Advances in the Surgical Management of Epilepsy

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Outline

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- Definitions
- Surgical evaluation pathway
- Surgical options
- Future directions

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Case

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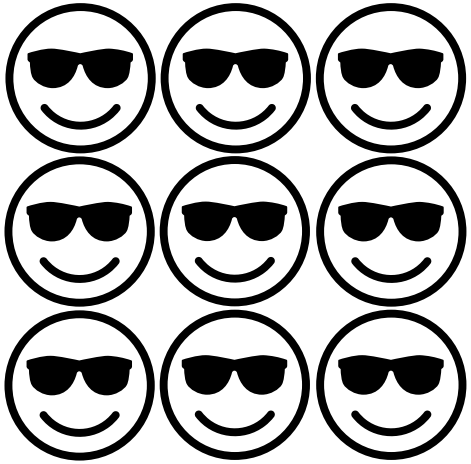
- 35yo RHM with a history of febrile seizures presents for further evaluation. Despite being on 3 anti-epileptic drugs, he continues to have focal seizures several times a week and convulsions every 1-2 months. He has suffered several concussions and has had repeated dislocations of his shoulder as a result. He is married with 2 young children. Over the last 3 years, he has lost his job, is unable to drive, and is afraid to care for his children alone. He endorses significant anxiety and depression.

Drug-resistant epilepsy



30-40% are drug-resistant

Only 5-10% will achieve complete seizure control with ongoing AED adjustments

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The New England Journal of Medicine

VOLUME 345 AUGUST 2, 2001 NUMBER 5

A RANDOMIZED, CONTROLLED TRIAL OF SURGERY FOR TEMPORAL-LOBE EPILEPSY

SAMUEL WIEBE, M.D., WARREN T. BLUME, M.D., JOHN P. GIRVIN, M.D., PH.D., AND MICHAEL ELIASZIW, PH.D., FOR THE EFFECTIVENESS AND EFFICIENCY OF SURGERY FOR TEMPORAL LOBE EPILEPSY STUDY GROUP*

Original Contribution

JAMA

March 7, 2012

Early Surgical Therapy for Drug-Resistant Temporal Lobe Epilepsy

A Randomized Trial

Jerome Engel, MD, PhD; Michael P. McDermott, PhD; Samuel Wiebe, MD; et al

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Surgical evaluation pathway

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- Initial evaluation:
  - MRI brain: evaluate for focal lesions
  - EMU evaluation: localization and characterization of seizures
- If we cannot definitively pinpoint the epileptogenic focus:
  - Advanced imaging modalities
  - Intracranial evaluation

Advanced imaging modalities

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- FDG-PET
- Ictal SPECT (single photon emission computed tomography)
- MEG (magnetoencephalography)
- 7T MRI
- fMRI

FDG-PET

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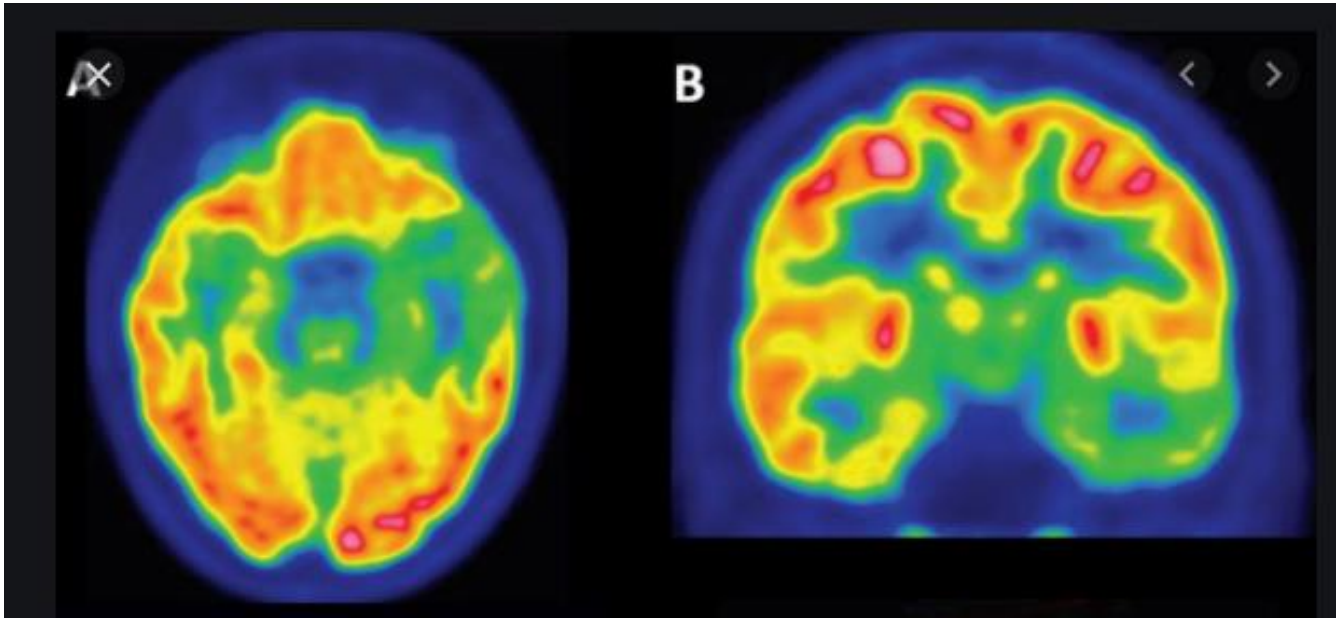
- Evaluate for areas of hypometabolism- best studied in temporal lobe epilepsy



Rugg-Gunn et al. Epilepsy surgery. Practical Neurology 2020;20:4-14.

Ictal SPECT

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- Single photon emission computerized tomography
  - inject radioactive substance into IV at onset of seizure
  - Area involved in seizure requires more blood flow, thus radioactive substance can be detected in this region
  - Compare interictal (baseline) and ictal scans

Ictal SPECT

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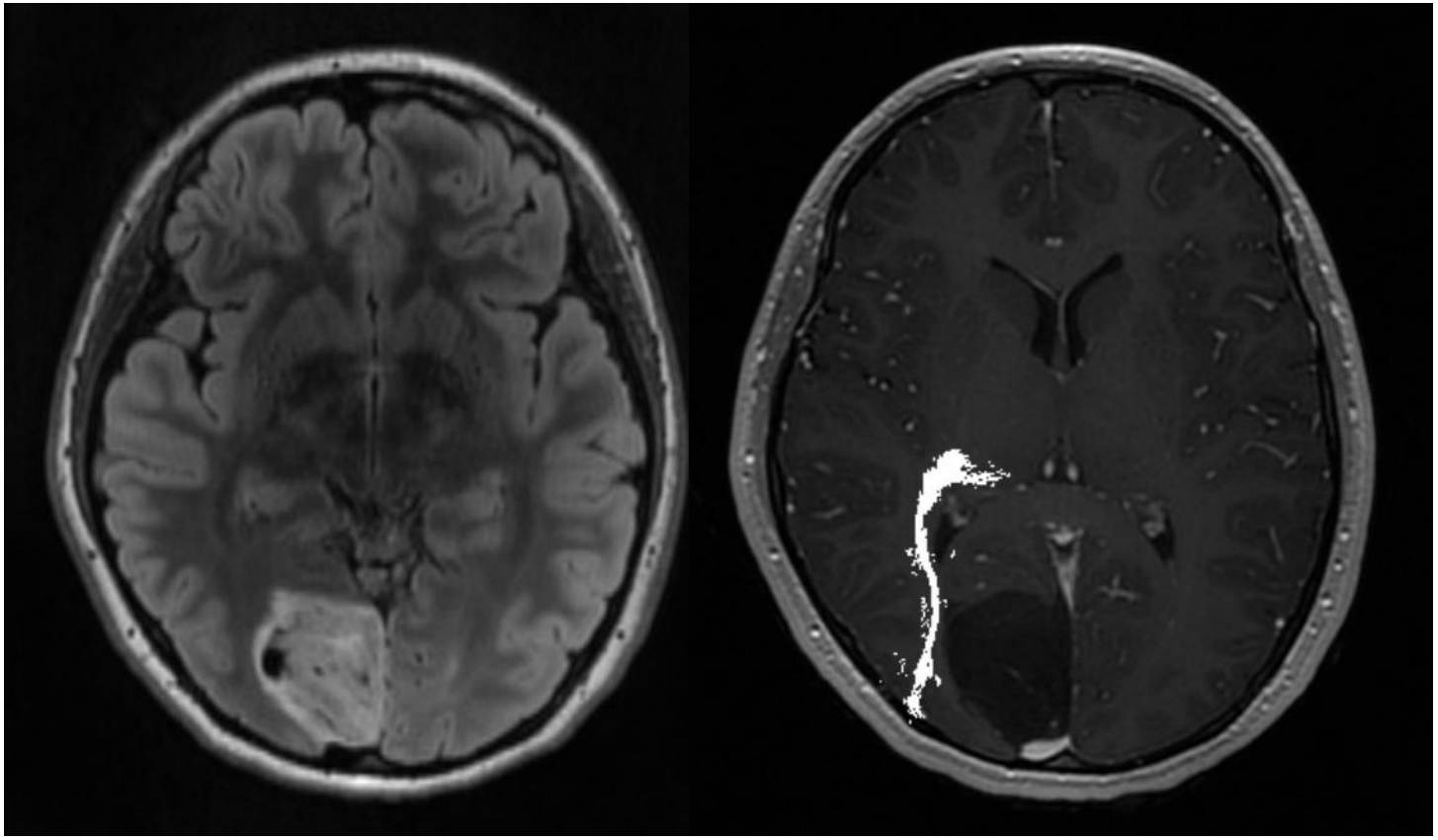
MRI demonstrating a R occipital mass



