NEUROIMAGING IN EPILEPSY

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EPILEPSY

- From the beginning of the disease, brain imaging assists in reaching the correct diagnosis, selective initial treatments and estimating the prognosis for treatment response.
- For the patients with drug-resistant epilepsy, neuroimaging becomes more important when considering epilepsy surgery.
- Localizing the epileptogenic onset zone, optimizing seizure freedom and minimizing the risk of neurologic impairment.

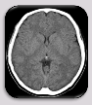
NEUROIMAGING IN EPILEPSY

- Computed tomography (CT)
- Magnetic resonance imaging (MRI) : Structural and functional MRI (fMRI), MR perfusion
- EEG combined with fMRI (EEG/fMRI)
- Positron emission tomography (PET)
- Ictal and interictal single photon emission computed tomography (SPECT)
- Magnetoencephalography (MEG)
- Wada Test (Cerebral angiography)

ANATOMIC NEUROIMAGING (MRI, CT)

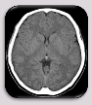
- Determination of the actual pathologic/structural lesion
- Determination of location and extent of the potential epileptogenic zone
- Surgical planning (type of resection or palliative surgery)
- Predicting operative outcome

INDICATION OF CT SCAN



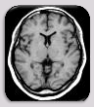
- Emergency/Acute situations
- New-onset seizure patients with symptoms (i.e. focal deficits, altered mental status, fever, trauma, persistent headache, history of cancer, anticoagulation, ventriculoperitoneal shunts, acquired immunodeficiency syndrome)
- New-onset seizures in elderly (acute stroke and tumors)
- Patients with MRI contraindication

INDICATION OF CT SCAN



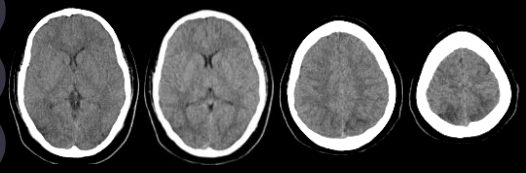
- CT can detect some tumors, large arteriovenous malformations, stroke and calcified lesions.
- CT with contrast is indicated in cases with suspicion for infection or neoplasms, if MRI is unavailable.

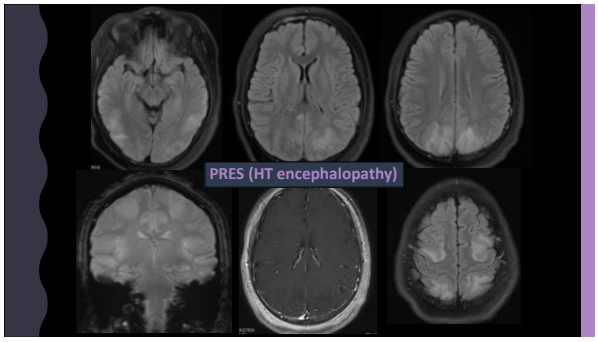
INDICATION OF MRI BRAIN



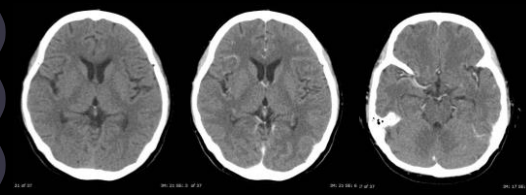
- Focal seizure, at any age
- Abnormal neurological examination (focal deficits, stigmata of neurocutaneous, cerebral malformation syndrome, developmental delay/arrest/regress)
- Generalized or unclassified seizures in the first year of life or in adulthood
- Difficulty obtaining seizure control with first-line AEDs
- Loss of seizure control or a change in the pattern of seizures

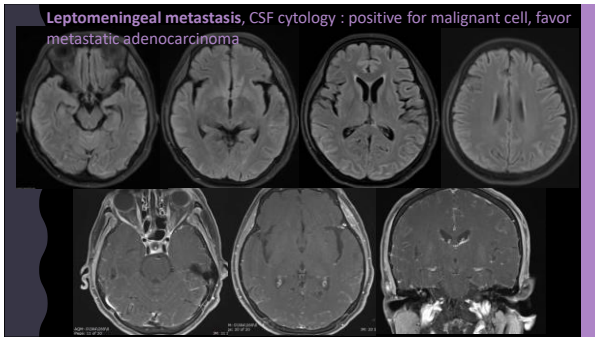
A 14-year-old boy with acute glomerulonephritis, HT and seizure (posterior reversible encephalopathy syndrome, **PRES**)





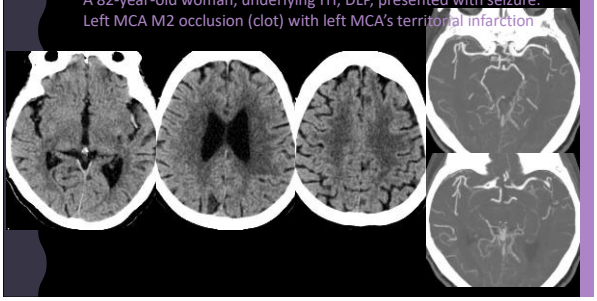
A 58-year-old woman with progressive headache, diplopia, seizure and stiffness of neck.





