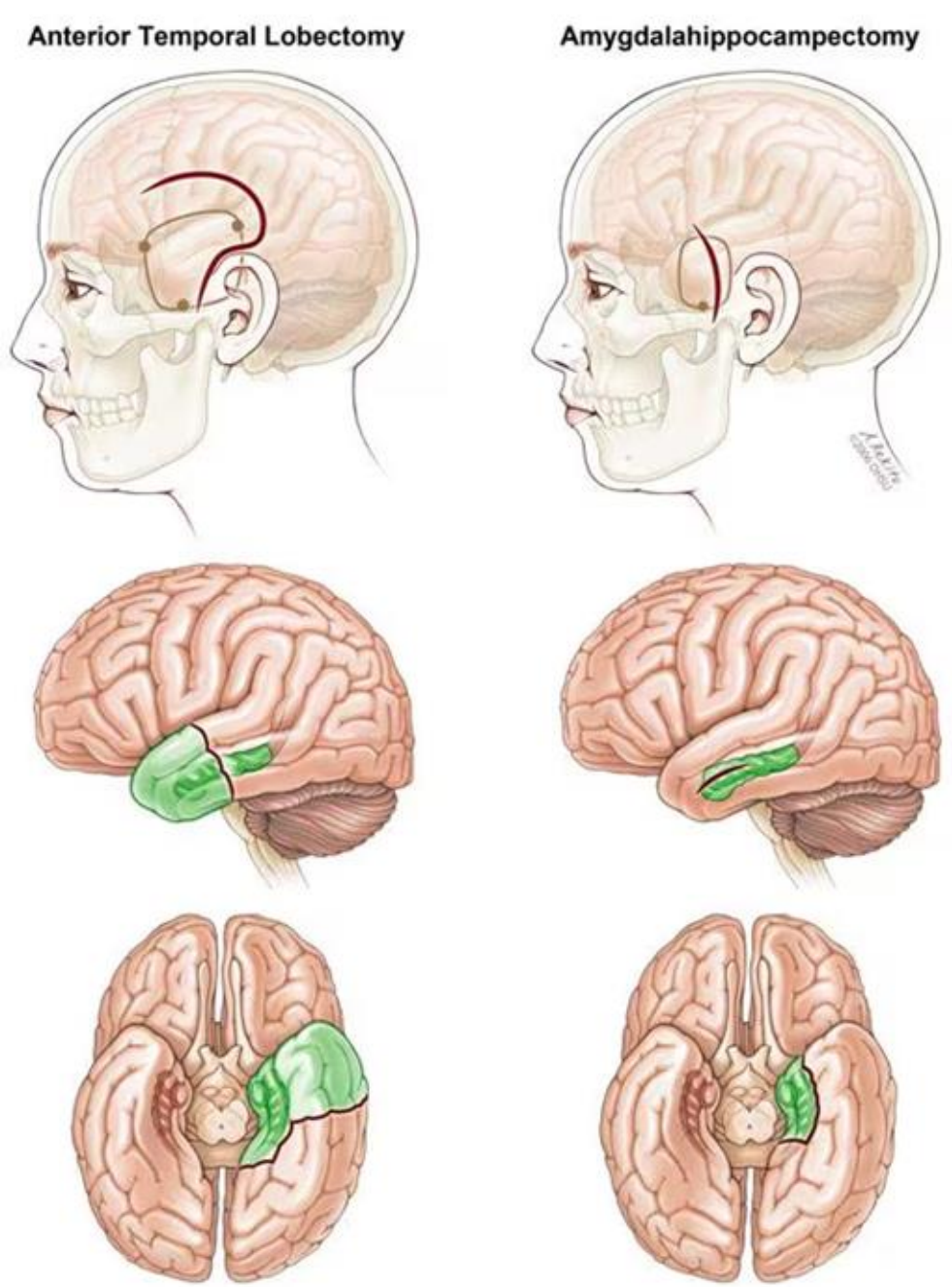


Temporal Resection

- w/ HS - ⅓ can achieve years or even decades of seizure freedom, but majority evolve into drug resistant
- Ablative/resective treatment - up to 60-80% seizure free with concordant data (vs. 30-60% when patient has two lesions or epileptiform discharges on both sides)
  - Usually keep patient on medication even if seizure free initially, after a year start decreasing medications – targeting medications with side effects or at high doses
  - Anterior temporal lobectomy (ATL) - been used for decades
  - Selective amygdalohippocampectomy (SAH)
  - LITT - laser interstitial thermal therapy - 1-2 year seizure freedom 55-60% - range 40-78%

