Drug-Resistant Epilepsy

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Learning Outcome

- “Outline and discuss the management of patients with refractory epilepsy, including when to refer to a comprehensive epilepsy centre.”

Definition

- *“Drug resistant epilepsy may be defined as failure of adequate trials of two tolerated and appropriately chosen and used AED schedules (whether as monotherapies or in combination) to achieve seizure freedom”.*

Kwan P, Arzimanoglou A, Berg A et al. Definition of drug resistant epilepsy: Consensus proposal by the ad hoc Task Force of the ILAE Commission on Therapeutic Strategies. Epilepsia 2009; 51(6)1069-1077.

Risk Factors

- Response to first AED
- Higher number of seizures prior to diagnosis
- Aetiology
- Possible risk factors
  - Presentation with status epilepticus
  - Family history of epilepsy.
  - Recreational drug use

Importance

- Increased mortality
  - Some of this may relate to aetiology
  - SUDEP 40x more likely in those who continue to have seizures.
- Increased morbidity
  - Seizure-related injuries
  - Reduced quality of life measures
  - Unemployment
  - Social isolation
  - Driving
  - Medication toxicity
  - Comorbid depression and anxiety

Evaluation of Drug-Resistant Epilepsy

- Re-evaluate diagnosis and management
  - Up to 25% of ‘drug-resistant epilepsy’ is due to misdiagnosis.
  - Medication issues – incorrect drug, inadequate dose, non-compliance.
  - Lifestyle factors – sleep, alcohol, drug use.

- Additional investigations
  - Many misdiagnosed cases are due to over-interpretation of EEG.
  - Video EEG is gold standard to identify seizure mimics (psychogenic non-epileptic seizures, other paroxysmal disorders), and helps further define epilepsy syndrome.
  - Dedicated epilepsy imaging.

Epilepsy Surgery

- Focal resection is potentially curative in appropriately selected patients.

- Most common potential candidates:
  - Mesial temporal lobe epilepsy.
  - Lesional epilepsy
  - Non-lesional focal epilepsy

Epilepsy Surgery Evaluation

- Clinical evaluation
- Routine and video EEG
- MRI
- FDG-PET
- SPECT
- Neuropsychological evaluation
- Neuropsychiatric evaluation
- Multi-disciplinary consensus

Key Points

- All drug-resistant epilepsy should be referred to a comprehensive epilepsy centre.
  - Facilitate additional diagnostic workup, confirmation of diagnosis.
  - Access to multi-disciplinary services (neuropsychiatry, neuropsychology, epilepsy nurse support).
- Additional aim is to identify potential surgical candidates early.
  - Streamline referral and investigations
  - Longer duration of epilepsy is associated with worse post-surgical outcomes, lower quality of life measures, risks of complications from frequent seizures.

