NEURO-IMAGING IN EPILEPSY

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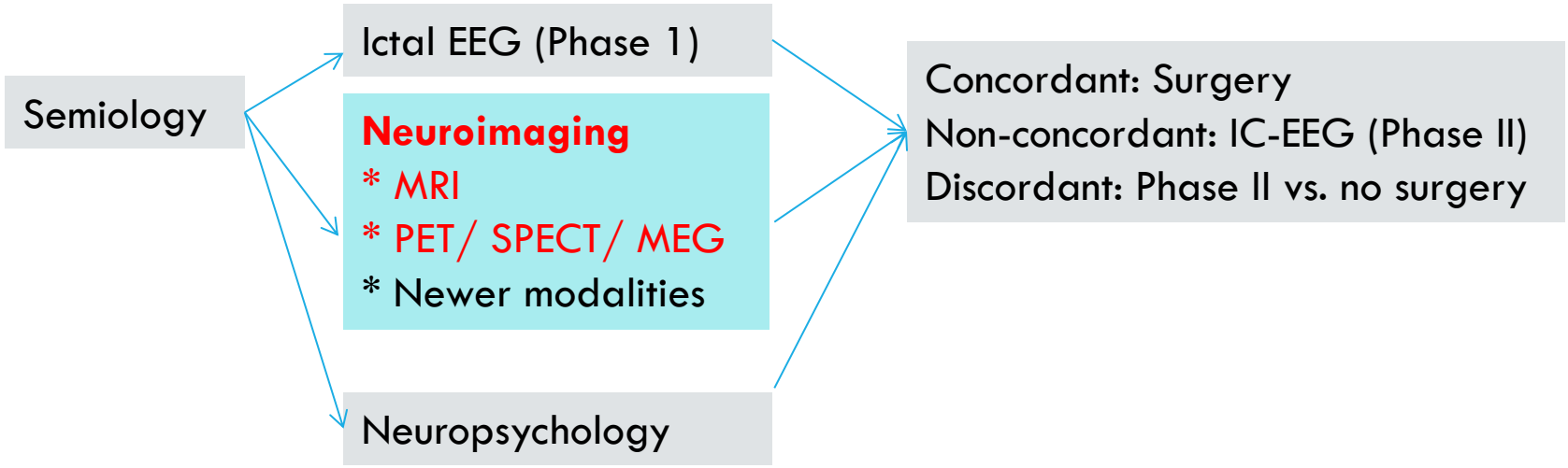
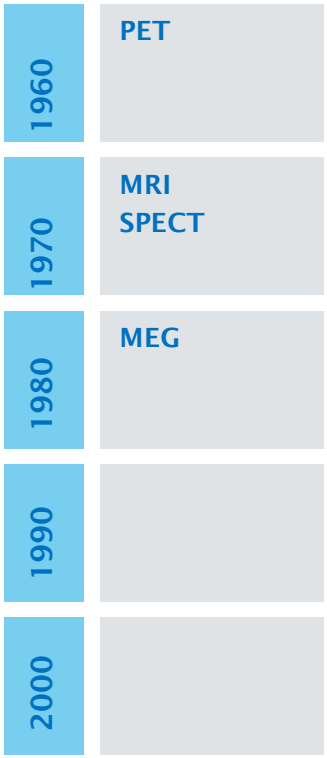
Baylor College of Medicine,
Houston, Texas

