UW Nuclear Medicine Clinical Case Conference – DS1226
CME Disclosure Statement

I, Dr. Irene Cruite have no financial relationships to disclose.

Epilepsy

Aims

- Outline the classification of seizures including epilepsy syndromes amenable to surgery
- Discuss determination of surgical candidacy and surgical planning
- Discuss the role of radionuclide functional imaging with SPECT and PET with respect to the ictal onset zone, seizure propagation pathways, functional deficit zone

Epilepsy - Introduction

- Chronic neurological disorder in 3% population.
  - Excessive abnormally synchronized neuronal activity affecting small or large neuronal networks
  - Results in sudden, transient, clinical manifestations
- After the first seizure, 80% of patients experience another seizure within 3 years.
- 60-70% of patients experience focal or partial seizures, 30-40% generalized seizures.
- Controlled with antiepileptics in 70% of cases.

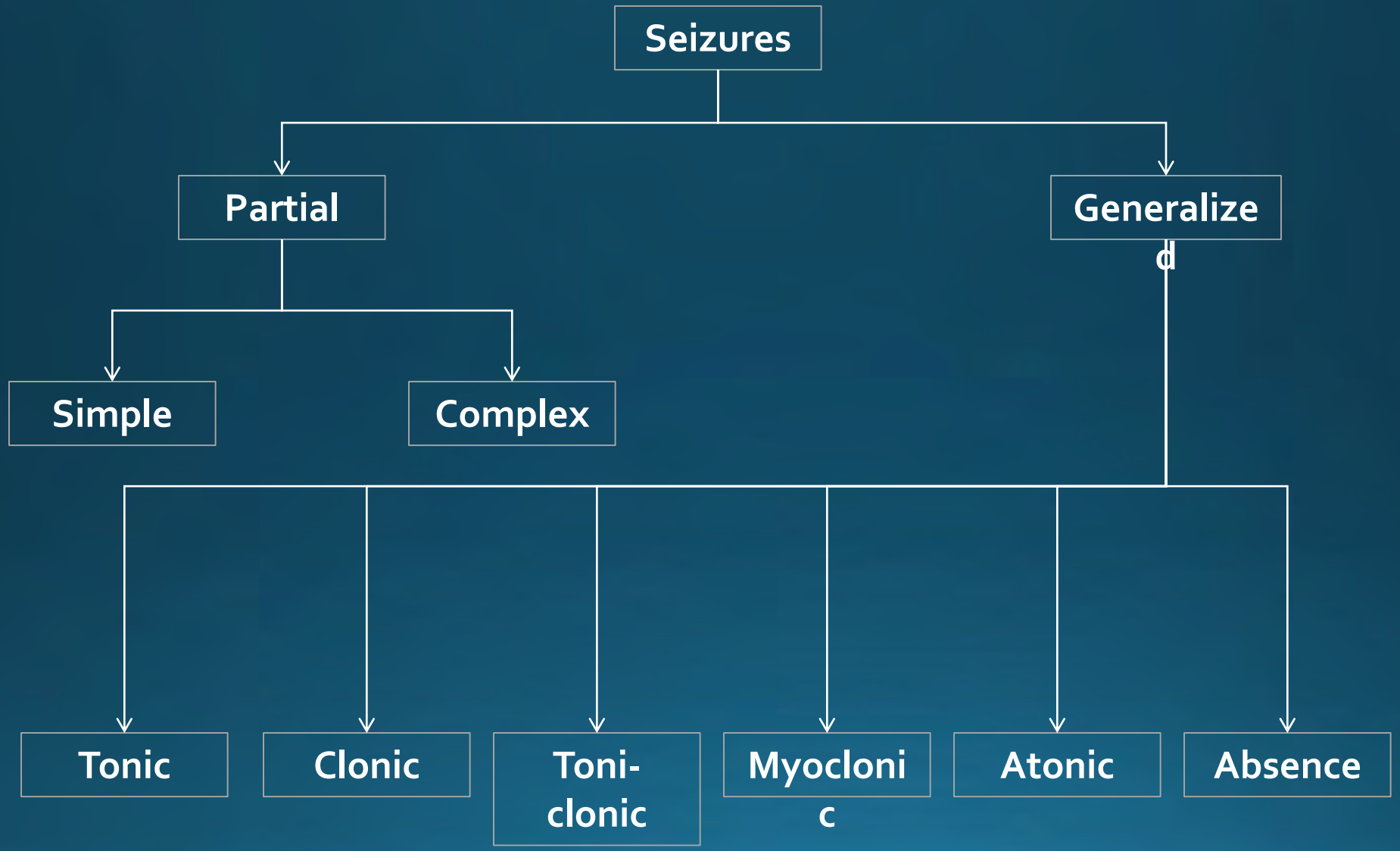
Epilepsy - Introduction

- Resection of epileptogenic cortex is considered when seizures refractory despite medical treatment.
- Nuclear medicine role is important in presurgical assessment of such patients.

Classification of Seizures

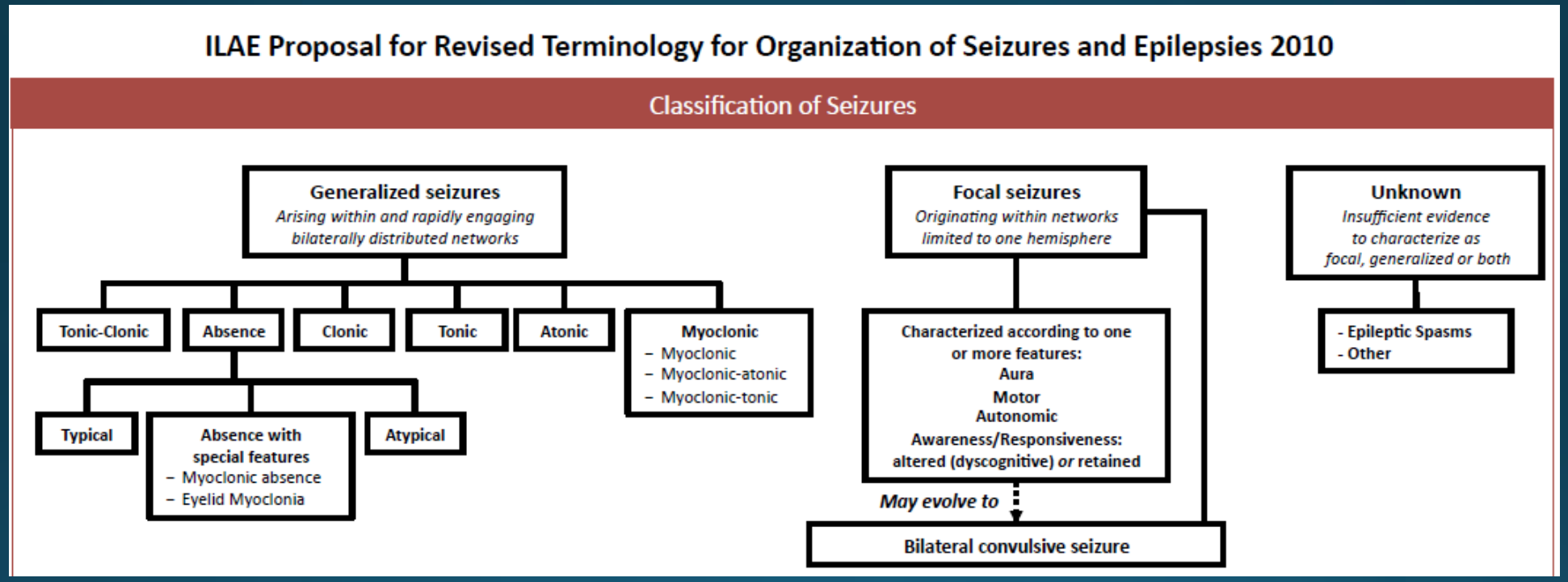
- May be based on various criteria.
- 1981 International League Against Epilepsy (ILAE) classification dichotomizes seizures into generalized and partial based on electroclinical features.

Classification of Seizures



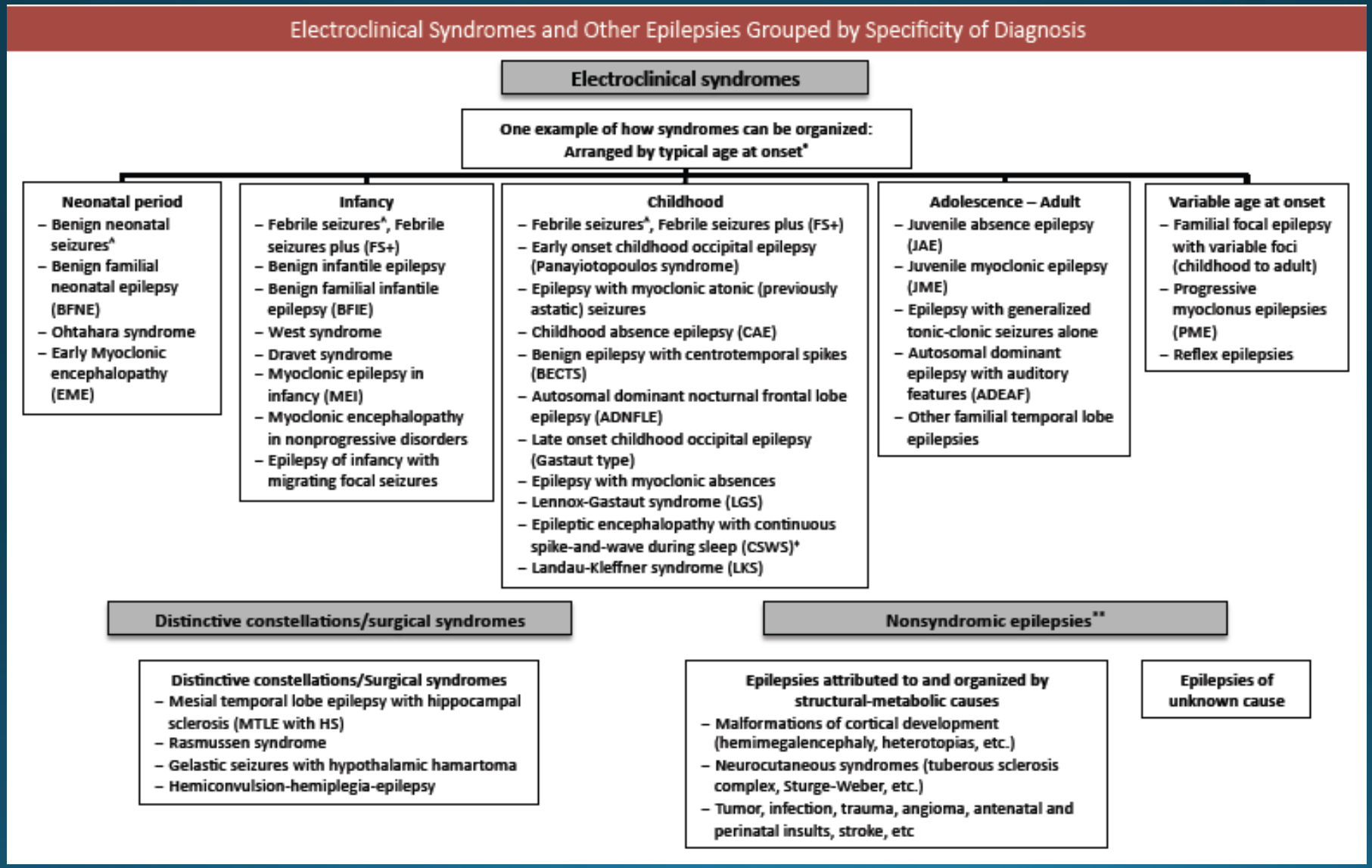
The 1981 International League Against Epilepsy classification.

Classification of Seizures



http://www.ilae.org/Visitors/Centre/ctf/documents/ILAEHandoutV10_000.pdf

Classification of Seizures



http://www.ilae.org/Visitors/Centre/ctf/documents/ILAEHandoutV10_000.pdf

Classification of Seizures

Syndrome	Remedy
Tuberous sclerosis	Surgery may be curative
Neurofibromatosis Type I	Surgery has no role
Sturge-Weber syndrome	Early surgery
Polymicrogyria	Surgical resection if well localized
Hemimegalencephaly	Surgery usually curative
Schizencephaly	Surgery usually difficult
Focal cortical dysplasia	Surgery in certain cases
Cortical migration abnormalities (agyria, pachygyria, lissenchephaly, subcortical band heterotopia)	Surgery generally not indicated
Periventricular nodular heterotopia	Surgery in isolated lesions
Acquired lesions	Surgery may be considered

Classification of Seizures

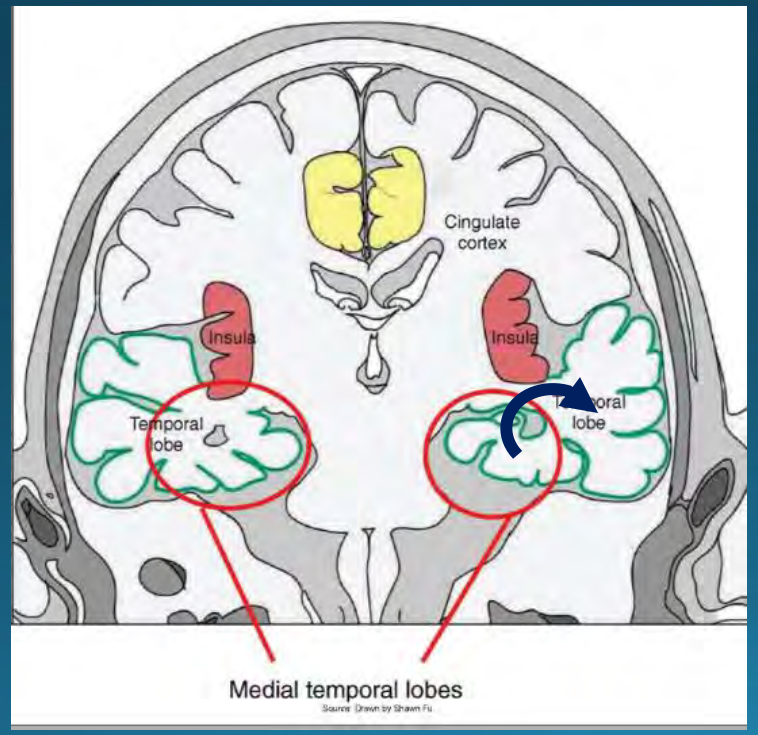
- Mesial temporal lobe epilepsy
  - Temporal lobe is a common location of seizure onset in adults, especially the medial temporal lobe (hippocampus).
  - It is also the seizure location most amenable to surgical cure.
  - Associated with childhood febrile convulsions.
  - Febrile convulsions, especially if prolonged or complex, damage the hippocampus with neuronal cell loss and gliosis (sclerosis).

Epilepsy – Seizure Propagation

- Although seizures arising in each region have characteristic clinical features, clinical seizure semiology/manifestation not always accurate:
  - Many epileptic symptoms are nonspecific.
  - Seizures arising in one cortical area rapidly spread to another.

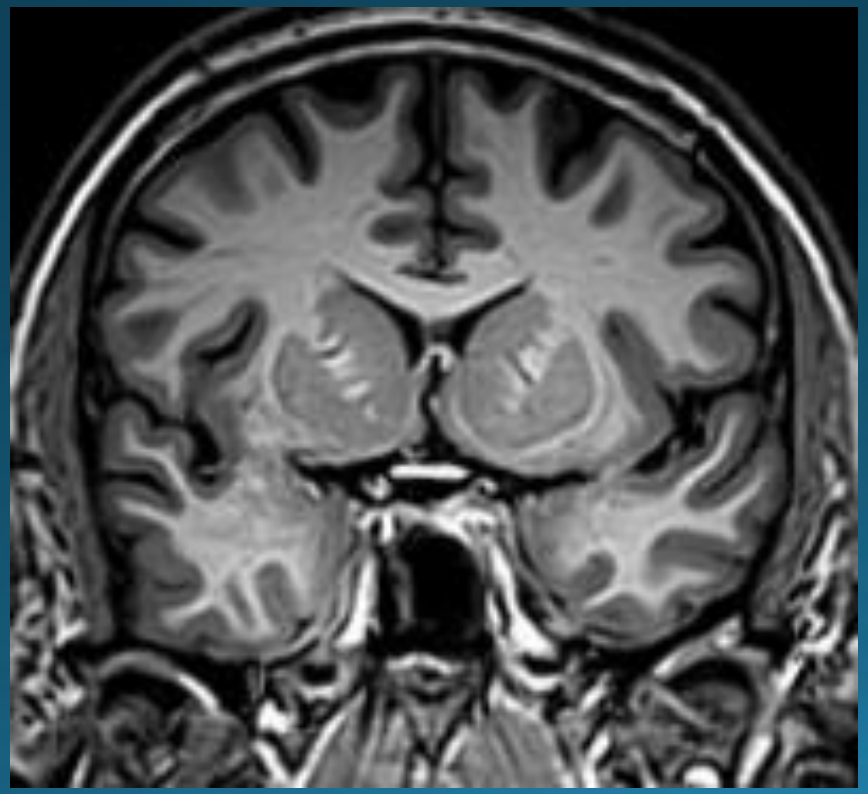
Epilepsy – Seizure Propagation

- Overlap of clinical and EEG changes associated with mesial temporal lobe and lateral temporal lobe seizures due to rapid spread of epileptiform discharges between the two areas.



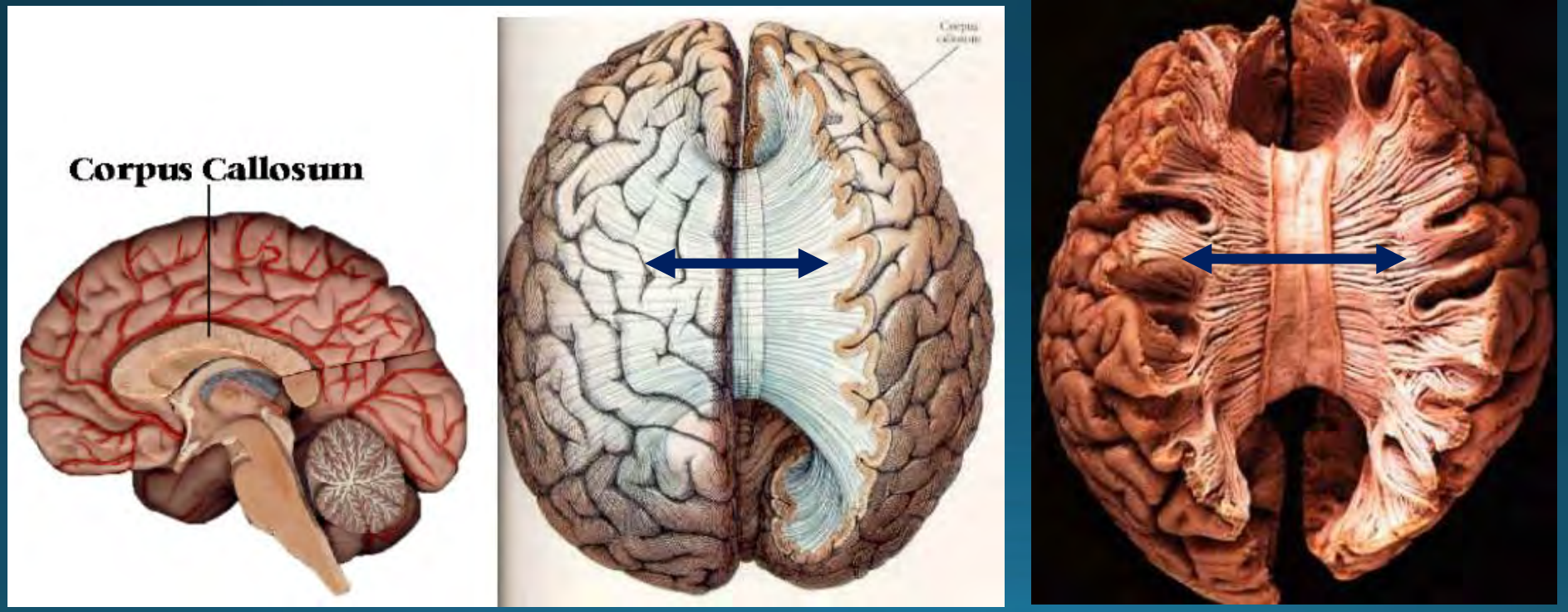
Epilepsy – Seizure Propagation

- Frontal lobe seizures may be mistaken for those arising in the temporal lobe owing to rapid spread of discharges between the 2 sites.



Epilepsy – Seizure Propagation

- Epileptiform discharges may rapidly spread from one hemisphere to the contralateral onevia corpus callosum.



Epilepsy - Management

Seizure

Epilepsy diagnosis

Medication trials

Imaging for pathology

CT
MRI

Medical intractability

Surgical Consideration

Surgical workup

Surgery

CT, MRI
Ictal/Inter-ictal SPECT
Inter-ictal FDG PET

Epilepsy – Surgical Candidacy

- Important concepts:
  - Epileptogenic lesion – anatomic lesion on imaging.
    - Should be resected for seizure freedom.
  - Epileptogenic zone – produces seizures.
    - Should be resected for seizure freedom.
  - Symptomatogenic zone – produces clinical symptoms.
    - Resection not necessary for seizure freedom.

Epilepsy – Surgical Candidacy

- Important concepts:
  - Irritative zone – produces inter-ictal symptoms.
    - Resection not necessary. Contains epileptogenic zone.
  - Ictal onset zone – origin of seizures on ictal EEG.
  - Functional deficit zone - abnormal function interictally
    - hypometabolic on functional imaging; larger than epileptogenic zone.

Epilepsy

Table 1 Important Concepts in Epilepsy Surgery

Term	Definition	Localization
Epileptogenic lesion	An anatomic abnormality visible on imaging, which is able to produce seizures, and should be included in the resection to achieve seizure freedom.	MRI
Epileptogenic zone	The area responsible for the generation of focal seizures. Its removal is necessary and sufficient to achieve seizure freedom. It usually includes, but can be larger than, the epileptogenic lesion.	Concordance of overall data
Symptomatogenic zone	The area necessary to produce clinical symptoms, but whose removal is not necessary for seizure freedom.	History and physical exam
Irritative zone	The area involved in generating interictal discharges, but whose resection is not necessary for seizure freedom. It usually contains the epileptogenic zone.	Interictal EEG
Ictal onset zone	The area from which seizures originate on ictal EEG.	Ictal EEG (noninvasive and/or invasive)
Functional deficit zone	An area showing hypometabolism on functional imaging, usually much larger than the epileptogenic zone.	PET

Pre-surgical Assessment

- Surgery has best results if the cortical zones are concordant on different studies, provided there is no overlap with eloquent cortex for complete resection of epileptic zone.
-
- 60-90% of patients with unilateral TLE and 70% of patients with a focal cortical malformation are seizure free after surgery.