Ictal SPECT

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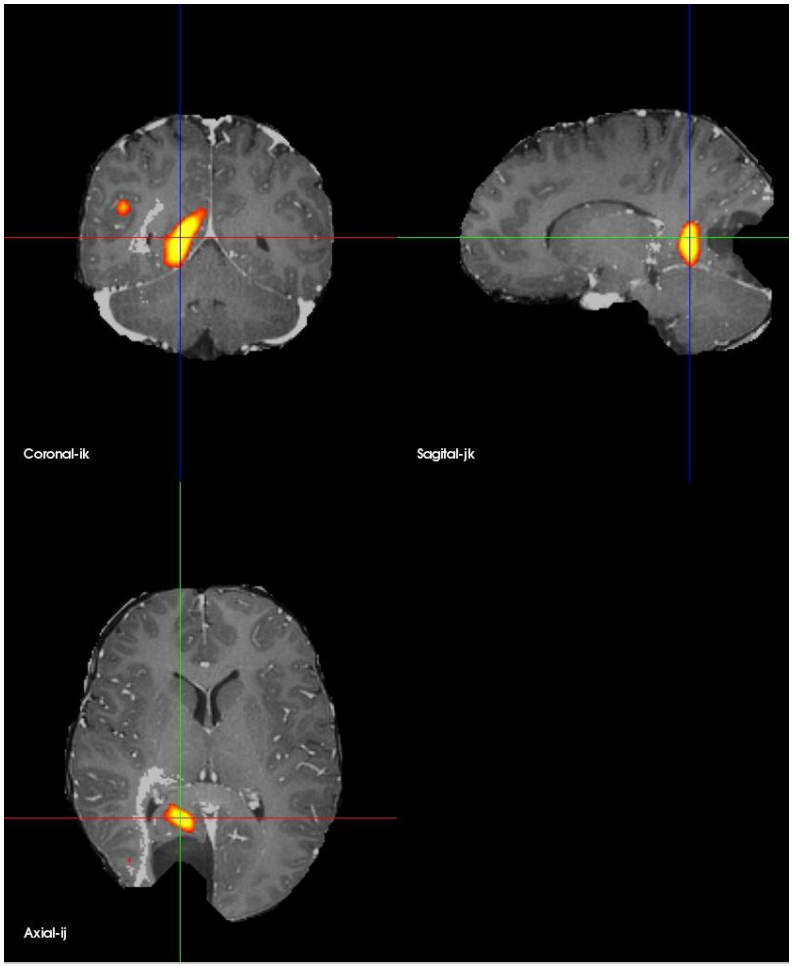

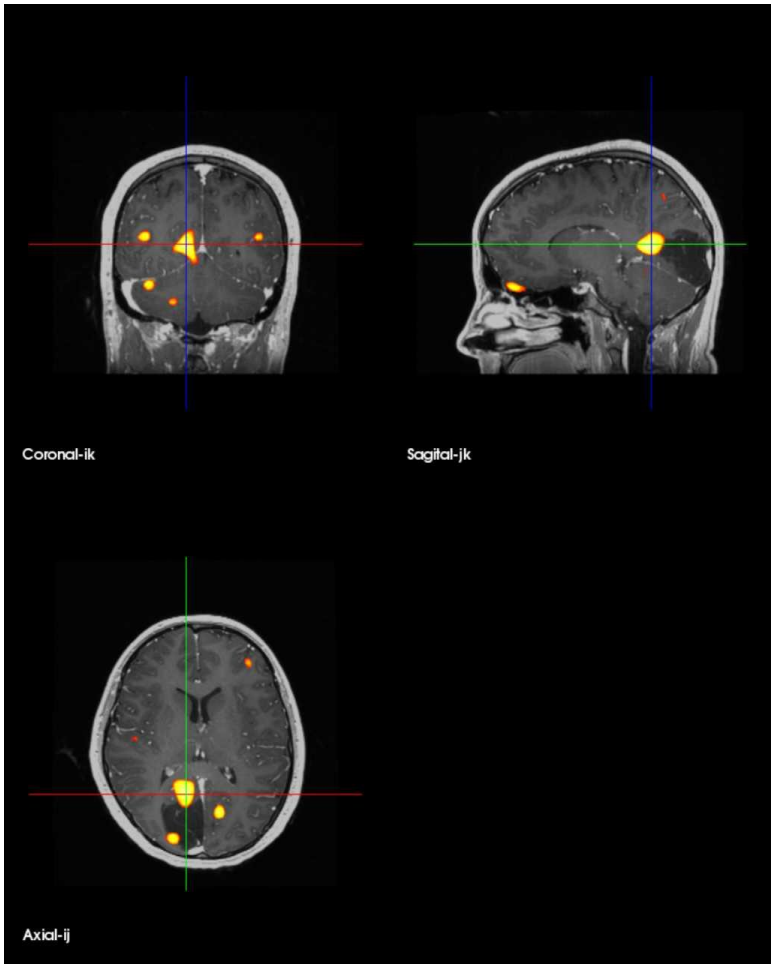

Ictal SPECT

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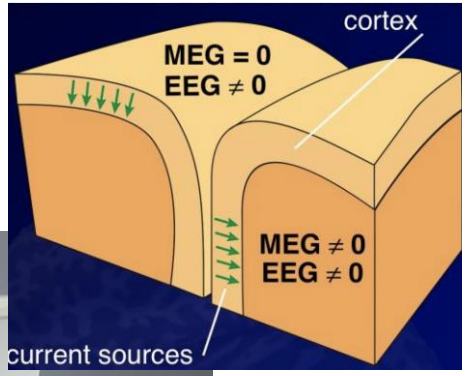
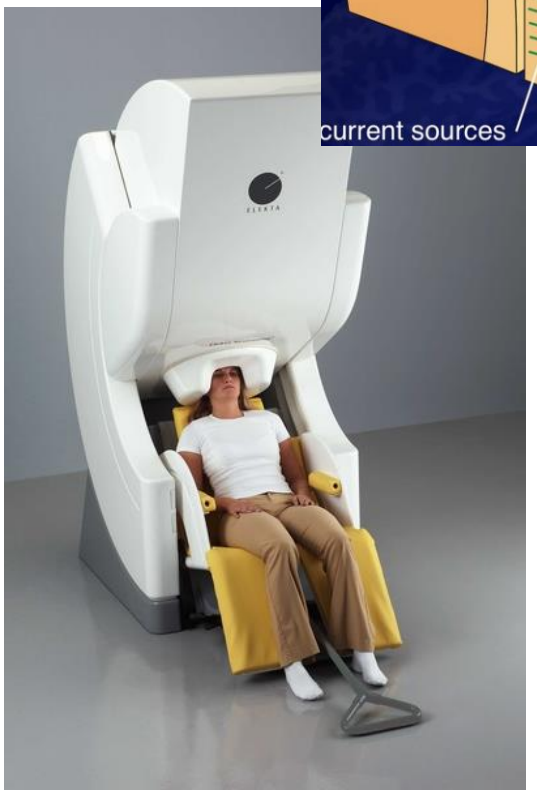
- Pros
  - Poorly lateralized/localized seizures on EEG

- Cons
  - Radioactive substance only usable for a certain window
  - Best in patients with very frequent and reliable seizures
  - Best for seizures that do not have very rapid spread
  - Requires significant post-analysis of the data

MEG

- Magnetoencephalography
  - Measures magnetic fields produced by electrical activity, can measure tangential dipoles parallel to the cortical surface (neurons in sulci)
  - Signal unaffected by skull/scalp
  - Spatial localization ~1mm





https://news.mit.edu/2010/mcgovern-institute-magnetoencephalography

MEG

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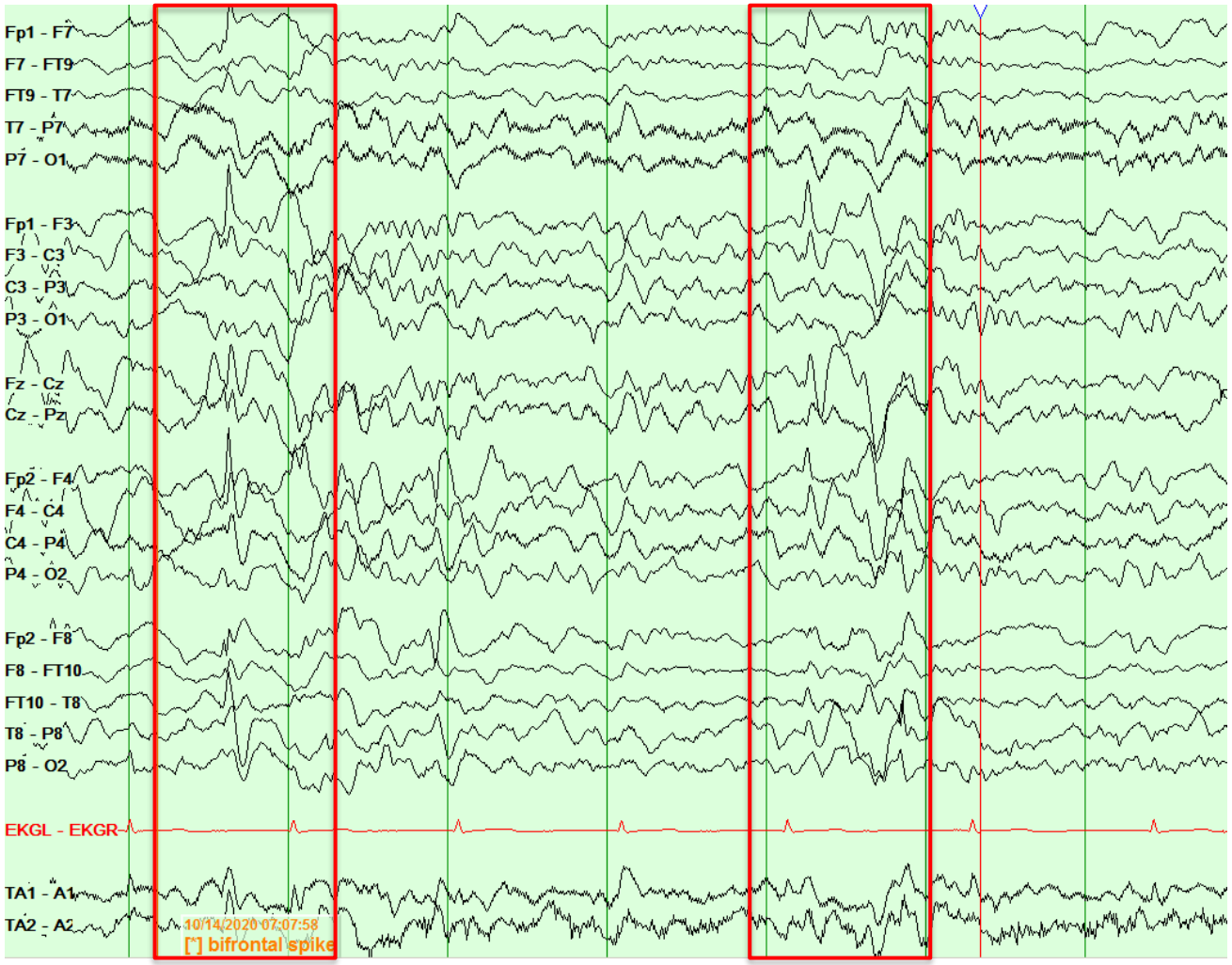
Poorly localized frontal spike on scalp EEG