THE CLINICAL APPROACH TO EPILEPSY SURGERY

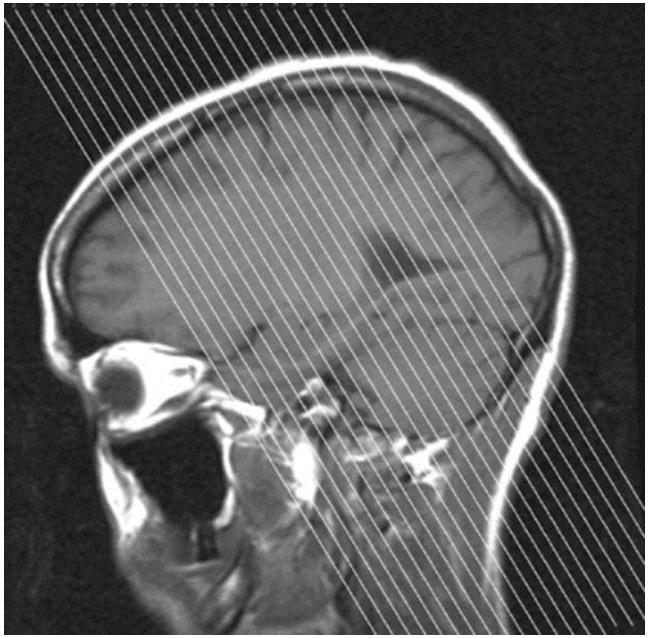


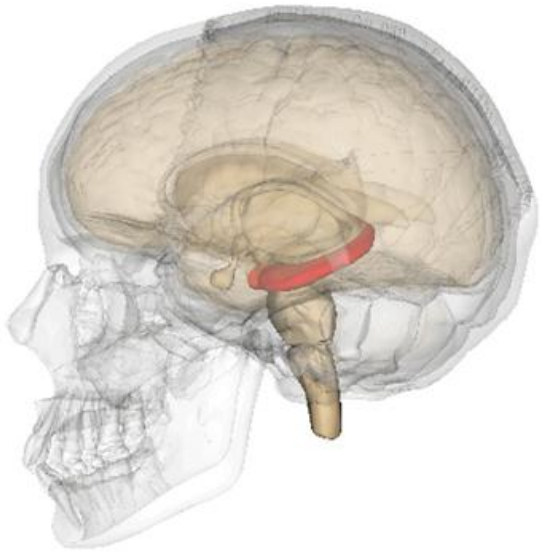
TRADITIONAL NEURO-IMAGING