Pre-surgical Assessment

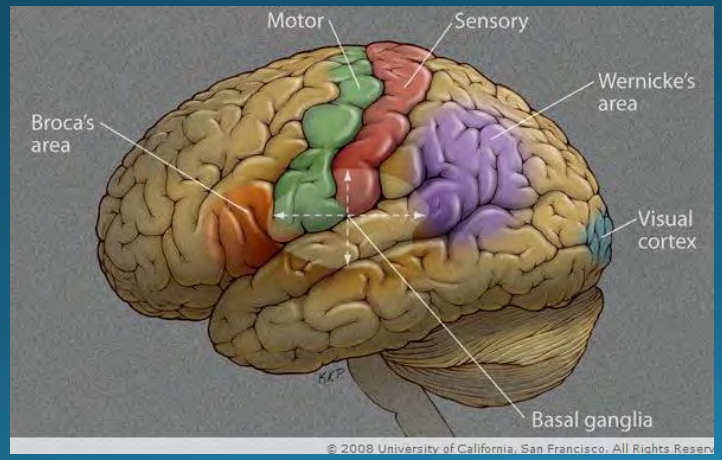
- Some investigations can be considered mandatory whereas others are supplementary when localization is difficult.
- There are no evidence-based guidelines regarding course of investigations.
- Most important is to have concordance - multiple investigations implying the same region of brain as the epileptogenic zone.

Pre-surgical Assessment

- Pre-surgical assessment encompasses:
  - complete seizure history
  - physical and neurological examination
  - scalp electroencephalography (EEG)
  - High-resolution brain MRI
- Complimentary tests include:
  - video-EEG monitoring,
  - interictal and ictal EEG
  - Ictal SPECT
  - Interictal PET
  - neuropsychological examination

Pre-surgical Assessment

- Goals of presurgical evaluation:
  - Determine if single epileptogenic focus
  - Lateralize and locate epileptogenic zone
  - Localize functional areas of the brain if indicated
  - Determine epileptogenic focus is not in "eloquent" cortex and can therefore be resected without causing an unacceptable neurological deficit.



Pre-surgical Assessment

- Pre surgical assessment can be achieved using noninvasive modalities in 85% of patients; 15% require invasive intracranial modalities.

Pre-surgical Assessment

- Clinical history on seizure semiology for seizure localization.
  - Ictal and postictal neurologic features may not indicate the area of initial seizure onset in all cases.
  - Clinical features only arise once electrical activity generated by an epileptogenic zone (usually silent) propagates to symptomatogenic zone.
  - Symptomatogenic zone may be remote from the site of seizure onset.

Pre-surgical Assessment

- Interictal EEG
  - Demonstrates epileptiform activity generated by the irritative zone.
  - May provide information on lateralization and localization of epileptogenic zone, as it theoretically resides within the irritative zone.
- Prolonged ictal video EEG
  - For identification of the ictal onset zone.

Pre-surgical Assessment

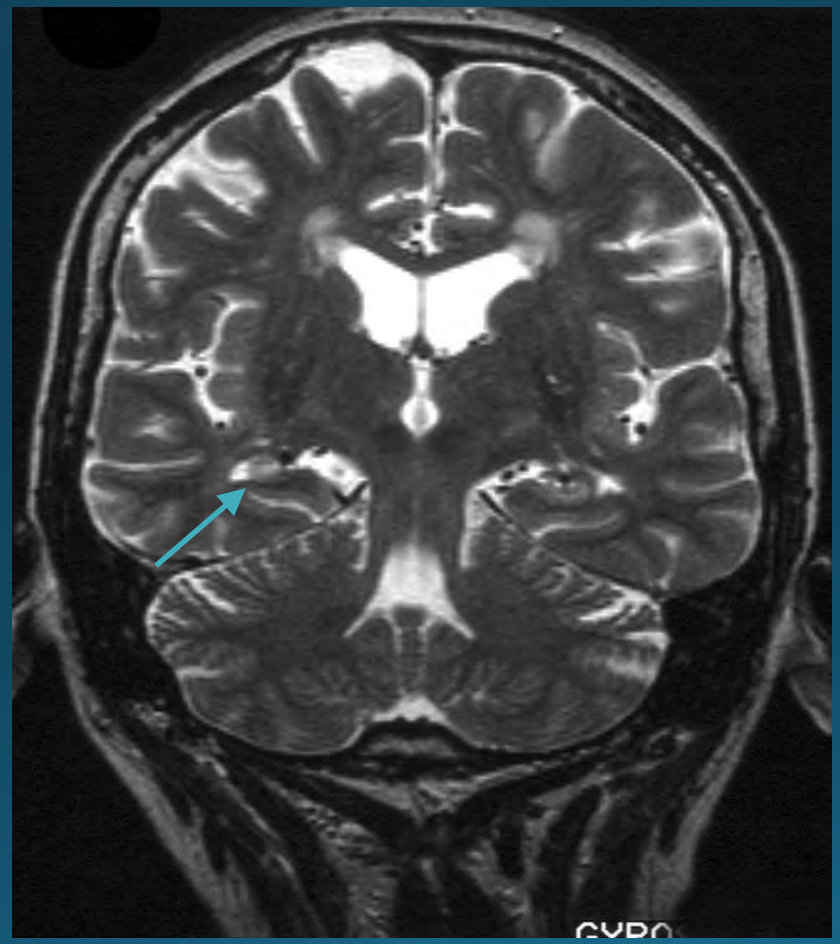
- Challenges in using EEG:
  - In deeply situated seizure focus, EEG may not capture the true ictal onset.
  - In some patients, the ictal onset is characterized by a bilateral pattern, and lateralization is not possible.

- Hence need for other investigations, including advanced imaging modalities and perhaps also a period of invasive EEG monitoring.

Pre-surgical Assessment - MRI

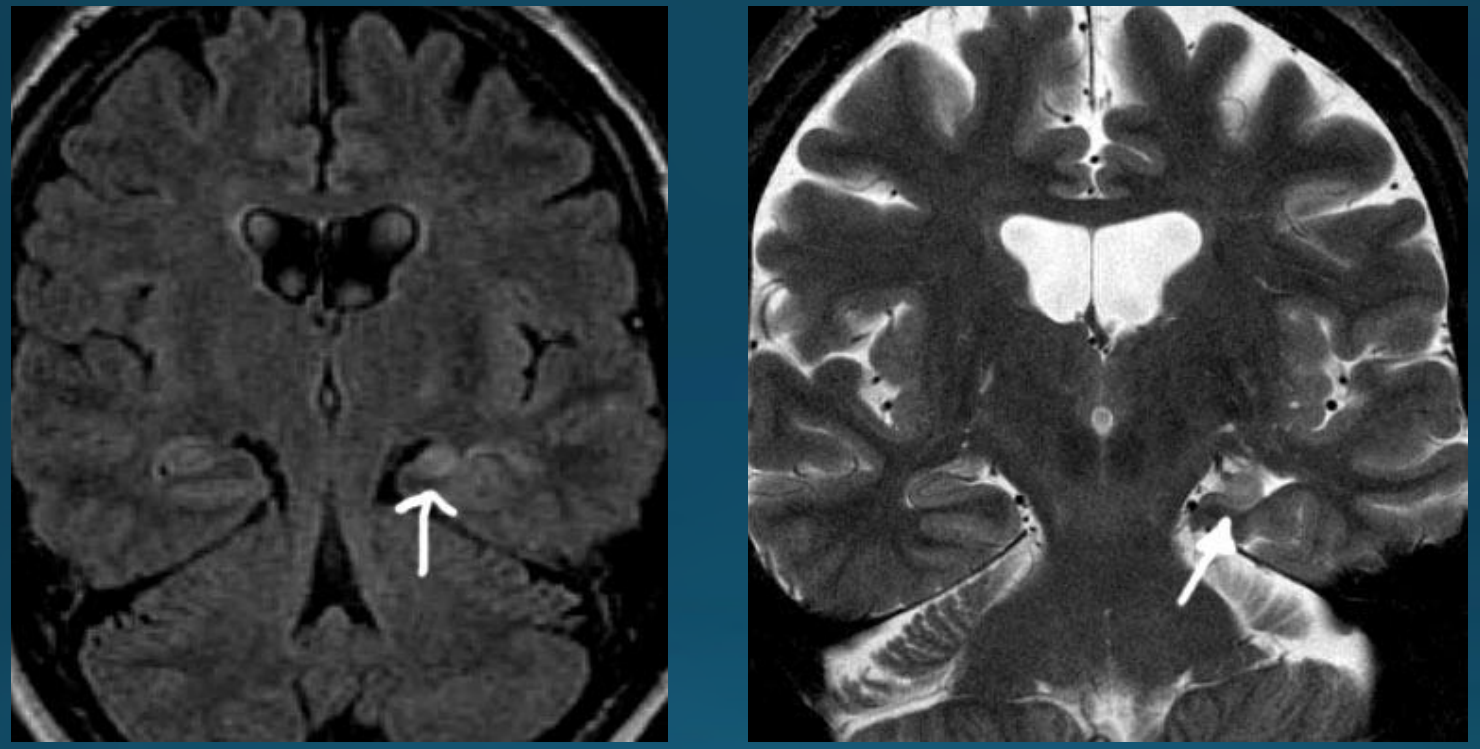
- Focal epileptogenic lesion on MRI increases chance of surgical cure.
- Lateralizes TLE in 80%-90% of cases
- TLE - hippocampal atrophy and increased T2 signal correlate with pathological evidence of hippocampal/mesial temporal sclerosis (neuronal loss and gliosis); 80% chance of seizure freedom after temporal lobectomy.

Pre-surgical Assessment - MRI



Right hippocampal sclerosis (arrow)

Pre-surgical Assessment - MRI



Left mesiotemporal sclerosis (arrows)

Pre-surgical Assessment - MRI

- MRI may also show
  - Tumors.
  - vascular malformations - AVMs or cavernous malformations.
  - cortical dysplasia - gray matter heterotopias, cortical thickening, and blurring of normal gray-white junction.

- MRS

Pre-Surgical Assessment - Functional Imaging with PET

- Measures brain metabolism/distribution of certain receptors.
- Interictal FDG PET shows hypometabolism in epileptogenic zone (localization of the epileptogenic focus).
- Ictal PET is not practical due to extremely short half life of PET radiotracers.

Pre-Surgical Assessment - Functional Imaging with PET

- PET is of assistance in:
  - MRI-negative TLE
  - Non-lesional neocortical epilepsy cases for general localization
  - Extra-temporal epilepsy
  - Guiding intracranial electrode placement

- PET cannot be used to refine surgical borders.

Pre-Surgical Assessment - Functional Imaging with PET

- Automated analysis and quantification is especially useful in extratemporal epilepsy.
- Sensitivity increases with use of 3-dimensional stereotactic surface projections (3-D SSP) instead of visual assessment.

Pre-Surgical Assessment - Functional Imaging with PET

- Localization accuracy is greatest in patients with neocortical TLE.
  - Hypometabolism ipsilateral to seizure focus is present in 60 to 90% of patients including those without a focal lesion on MRI.
- In extratemporal epilepsy, detection rate of hypometabolism relevant to the focus is in 67% of patients.

Pre-Surgical Assessment - Functional Imaging with PET

- **Surgical Outcomes. In TLE:**
  - unilateral temporal hypometabolism correlates with a better surgical outcome than extended hypometabolism.
  - >75% of patients with TLE and ipsilateral hypometabolism are seizure free after surgery.
  - 45% of patients with ipsilateral extratemporal cortical hypometabolism are seizure free after surgery.
  - 20% of patients with hypometabolism in contralateral cerebral cortex are seizure free after surgery.

Epilepsy – Functional Imaging PET

- Hypometabolic areas often extend beyond the epileptogenic zone - functional deficit zone.
  - Reflect neuronal activity at the site of ictal onset and in areas of ictal spread and postictal depression.

- Cause of inter-ictal hypometabolism is unclear:
  - Effects of repeated seizures on the brain.
  - Reflection of underlying pathologic process.
  - Sequela of an initial insult eg. early status epilepticus.

Pre-Surgical Assessment - Functional Imaging with PET

- Hypometabolism on FDG-PET has specifically been ascribed to:
  - neuronal loss
  - diaschisis
  - inhibitory processes
  - reduction in synaptic density
  - decreased BBB glucose transporter activity.
- Possible synaptic mechanisms are what contribute to hypometabolism.

Epilepsy – Functional Imaging SPECT

- Utilizes blood flow radiotracers that bind on first-pass through the brain - brain perfusion snapshot at injection time.
- Tracer stable for several hrs - delayed imaging.
- Ictal SPECT – hyperperfusion at seizure onset site
  - most useful study for presurgical evaluation.
- Interictal SPECT - hypoperfusion at the site of seizure onset.

Epilepsy – Functional Imaging SPECT

- SPECT localizes seizure foci if performed ictally.
  - Increased blood flow ictally with decreased blood flow inter-ictally in epiloptogenic area.
  - In complex partial seizures, seizure focus is identified in 71-93% of ictal SPECT with 95% PPV and
    in 40-58% of inter-ictal SPECT with 80-87% PPV.
- Increased blood flow is an autoregulatory response to local neuronal hyperactivity.
- Accuracy is greatest when ictal perfusion images are compared to interictal perfusion images.

Epilepsy – Functional Imaging SPECT

- SPECT Brain perfusion radiopharmaceuticals:
  - 99mTc ECD, Neurolite
    - Rapid blood clearance thus high brain to soft tissue contrast early after injection and with time.
    - Chemically stable for 6 hours thus can be used for episodic seizures.
  - 99mTc HMPAO, Ceretec
    - Rapid brain uptake, maximal within 10 mins, distribution constant over may hours.
    - Chemically unstable in vitro 30 mins after preparation.
  - 133Xe inert gas
  - 123I (IMP, Spectamine)

Ictal and Interictal Perfusion SPECT Imaging

- Ictal brain perfusion images display both ictal onset zone and areas of seizure propagation.
- When interpreting ictal perfusion images, must be aware of:
  - Seizure propagation patterns
  - time of tracer injection relative to start of seizure
  - type of seizure, and
  - ictal EEG recording.

Ictal and Interictal Perfusion SPECT Imaging

- For example, patients with TLE, seizure activity may propagate to the contralateral temporal lobe, and ipsilateral insula, basal ganglia, and frontal lobe and parieto-occipital region may occur.

Ictal and Interictal Perfusion SPECT Imaging

- Early tracer injection after beginning of seizure is therefore very important.
- Injection delay of <20 secs is significantly correlated with a correct localization.
- With early injections, the largest and most intense cluster is more likely to represent the seizure onset zone, and not seizure propagation.

Ictal and Interictal Perfusion SPECT Imaging

- Perfusion changes after the termination of a seizure can be assessed by injection of the tracer in the early postictal (1-60 secs after seizure termination) or in the late postictal phase (1-10 mins after seizure termination).
- Postictal phase is characterized by a postictal switch, i.e., hyperperfusion at seizure onset zone switches to hypoperfusion.

Ictal and Interictal Perfusion SPECT Imaging

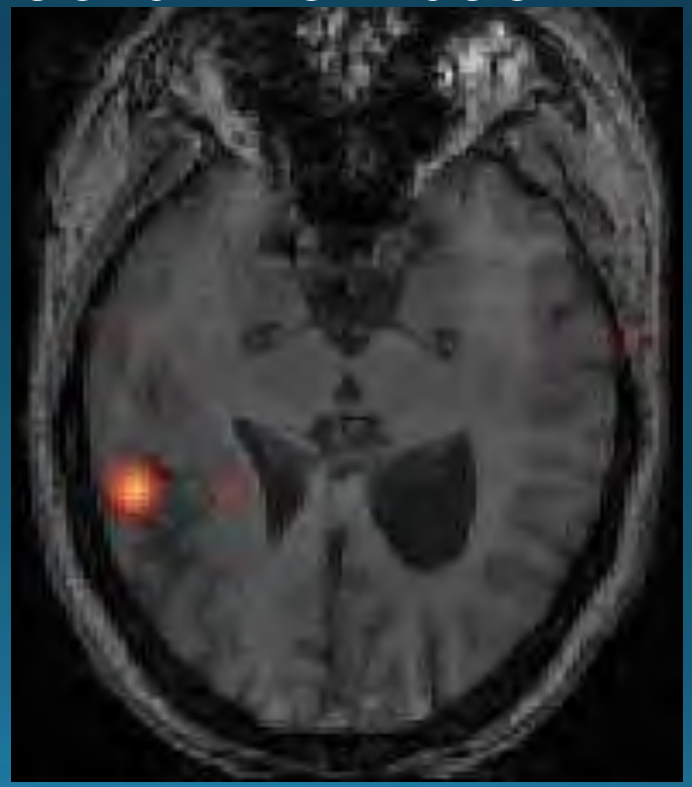
- Postictal switch occurs about 60 seconds after the seizure termination.
- When tracer injection is performed in the first 100 seconds after the end of the seizure, there is still a hyperperfusion present in more than 60% of patients.
- When tracer injection is performed after the first 100 seconds after the end of the seizure, hypoperfusion is present in all patients.

Ictal and Interictal Perfusion SPECT Imaging

- In TLE, early postictal SPECT has a sensitivity of 75% (poor) in localizing the seizure onset zone based on either perfusion increases or decreases, often because changes are similar in multiple brain regions.
- Interictal SPECT perfusion imaging on its own is inefficient in localizing the seizure onset zone and should only be used as a baseline perfusion measure in the comparison of ictal perfusion images.

Epilepsy – Functional Imaging SPECT

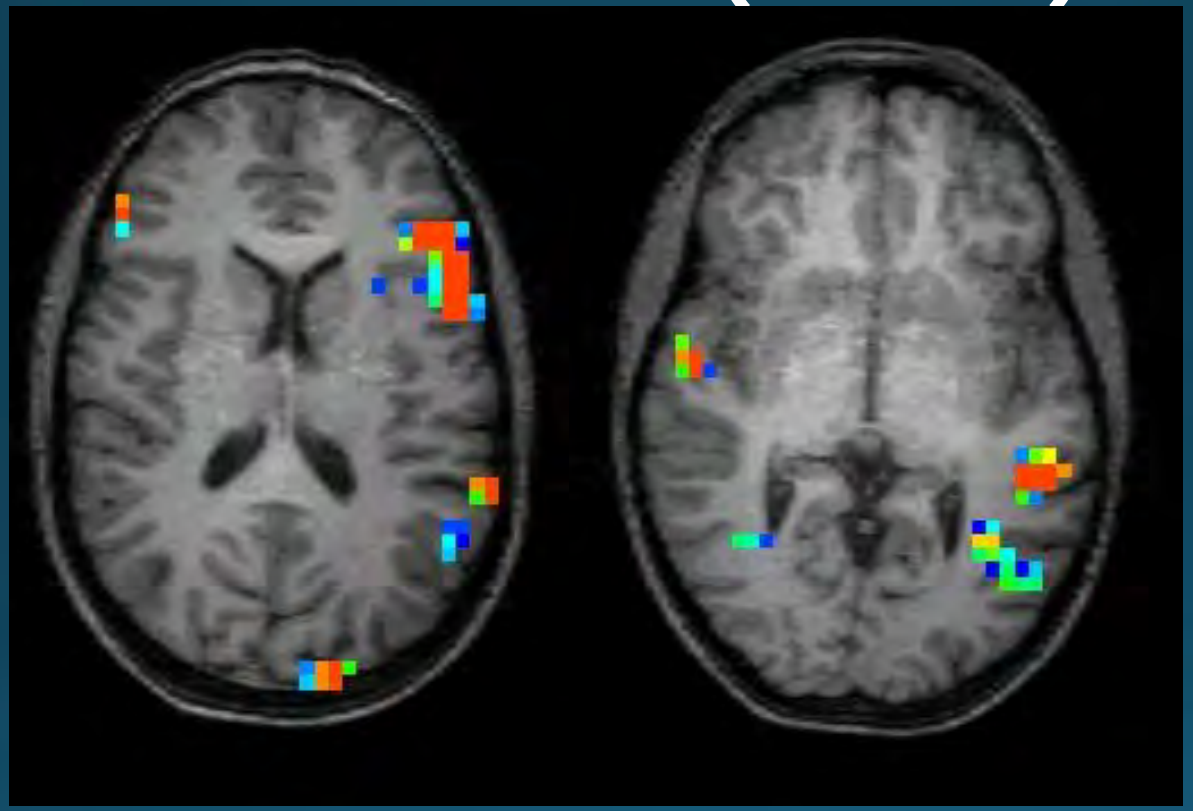
- Comparing ictal and interictal studies with quantitative subtraction and co-registration of the subtraction images with MRI can add additional information.



Epilepsy – Functional Imaging Functional MRI (FMRI)

- Used for non-invasive motor, sensory and language mapping, and is most commonly used as part of surgical planning.
- Detects focal changes in blood flow and oxygenation levels that occur when an area of the brain is activated.
- Possible future applications include localizing epileptiform discharges or seizures (EEG/fMRI), and lateralizing memory function.

Epilepsy – Functional Imaging
Functional MRI (FMRI)



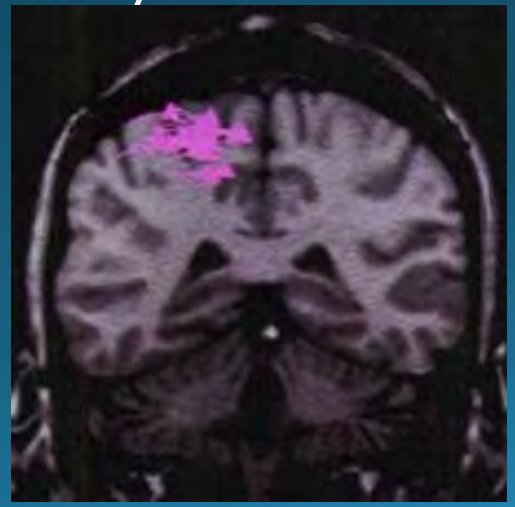
Patient with left temporal lobe epilepsy.
Left: Language mapping with verb generation task - activation in Broca's and Wernicke's areas.
Right: Memory localization with picture encoding task - decreased activation in the left hippocampus.

Epilepsy – Functional Imaging Magnetoencephalography (MEG)

- Relatively new diagnostic technique for localization of interictal epileptiform discharges.
- Similar to EEG, but it detects magnetic rather than electric signals from the brain.
- Complementary to EEG in normal scalp EEGs.
- Also for functional mapping and for evaluation of extratemporal, neocortical epilepsies.
- Concordance between MEG and intracranial monitoring positive predictive value for epilepsy surgery outcome.