Leptomeningeal metastasis, CSF cytology : positive for malignant cell, favor metastatic adenocarcinoma

A 82-year-old woman, underlying HT, DLP, presented with seizure. Left MCA M2 occlusion (clot) with left MCA's territorial infarction



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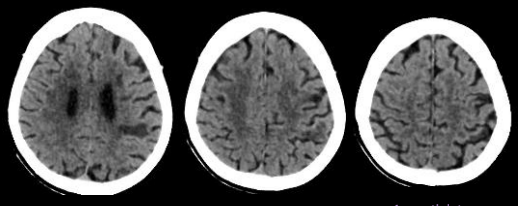


1 month later

THE GOALS OF NEUROIMAGING IN PRESURGICAL EVALUATION

- To identify structural, and if possible, functional abnormalities
- To aid in formulating a syndromic or etiologic diagnosis
- To detect additional abnormalities
- To depict the relationship of the abnormalities to the eloquent regions of the brain (mapping of sensorimotor, language and memory functions)

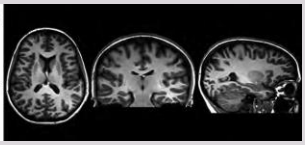
HARMONIZED NEUROIMAGING OF EPILEPSY STRUCTURAL SEQUENCES (HARNESS-MRI PROTOCOL)

- High-resolution 3D T1W MRI :
  for optimal evaluation of brain anatomy and morphology

EPILEPSY PROTOCOL – 3D MRI

T1-weighted

Sequence type: gradient echo
Voxel size (mm): 1 x 1 x 1
Best to evaluate: anatomy and morphology (volume, thickness, sulco-gyral shape, grey-white matter interface integrity)



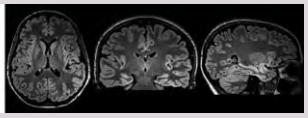
Epilepsia. 2019;60:1054-1068

HARMONIZED NEUROIMAGING OF EPILEPSY STRUCTURAL SEQUENCES (HARNESS-MRI PROTOCOL)

- High-resolution 3D FLAIR : for assessing signal anomalies, particular hyperintensities related to gliosis, enhancing the visibility of hyperintense cortical lesions

FLAIR

Sequence type: turbo spin echo
Voxel size (mm): 1 x 1 x 1
Best to evaluate: signal intensity
Caveat - Not sensitive in neonates and children <24 months of age due to incomplete myelination



Epilepsia. 2019;60:1054-1068

HARMONIZED NEUROIMAGING OF EPILEPSY STRUCTURAL SEQUENCES (HARNESS-MRI PROTOCOL)

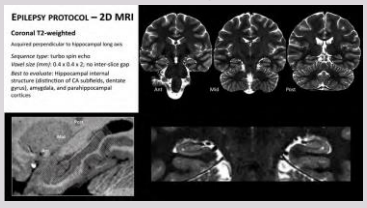
- High in-plane resolution 2D coronal T2W MRI : for assessing the hippocampal internal structure

EPILEPSY PROTOCOL – 2D MRI

Coronal T2-weighted

Acquired perpendicular to hippocampal long axis

Sequence type: turbo spin echo
Voxel size (mm): 0.4 x 0.4 x 2; no inter-slice gap
Best to evaluate: Hippocampal internal structure (distinction of CA subfields, dentate gyrus), amygdala, and parahippocampal cortices



(The images are acquired perpendicular to the long axis of the hippocampus, using submillimetric voxel resolution.)

Epilepsia. 2019;60:1054-1068

ETIOLOGY OF EPILEPSY

Etiology of epilepsy (ILAE 2017 classification)
→ structural, genetic, infectious, metabolic, immune, unknown

- **Structural** : hippocampal sclerosis, congenital malformation, stroke, tumor, infection, tuberous sclerosis (genetic)
- **Genetic** : autoimmune encephalitis, inborn errors of metabolism
- **Metabolic** : inborn errors of metabolism
- **Infectious** : neurocysticercosis, TB, SSPE, CMV

TABLE 2: Cause of Epilepsy Categorized by Age at Onset of Seizures

Cause	Age (yr)				
	0–2	3–20	21–40	41–60	>60
Anoxia	Yes				
Metabolic abnormalities or inborn error of metabolism	Yes				
Congenital or developmental malformations	Yes	Yes			
Infection	Yes	Yes			
Phakomatosis	Yes	Yes			
Primary generalized seizures		Yes			
Hippocampal sclerosis		Yes			
Trauma	Yes	Yes	Yes	Yes	
Vascular malformation			Yes		
Tumor			Yes	Yes	Yes
Cerebrovascular accident				Yes	Yes

Note.—Phakomatoses include tuberous sclerosis, Sturge-Weber syndrome, and neurofibromatosis.

AJR 1992;159:1165-1174

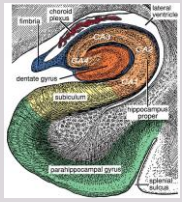
PATHOLOGIC ENTITIES OF EPILEPSY

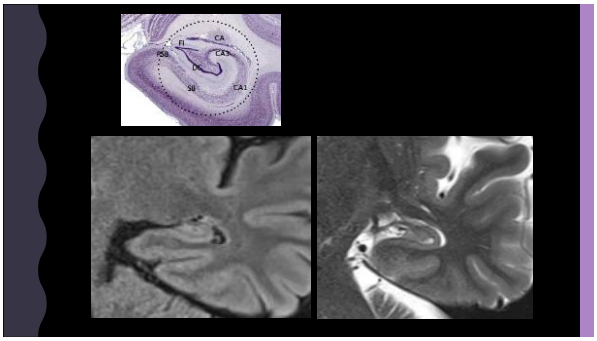
- Malformation of cortical development
- Mesial temporal/hippocampal sclerosis
- Neoplasm
- Vascular abnormalities
- Gliosis and miscellaneous abnormalities

