# Neuroimaging for Neuropsychologists

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Thanks to Bill Lynch, Frank Hillary, Mohamed El Safwany, Grant J. Linnel, Scott Huettel, Aaron S. Field & John DeLuca

# Download NP Seminars

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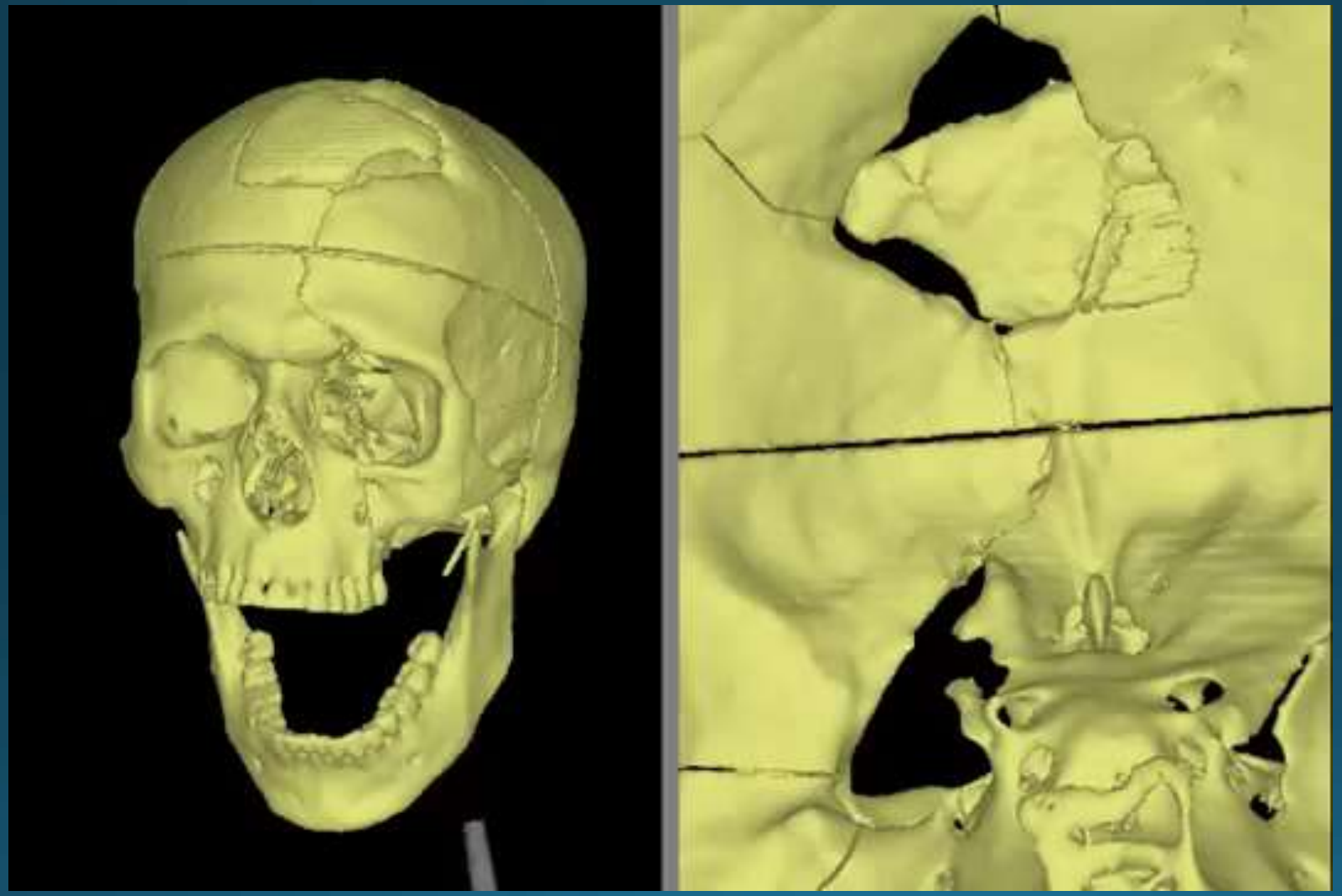
# The Phineas Gage Event

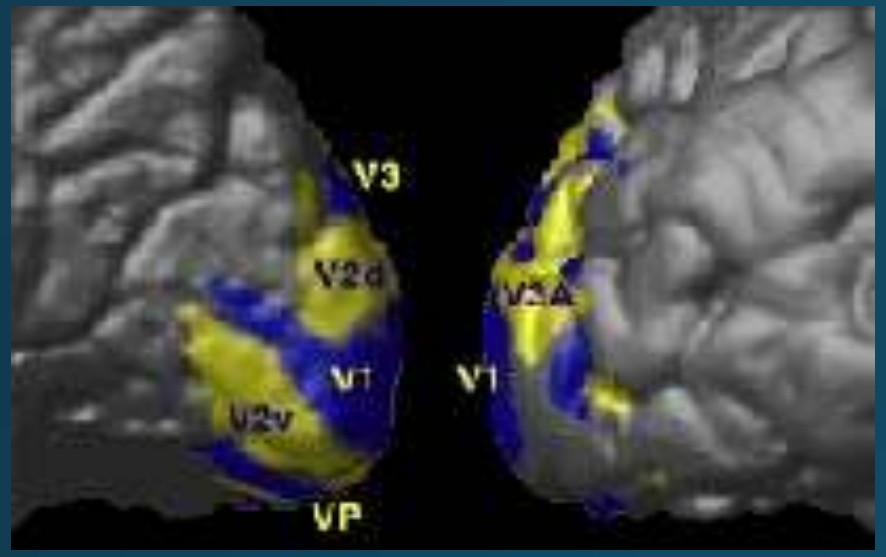


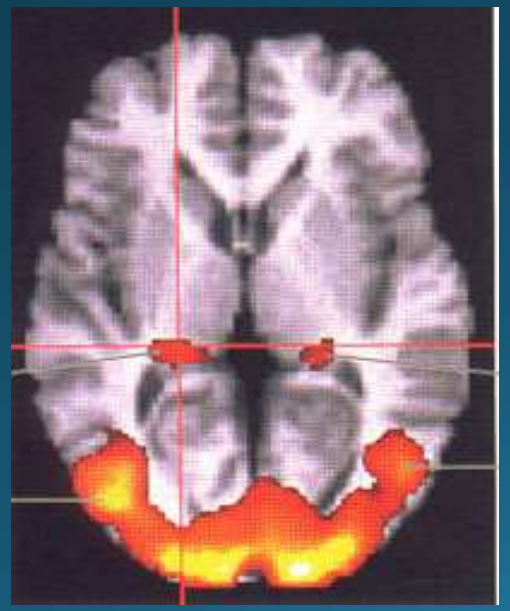
Arrow on picture to start

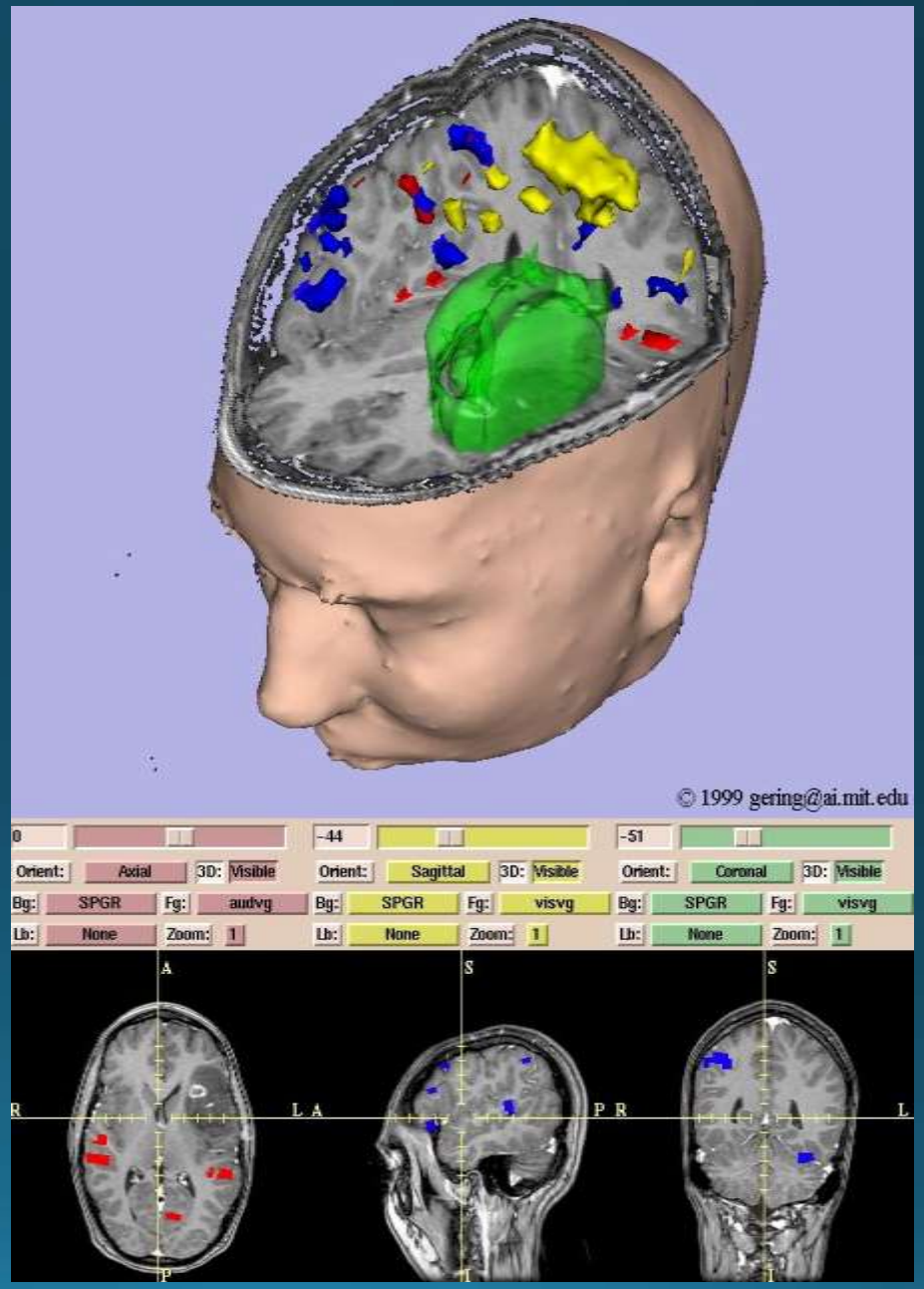
# Disclosure

- I am not a neuroradiologist. I am a clinical neuropsychologist.
- This is one neuropsychologist's attempt to review what the typical neuropsychologist should know about basic neuroimaging.
- I have summarized many internet presentations of this material.
- There will be more repetition of some points because the physics is complex.
- I will be less spontaneous than usual; I will read more slide material this time because I want to get it right.

# Modern Phrenology?

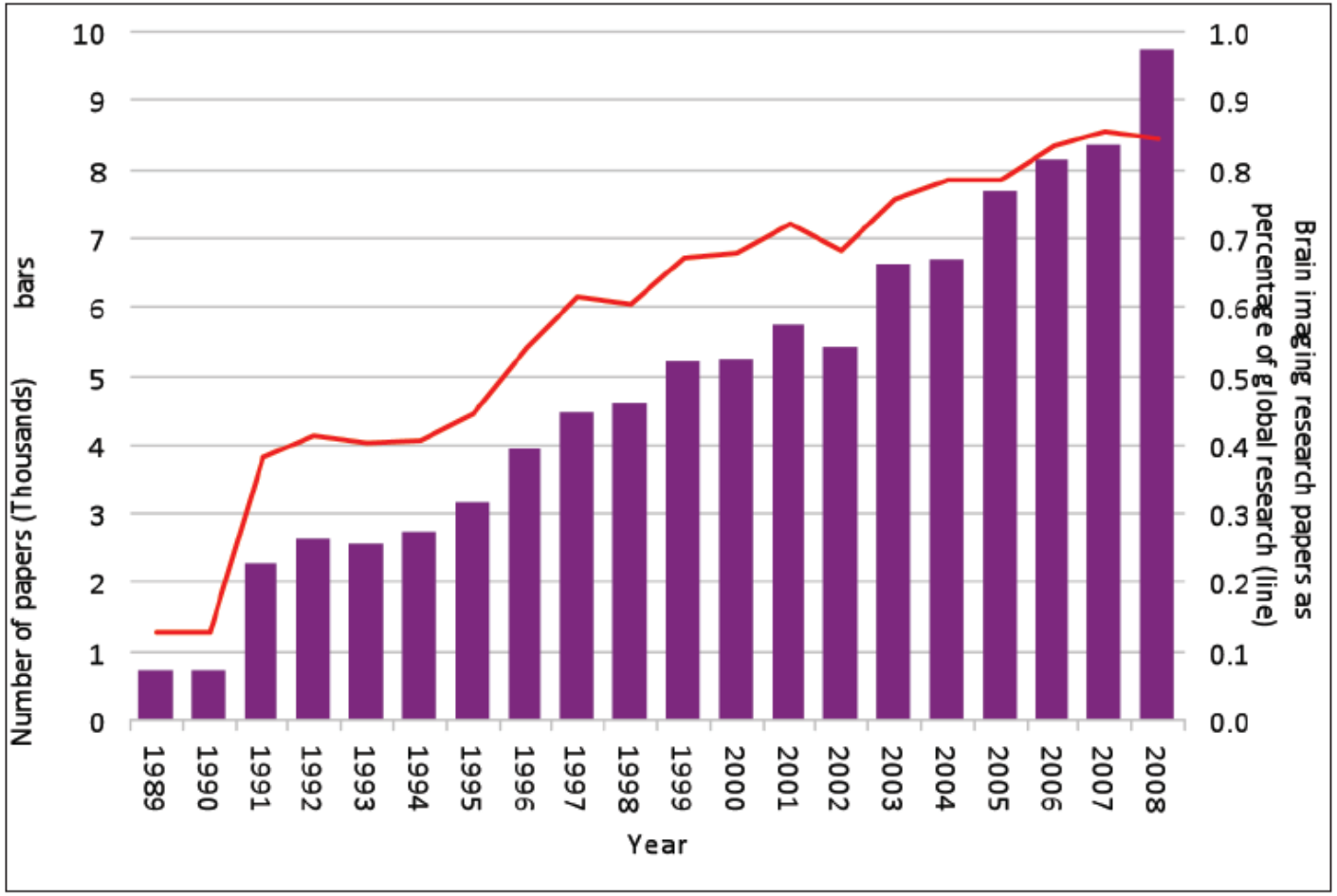




# Number of neuroimaging papers: 1989-2008

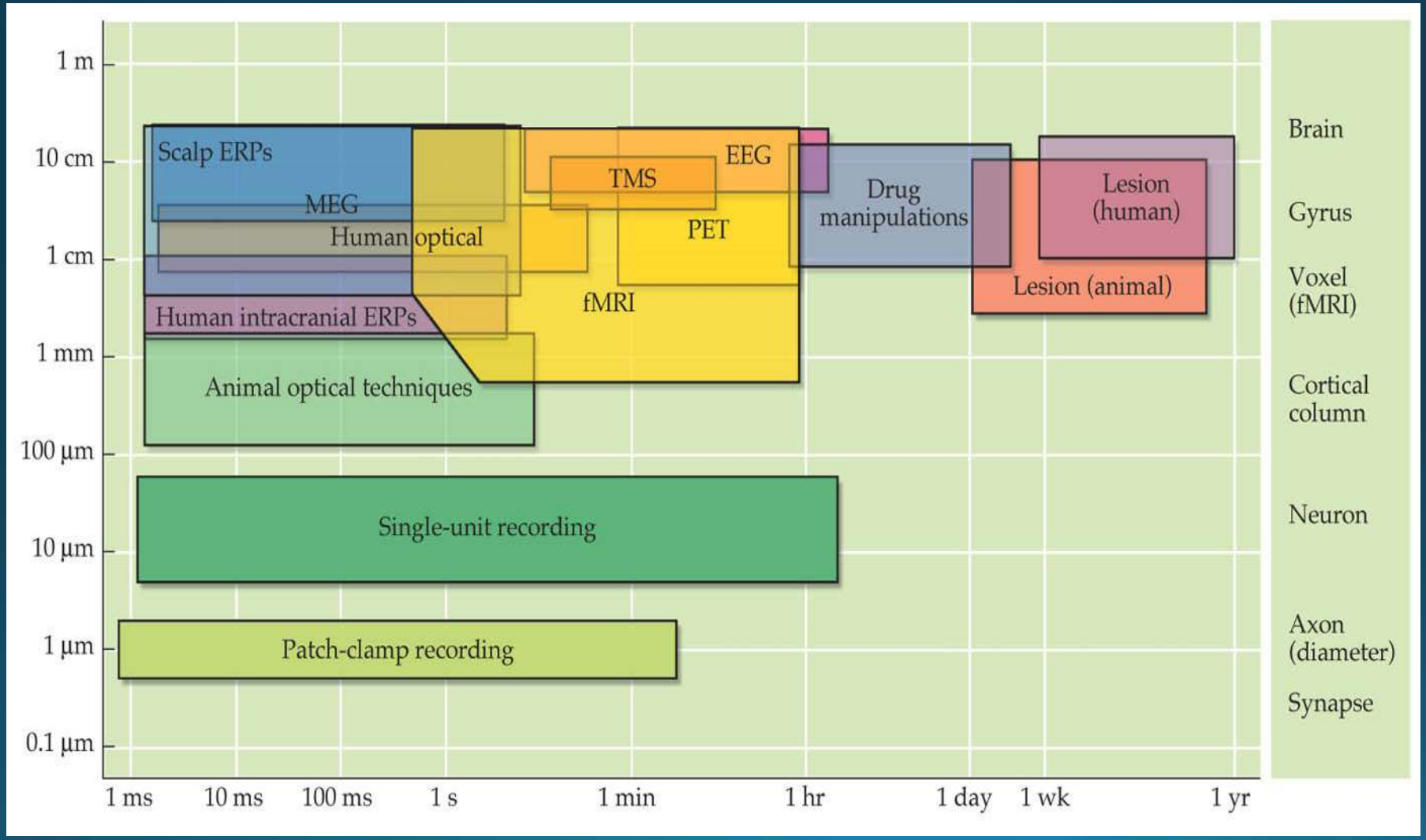
Figure 1 Number of brain imaging papers and as percentage of all research papers, 1989–2008



# The major brain study methods

- Lesion studies
- 1960s  - Single-unit neuron recording
- Neurosurgery-related methods
  - Direct cortical stimulation
  - Split-brain
  - WADA
- Functional imaging
  - 1970s - Electromagnetic: EEG, MEG
  - Hemodynamic: PET, fMRI
- Transcranial magnetic stimulation (TMs  1 tesla jolt)

# Temporal & Spatial Scale in studying the nervous system



| Structural Neuroimaging | Functional Neuroimaging |
| --- | --- |
| Skull X-rays | |
| CT - Computed Tomography | SPECT - Single-Photon Emission Computed Tomography |
| MRI - Magnetic Resonance Imaging | PET - Positron Emission Tomography |
| Diffusion-weighted MRI | fMRI - Functional Magnetic Resonance Imaging |
| Perfusion-weighted MRI | EEG - Electroencephalography |
| DTI - Diffusion Tensor Imaging | MEG - Magnetoencephalography |
| MRS - Magnetic Resonance Spectroscopy | |
| MRA - Magnetic Resonance Angiography | |

# Brain Imaging

| Structural | Functional |
|---|---|
| | Direct measures of neural activity: |
| CT – Computed tomography | EEG - Electroencephalography |
| MRI - Magnetic resonance imaging | MEG – Magnetoencephalography<br>Optogenetics: ofMRI |
| VBM - Vox-based morphometry | PET - Positron-emission-tomography |
| DTI - Diffuse Tensor Imaging<br>DSI – Diffuse Spectrum Imaging | SPECT - Single Photon emission computed tomography |
| Hybrid modalities: | fMRI - Functional magnetic resonance imaging |
| PET-CT | |
| MRI-PET | |
| fMRI-EEG/MEG | NIRS - Near infrared spectroscopy |
| PET-SPECT | |
| CT-SPECT | |
| | |

# MRI variations:

| | |
|---|---|
| T1-weighted | Important for discriminating lacunes from dilated perivascular spaces; for discriminating grey from white matter, and for studying brain atrophy |
| DWI | The most sensitive sequences for acute ischaemic lesions; positive for up to several weeks after cerebrovascular event |
| T2-weighted | To characterise brain structure; to differentiate lacunes from white matter hyperintensities and perivascular spaces; to identify old infarcts |
| FLAIR | To identify white matter hyperintensities and established cortical or large subcortical infarcts; to differentiate white matter lesions from perivascular spaces and lacunes |
| $T2^*$-weighted GRE | To detect haemorrhage, cerebral microbleeds, siderosis; for measurement of intracranial volume |

| | | | | |
|---|---|---|---|---|
| **Other routine sequences, available on most MR scanners** | | | | |
| Proton density-weighted | To detect white matter hyperintensities, infarcts, perivascular spaces (with T2-weighted dual echo), or other pathologies | 2D axial | 3–5 mm, and 2 mm × 2 mm | Mostly replaced by FLAIR |
| MRA | To detect stenosis of vertebral, basilar, internal carotid, middle cerebral, anterior cerebral, or posterior cerebral artery, or other pathologies | Post-contrast or 3D time-of-flight for intracranial arteries | 3D, axial, coronal, sagittal reconstruction; 1 mm isotropic voxels | Only large vessels visible at 1·5 T or 3·0 T; see below for perforating arterioles |
| **Sequences commonly available on commercial clinical MR scanners; at present, used more for research studies, but some techniques are increasingly used in clinical protocols** | | | | |
| DTI with six-gradient direction diffusion encoding | To diagnose recent infarct; measurement of mean diffusivity and fractional anisotropy | 2D axial | 3–5 mm, and 2 mm × 2 mm | More detailed characterisation than with DWI; acquisition time is double that for DWI |
| SWI or equivalent | Very sensitive to haemosiderin, measurement of intracranial volume | 2D or 3D axial | 2D: 3–5 mm, and 2 mm × 2 mm; 3D: 1 mm isotropic voxels | Enables visualisation of more cerebral microbleeds than $T2^*$-weighted GRE imaging and is more sensitive to artifacts including motion |
| **Research-only sequences; require research expertise** | | | | |
| Isotropic volumetric T2-weighted | To display fine detail of perivascular spaces | 3D axial | 1 mm isotropic voxels | Allows post-acquisition reformatting; could potentially replace 2D T2-weighted imaging if signal-to-noise ratio is adequate |

# Research-only Types of MRI

| Research-only sequences; require research expertise | |
|---|---|
| Isotropic volumetric T2-weighted | To display fine detail of perivascular spaces |
| Isotropic volumetric 3D T1-weighted (eg, MP-RAGE) | Provides improved global and regional volumetric brain measurements |
| Isotropic volumetric FLAIR | Enables identification of white matter hyperintensities; used for imaging cortical or subcortical infarcts |
| Advanced DTI with more than six-direction diffusion encoding (eg, 32 or more diffusion-encoding directions) | Provides refined and superior quantitative measurements of microscopic tissue changes |
| MTR | To detect demyelination and axonal loss |
| T1 mapping | To measure water content of tissue |

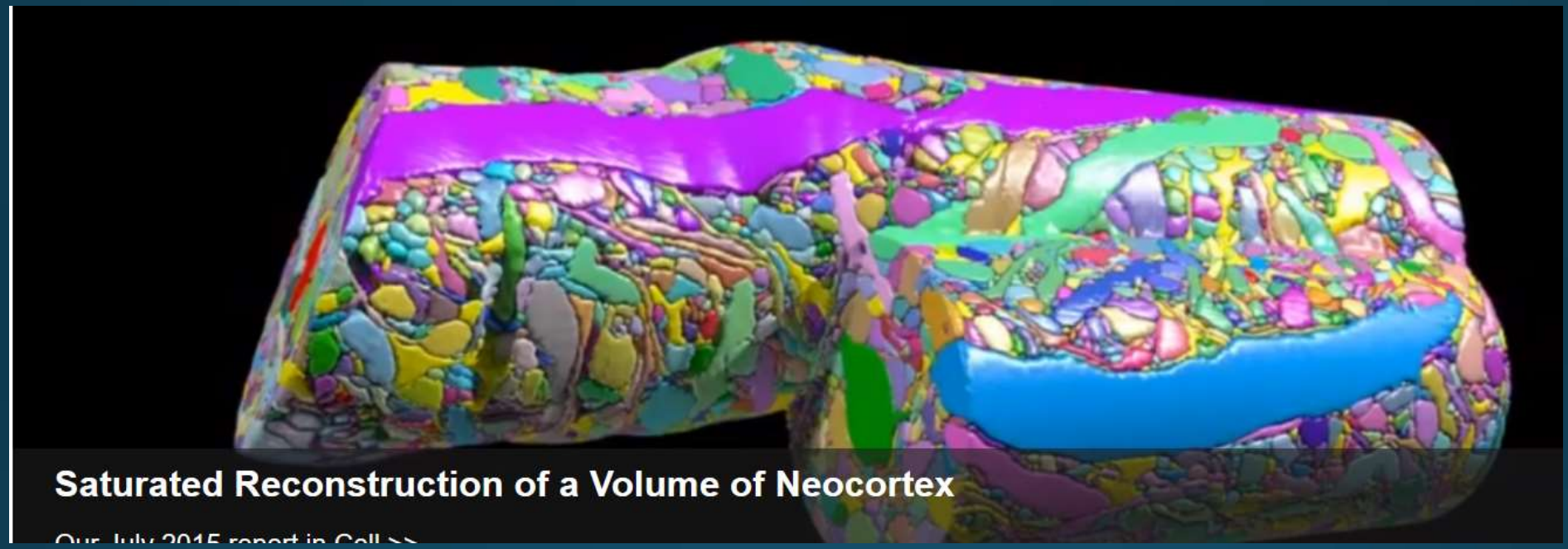
| | |
|---|---|
| MTR | To detect demyelination and axonal loss |
| T1 mapping | To measure water content of tissue |
| Permeability imaging | To estimate permeability of the blood–brain barrier |
| ASL perfusion imaging | To measure tissue perfusion; quantitative, with assumptions |
| Perfusion imaging (DCE or DSC) | To semiquantitatively measure blood perfusion in tissue |
| fMRI | To measure brain function in response to tasks or stimuli, or at rest for default mode networks |
| QSM | To provide quantitative measures of susceptibility changes, independent of scanner or acquisition variables |

| | | | | |
|---|---|---|---|---|
| Perfusion imaging (DCE or DSC) | To semiquantitatively measure blood perfusion in tissue | 2D axial | 3–5 mm, and 2 mm × 2 mm | Needs intravenous injection of contrast agent and post-processing; optimum acquisition and processing not yet confirmed for T1 (DCE) or $T2^*$-weighted (DSC) approaches |
| fMRI | To measure brain function in response to tasks or stimuli, or at rest for default mode networks | 2D axial | 3–5 mm, and 2 mm × 2 mm | Complex set-up, acquisition, and processing |
| QSM | To provide quantitative measures of susceptibility changes, independent of scanner or acquisition variables | 2D or 3D axial | 2D: 3–5 mm, and 2 mm × 2 mm; 3D: 1 mm isotropic voxels | Uses an SWI-like acquisition, but needs very complex post-processing methods; post-processing strategies currently under investigation |
| Microatheroma and arteriolar imaging | To visualise perforating arteriolar anatomy and atheroma | Uncertain, emerging method | Uncertain, emerging method | Promising experimental approach that needs a scanner that is more than 3·0 T |

DWI=diffusion-weighted imaging. FLAIR=fluid-attenuated inversion recovery. GRE= gradient-recalled echo. MRA=magnetic resonance angiography. DTI=diffusion ensor imaging. SWI=susceptibility-weighted imaging. MP-RAGE=magnetisation-prepared rapid acquisition with gradient echo. MTR=magnetisation transfer ratio. ASL=arterial spin labelling. DCE=dynamic contrast-enhancement. DSC=dynamic susceptibility contrast. fMRI=functional MRI. QSM=quantitative susceptibility mapping.

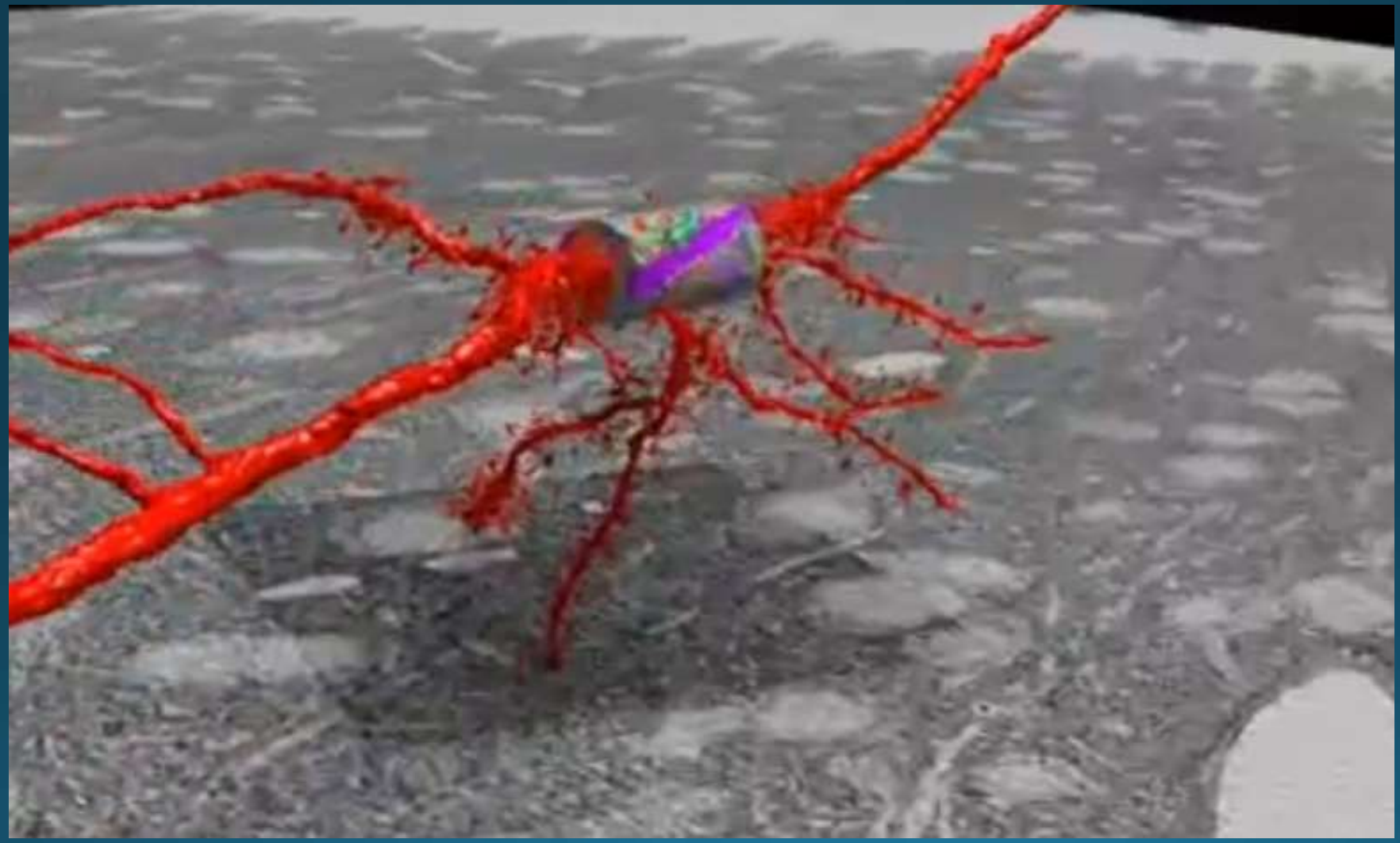
MRI at 3·0 T is preferred to 1·5 T. However, these standards are listed as minimum and essential to research-only applications. These categories are not absolute; urposes are variable, and will vary with investigators' interest, expertise, and available technology.

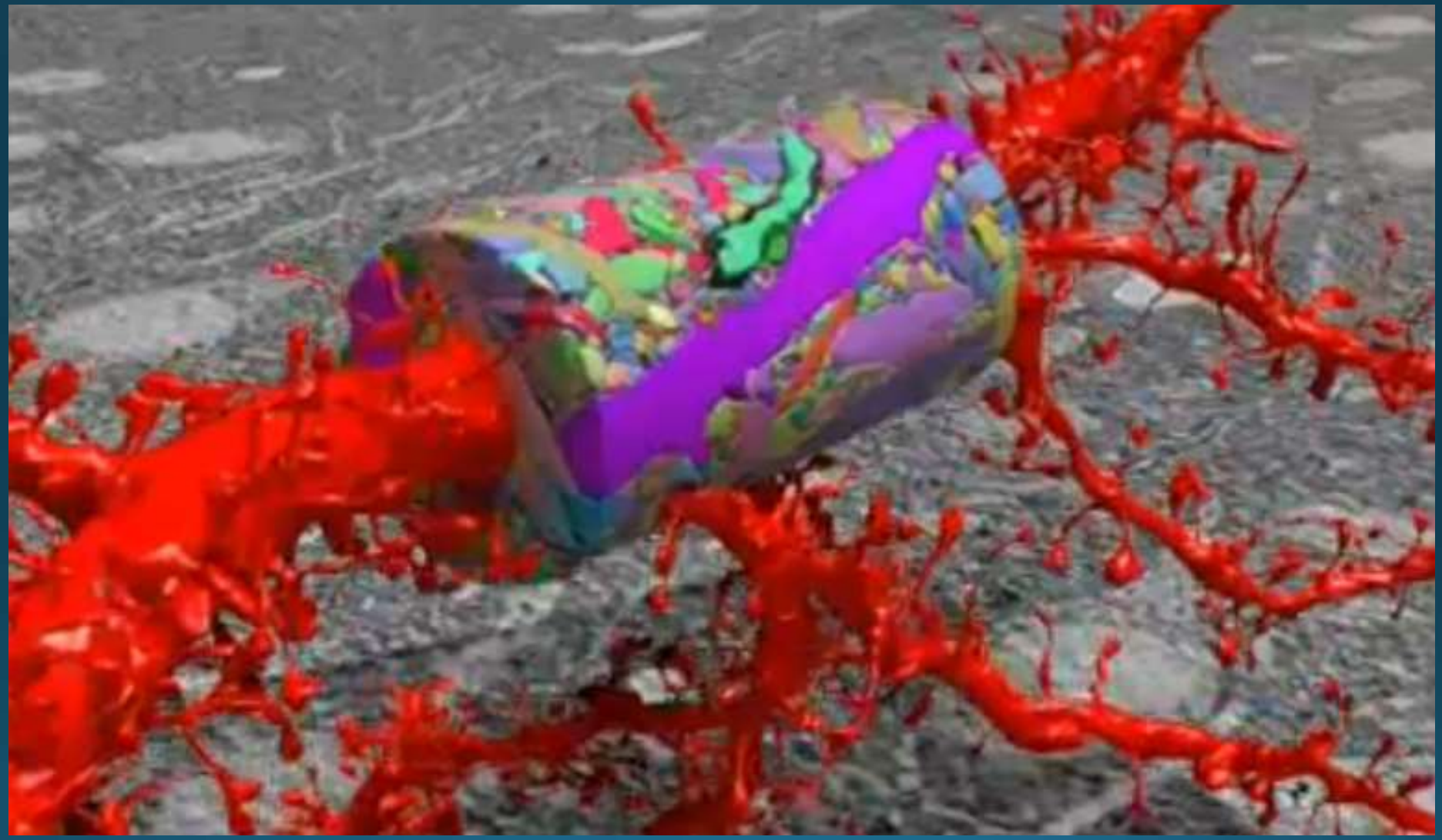
# Jeff Lichtman from Harvard University 1 section of mouse brain

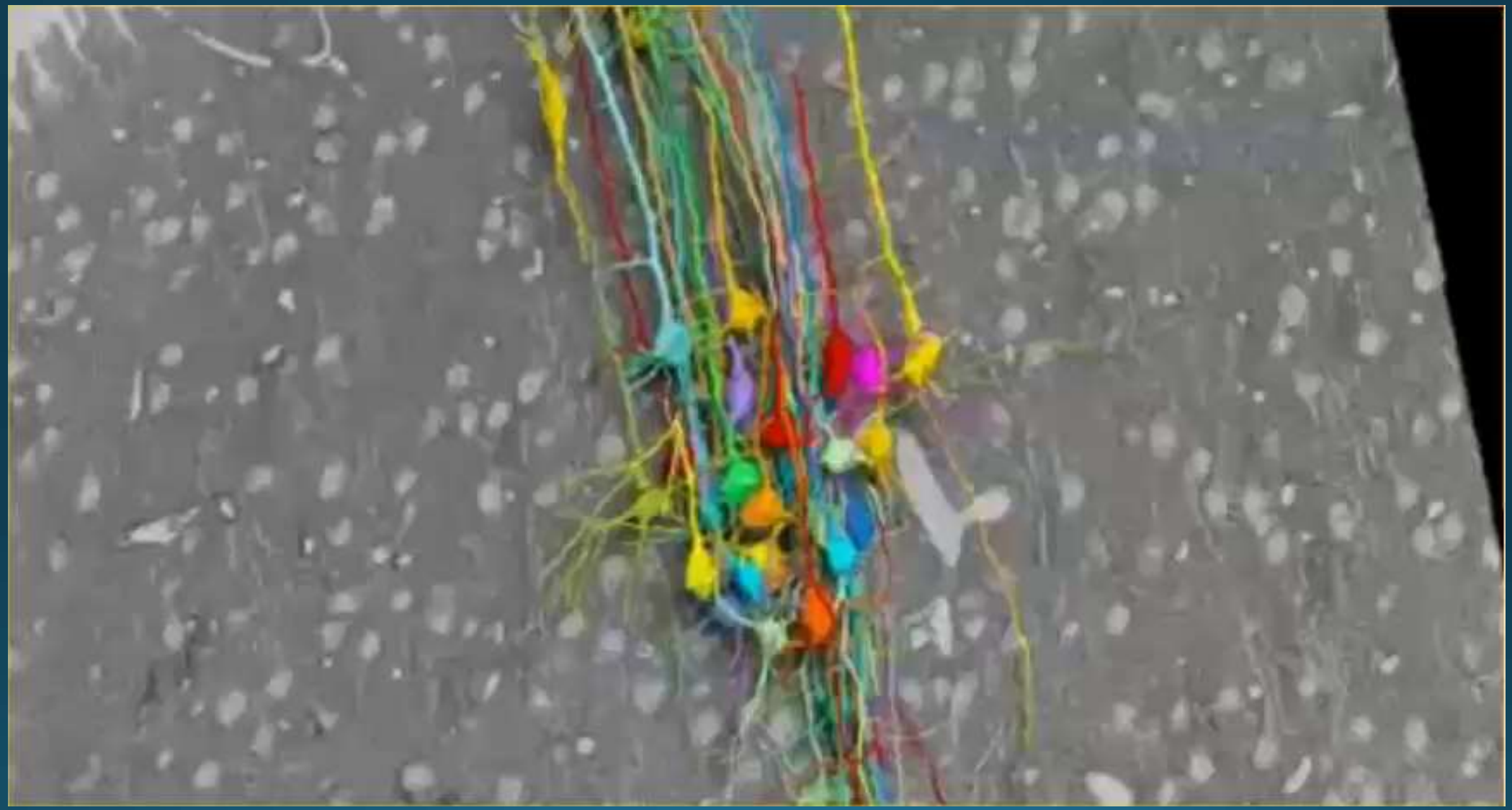



- Cylindrical EM reconstruction of a piece of mouse brain smaller than a grain of sand. In the center of this volume was the proximal shaft of a pyramidal cell apical dendrite surrounded by all manner of synaptic elements
- In this volume there are around 680 nerve fibers that can be resolved, together with 774 synapses. A key finding by Lichtman is that mere contact alone, does not a synapse make.
- Per mm, 33,000 sections

# Crumb of mouse brain reconstructed in full detail

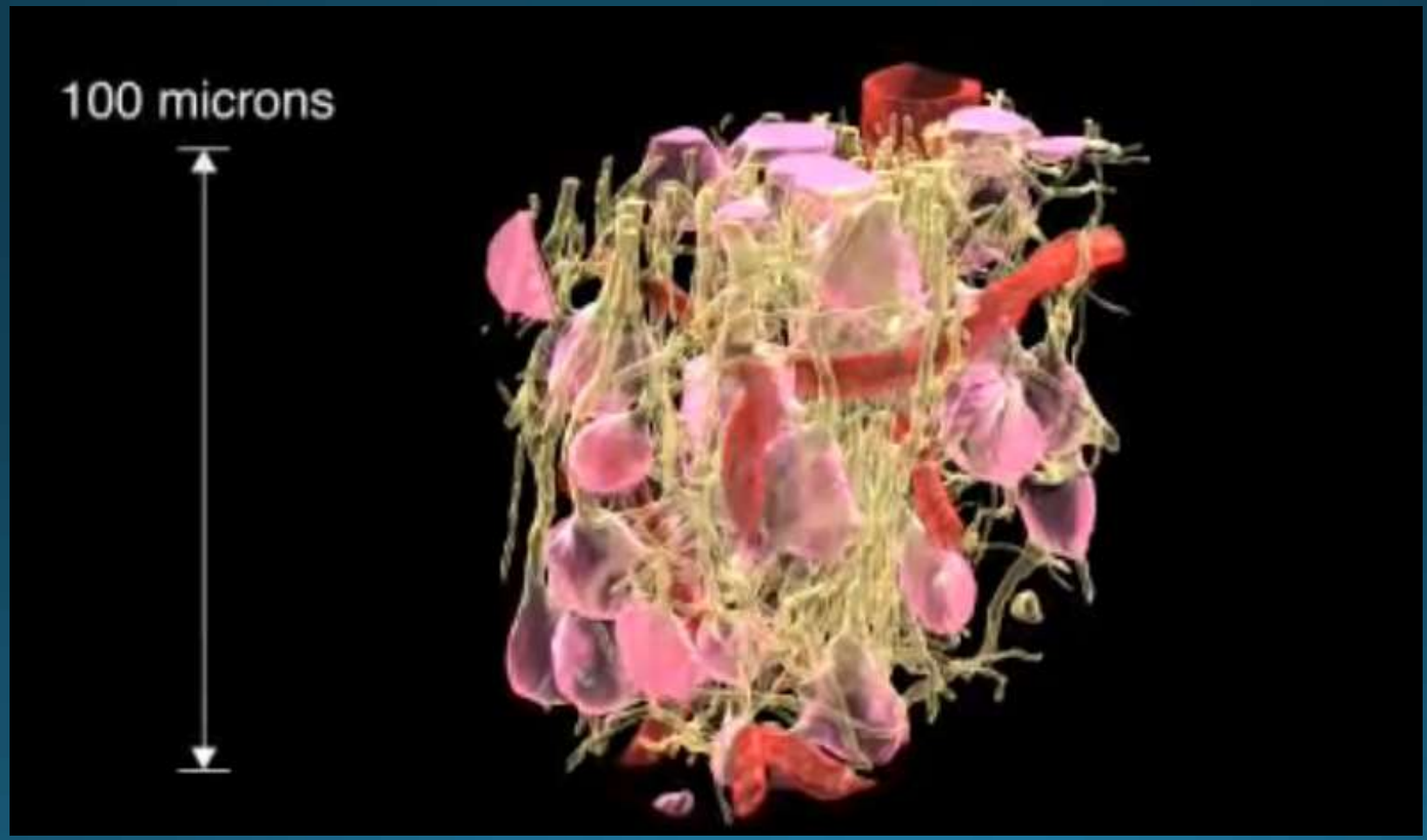




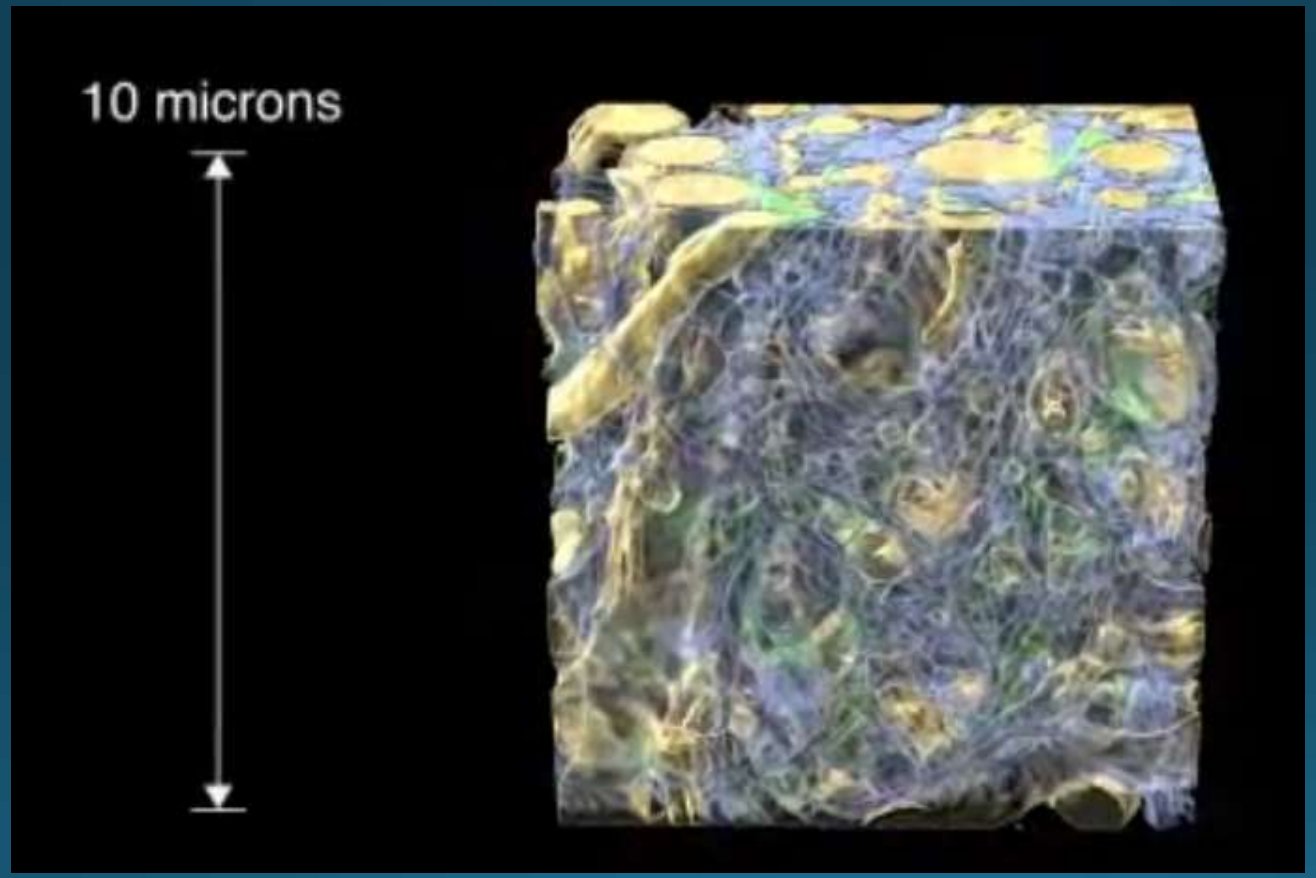


Film

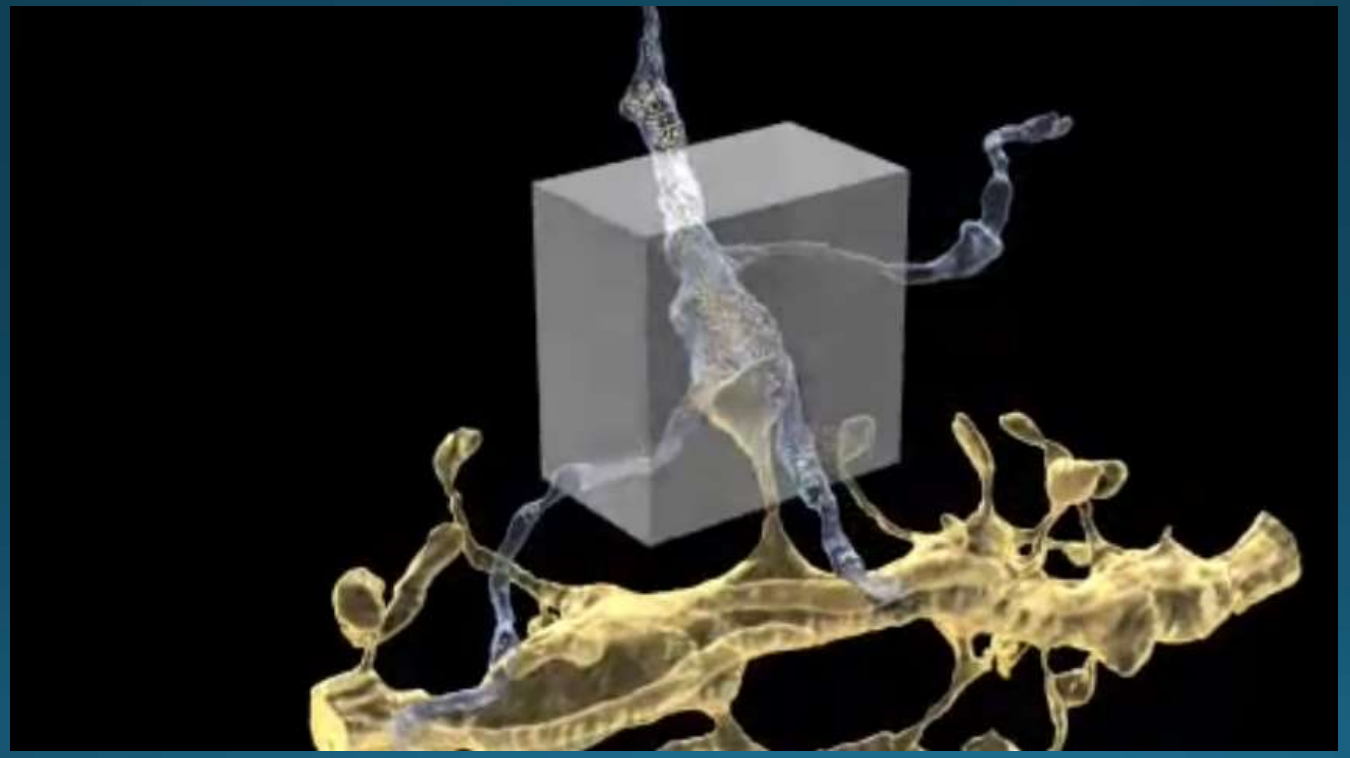
100 microns: pink = nerves; red = blood vessel; yellow =  dendrites



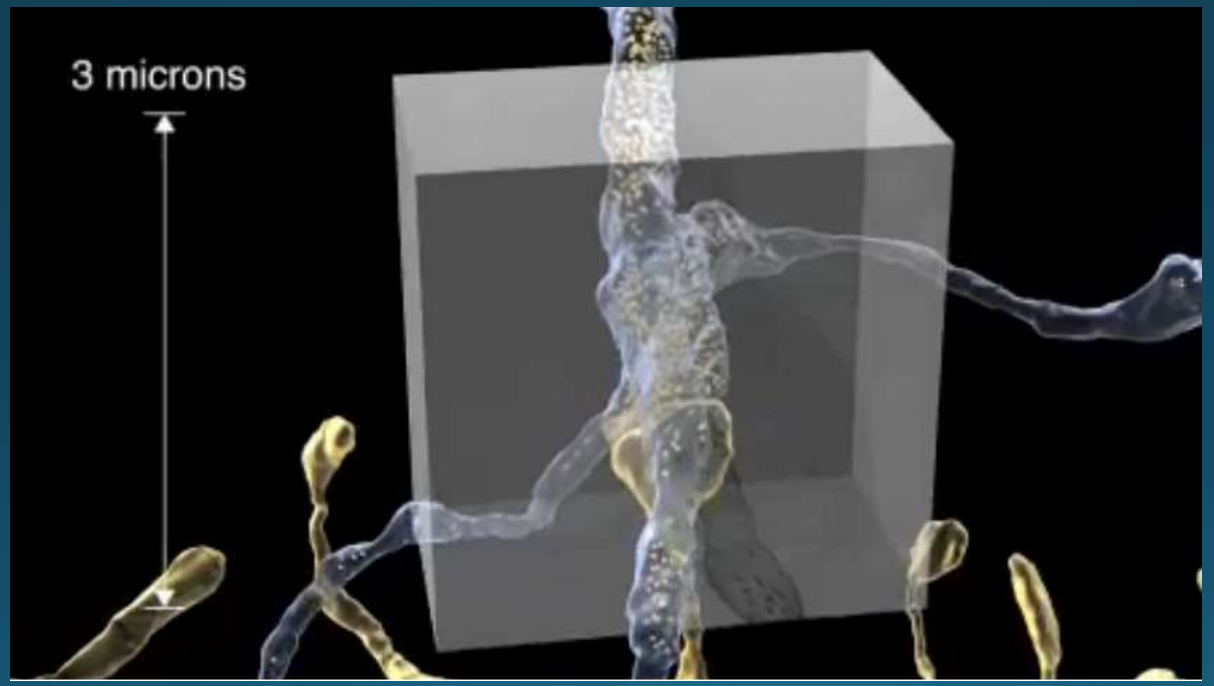
# 10 microns: yellow = dendrites; blue = axons



# Yellow = dendrite

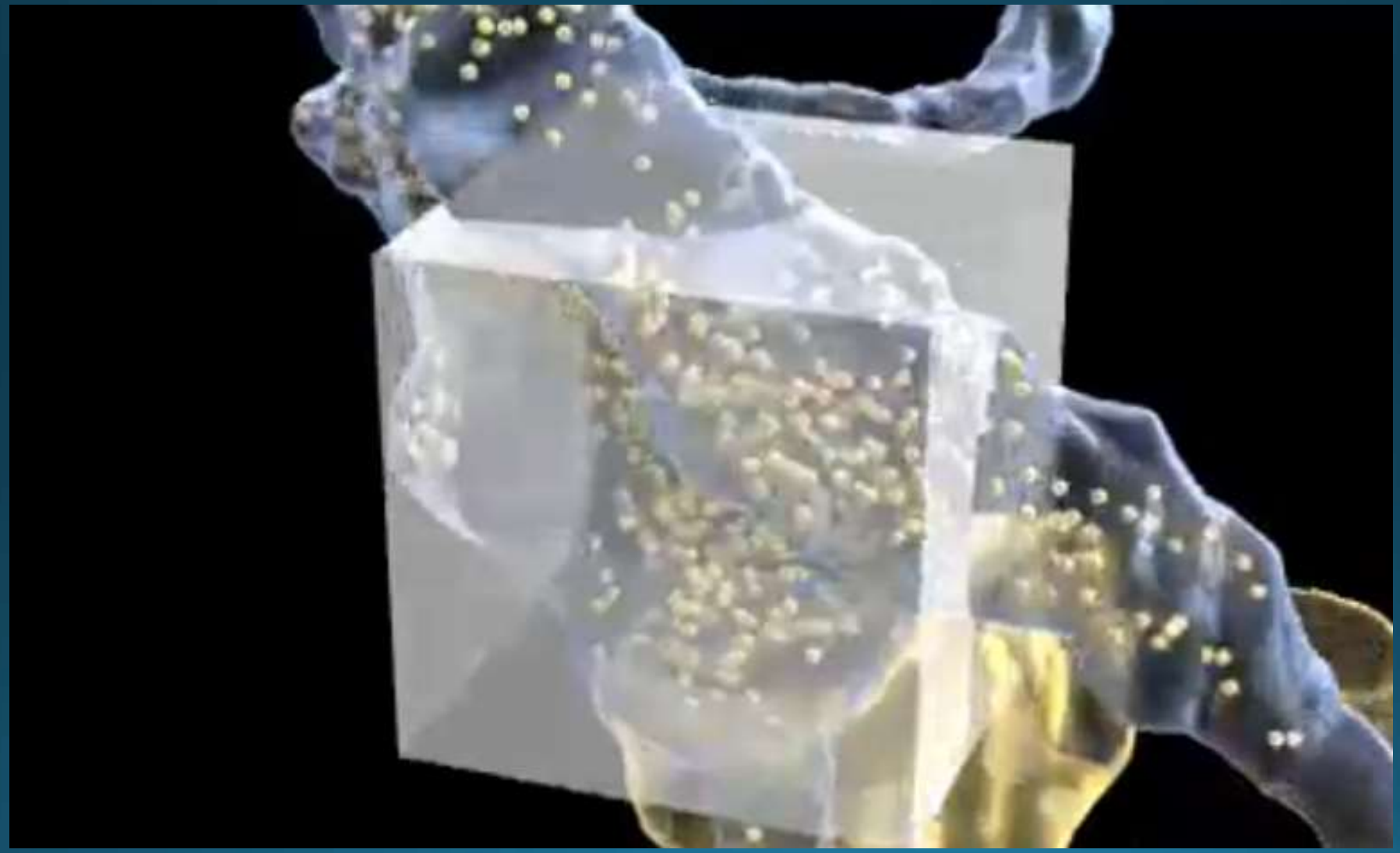


# 3 microns

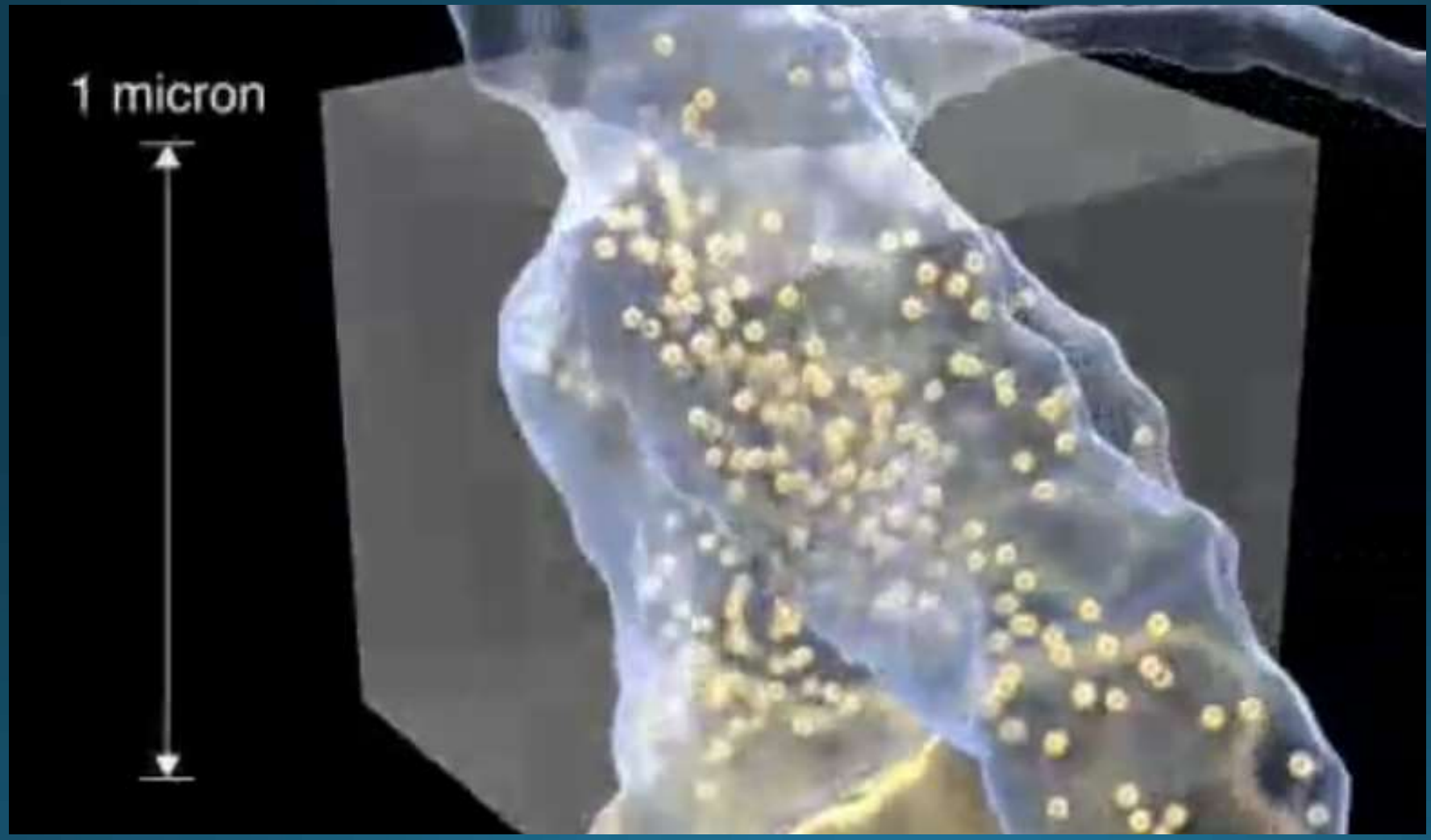


# A synapse: dendrite meets axon

# Synapse



# 1 micron

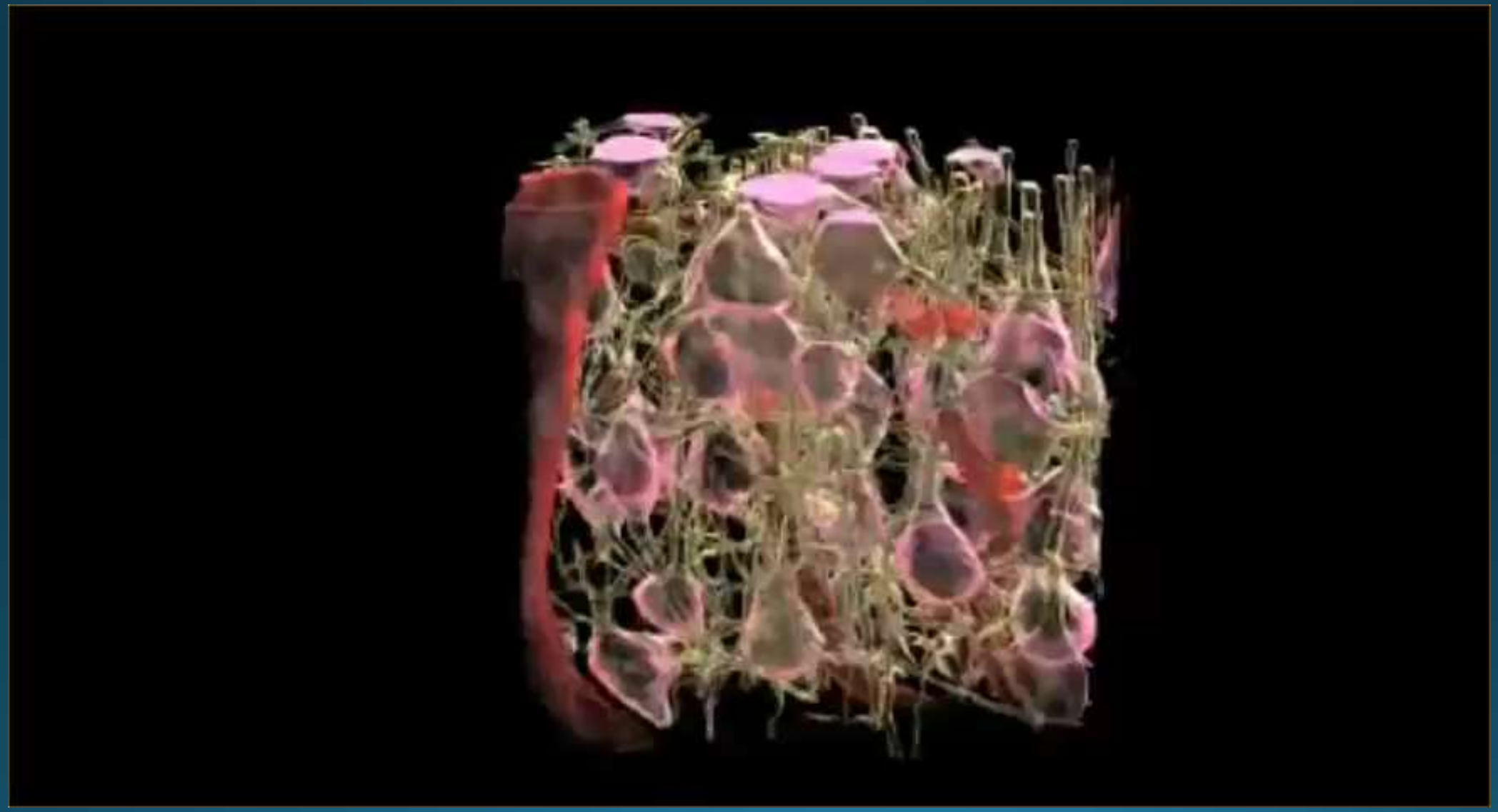


# Neurotransmitter packets

# Synapse

# 10 trillion of these synapses

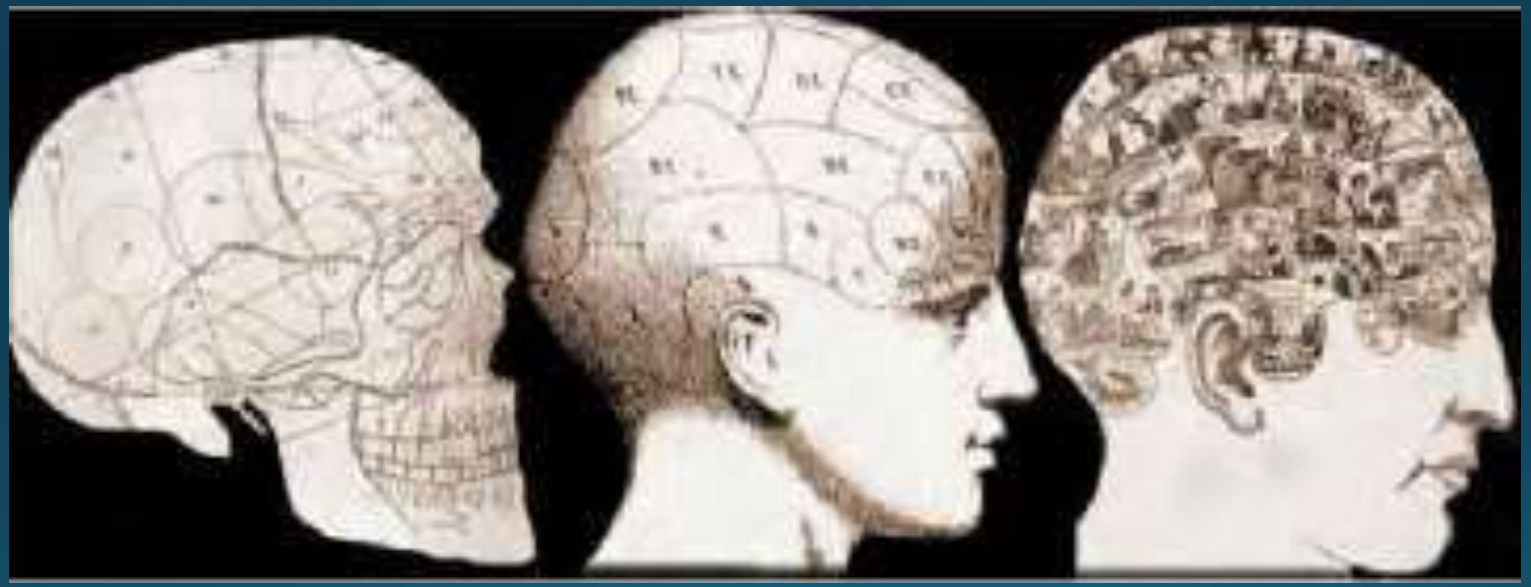
# Column of synapses Film



# When to request Neuroimaging

- Mental Status changes
- Personality changes [esp. age 50+]
- History of Seizures, Alcohol Abuse, Trauma
- Abnormal actions /movements
- Focal Neurological signs

# Early Speculative Pictures: Phrenology



# Neuropsychological (Phrenology) Test, 1905

# Psychoanalysis Device, 1931


A demonstration of a new “psychoanalyzing apparatus” in 1931

# Neuroimaging: History

## Historical overview

– The quest for an image of the brain

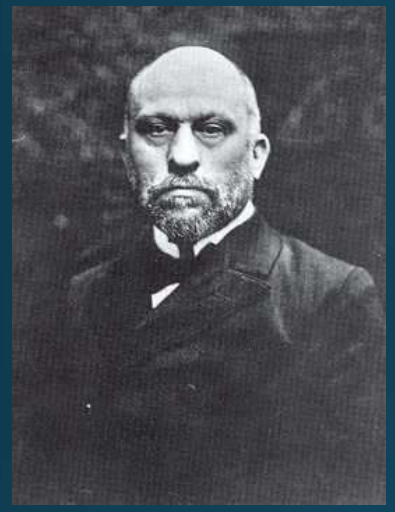
Ancient Times:  Autopsy or Injury

– Early Methods

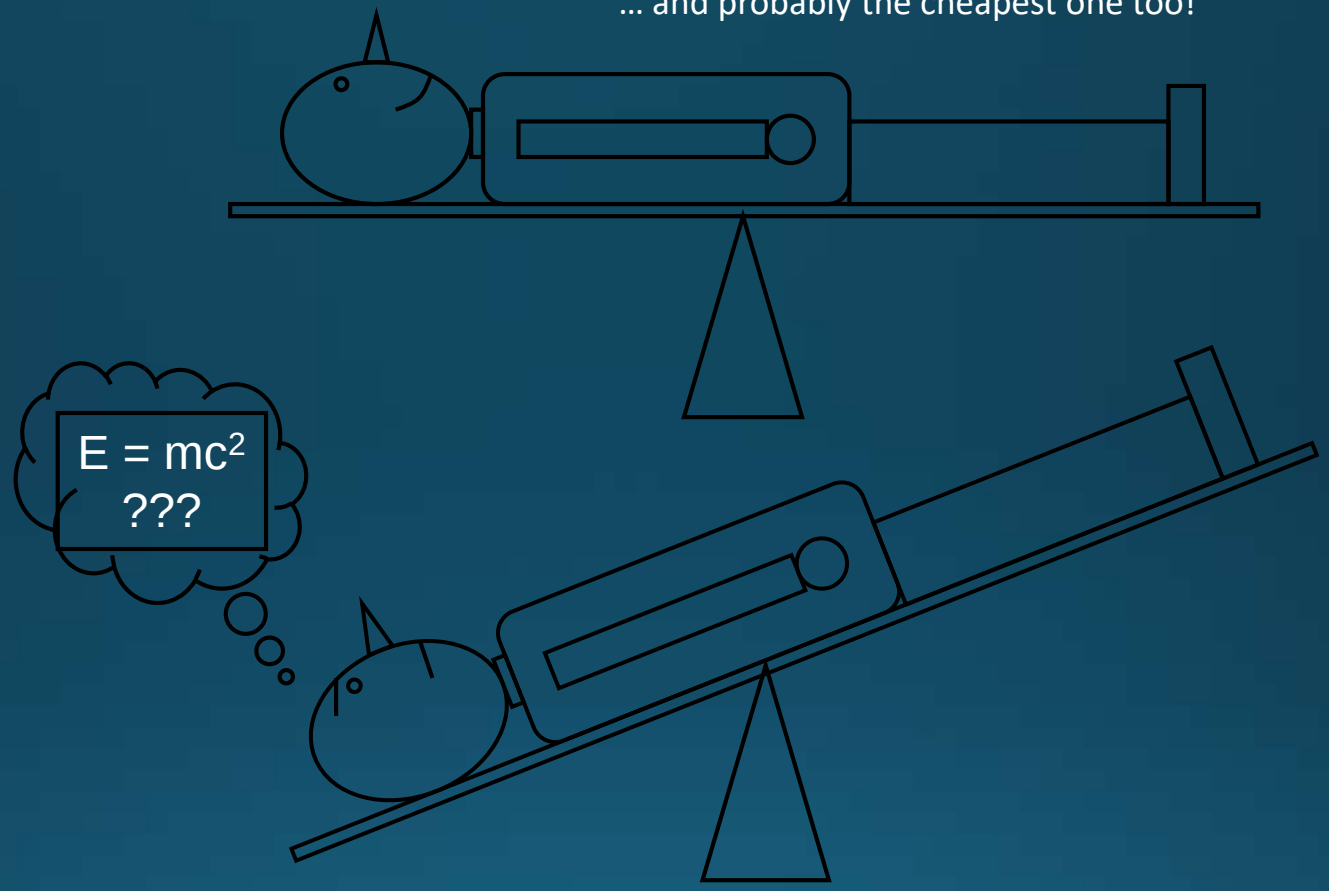
- X-Ray
- EEG
- Pneumoencephalography
- Angiography
- Isotope Brain Scan

# 1901: The First “Brain Imaging Experiment”

… and probably the cheapest one too!



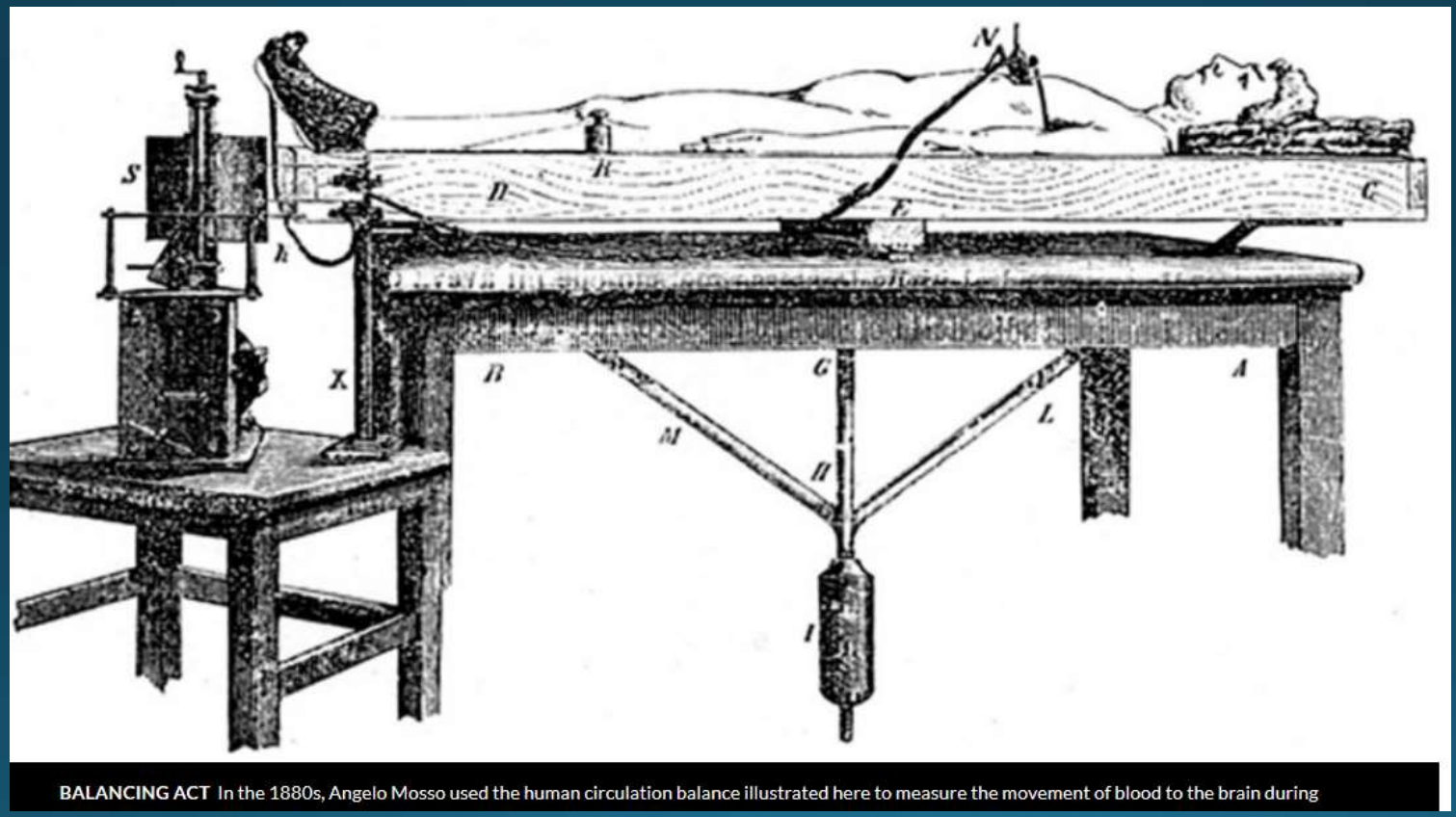
*Angelo Mosso*
*Italian physiologist*
*(1846-1910)*




“[In Mosso’s experiments] the subject to be observed lay on a delicately balanced table which could tip downward either at the head or at the foot if the weight of either end were increased. The moment emotional or intellectual activity began in the subject, down went the balance at the head-end, in consequence of the redistribution of blood in his system.”

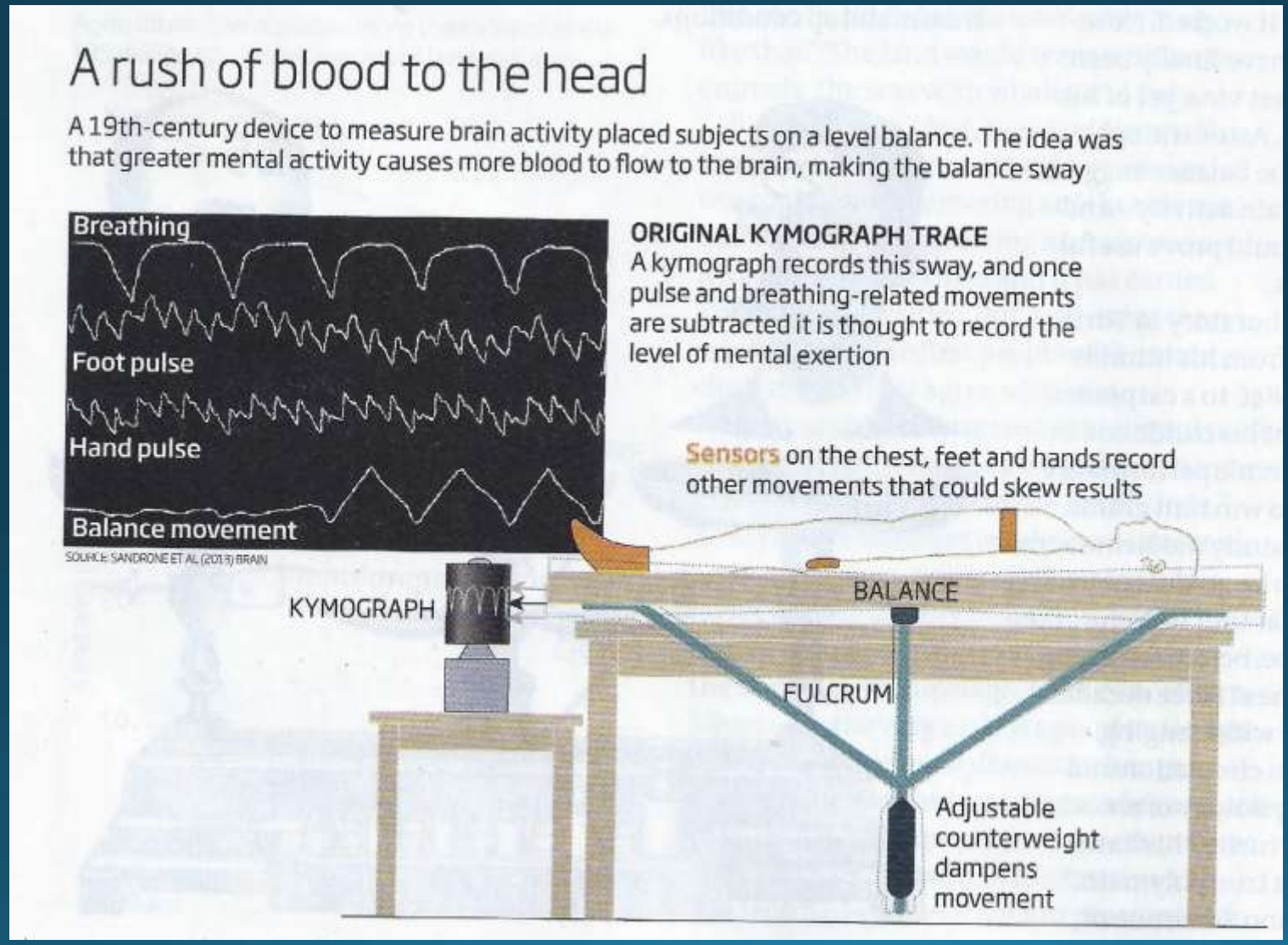
-- William James, *Principles of Psychology* (1890)

# Angelo Mosso in 1901: 1st Brain Activity Device




Reading math text tips balance more than reading newspaper

# First Hemodynamic Brain Imaging



# Pneumoencephalography: Air in Ventricles

- Discovered by accident in 1912

- A 47 year old man was hit by NYC trolley car and  had a fracture of frontal bone

- Initial x-ray: Normal

- Subsequent x-ray: Ventricles visible due to leakage of air through fracture

- Autopsy: Air leak from sneeze or blowing nose

# Pneumoencephalography

- Procedure in which
  - most of the cerebrospinal fluid (CSF) was drained from around the brain by means of a lumbar puncture
  - replaced with air, oxygen, or helium to allow the structure of the brain to show up more clearly on an X-ray image.

- It was derived from ventriculography, an earlier and more primitive method where the air is injected through holes drilled in the skull.

# Pneumoencephalography: Dr. Walter Dandy

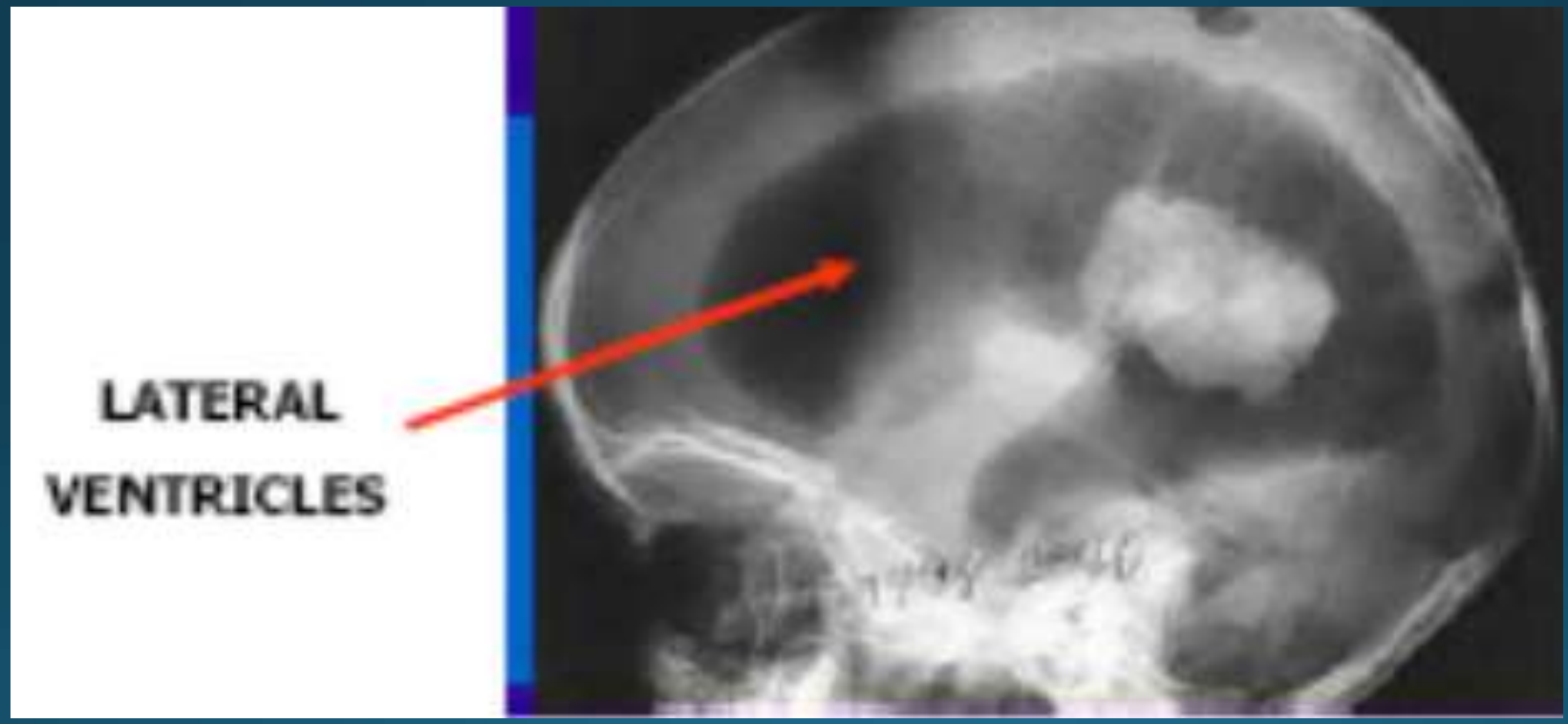
Initial research: 1918 by Walter Dandy, neurosurgeon, Johns Hopkins

Basic procedure: Inject 15 cc air through lumbar puncture into subarachnoid space

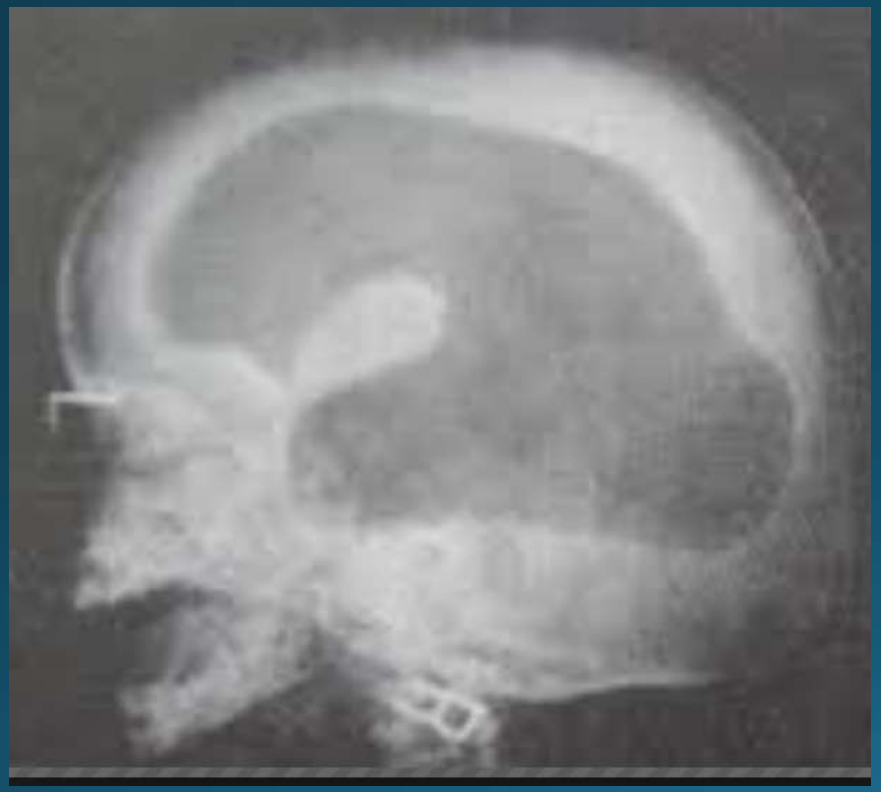
Air migrates up to the ventricles, patient tilted to accommodate different view.

Performed until the late 1970s.

# Pneumoencephalography



# Pneumoencephalography



See one being done in film The Exorcist

# Pneumoencephalography

What it images:
Location of cerebral spinal fluid – size and position of ventricles

Utility: Rarely used now; excruciating discomfort

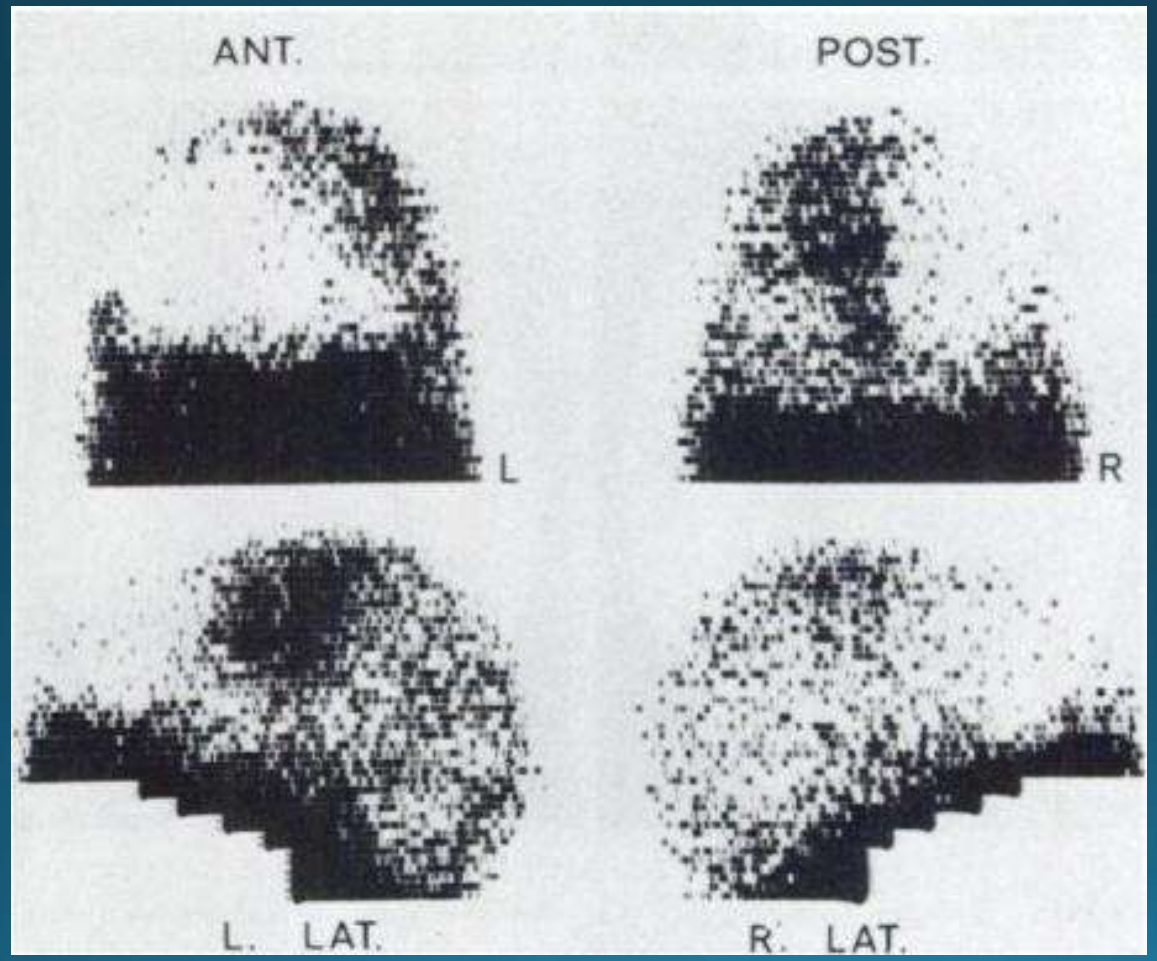
Advantage: None

Early Schizophrenia research by Seidman: atrophy before modern antipsychotic medications

# Isotope Brain Scan: Old radioactive technology

- 1947: Minnesota surgeon George Moore published first paper on locating brain tumor by radioactive labeling.
- Basic process: Patient injected with isotope, scanner moves over surface of head looking for “hot spots.”
- Same basic process used for thyroid scans

# Isotope Brain Scan

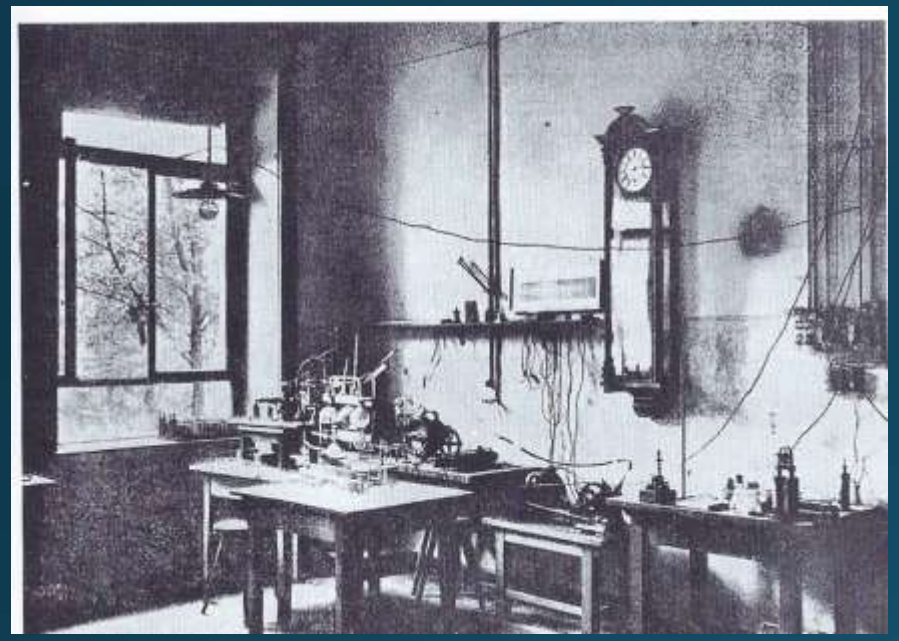


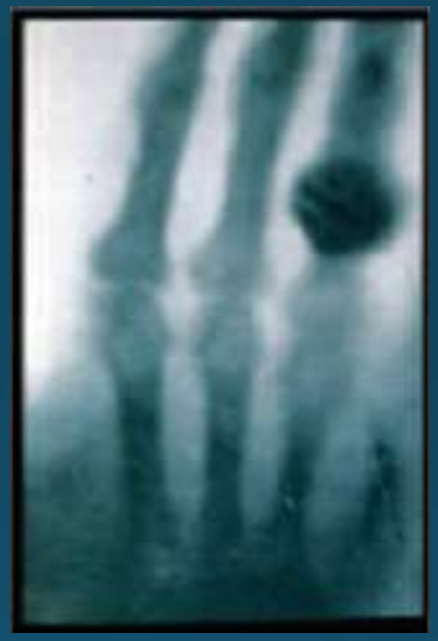
# Isotope Brain Scan

- What it images: Distribution of breakdown of blood brain barrier (capillary level restricted permeability of brain blood vessels)
- Utility: Not in general use since mid 1970s
- Advantages?: Originally, noninvasive and fairly sensitive

# Wilhelm Konrad Roentgen: 1845-1923
# Inventor of the X-ray 1895

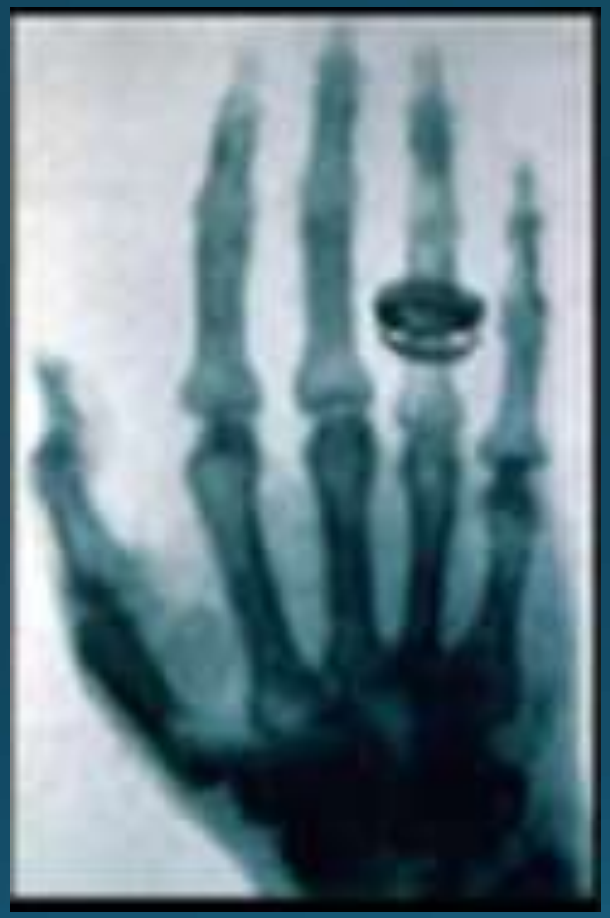
# First X-ray 1895





The famous radiograph made by Roentgen on Dec. 22 1895 in his lab. Sent to physicist Franz Exner in Vienna. Known as the "first X-ray picture" and "the radiograph of Mrs. Roentgen's hand."
It is certainly not the previous, and was not labeled as the latter at the time

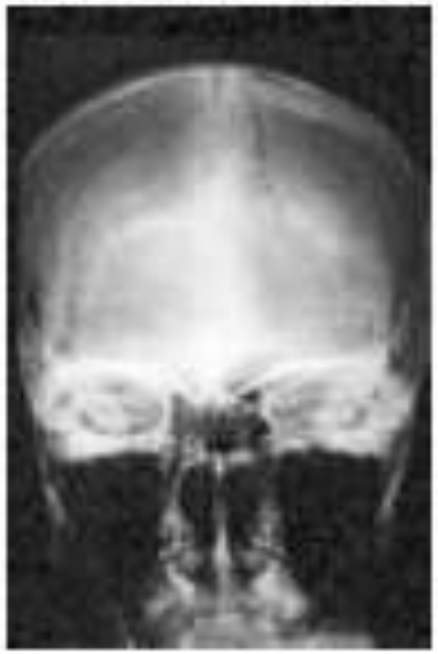
# X-rays: 1896

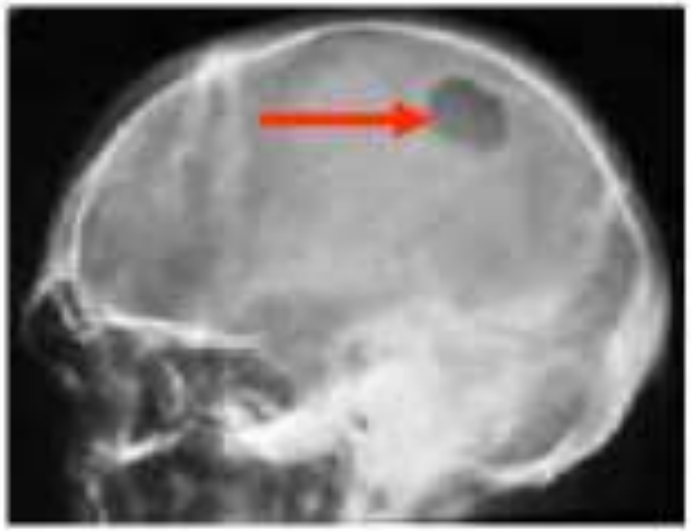


Radiograph of the hand of Albert von Kolliker, made
at the conclusion of Roentgen's lecture and demonstration
At the Wurzburg Physical-Medical Society on Jan. 23, 1896

# Skull Radiography: skull injuries

- **Skull Radiography** (X-ray)- examples





Lateral plain radiograph of skull. The dark "hole" is an erosion made by a slowly growing benign tumor.

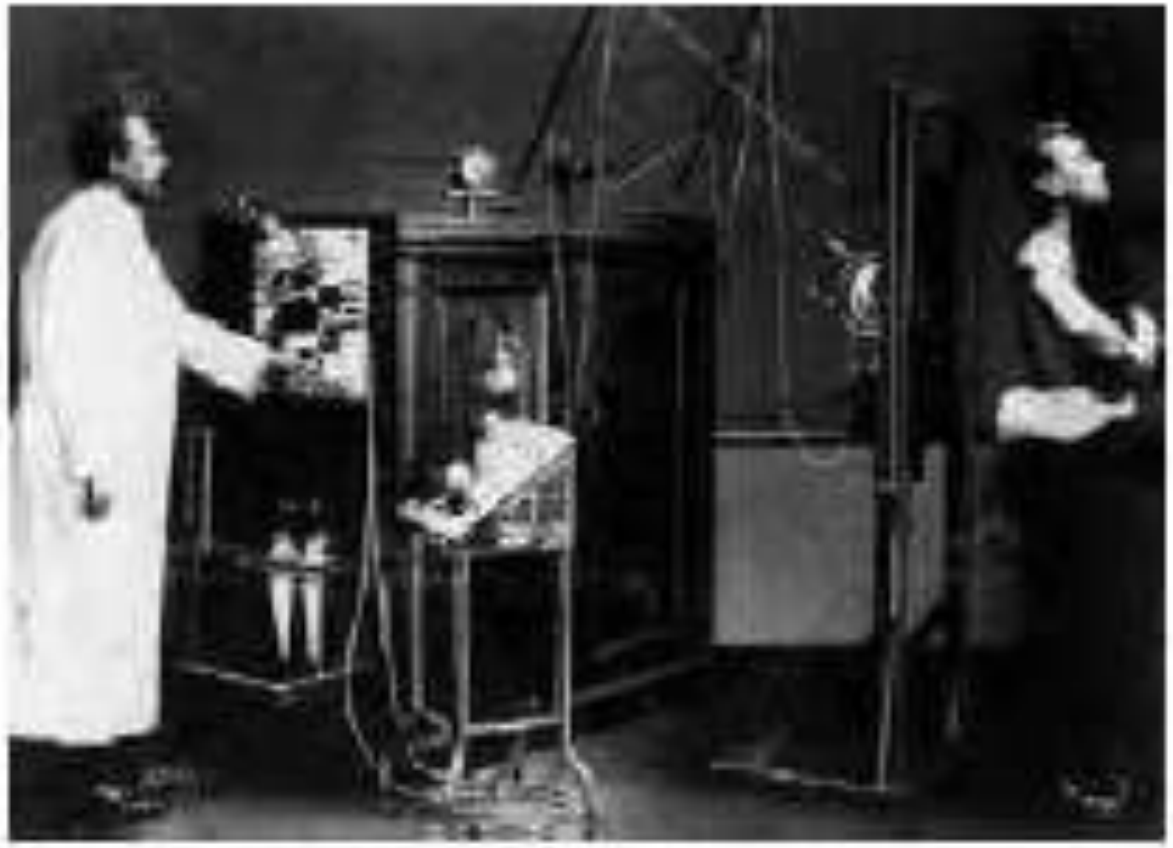
Conventional skull X-rays used in rapid exam of skull injuries; but CT may be more useful in characterizing skull fractures.

# Skull Radiography (X-ray): Calcium & Bone

Skull Radiography (X-ray):

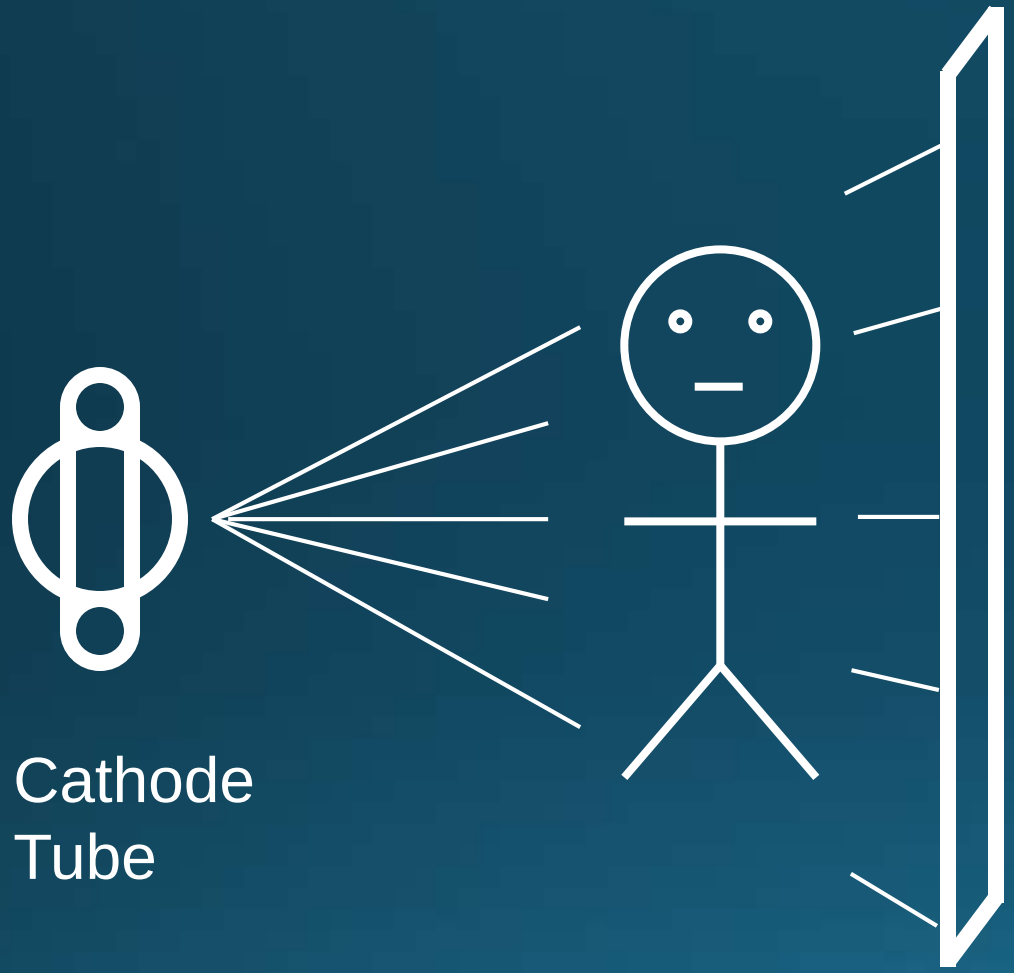
- Introduced in 1895 by Roentgen
- First published skull x-ray: 1896 by William Morton
- What it images: Distribution of solid calcium, i.e. the skull or any other structure within or on the brain
- Utility: Minimal: can't visualize tissue, only bone
- Advantage?: Inexpensive, universally available

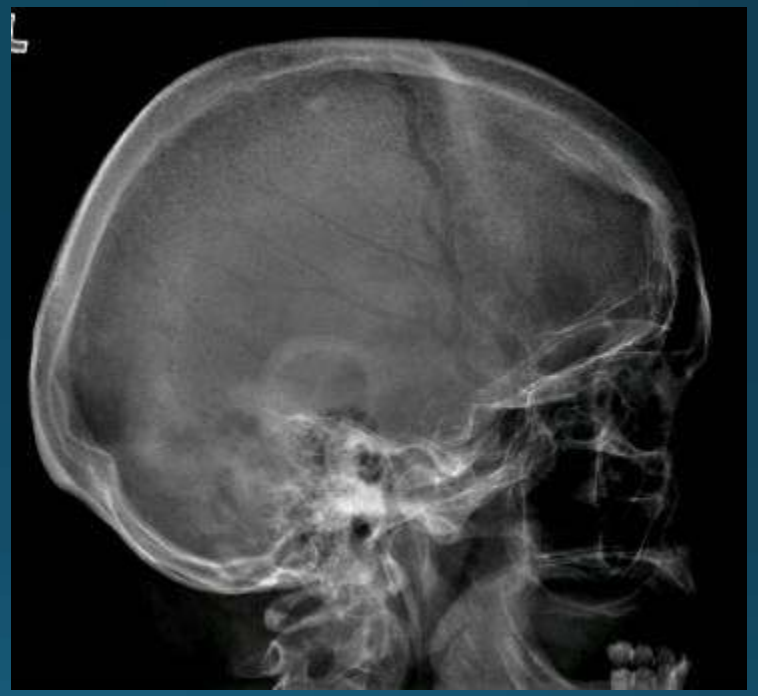
# Early X-Ray: You got to hold the film.



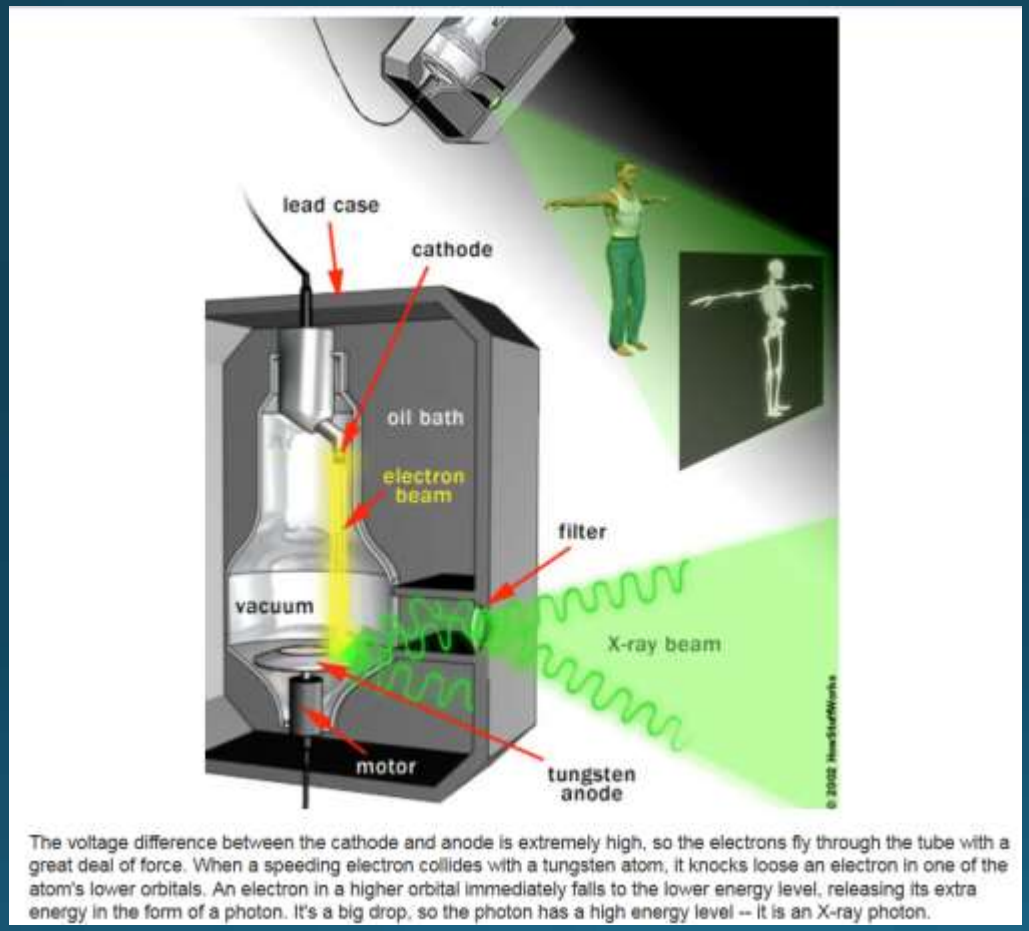
An x-ray system from the pioneering days.
Patients still had to hold the cassettes themselves.

# Radiography (X-Ray)



# Modern X-Ray Machine




The voltage difference between the cathode and anode is extremely high, so the electrons fly through the tube with a great deal of force. When a speeding electron collides with a tungsten atom, it knocks loose an electron in one of the atom's lower orbitals. An electron in a higher orbital immediately falls to the lower energy level, releasing its extra energy in the form of a photon. It's a big drop, so the photon has a high energy level -- it is an X-ray photon.

Electron meets tungsten atom; produces X-ray photon

# 1907 Fluoroscope (constant xray)

# Ill fitting shoes more dangerous than x-rays!

Buster Brown Shoe Stores in 1950s:
Shoe-fitting Fluoroscope
Charlie's first x-ray.

FDA banned it in 1953

# Modern Fluoroscopy (Real-Time X-Ray)

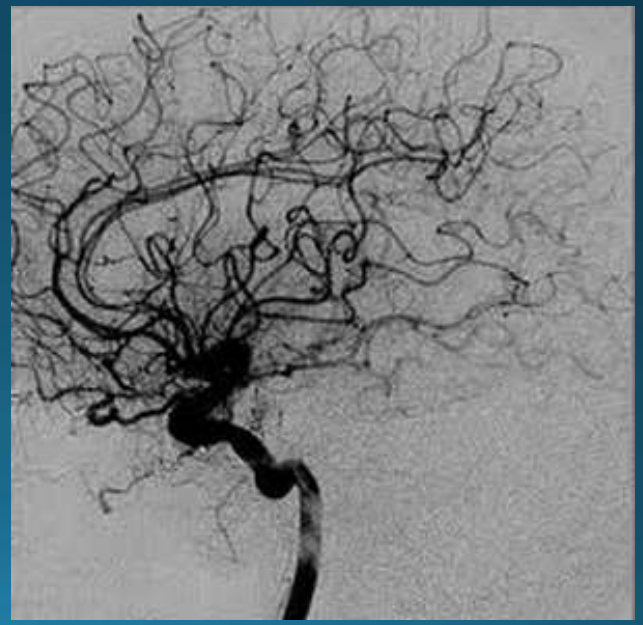
Fluoro-guided procedures:

- Angiography (blood vessels)
- Myelography (spinal cord)

# Angiography: Dr. Egaz Moniz

1896: E. Hascheck of Vienna injected the brachial artery of a cadaver with lime, mercuric sulfide, and petroleum and visualized blood vessels of arm and hand

1927: Dr. Egas Moniz publishes first arteriogram of living human (1926)
1936: Published first article on prefrontal lobotomy
1949 Only Nobel Prize in Psychiatry



# CT/MR Angiography

MR Angiography = designed to enhance arterial blood (moving $H_20$) — sometimes with Gd contrast

Much more commonly used than MR Venography

Useful in diagnosing blood supply problems (i.e. occlusions)

# CT Angiography - Indications

- Atherosclerosis
- Thromboembolism
- Vascular dissection
- Aneurysms
- Vascular malformations
- Penetrating trauma

# Angiography: brain vasculature

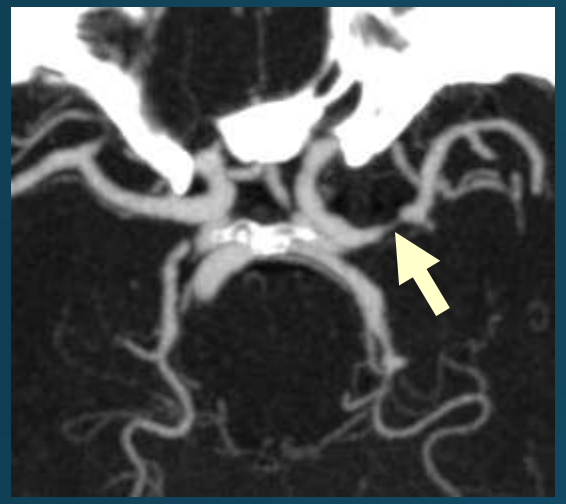
- What it images: Location and size of brain blood vessels

- Utility: Identification of:
  - vessel narrowing (e.g. stenosis),
  - distortion (e.g. AV malformations),
  - aneurysms

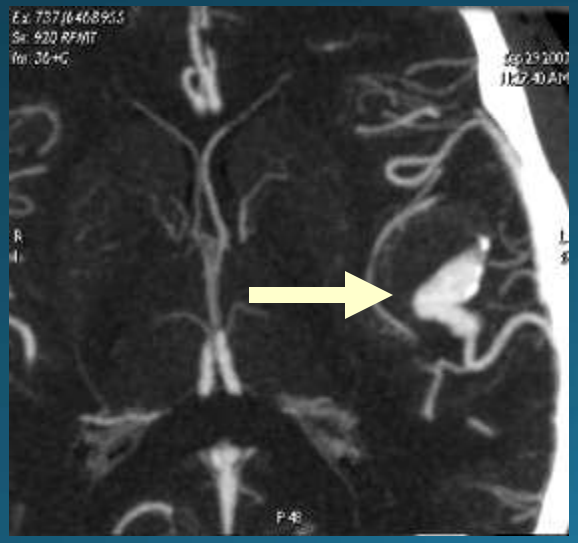
- Advantages?: Especially with new digital techniques, best way to visualize distribution and state of brain vasculature

# CT Angiography - Head

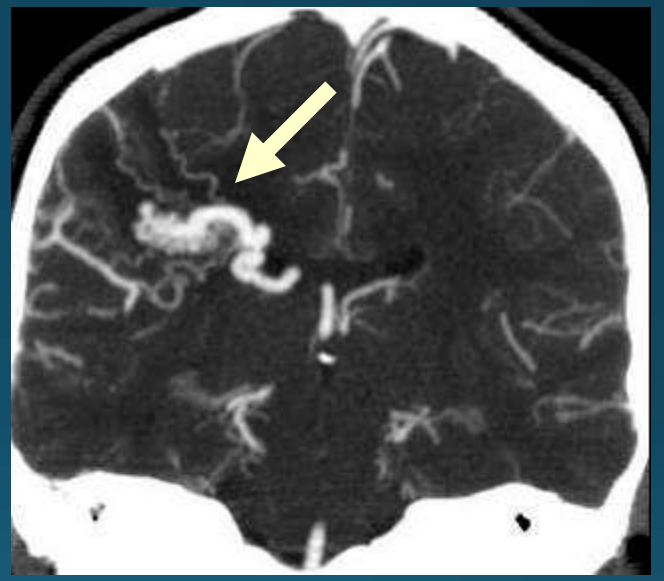
Circle of Willis



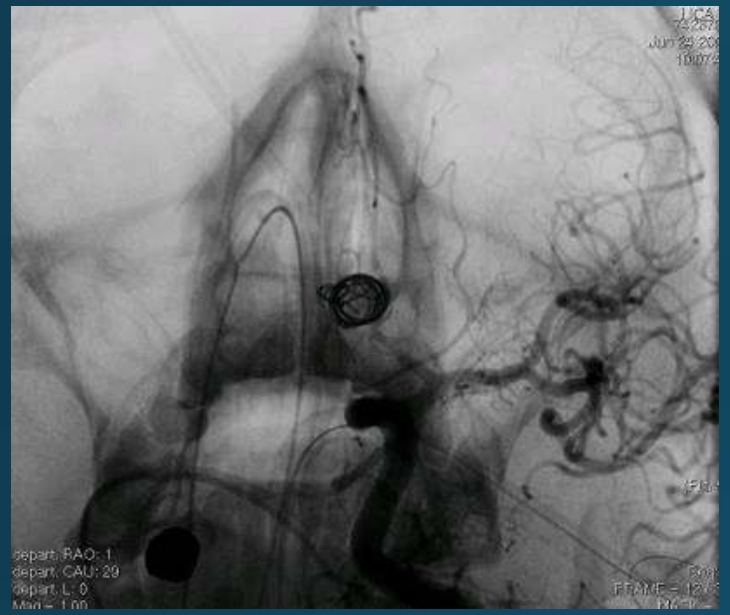
Aneurysms

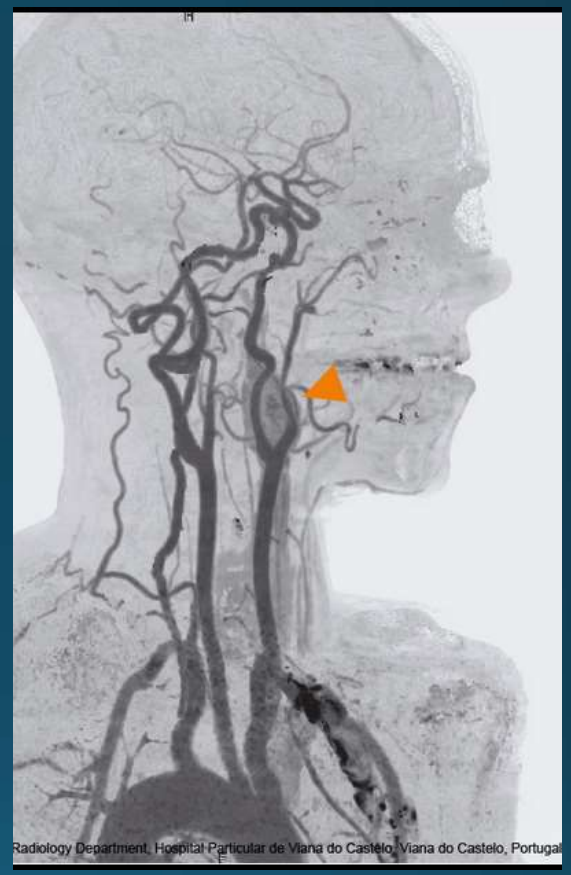


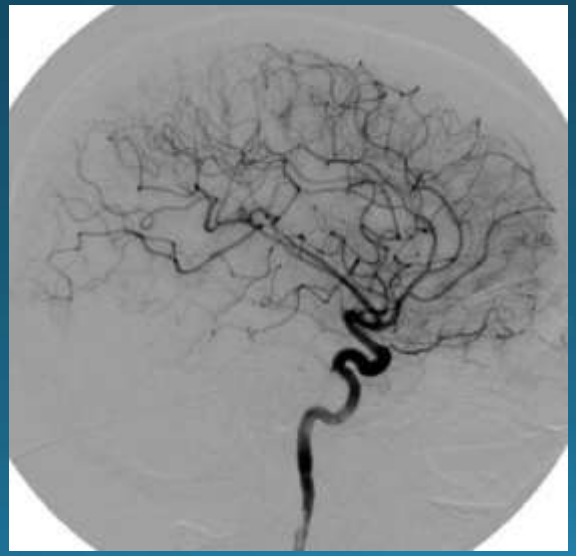
Vascular Malformations



# Angiography





45 year old female presented with right arm weakness and a Head CT with and without contrast was performed. CT demonstrates subarachnoid hemorrhage with a left MCA aneurysm.

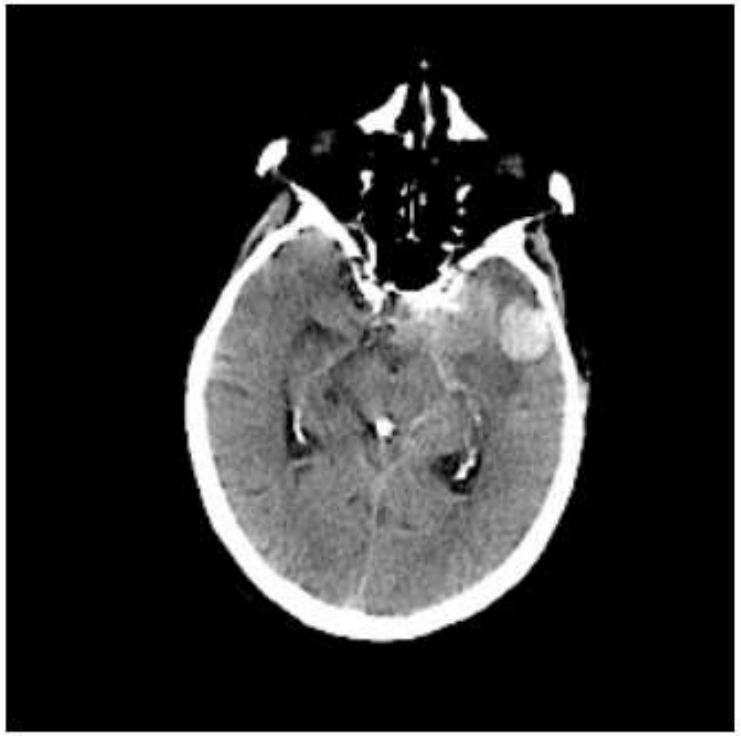


Image 1 - Non Contrast CT

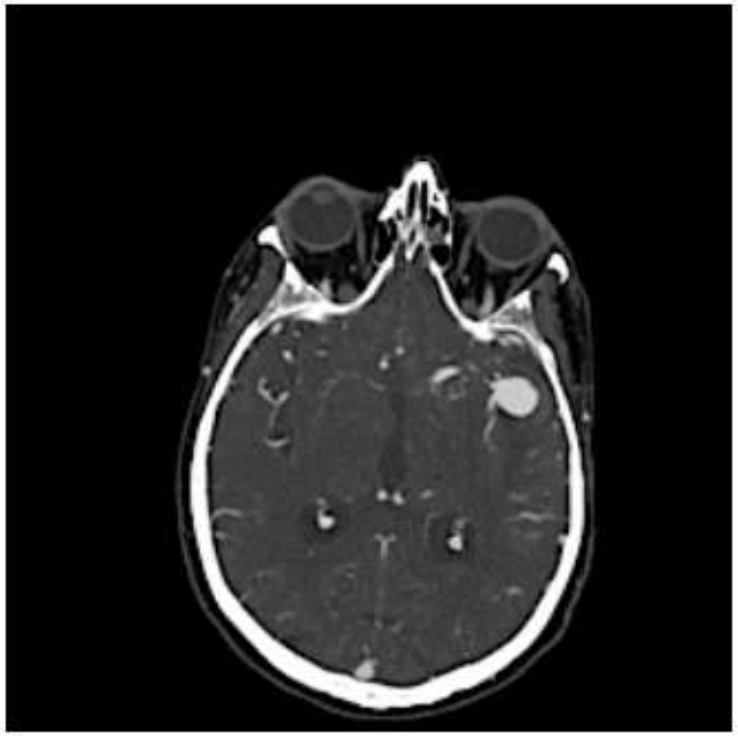


Image 2 - CT Angiogram

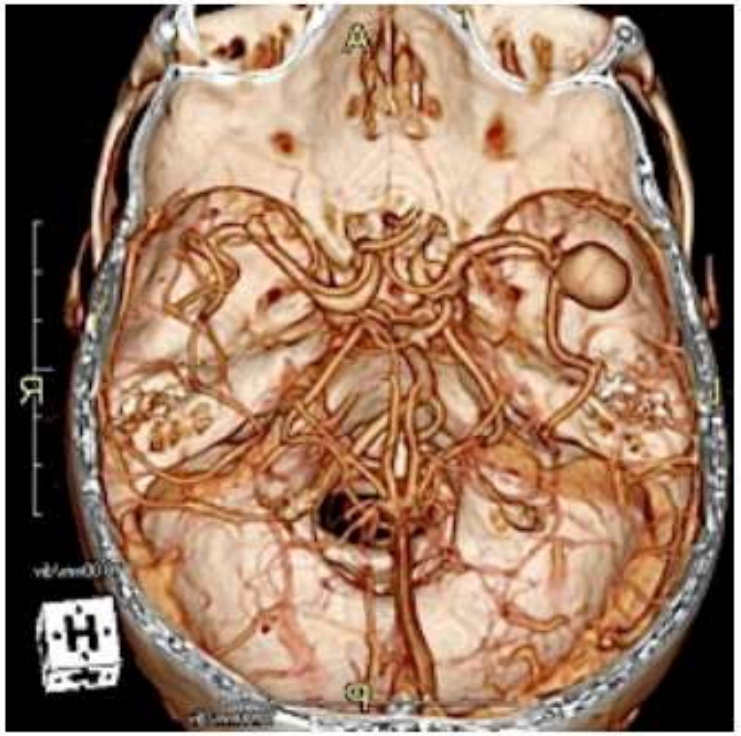



Image 3 - CTA 3D Reformat

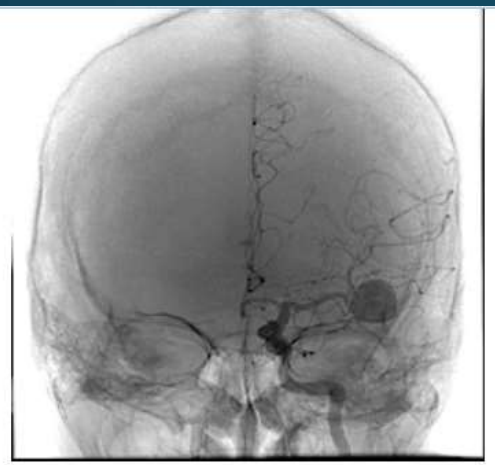


Image 4 - Cerebral Angiogram

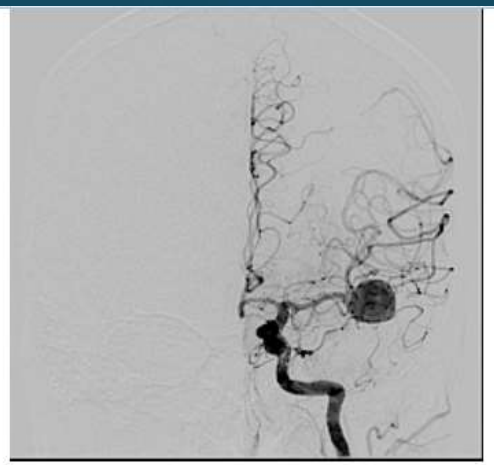


Image 5 - Cerebral Angiogram

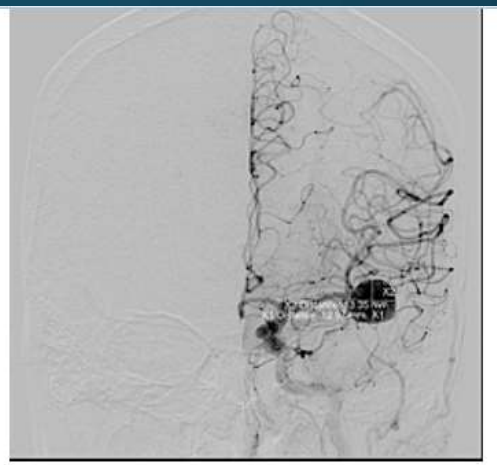


Image 6 - Measurements

A microcatheter was advanced into the aneurysm and coils deployed (Images 7 and 8). Post procedure images demonstrate occlusion of the aneurysm (Image 9).

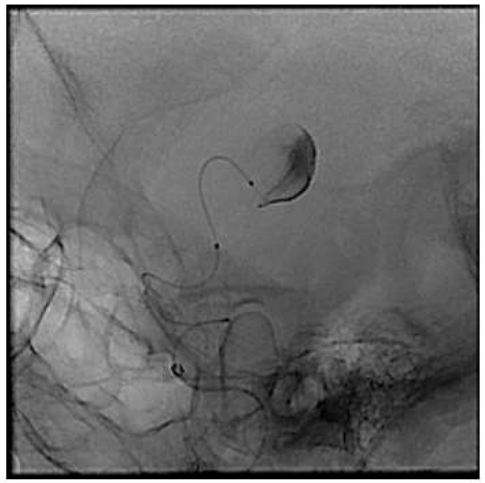


Image 7 - Microcatheter

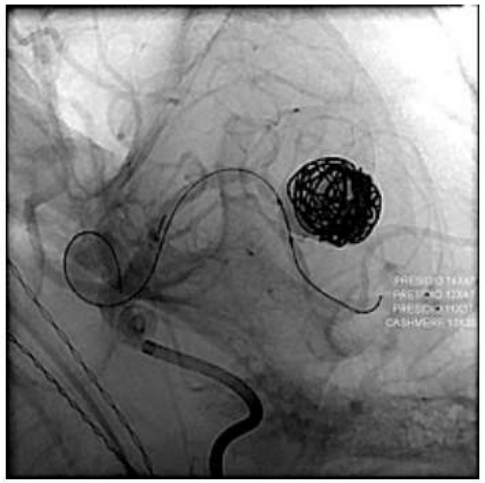


Image 8 - Coil Deployment

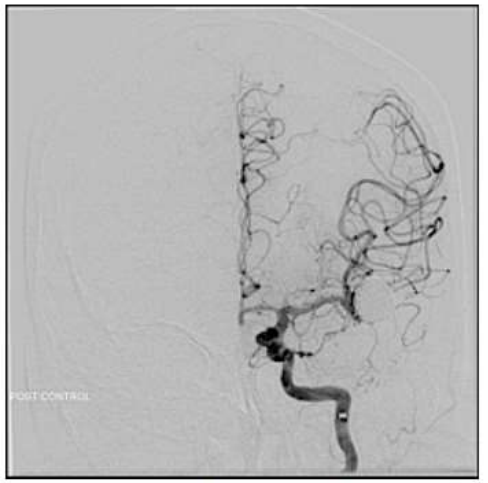


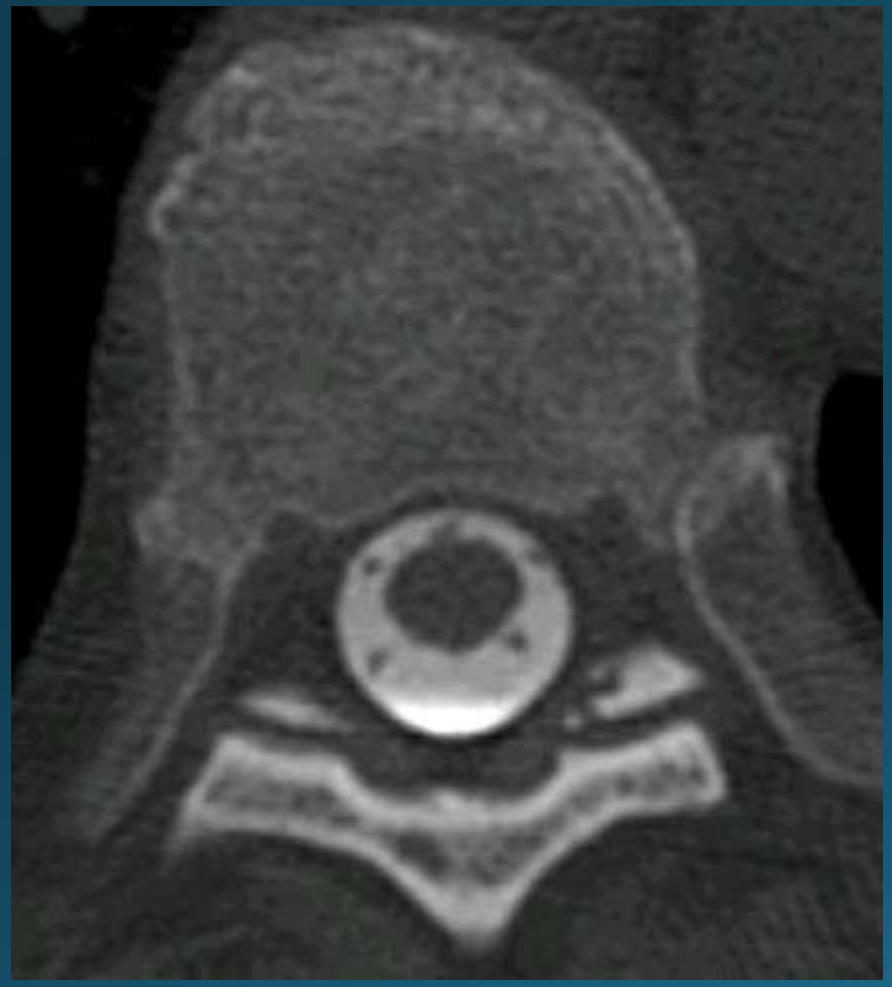
Image 9 - Final Result

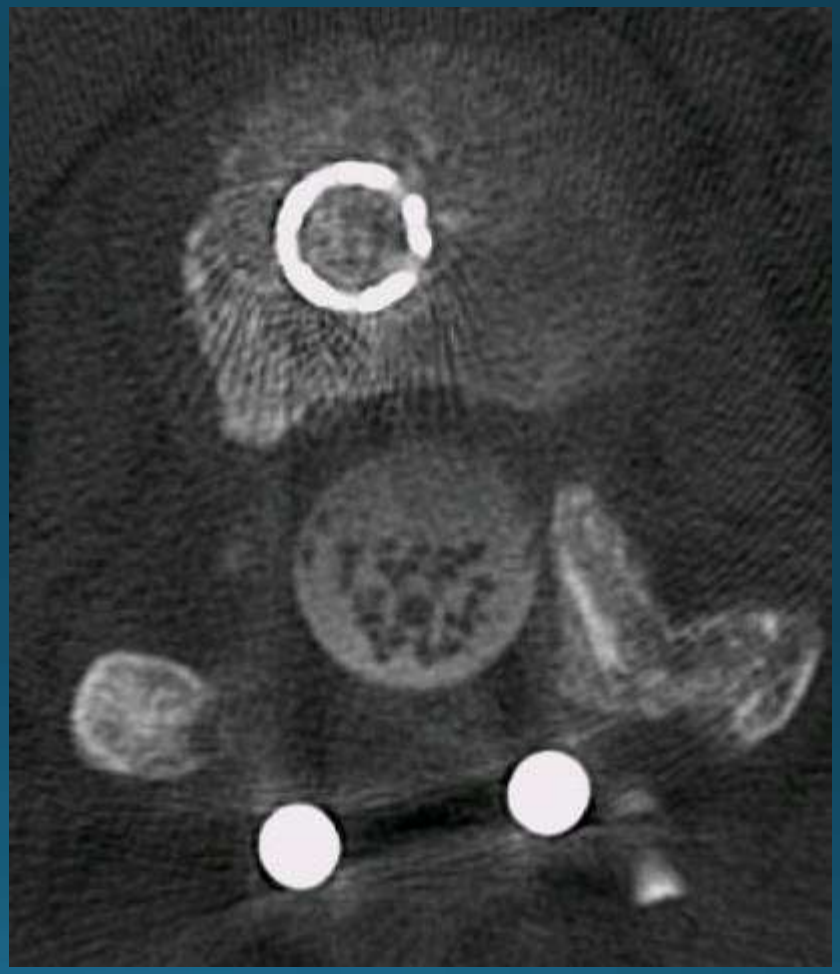
45 year old female presented with right arm weakness.
Prior CT demonstrated subarachnoid hemorrhage with a left MCA aneurysm.