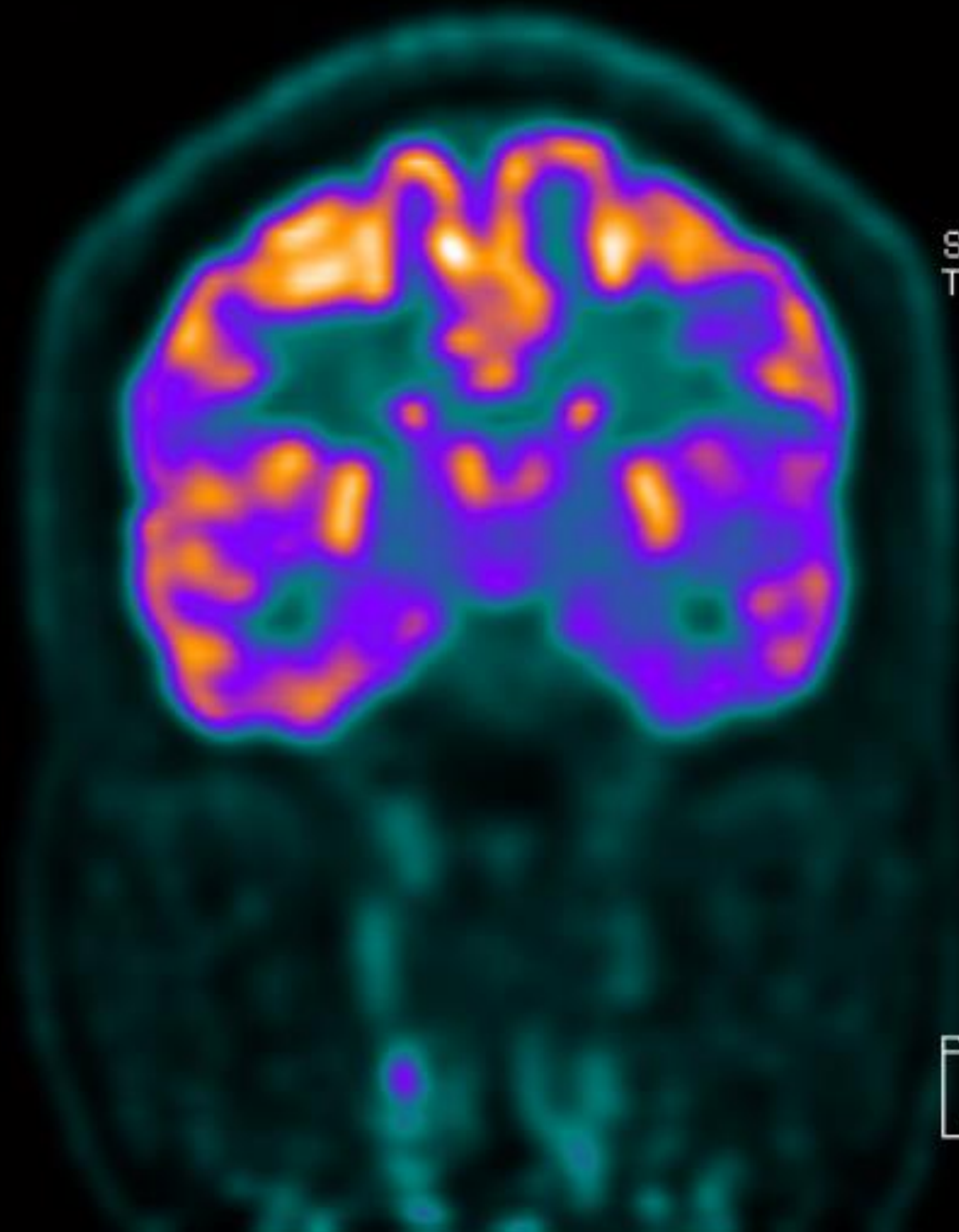
Case 1

- 40 year-old lady referred to epilepsy clinic with long-standing epilepsy, lost to follow up.
- GTCS at age 17. Frequent events since, current frequency 2-3/week.
  - Somatosensory phenomena in right flank, migrating down right leg, followed by clonic jerks lasting up to one minute.
  - A few atypical features eg episodes aborted with startle or change in position.
- LEV 1000/1000, CBZ CR 400/400. Previously tried LTG, TOP.
- Not working. Not driving. Smokes 2 cones/day. Background of amphetamine abuse.
- MRI x2 previously showing non-specific white matter hyperintensities. Routine EEG x2 normal.

Case 2

- 28-year-old man referred from general neurology for evaluation of drug-resistant epilepsy and workup for epilepsy surgery.

- Background:
  - Febrile seizures 8mths and 18mths of age, each lasting >30 minutes.
  - Focal dyscognitive seizures since age three.
  - Managed well with Valproate. Carbamazepine ineffective.
  - MRI demonstrating left mesial temporal sclerosis.
  - Seizures increasingly frequent throughout adulthood, with rare secondary generalised tonic-clonic seizures.
  - 2-3 events each week despite addition of Levetiracetam



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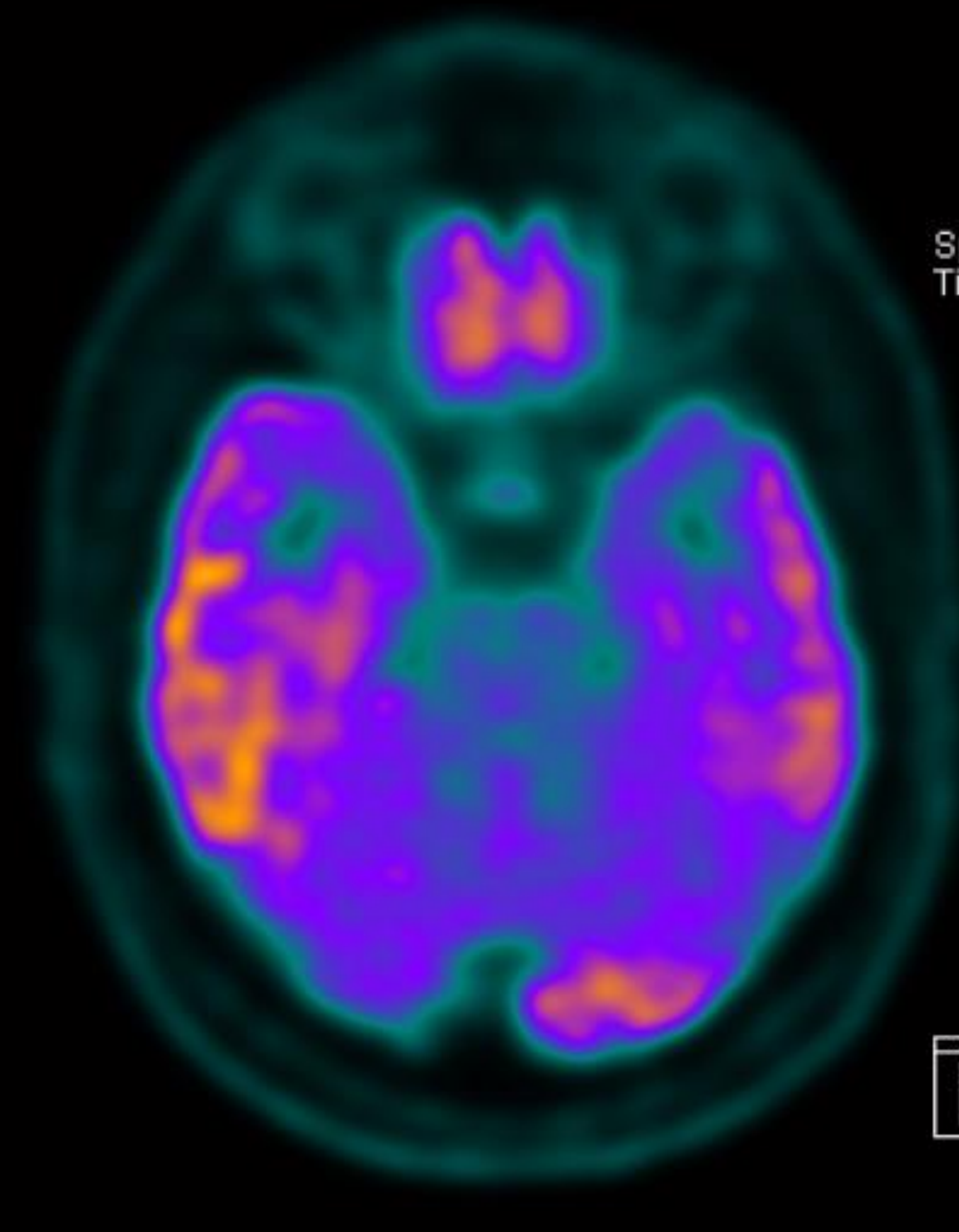