MEG

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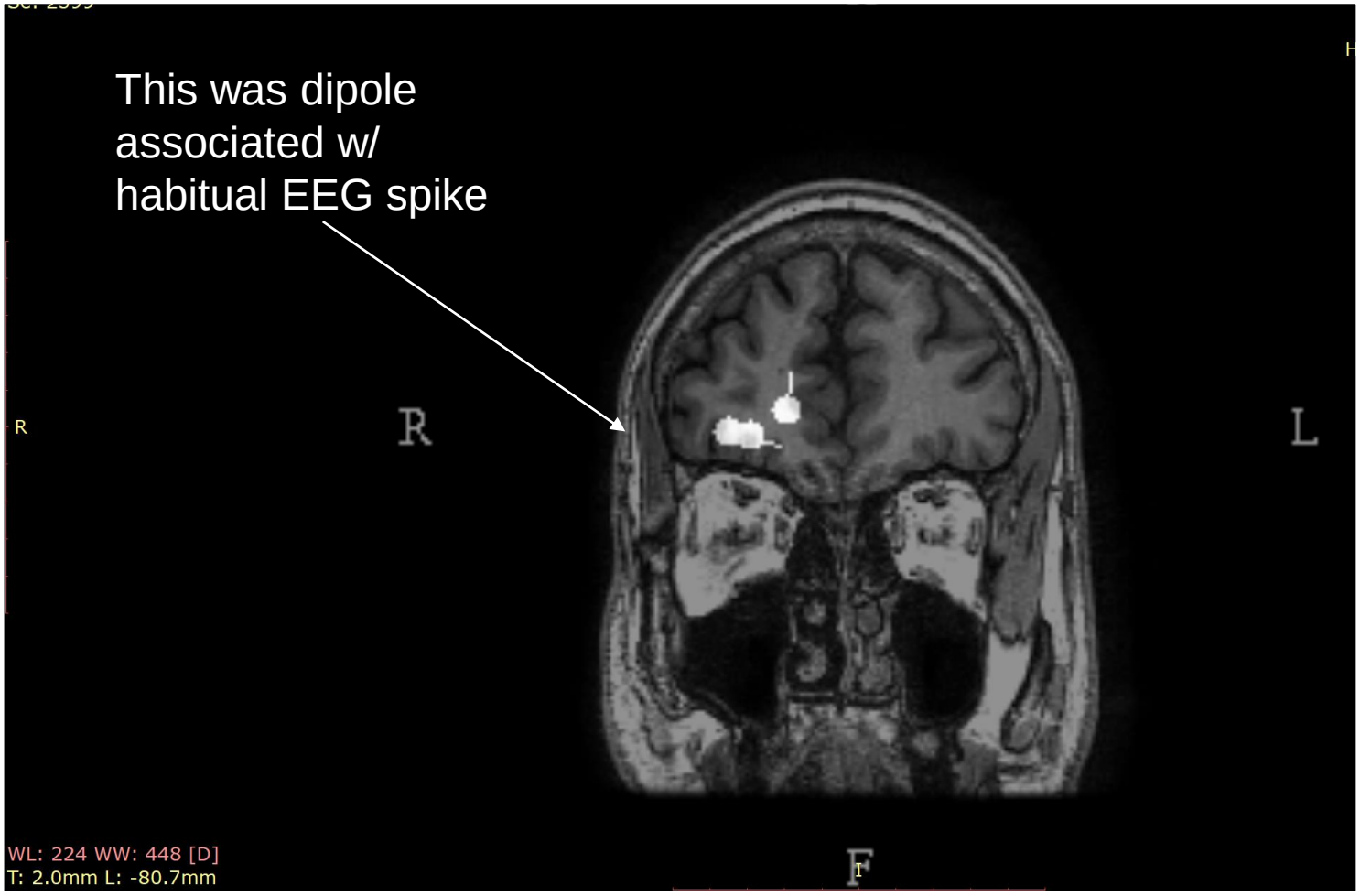

7T MRI

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- About 1/3 of patients with drug-resistant epilepsy are non-lesional on conventional MRI (1.5T or 3T)
- 7T MRI: better image contrast, higher spatial resolution, stronger susceptibility contrast
- Can detect lesions in 16-32% of previously non-lesional cases, especially focal cortical dysplasias and other malformations of cortical development

7T MRI

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- 3T MRI negative cases
- Lesion typing
  - Hippocampal sclerosis
  - Focal cortical dysplasias
  - Polymicrogyria
  - Tuberous sclerosis complex
  - Vascular malformations
  - Long-term epilepsy-associated tumor (LEAT)- gangliomas, DNETs
- Intracranial electrode positioning

7T MRI

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MP2RAGE

7T MRI

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- Need experienced radiologists to evaluate (many benign variabilities that can be seen that are not present on 3T scans)
- Increased artifact in temporal lobes, cerebellum, skull based region
- Pt needs to be very still in the machine

fMRI

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- Task functional MRI (tfMRI) can map the location of important cognitive functions such as memory and language
- Help lateralize language dominance and identify functionally eloquent brain areas that may be at risk
- Significantly less invasive than WADA tests (intracarotid sodium amobarbital procedure)

Source localization

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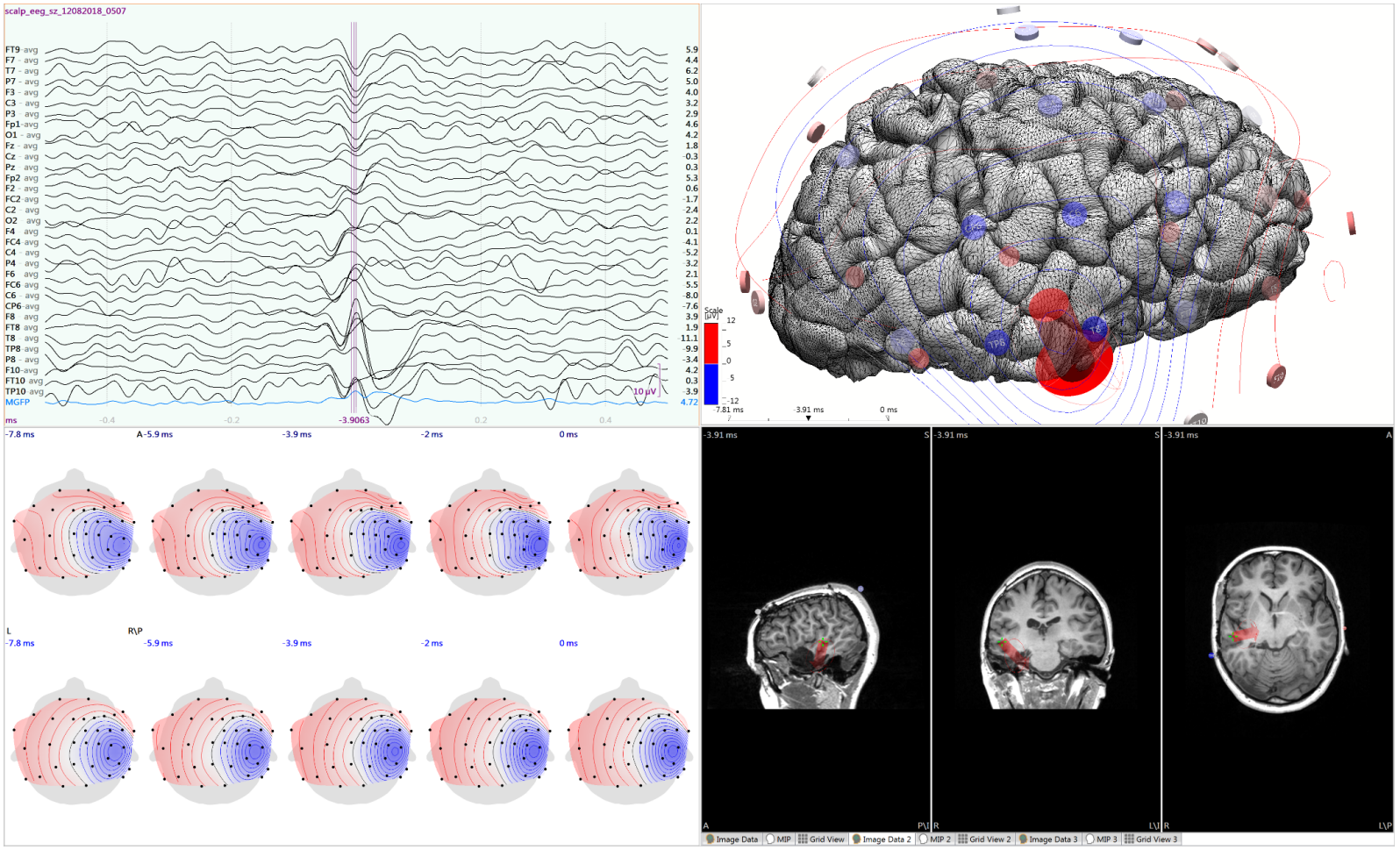
Ictal source localization post-ATL



Intracranial EEG evaluations

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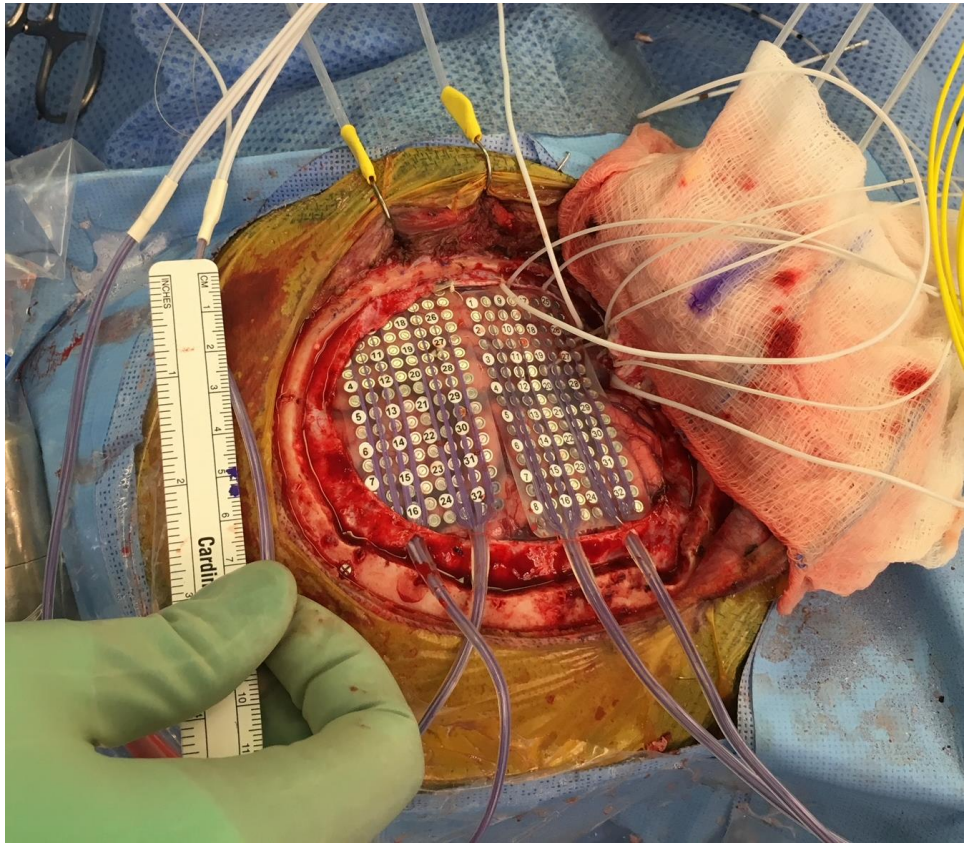
Subdural grids

- Requires a craniotomy
- Increased morbidity
- Allows for cortical mapping (language)
- Miss significant cortical coverage due to sulci
- Resection usually occurs on same admission