# CT Myelography: Spinal Cord

- **Myelography** is a type of radiographic examination that uses a contrast medium to detect pathology of the spinal cord, including the location of a spinal cord injury, cysts, and tumors.
- The procedure often involves injection of contrast medium into the cervical or lumbar spine, followed by several X-rays. A myelogram may help to find the cause of pain not found by an MRI or CT.
- Spinal CT immediately following conventional myelogram
- Cross-sectional view of spinal canal along with spinal cord and nerve roots; assess spinal stenosis/nerve root compression (e.g. disc herniation, vertebral frx, neoplasm)

# CT Myelography





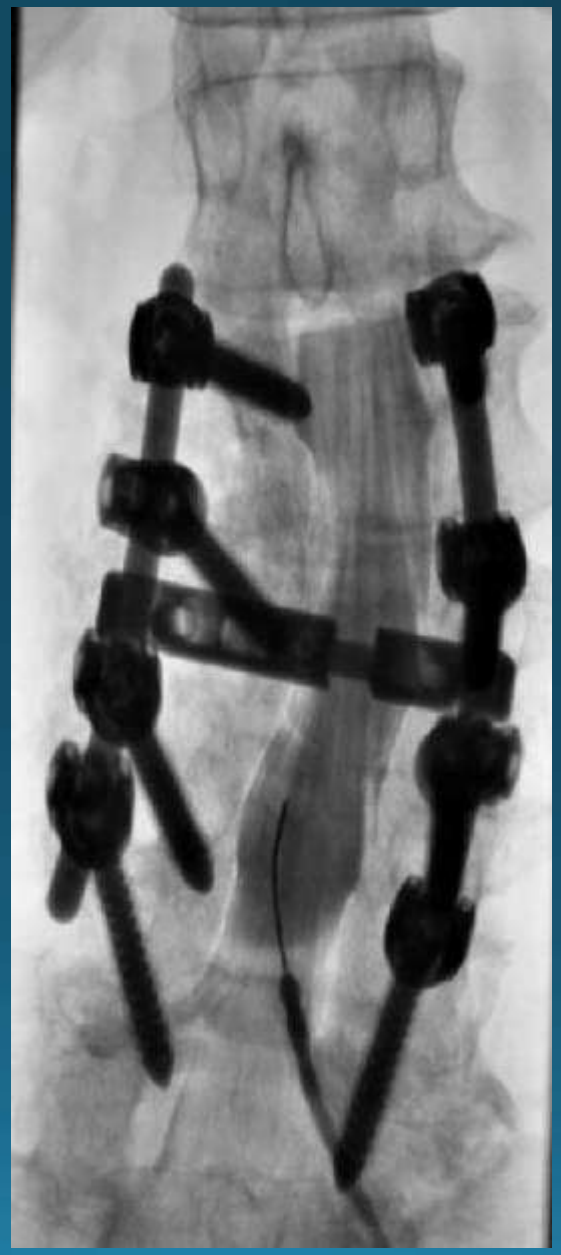
# Fluoroscopy (Real-Time X-Ray)

## Myelography

Lumbar or cervical puncture

Inject contrast intrathecally with fluoroscopic guidance

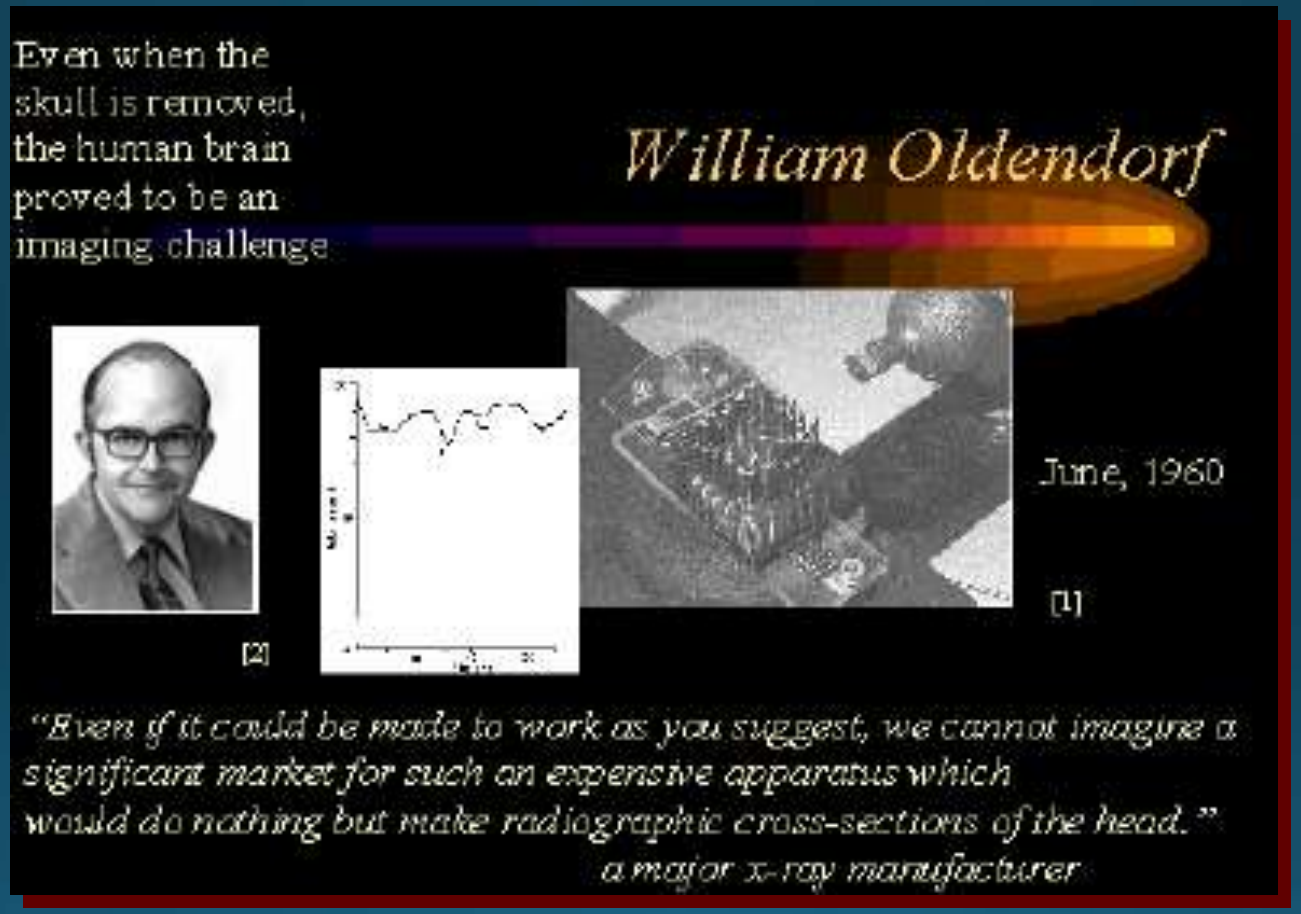
Follow-up with post-myelo CT (CT myelogram)



# Computed Tomography (CT) Basics

# CT: William Oldendorf, 1963 patent, but no Nobel Prize

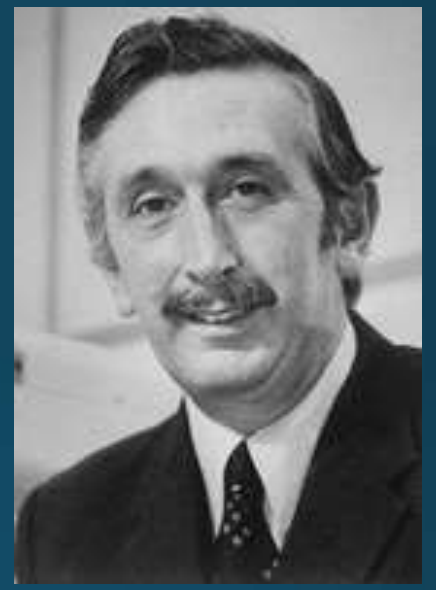
*Even when the skull is removed, the human brain proved to be an imaging challenge*




*"Even if it could be made to work as you suggest, we cannot imagine a significant market for such an expensive apparatus which would do nothing but make radiographic cross-sections of the head."*

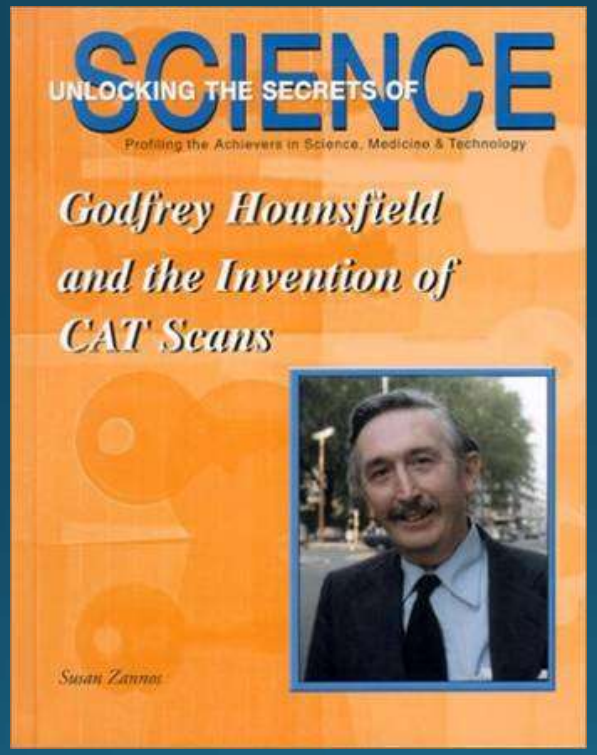
*A major x-ray manufacturer*

# Sir Godfrey Hounsfield and EMI & Beatles



Hounsfield built a prototype head scanner and tested it first on a preserved human brain, then on a fresh cow brain from a butcher shop, and later on himself. In September 1971, CT scanning was introduced into medical practice with a successful scan on a cerebral cyst patient at Atkinson Morley's Hospital in London, UK.

# CT History: Sir Godfrey N. Hounsfield




- **1979 Nobel Laureate in Medicine**

# X-ray and CT

- Computerized tomography was developed from X-ray technology, and many of the principles are the same.
- In CT, rather than just taking one shot of the patient, the X-ray beam is rotated around the head at different levels.
- The X-ray information is compiled by a computer to create a series of images that look as if the brain had been sliced somewhat like a loaf of bread.

# CAT: Computed Axial Tomography


**CT (roentgen-ray computed tomography)**

A beam of x-rays is shot straight through the brain. As it comes out the other side, the beam is blunted slightly because it has hit dense living tissues on the way through.

Blunting or "attenuation" (absorption) of the x-ray comes from the density of the tissue encountered along the way. Density of tissue absorbs differentially.

Very dense tissue like bone blocks lots of x-rays (white); tissue blocks some (grey) and fluid even less (dark).

X-ray detectors positioned around the circumference of the scanner collect attenuation readings from multiple angles. A computerized algorithm reconstructs an image of each slice.

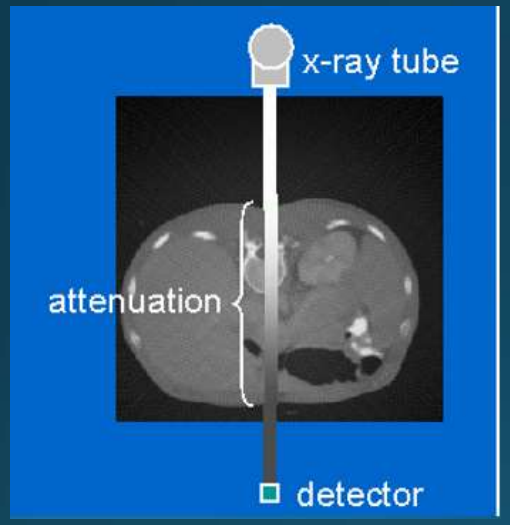
1.5 to 7 Tesla

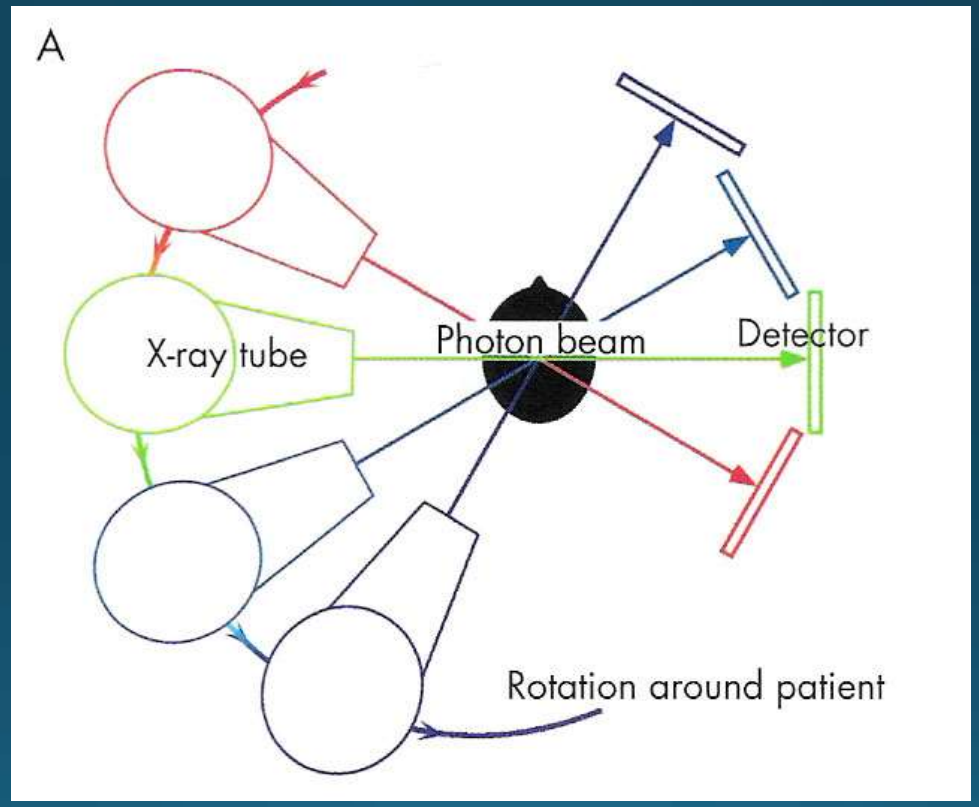
Head CT: 2 mSv (8 months of background rad)

20 x radiation of chest x-ray (0.1 mSv)

# Computed Tomography

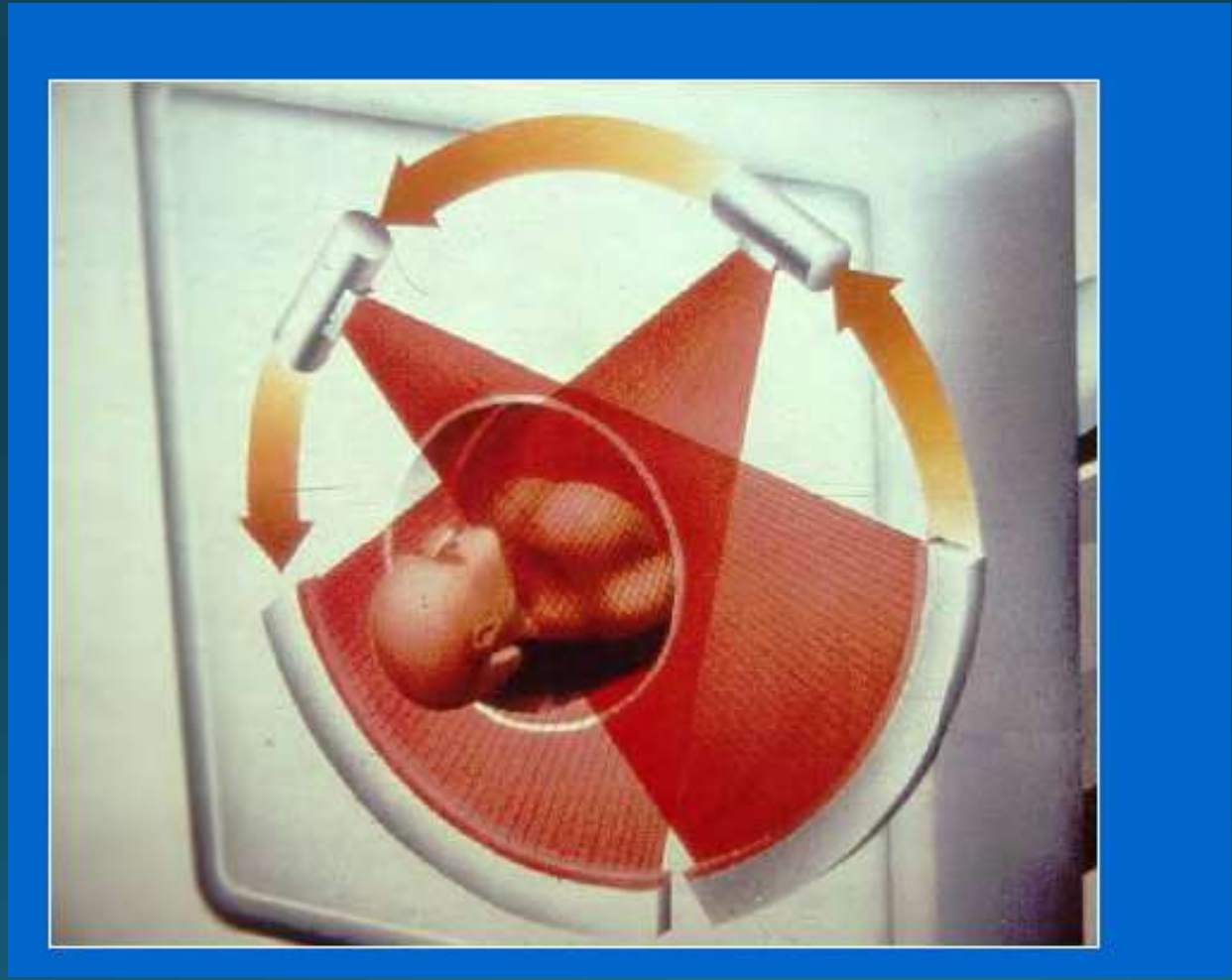
Based upon X-rays and attenuation




Images record tissue density as measured by variable attenuation

Rotating X-ray tube and detector array allows multiple projections at different angles.



# Computed Tomography

A CT image is a pixel-by-pixel map of X-ray beam attenuation (degree to which the X-ray intensity is reduced by density of the material) in Hounsfield Units (HU)

$HU_{water} = 0$

Bright = “hyper-attenuating” or

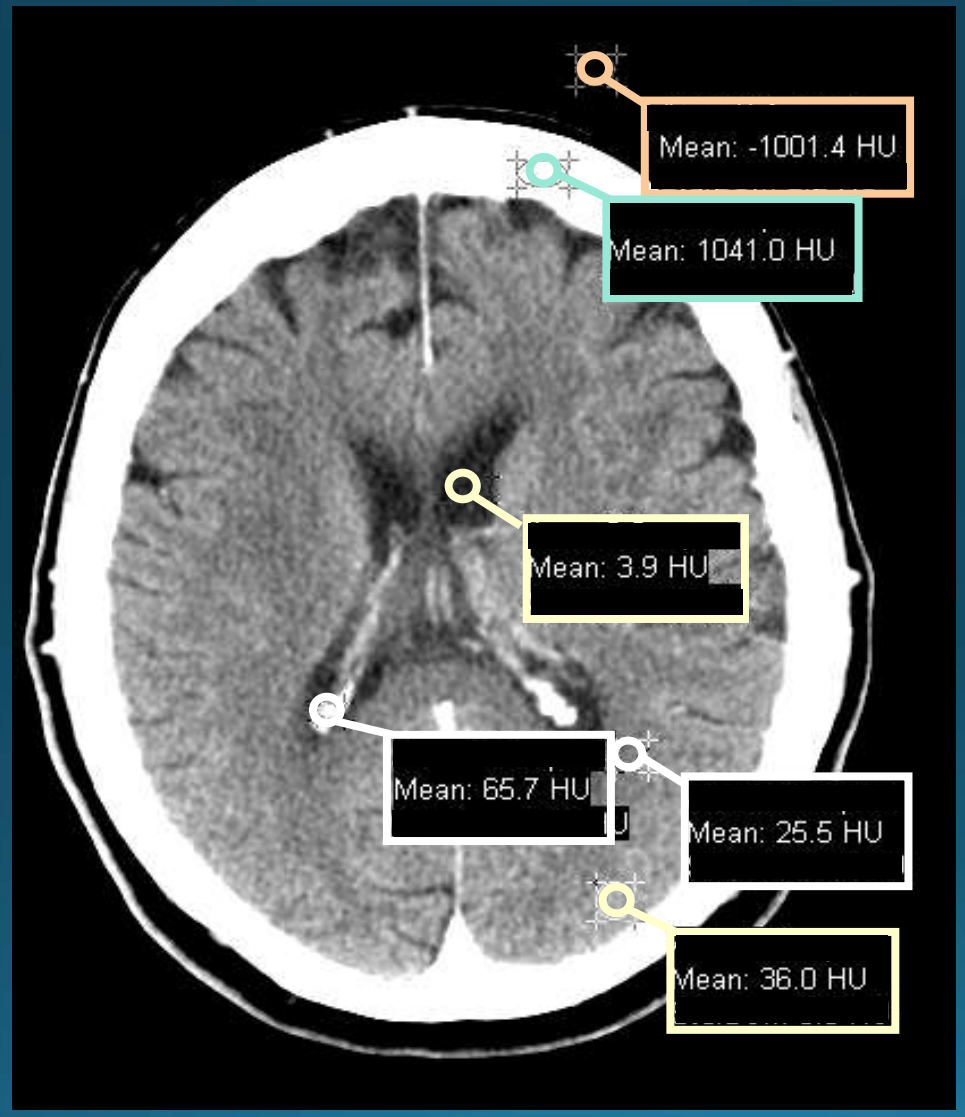
“hyper-dense”

# Computed Tomography

## Typical HU Values:

| | | |
|---|---|---|
| | Air | –1000 |
| | Fat | –100 to –40 |
| | Water | 0 |
| | Other fluids (e.g. CSF) | 0–20 |
| Brain | White matter | 20–35 |
| Brain | Gray matter | 30–40 |
| | Blood clot | 55–75 |
| | Calcification | >150 |
| | Bone | 1000 |
| | Metallic foreign body | >1000 |

# Different HU values in the Brain: 3.9 to 1041



# Grey-scale appearance on CT

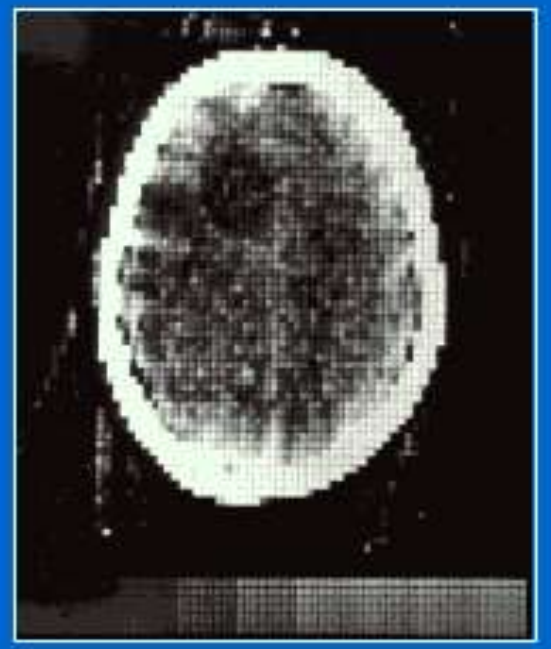
| Tissue | Appearance |
| --- | --- |
| **Bone** | **White** |
| **Calcified Tissue** | **White** |
| **Clotted Blood** | **White** |
| **Grey Matter** | **Light Gray** |
| **White Matter** | **Medium Grey** |
| **CSF** | **Near Black** |
| **Water** | **Near Black** |
| **Air** | **Black** |

# CT History

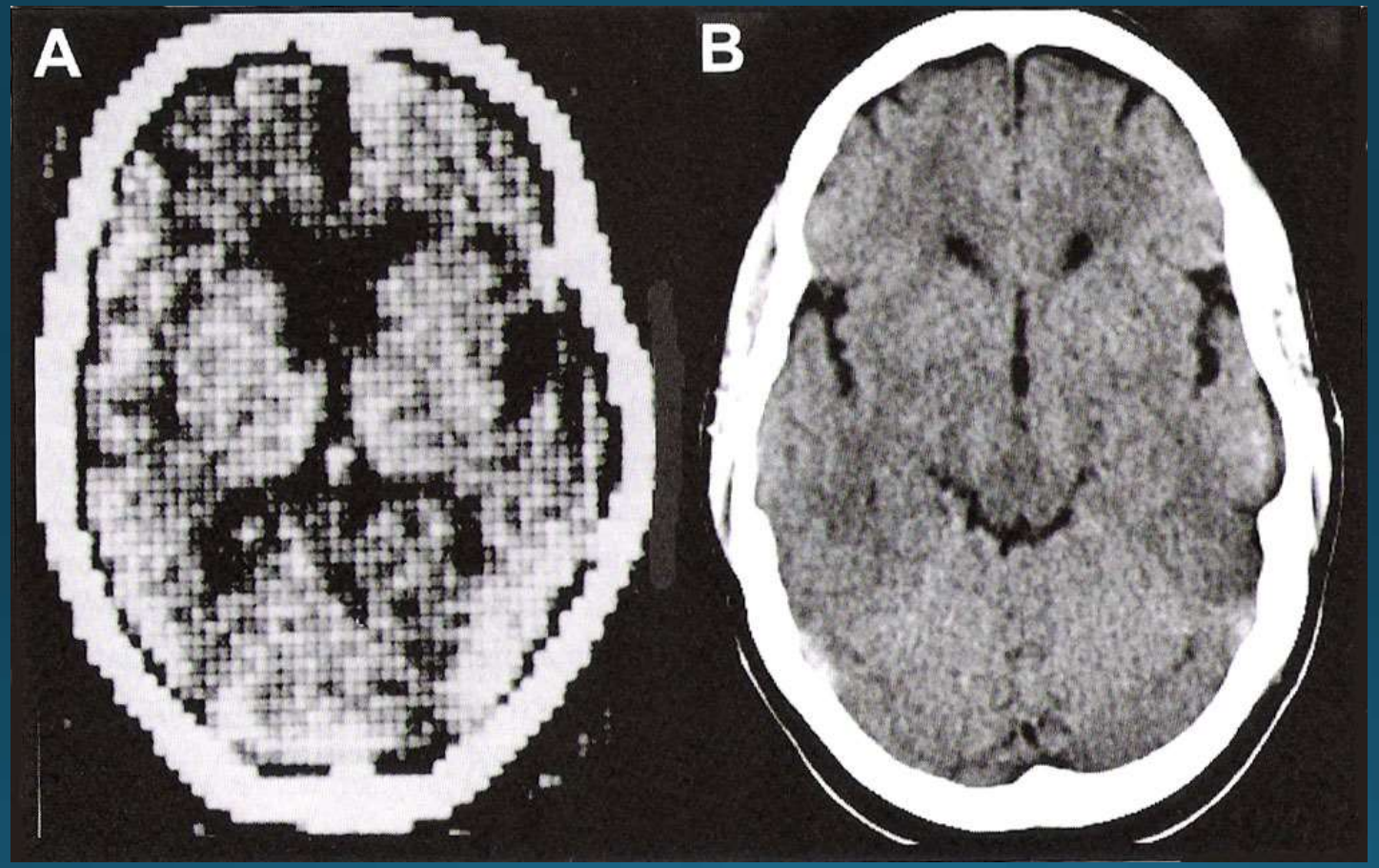
- 1972 – First clinical CT scanner use
  - Used for head examinations
  - Water bath required
  - 80 x 80 matrix
  - 4 minutes per revolution
  - 1 image per revolution
  - 8 levels of grey
  - Overnight image reconstruction

# 1972 image: wait overnight

- 1972: 80 x 80 matrix, 4 min per rotation, 8 grey levels, overnight image reconstruction.



# Computed Tomography (CT)



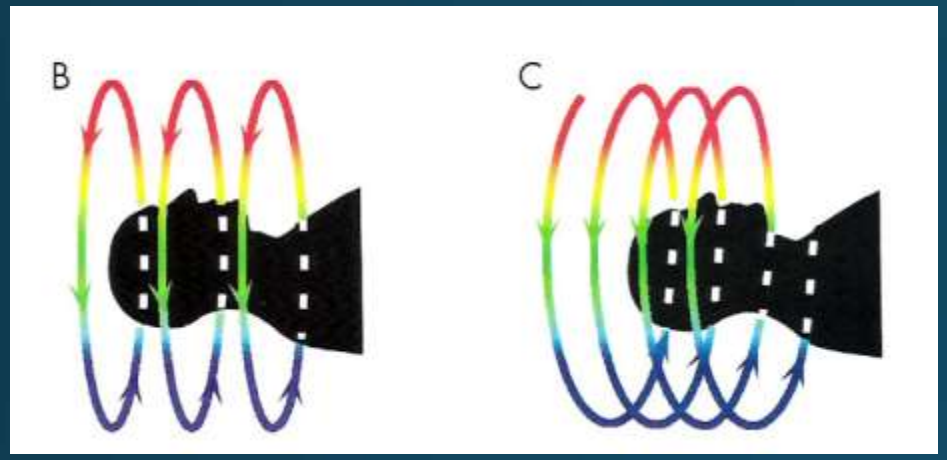

**1st Generation (1975)**

**Modern CT**

# CT History

- 2004 – 64 slice scanner
  - 1024 x 1024 matrix
  - 0.33s per revolution
  - 64 images per revolution
  - 0.4mm slice thickness
  - 20 images reconstructed/second

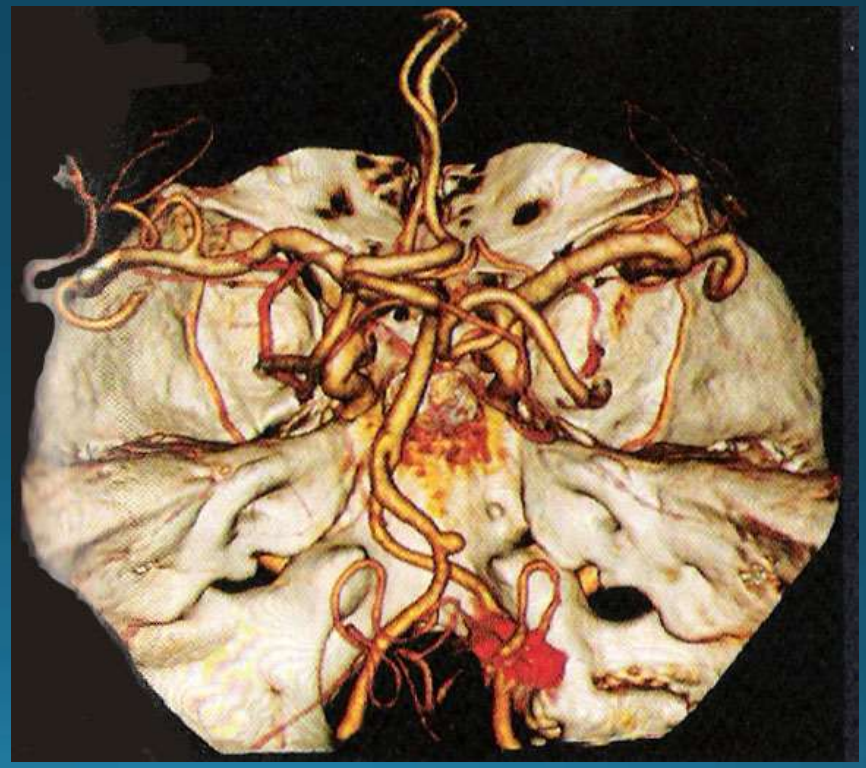
# Newer Models: Faster Speed and More Dimensions




**Spiral scanners introduced in the 1990's**

**Rapid image acquisition and ability to reconstruct coronal, sagittal, and 3D images.**

**3D image revealing vertebral artery aneurysm.**

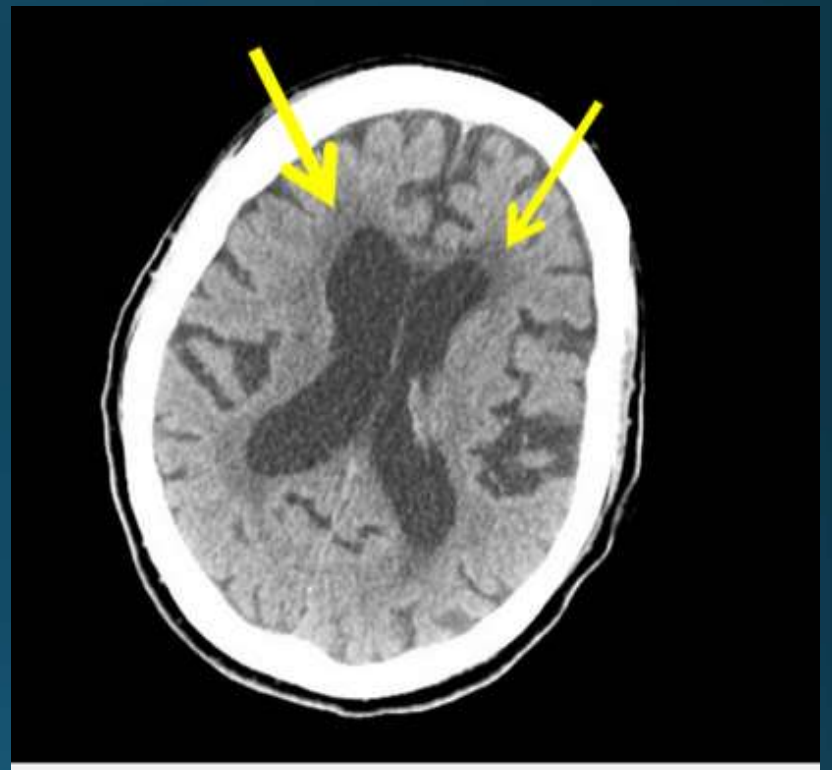


# CT: Radiation

- Exams using ***Ionizing radiation***
  - Plain film & digital
  - CT
    - 1/10 of all medical exams
    - ***2/3 OF ALL MEDICAL RADIATION EXPOSURE***
  - Fluoroscopy: most radiation
    - Angiography, barium studies

# CT Attenuation =  measure of tissue density

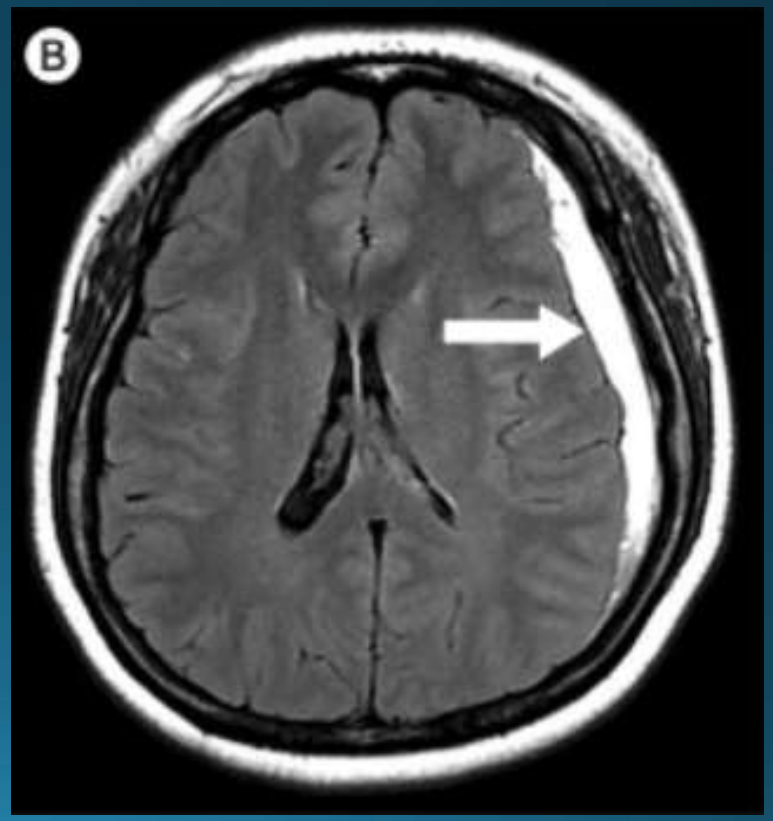
- Attenuation
  - Hyperattenuating (hyperdense) (bright) (bone)
  - Hypoattenuating (hypodense) (dark) (fluid)
  - Isoattenuating (isodense) (identical)
- Attenuation is measured in Hounsfield units
  - Scale -1000 to 1000
    - -1000 is air
    - 0 is water
    - 1000 is cortical bone



**Periventricular white matter hypoattenuation:** Axial CT

# CT viewing

- What we can see
  - The brain is grey
    - White matter is usually dark grey (HU = 40)
    - Grey matter is usually light grey (45)
    - CSF is black (0)
    - Things that are bright on CT
      - Bone or calcification (>300)
      - Contrast
      - Hemorrhage (Acute ~ 70)
      - Metallic foreign bodies



# CT Scan: Modality of first choice in acute care

Advantage: very quick, less expensive; good at differentiating very different tissue (blood vs brain vs bone)

Disadvantages: good but not great in delineation of similar soft tissue anatomy and pathology; Less useful in white matter conditions (e.g. MS) or  differential diagnosis (tumor vs other mass)

Uses x-ray radiation

# CT noncontrast uses

Modality of first choice in acute care

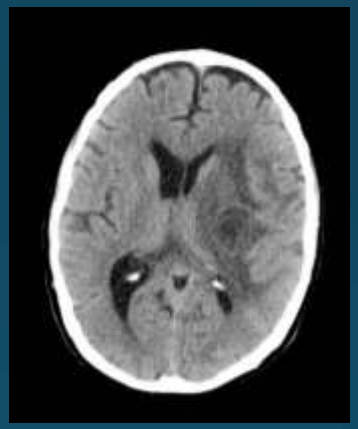
Initial evaluation of: stroke/hemorrhage, skull fracture, mass effect

Head injury – acute intracranial hemorrhage especially subarachnoid hemorrhage – superior in evaluating cortical bone structures and spine

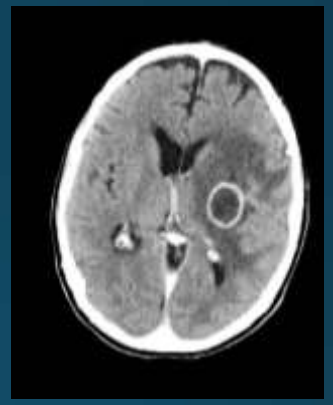
Stroke -Less sensitive than MRI during first 48 hours

# Contrast enhanced CT

Intravenously (IV) delivered contrast media enhances CT in depicting vasculature, and hyper vascular tumors (resulting in the “ring enhancing” phenomenon).

No contrast



Contrast

Iodinated water soluble contrast agents can be given intravenously to enhance differences in tissue density

Intravenous CT contrast agents are based on iodine

# CT Indications

- Skull and skull base, vertebrae
  (trauma, bone lesions)
- Ventricles
  (hydrocephalus, shunt placement)
- Intracranial masses, mass effects
  (headache, N/V, visual symptoms, etc.)
- Hemorrhage, ischemia
  (stroke, mental status change)
- Calcification
  (lesion characterization)

# Imaging of Stroke: CT vs MRI

- CT
  - Better identification of acute hemorrhage
  - Availability
  - Decrease expense
  - Decreased time
  - Less contraindications (i.e. metal in body)
  - In the ED setting CT remains the primary screen based on consideration of hemorrhage

- MRI
  - More sensitive to early changes of stroke, i.e. edema

# Stroke

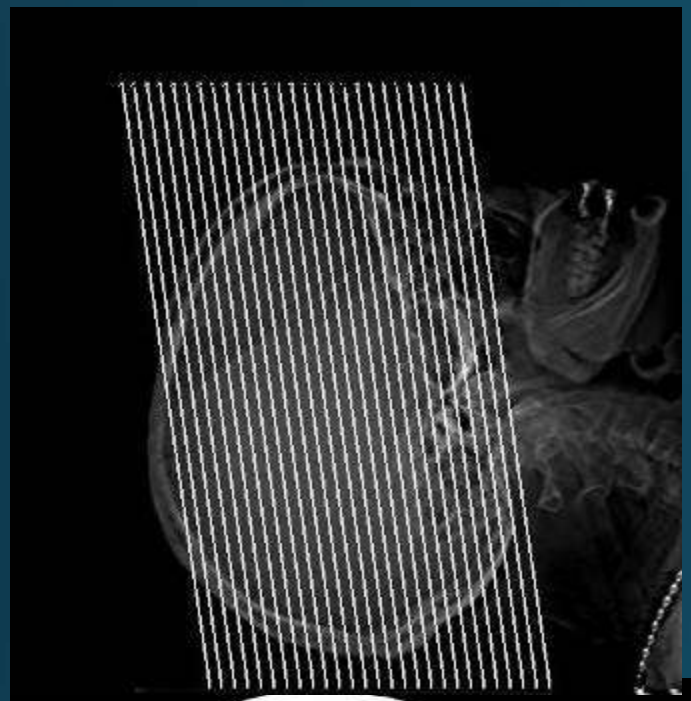
CT remains the initial study in suspected stroke case

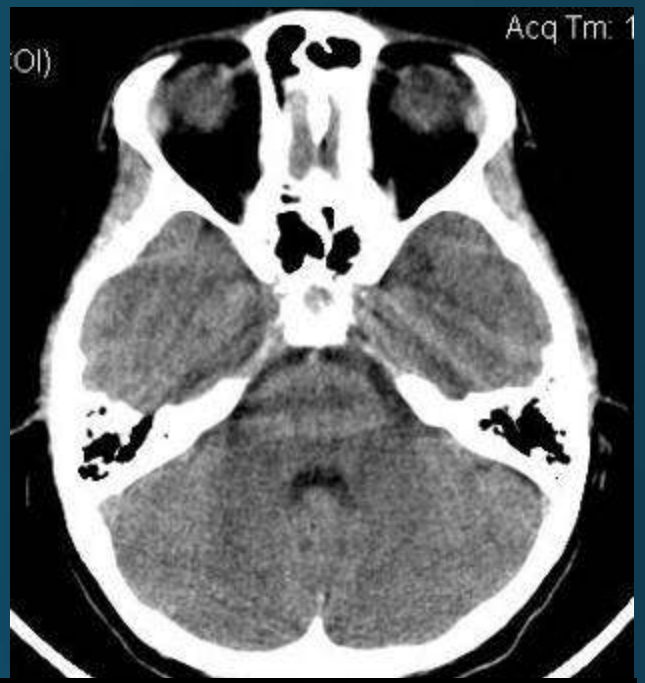
Quick
Excludes hemorrhage
Evaluates for possible mass effect (displacement of surrounding tissue)

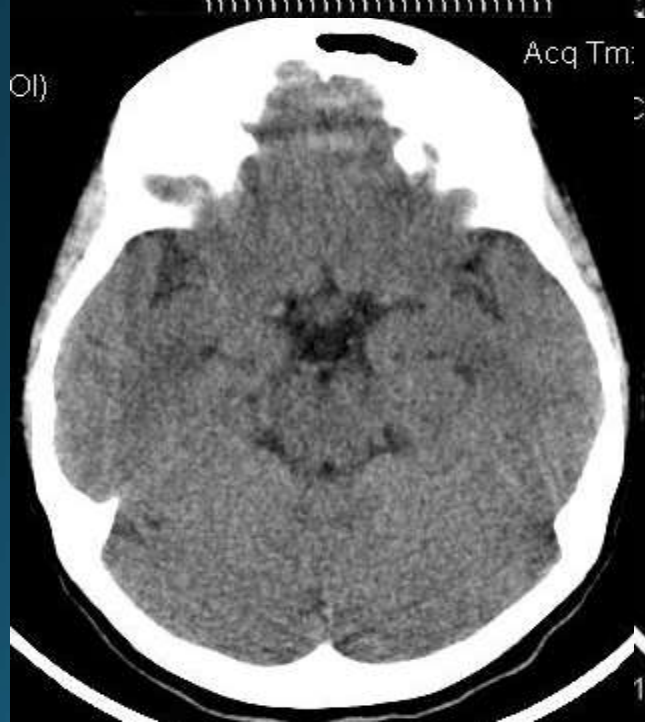
Early cerebral infarct may not be visible on CT

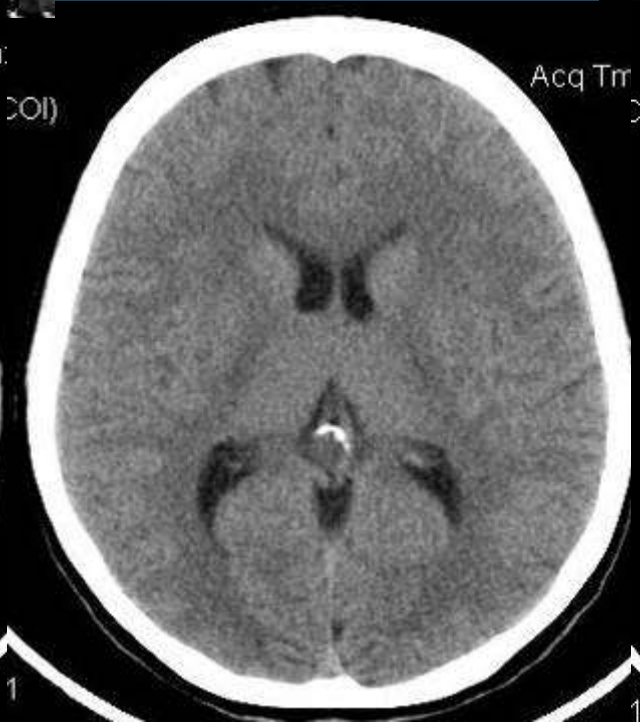
Conventional CT has a 42% sensitivity and 91% specificity in the diagnosis of hyperacute stroke.

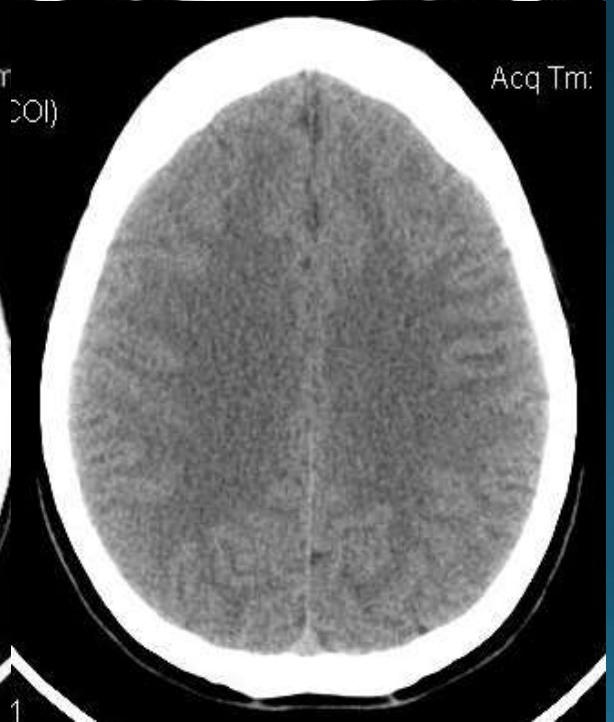
# Normal CT



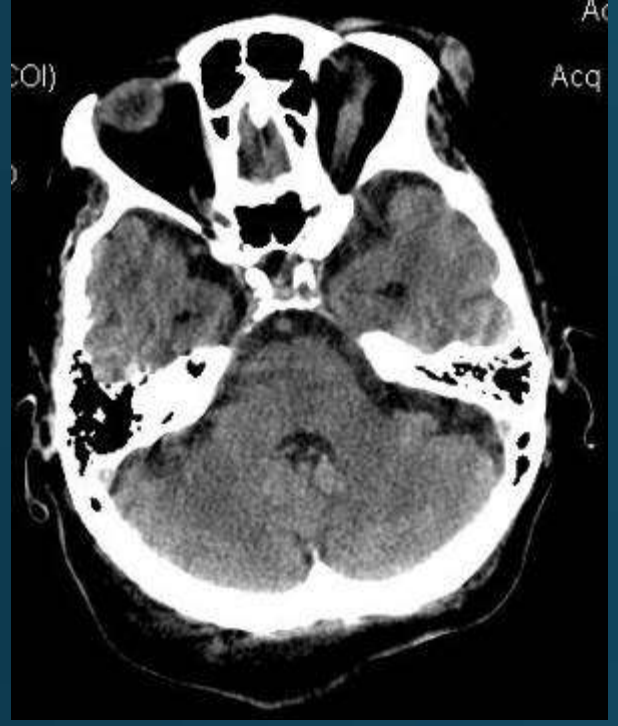


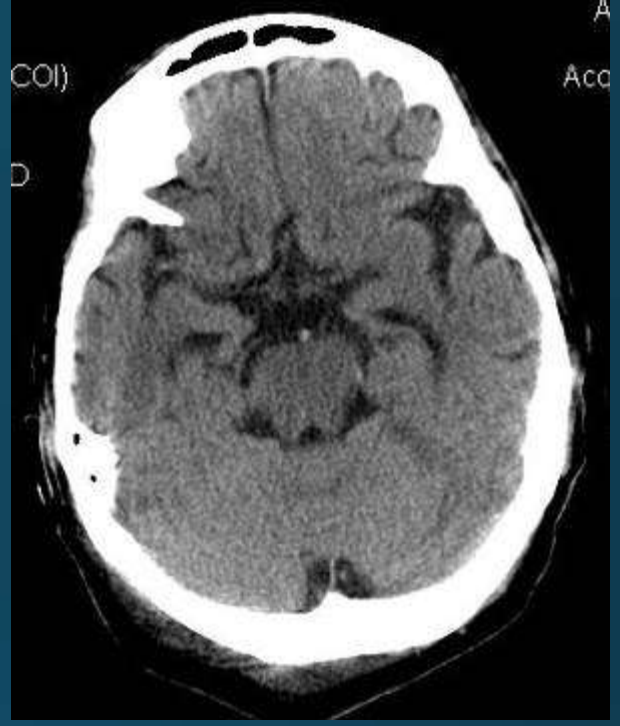



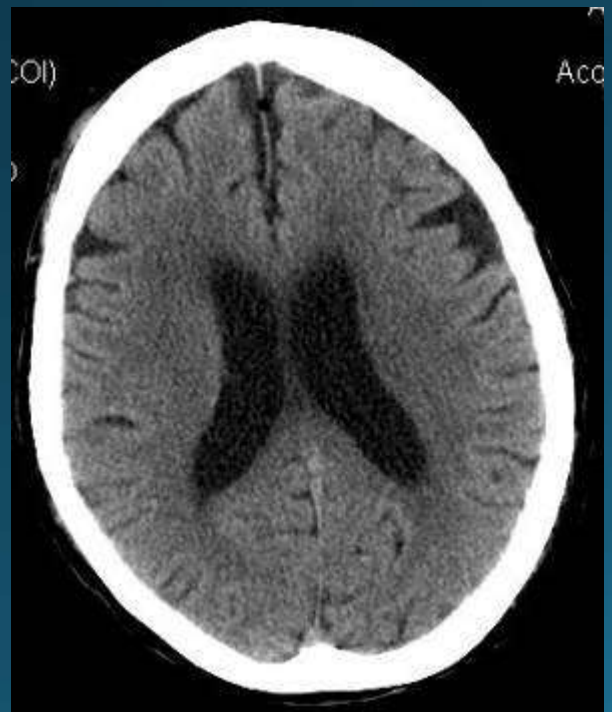



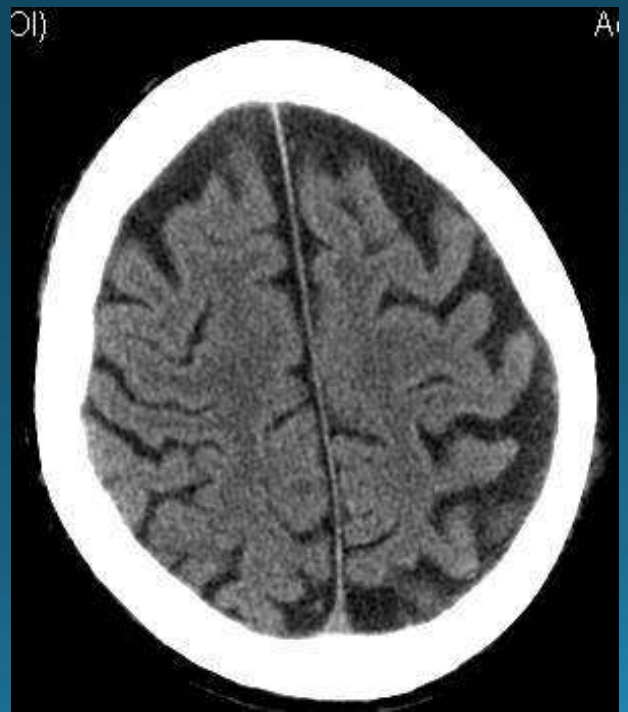



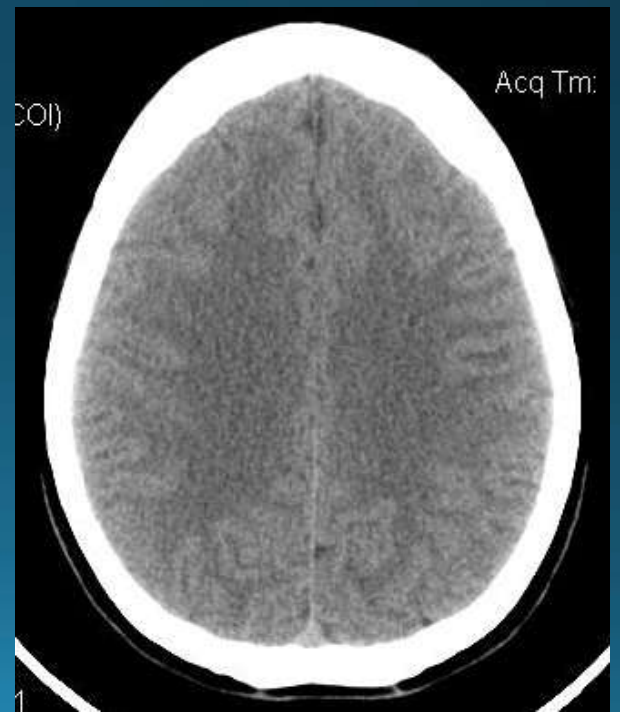
# Normal CT
# Older person



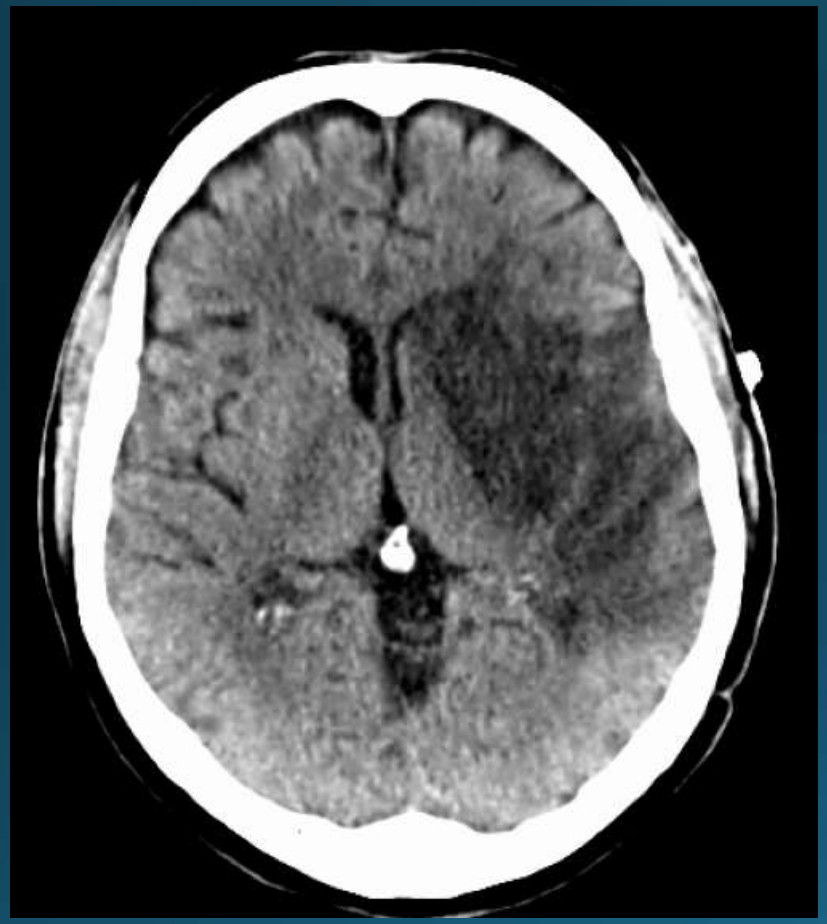


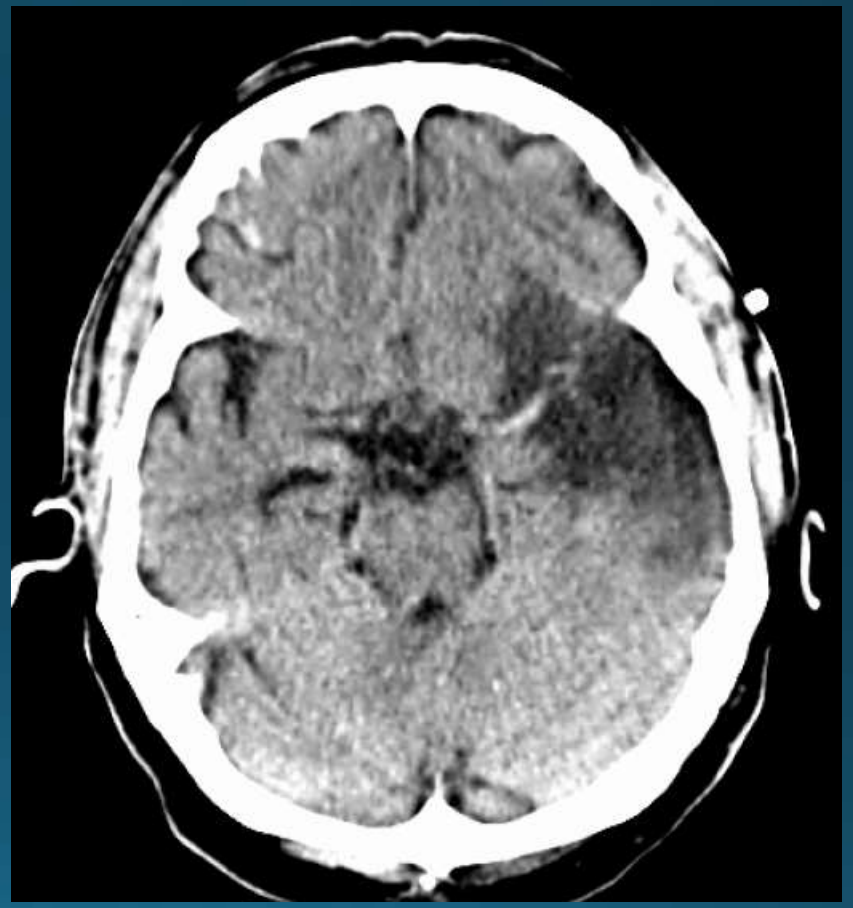




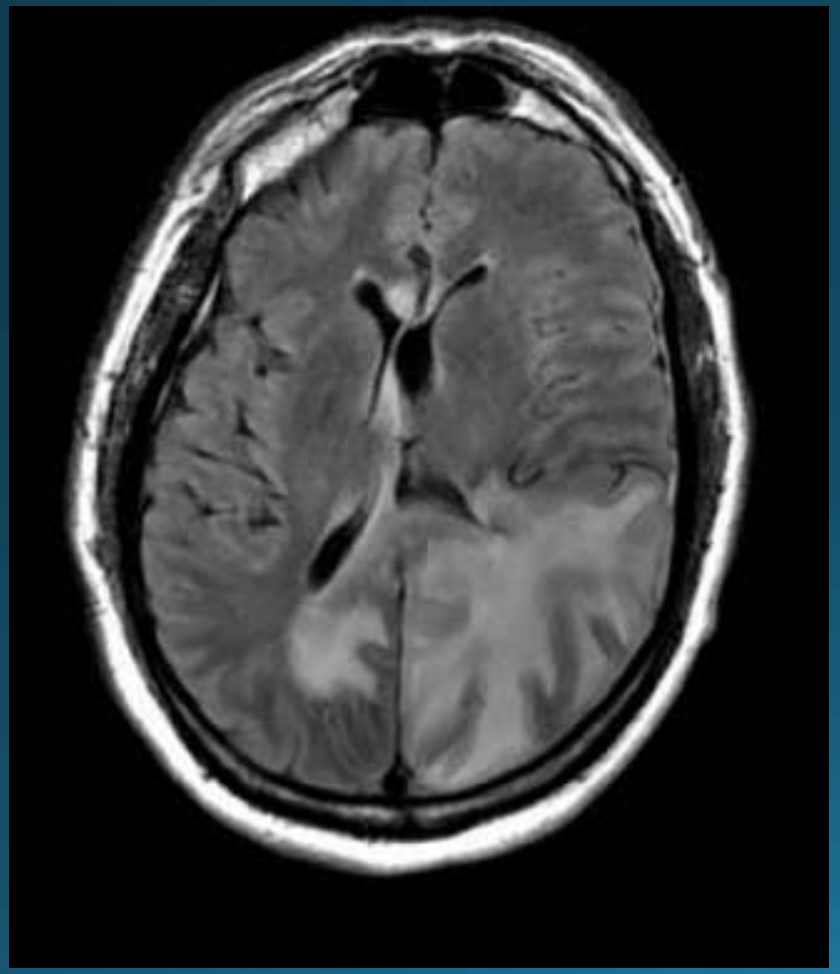


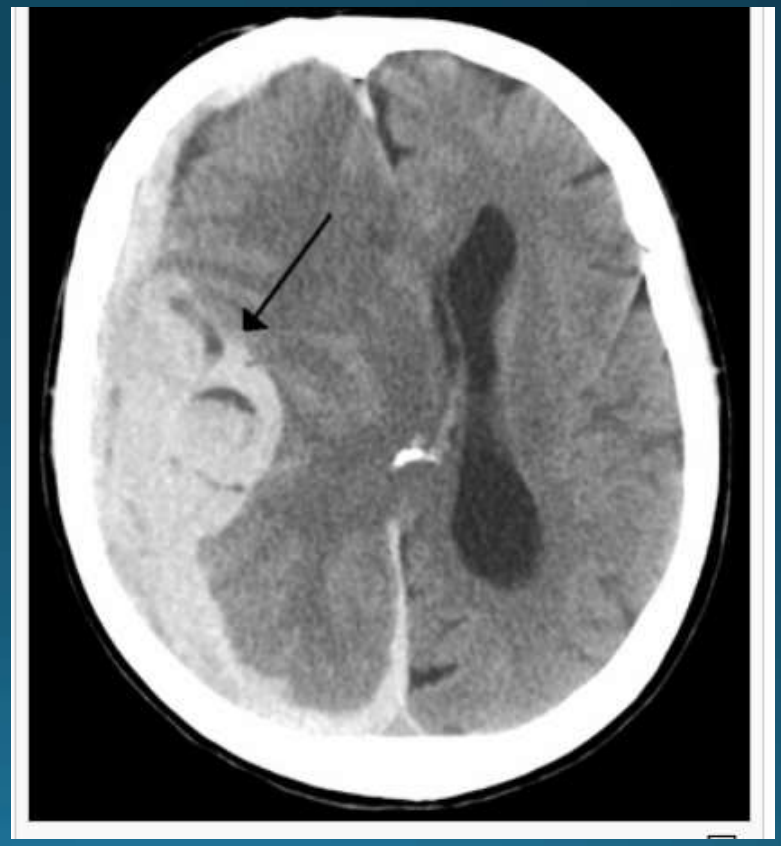
# Stroke



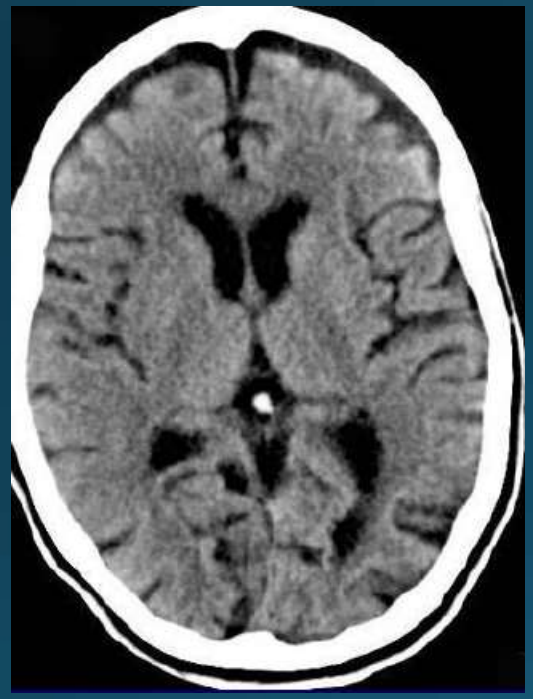


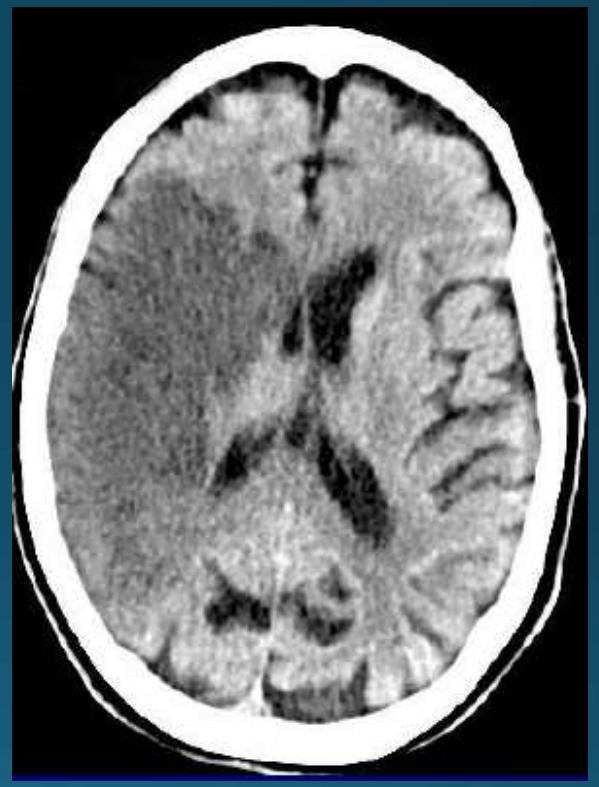
# Severe Mass Effect from Tumor & Subdural





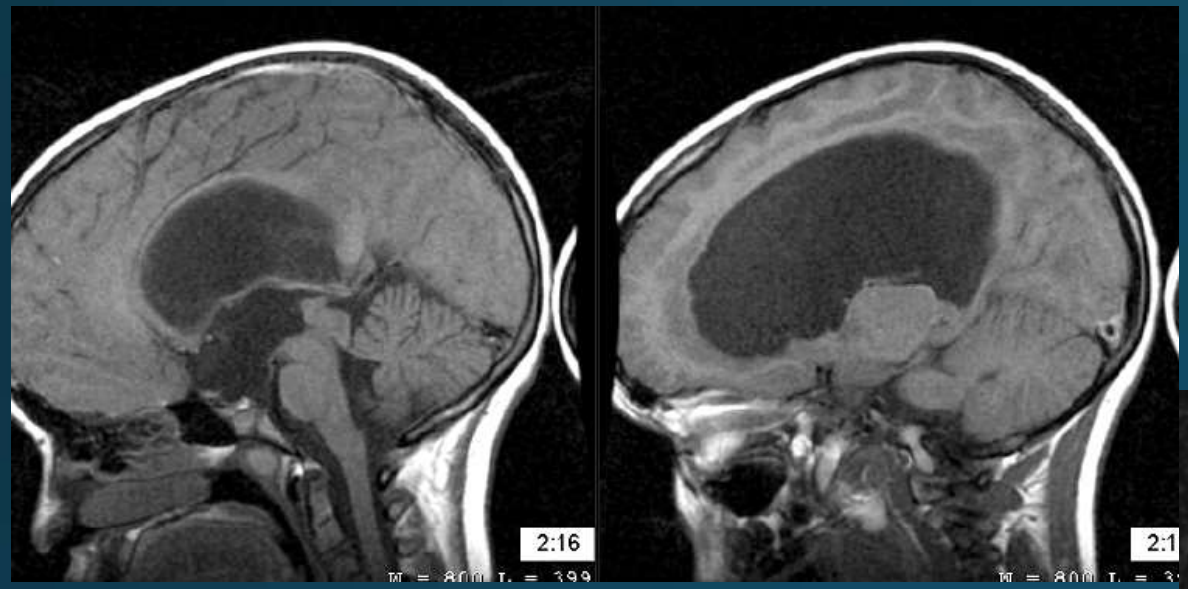
# 78 year old male AMS:  MCA stroke

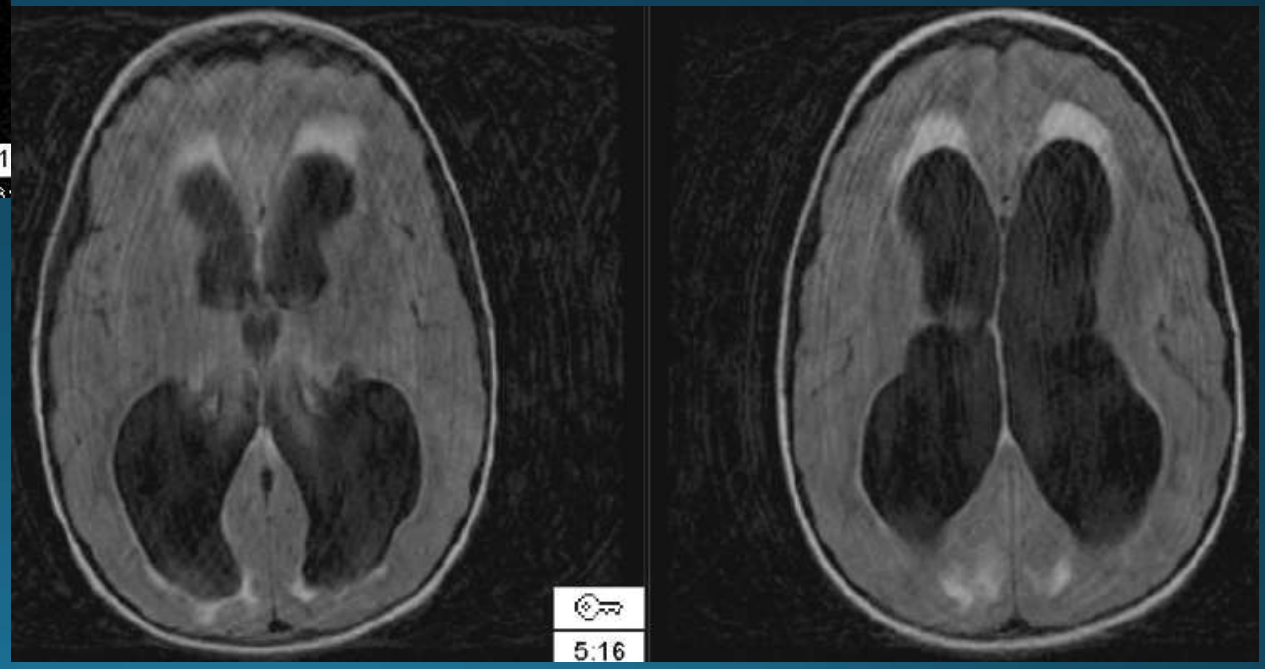




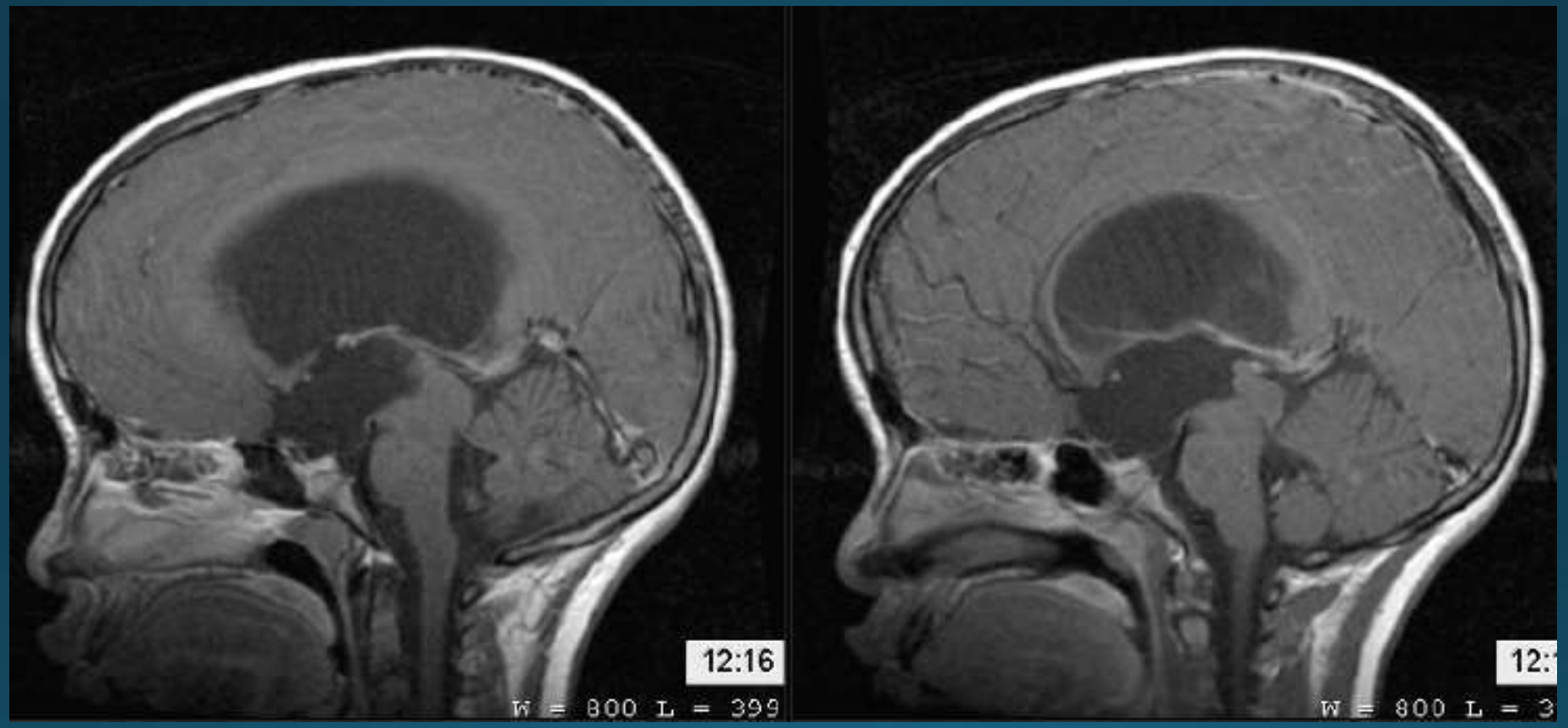
Initial 48 Hours later

# 7 yo, right sided weakness, mild ataxia



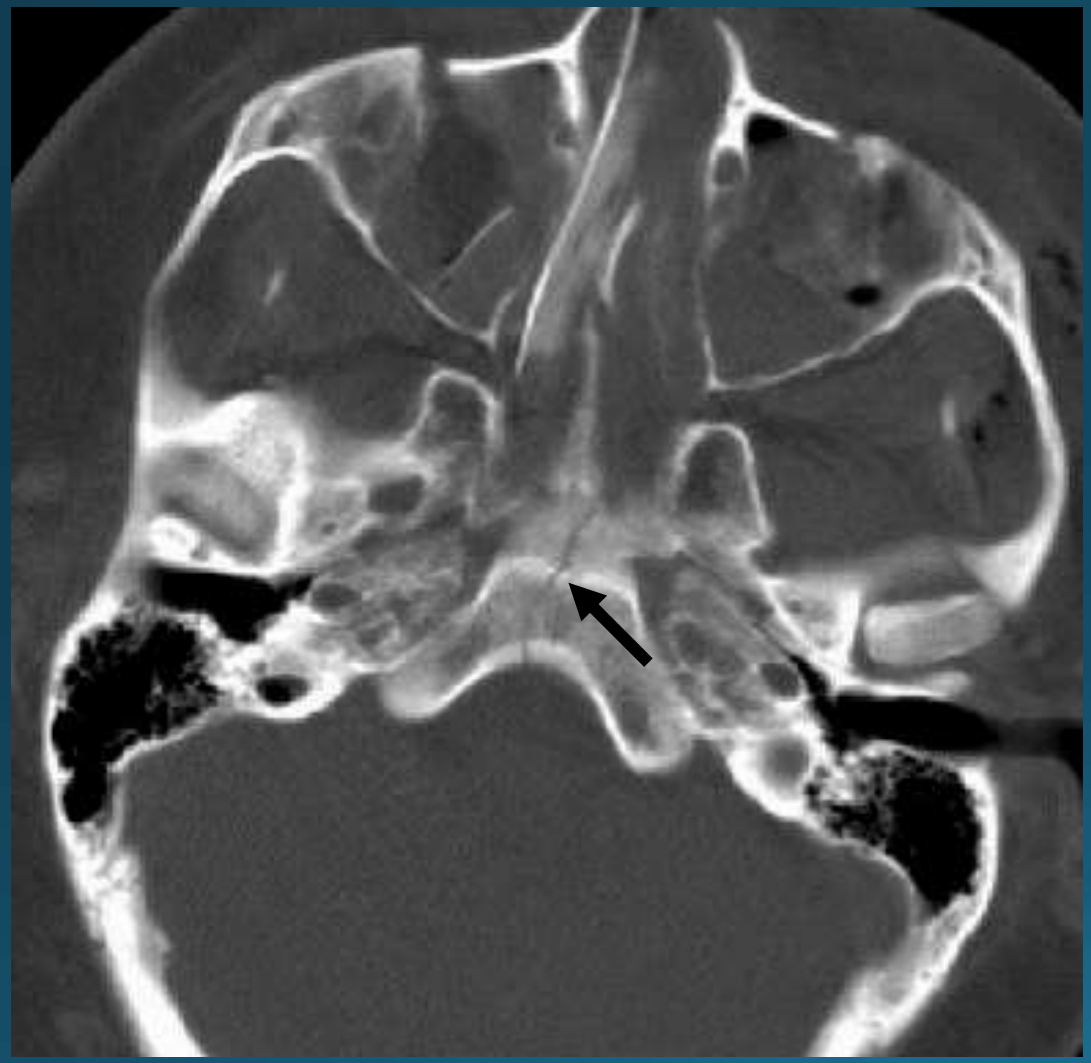



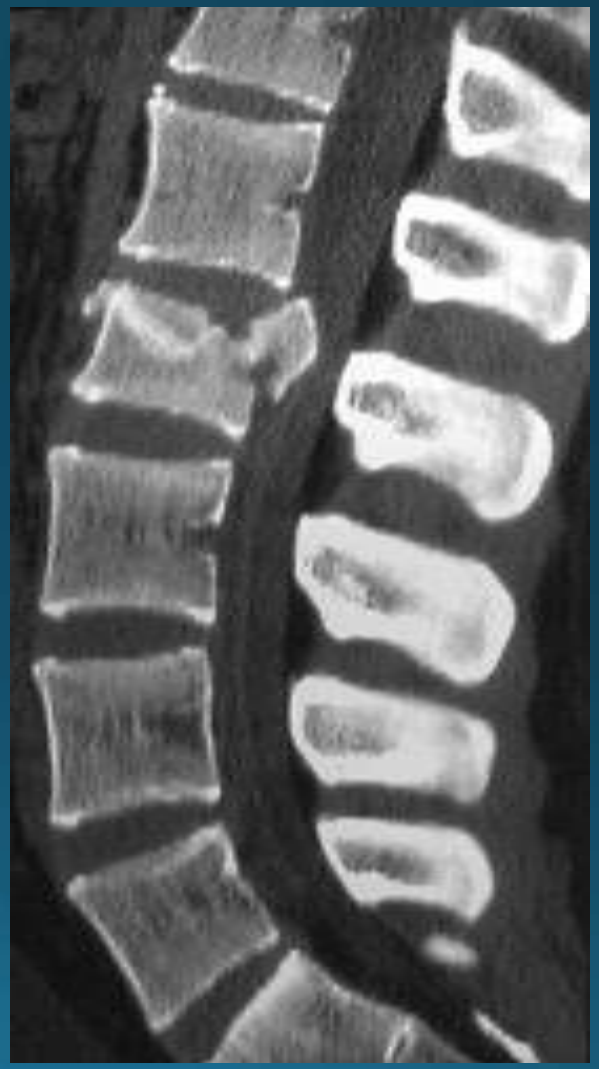
# Same 7 y o




Midbrain – Tectal glioma – low grade

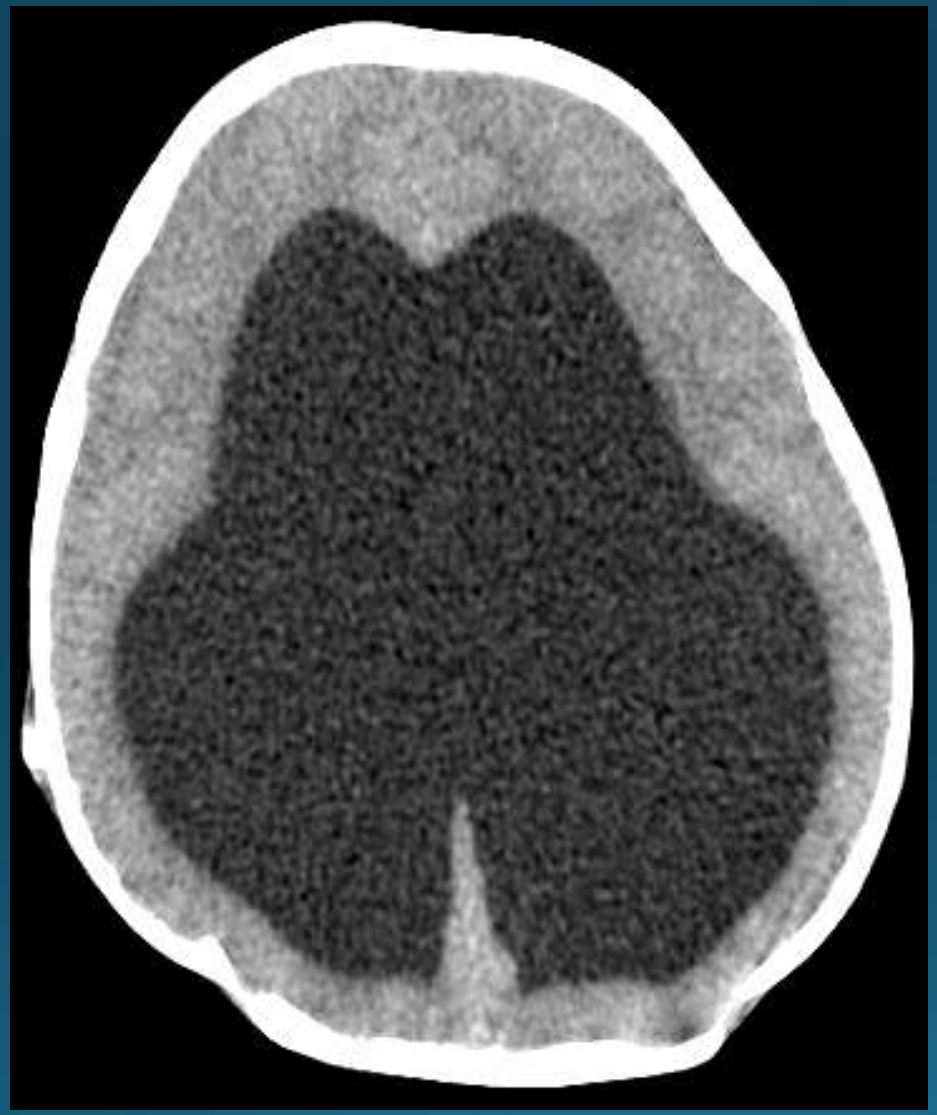
# Fractures: Skull and skull base, vertebrae: CT not MRI!





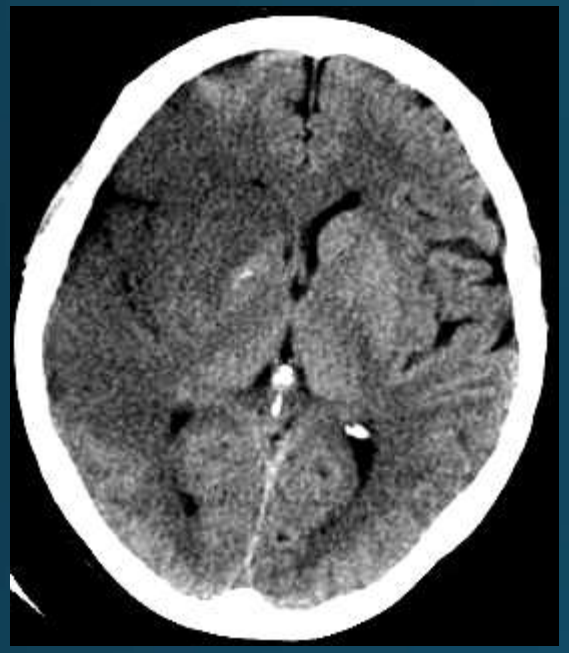
Fractures

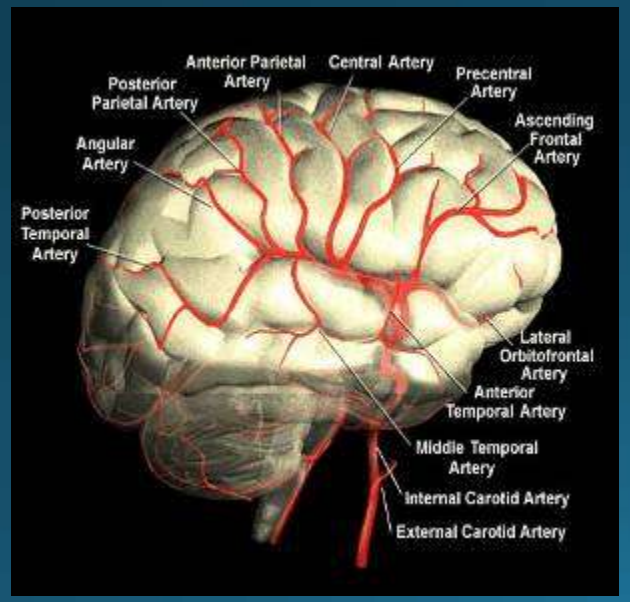
# Ventricles

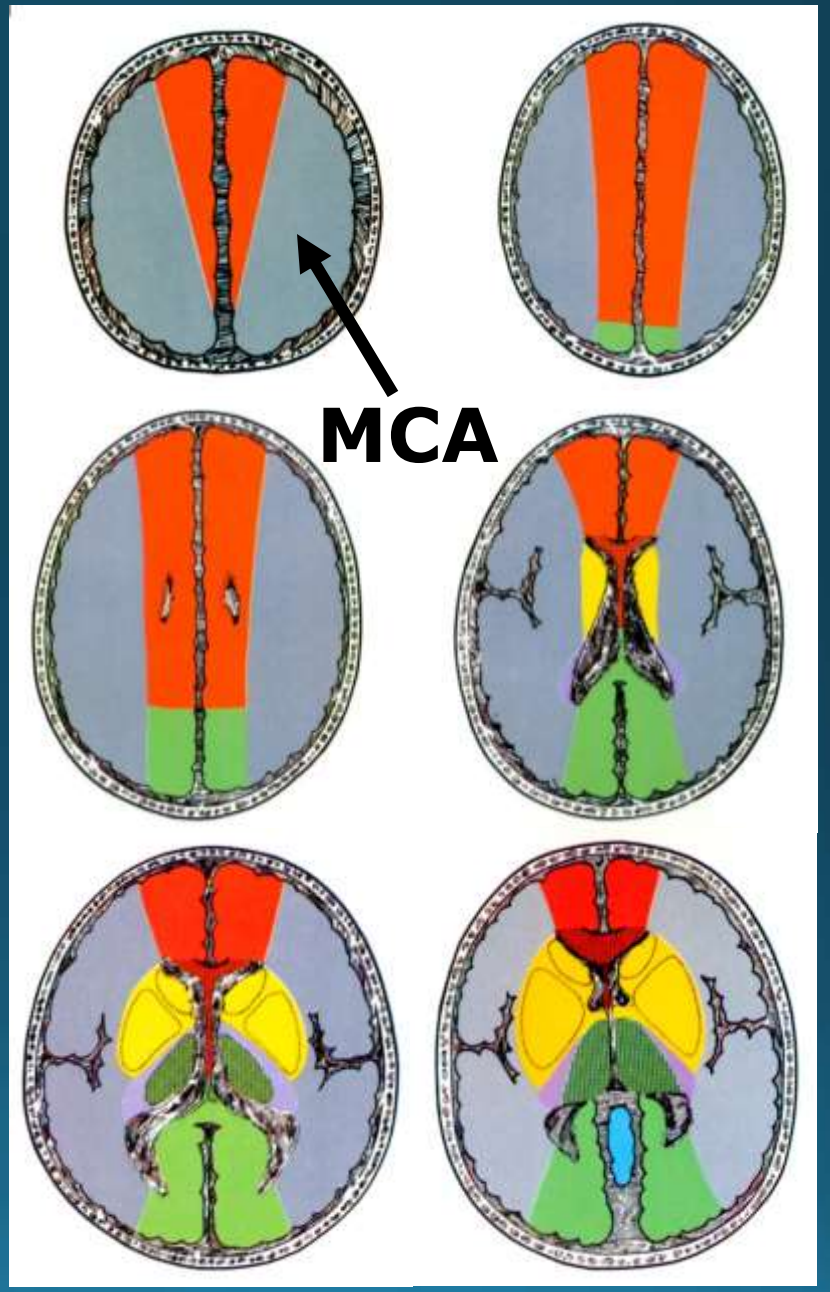


Hydrocephalus

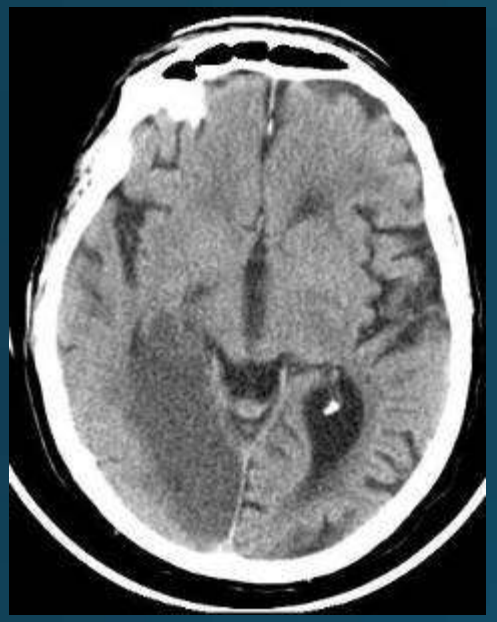
# MCA Infarct

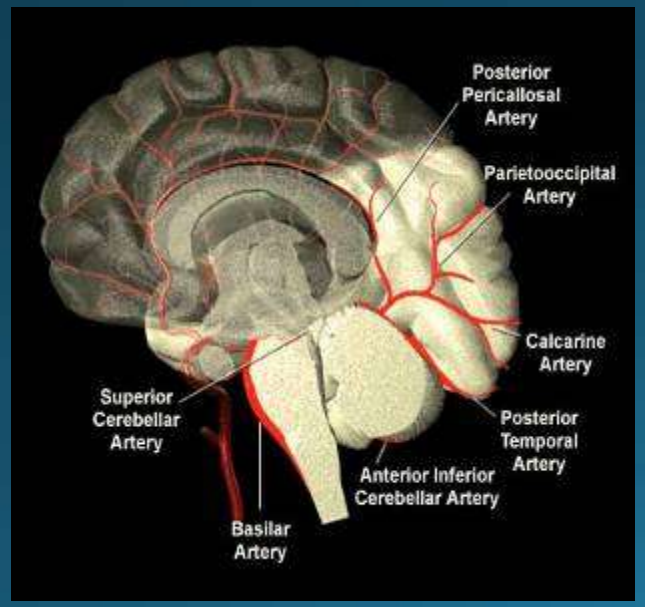


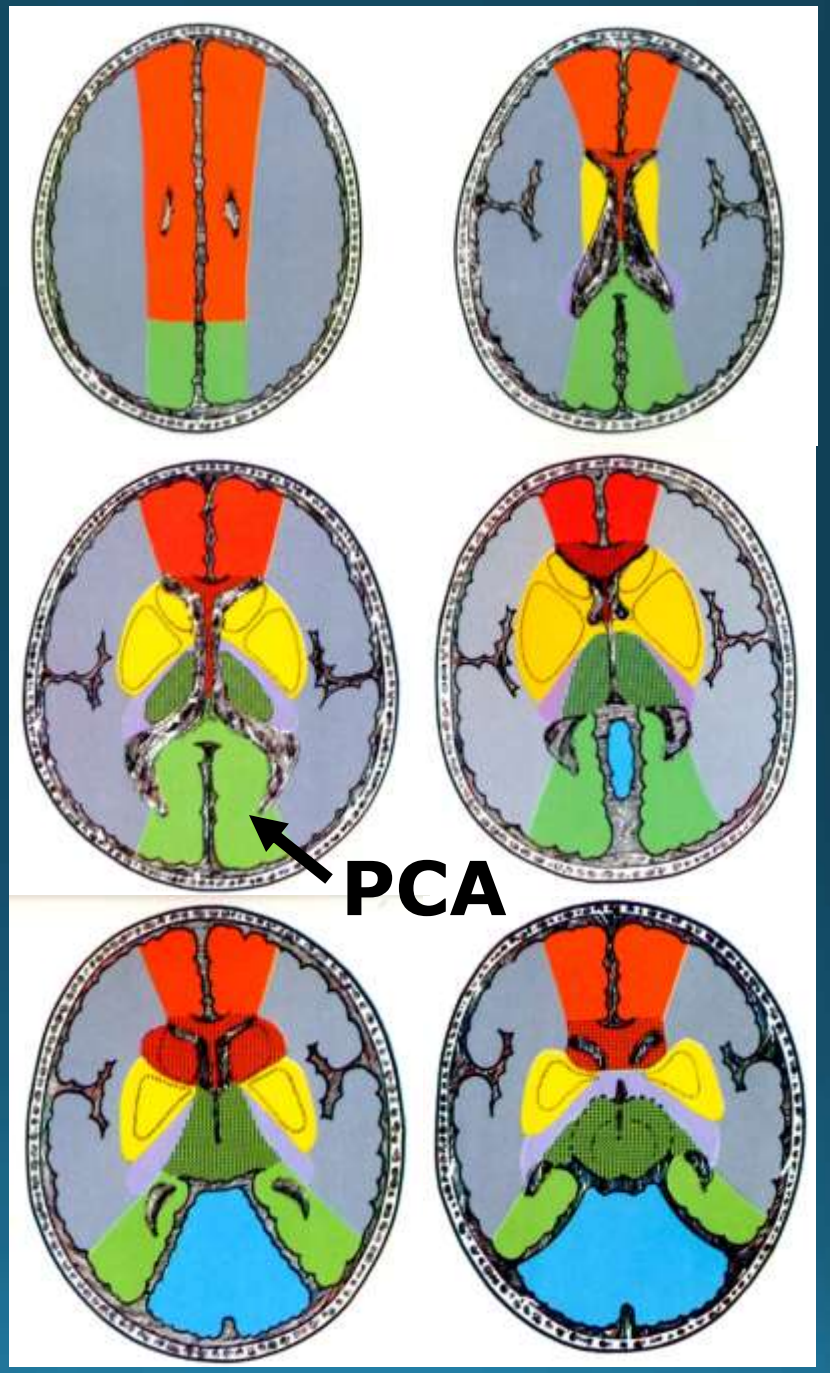

Anterior Parietal Artery
Central Artery
Precentral Artery
Posterior Parietal Artery
Ascending Frontal Artery
Angular Artery
Posterior Temporal Artery
Lateral Orbitofrontal Artery
Anterior Temporal Artery
Middle Temporal Artery
Internal Carotid Artery
External Carotid Artery


MCA

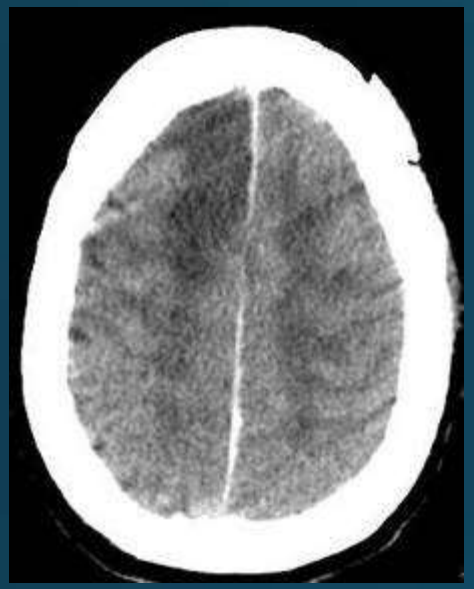
# PCA Infarct

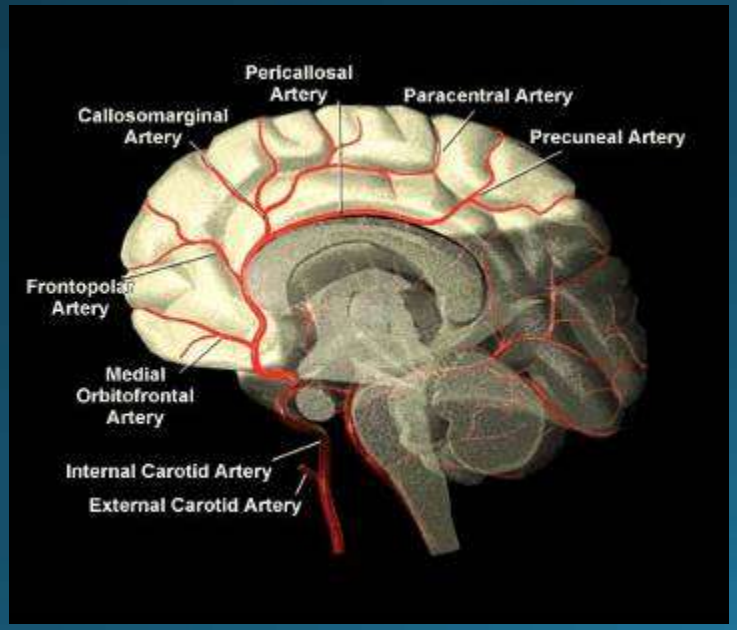


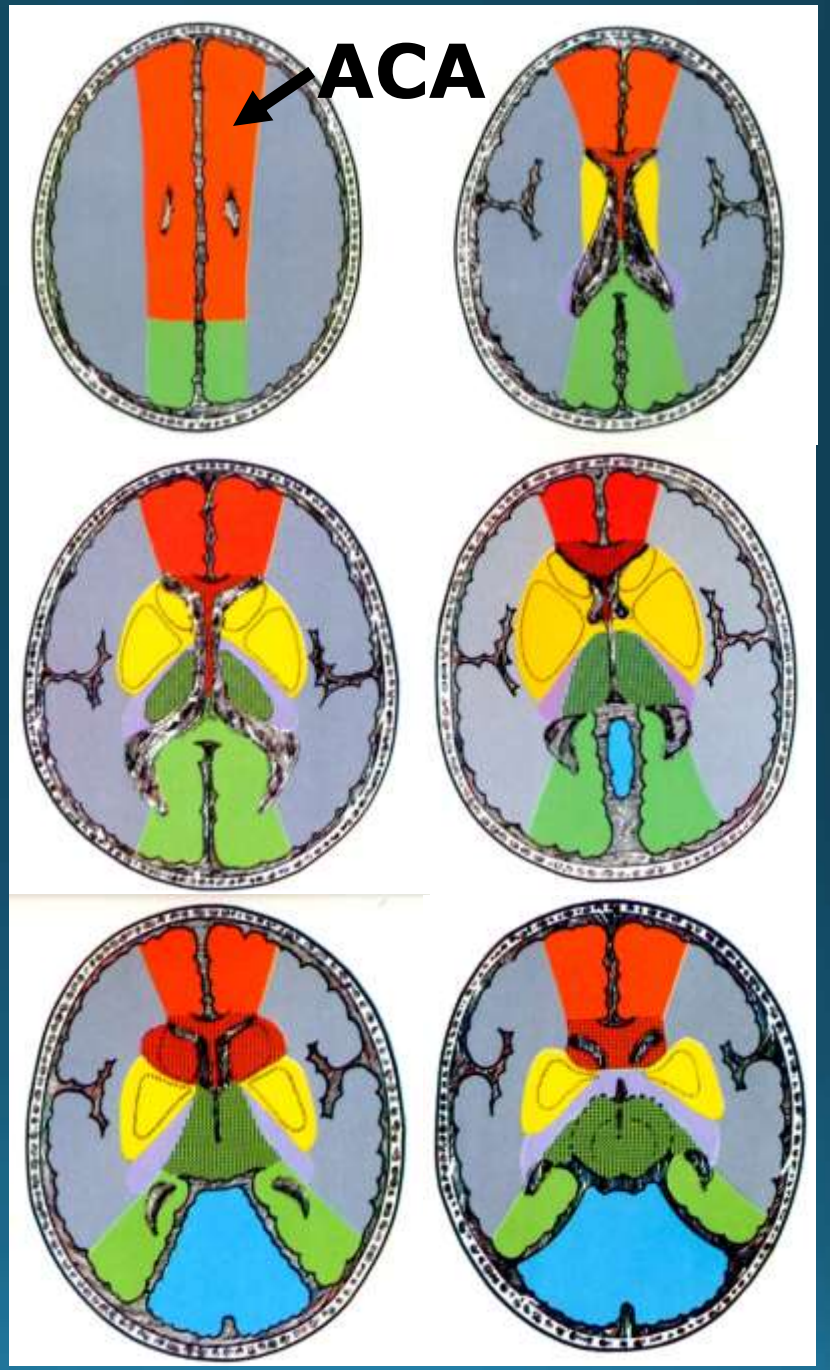

Posterior Pericallosal Artery
Parietooccipital Artery
Calcarine Artery
Posterior Temporal Artery
Anterior Inferior Cerebellar Artery
Superior Cerebellar Artery
Basilar Artery


PCA

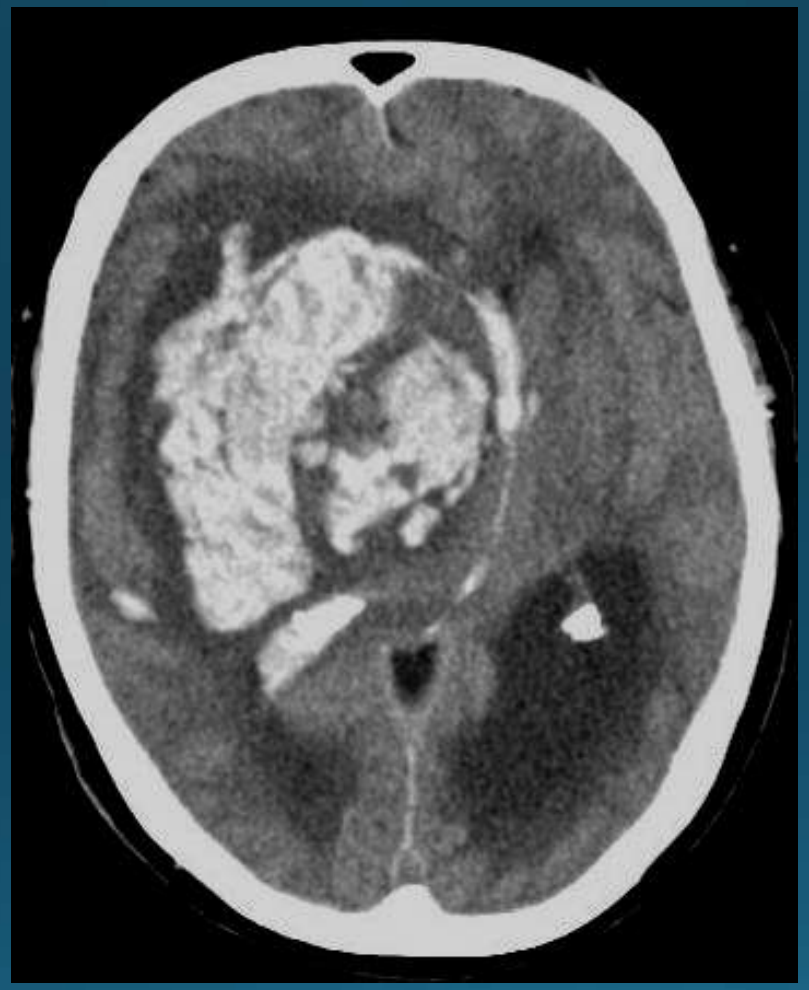
# ACA Infarct




Pericallosal Artery
Paracentral Artery
Callosomarginal Artery
Precuneal Artery
Frontopolar Artery
Medial Orbitofrontal Artery
Internal Carotid Artery
External Carotid Artery

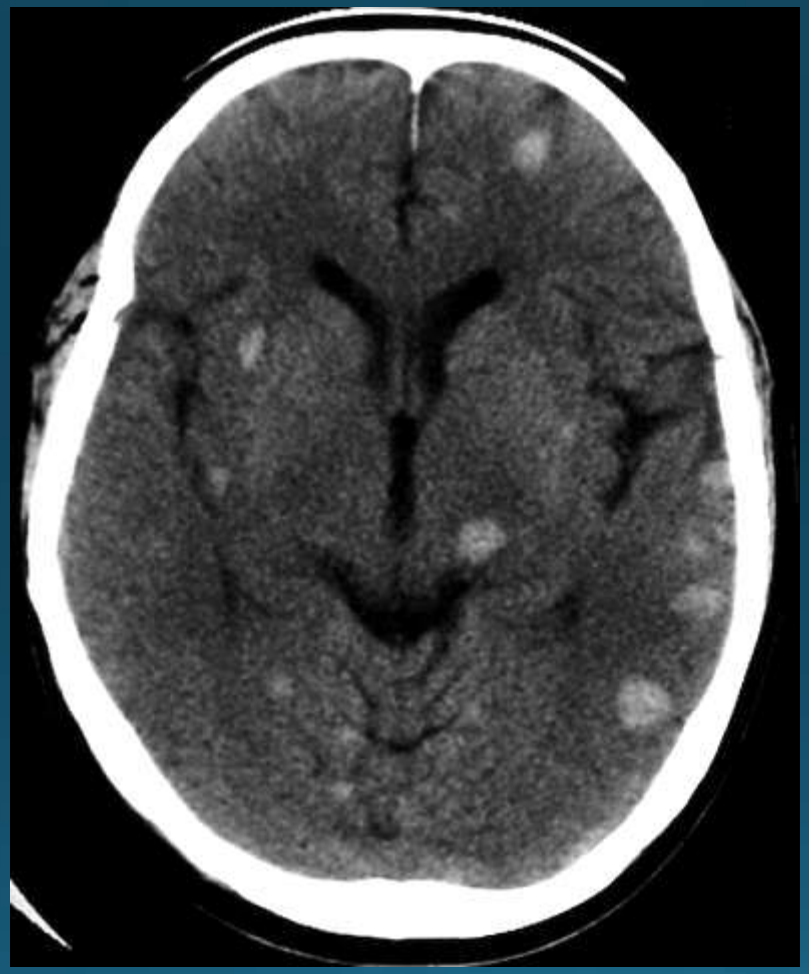

ACA

# Cerebral Hemorrhage



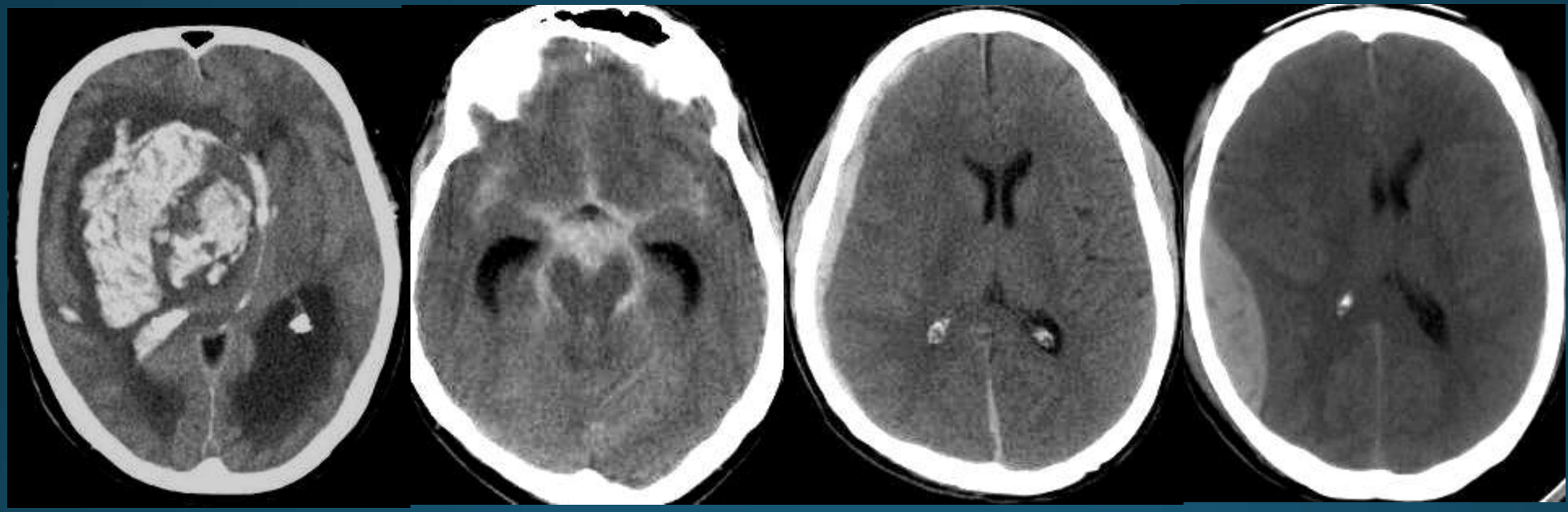
Acute intraparenchymal hematoma

# Cerebral Hemorrhage



Hemorrhagic melanoma metastases

# Acute Hemorrhage



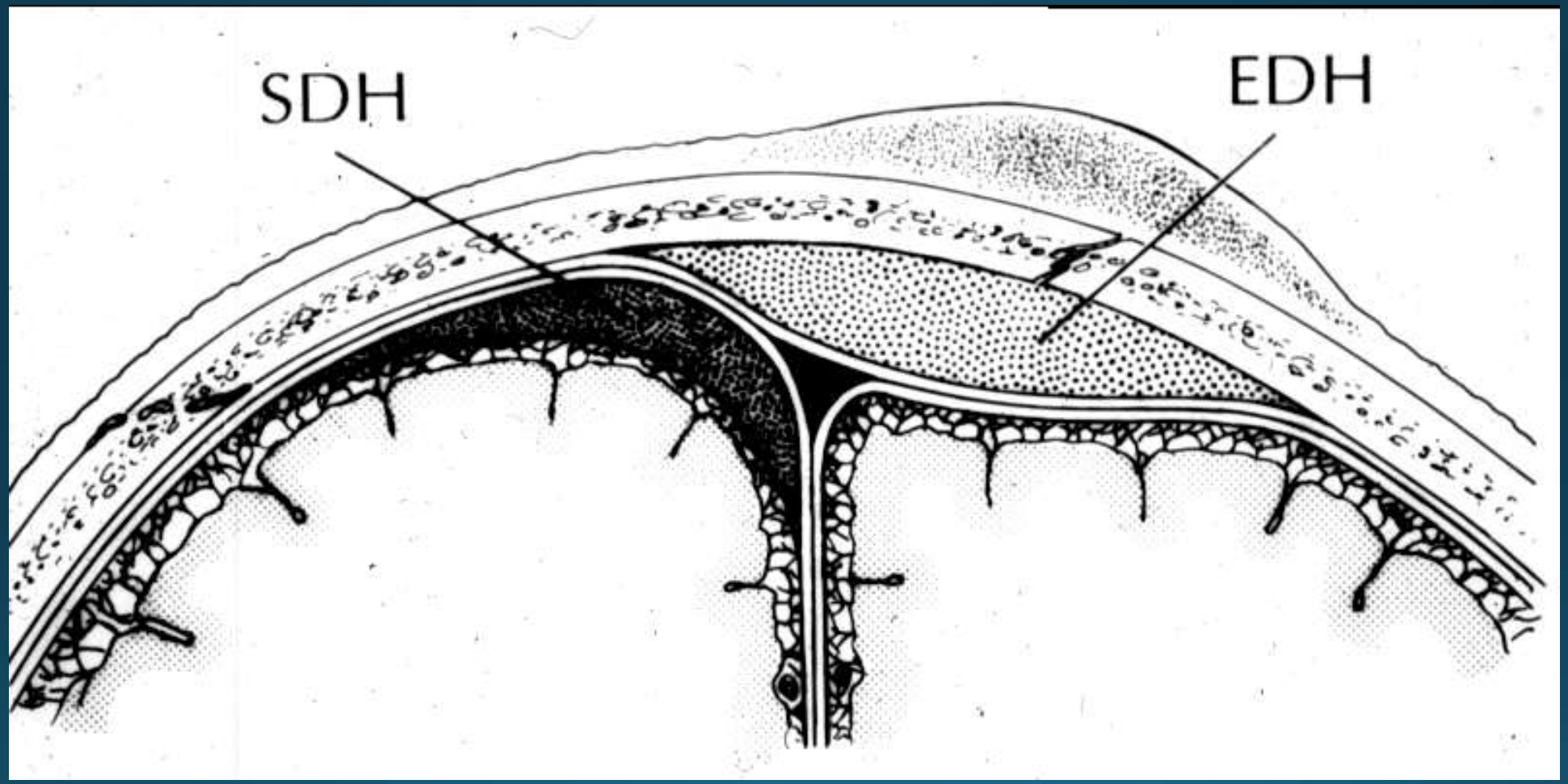
Intraparenchymal (intracerebral)

Subarachnoid

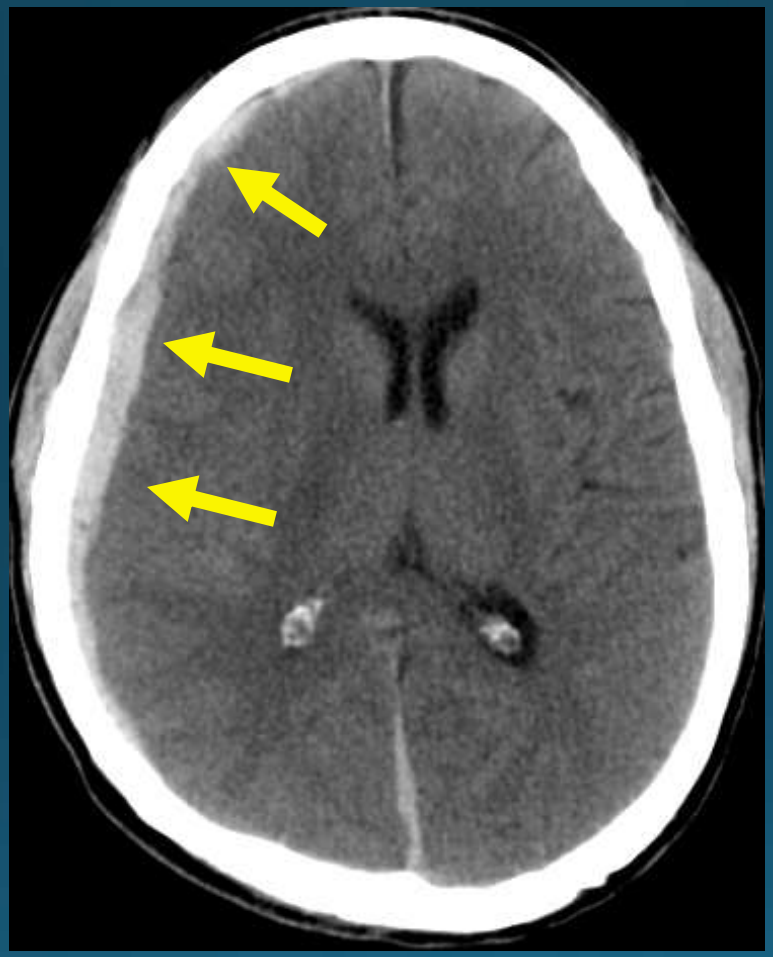
Subdural

Epidural

# Subdural vs. Epidural Hematoma

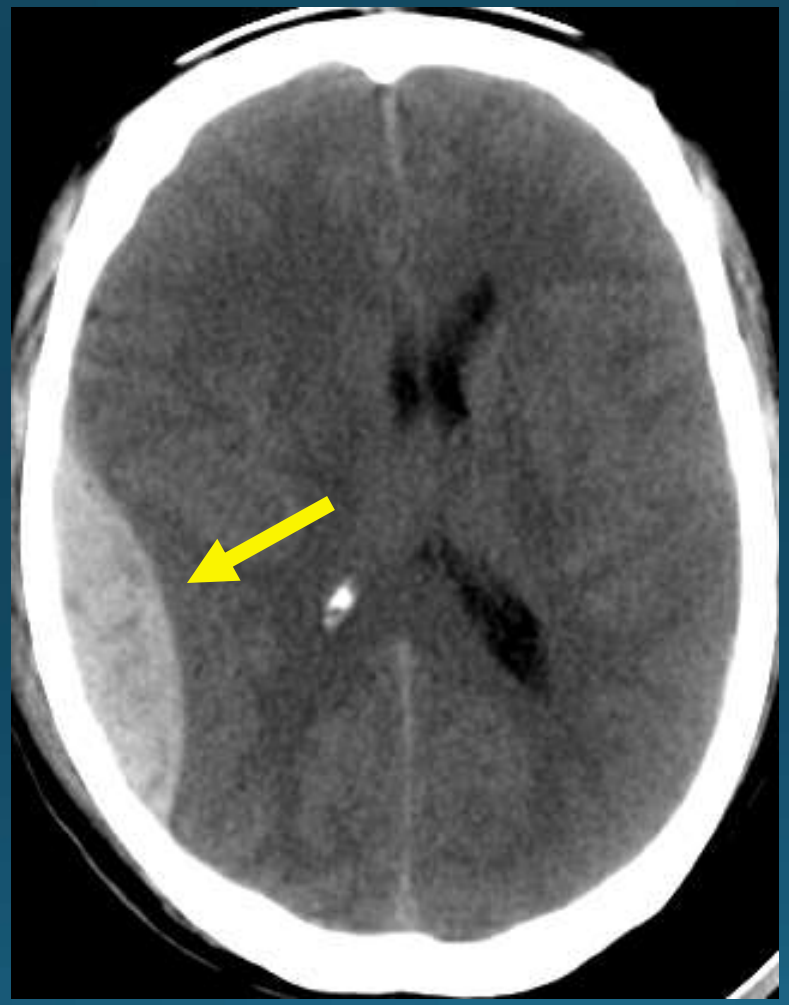


# Cerebral Hemorrhage



Acute subdural hematoma

# Cerebral Hemorrhage

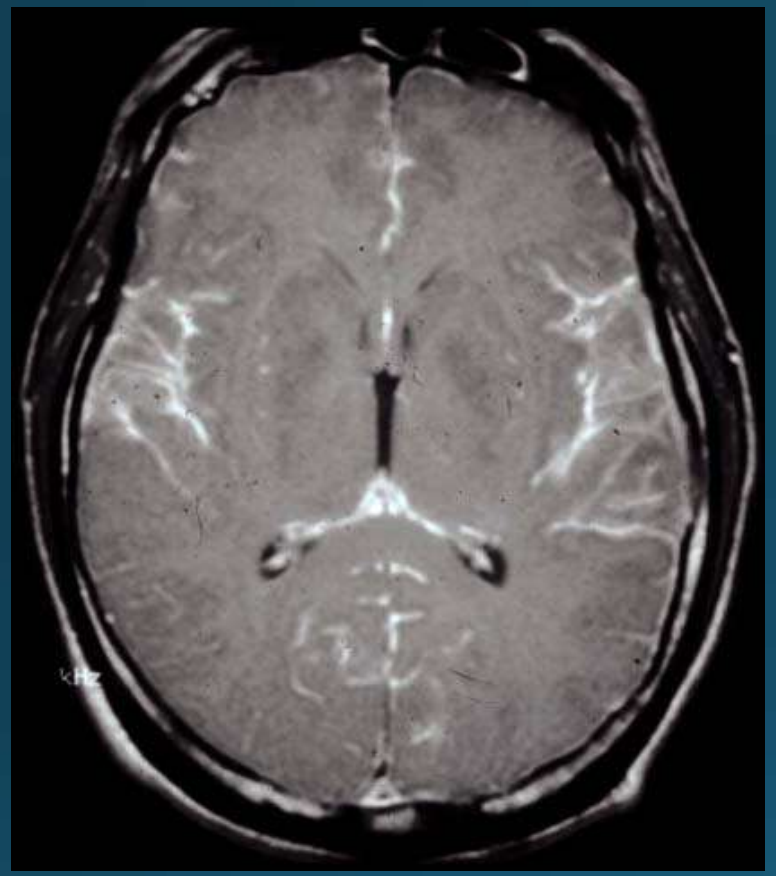


Acute epidural hematoma

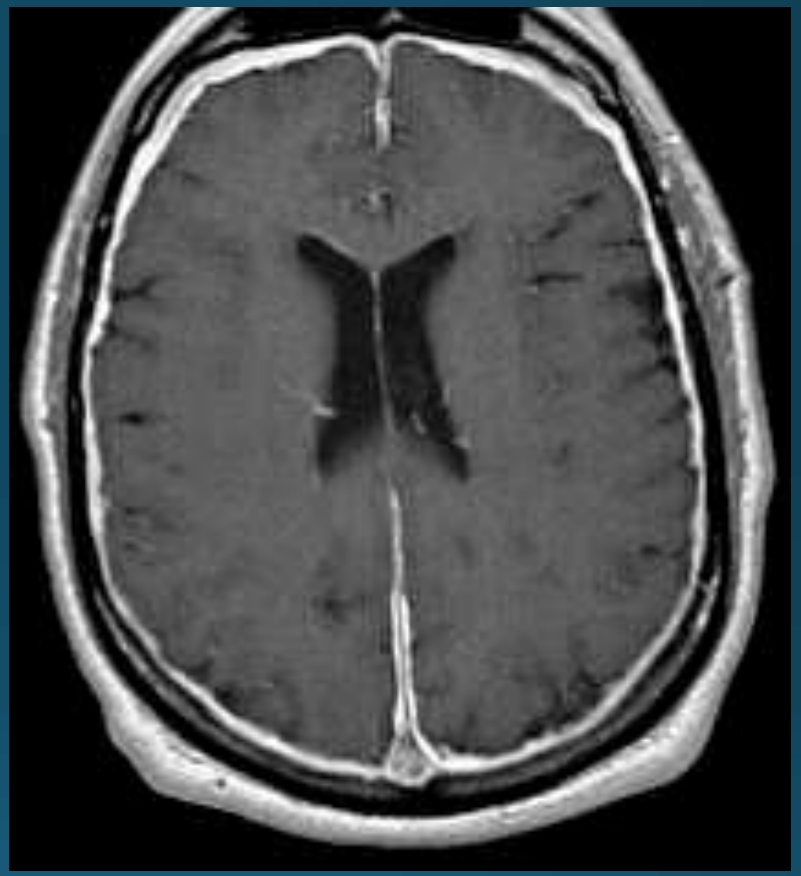
# Infections

- Meningitis
- Encephalitis
- Cerebritis and parenchymal abscess

# Meningitis



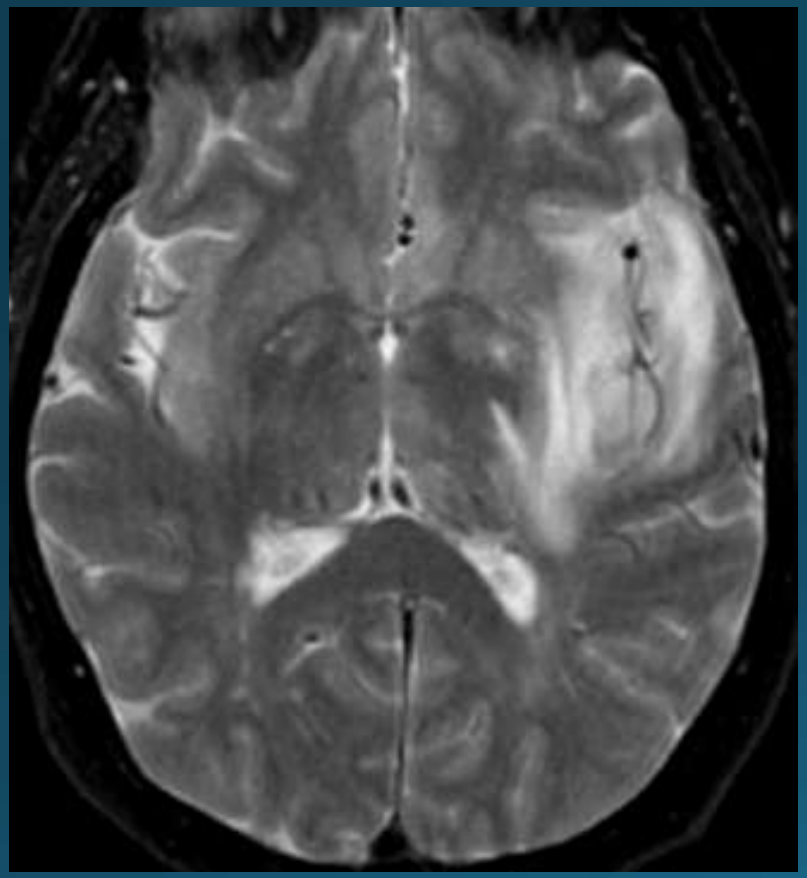
**Leptomeningitis: pia-arachnoid**

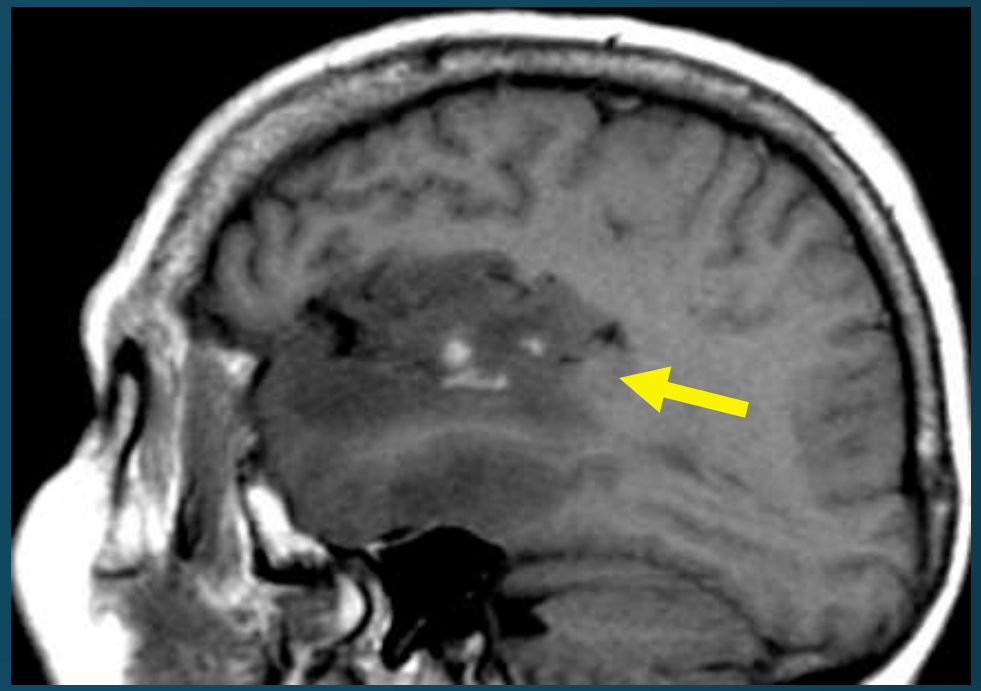


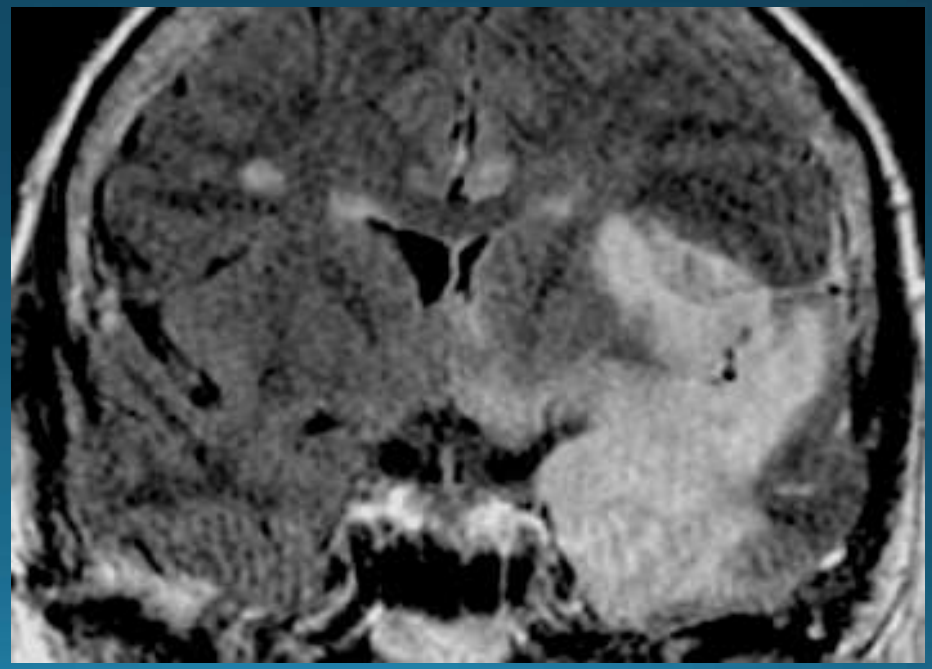
**Pachymeningitis: dura**

**Most common imaging findings in meningitis: NONE !!**

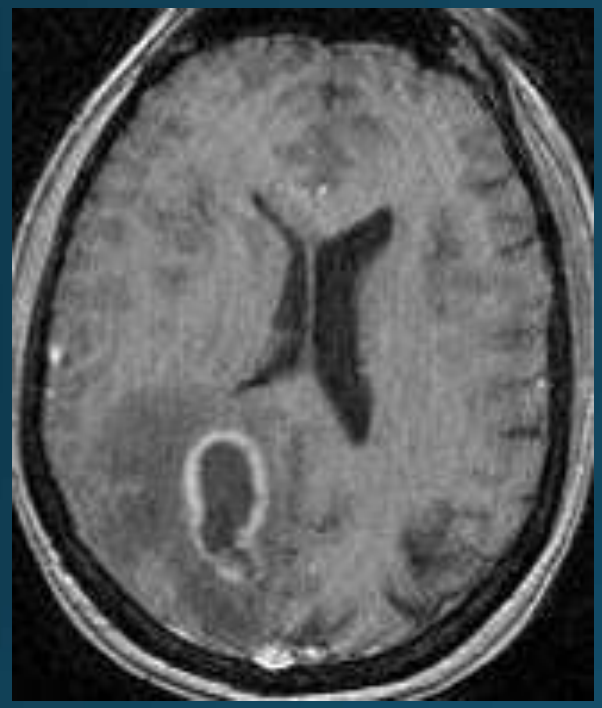
# Herpes Encephalitis

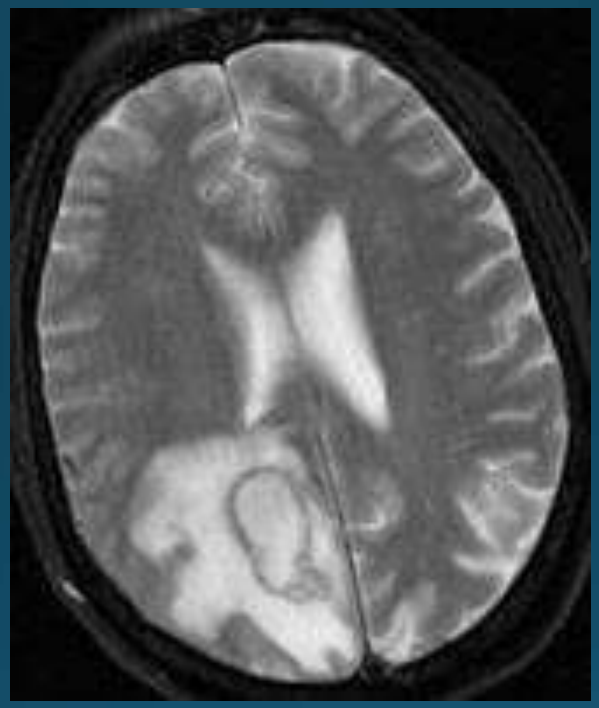


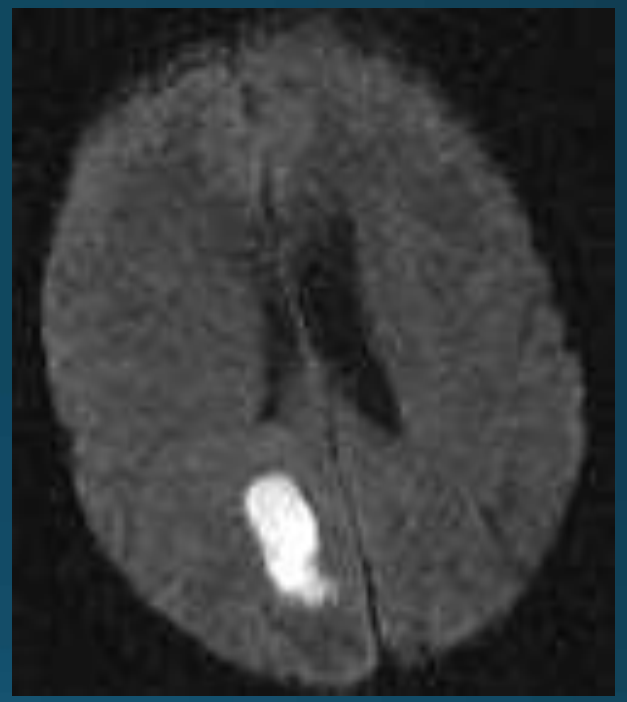




# Cerebritis w/ Bacterial Abscess



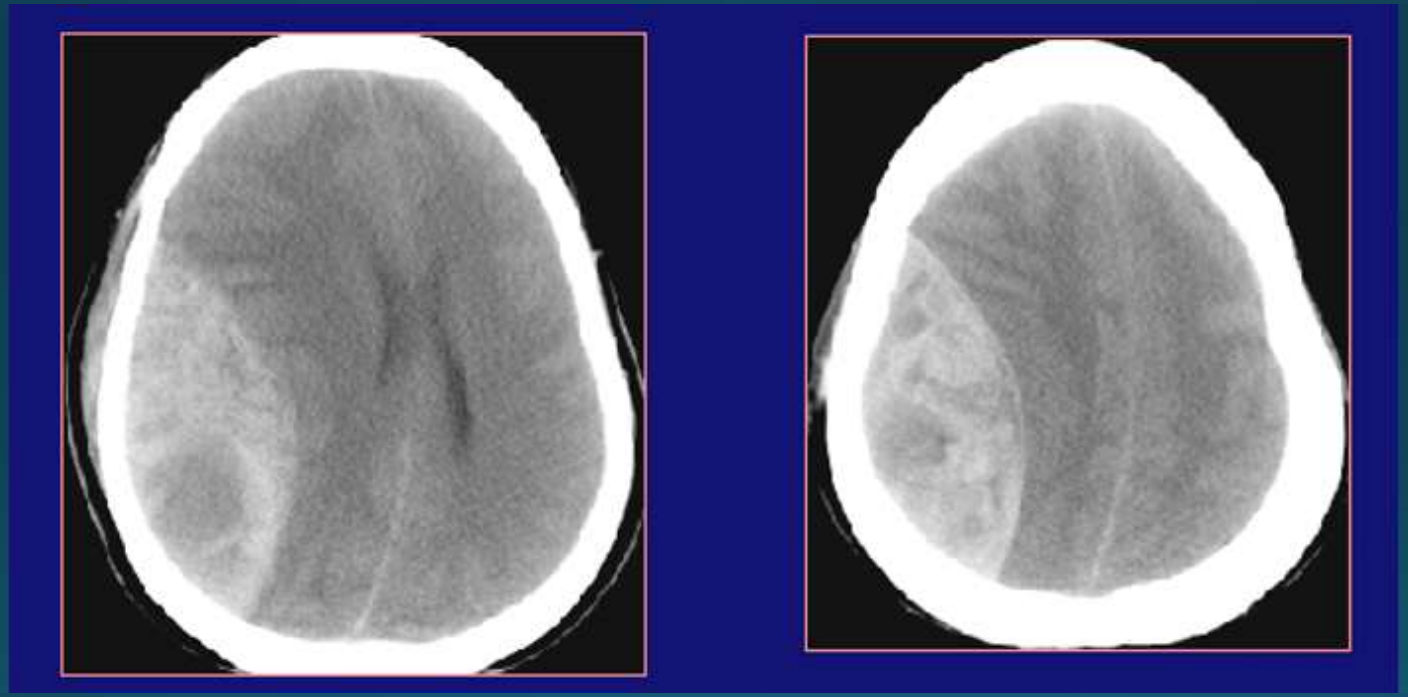




**T1 + Gd** **T2** **Diffusion**

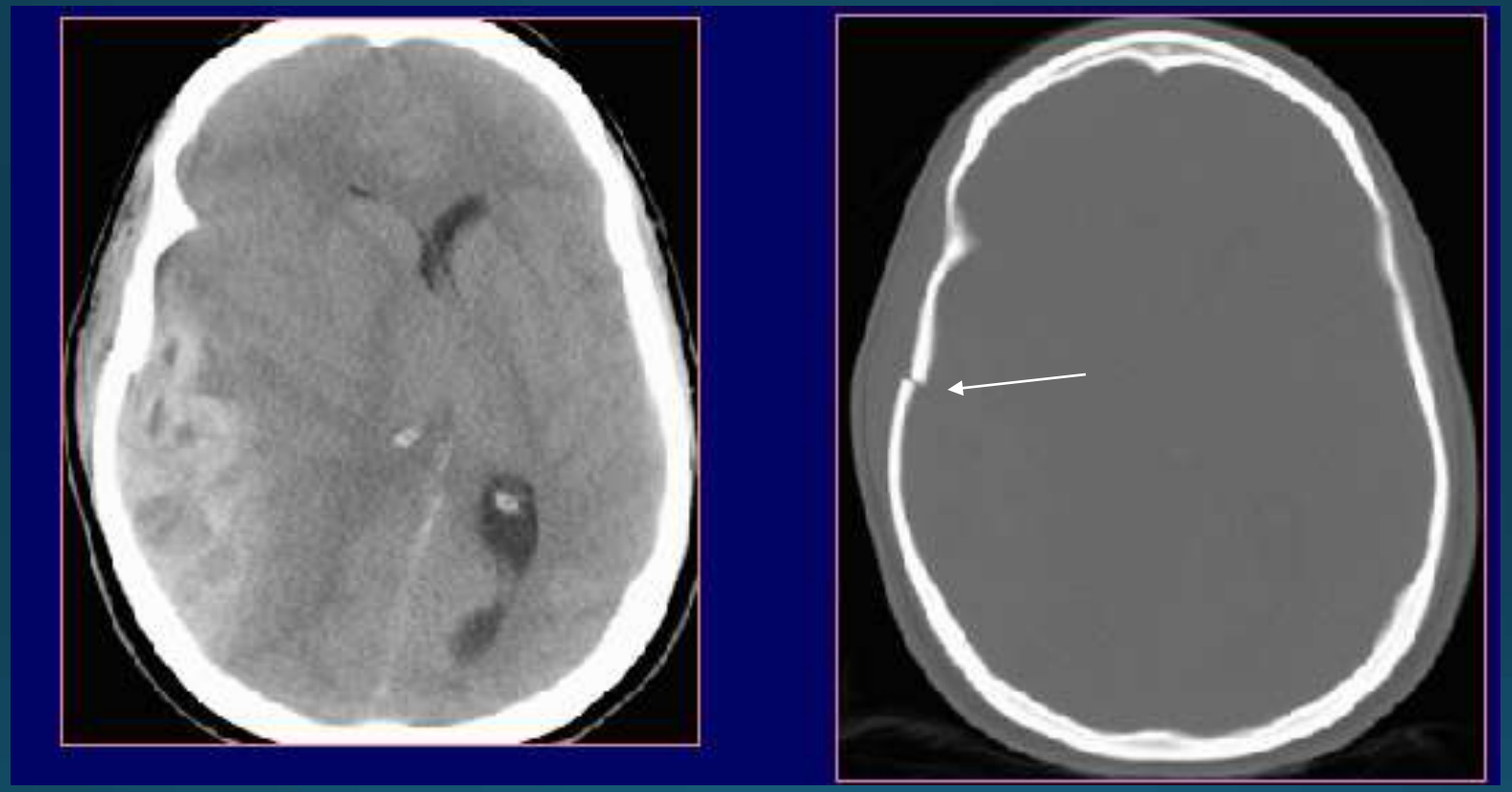
Brain inflammation that leads to abscess

# 28 y.o. woman found comatose following MVA



Scans show a lentiform hyperdense extra-axial collection of fluid pressing on the right cerebral hemisphere (your left, the patient's right), diagnostic of an epidural hematoma.