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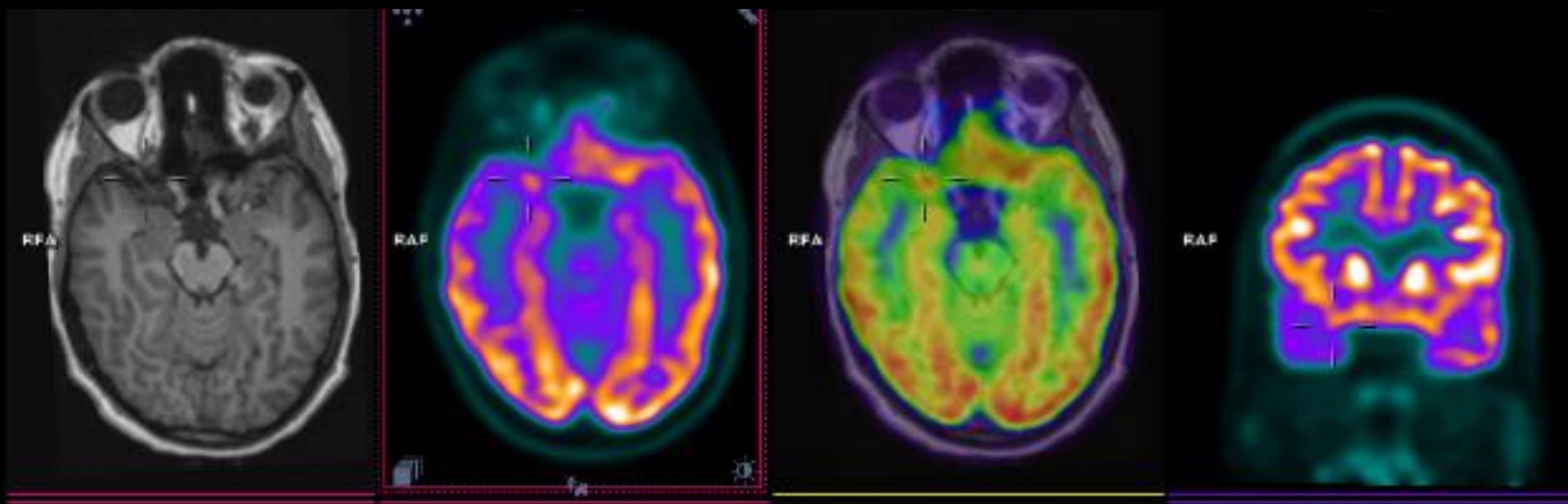
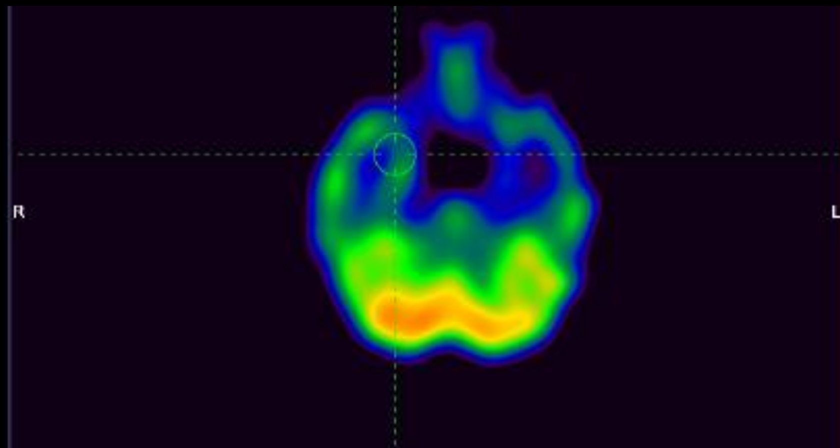
Case 3

- 30-year-old lady referred from general neurology clinic with drug-resistant epilepsy.
- No risk factors for epilepsy
- Smoker. Otherwise well.
- Medications: VPA 500/500, LEV 1000/1000
- Diploma in social services. Not driving.

- Onset of seizures 4 years ago
  - GTCS in setting of acute illness
  - Two months later, two further unprovoked seizures
  - Commenced on VPA, which after titration to 500/500 controlled the GTCS
- However, continues to have smaller episodes –
  - Gustatory aura and associated déjà vu
  - Followed by loss of awareness with oral and manual automatisms
  - Head consistently turns to left
  - Duration typically ~60 seconds
- Identified as surgical candidate and proceeded to surgical workup.