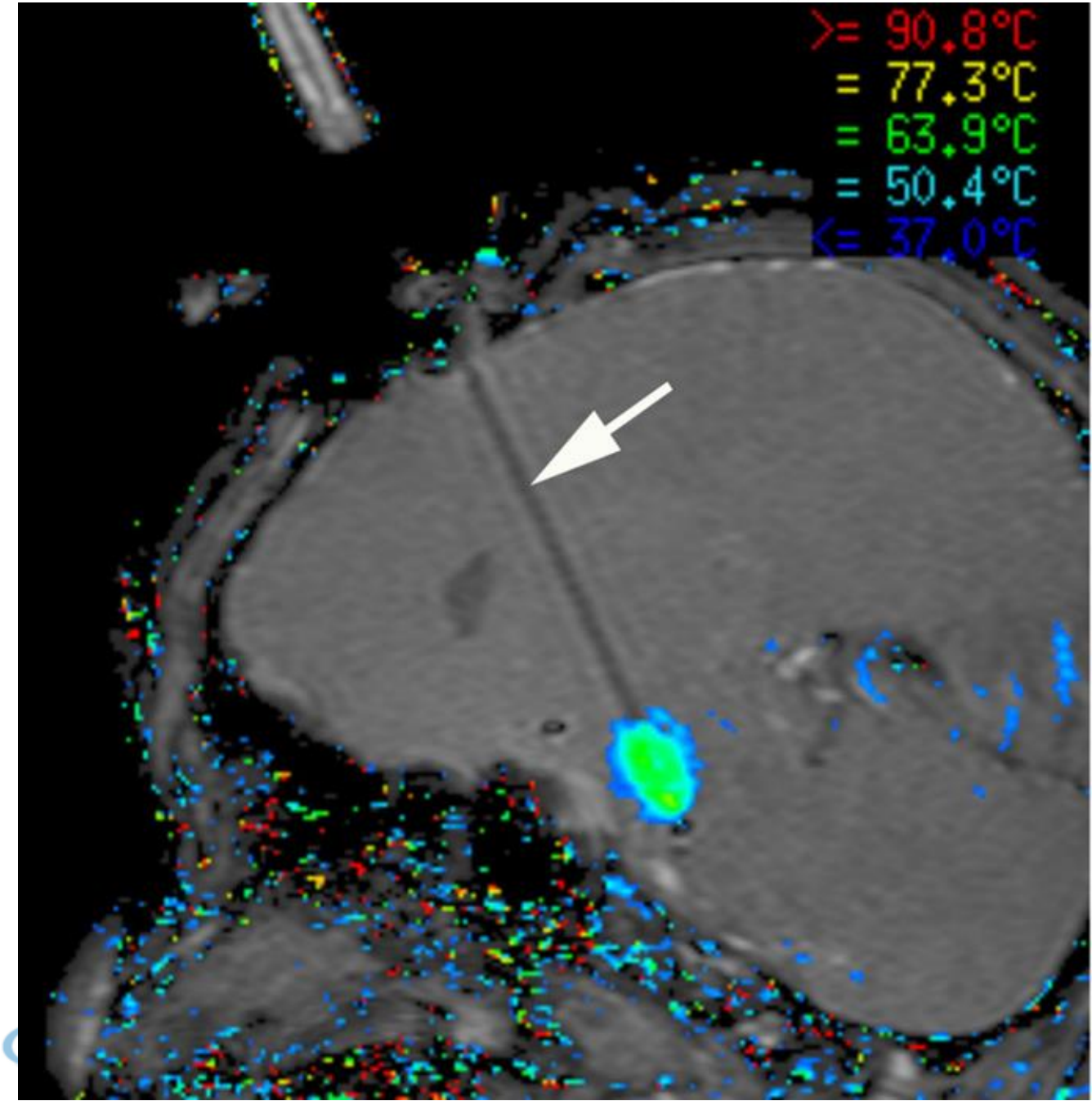
Resection

- **Naming deficits**
- **Visual field deficit**
- ATL - Meyer loop - up to 50% superior/contralateral quadrantanopia - should not affect driving or ADLs, most learn to ignore the deficit over time
- Meta-analysis comparing SAH to ATL VFD - (Xu et al, 2020)
  - Twenty-six articles which included 2930 cases (1390 SAH and 1540 ATL)
  - 6 studies included in meta-analysis for VFD - relative risk 0.87 SAH compared to ATL
- **Cranial nerve palsies**
- Transient postoperative **aphasia** improving within 1-2 days
- Running down phenomenon - up to 33% of patients have rare postoperative seizures that resolve after ~6 months
- Risks - low - infection, hemorrhage, DVT