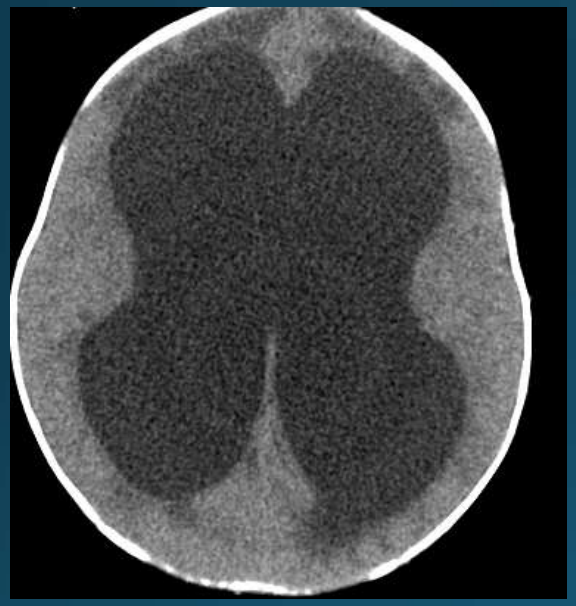
There is significant mass effect on the lateral ventricles and midline shift.

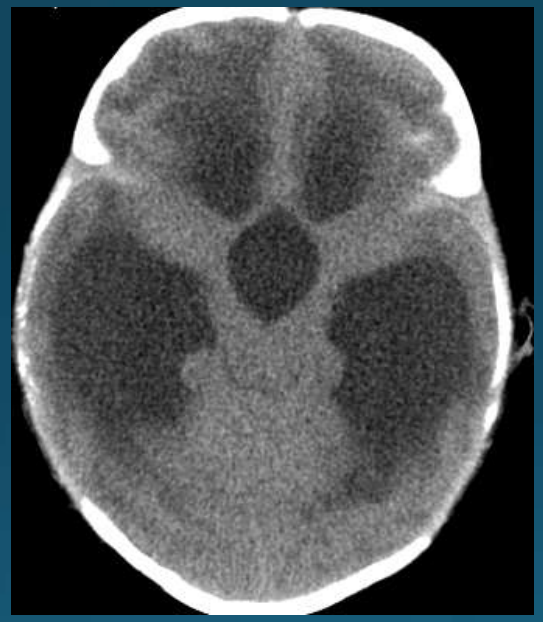


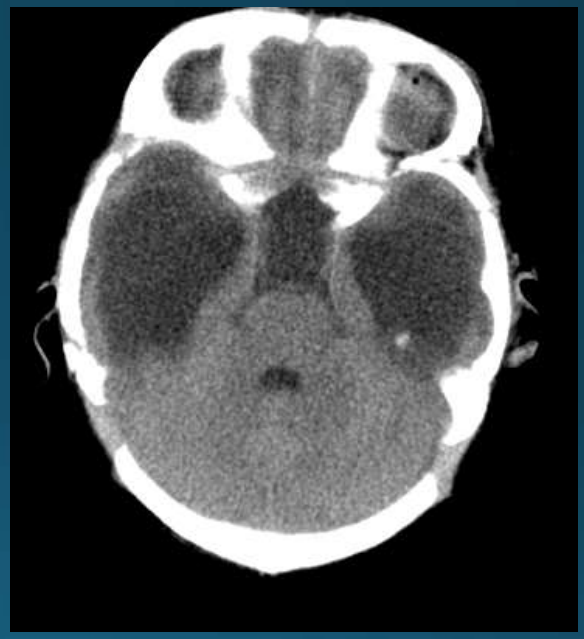
Mass effect

fracture (arrow)

# Baby with big skull: Diagnosis?

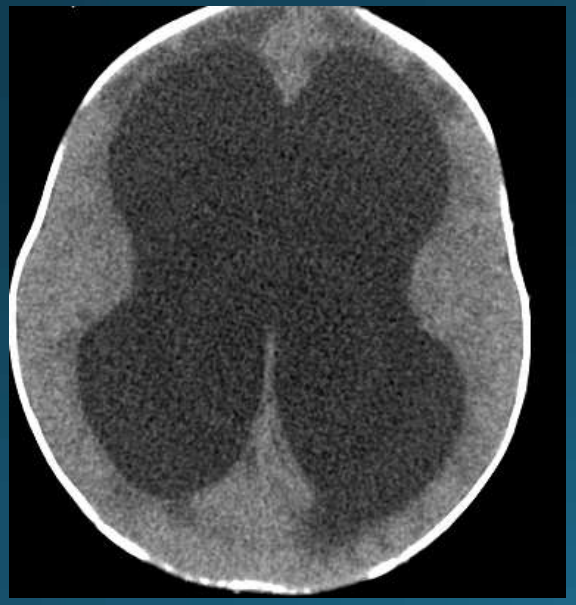


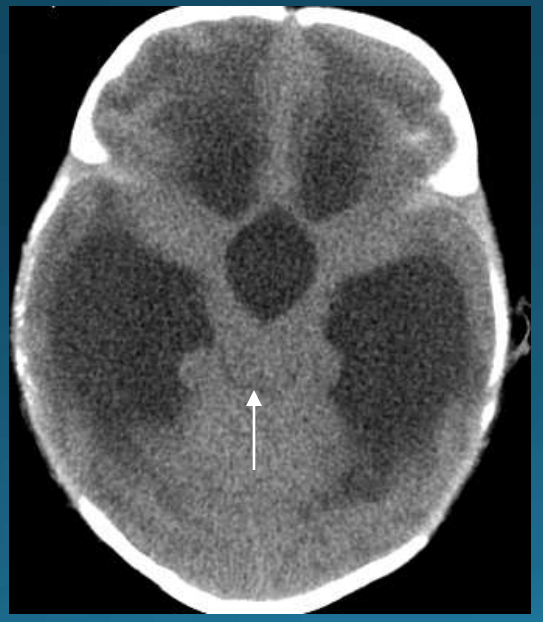


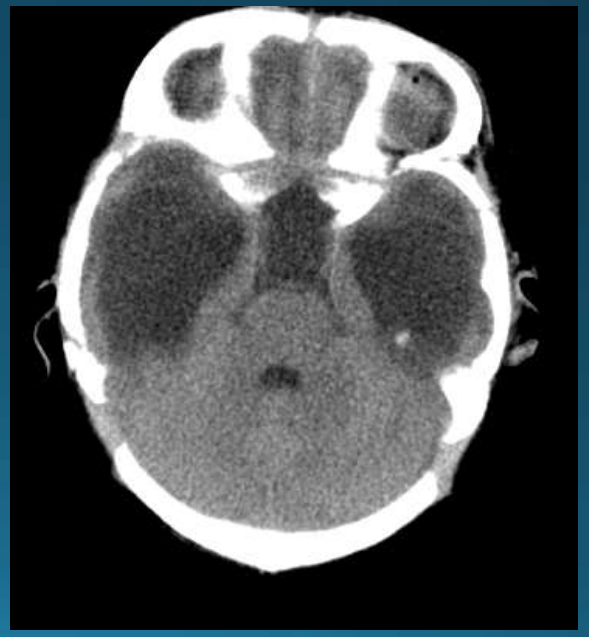


The ventricles are too big = Hydrocephalus.

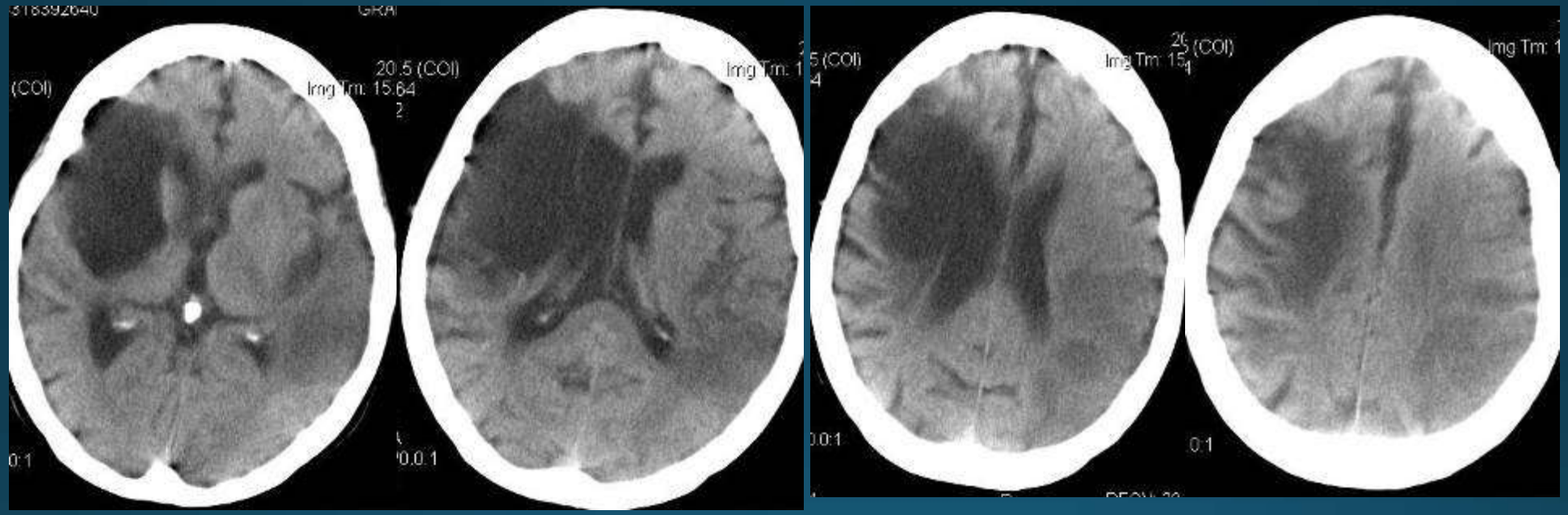
Notice – the aqueduct of Sylvius is missing (arrow).
Diagnosis: Congenital aqueductal stenosis.





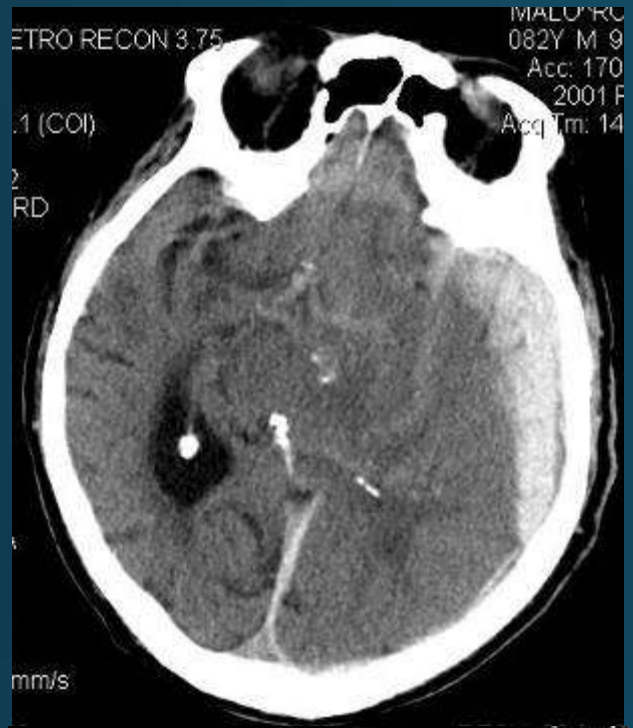


# Chronic Ischemic change = Encephalomalacia



# Case 1

- 82 yo male with mental status change after a fall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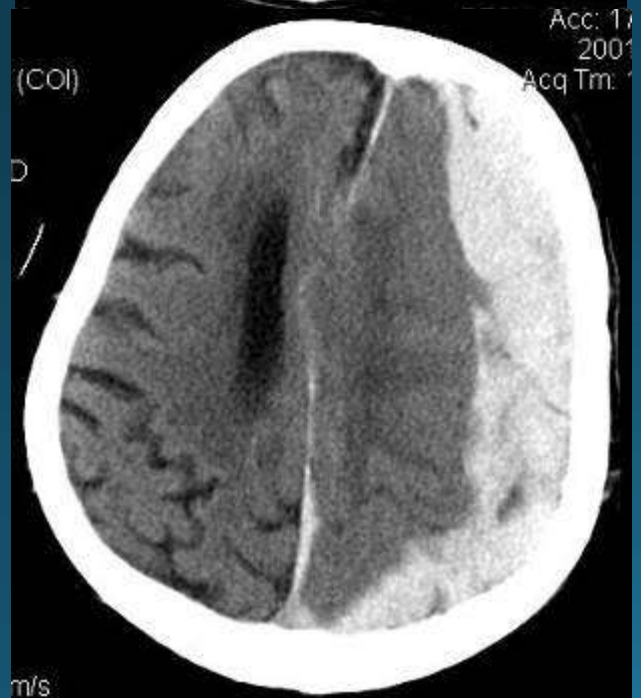
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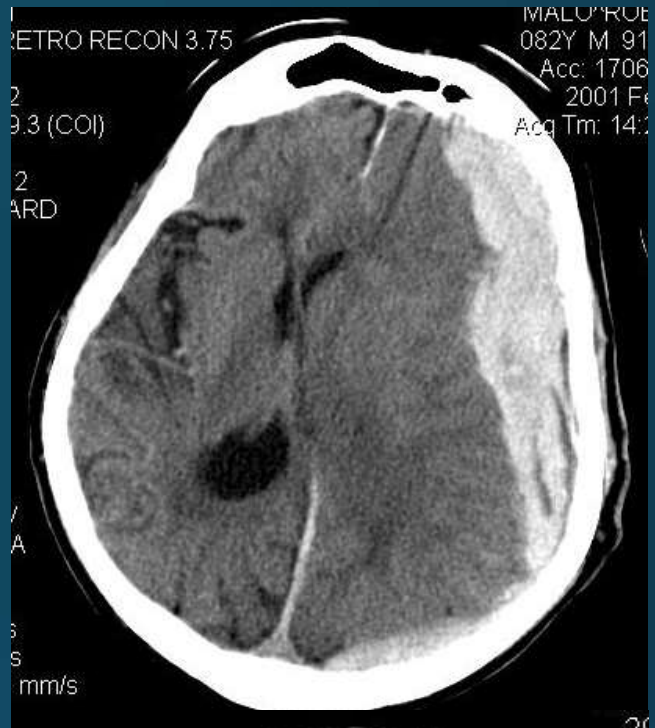
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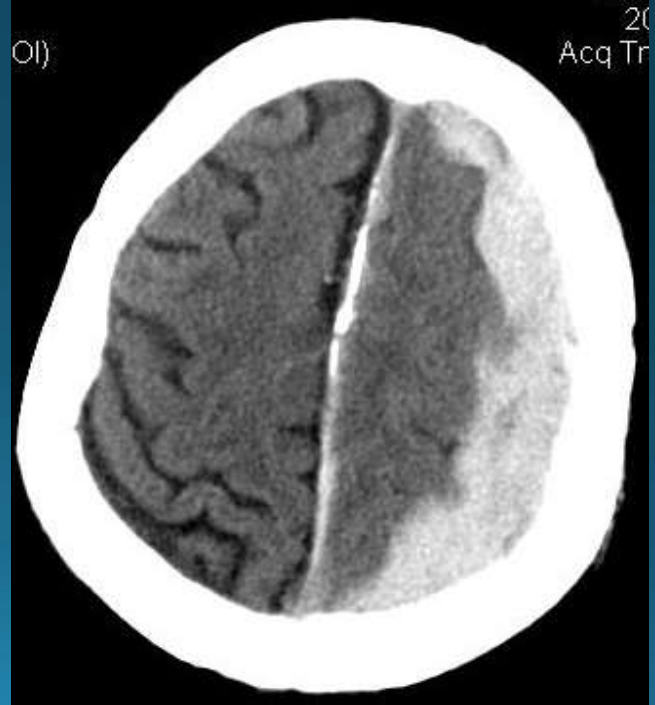
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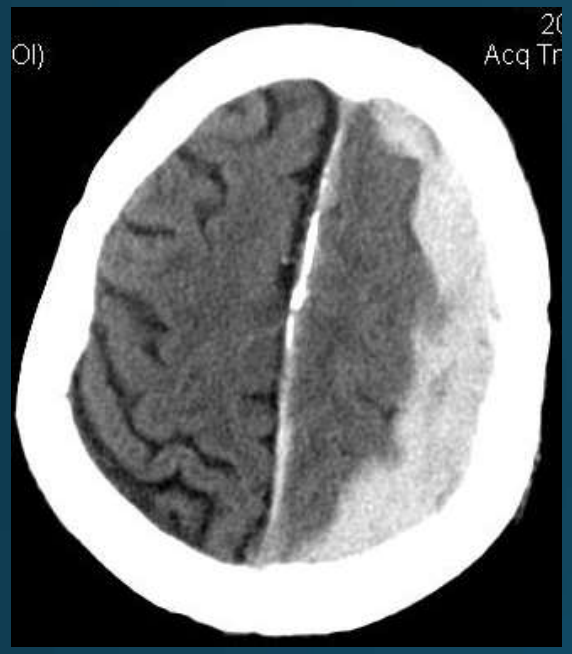
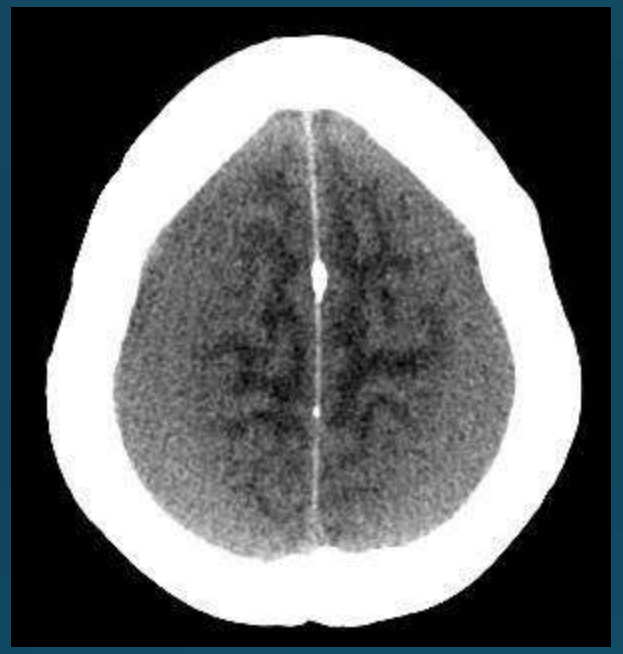
# Case 1

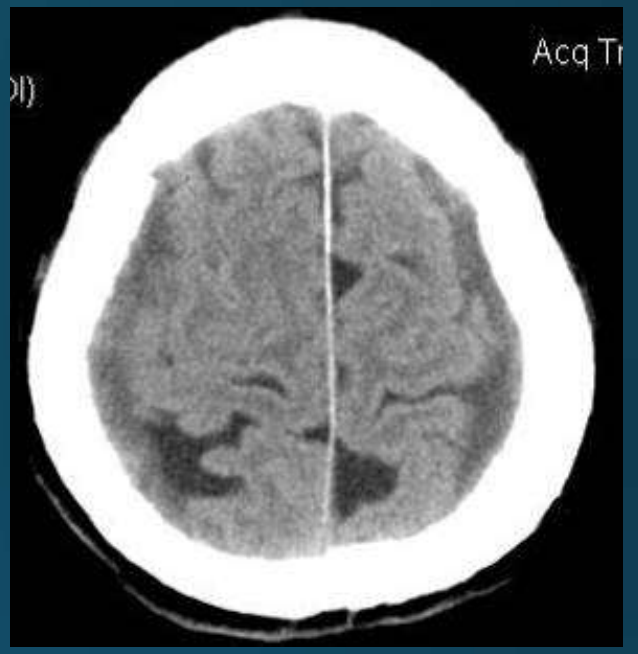
- Subdural hematoma
- Venous bleeding from bridging veins

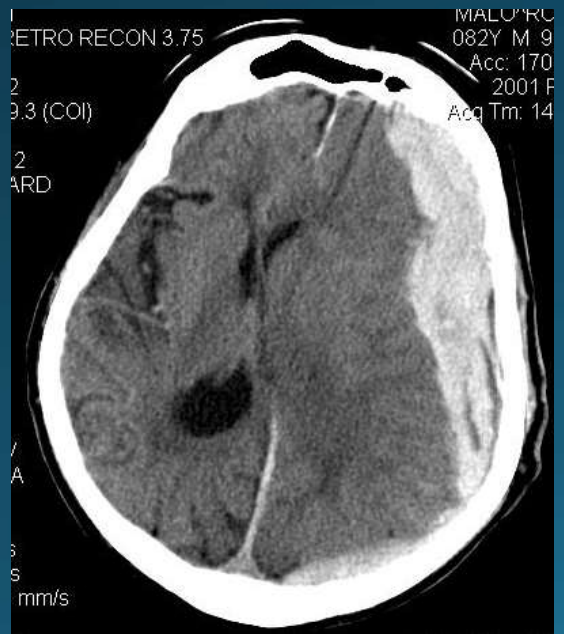
- General presentation
  - Older age group
  - Mental status change after fall
  - 50% have no trauma history

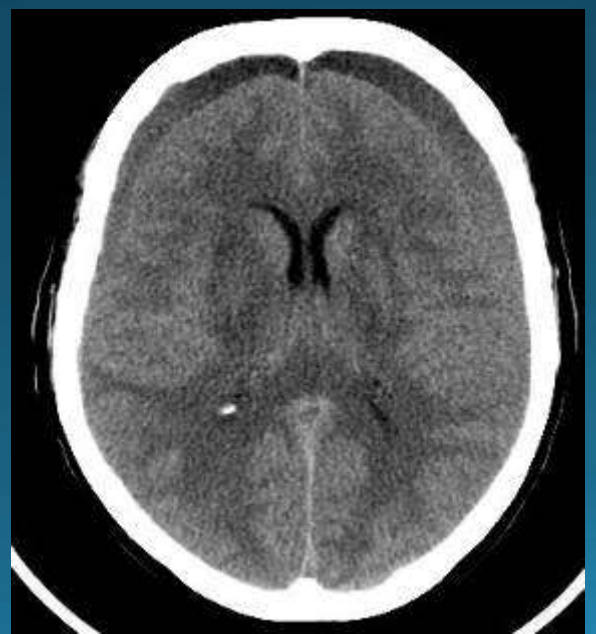
# Another Subdural Hematoma

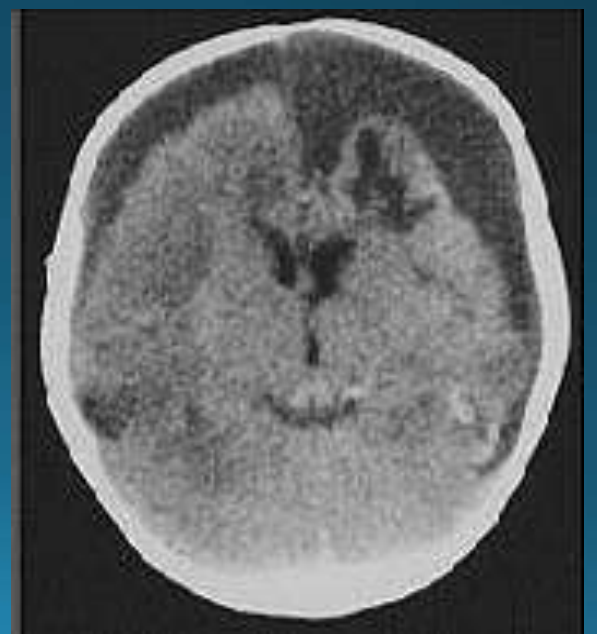






# Subdural Hemorrhages

Usually secondary to trauma

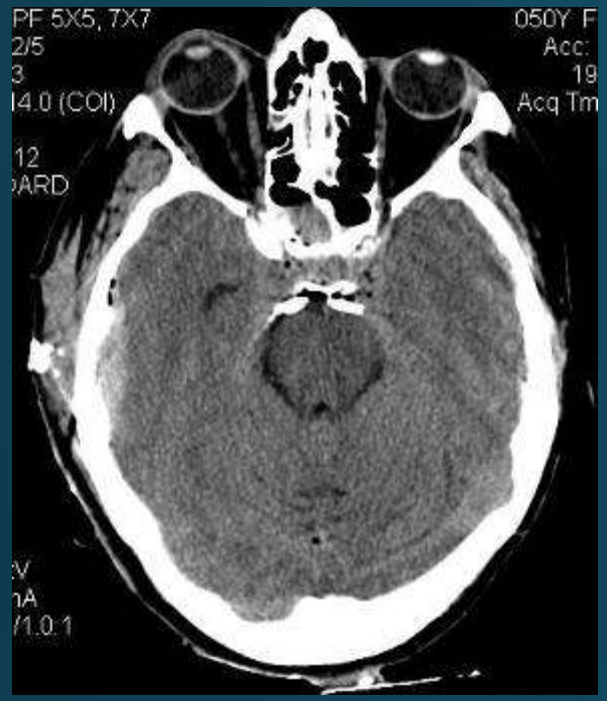
In young patient this is usually secondary to an MVA

Results from shearing of bridging veins

In the elderly it is most common secondary to a fall (40% of all TBIs)

# Case 2

- 50 yo male post head trauma.
- Pt was initially conscious but now 3 hours post trauma has had a sudden decrease in his neurological function.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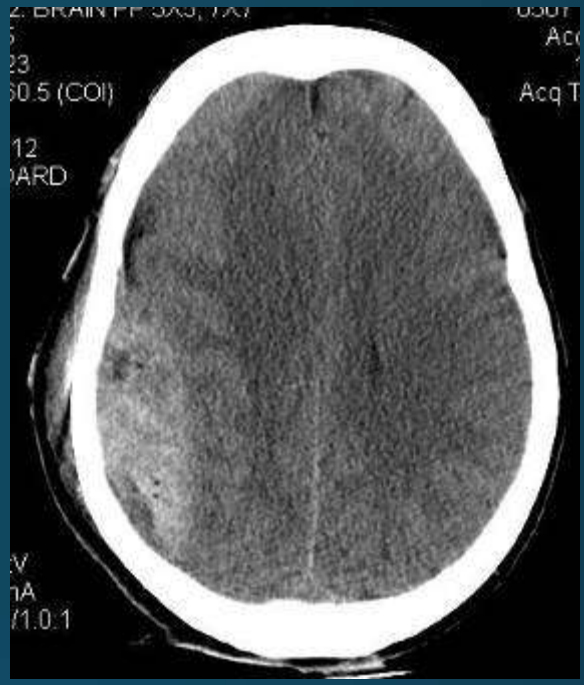
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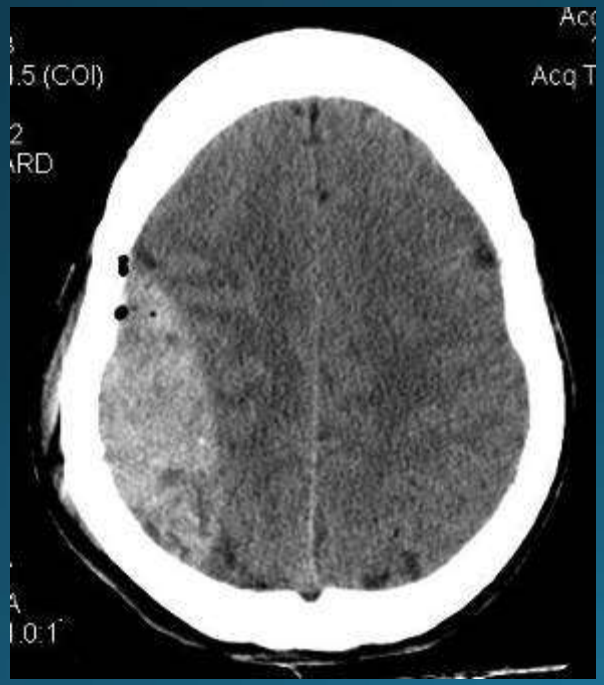
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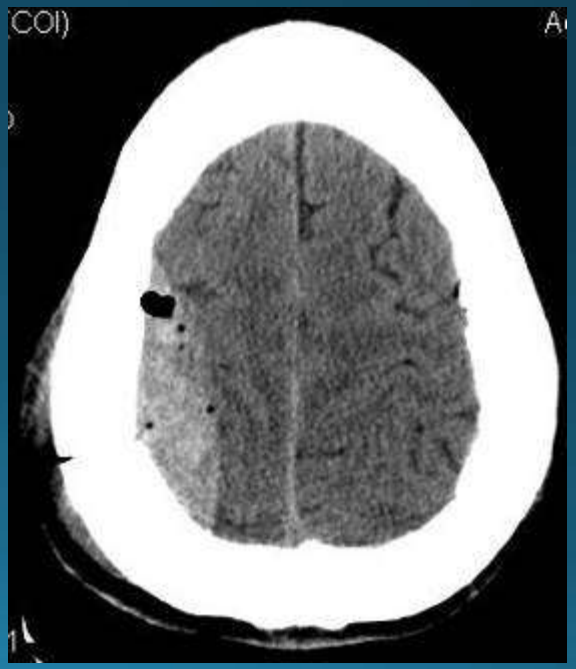

(COI)

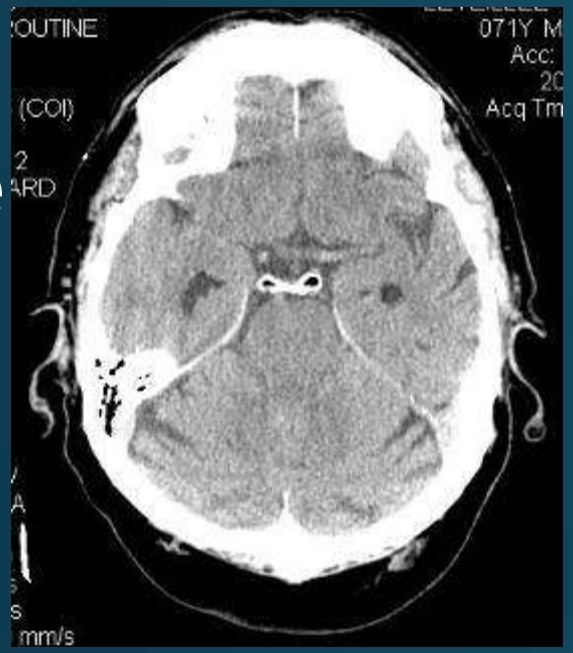
# Case 2

- **Epidural hematoma**
  - Typical history is a patient with TBI who has a period of lucidity after trauma but then deteriorates rapidly.
  - Hemorrhage is a result of a tear through a meningeal artery.

# Case 3

- 71 yo male who initially complained of incoordination of his left hand and subsequently collapsed

# Case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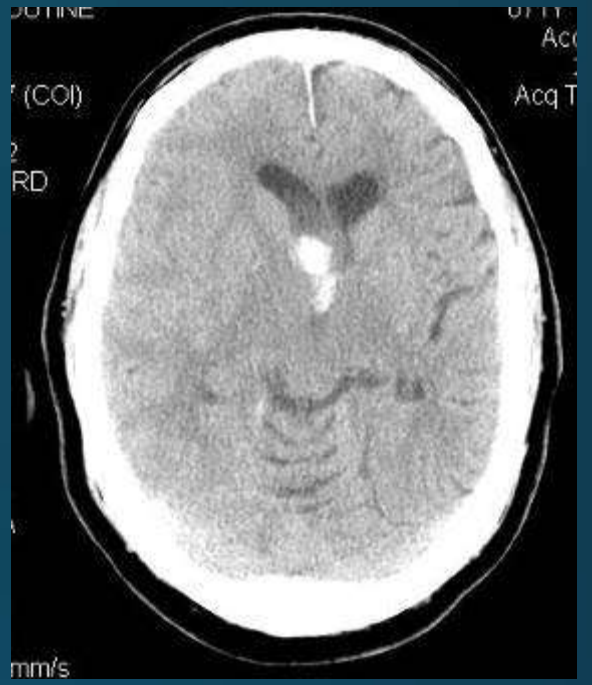
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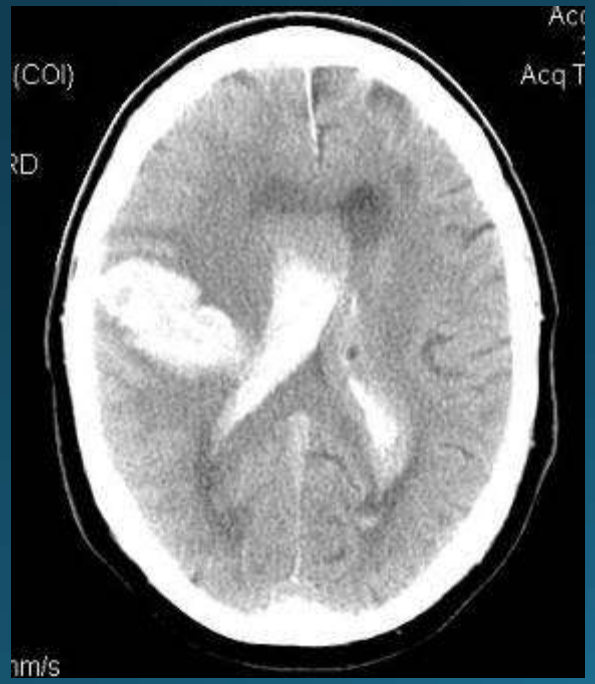
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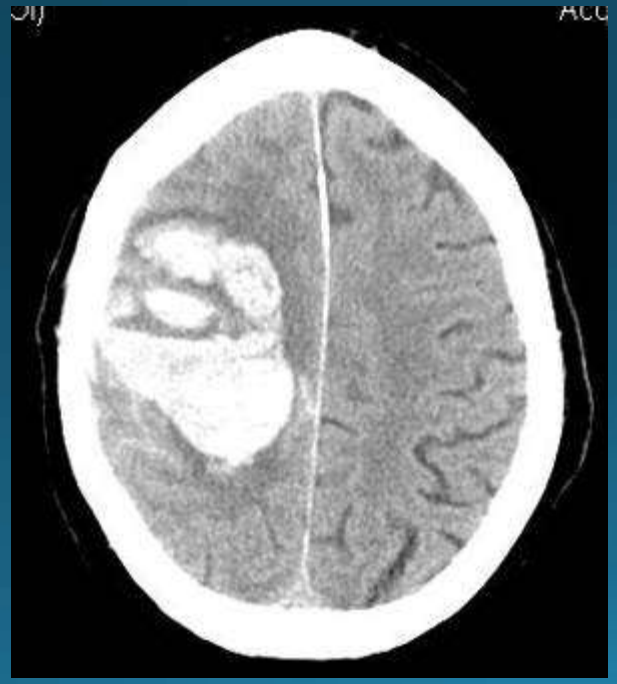
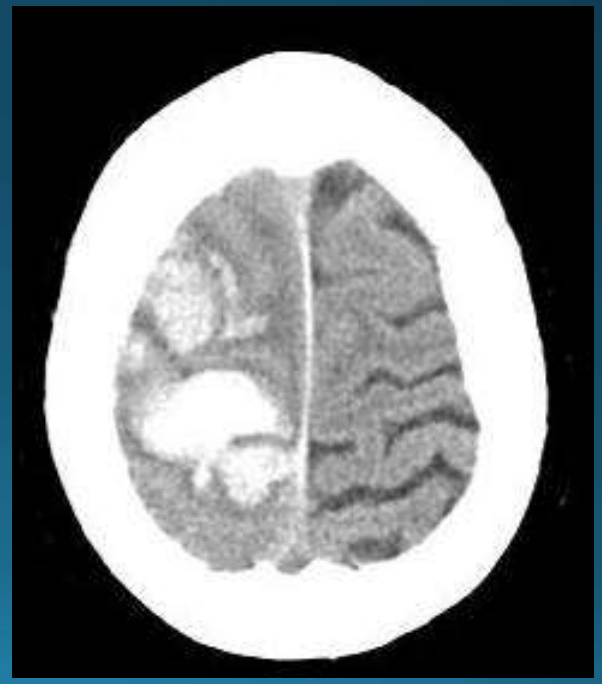




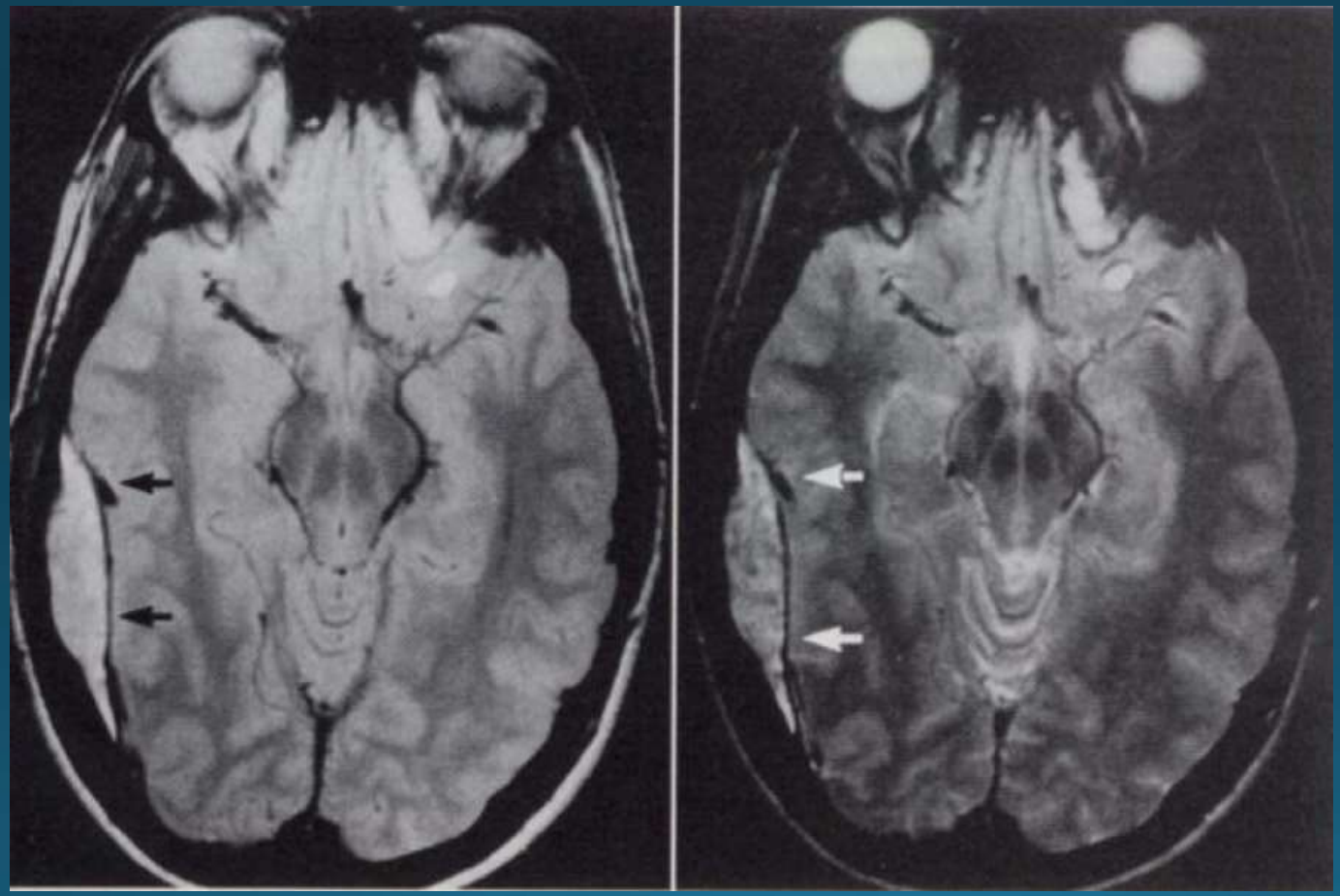
# Case 3

- **Intraparenchymal (intracerebral) hemorrhage**
  - Hypertensive
  - Amyloid angiopathy
  - Tumor
  - Trauma

# Case 4

30 y/o s/p head trauma with no immediate neurologic findings, rapid clinical deterioration 20 minutes later

# Epidural



# Epidural Hemorrhage

Usually secondary to trauma

Arterial epidural

Most common from laceration of the **middle meningeal artery**

Associated with a temporal bone **fracture**

## Dosimetry – typical effective doses from CT

| | | | |
|---|---|---|---|
| • CT head | ~ 2 mSv | • X-ray skull | ~ 0.03 mSv |
| • CT chest | ~ 8 mSv | • X-ray chest | ~ 0.02 mSv |
| • CT abdo | ~ 10 mSv | • X-ray abdo | ~ 0.7 mSv |
| • CT pelvis | ~ 10 mSv | • X-ray pelvis | ~ 0.7 mSv |

- These doses are approximations only – actual values depend on large number of factors
- Big differences between the information available in CT and planar x-ray images!

Like X-rays and PET scans, CT scans use ionizing radiation, which can damage DNA and cause cancer. Two other imaging technologies, MRI scans and ultrasound, do not use radiation.

The added information of CT comes at a high price:
Some big radiation doses! An abdominal CT scan, which contains about 10 milliSieverts (mSv) of radiation, the rough equivalent of 200 chest X-rays or 1,500 dental X-rays.
One sievert equals 100 rem (1 Sv = 100 rem). One milliSievert equals one hundred millrems (1 mSv = 100 millrems).

# Radiation Safety

- 1 Chest XR approximates the same risk as:
  - 1 year watching TV (CRT)
  - 1 coast to coast airplane flight
  - 3 puffs on a cigarette
  - 2 days living in Denver (higher on earth, more radiation)
- 1 Head CT scan (2000 milliSv) is approximately 20 CXR
- Amer. College of Radiology – Appropriateness Criteria - determine the best imaging study for a given clinical question and also gives some general information about dosage for each study type: https://acsearch.acr.org/list

Health Physics Society on the web--http://hps.org

# Radiation danger

- Food and Drug Administration reports that an estimated 30 to 50 percent of imaging tests are believed to be medically unnecessary.
- The National Cancer Institute (NCI) estimates that the additional risk of developing a fatal cancer from a scan is 1 in 2,000, while the lifetime risk of dying of cancer is 1 in 5.
- 2009 study: Among 31,000 patients who had a diagnostic CT scan in 2007, 33 percent had more than five during their lifetime, 5 percent received 22 or more and 1 percent underwent more than 38 scans.
- Doctors who have a financial stake in radiology clinics or who own scanners use imaging substantially more often than those who don't
- Radiation exposure is cumulative, and children, who undergo between 5 million and 9 million CT scans annually, are much more vulnerable to its effects.
- Except for mammography, there are no federal regulations governing radiation doses.

# Radiation in medical diagnostic tests: Number of millirems per procedure

- **Ave. daily background radiation = 9 mSV**
- **Dental x-ray = 9 mSV**
- **X-Rays:**
- **Chest-10 mrem,**
- **Mammography (2 views)-72,**
- **Skull-10,**
- **Cervical Spine-20,**
- **Lumbar Spine-600,**
- **Upper GI-600,**
- **Abdomen (kidney/bladder)-700,**
- **Barium Enema-800**
- **Pelvis-60, Hip-70,**
- **Dental Bitewing/Image-0.5,**
- **Extremity (hand/foot)-0.5**

**CT Scans:**

**Head-2000 mSV**
**Chest-7000 mSV**
**Abdomen/Pelvis-10000 mSV**
**Angiography (heart)-20000 mSV**
**Angiography (head)-500**
**Spine-1000**
**Whole Body-1000**
**Cardiac-20**

Conversion base : 1 mrem = 0.01 mSv

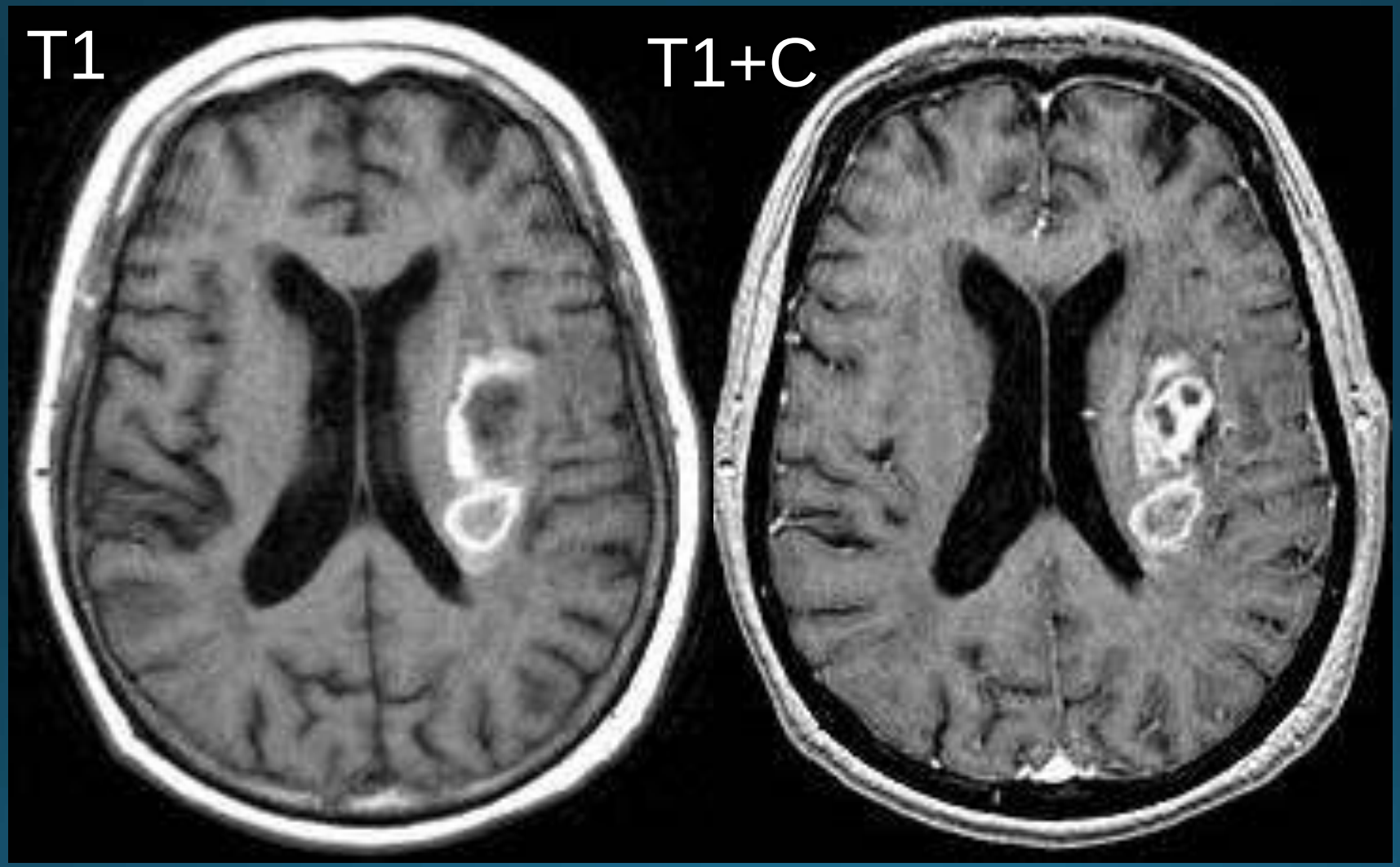
| Type of Radiation (dose in mSv)† | Equivalent Period of Natural Background Radiation‡ | Estimated Lifetime Risk of dying from cancer that results from a single exposure§ |
|---|---|---|
| Airport Security x-ray scanner [23] (~0.0001mSv) | less than one hour | Almost 0 (less than 1 in 100,000,000) |
| 7 hour airplane flight [9] (~0.03 mSv) | a few days | Almost 0 (1 in 1,000,000 – 100,000) |
| Chest x-ray [6] (~0.1 mSv) | ~ one week | Almost 0 (1 in 1,000,000 – 100,000) |
| Mammogram [27] (~0.4 mSv) | a few months (~2 months) | 1 in 100,000 to 10,000 |
| CT of chest [27] (~7 mSv) | a few years (~2.3 years) | 1 in 10,000 to 1,000 |
| Fluoroscopy: colon (barium enema) [27] (~8 mSv) | a few years (~2.7 years) | 1 in 10,000 to 1,000 |
| CT of heart (angiography) [27] (~16 mSv) | a few years (~5.3 years) | 1 in 10,000 to 1,000 |
| PET scan, whole body [5] (~14 mSv) | a few years (~4.6 years) | 1 in 10,000 to 1,000 |
| Fluoroscopy: kidneys, ureters and bladder [5] (~15mSv) | a few years (~5 years) | 1 in 10,000 to 1,000 |
| Whole-body CT scan [5] (~22.5 mSv) | several years (~7.5 years) | 1 in 1,000 |
| Nuclear Medicine: Cardiac stress-rest test (thallium) [27] (~40.7mSv) | many years (~13.6 years) | ~2 in 1,000 |
| Transjugular intrahepatic portosystemic shunt placement [27] (~70mSv) | many years (~23.3 years) | 1 in 100 – 1,000 |
| Lifetime risk of cancer death NOT caused by radiation§§ | | 1 in 5 |

# Contrast media

CT: Iodine-based - Iodine is highly attenuating of X-ray beam (bright on CT)

MRI: Gadolinium-based  - Gadolinium is a paramagnetic metal that hastens T1 relaxation of nearby water protons (bright on T1-weighted images)

# Enhancement




Hemorrhagic melanoma metastasis

# Contrast risks

- What are the risks of iodinated contrast?
  - Contrast reaction
    - 1 in 10,000 have true anaphylactic reaction
    - 1 in 100,000 to 1 in 1,000,000 will die
  - Medical Issues
    - Acute renal failure
    - Lactic acidosis in diabetics
      - If on Glucophage, patient must stop Glucophage for 48 hours after exam to prevent serious lactic acidosis
    - Cardiac
  - Extravasation: contrast dye leaks into the tissue around the vein where the IV was placed

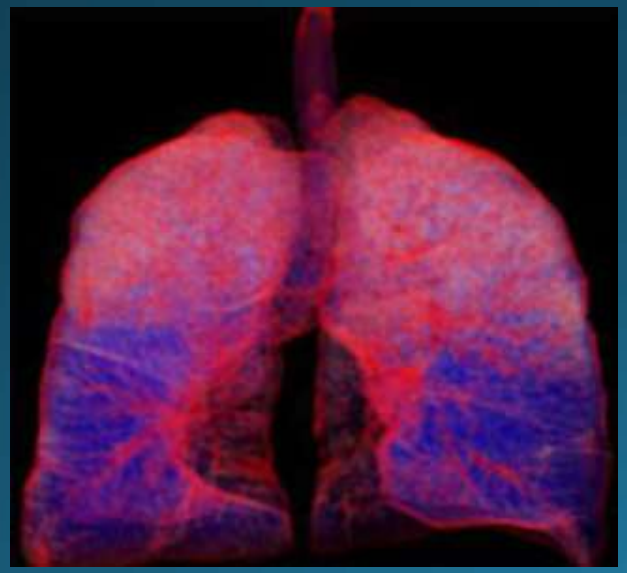
# Risks

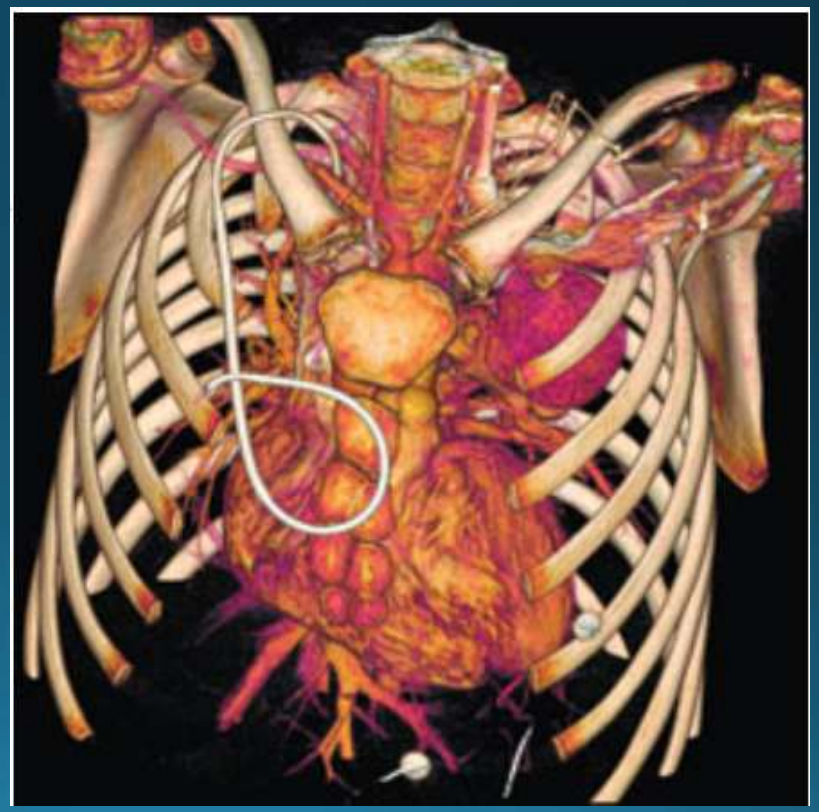
- Hyperintensity, in two brain regions (the dentate nucleus (DN) and globus pallidus (GP)), which correlated with the number of gadolinium-based enhanced MRIs.
- Use of gadolinium at UCSF is based on the GFR (a lab measure of kidney function). If the GFR is <30 or the patient is on dialysis, no gadolinium. If the GFR is 30-40 then it becomes a risk/benefit discussion with the patient. Ok if >40.
- Among patients with severe kidney disease (especially dialysis patients), the use of gadolinium-based contrast agents is linked to the development of Nephrogenic Systemic Fibrosis, or NSF.
- NSF causes skin thickening that can prevent bending and extending your joints. It can also develop in your diaphragm, thigh muscles, lung vessels, and lower abdomen. Along with causing decreased mobility of joints, NSF is irreversible, extremely debilitating, and can be fatal.

# CT better than MRI

- When MRI contradicted [pregnancy, metal in body]
- No Localizing signs
- Meningeal Tumors
- Pituitary Tumors
- Calcified Lesions
- Acute Vascular Lesions

# CT - Multidetector Imaging





# MRI Basics and Interpretation

# The Cardinal Principles in Neuroimaging

- Functional neuroimaging comprises methods for mapping information processing within the brain.

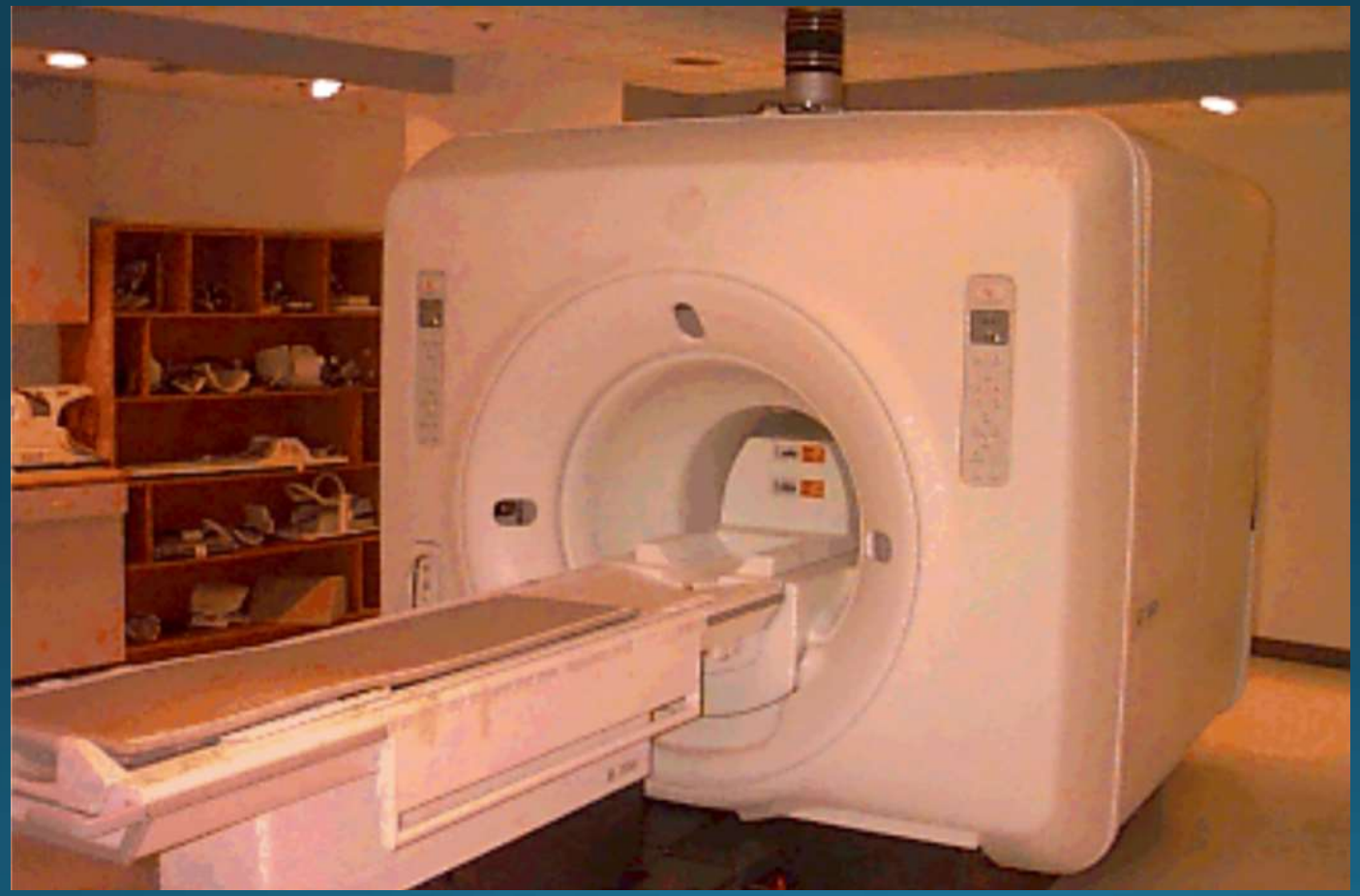
- All functional neuroimaging is limited by two factors:
  - physical properties of the recording system
  - physiological constraints of the brain.

- Images of brain activity only have meaning when acquired using the correct experimental design & interpreted using the correct analysis.

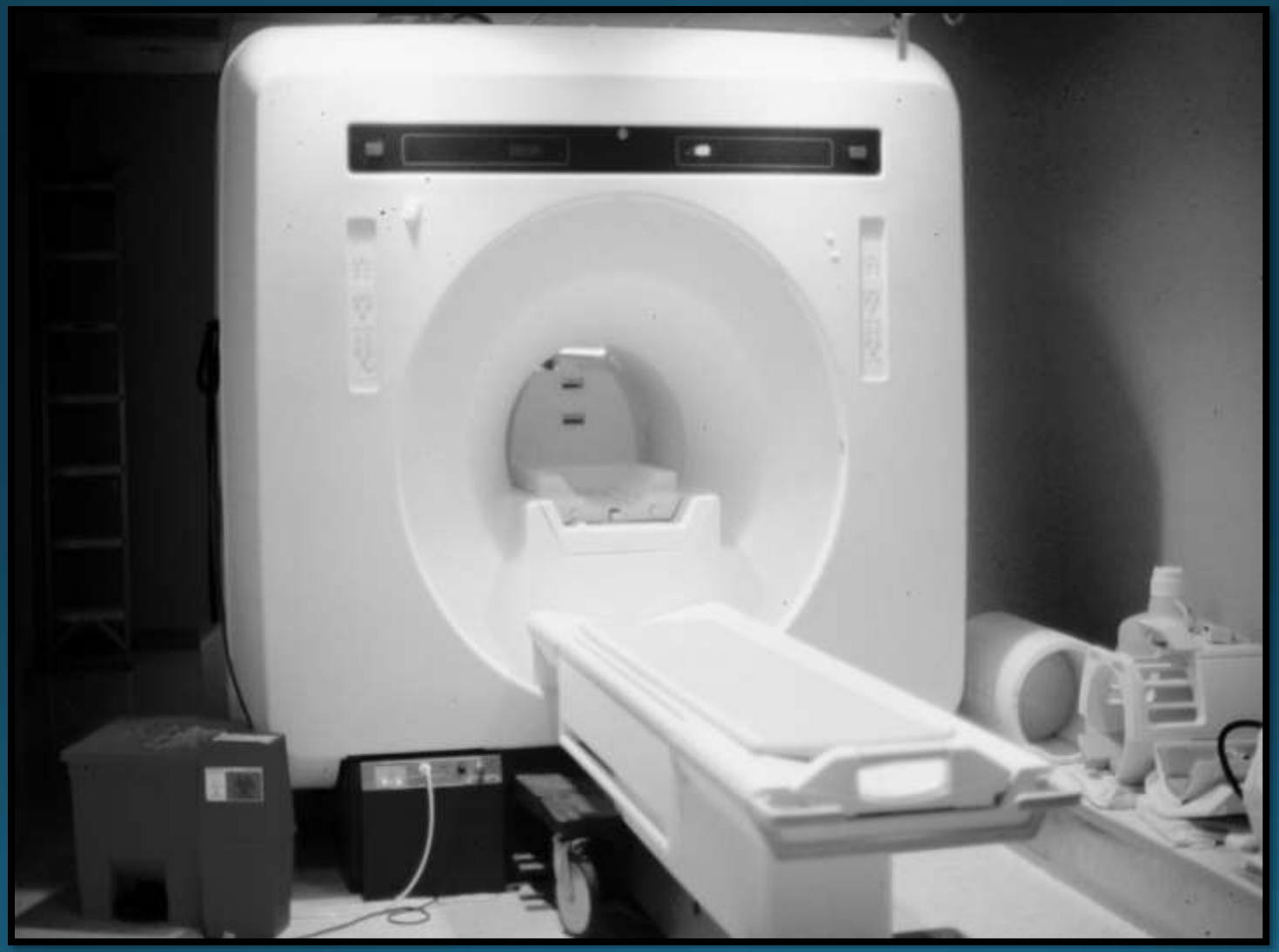
# MRI

- MRI is a structural imaging procedure, like CT.
- Greater resolution of anatomy & tissue differentiation compared to CT
- Unlike CT, does not use ionizing radiation.
- MRI can detect reaction of water molecules within a strong magnetic field after the introduction of a radiowave signal.

# MRI

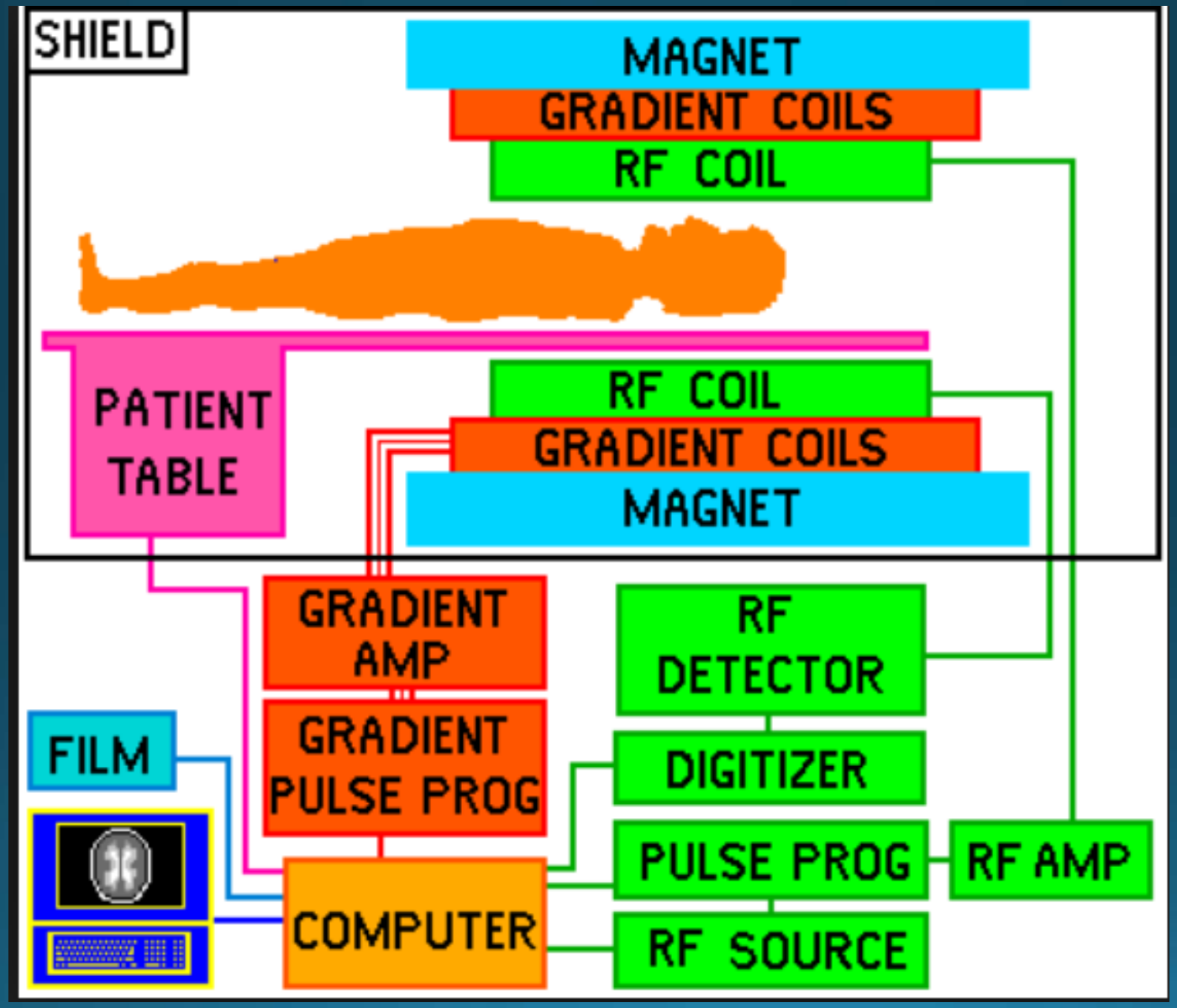


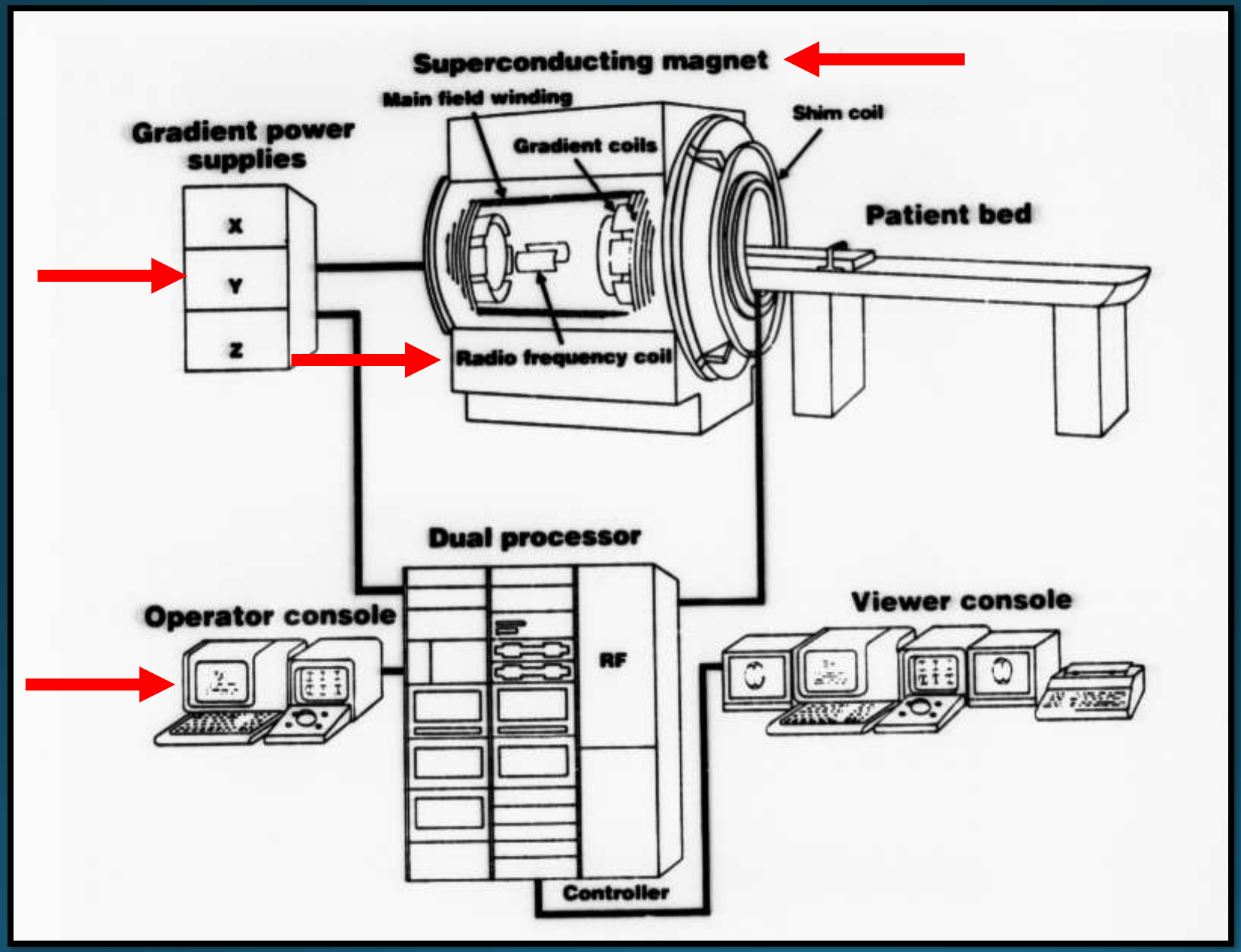
# Superconducting magnet



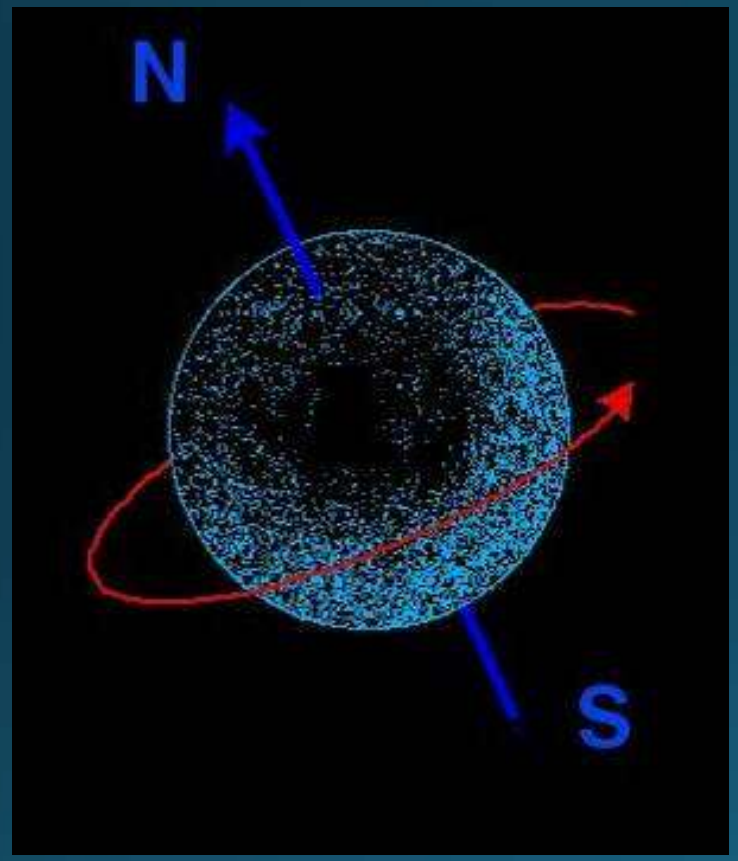
# 7 Tesla Siemens Magnetom: second best

# MRI Hardware

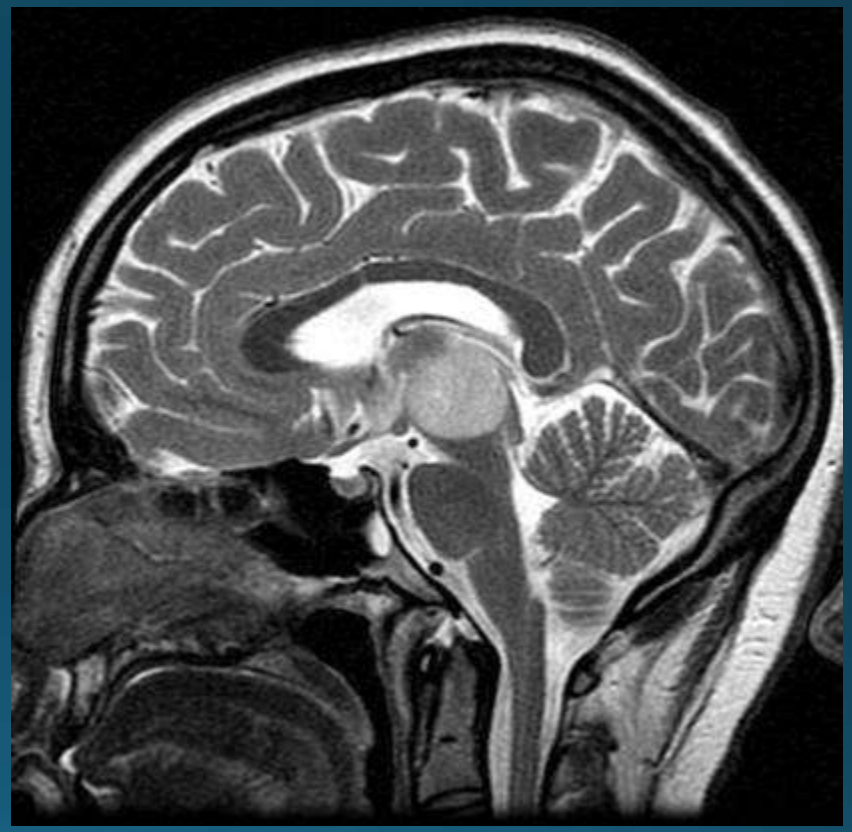



Superconducting magnet
Main field winding
Gradient coils
Shim coil
Gradient power supplies
X
Y
Z
Patient bed
Radio frequency coil
Dual processor
Operator console
RF
Viewer console
Controller

# Magnetic Resonance (MR)

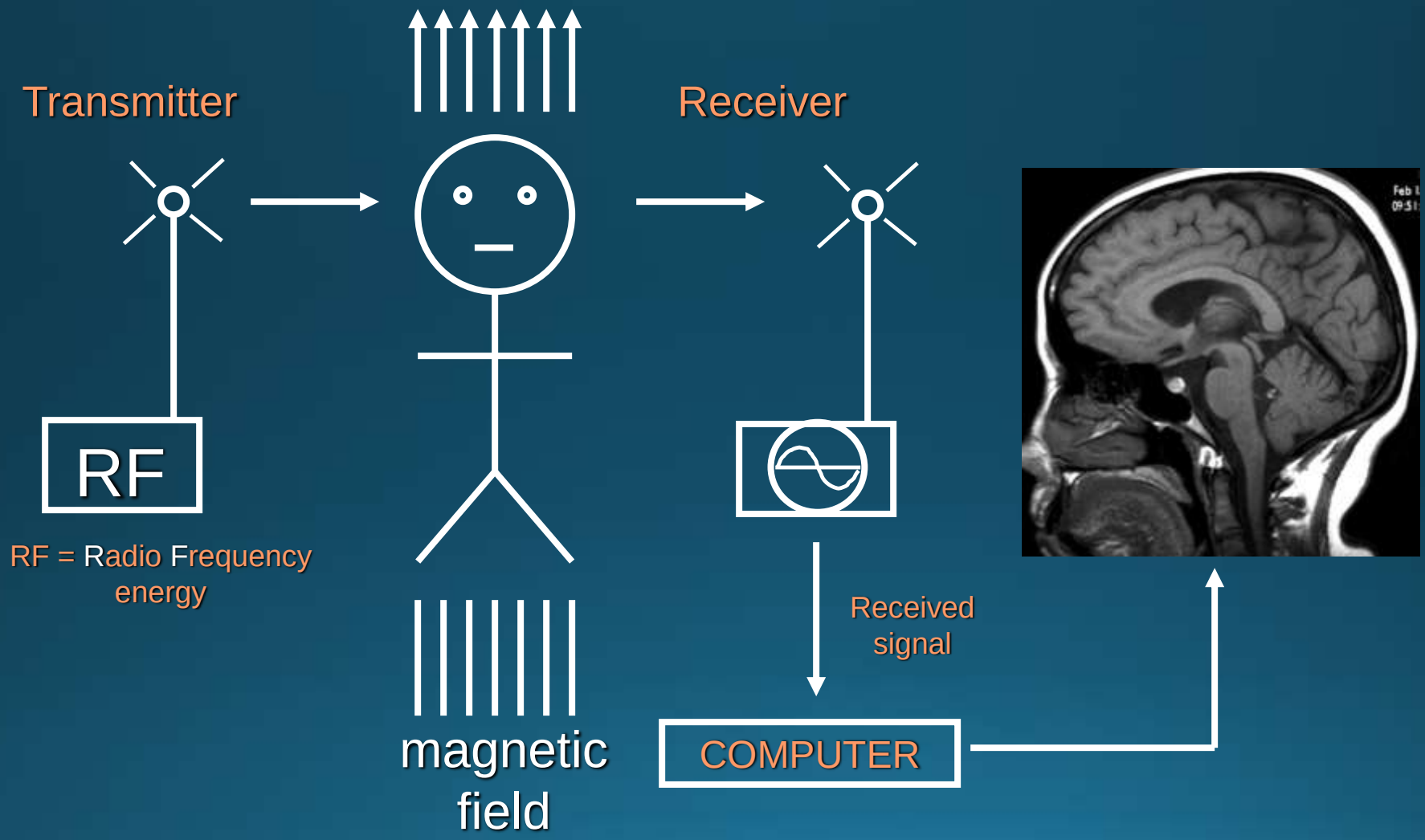



Hydrogen proton in water or fat



MRI

# Magnetic Resonance Imaging



# Physical Principles

- Based on the absorption and emission of radiofrequency energy.
- No ionizing radiation.
- Uses magnets ranging in strength based on units of Tesla  (1.5T, 3T, 7T, 9.4T, 10.5T).
- Magnetic field causes protons in the body to align and then pulsed radiowaves are directed at the patient causing a disturbance of the proton alignment.
- Atoms then realign and in doing so, emit the absorbed radiofrequency.
- Different tissues realign (relax) at different frequencies.

# Synopsis of MRI

**1**) Put subject in big magnetic field [and leave him there]

⇒ Magnetizes the H nuclei in water (**$H_2$**O)

**2**) Transmit radio waves into subject [about 3 ms]

⇒ Perturbs the magnetization of the water

**3**) Turn off radio wave transmitter

**4**) Receive radio waves re-transmitted by subject's H nuclei

⇒ Manipulate re-transmission by playing with H magnetization with extra time-varying magnetic fields during this readout interval [10-100 ms]

⇒ Radio waves transmitted by H nuclei are sensitive to magnetic fields — those imposed from outside and those generated inside the body:

⇒ Magnetic fields generated by tissue components change the data and so will change the computed image

**5**) Store measured radio wave data vs time

⇒ Now go back to **2**) to get some more data [many times]

**6**) Process raw ("*k*-space") radio wave data to reconstruct images

# MRI: strengths and limitations

- Strengths
  - Widely available (9000+ scanners in USA)
  - Harmless to subject ***if*** proper safety precautions are used
  - Very flexible: can make image intensity (contrast) sensitive to various sub-voxel structures
  - Still advancing in technology and applications
  - Still in a growth phase for brain research
  - High resolution imaging
  - Can register water content, inflammation and bleeding
- Limitations on spatial resolution and contrast types
  - e.g., little chemical information is available with even the most sophisticated scanning methods
    - Novel contrast agents making some inroads in this direction
    - Can only register structure, and not function

# MRI: Strengths & Limitations

Advantages:

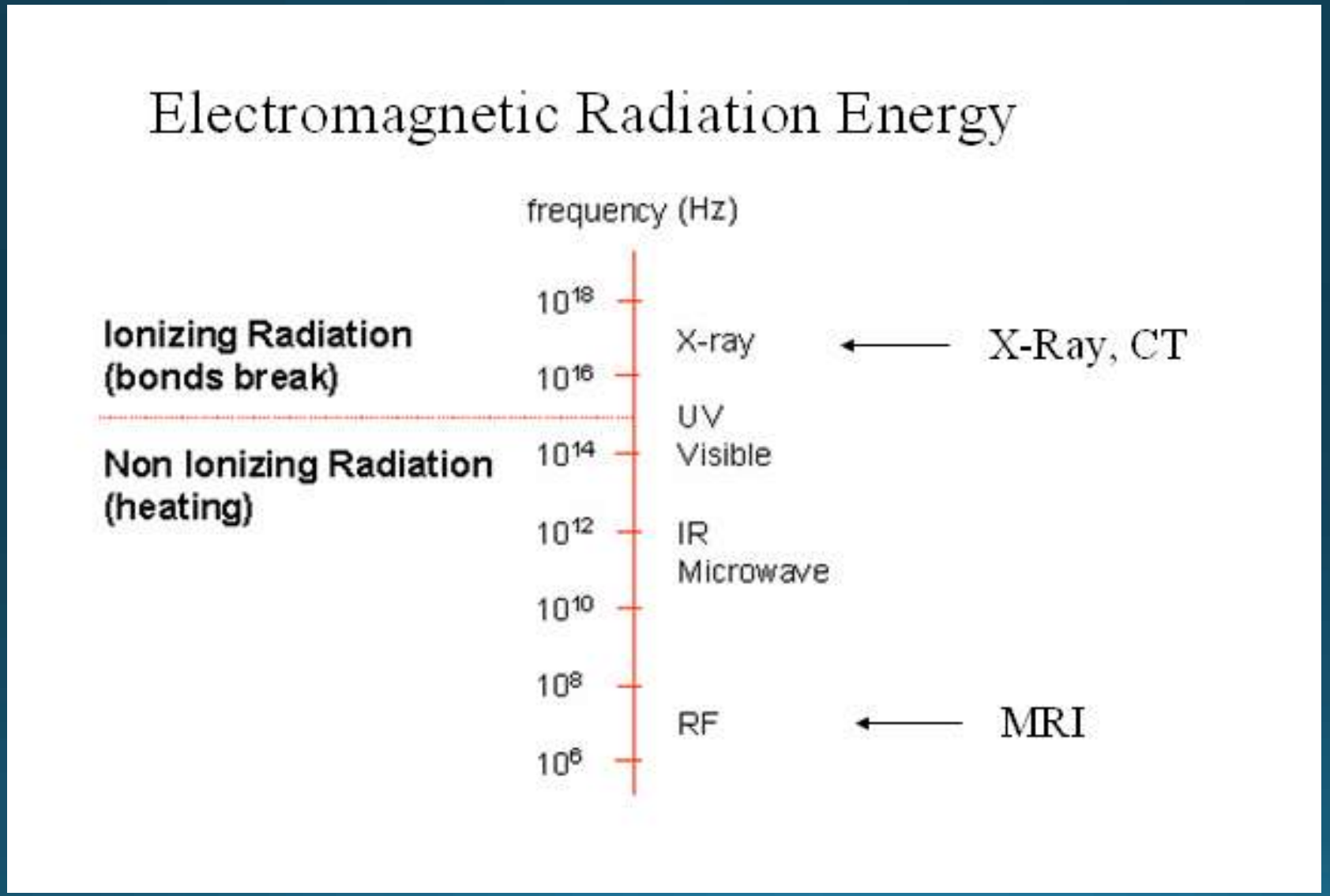
Superior to CT for the detection of most CNS diseases due to its high soft tissue contrast resolution

Multiplanar capability

Disadvantages

Typical brain MR study takes approx. 30 min
Patient must be able to hold still
No metal in body
Caution – Pacemaker

# Another benefit of MR: no ionizing radiation!



# Magnetic Resonance Imaging

## Limitations

1. ICU patients (have multiple electronic devices) and Claustrophobia
2. Metal artifact

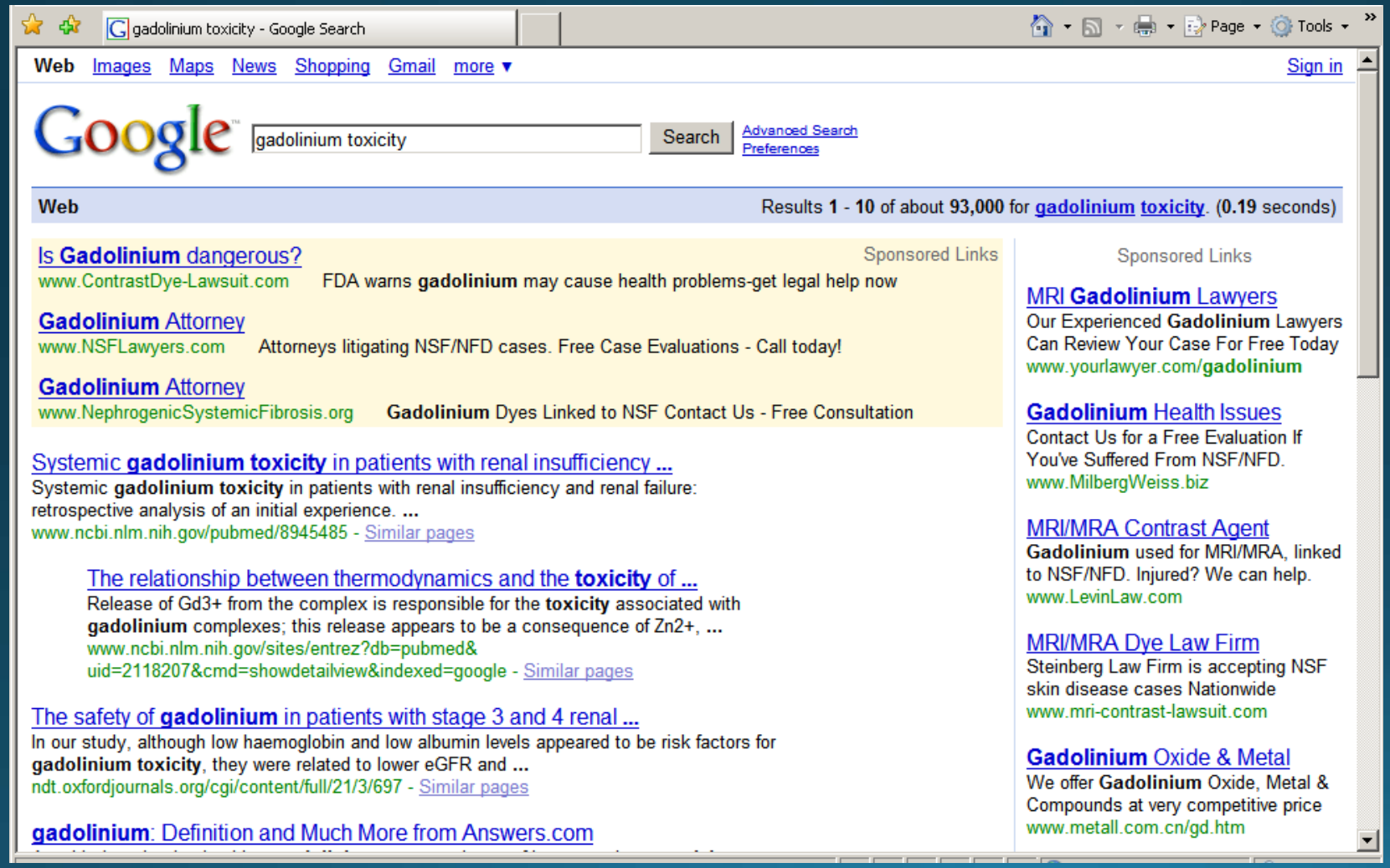
1. RF Energy – pacemaker override
2. Magnetic field - aneurysm clips - ocular metal - missile effect
3. Nephrogenic Systemic Fibrosis- gadolinium toxicity in renal failure

# Child Dies in MRI Machine


**The Associated Press**
**Monday, July 30, 2001: 2:42 p.m. EDT**

A child undergoing an MRI exam received a fatal head wound when the machine's powerful magnet pulled a metal oxygen canister inside.

# **Gadolinium Toxicity:** Google searches show the attorneys are interested at least.



# Typical MRI indications

- Ischemia
- Tumor
- Infection
- Dating blood products
- Congenital abnormalities

MRI better than CT

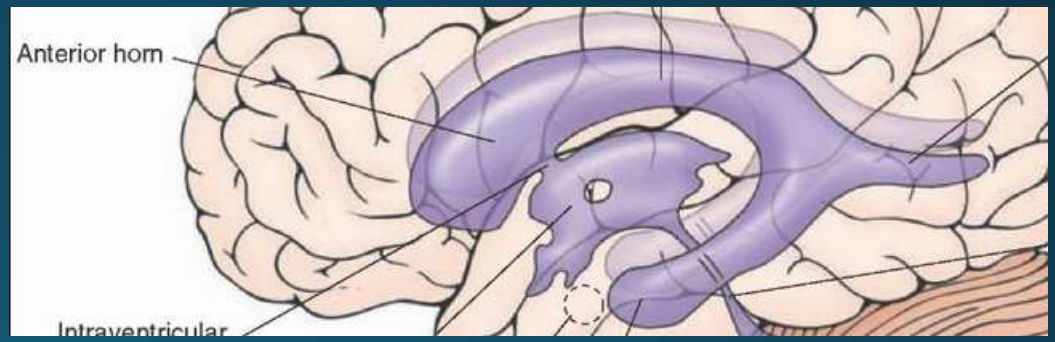
- CT contradicted [radiation, contrast]
- Clear Localizing signs
- Temporal Lobes, Cerebellum, Subcortical
- Brain Stem, Spinal Cord
- Dementia; Non-meningeal tumors
- AVMs; Huntington’s; Infarctions

# Erin Bigler: Imaging advice

Look at MRIs when you do NP testing

Ventricular dilation is window to brain pathology: atrophy going on

Anterior horn of lateral ventricle points to greatest atrophy

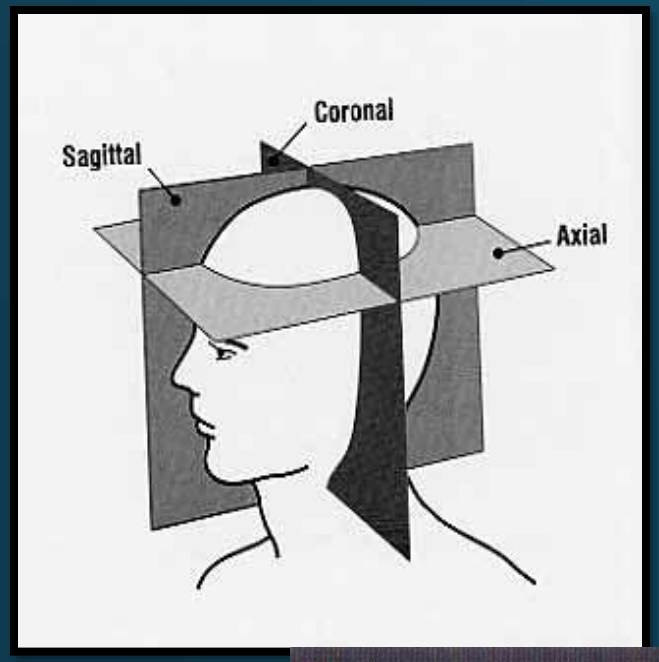



Any bright area is important

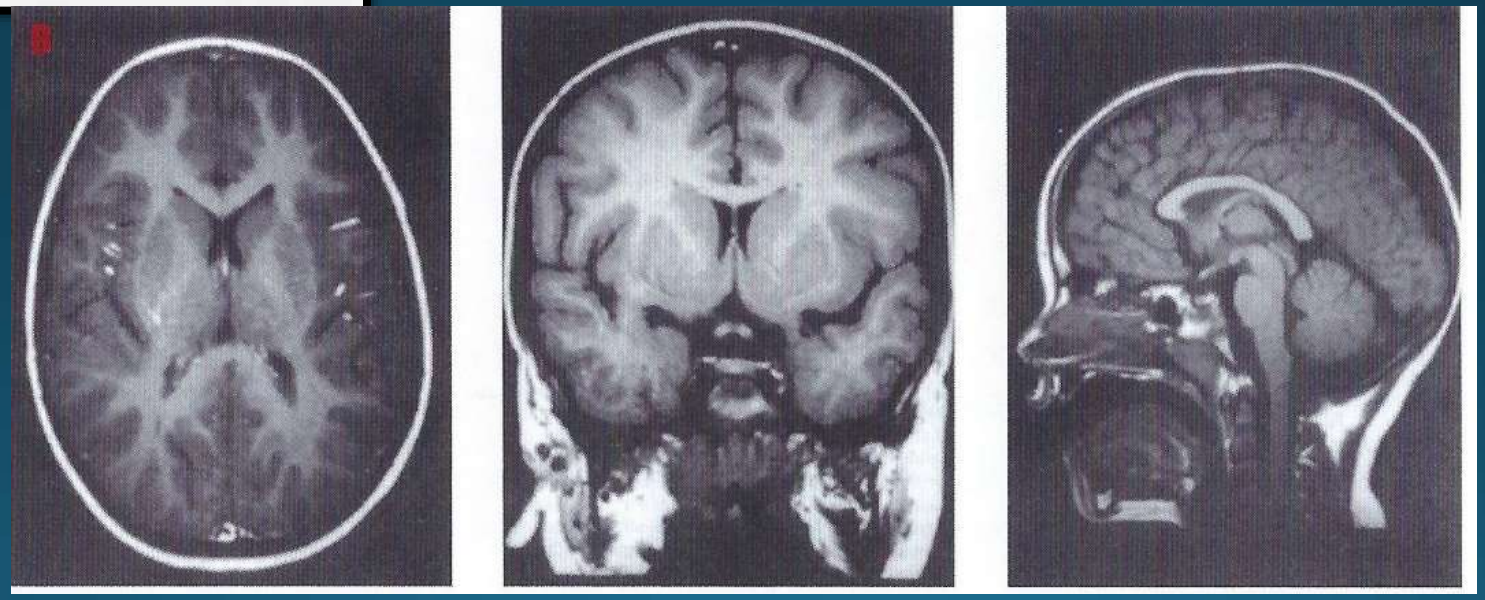
Look for any asymmetry

TBI is teaching model for all other neurological disorders

Optimal neuroimagery time for NP is 3-6 months post event

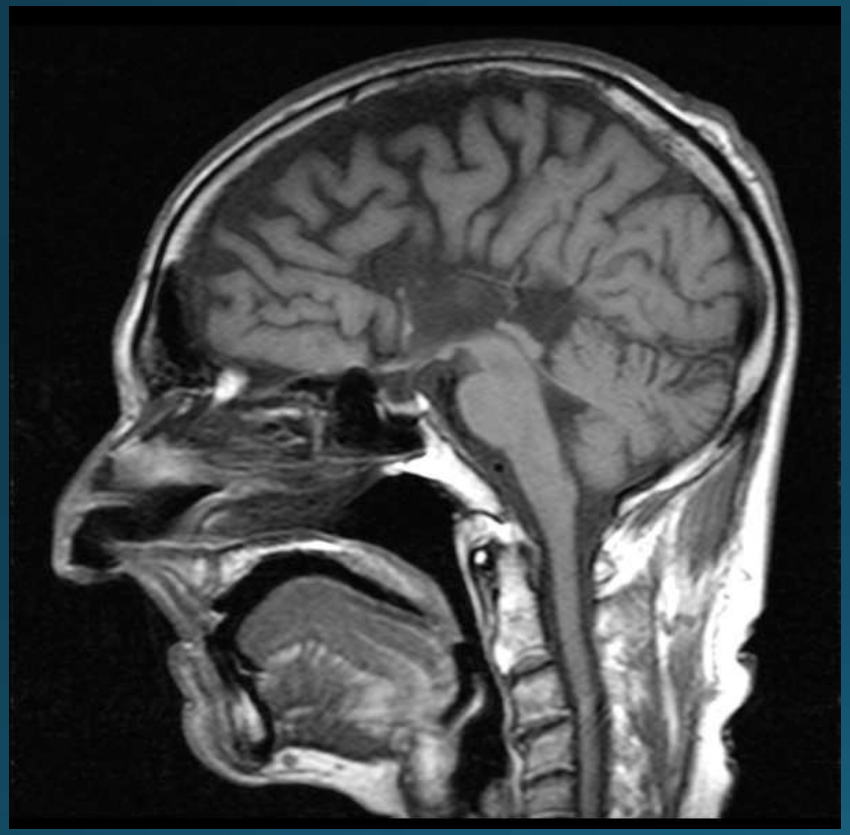


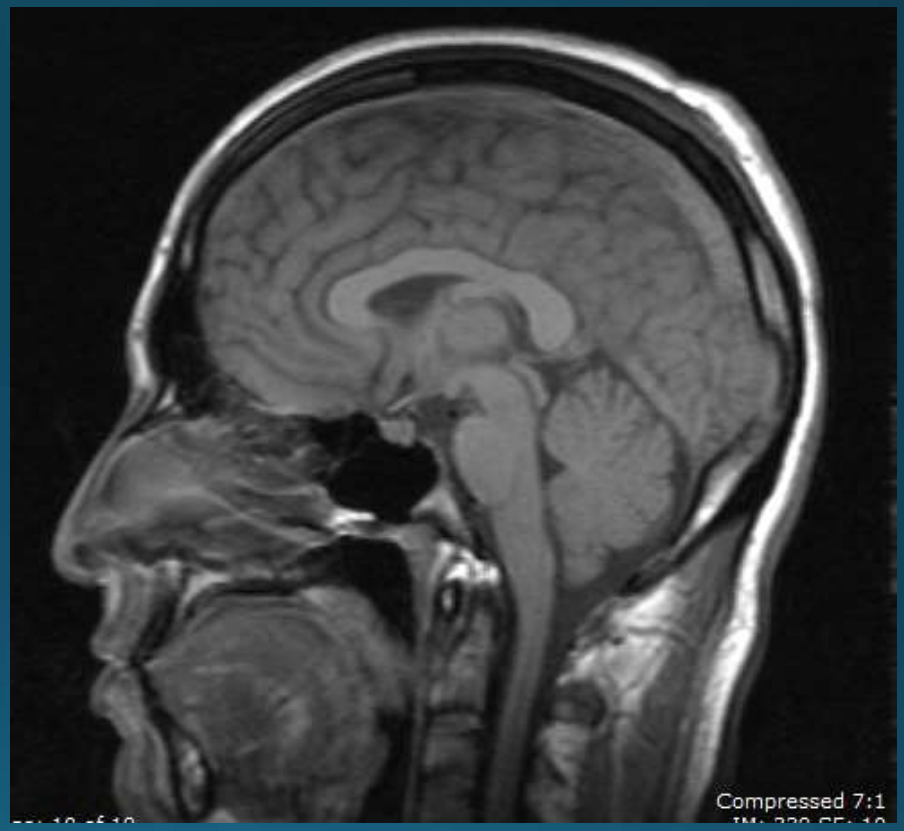

MR has advantage of multiplanar imaging: any plane of section possible



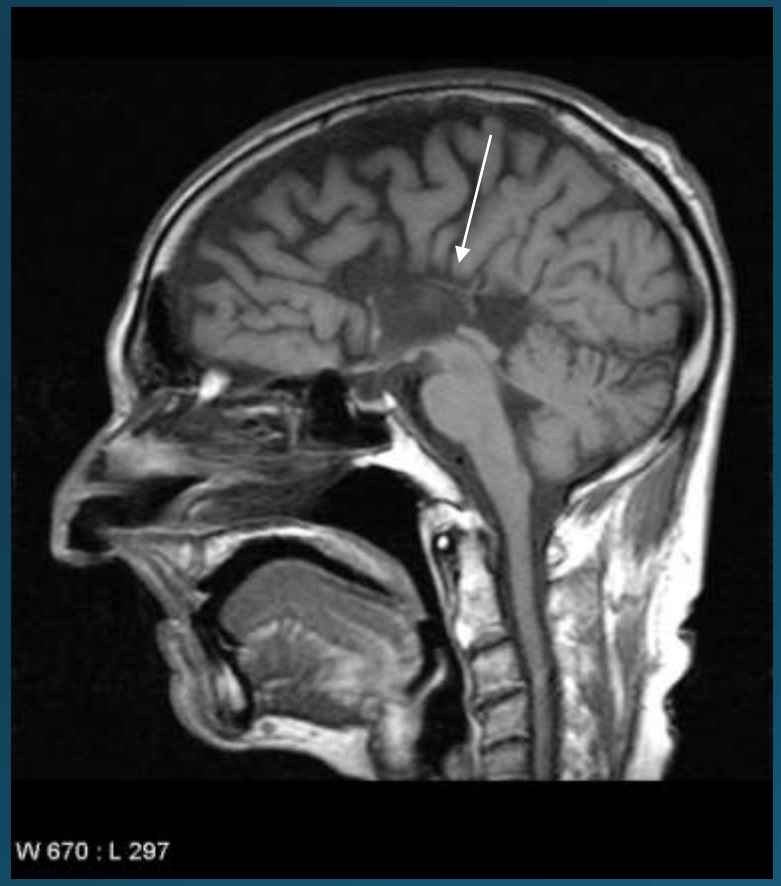
Axial Coronal Sagittal

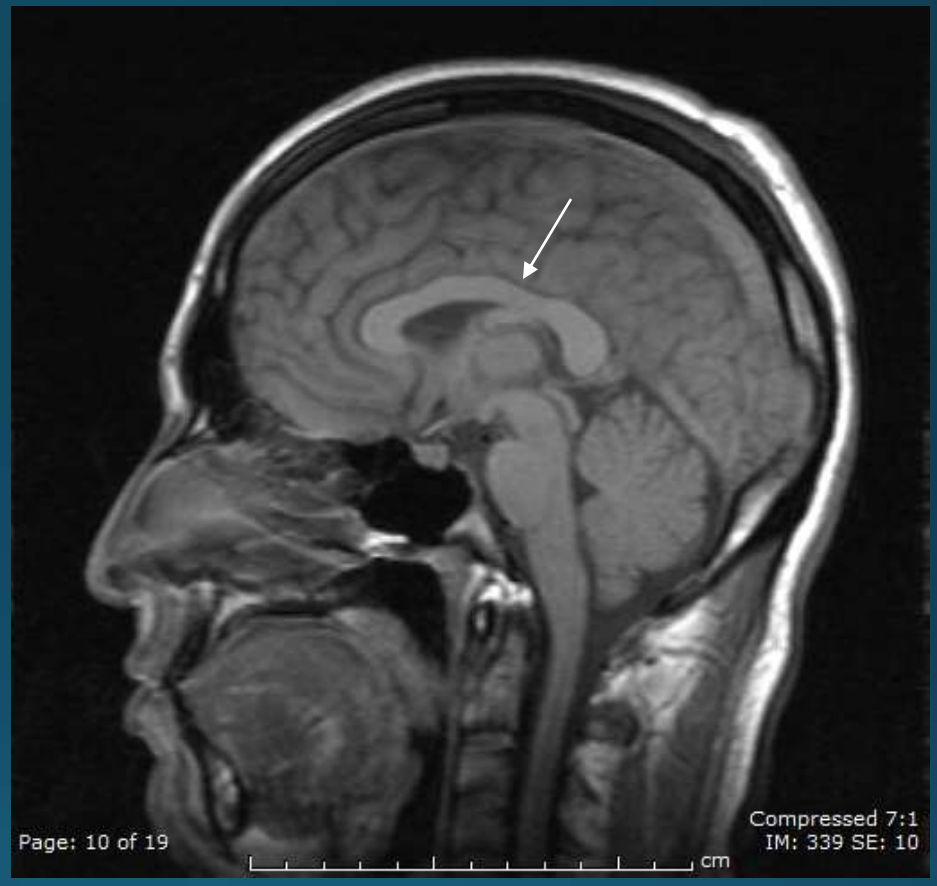
# The benefits of multiplanar imaging





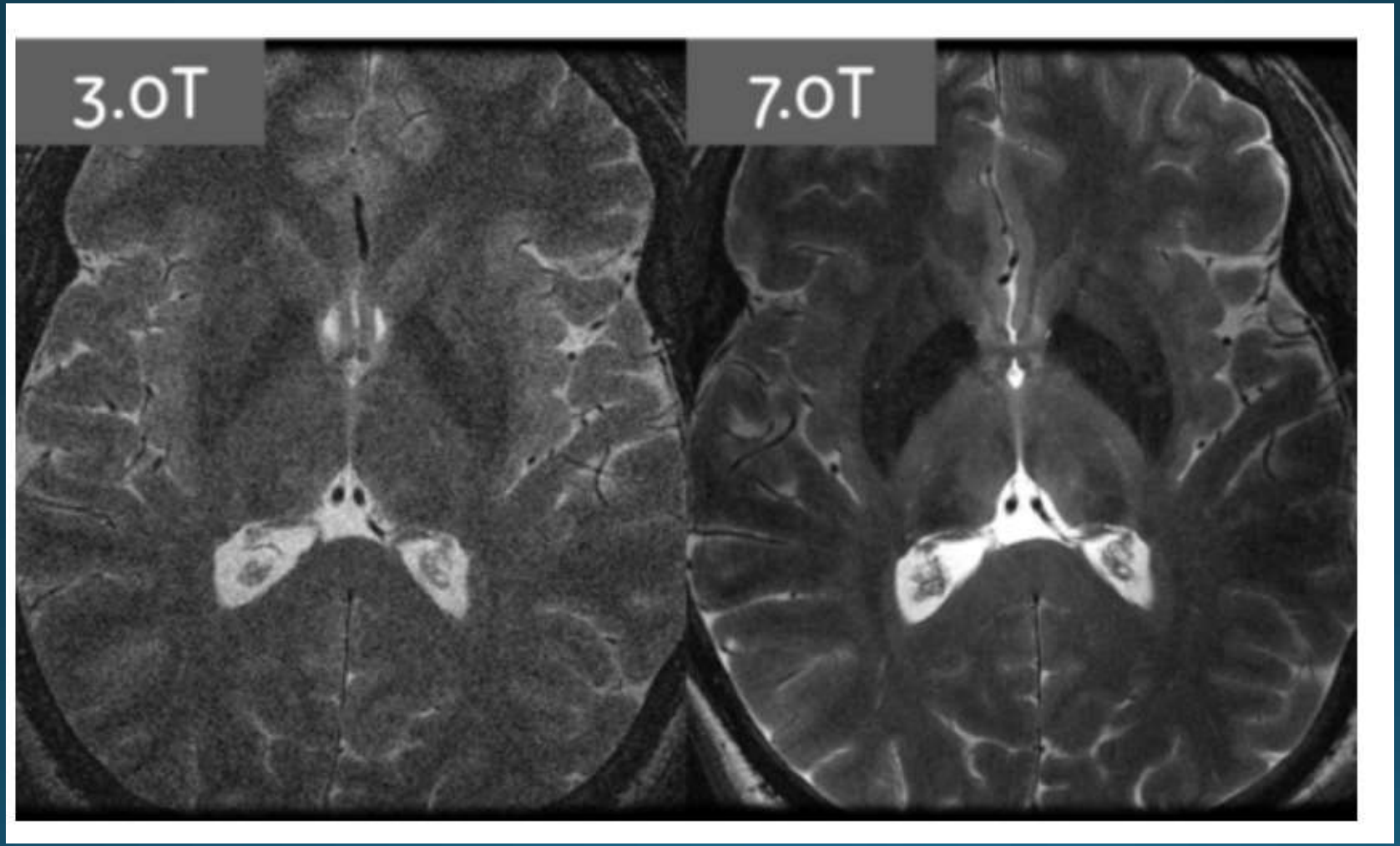

Anything missing? (Patient on your left, control on right)



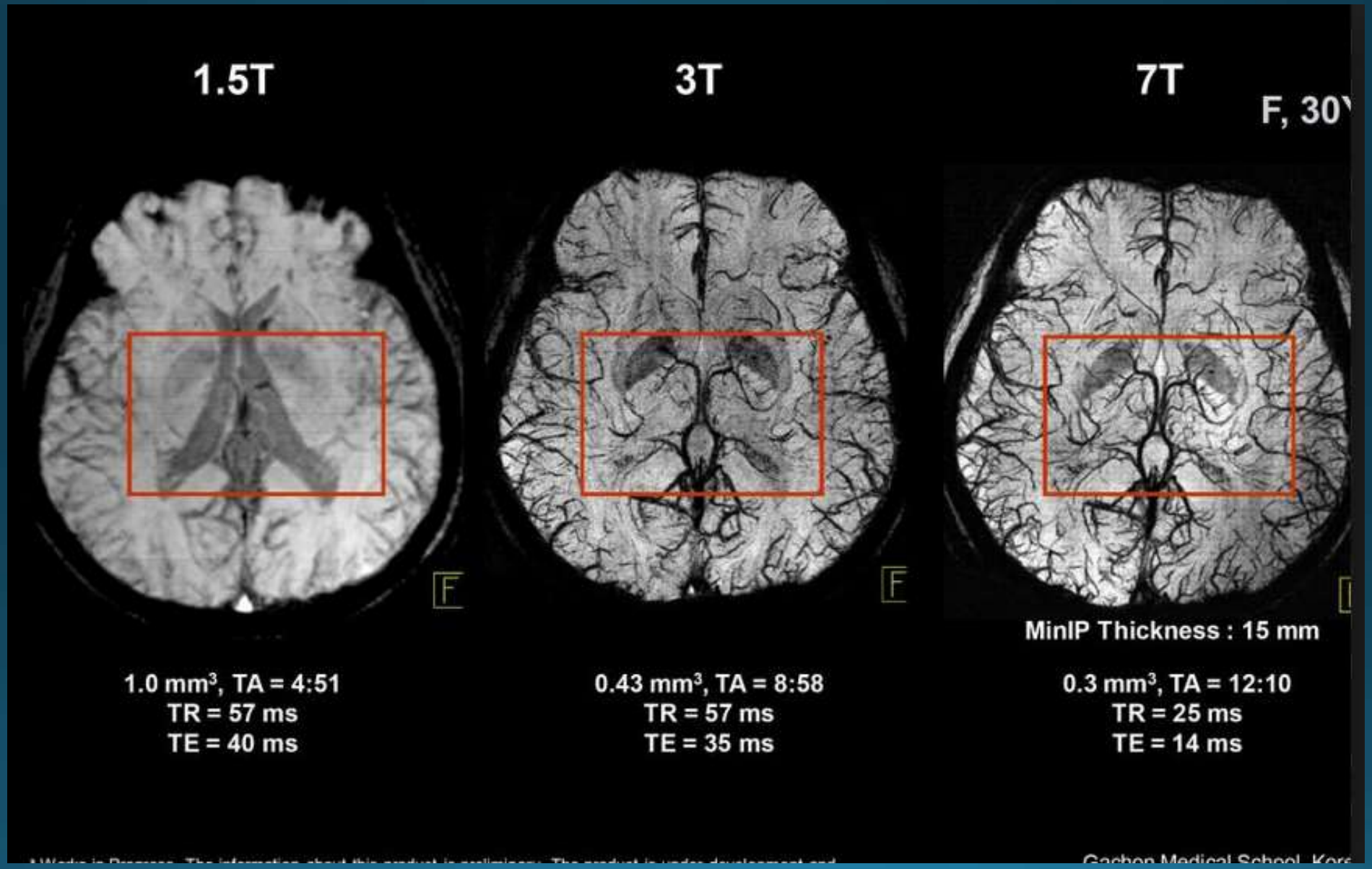

Patient is missing his corpus callosum.
Diagnosis: Agenesis of the corpus callosum

# 3 vs 7 Tesla




7 Tesla: 140,000 times stronger than the Earth's magnetic field;
must cool the 7T's wiring to just 4 degrees Kelvin above absolute zero,

# Tesla Comparison



# 10.5 Tesla at U of Minnesota

Prof. Kamil Ugurbil: 7-Tesla resolution = cubic millimeter, or about 80,000 neurons.
10.5-Tesla =  tenths of a cubic millimeter.

# 16.4 Tesla Varian Console for animal models


Scientists at the Los Alamos National Laboratory campus of the National High Magnetic Field Laboratory have successfully produced the world's first 100 Tesla non-destructive magnetic field.

# MRI Physical Principles 2

- The time it takes the protons to regain their equilibrium state = relaxation time.
- Two types of relaxation time:

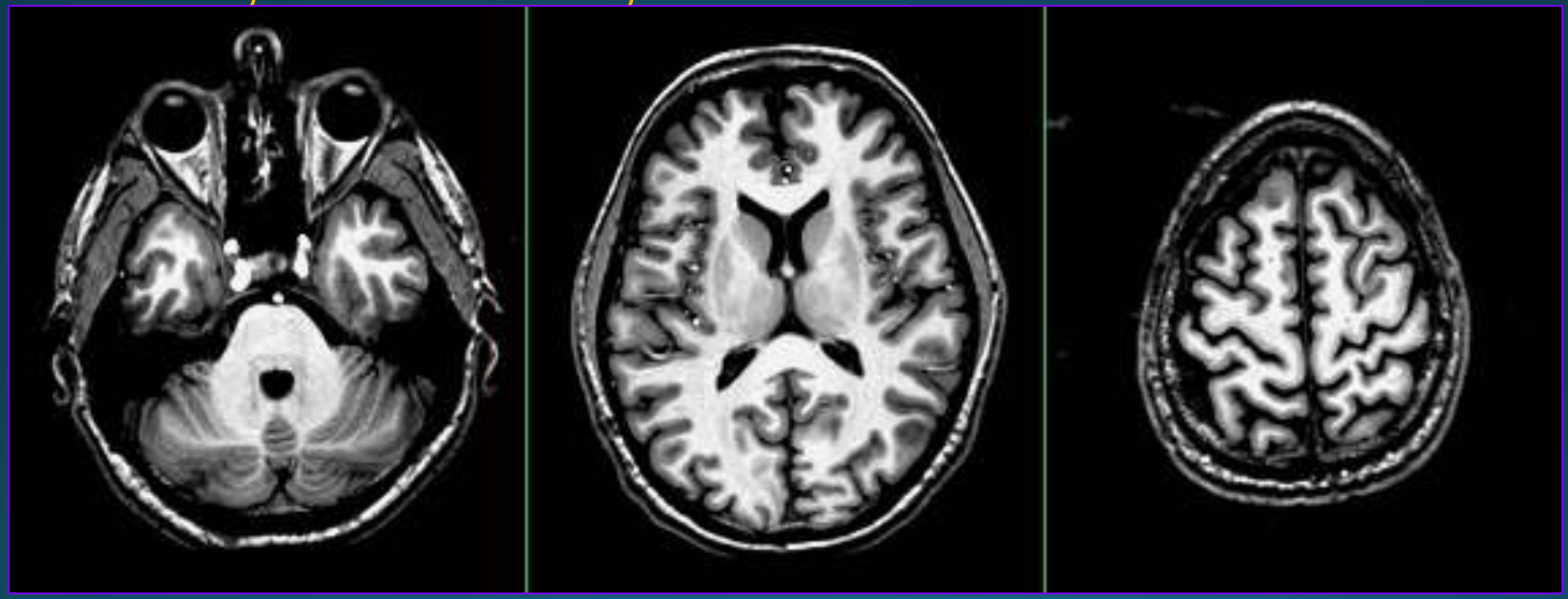
- T1 - Longitudinal (parallel to the magnetic field; reflects how quickly vertical magnetization recovers in that tissue); greater anatomic detail, but less tissue contrast

- T2 - Transverse (perpendicular to the magnetic field; how quickly horizontal magnetization disappears in that tissue); enhanced contrast & better differentiation of types of brain tissue (pathology looks brighter)

- Relaxation time and proton density are the main determinants of signal strength.

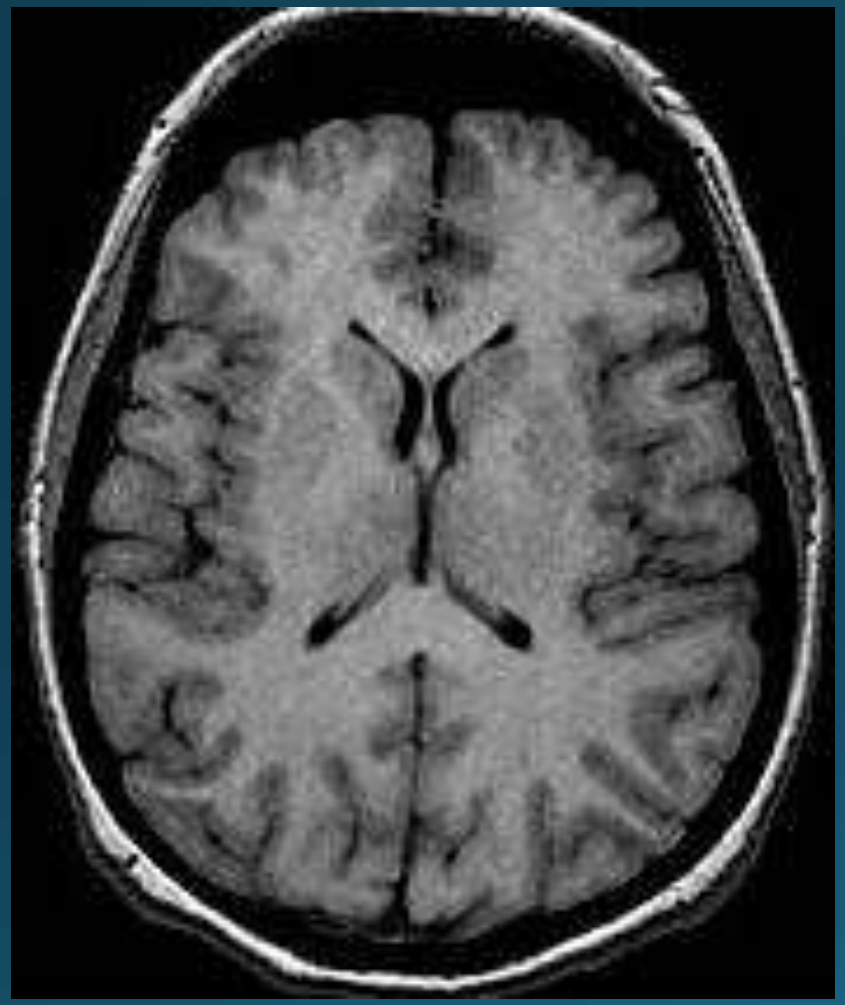
# T1-Weighted Images:
# Best for visualizing normal neuroanatomy

- Images designed to produce ***contrast*** between gray matter, white matter, and CSF

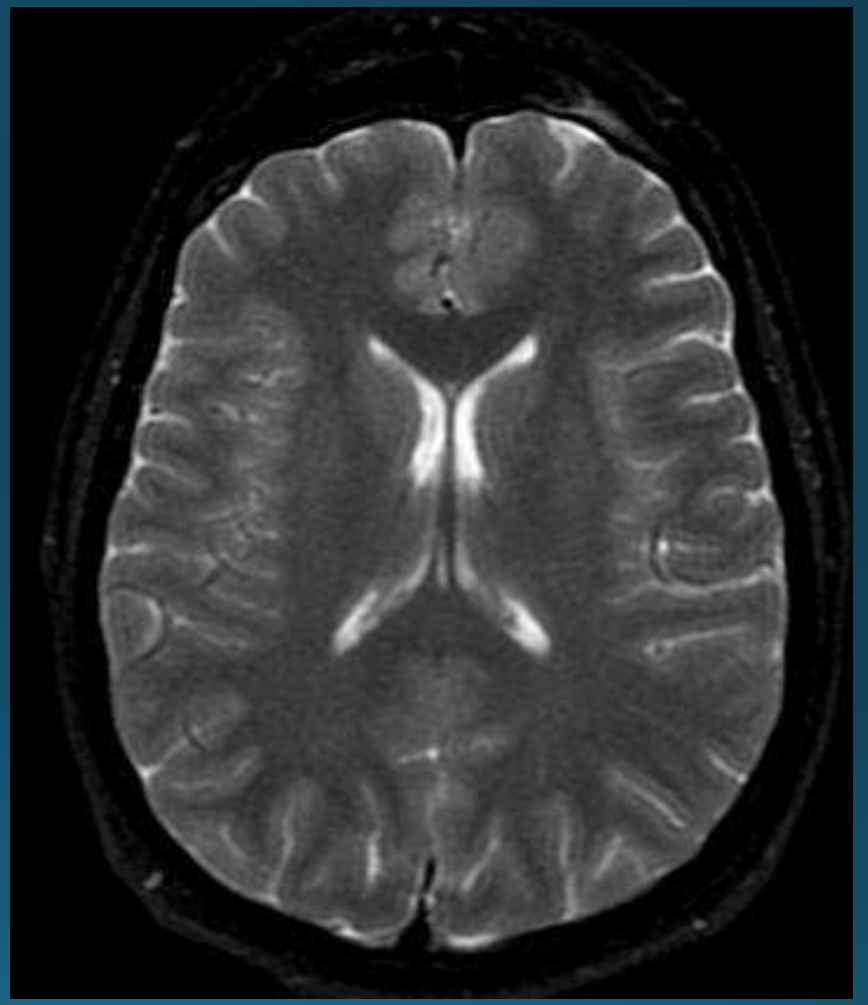


Three axial (AKA transaxial or horizontal) slices:
Spatial resolution is about 1 $mm^3$
Acquisition time for whole head is 5-10 minutes

# Magnetic Resonance



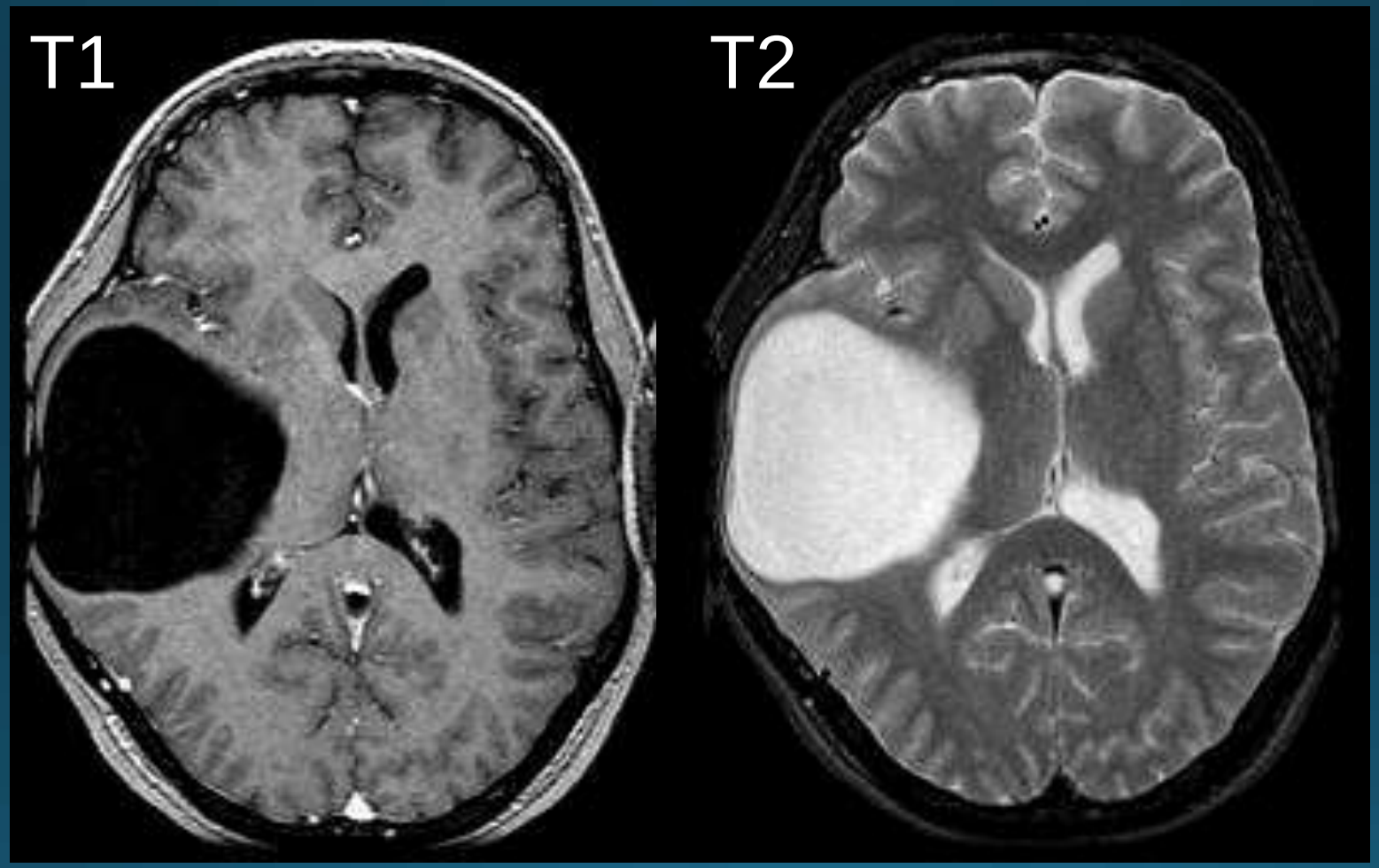
“T1-weighted”



“T2-weighted”

w/ fat suppression

# Magnetic Resonance



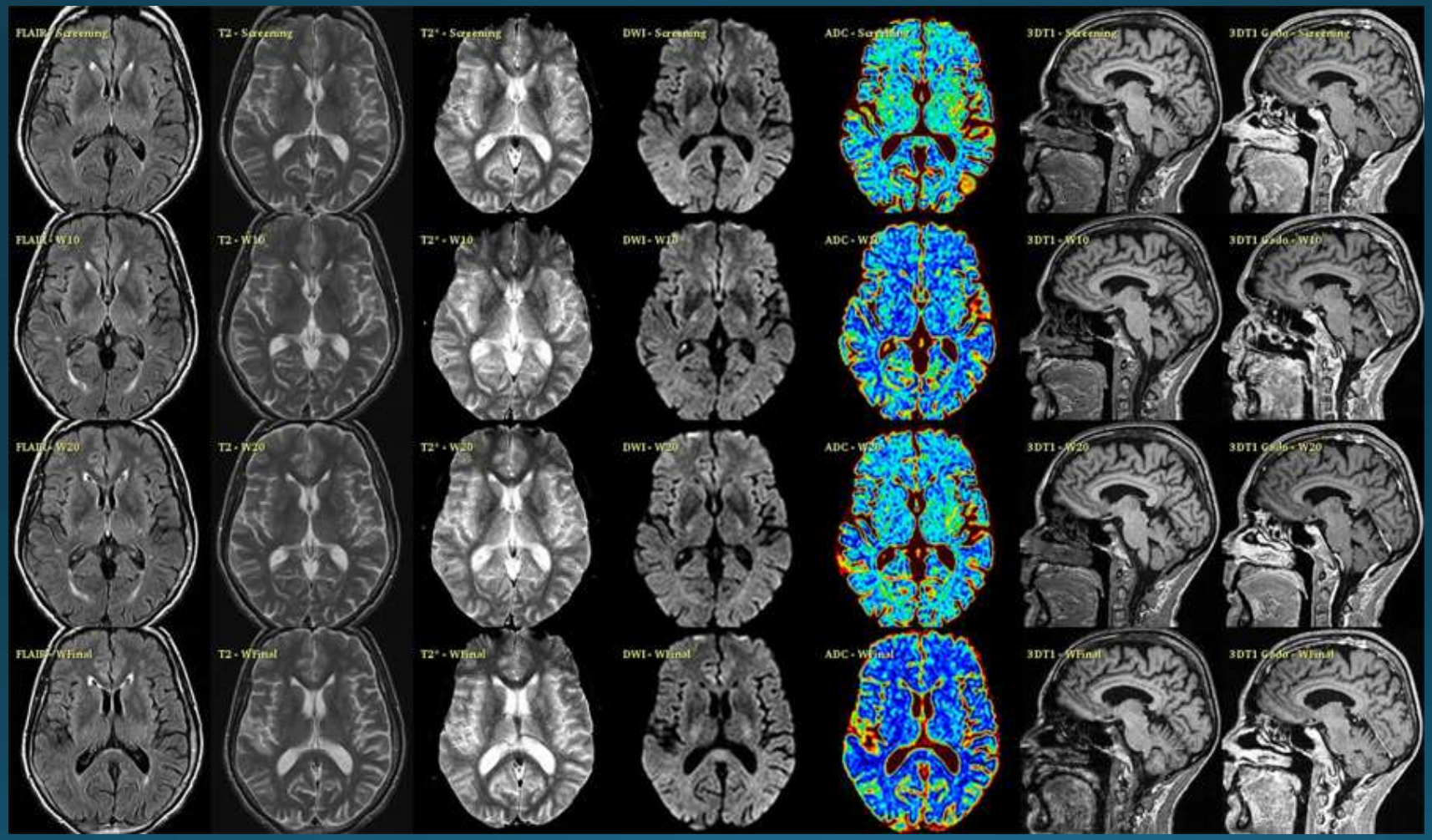

Arachnoid Cyst: water is bright on T2

# MRI Pulse Sequences

- Pulse sequences describe the type of MR scan that is obtained. They are determined by the time used to sample the tissue after the exciting radiowave has been emitted and how quickly a repeat radiowave is used to reexcite the tissue for a subsequent pulse. They are variously described as T1 weighted, T2 weighted, FLAIR, Diffusion etc.