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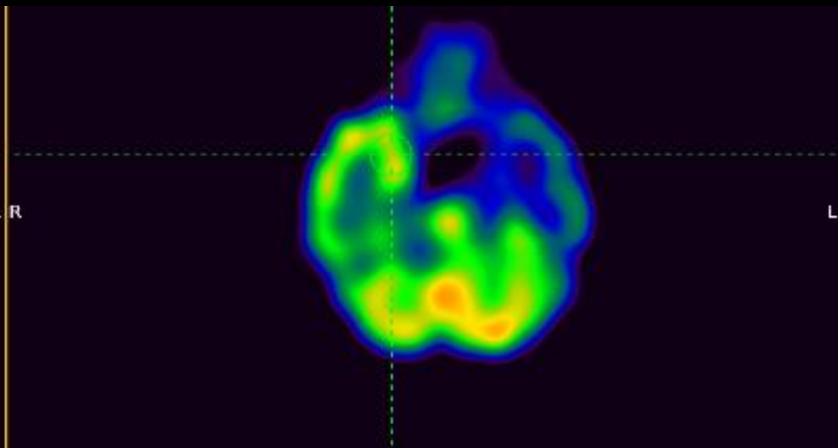
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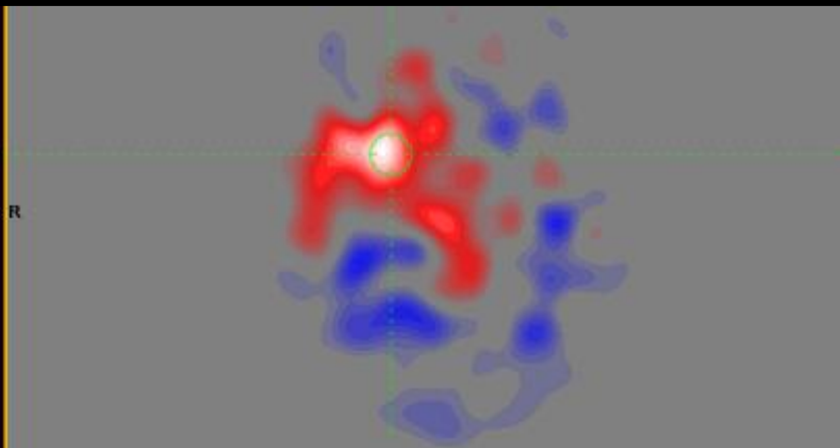
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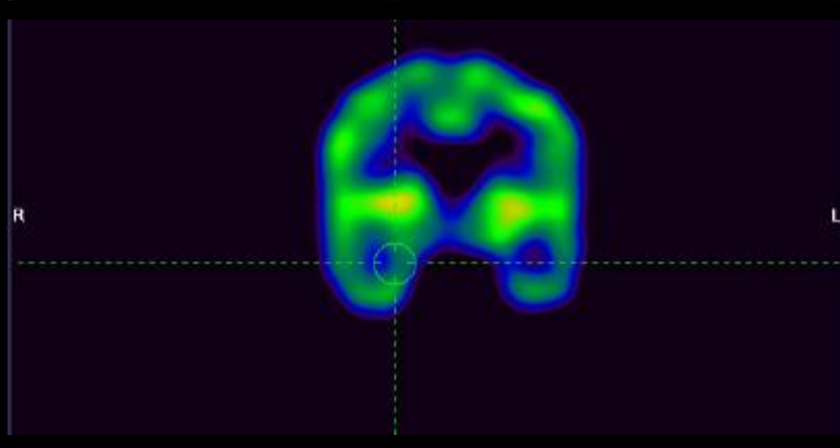