Intracranial EEG evaluations

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Stereotactic EEG

- “minimally invasive”
- Requires a burr hole per electrode
- Each electrode has on average 5-10 electrode contacts
- On average implant between 7-14 electrodes
- Must have clear clinical hypothesis – do not want to do a “fishing expedition
- Implantation scheme is individualized, based on underlying circuitry/network

Intracranial EEG evaluations

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Robotic Stereotactic Assistance Unit (ROSA)

https://www.neurosurgery.pitt.edu/centers/epilepsy/rosa

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Epilepsy Surgery

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- Goal of epilepsy surgery is to control seizures and to improve quality of life
- Seizure-freedom achieved in ~60% of patients, best outcomes seen in lesional patients (2.5x) and temporal lobe epilepsy
- ~25% able to come off of all seizure medications

Jobst et al 2015 JAMA

Resection

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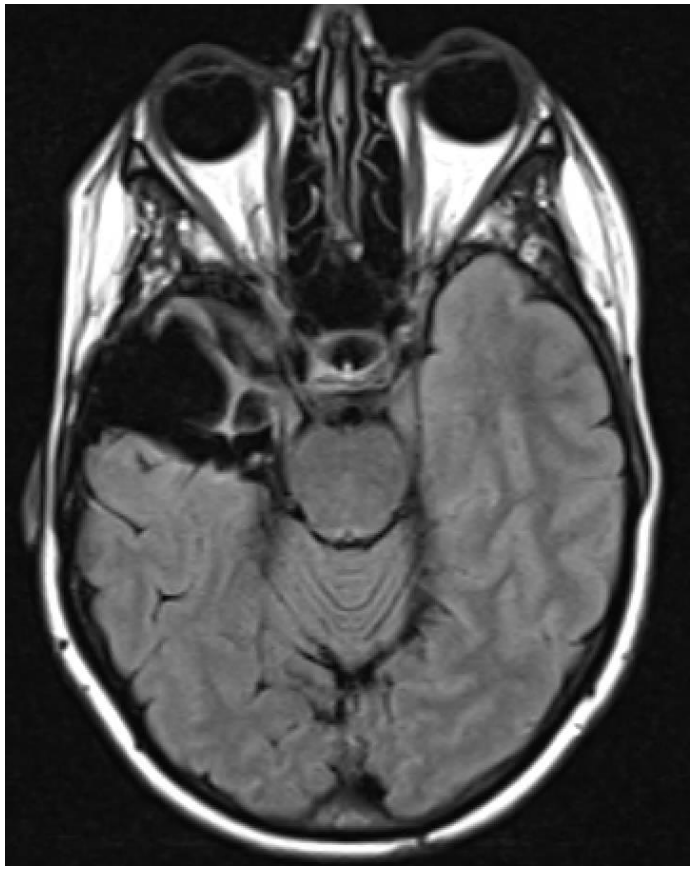
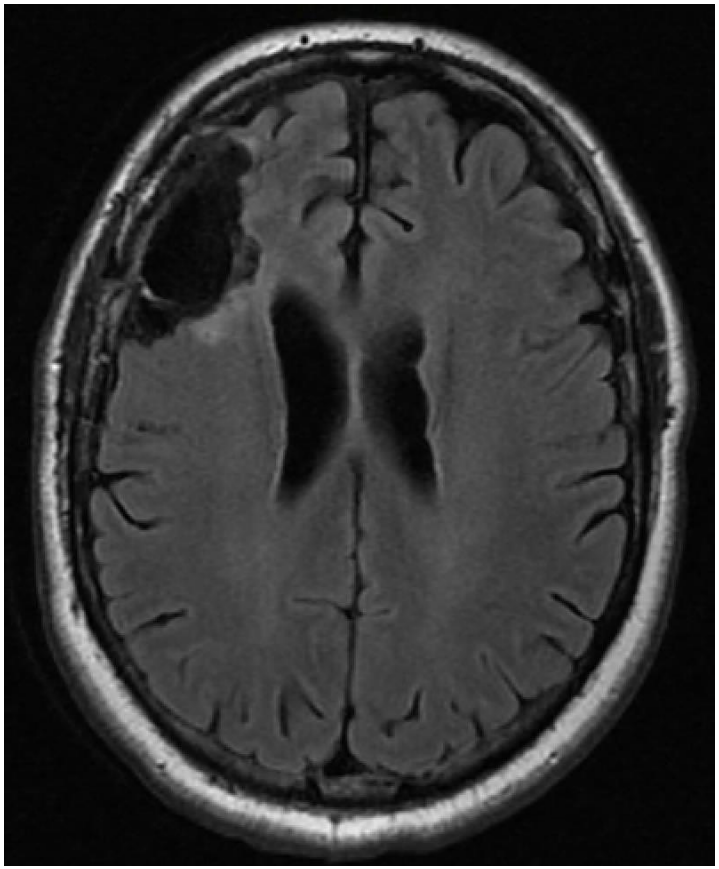
R ATL



R frontal lesionectomy



Surgical outcomes/recovery

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- Temporal lobectomies: ~75% achieve seizure freedom
  - Verbal memory decline in 44% of left and 20% of right temporal resections
  - Naming deficits in 34% of left resections
  - Right sided temporal lobe resections not associated with nonverbal memory decline
- Extratemporal resections: 34-56% seizure free

Jobst et al 2015. JAMA

Surgical outcomes/recovery

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- Health related quality of life (HRQOL) improved in patients in remission at 2-year and 5-year follow up, regardless of memory outcome
- In those not in remission
  - HRQOL remained stable when memory did not decline
  - HRQOL decreased when memory did decline
- Most notable areas: role limitations, limitations in work, driving, and social activities

Langfitt et al. 2007 Neurology

Surgical outcomes/recovery

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- Cognitive rehabilitation
  - Internal compensatory strategies, external memory aids, psychoeducation, verbal and visual memory training, exercises of attention and executive function
- Goal is to help improve verbal memory and functional and life outcomes
- Better outcomes in right vs left temporal resections
- Risk of losses in verbal memory may be up to 4x higher without rehabilitation

Mazur-Mosiewicz et al 2015. Epilepsia

Epilepsy surgery in children

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- Seizure-free patients were significantly more likely to work full time
- Educational attainment and rates of full-time employment of seizure-free patients with IQ≥70 similar to the general population

Reinholdson et al 2020. Neurology

Stereotactic laser ablation

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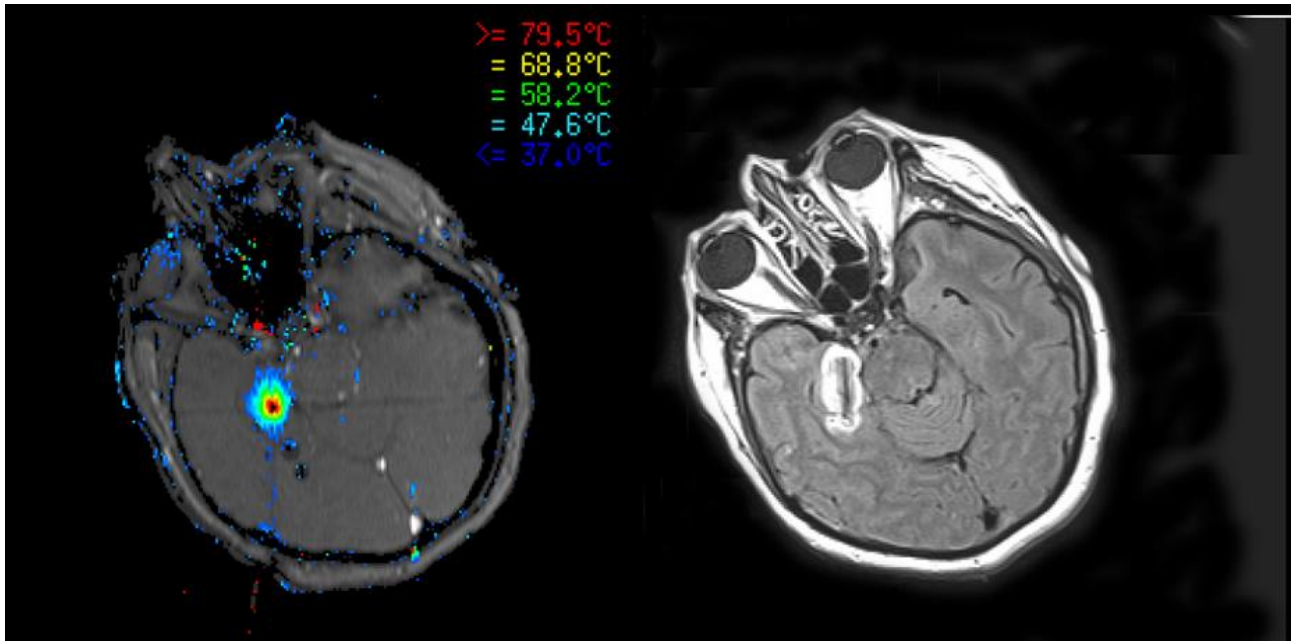
- MRI-guided LITT (laser interstitial thermal therapy) procedure
- Thermal energy used to target a discrete epileptogenic focus
- Less invasive, potentially better cognitive outcomes