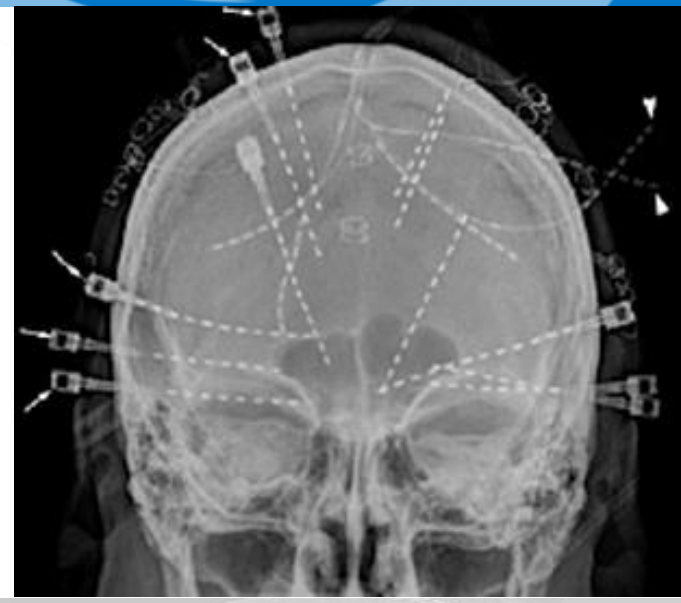
Ablation / LITT

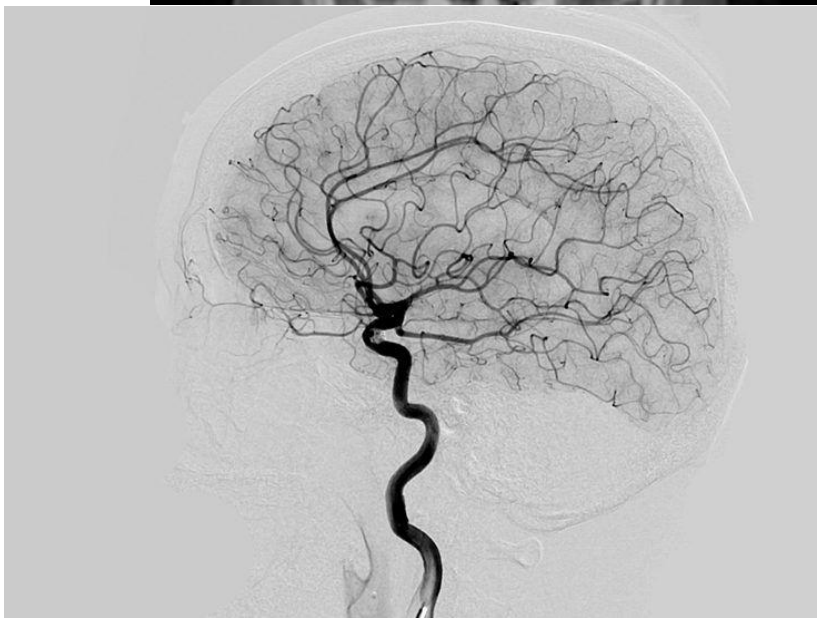
- LITT – intubated/sedated, catheter introduced near MRI scanner
- ability to monitor ablation volumes in near real time w/ MRI thermography
    - → (brain tumor case, not epilepsy) →
- 2-3 cm diameters - can plan multiple trajectories
- Became popular in 2010s
- Images of heat changes refresh every 3-8 seconds
- 43°C for 10 minutes - cell death, protein denaturation
- 60°C - instantaneous
- Do not routinely shave hair
- Observe overnight, discharge home next day