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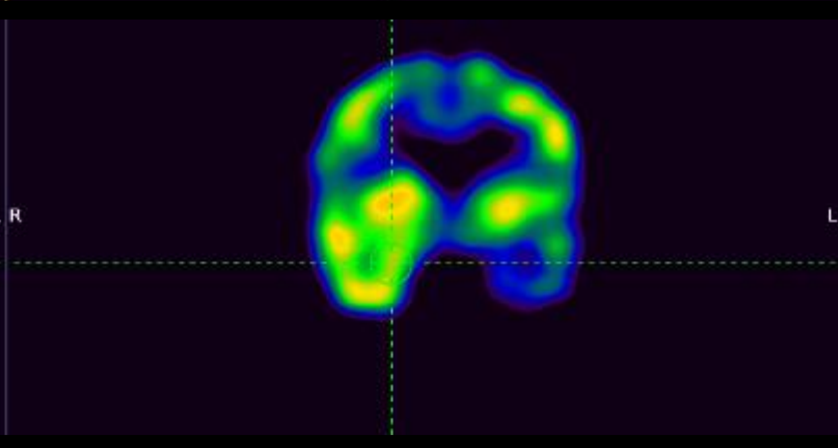
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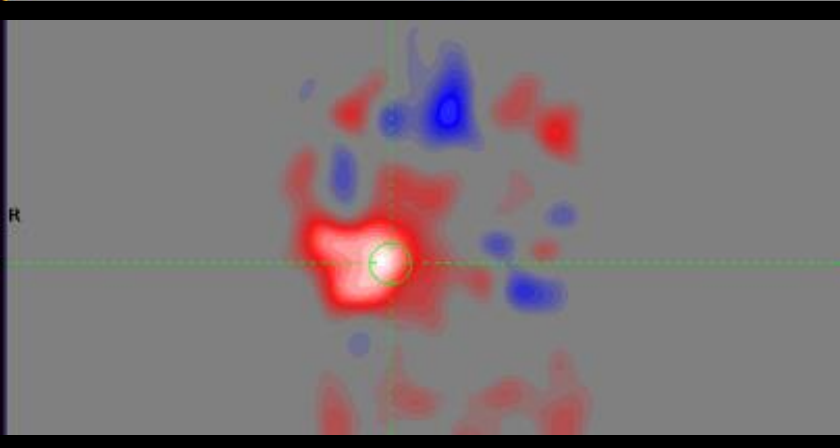
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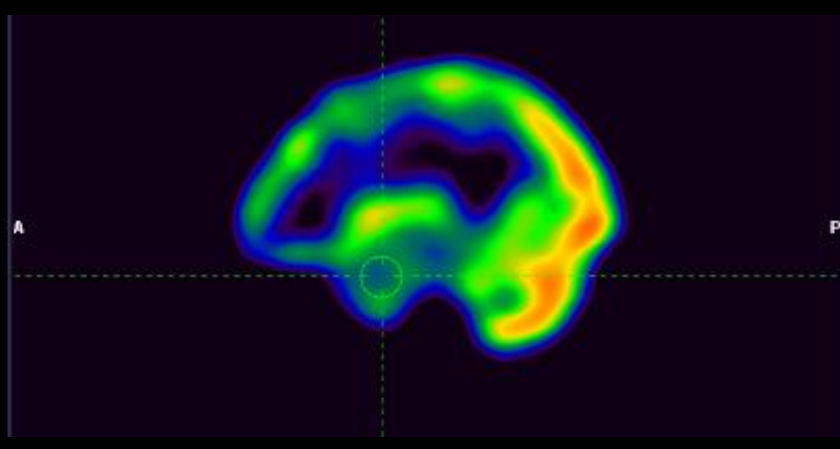
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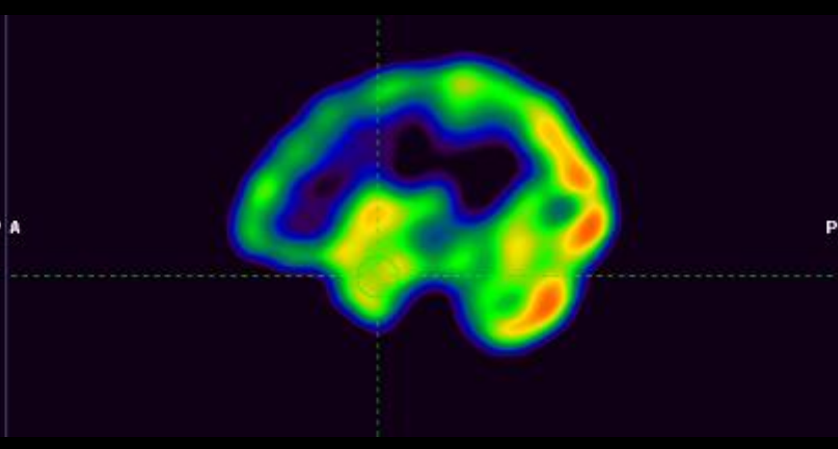