1. MRI
2. PET & Co-registration
3. SPECT
4. MEG/ MSI

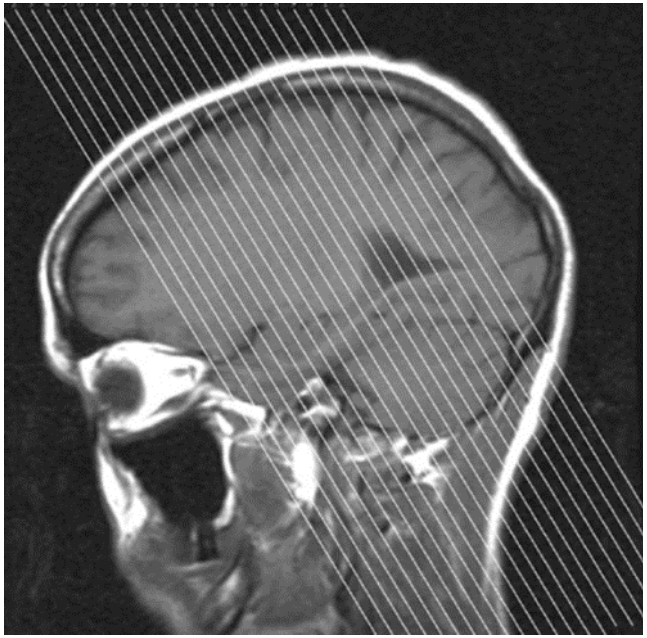


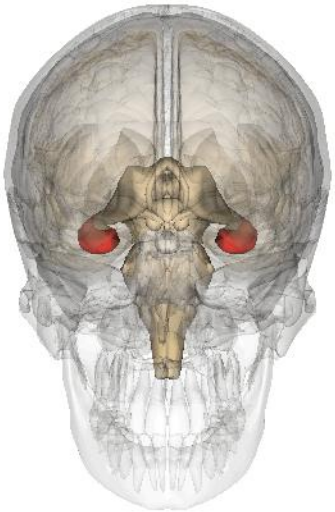