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Neuromodulation

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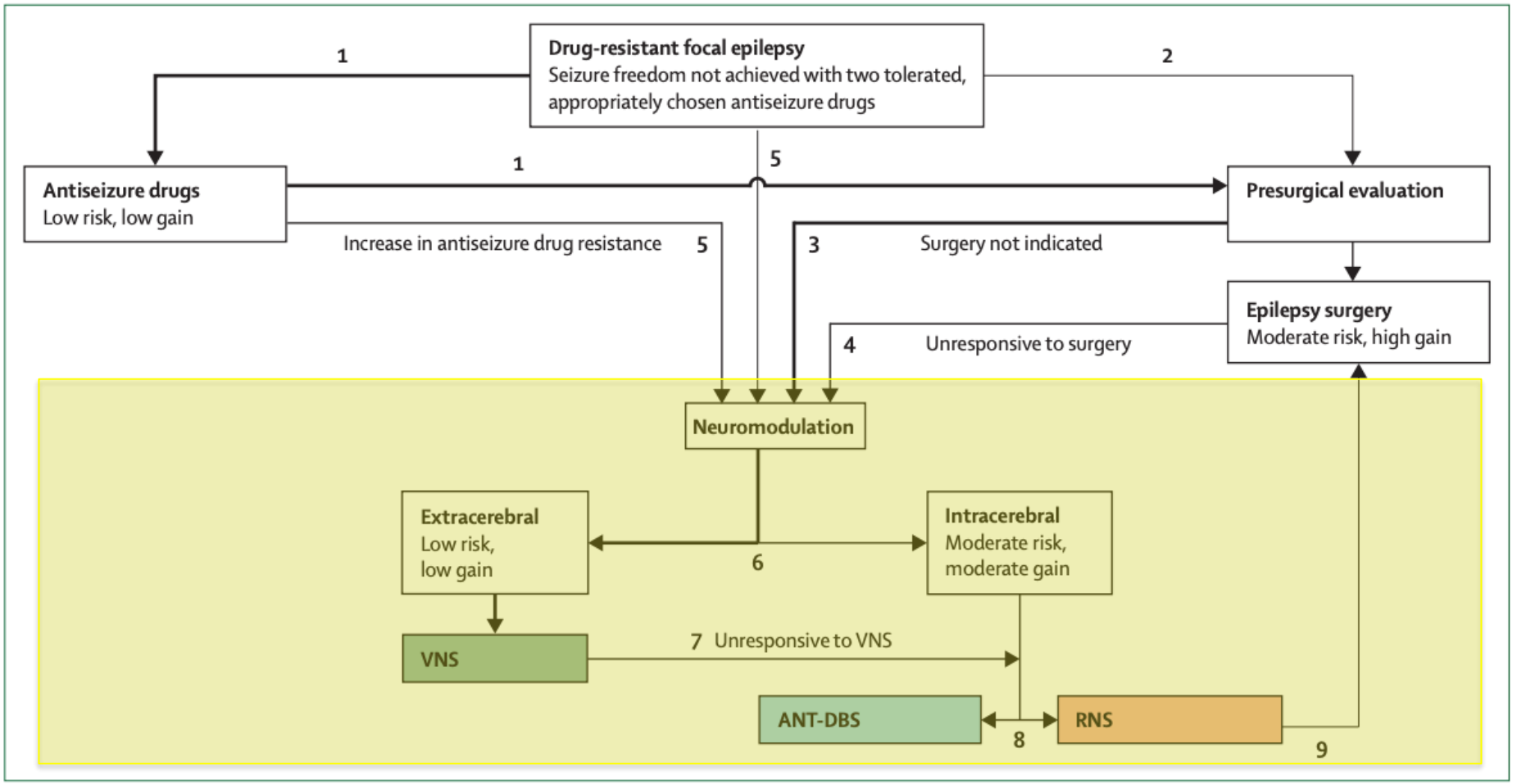

Ryvlin et al 2021. Lancet Neurol

Neuromodulation

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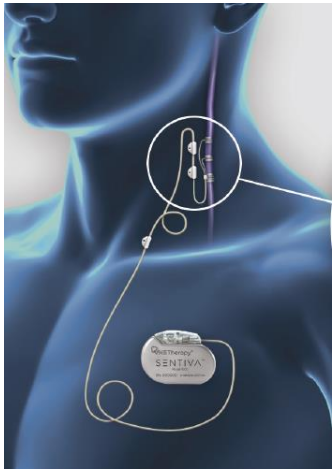
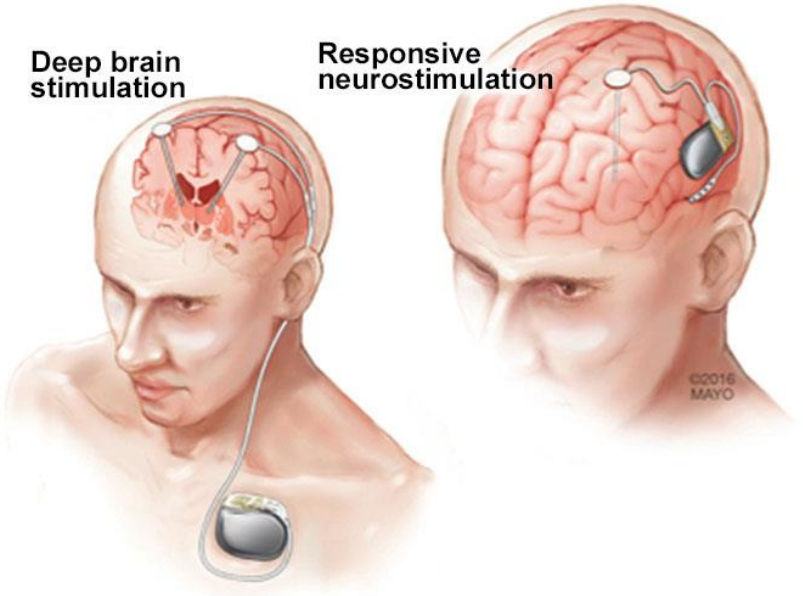
Unresectable foci

Bilateral or widespread epileptogenic foci

Generalized epilepsy

Vagal nerve stimulation





https://www.ninds.nih.gov/About-NINDS/Impact/NINDS-Contributions-Approved-Therapies/Brain-stimulation-therapies-epilepsy
https://www.epilepsy.com/learn/treating-seizures-and-epilepsy/devices/vagus-nerve-stimulation/placement-programming-and

Vagal Nerve Stimulation

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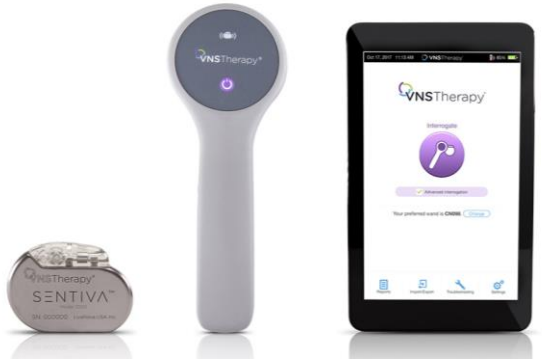
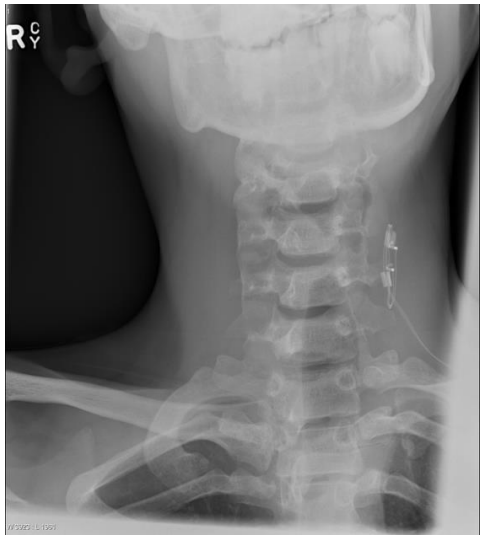
VNS
Small neck incision
(-) seizure localization
Multifocal or generalized epilepsy
Vagus nerve
Open-loop, scheduled intermittent therapy
Titration and Adjustment: Minimal physician time
SE: coughing, hoarseness, dysphonia





https://radiopaedia.org/articles/vagal-nerve-stimulator

Responsive Neurostimulation

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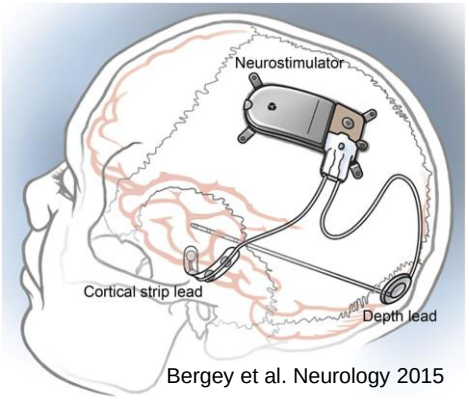
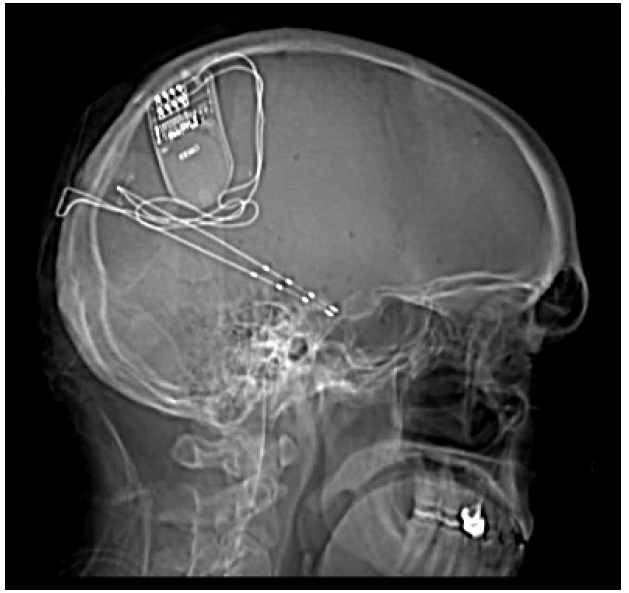
RNS
Craniotomy
(+) seizure localization
Multifocal epilepsy
Epileptogenic focus
Closed-loop, responsive therapy
Titration and Adjustment: Significant patient involvement Physician time-intensive
SE: minimal



Bergey et al. Neurology 2015



Deep Brain Stimulation

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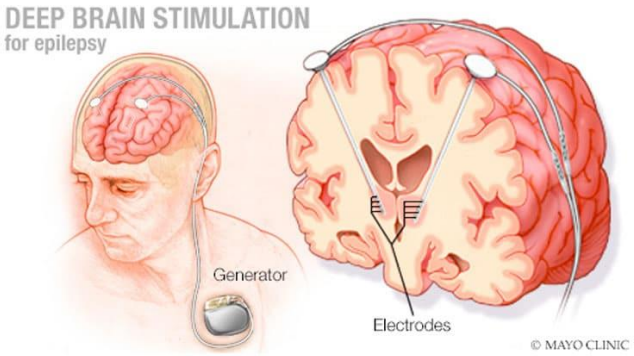
DBS
Burr holes
(-) seizure localization
Multifocal or generalized epilepsy
Anterior nucleus of the thalamus
Open-loop, scheduled intermittent therapy
Titration and Adjustment: Minimal physician time
SE: minimal