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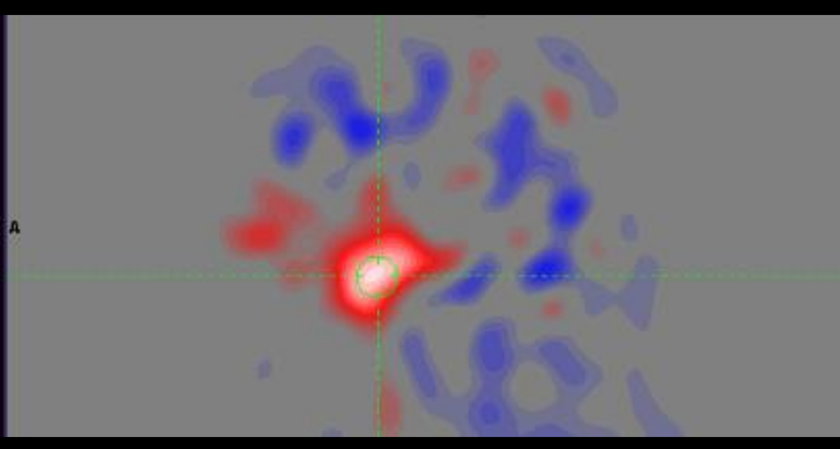
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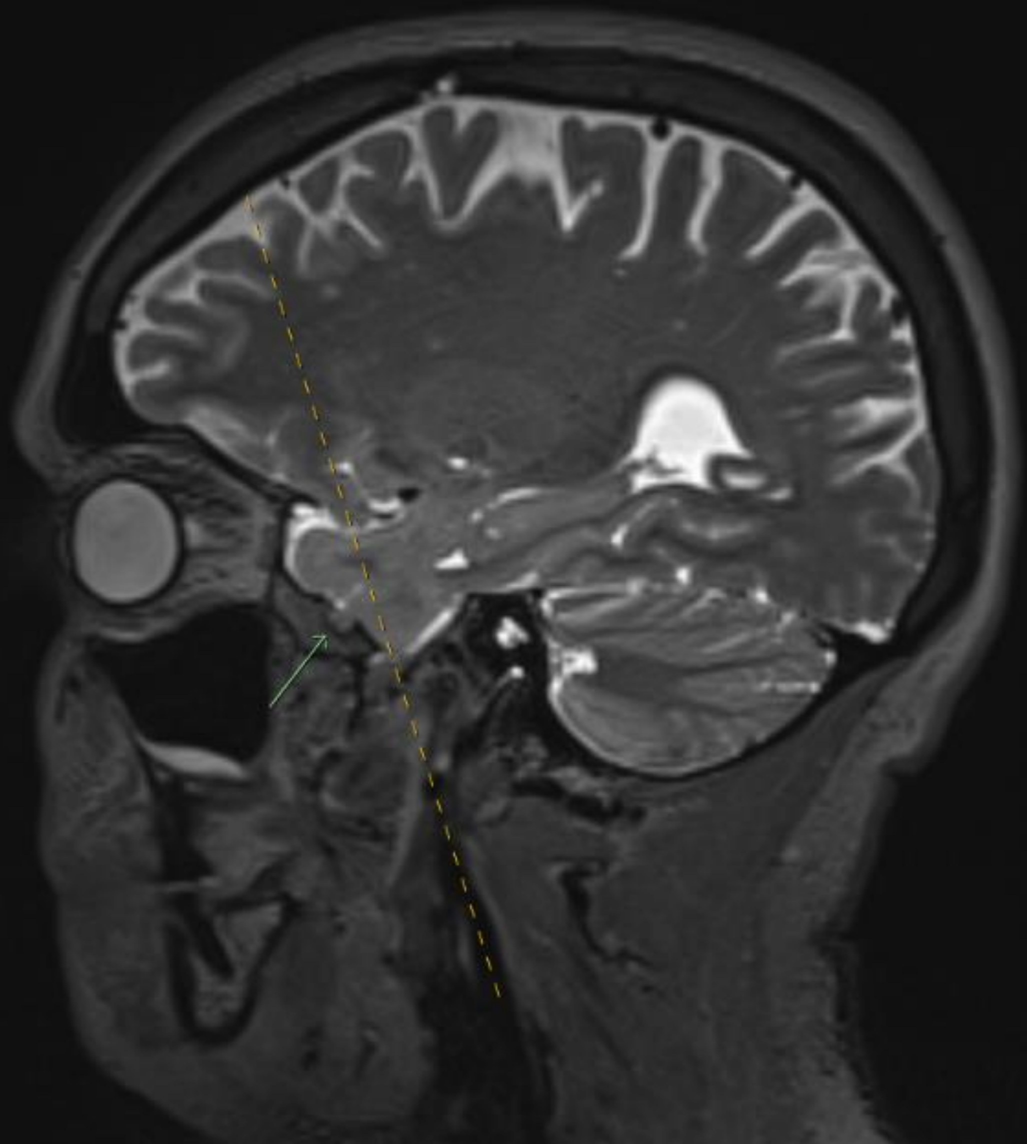
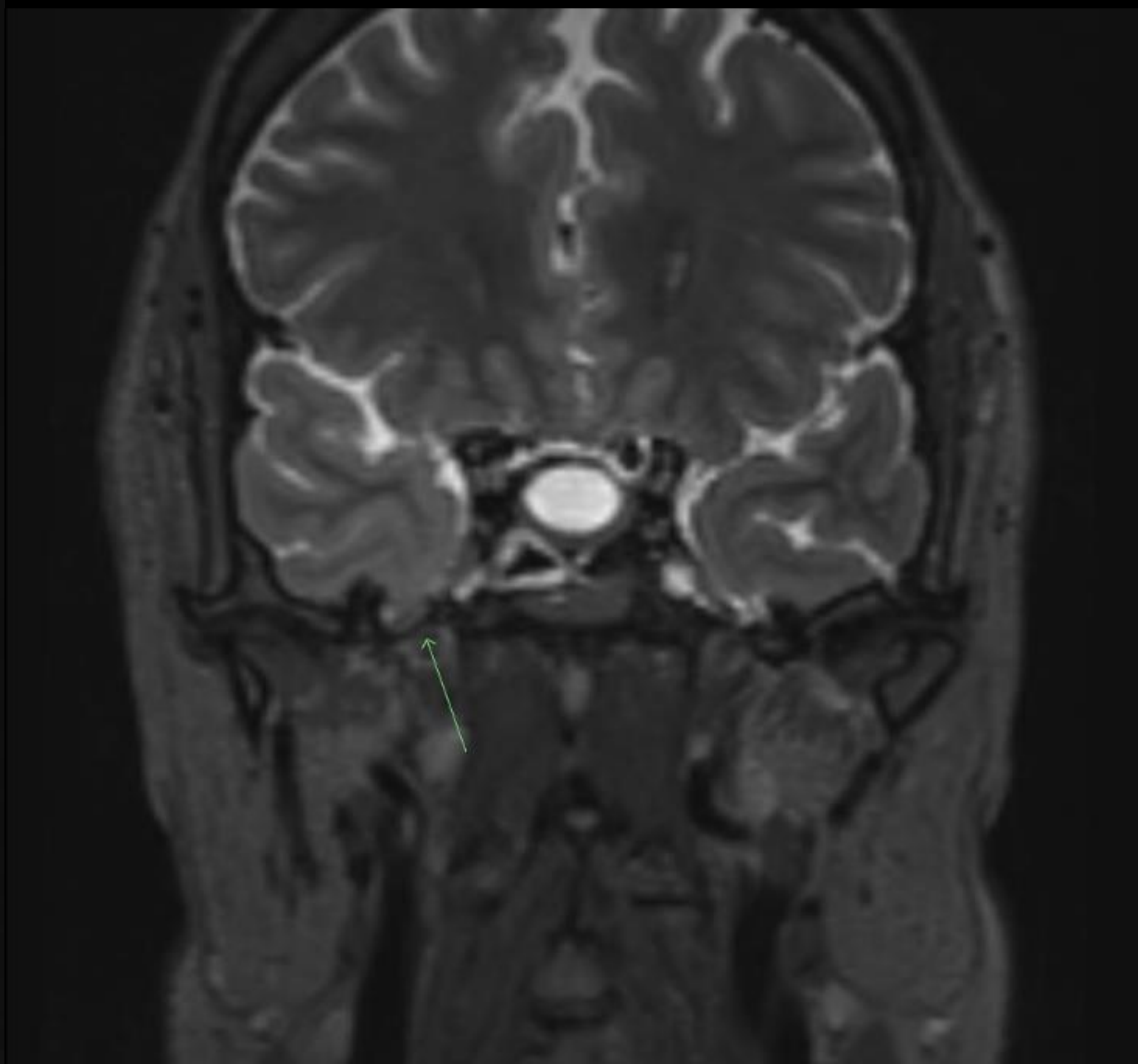
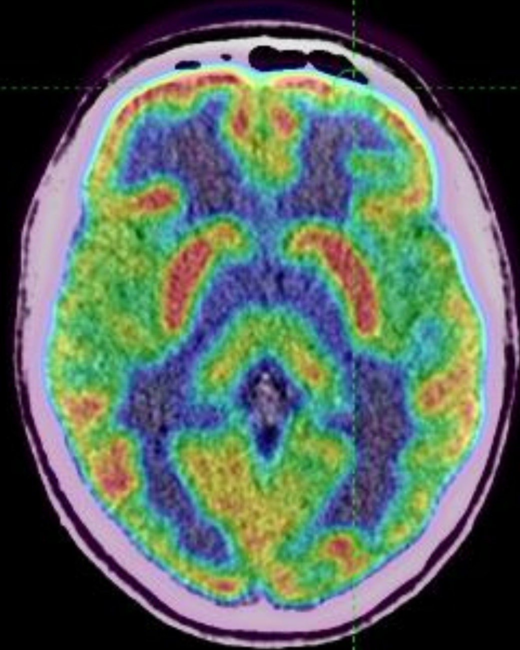