MRI



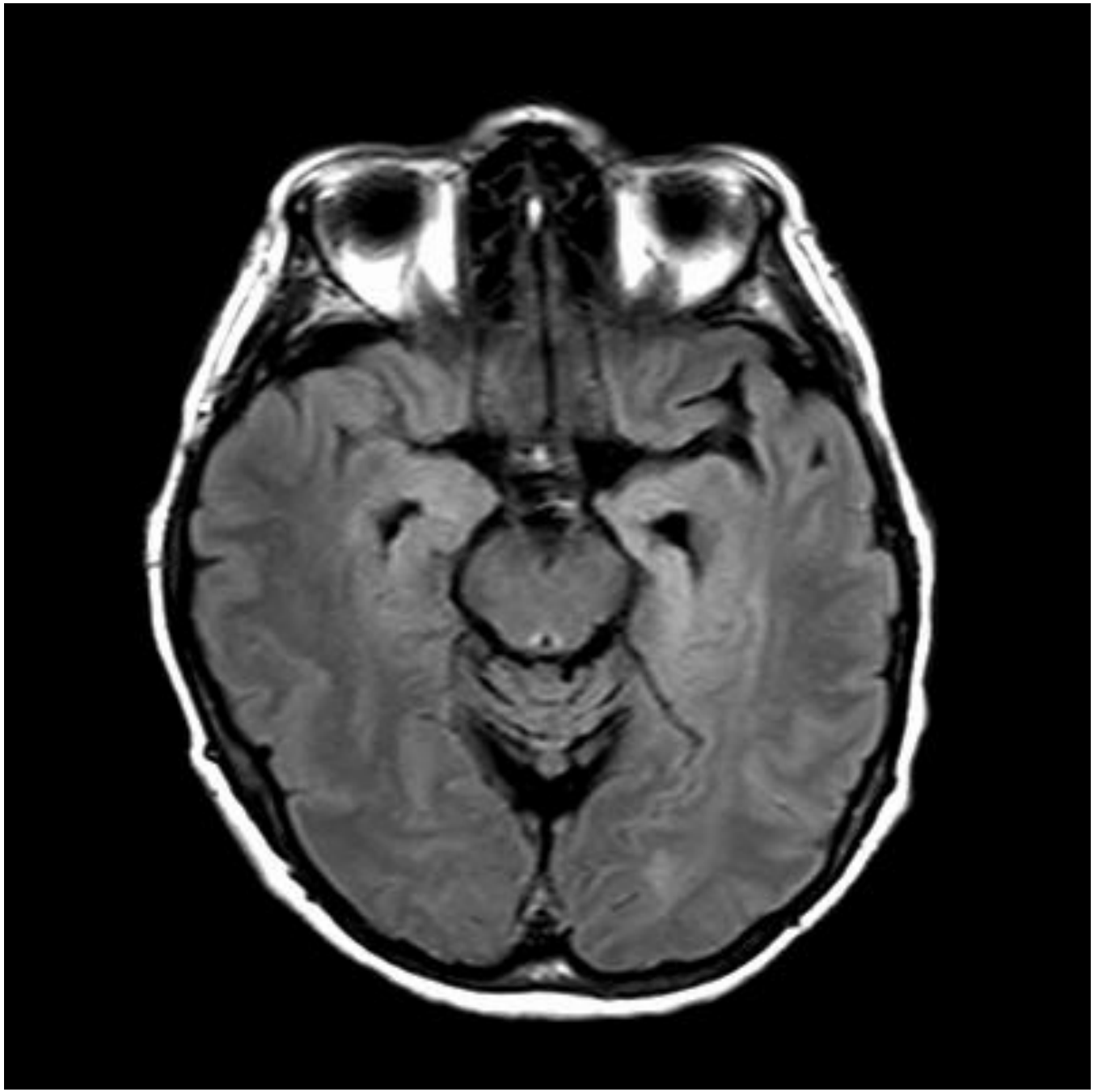


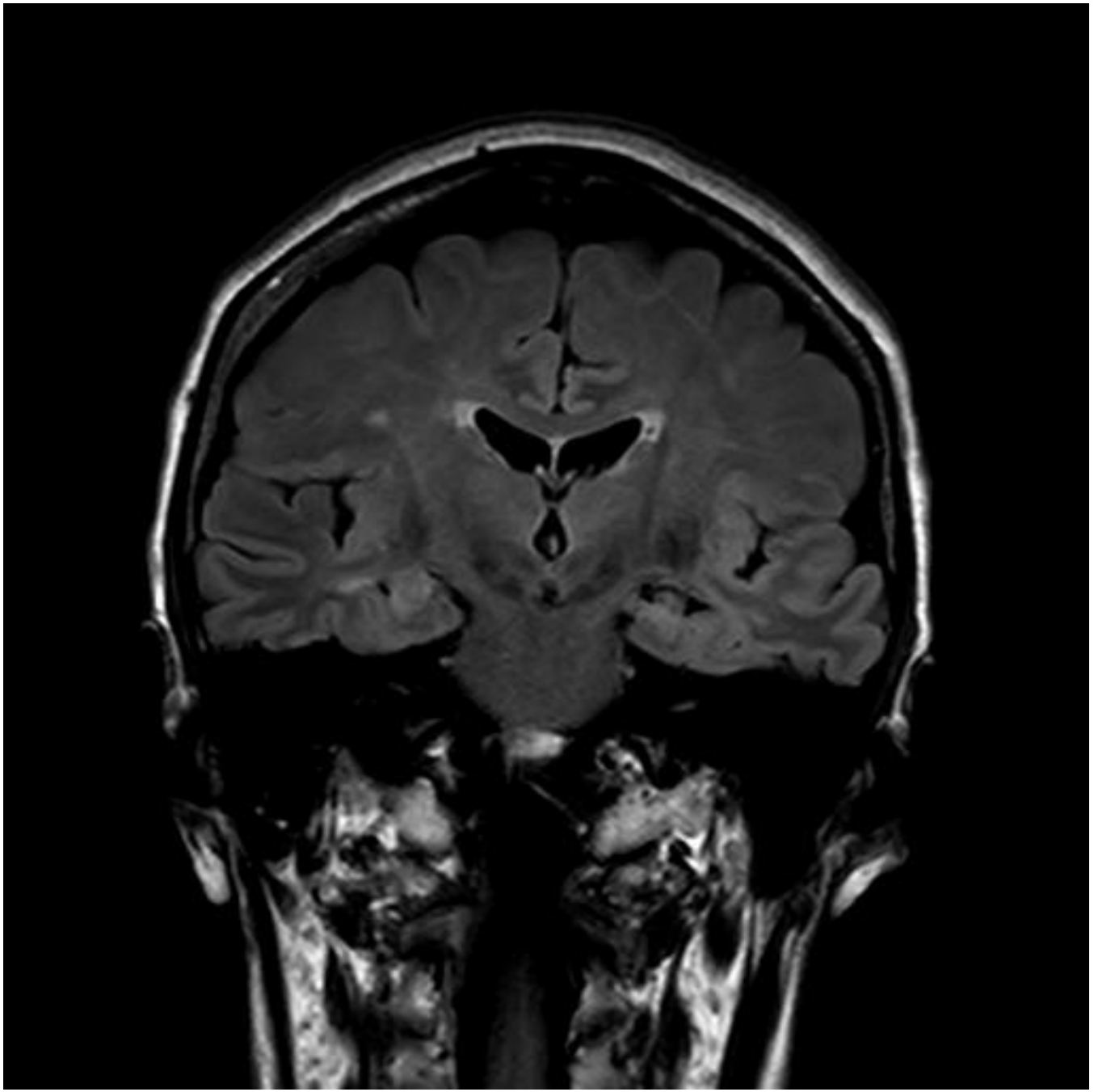
MRI plane perpendicular to long axis of hippocampus