Lesional focal epilepsy

- Often will do intracranial EEG
- 15-25 wires placed in OR under anesthesia, targeting few in lesion, often also coverage in temporal lobe/hippocampus, surrounding areas
- Patient in hospital for 1-2 weeks, come off ASMs to make seizures more likely, pinpoint exactly where seizures are coming from, if limited to just lesion or also involving surrounding tissue
  - address rather than just zip code
- Will often do:
  - neuropsychological testing to assess for verbal (dominant) vs visuospatial (nondominant) dysfunction
  - Wada – intracarotid anesthetic procedure – assess if the contralateral hemisphere can support memory with the other hemisphere temporarily turned off – also assesses language
  - fMRI – only good for assessing language lateralization, not memory



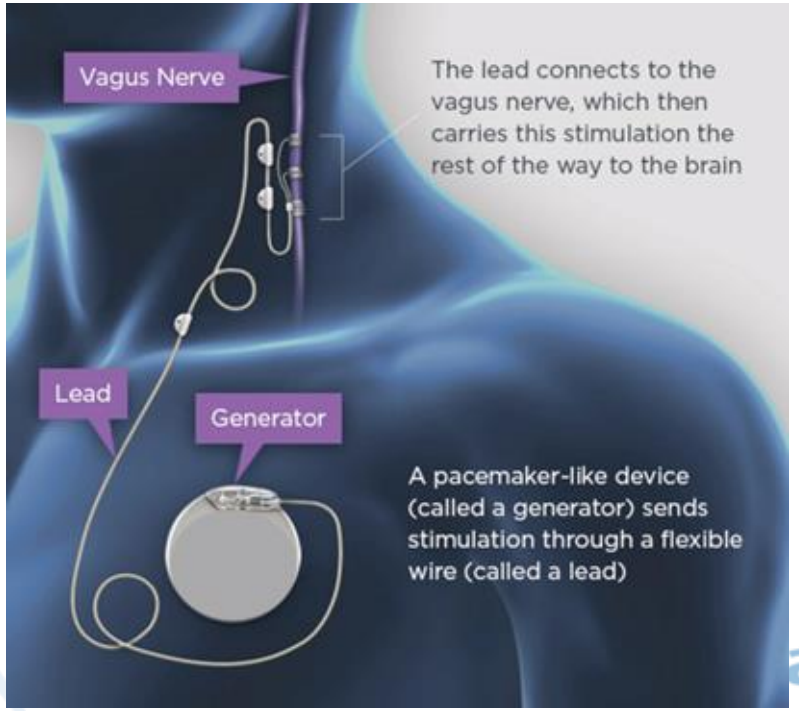