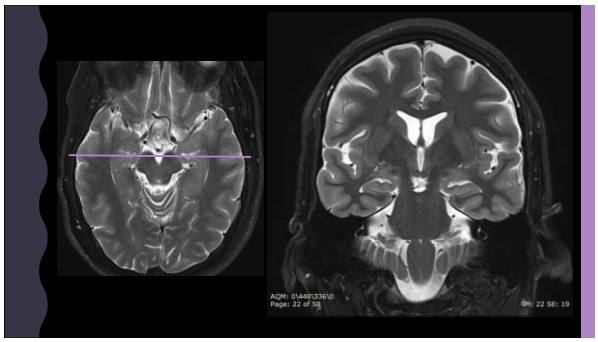
HIPPOCAMPAL SCLEROSIS

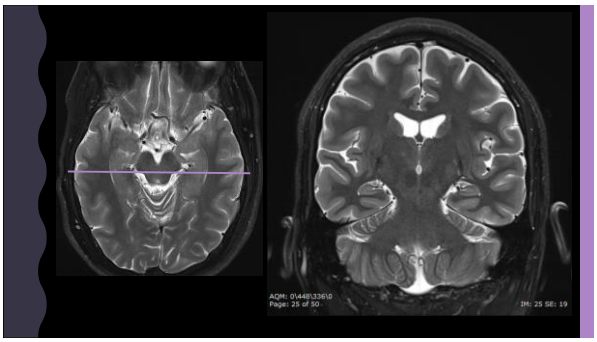
Hippocampus

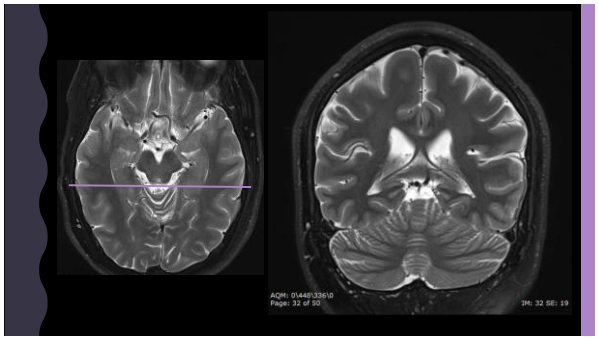
- curved structure on the medial aspect of the temporal lobe
- consisting of complex U-shaped layers of the dentate gyrus and cornu amonis, interlocked together
- cornu amonis : CA 1 through CA 4
- cornu amonis → subiculum → parahippocampal gyrus



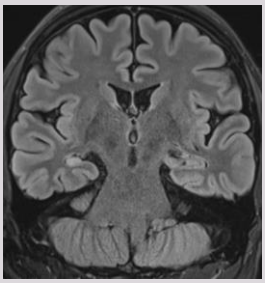








MR FEATURES OF HIPPOCAMPAL SCLEROSIS



Principle hippocampal findings

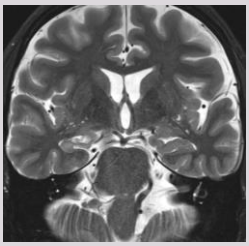
- Hippocampal atrophy
- Signal alterations (hyperintense on T2WI and FLAIR)
- Loss of internal architecture

MR FEATURES OF HIPPOCAMPAL SCLEROSIS

Secondary findings

Temporal lobe

- Ipsilateral loss of hippocampal head digitations
- Dilation of temporal horn
- Temporal lobe atrophy
- Collateral WM atrophy
- Anterior temporal WM change

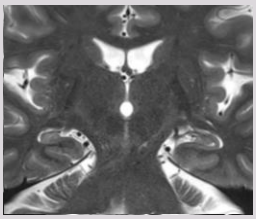


MR FEATURES OF HIPPOCAMPAL SCLEROSIS

Secondary findings

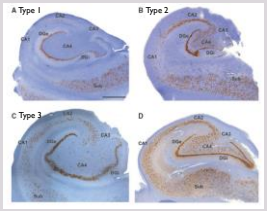
Extratemporal lobe

- Fornix atrophy
- Mammillary body atrophy
- Thalamic atrophy
- Caudate atrophy

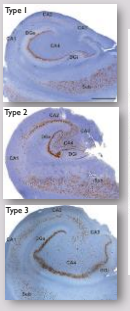


THE ILAE CLASSIFICATION OF HS IN PATIENTS WITH TLE

- **HS ILAE type 1** = severe neuronal loss and gliosis predominantly in CA1 and CA 4 regions
- **HS ILAE type 2** = CA 1 predominant neuronal cell loss and gliosis
- **HS ILAE type 3** = CA 4 predominant neuronal cell loss and gliosis



Epilepsia, 54(7):1315-1329, 2013



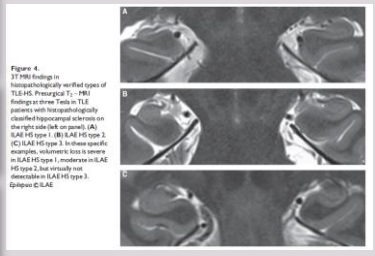
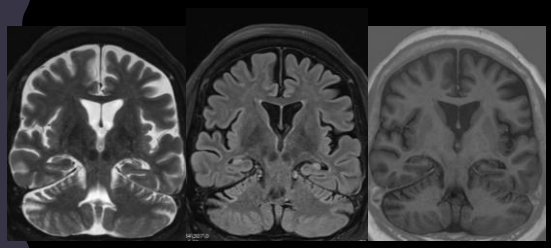


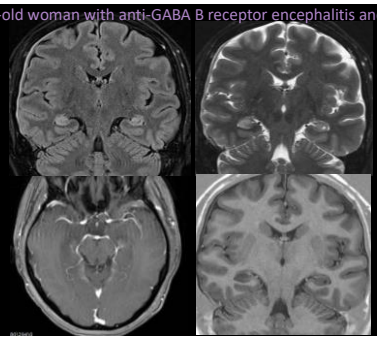
Figure 4.
3T MRI findings in histopathologically verified types of TLE-HS. Presurgical T_2 – MRI findings at three Tesla in TLE patients with histopathologically classified hippocampal sclerosis on the right side (left on panel). (A) ILAE HS type 1. (B) ILAE HS type 2. (C) ILAE HS type 3. In these specific examples, volumetric loss is severe in ILAE HS type 1, moderate in ILAE HS type 2, but virtually not detectable in ILAE HS type 3.
Epilepsia © ILAE