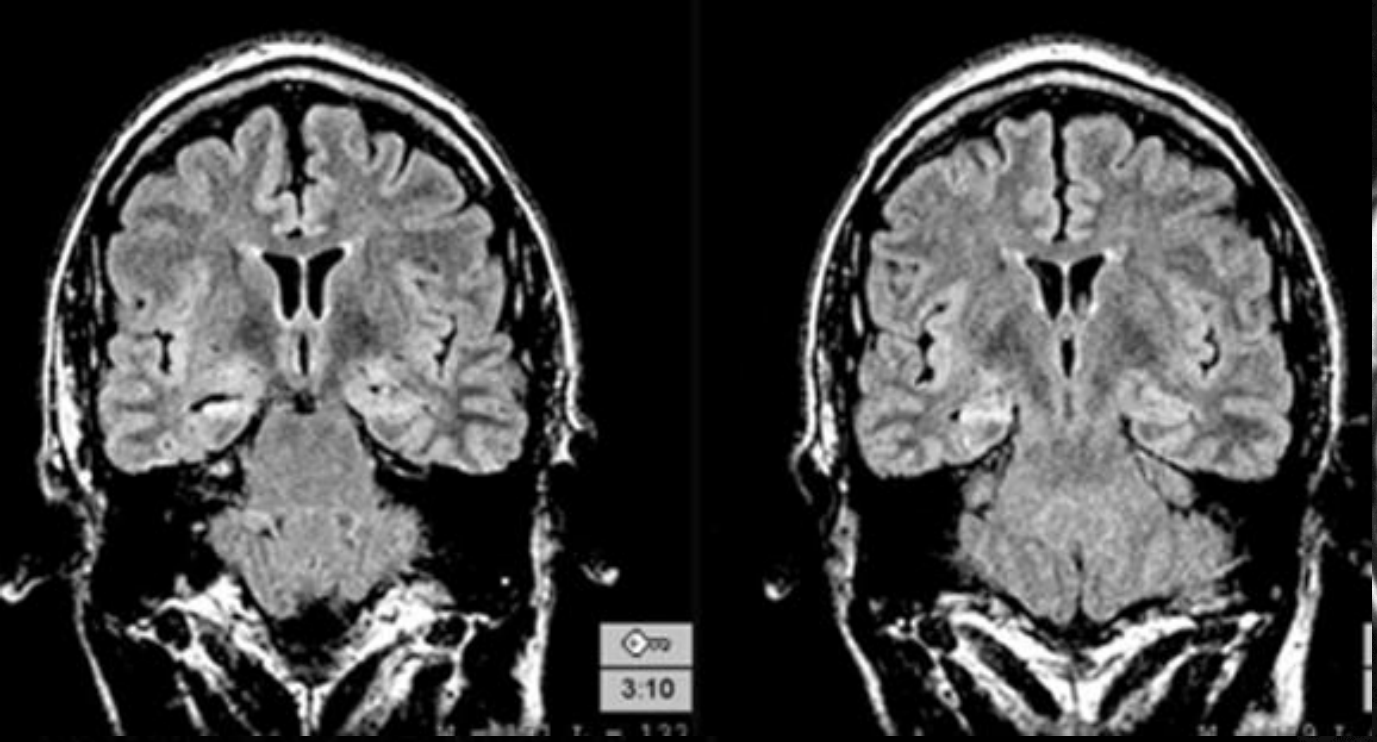


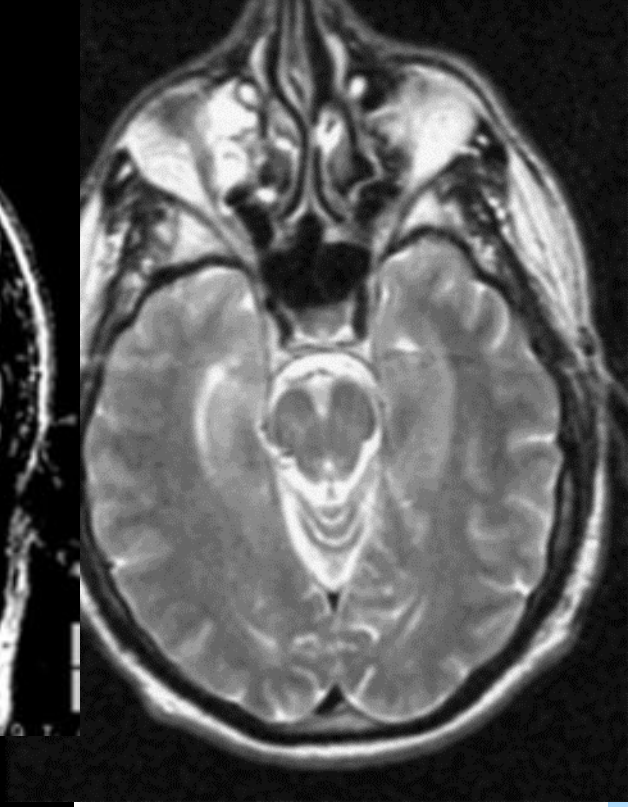