- Pulse Sequences-
  - T1 weighted-- (Fat, Melanin, Hemosiderin, Methemoglobin= bright)
  - T2 weighted-- (Water, Oxyhemoglobin, Hemosiderin= bright)
  - FLAIR-- (Pathology bright, CSF dark)
  - Diffusion Weighted - (recent infarction, bright)

# MRI Types



Flair T2 T2 DWI ADC 3D T1

Diffusion

# Types of MRI Imaging: all valuable

T1: CSF in brain is dark, best anatomic image

- Discriminate lacunes in perivascular spaces
- Discriminate grey from white matter
- Study of brain atrophy

T2: CSF is bright; best for pathology view (i.e. MS)

- Characterizes brain structure
- Differentiate lacunes from WMH & perivascular spaces
- Identification of old infarcts

# Types of Images

- DWI:
  - most sensitive for acute ischemic lesions; positive for up to several weeks after stroke event

- FLAIR: white matter changes
  - Identify WMH
  - Establish cortical or large subcortical infarcts;
  - Differentiate WM lesions from perivascular spaces & lacunes

- GRE: hemosiderin deposits (following hemorrhage)
  - Detection of hemorrhage, microbleeds, siderosis
  - Measurement of intracranial volume

- SPECT: metabolic perfusion

# Types of Images 3

- MRA:
  - Detection of stenosis of vertebral, basilar, internal carotid, MCA, ACA, PCA

- Proton density:
  - Detection of WMH, infarcts, perivascular spaces, other pathologies

# MRI types for research

- fMRI:
  - Measure brain function response to tasks or stimuli or at rest for default mode networks
- DTI (6-gradient direction diffusion encoding):
  - Diagnose recent infarct
  - Measurement of me and diffusivity and fractional anisotropy
- DTI (more than 6-gradient direction):
  - Refined & superior quantitative measurements of microscopic tissue changes
- SWI:
  - Very sensitive to hemosiderin
  - Measurement of intracranial volume
- Isotropic volumetric T2-weighted:
  - Fine detail of perivascular spaces
- Isotropic volumetric 3D T1-weighted (MP-Rage):
  - Improved global and regional volumetric brain measurements

# MRI types for research

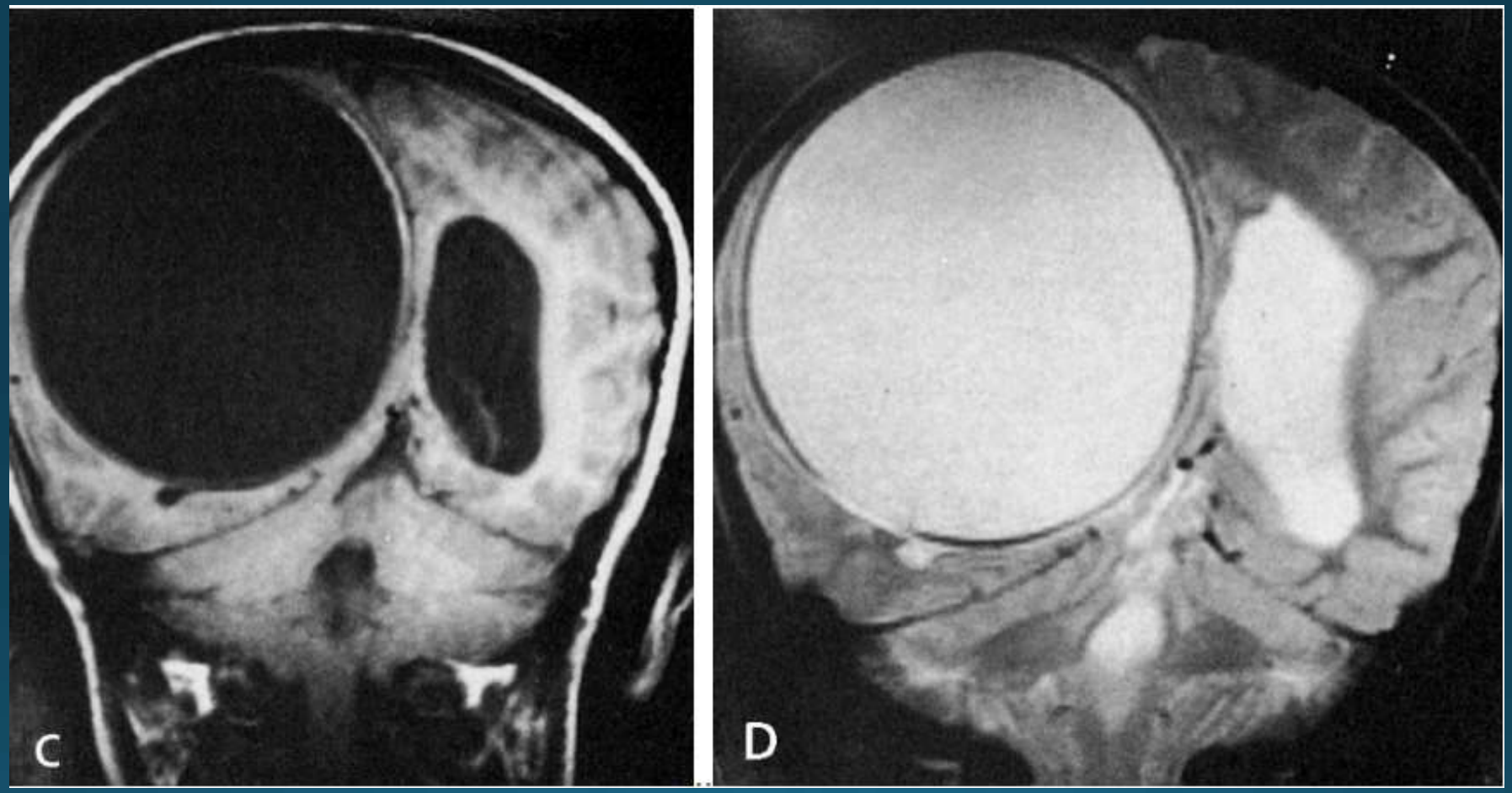
- Isotropic volumetric FLAIR:
  - Identification of WMH
  - Imaging cortical or subcortical infarcts
- MTR:
  - Detection demyelination and axonal loss
- TI mapping:
  - Measure water content of tissue
- Permeability imaging:
  - Estimate permeability of the blood-brain barrier (BBB)
- ASL perfusion imaging:
  - Measure permeability of the BBB

# MRI types for research

- Perfusion imaging (DCE or DSC):
  - Semi-quantitatively measure blood perfusion in tissue
- QSM:
  - Provide quantitative measures of susceptibility changes, independent of scanner or acquisition variables

- Microatheroma and arteriolar imaging:
  - Visualize perforating arteriolar (smallest arteries) anatomy and atheroma (artery wall degeneration)

# T1 & T2: Abscess

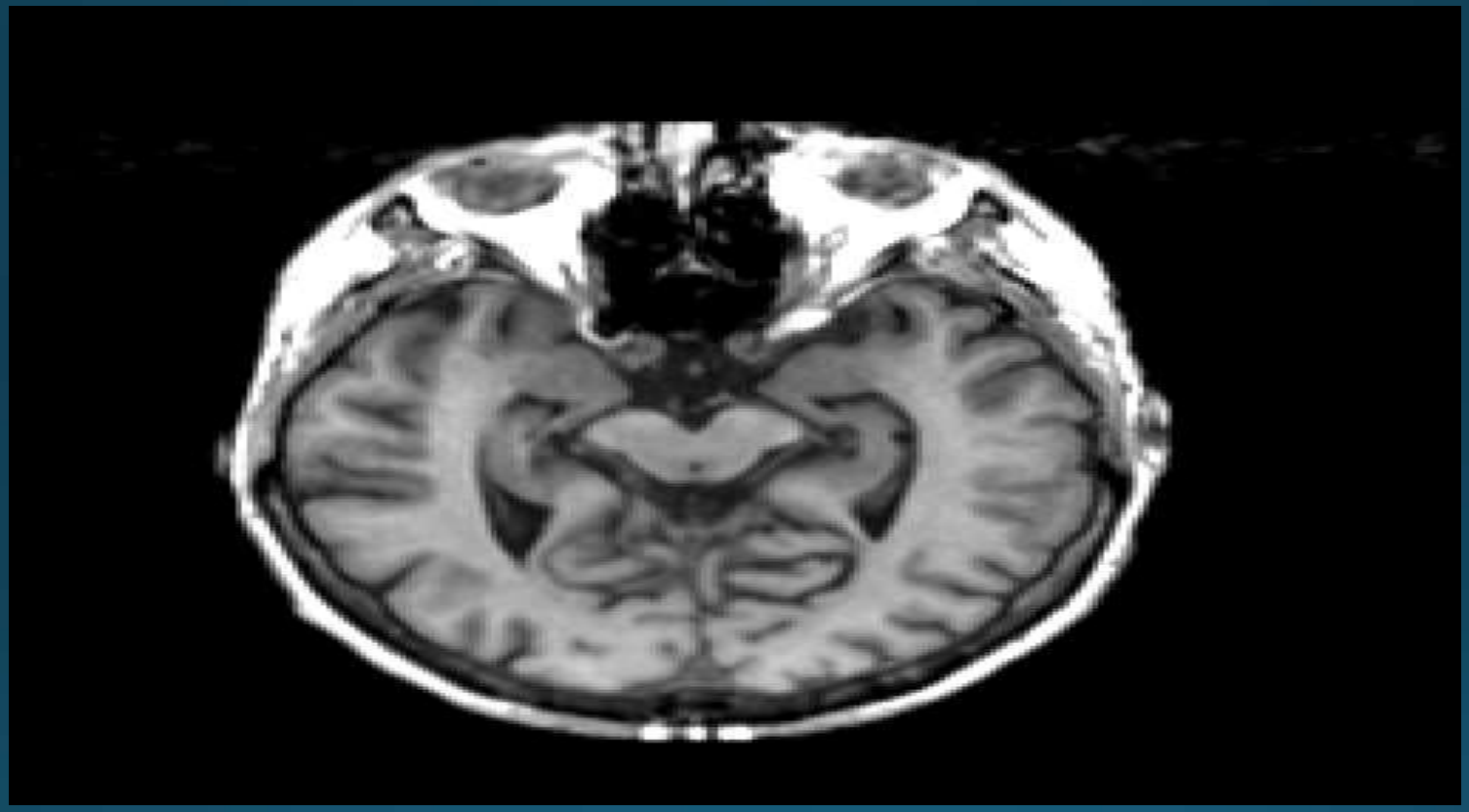



(**C**) MRI T1-weighted and (**D**) MRI T2-weighted; coronal image

CSF = Dark

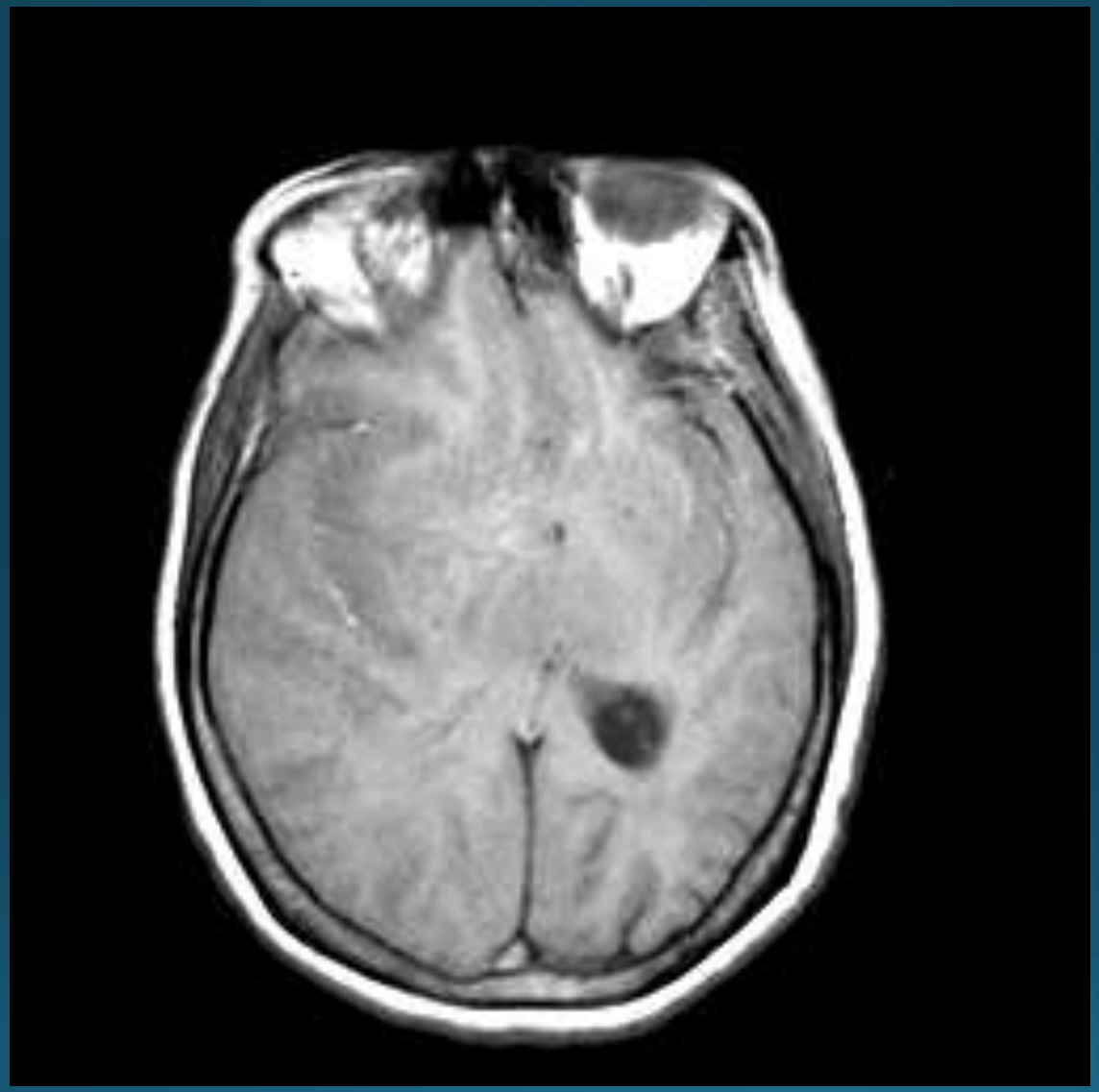
CSF= Bright

# MRI-T1 (CSF = dark): Best anatomic image

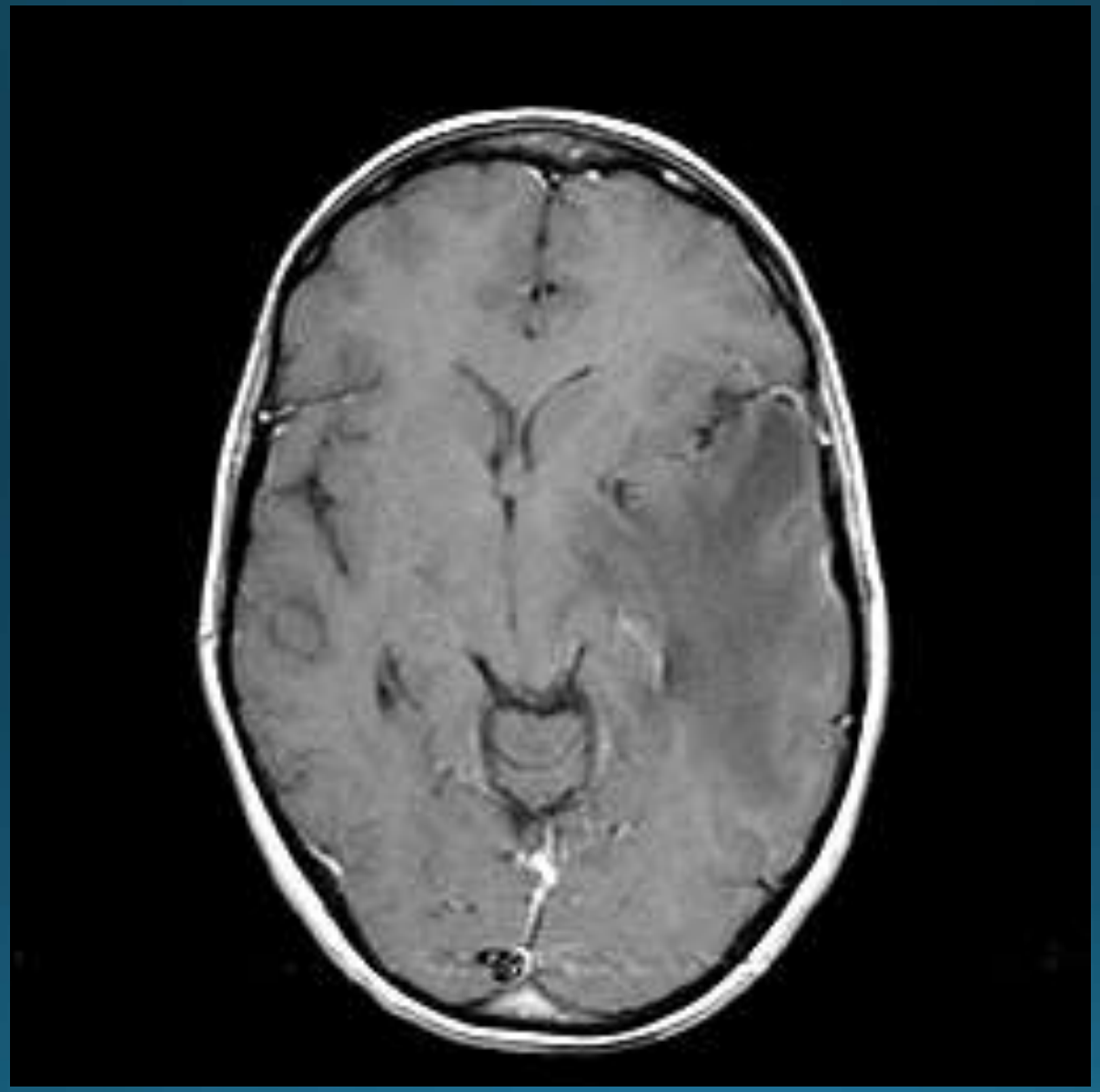


T1: cerebrospinal fluid (CSF) has a low signal intensity in relation to brain tissue; best anatomic image; least sensitive to pathology

# T1- Infarct

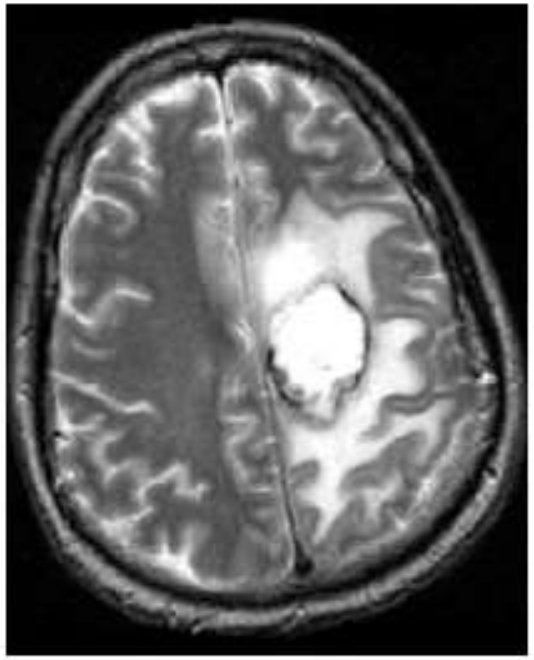


# T1- Tumor

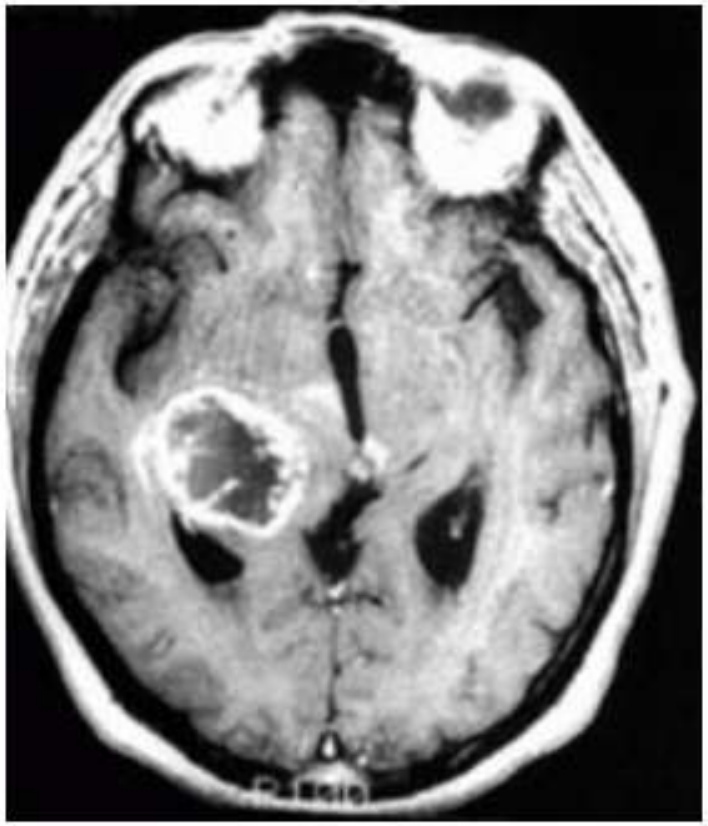


# T2 Weighted MRI: best for pathology

- Less distinct boundaries between white and grey matter
- Best for displaying pathology
- Pathology appears bright, reflecting water/edema
- Gray matter medium gray, white matter dark grey, CSF and water white

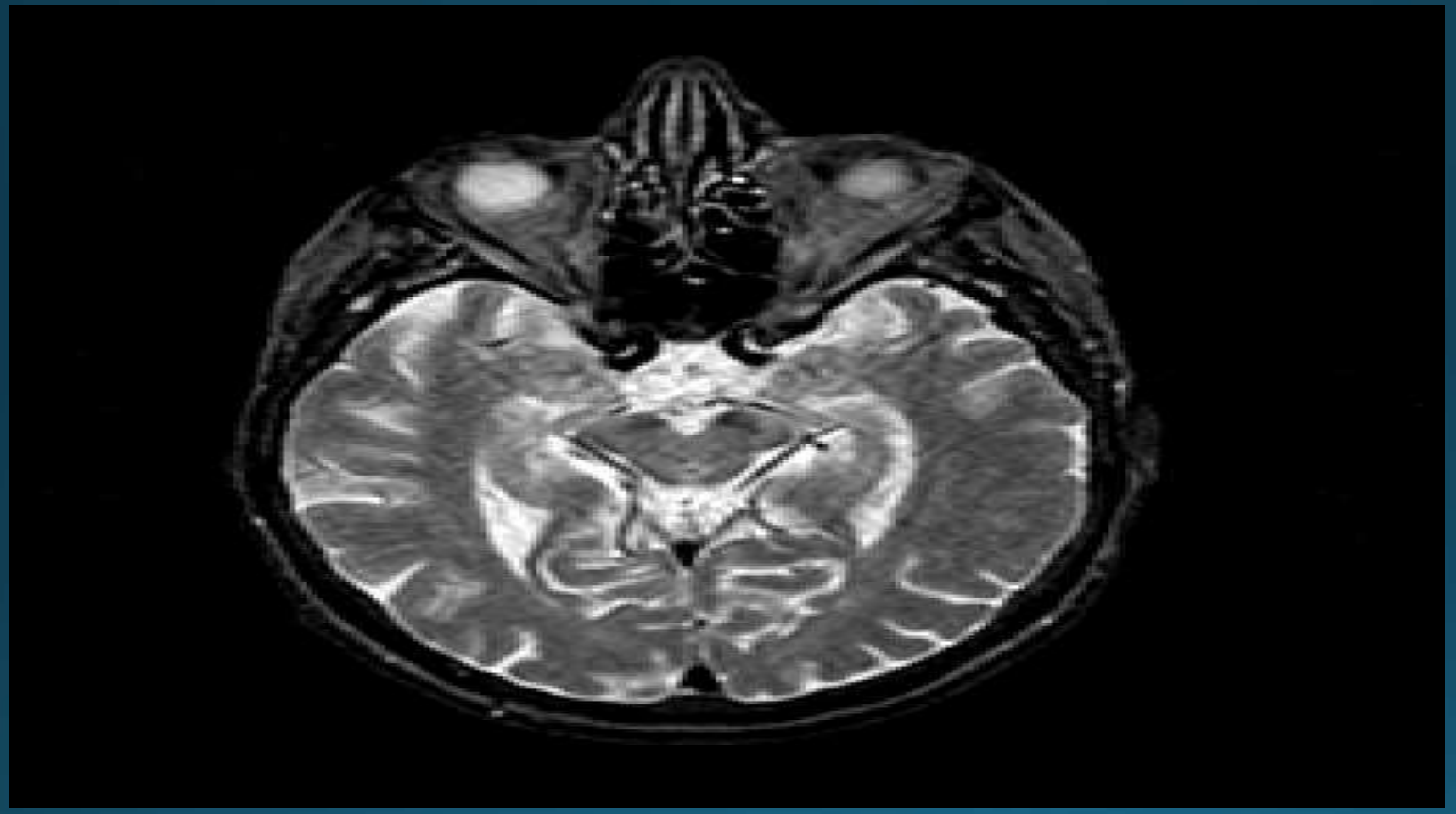


T2 weighted MRI



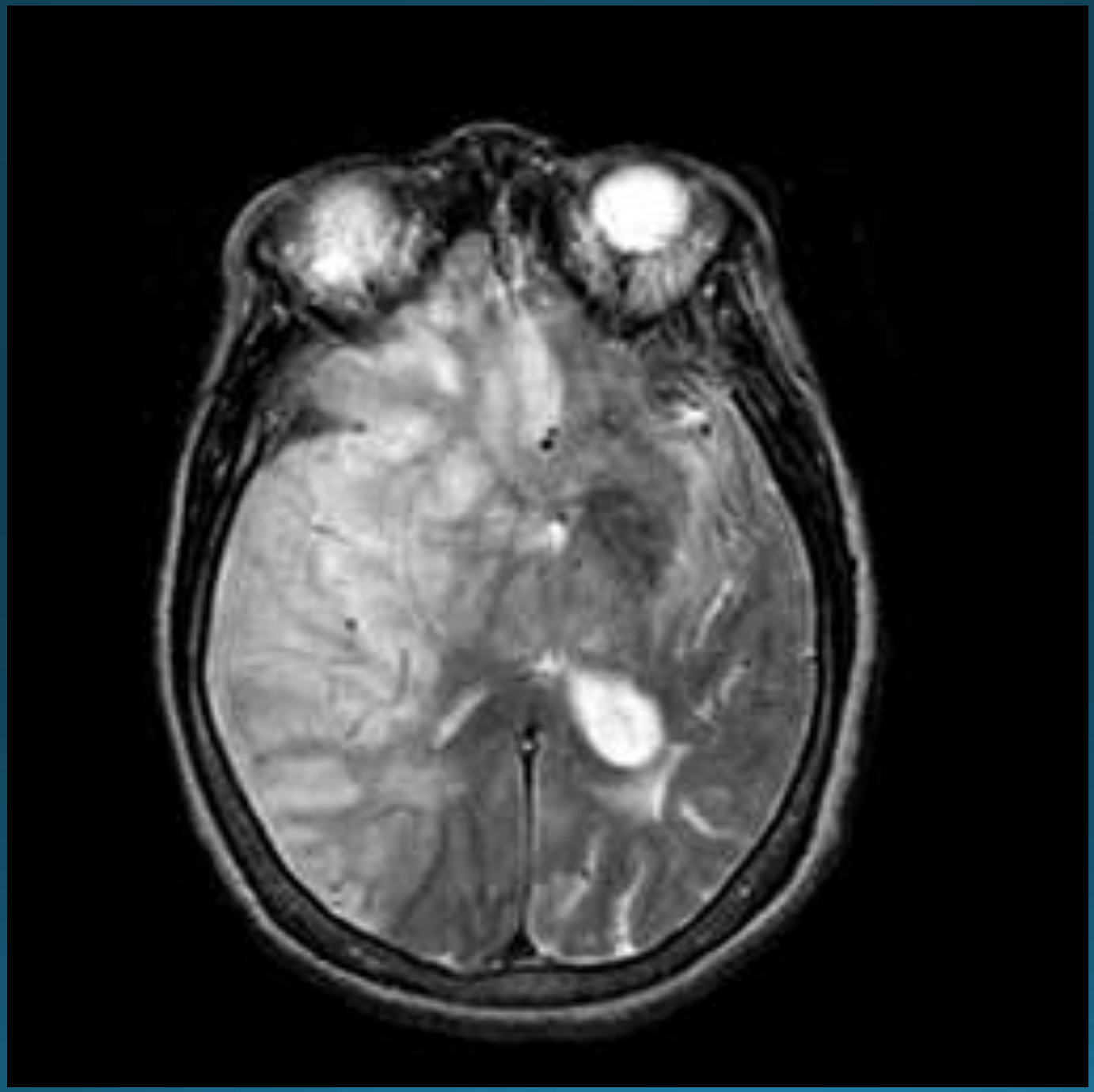
T1 weighted MRI after Gadolinium infusion

# MRI-T2 (CSF=bright)

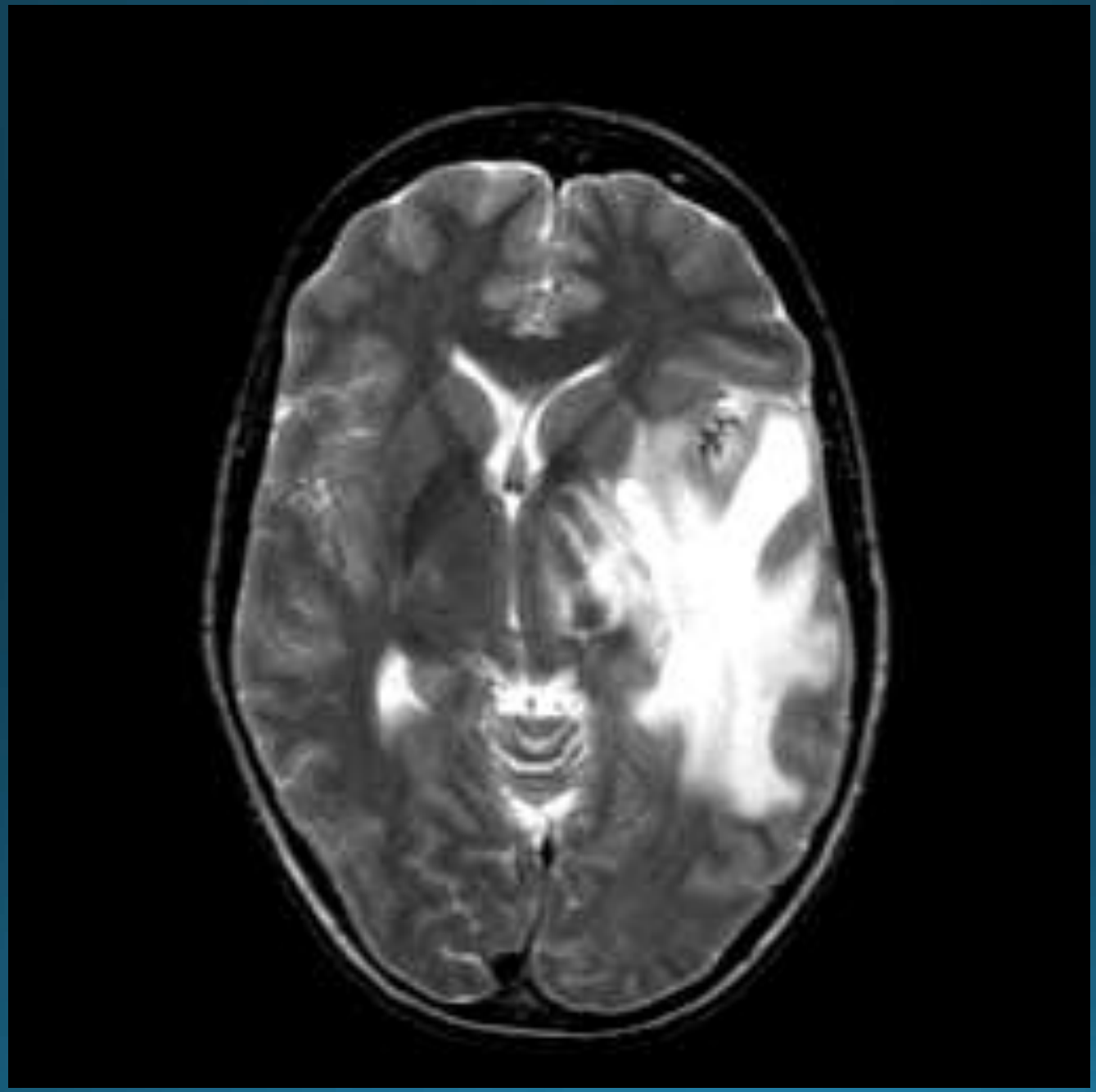


T2: CSF has a high signal intensity in relation to brain tissue;
Water content highlighted; bright is highest water content

# T2- Infarct



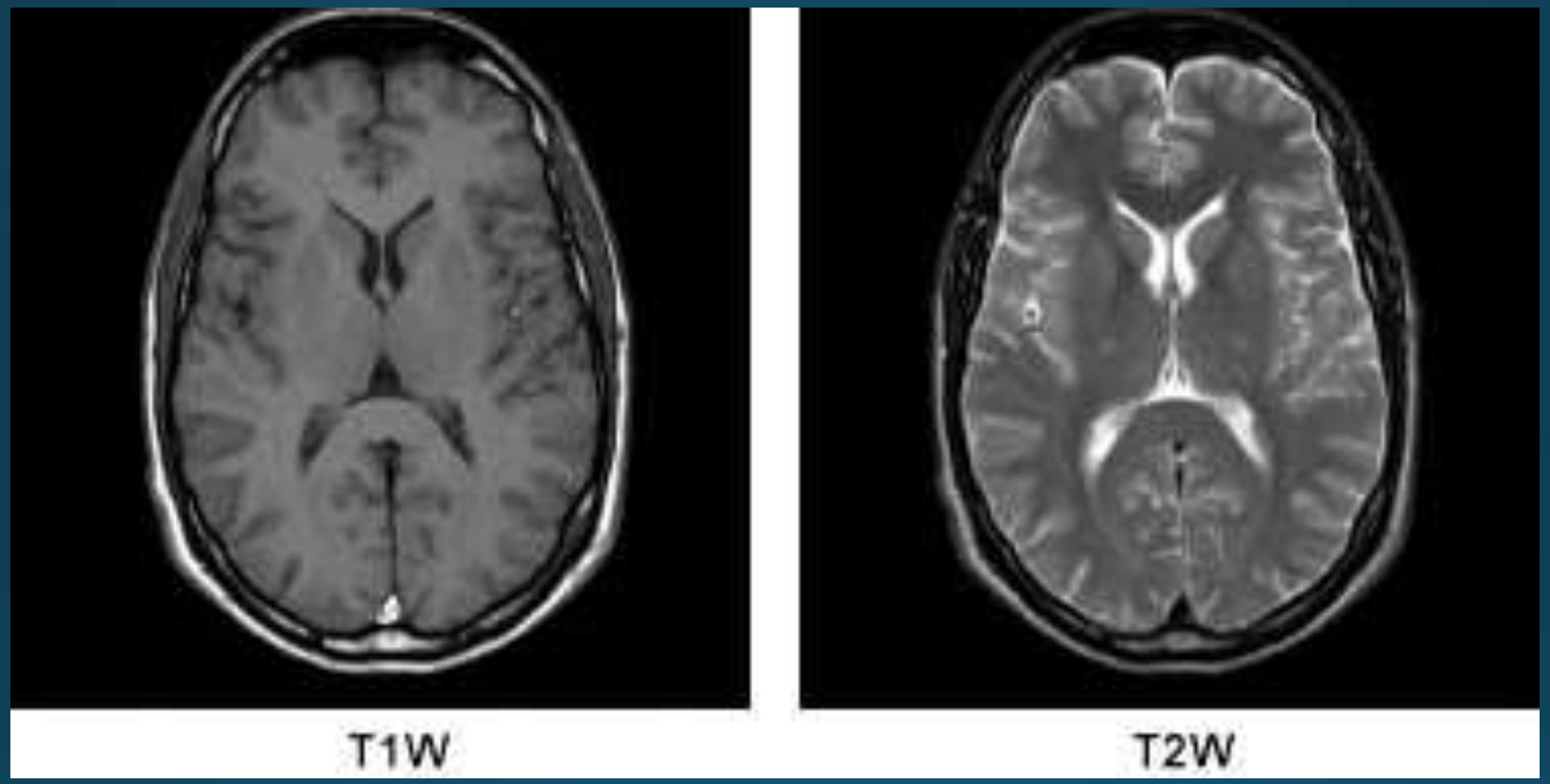
# T2- Tumor



Take home message:

*On T1 weighted images, tissues with SHORTER T1 times are brighter; better anatomy

*On T2 weighted images, tissues with LONGER T2 times are brighter; better pathology view

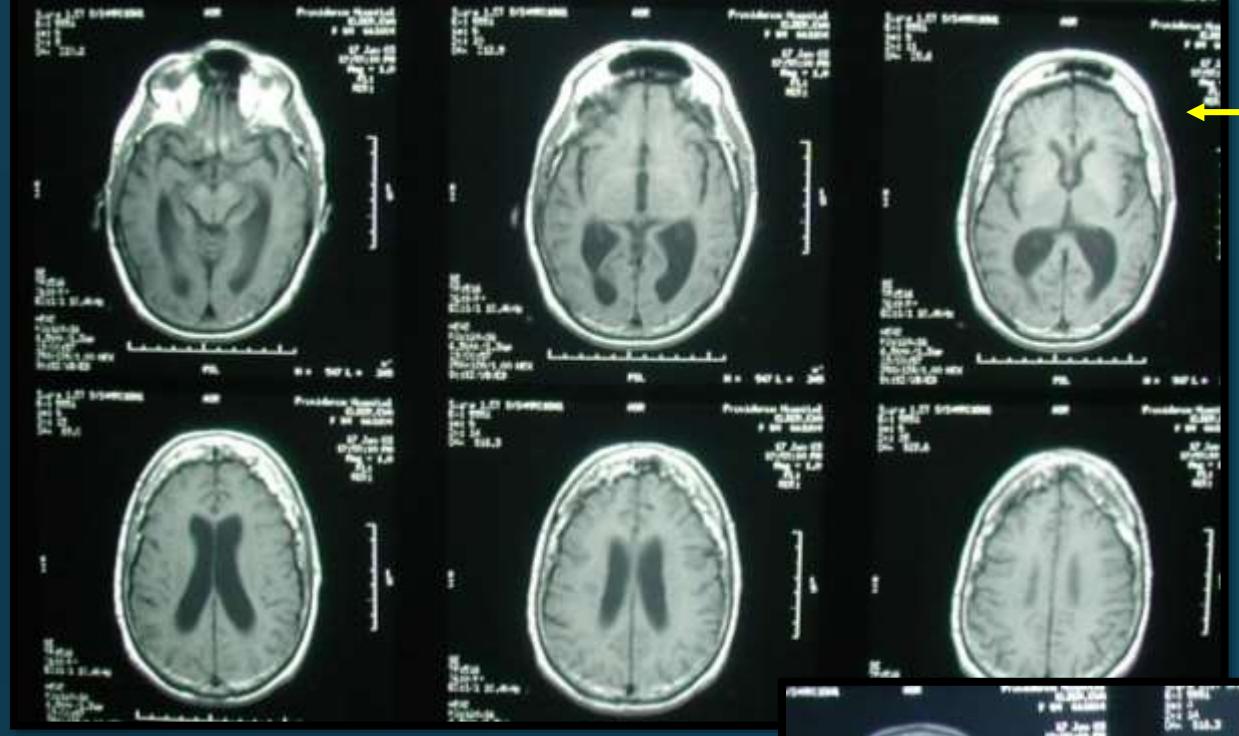



On a T1 weighted image, white matter is brighter than gray matter

On a T2 weighted image, white matter is darker than gray matter.

# MRI Flow cart

- CSF
  - Bright CSF = T2
  - Dark CSF = T1
    - Low Resolution =  DWI
    - High Resolution =
      - Gray matter darker than White matter  = T1
      - GM lighter than WM = Flair



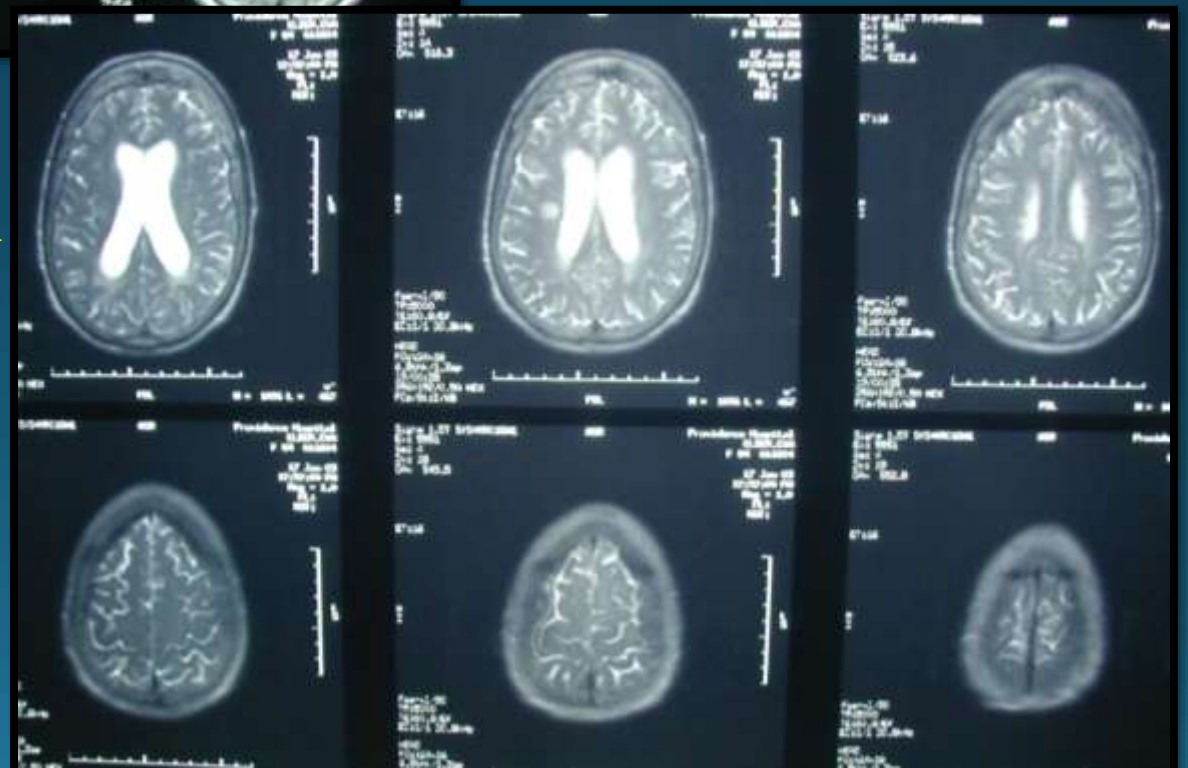
# T1 SCAN

Anatomic structures

Fat = bright

Water = dark

# T2 SCAN



Water weighted sequence

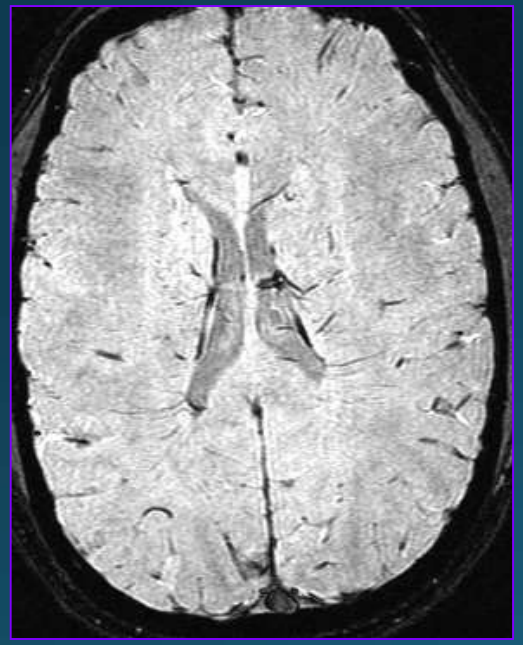
Water = bright

Fat = relatively hypo intense

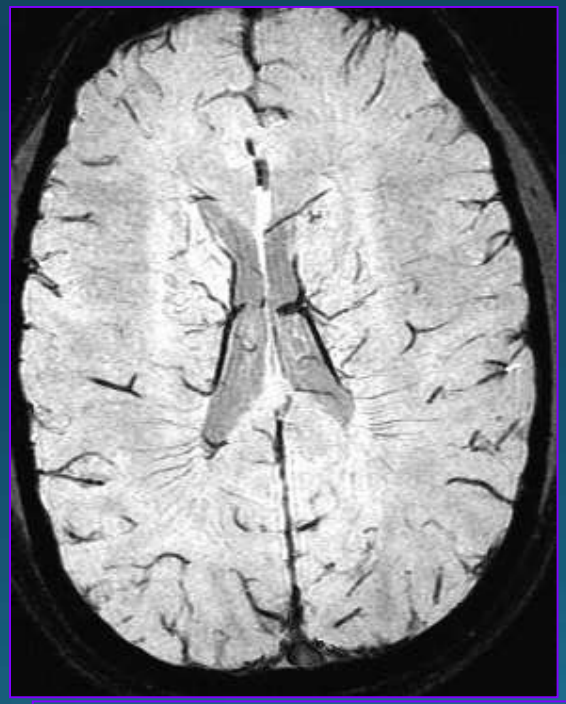
Good for seeing pathology

# T2*-Weighted Images: venous blood darker

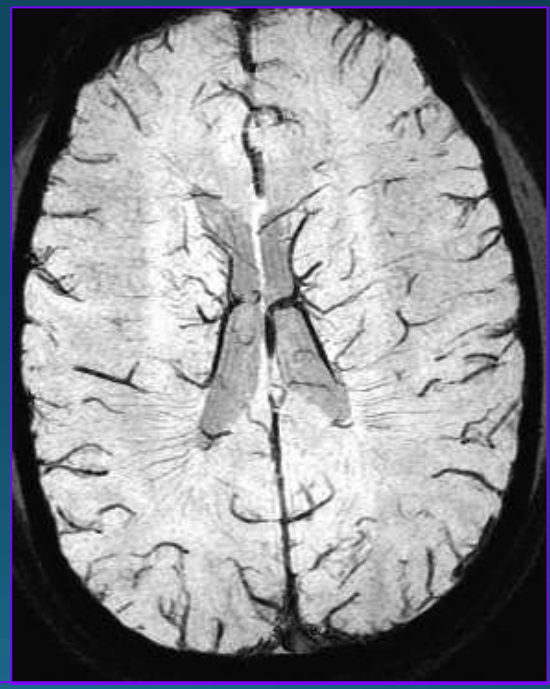
- Designed to make venous blood (with lots of deoxy-hemoglobin) darker than normal tissue = *venography*



Output image



minIP ±1 slice

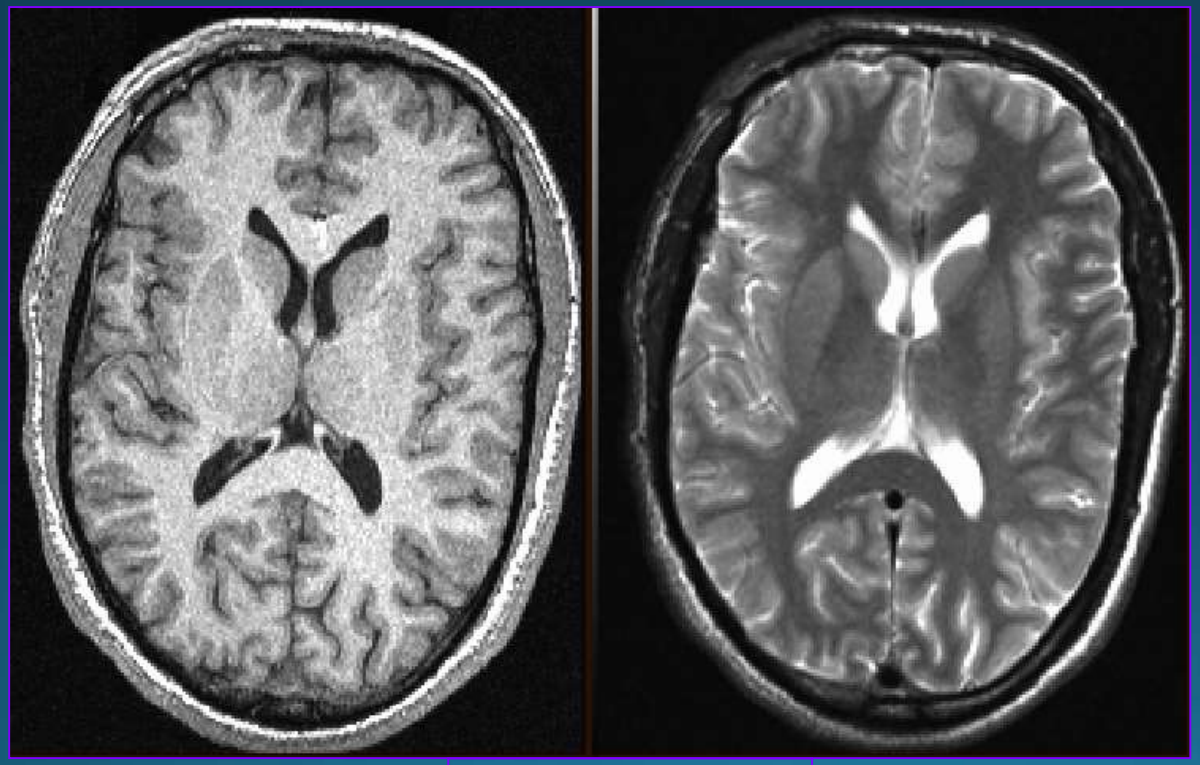


minIP ±2 slices

Images post-processed to enhance small effects

# T2-Weighted Images

- Often better than T1-weighting in detecting tumors and infarcts (usually radiologists look at both types of scans)



Same subject

# FLAIR: Fluid Attenuated Inversion Recovery

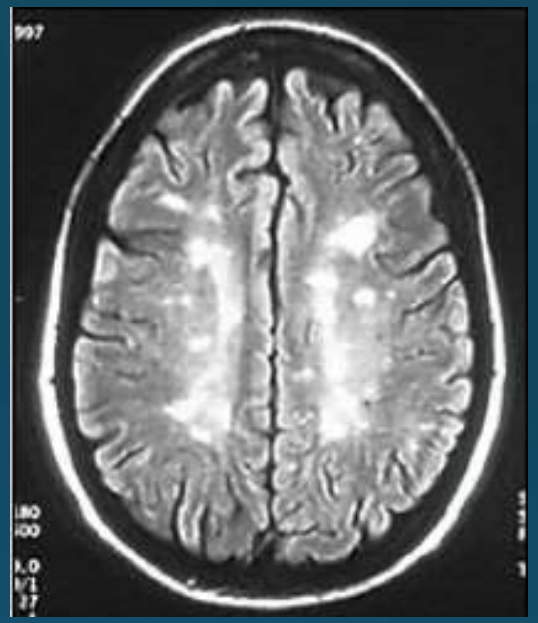
- T1 - This image weighting is useful for assessing the cerebral cortex, identifying fatty tissue, and for post-contrast imaging

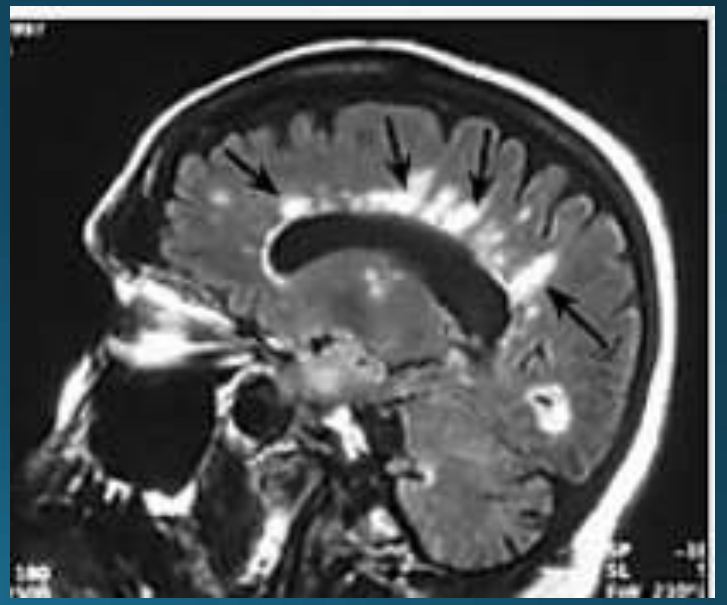
- T2 - This image weighting is useful for detecting edema, and revealing white matter lesions.

- FLAIR - an inversion-recovery pulse sequence used to nullify the signal from fluids. Used to suppress CSF so as to bring out periventricular hyperintense lesions, such as multiple sclerosis (MS) plaques. Better contrast than above T1 & T2.

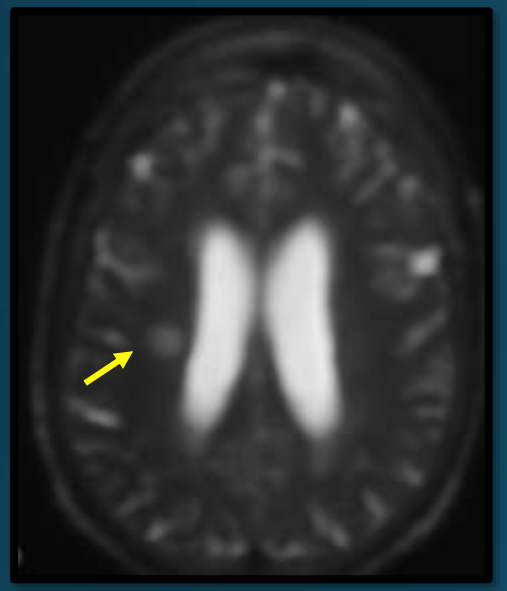
# Fluid Attenuated Inversion Recovery (FLAIR)

- Variant of T2 with intense CSF signal nullified
- Improved identification of subtle lesions; ideal for MS
- Method which provides greater visibility of white matter abnormalities
- Easier to see pathology adjacent CSF-filled spaces

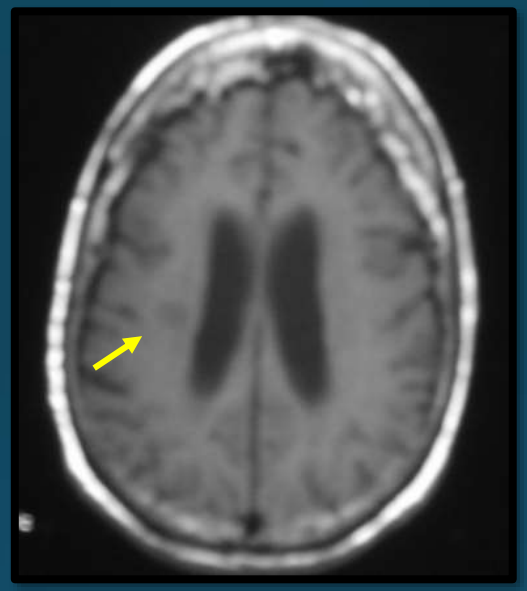




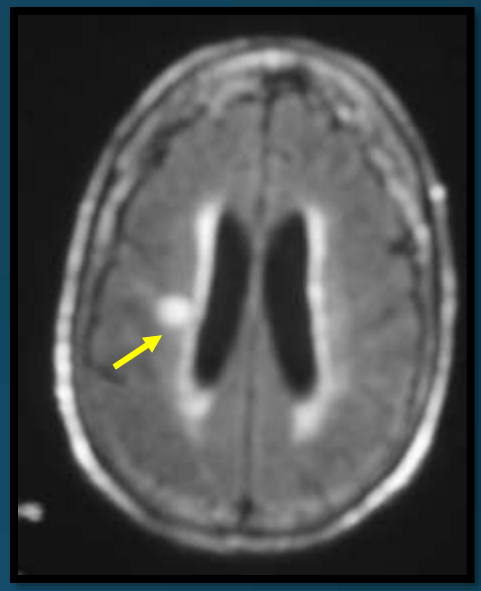
# MRI Findings of acute ischemic stroke



T1 (hypo intense)



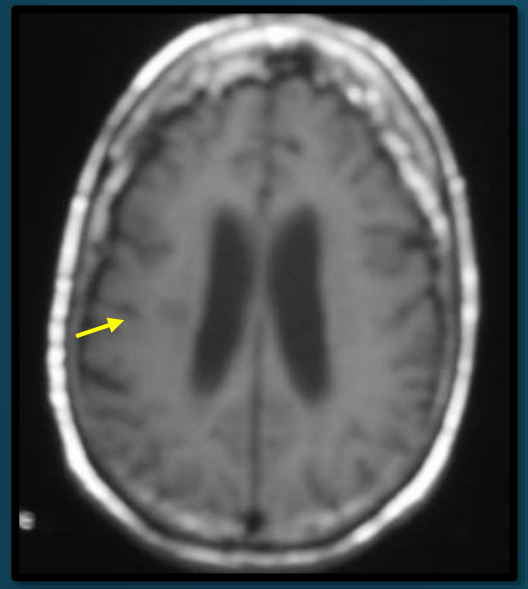
T2 (hyper intense)



FLAIR (hyper intense)

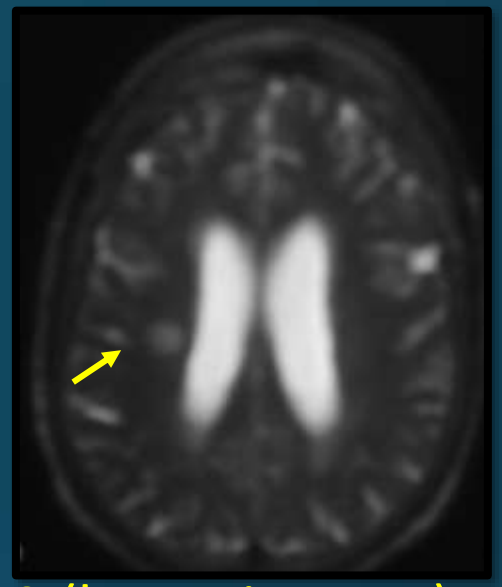
**FLAIR scans are T2 scans with the free water signal nulled;** so that the only bright T2 signal comes from edema. This makes visualization of pathology easier.

# MRI findings of acute stroke

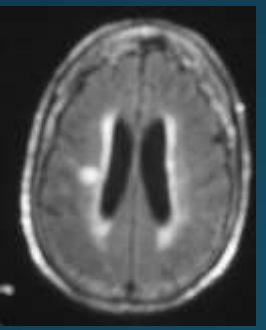


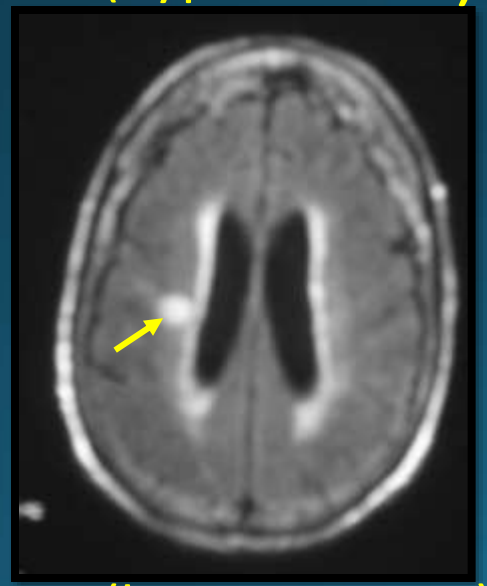
T1 (hypo intense)

Same pt.



T2 (hyper intense)

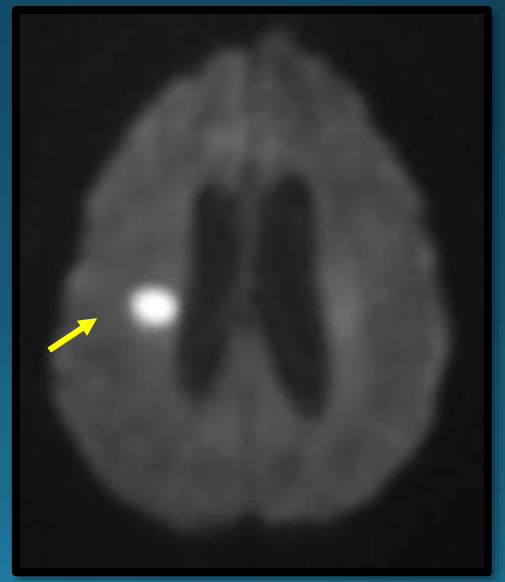




FLAIR (hyper intense)

T2 weighted scan and FLAIR will not separate acute infarction from chronic infarction.

Diffusion scan helps in this.



Diffusion (hyper intense)

# Microvascular ischemic disease

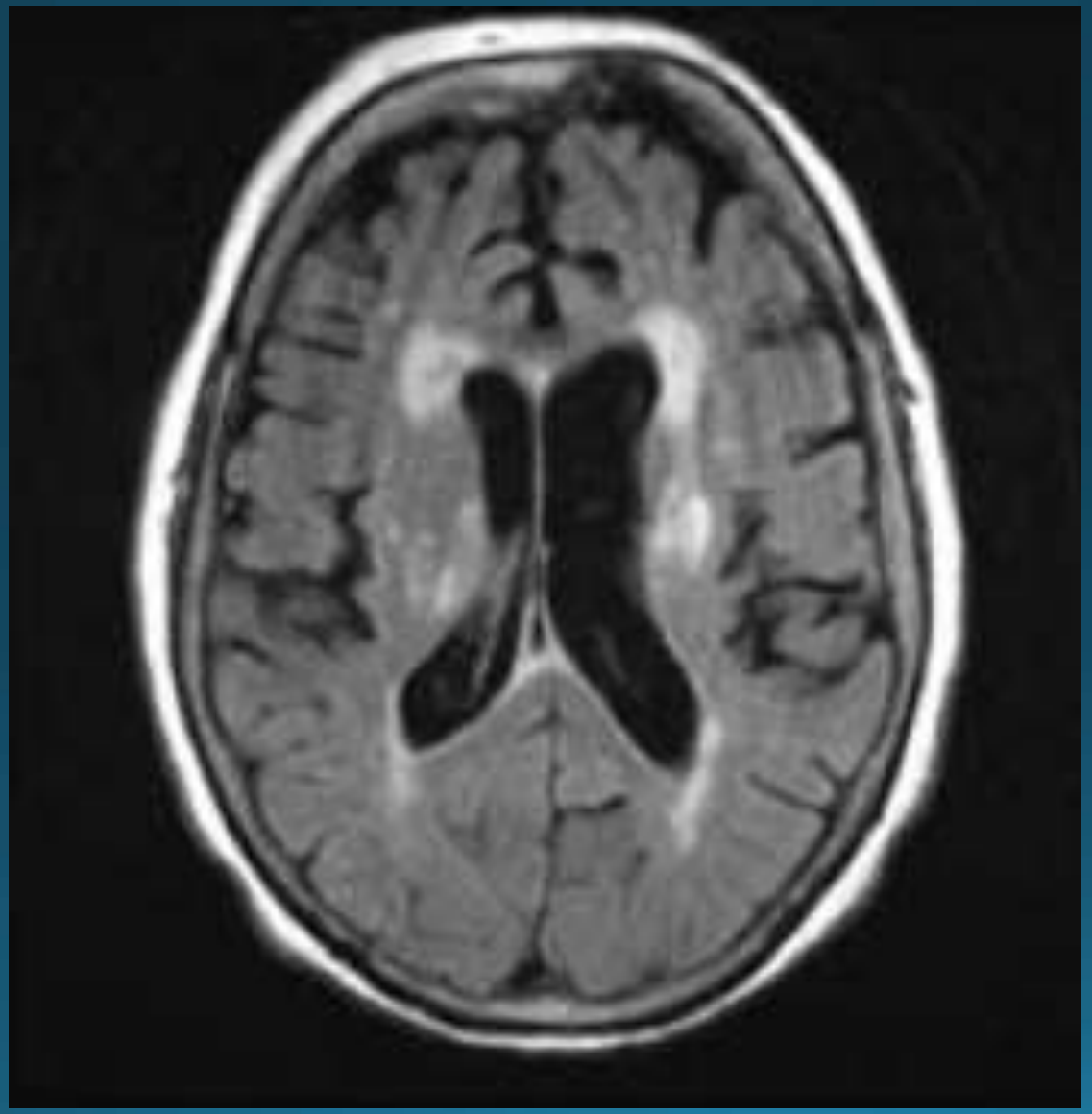
- Common in elderly: may or may not correlate with neurological deficits; Part of normal aging?
- Often read by radiologist as “normal MRI” “age related”, when NP data indicates significant NP deficits

- Due to Hypertension, diabetes
- Patchy, multifocal, periventicular and deep white matter (Hyperintensities, UBOs)
  Basal ganglia

- When extensive, some correlation between white matter ischemic disease and dementia (Binswanger encephalopathy)

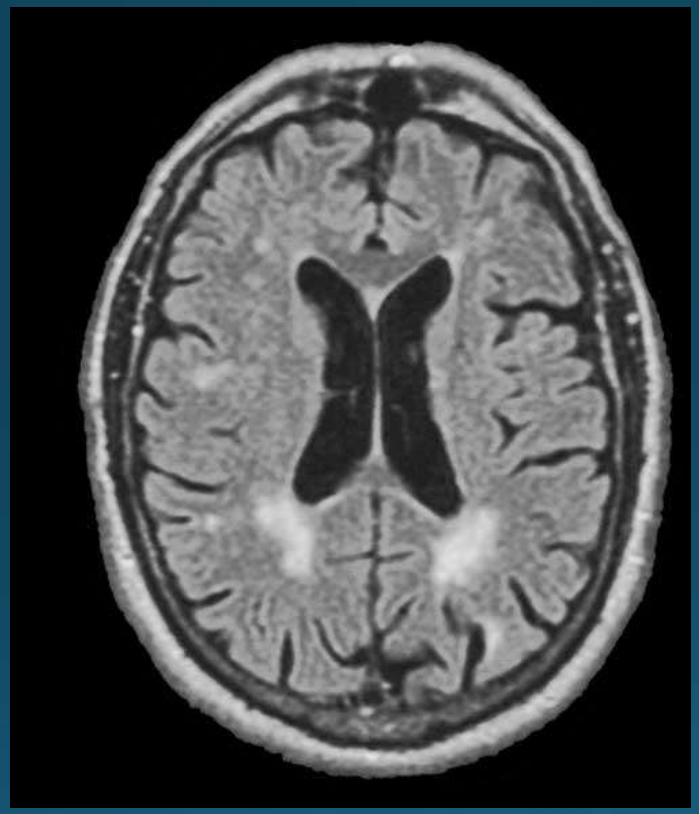
- Lothian Study: correlation with cortisol level and stress

# Microvascular ischemic disease: UBOs



# Periventricular white matter lesions

Periventricular: immediately to the side of the two lateral ventricles

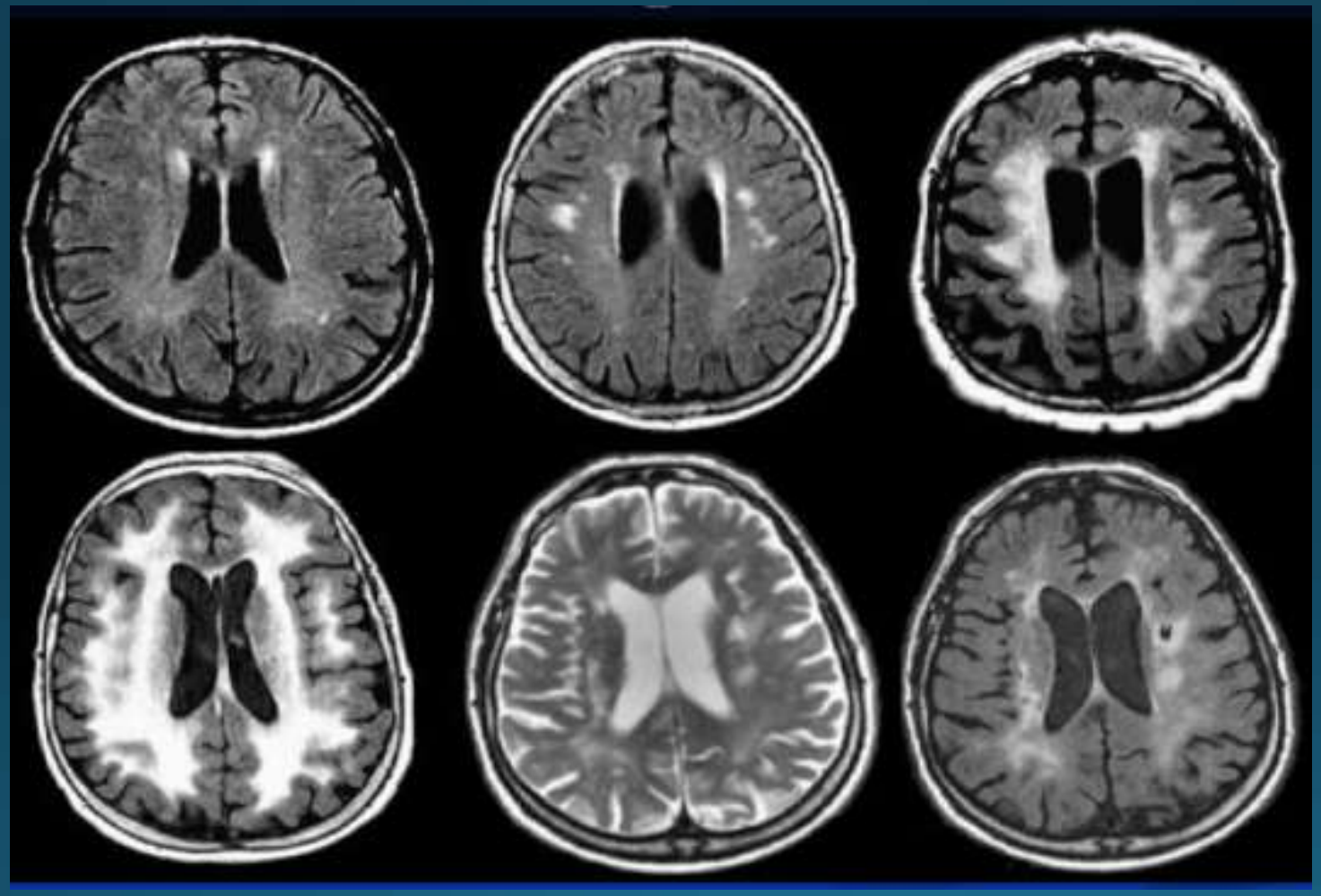


Most common cause of periventricular white matter changes is normal aging (that is not associated with a disease process?)

# MRI: Leukoaraiosis = white matter hyperintensities (WMHs)

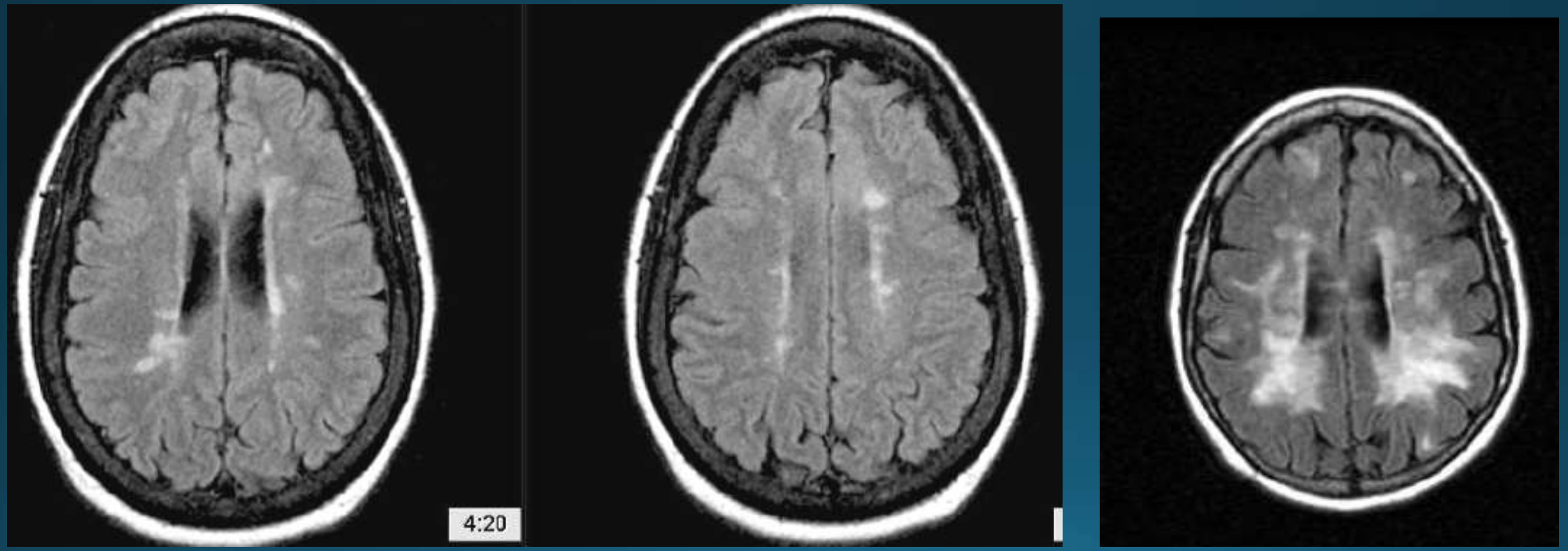
- Diffuse UBO in periventricular, centrum semiovale, and subcortical areas
- Leukoaraiosis: patchy or diffuse WM hyperintensities on T2
- Normal leukoaraiosis: pencil-thin line periventricularly, rounded foci at angles of frontal or occipital horns
- Pathological leukoaraiosis: intense halo periventricularly, patchy distribution, irregular margins, bilateral; lesions >2x2mm

# Spectrum of Small Vessel Disease

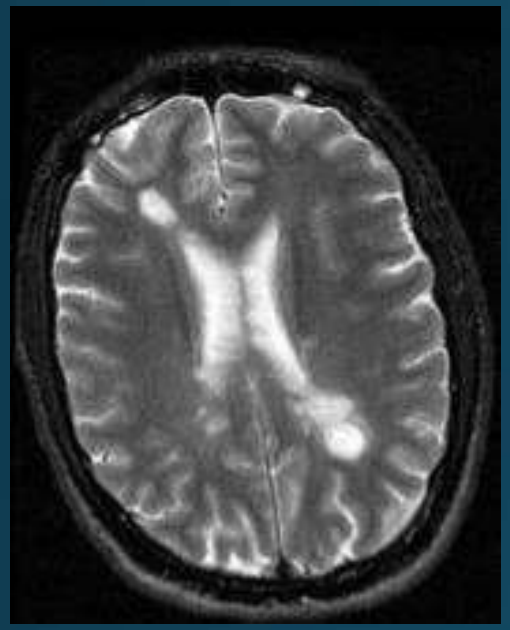


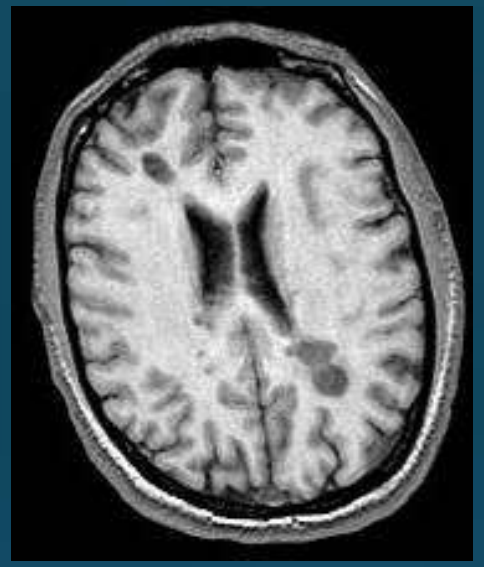
Ranging from punctate loci (upper left) to extensive abnormalities (lower left) & lacunar infarcts (lower right)

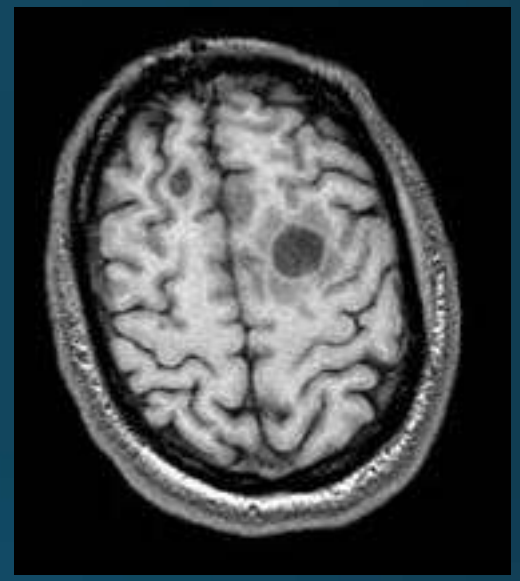
# Multiple Sclerosis: lesions in space and time

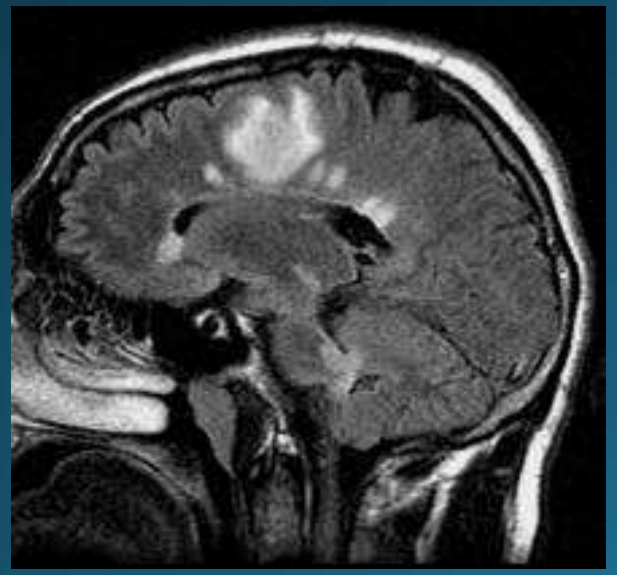


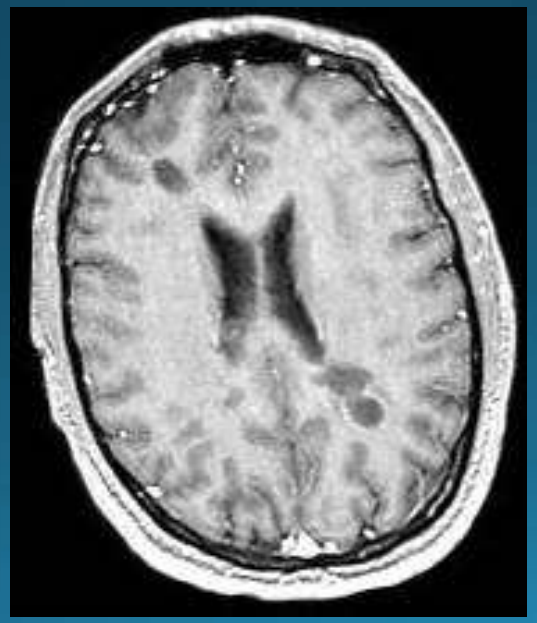
# Multiple Sclerosis

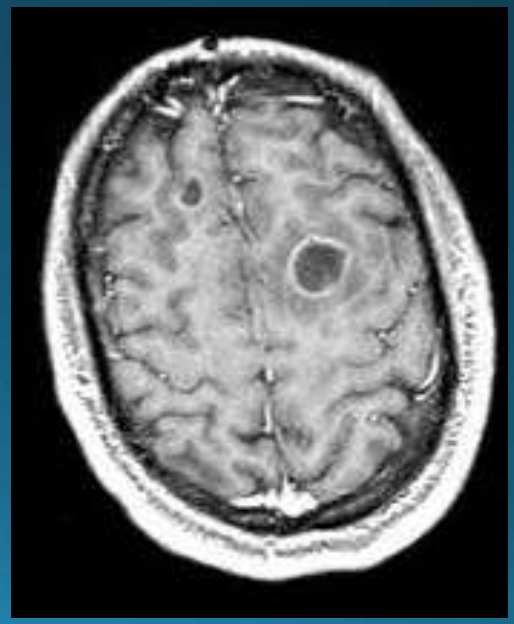




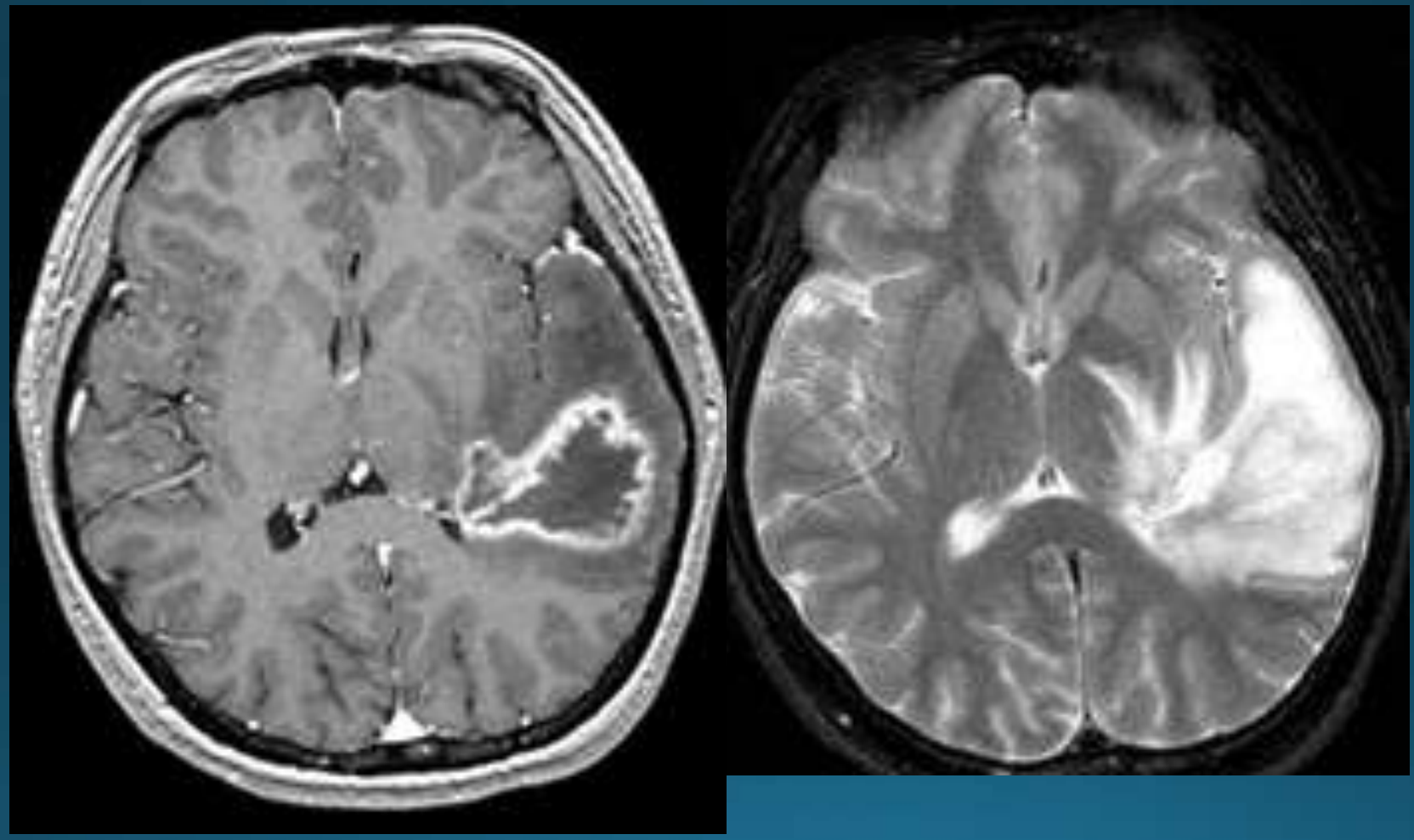






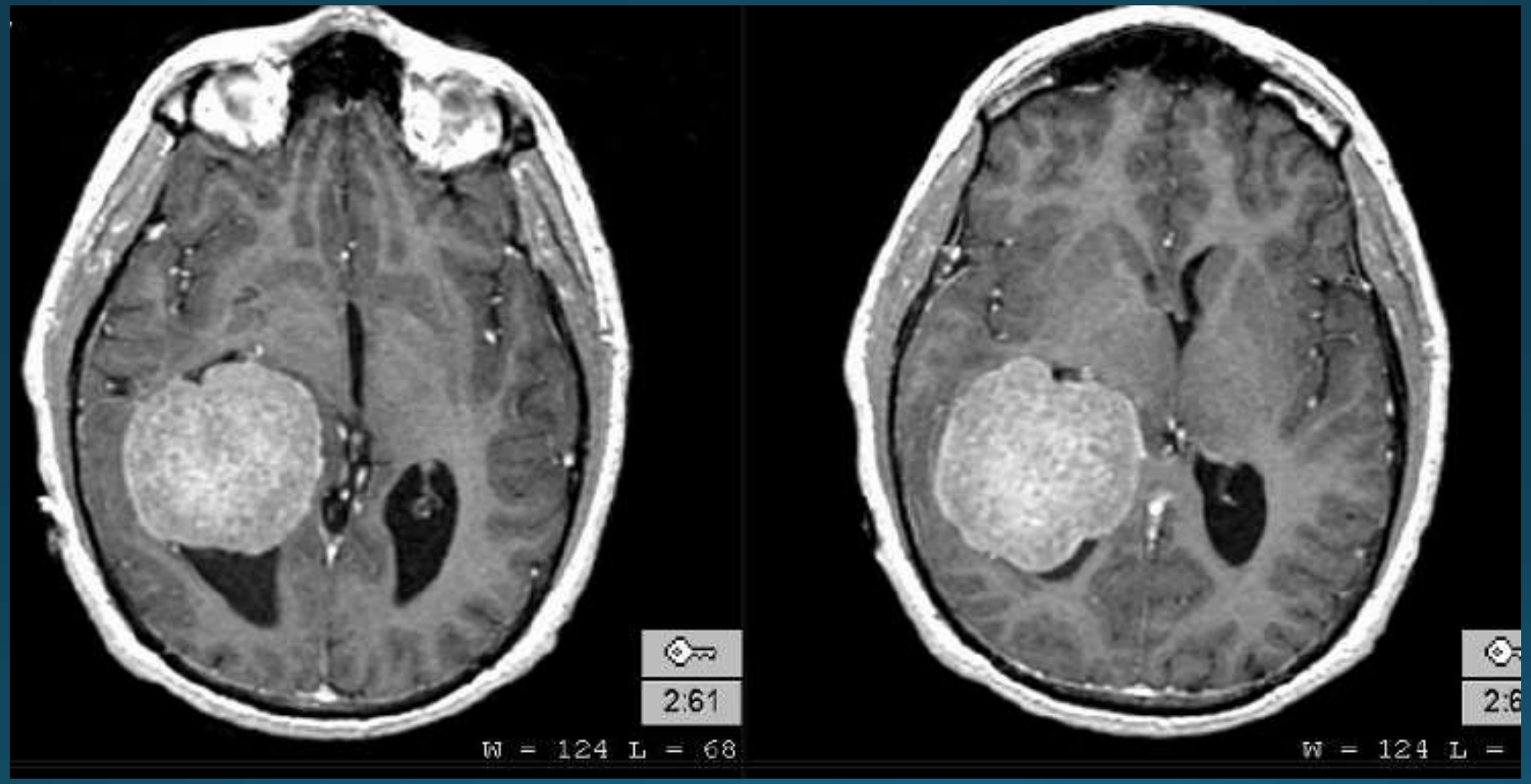


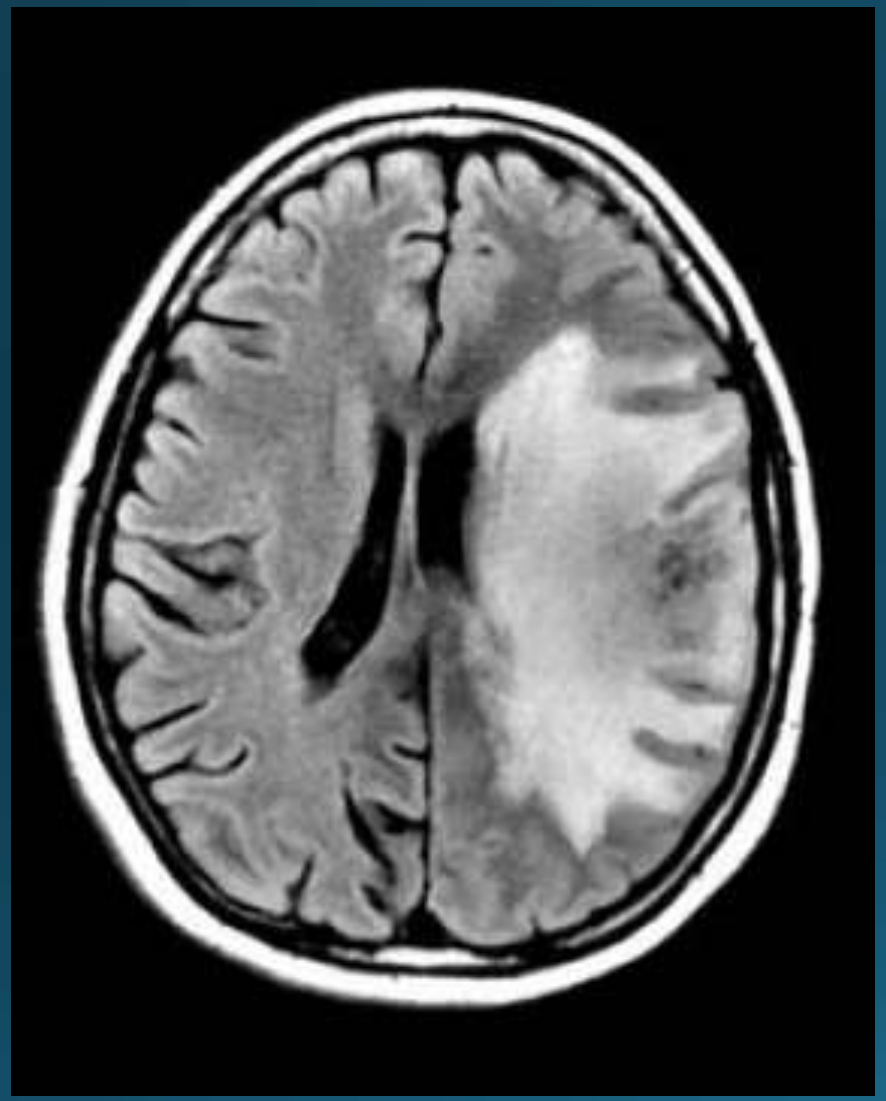
# Tumefactive MS

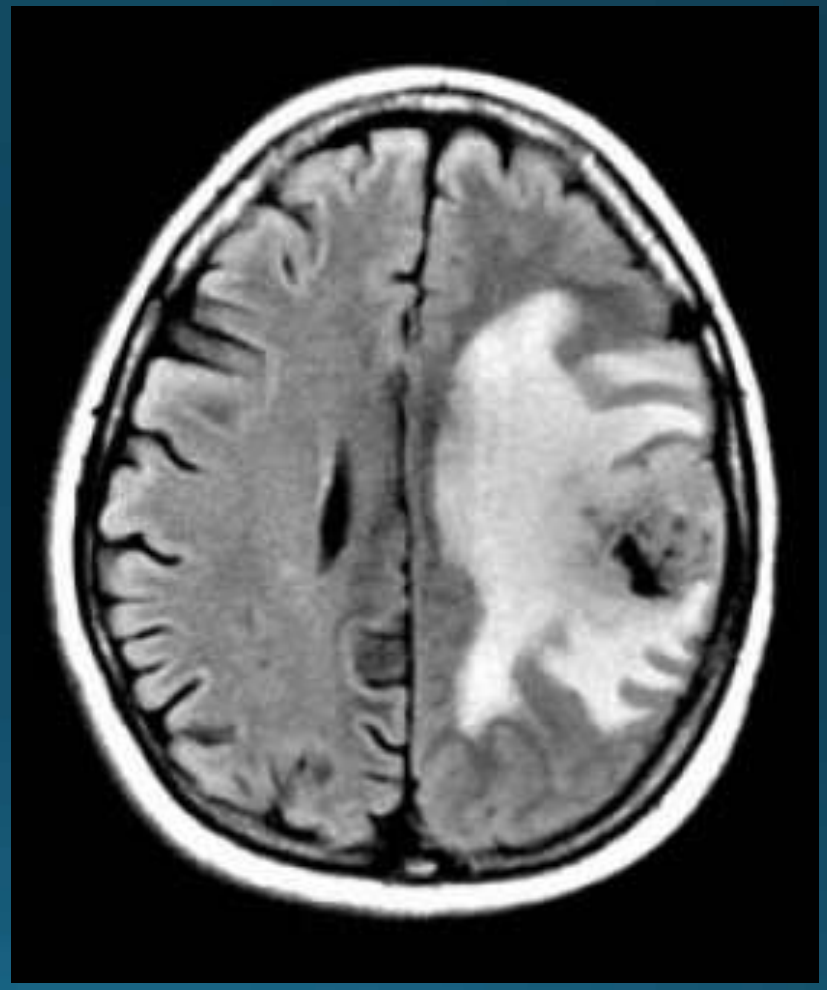


Locally aggressive form of demyelination

# Meningioma

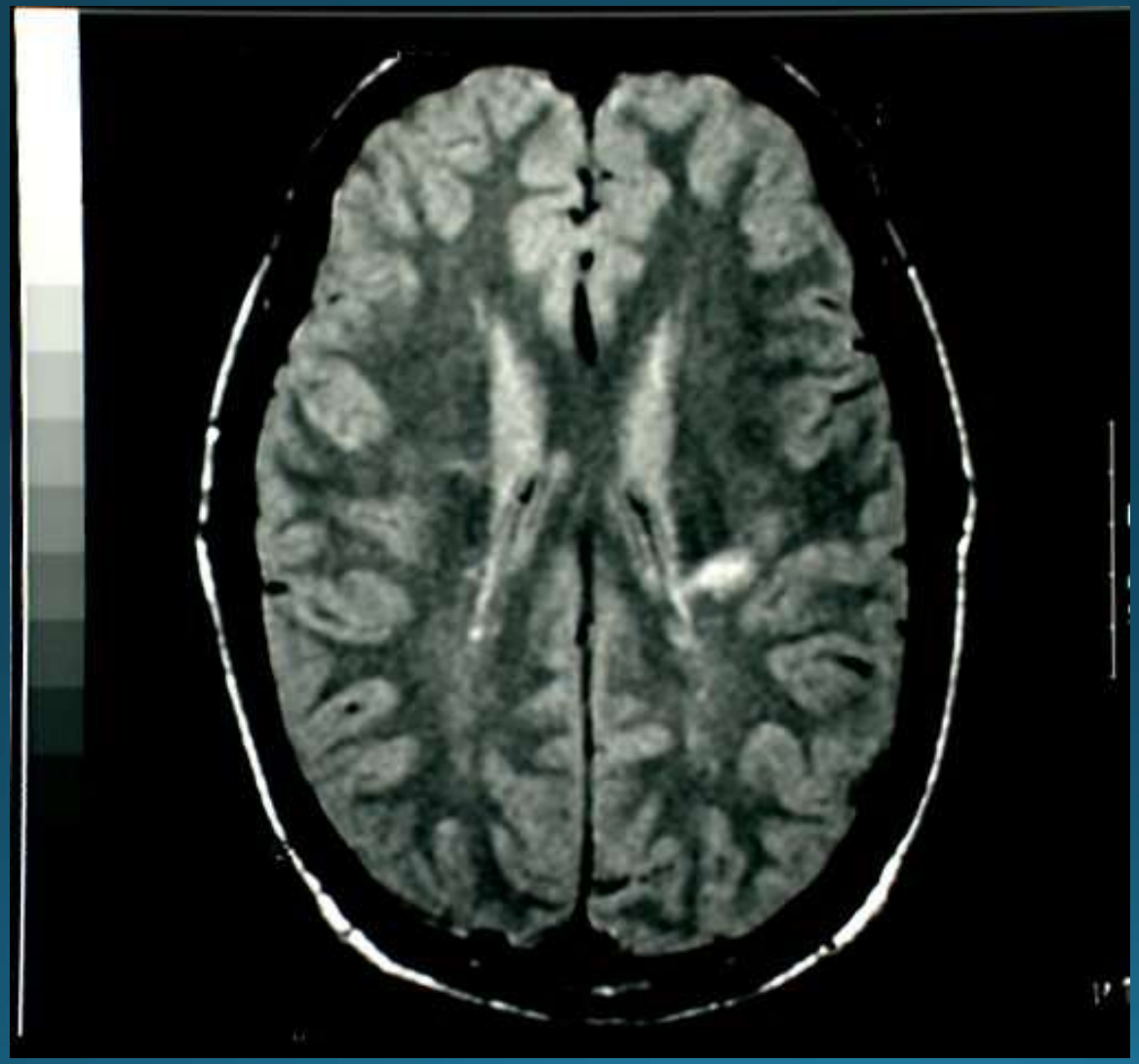




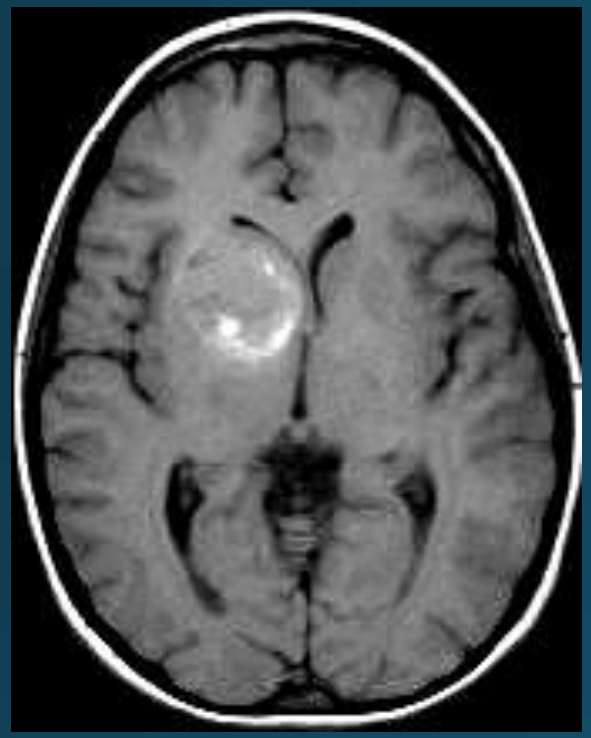


Glioblastoma Multiforma

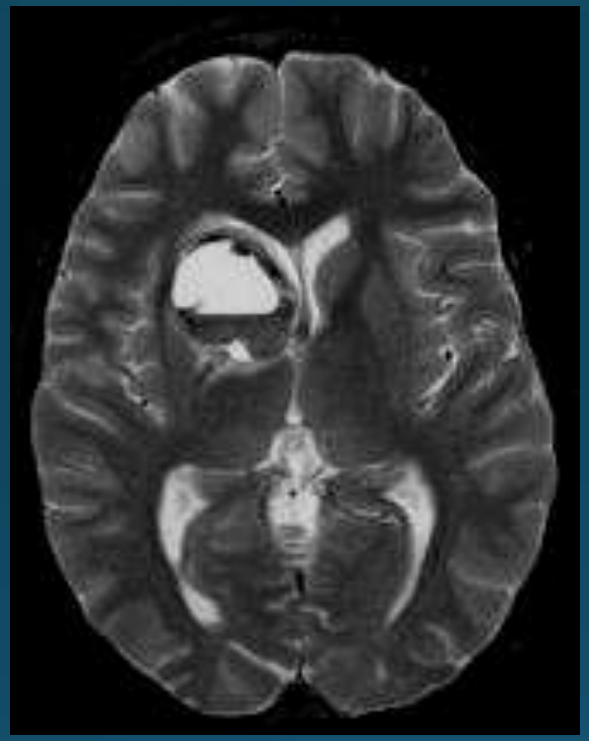
# White Matter: Lyme Disease



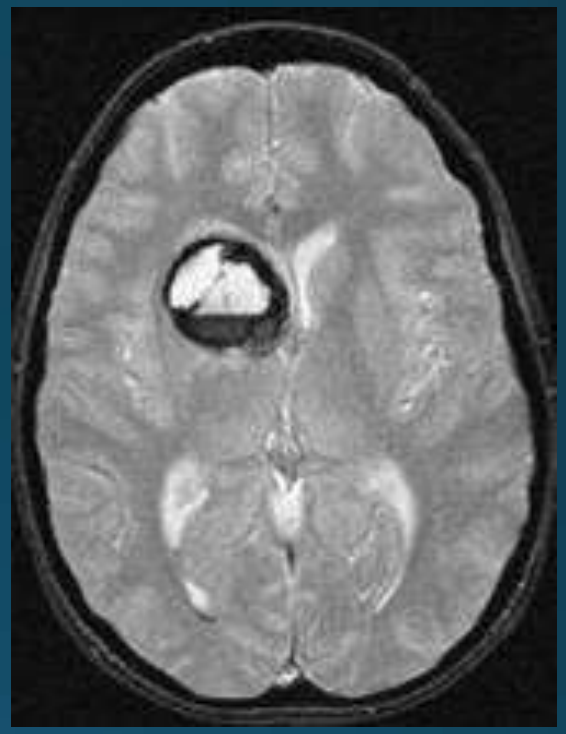
# MRI of Hemorrhage



**T1**



**T2**

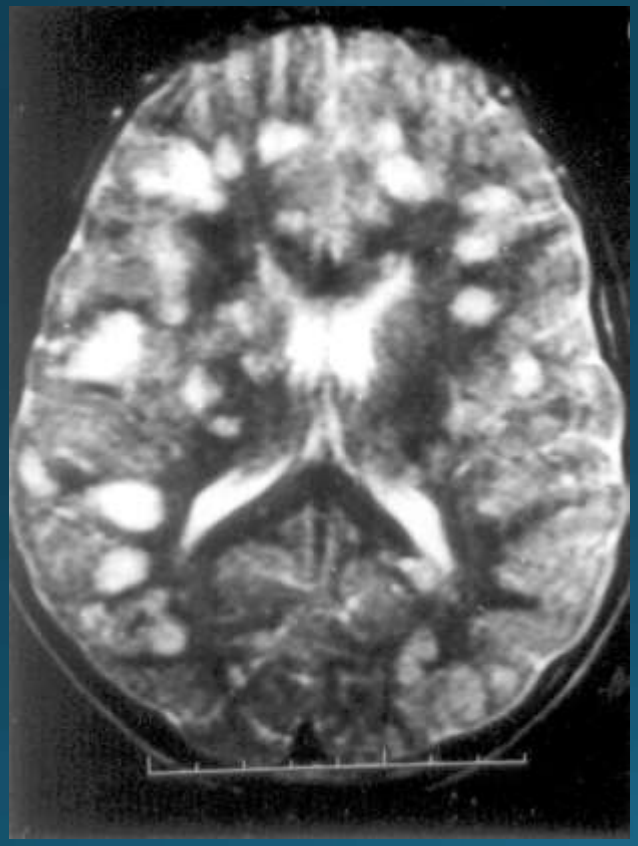


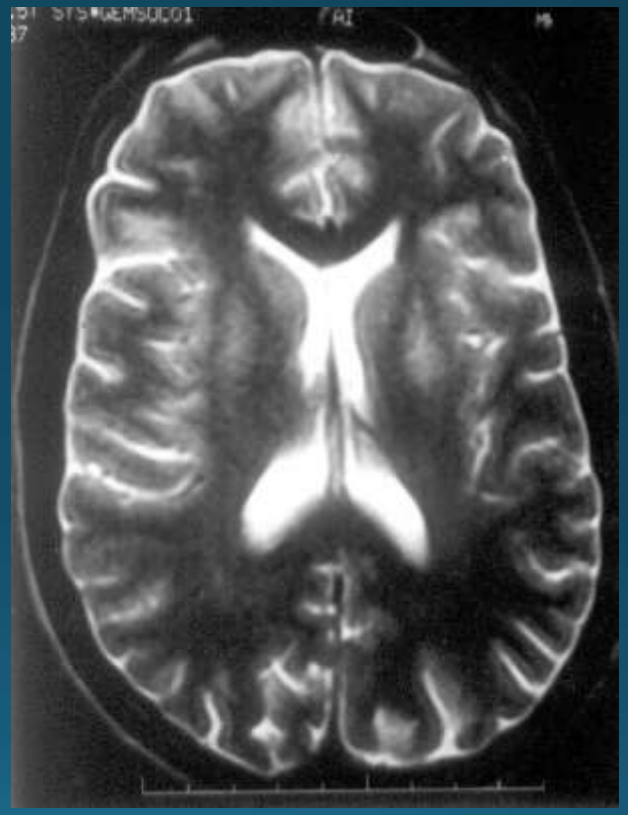
**T2***

MR appearance of hematomas depends on image type.

Magnetic properties change over time (Hgb breakdown products), allowing approximate dating

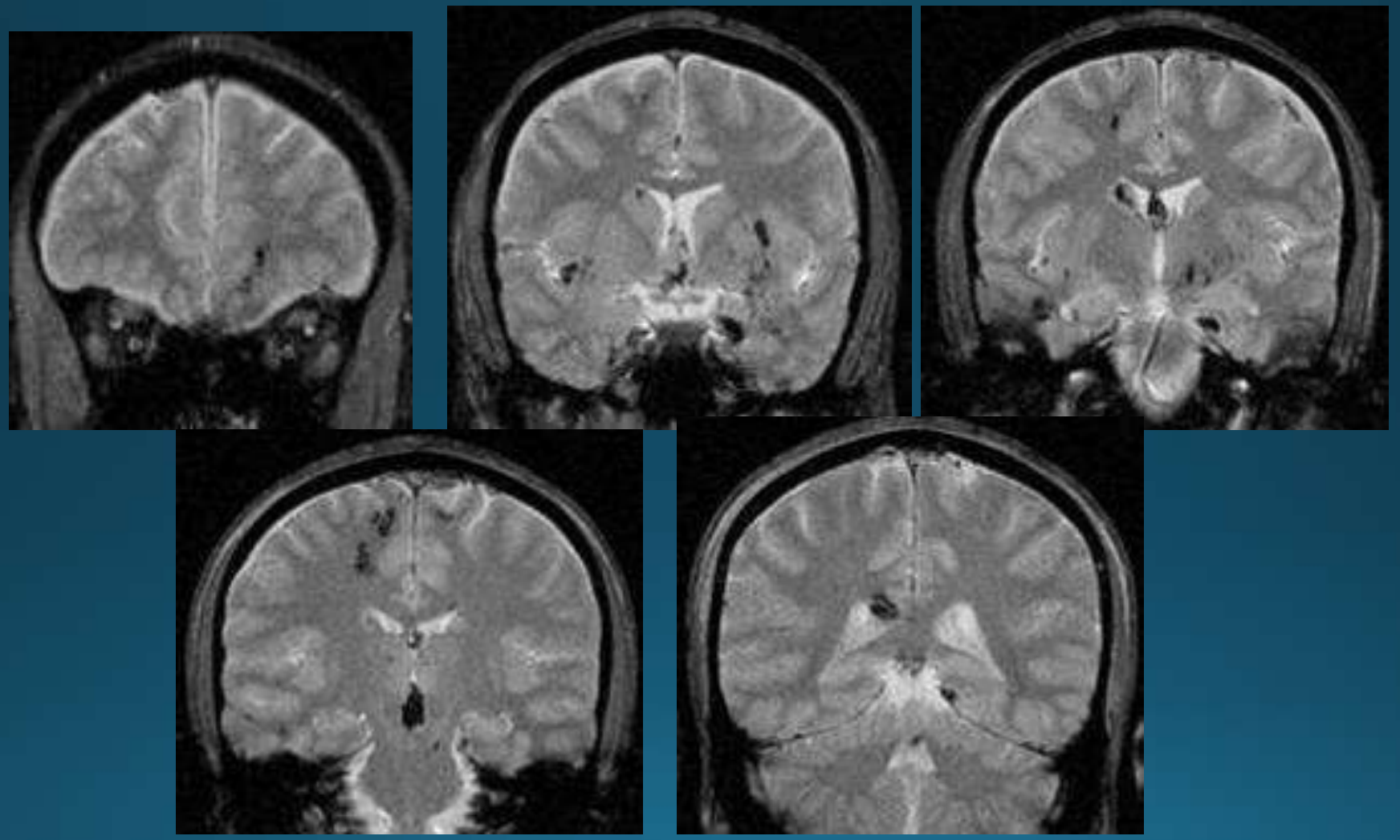
# MRI: demylinization in encephalomyelitis (brain inflammation)





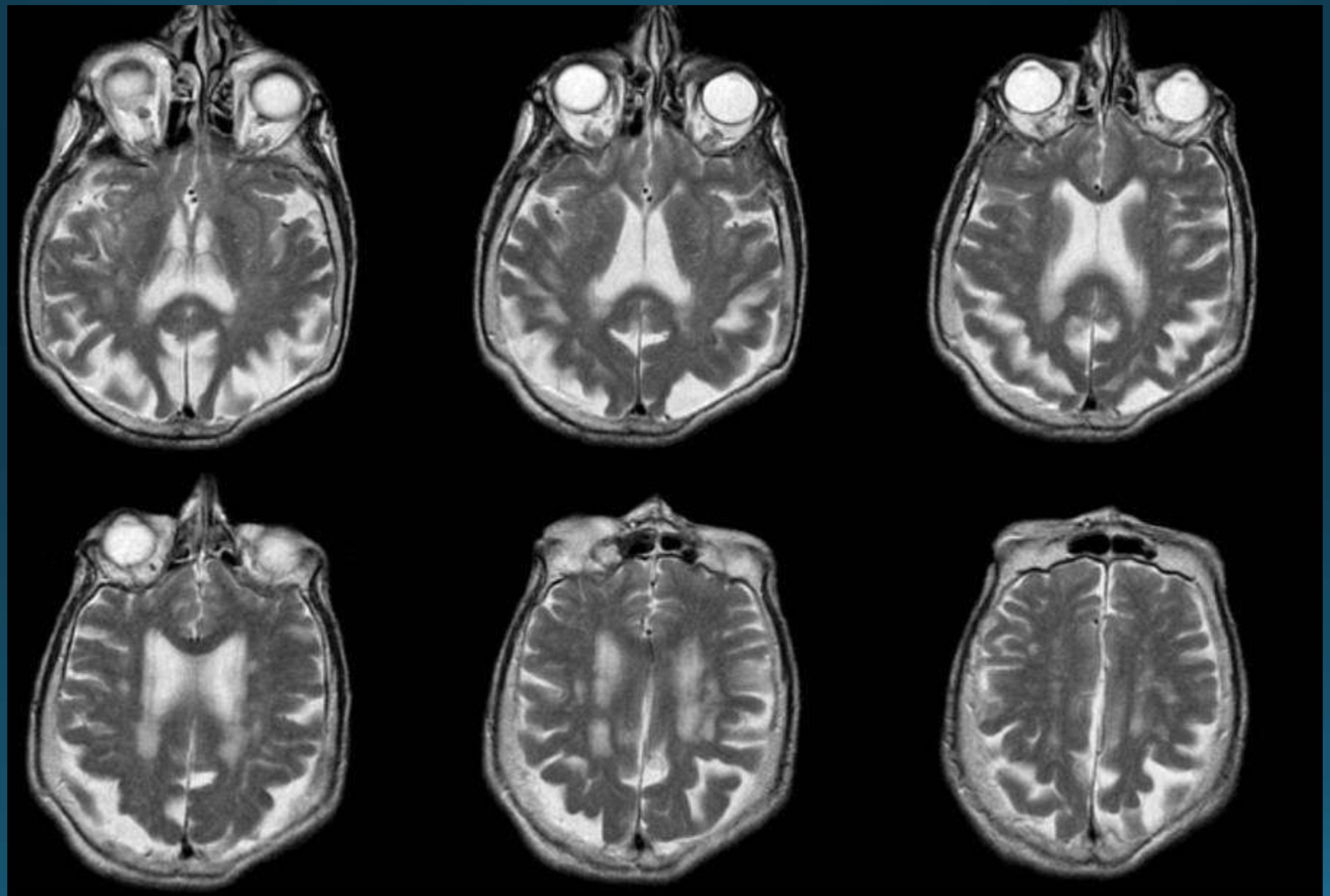
Autoimmune Chronic Fatigue: Multiple hypertense lesions

# Diffuse Axonal (Shear) Injury (DAI)

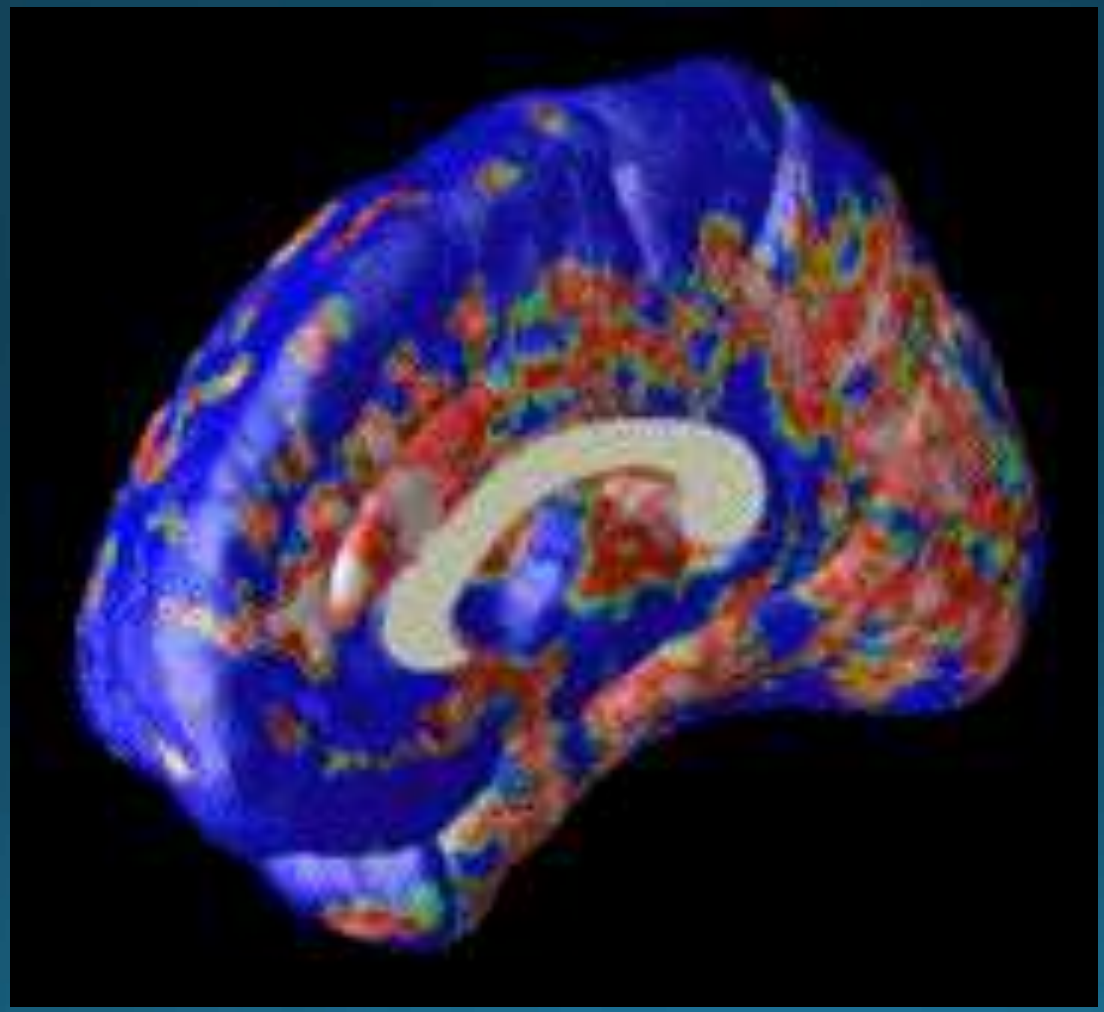


T2*: Increased sensitivity to hemorrhage

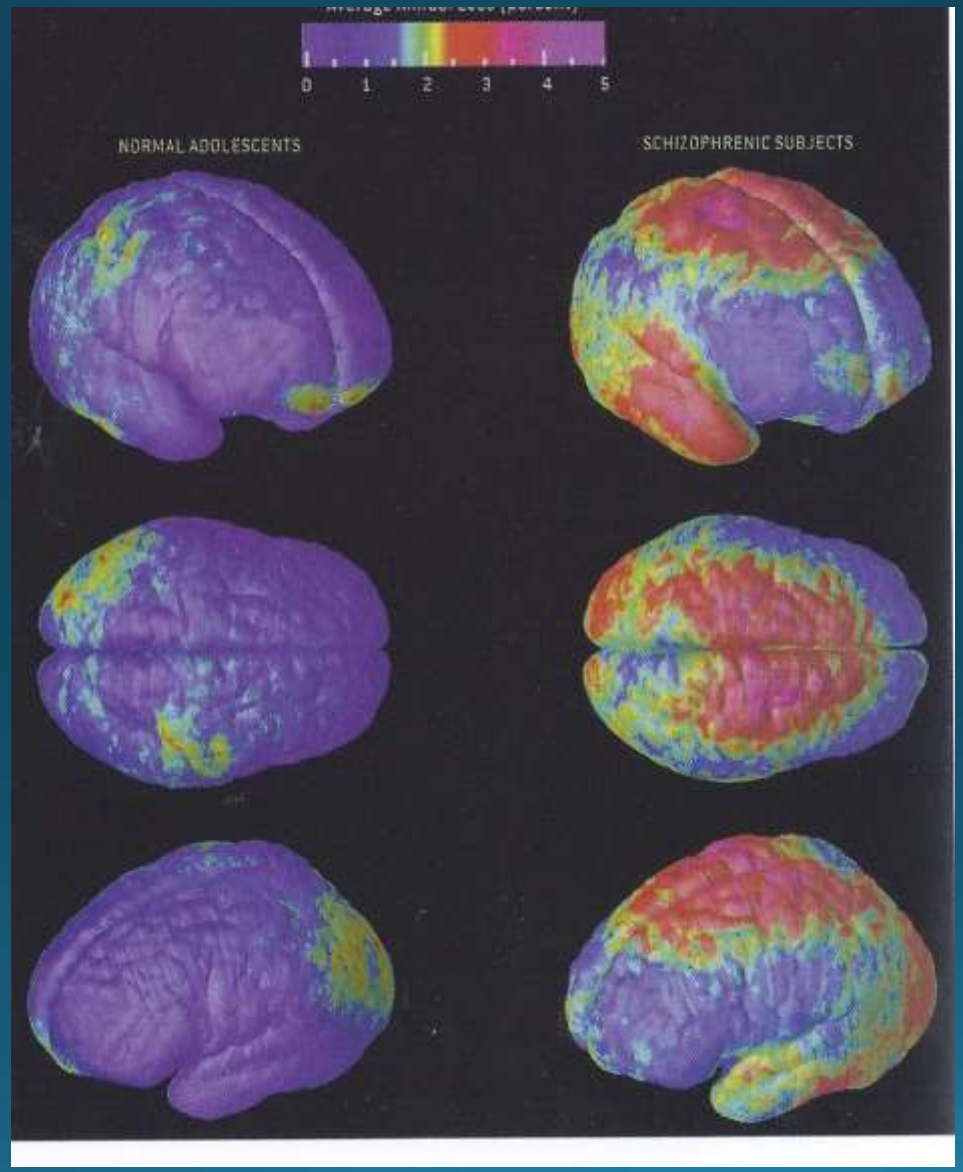
# Alzheimer’s: Temporal-Parietal Lobe Atrophy (Late)



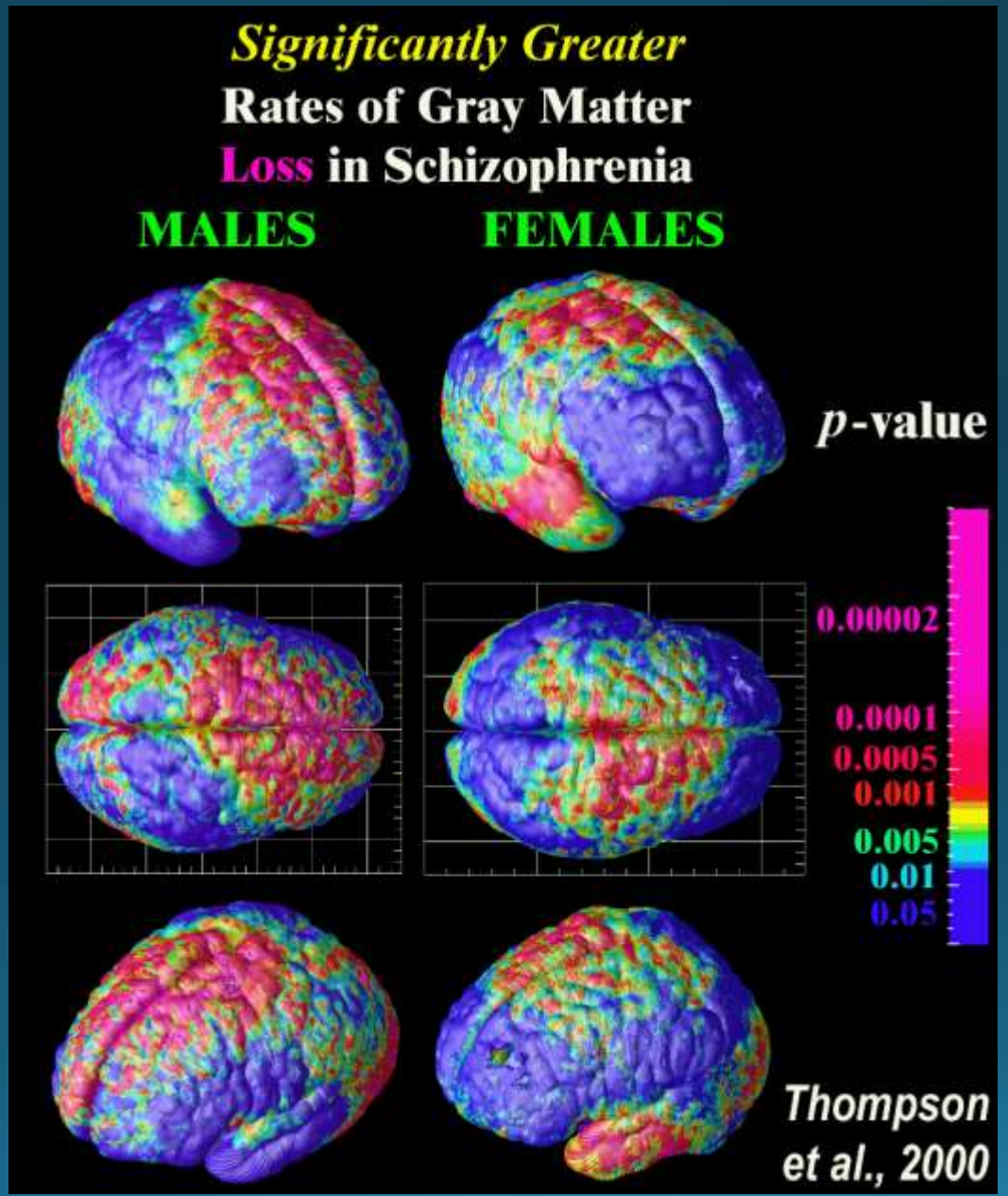
# Alzheimer’s atrophy over 18 months



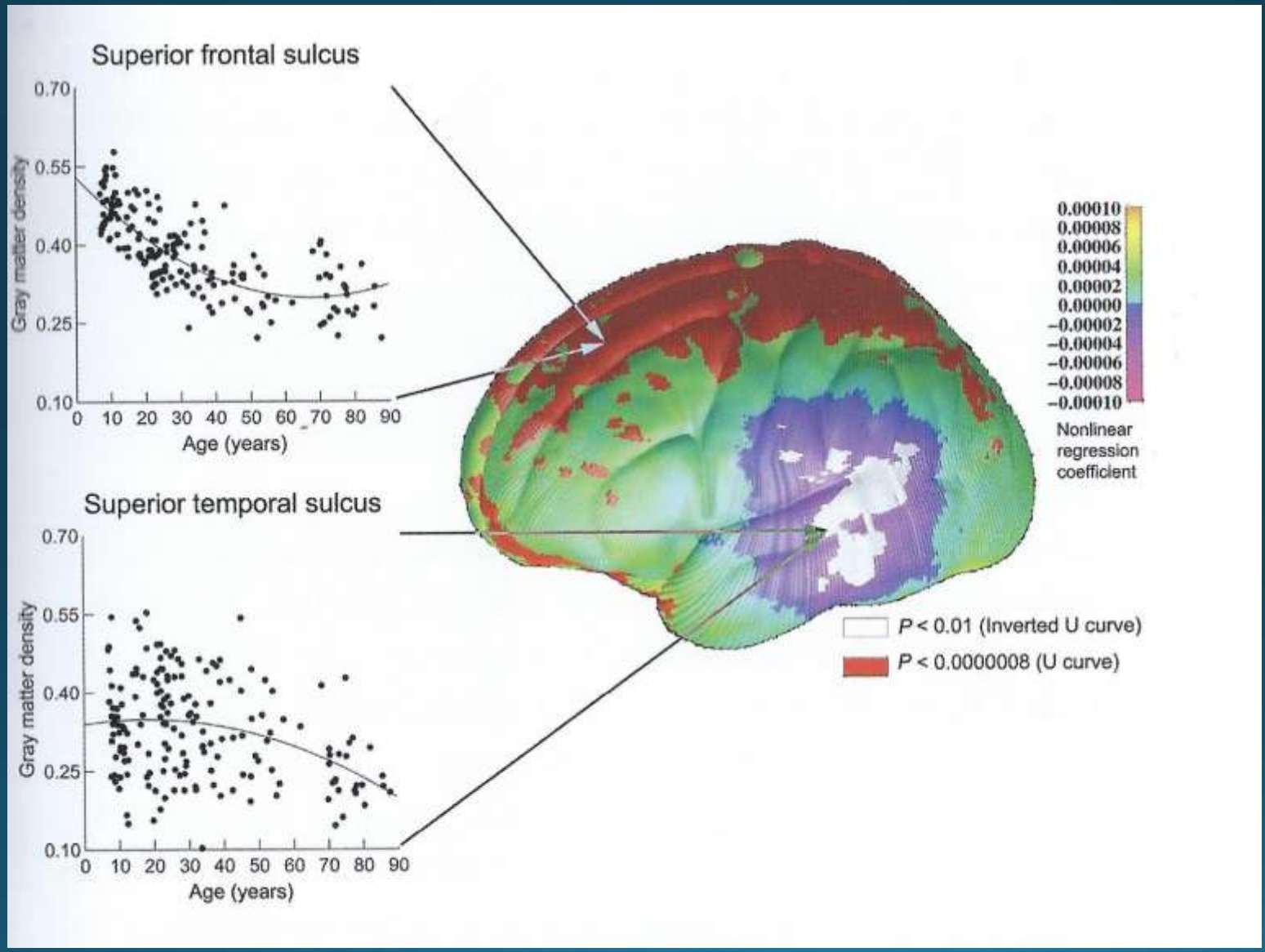
# MRI: Childhood onset Schizophrenia – grey matter loss