https://www.mayoclinic.org

Neuromodulation

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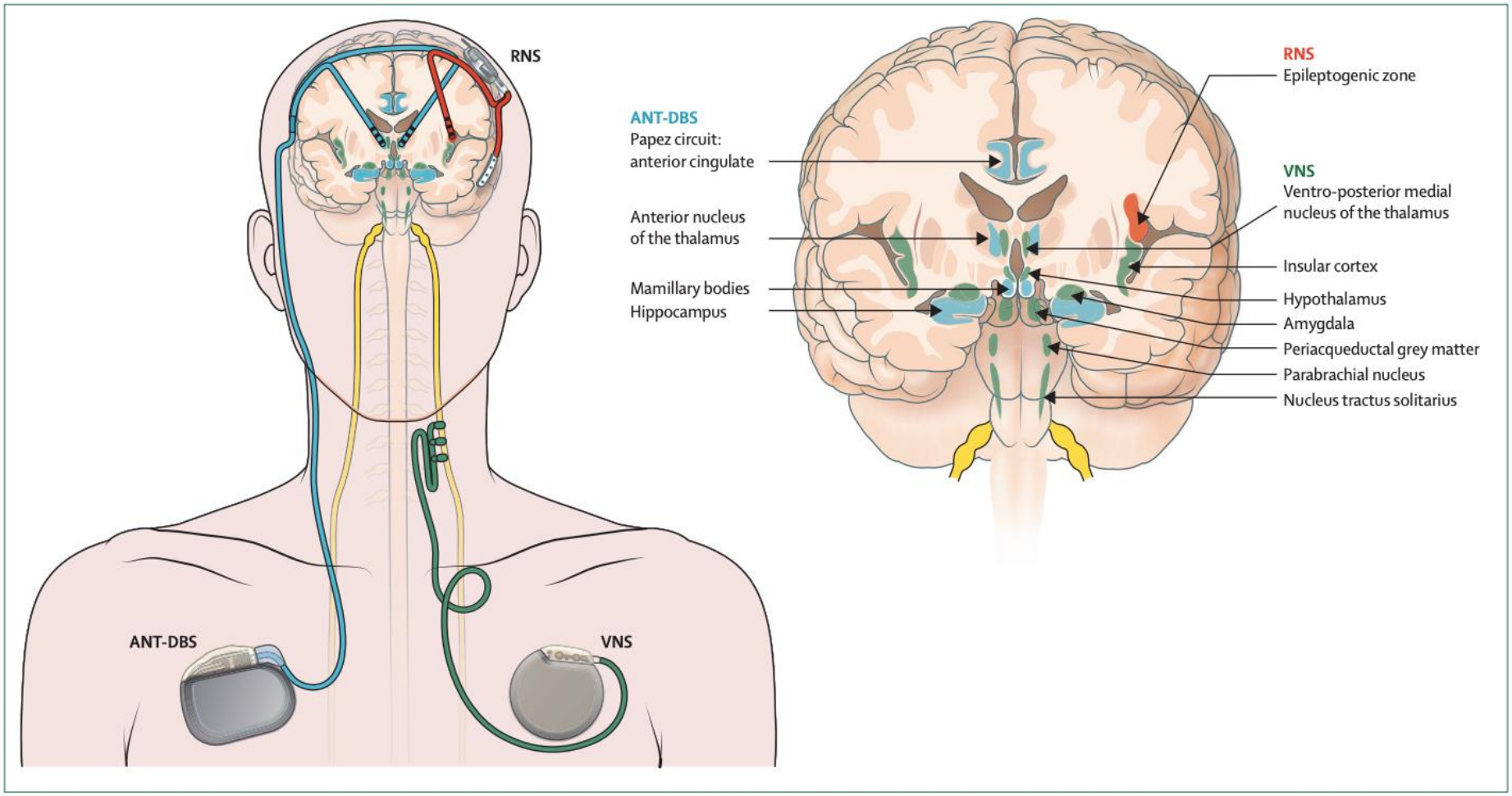


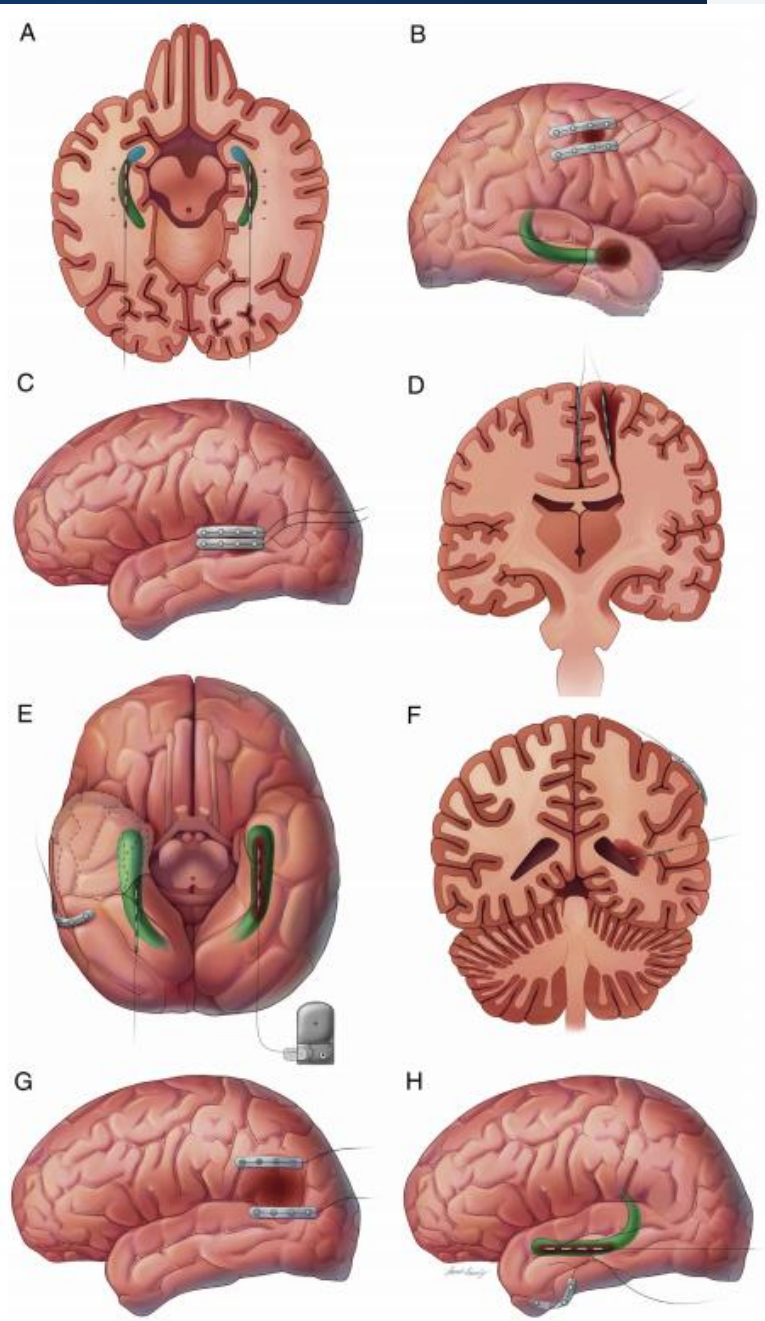
Ryvlin et al 2021. Lancet Neurol

RNS

- RNS continuously senses neural activity, and in response to patterns of epileptiform activity, will deliver electrical pulses intended to terminate seizures
- Long-term efficacy- median % reduction in seizure frequency at 9 years was 75%, responder rate 73%
- Overall quality of life remained improved long-term