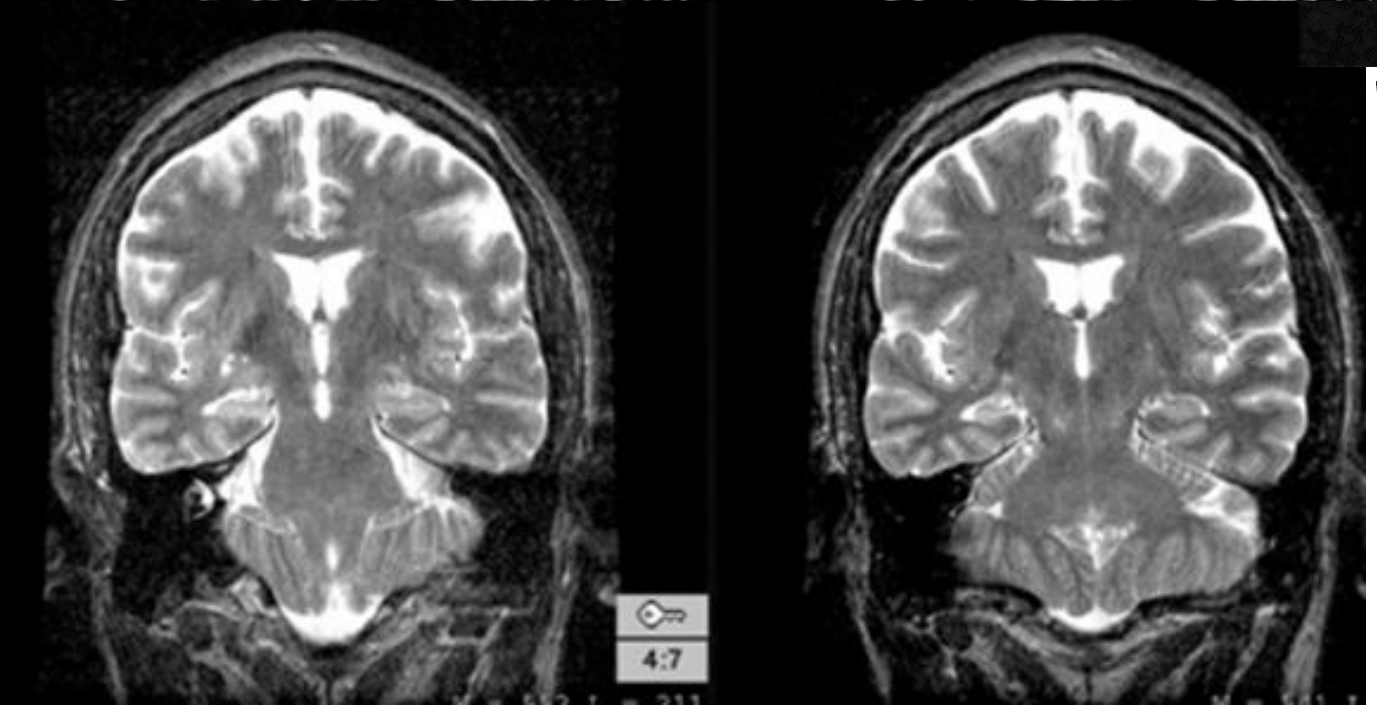
MRI plane perpendicular to long axis of hippocampus