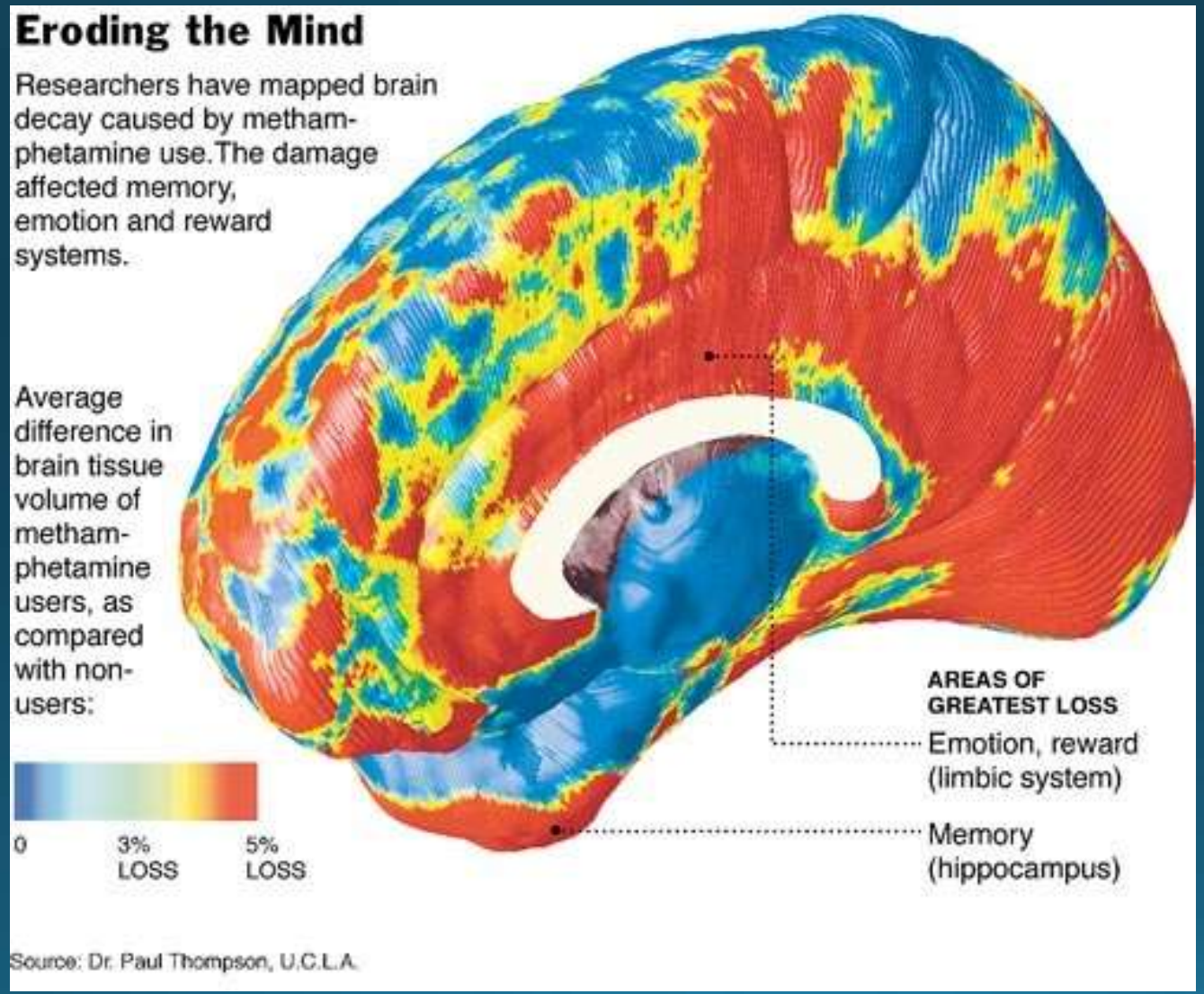
# Neuronal Loss in schizophrenia



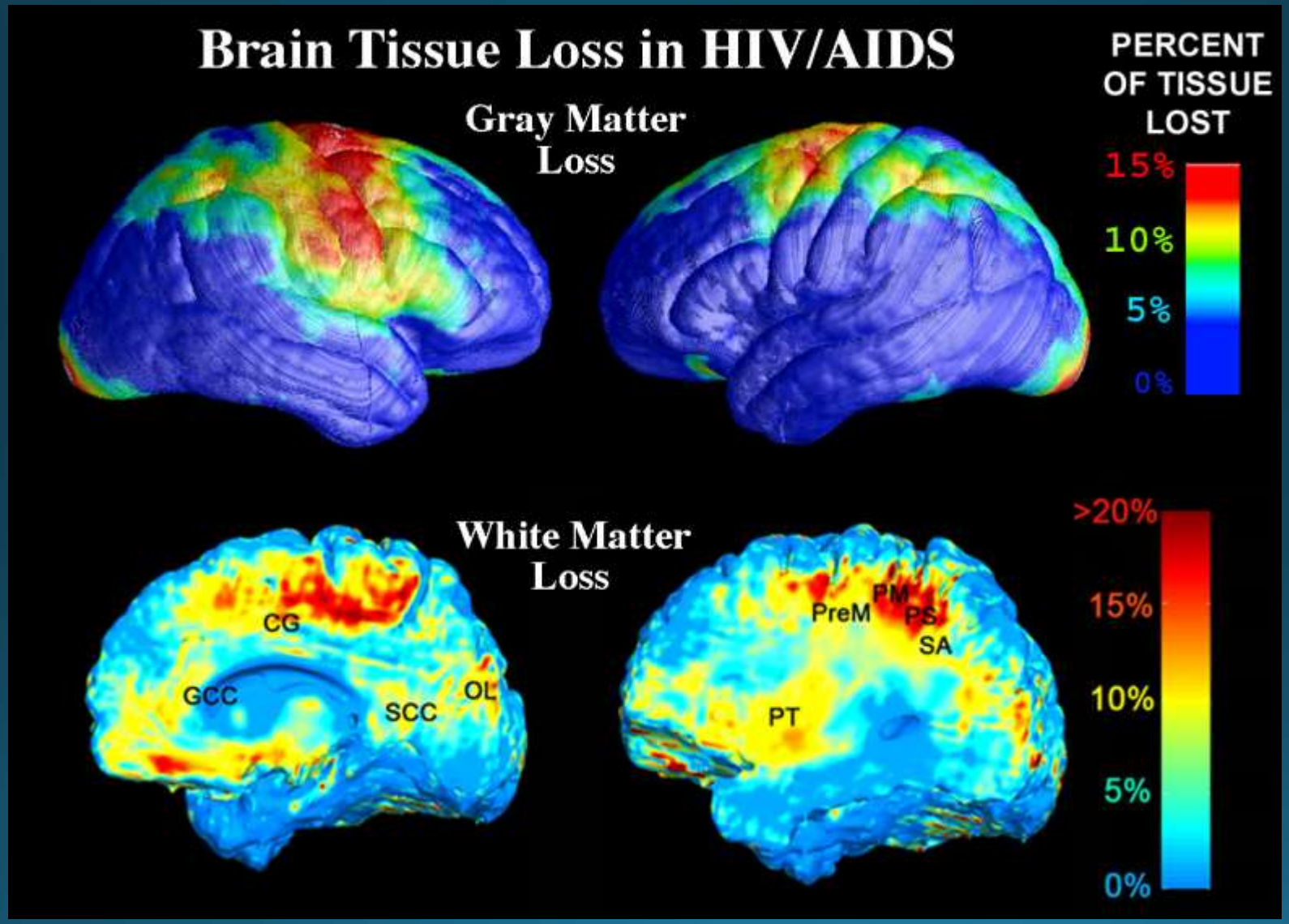
# Loss of grey matter density between childhood and old age



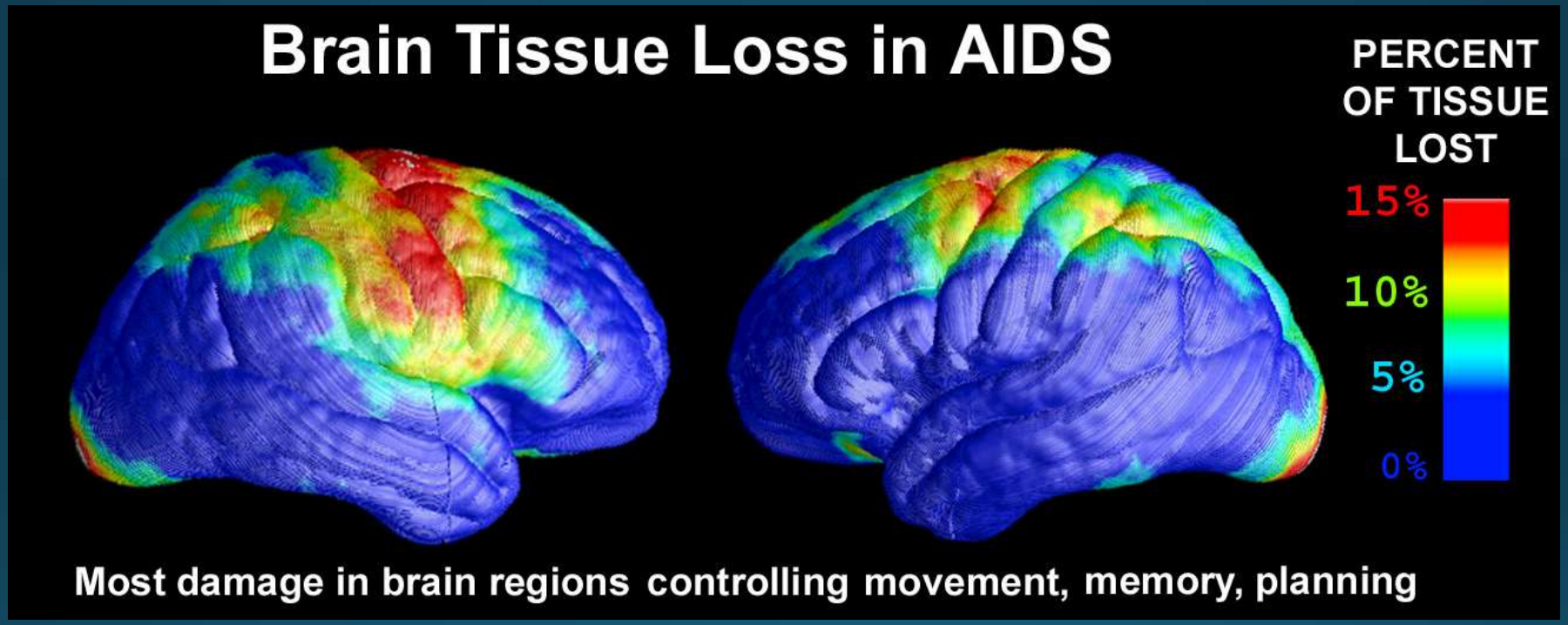
# Methamphetamine Use & brain atrophy



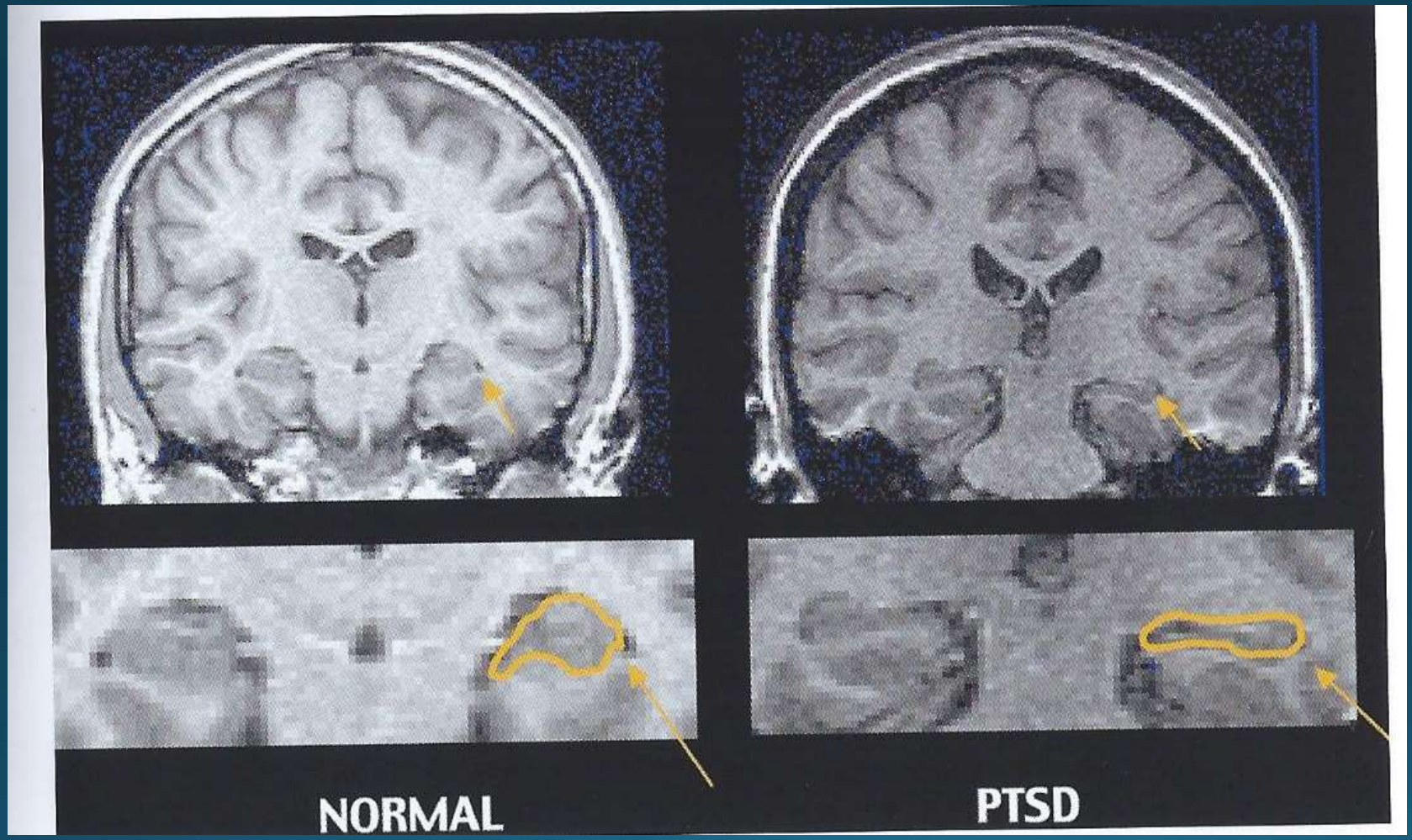
# HIV / AIDS Neuronal Loss



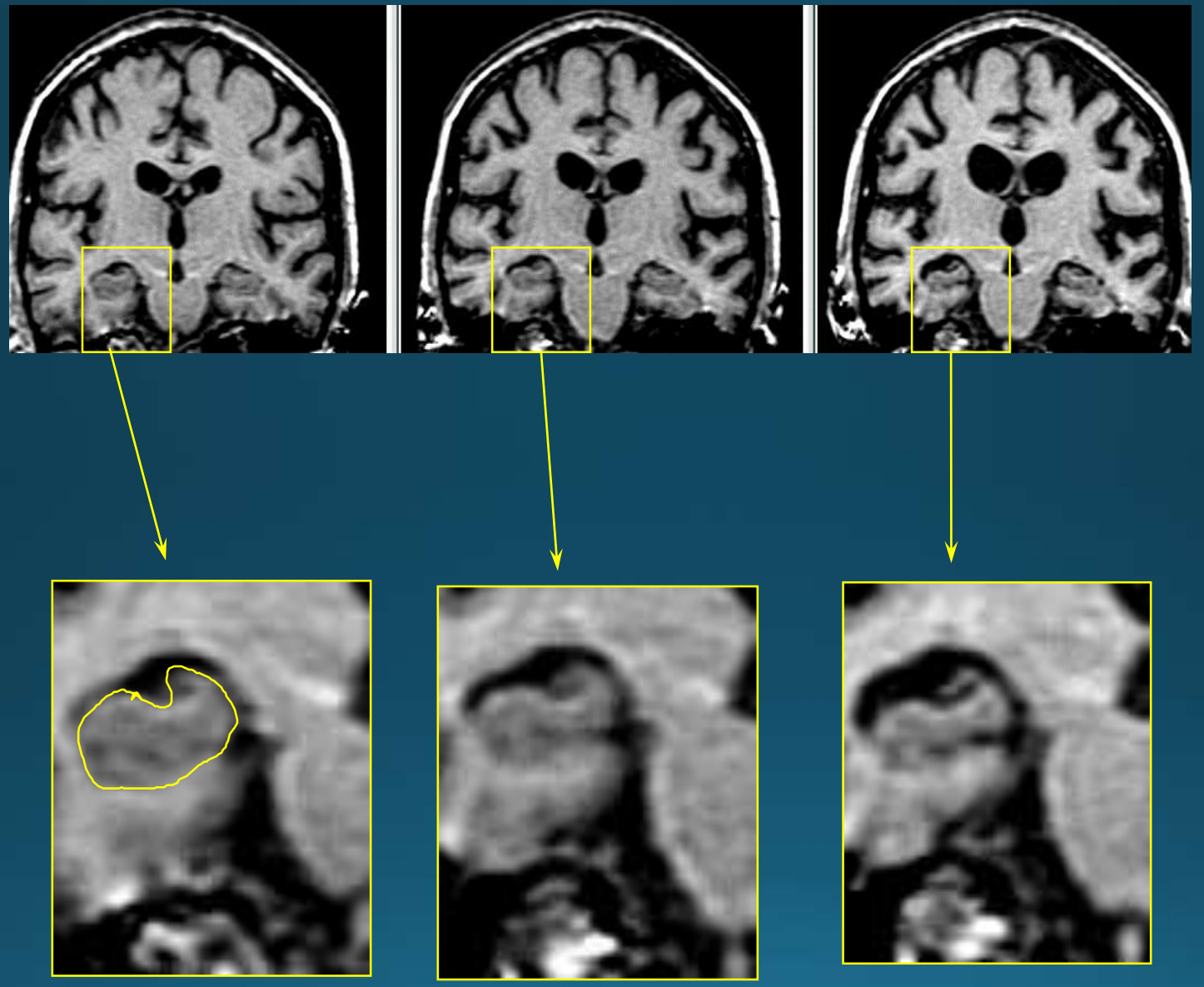
# Brain Tissue Loss in AIDS



# MRI: hippocampal volume decrease in PTSD



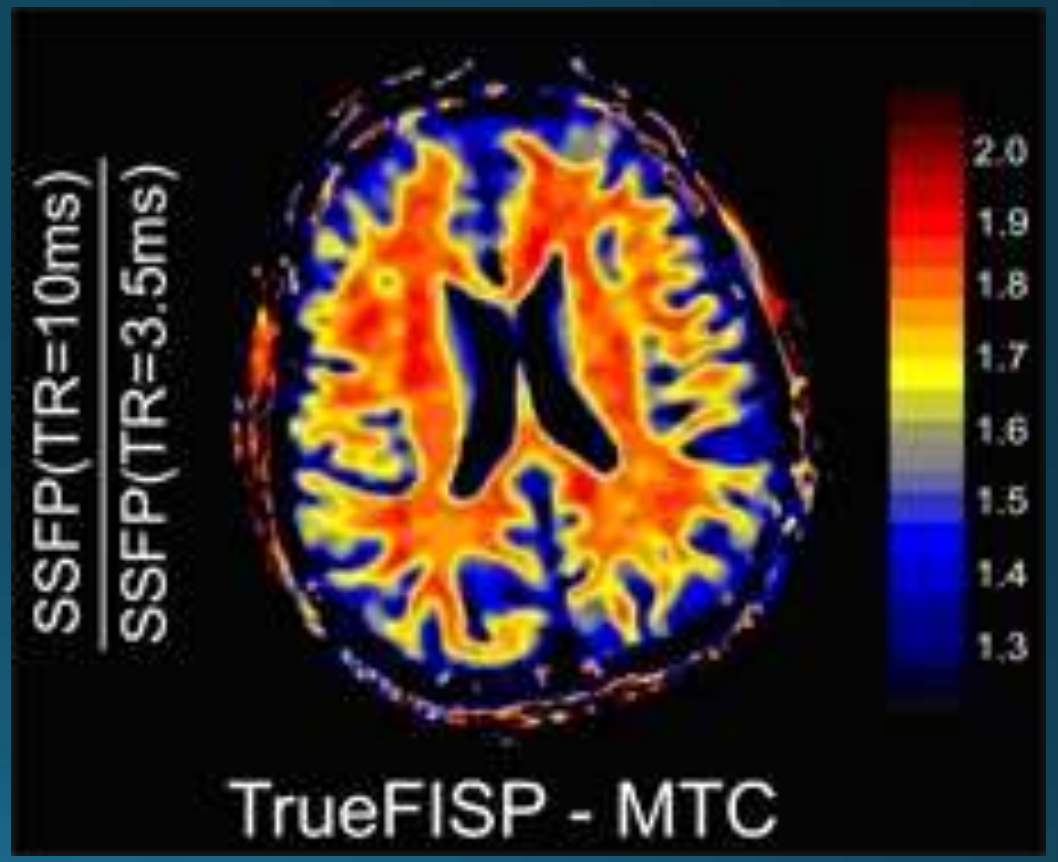
# Hippocampal Loss in AD



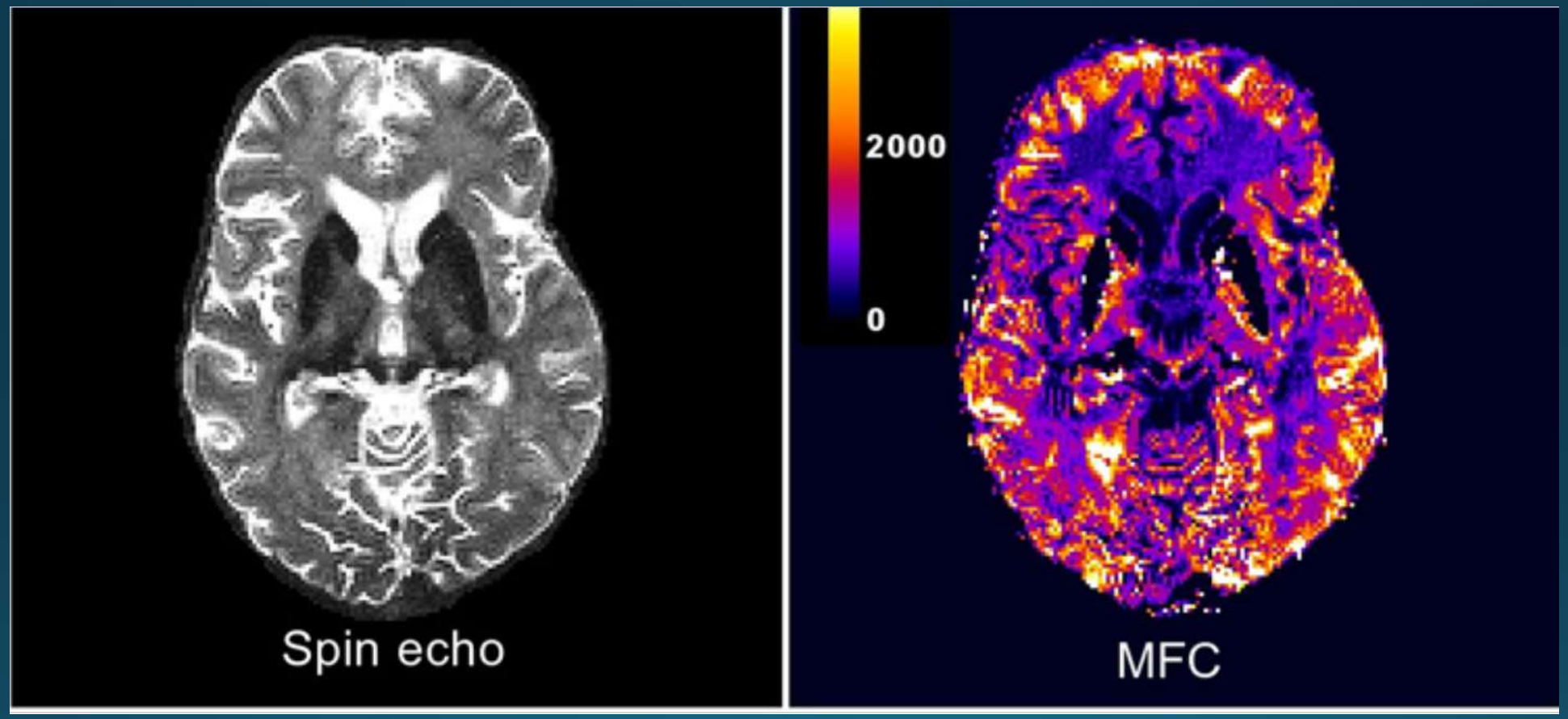

Serial coronal MRI of an individual with initially mild AD

# MTI -Magnetization Transfer

- Magnetization Transfer = designed to indirectly image H in proteins (not normally visible in MRI) via their magnetic effects on magnetized H in water
  - Useful in diagnosing MS and ALS abnormalities in WM
    - Especially when used with Gd contrast agent
  - Possibly useful in detecting Alzheimer's plaques

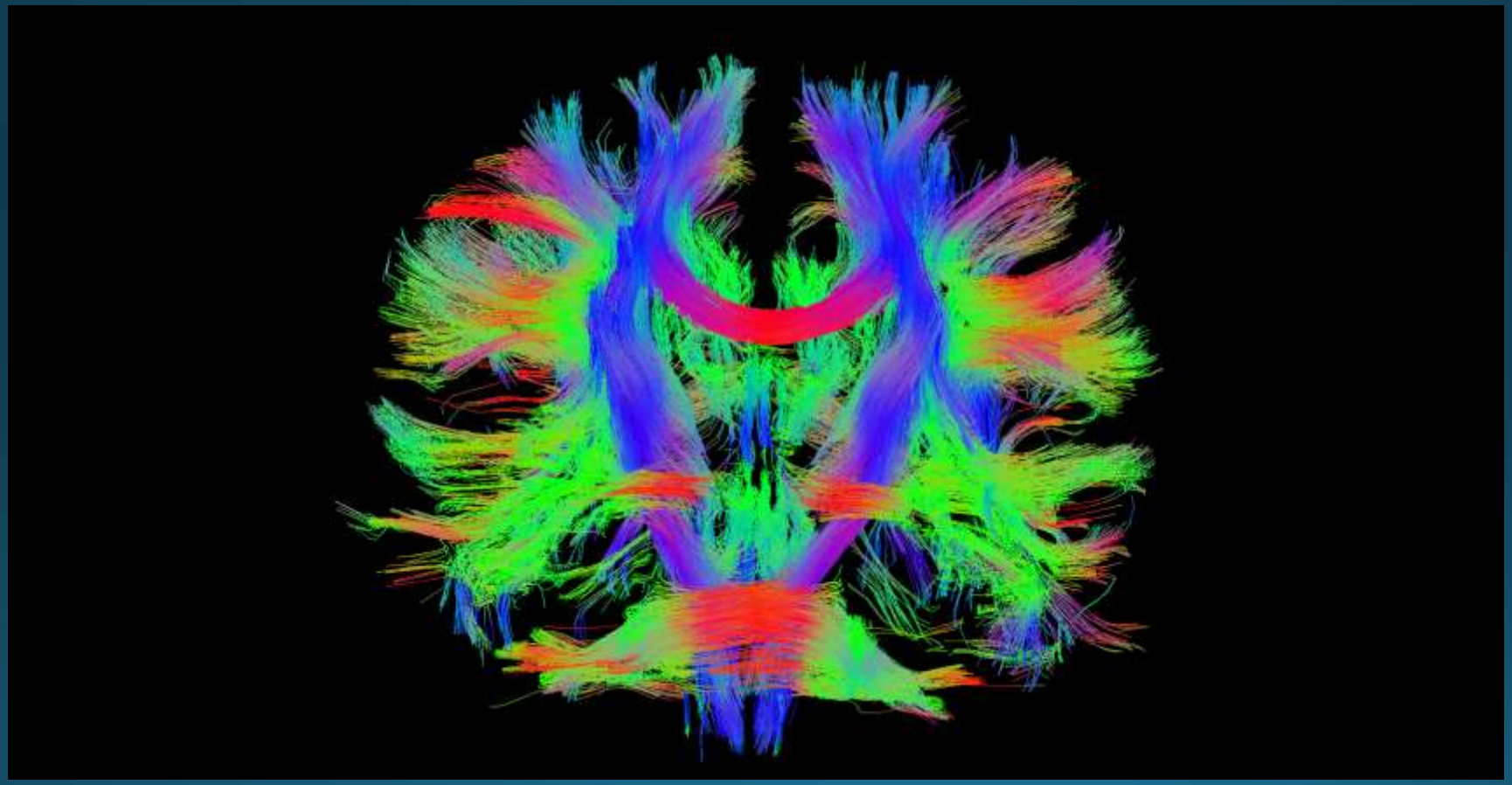


# MRI - MFC: 2009, iron detection




Magnetic Field Correlation imaging

# Diffusion MRI



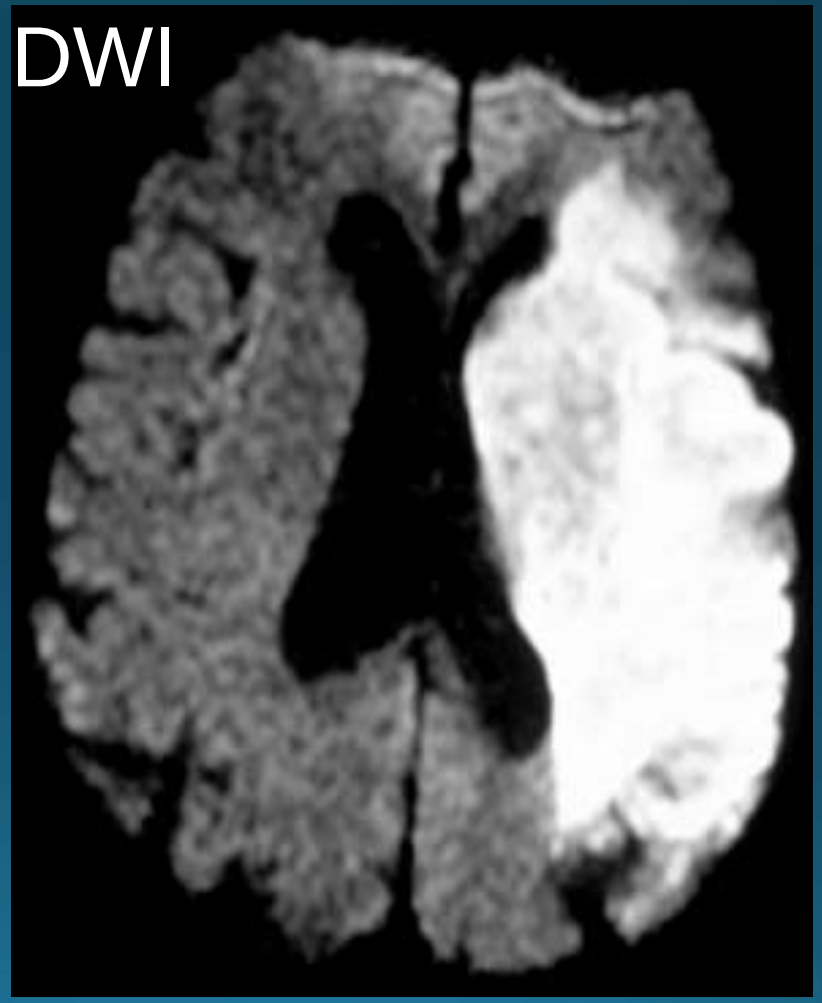
# Magnetic Resonance

## Diffusion Imaging

Highly sensitive to acute ischemia

+ within a few hours!

No other imaging is more sensitive to acute ischemia




Acute left MCA infarction

# Diffusion Weighted Imaging (DWI) vs Diffusion Tensor Imaging (DTI)

- **Diffusion Weighted Imaging (DWI)** contrast is based on the rate of water diffusion in the tissue described by a parameter called apparent diffusion constant (ADC). It is used for evaluation of stroke and many other diseases.

- **Diffusion Tensor Imaging (DTI)** is used to map the "anisotropy" of the water diffusion in the tissues. This provides a powerful tool to visualize the brain white matter tracts and to assess the changes due to diseases or trauma. Fractional anisotropy (FA) is used to characterize the DTI changes.

# DTI - Diffusion Weighted Imaging

- Tool for evaluating brain structure, especially white matter

- Exploits water's differential diffusion along versus across axons; provides information on axonal direction and integrity

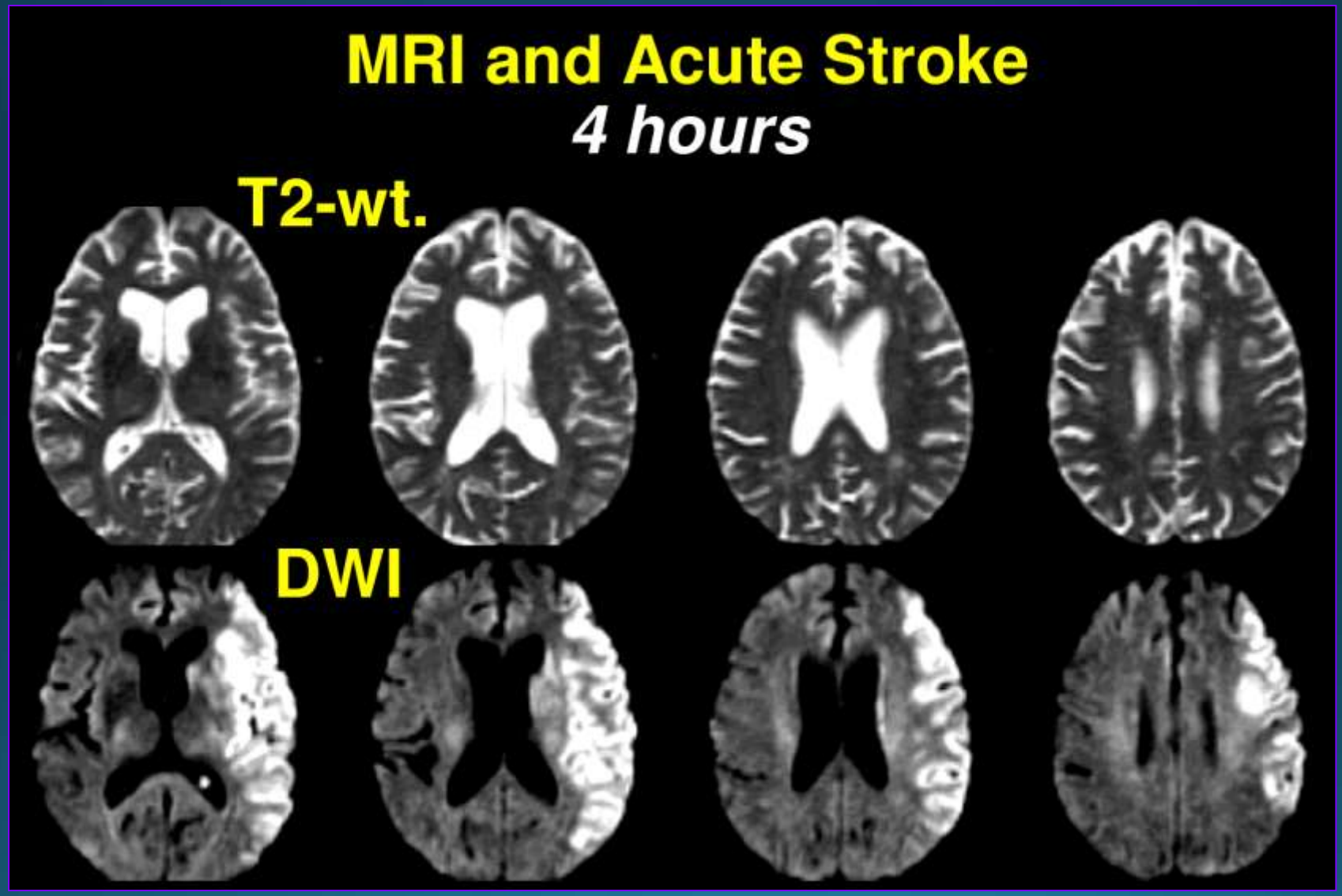
- Images modified for sensitivity to water movement in different directions
- Evaluation of stroke:
  - differentiates cytotoxic edema (in stroke; BBB intact) vs vasogenic edema (in other lesions);
  - identification of acute brain ischemia after stroke;
  - differentiation of acute vs chronic strokes

# DWI in Stroke

- Stroke damage doesn't show up on T1- or T2-weighted images for 2-3 *days* post-blockage

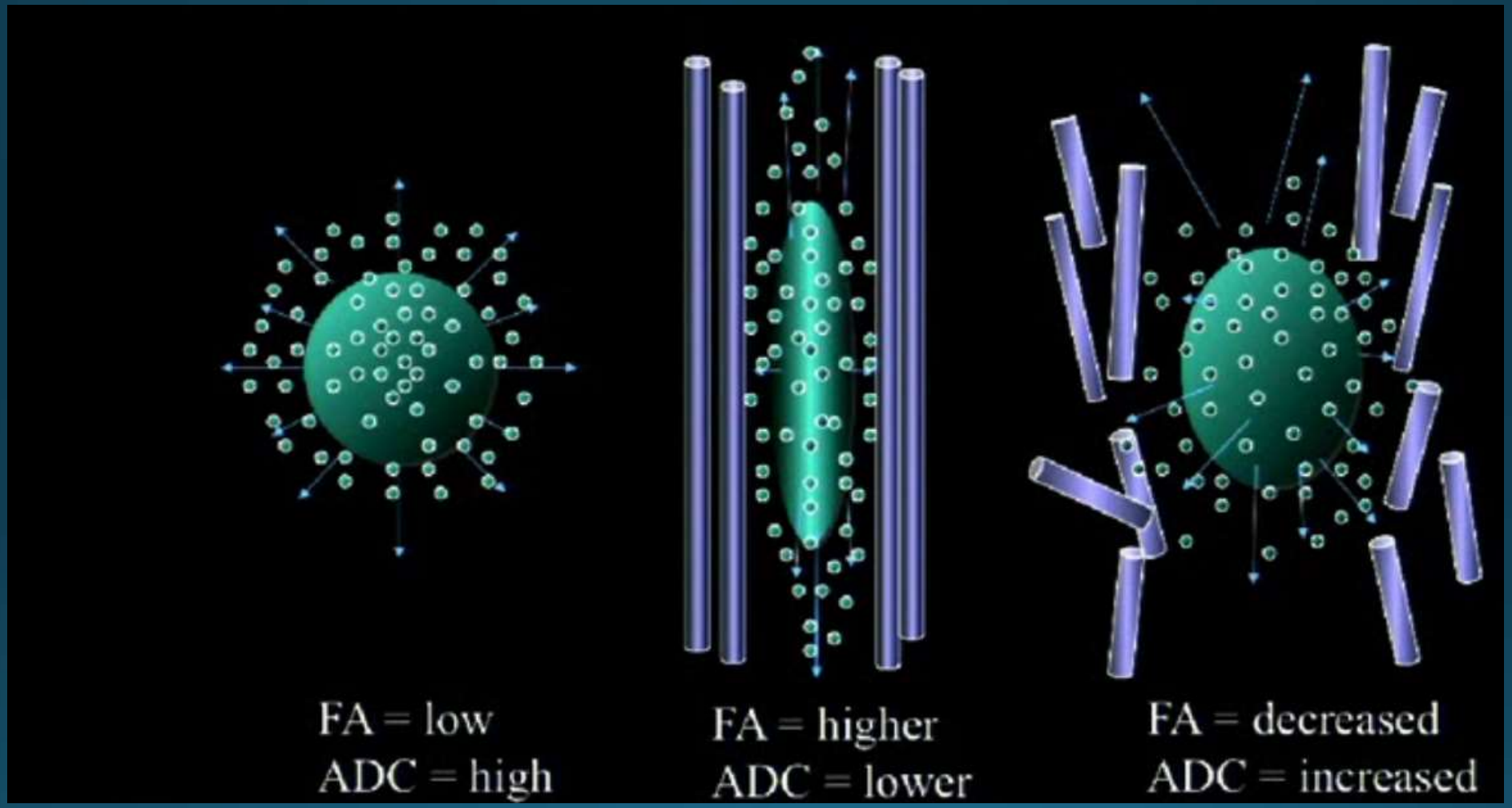
- DWI is now commonly used to assess region of damage in stroke emergencies
  - And whether to administer TPA (clot dissolving agent with many bad side-effects)

# DWI gives better stroke contrast



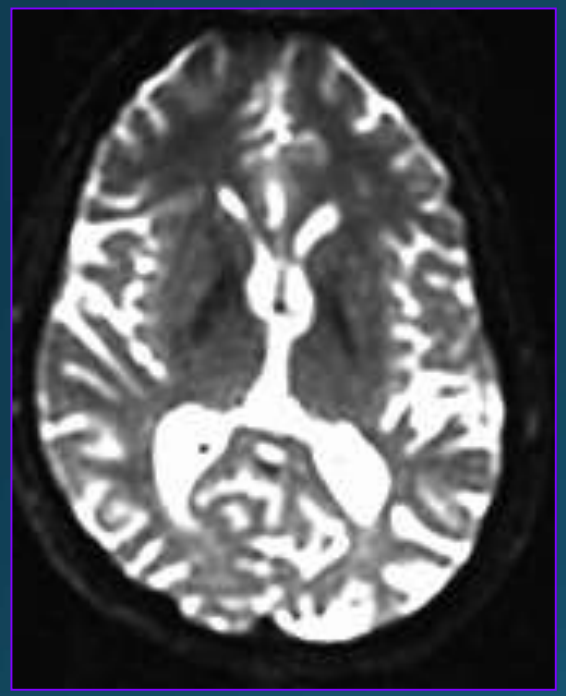

From Mike Mosely (Stanford Radiology)

# DTI (FA= Fractional anisotropy (direction)  & ADC= Average Diffusion Coef)

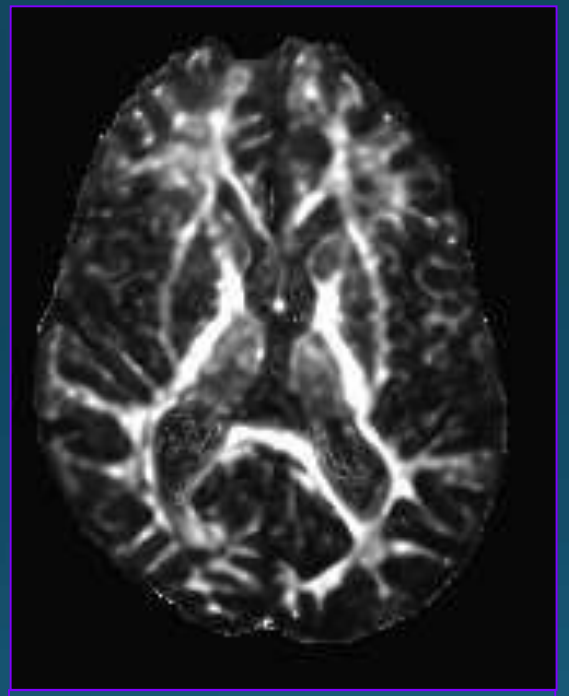



Bucket of water  Normal Cell  Abnormal Cell

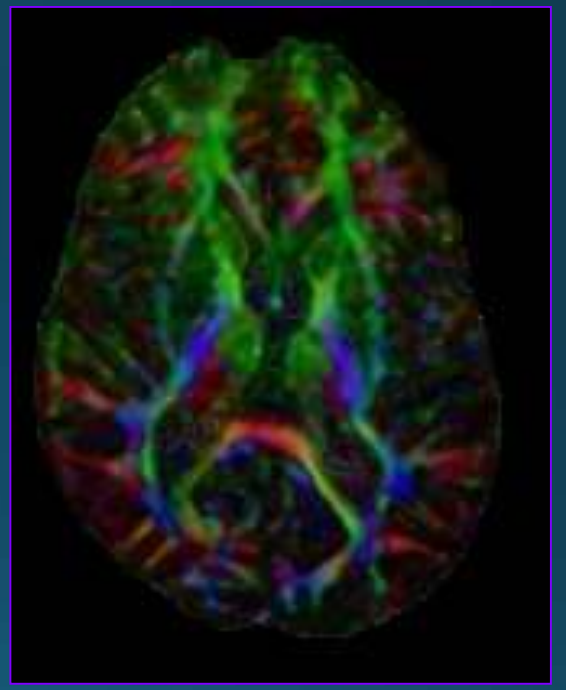
# DTI Results



Unweighted (baseline b=0) image



Fractional Anisotropy (FA):
Measures how much ADC depends on direction



FA Color-coded for fiber directionality:
*x* = Red *y* = Green
*z* = Blue

# Fractional anisotropy: Higher FA is better

- **Anisotropy** ("not/the same/in all directions") is property of being directionally dependent, as opposed to isotropy, which implies identical properties in all directions

- **Fractional anisotropy (FA)** is a scalar value between zero and one that describes the degree of anisotropy (directionality) of a diffusion process.
- FA = underlying fiber tract orientation
- A value of zero means that diffusion is isotropic, i.e. it is unrestricted (or equally restricted) in all directions.
- A value of one (good, normal) means that diffusion occurs only along one axis and is fully restricted along all other directions.

# Fractional anisotropy 2

- Low FA = random direction (abnormal cell)
- High FA = highly directional (normal cell)

- FA is higher in more highly organized and densely myelinated areas of brain (i.e. corpus callosum, pyramidal tracts)

- FA is a measure often used in diffusion imaging where it is thought to reflect fiber density, axonal diameter, and myelination in white matter.

# ADC: apparent diffusion coefficient;
# higher value = bright = abnormal; opposite of FA

- ADC = An average of all directions acquired, when performing DTI.
- The ADC in anisotropic tissue varies depending on the direction in which it is measured. The stronger the diffusion, the greater the diffusion coefficient.
- Diffusion (the random movement of molecules) is fast along the length of (parallel to) an axon, and slower perpendicularly across it.
- On an ADC map, lots of diffusion is bright. Water molecules cannot move as far in the damaged tissue as in normal tissue. As a result, ADC is lower and appears darker than the surrounding normal tissue. low ADC, suggestive of cytotoxic edema.
- This is opposite to the diffusion weighted images, where good diffusion is dark.

# DWI (Bright) & ADC (Dark): Trouble

| | Restricted Diffusion of molecules appears: | Normal Diffusion of molecules appears: |
|---|---|---|
| **On DWI** | Bright (More spins stuck in one area = more signal) | Dark (Less/No spins = No signal) |
| **On ADC map** | Dark (Traffic Jam) | Bright (Highway without traffic) |

A high D value will come up bright on the ADC because it is showing that there is quick, proper diffusion taking place (i.e. normal blood flow). A low diffusion value will come up dark on the ADC and mean there is no diffusion taking place in that area (i.e. restricted by a blood clot)

# DTI vs ADC: bacterial brain abscesses

DWI ADC DWI ADC

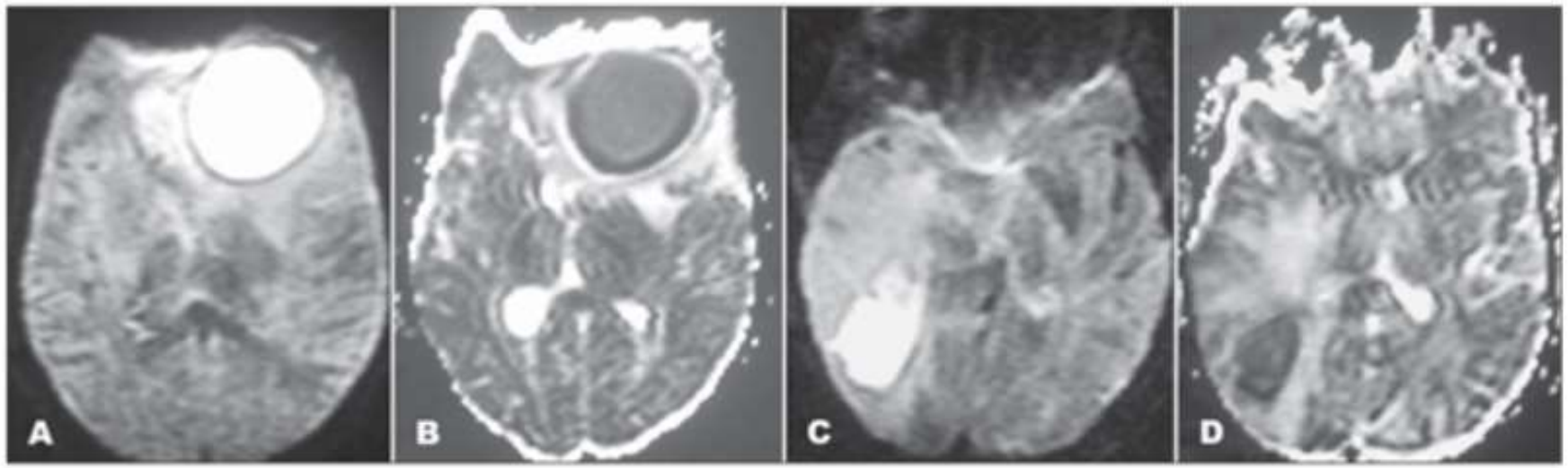
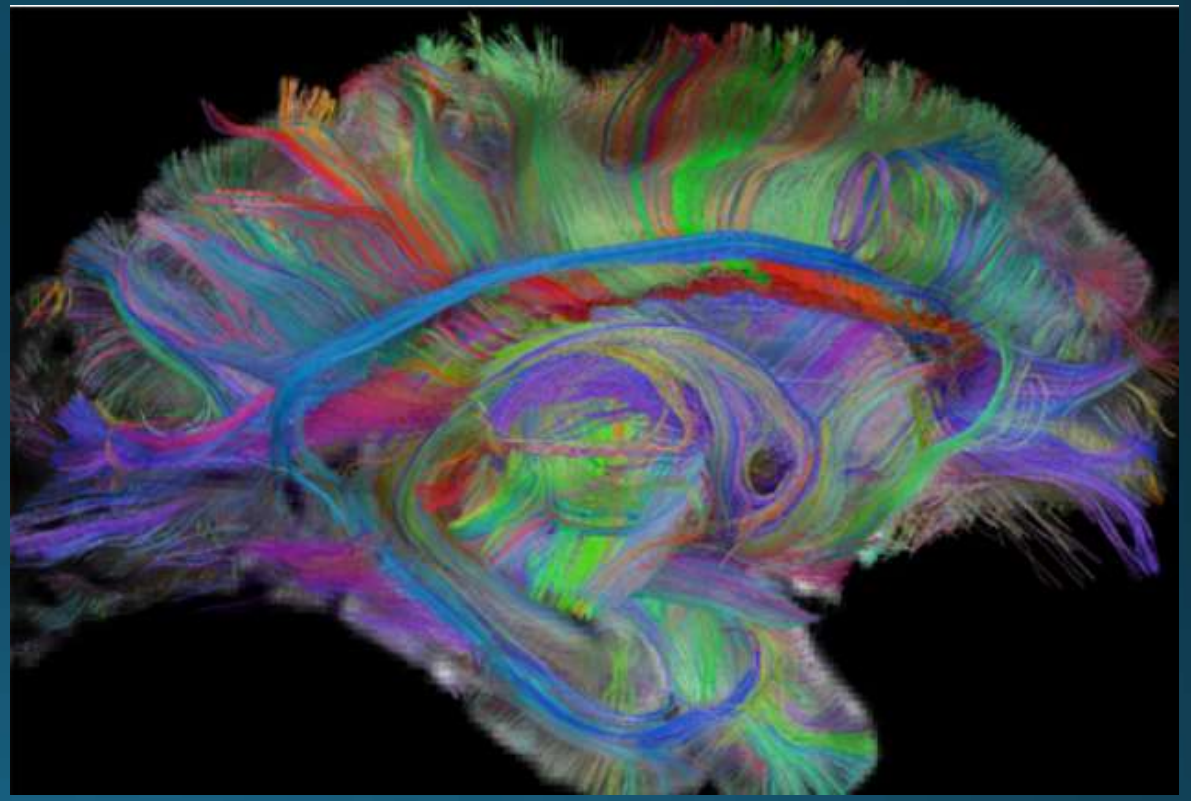



*Fig 2. Patient 1 (A and B) and patient 2 (C and D) show lesions with restricted diffusion on DWI (A and C) and ADC map (B and D).*

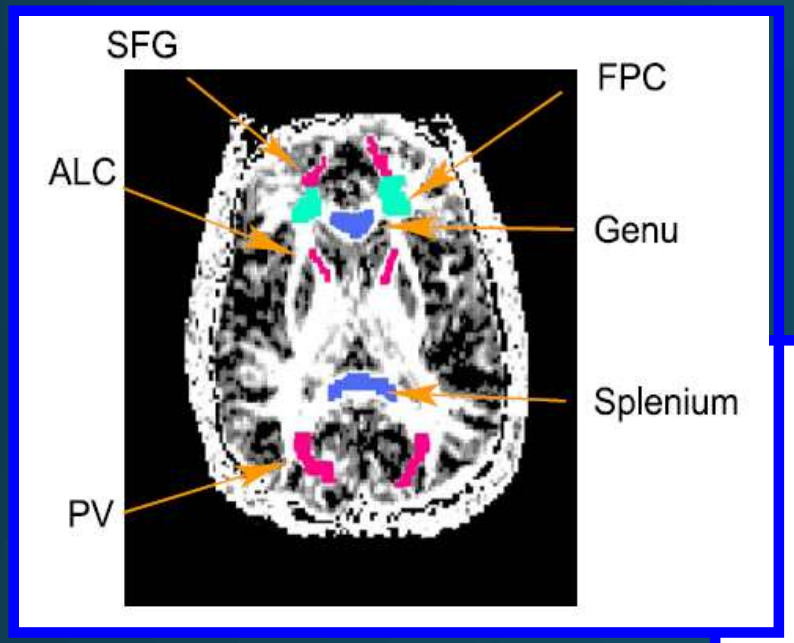
Abnormal: White Dark

# DSI: Diffuse spectrum imaging

- (DTI) cannot directly image multiple fiber orientations within a single voxel.
- Diffusion spectrum MRI (DSI) and related methods were developed to image complex distributions of intravoxel fiber orientation.
- Tractography based on DSI has the capacity to image crossing fibers in neural tissue.
- Allows researchers to continue tracing fiber bundles even when one seems to pass behind another

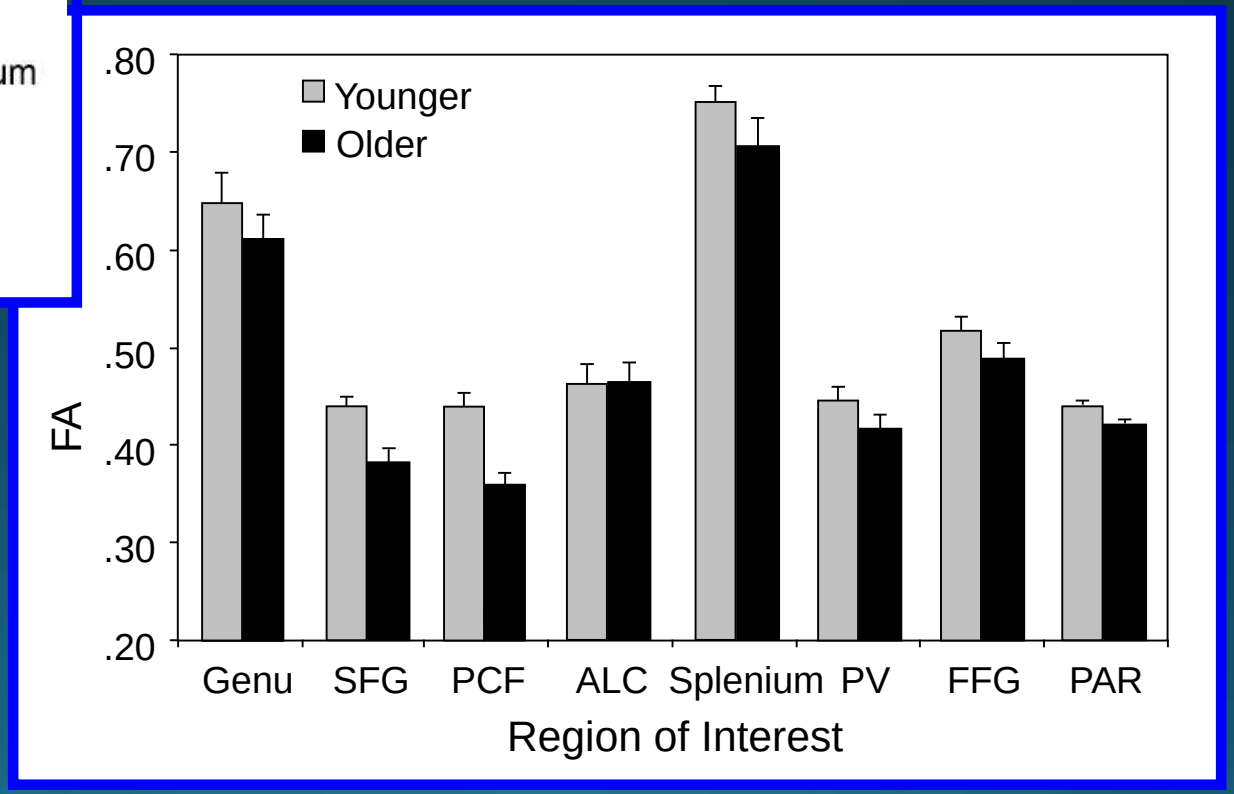


# DTI: White-Matter Changes with Aging :*Reduced Fractional Anisotropy*




Key fiber tracts in the human brain

White matter integrity, assessed in central voxels, decreases in the elderly



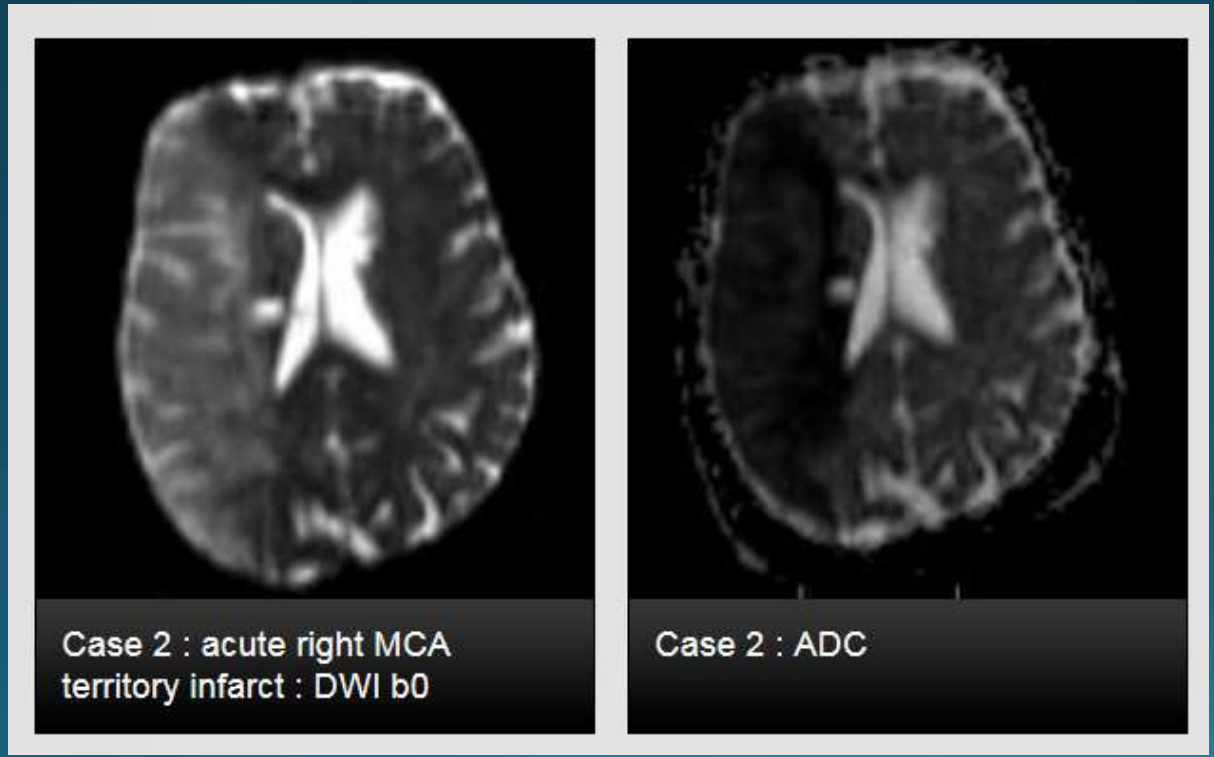

Data from Madden et al. (2004)

# Diffusion Imaging

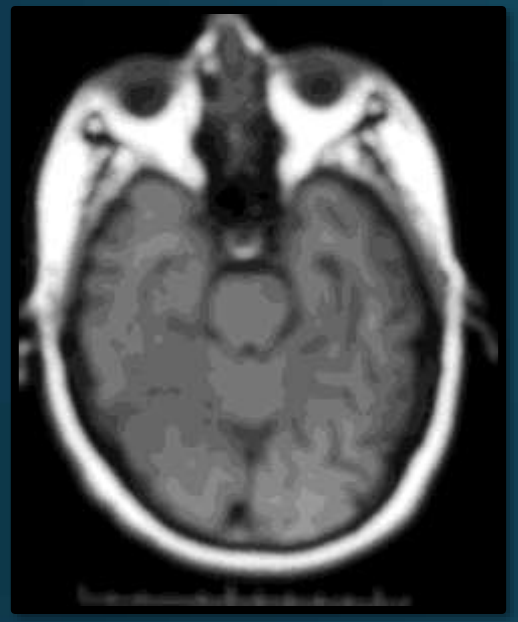
- Diffusion imaging separates infarction on acute or chronic basis.
- The acute infarct has a different diffusion signal due to edema.
- Conventional (T1/T2) MRI sequences may not demonstrate an infarct for 6 hours; DWI has increased sensitivity for early changes of edema
- Distinguish b/w old and new stroke
    - New stroke = bright on DWI
    - Old stroke (encephalomalacia) = low Signal Intensity on DWI

# Diffusion Imaging: Early stroke

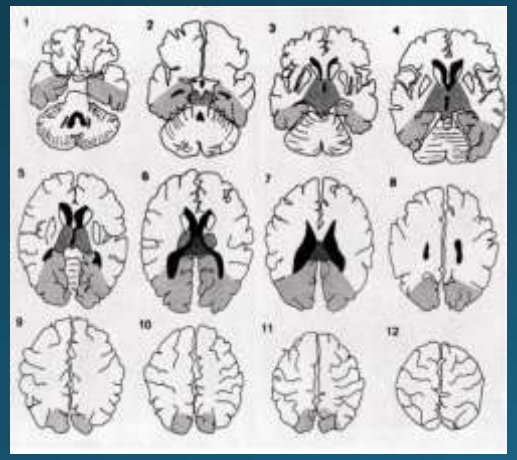
- Increased DWI signal in ischemic brain tissue is observed within a few minutes after arterial occlusion and progresses through a stereotypic sequence of apparent diffusion coefficient (ADC) reduction followed by subsequent increase



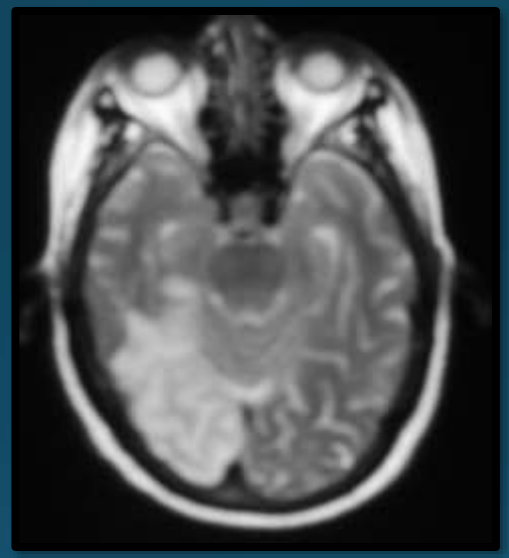
# MRI acute stroke



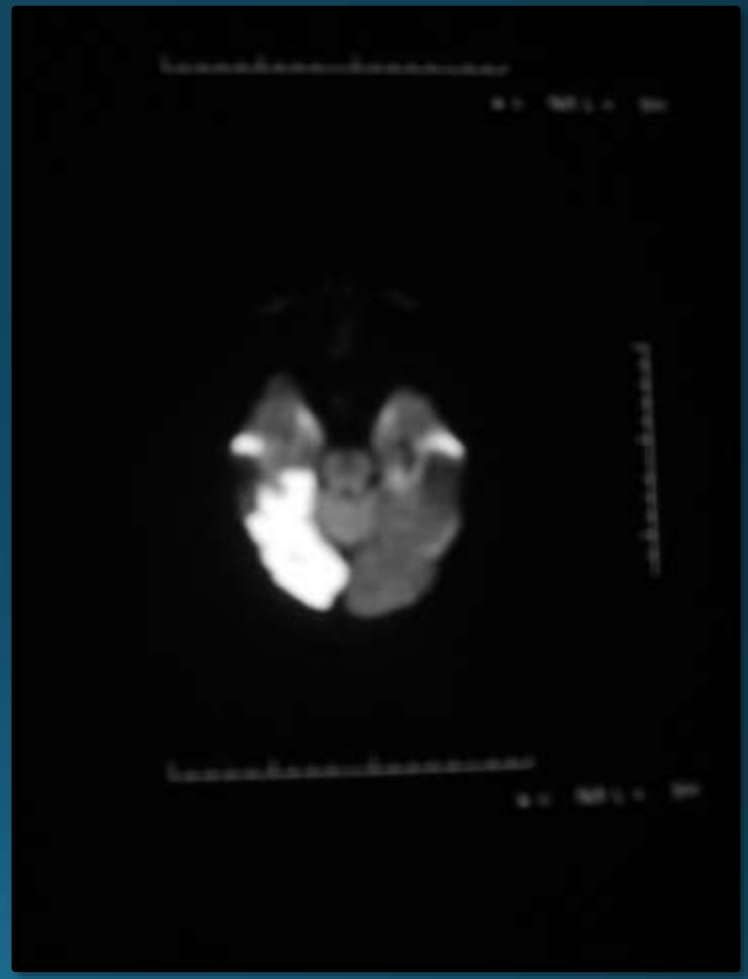
T1



PCA DISTRIBUTION



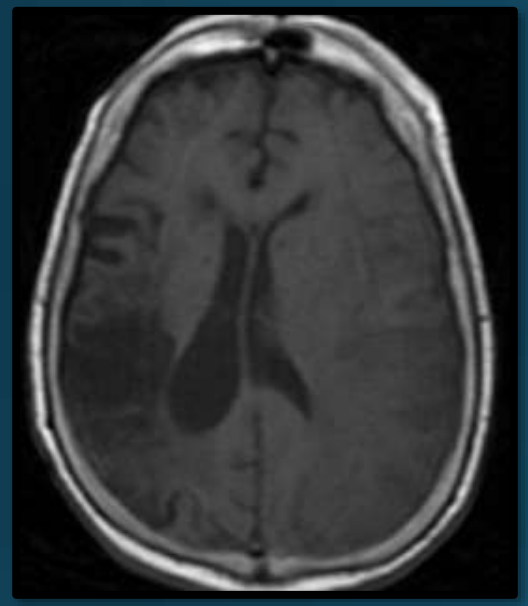
T2



Diffusion

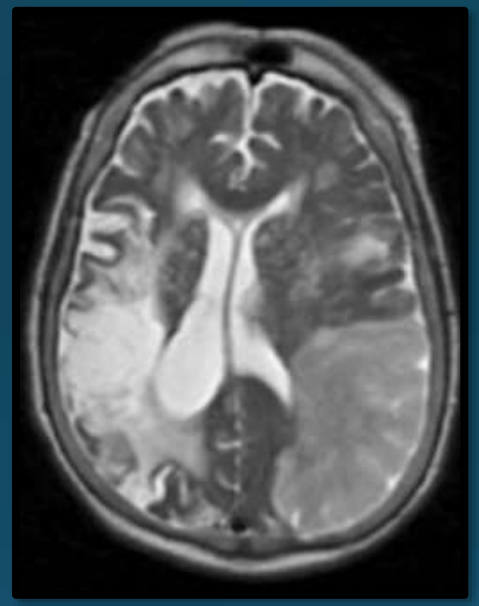
# MRI Old -vs- New ischemic infarct

Old

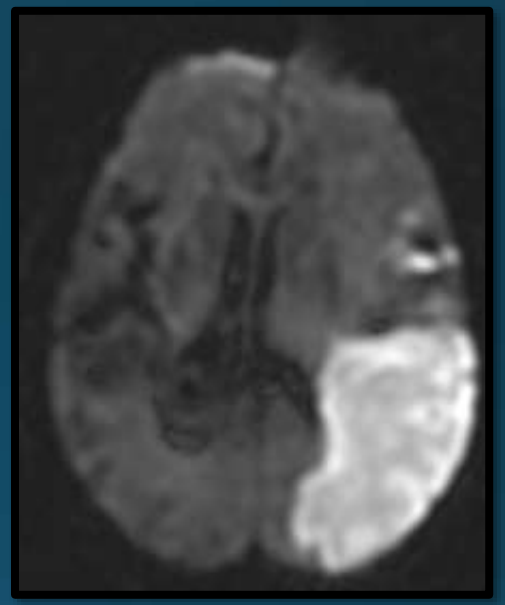


T1

Old



T2



New

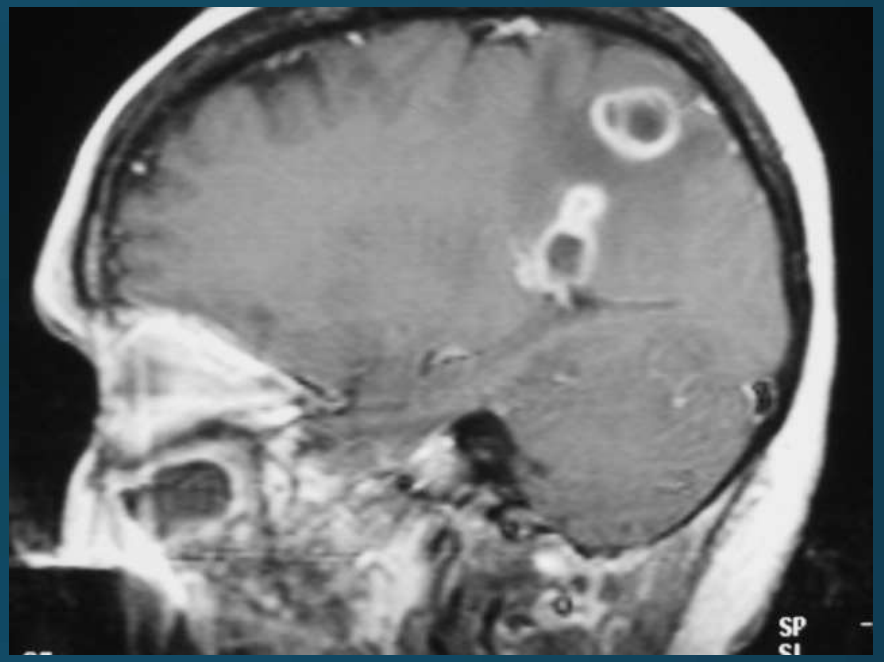
Older vs Newer stroke

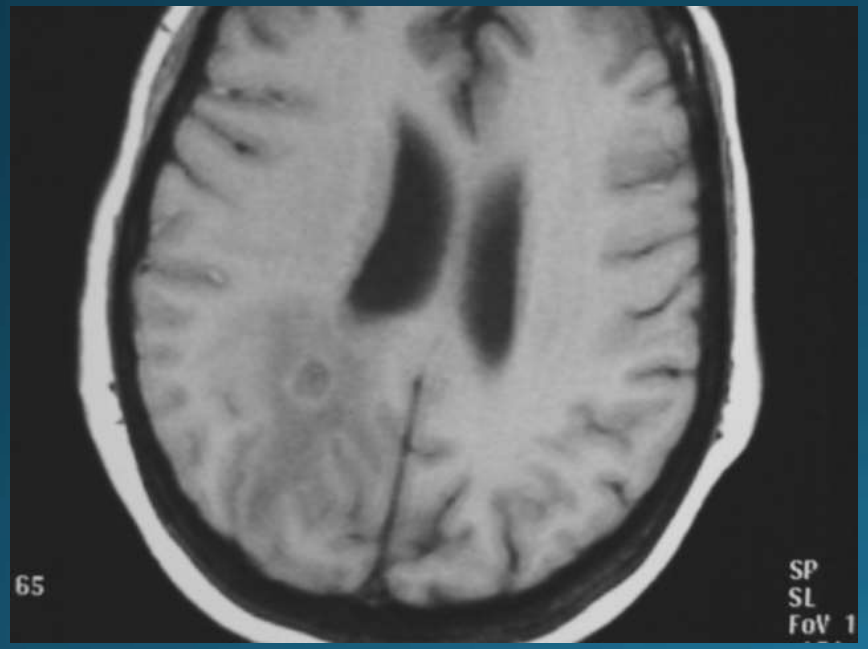
**DIFFUSION**

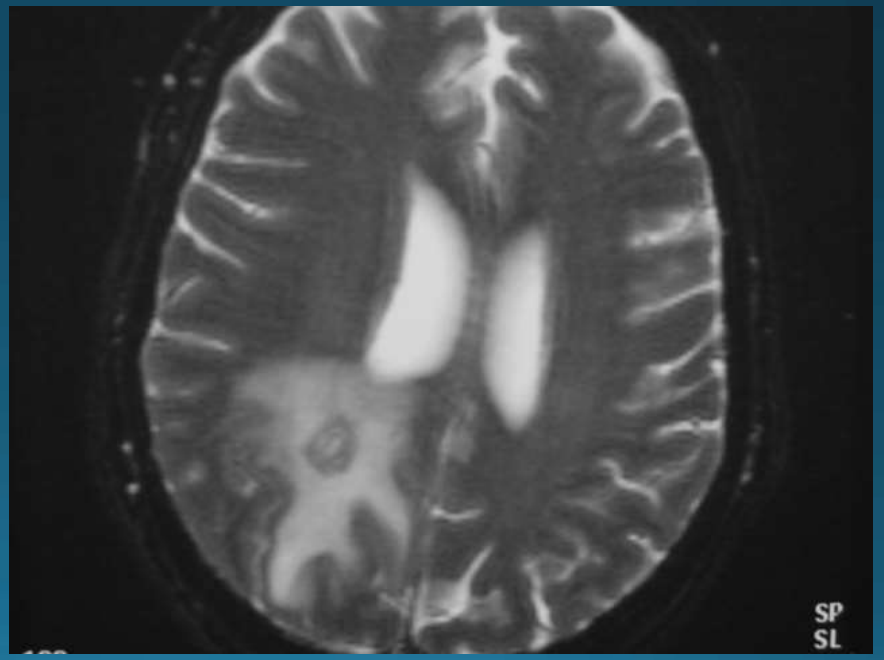
# 42 year old with headache

Ring enhancing lesions in right parietal lobe with edema.

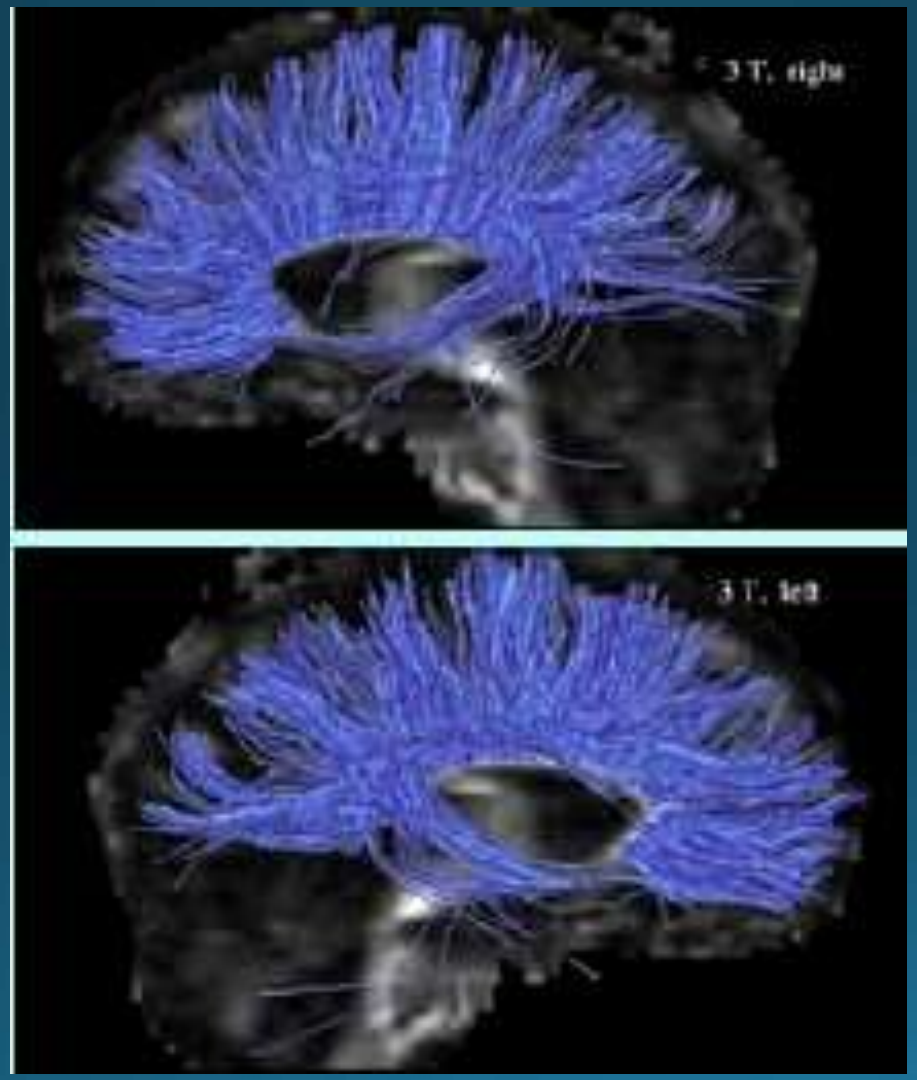
Ddx: abscess vs. tumor



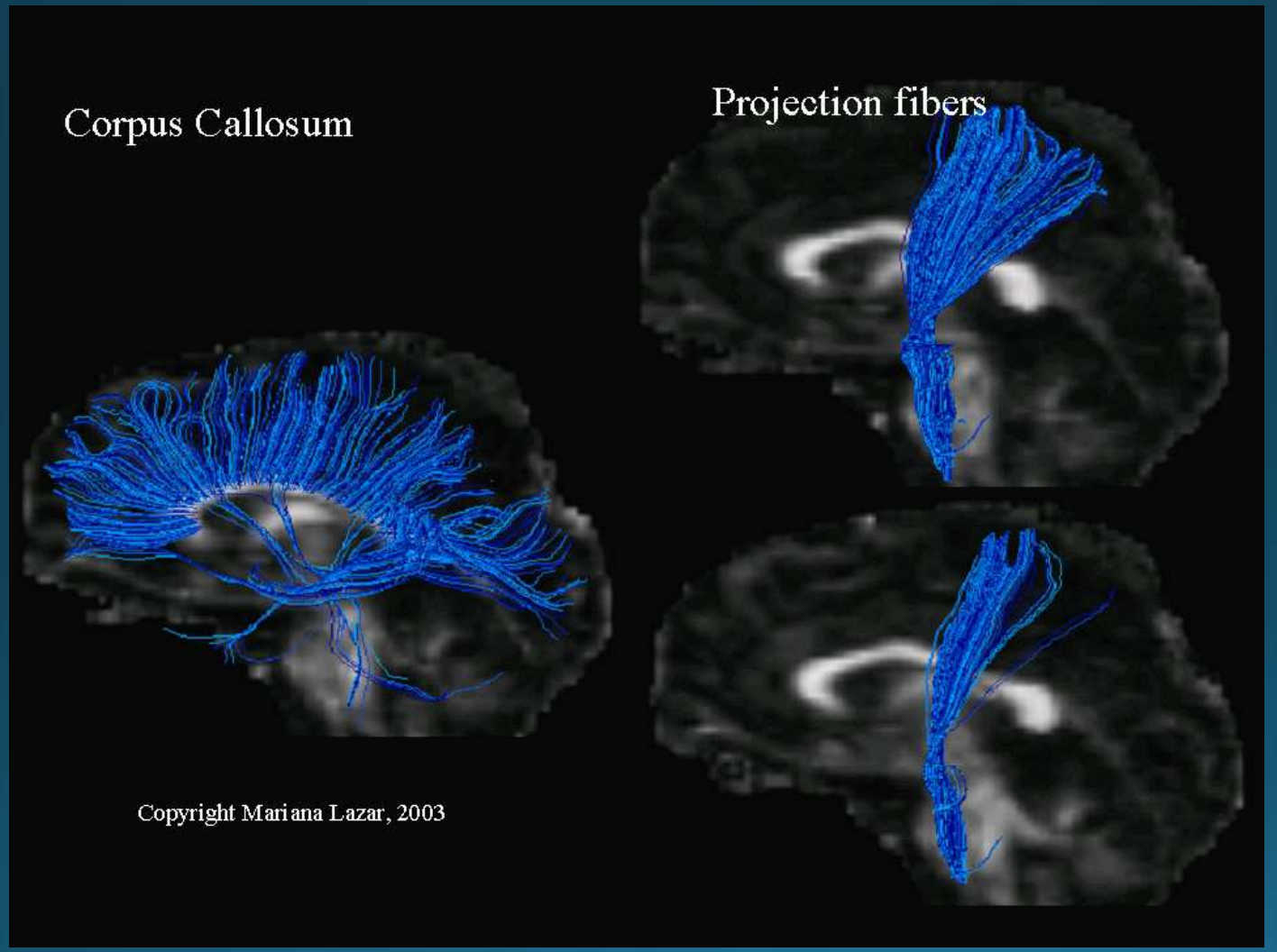



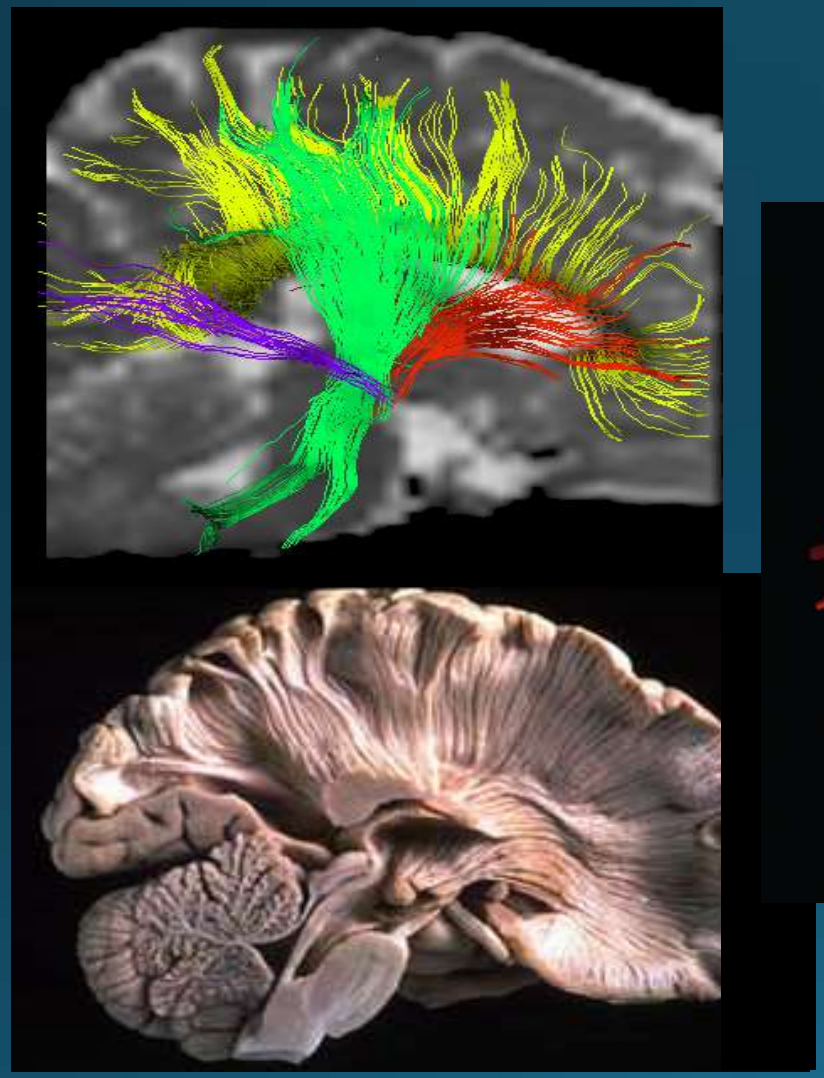
# White Matter: Diffusion Tensor MRI



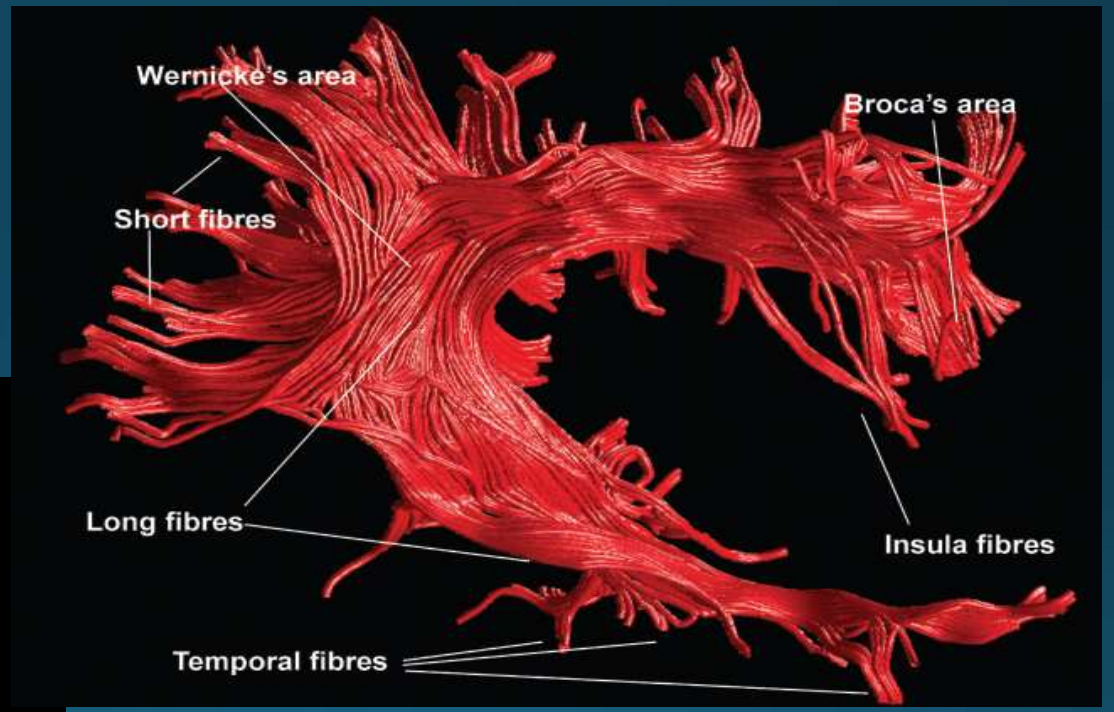
# Diffusion Tensor MRI



# DTI – Tractography

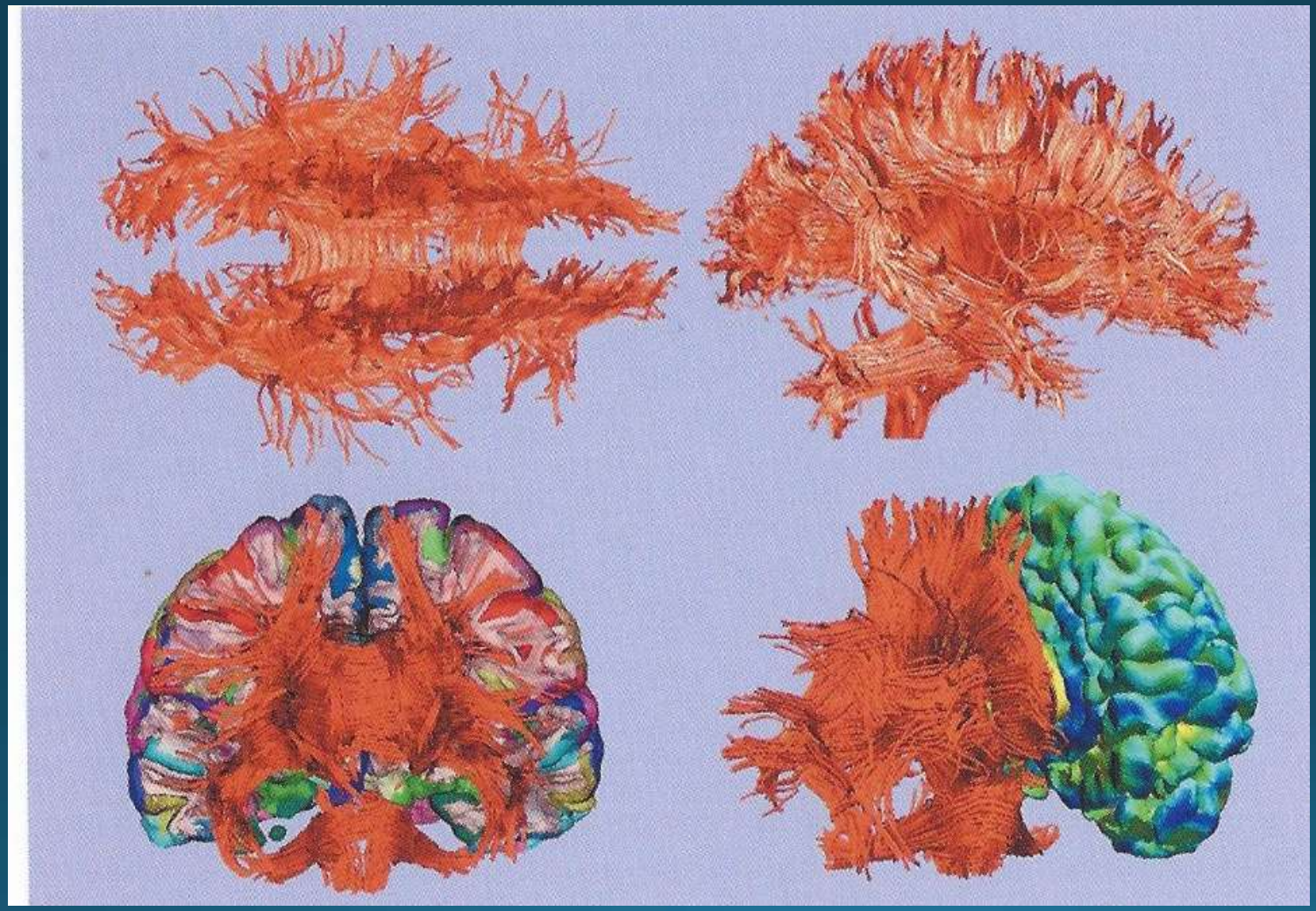


S. Mori - JHU

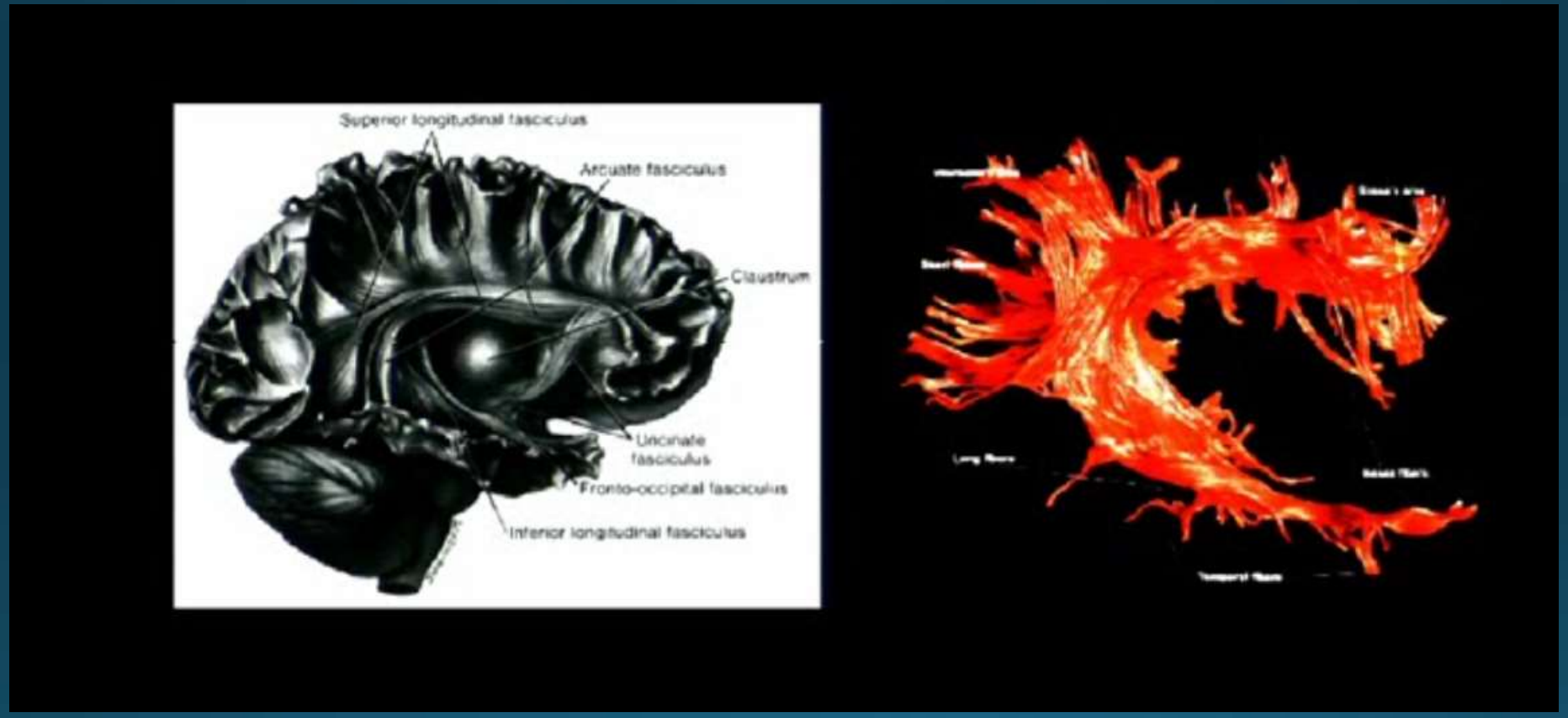



D. Jones – U Nottingham, UK

# DTI: White Matter tracts

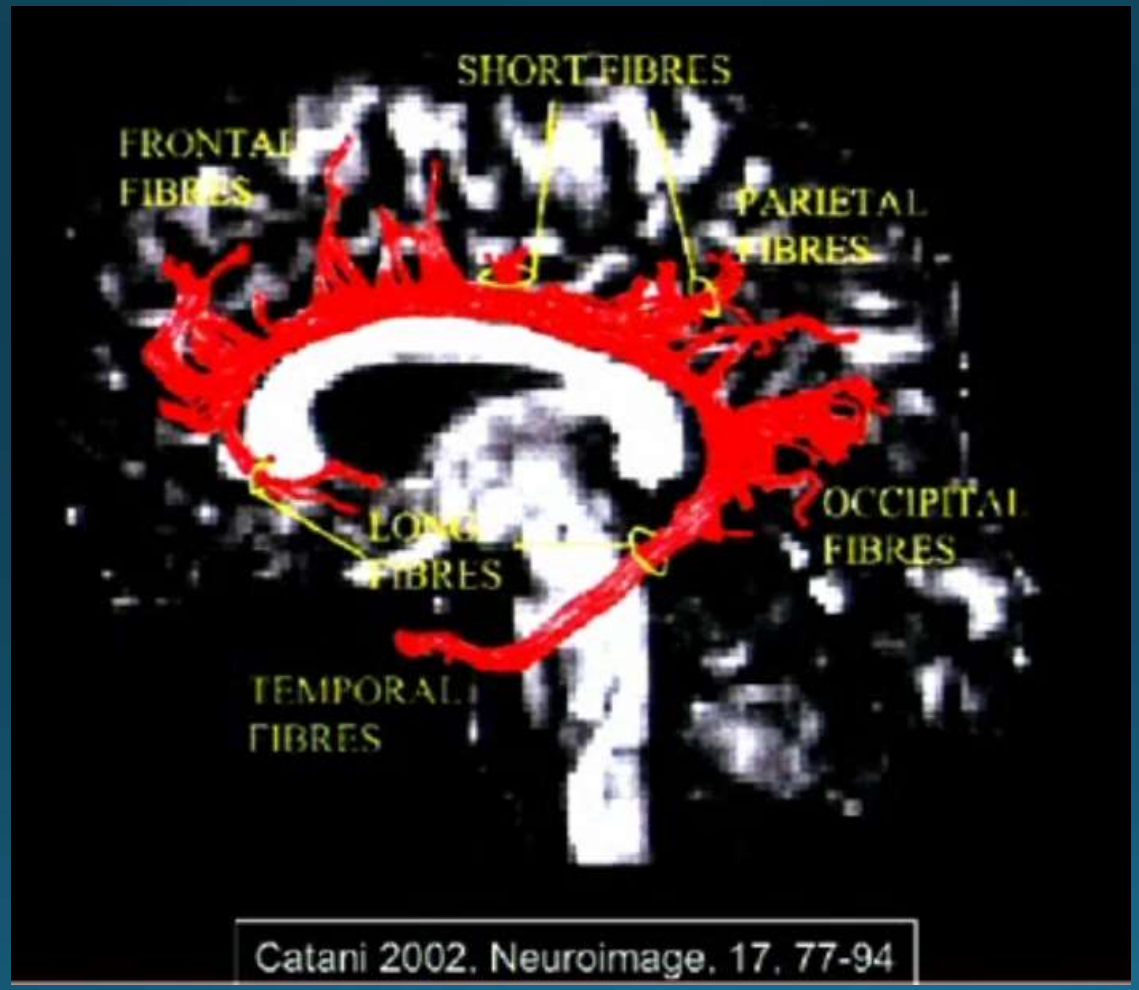


# Major fiber tracts can be mapped

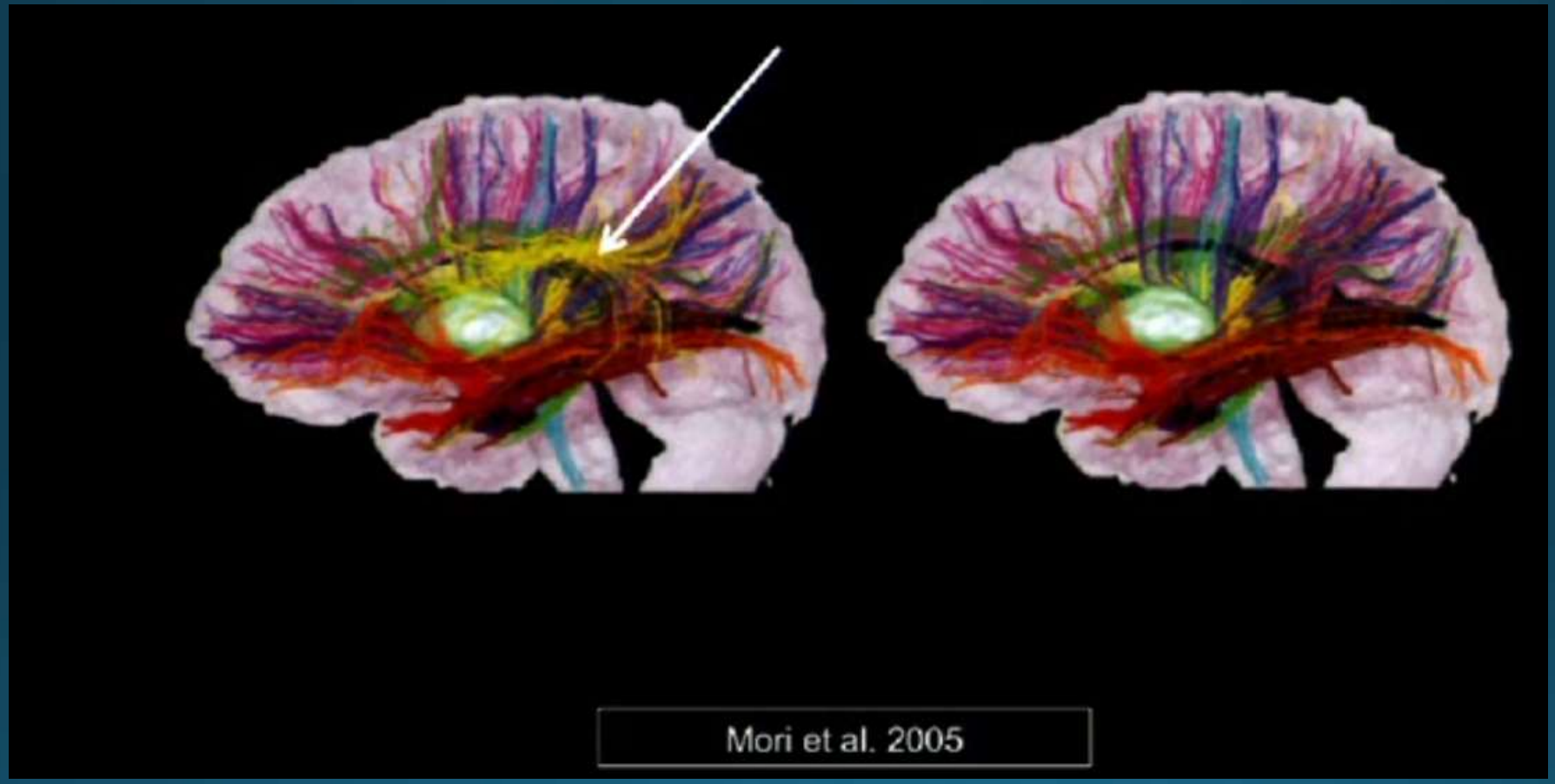



Superior Longitudinal Fasciculus & Arcuate Fasciculus

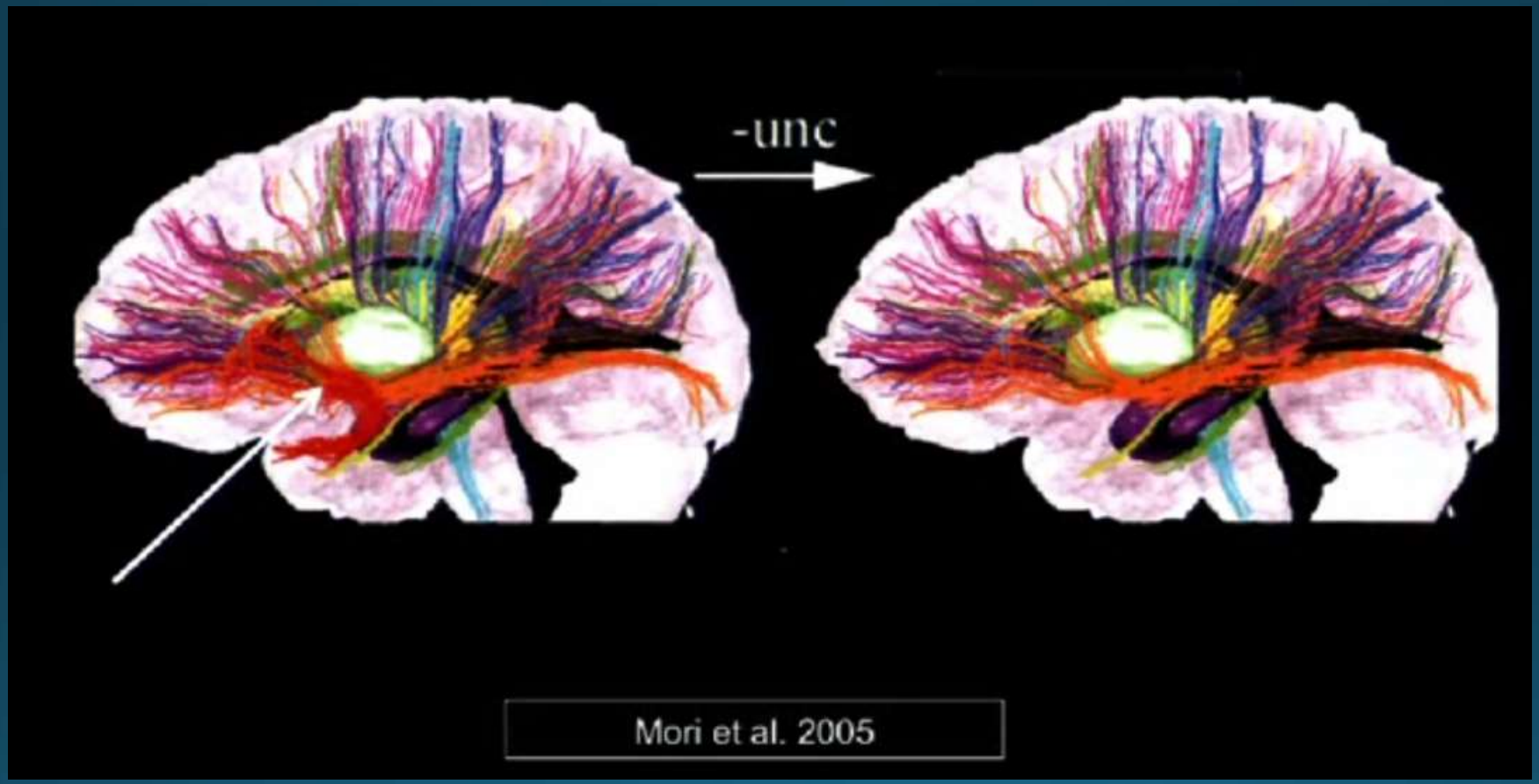
# Cingulum: Diffuse connections



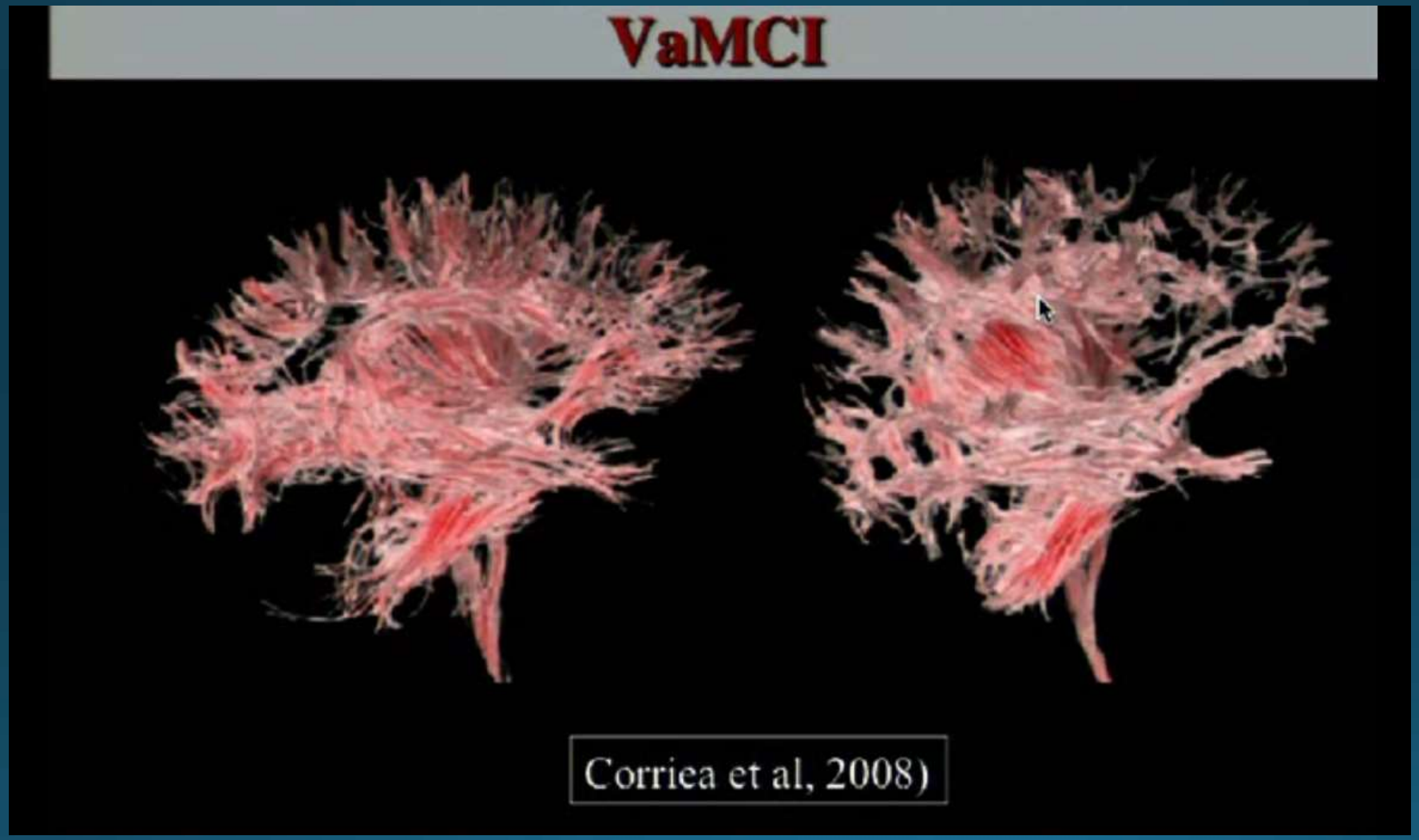
# Superior Longitudinal Fasciculus



# Uncinate Fasciculus: Limbic/memory to OFC

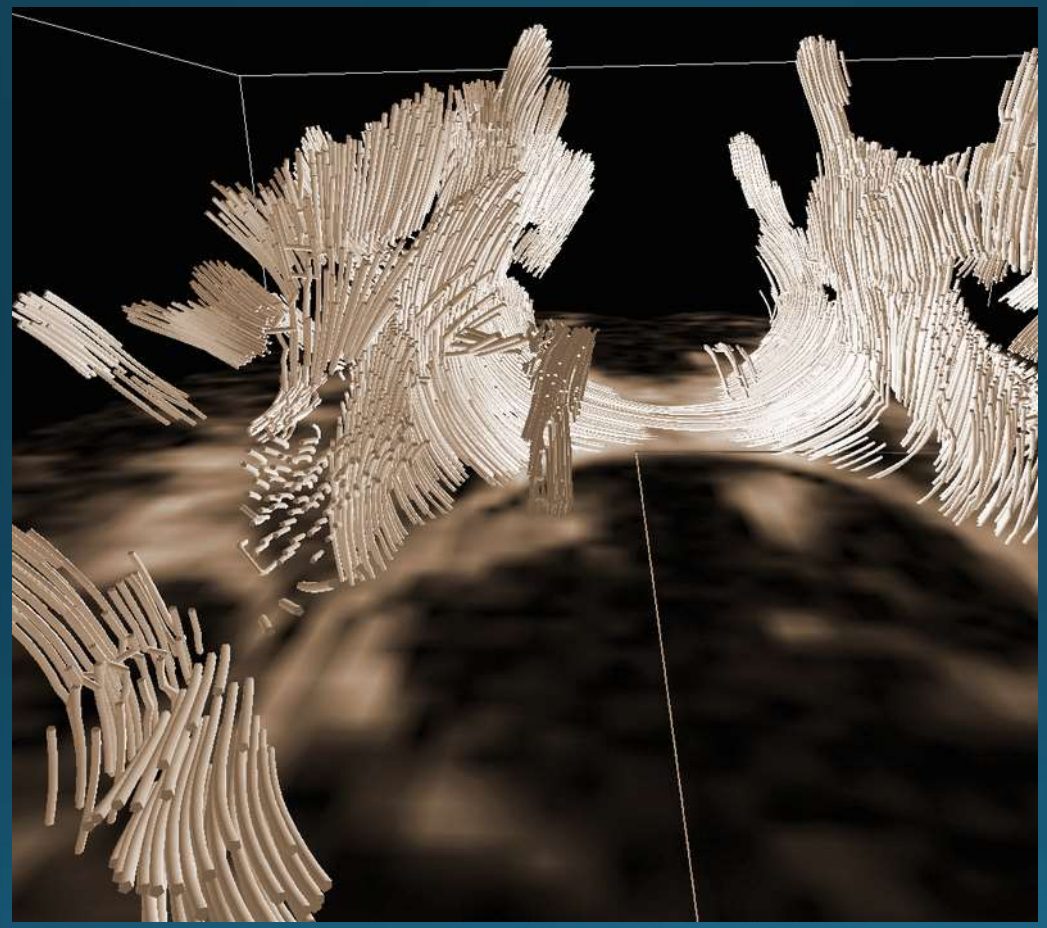


# Vascular Mild NCD (L) & Healthy Aging (R)

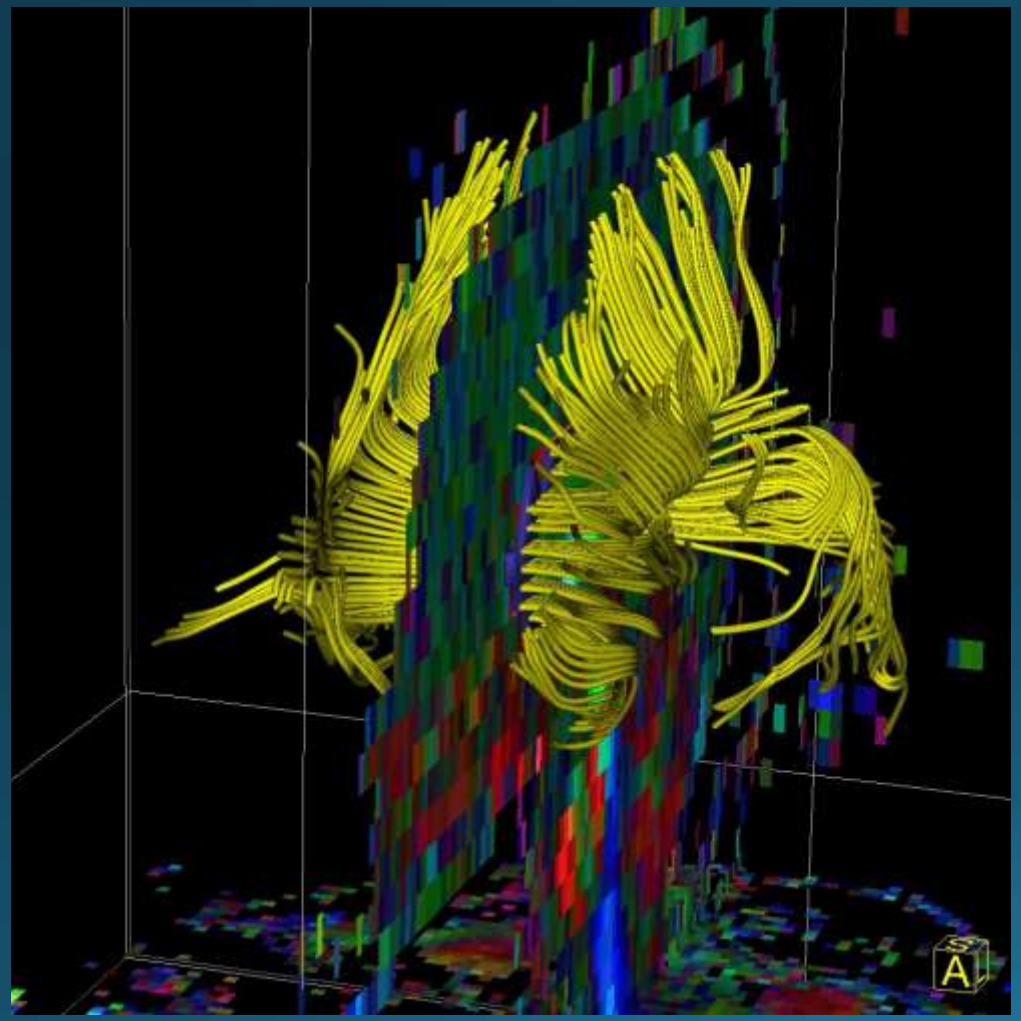


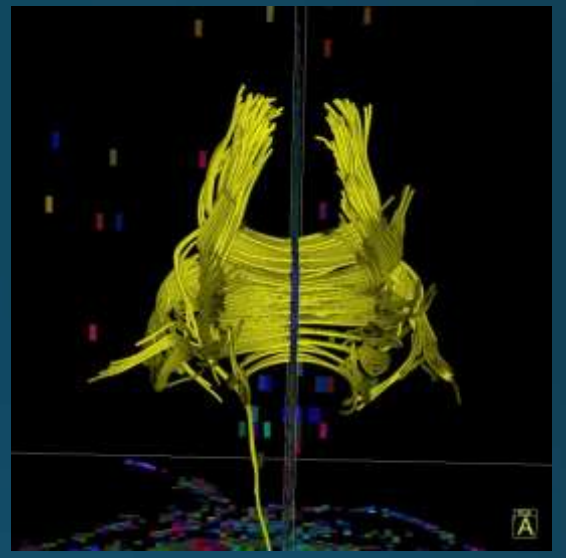

Reduction in WM correlated with PS and EF, indep. of atrophy

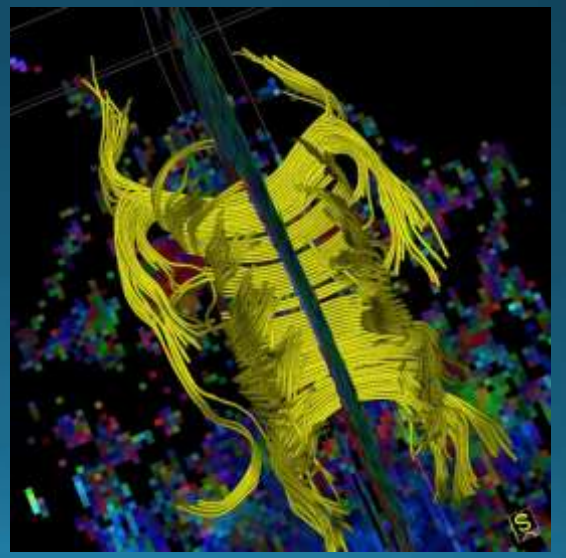
# White Matter: Diffusion Tensor MRI



# DTI-Tractography:  Corpus Callosum

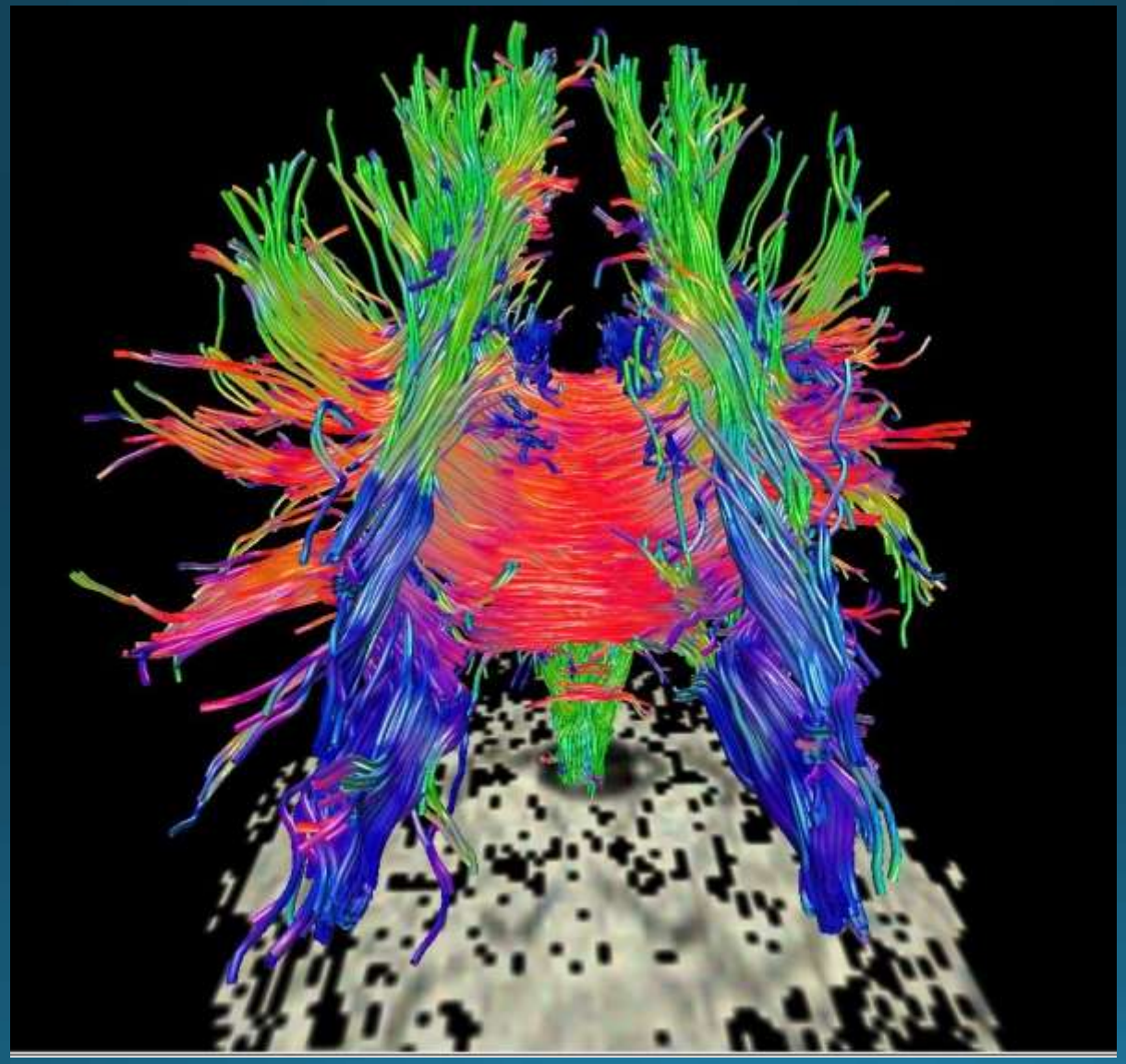




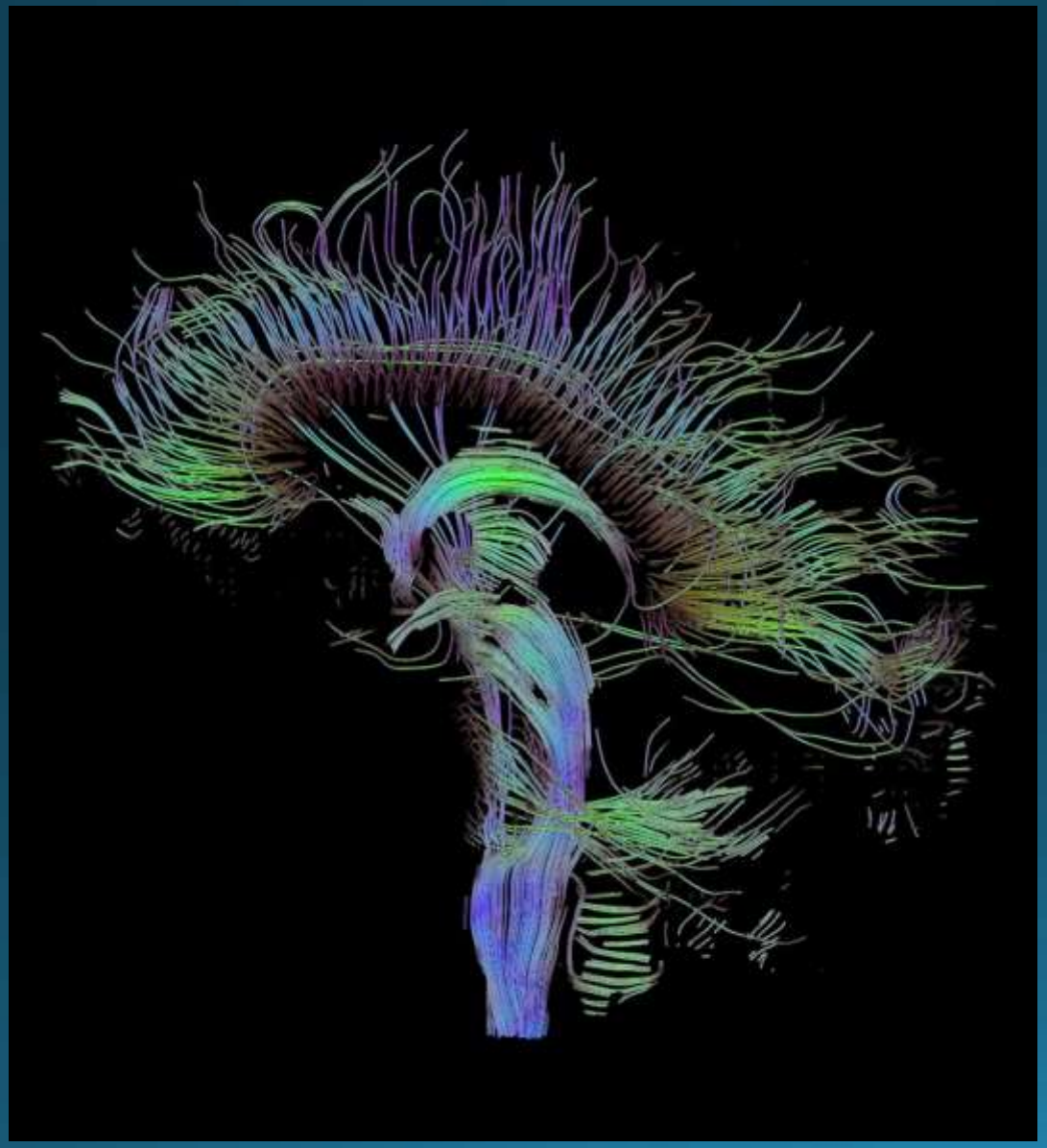


W. Zhan et. al.

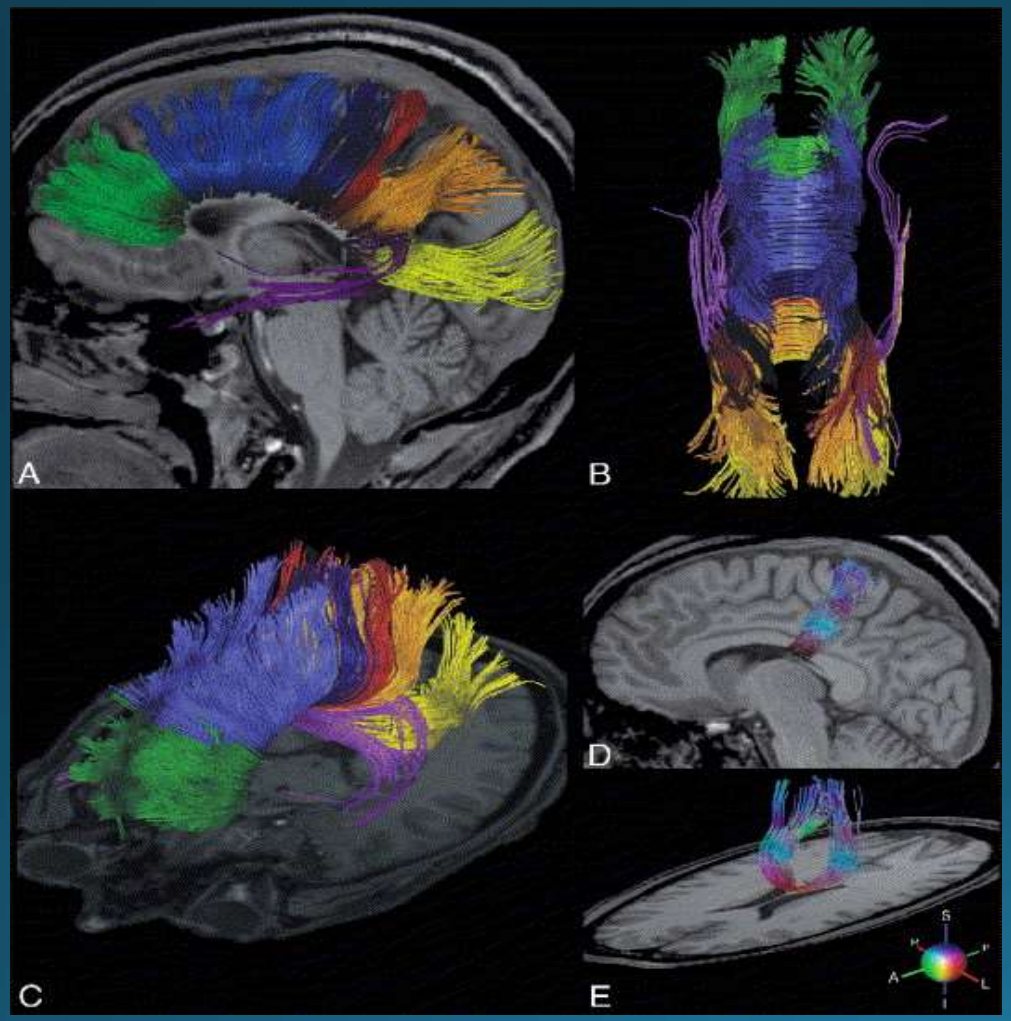
# DTI: Corpus Callosum



# MRI: Corpus Callosum and Brain Stem

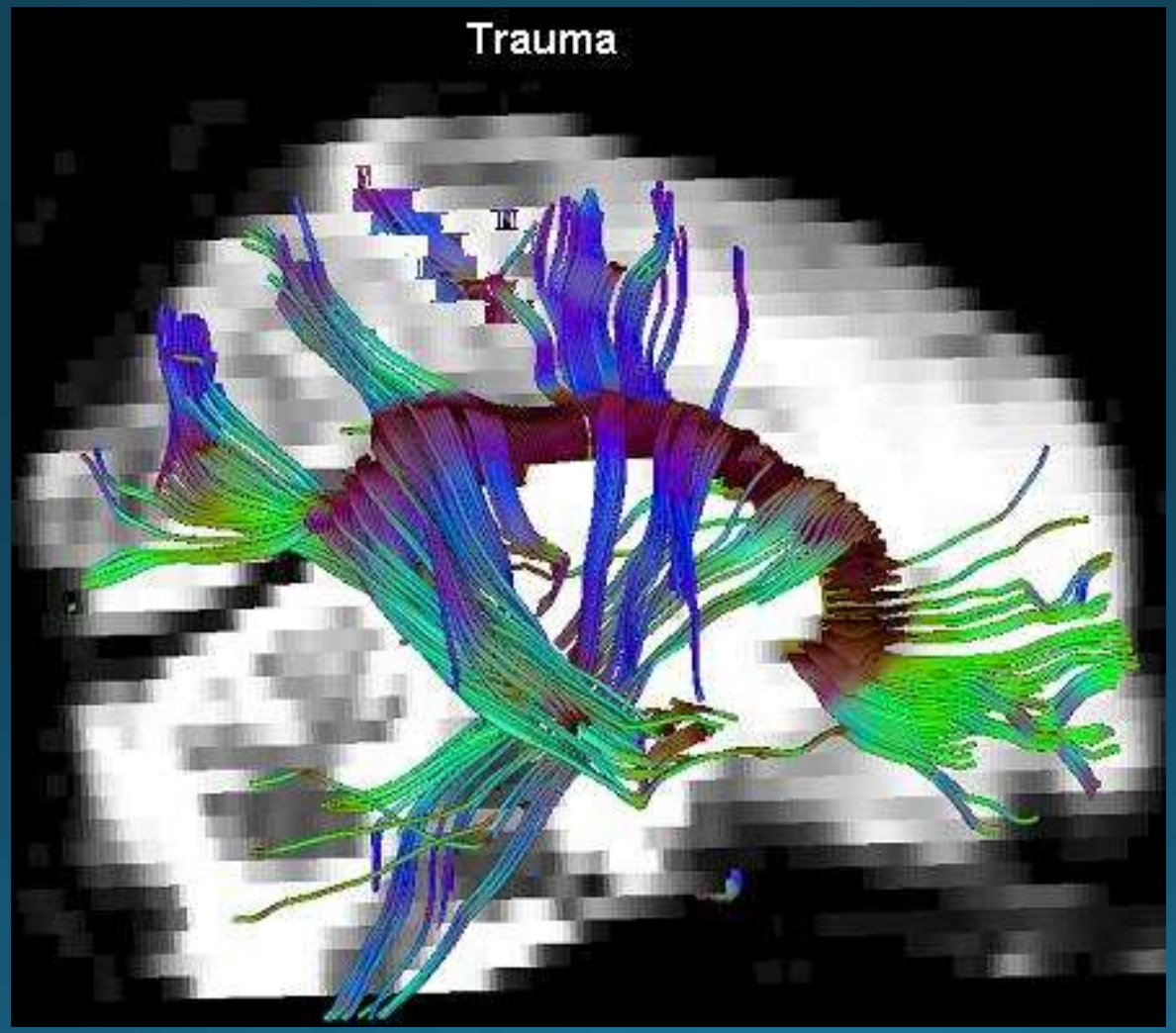


# DTI: Corpus Callosal Projections; Color Coded for Destination

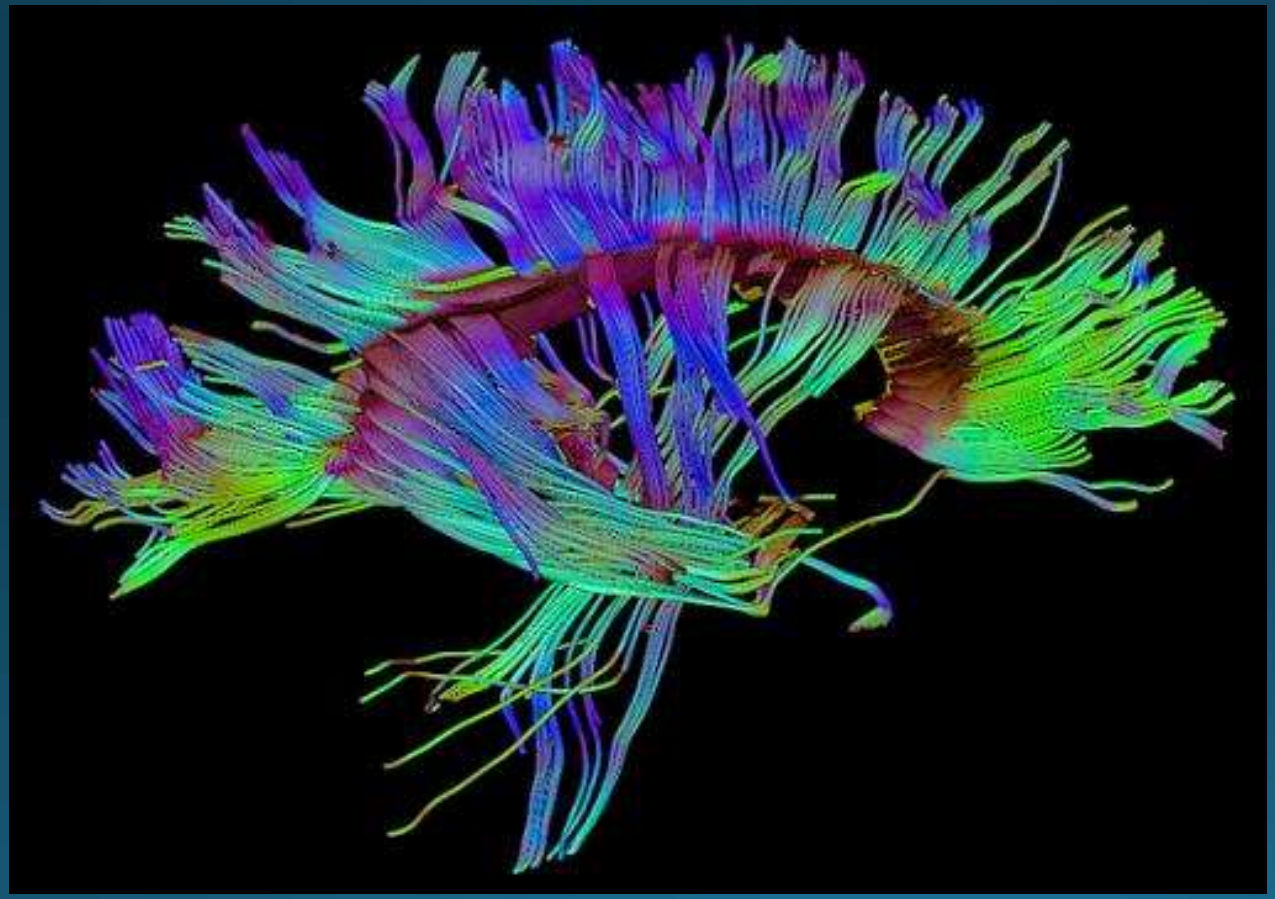



Green: Prefrontal
Blue: Premotor
Dark Blue: Motor
Red: Sensory
Orange: Parietal
Yellow: Occipital