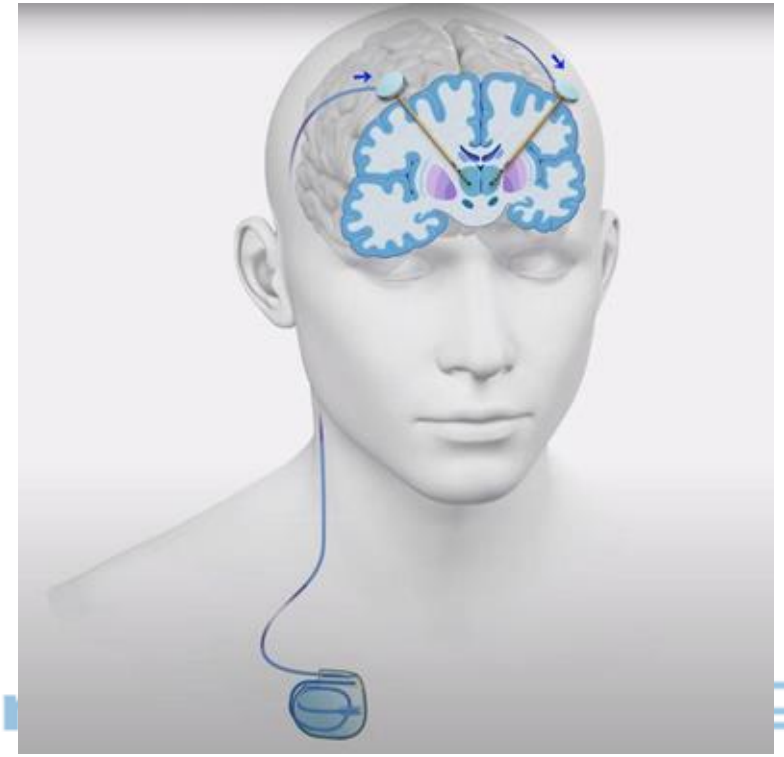
If resective surgery is not an option

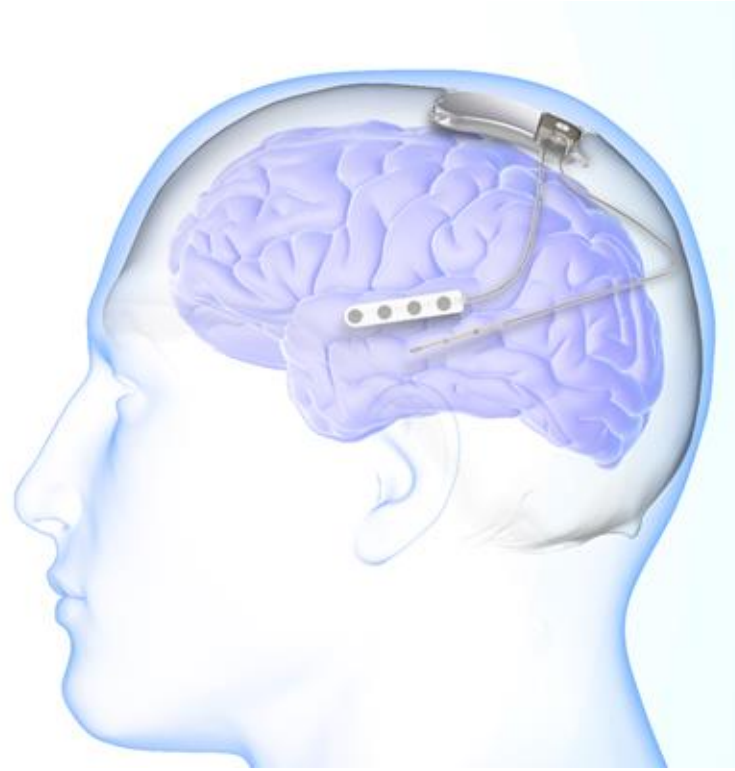
- Large lesion, not sufficiently able to localize on intracranial EEG
- Two lesions far apart, concern for 2 seizure foci
- Generalized epilepsy not completely ruled out
  - Can go straight to VNS
- Other options – deep brain stimulation (DBS) and responsive neurostimulation (RNS)
- Neuromodulation - RNS, DBS, VNS - 10% chance seizure freedom, 60-70% chance of 50% reduction in seizure frequency

Devices for Epilepsy

VNS	DBS – targeting bilateral thalamus – relay centers	RNS – two leads, anywhere in brain, for 1-2 seizure foci
LivaNova (VNS Therapy brand)	Medtronic	Neuropace
Also treatment-resistant depression	Also essential tremor, Parkinson's (Boston Scientific, Abbott)	-none-