Epilepsia, 54(7):1315-1329, 2013

A 32-year-old woman with bilateral MTS

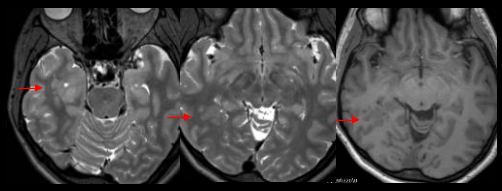


A 39-year-old woman with anti-GABA B receptor encephalitis and seizure



DUAL PATHOLOGY

A 36-year-old woman with focal epilepsy, onset at the age of 25
Subcortical-subependymal heterotopia at right temporal lobe and right MTS



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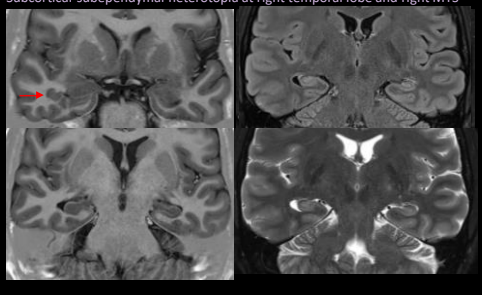
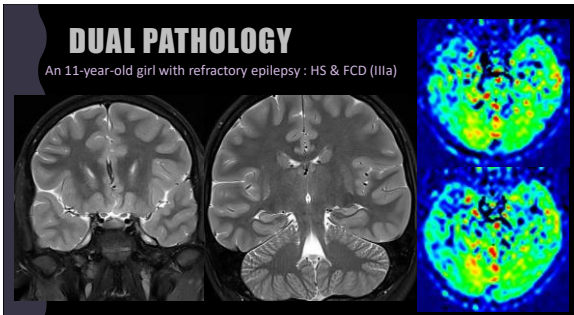


DUAL PATHOLOGY

An 11-year-old girl with refractory epilepsy : HS & FCD (IIIa)



MR FEATURES OF MALFORMATIONS OF CORTICAL DEVELOPMENT

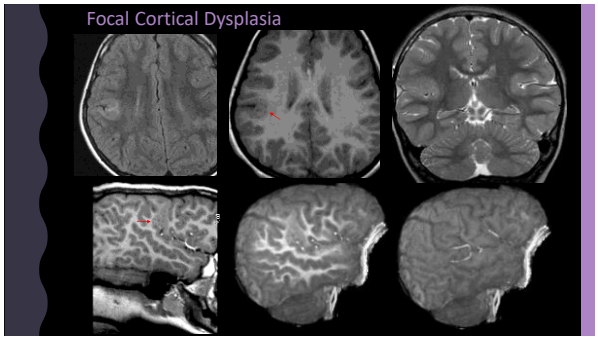
- Cortical thickening
- Blurring or indistinctness of gray-white matter junction
- Hyperintensity of gray matter
- Irregularity of gray-white matter junction
- Macrogyria
- Paucity of gyri (pachygyri)
- Polymicrogyria (multiple small gyri)
- CSF cleft and cortical dimple
- Altered sulcal morphology
- Radial bands
- Heterotopic GM, ependymal or subcortical
- Band heterotopia
- Transmantle heterotopia
- Hemispheric enlargement

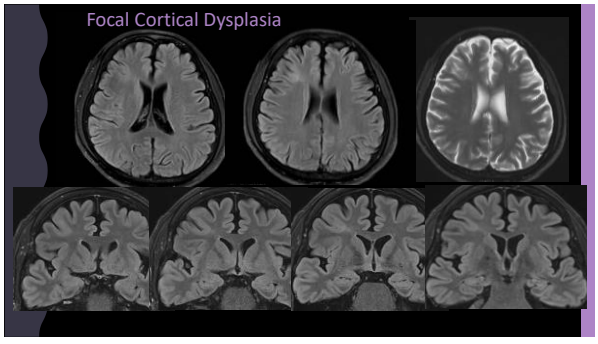
FOCAL CORTICAL DYSPLASIA

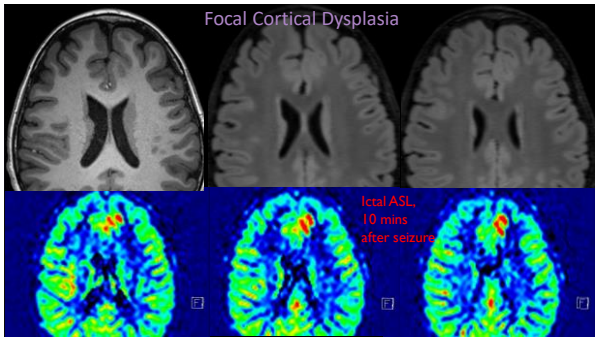
MRI findings:

- cortical thickening
- blurring of WM-GM junction with abnormal architecture of subcortical layer
- altered signal from WM with or without the penetration through cortex (transmantle sign)
- altered signal from GM
- abnormal sulcal or gyral pattern
- segmental and/or lobar hypoplasia/atrophy

Pol J Radiol, 2012; 77(2): 35-43







FOCAL CORTICAL DYSPLASIA

Table 2. New classification system of focal cortical dysplasia by Blumcke et al. 2011.