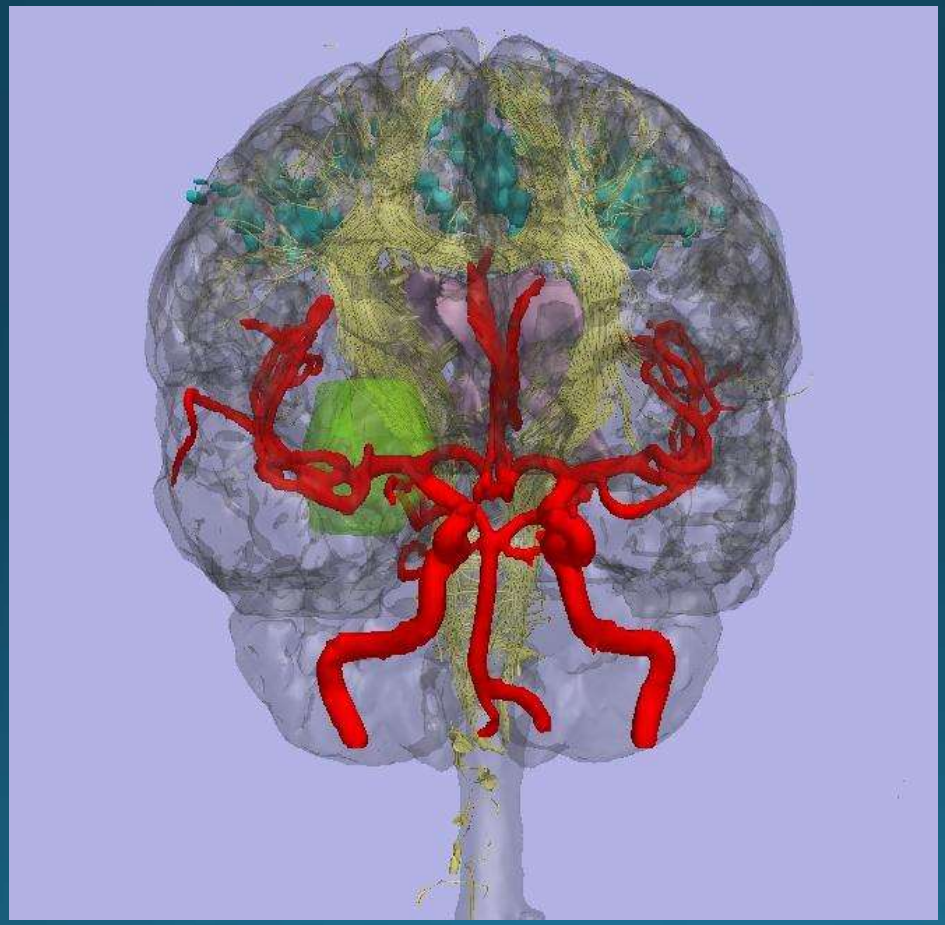
# DTI: Trauma



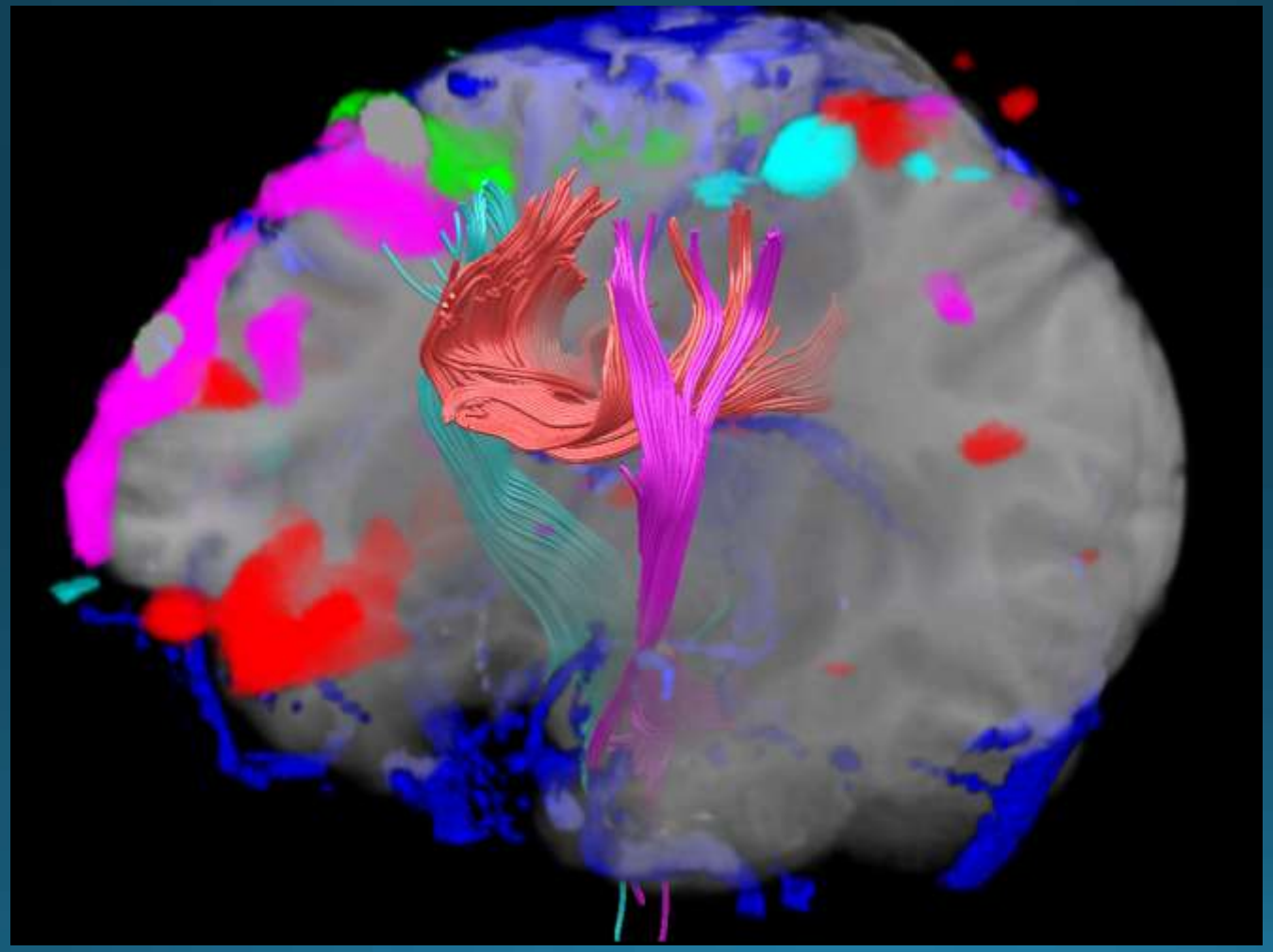
# White Matter: Diffusion Tensor MRI in TBI



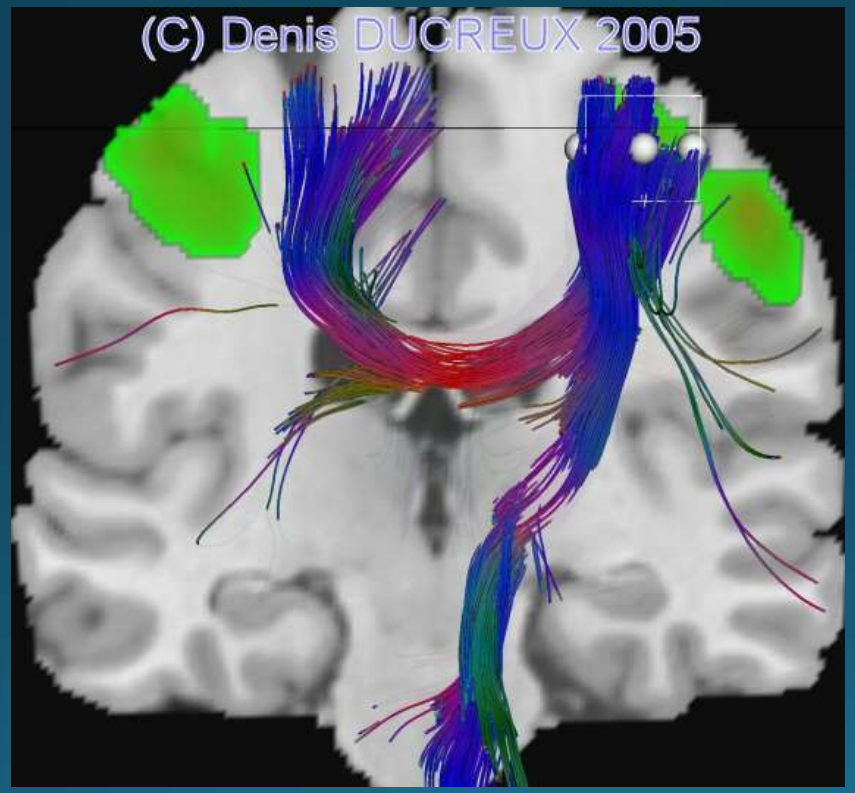
# DTI: Use in Neurosurgery



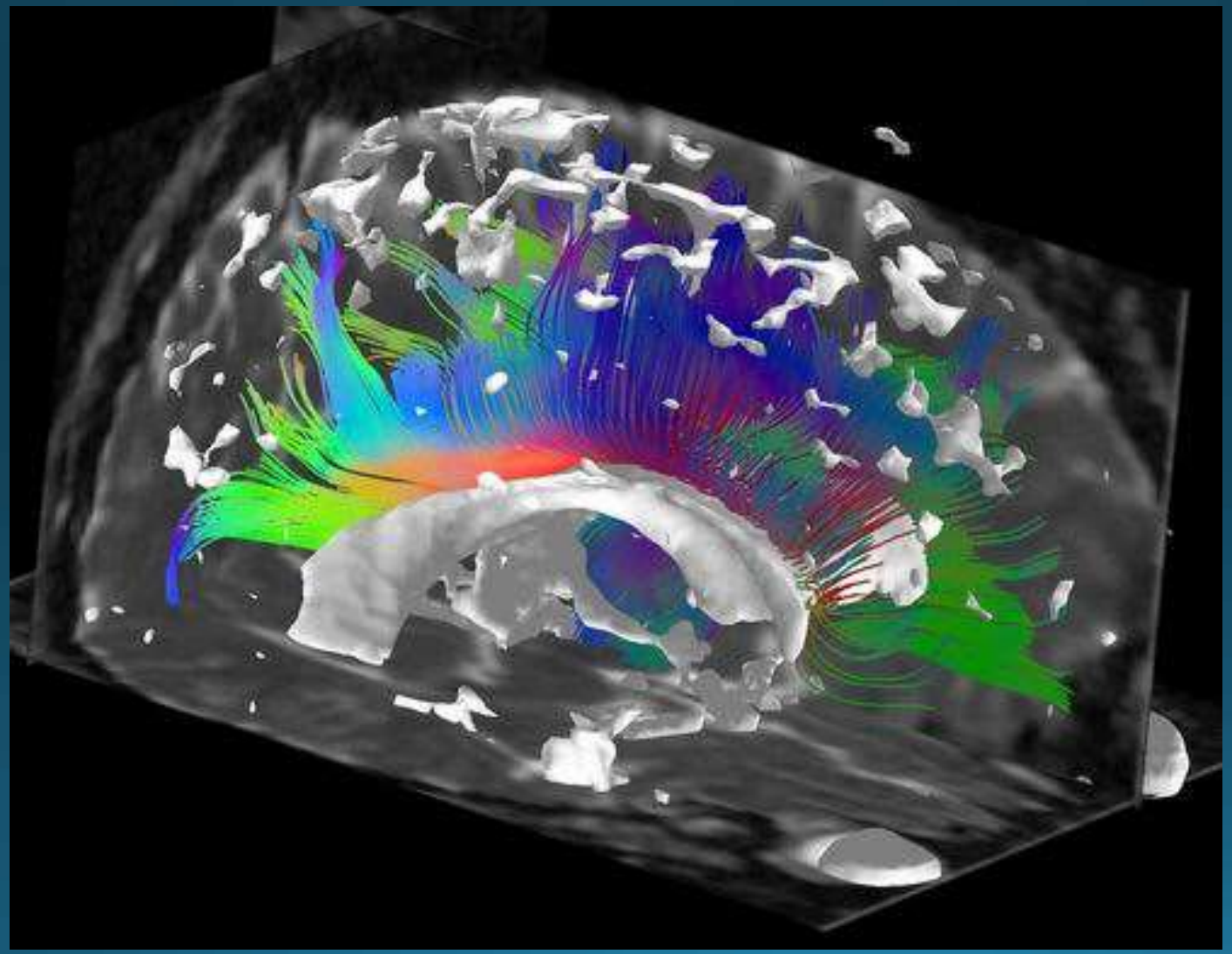
# FMRI + DTI



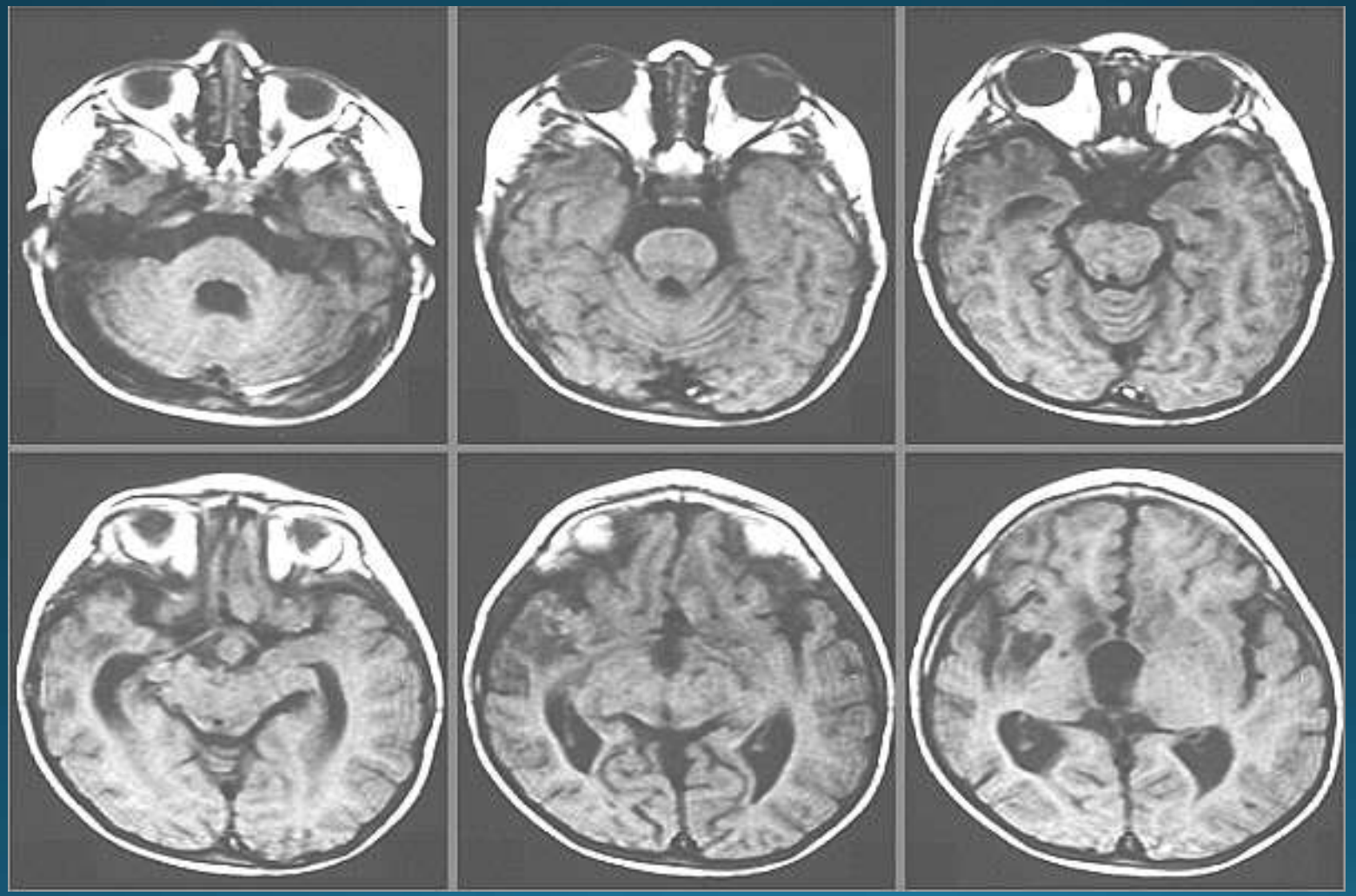
# White Matter: Diffusion Tensor MRI



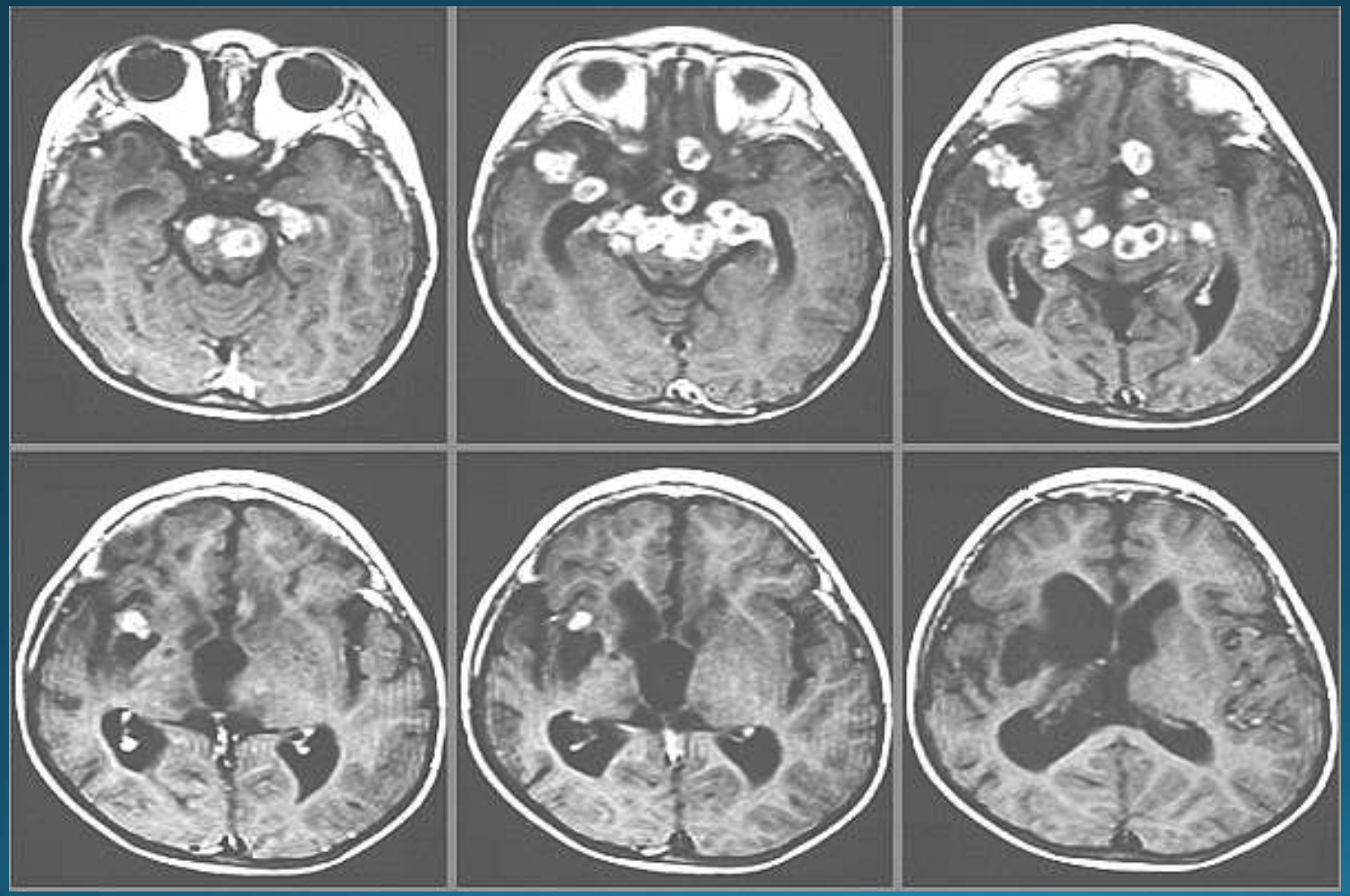
# White Matter: Diffusion Tensor MRI



T1 weighted MR images of a child – no obvious pathology visible.



After contrast administration, numerous ring enhancing abscesses are visible at the base of the brain. *Diagnosis*: CNS tuberculosis.
*Teaching point:* Utility of gadolinium contrast in MRI.



# MRI with contrast

Contrast increases tissue differentiation: Makes T1-weighted images brighter where it accumulates and makes T2-weighted images darker

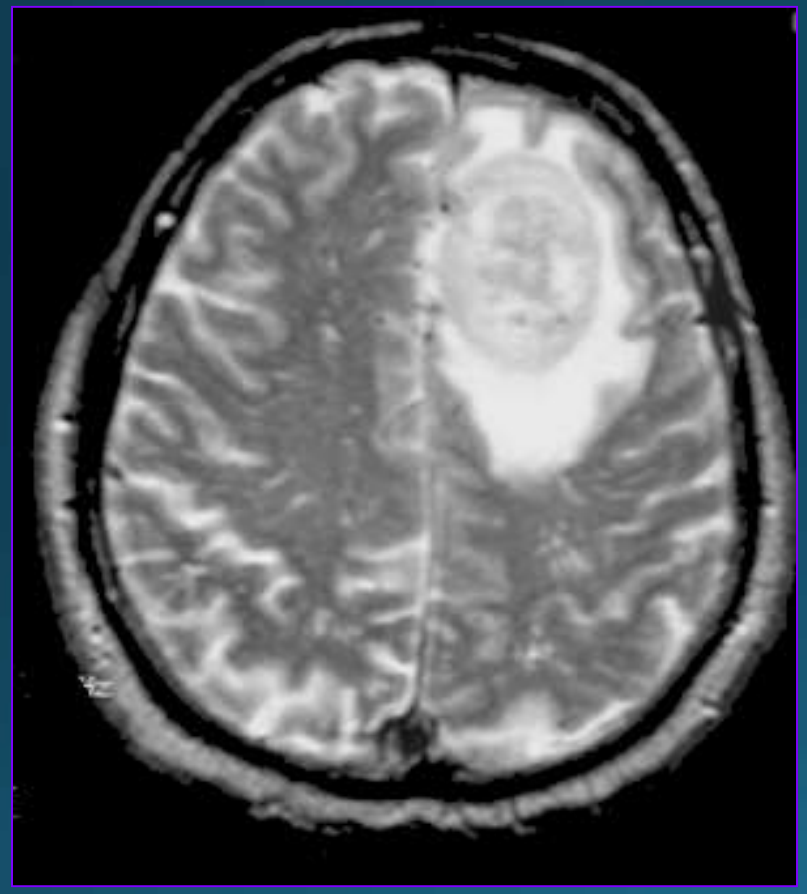
Administer Gadolinium

Useful for infection, inflammatory process, neoplasm

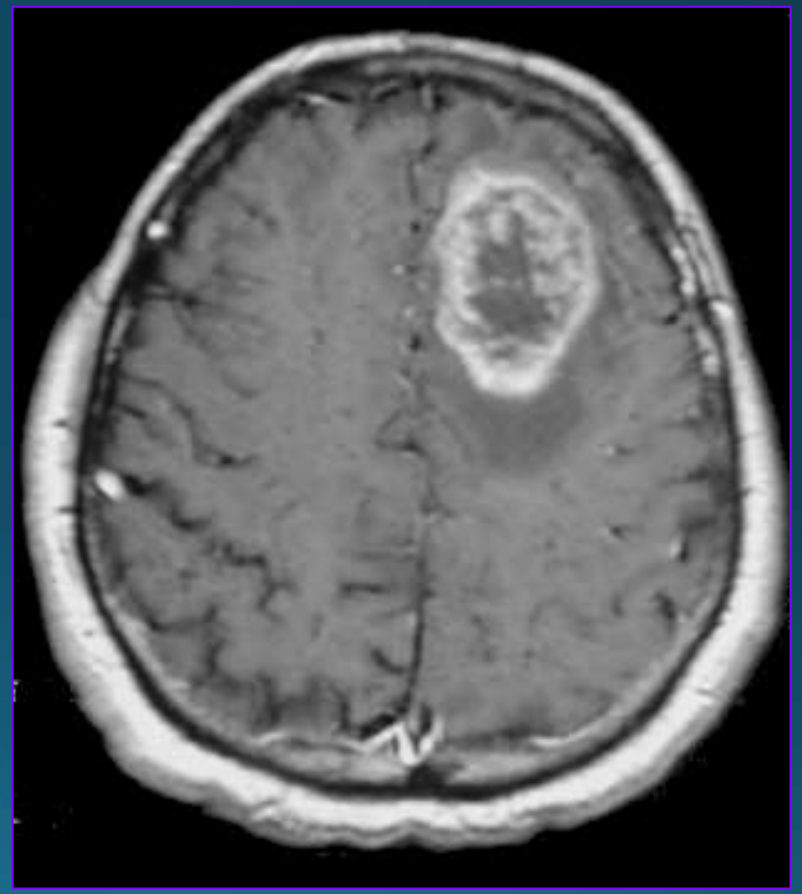
Does not significantly affect renal function – unlike CT contrast

Less risk of allergic reaction than with iodinated (CT) contrast; About 1 person in 100,000 has allergic reaction

# Tumor: T2 and T1+contrast

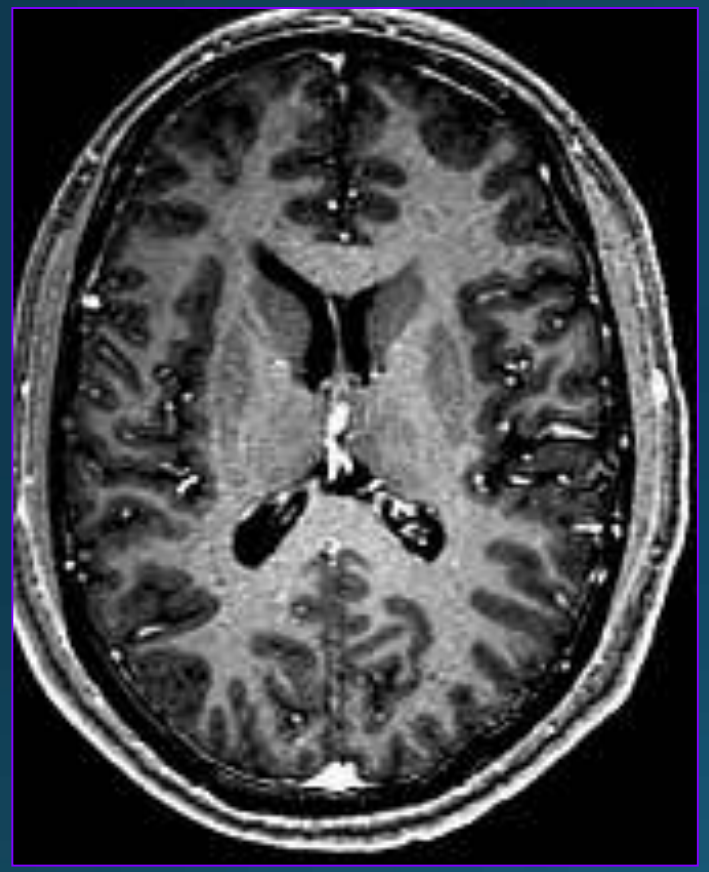


T2-weighted



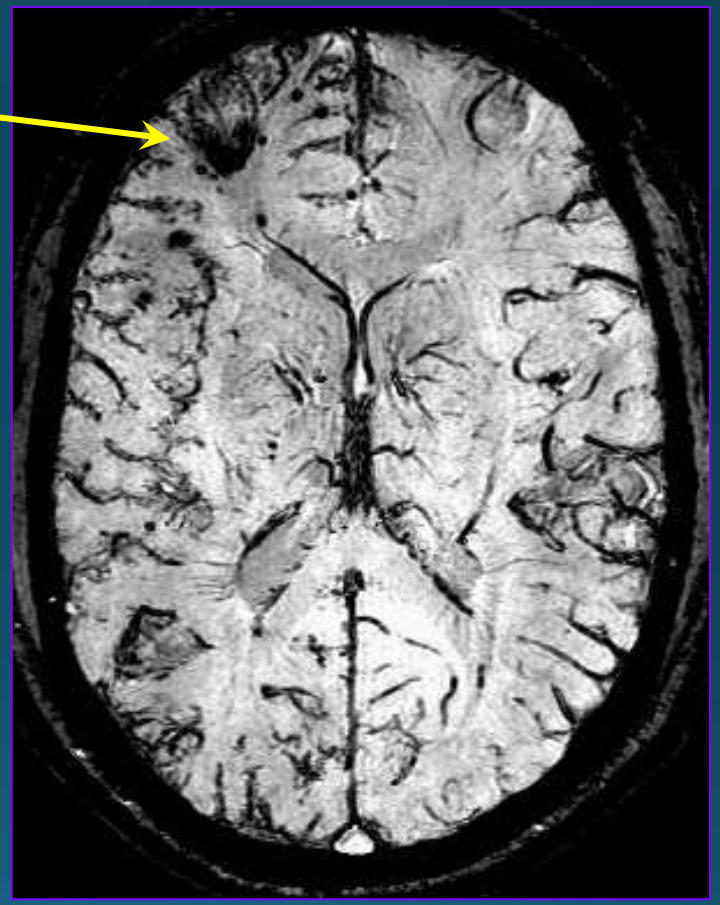
T1-weighted post-contrast

# T2* MR Venography on a Seizure Patient



Gd-enhanced T1-weighted

Lesion



Gd-enhanced T2*-weighted

# MRI: Gradient Echo/Gradient Recall Image (GRE)

T2* decay underlies all gradient echo imaging

Bleeds (even microbleeds) leave behind iron (hemosiderin): GRE detects iron

GRE has highest sensitivity in detecting early hemorrhagic changes

Hemorrhagic shear lesions (in TBI) leave hemosiderin deposits; all brain cells have capillaries, which can be sheared

# Microbleeds in TBI

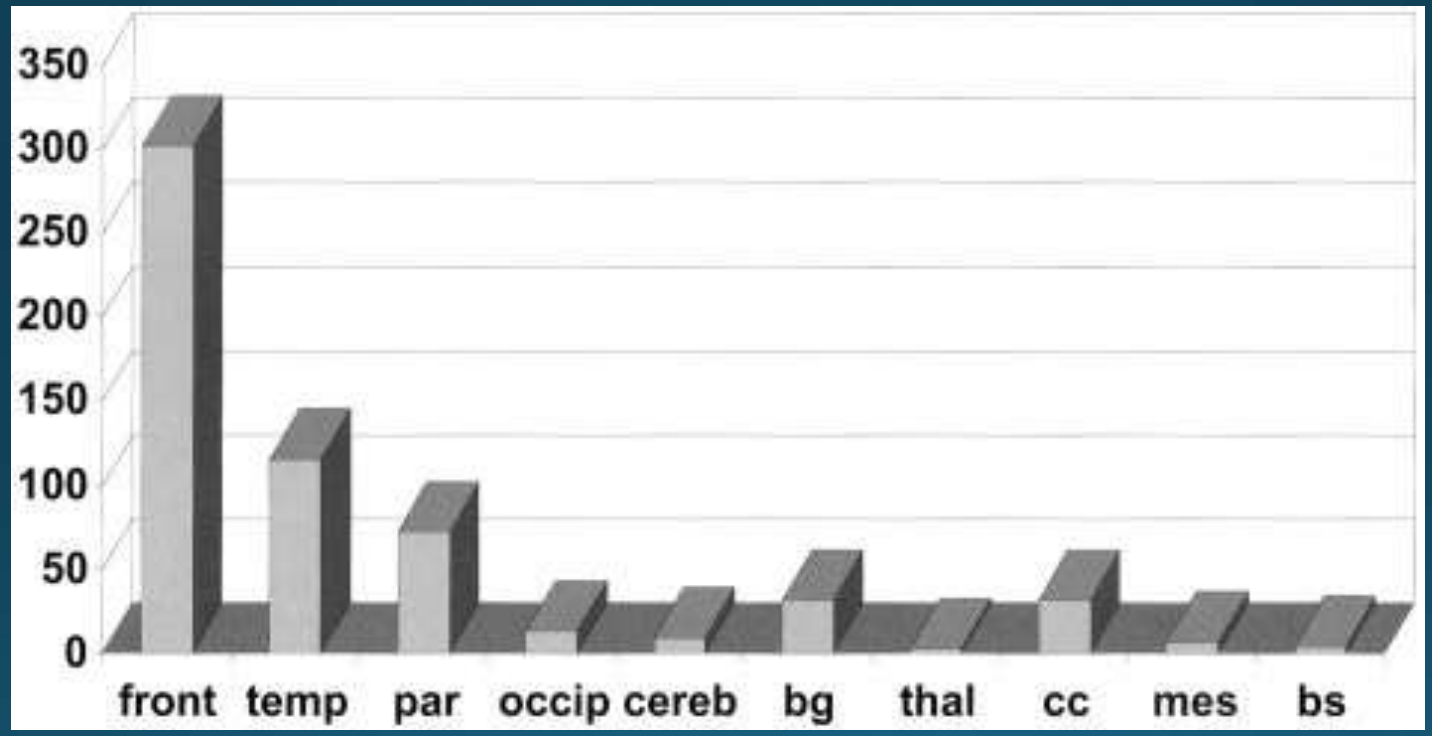
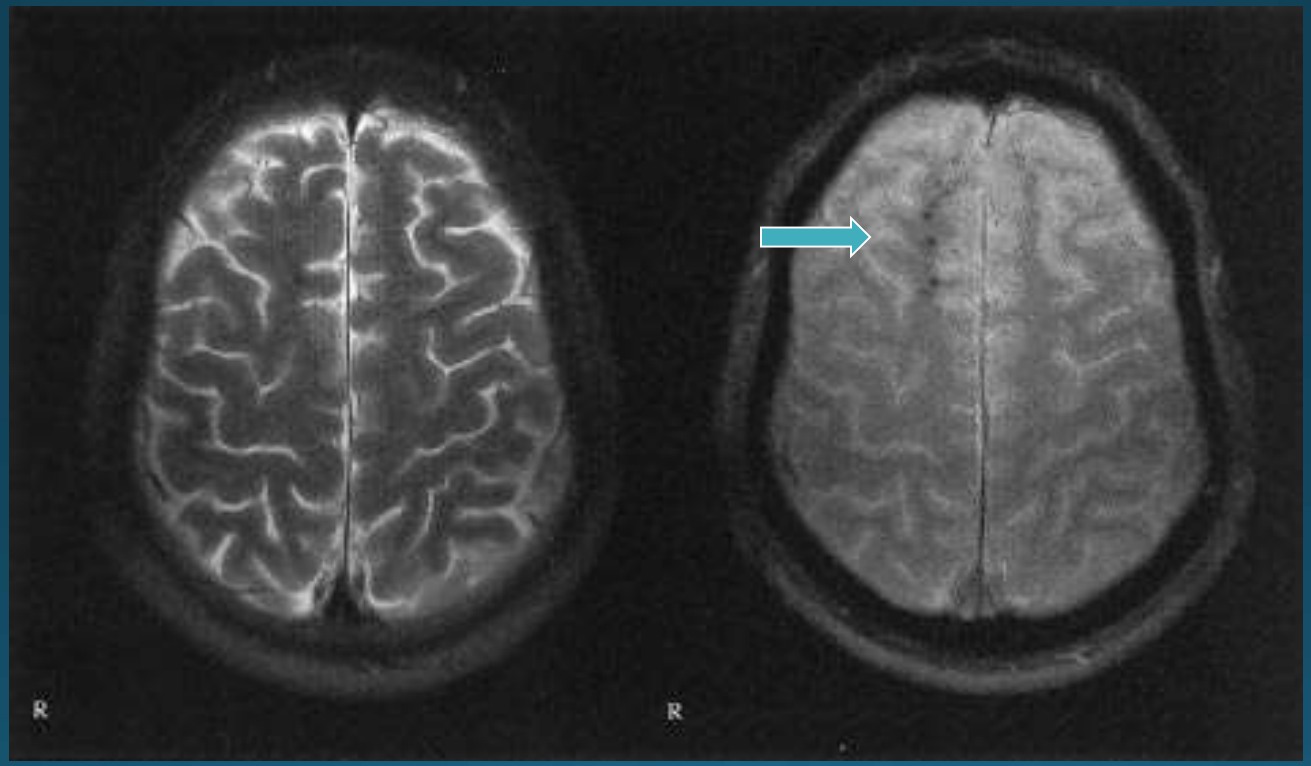



FIG 1. Frequency and site of traumatic microbleeds according to 10 brain areas. Shown is the total number of traumatic microbleeds in each brain area

AJNR: 24, June/July 2003

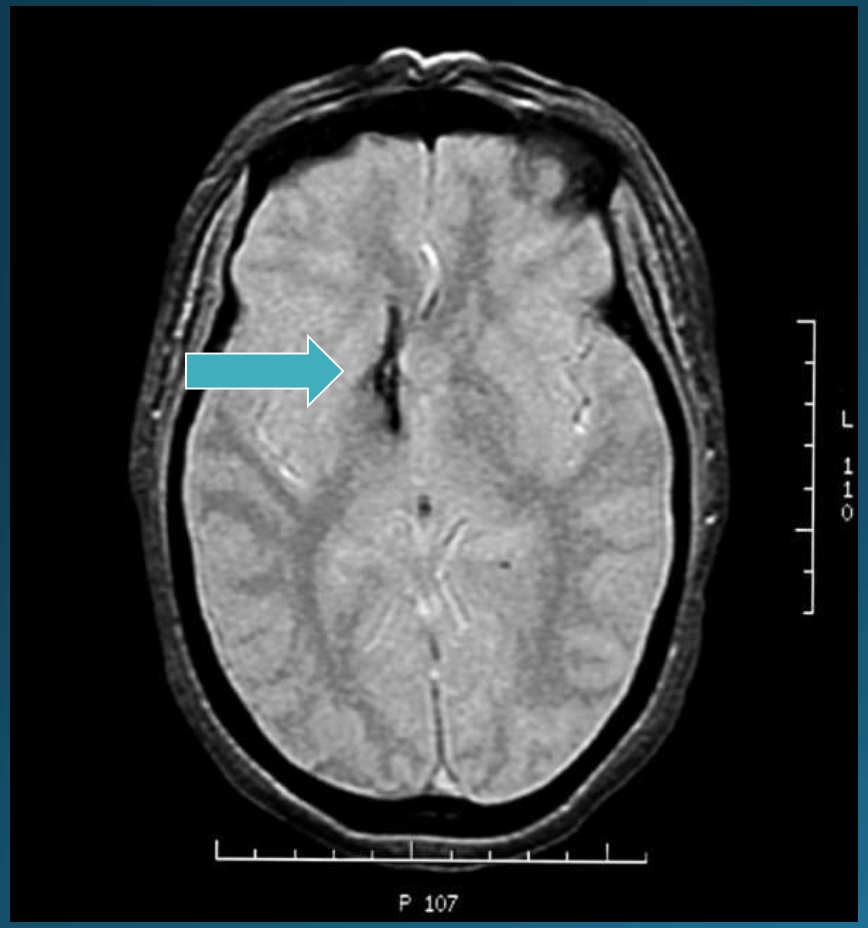
# Microbleeds

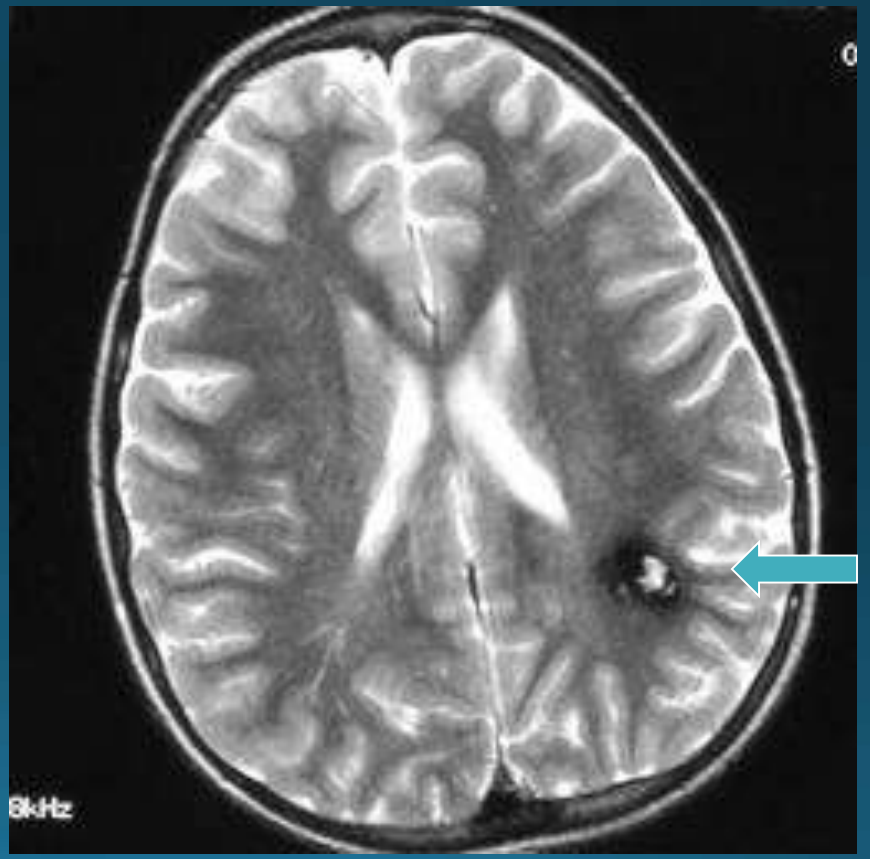
*Left*, T2-weighted image; *right*: T2*GRE-weighted image



20-year-old man in MVA: Multiple traumatic microbleeds are shown in the white matter of the right superior frontal gyrus.

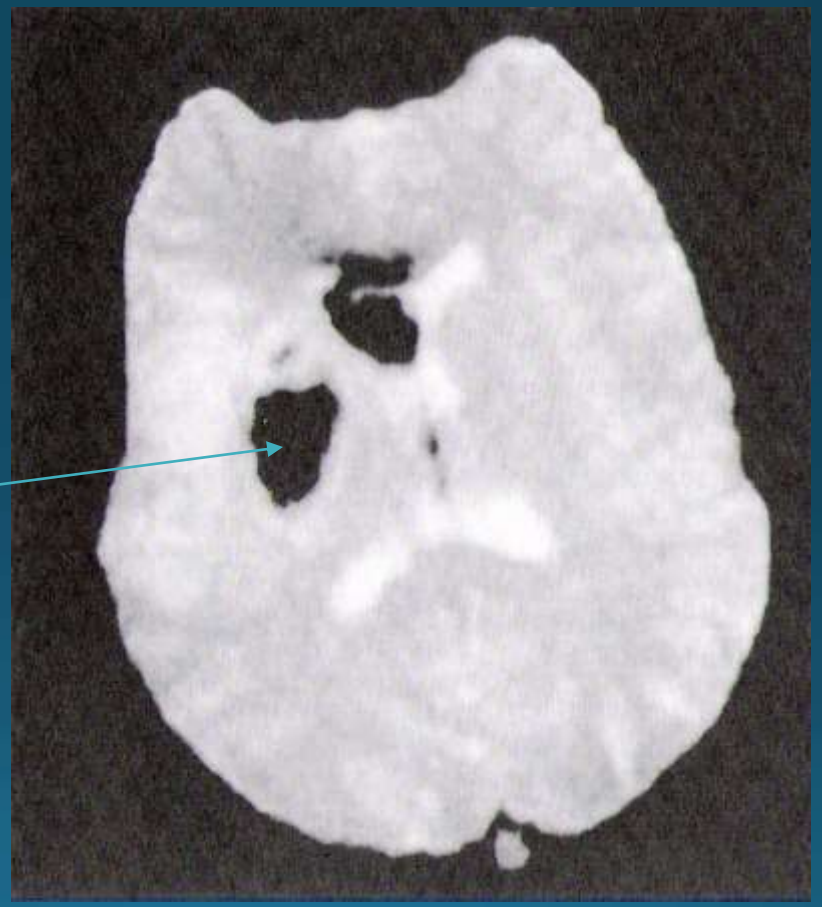
# MRI: Gradient Echo:
# Hemosiderin



# Gradient Echo (GE) MRI with hemorrhage

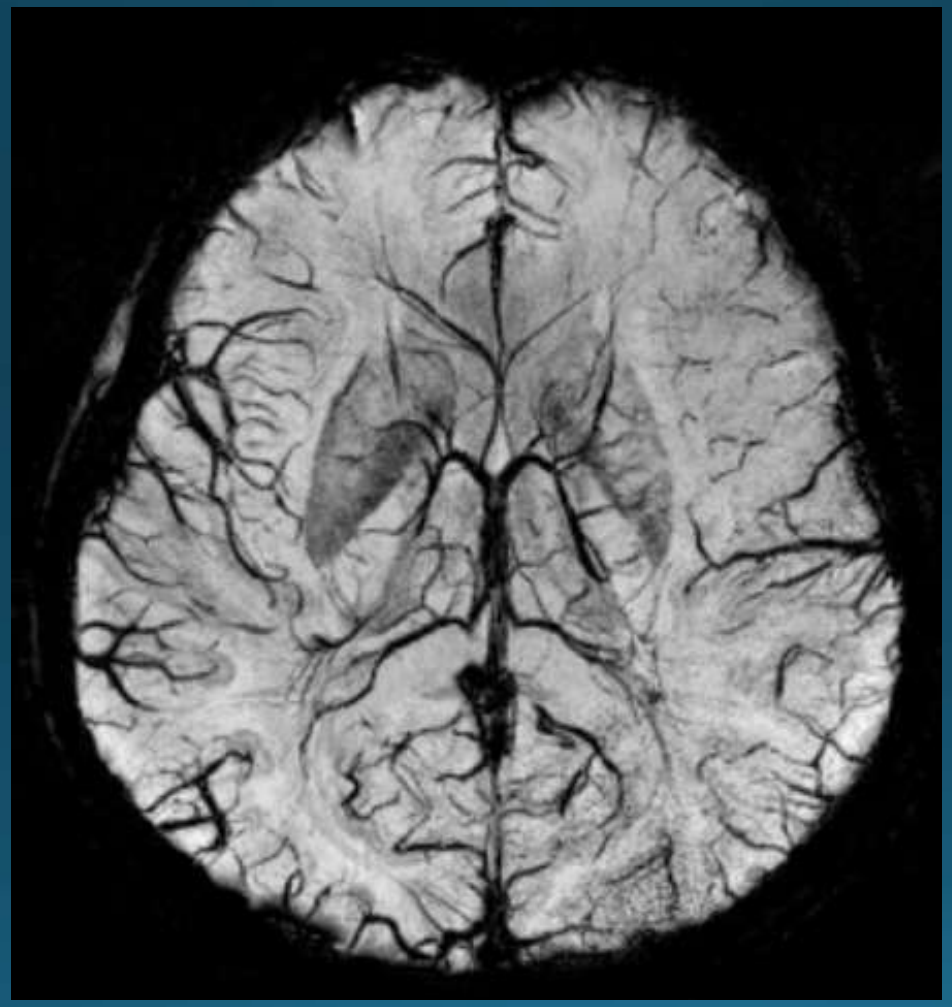
- Enhanced ability to detect fresh blood or chronic hematoma
- Acute and chronic hemorrhage as very low signal (black)



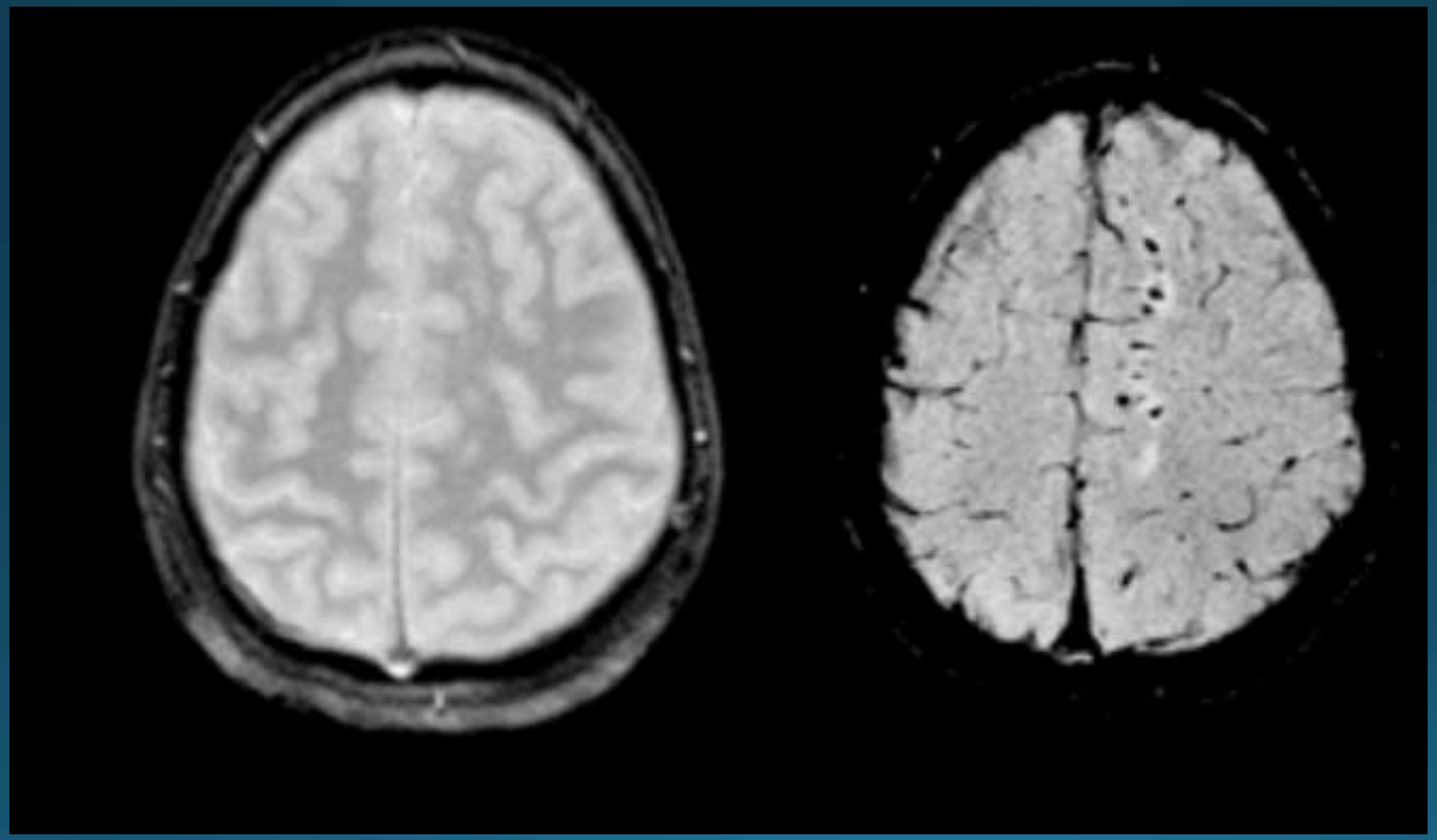
# Susceptibility weighted imaging (SWI)

- SWI uses a fully flow compensated, long echo, gradient recalled echo (GRE) pulse sequence to acquire images. This method exploits the susceptibility differences between tissues.
- Exquisitely sensitive to venous blood, hemorrhage and iron storage.
- The imaging of venous blood with SWI is a blood-oxygen-level dependent (BOLD) technique,  referred to as BOLD venography.
- Due to its sensitivity to venous blood SWI is commonly used in traumatic brain injuries (TBI) and for high resolution brain venographies
- Uses: TBI, stroke & hemorrhage, tumors, MS

# Susceptibility weighted imaging (SWI) of veins in brain



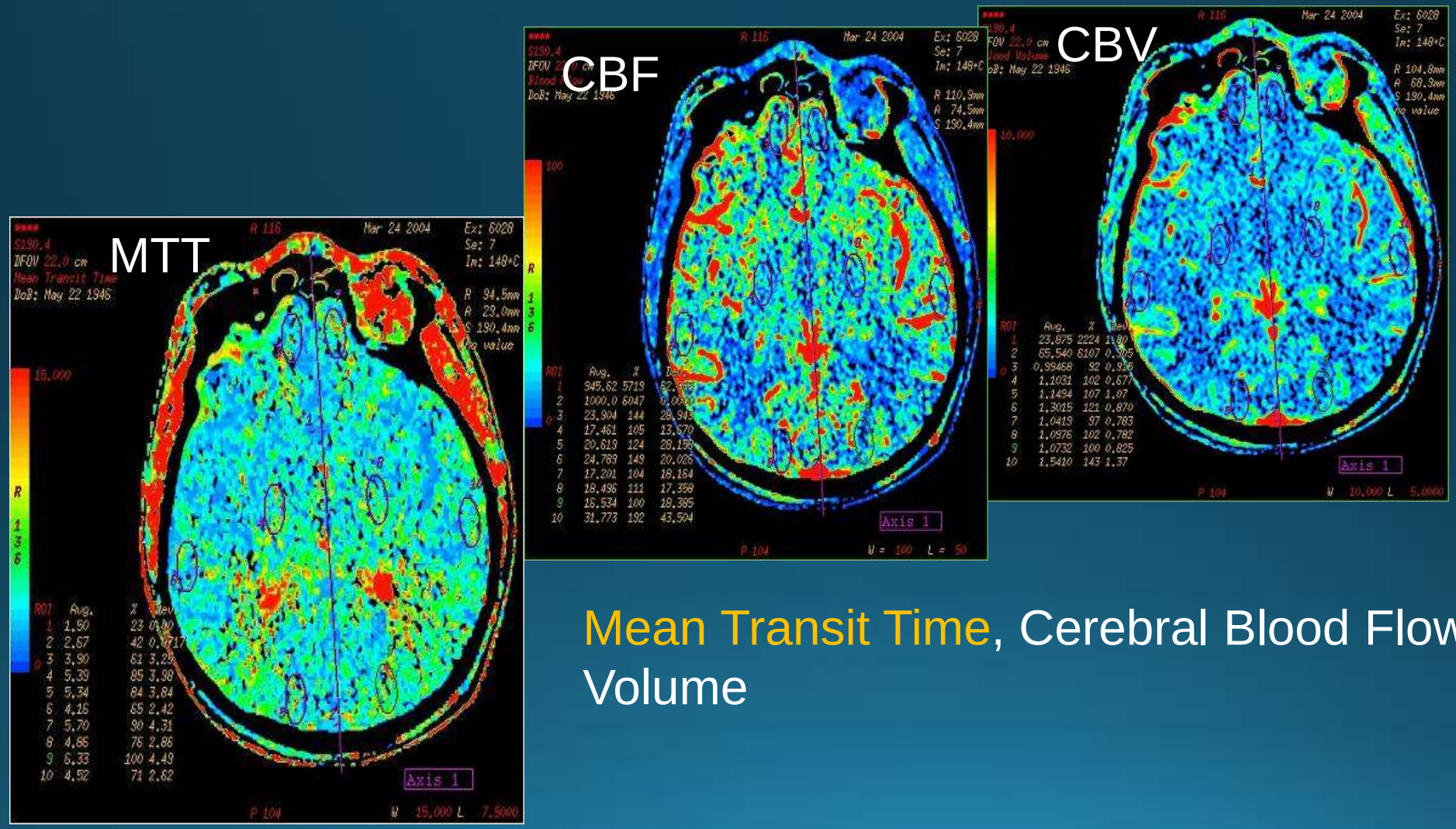
# GRI vs SWI: Diffuse axonal injury



# DSC & ASL: Perfusion MRI

- Perfusion refers to the delivery of blood flow to a tissue or organ. Brain perfusion is also termed CBF.
- The two most common methods for measuring perfusion with MRI are based on dynamic susceptibility contrast (DSC) and arterial spin labeling (ASL).
- ASL: completely noninvasive; absolute cerebral blood flow (CBF) measurements are possible; utilizes magnetically labeled arterial blood water as a diffusible flow tracer
- DSC: detects the first passage of an intravascular contrast agent such as a gadolinium chelate
- DSC perfusion MRI is more widely applied clinically

# CT Perfusion




Mean Transit Time, Cerebral Blood Flow & CB Volume

# Perfusion Imaging
# Brain Imaging/Physiology

Large Vessels - Angiography

DSA - Digital subtraction
MRA - Magnetic resonance
CTA - Computed tomography

Small Vessels - Perfusion Methods - Tracers

Diffusion - PET (FDG, $O_2$, rubidium)
SPECT (99mTc-HMPAO)
CT (xenon)

Kinetics - MR (gadolinium)
CT (iodine)

Multiple types of imaging in vascular dx

# MRA: MR Angiography

MR Angiography (MRA): MRI study of the blood vessels

Used to detect, diagnose and aid in treatment of heart disorders, stroke and blood vessel diseases

MRA provides detailed images of blood vessels without using any contrast material.

Procedure is painless.

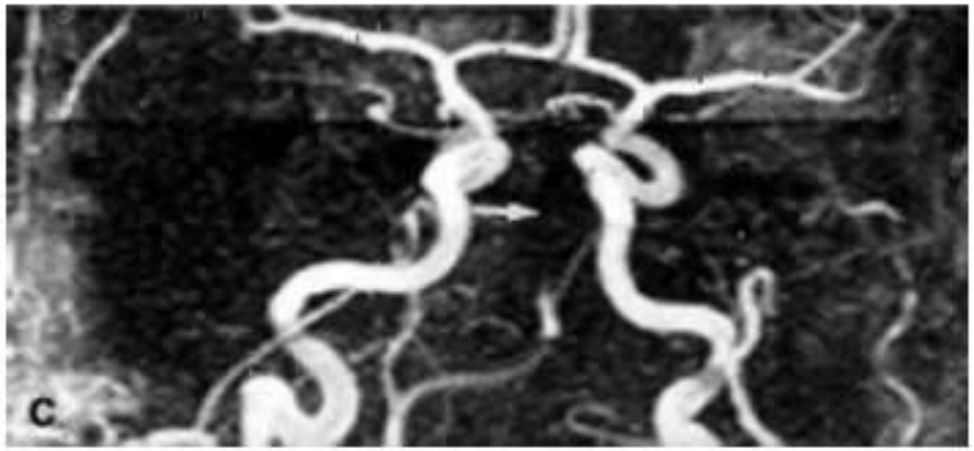
# MRA

Brain MR angiogram

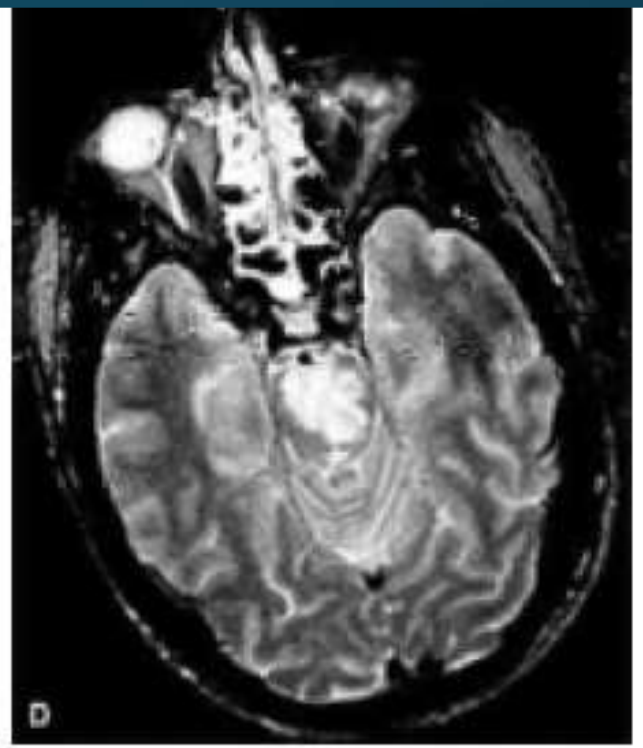
delineates circle of Willis
evaluates for major vessel stenosis or aneurysm

resolution is approximately 3 mm

# MRA: images

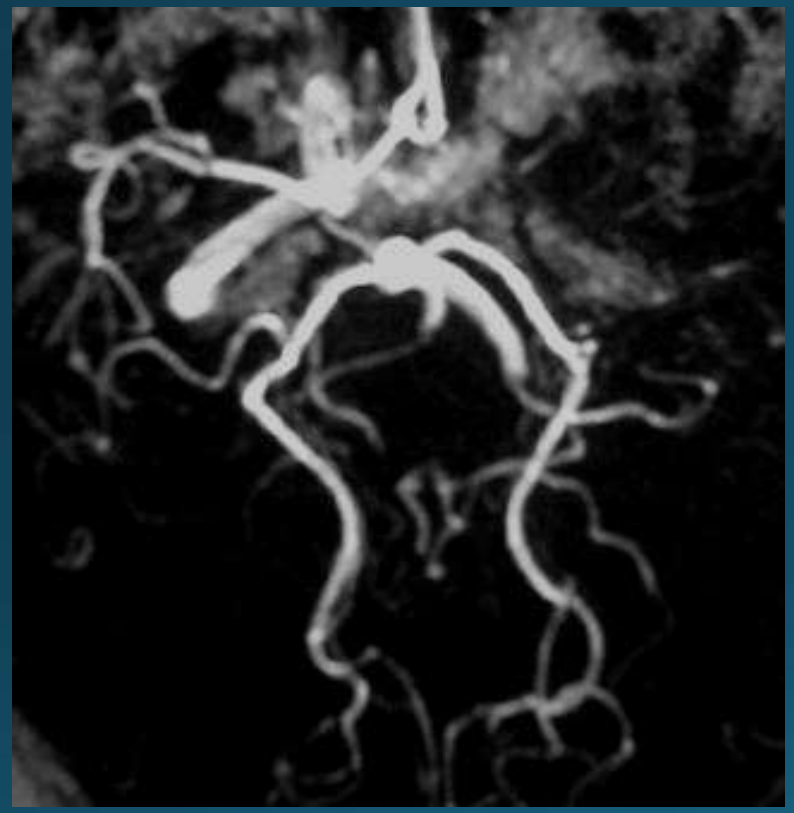



**MRA**. (**C**) Anteroposterior projection 3D time-of-flight MRA displays absence of flow signal in basilar artery (*arrow*). (**D**) T2WI [**MRI**] in same patient large paramedian pontine infarction.

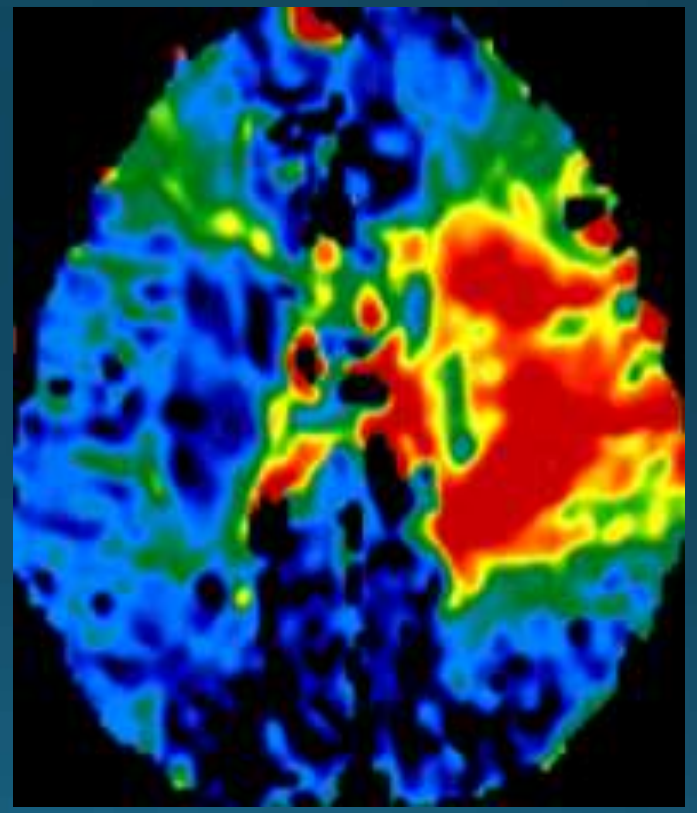



**MRI-Same Pt**

# MR Angiography with Perfusion MR



MRA



Perfusion MR

# MRS: MR Spectroscopy

Images tissue biochemistry non-invasively

Substances must be in motion, not static

Enables interrogation of tissues' chemical  environment

Provides relative quantification of particular compounds and their constituents

Example: Inhibitory GABA deficiency in autism

# MR spectroscopy

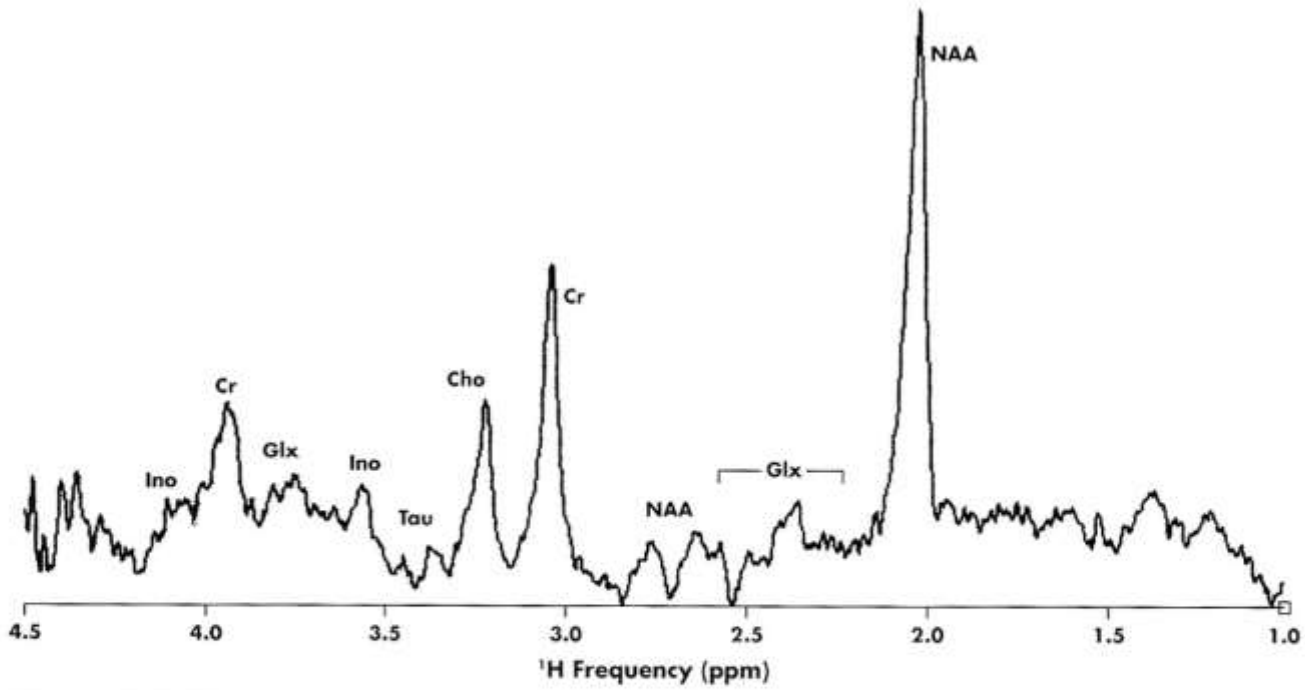
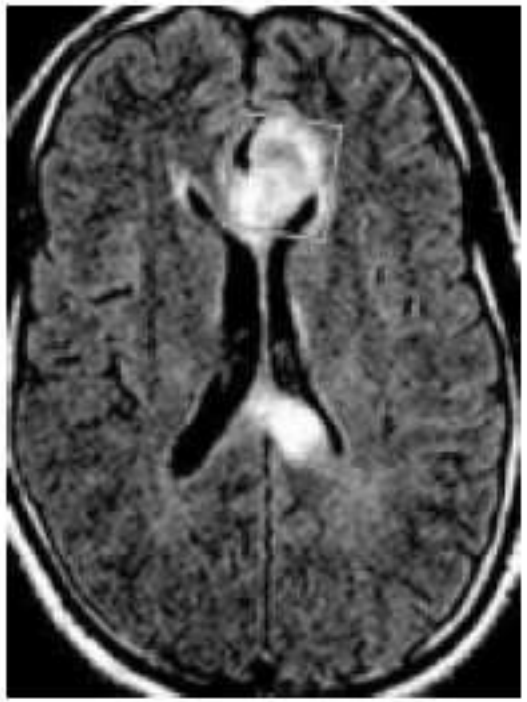
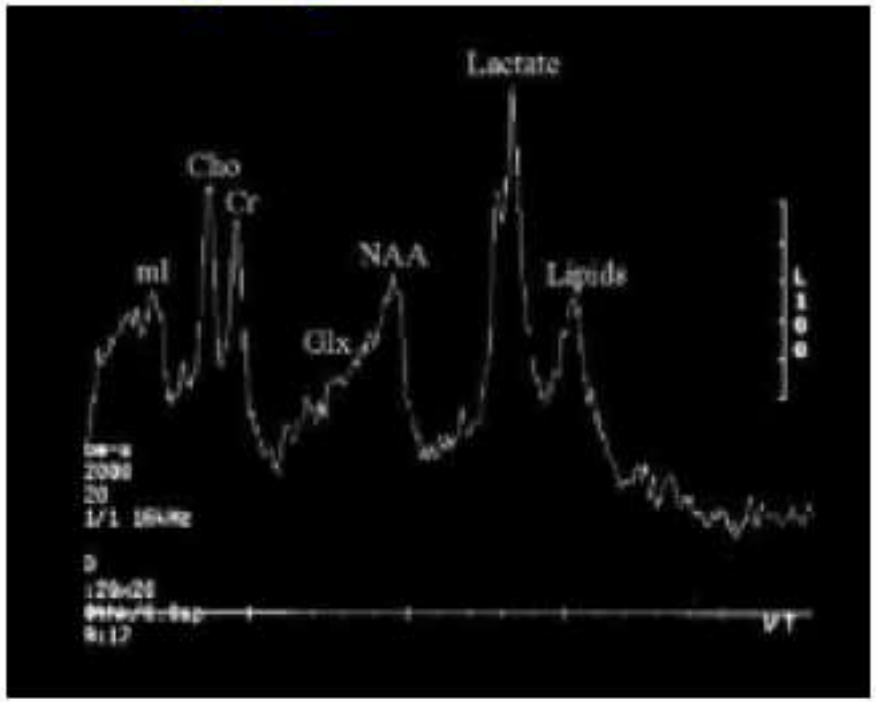



**Figure 5–1.** Proton spectrum recorded on a 4-tesla magnetic resonance scanner of brain tissue in vivo from a healthy 21-year-old man.
Point-resolved spectroscopy (PRESS) recording from a 6-mL volume localized in the motor cortex, right hemisphere; volume size=6 mL, echo time=23 msec, repetition time=3000 msec, 64 averages. Apodization with line broadening of 2.5 Hz applied. Abbreviations for peaks: Cho=choline compounds (choline, phosphocholine, glycerophosphocholine); Cr=creatine and phosphocreatine; Glx=spectral region of peaks for glutamate, glutamine, and GABA; Ino=myoinositol; NAA=*N*-acetyl-aspartate; Tau=taurine.

NAA = N-acetyl-aspartate: most prominent compound detectable with MR spectroscopy in the human brain;
Decrease in NAA levels characterizes most neurological damage

# MRA vs. MRS: Infarct






**CASE**: Stroke. A 47-year-old man with history of cocaine abuse and sudden onset of confusion. **MRA** showed significant decrease of the flow in the left anterior cerebral artery. **A. FLAIR** image shows the location of the voxel on the high signal area. **B. MRS** shows increased lactate with significantly decreased N-acetyl-aspartate peak. Increased lipid is seen at 0.9 ppm. Findings are consistent with infarction. His condition improved gradually.

# MRS: MR Spectroscopy – drug development

- In vivo measurement of psychoactive drugs in the human brain
- In vivo measurement of GABA levels
- Observe changes induced by experimental agents, explore mechanisms of action, develop new medications
- Characterize neurochemical effects in a specific brain area and help evaluate treatment efficacy

# MRS

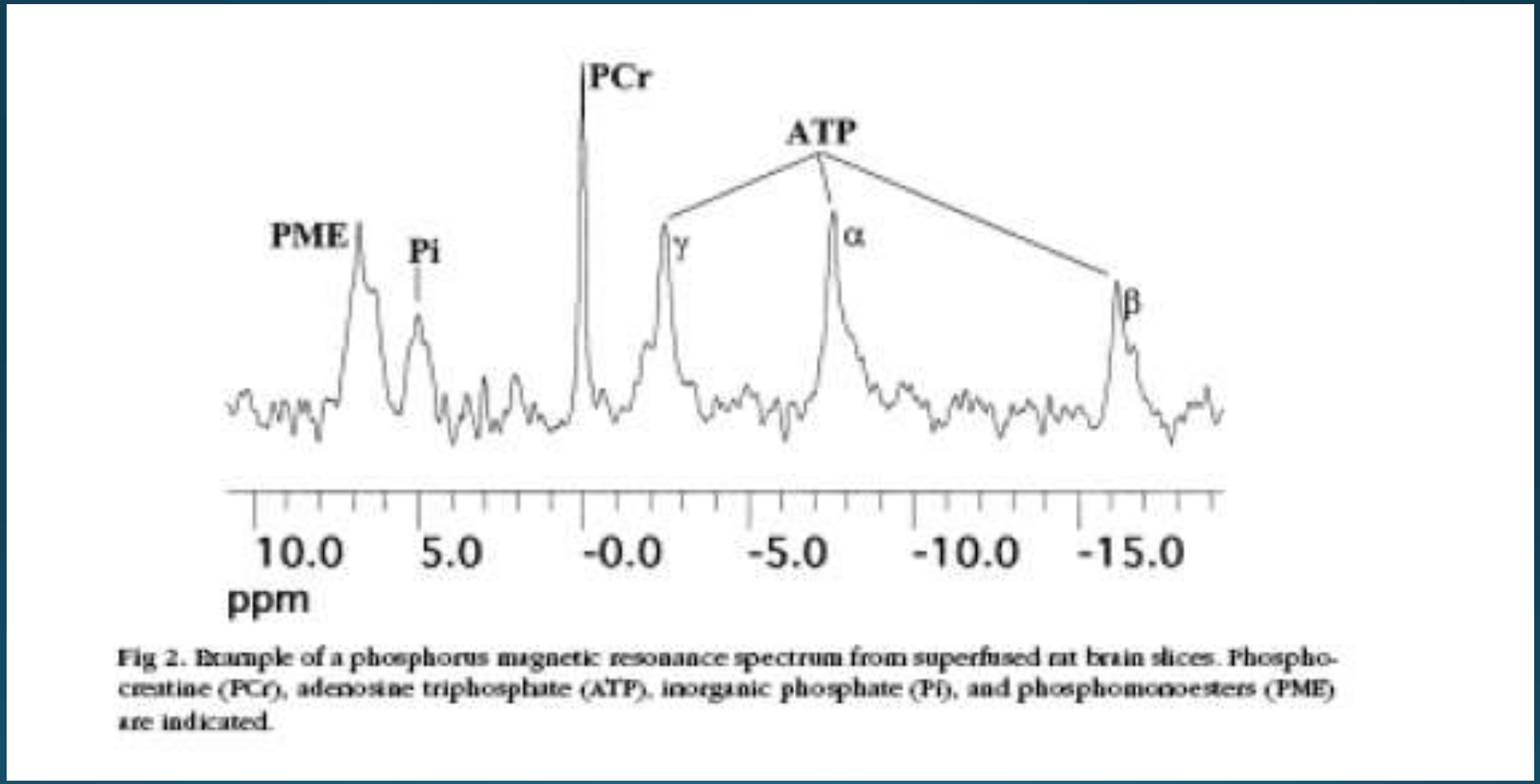
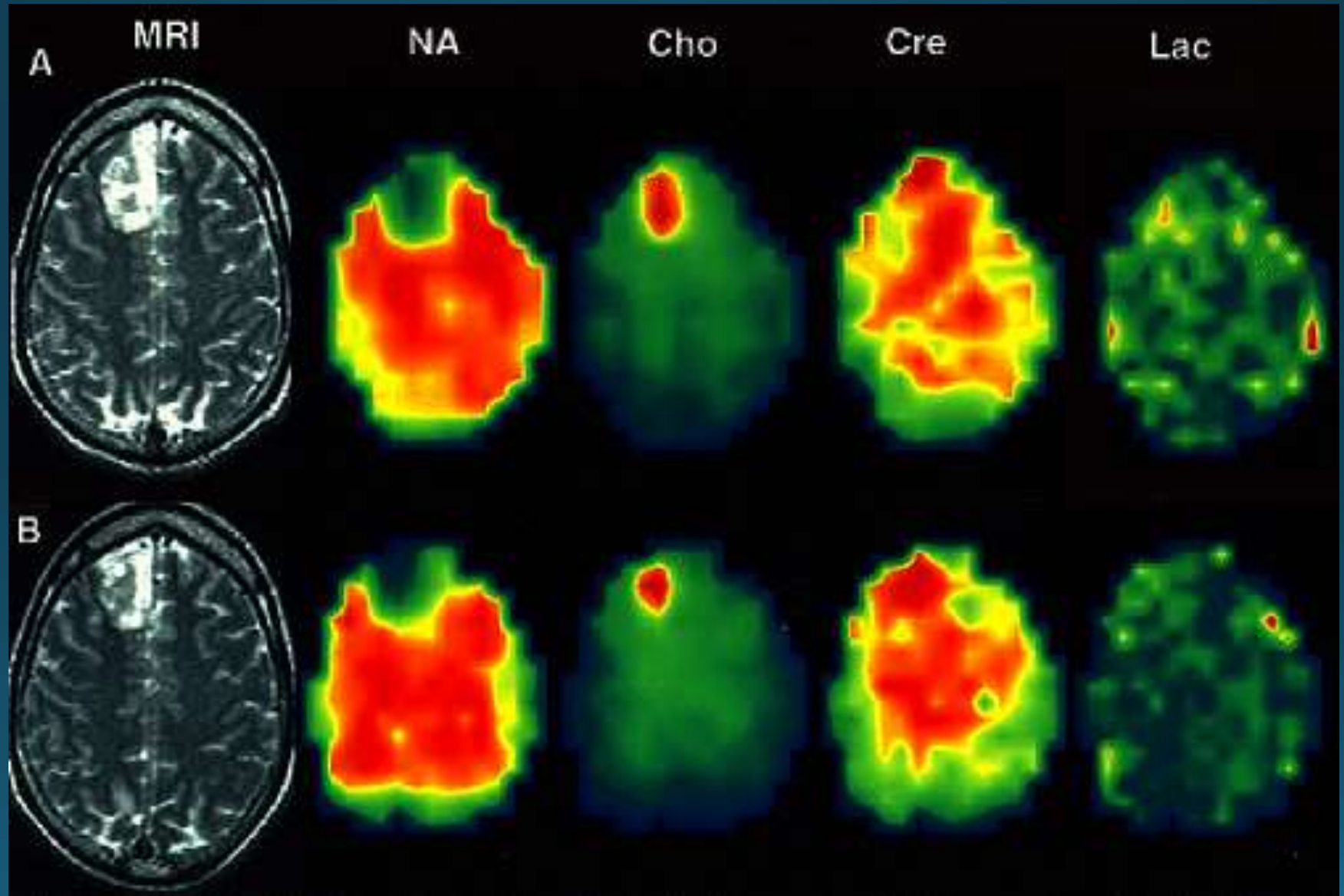



Fig 2. Example of a phosphorus magnetic resonance spectrum from superfused rat brain slices. Phosphocreatine (PCr), adenosine triphosphate (ATP), inorganic phosphate (Pi), and phosphomonoesters (PME) are indicated.

# MRS: brain chemistry



# rs-fMRI: resting-state functional MRI

- Resting-state functional MRI (rs-fMRI), in which people think about nothing in particular while their brain activity is measured
- There is no task, and researchers look for correlations among the activity levels in different areas. The presumption is that any two regions with a consistently high correlation are linked — perhaps by an actual bundle of nerve fibers, but certainly by working together in some way.
- what is actually measured isn't neural activity itself, but blood flow
- vascular fluctuation “remains a concern”.

# fMRI - Statistical Neuroanatomy: where is the function

- Attempts to summarize and describe populations (and differences between populations) from MRI scans

- Example: Voxel Based Morphometry (VBM)
  - Try to characterize “gray matter density” as a function of location in brain, then map differences between patients and normals, …

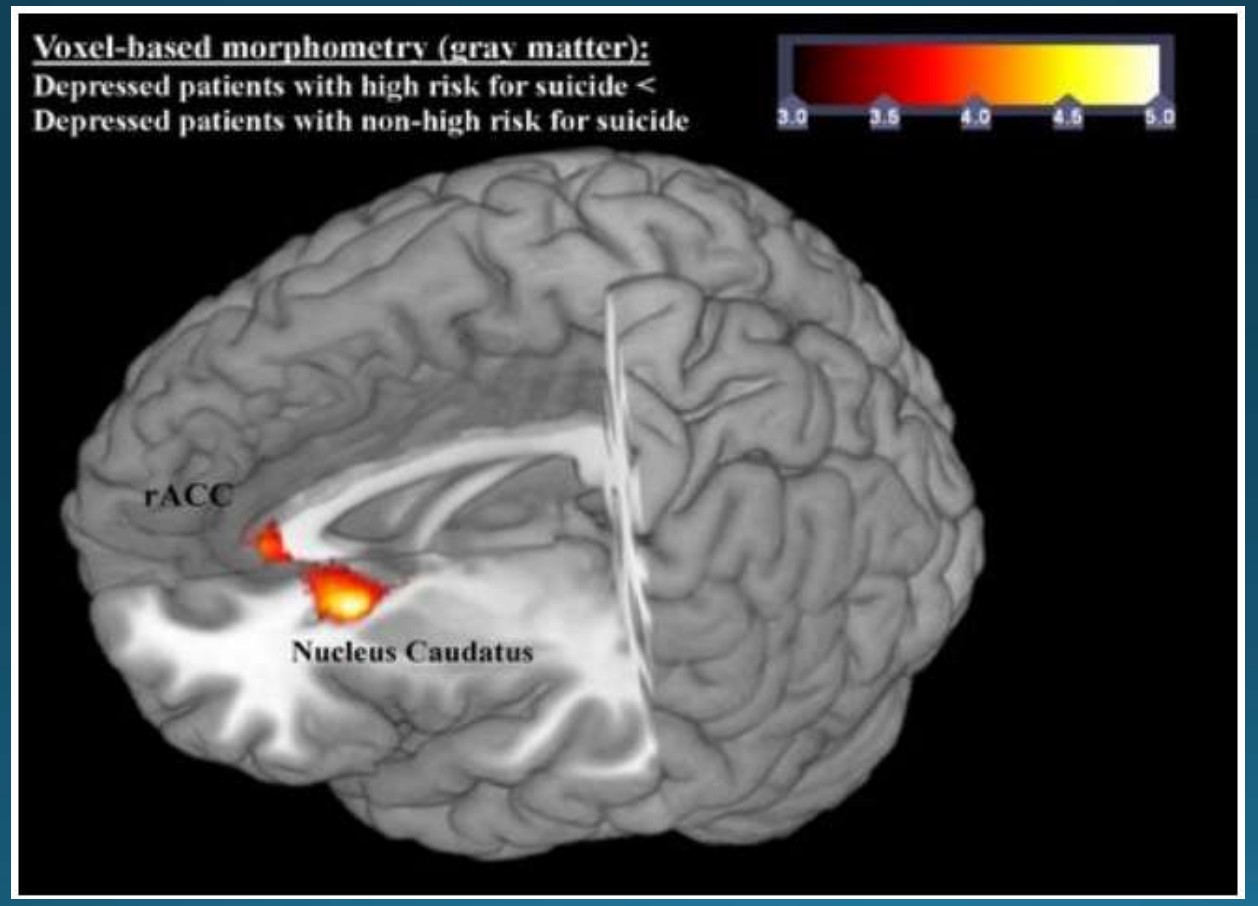
- Example: Cortical thickness maps
  - Extract gray matter cortical ribbon from images and measure thickness at each location
  - Map vs age, disease condition, …

- Biggest practical issue: Spatial Alignment

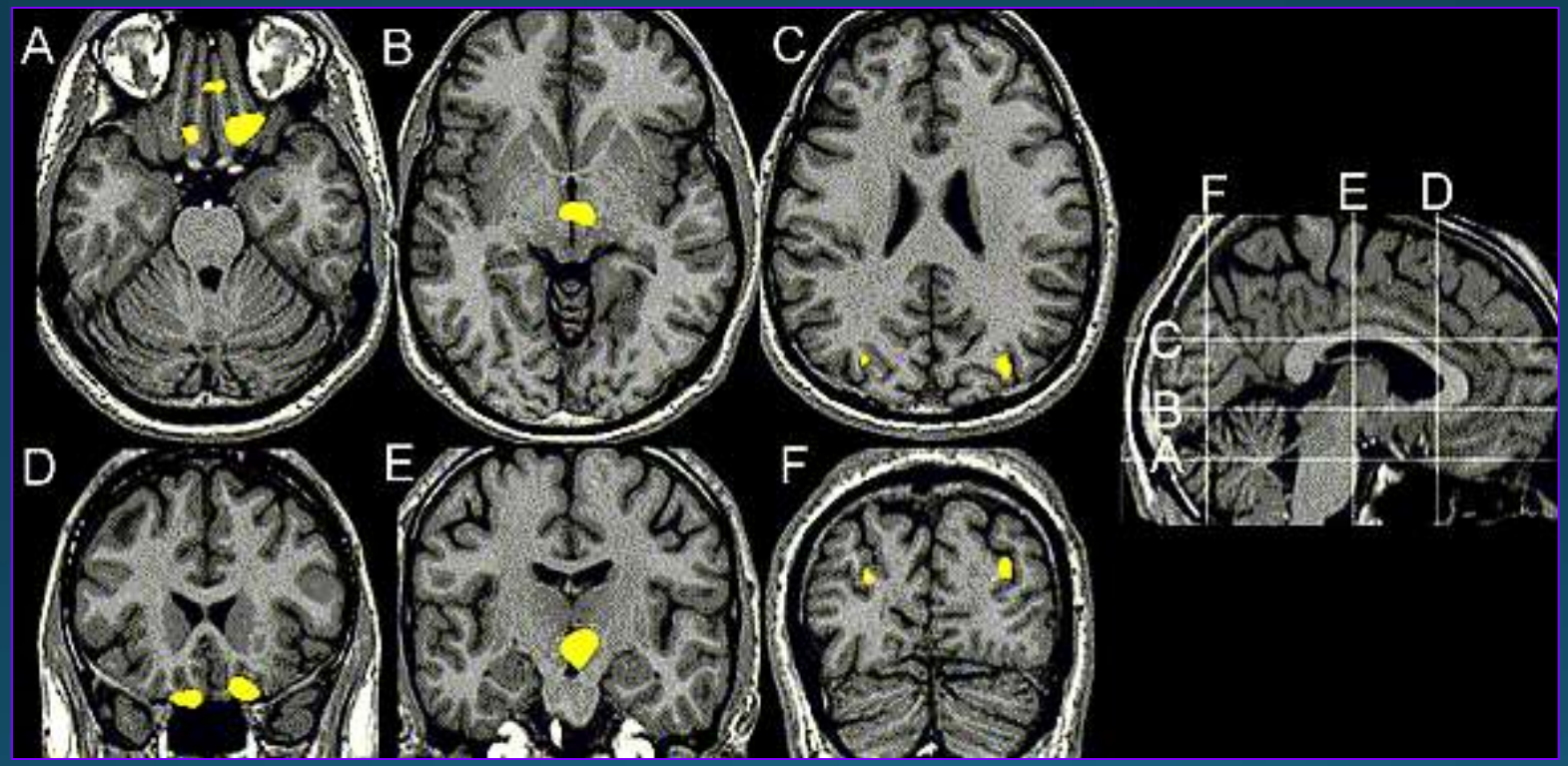
# Voxel-based morphometry

- Voxel-based morphometry (VBM) is a neuroimaging analysis technique that allows investigation of focal differences in brain anatomy, using univariate and multivariate statistical approaches by means of statistical parametric mapping (SPM). VBM represents an unbiased, objective and comprehensive method for testing differences in local composition of brain tissue after discounting global shape differences.
- Shows regions where certain tissue type differs significantly between groups or correlates with a special parameter i.e. age, test score, condition

# Voxel-based morphometry: what area is different in a suicidally depressed pt



# VBM in Williams Syndrome: loss of gray matter




Yellow overlay shows regions with gray matter volume reduction in WS
(13 WS patients vs 11 normals)

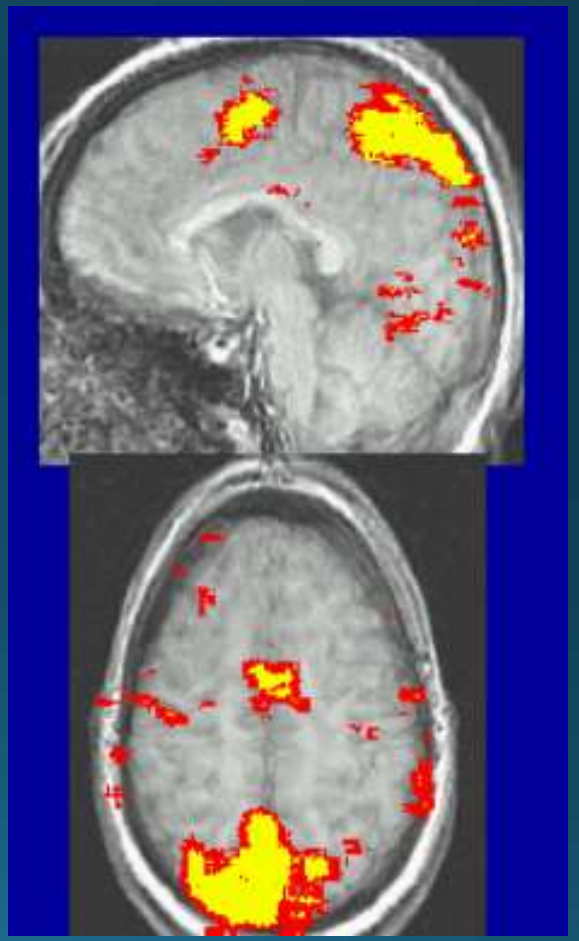
# Functional MRI (fMRI)

Developed in 1991

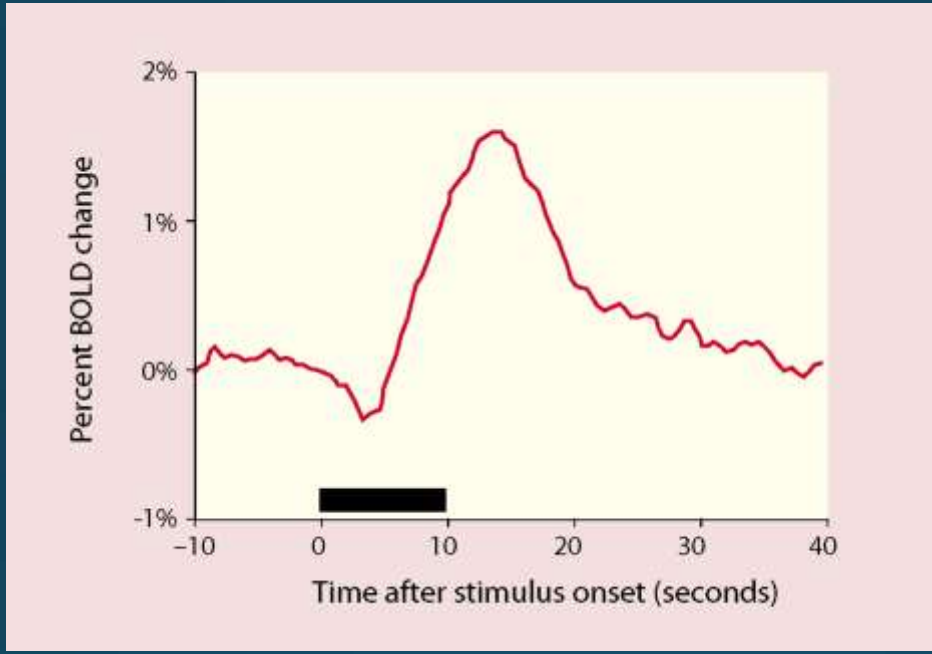
Uses MR to detect changes in blood flow during functional states

Uses Blood oxygen level dependent (BOLD) response

Good spatial and temporal resolution



# Functional MRI



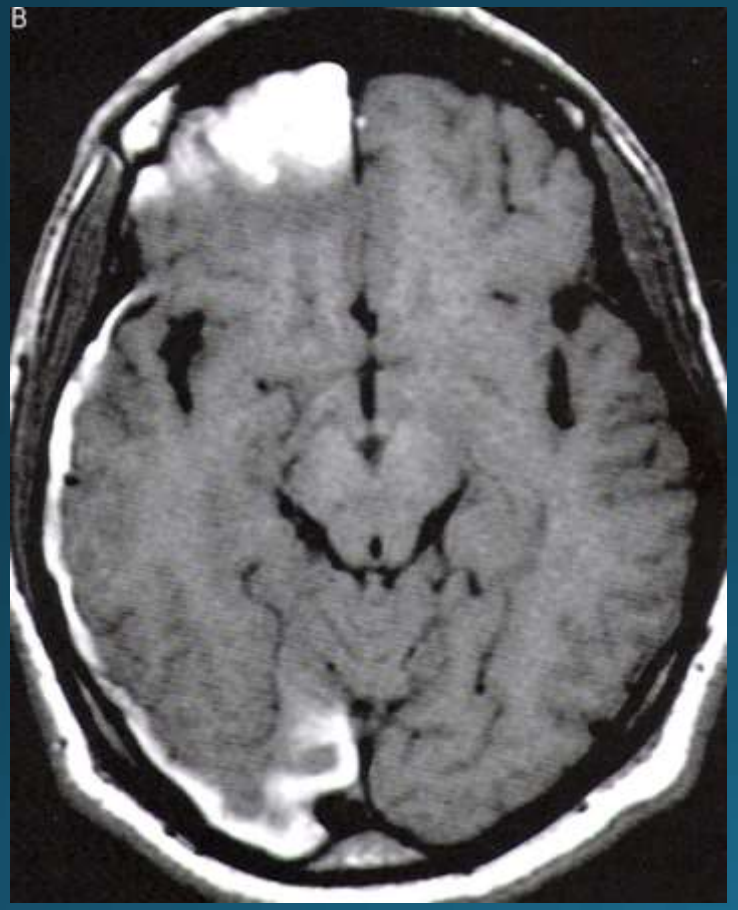

- Takes advantage of the fact that neural activity is followed by blood flow in a highly predictable manner
- Altered blood flow alters RF signal from active brain regions

# Functional MRI

- Permits examination of brain regions that become active during cognitive performance

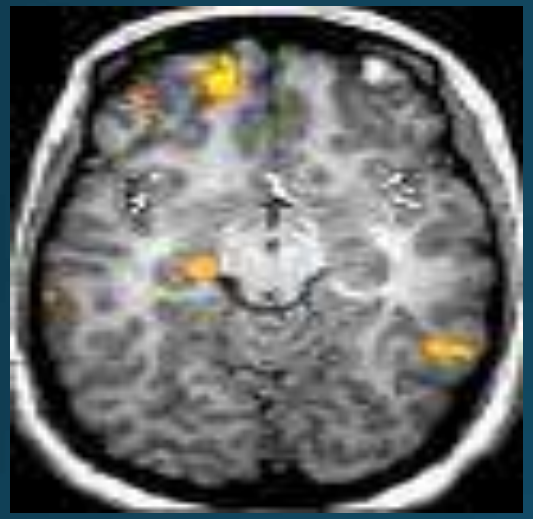

Facilitates comparison of brain activity in multiple groups

# MRI: Structural



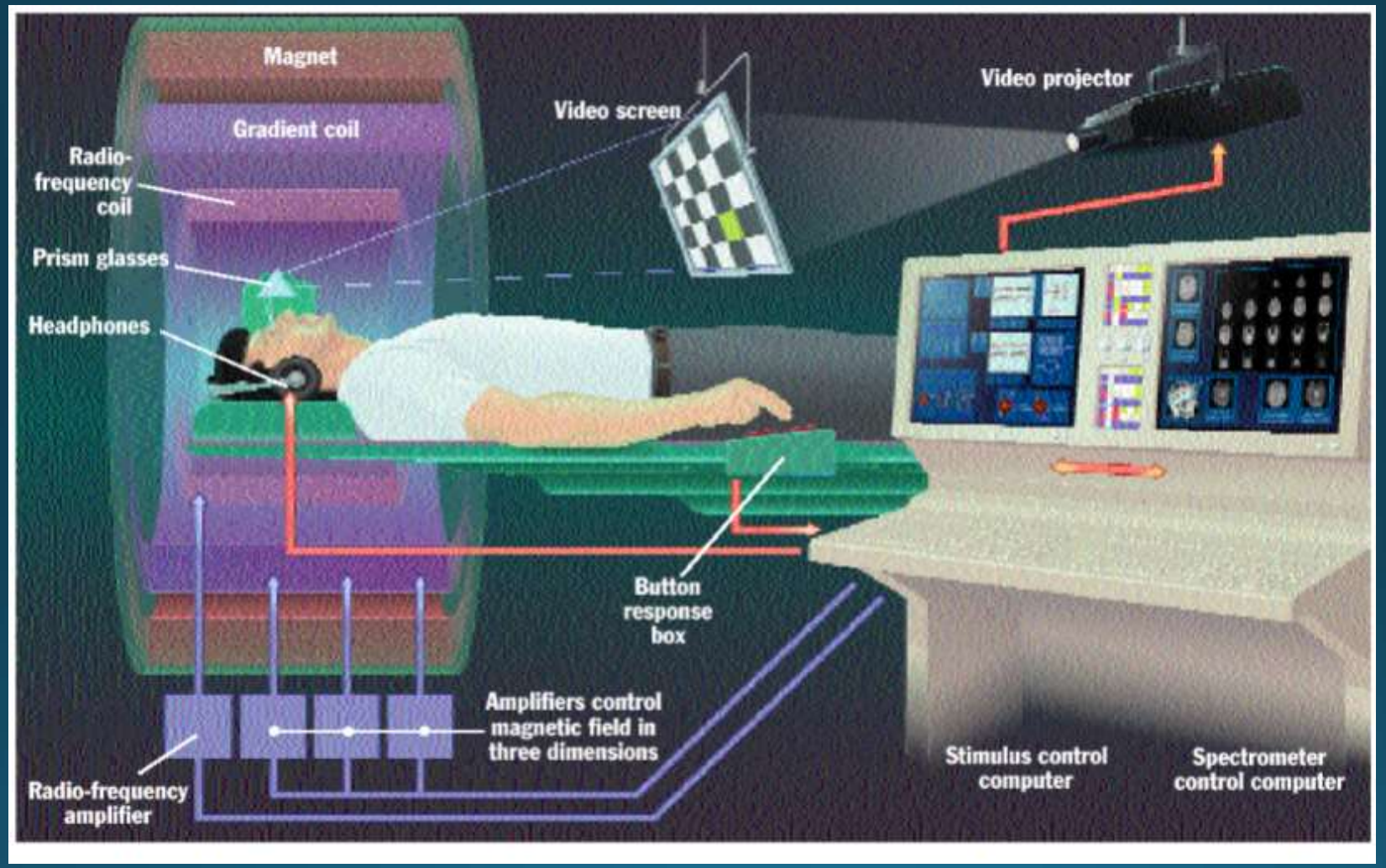

# fMRI: Functional

# Seiji Ogawa, 1990 & Kamil Ugurbil: FMRI



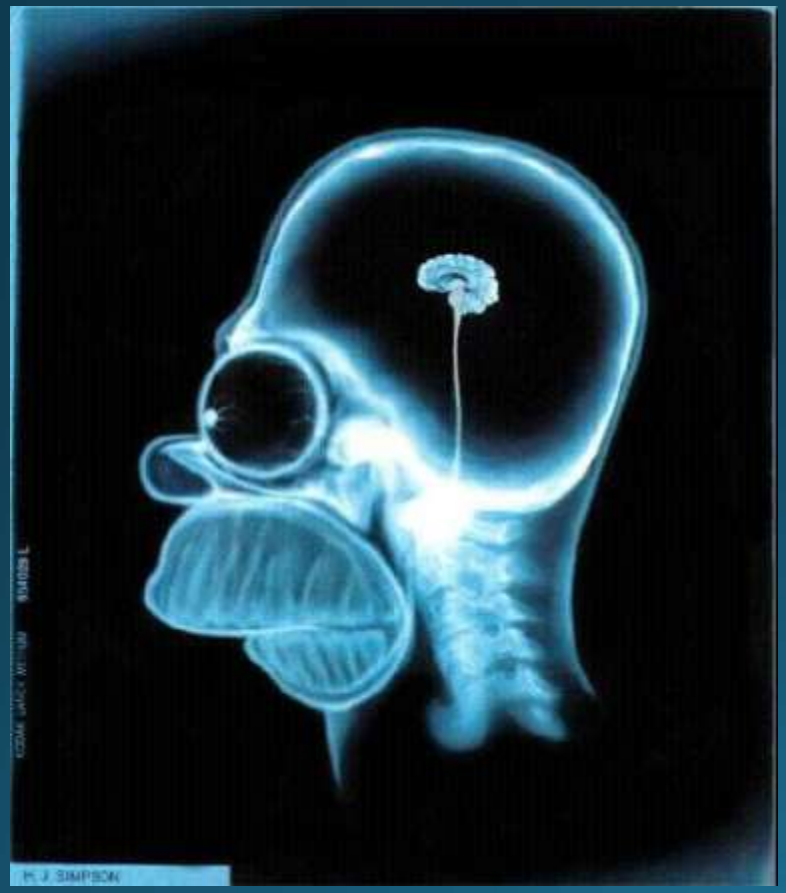
Ogawa, S., D.W. Tank, R. Menon, J.M. Ellermann, S.G. Kim, H. Merkle, and K. Ugurbil, Intrinsic signal changes accompanying sensory stimulation: functional brain mapping with magnetic resonance imaging. Proc Natl Acad Sci U S A, 1992. 89(13): p. 5951-5.

# fMRI setup

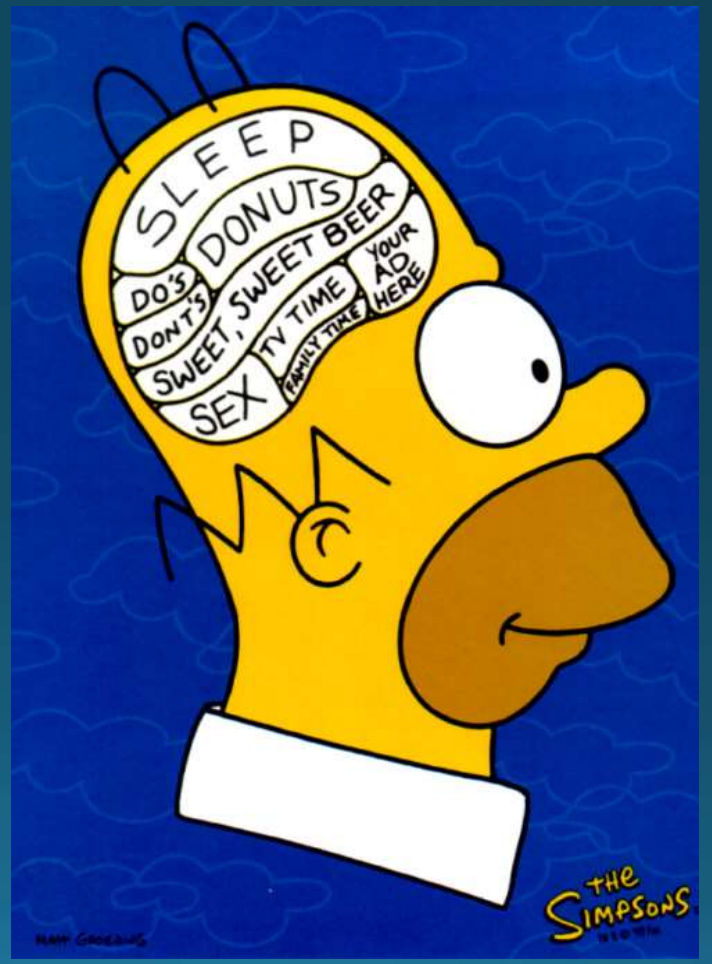

Magnet
Gradient coil
Radio-frequency coil
Prism glasses
Headphones
Video screen
Video projector
Button response box
Amplifiers control magnetic field in three dimensions
Radio-frequency amplifier
Stimulus control computer
Spectrometer control computer

# MRI vs. fMRI

MRI studies brain anatomy.



FMRI studies brain function.




Source: Jody Culham's fMRI for Dummies web site

# Caution

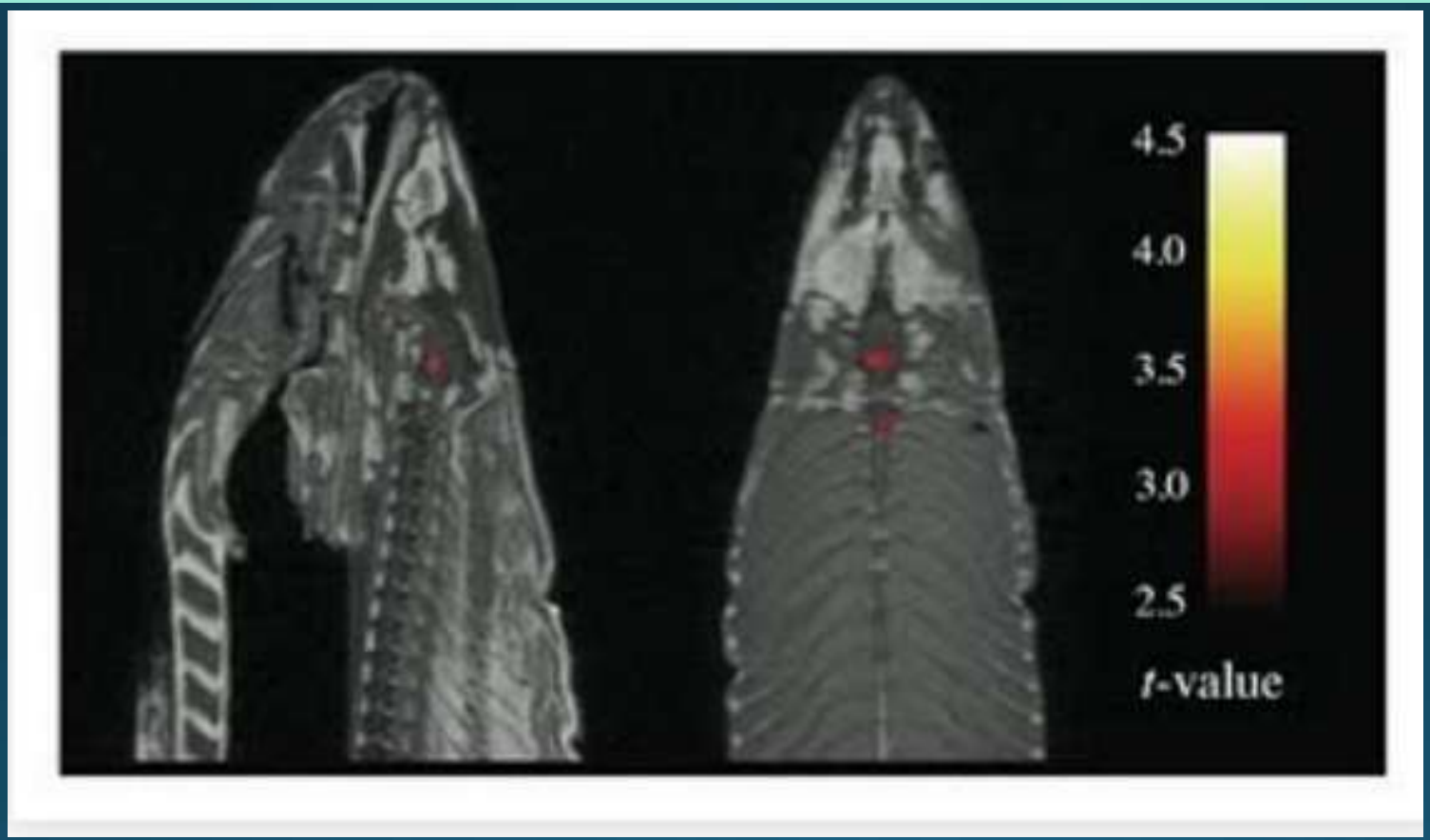
- Pretty Images are statistically derived; colors are imaginary
- fMRI measure hemodynamics, not exact neuronal activity
- fMRI provides information about what's active, not what's not active
- Studies often tend to be underpowered (n=15-20): fMRI analysis detects only a small minority of true effects while producing a high rate of false positives
- Replication always needed!!

# Caution 2

- Voxel equals 1 cubic mm in size = 1 million neurons
- Best DTI of 1 fiber bundle = 200 thousand axons
- MRI = 200 micron resolution (edge of 2 sheets of paper; cell = 100 x smaller);
- The smallest spatial features distinguishable through PET or fMRI are two to three millimeters across

Cautionary Tale:  Post-Mortem Atlantic Salmon: false positives in MRI phantom data

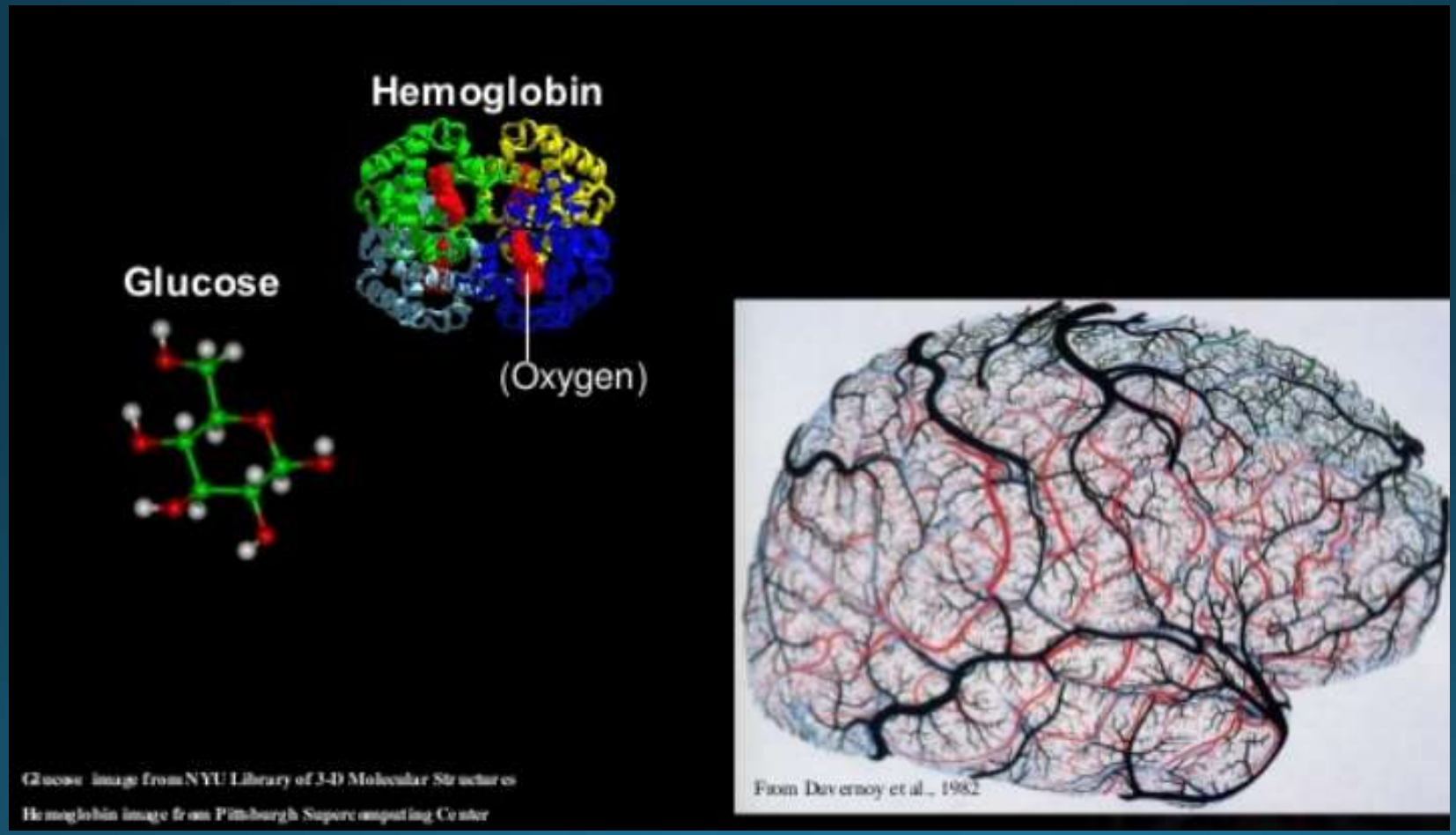
**Neural correlates of interspecies perspective taking in the post-mortem Atlantic Salmon: An argument for multiple comparisons correction**



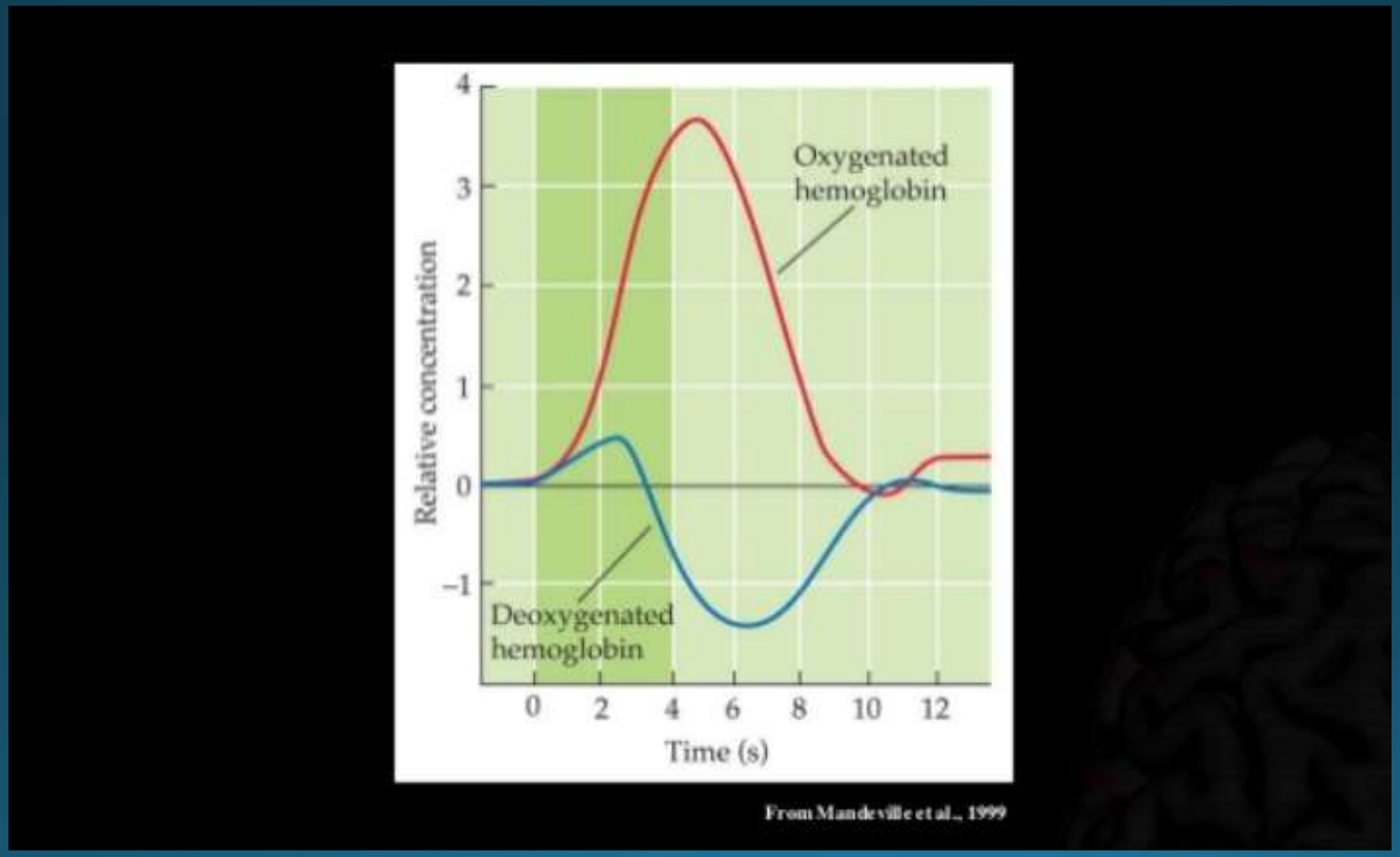

This is a lesson in statistics, not in fMRI. Which is why this was never published in a peer-reviewed journal.  It is a lesson about how probability indicates that you certainly can get activation in a dead salmon by chance, and that if you only have one salmon and no corrected threshold in 2 million samples, you will get about 100000 false positives.

Bennett, 2009

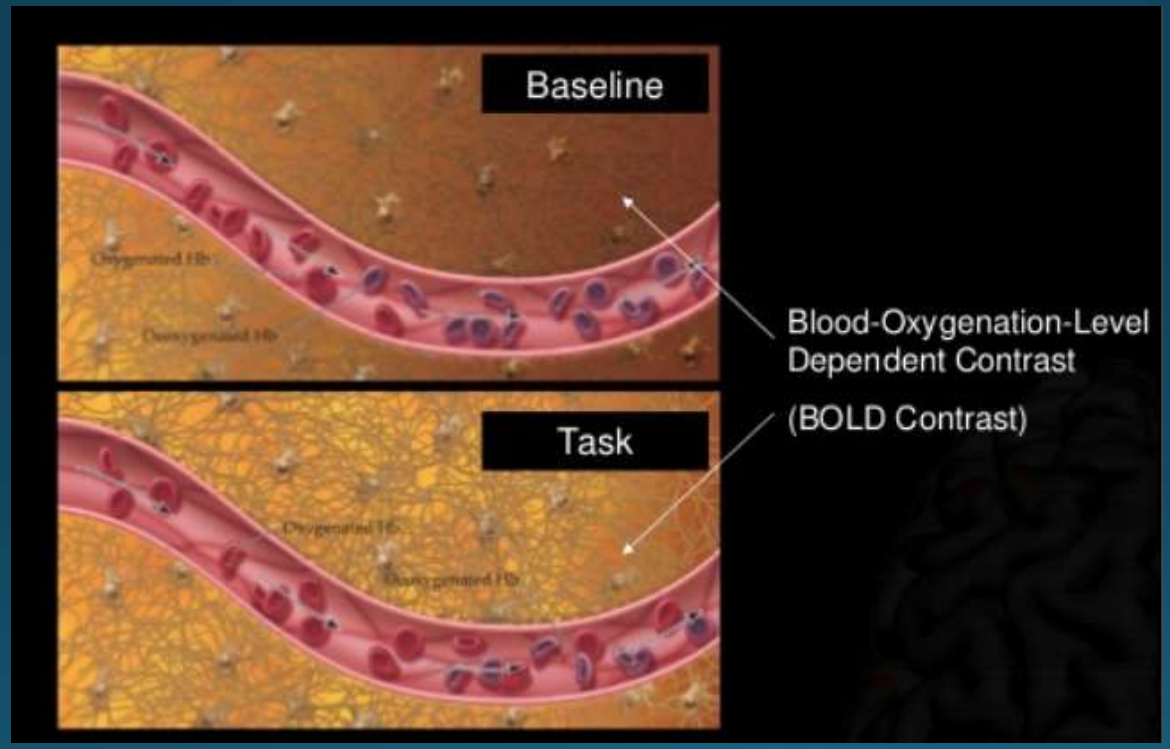
# Fact 1: Energy is supplied to the brain through the vascular system



# Fact 2: More hemoglobin is supplied than is needed causing a decrease in deoxygenated hemoglobin

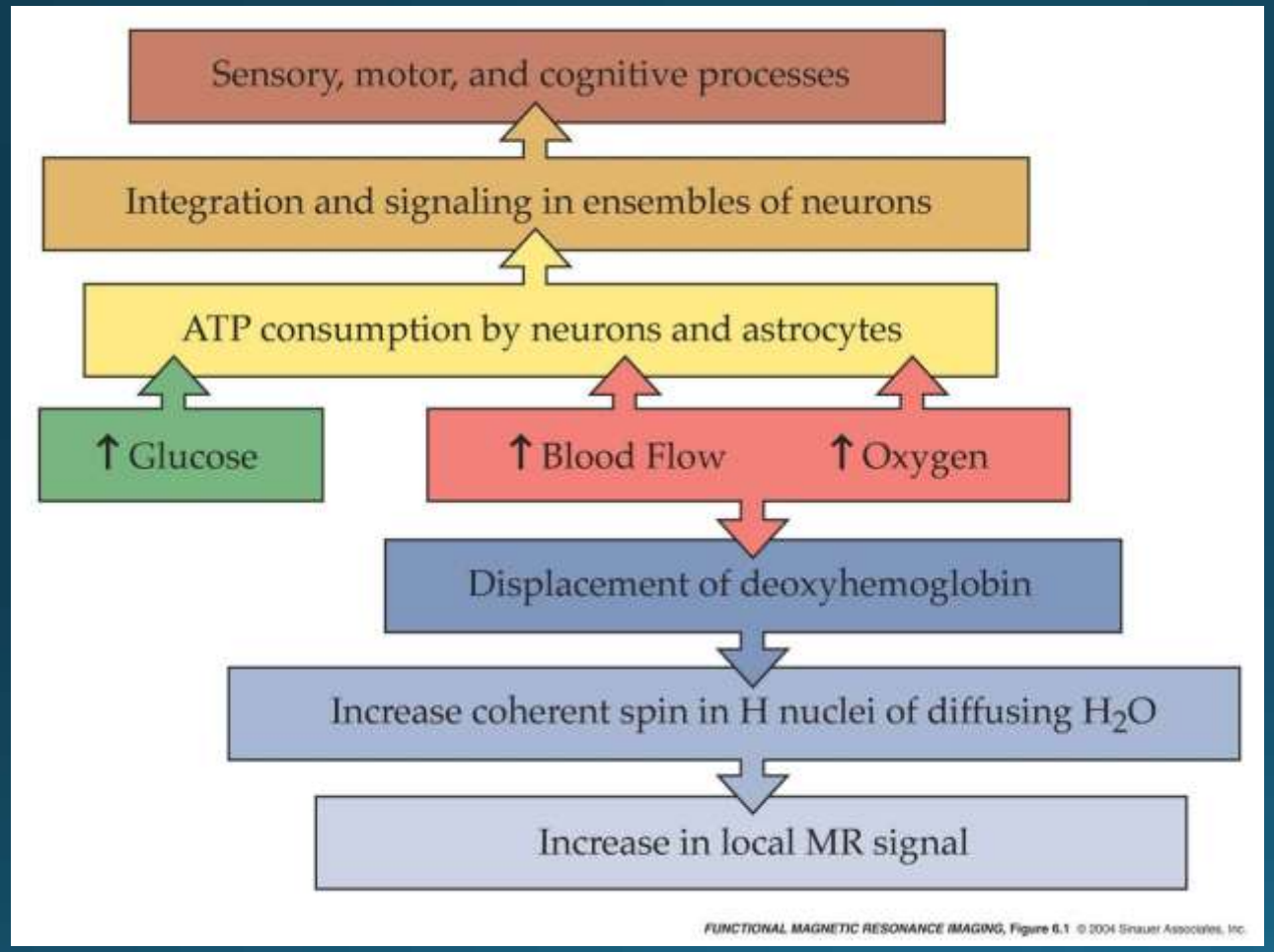


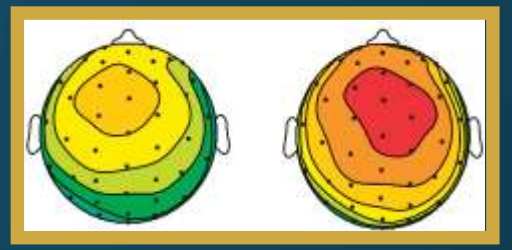
# Fact 3: Deoxygenated hemoglobin reduces some forms (T2*) of MR signal

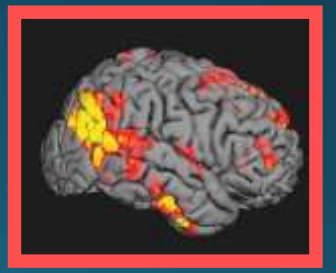



BOLD contrast = The difference in signal on T2*- weighted images as a function of the amount of deoxygenated hemoglobin.

# Neuronal activity vs. Metabolism





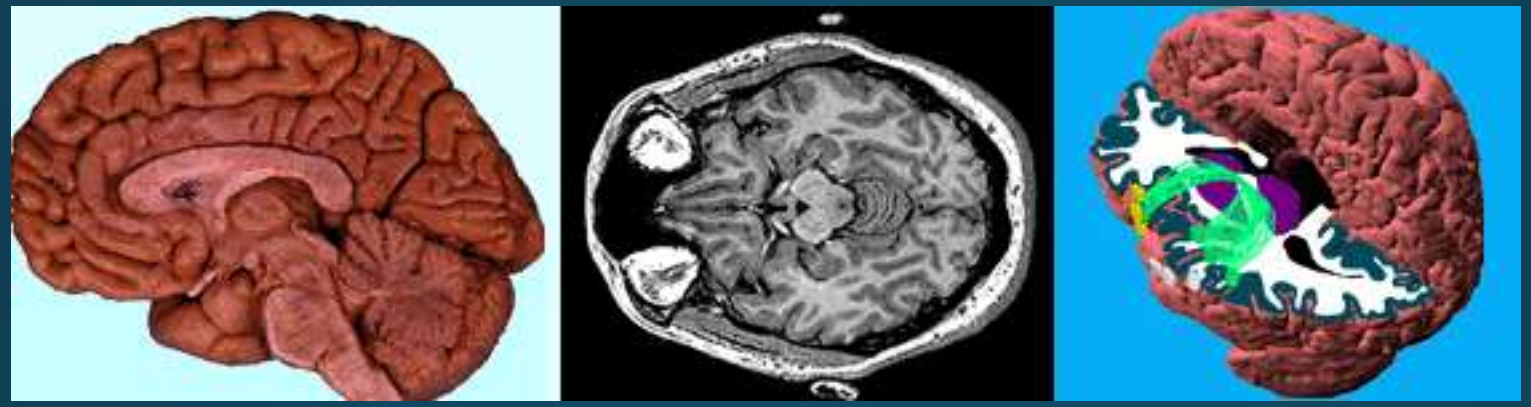
**Key idea: distinguish changes in our measure from changes in function.**

Scott Huettel, Duke University

# Functional imaging

- Functional magnetic resonance imaging (fMRI)
  - Like PET, fMRI measures regional changes in blood flow, but does it very differently
  - As blood flow increases, so does the oxygen concentration in the blood.  MRI is sensitive to these Ox concentration changes
  - Excellent spatial resolution (3-6mm), relatively poor temporal resolution (on the order of seconds)

# Structural MRI



- Takes advantage of the fact that different types of tissue produce different radio-frequency (RF) pulses

# fMRI vs. PET

- Both fMRI & PET: blood flow to brain provides the signals detected
  - when resting neurons become active, blood flow to them increases

- fMRI - detects changes in oxygen levels, which rise in nearby blood vessels when they are at rest

- PET - relies on increased delivery of injected radioactive water, which diffuses out of the vessels to reach rest of brain.

# Hemodynamic (fMRI) vs Electrical (EEG, MEG)

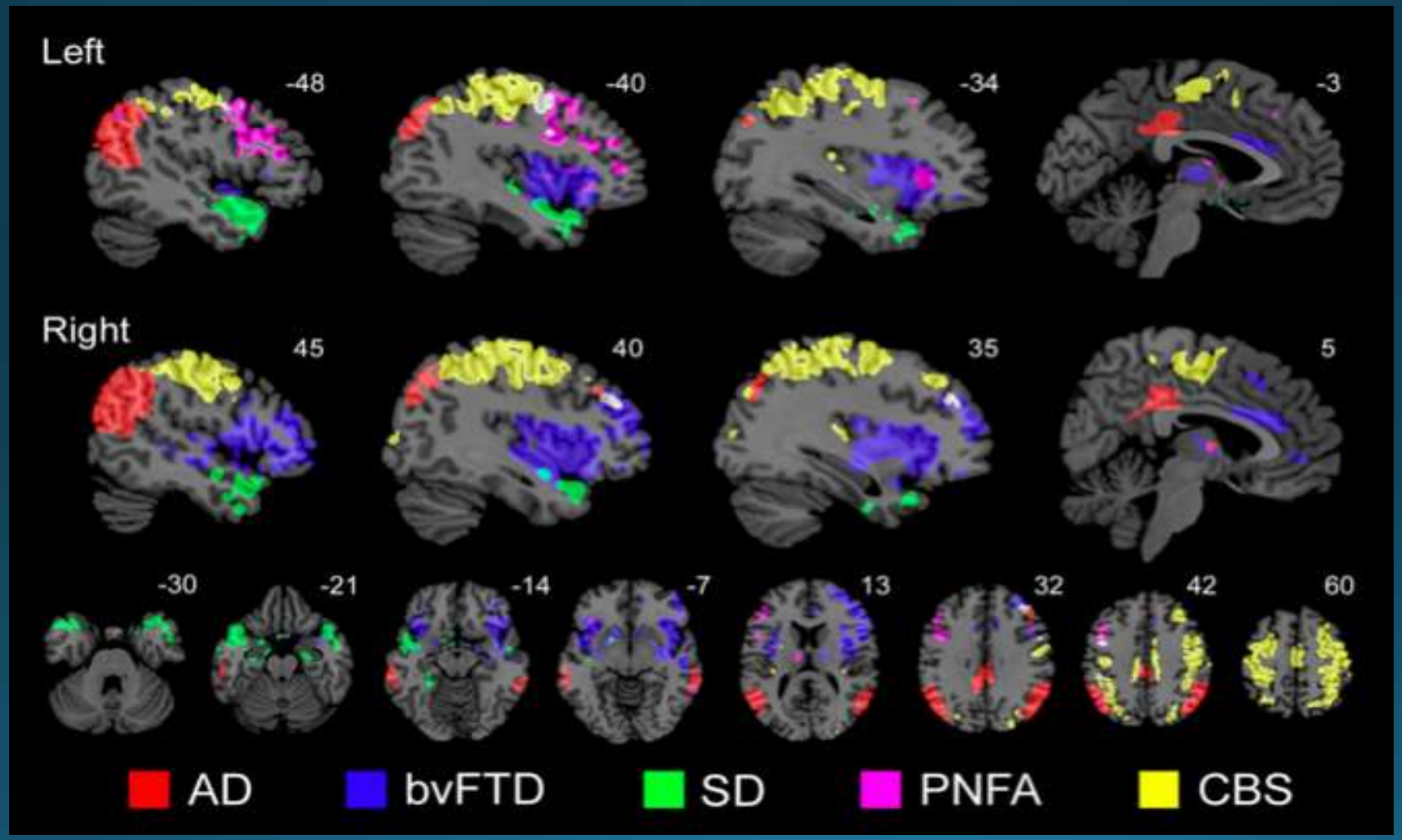
- Hemodynamic (Blood):
  - increase in neuronal activity
  - increase in metabolic demand for glucose and oxygen
  - increase in cerebral blood flow (CBF) to the active region

- Electricity: the brain works because neurons communicate with each other via electrical impulses

- Blood is an indirect, slow measure of neural activity.