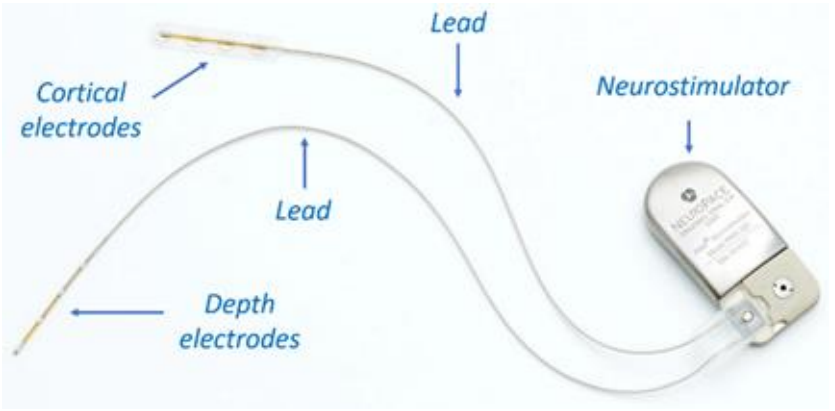


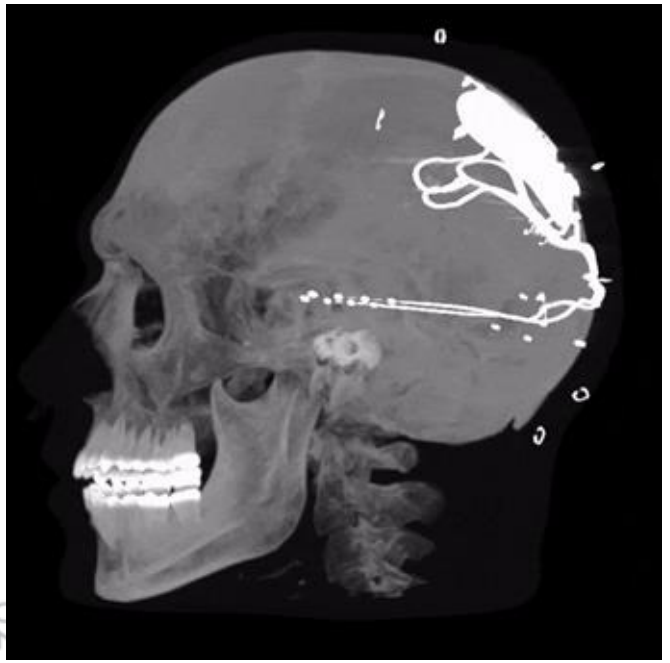




What do non-neurologists need to know for RNS?

- Initial goal was to detect seizures and stop them, this is not the main way it works – detects epileptiform discharges and stimulates in response to these
- Long-term - gene expression changes, synaptic plasticity, cortical reorganization, neurogenesis (Wong et al., 2019)
- One phase surgery - template of neurostimulator used to cut a craniotomy the exact shape of the stimulator
    - Stimulator curved to be flush with the skull
- Record for 2-4 weeks, then initial programming
- Magnet can be swiped to mark the record and save electrocorticography (ECoG)
    - Magnet does not deliver higher current or help seizure resolve more quickly (unlike VNS)





Differences between devices

- All devices require visits, usually every 3 months initially, to adjust stimulation parameters.
- **Battery life** - VNS median 4-8 years
  DBS Activa 3-5 years, rechargeable - 9 years
  RNS post-2018 - 8.4 years under “medium” stim settings
- **MRI** - VNS is easily turned off – ask your neurologist if they have a programmer, or call rep
  DBS patient turns off
  RNS - pre-2018 - no MRI. 320 model - needs to be set to MRI mode, only 1.5 T (MRI conditional whole body)

(Wong et al., 2019, neuropace.com)

Psychogenic nonepileptic seizures/spells (PNES)

- A type of functional neurologic disorder (FND)
  - Other FNDs – functional movement disorder, gait disorder
  - There isn't a structural problem like a tumor that is causing symptoms, but rather a problem with the "software" or how the brain functions, more psychologically-based
- Nonepileptic – not associated with abnormal electrical activity in the brain – not a seizure in the typical sense meaning associated with abnormal electrical activity
- Patient usually not purposely doing this behavior, may not have complete memory of episodes, but often than can develop better awareness before/during episodes
- PNES can be mistaken for epileptic seizures and vice versa, sometimes can be clear with a video, or with data all fitting with PNES
- Gold-standard is video EEG of an episode – EMU or 2-day ambulatory EEG
- Presentation of the diagnosis is crucial to treatment – If there are tests upcoming, consider waiting to present diagnosis until after test is done, schedule a separate visit to present diagnosis
- Often having family present is helpful