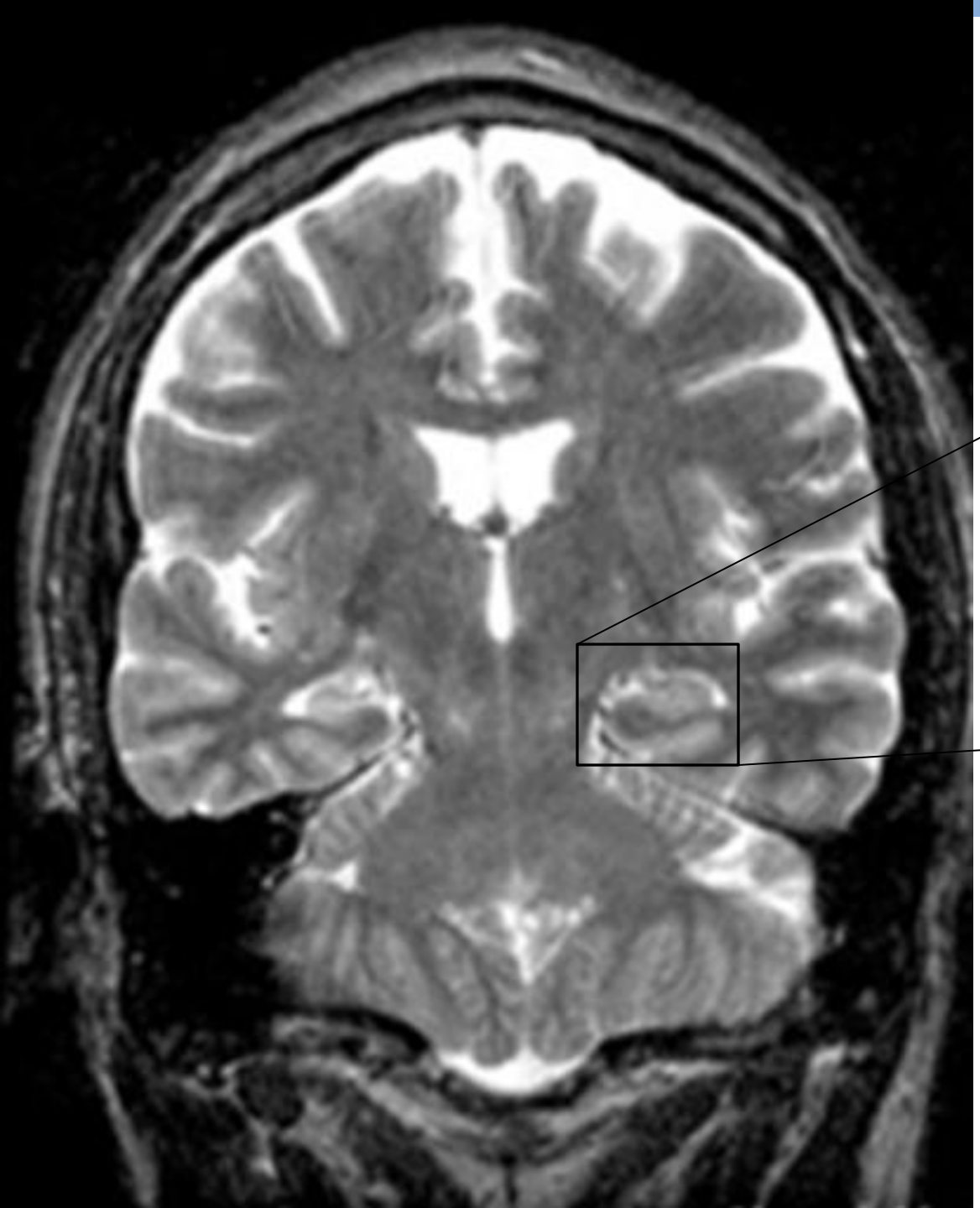


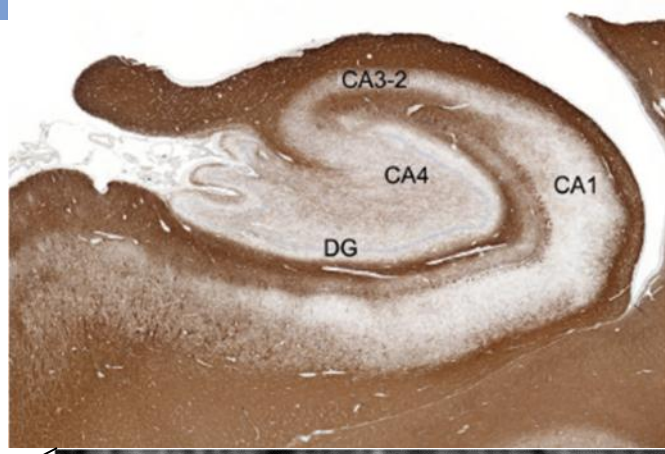


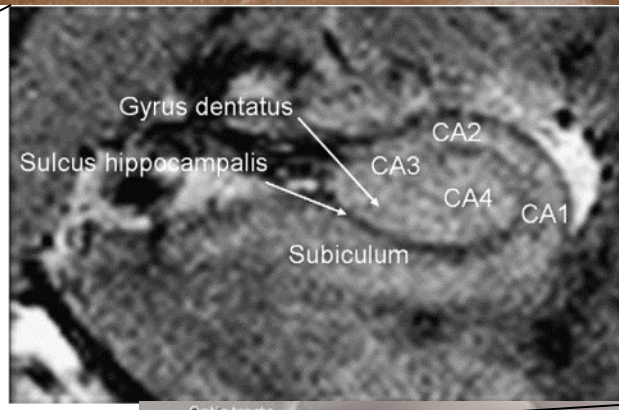


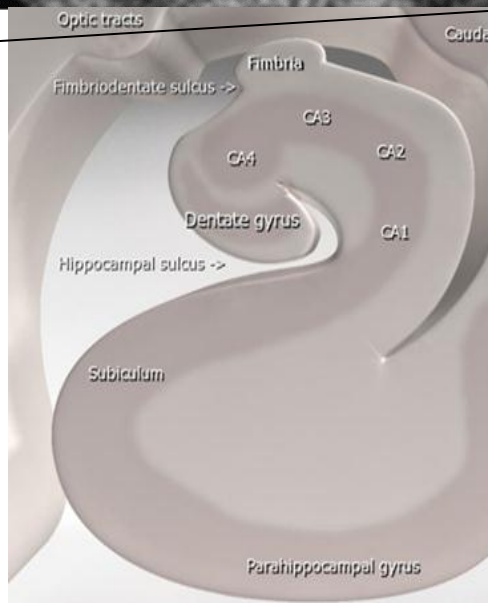