Epilepsy – Functional Imaging Magnetoencephalography (MEG)

- fMRI has a good spatial resolution but poor temporal correlation.
- EEG provides timed waveforms (good temporal correlation) with poor localization.
- MEG jointly records function and signal, providing spatially and temporally correlated images.



Epilepsy – Additional Tests

- Visual fields
  - Formal testing if resection will endanger vision
- Intracarotid Amobarbital Procedure (Wada)
  - Language dominance
  - Verbal memory
  - Prediction of postoperative decline

Epilepsy – Additional Tests

- Phase II monitoring with intracranial electrodes if necessary
  - Subdural/depth electrodes
  - Identification of ictal onset and epileptogenic zone
  - Allows for cortical mapping if needed

- Cortical mapping
  - Intraoperative (phase III) or during phase II monitoring
  - Identification of eloquent areas of cortex

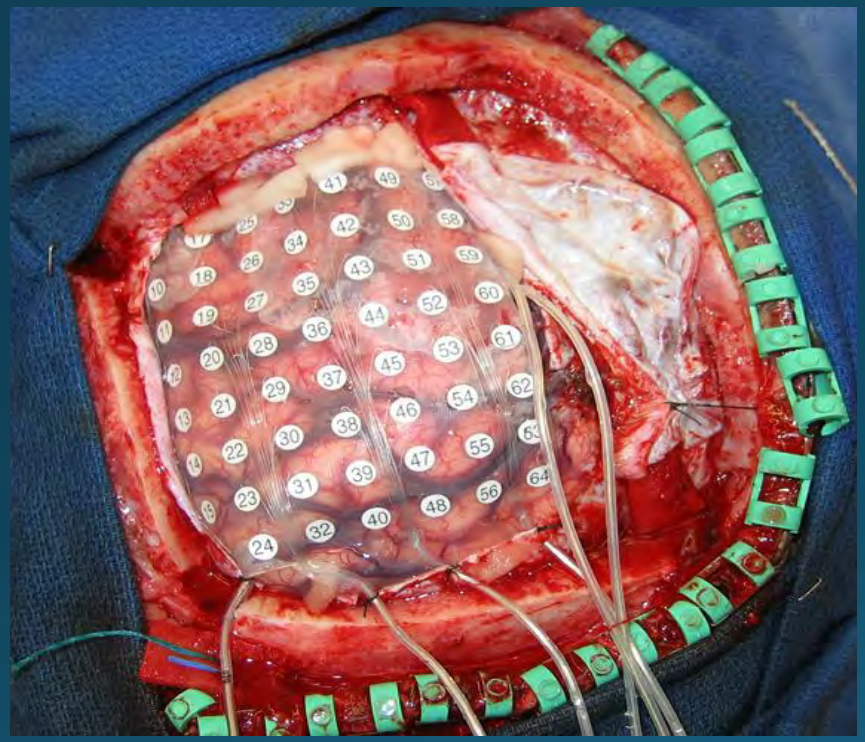
Epilepsy – Invasive Tests

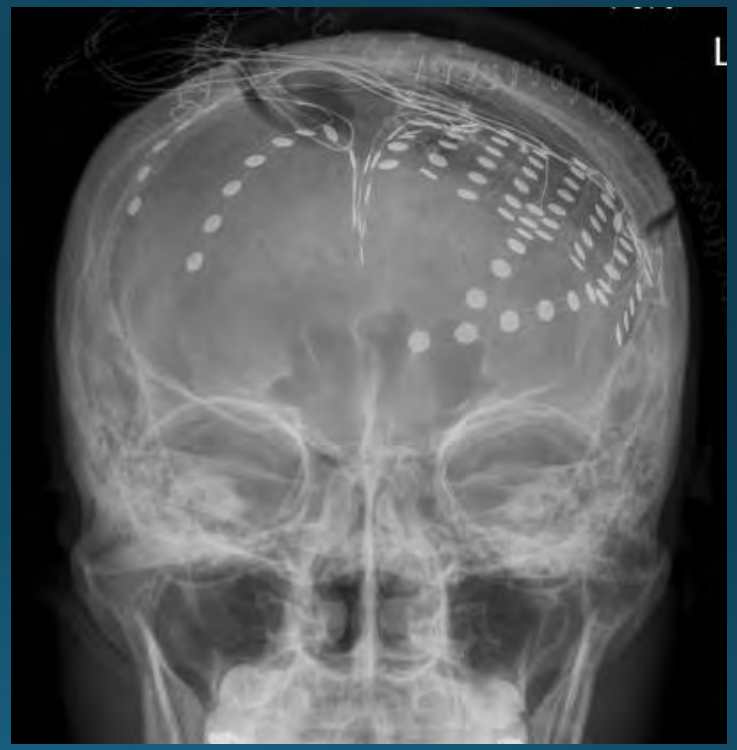
- If seizure focus cannot be adequately localized and safely resected based on the above studies, intracranial EEG may be necessary.
- Intracranial electrodes are inserted surgically and include
  - subdural (or less common epidural) strips or grids of electrodes, or
  - intraparenchymal "depth" electrodes
  - often do not localize epileptogenic area in cortical developmental disorders

Epilepsy – Invasive Tests

- Depth electrodes –
  - thin probes with electrodes along their length;
  - commonly used to record hippocampus.
- Intracranial electrodes, especially subdural grids, can also be used for cortical mapping via cortical stimulation and/or recording of evoked potentials.

Epilepsy – Invasive Tests





Subdural electrodes for intracranial monitoring

Epilepsy – Depth Electrodes

- Thin cables placed in the hippocampus, amygdala, and cingulate cortex via burr holes.
- Sometimes used to assess cortical dysplasias.
- Used primarily when medial temporal lobe epilepsy is suspected but cannot be reliably lateralized, and to distinguish medial from lateral (neocortical) temporal lobe seizure onset.

Epilepsy – Depth Electrodes

- May be used with subdural strip electrodes to record from the lateral temporal cortex as well.
- Disadvantage is limited spatial sampling (localization) - ? Are electrodes in the center of the epileptogenic zone and ?do the seizures really originate from the detected area.
- Concurrent scalp EEG is sometimes used to overcome this limitation.

Epilepsy – Subdural Electrodes

- Subdural electrodes - strips, grids or both.
- Used to record from the surface of the brain.
- Useful in localizing the epileptogenic zone and in mapping of cortical function.
- Require a craniotomy for placement.

UW Nuclear Medicine Clinical Case Conference – DS 1524
CME Disclosure Statement - 2015

I, Dr. Megan Zare have no financial relationships to disclose.

Planning Committee:

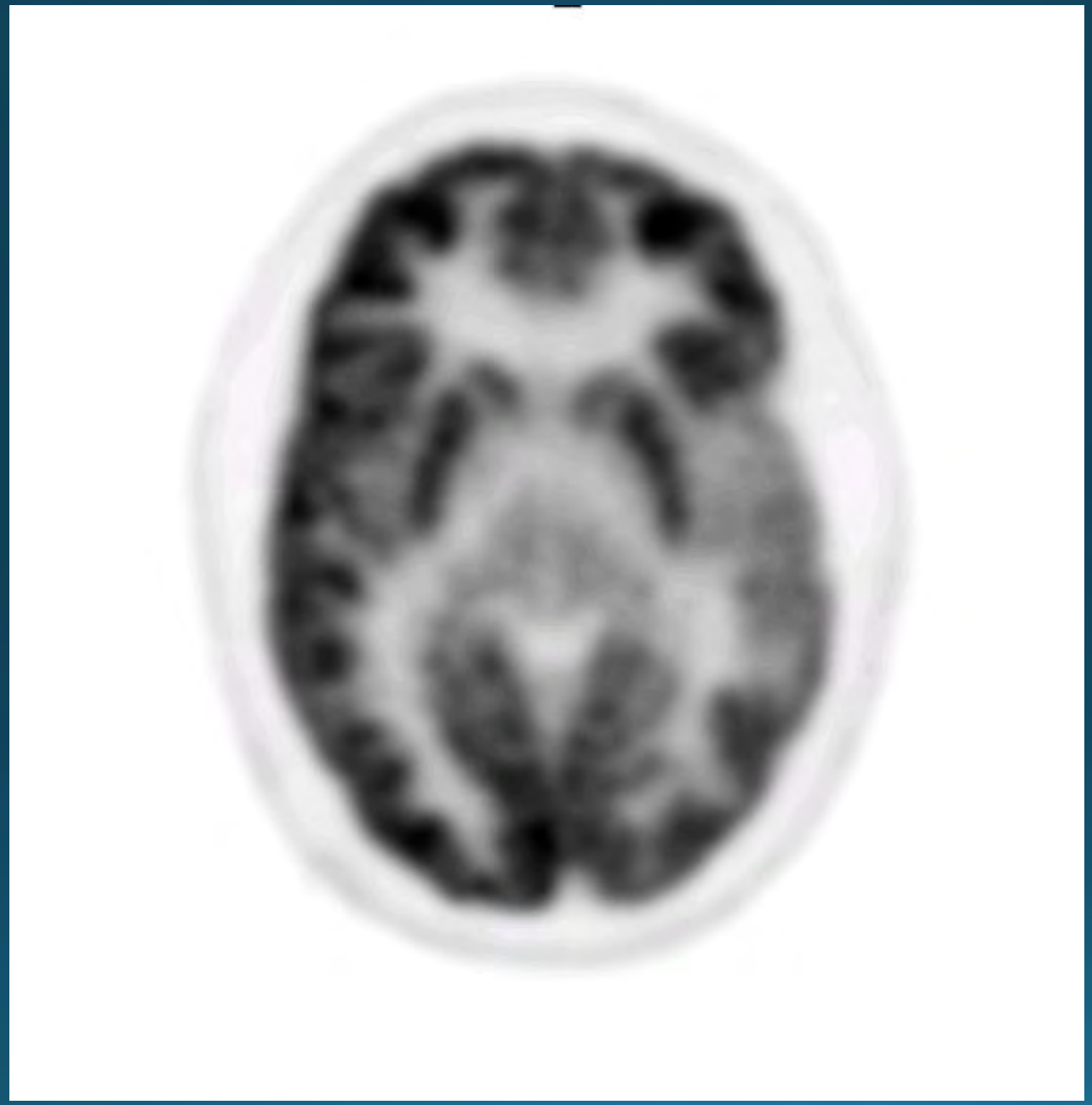
Dr. Hubert Vesselle has disclosed his financial relationship with MIM Software for consulting.

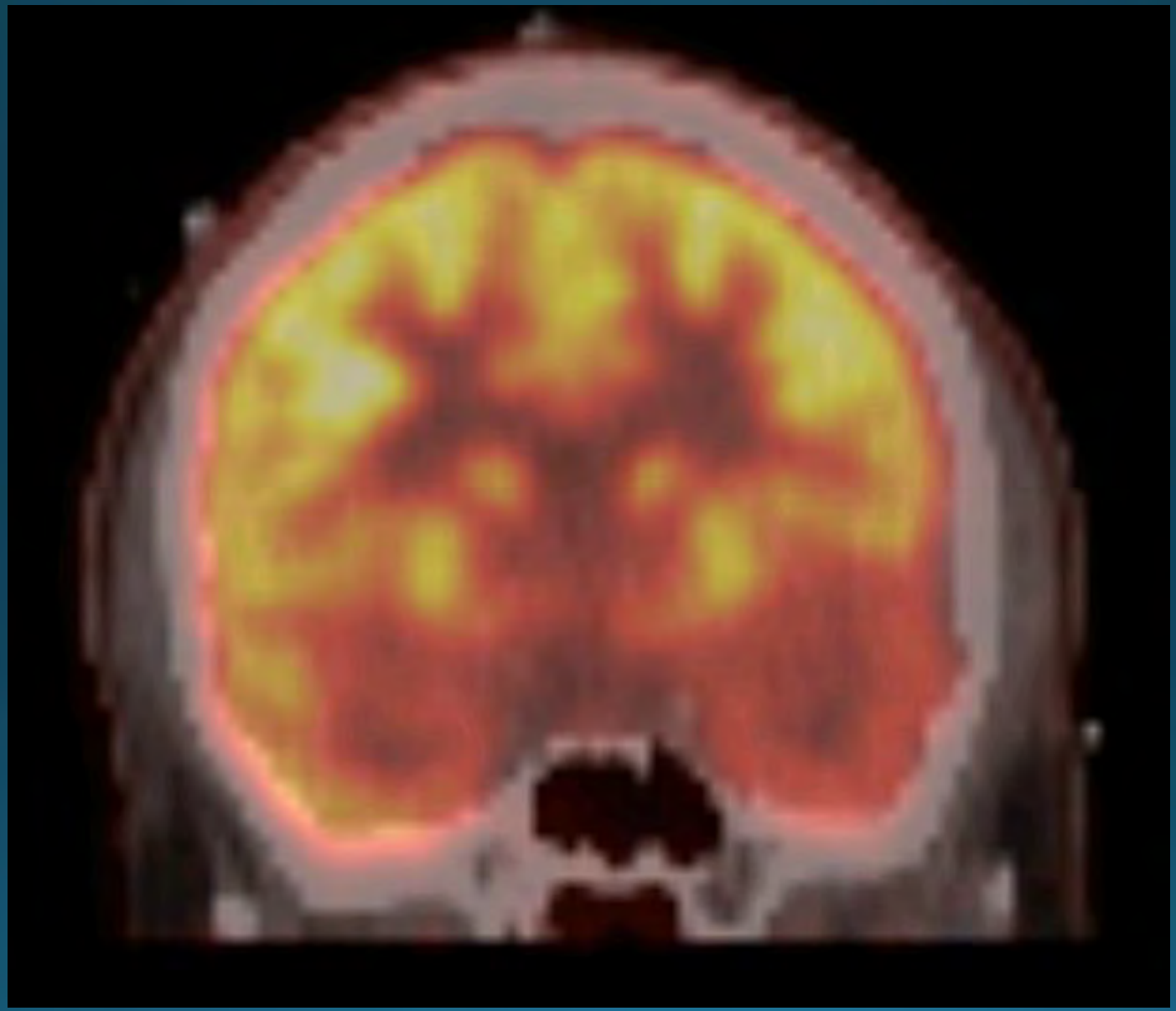
Dr. Lewis has no financial relationships to disclose.

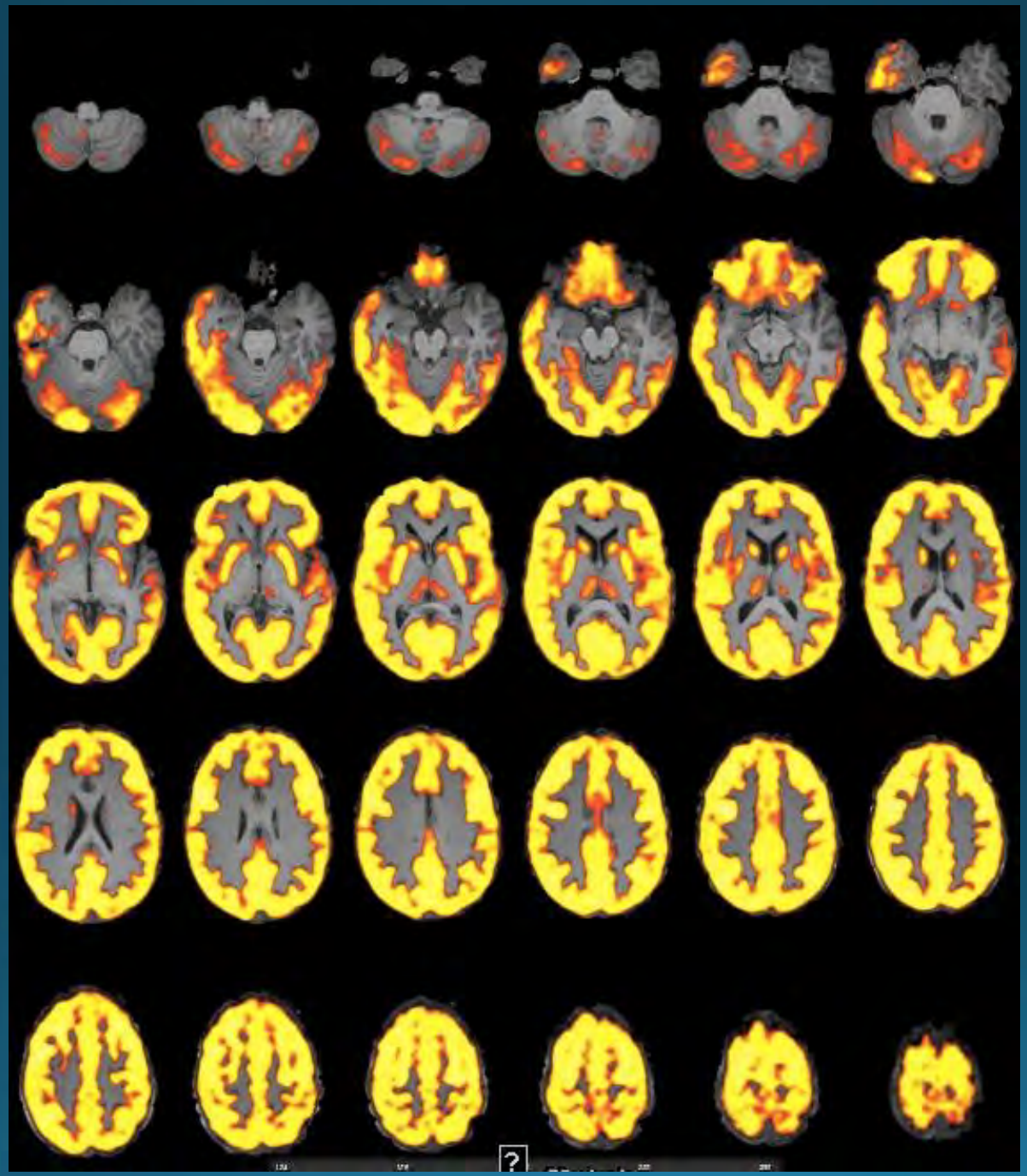
*If there is a financial relationship to disclose, please replace “no financial relationships” with the name of any commercial entity and the type of relationship with which you or your spouse/partner have an affiliation. Otherwise, delete this smaller print before including as the first slide in your case conference presentation.