Type	Characteristic features
I	a – focal cortical dysplasia with abnormal radial cortical lamination b – focal cortical dysplasia with abnormal tangential 6-layer cortical lamination c – focal cortical dysplasia with abnormal radial and tangential cortical lamination
II	a – focal cortical dysplasia with dysmorphic neurons b – focal cortical dysplasia with dysmorphic neurons and balloon cells
III	a – architectural distortion of cortical layer in temporal lobe with hippocampal atrophy b – architectural distortion of cortical layer adjacent to glial or glioneuronal tumor c – architectural distortion of cortical layer adjacent to vascular malformation d – architectural distortion of cortical layer adjacent to other lesions acquired in early childhood such as trauma, ischemic event, encephalitis

The histopathology-based FCD classification update

(new categories highlighted in gray)

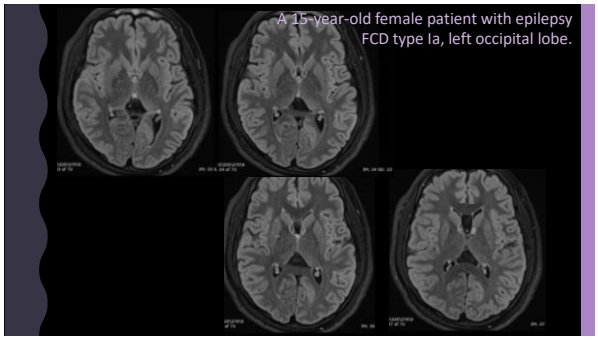
FCDI [a]	FCDIa abundant microcolumns	FCDIb abnormal layering	FCDIc vertical and horizontal abnormalities	
FCDII [a]	FCDIIa dysmorphic neurons		FCDIIb dysmorphic neurons and balloon cells	
FCDIII [a]	FCDIIIa cortical dyslamination associated with hippocampal sclerosis	FCDIIIb cortical dyslamination adjacent to brain tumor	FCDIIIc cortical dyslamination adjacent to vascular malformation	FCDIIId cortical dyslamination adjacent to lesion acquired during early life, e.g. stroke
White Matter [a]	mMCD [b] with excessive heterotopic neurons [a]		mMCD with oligodendroglial hyperplasia in epilepsy (MOGHE) [c]	
No definite FCD on histopathology [a]	Abnormality of cortical organization remains ambiguous and histopathological findings not compatible with FCDI, II or III [d]			

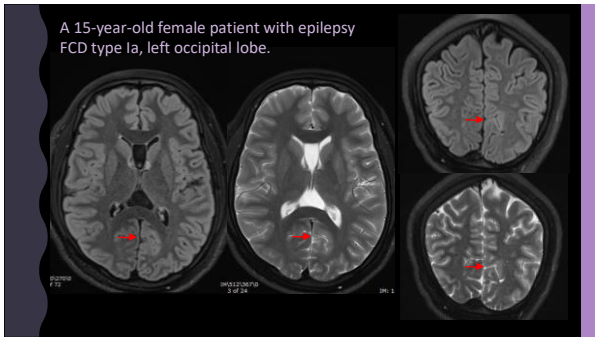
Epilepsia. 2022;63:1899-1919

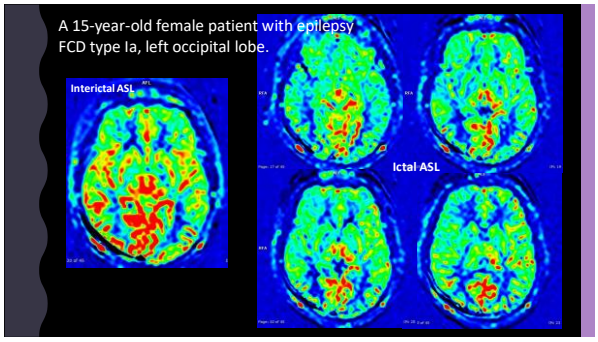
FCD TYPE I

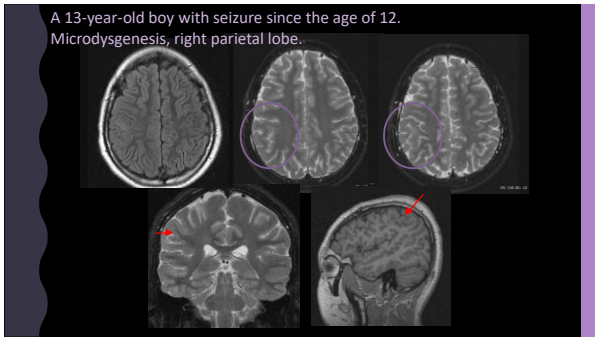
- Significant segmental or lobar hypoplasia/atrophy
- Often with reduced volume of subcortical WM, which may reveal increased signal on T2WI/FLAIR and decreased on T1WI/IR.
- Slight blurring of GM/WM junction
- Abnormal sulcal and gyral pattern
- Frequently found in the temporal lobe with coexist hippocampal atrophy (IIIa)

Pol J Radiol, 2012; 77(2): 35-43







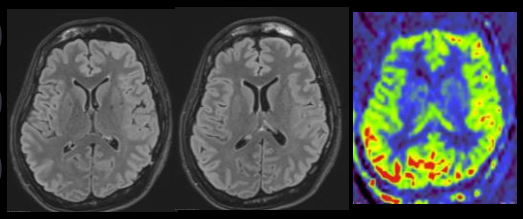


FCD TYPE II

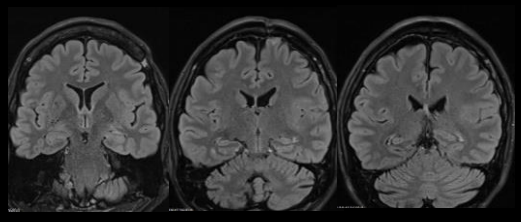
- Cortical thickening
- Marked blurring of GM/WM junction (more evident than in type I)
- An increase WM signal on T2WI, FLAIR (more evident than in type I) and decrease on T1WI
- Altered WM signal, often towards the ventricle (**transmantle sign**)
- Often abnormal sulci, gyri, which clearly visualized by surface 3D
- Perivascular space may be enlarged.
- More often found in extratemporal location, predilection toward **frontal lobe**

Pol J Radiol, 2012; 77(2): 35-43

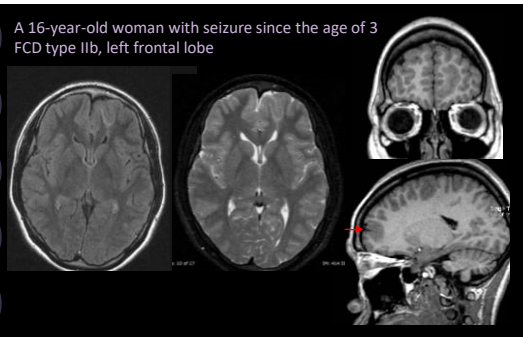
A 36-year-old woman with refractory seizure.
FCD type IIa, left insular lobe.