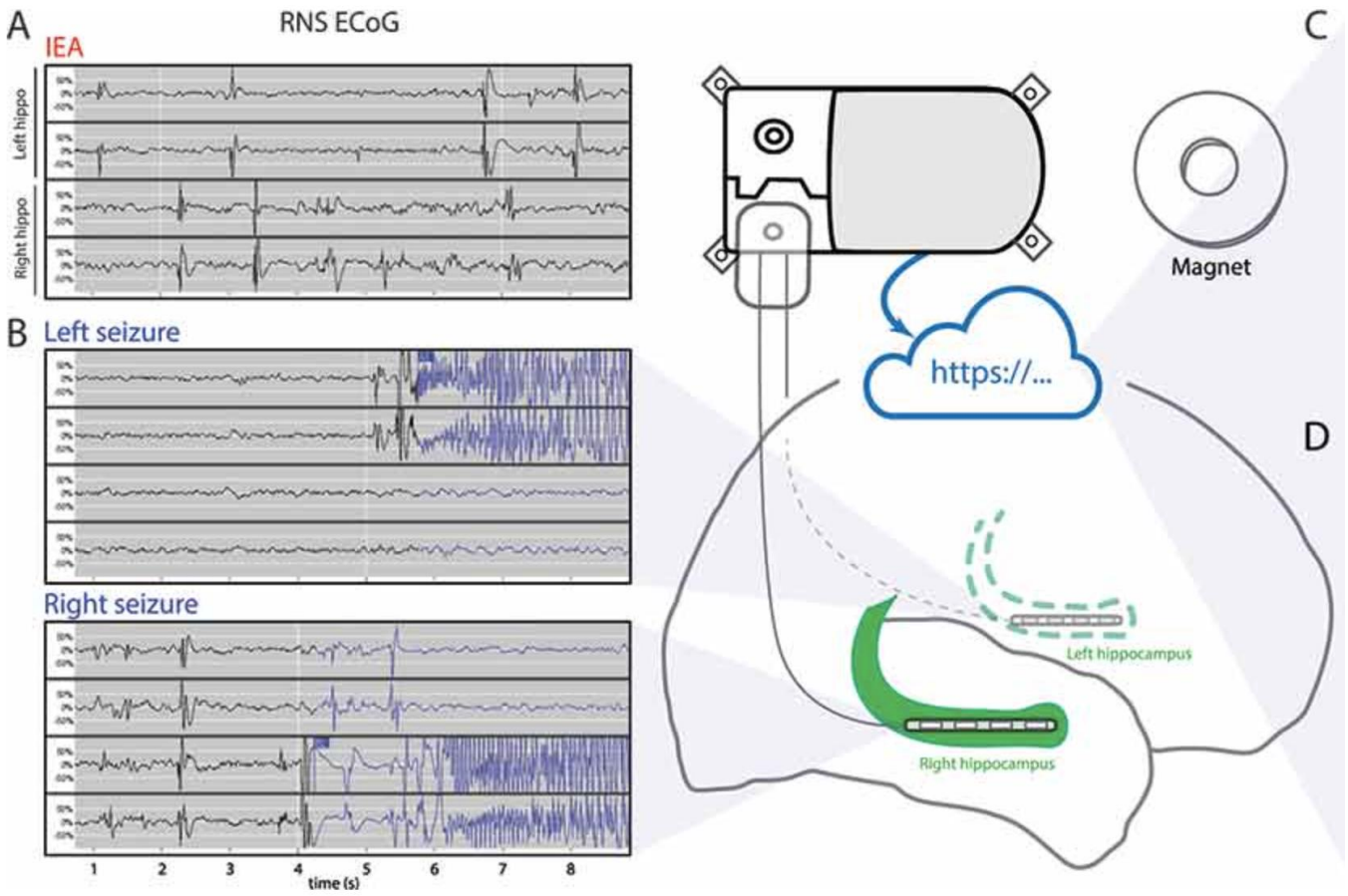
Nair et al 2020. Neurology

RNS



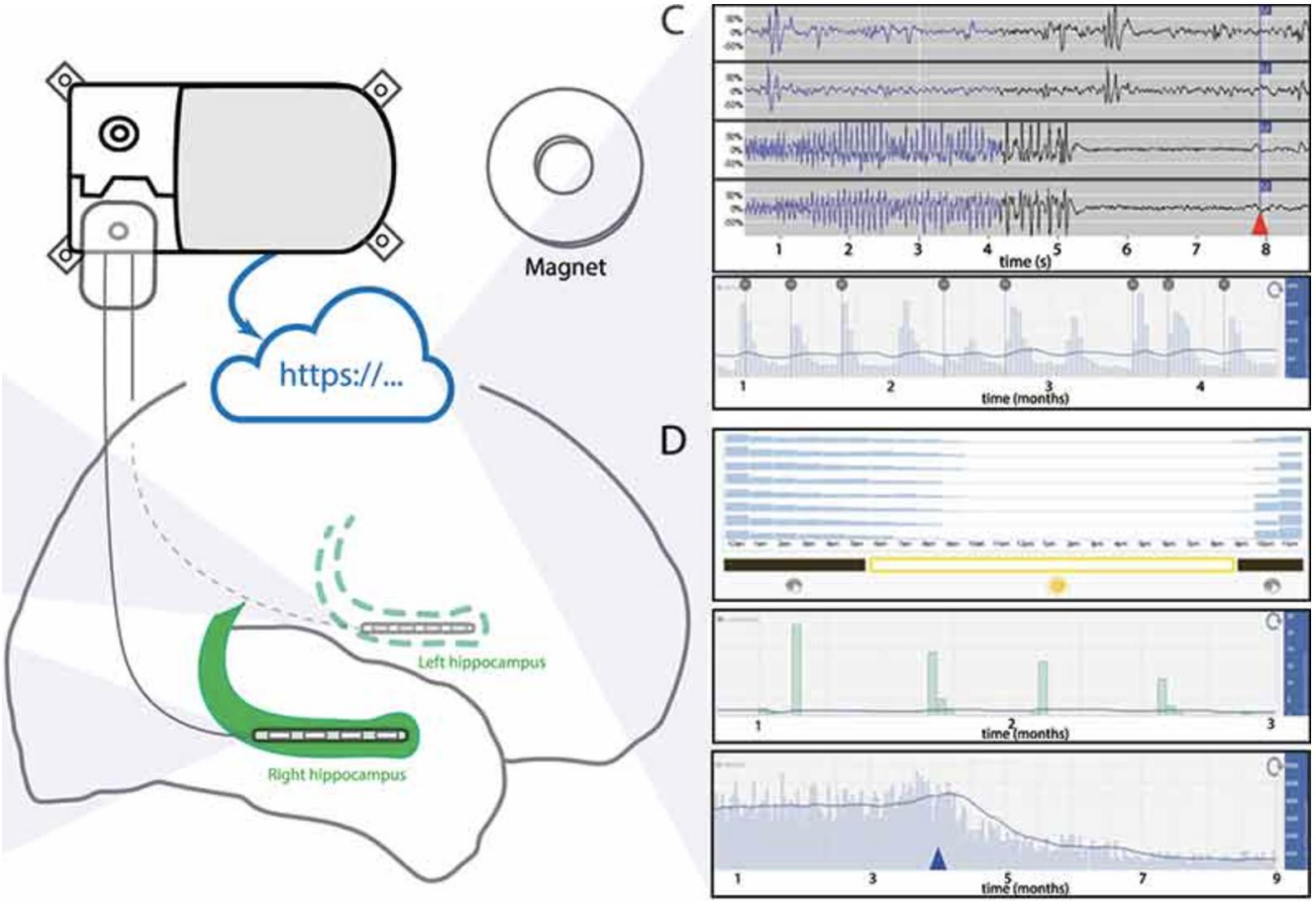
Ma & Rao 2018. Epilepsia

RNS



Rao 2021. Expert review of medical devices

RNS



Rao 2021. Expert review of medical devices

RNS

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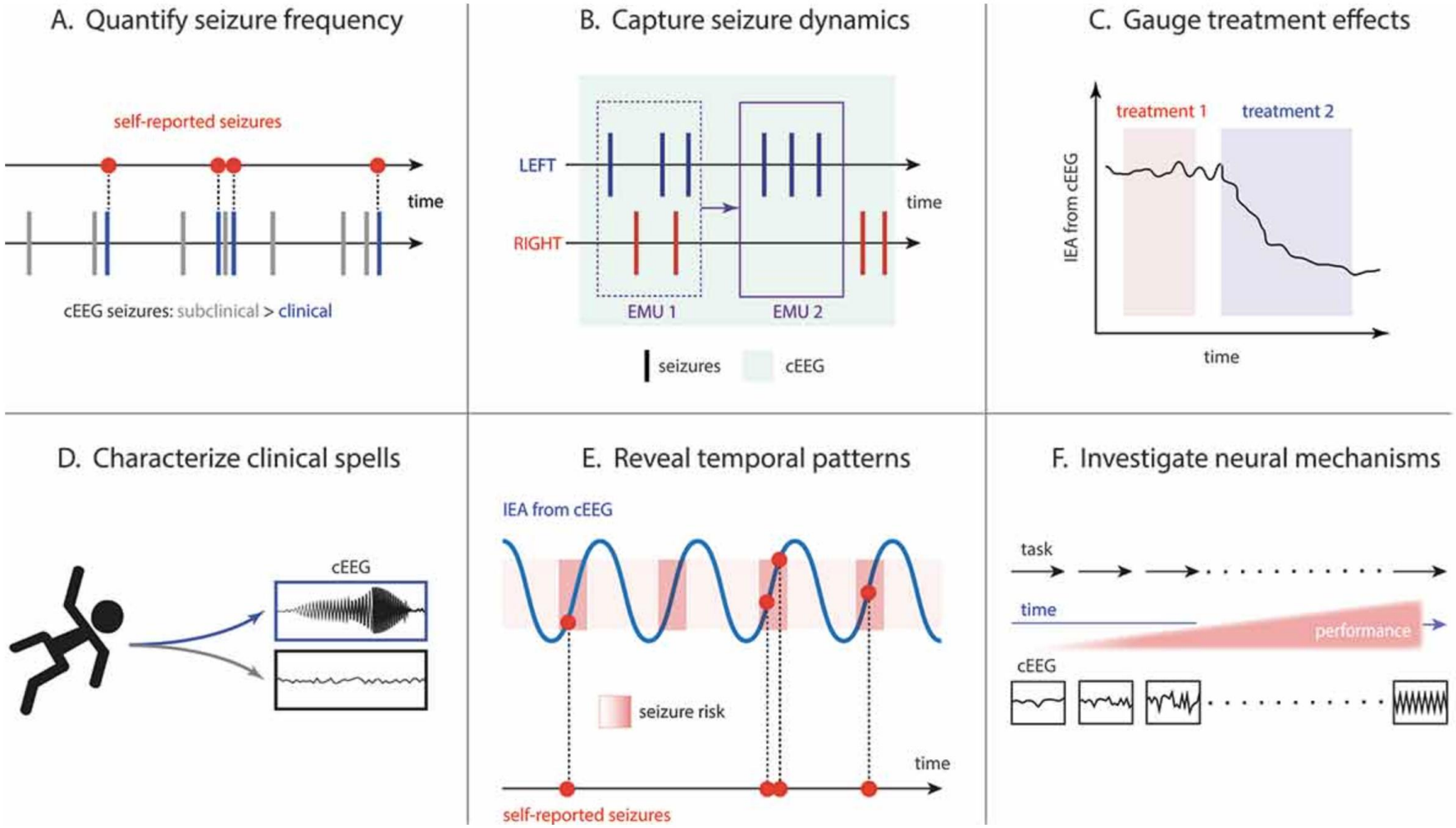
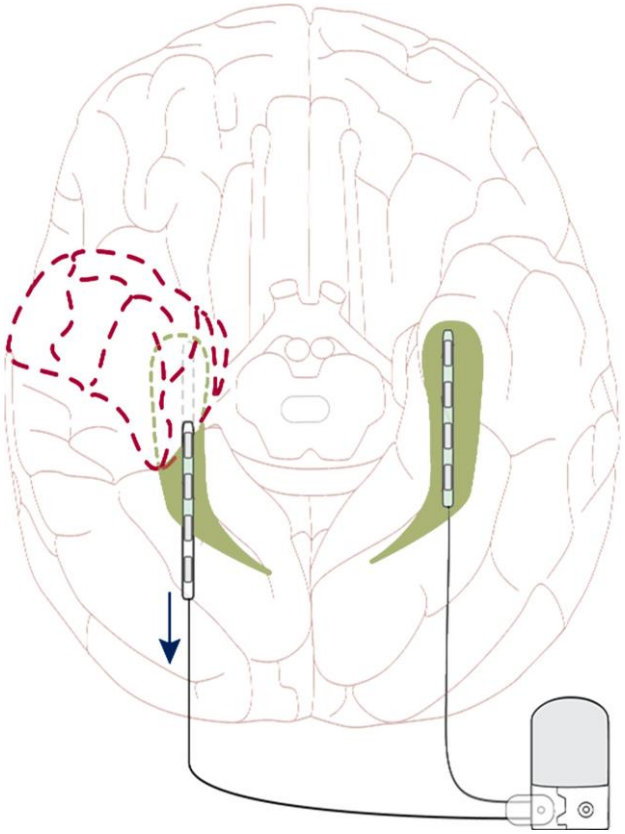


Rao 2021. Expert review of medical devices

RNS

- In bilateral mesial temporal lobe cases, RNS can help lateralize predominant seizure type over time
- Allow for resections in individuals previously thought to not be candidates



Hirsch et al 2020. Epilepsia

DBS

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- Anterior nucleus of the thalamus- part of the medial limbic circuit
- Results of SANTE trial
  - Median percent seizure reduction: 1 year = 41%, 5 years = 69%
  - Responder rate (≥ 50% reduction in seizure frequency): 1 year = 43%, 5 years = 68%
  - Treatment efficacy varied with region of seizure origin, best in temporal lobe epilepsies (76% vs 59% improvement for frontal lobe epilepsies)