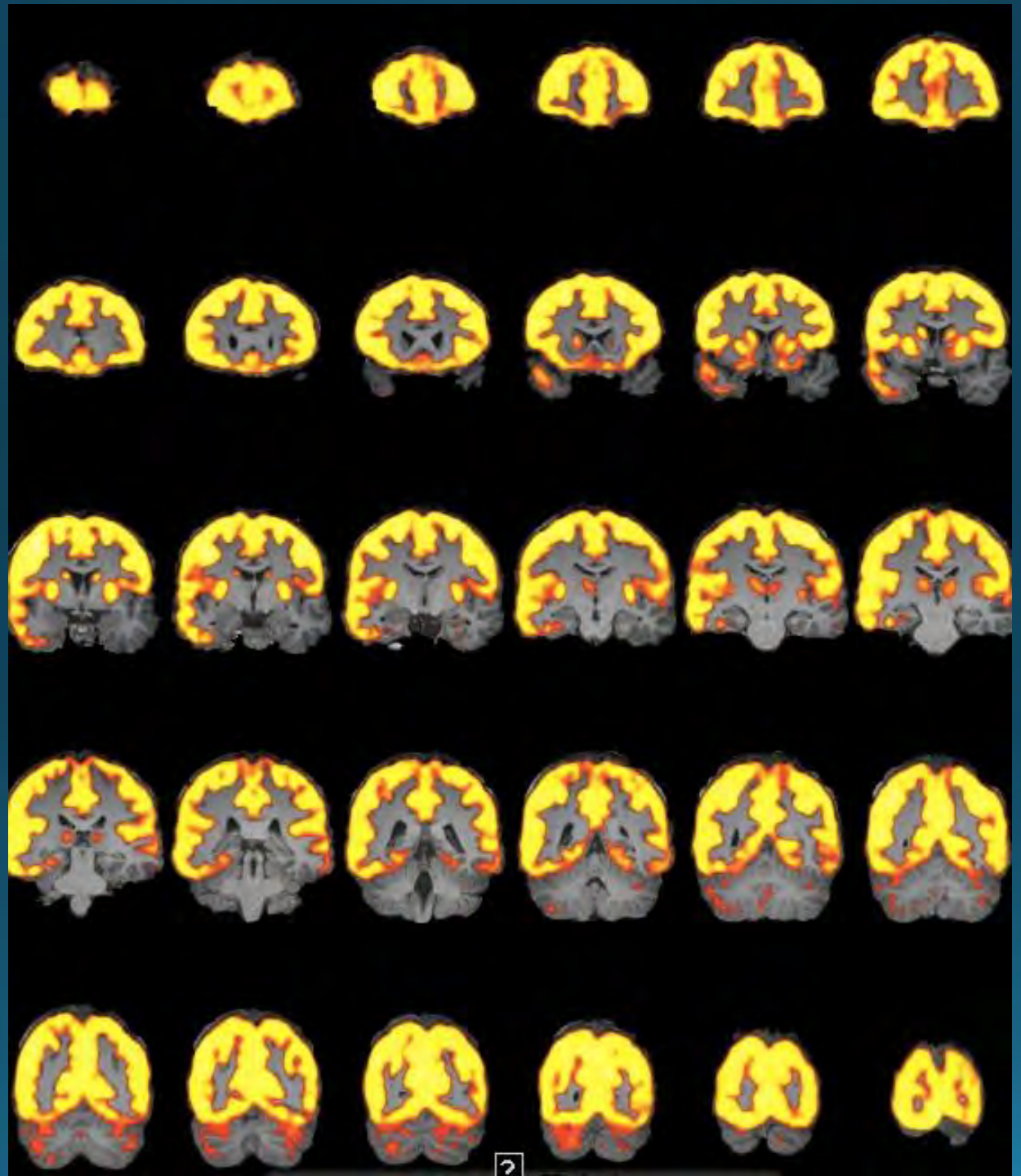
Epilepsy

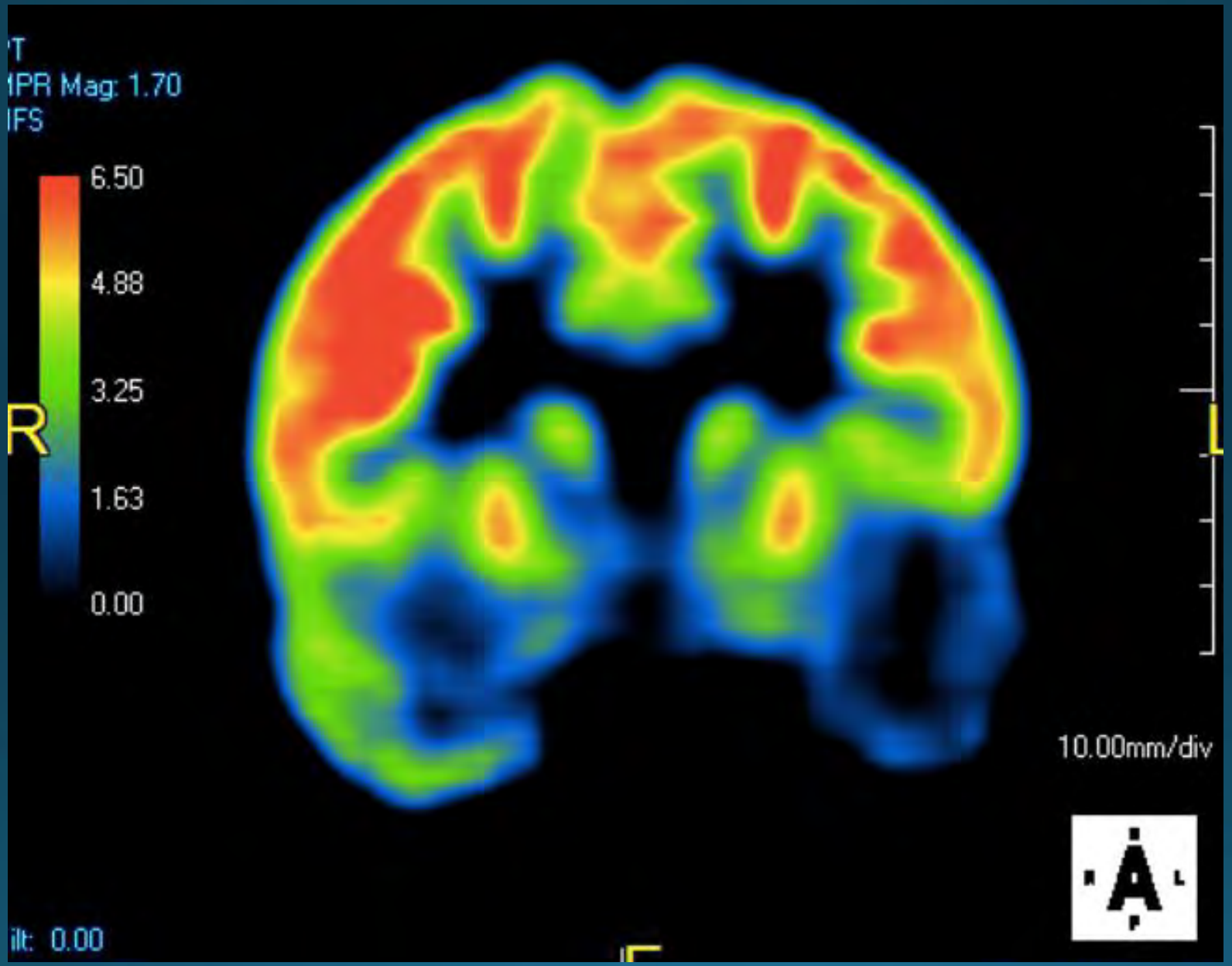
13 year old boy with seizure

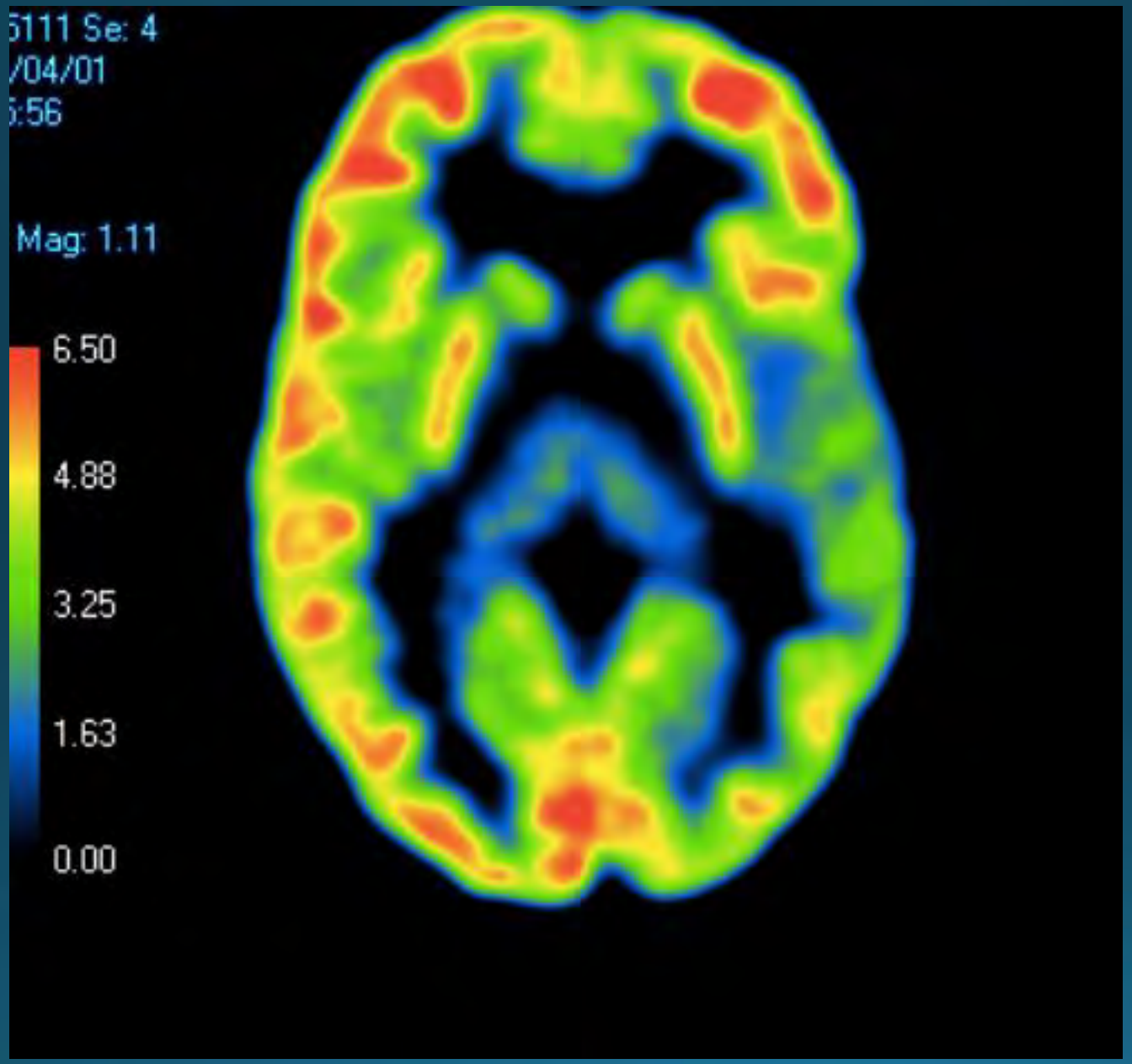


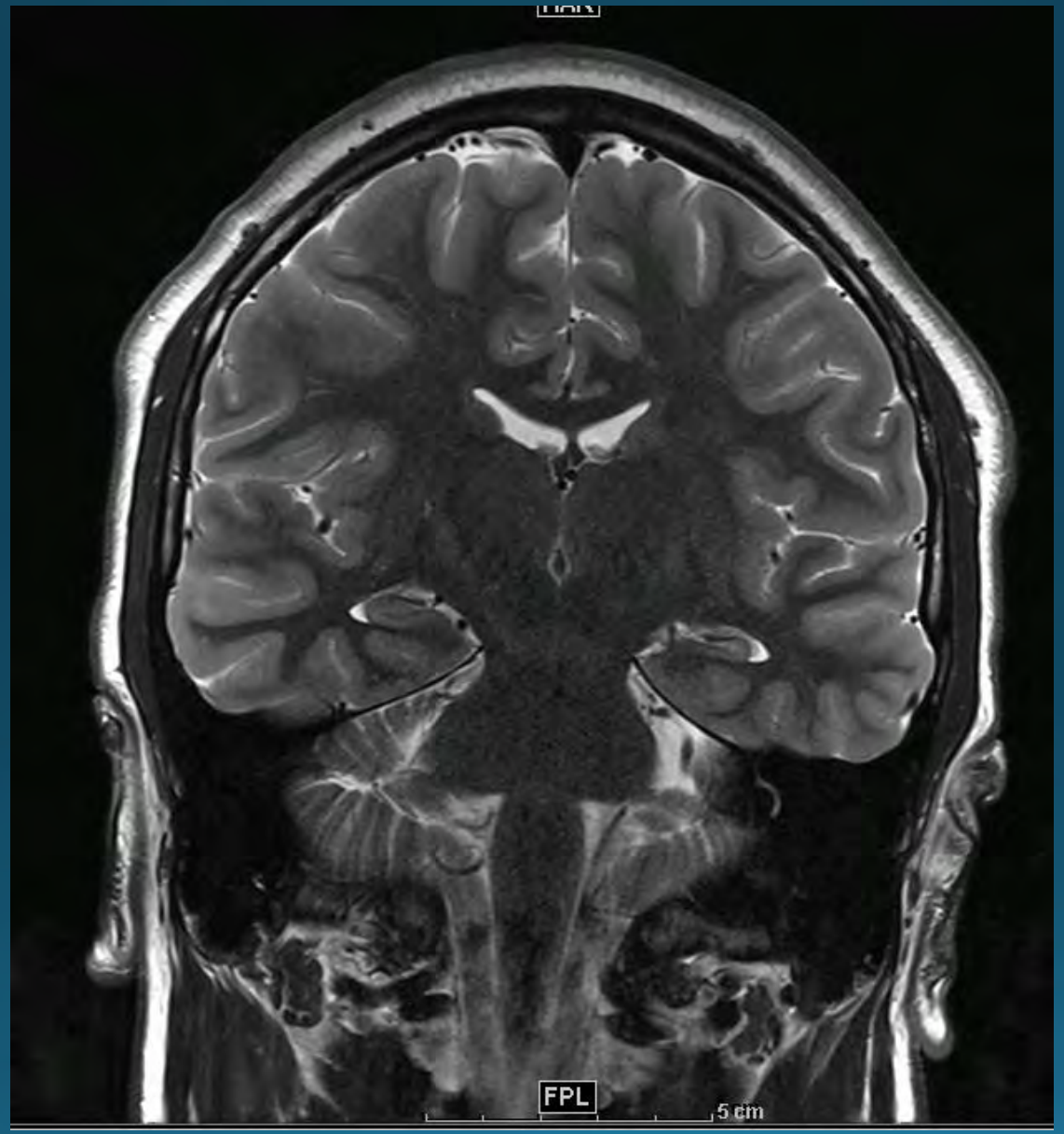







T
IPR Mag: 1.70
IFS
6.50
4.88
3.25
1.63
0.00
R
L
10.00mm/div
A
P
ilt: 0.00


5111 Se: 4
/04/01
:56
Mag: 1.11
6.50
4.88
3.25
1.63
0.00


FPL
5 cm

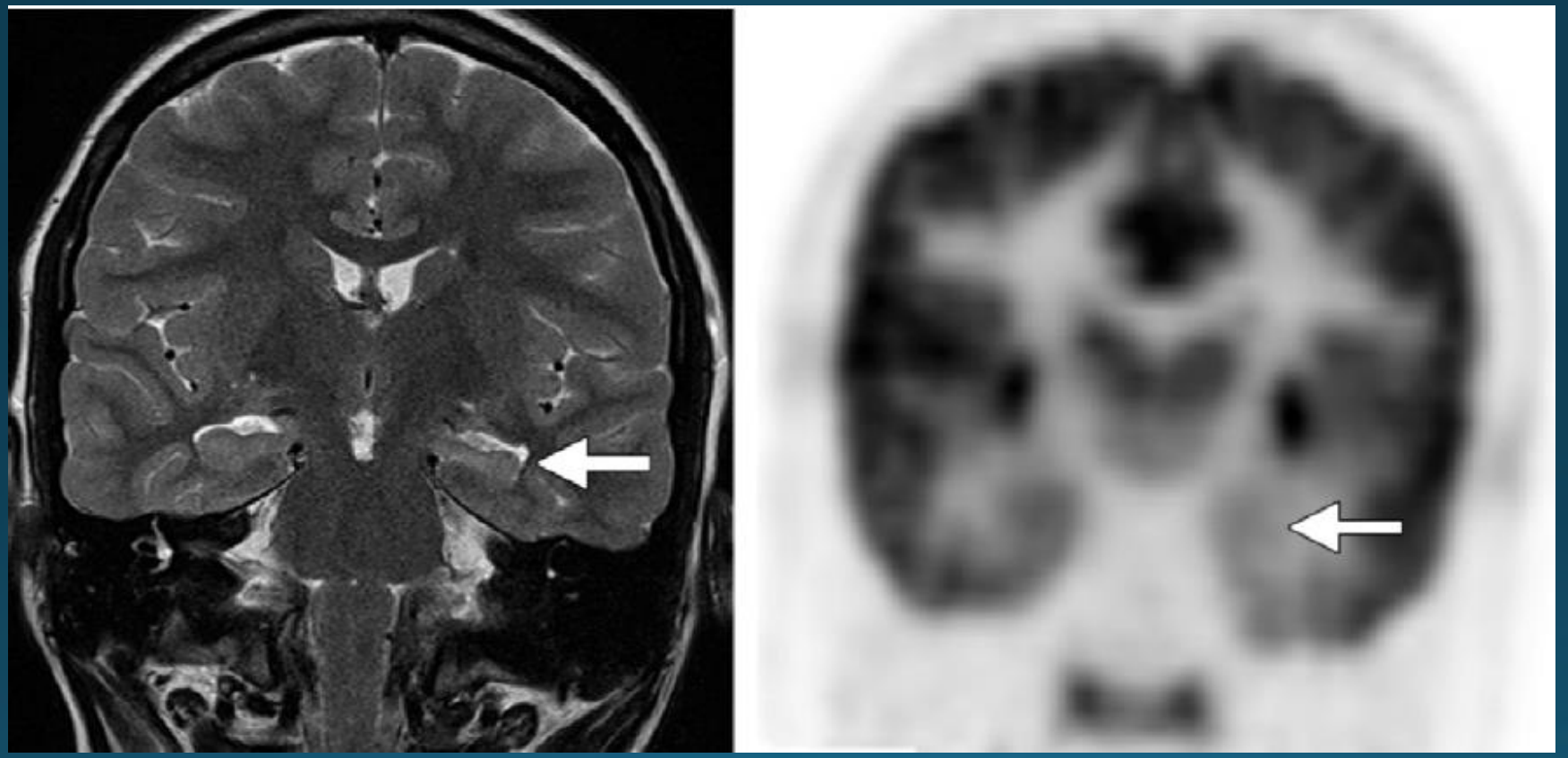
Diagnosis: Mesial temporal sclerosis

- PET/CT findings: Diffuse left temporal lobe hypometabolism extending to left parietal and left occipital lobes consistent with interictal epileptogenic area
- MRI findings: Left hippocampus shows volume loss and distortion of architecture, left anterior temporal lobe volume loss

Temporal lobe epilepsy

- Focally decreased FDG uptake in the ipsilateral hippocampal structures in 85% of patients
- In children the etiology of temporal lobe epilepsy is **multifactorial** and includes mesial temporal sclerosis and other entities, such as focal cortical dysplasia and developmental tumors
- A prior insult such as infection or trauma is often noted in the patient's history

Mesial temporal sclerosis



- Increased T2 signal intensity within the left hippocampus, which also appears asymmetrically smaller than the right
- hypometabolic area (arrow) in the region of the left hippocampus -

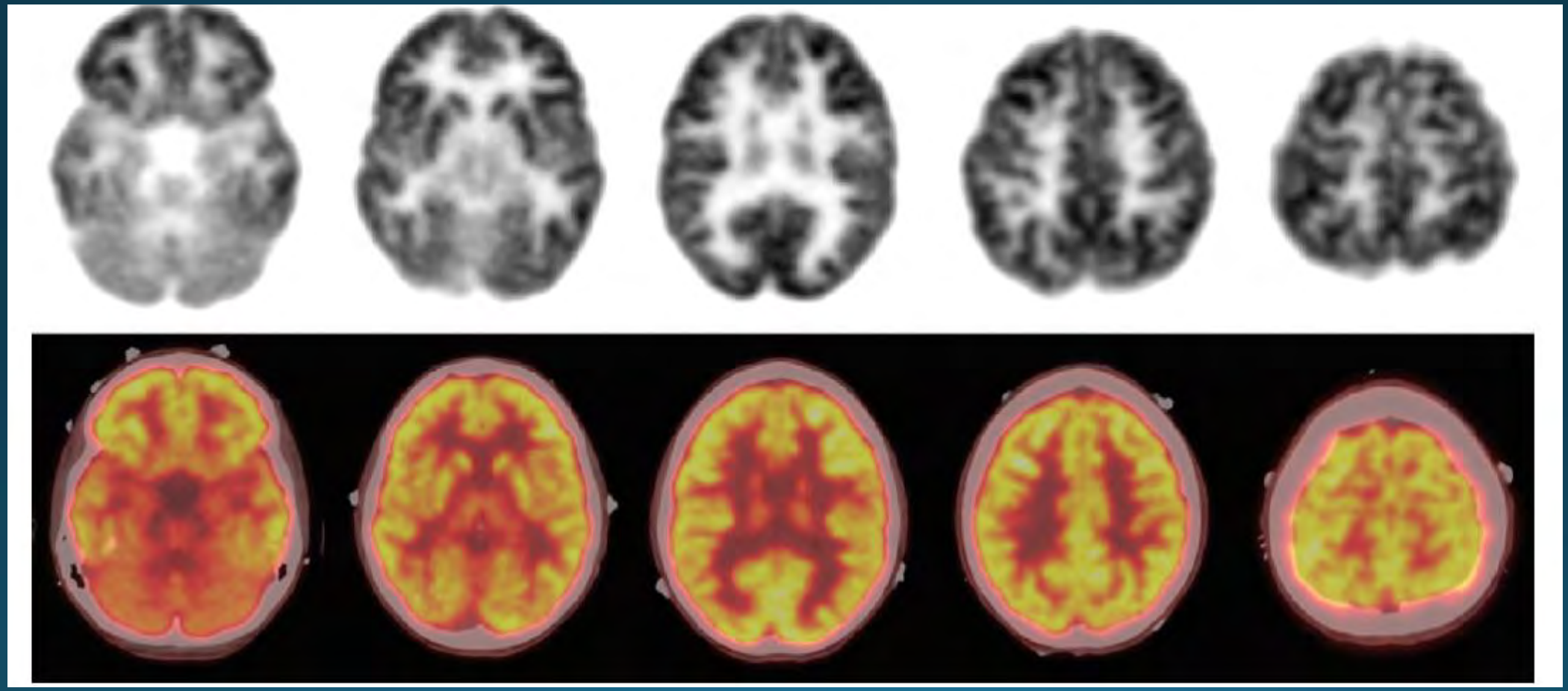
FDG PET imaging of the Brain in Pediatric Patients

Luana Stanescu, MD • Gisele E. Ishak, MD • Paritosh C. Khanna, MD
Deepa R. Biyyam, MD • Dennis W. Shaw, MD • Marguerite T. Parisi, MD, MSEd , Radiographics. RSNA , 2013

Brain glucose metabolism

- Infants : 30% of adult brain metabolism
- Rapid increase after 4 months of age
- Peak level by about 4 years of age (30% higher than that of adults)
- Plateau 4- 9 years of age
- After 9 years of age there is a steady decline, with brain glucose metabolism reaching adult levels by the age of 20 years

Normal Brain PET



FDG PET in Childhood Epilepsy

- Epilepsy causes: genetic, unknown, metabolic-structural
- Occurs in 0.5-1% of the population
- During an epileptic seizure, cerebral glucose metabolism and blood flow in the epileptogenic focus are **increased**
- During interictal or postseizure (postictal) period, both will be **decreased**

Causes for high FDG uptake during interictal

- Clinically overt seizure
- Subclinical seizure
- Restoration of resting membrane potential and chemical equilibrium after the seizure event, with an increased permeability of the blood-brain barrier for glucose transporters

False positive brain hypometabolism

- Depression and certain antiepileptic drugs, such as phenobarbital and valproate sodium, have been shown to cause diffusely decreased cerebral metabolic activity
- Phenytoin can lead to decreased glucose metabolism in the cerebellum

Epilepsy

- The functional deficit zone is defined as the cortex with abnormal function in the interictal period, which is due to morphologic or functional physiologic causes.
- More extensive than the focal epileptogenic zone and can be assessed by using FDG PET or carbon 11 (11 C)- labeled flumazenil

Extratemporal hypometabolism

- Usually in the frontal lobes
- represents a preferential pattern of seizure extension.
- inhibition process acting as a defense mechanism against seizure propagation.
- This hypothesis is supported by improvement in both cognitive impairment and glucose metabolism after surgery

References

Lateralization phenomenon

- Hypometabolism in the contralateral temporal lobe
- usually less severe than the seizure focus
- attributed to various factors, including distant spread of seizures or medication effects

Brain SPECT/CT

- 99mTc-exametazime (99mTc- [HMPAO]; Ceretec or
- 99mTc-bicisate (ie, 99mTc-ethyl cysteinate dimer [ECD]; Neurolite