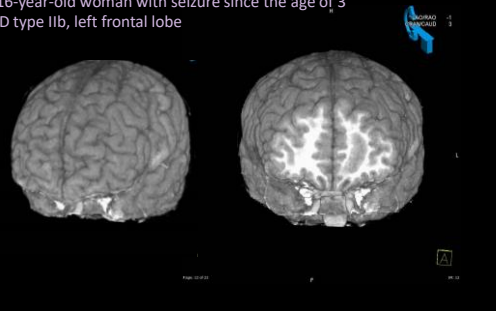
A 36-year-old woman with refractory seizure.
FCD type IIa, left insular lobe.

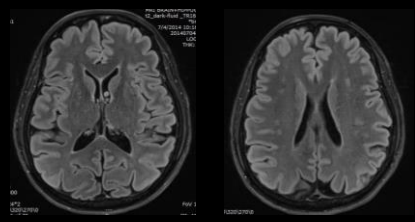


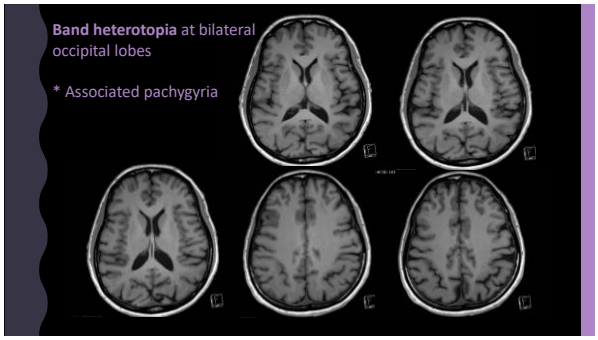
A 16-year-old woman with seizure since the age of 3
FCD type IIb, left frontal lobe

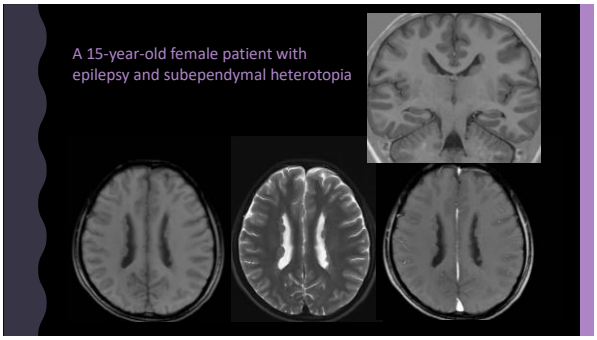


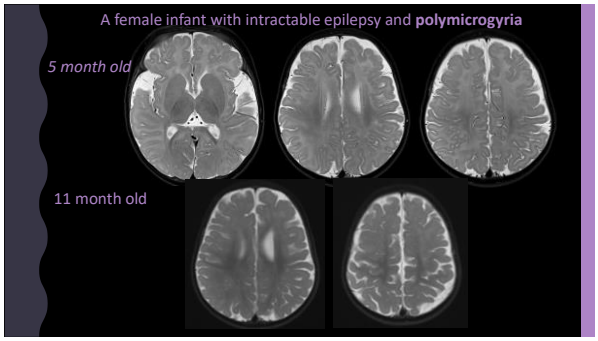
A 16-year-old woman with seizure since the age of 3
FCD type IIb, left frontal lobe