Case 4

- 26-year-old man. No risk factors for epilepsy.
  - Onset of seizures in childhood, well managed with Carbamazepine.
  - Re-emerged in early adulthood.
- Mostly nocturnal events. Eyes open, stiffening of trunk and limbs, vocalisation, inconsistent lower limb movements. Frequency of 1-3 every night; daytime events ~monthly.
- Medications: OXC 600/900, TOP 100/200, Clonazepam 3mg nocte
- Routine EEG x2 – normal; MRI x2 – normal



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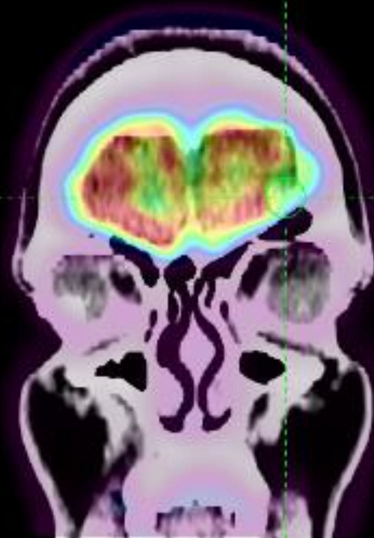

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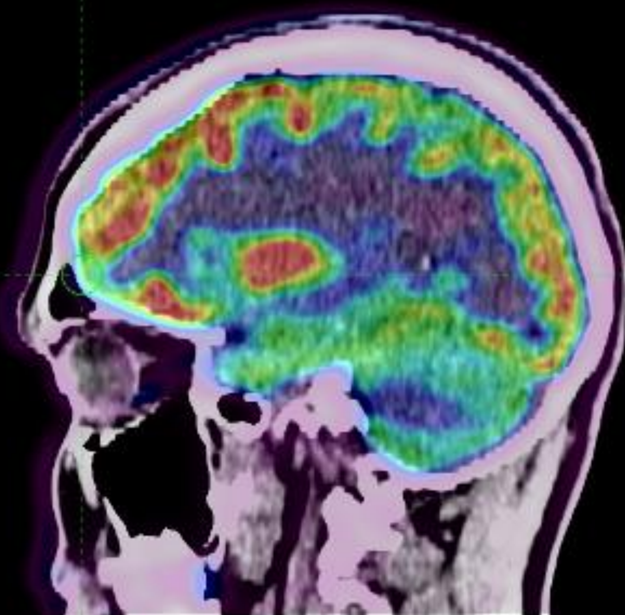

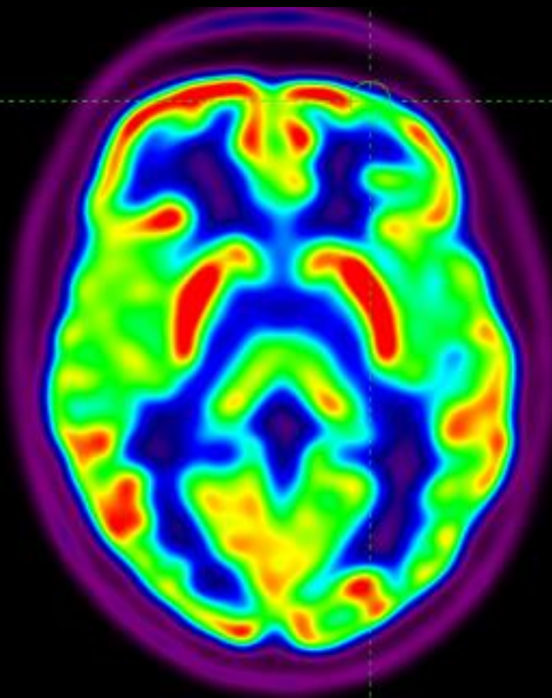

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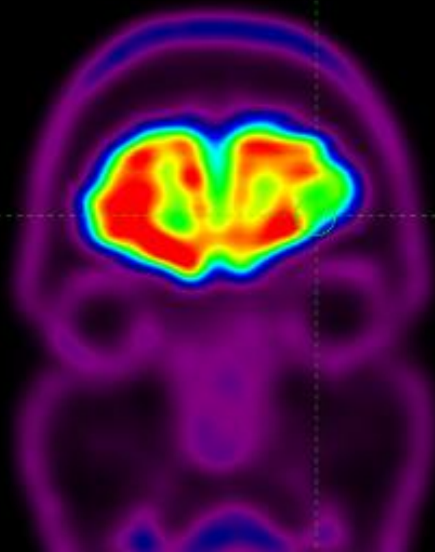

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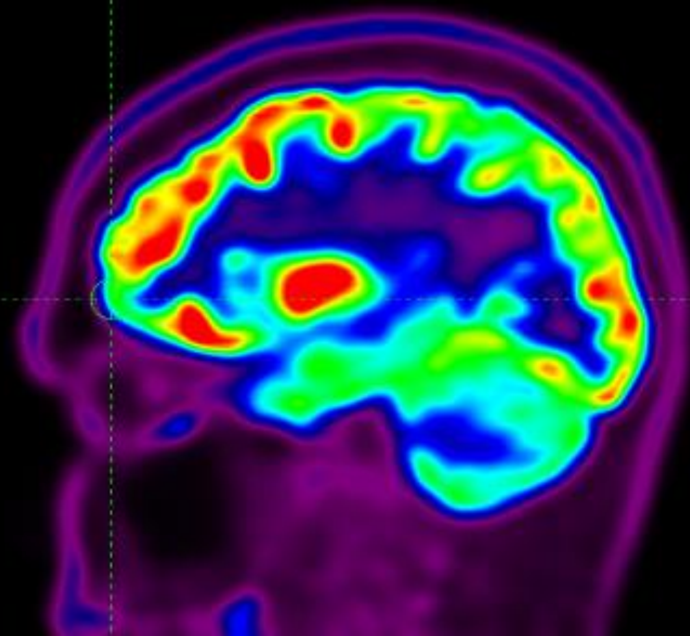