Brain PET/CT

- 18F FDG : 0.1 mCi/kg maximum dose of 10 mCi
- carbon 11 (11 C) methionine

Common causes

- Neuronal proliferation anomalies
- Arrested neuronal migration
- Tumors

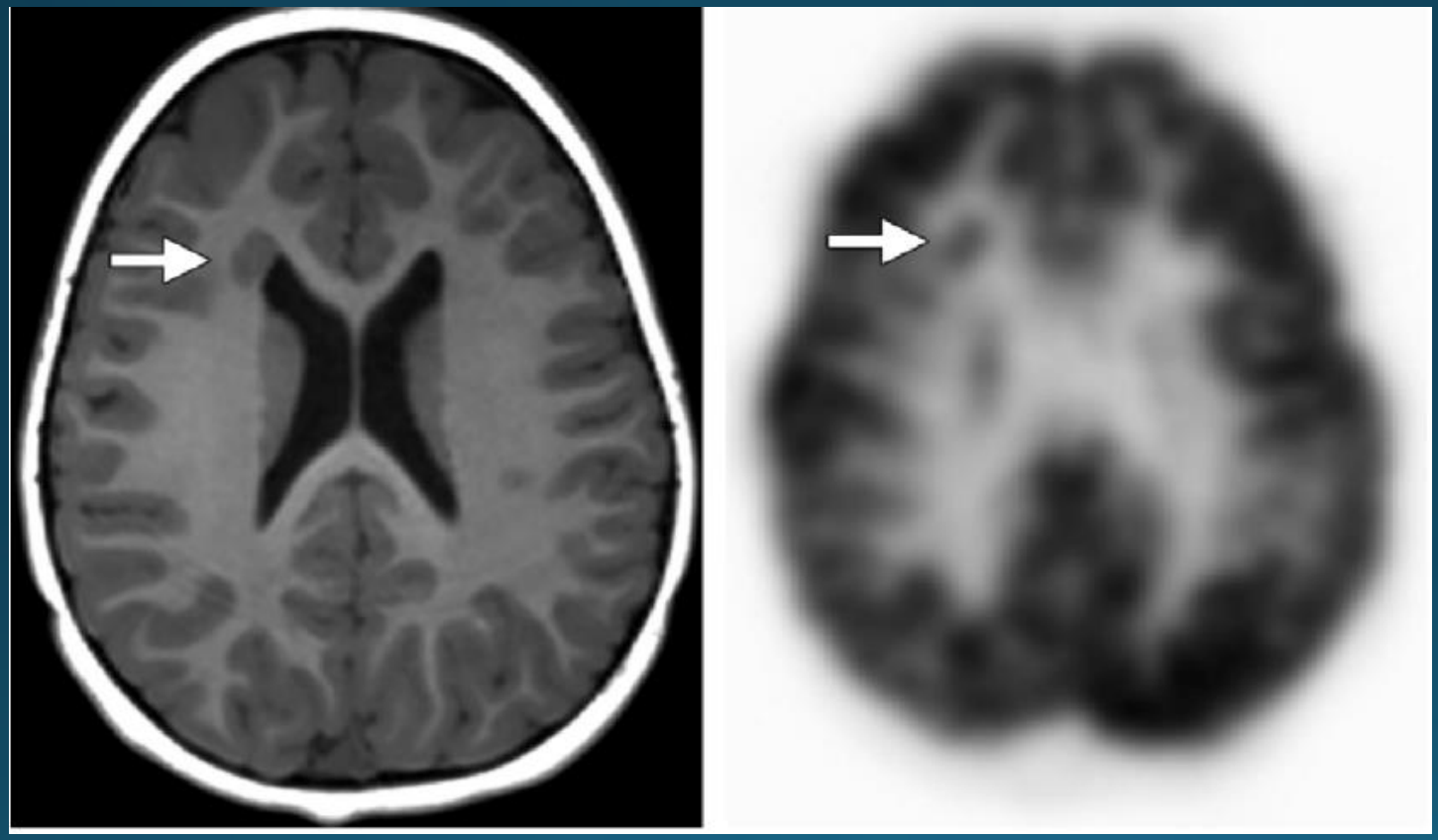
Neuronal Proliferation Anomalies

- Focal cortical dysplasia,
- Hemimegalencephaly,
- Tuberous sclerosis,
- Other Phacomatoses

Arrested neuronal migration

- gray matter heterotopias
- lissencephaly (agyria)
- polymicrogyria
- schizencephaly

Heterotopic Gray Matter



- right frontal focus of gray matter heterotopia in a 1yo girl with infantile spasms
- increased metabolic activity that is slightly less than that of the adjacent cortical gray matter

Heterotopic Gray Matter

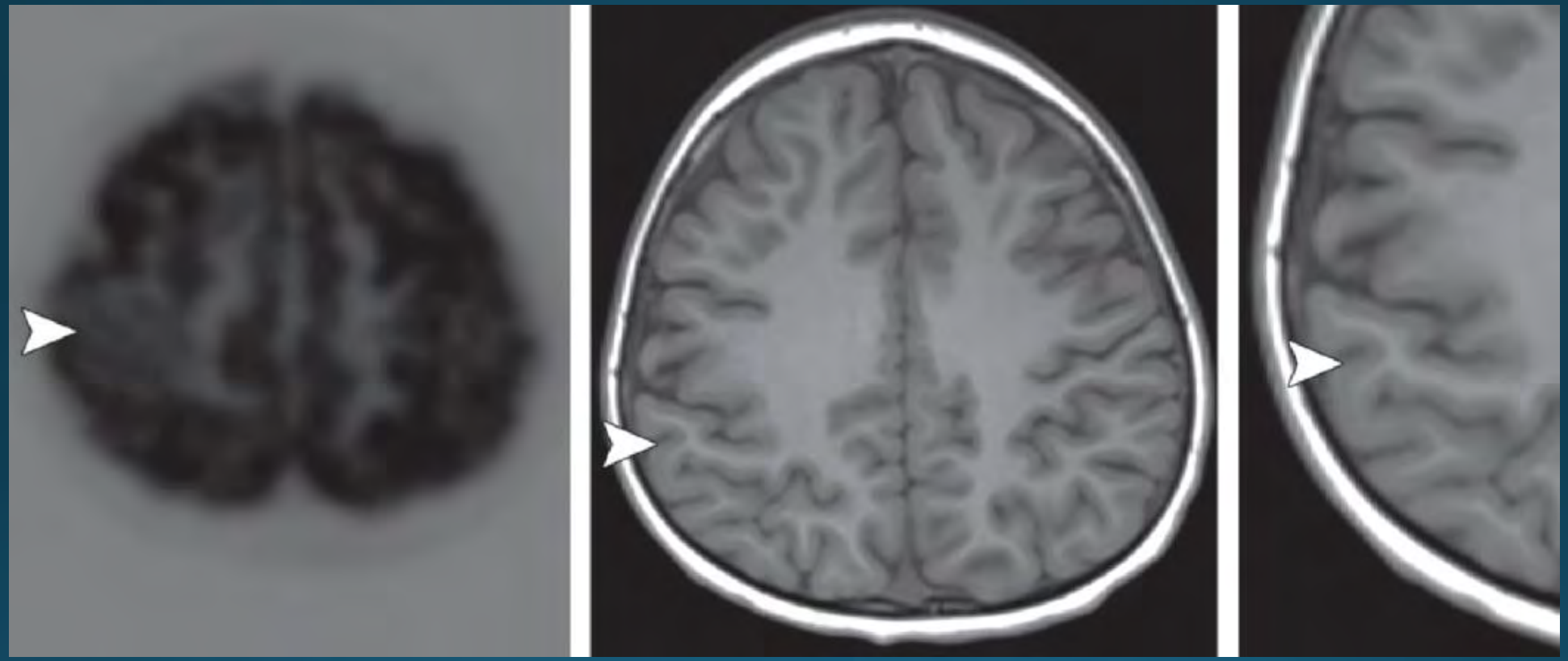
- Arrested neuronal migration along the pathway from the germinal matrix to the cortex
- large neuronal conglomerates are present in an ectopic location

Heterotopic Gray Matter

- subependymal (periventricular) (most common)
- subcortical heterotopia
- band heterotopia ("double cortex" sign)

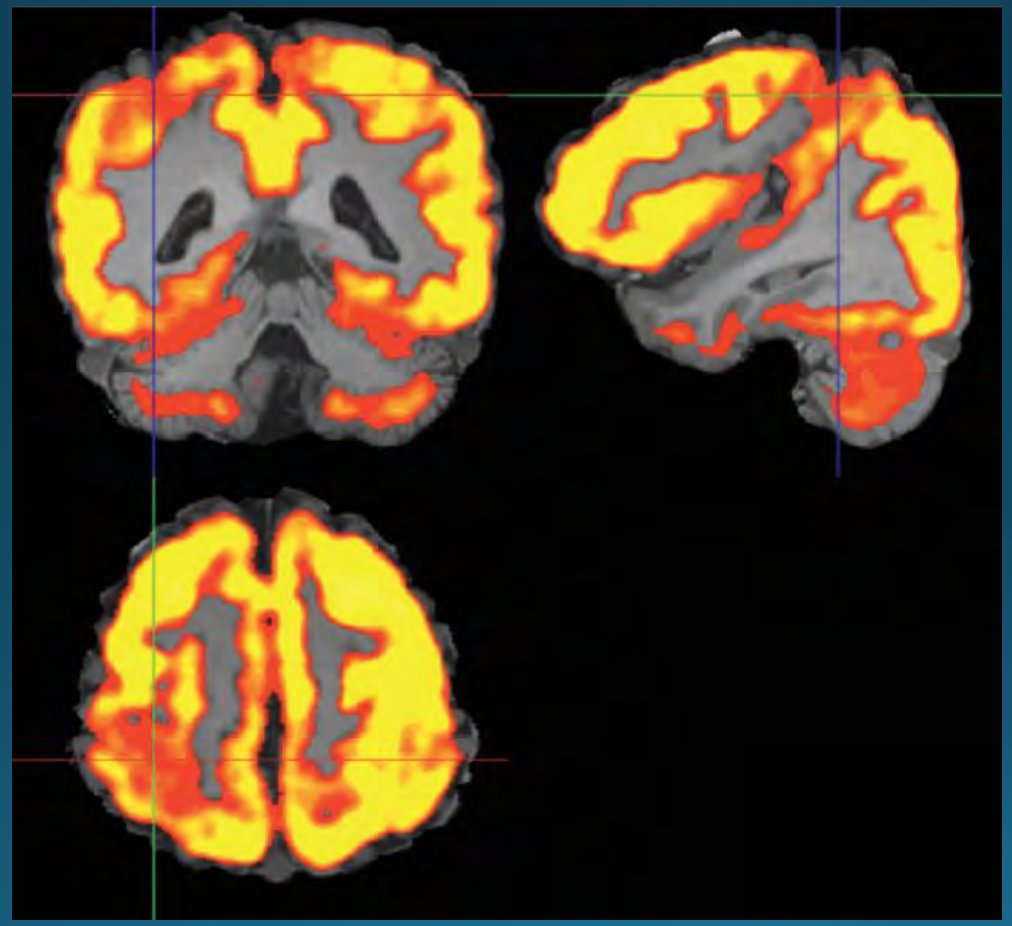
Can be in association with other structural anomalies, such as Chiari malformations or callosal dysgenesis.

Polymicrogyria

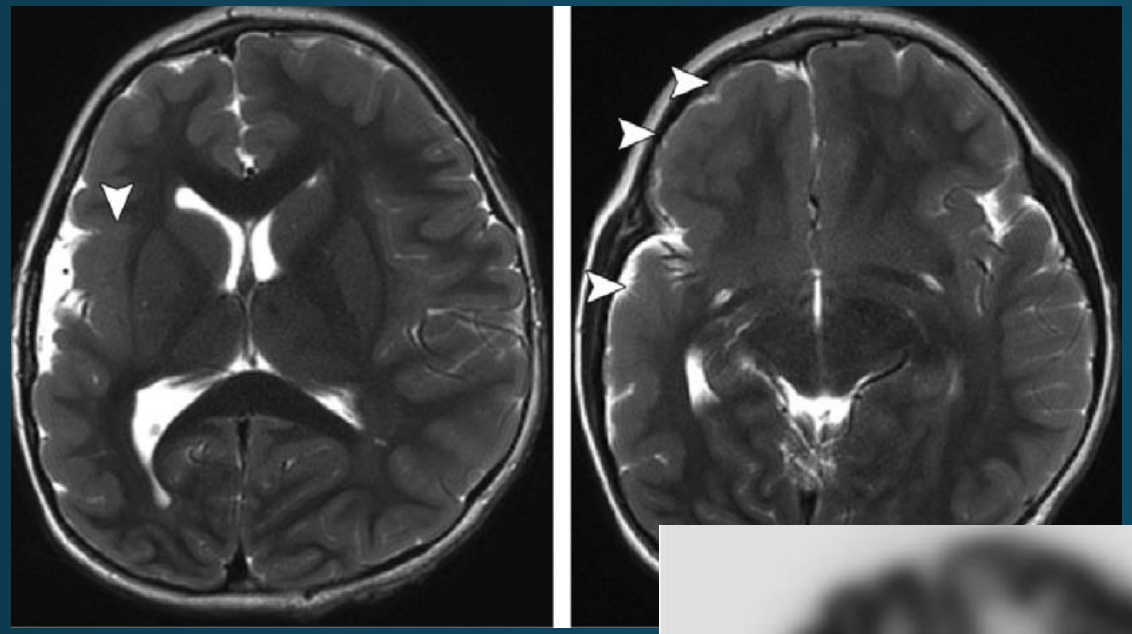


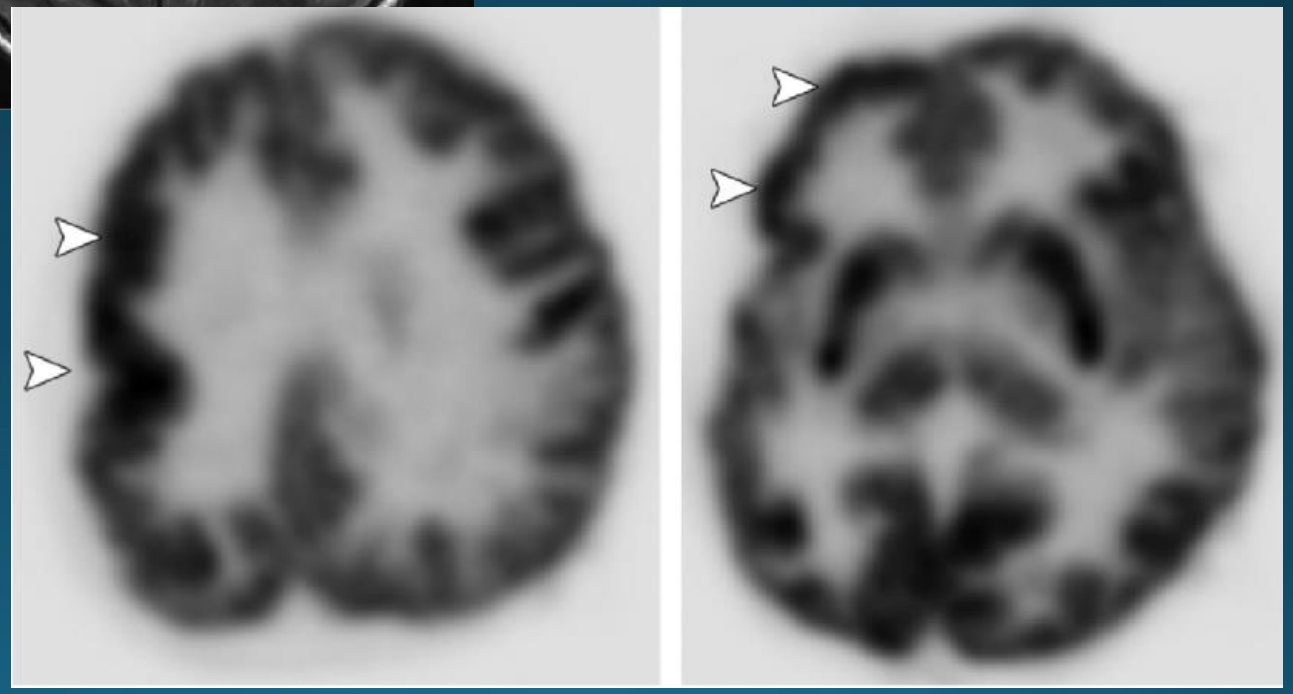
focal hypometabolism in the right perirolandic region,

Polymicrogyria



hypometabolism in the right perirolandic region





Polymicrogyria, show diffuse hypermetabolism (arrowheads) within the dysplastic right frontal, temporal, and parietal lobes.

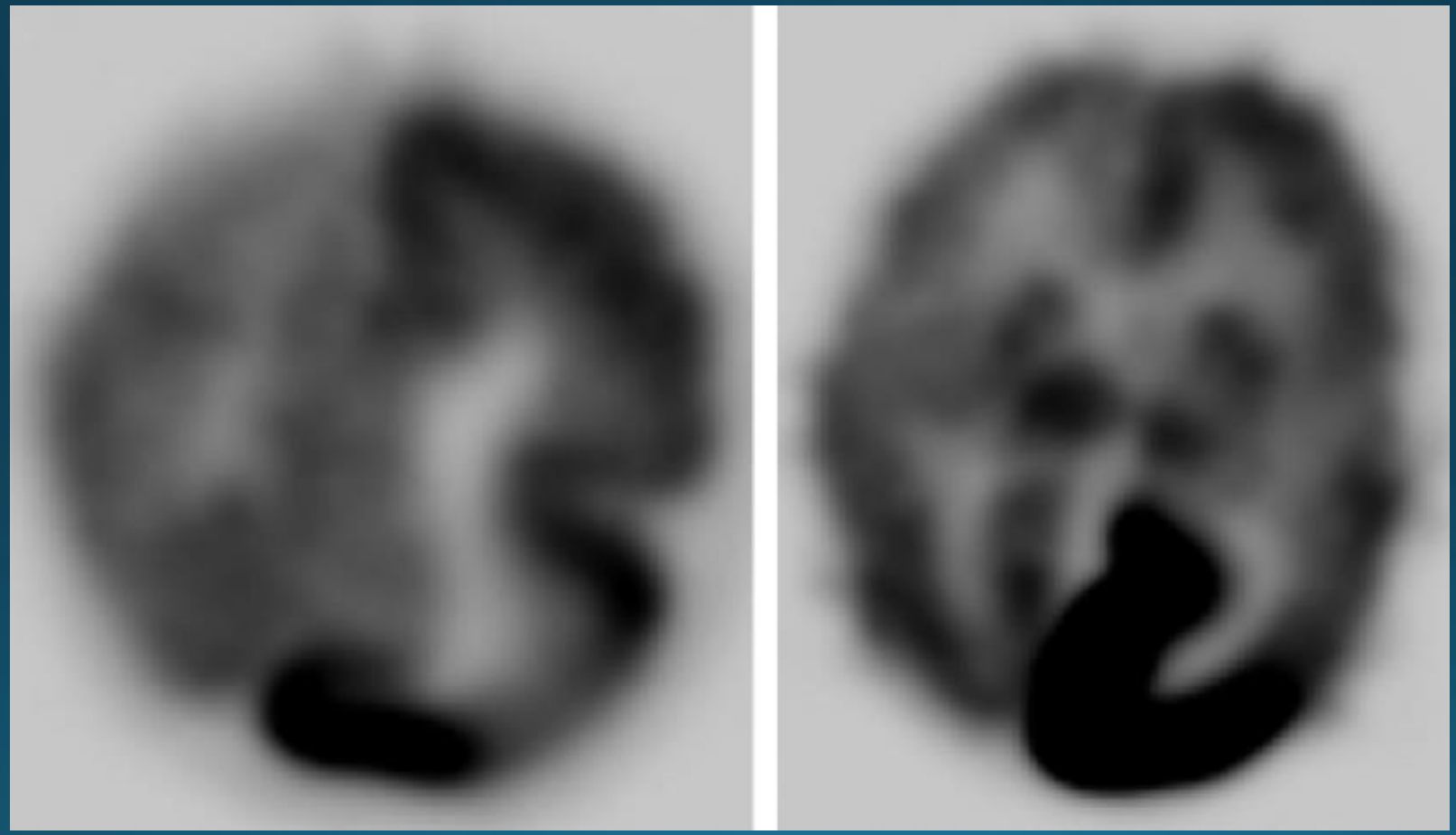
Polymicrogyria

- A variable pattern of FDG uptake occurs in patients with polymicrogyria, ranging from normal to either increased or decreased uptake

Polymicrogyria

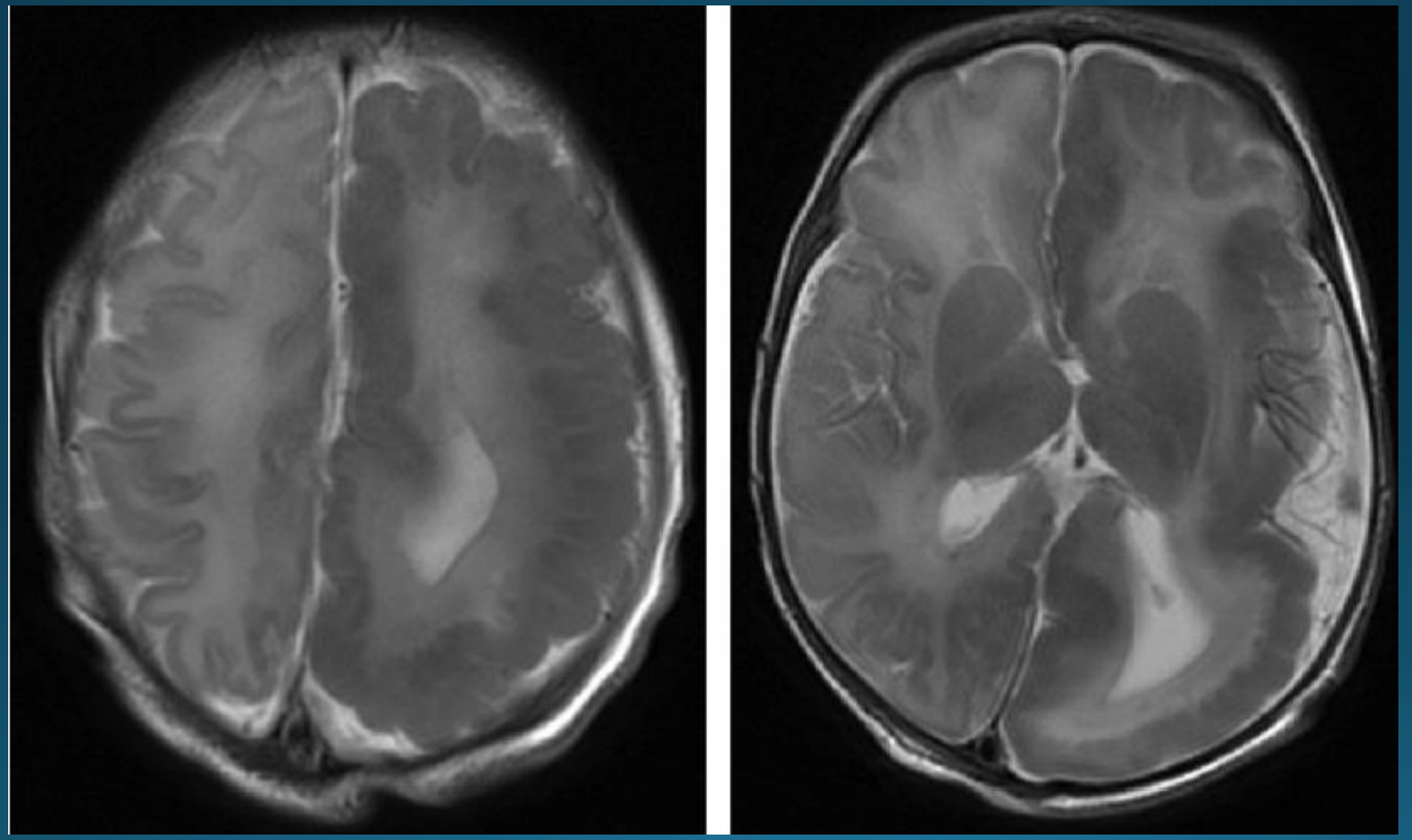
- occurs in the later stages of brain development
- neurons reach the cortex but organize atypically in small, crowded gyri because of disruption of the normal six-layered cortical lamination