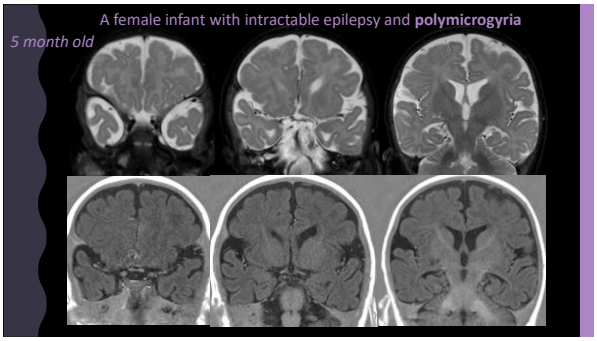


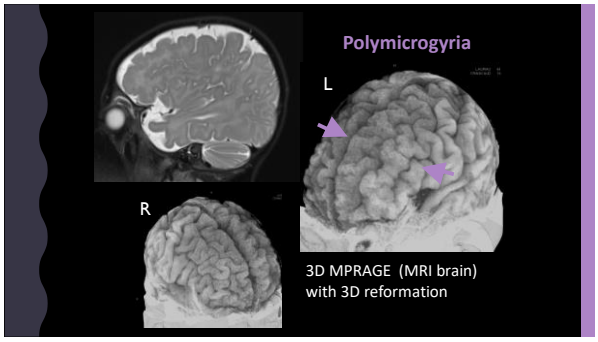






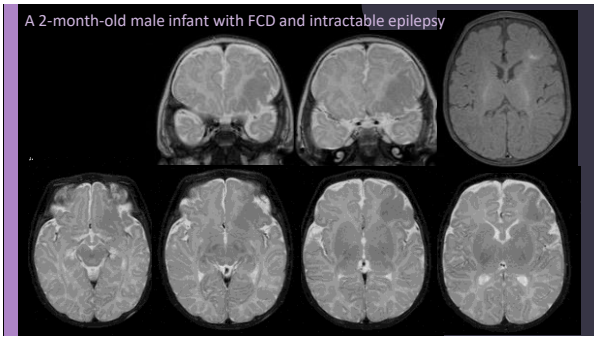






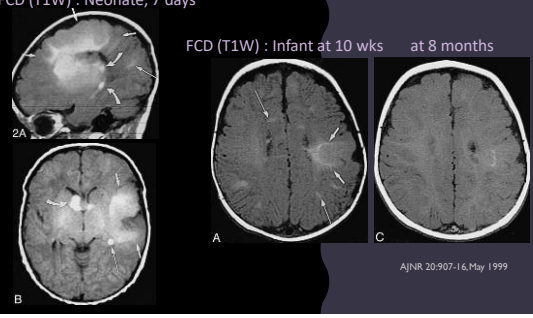
MYELINATION

A 2-month-old male infant with FCD and intractable epilepsy



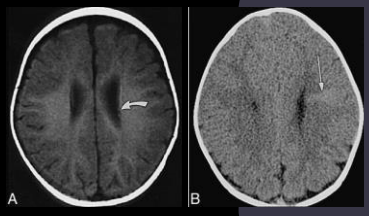
FCD (T1W) : Neonate, 7 days

FCD (T1W) : Infant at 10 wks at 8 months



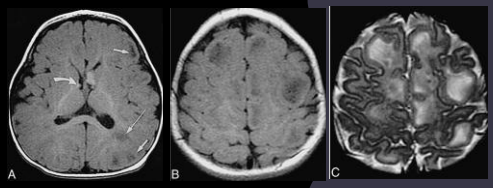
AJNR 20:907-16, May 1999

FCD : Infant, 6 months



AJNR 20:907-16, May 1999

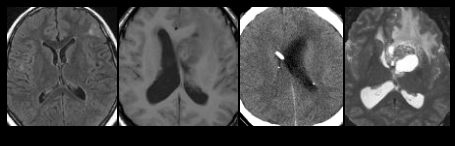
FCD : Infant, 8 months, "adult" signal pattern



AJNR 20:907-16, May 1999

TUBEROUS SCLEROSIS

- Autosomal dominant genetic disease with hamartomas in multiple organs
- Clinical triad: mental retardation, epilepsy and adenoma sebaceum



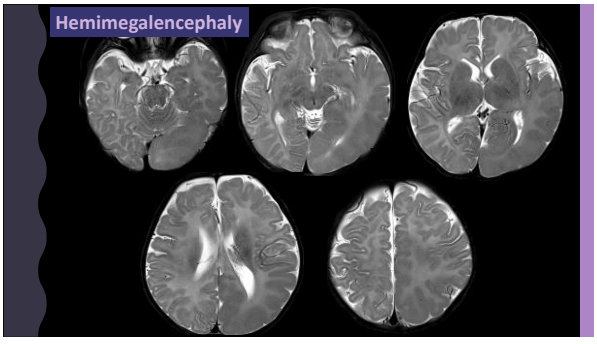
A 5-year-old boy with tuberous sclerosis and intractable epilepsy

mTORopathies

- Tuberous sclerosis complex (TSC)
  - Mutations in the TSC1 or TSC2 genes causes loss of normal inhibition of mTORC1, leading to cell overgrowth and disruptions in synaptogenesis.
  - Cortical malformations, subependymal giant cell astrocytoma (SEGAs) and drug-resistant epilepsy

mTORopathies

- Hemimegalencephaly : HME occurs following somatic mutation (AKT3, PI3K, PTEN, mTOR) leading to hyperactivation of mTOR pathway during brain development.
- Focal cortical dysplasia : Growing evidence for germline and somatic mations in the mTOR pathway leading to FCD

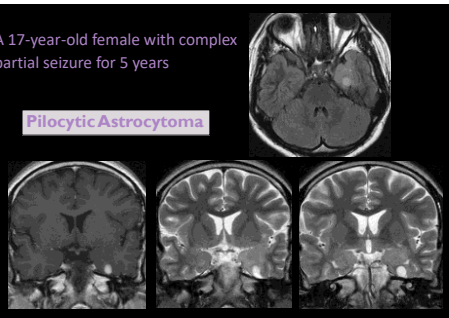


NEOPLASMS

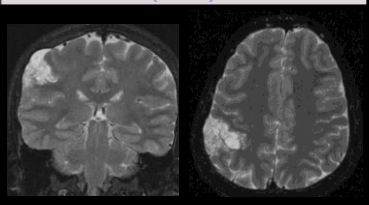
- Involved region: usually temporal lobe (70%), in or adjacent to the cerebral cortex
- MRI 96-99% sensitivity
- Indolent tumors: Ganglioglioma, dysembryoplastic neuroepithelial tumor (DNET), and low-grade gliomas
- Metastasis (elderly, late-onset seizure)
- Chronic recurrent seizures: small, well localized, little or no perilesional edema, +/- mass effect and calvarial remodelling

A 17-year-old female with complex partial seizure for 5 years

Pilocytic Astrocytoma

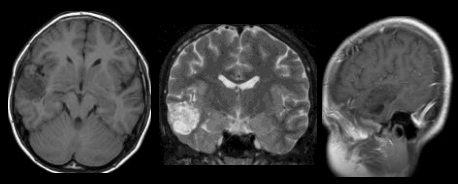


Dysembryoplastic Neuroepithelial Tumor (DNET)



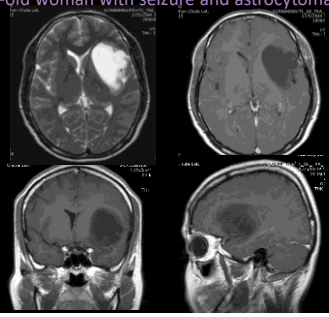
A 13-year-old boy with right-sided headache and left-sided numbness prior to generalized epilepsy

Dysembryoplastic Neuroepithelial Tumor (DNET)