- Electricity is a direct measure of neural activity

# Functional MRI: Neurodegeneration Types



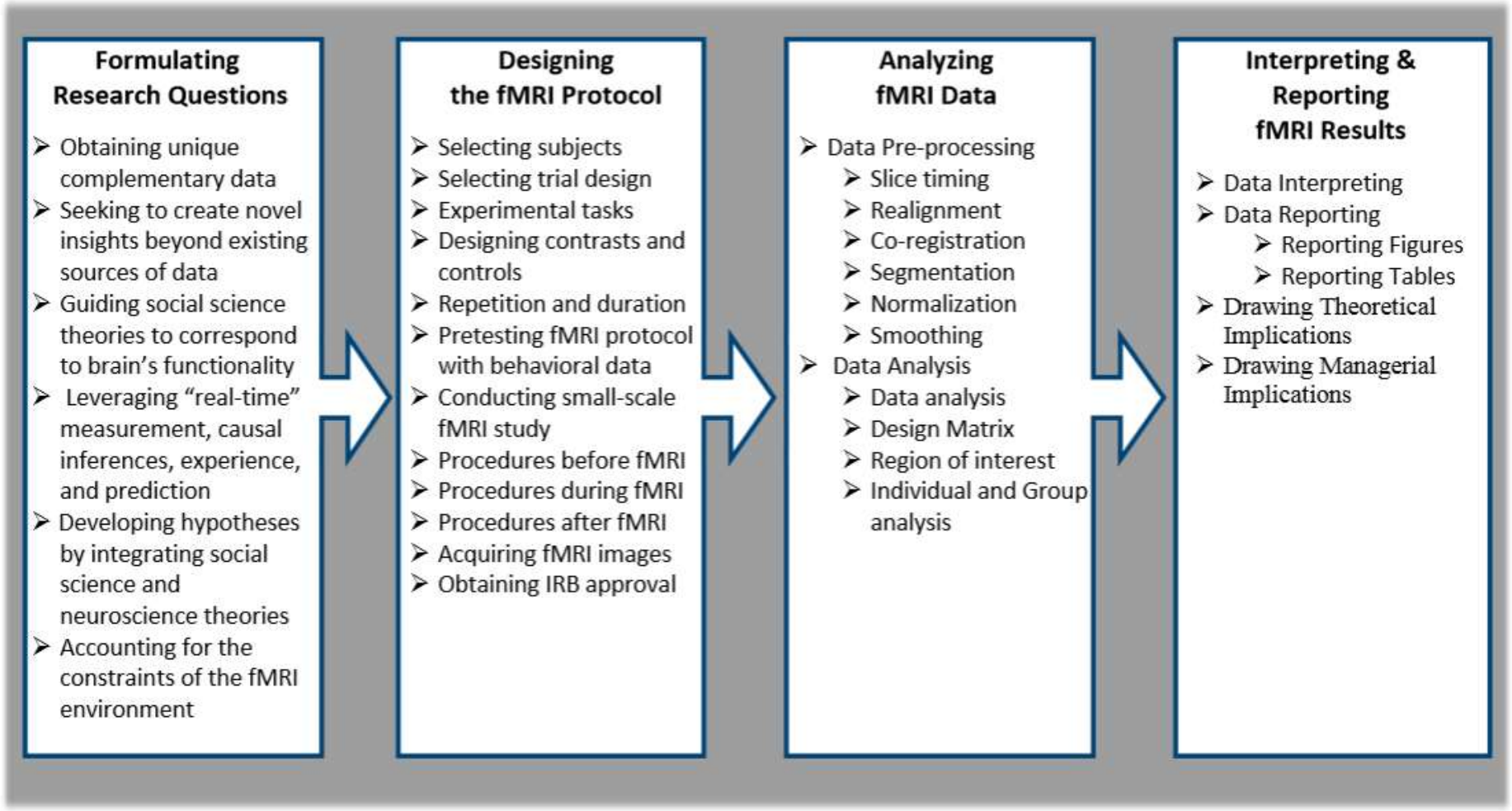
# Applications of FMRI

- Clinical (in individuals):
  - Pre-surgical mapping of language cortex to help the surgeon avoid resecting viable tissue
  - Can combine with DTI to help surgeon avoid important white matter bundles (e.g., cortico-spinal tract)
  - Measure hemispheric lateralization of language prior to temporal lobe surgery for drug-resistant epilepsy

- Neuroscience (in groups of subjects):
  - Segregation of brain into separate functional units
    - What *are* the separate functions of the brain subunits?
  - Discover differences in activity between patients and normals (e.g., in schizophrenia)
  - Map functional (i.e., temporal) connectivity
    - vs. anatomical connectivity (e.g., via DTI)

# How to conduct an fMRI study

Figure 1. The Four Basic Steps for Conducting an fMRI Study




Angelika Dimoka, 2011

# fMRI statistical tools

- There are many statistical tools for analyzing fMRI data:
  - SPM (www.fil.ion.ucl.ac.uk/spm)
  - FSL (www.fmrib.ox.ac.uk/fsl)
  - AFNI (afni.nimh.nih.gov/afni)
  - Brain Voyager (www.brainvoyager.com).

# Processing the fMRI data:
## Complex Statistical processing

| Step | Guidelines |
|---|---|
| Slice-Timing Correction | Compensate for delays from time differences among fMRI images |
| Realignment | Specifying realignment parameters to be used as confounds in analysis |
| Spatial Co-Registration | Aligning all fMRI images to first image to account for subject movement |
| Segmentation | Enhancing probability that voxels belong to appropriate brain tissue |
| Normalization | Normalizing all subjects to a template or "average" brain for group analysis |
| Smoothing | Smoothing images to account for spatial and temporal variation |

# Example of an fMRI experiment

- Question:
- Which regions in the brain are involved in the representation and perception of objects?

# Review of Neuroscience Literature related to Constructs of Interest to the Social Sciences

| Construct/Process | Sample Brain Areas[15] | Key References |
|---|---|---|
| Ambiguity | Insular cortex, Parietal cortex | Krain et al. 2006 |
| Anger | Lateral Orbitofrontal cortex | Murphy et al. 2003 |
| Anxiety | Amygdala–prefrontal circuitry, Inferior Frontal gyrus (Brodman Area 45), Ventromedial Prefrontal cortex | Bishop 2007, Mujica-Parodi 2007, Wager 2006 |
| Attention | Right Frontal and Parietal cortices and Thalamus | Coull et al. 1998 |
| Automaticity | Frontal and Striatal cortex, Parietal lobe (Deactivation) | Kubler et al. 2006 Poldrack et al. 2005 |
| Calculation | Anterior Cingulate cortex, Prefrontal cortex limbic system (mainly anterior cingulate cortex and amygdala) | Ernst & Paulus 2005, McClure et al. 2004b |
| Cognitive Effort | Dorsolateral prefrontal cortex, Parietal cortex | Owen et el. 2005, Linden et al. 2003 |
| Competition | Inferior parietal cortex, Medial Prefrontal cortex | Decety et al. 2004 |
| Consciousness | Parietal and Dorsal Prefrontal cortex, Striate cortex, Extrastriate cortex | Rees et al. 2002 |
| Cooperation | Orbitofrontal cortex | Rilling et al. 2002 |
| Disgust | Insular cortex | Britton et al. 2006, Lane et al. 1997, Murphy et al. 2003, Phan et al. 2002 |

Angelika Dimoka, 2011

# Review of Neuroscience Literature related to Constructs of Interest to the Social Sciences

| | | |
|---|---|---|
| Displeasure | Amygdala, Hippocampus, Insular cortex, Superior Temporal gyrus | Britton et al. 2006, Casacchia 2009 |
| Distrust | Amygdala, Insular cortex | Winston et al. 2002, Dimoka 2010 |
| Emotion in Moral Judgment | Medial Prefrontal cortex, Posterior Cingulate, and angular gyrus | Greene et al. (2001) |
| Emotional Processing | Anterior Cingulate cortex, Medial Prefrontal cortex (Emotional Information- dorsal frontomedial cortex) | Damasio 1996, Ferstl et al. 2005, Phan et al. 2002 |
| Envy | Anterior Cingulate cortex | Takahashi et al. 2009 |
| Fear | Amygdala | LeDoux 2003, Murphy et al. 2003, Phan et al. 2002 |
| Flow | Dorsomedial Prefrontal cortex, Medial Parietal cortex | Katayose 2006, Iacobini et al. 2004 |
| Frustration | Right Anterior Insula, Right Ventral Prefrontal cortex | Abler et al. 2005 |

# Review of Neuroscience Literature related to Constructs of Interest to the Social Sciences

| | | |
|---|---|---|
| Habit | Basal Ganglia, Medial Prefrontal cortex, Medial Temporal lobe | Graybiel 2008, Salat et al. 2006 |
| Happiness | Basal Ganglia (Ventral Striatum and Putamen) | Murphy et al. 2003, Phan et al. 2002 |
| Hate | Medial Frontal gyrus, Right Putamen, Bilaterally in Premotor cortex, Frontal Pole and bilateral Medial Insula, Right Insula, Right Premotor cortex , Right Fronto-Medial gyrus | Zeki and Romaya 2008 |
| Information Processing | Anterior Frontal cortex, Lateral Prefrontal cortex, Medial Orbitofrontal cortex Hippocampus, Amygdala (Emotional Information- Dorsal Frontomedial cortex) | Dimoka et al. 2008, Elliot et al. 1997, Ferstl et al. 2005 |
| Intentions | Ventrolateral Prefrontal cortex, Brodmann Area 47 | Dove et al. 2008, Okuda et al. 1998 |
| Jealousy | Left Prefrontal cortex | Harmon-Jones and Peterson 2009 |
| Language function | Broca's area | McDermott et al. (2003) |
| Loss | Insular cortex | Paulus and Frank 2003 |
| Love (maternal) | Ventral part of Anterior Cingulate cortex | Bartels and Zeki 2004 |
| Love (overlap of maternal and romantic) | Striatum (Putamen, Globus Pallidus, Caudate Nucleus), Middle Insula and Dorsal Anterior Cingulate cortex | Bartels and Zeki 2004 |

# Review of Neuroscience Literature related to Constructs of Interest to the Social Sciences

| | | |
|---|---|---|
| Love (romantic) | Dentate gyrus/Hippocampus, Hypothalamus, Ventral Tegmental area | Bartels and Zeki 2004 |
| Moral Judgments | Frontopolar cortex (Brodmann Area 10), Posterior Superior Temporal Sulcus | Borg et al. 2006, Moll et al. 2005 |
| Moral Sensitivity | Amygdala, Thalamus, Upper Midbrain, Medial Orbitofrontal cortex, Medial Prefrontal cortex, Superior Temporal Sulcus | Moll et al. 2002 |
| Motor Intentions | Premotor and Parietal cortex | Desmurget et al. 2009, Lau et al. 2007 |
| Multi-Tasking | Fronto-polar cortex (Brodman Area 10) | Dreher et al. 2008 |
| Optimism | Rostral Anterior Cingulate cortex, Amygdala | Sharot et al. 2007 |
| Person Recognition | Left Hippocampus, Left Middle Temporal gyrus, Left Insula, and Bilateral Cerebellum | Paller et al. 2003 |
| Pleasure/Enjoyment | Anterior Cingulate cortex, Putamen, Medial Prefrontal cortex ,Nucleus Accumbens | Klasen 2008, Sabatinelli et al. 2008, McLean et al. 2009 |
| Priming | Parietal cortex, Middle Temporal cortex, Posterior Superior cortex | Naccache and Dehaene (2001), Wible et al. 2006 |
| Rewards and Utility | Anterior Cingulate cortex, Caudate Nucleus, Nucleus Accumbens, Putamen | Bush et al. 2002, McClure et al. 2004c, Delgado et al. 2005 |

# Review of Neuroscience Literature related to Constructs of Interest to the Social Sciences

| | | |
|---|---|---|
| Sadness | Subcallosal Cingulate cortex | Murphy et al. 2003, Phan et al. 2002 |
| Self-reflection | Medial Prefrontal cortex, Posterior Cingulate | Johnson et al. 2002 |
| Self-regulation of emotion | Amygdala, Dorsolateral Prefrontal cortex, Hypothalamus | Beauregard et al. 2001 |
| Social Cognition | Amygdala, Cingulate cortex, Temporal lobe, Orbitofrontal cortex, Right Somatosensory cortex, Ventromedial Frontal cortex | Adolphs 1999, 2001 |
| Social Cooperation | Amygdala, Orbitofrontal cortex, Dorsolateral Prefrontal cortex | Rilling et al. 2007 |
| Spatial Cognition | Hippocampus, Medial Temporal Lobe | Moser et al. 2008, Shrager et al. 2008 |
| Sympathy | Anterior Superior Frontal gyrus, Inferior Frontal gyrus, Temporal pole, Amygdala, Left Central Sulcus, Right Dorsal Premotor cortex, Dorsomedial prefrontal cortex, pre-SMA, and Inferior Parietal lobule | Decety et al. 2002 |
| Task Intentions | Anterior Cingulate cortex, Medial and Lateral Prefrontal | Haynes et al. 2007, Winterer et al. 2002 |
| Theory of Mind | Anterior Paracingulate cortex, Medial Prefrontal cortex | McCabe et al. 2001 |
| Trust | Anterior Paracingulate cortex, Caudate Nucleus, Putamen | King-Casas et al. 2005, Dimoka 2010 |

Caution: same brain areas are activated in response to several constructs

# fMRI: strengths & limitations

Strengths:

Non-invasive, replicable

Can see activation in addition to high res brain structures

Scanners can be fitted to present stimuli

Higher spatial and temporal resolution than PET

Cons:

Cannot trace neurotransmission like PET

Blood flow is, again, only an indirect correlate of brain activity

Mediocre temporal resolution (seconds)

Complex, highly variable data analyses

Expensive and time-consuming

# fMRI

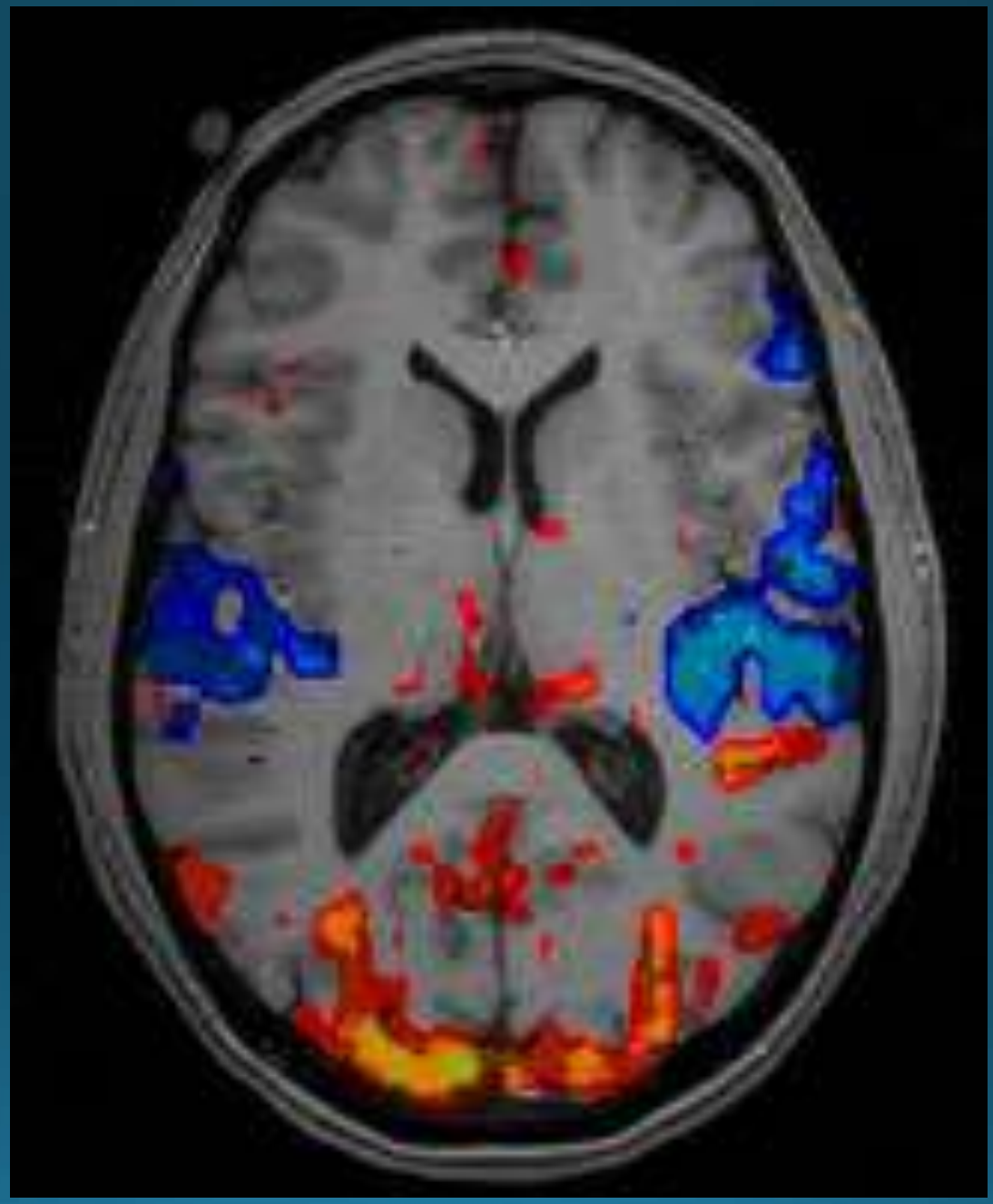
- Excellent spatial resolution
- Most MRI scanners can be modified for fMRI
- Subject to artifact, especially movement
- Data analysis remains time-consuming and controversial
- Should be considered a research technique, though a powerful one

# Caution about fMRI results: Correlation, not necessarily causation

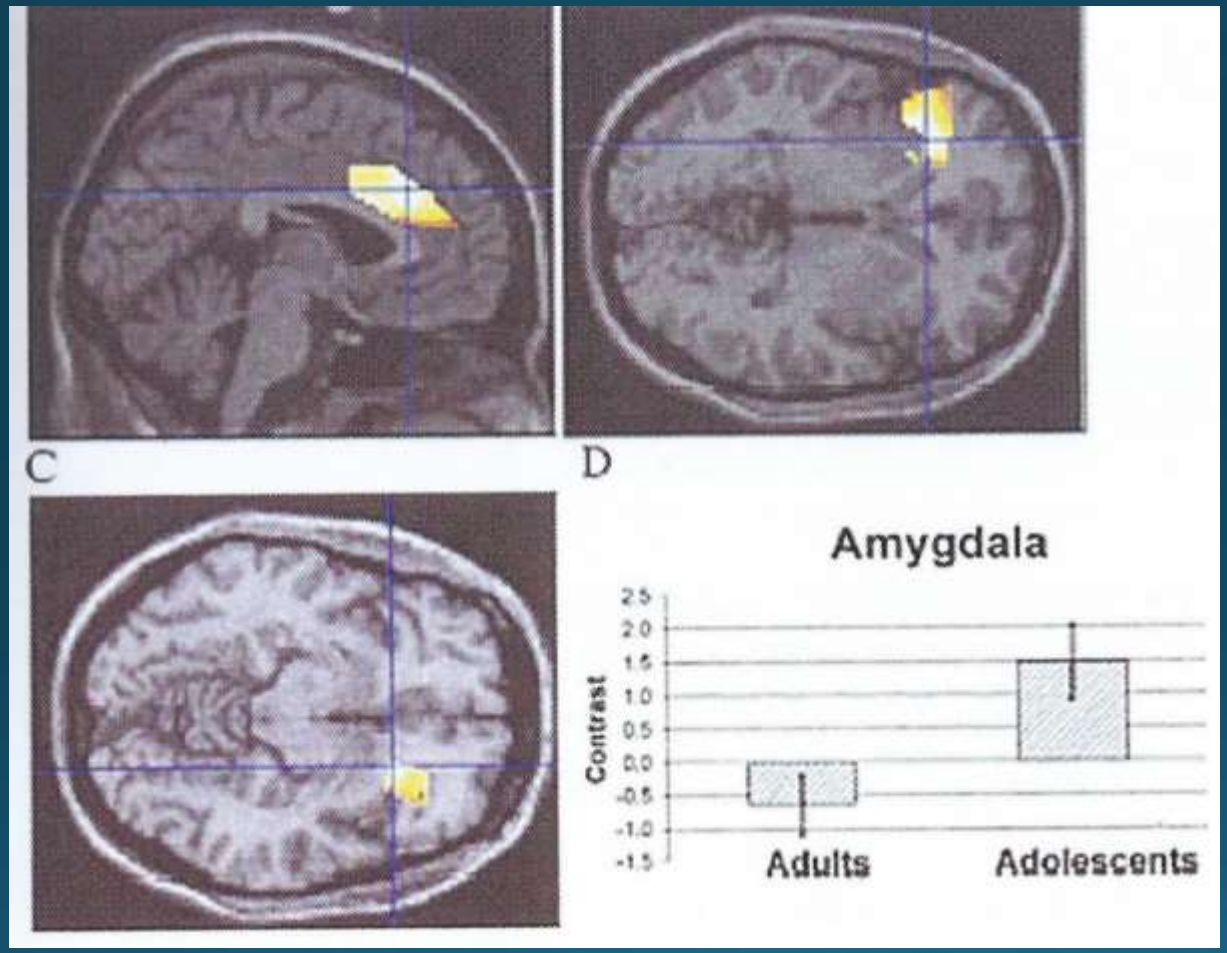
- fMRI can show only what neural activity occurs in particular task; not when such activity is necessary for the task at hand.
- When an area is selectively involved in a function, but not necessarily causative
- Brain imaging can't tell you if the region is necessary for anything.
- Neuroimaging reveals only correlations. Presence of a correlation between regional changes in brain activity and some outcome variable provides little evidence of a direct causal relationship
- You cannot test causality of an area without disrupting it. Area's necessity for a function can only be established through the use of disruption techniques (TMS, lesion studies).

fMRI:

- Activation with visual stimulus v. darkness (blue)

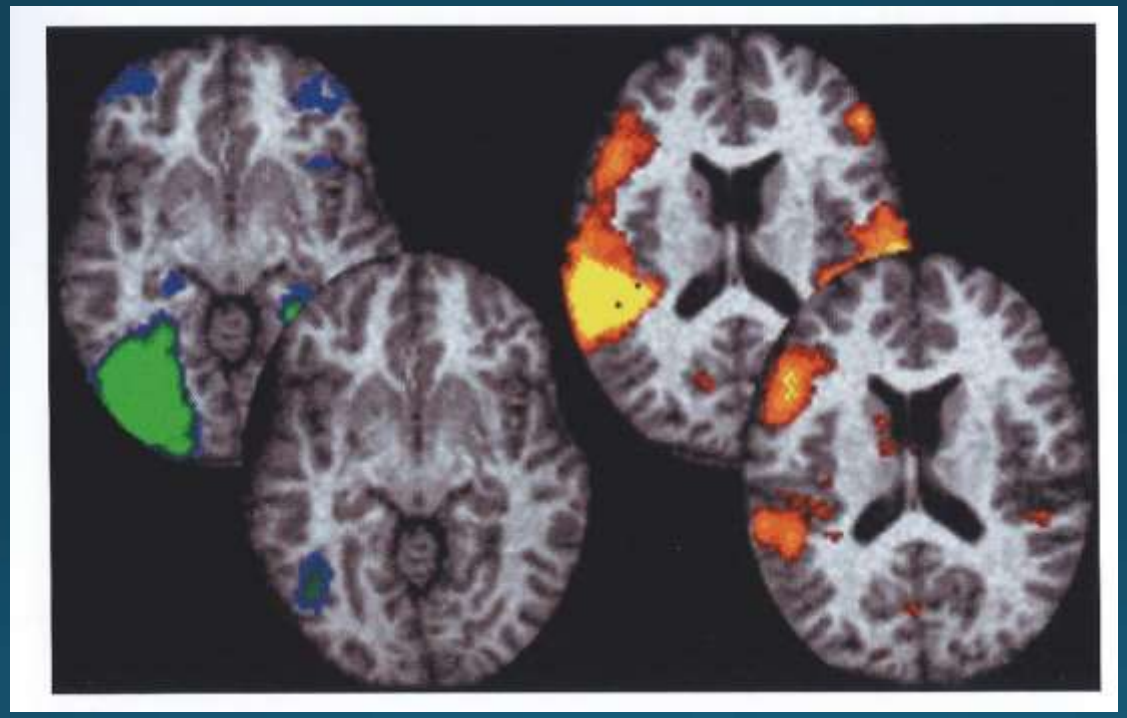


# fMRI: viewing fearful faces & amygdala



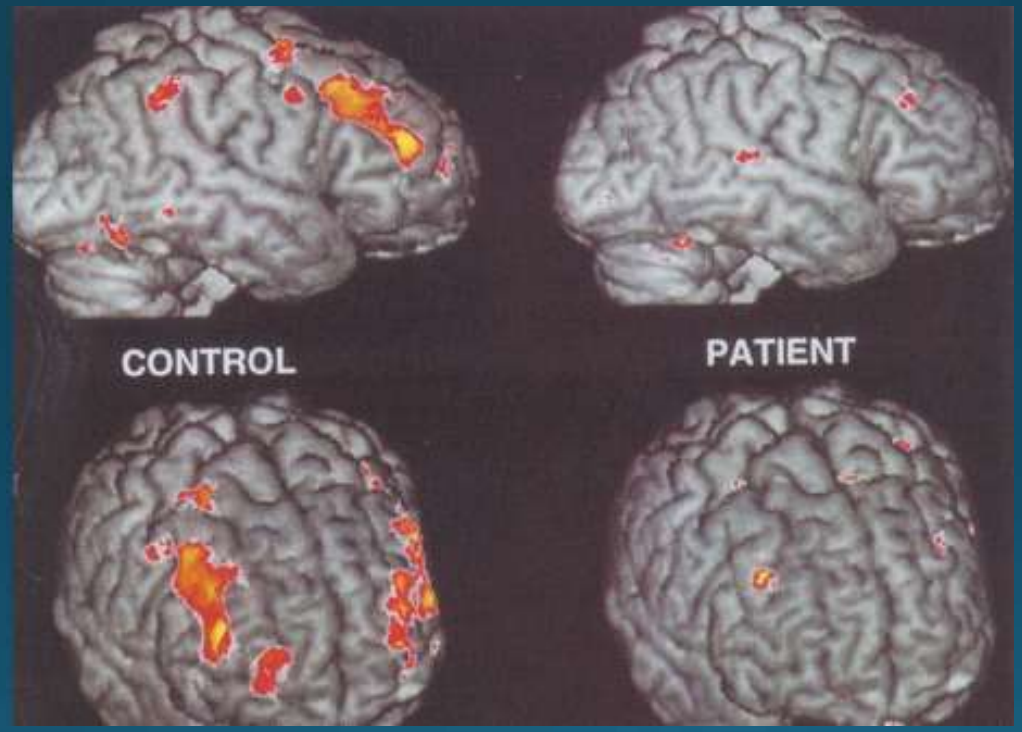

Normal adolescents show greater amygdala activation than adults.

# fMRI: Perception vs verbal and visual memory



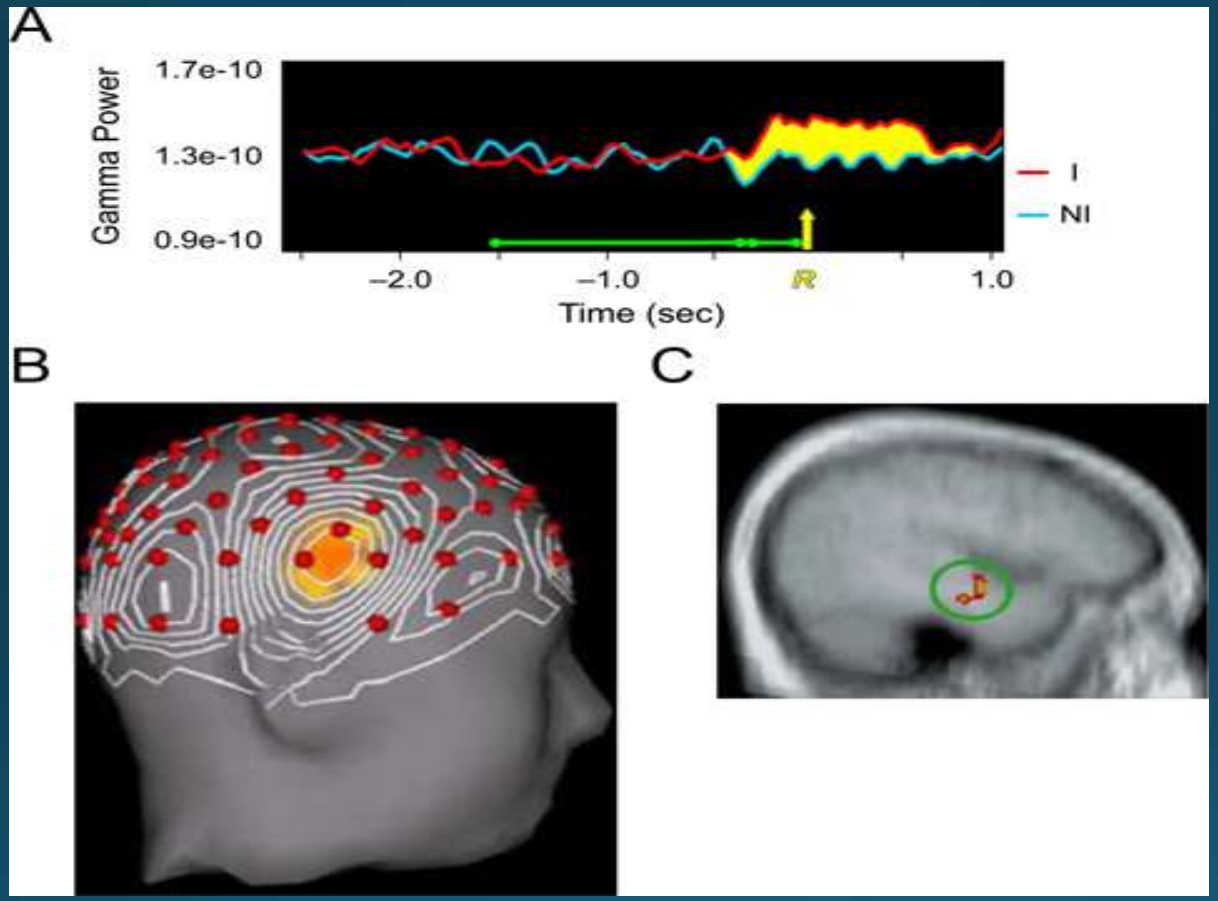
Top left: picture perception; top right: sounds
Bottom left: LTM retrieval of picture; bottom right: retrieval of sound

# fMRI: Reduced working memory in schizophrenia




Reduction in blood flow in dlPFC in schizophrenia

# “Aha” moment of insight: EEG & FMRI – right anterior TL

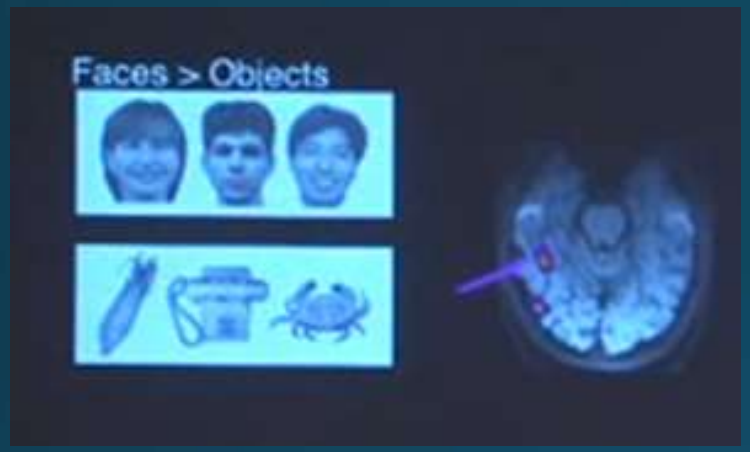



- EEG showed that insight solutions were associated with a burst of high-frequency (i.e., 40-Hertz gamma-band) activity starting about 300 milliseconds before the button-press signaling that a solution was derived. This burst of EEG activity was detected at electrodes located over the right anterior temporal lobe, just above the right ear. The only insight effect reliably detected with fMRI in this initial study occurred in a brain region called the right anterior superior-temporal gyrus, which was underneath the electrodes showing the corresponding EEG effect.
- M. Jung-Beeman,  et al., 2004, PLoS Biology, 2, pp. 502 and 505.

# Nancy Kanwisher at MIT

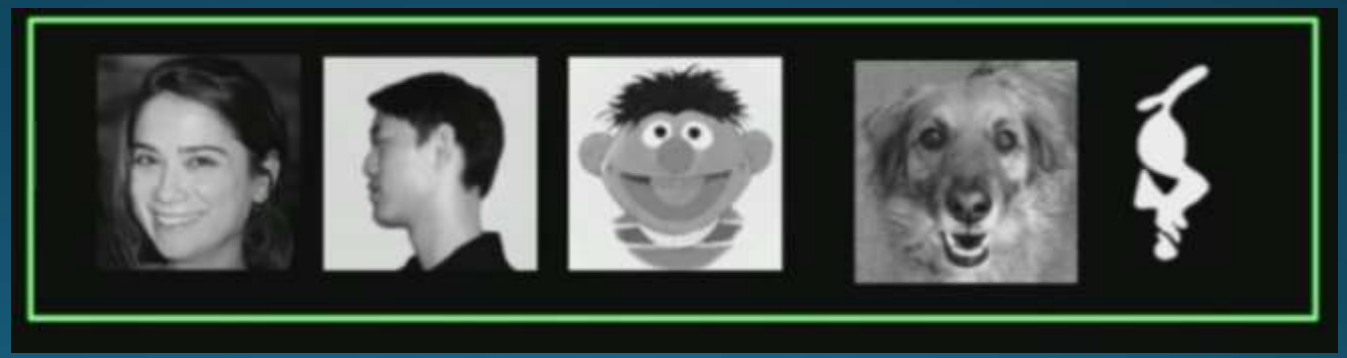
# Fusiform Face Area (FFA): Face Recognition

## Brain regions for face vs. object recognition




Genetic: Face perceptual abilities are inherited

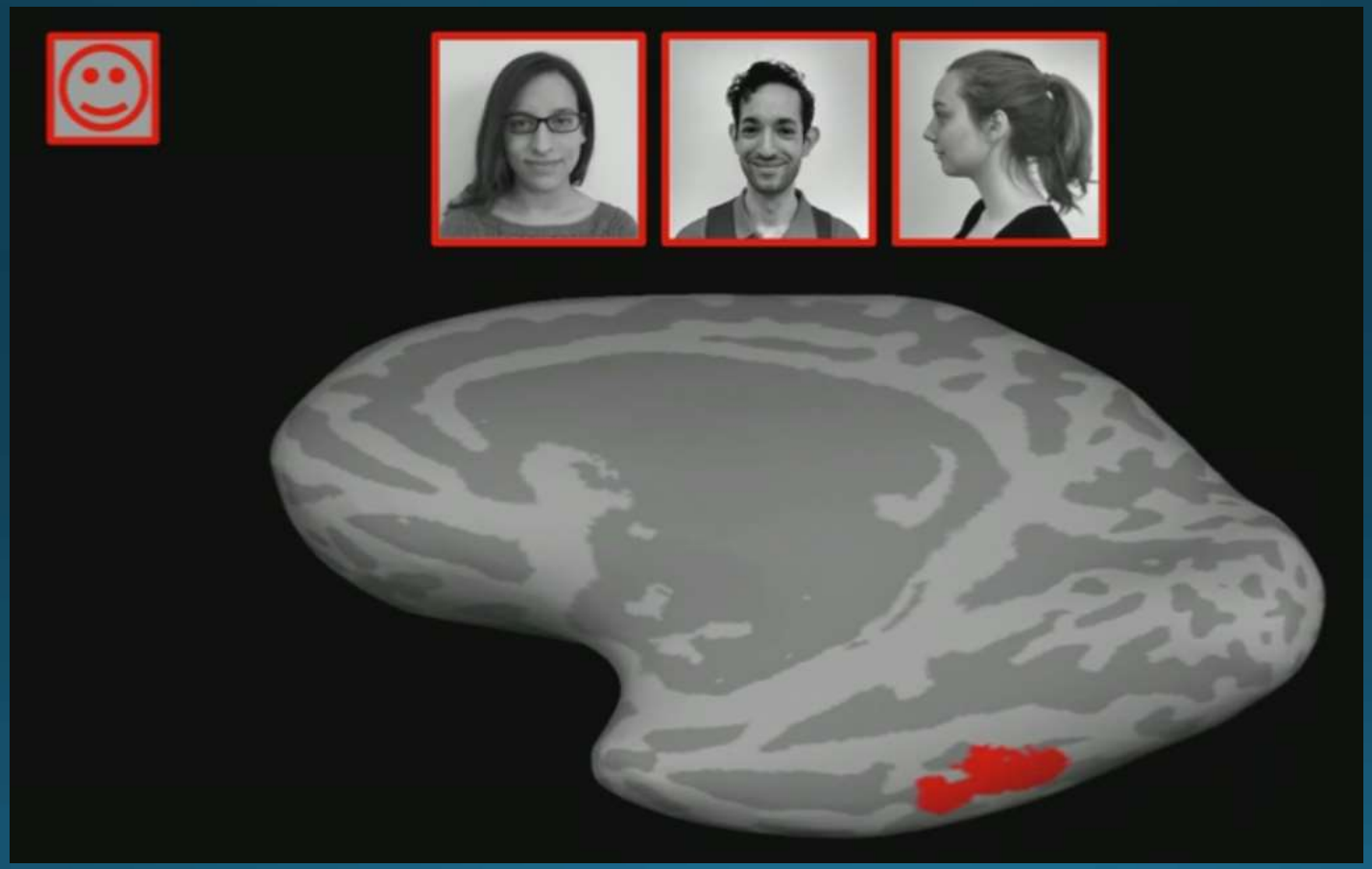
No correlation between IQ & face recognition



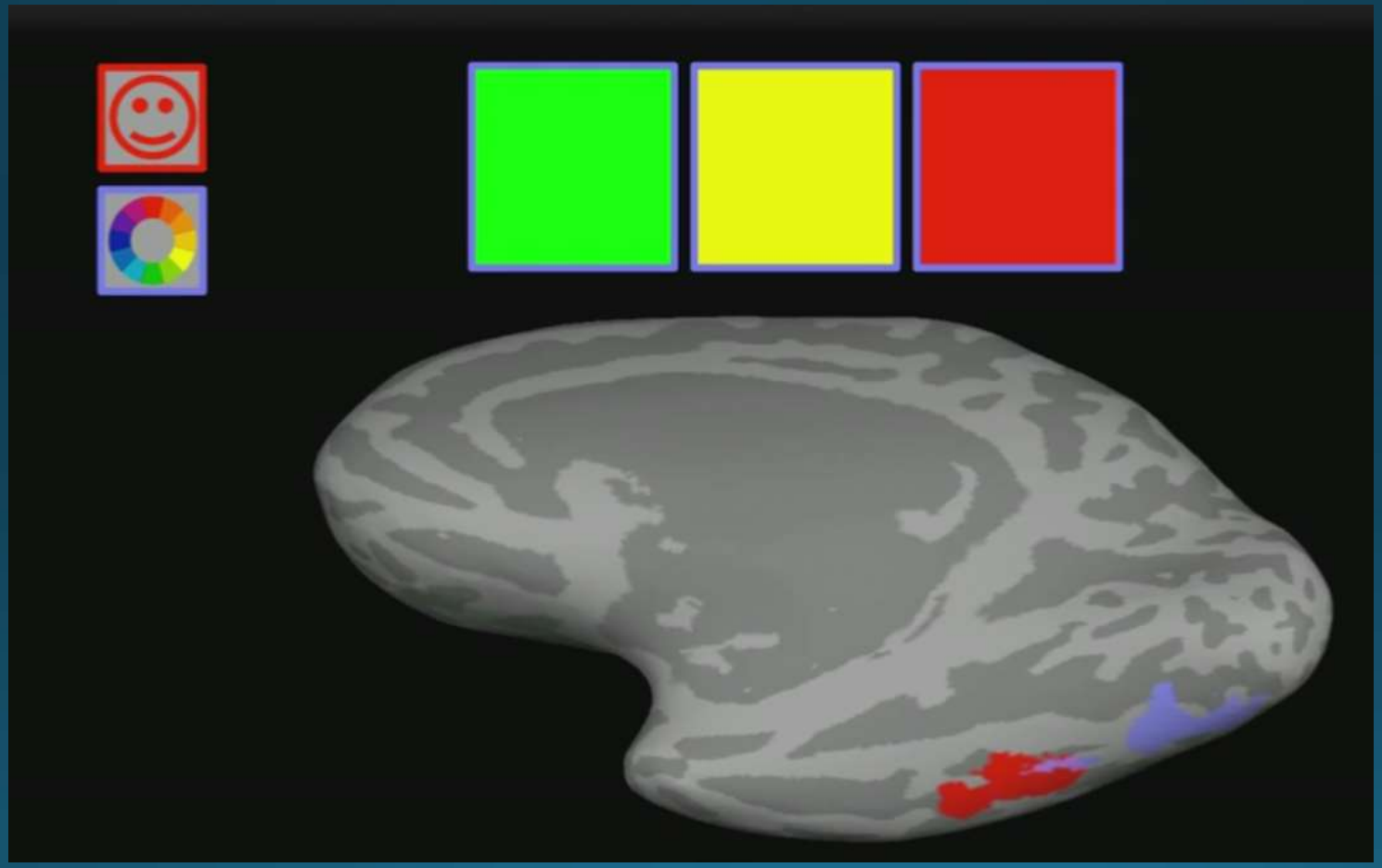
Confirmed in epileptic pt with 2 electrodes on FFA

**Nancy Kanwisher at MIT**

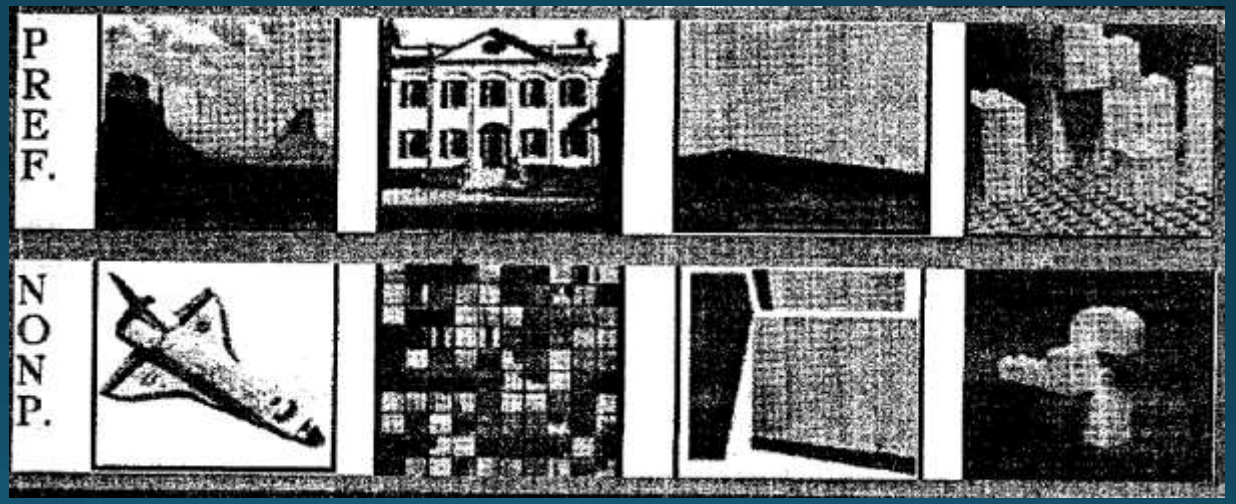
# FFA: Face Recognition



# Color Processing Area

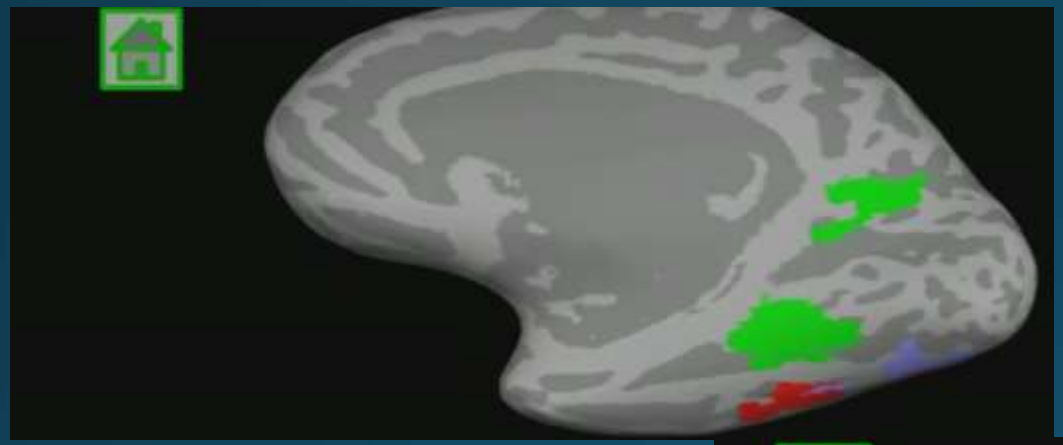


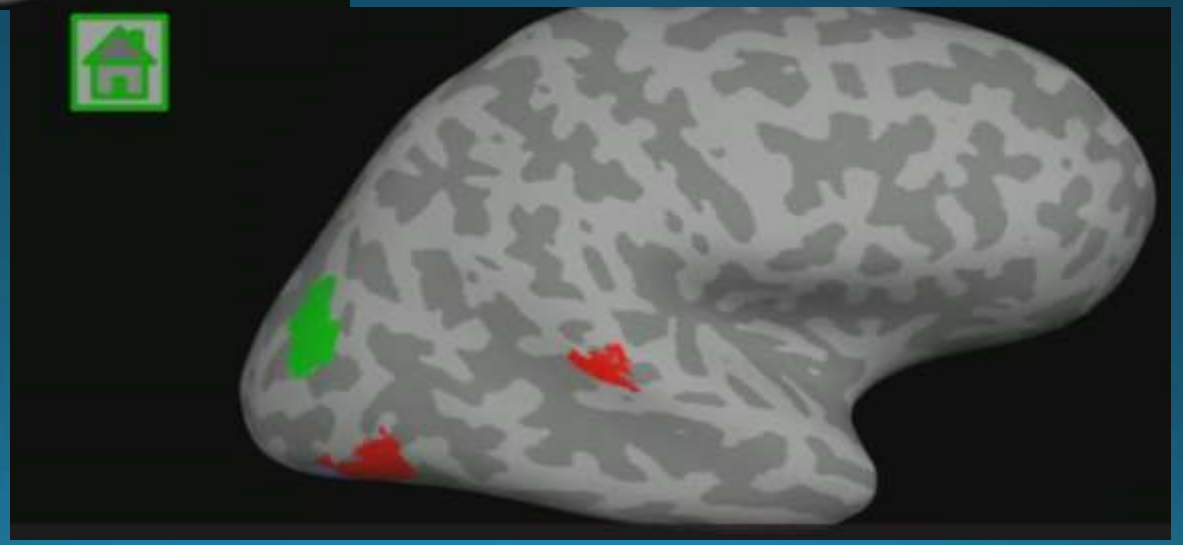
# Parahippocamal gyrus: Recognition of places



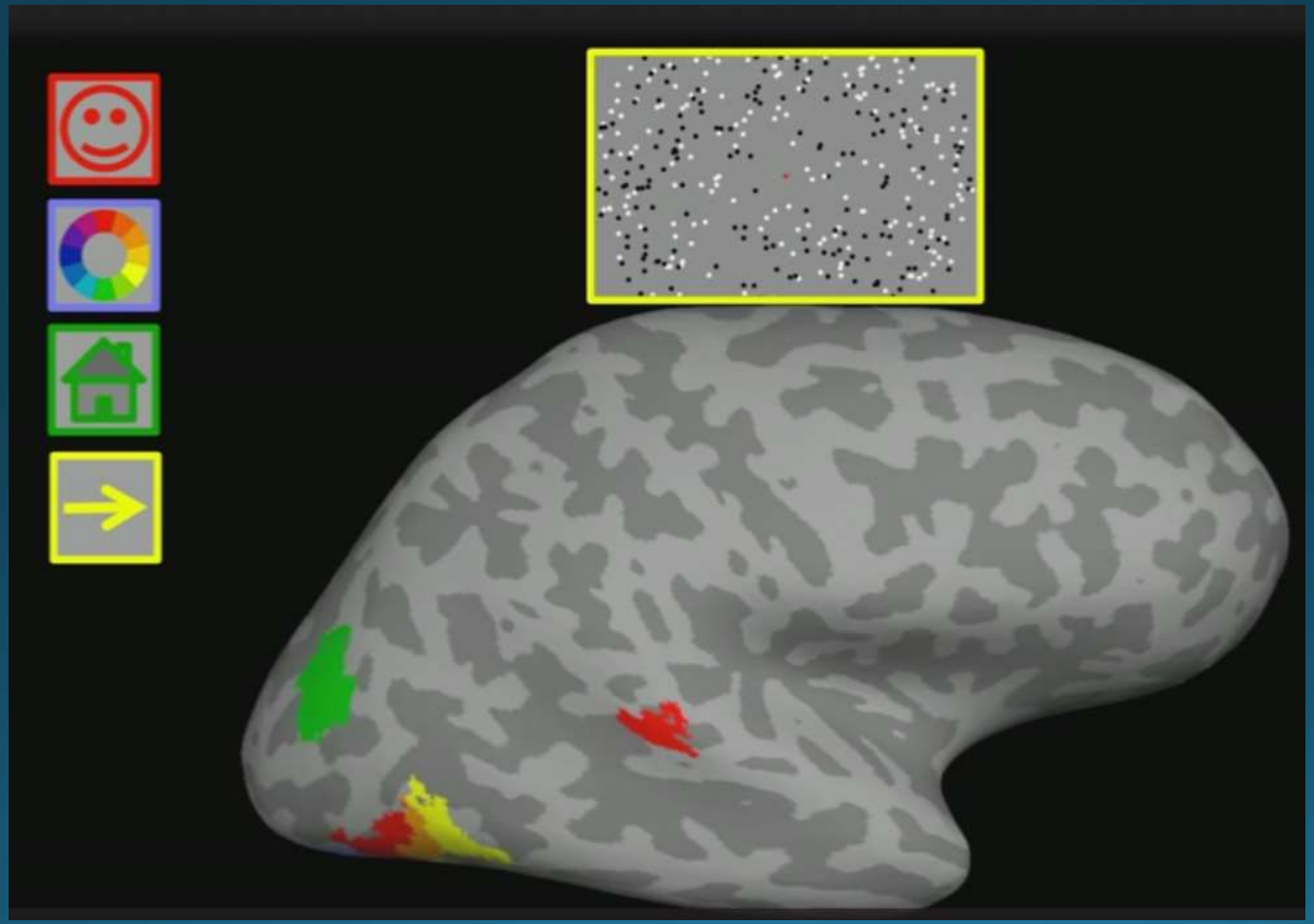

**Parahippocampal place area (PPA):**
**Place area of brain**: Recognition of spatial layouts

# PPA: Place area

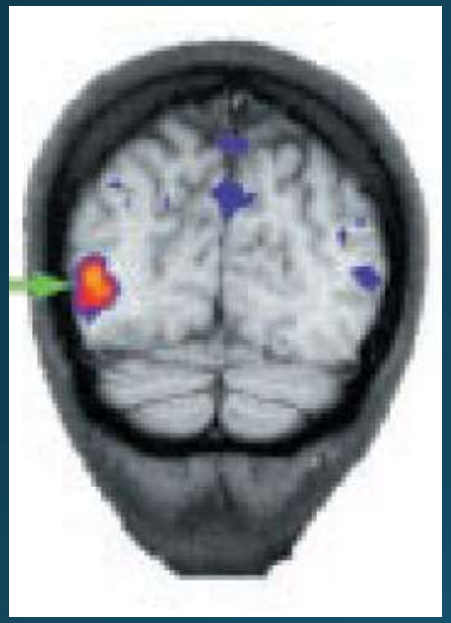


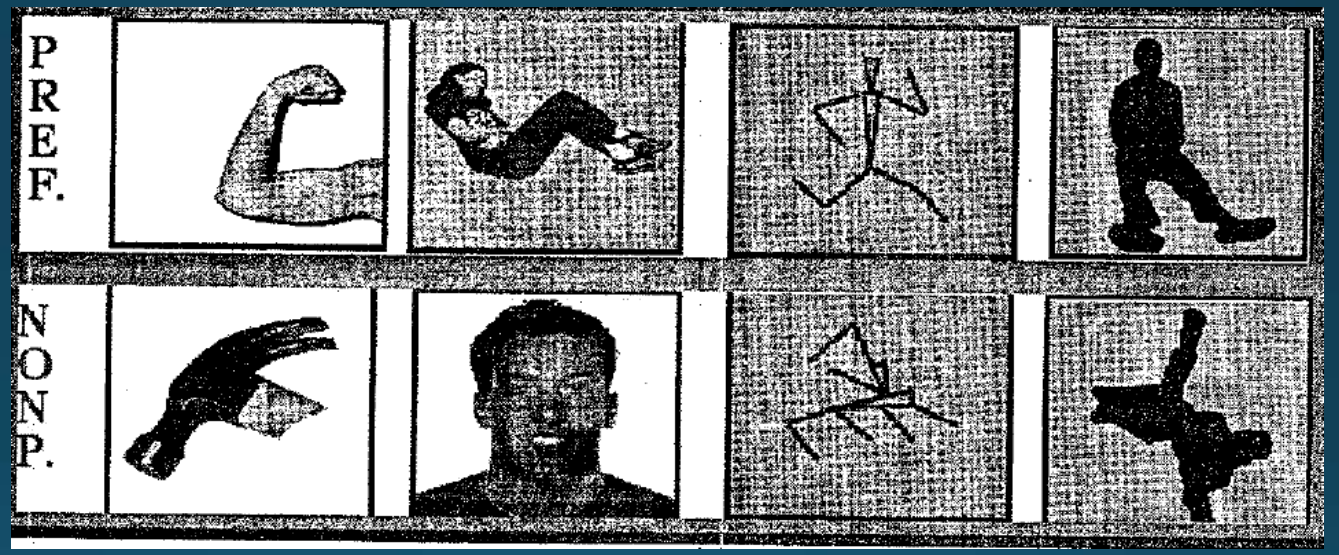


# Visual Motion area



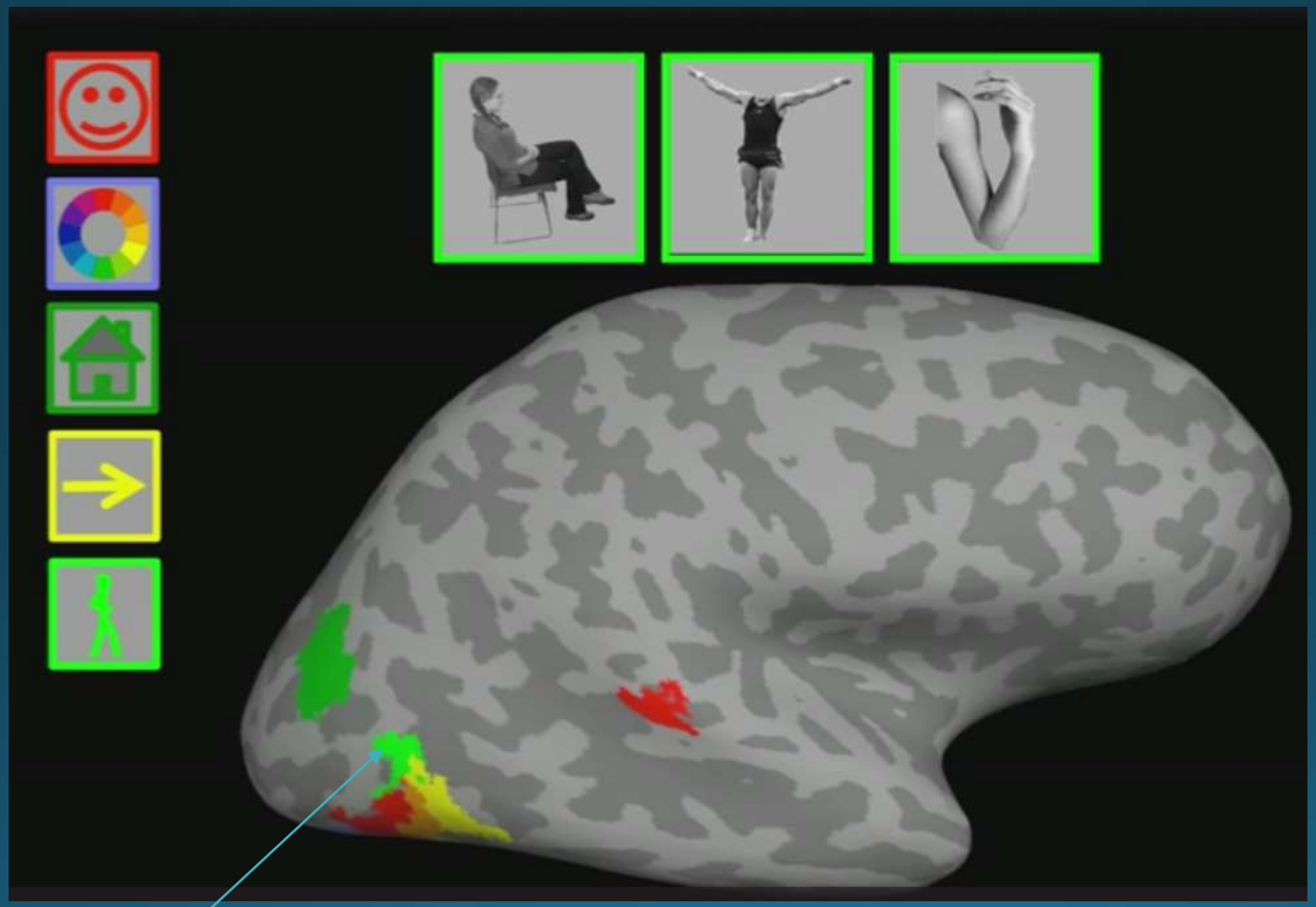
# Extrastriatal Body Area





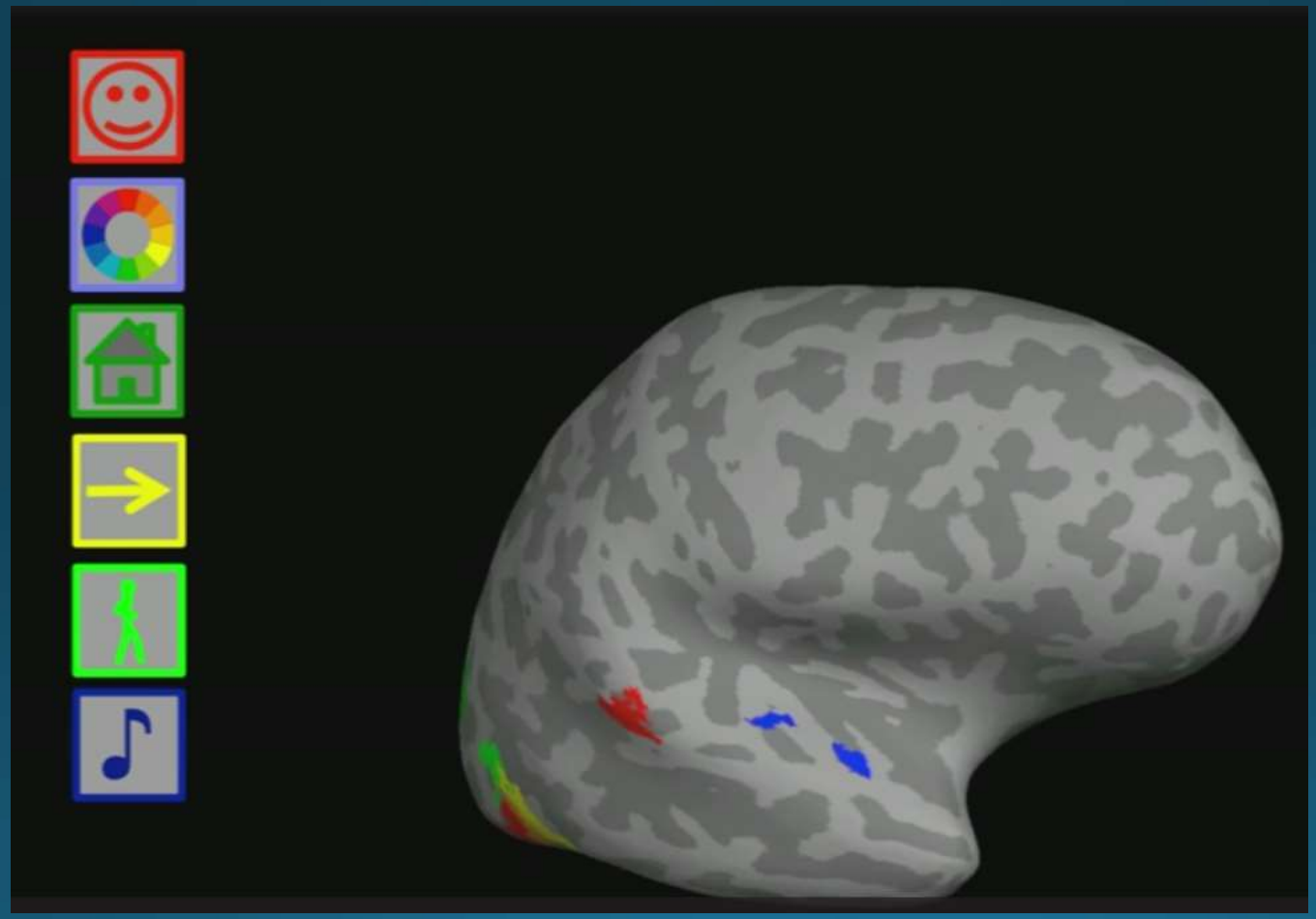

EBA: Only responds to **bodies and body parts**

# Body Parts Area



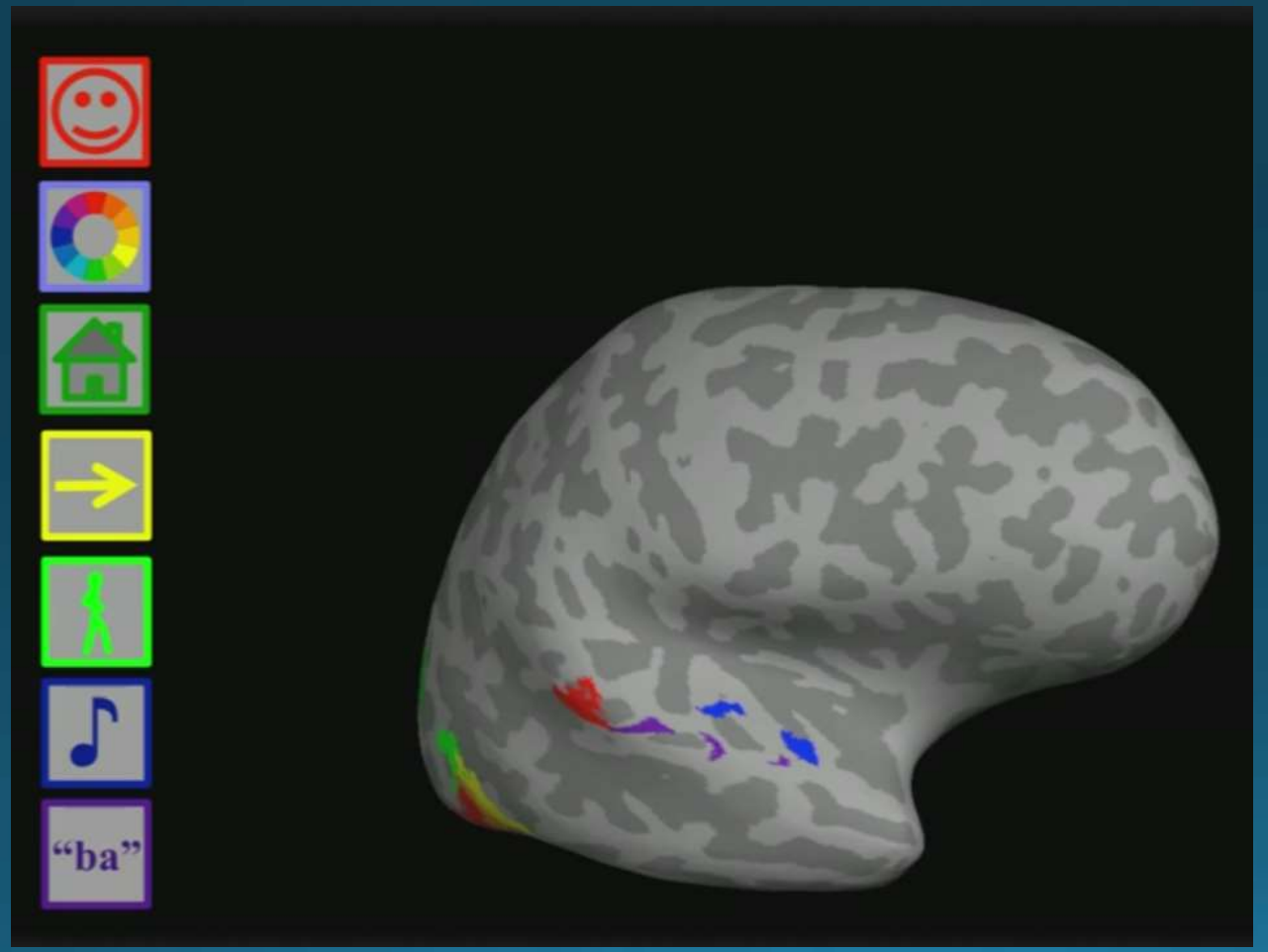
EBA

# Hearing pitch area

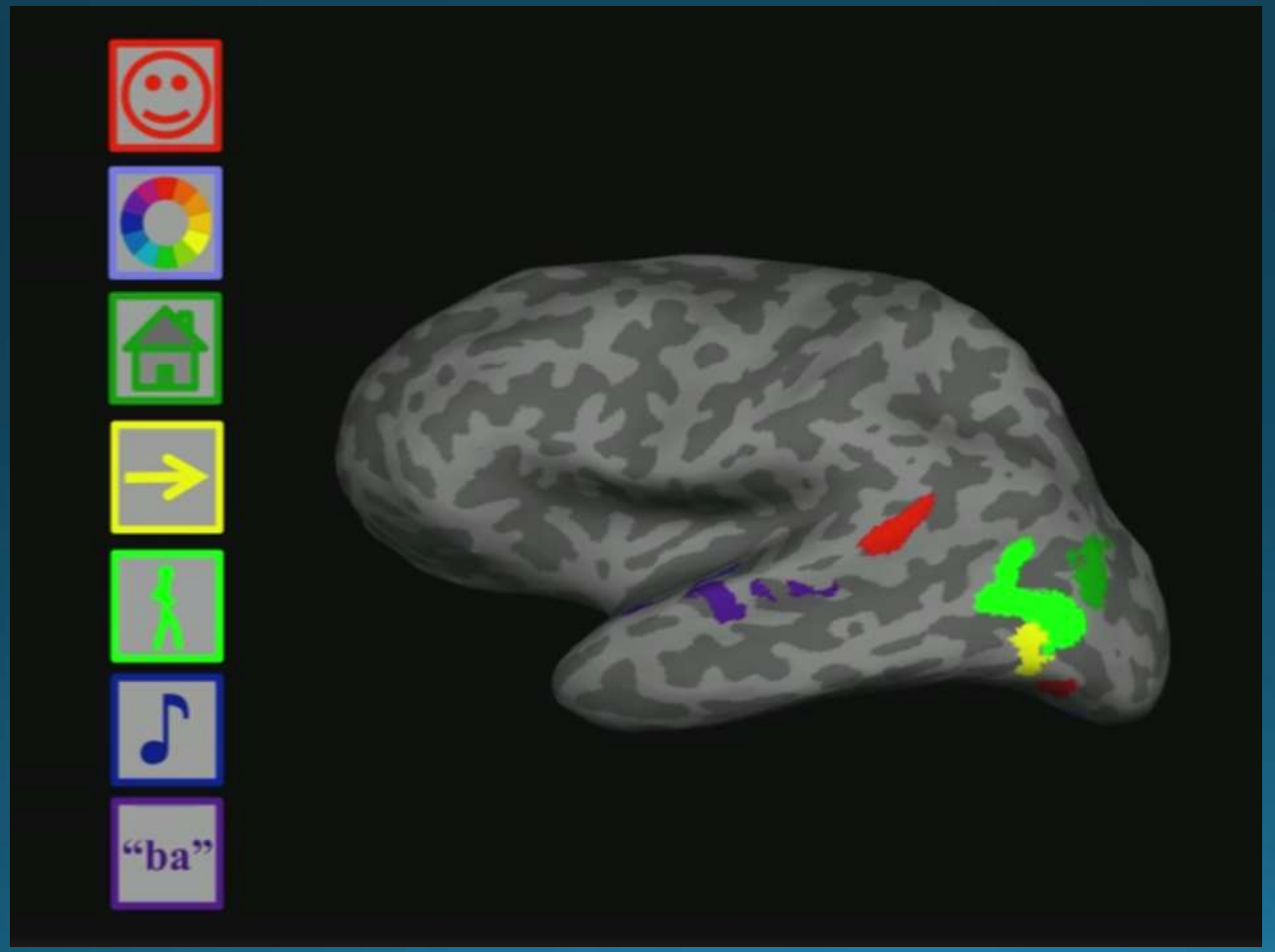


Sounds with pitch i.e. police siren

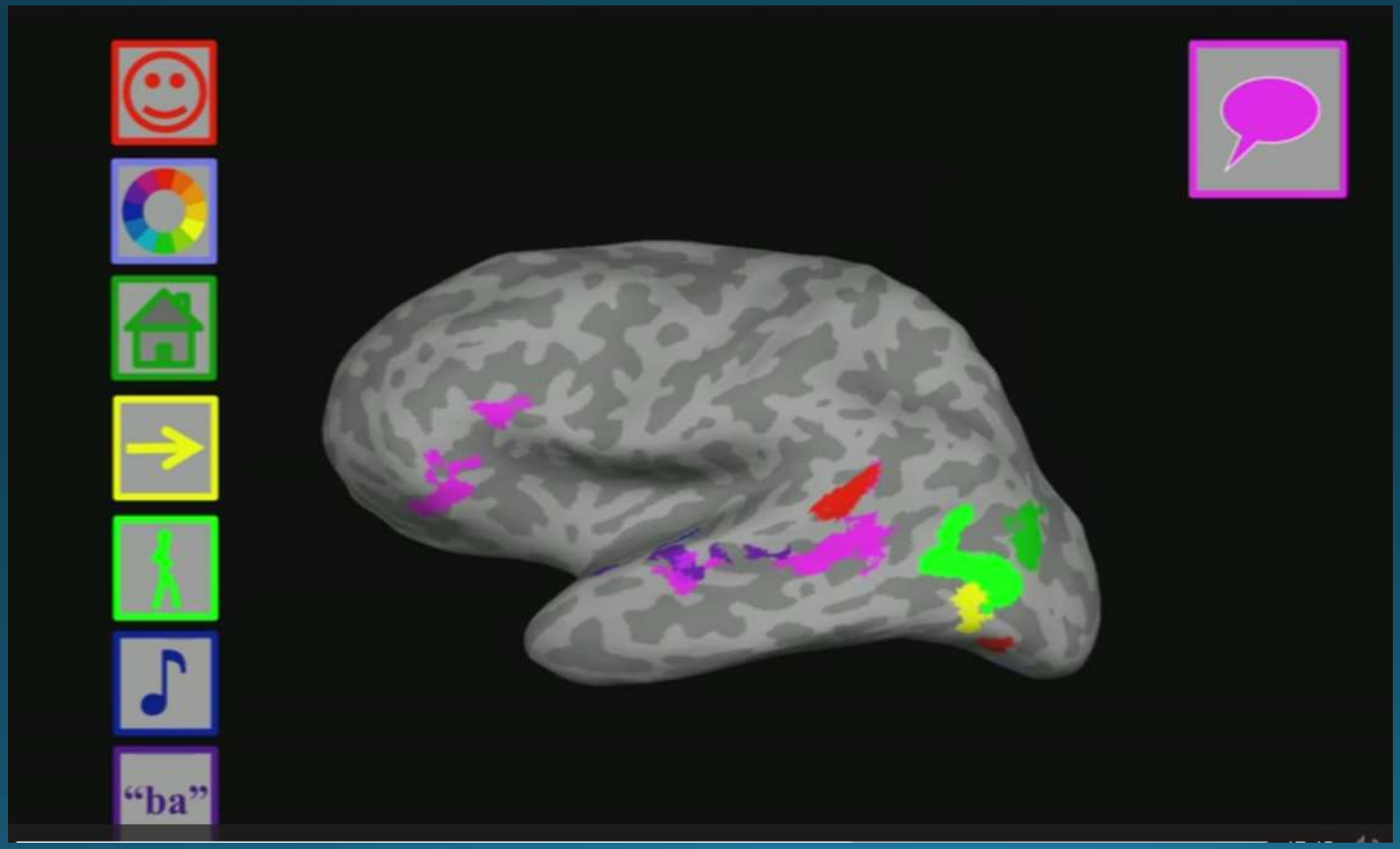
# Speech Sound area



# Left Hemisphere versions of 7 areas



# Language regions



# Visual Word Area: Experience counts

FFA

VWFA
Left ventral occipitotemporal cortex

PPA

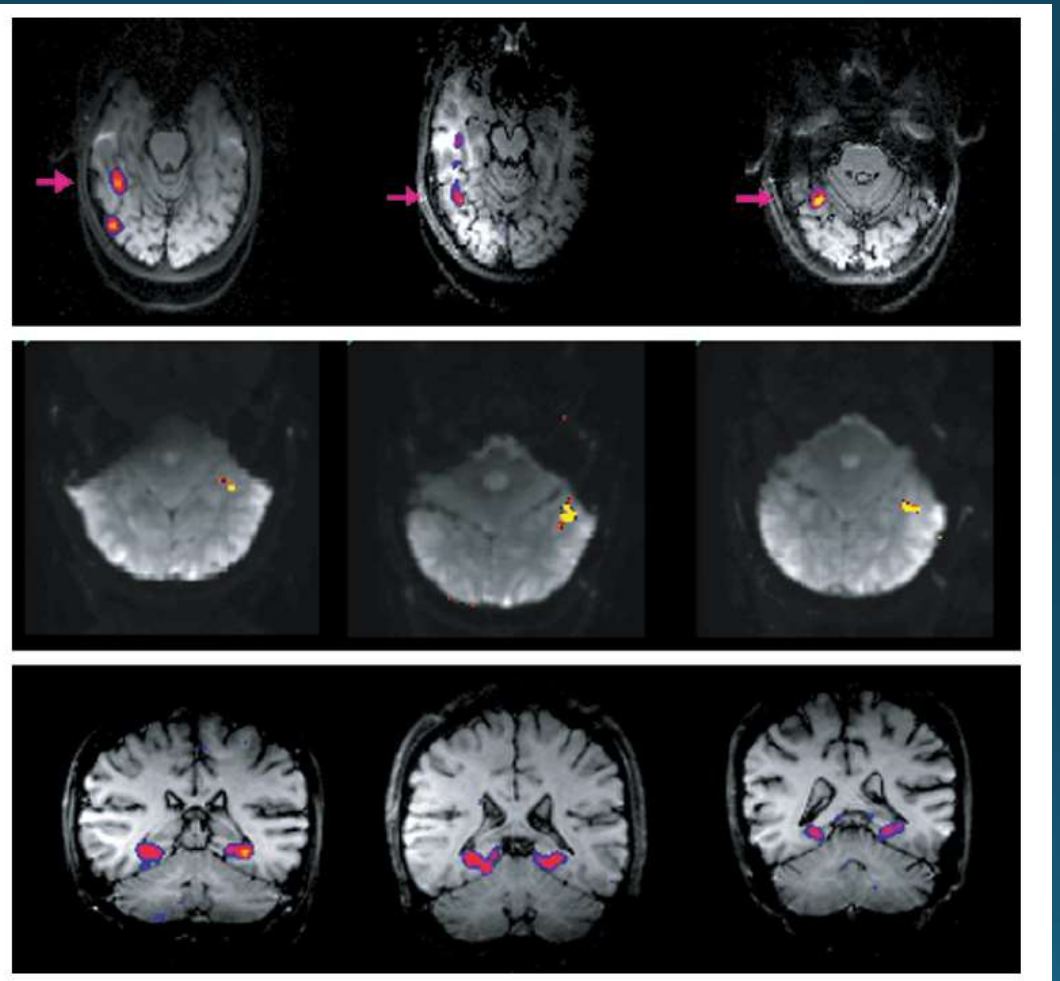


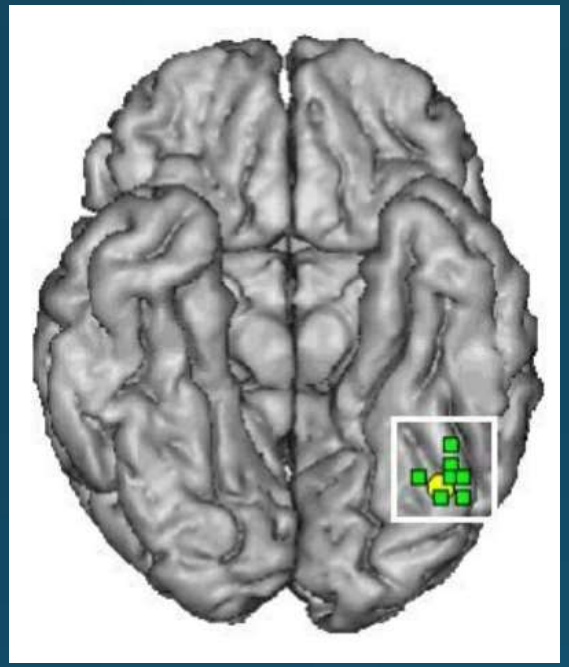
Fig. 6. Three of the functionally specific regions that have been discovered using the individual-subjects functional ROI approach. Top panel: the fusiform face area (FFA), which is defined by a higher response to faces than objects shown in three individual subjects (data from Kanwisher et al. 1997). Middle panel: a word and letter-string selective region, which is defined by its higher response to visually presented words than line drawings of objects shown in three individual subjects (data from Baker et al. 2007). Lower panel: the parahippocampal place area (PPA) which is defined by a higher response to scenes than objects shown in three individual subjects (data from Epstein et al. 1999).

Faces

Visual Words based on experience

Scenes

# Reading letters area: literacy changes brain



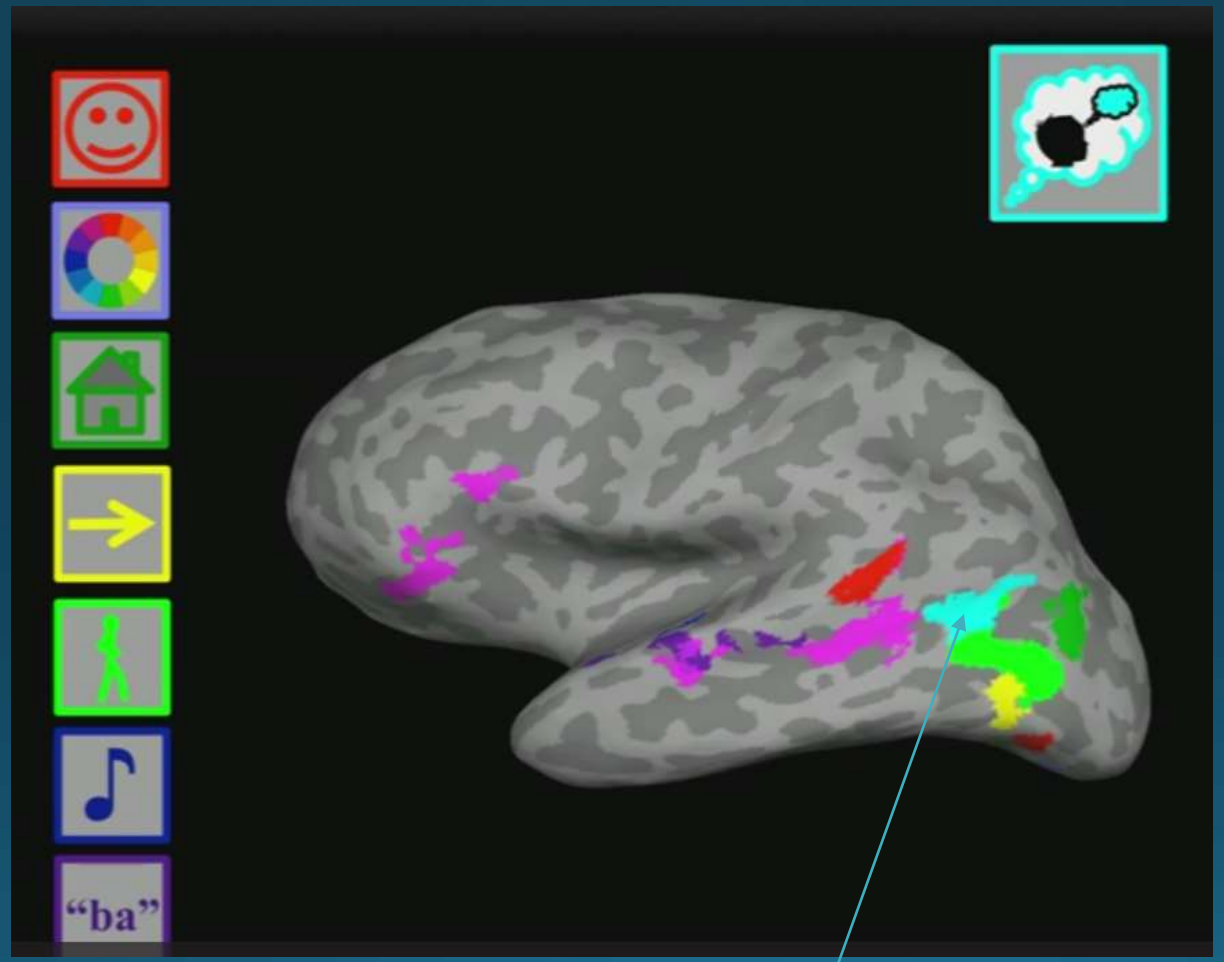
Result of experience

Visual Word Form Area localized to the left occipito-temporal region that is responsible for recognizing visual letters and words (reading written words). VWFA is the highest stage in a hierarchy of visual feature extraction for letter and word recognition. Brain circuits originally evolved for object recognition to become tuned to recognize frequent letters

Both Hebrew & English Words

Kanwisher; Dehaene

# Thinking about thoughts of others




Other's Thoughts

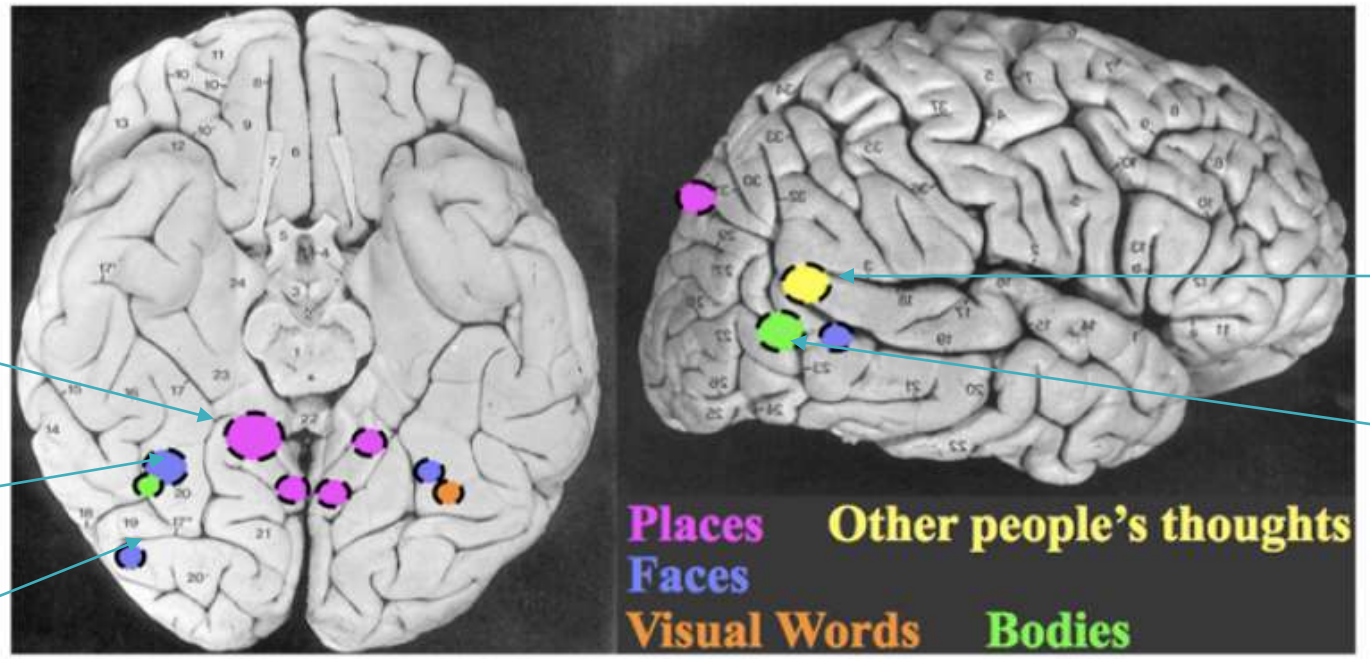
# Functionally specific areas:
## Faces, Places, Bodies, Visual Words, Thoughts

Ventral Visual Pathway:

PPA

FFA

EBA




rTPJ

EBA

**Fig. 1.** This schematic diagram indicates the approximate size and location of regions in the human brain that are engaged specifically during perception of faces (blue), places (pink), bodies (green), and visually presented words (orange), as well as a region that is selectively engaged when thinking about another person's thoughts (yellow). Each of these regions can be found in a short functional scan in essentially all normal subjects.

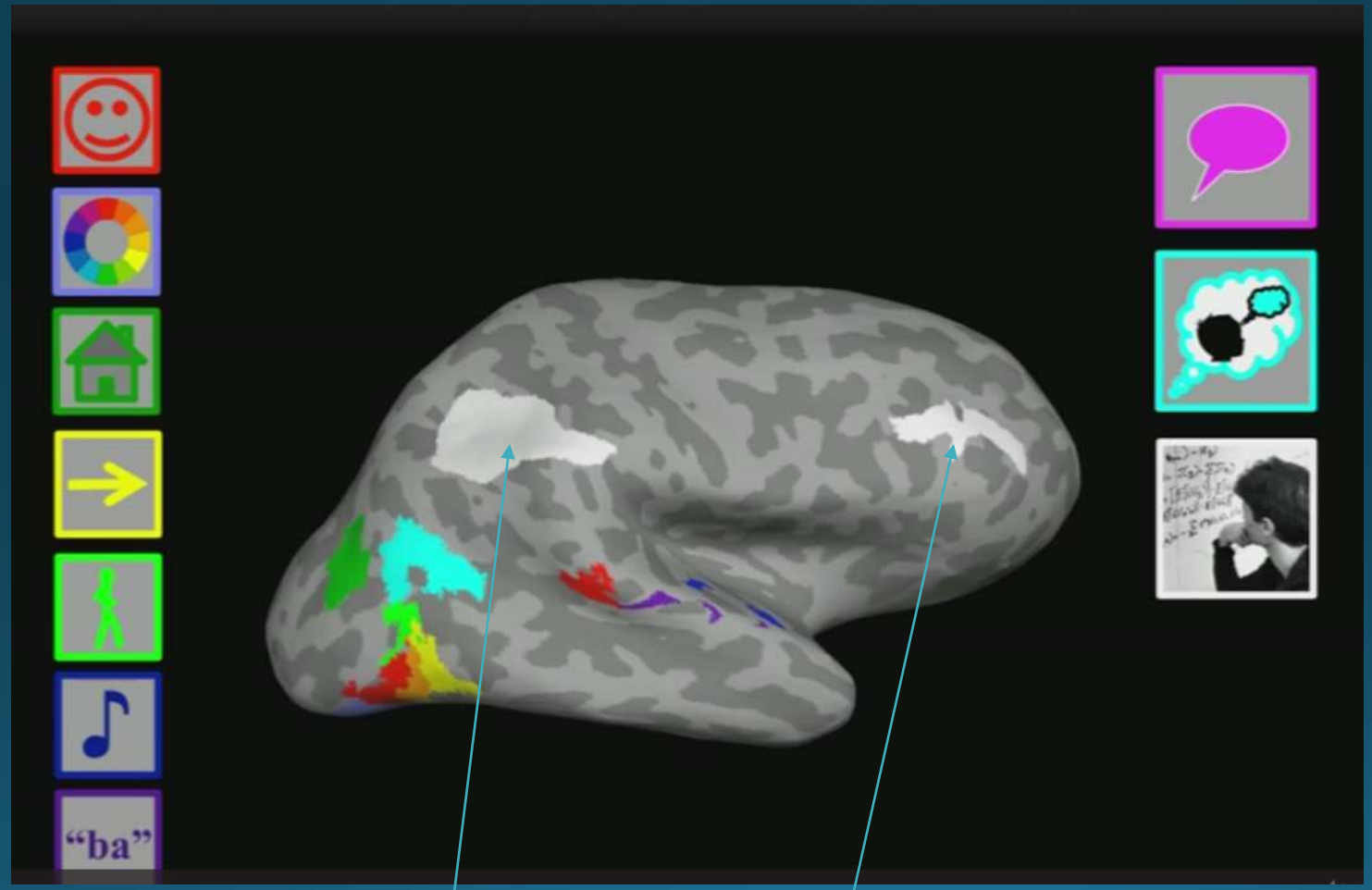
Nancy Kanwisher1, 2010

# Seeing = Imaging

- Same areas are active when participants are imagining faces and places, with no physical perception, as when they are actually looking at faces and places.

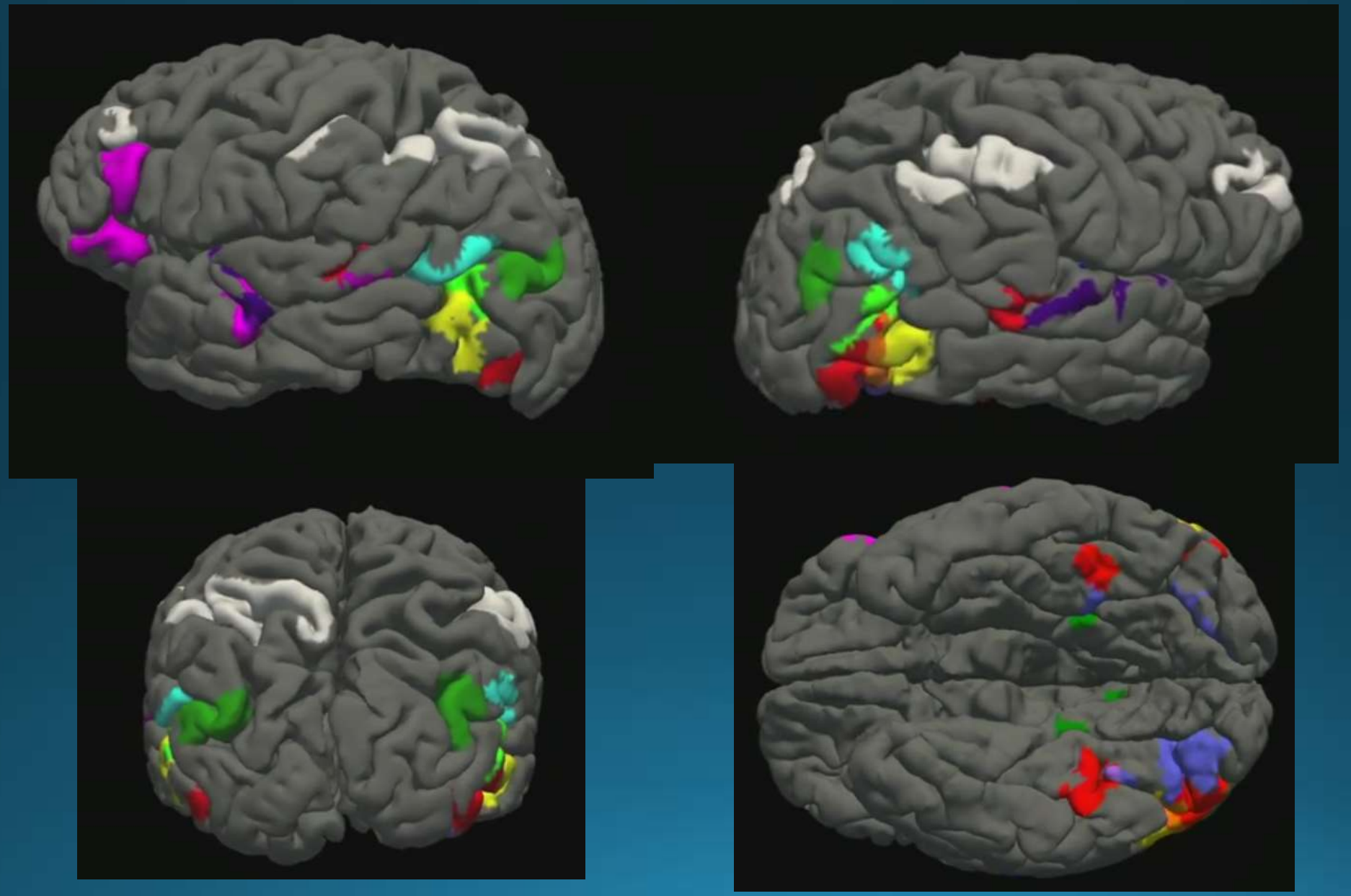
- It’s not just what you are physically seeing, but what you are consciously aware of that is processed by these areas.

# 2 General Purpose Processors




Respond to any difficult mental task

# All of these processors are in the same places in everyone



# New Couples fMRI Machine:
# Brain areas sync when we interact

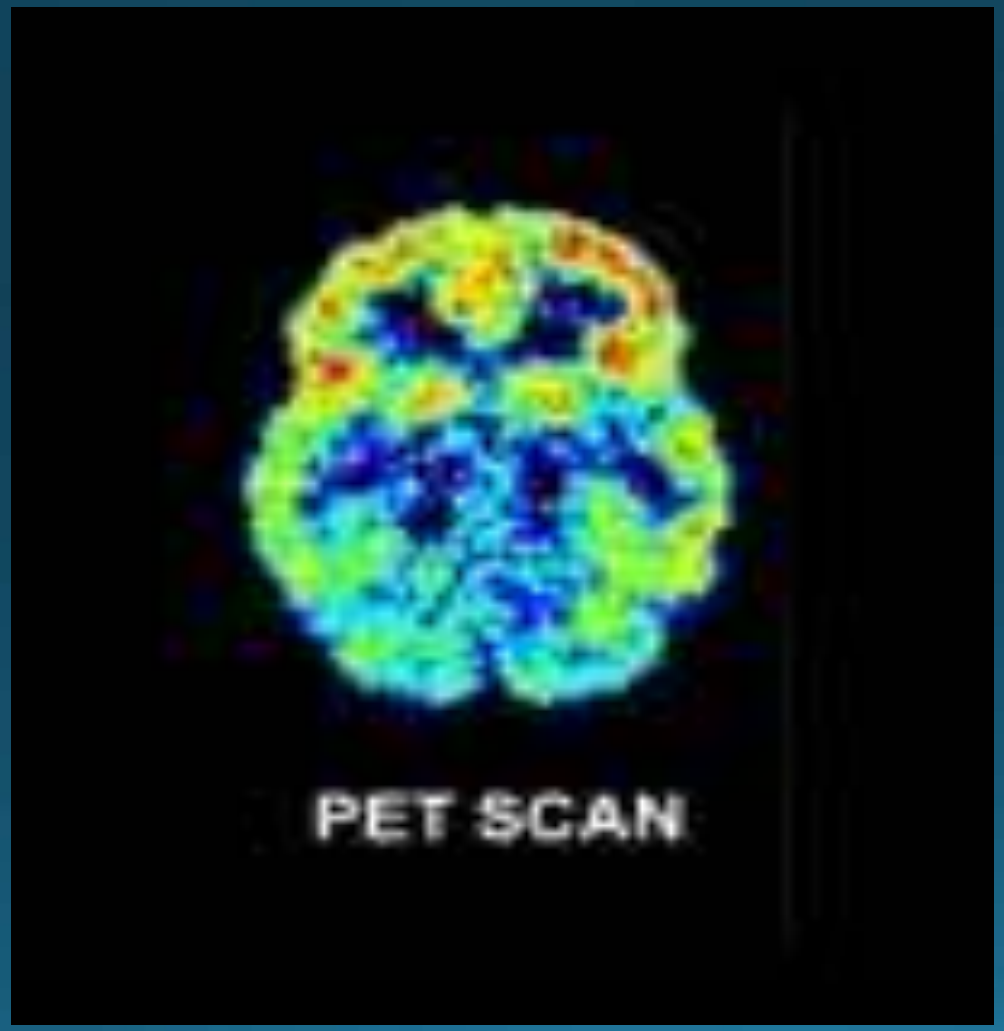
Friends: basal ganglia
Lovers: pCC

When touched:
toucher's motor and somatosensory cortex couples to the other person's STS and somatosensory cortex.

When people communicate: activates mPFC, TPJ, ACC

Ray Lee at Princeton University

# Phelps and Hoffman, 1974: Pet Scan



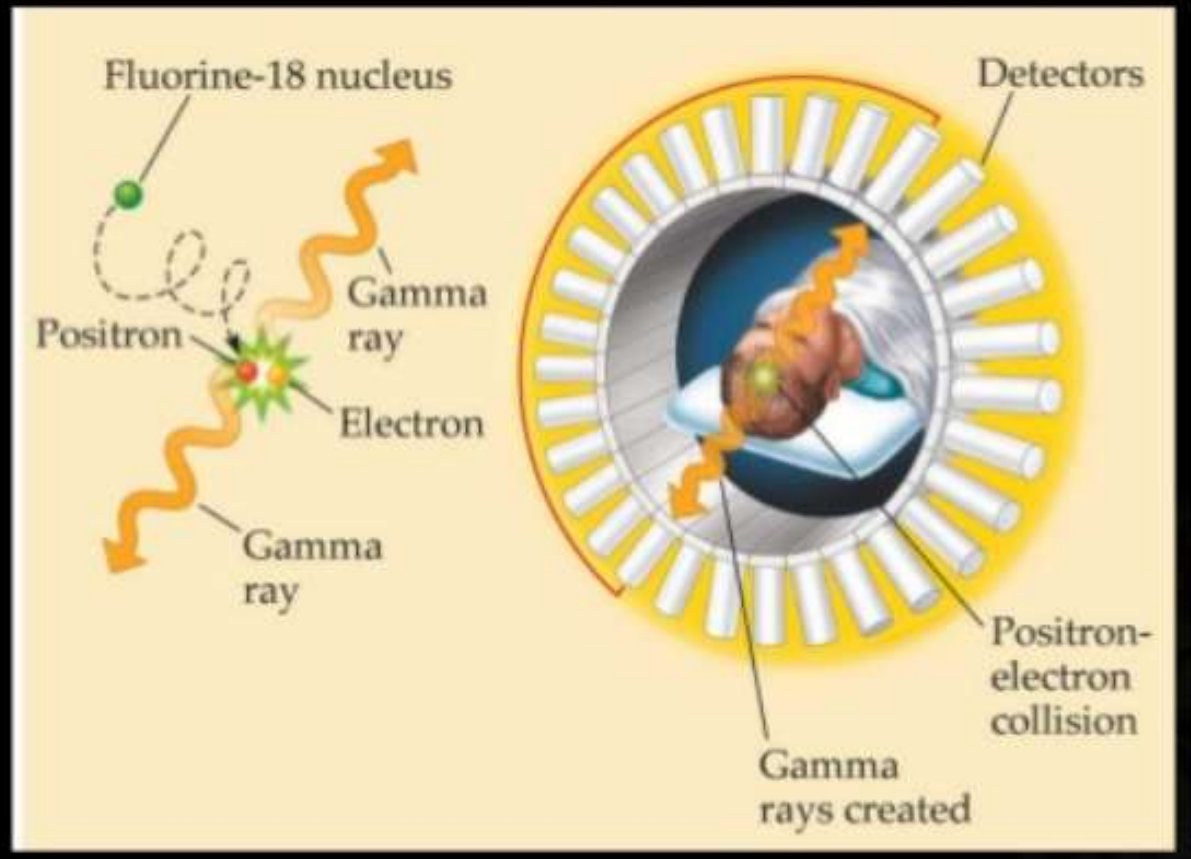
# Positron Emission Tomography (Pet)

- Developed in 1950s; applied to humans 1970s
- Label compounds with positron tracers (glucose, oxygen, water)
- Tracers distribute in brain, measure radioactive decay of tracer
- How it works: A scanning device reads the positron emissions that are released as a previously injected sugar decays. Thus, it can assess the blood flow, oxygen and glucose consumption in different parts of the brain.

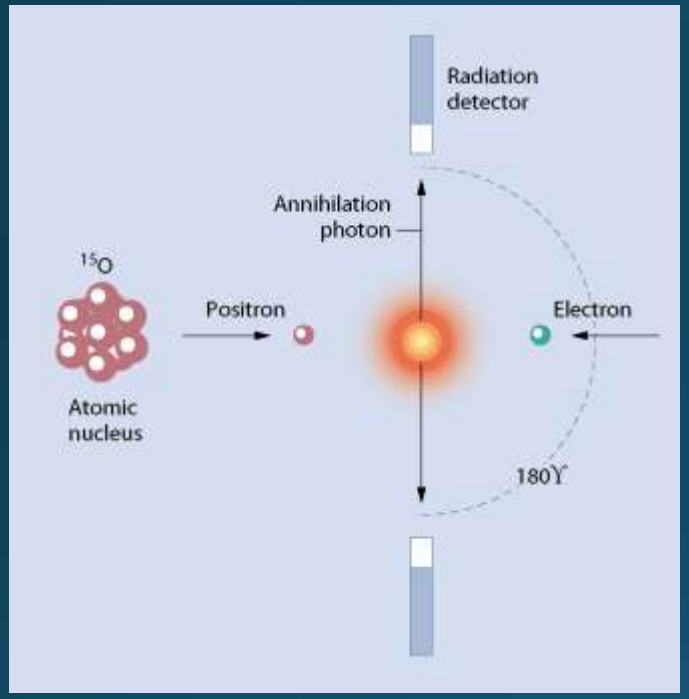
# PET - Positron Emission Tomography: The world of metabolic imaging

# PET Scanner

# PET Scanning: Principles



# Positron Emission Tomography: hemodynamic




Capitalizes on blood-flow or “hemodynamic” properties of brain

- Subjects injected with radioactive isotope
- Measures local changes in blood flow that are linked to neural activity
- Neural activity => increased metabolic demand => local increase in blood flow the active region

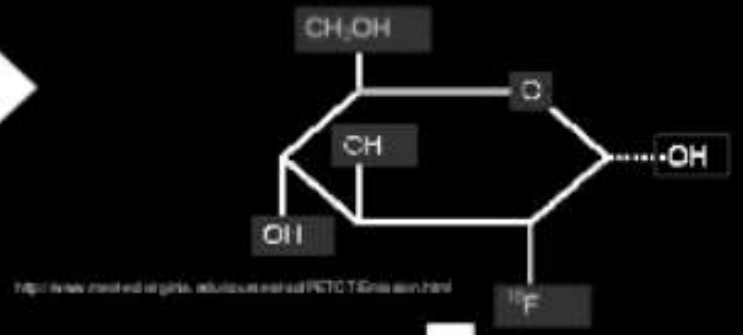
| Elements of Life | PET-nuclide |
| --- | --- |
| Hydrogen | $^{18}F$ (110 min) |
| Carbon | $^{11}C$ (20 min) |
| Nitrogen | $^{13}N$ (10 min) |
| Oxygen | $^{15}O$ (2 min) |

List of elemental radioactive isotopes that are positron emitters and can be used for PET imaging.

# Positron Emission Tomography

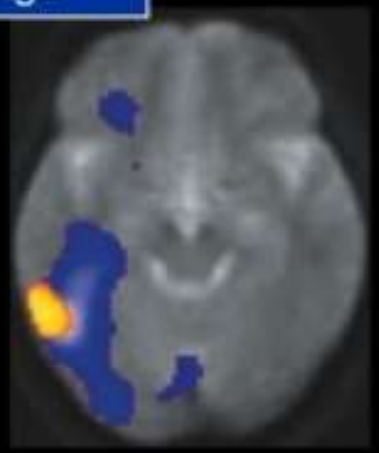
Cyclotron

Radio-isotope (FDG)

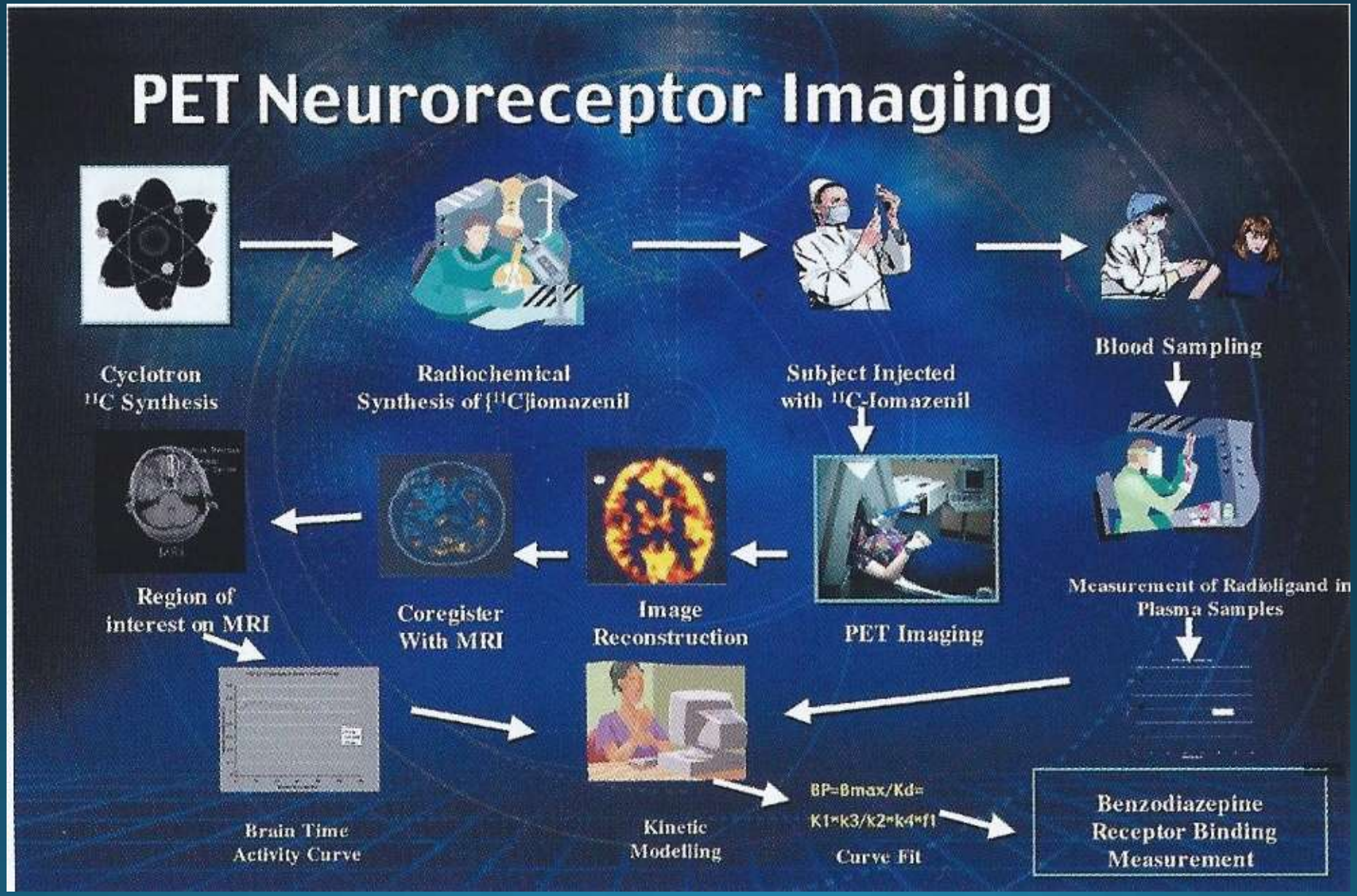



Scanner


Image



# Total Pet Process



# PET & SPECT

- Measure radioactive decay to create images of tissue function
- Unstable nuclides incorporated into desired molecules
- Emit photons as they return to more stable state
- Captured by detectors, processed by computer, to yield functional image of tissue

- In cardiac scanning, PET offers a resolution of 5 to 7 mm, compared with a cardiac SPECT resolution of 12 to 15 mm.

- SPECT radiotracers last longer in the patient; used in cardiology; stress testing takes  three to four hours; PET radiotracers emit gamma rays with shorter lives and higher energies and are more useful in brain imaging where scans last about 30 minutes.

# PET: What's measurable

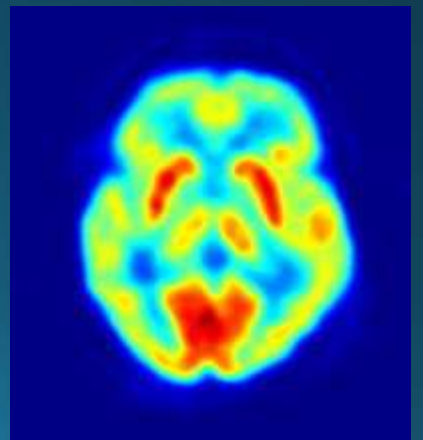
In principle, any brain function can be measured by labeling compound that crosses blood-brain barrier and interacts with relevant cellular machinery:

Neurotransmitter function
Blood Flow
Protein Synthesis, Gene expression
Molecular diffusion
Metabolism of oxygen, glucose, amino acids
Receptor and transport systems: uptake, binding, distribution

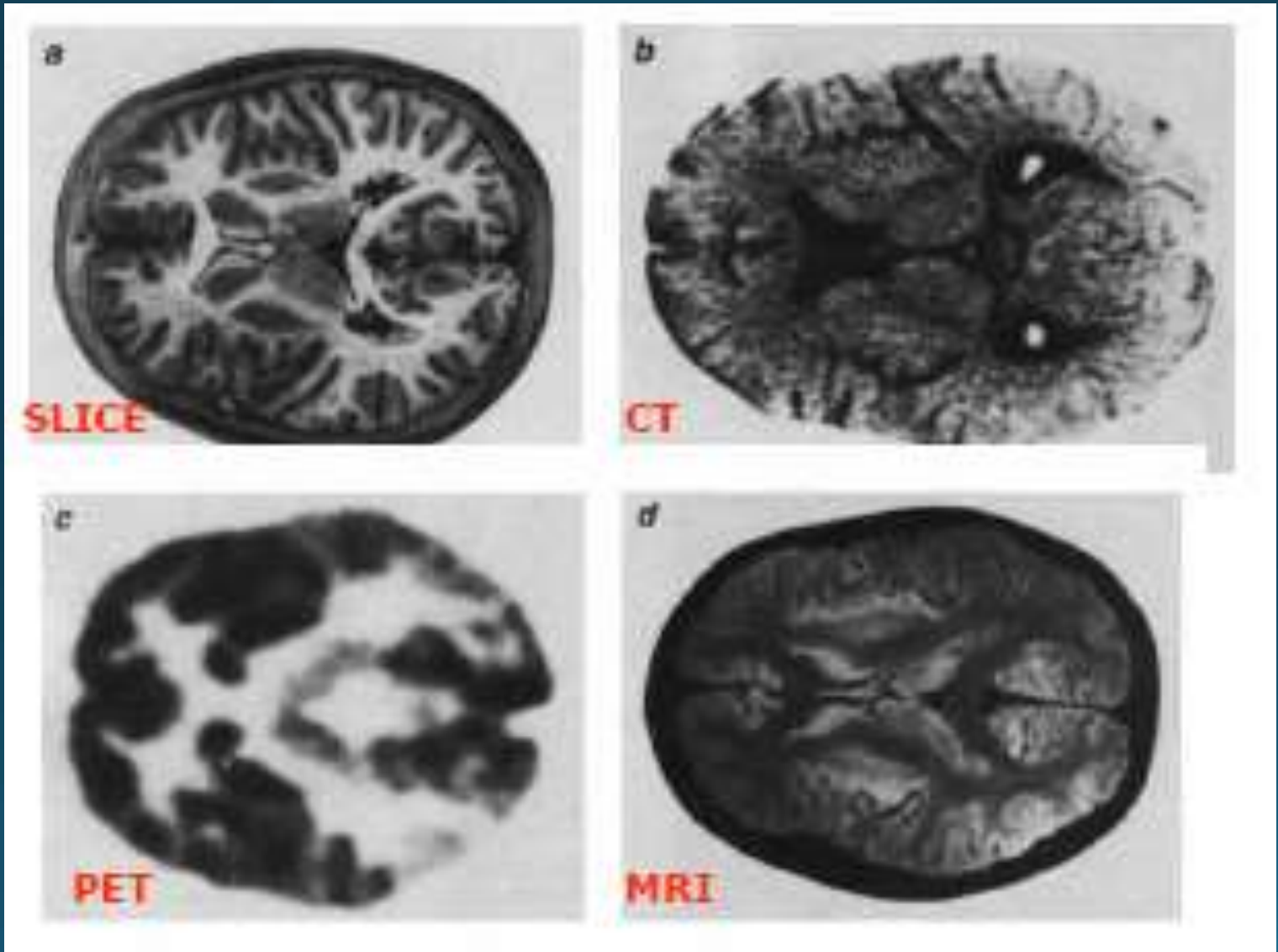
# PET: Pros & Cons

- Pros:
  - Unlike EEG, offers 3D resolution
  - Can measure several metabolic indicators
  - Tracers can reveal neurotransmitter receptors/transporters
  - Can image anything that can be tagged

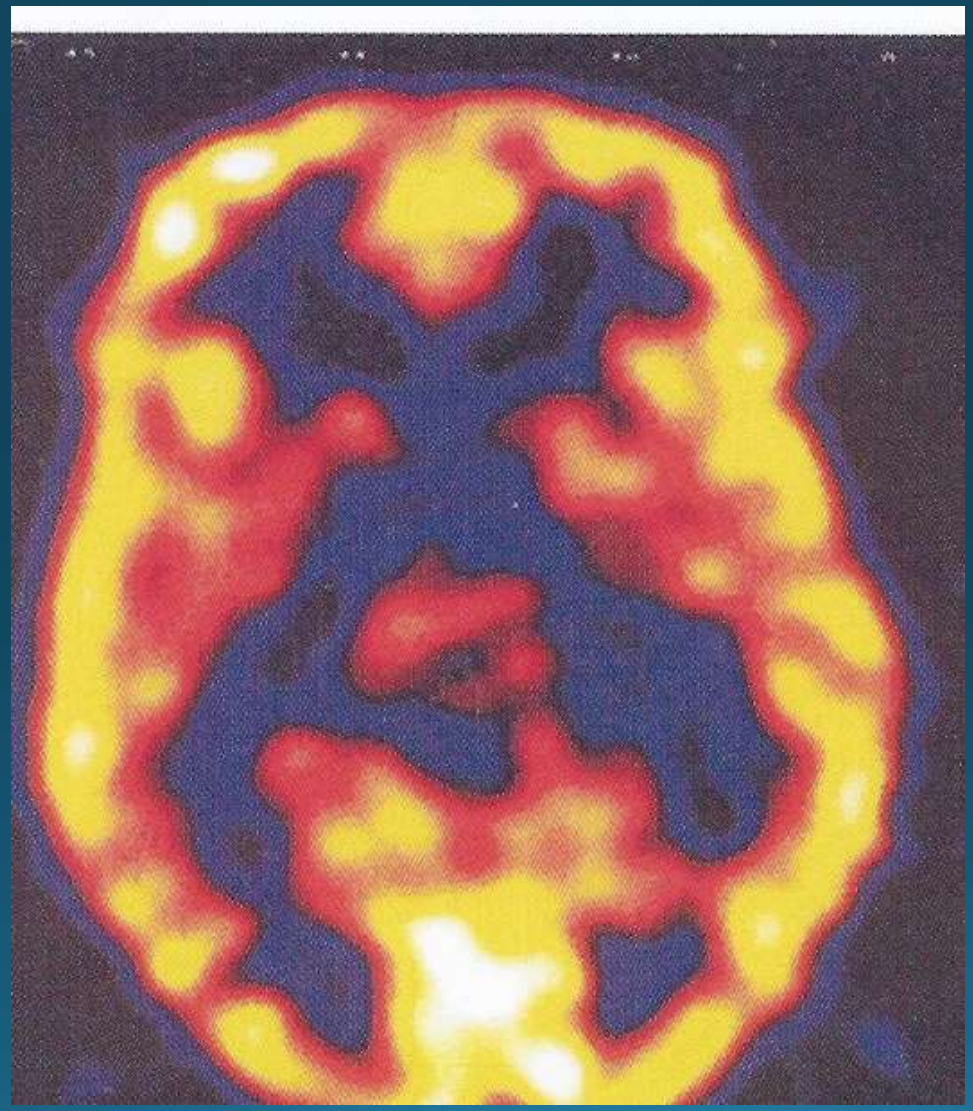
- Cons:
  - Requires radioactive injections
  - Radioactive half life means only short tasks can be measured
  - Blood flow, oxygen and glucose consumption are all indirect correlates of brain activity
  - Expensive
  - Poor temporal (minutes) & spatial (cms) resolution
  - Setbacks with radiopharmaceutical supply problems



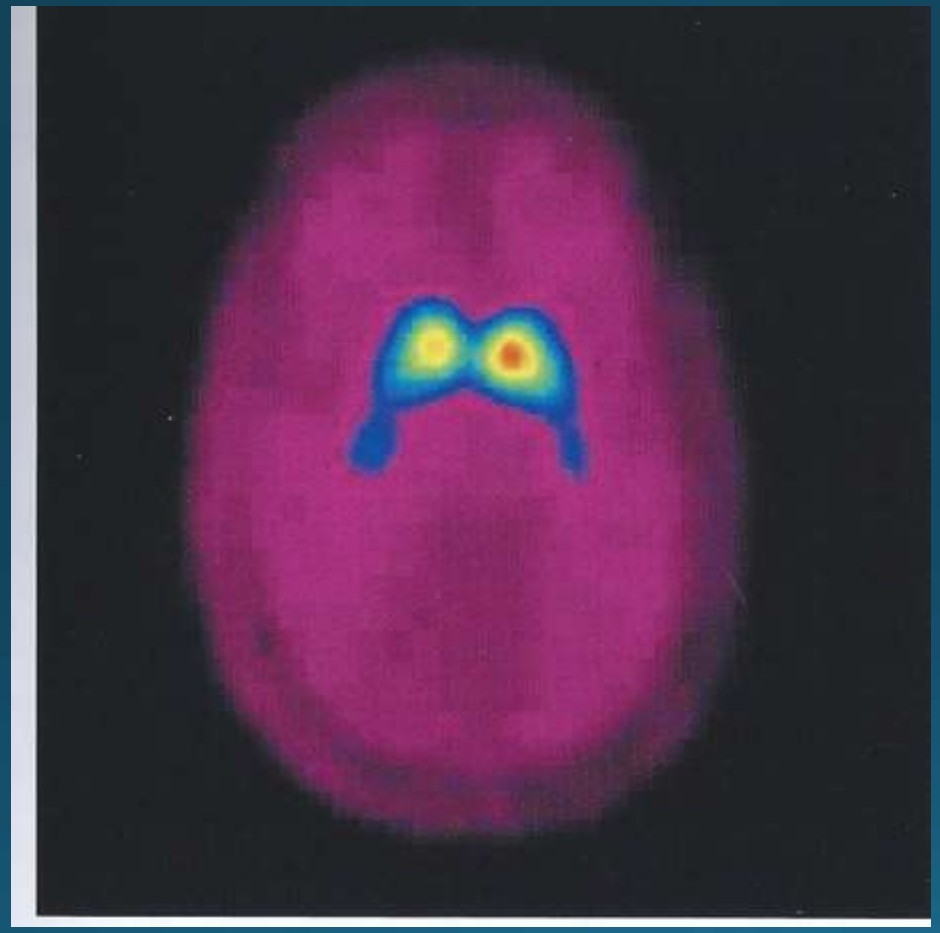
# Comparison: Real, CT, MRI, PET



# PET: Benzodiazepine receptor binding



# PET: Dopamine transporters



Highest concentrations in striatum

# PET: Language

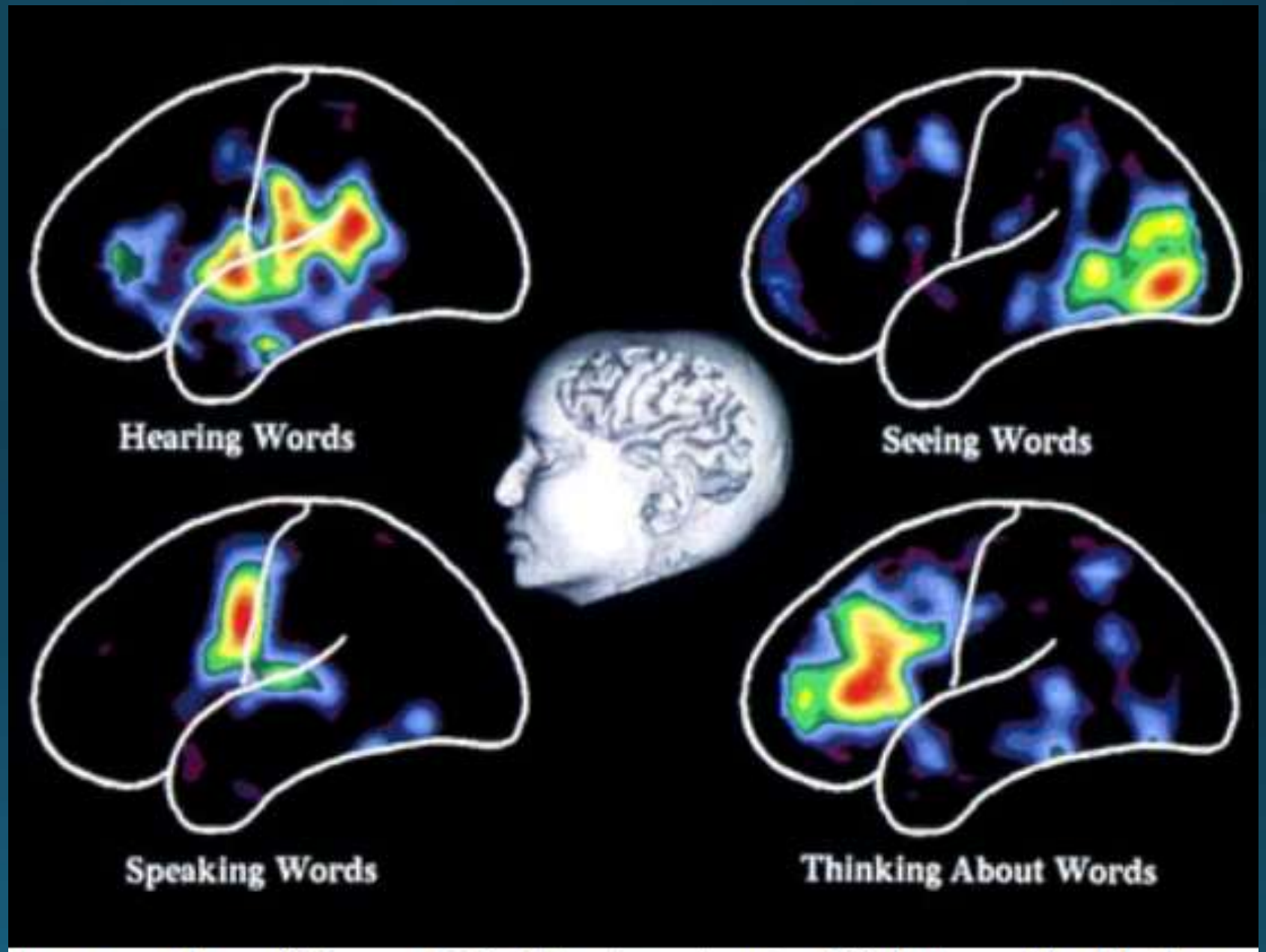



Image courtesy of Marcus E. Raichle, Department of Radiology, Washington University School of Medicine, St. Louis, Missouri

PET of Glucose Metabolism uptake in Normal v. Alzheimer's Disease

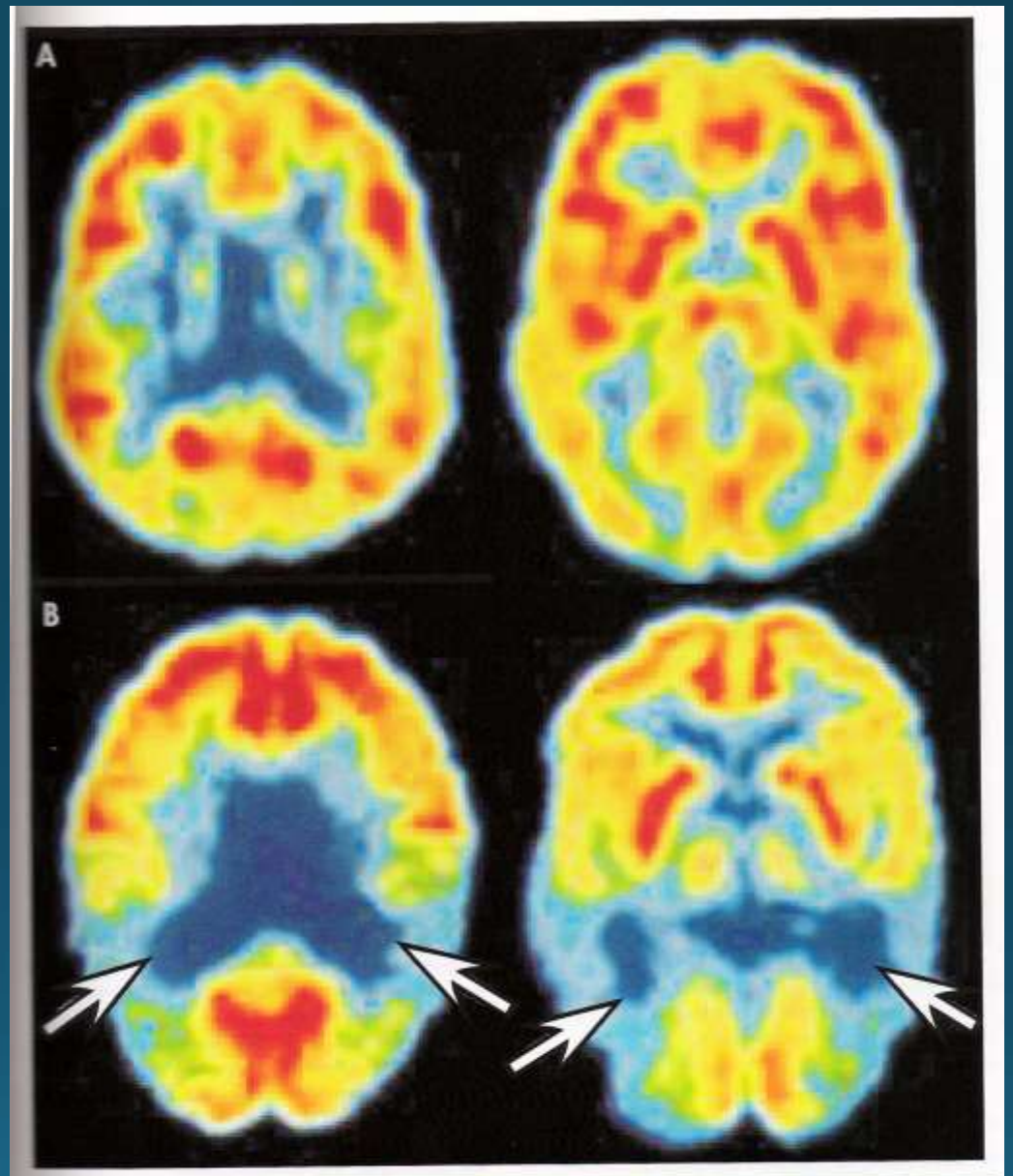
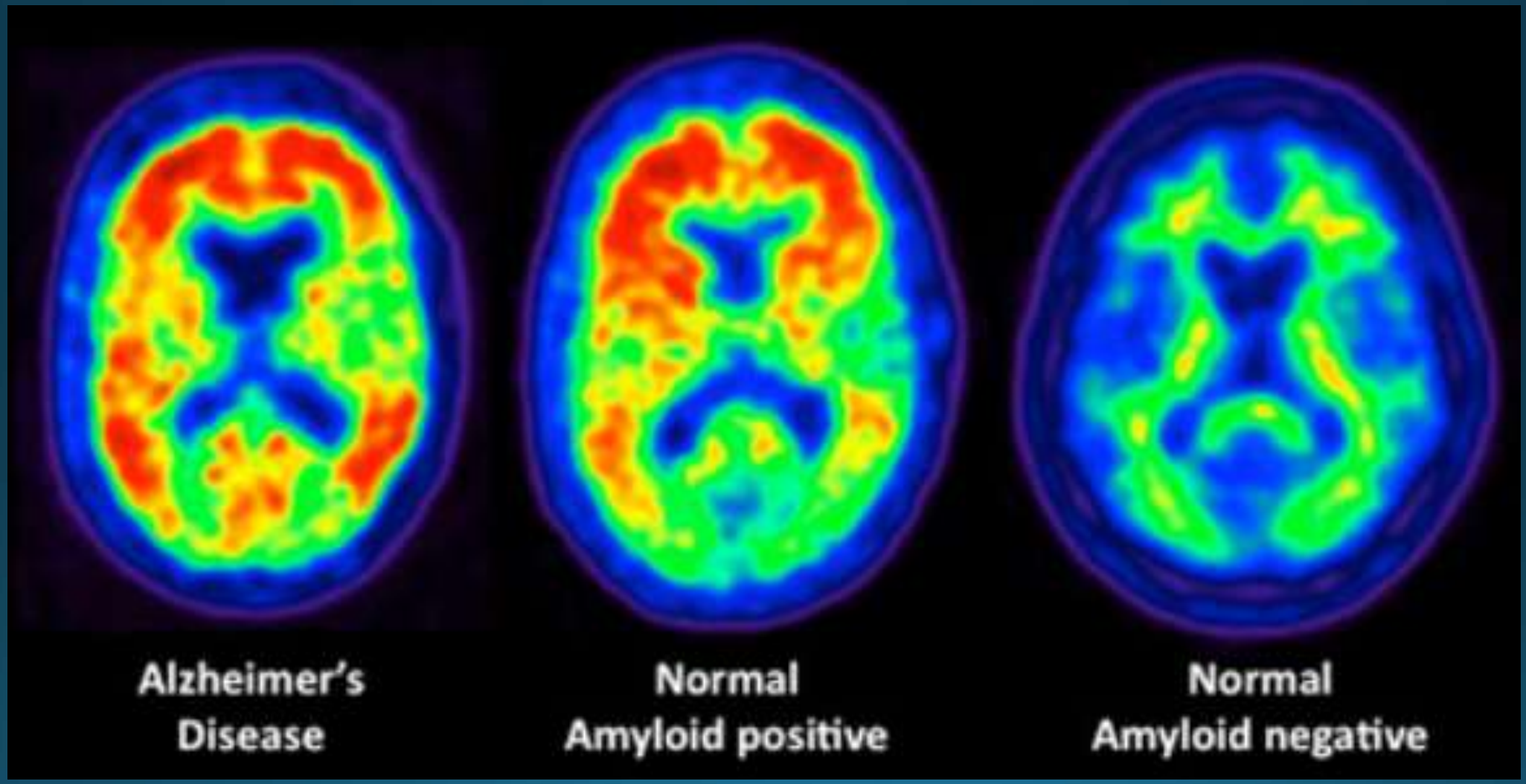



FIGURE 7–20. Positron emission tomographic imaging of cerebral metabolism is quite useful in diagnosis of Alzheimer's disease. (A) In individuals without Alzheimer's disease, uptake of [$^{18}$F]-fluorodeoxyglucose (FDG) is high (*orange-red*) throughout the cerebral cortex. (B) Uptake is reduced (*blue*) regionally, usually symmetrically (*arrows*), in patients with Alzheimer's disease. Source: Pictures courtesy of Siemens Medical.

# PET: beta amyloid binding



# PET-FDG (Fludeoxyglucose (18F))

- Discovery in 1980 that $^{18}$F-FDG accumulates in tumors underpins the evolution of PET as a major clinical tool in cancer diagnosis.

- $^{18}$F-FDG is now the standard radiotracer used for PET neuroimaging and cancer patient management.