Hemimegalencephaly



Hypermetabolic foci were related to ongoing seizure activity detected with concurrent EEG performed during

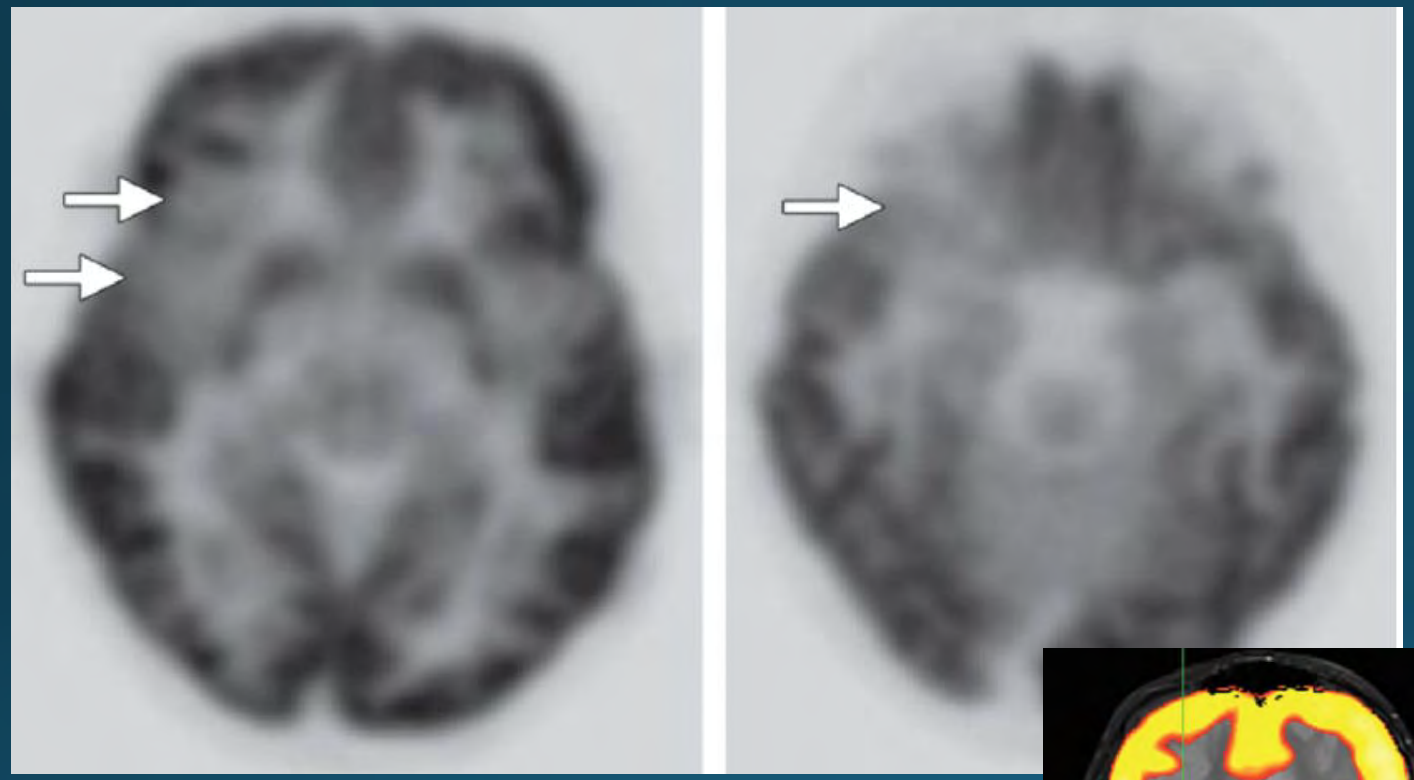
Hemimegalencephaly

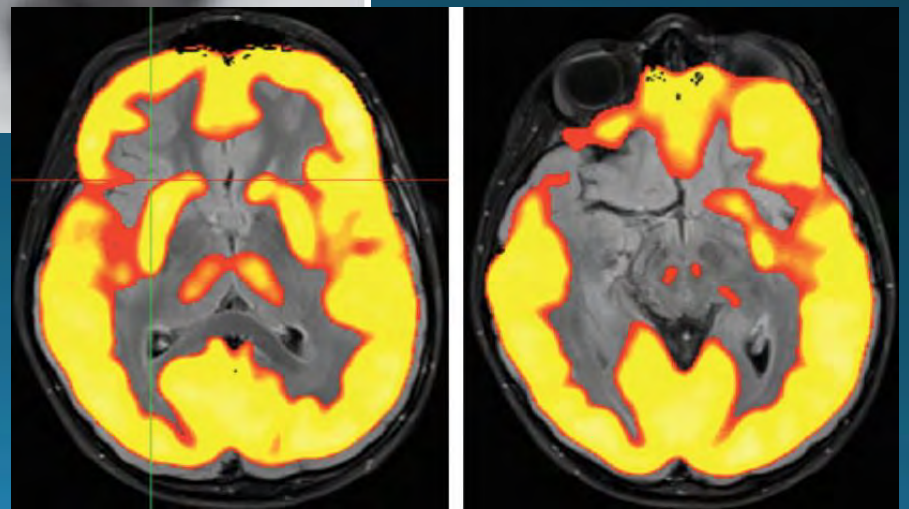


Hemimegalencephaly

- Isolated or in association with other syndromes, including hemihypertrophy syndromes, neurofibromatosis, and tuberous sclerosis
- Symptoms : intractable seizures, hemiplegia, and severe developmental delay

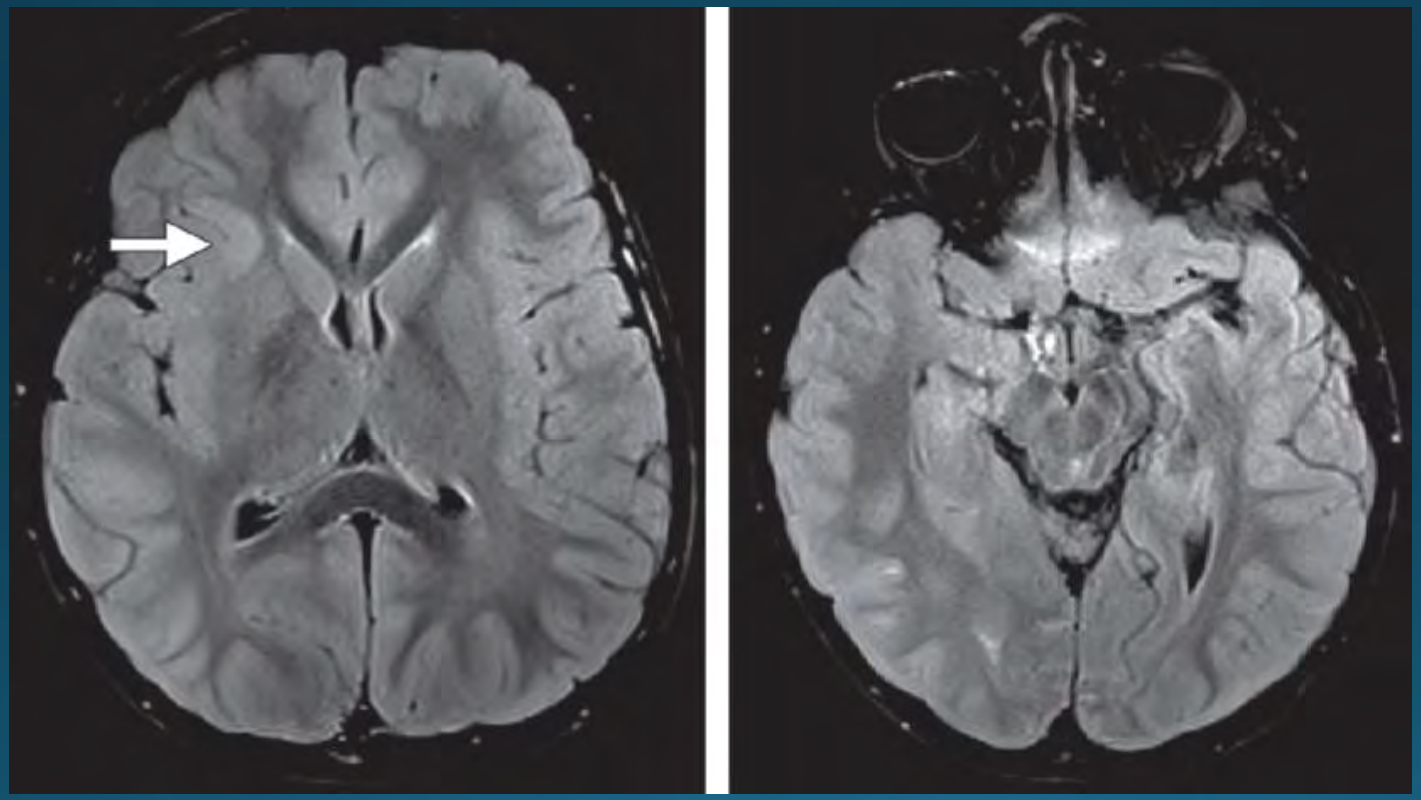
Focal Cortical Dysplasia





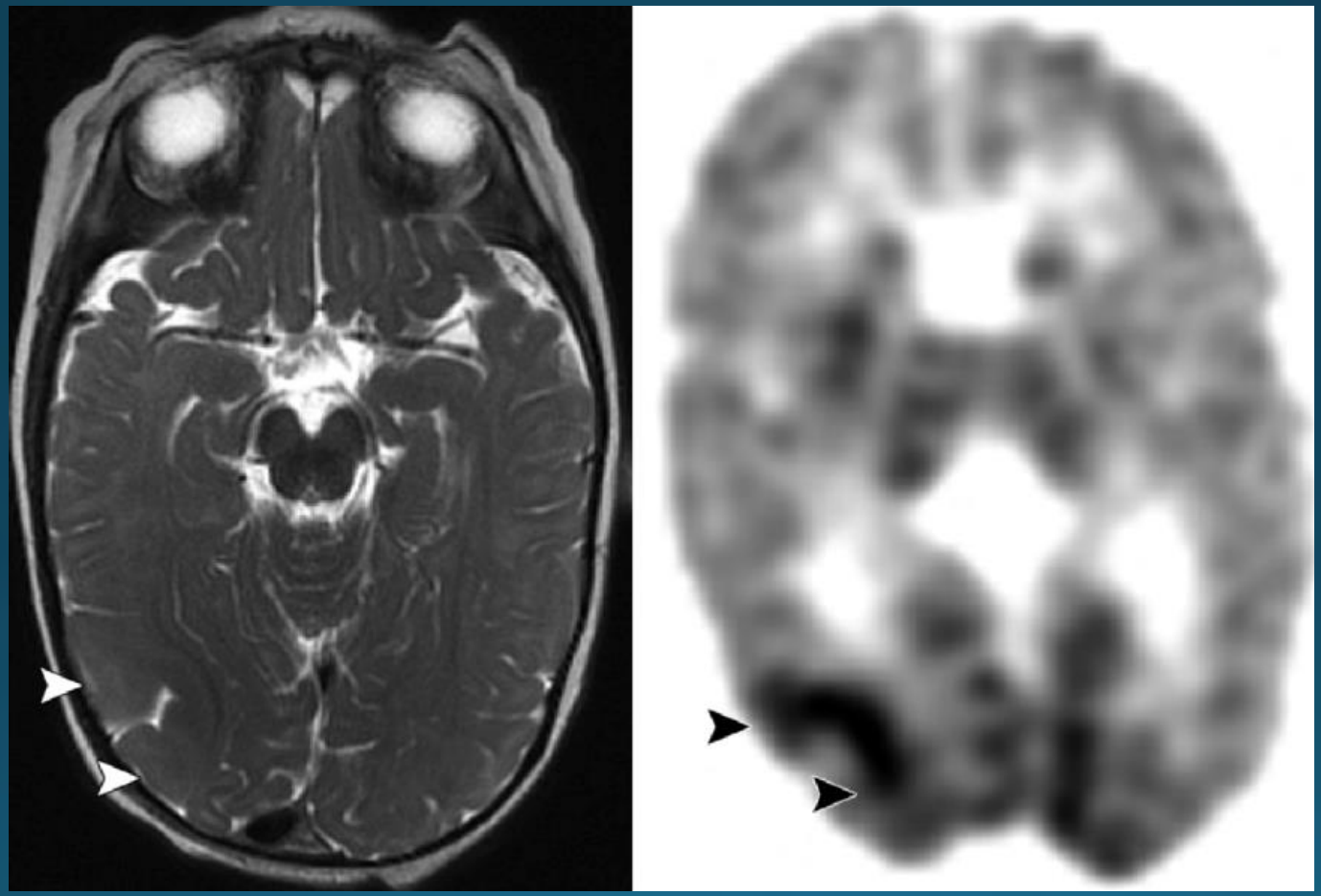
decreased avidity in the right inferomedial temporal, right superolateral temporal, and right inferior frontal regions

Focal Cortical Dysplasia



MR images show focal cortical dysplasia with increased signal intensity in the right frontal lobe

Focal Cortical Dysplasia

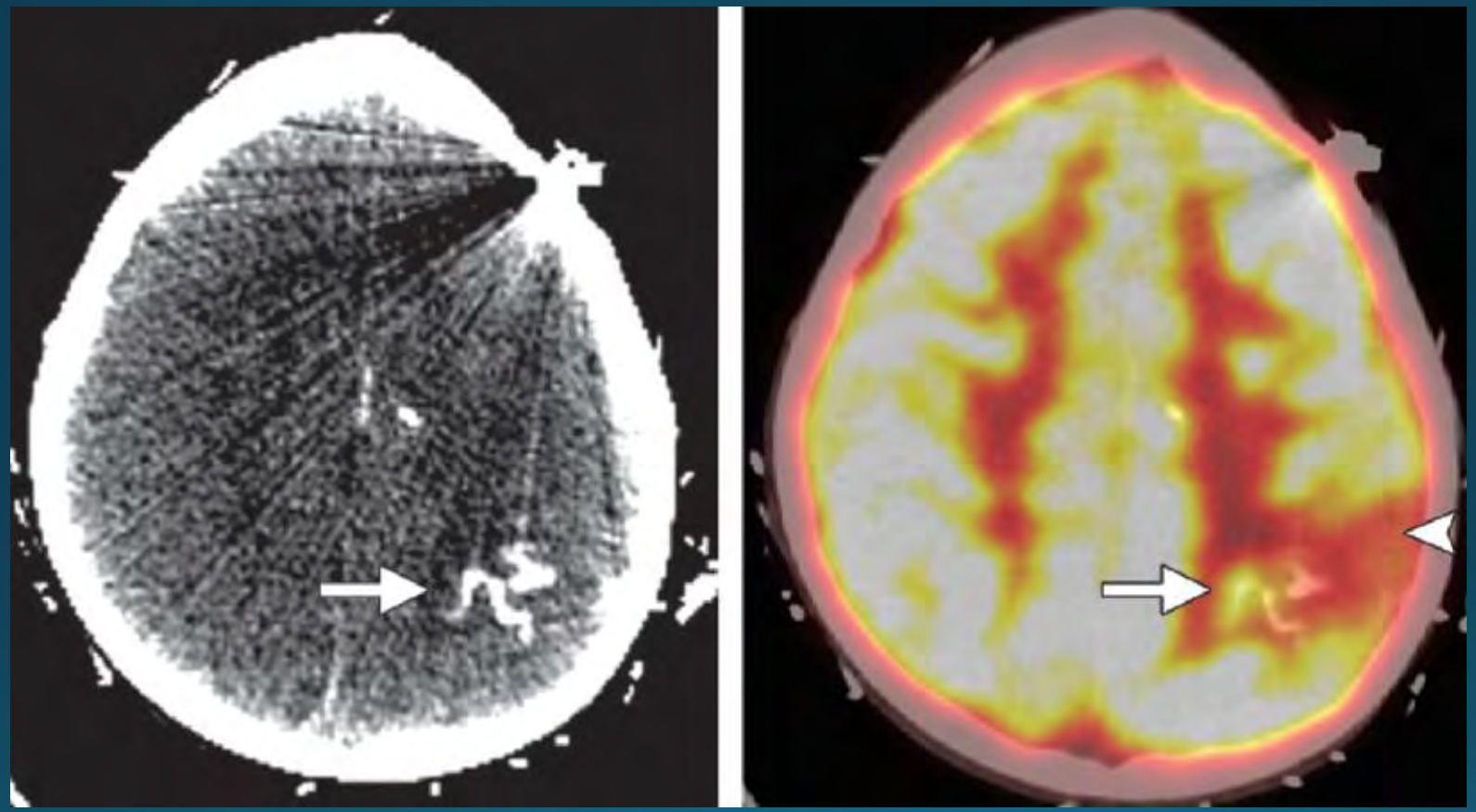


MRI: focally thickened cortex in the right parieto-occipital lobe
FDG PET : hypermetabolism corresponding to the focal cortical dysplasia

Focal Cortical Dysplasia

- From microscopic abnormalities not detectable with imaging to tumorlike lesions
- associated with seizures and variable degrees of neurologic and cognitive deficits
- At FDG PET, the lesions will typically exhibit hypometabolism

Parry-Romberg Syndrome

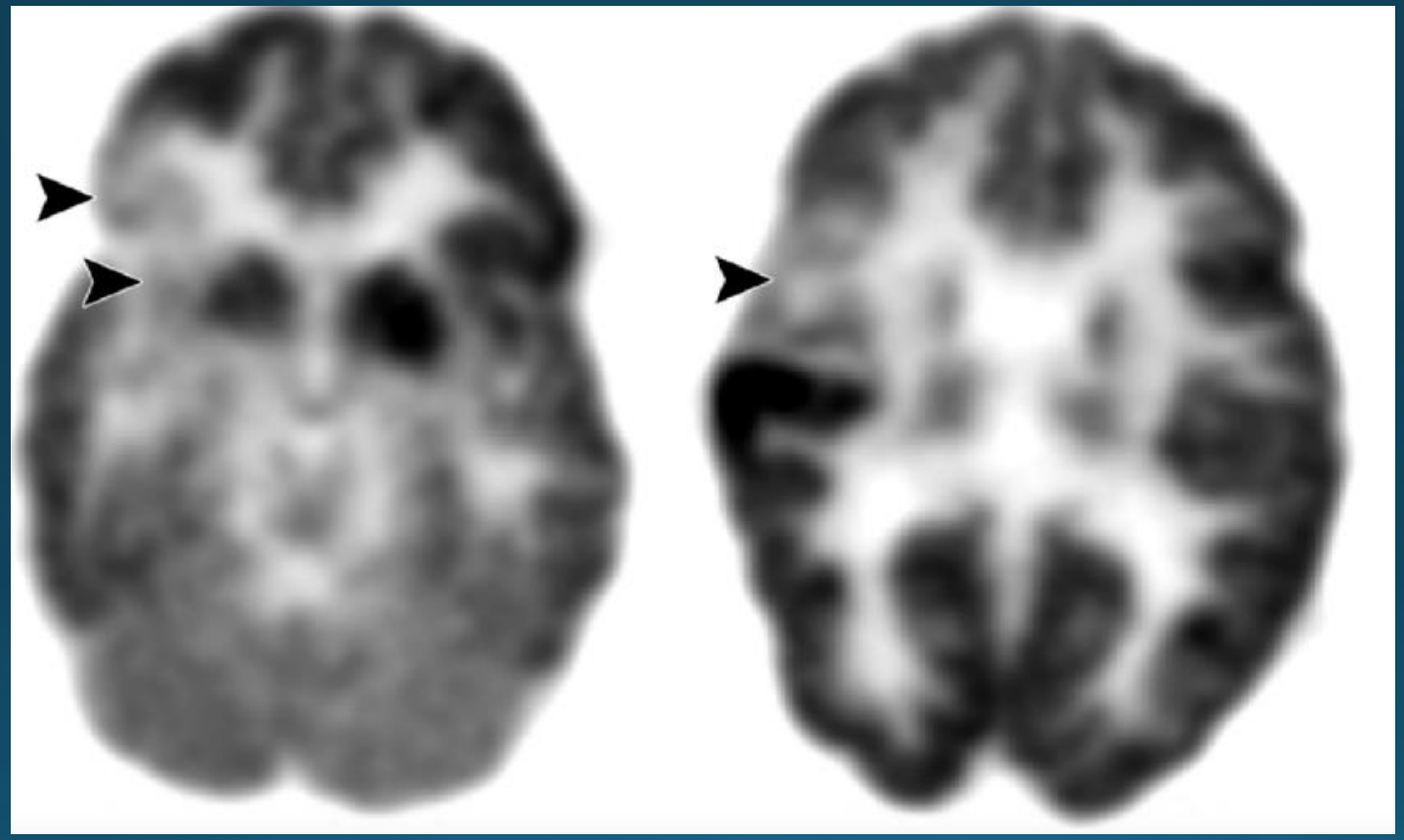


CT attenuation : gyriform calcified areas in the left parietal lobe
Increased FDG uptake due to seizure activity