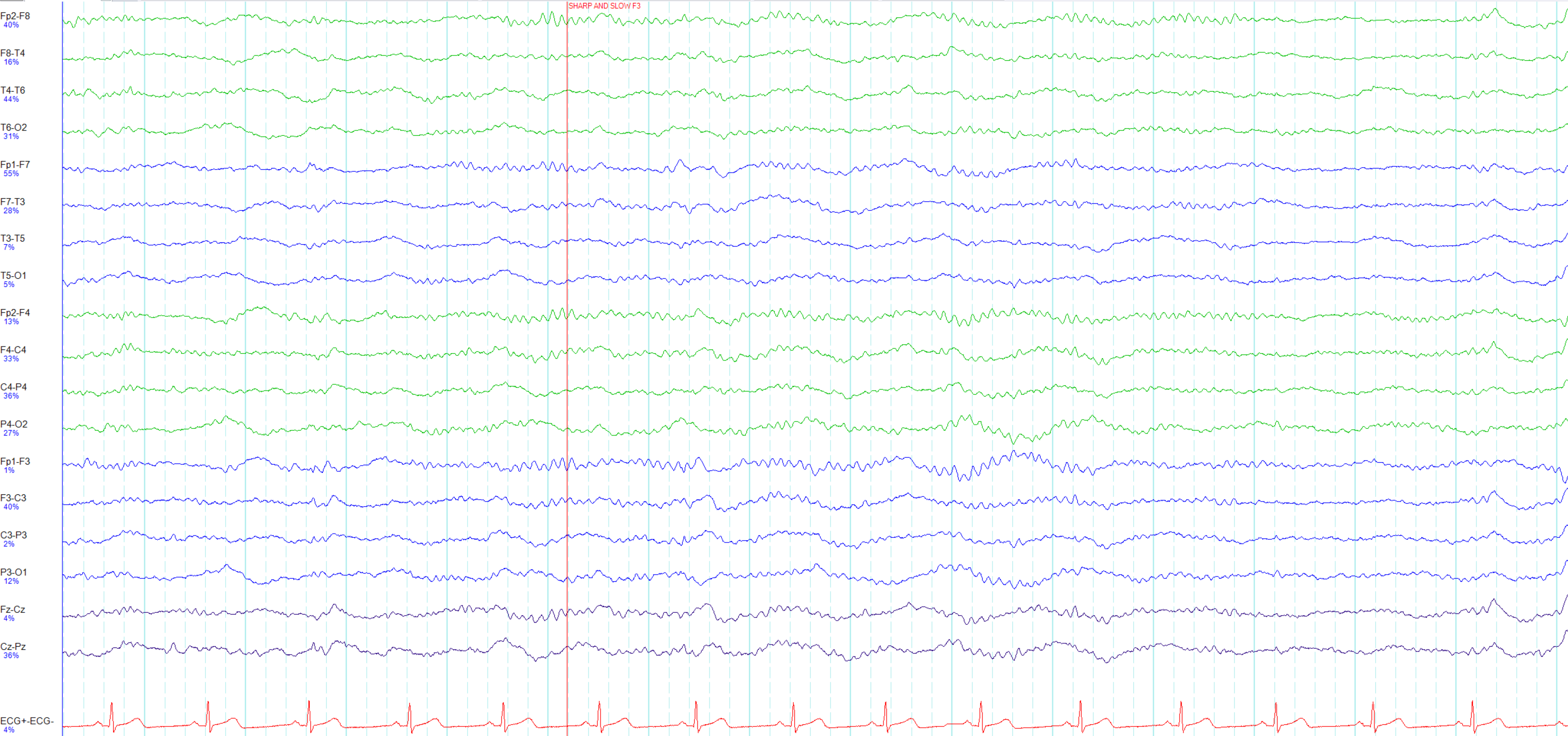

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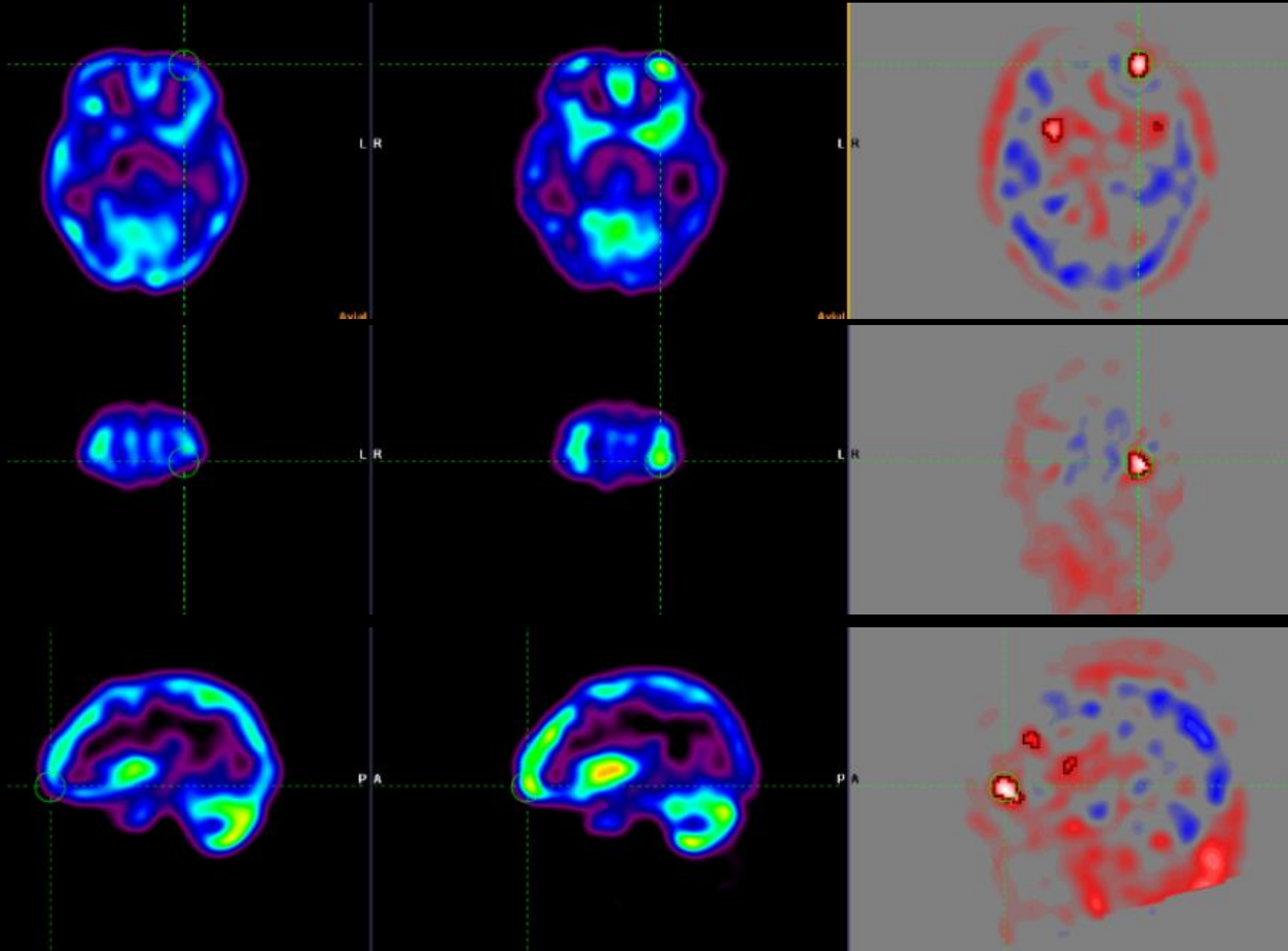

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