PNES

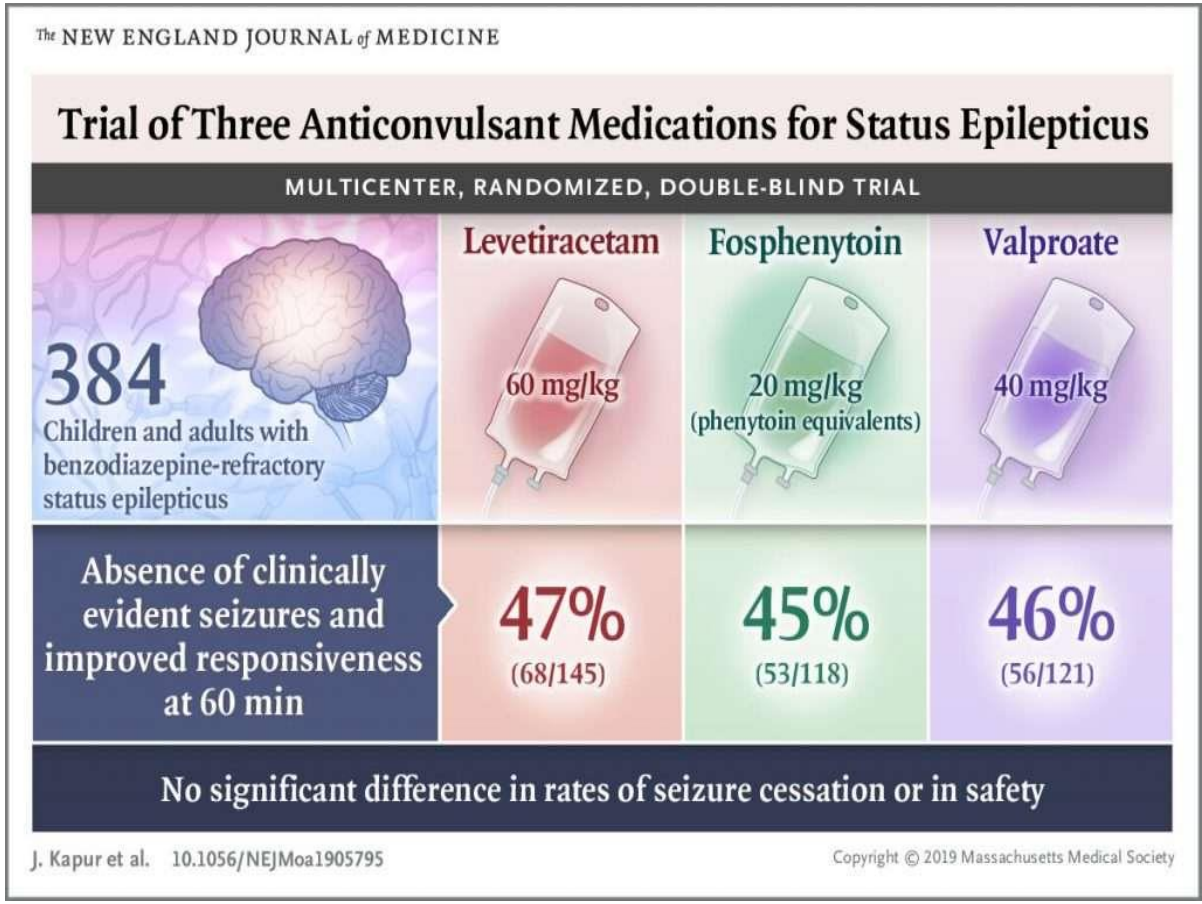
- Mainstay of treatment is psychotherapy
- If patient is already seeing a therapist, tell them they need to talk with their therapist specifically about these episodes, techniques when patient feels an episode coming on in order to keep it from progressing or decrease duration/severity
- Also keeping track of triggers, stressors, noticing on days/weeks when episodes less frequent/prolonged/severe, what are things I was doing differently or things that were going well
- If comorbid depression, anxiety, PTSD, etc. treat these, medications can be used
- No medication just for PNES by itself
- ASMs are not effective for PNES

PNES

- If not a solid diagnosis, but suspicious, but no need for new/repeat neurology referral and no further workup needed, consider introducing the possibility of this diagnosis
- "You've already had an MRI which rules out a tumor as a cause for this, you haven't had any episodes recently, it could have been that the stress you identified was a major factor to this episode. Sometimes people can have episodes that look like seizures but are more related to stress as the primary cause. That could have been what you experienced, sometimes patients have very frequent episodes and we'll do more workup, other times patients have just a few and don't have further episodes, particularly if the stress they were under has decreased"
- Some patients are looking for reassurance that they don't have a neurologic problems, whereas other patients might take this as dismissive

Status epilepticus treatment

- Lorazepam 2-4mg IV, can repeat once
- Midazolam 10mg IM, can repeat once
- Non-benzodiazepine ASMs – brivaracetam, lacosamide, more often used second-line
- Convulsive status epilepticus – quickly escalate to intubation and sedation
- Propofol and midazolam – if still clinical seizures, can keep increasing dose, try to get on EEG



Status epilepticus

- Some use of ketamine as an alternative to propofol/midazolam
- Focal status epilepticus requires more nuanced treatment, may be able to avoid intubation
- Any lack of return to baseline, conversational -> continuous EEG – subclinical seizures – guide further medication changes – escalate anesthetic medications to target burst-suppression pattern – very high doses
- Some rapid response EEGs becoming available – no need for EEG tech coverage, can be placed by nurses
- Can be useful to rule out nonconvulsive status epilepticus in patients who are encephalopathic without a high suspicion for ongoing seizures

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