Parry-Romberg Syndrome

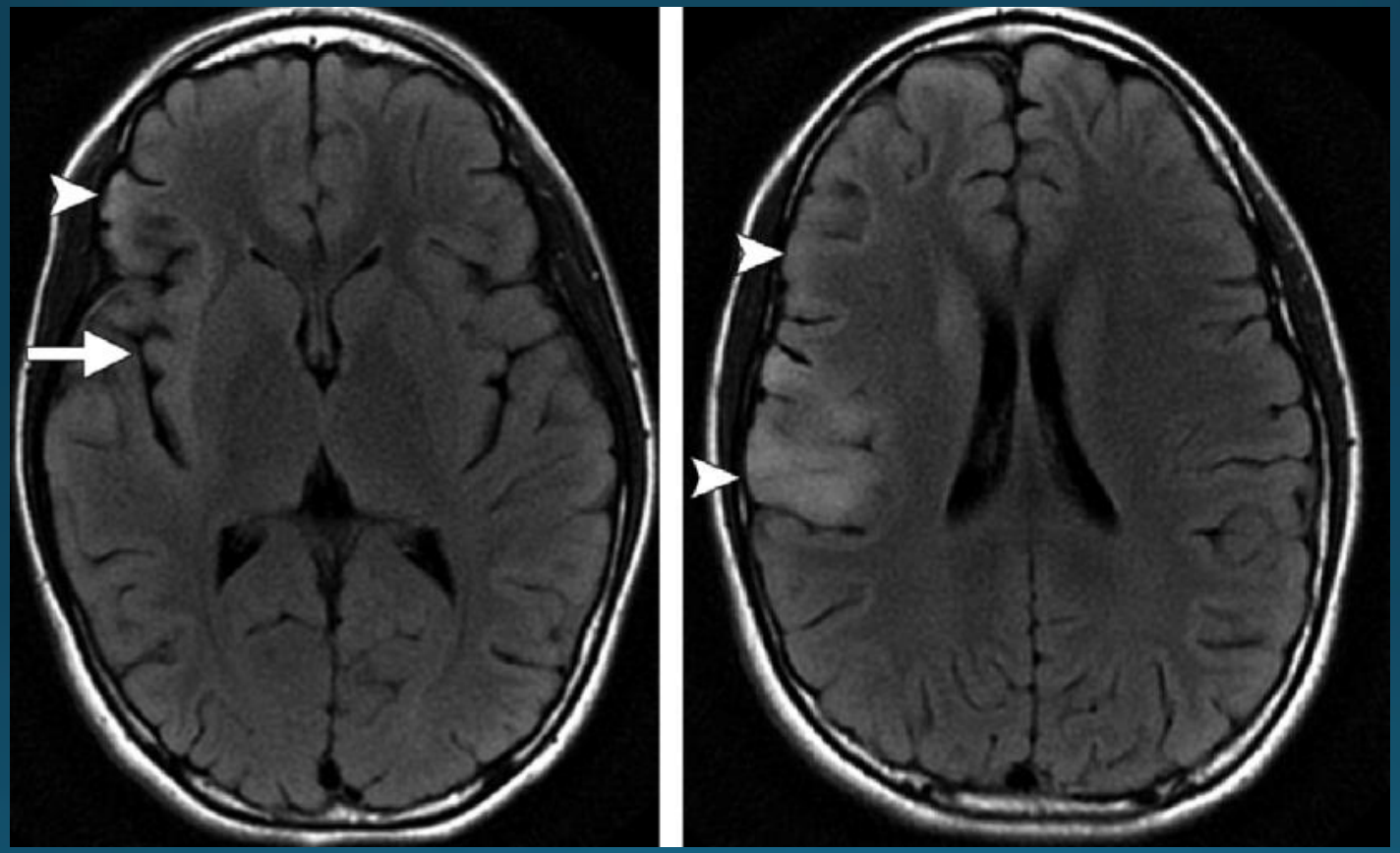
- Neurocutaneous syndrome of unclear etiology
- slow and progressive hemifacial atrophy
- 10% of patients present with epilepsy
- focal cerebral atrophy with variable degrees of high T2 and FLAIR signal intensity abnormalities in the ipsilateral white matter

Rasmussen Encephalitis



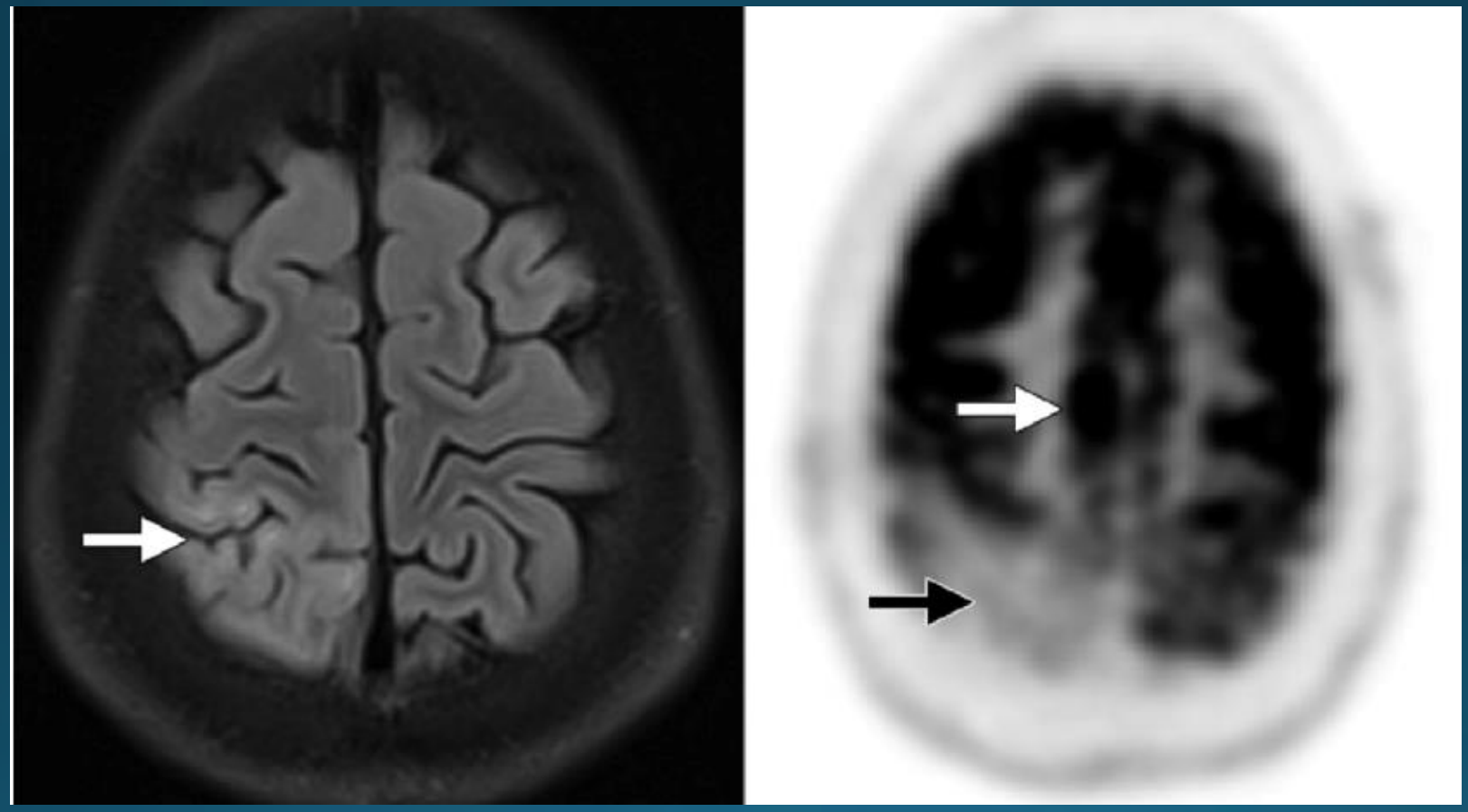
hypometabolism involving the right insula, inferior frontal region and right caudate and lentiform nuclei, findings likely representing abnormal interictal areas.

Rasmussen Encephalitis



focal hyperintensity and volume loss in the right peri-insular cortex
inferior right frontal lobe and superior right frontoparietal region

Rasmussen Encephalitis



- Regional parieto-occipital hypometabolism with a medial posterior frontal hypermetabolic focus, likely representing an ictal focus
- FLAIR MR: right posterior parietal atrophy and signal abnormality

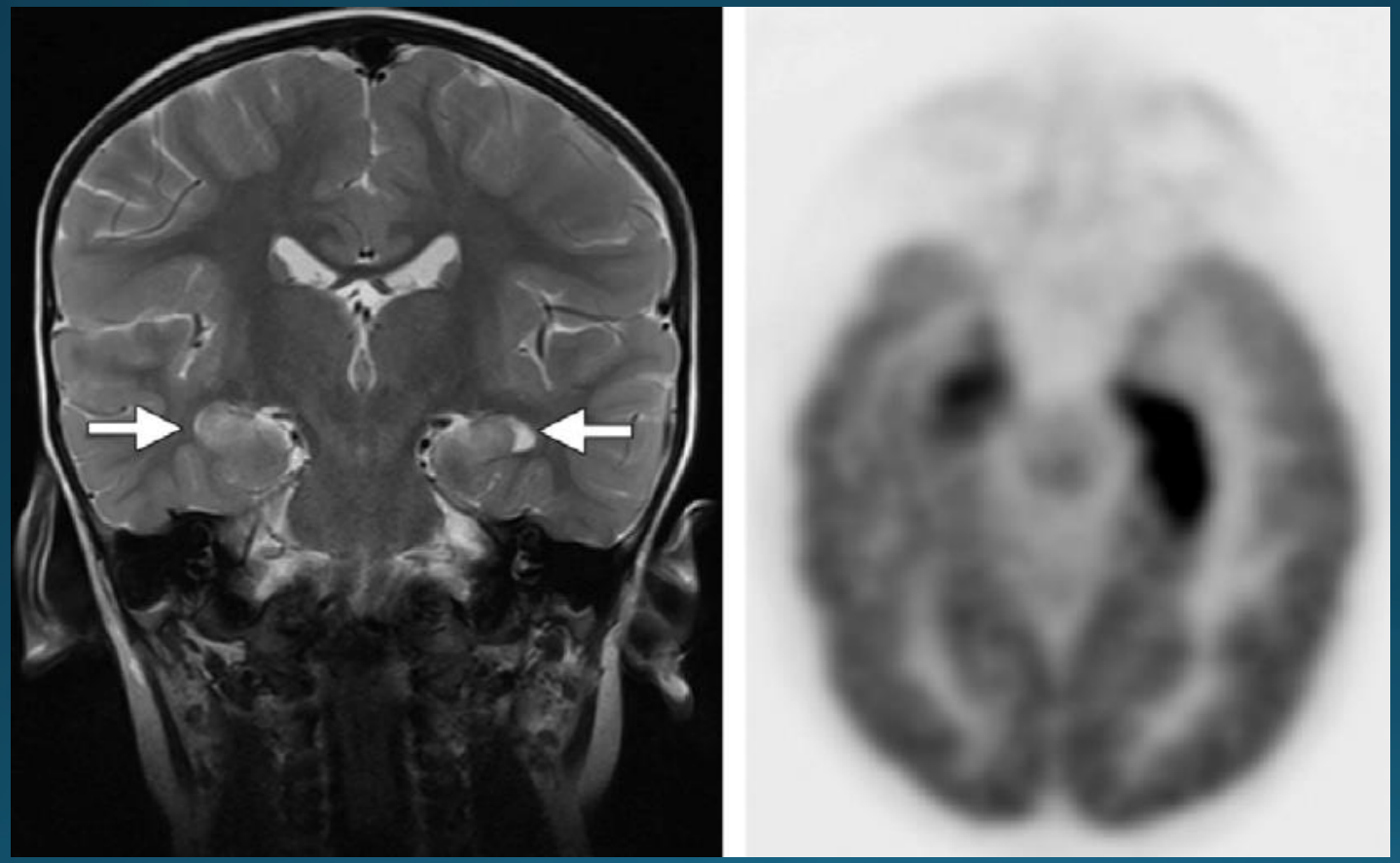
Rasmussen Encephalitis

- Autoimmune or viral etiology
- Intractable seizures
- Swelling of gyri, blurring of the cortical ribbon, and abnormal high T2 and FLAIR MR signal intensity in underlying white matter
- May progress to unilateral cortical atrophy, usually within the first 12 months

Rasmussen Encephalitis

- The decreased FDG uptake is presumed to be due to the reduced neuronal activity caused by recurrent seizures, as well as the diffuse inflammatory process itself causing neuronal loss and gliosis

Limbic Encephalitis



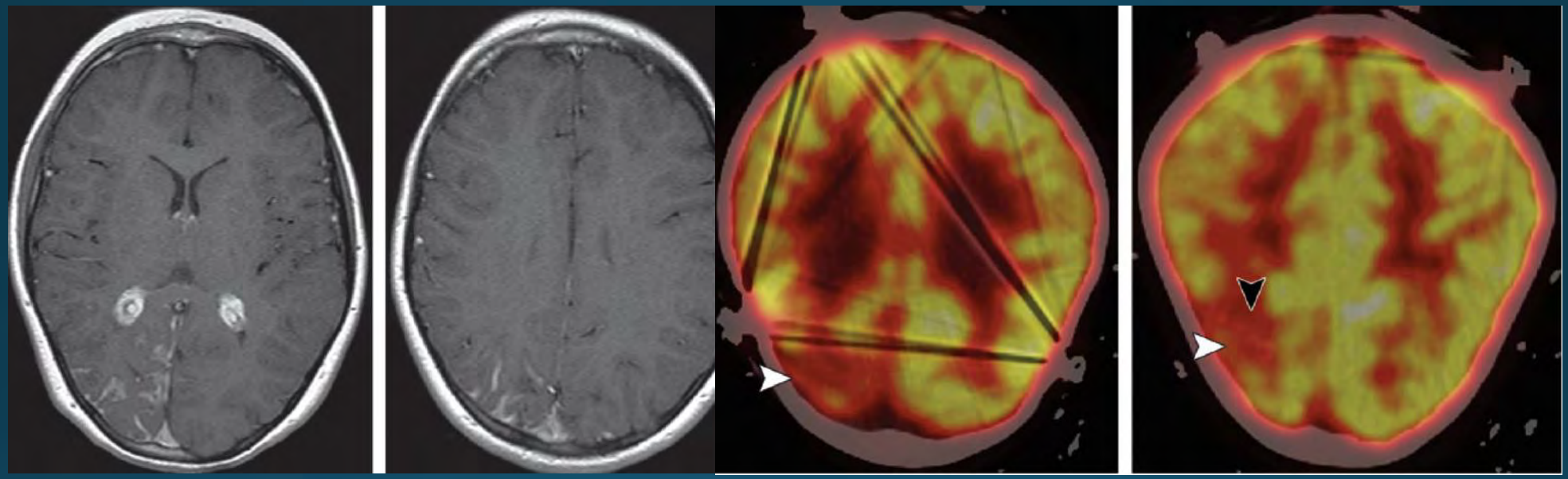
T2-weighted MR image shows bilateral areas of T2 hyperintensity in the hippocampal formations

Increased metabolism bilaterally in the mesial temporal lobes that was confirmed by the presence of anti- NMDA receptor antibodies

Limbic Encephalitis

- Subacute onset of psychiatric symptoms, seizures, and memory loss .
- traditionally described to be a paraneoplastic syndrome associated with carcinomas
- In pediatric population, underlying neoplasm is only identified in less than 25%
- Anti-NMDA (N-methyl D-aspartate)and anti-Hu (Small cell lung CA) are two types of receptor antibodies

Sturge-Weber syndrome

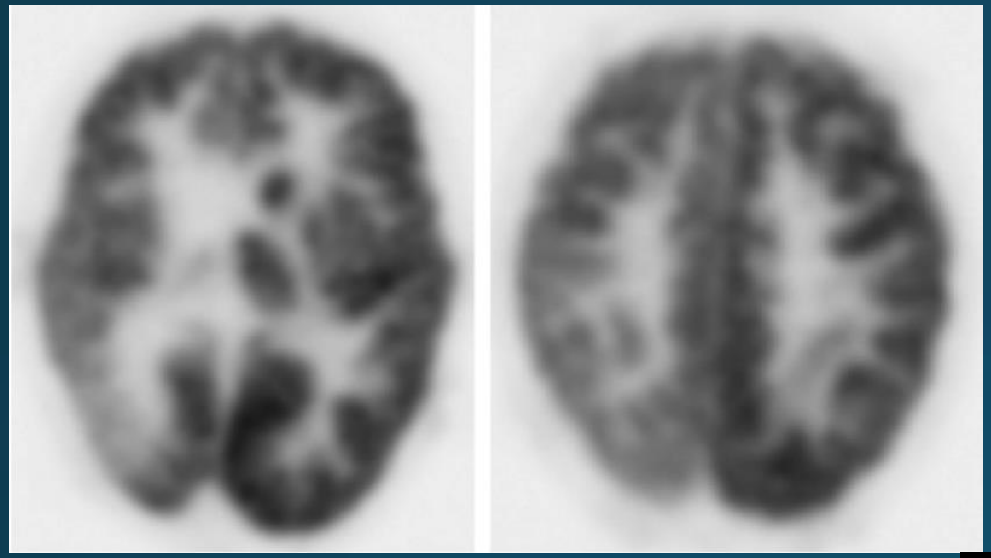


- T1-weighted : right parieto-occipital volume loss with overlying leptomeningeal enhancement, bilateral choroid plexus enhancement
- hypometabolism in the corresponding regions with areas of parenchymal calcification

Sturge-Weber syndrome

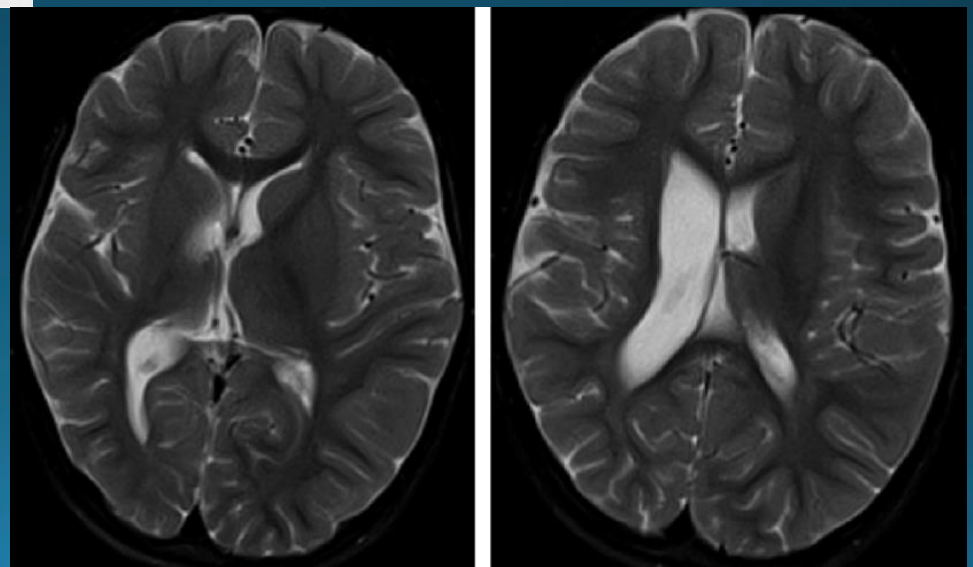
- cortical pial angiomatous malformation
- facial telangiectatic nevi in the trigeminal distribution,
- epilepsy and mental retardation
- MR imaging :pial angiomatosis and serpentine leptomeningeal enhancement, followed by white matter atrophy, gliosis, and calcification

Perinatal Arterial Stroke



Perinatal arterial stroke hypometabolism in the right hemisphere, with sparing of the right frontal lobe

Axial T2- weighted MR images show diffuse white matter loss in the right cerebral hemisphere, with relative sparing of the right frontal lobe, and ex vacuo dilatation of the right ventricle.



Perinatal Arterial Stroke

- Cerebral arterial infarction occurring around the time of birth will show variable degrees of signal abnormality in the affected arterial territory, depending on the timing of the examination in relation to the injury

FDG PET in Childhood Brain Tumors

- Third most common type of pediatric cancer after leukemia and lymphoma
- In low grade tumors the FDG uptake may be similar to that in normal white matter
- The exception is low-grade tumor recurrence associated with dedifferentiation to a higher-grade tumor, which will show increased FDG uptake

Hot spot- brain index

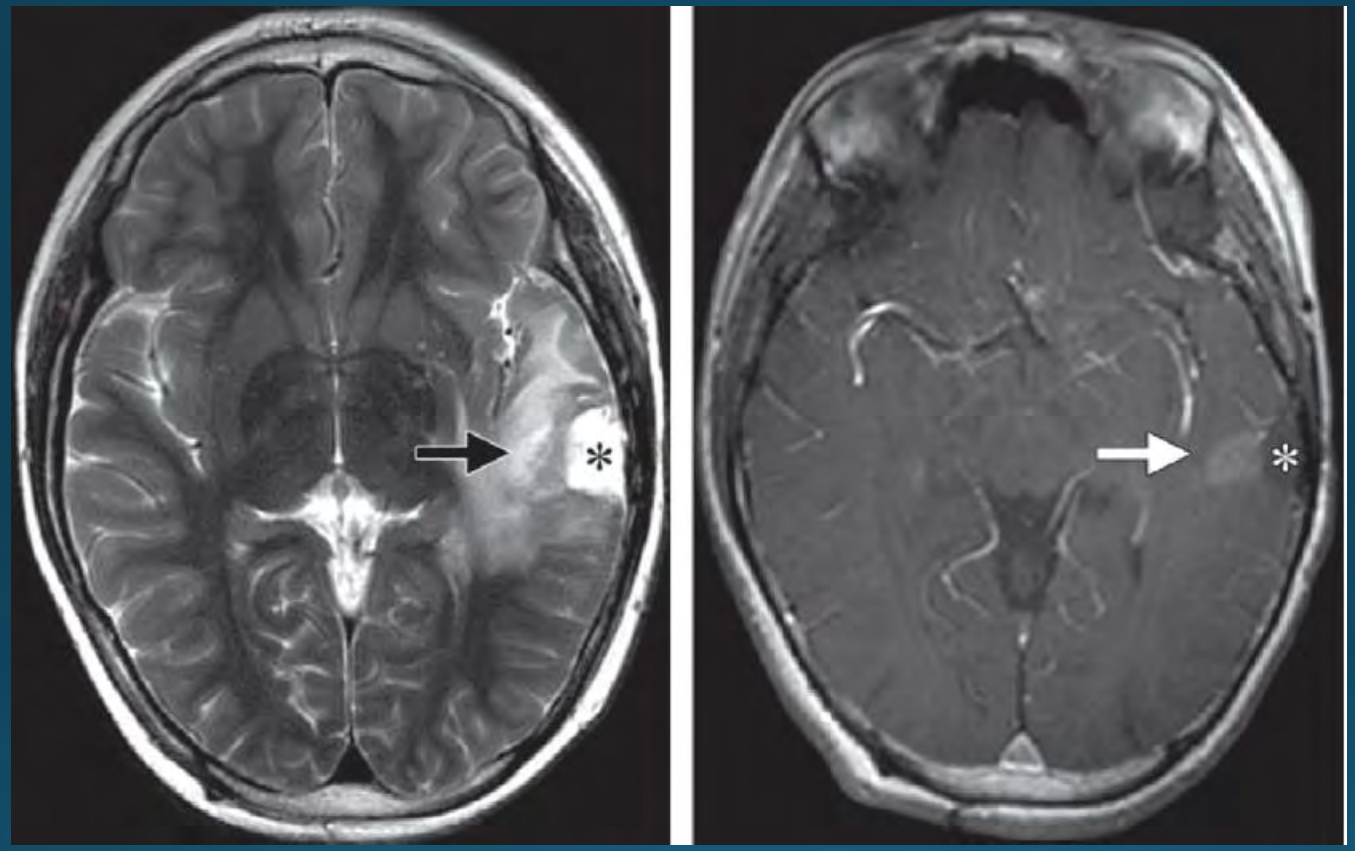
- Correlation of the tumor hot spot with contralateral white and gray matter
- There is a positive correlation between FDG uptake and malignancy grade by using fusion of PET and MR images
- Hypermetabolic benign lesions : such as pilocytic astrocytoma or choroid plexus papilloma