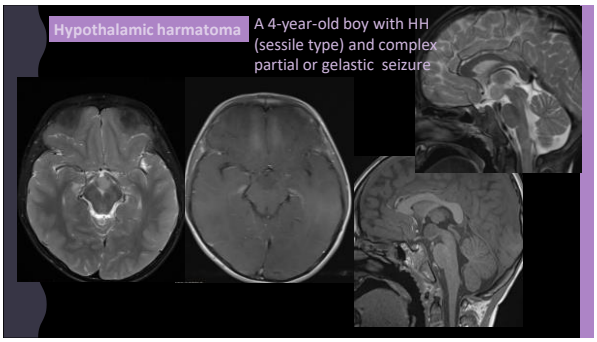
An 11 year-old boy with complex partial seizure for more than a year

A 34-year-old woman with seizure and astrocytoma, grade II

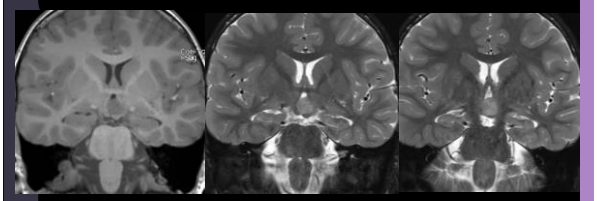


Hypothalamic harmatoma

A 4-year-old boy with HH (sessile type) and complex partial or gelastic seizure



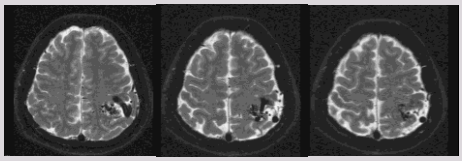
A 4-year-old boy with **hypothalamic harmatoma** (sessile type) and complex partial or gelastic seizure



VASCULAR MALFORMATION

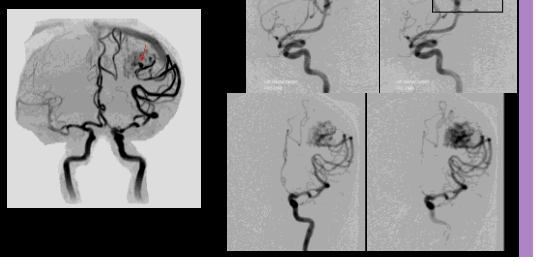
- Brain arteriovenous malformation (BAVM)
- Cavernous angioma or cavernoma: central hyperintensity due to haemoglobin products surrounded by a hypointense rim resulting from hemosiderin
- Most capillary telangiectasia and venous angiomas are clinically silent.

CORTICAL-SUBCORTICAL BRAIN AVM WITH SEIZURE

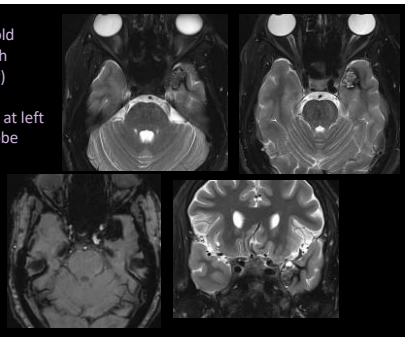


Seizure; a common clinical manifestation of intracranial AVMs (20-60%)
Often associated with the AVMs in the temporal and frontal regions

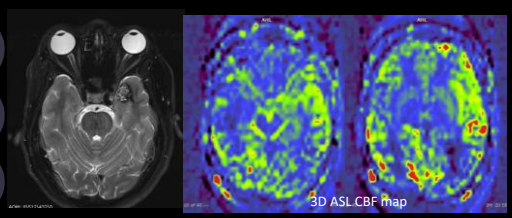
3D TOF MRA brain and DSA images :
Cortical-subcortical AVM, lt parietal lobe
* Intranidal aneurysm



A 35-year-old woman with (automotor) seizure and **cavernoma** at left temporal lobe

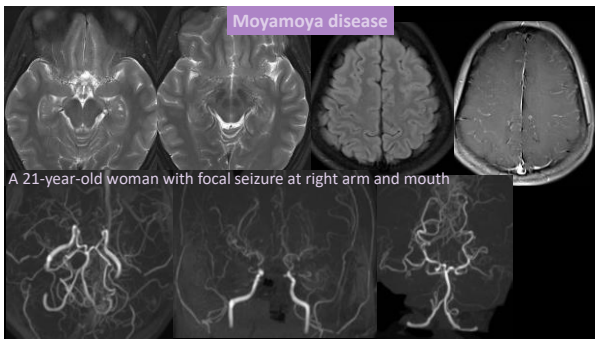


A 35-year-old woman with (automotor) seizure and **cavernoma**



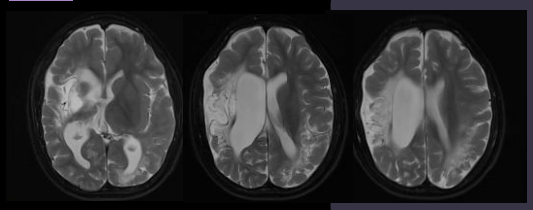
3D ASL CBF map

Moyamoya disease



A 21-year-old woman with focal seizure at right arm and mouth

Gliosis A 4-year-old boy with epilepsy and history of neonatal stroke



Gliosis A 55-year-old man with bilateral temporal lobe epilepsy (post traumatic epilepsy)

ROLE OF NEUROIMAGING IN POSTOPERATIVE EVALUATION

- Determine the adequacy of resection, reasons for operative failure, complications
- Monitor tumor resections for recurrence, follow-up of other substrates
- Prognosticating the postoperative seizure control
- To identify any other previously unrecognized epileptogenic substrates at other location in the brain
- Intracranial EEG: verify the exact anatomic distribution of contacts.

MR AND CT FUSION

SUBDURAL GRID IMPLANTATION FOR INTRACRANIAL EEG

STEREOTACTIC EEG(SEEG)