Salanova et al 2015. Neurology

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Seizure forecasting

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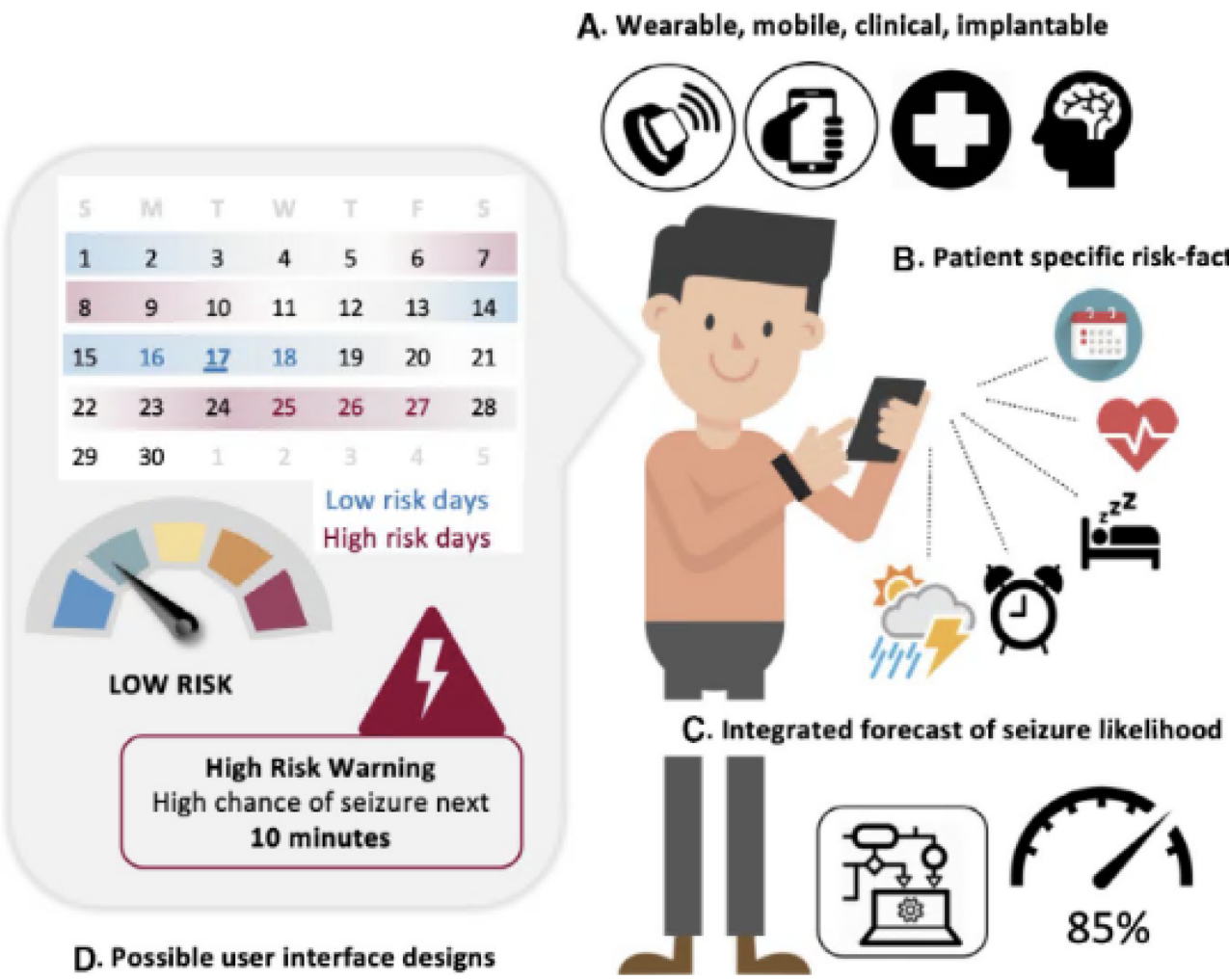

Stirling et al 2020. Epilepsia

Seizure forecasting

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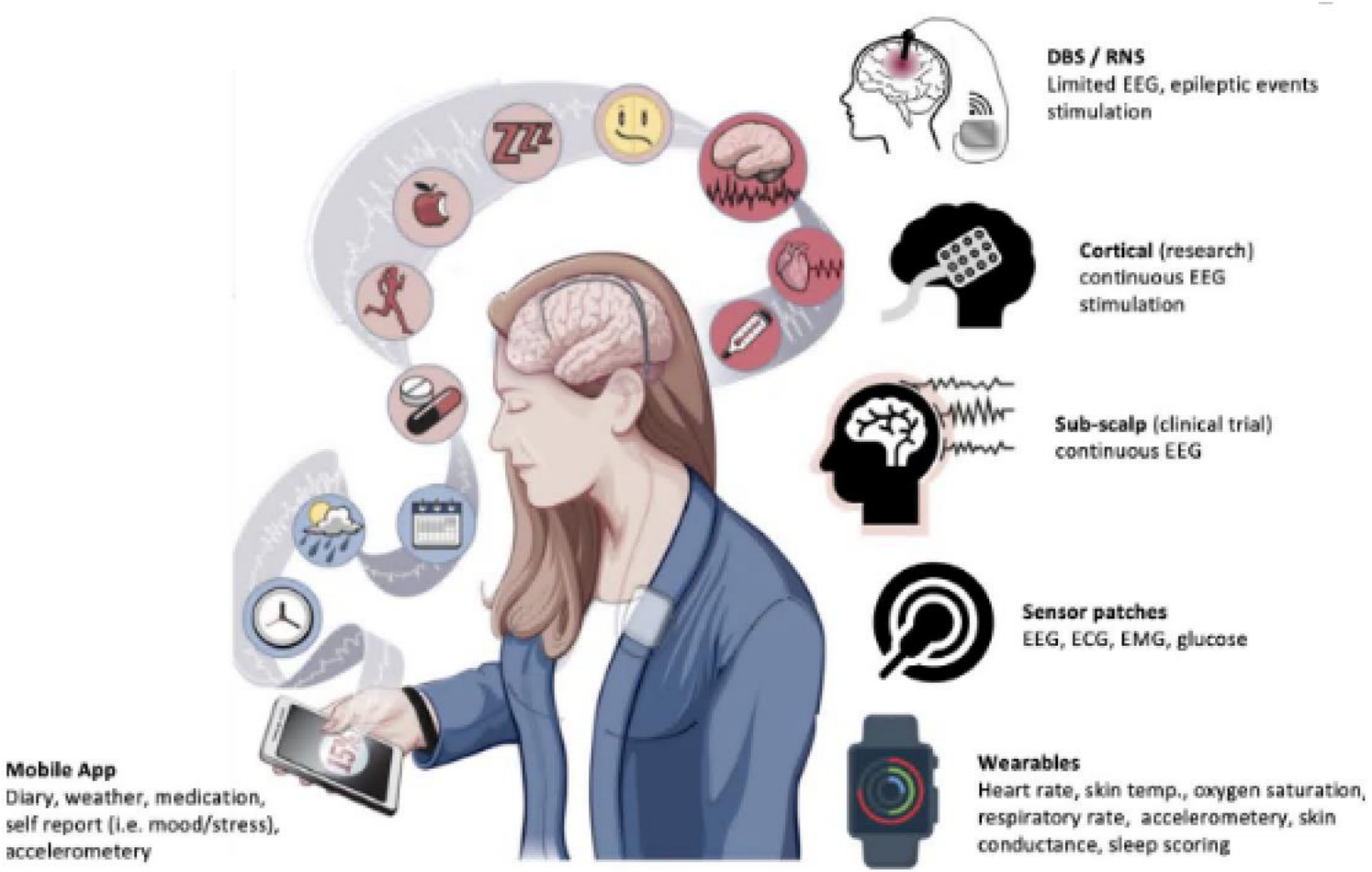

Stirling et al 2020. Epilepsia

Seizure forecasting

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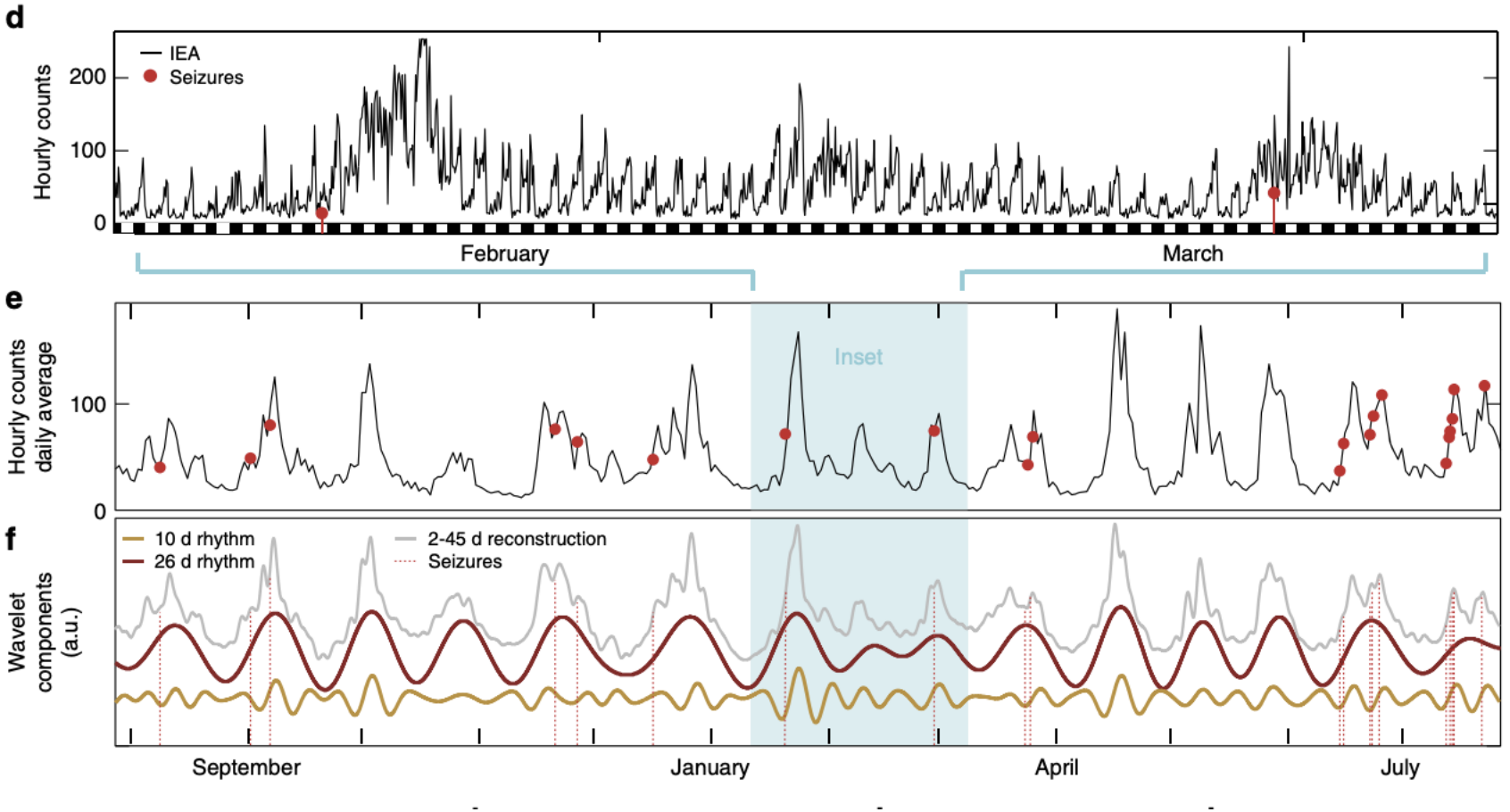

Baud et al. Nat Commun 2018

Seizure forecasting

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- Critical phases of these cycles help determine periods of highest seizure risk, with a goal of real-time seizure prediction with high sensitivity and specificity
- Chronotherapy- tailoring medication to periods of highest seizure risk
- Timing of adjunctive abortive treatments

Key points

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- Drug-resistant epilepsy occurs in 30-40% of people with epilepsy, and only 5-10% of these will achieve seizure freedom with continued medication adjustments
- The majority of patients will benefit from advanced imaging and intracranial evaluations for further localization of epileptogenic foci
- A variety of surgical options are available outside of resections, including thermal ablation and neuromodulation
- A main determinant of quality of life after surgery is memory decline, which can be improved with cognitive rehabilitation
- The unpredictability of seizures is one of the most limiting aspects of the condition. Chronic intracranial EEG technology has demonstrated the unique temporal patterns seen in most patients, which can aid in seizure forecasting

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