Borgwardt et al, J clinical oncology 2005

FDG PET in Childhood Brain Tumors

- In general, focal increased FDG uptake is present in the majority of residual or recurrent brain tumors.
- PET findings sometimes are apparent even before morphologic changes become evident at MR imaging

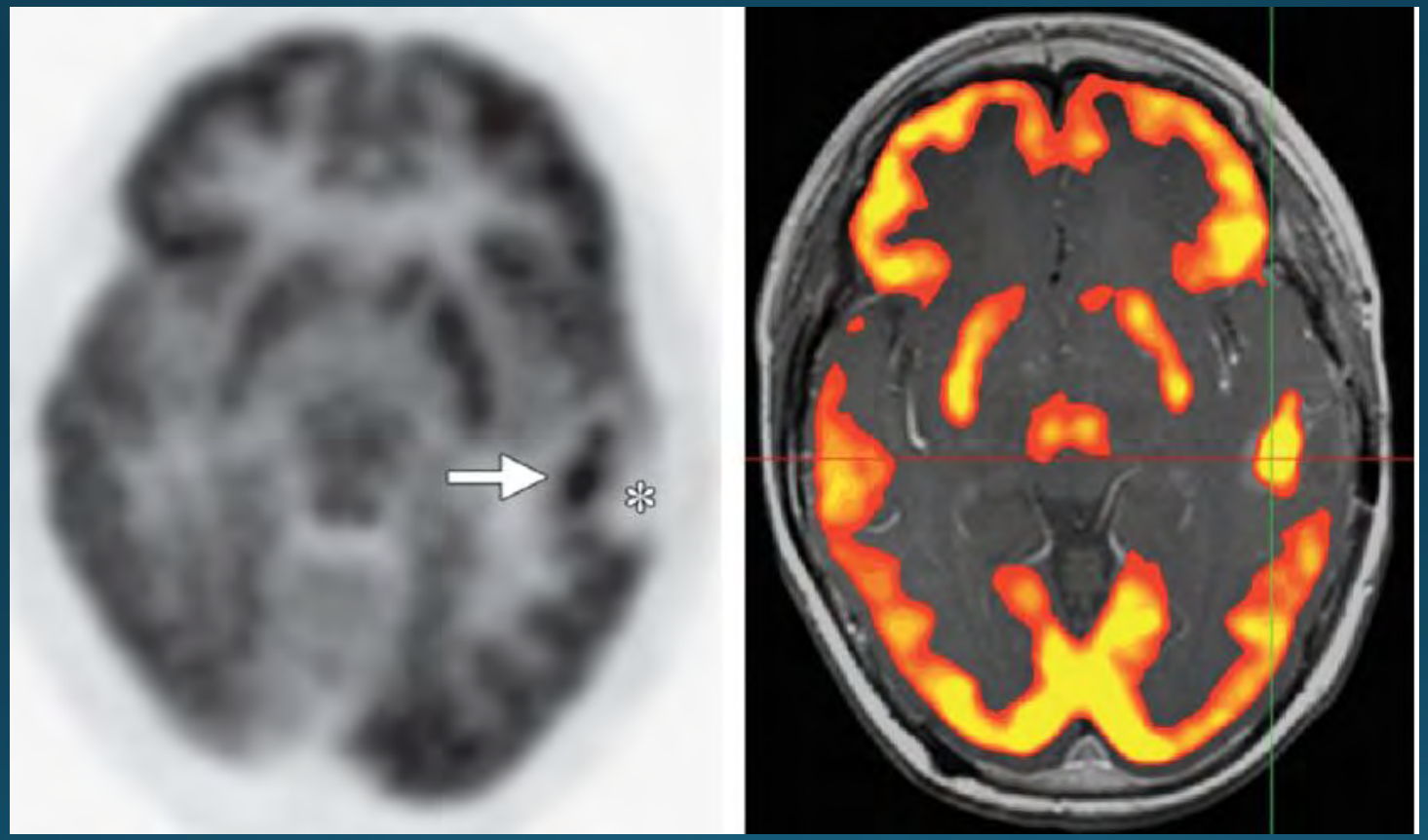
Neurofibromatosis type 1



History of posterior fossa ependymoma resection , recent resection of a secondary left temporal lobe grade III anaplastic astrocytoma.

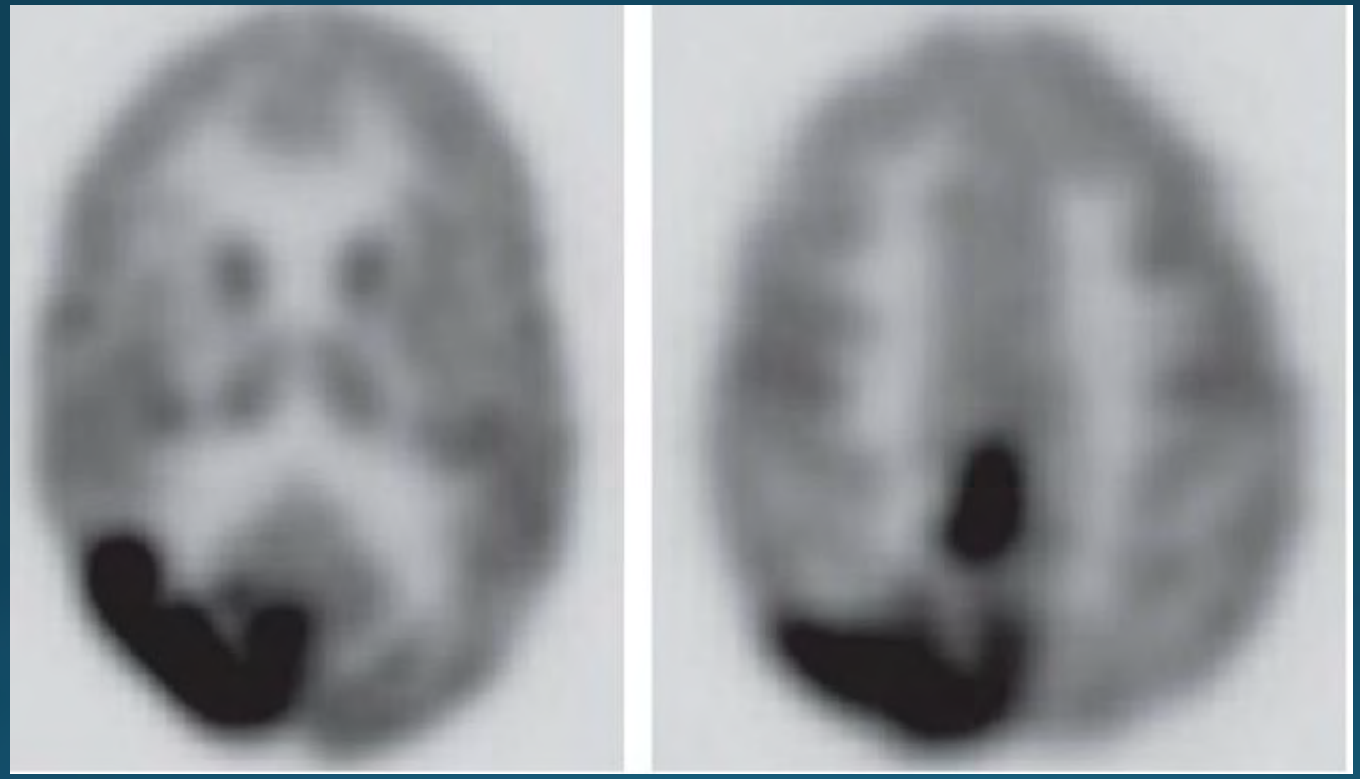
- Increase in T2 signal intensity surrounding the left temporal resection cavity
- Contrast enhanced T1: focal increased enhancement , concerning for recurrent tumor or a radiation-induced effect

Neurofibromatosis type 1



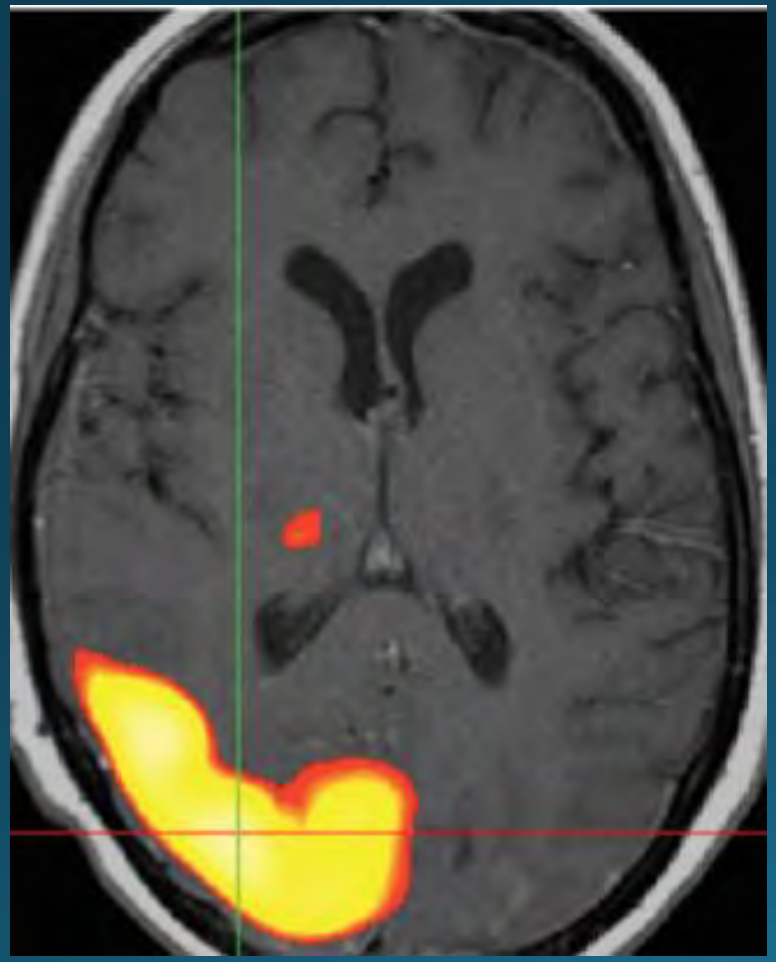
Increased uptake helps differentiate between residual or recurrent tumor and radiation necrosis : consistent with tumor recurrence

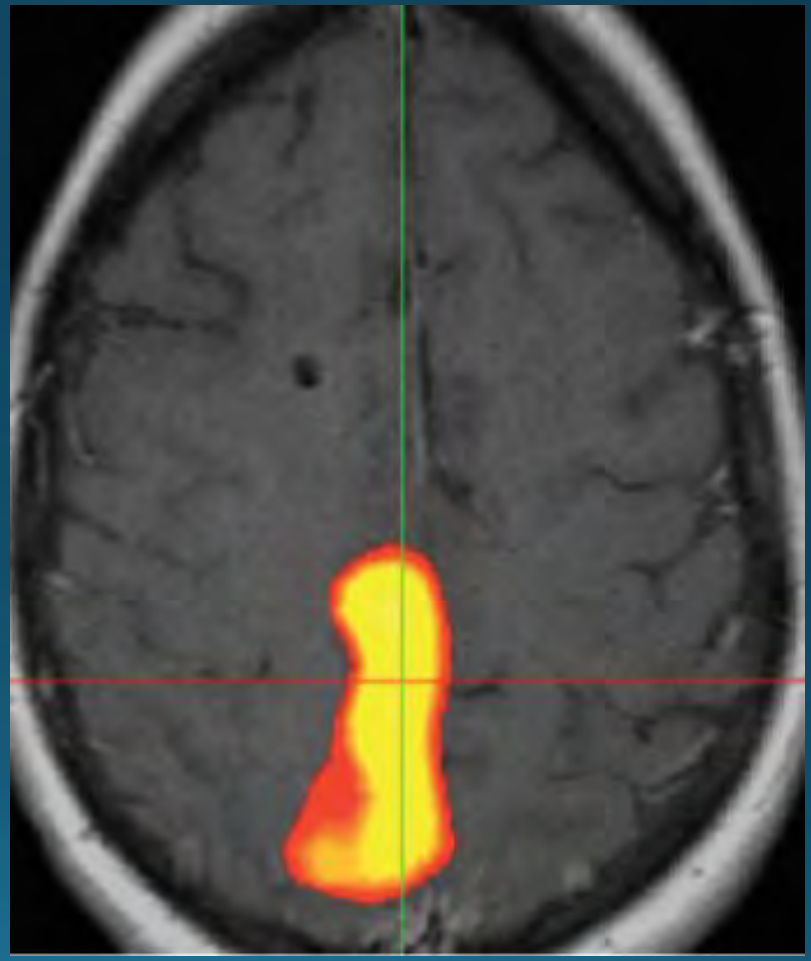
Recurrent Burkitt lymphoma



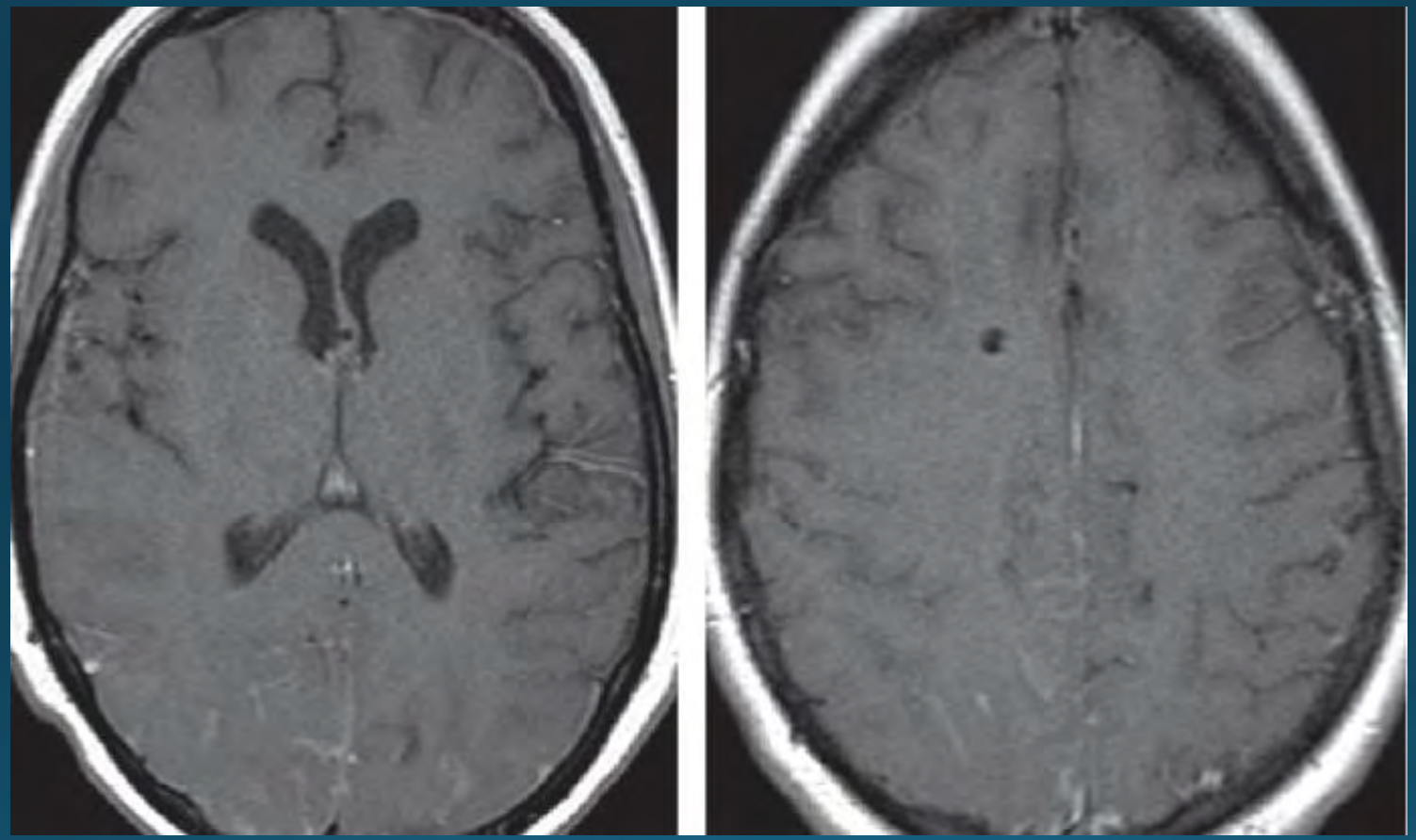
FDG PET : extensive hypermetabolic activity in posterior right temporoparietal and occipital regions extending to interhemispheric dura

Recurrent Burkitt lymphoma



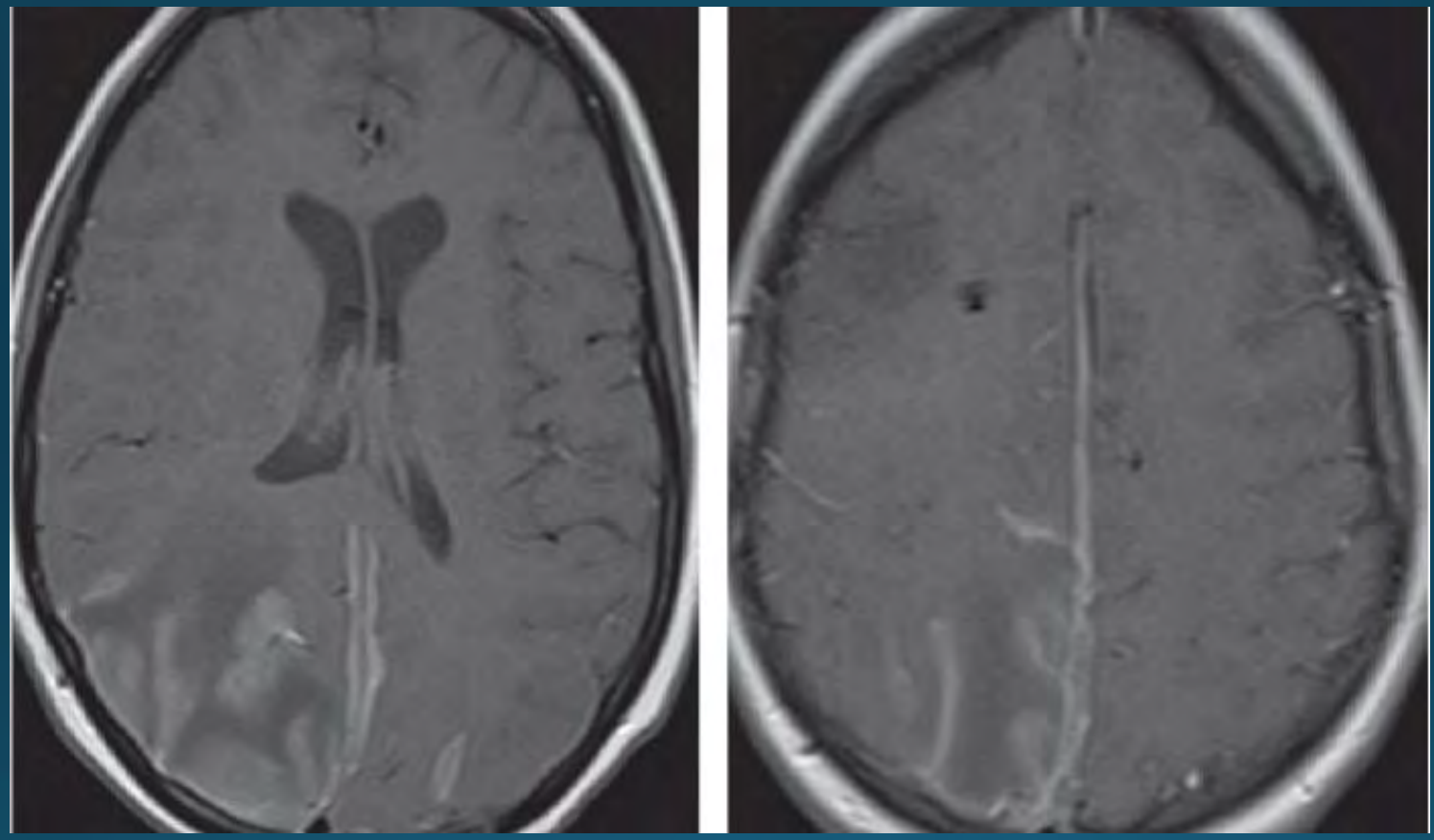


Recurrent Burkitt lymphoma



contrast-enhanced T1-weighted MR : very subtle leptomeningeal enhancement along the posterior right temporoparietal and occipital regions

Recurrent Burkitt lymphoma



1 month later show considerable worsening of the leptomeningeal and dural enhancement, with adjacent parenchymal edema, consistent with disease progression

PET pitfall in brain tumor

- Unfortunately, after treatment, the FDG uptake in high-grade tumors may be similar to that in adjacent white matter or minimally increased
- In these cases, fusion of FDG PET and MR images can play a crucial role, and any uptake higher than that of the adjacent brain background level that corresponds to the region of concern at MR imaging should be considered suspicious for recurrence.

MR perfusion imaging versus FDG PET

- MR perfusion imaging and FDG PET are similar in effectiveness for differentiating radiation necrosis from tumor recurrence.
- The current recommendation is to perform FDG PET at least 6 weeks after the patient completes radiation therapy

Hatzoglou et al, Clin Imaging 2013

Amino acid PET radiotracers

- 11C-methionine (l-[methyl-11C]methionine), which evaluate local protein metabolism, are increasingly useful in assessing pediatric brain tumors, given the low uptake of these tracers in normal brain tissue, which leads to a high tumor-to–normal brain tissue contrast.
- particularly helpful in low-grade tumors
- Short half life(20 minutes)

Conclusion

- FDG PET can be used as a problem-solving tool in the evaluation and management of pediatric patients with :
- Epilepsy (identify the focal epileptogenic zone, as well as the functional deficit zone)
- Brain tumors (distinguishing residual or recurrent malignancies from post therapeutic changes)

In all cases, correlation or coregistration of PET images with MR images provides added diagnostic value.

References

- *Luana Stanescu, MD • Gisele E. Ishak, MD Paritosh C. Khanna, MD Deepa R. Biyyam, MD Dennis W. Shaw, MD • Marguerite T. Parisi, MD, MSEd ,* ***RSNA , 2013***