# PET FDG: stroke hypometabolism in normal tissue

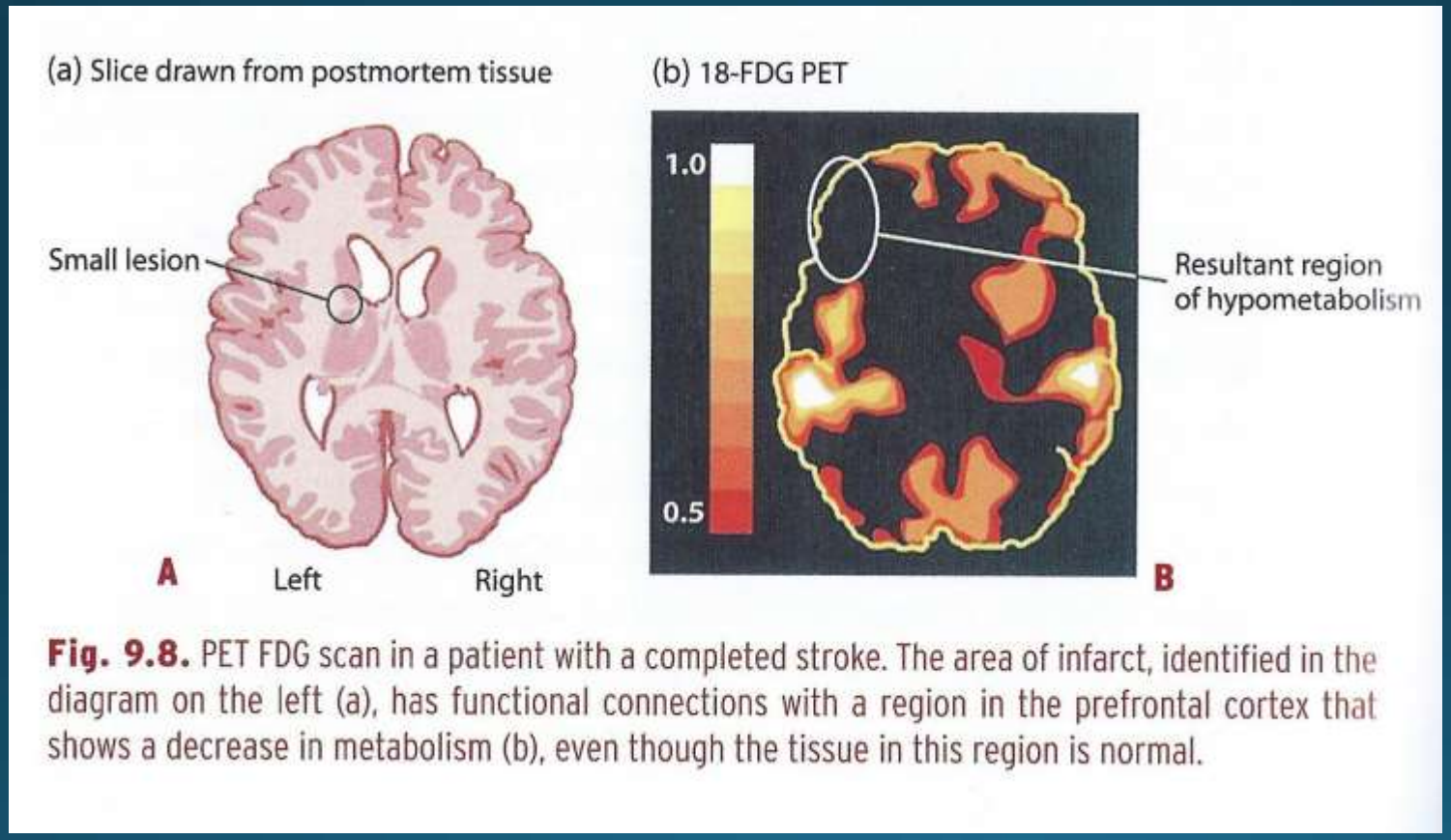
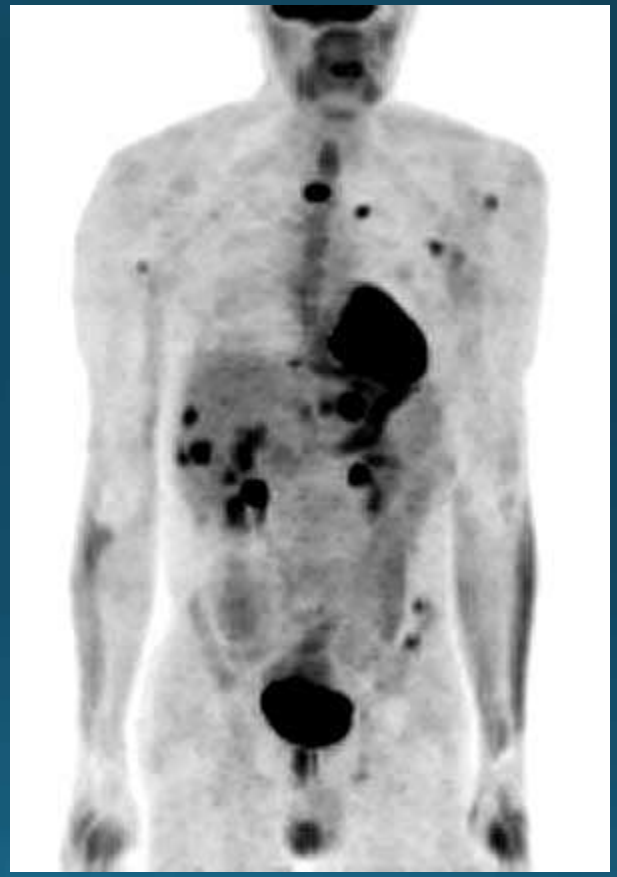


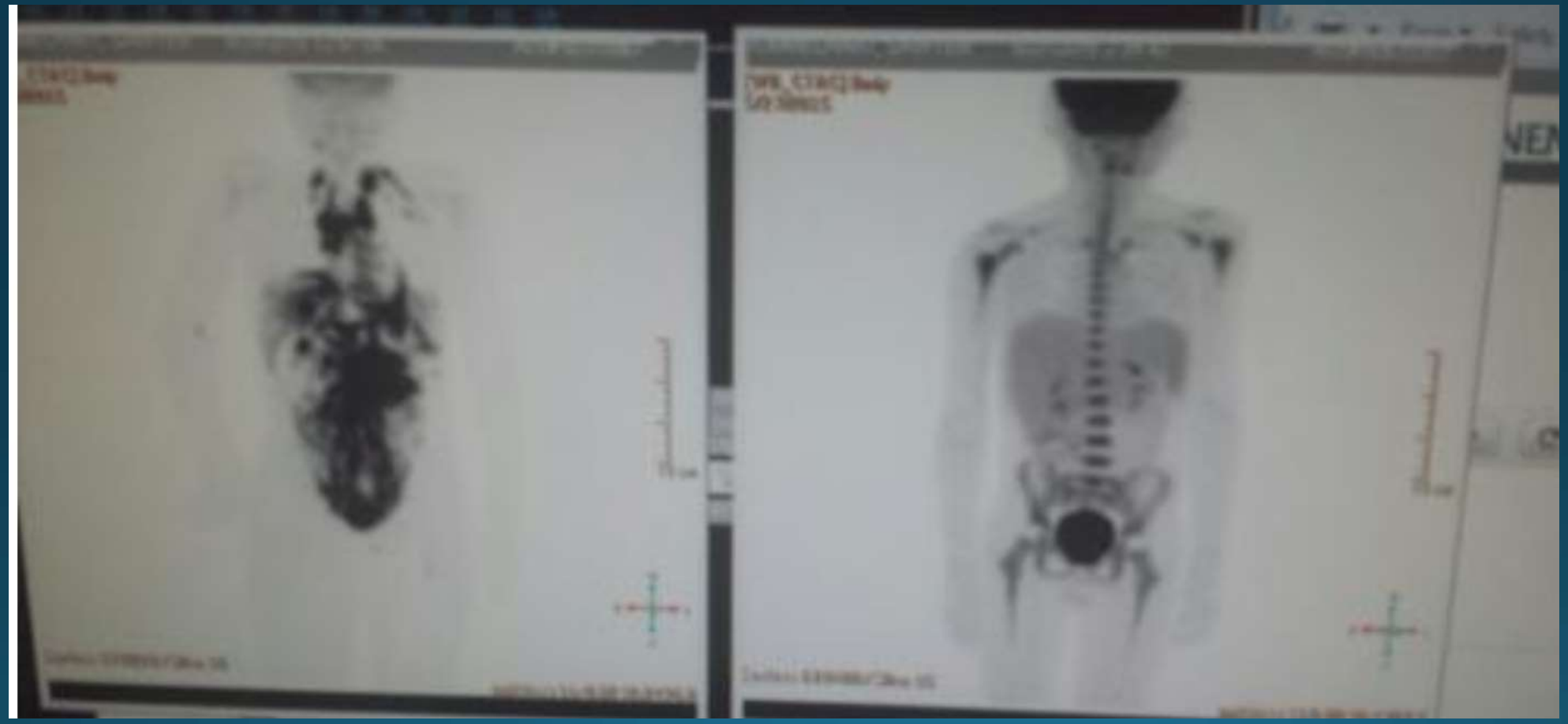

**Fig. 9.8.** PET FDG scan in a patient with a completed stroke. The area of infarct, identified in the diagram on the left (a), has functional connections with a region in the prefrontal cortex that shows a decrease in metabolism (b), even though the tissue in this region is normal.

# Fluorodeoxyglucose PET: Cancer

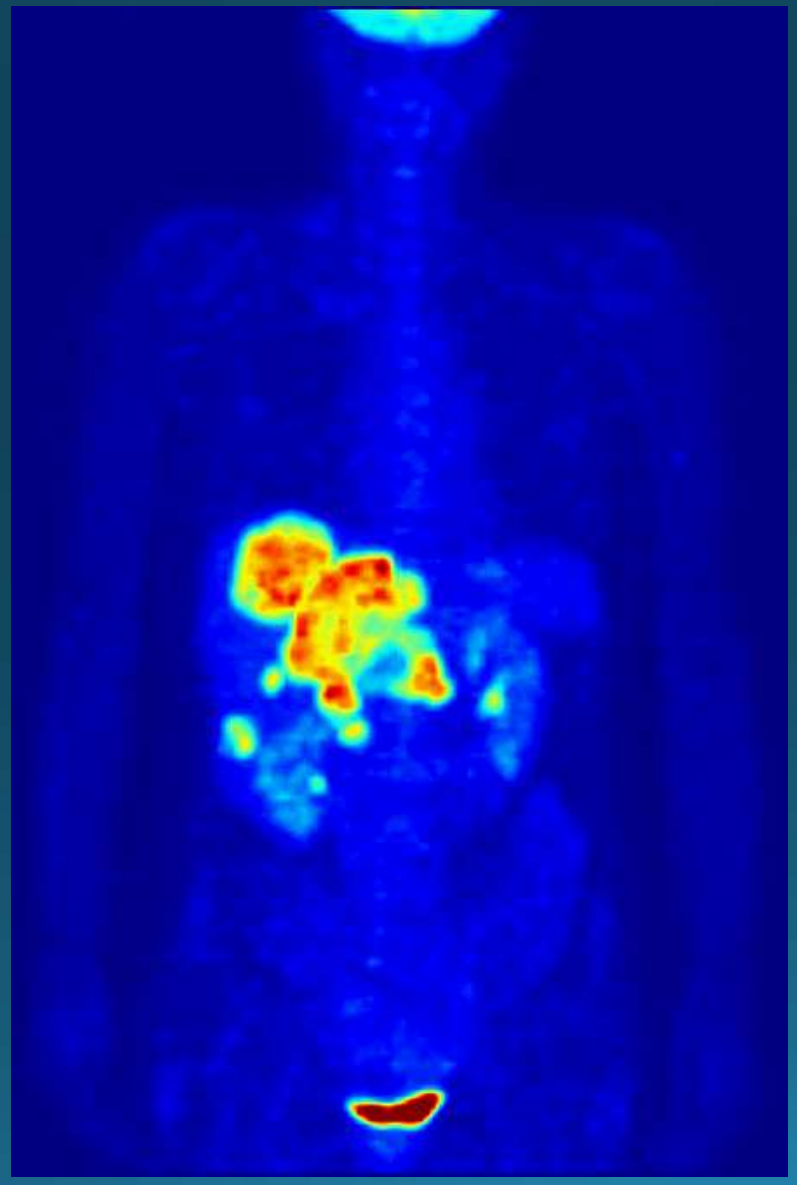
- The role of this procedure is to detect metabolically active malignant lesions



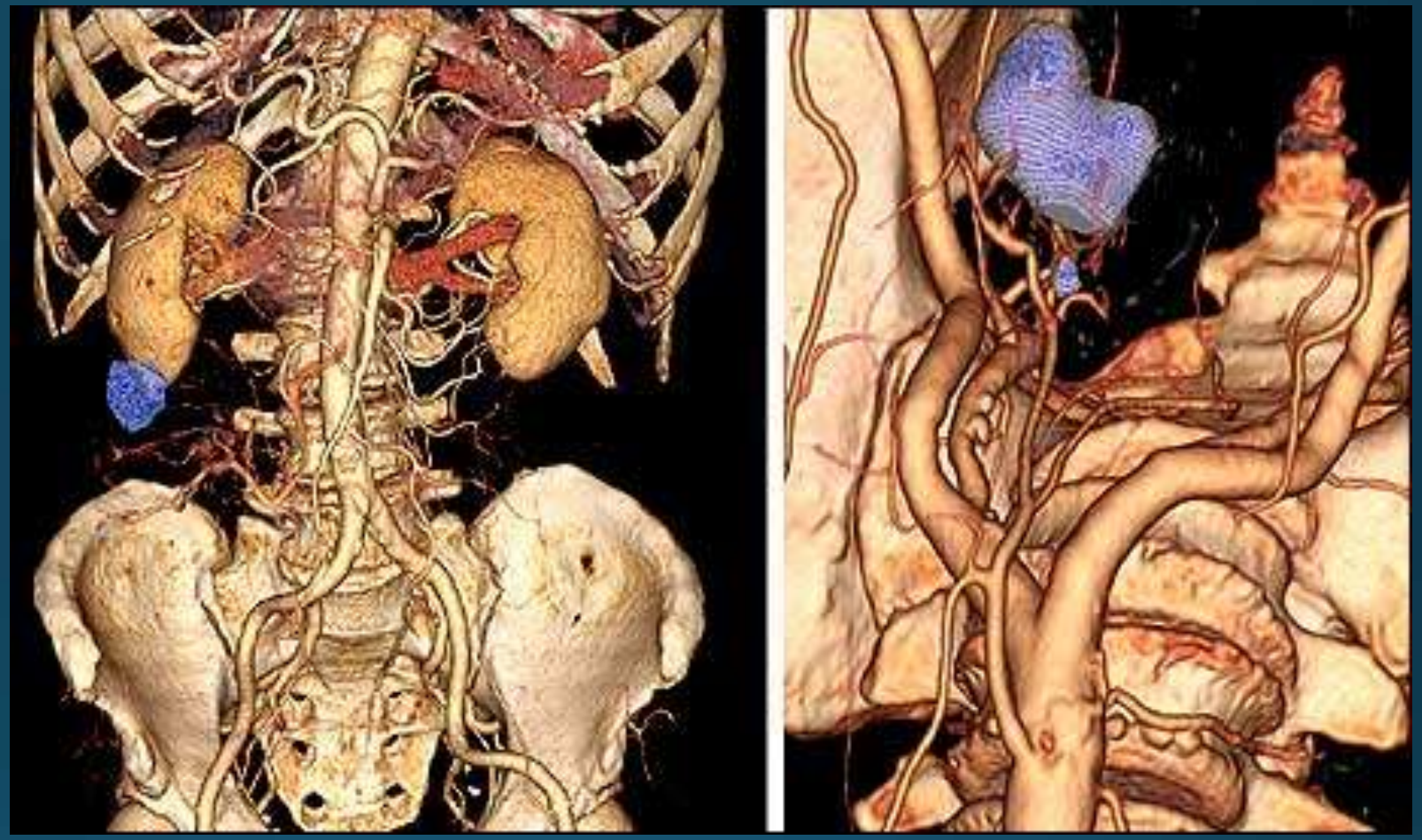
# 8 yo, dx Burkett's Lymphoma;
# 1st PET; 1 month of chemo – 2nd PET



# Whole-body PET scan using 18F-FDG to show liver metastases of a colorectal tumor



# PET and surgery



Both colon cancer scans shown here were captured with GE Healthcare's Discovery PET/CT at the National Cancer Center in East Japan. The fused volume rendering of a PET/CT angiography (above left) provides vascular and metabolic visualization for surgical planning. In the zoomed view (above right), the surgeon is able to better understand the blood supply and vascular involvement of the tumor

# SPECT (Single Photon/positron Emission Computed Tomography)

When radiolabeled compounds are injected in tracer amounts, their photon emissions can be detected much like x-rays in CT.

The images made represent the accumulation of the labeled compound. The compound may reflect, for example, blood flow, oxygen or glucose metabolism, or dopamine transporter concentration.

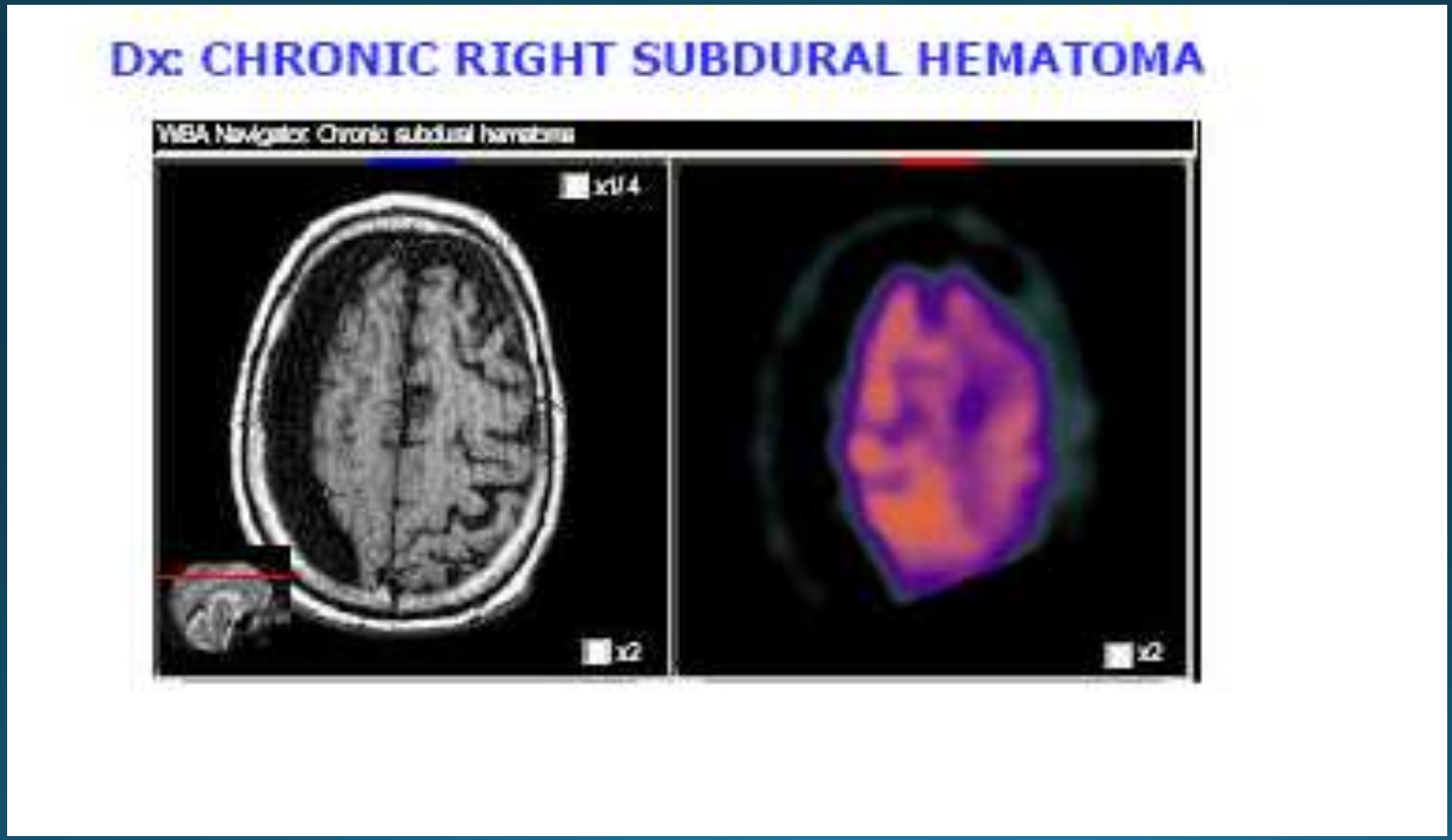
Often these images are shown with a color scale

# SPECT

- Uses radioactive tracer with brief half-life
- Injected
- Tracer not absorbed into tissue
- Hemodynamic: Detectors determine blood flow
- Both increases and decreases are relevant

# Siemens  510(k)-pending Symbia Intevo SPECT/CT: latest SPECT machine

# MRI vs. SPECT: Subdural Hematoma



# SPECT of rCBF in Alzheimer's Disease:

## A: early decrease in posterior; B – later frontal

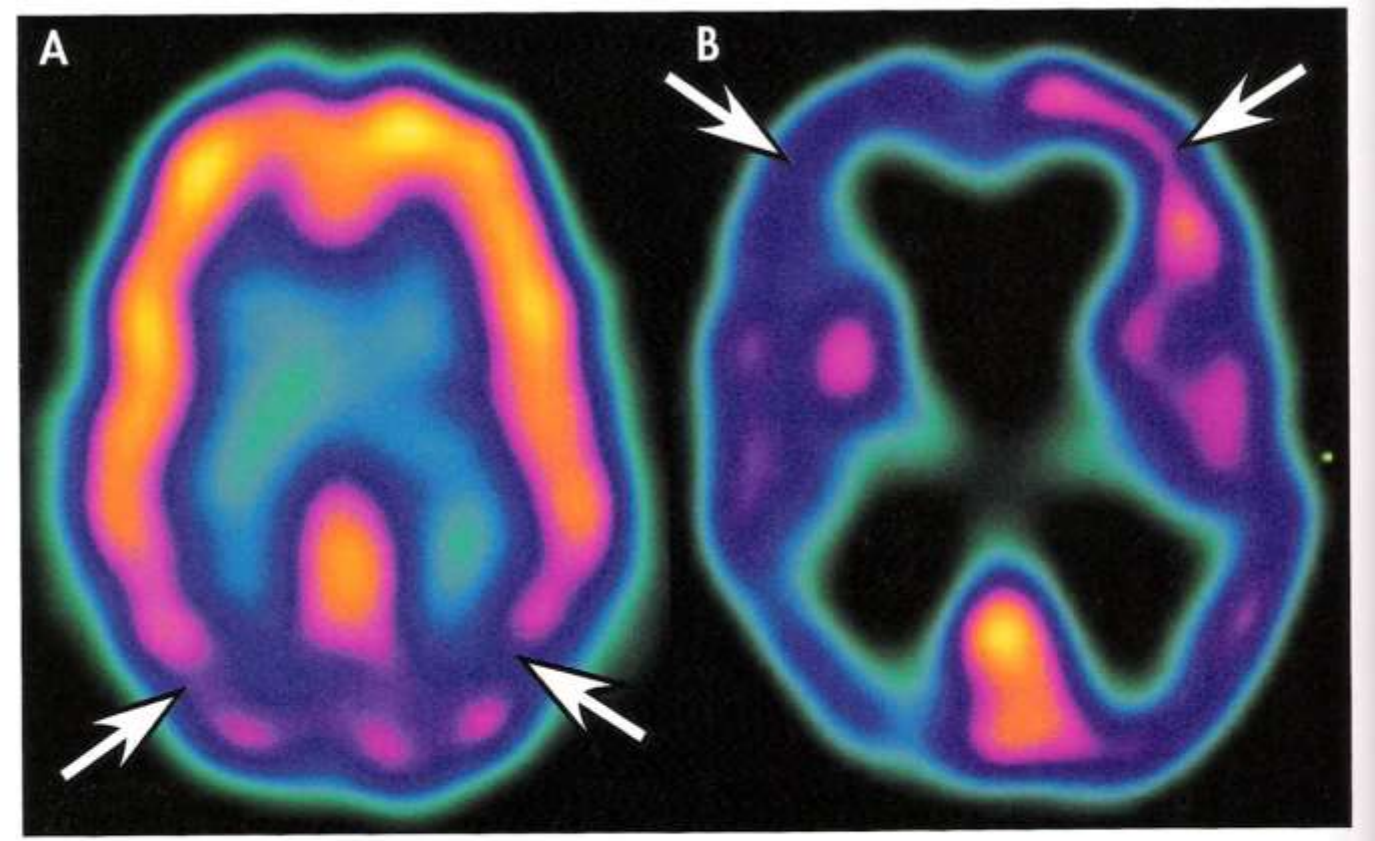



FIGURE 7–21. Regional cerebral blood flow (rCBF) in Alzheimer's disease. (*A*) As imaged here with single-photon emission computed tomography, rCBF is decreased in posterior temporoparietal cortex in early Alzheimer's disease (*arrows*). (*B*) As the disease progresses, frontal lobe involvement is common (*arrows*).

(Cummings and Mega, 2003)

# SPECT of Epileptic Focus:

A: ictal increased metabolism; B: normal hypometabolism

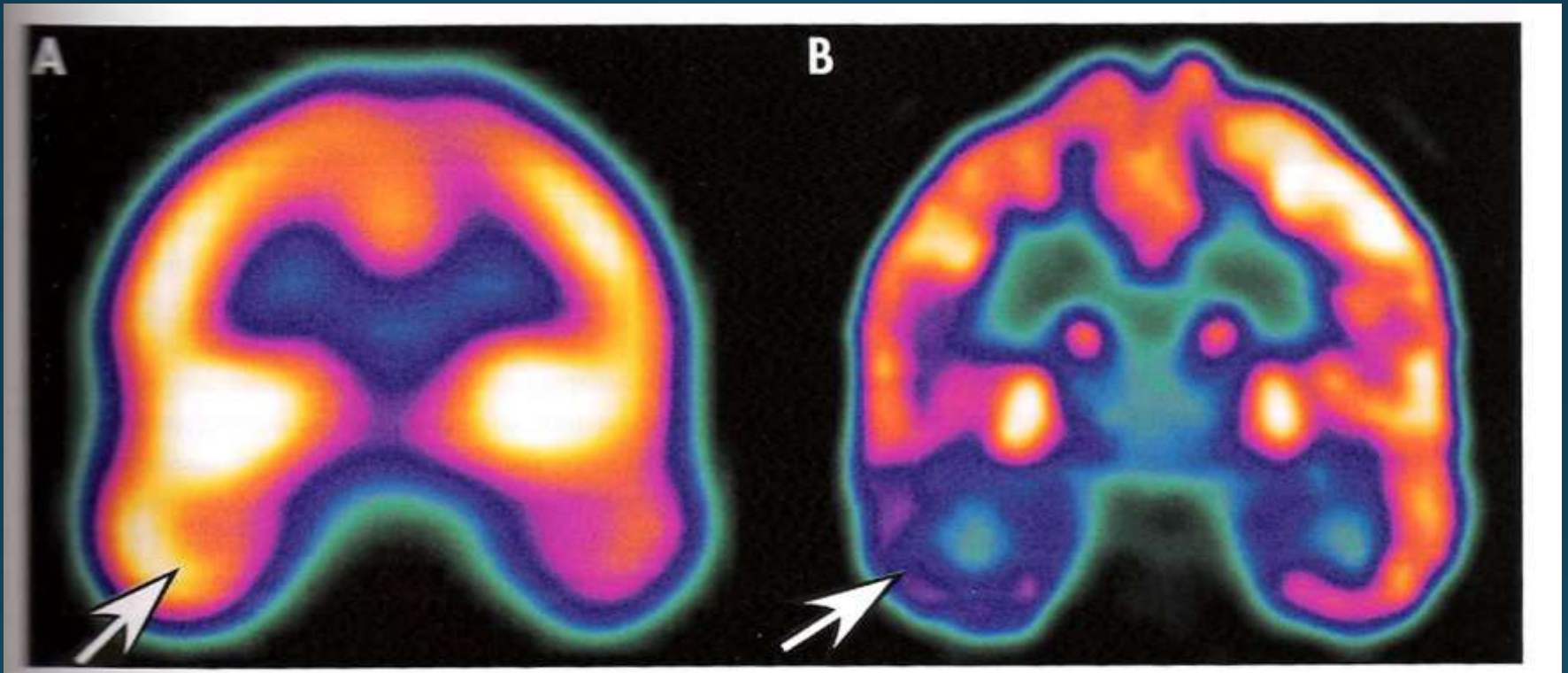
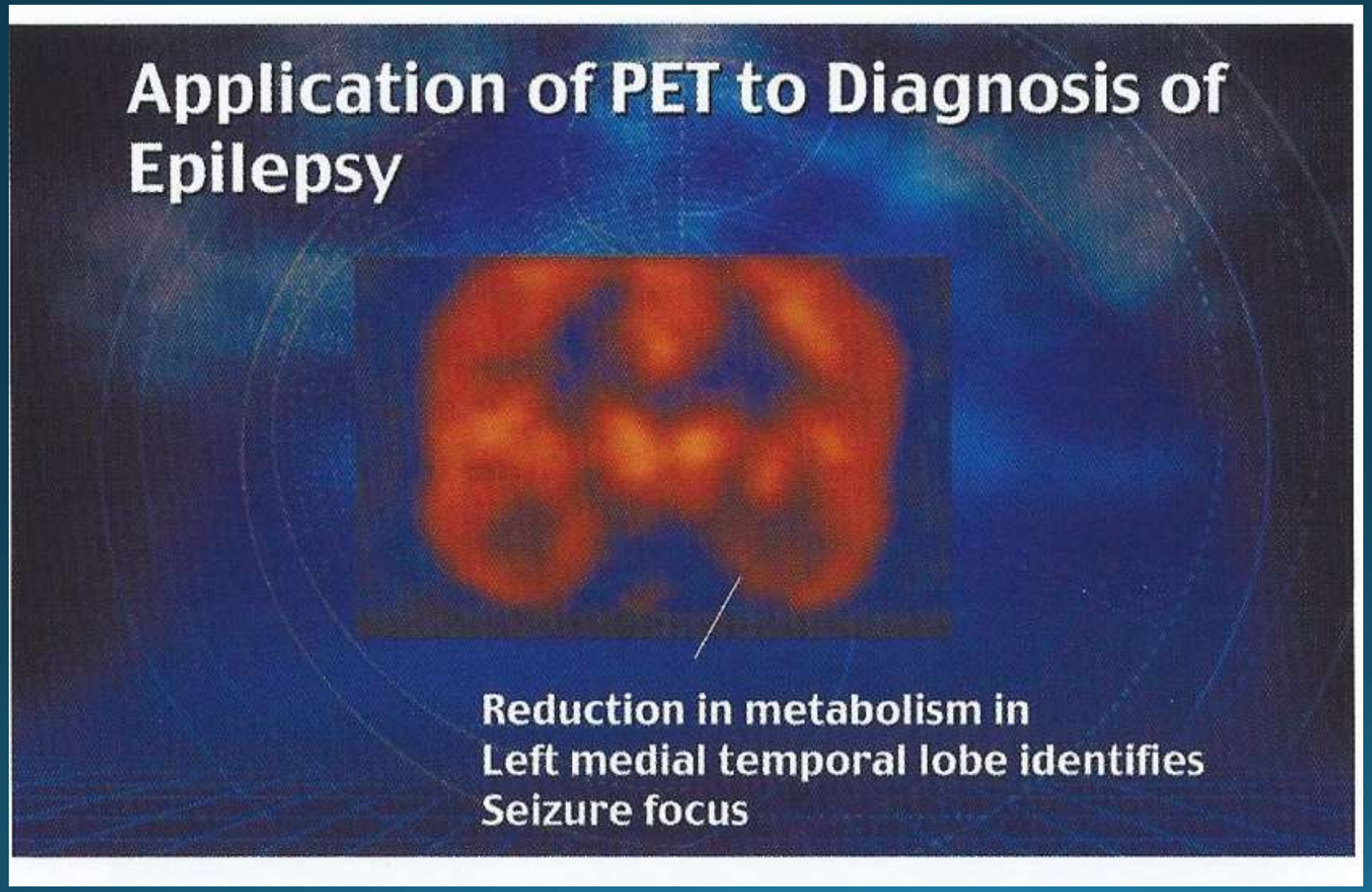


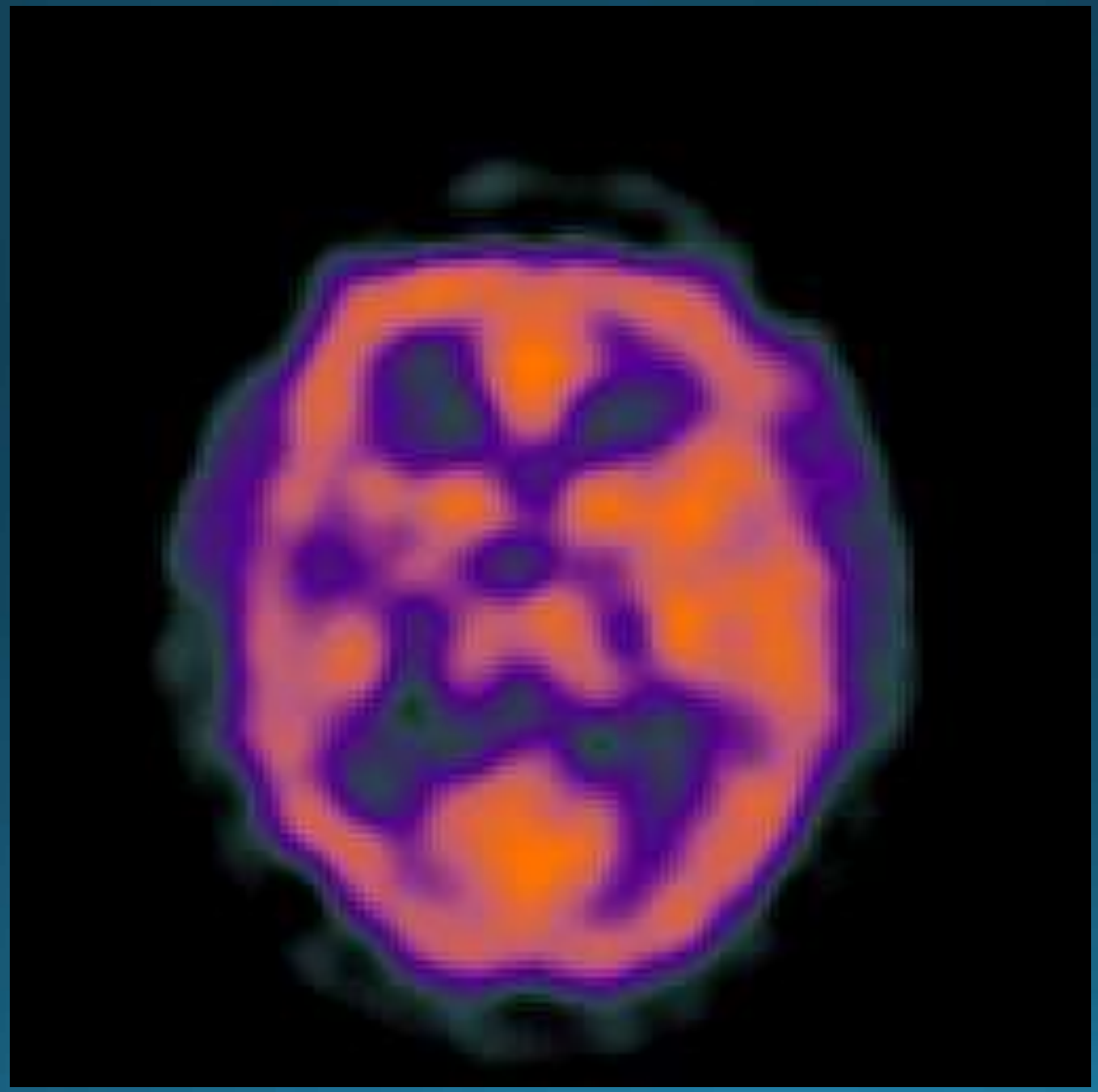

**FIGURE 7–27.** Nuclear medicine imaging is useful for visualizing the area of an epileptic focus. (*A*) Scans obtained during a seizure (ictal scan) will show increased perfusion or metabolism, as illustrated here with a coronal single-photon emission computed tomographic image of cerebral blood flow (*arrow*). (*B*) Scans obtained in the absence of seizure will show decreased perfusion or metabolism, as illustrated here with a coronal positron emission tomographic image of cerebral metabolism (*arrow*).

(Cummings and Mega, 2003)

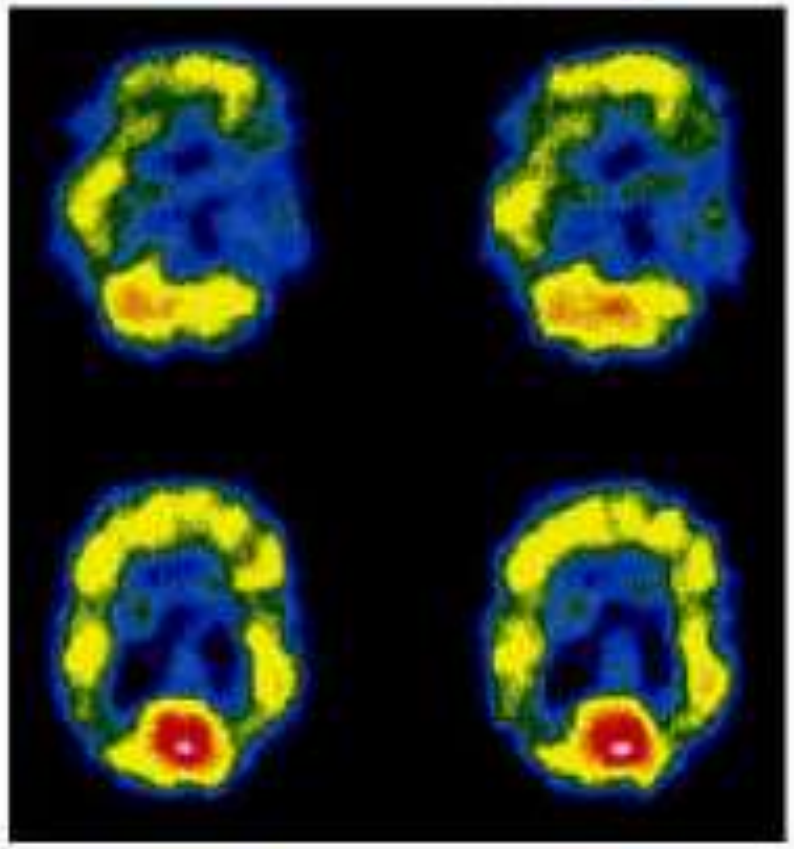
# SPECT: Seizure focus – hypometabolism site



# SPECT: blue = lack of perfusion

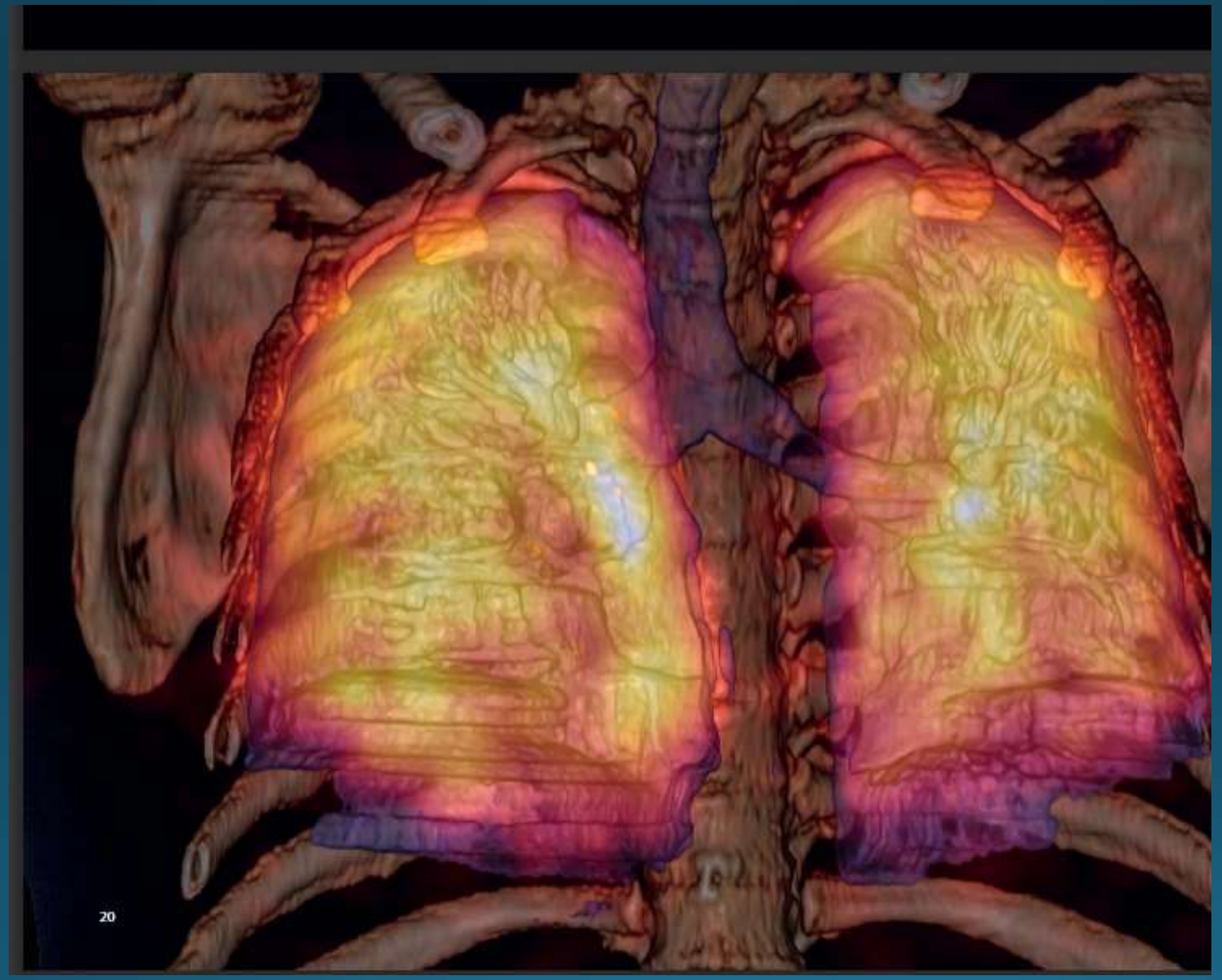


# SPECT: Seizure location

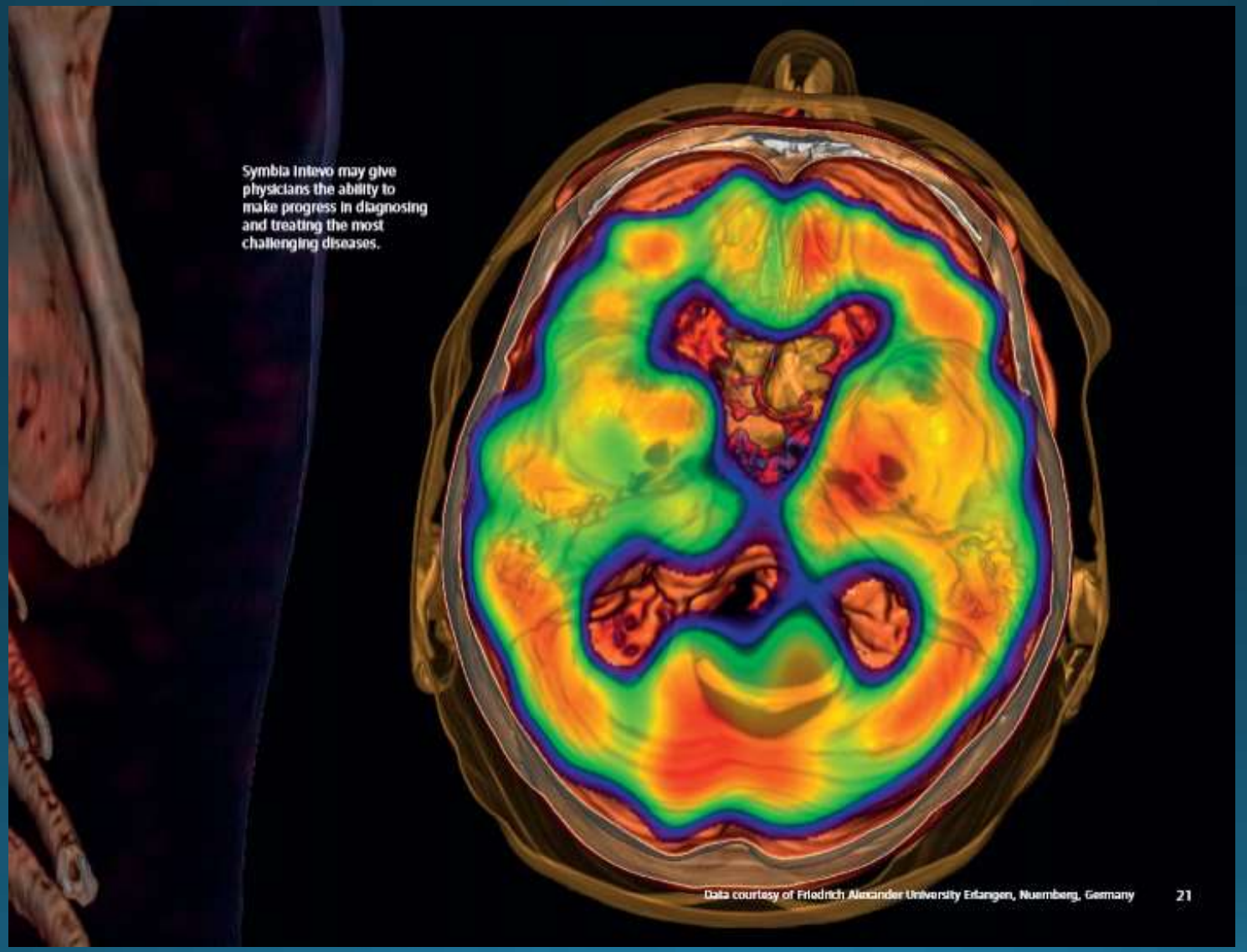



A SPECT scan of a patient with medically uncontrolled complex partial seizures. The temporal lobe on the left side of the brain shows less blood flow than the right, confirming for the surgeon the nonfunctioning area of the brain causing seizures.

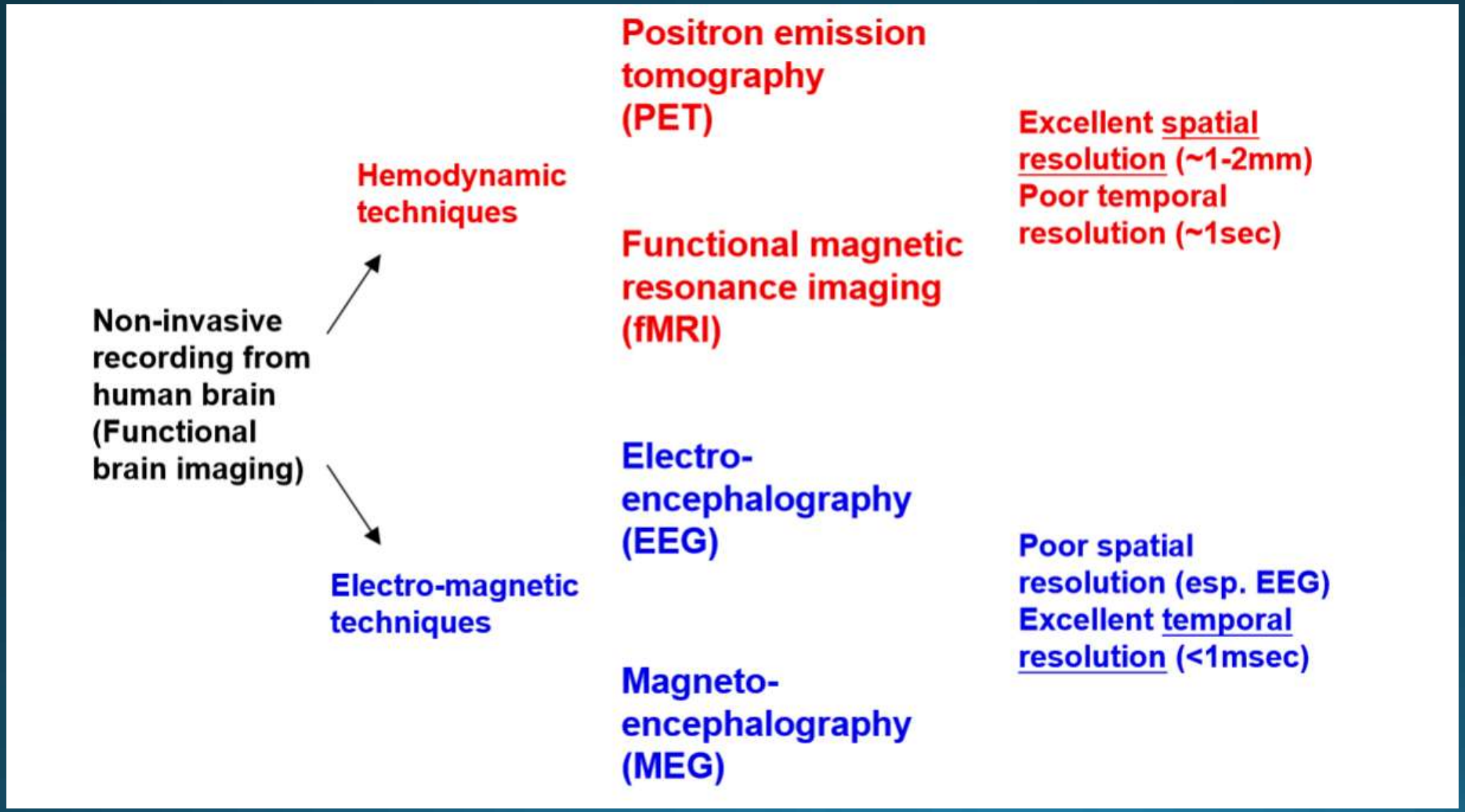
# Latest Siemens SPECT



# Latest Siemens SPECT

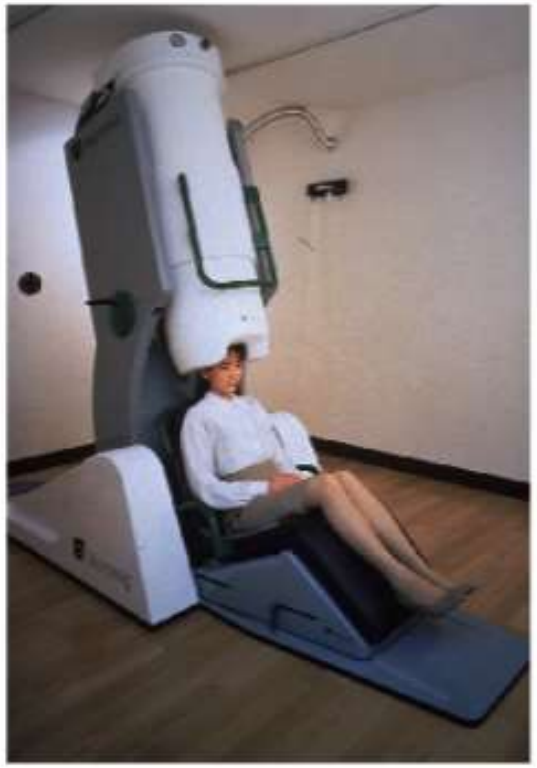


# Hemodynamic (best spatial) vs Electromagnetic (best temporal)



# MEG & EEG: electromagnetism

**MEG**



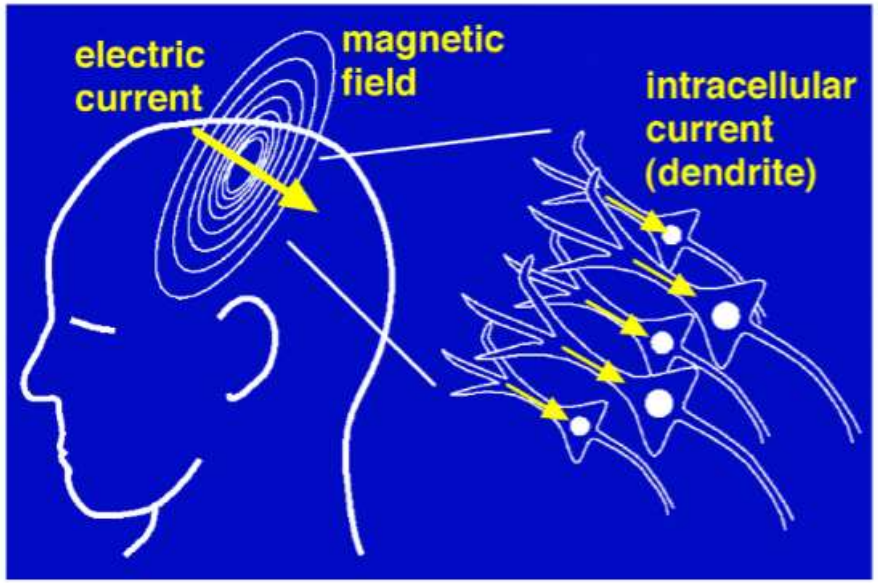
**EEG**

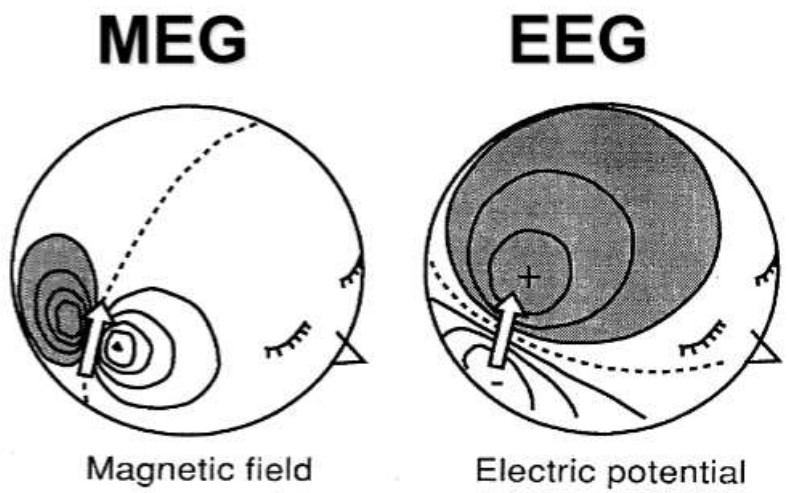
# Electromagnetic techniques (EEG, MEG)

- EEG and MEG: signal is from neural electrical activity
- Very good temporal resolution (milliseconds)
- Generally poor spatial resolution (roughly on the order of the size of a cerebral lobe)
- For simple sensory or motor events resolution can be better (closer to 1 cm), particularly for MEG

# Electromagnetism

- EEG (electroencephalography): electric potentials
- MEG (magnetoencephalography): magnetic fields



# Needs Magnetically shielded room (MSR)

**Magnetically shielded room (MSR)**

**Magnetically shielded room (MSR)**

# MEG

- Magnetoencephalography records magnetic fields produced by intraneuronal electric current
- Magnetic fields essentially unaffected by scalp and skull
- Better for deep-brain sources
- Detects tangential current sources, neurons in sulci running parallel to scalp

# MEG

- Good localization (relative to EEG) and temporal resolution
- Magnetic source imaging combines MEG and MRI, used to evaluate seizure foci
- Expensive shielding required to contend with ambient magnetic noise; Earth's field billionfold stronger
- Essentially research tool at present

# MEG: Magnetoencephalography
# “Hairdresser from Mars”

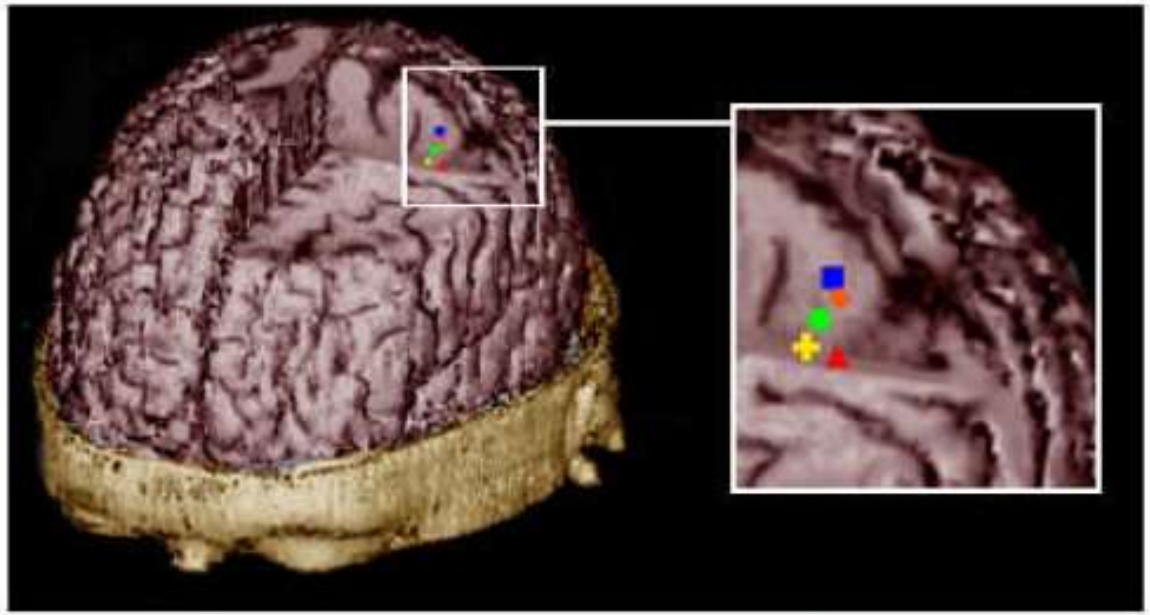
Temporospatial resolution of MEG surpasses that of all other neuroimaging techniques, in real time; direct measure of neuronal activity; magnetic equivalent of EEG.

# MEG: Magnetoencephalography

No Magnets; a technique for mapping brain activity by recording magnetic fields produced by electrical currents occurring naturally in the brain, using arrays of SQUIDs (superconducting quantum interference devices) which can measure extremely weak signals,

# MEG: Magnetoencephalography

## Direct measure of neuronal activity



MAGNETOENCEPHALOGRAPHY, or MEG, captures neural activity too brief to be detected by PET or MRI. Above, MEG has located the areas in the normal adult somatosensory cortex associated with the digits of the right hand (*colored symbols*). The symbols on the MRI image of the brain correspond to those on the fingers.

## Magnetoencephalography (MEG)

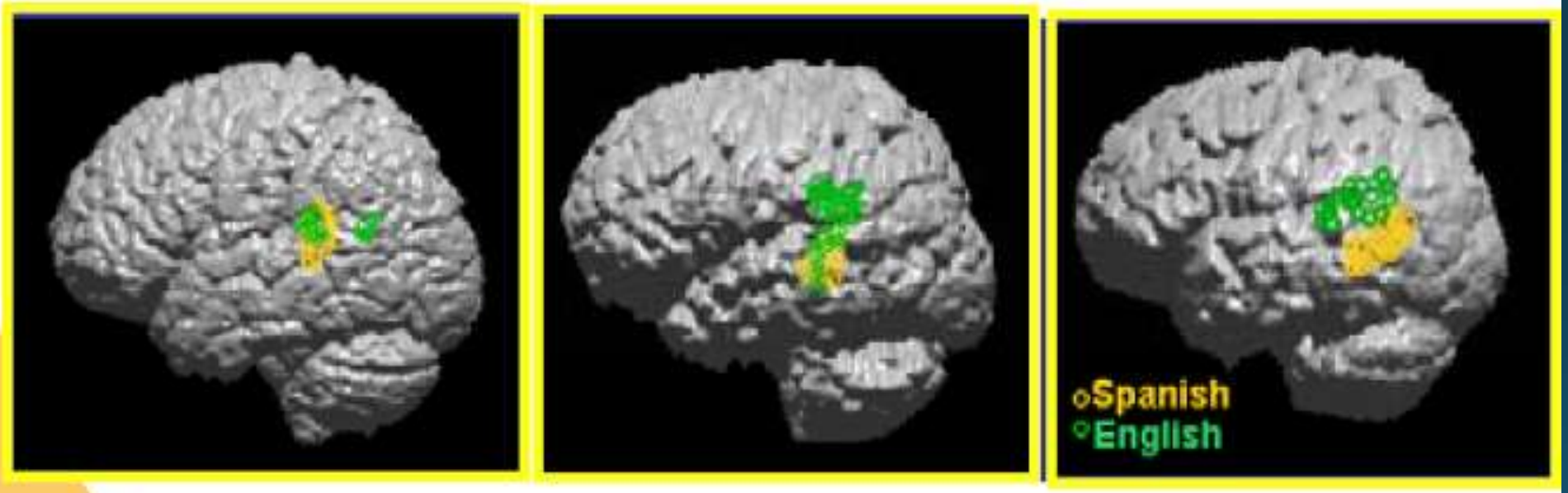
Pt can move



Silent; mm & ms accuracy

# MEG: Bilinguals

## Receptive Language-Specific Cortex in Bilinguals




Patient #1 Patient #2 Patient #3

# First EEG: Dr. Richard Catton

- Introduced: Dr. Richard Catton
  Liverpool physician first identified electrical brain signals in animals in 1875

- In 1887, using a flame, he demonstrated, at 9th International Medical Conference, the cerebral response to light in contralateral brain

- Work was expanded by Polish and Russian researchers

# First Human EEG: Dr. Hans Berger

- First published EEG of human:
  - 1929 by Austrian psychiatrist **Dr. Hans Berger**
  - Found brain waves appear at 2 months of age (myelinization)
  - Berger's work confirmed in British journal *Brain* 1934
  - Despite international renown, forced by Nazis to retire 1938
  - Suicide in 1941

# EEG

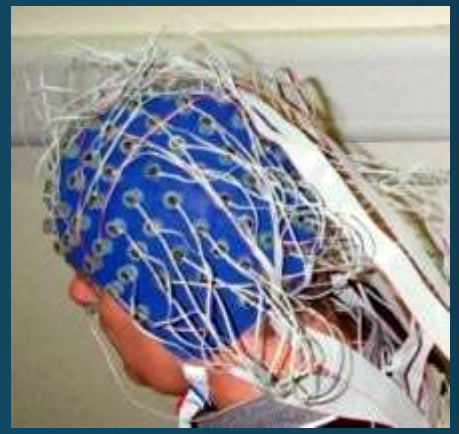
What it images: Distribution of brain electrical activity at rest, or when stimulated (“evoked potential”)

Utility: Most useful in identifying seizure  disorders, sleep disorders

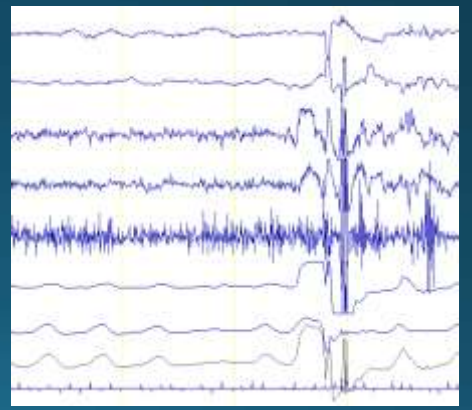
Advantages: Noninvasive, inexpensive, flexible, repeatable

# EEG (Electroencephalogram)

- How it works: Electrodes placed on the scalp record voltage differences between different parts of the brain



- Pros:
  - High temporal resolution,
  - Measures neuronal activity directly (via electrical output),
  - Relatively easy to use.

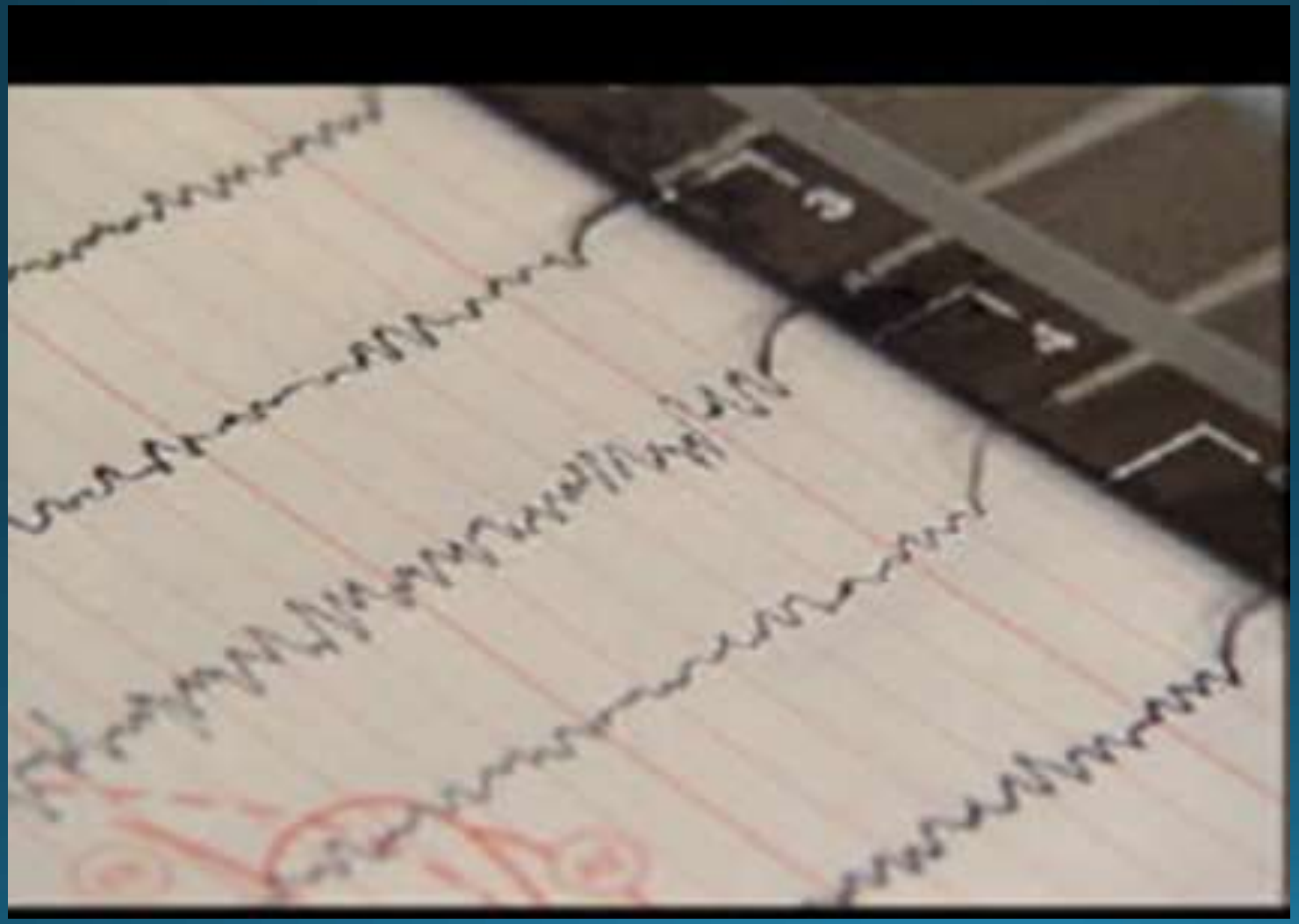


# Limitations and Disadvantages Of EEG

Limited to surface (cortical) activity
Limited spatial resolution/anatomical specificity

- Detects cortical dysfunction but rarely discloses its etiology
- Relatively low sensitivity and specificity
- Subject to both electrical and physiologic artifacts
- Influenced by state of alertness, hypoglycemia, drugs
- Small or deep lesions might not produce an EEG abnormality
- Limited time sampling (for routine EEG) and spatial sampling
- May falsely localize epileptogenic zone

# Classic Electroencephalograph



# EEG

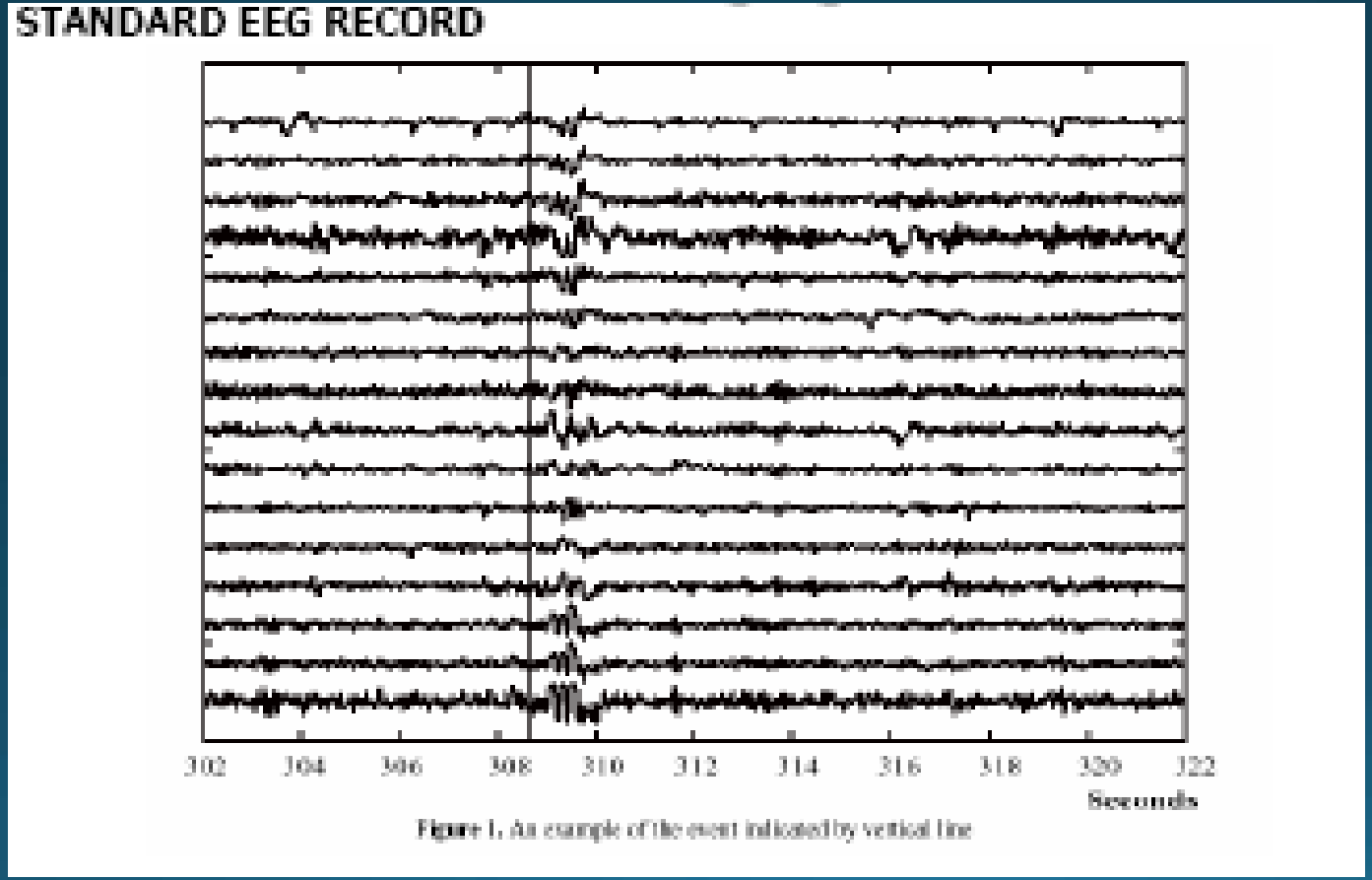
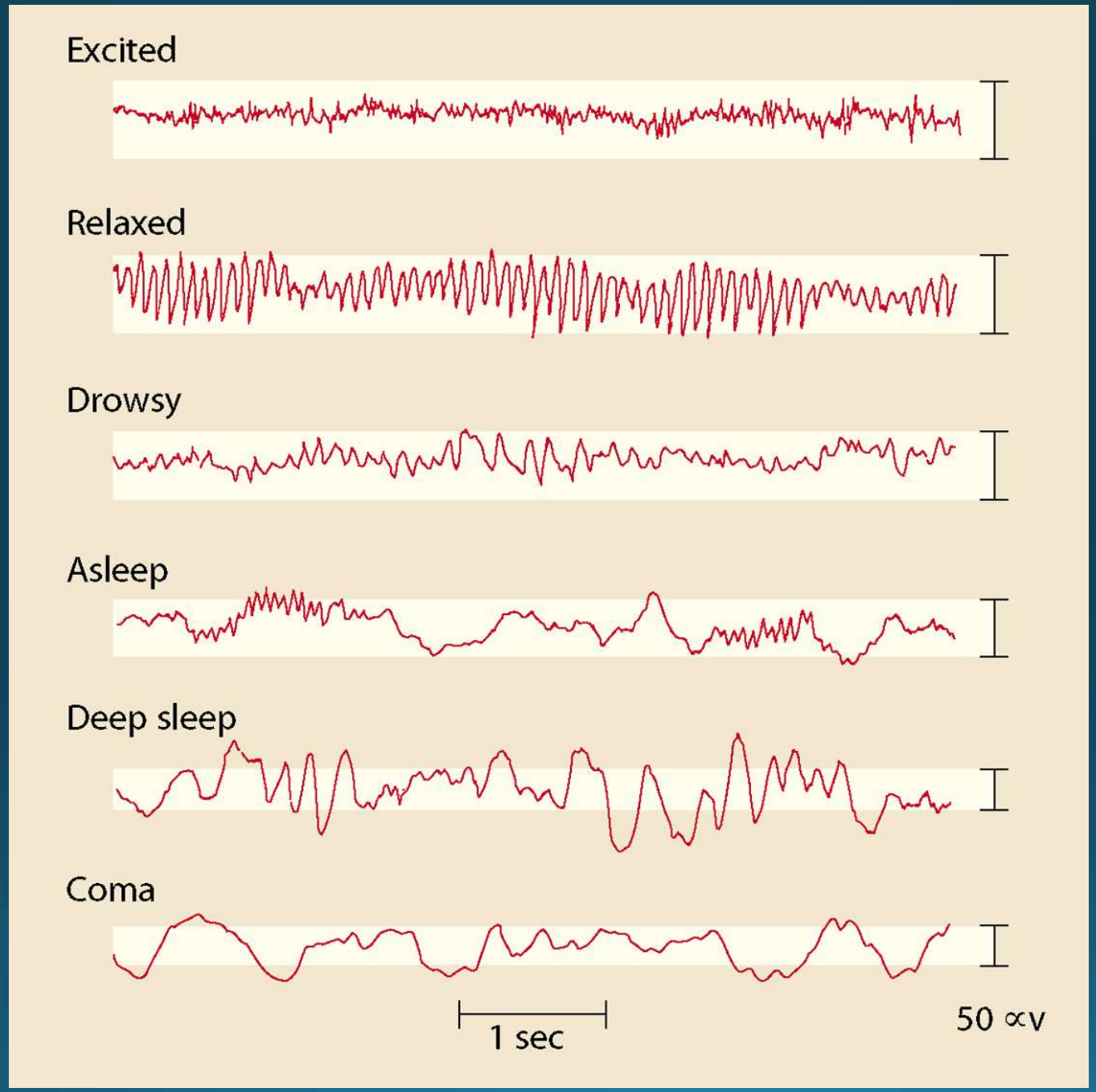


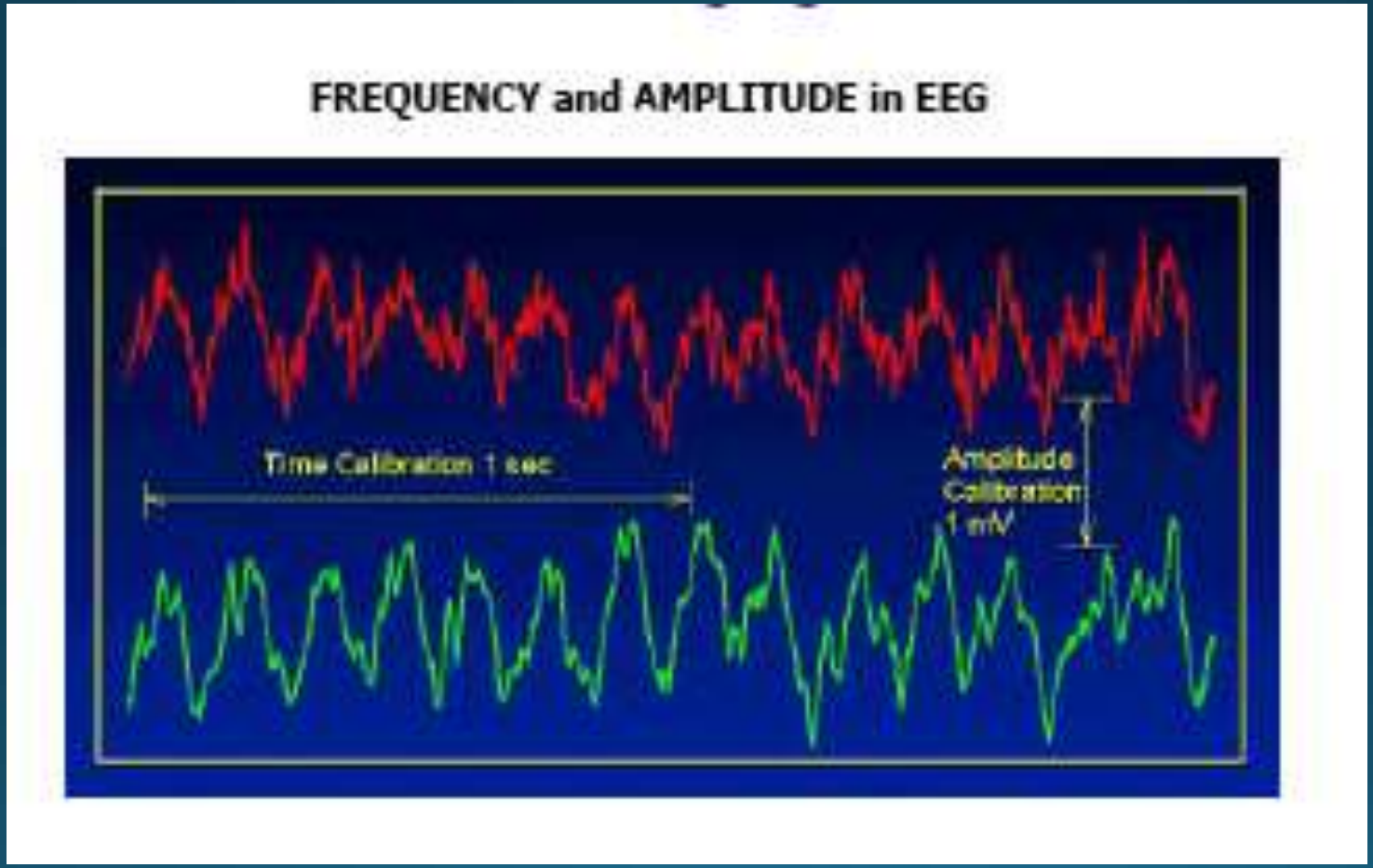

Figure 1. An example of the event indicated by vertical line



# Basic EEG Frequencies

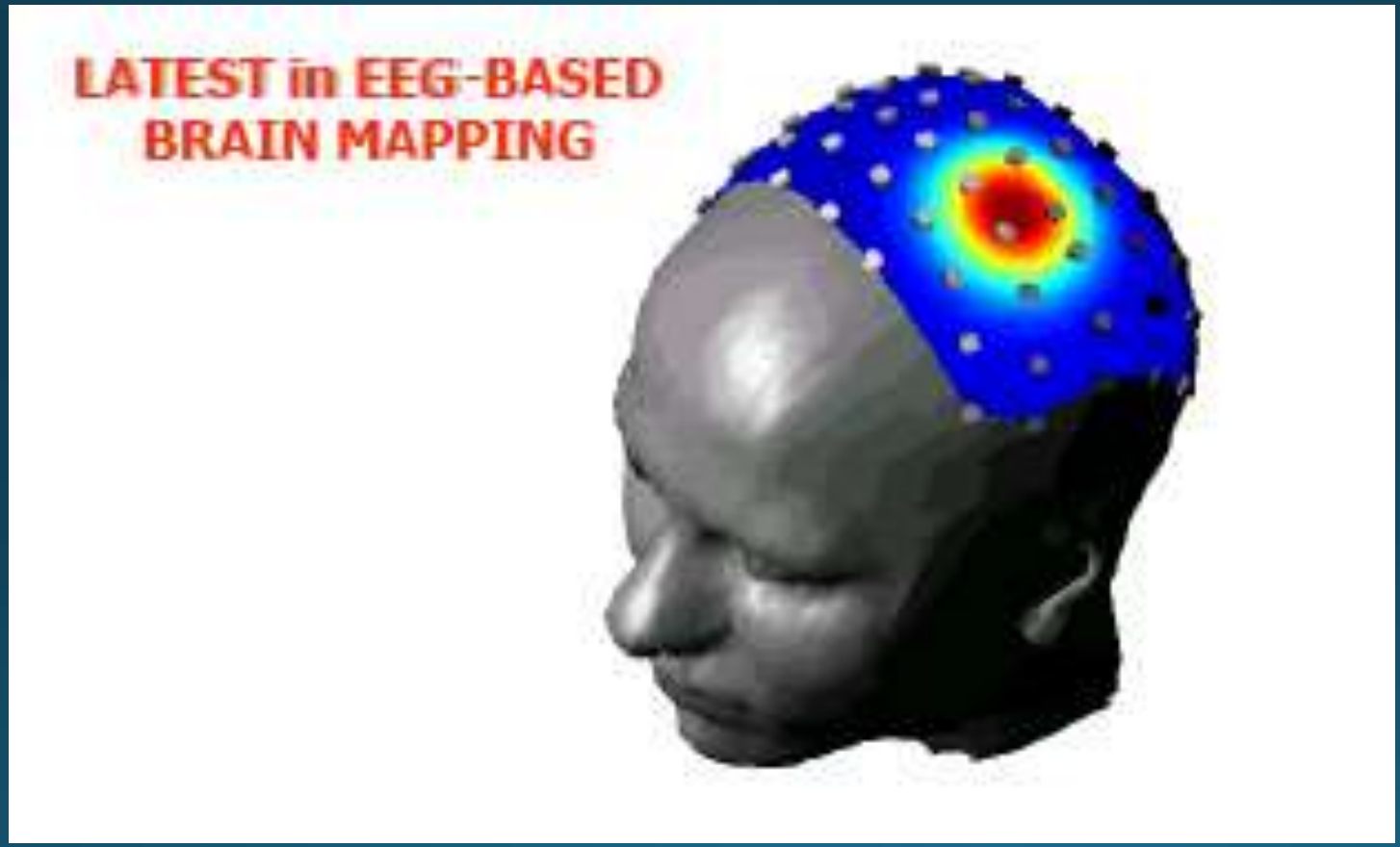
| *TYPE:* | *FREQUENCY:* |
|---|---|
| Delta | 1 – 4 Hz |
| Theta | 4 – 8 Hz |
| Alpha | 8 – 13 Hz |
| Beta | 14 + Hz |

# Frequency and Amplitude

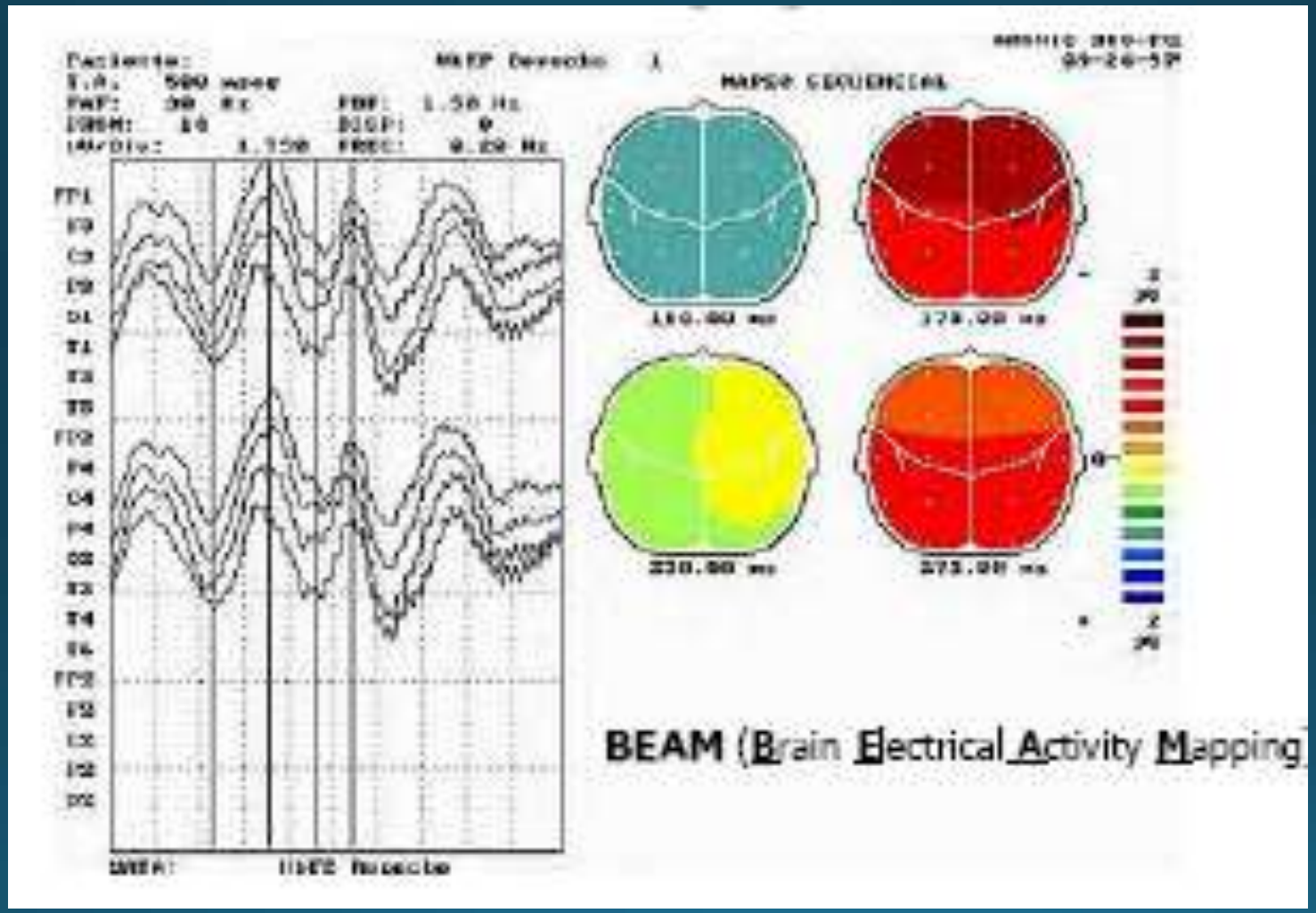


# 3-D Reconstruction of Electrode Placement

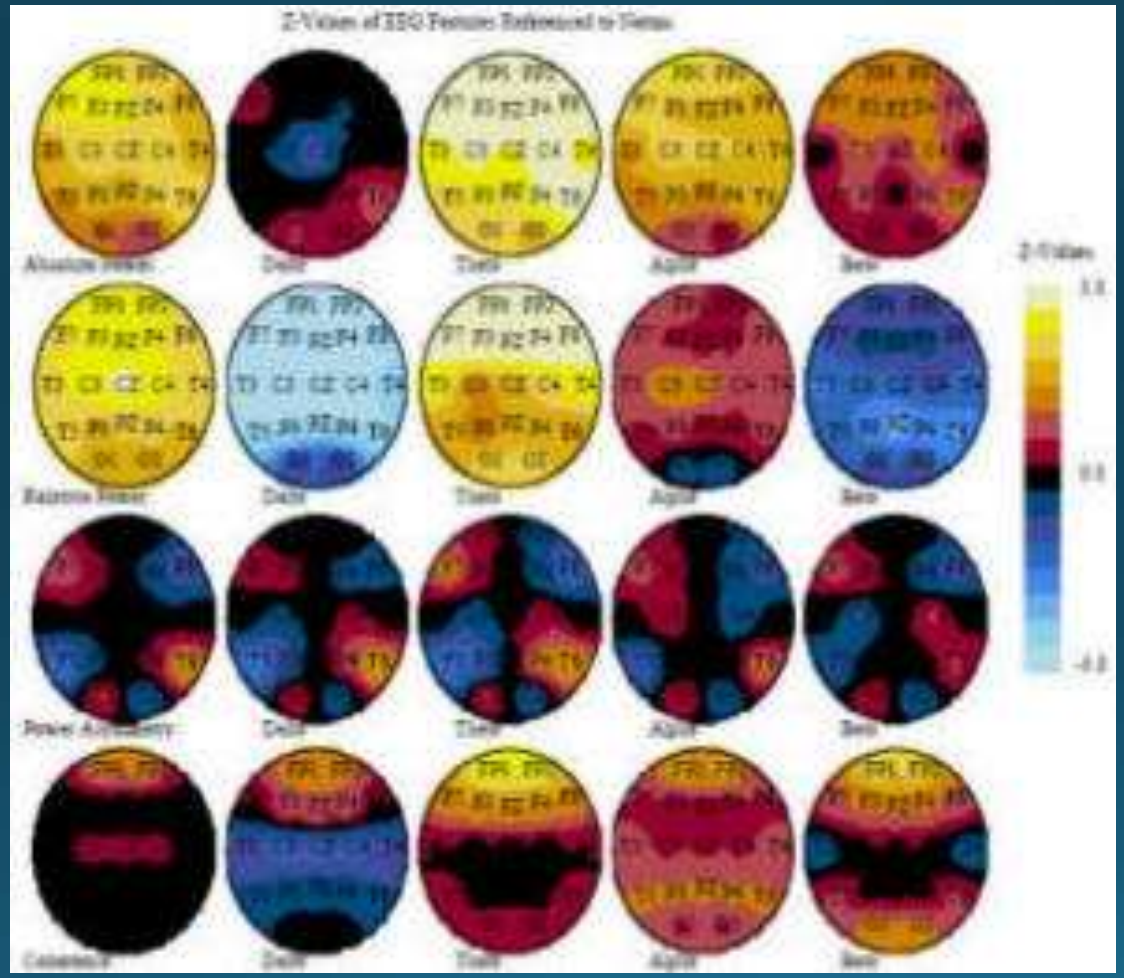
# EEG Brain Mapping



# BEAM: Brain Electrical Activity Mapping



# QEEG



Neurofeedback use: controversial

# QEEG/Brain Mapping

- Provides information that cannot be extracted by visual inspection
- Potentially enhances intra- and interrater reliability
- Absolute power- measure of energy intensity in frequency bands
- Coherence-measure of phase consistency of two sources

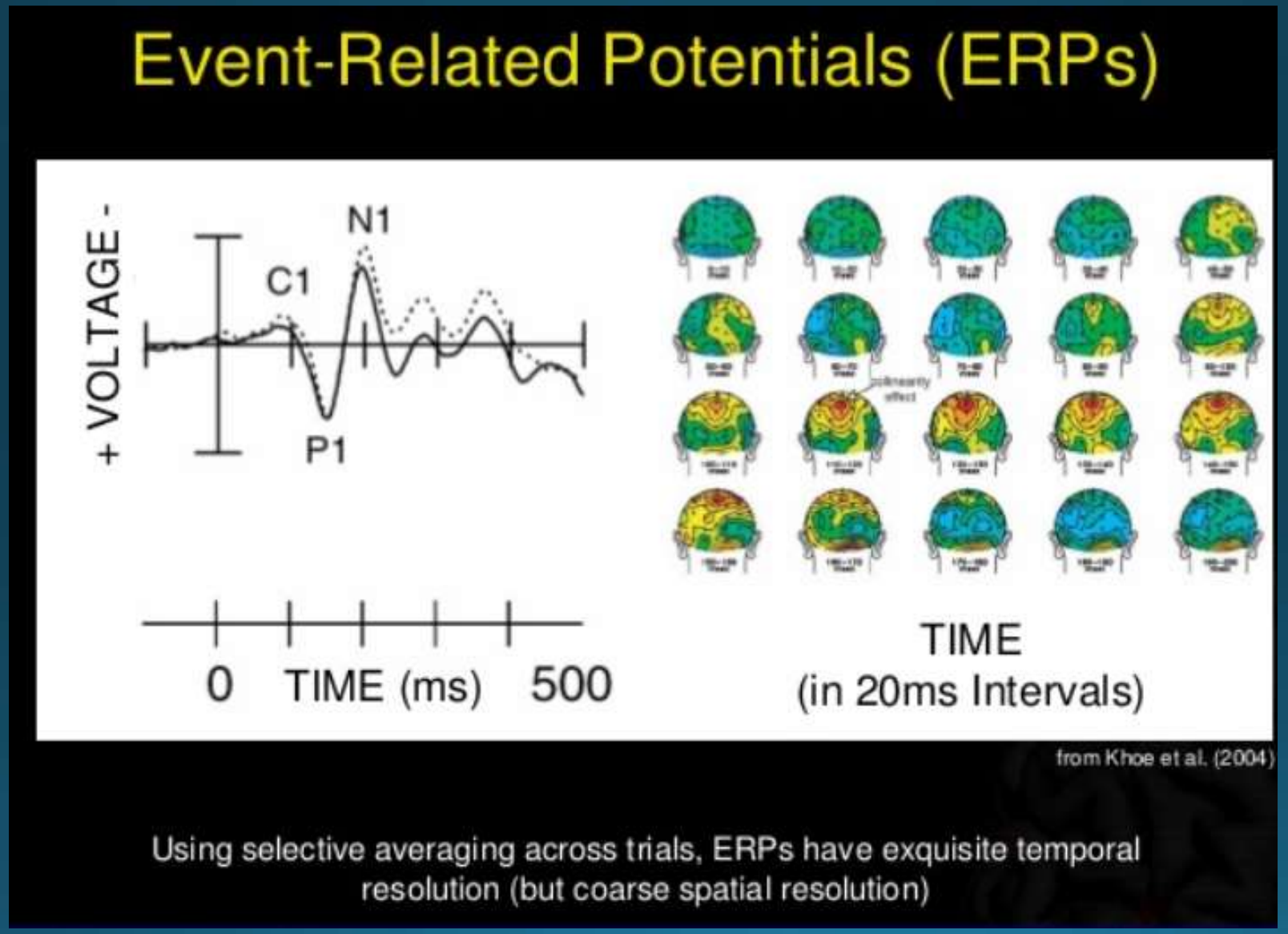
# QEEG

- Pharmaco-electroencephalography: QEEG use to detect drug-induced changes
- Potential uses in drug development and early prediction of clinical response

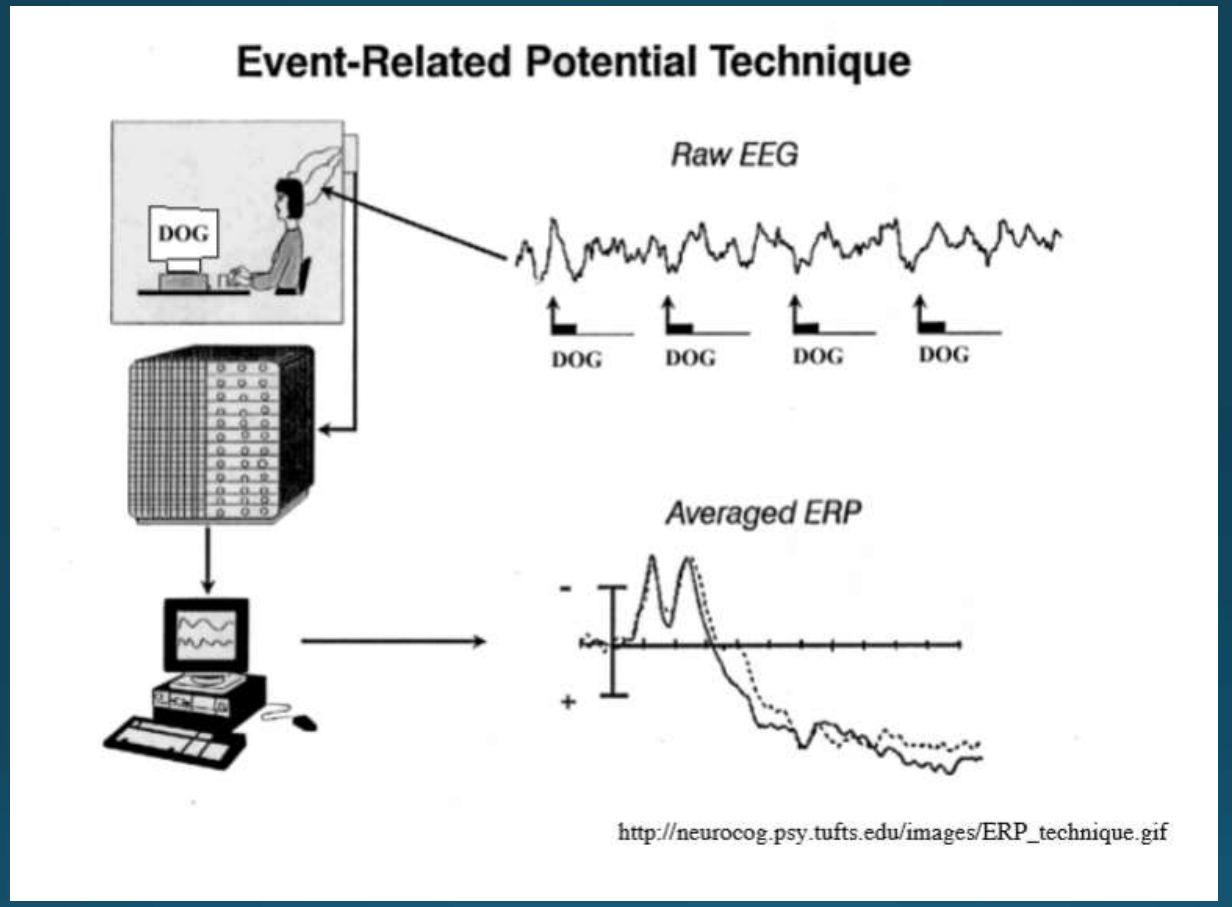
- Somewhat controversial; more research is needed

- ANPA's research committee (2006):
  "*As a clinical laboratory test, qEEG's cautious use is recommended in attentional and learning disabilities of childhood, and in mood and dementing disorders of adulthood.*"

# ERPs

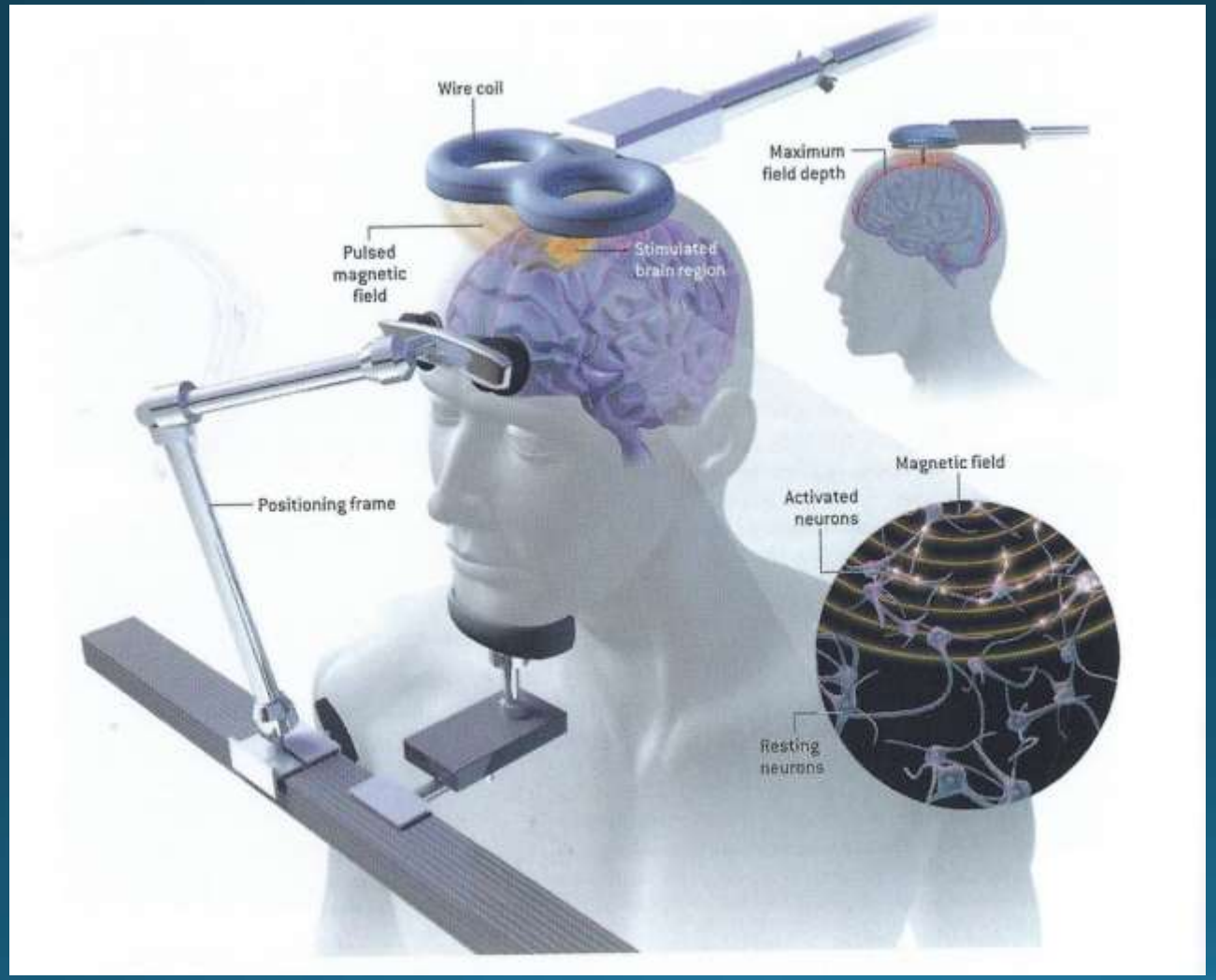

Event-Related Potentials (ERPs)
+ VOLTAGE -
N1
C1
P1
0
TIME (ms)
500
TIME
(in 20ms Intervals)
from Khoe et al. (2004)
Using selective averaging across trials, ERPs have exquisite temporal resolution (but coarse spatial resolution)

# ERP

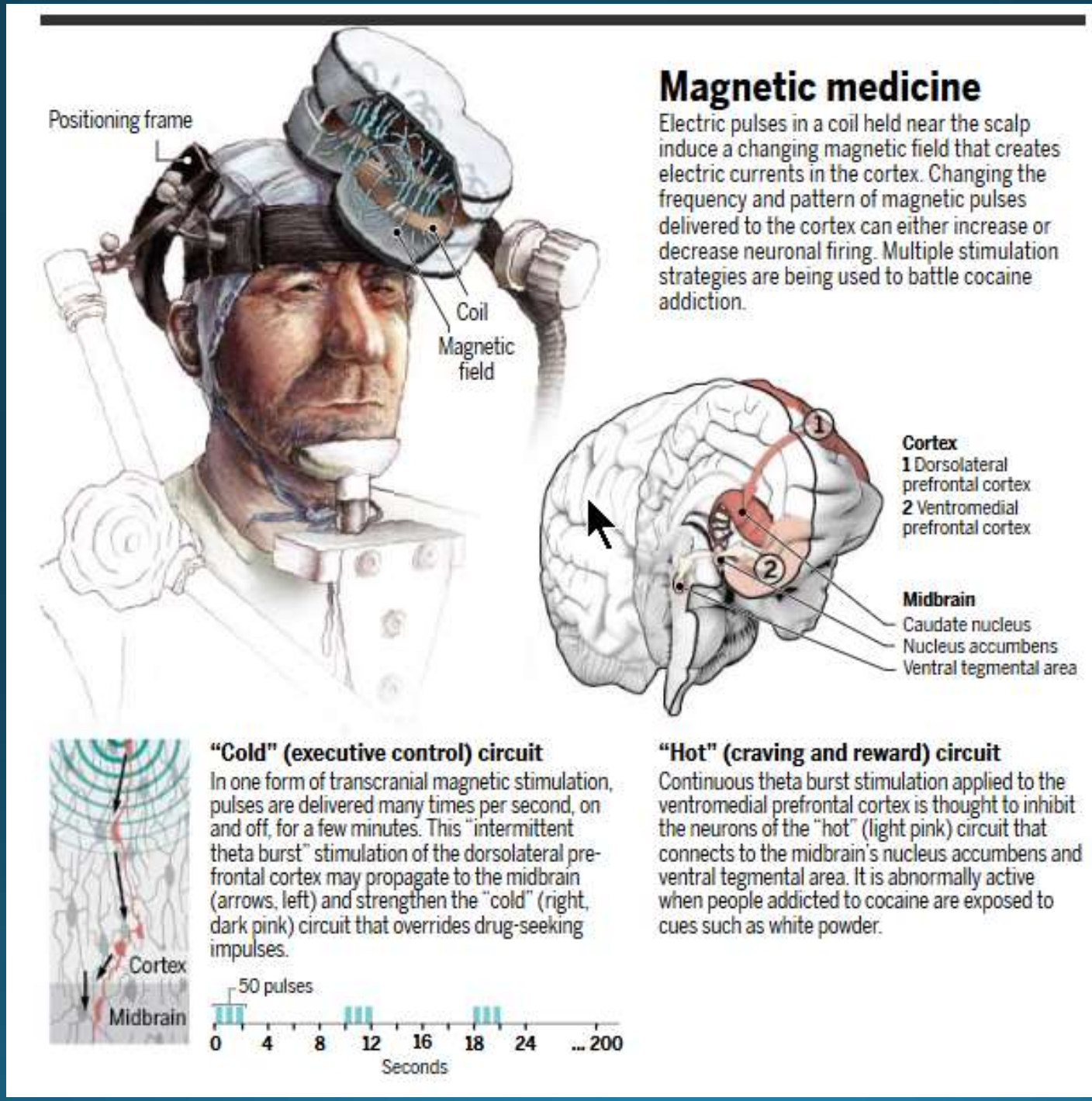



An **evoked potential** or **evoked response** is an electrical potential recorded following presentation of a stimulus.

# Transcranial Magnetic Stimulation (TMs)



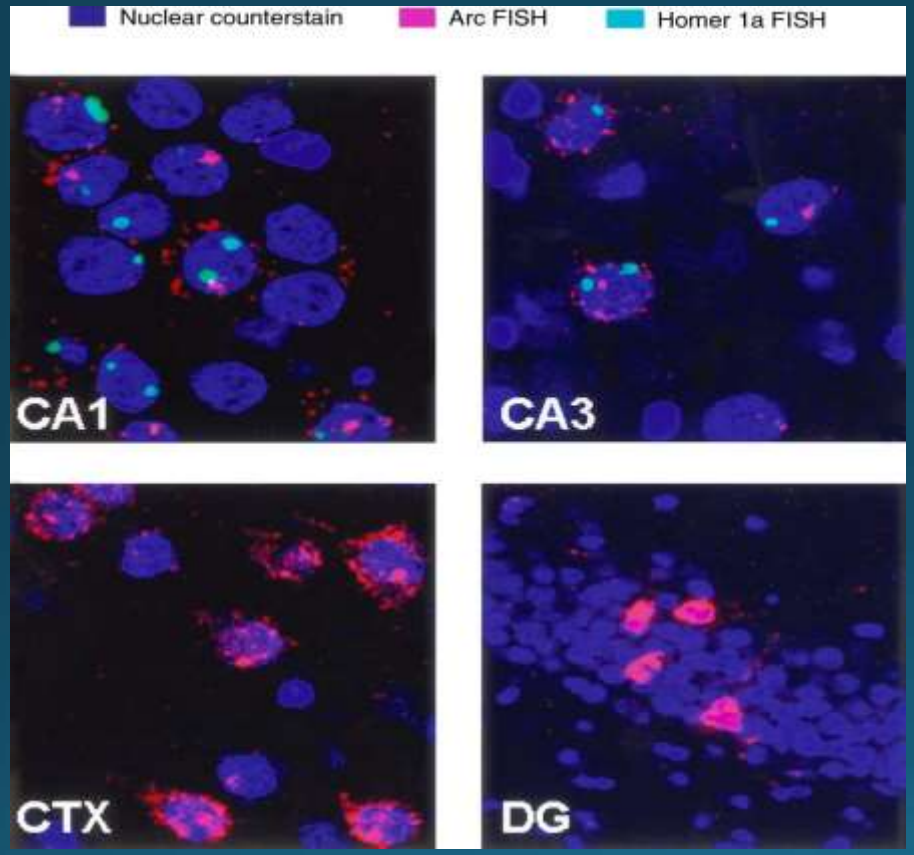
# TMs treatment of addiction



# TMs (Transcranial Magnetic Stimulation): Causality

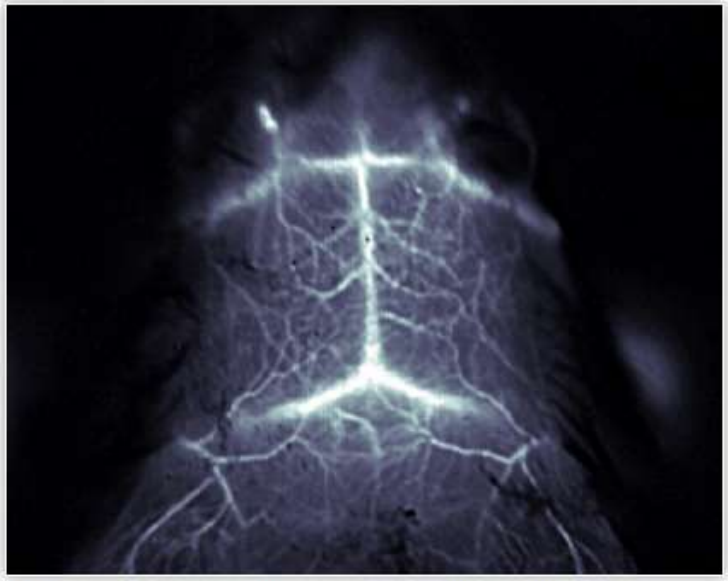
- How it works: Targeted magnetic pulse (1 tesla) temporarily excite sugar-cube sized groups of neurons, allowing increases or decreases in neuronal excitability
- Pros:
  - Can manipulate activation rather than just image it, allowing causality to be inferred
  - Temporary with no lasting damage
- Cons:
  - Researchers still unclear on how it works, exactly

# Arc catFISH: Cellular level hippocampal MRI




Fluorescence in situ hybridization (FISH) of neural activity-regulated, immediate-early gene (IEG) expression

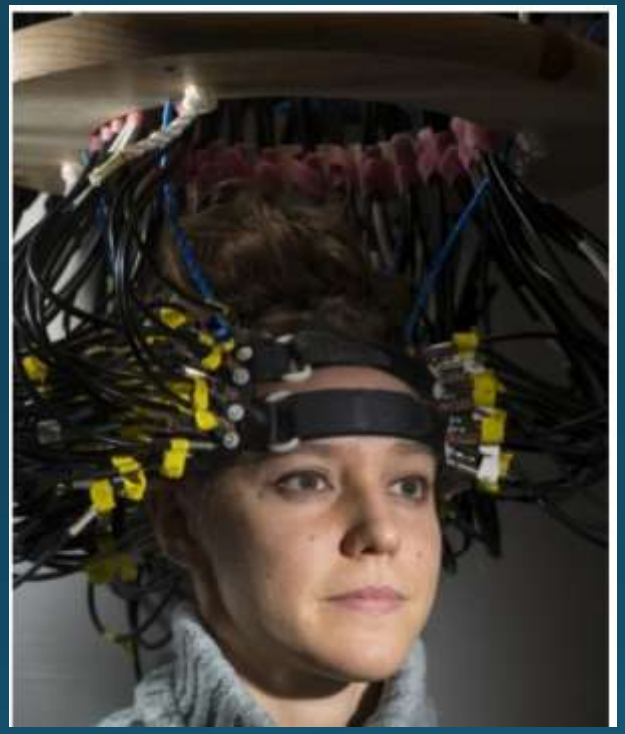
# Through-the-skull Near Infrared-IIa imaging (NIR-IIa*)



*A fluorescent image of the mouse brain taken with a near-IR laser through the skull, clearly showing the brain vasculature of a live mouse through the intact scalp and skull (credit: Stanford Dai lab)*

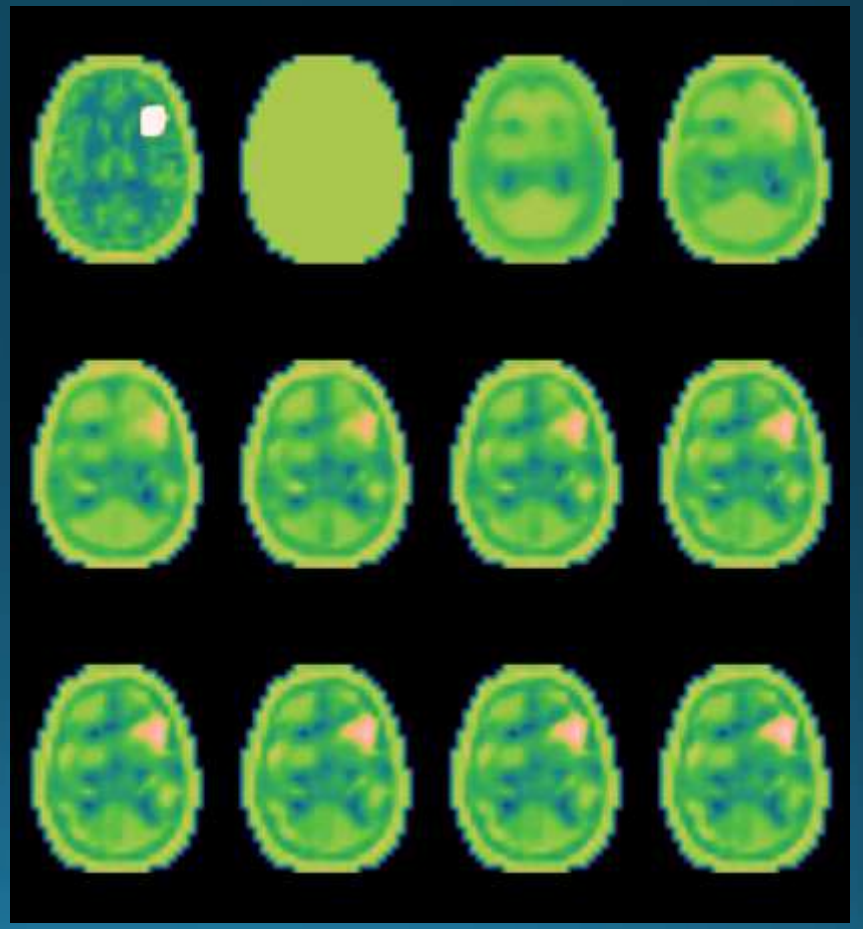
Water-soluble carbon nanotubes are injected into a live mouse's bloodstream. Then shine near-infrared laser light (at 808 nm wavelength) into the brain from outside the skull. That light causes the nanotubes to fluoresce at wavelengths of 1,300–1,400 nanometers. View about three millimeters underneath the scalp

# Diffuse optical tomography

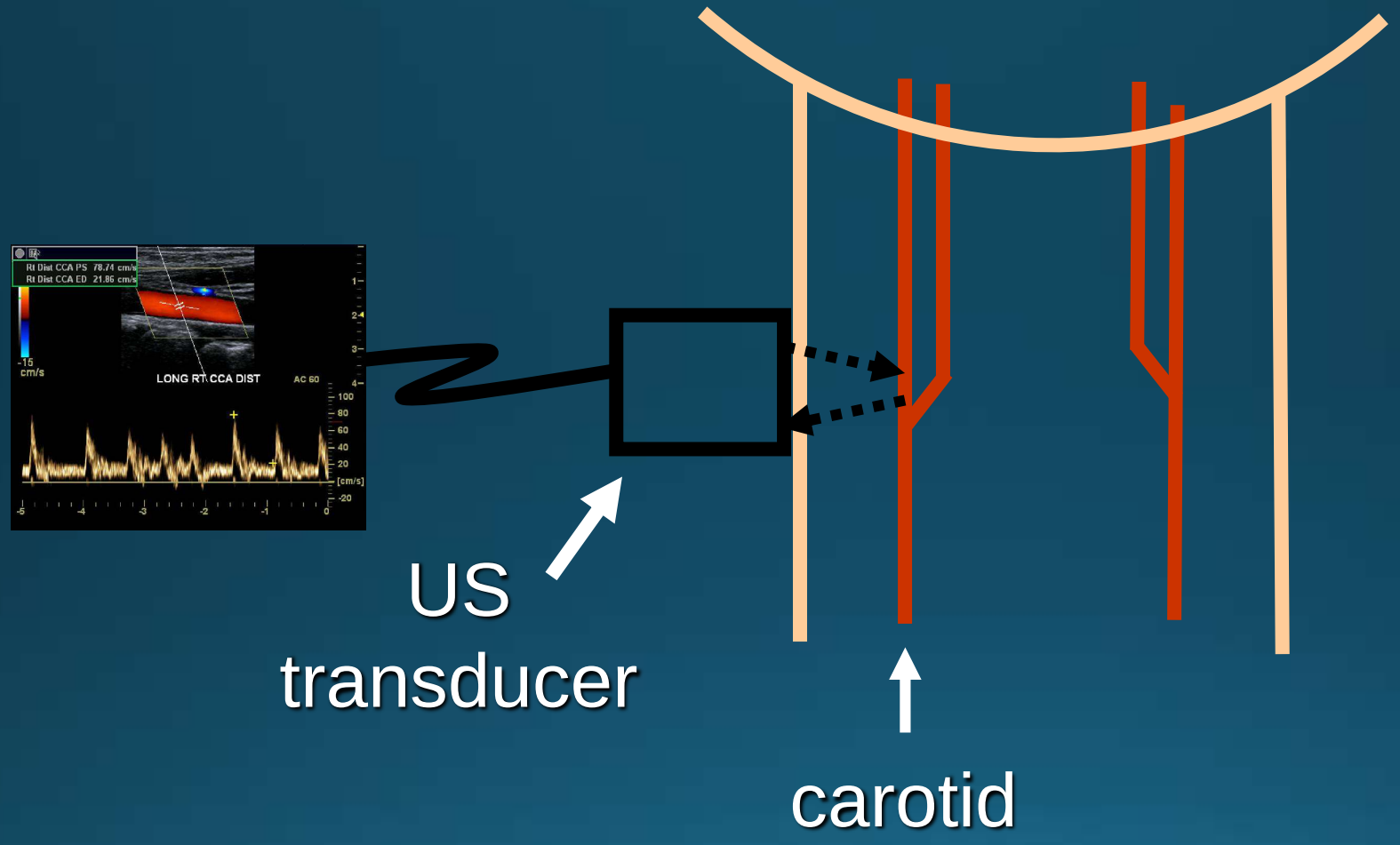


Shining LEDs into the subject's head; latest system able to monitor up to two-thirds of the head at once. Can only reliably image the brain down to a depth of about one centimeter – it can't be used for deep brain scans. Has done four hierarchical language tasks and multiple resting-state networks including the dorsal attention and default mode networks.

# Monstir: Optical Tomography



# Ultrasound


Rt Dist CCA PS 78.74 cm/s
Rt Dist CCA ED 21.86 cm/s
LONG RT CCA DIST
AC 60
US
transducer
carotid

# Ultrasound

## Indications:

- Carotid stenosis
- Vasospasm - Transcranial Doppler (TCD)
- Infant brain imaging (open fontanelle = acoustic window)

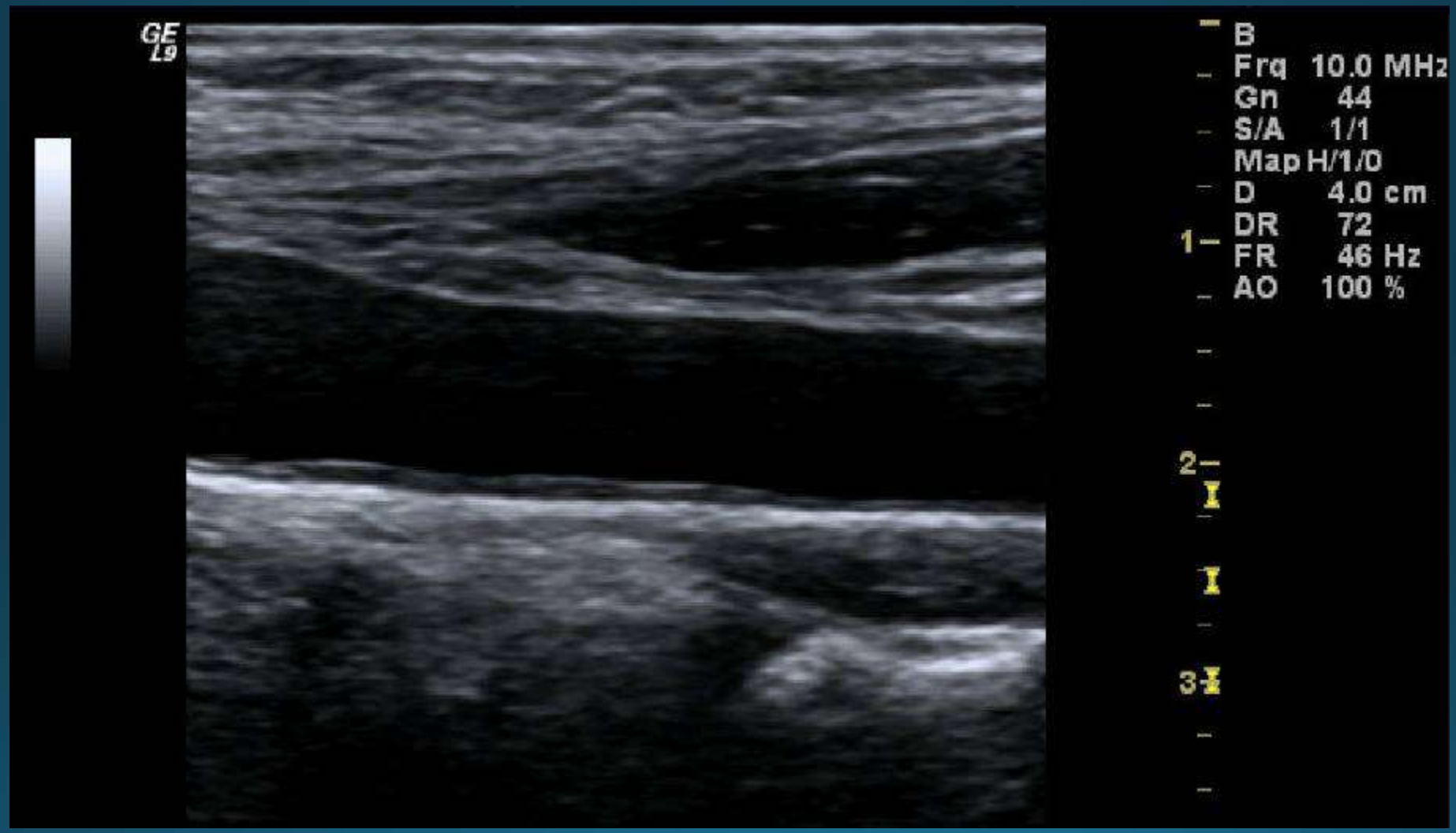
## Advantages:

- Noninvasive, well-tolerated, readily available, low cost
- Quantitates blood velocity
- Reveals morphology (stability) of atheromatous plaques

## Disadvantages:

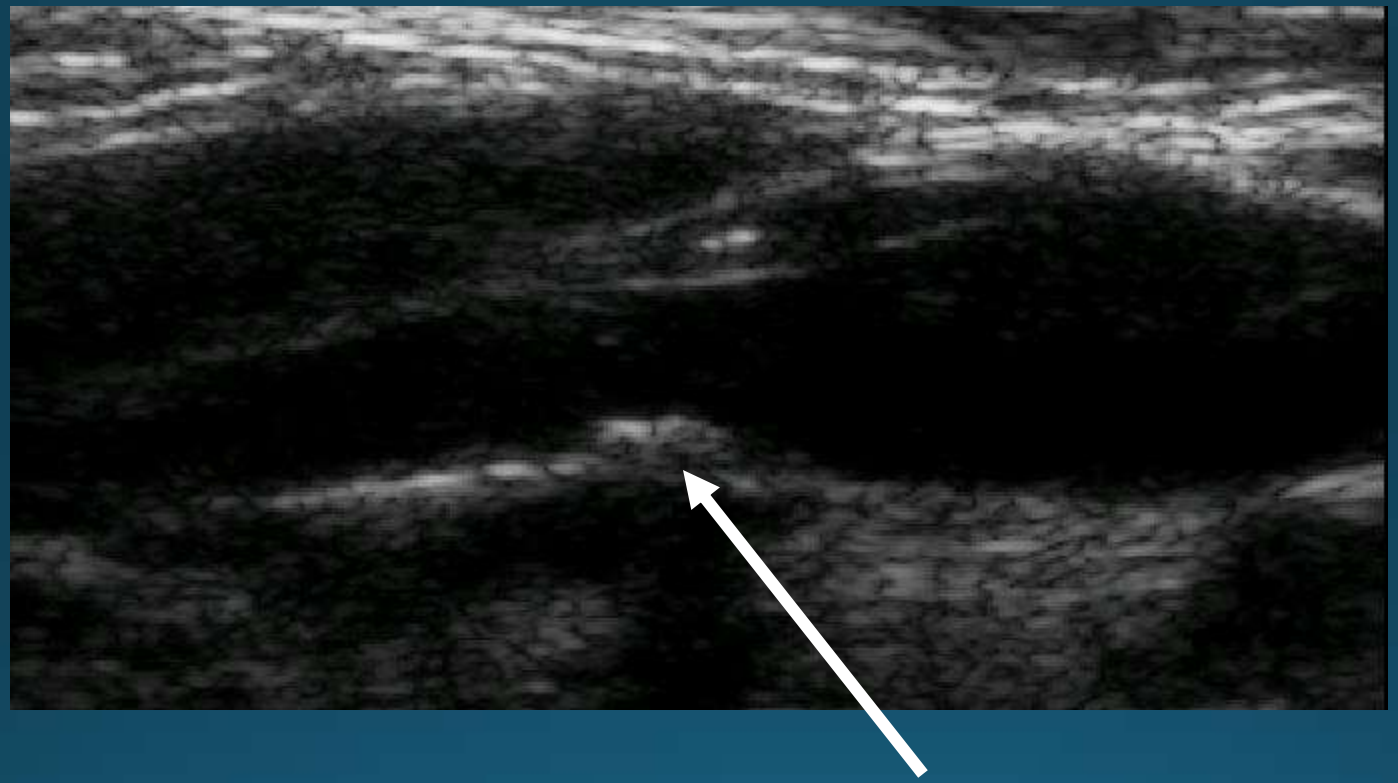
- Severe stenosis may appear occluded
- Limited coverage, difficult through air/bone
- Operator dependent

# Ultrasound – Gray Scale



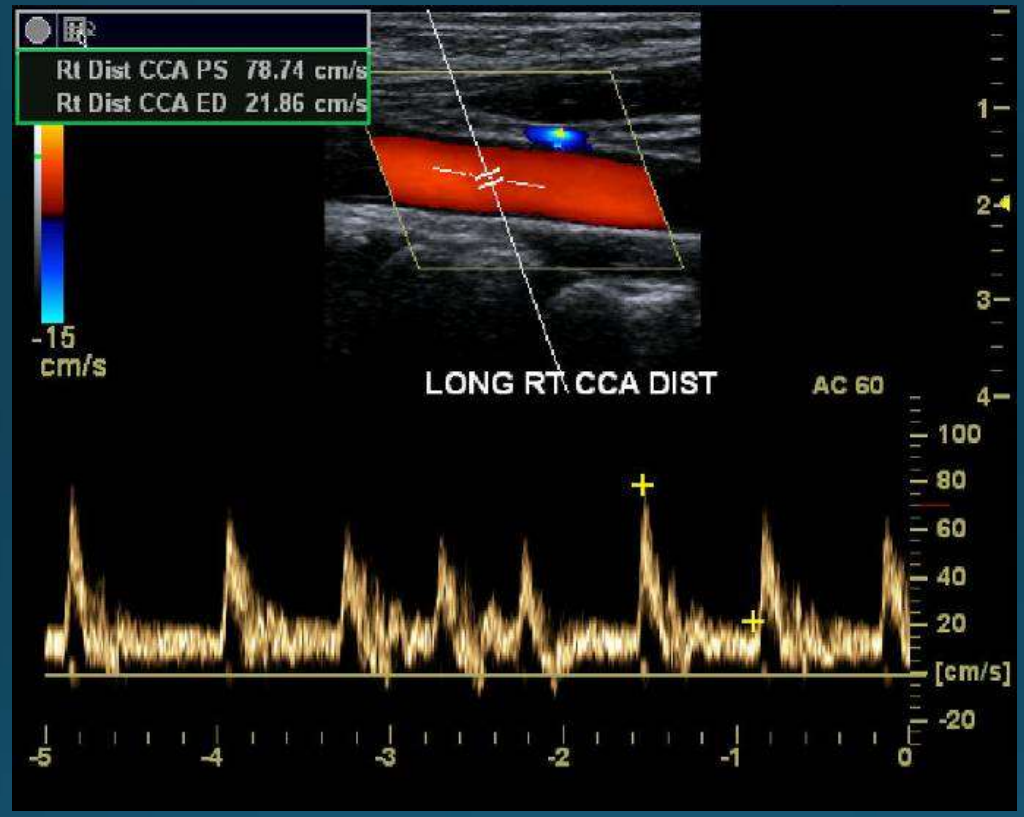

Gray-scale image of carotid artery

# Ultrasound – Gray Scale




Gray-scale image of carotid artery

# Ultrasound - Color Doppler

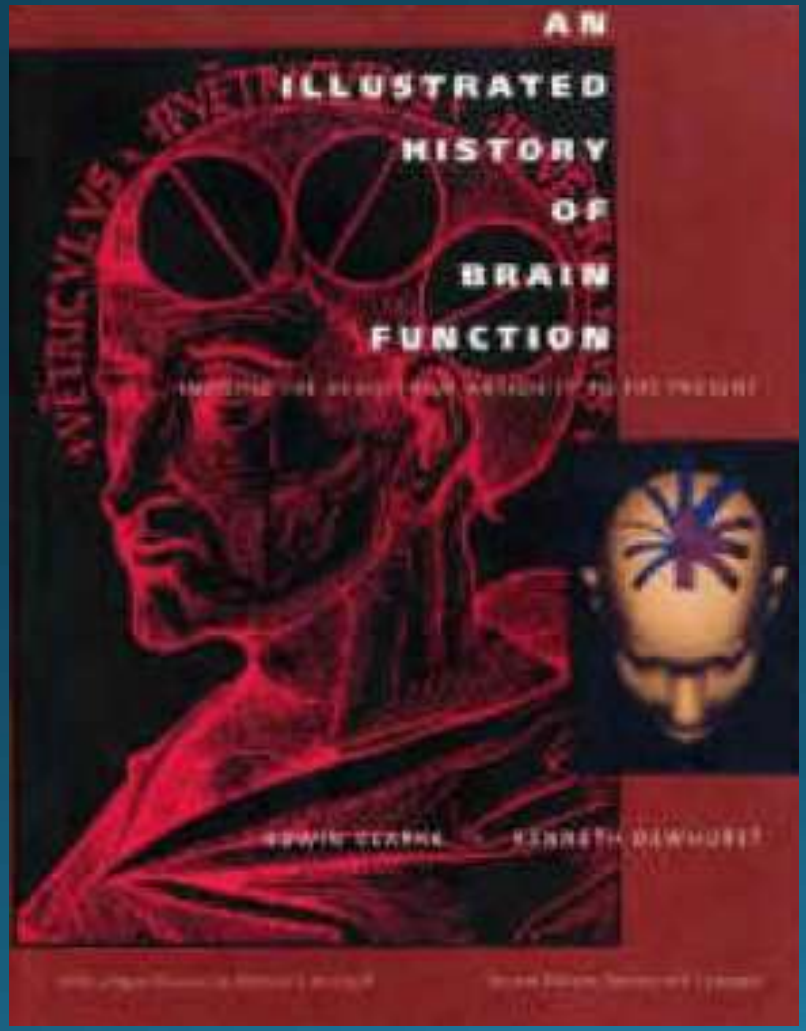



| Peak Systolic Velocity (cm/sec) | ICA Stenosis (% diameter) |
|---|---|
| 125 – 225 | 50 – 70 |
| 225 – 350 | 70 – 90 |
| >350 | >90 |

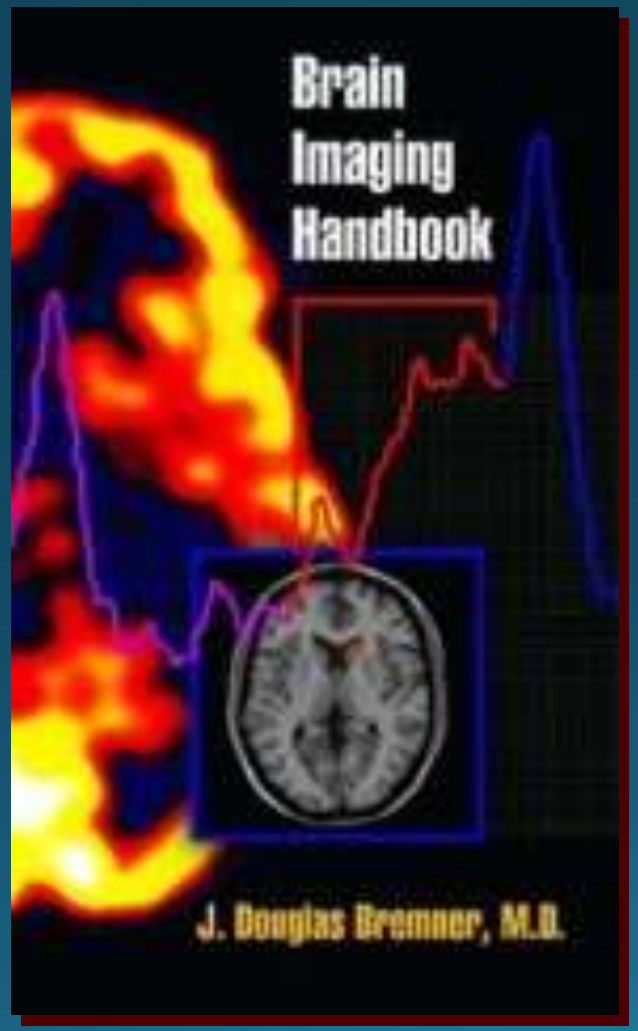
“It's interesting that they are having you give this talk at SFGH and not one of neuroradiologists. If they want more specifics I know the neuroradiology attendings at SFGH would be happy to talk with the neuropsych postdocs as well. They would have much better and more specific answers than me as this is what they do every day.”

Maya Vella, MD, 2nd year UCSF radiology resident

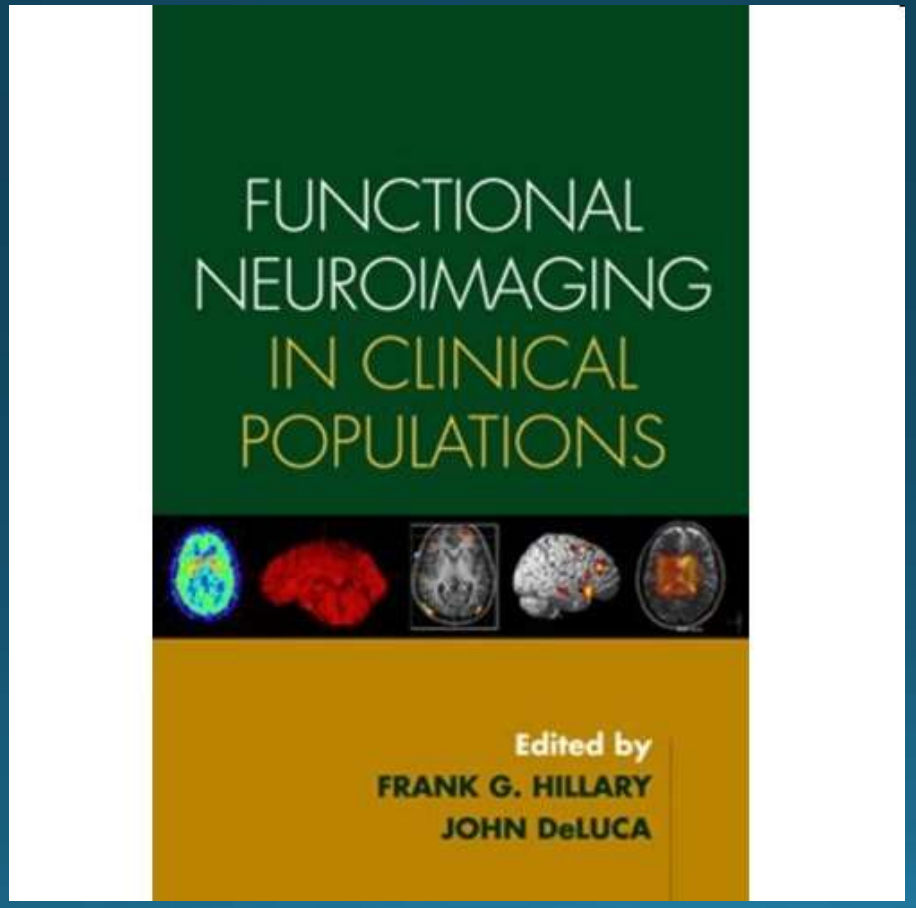
# Illustrated History of Brain Function: Clarke & Dewhurst



# Brain Imaging Handbook – J. Bremner



# Functional Neuroimaging in Clinical Populations



# Whole Brain Atlas