Coronal FLAIR:
Hippocampal sclerosis/ atrophy

← **Coronal T2:**
Internal architecture.

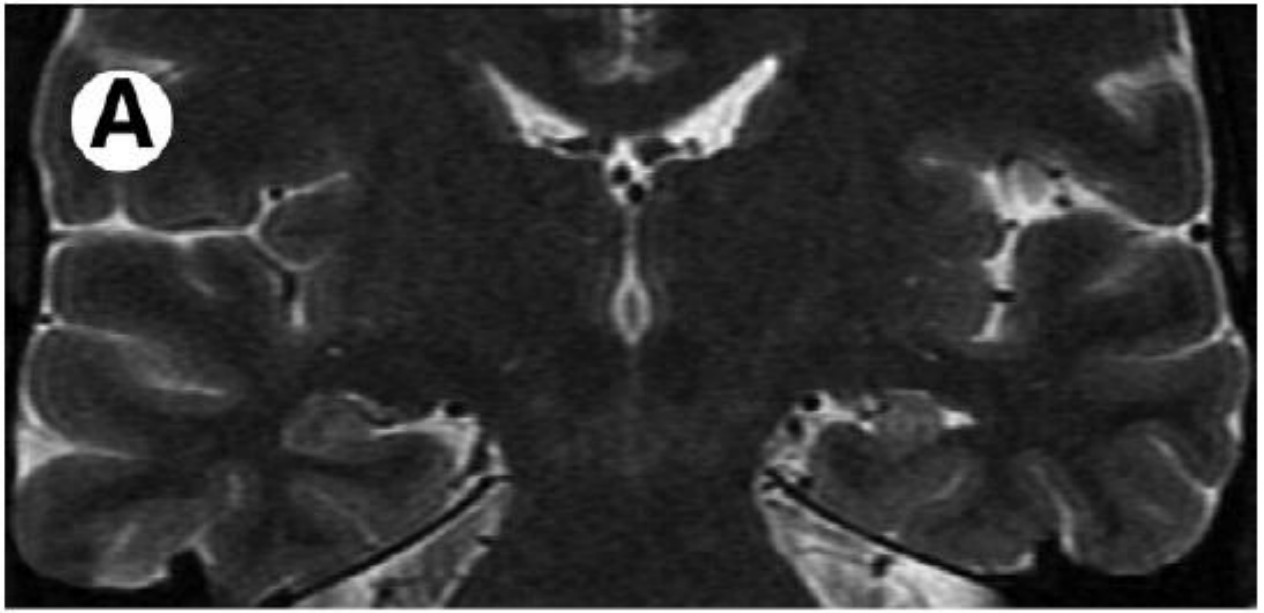



CA3-2
CA4
CA1
DG

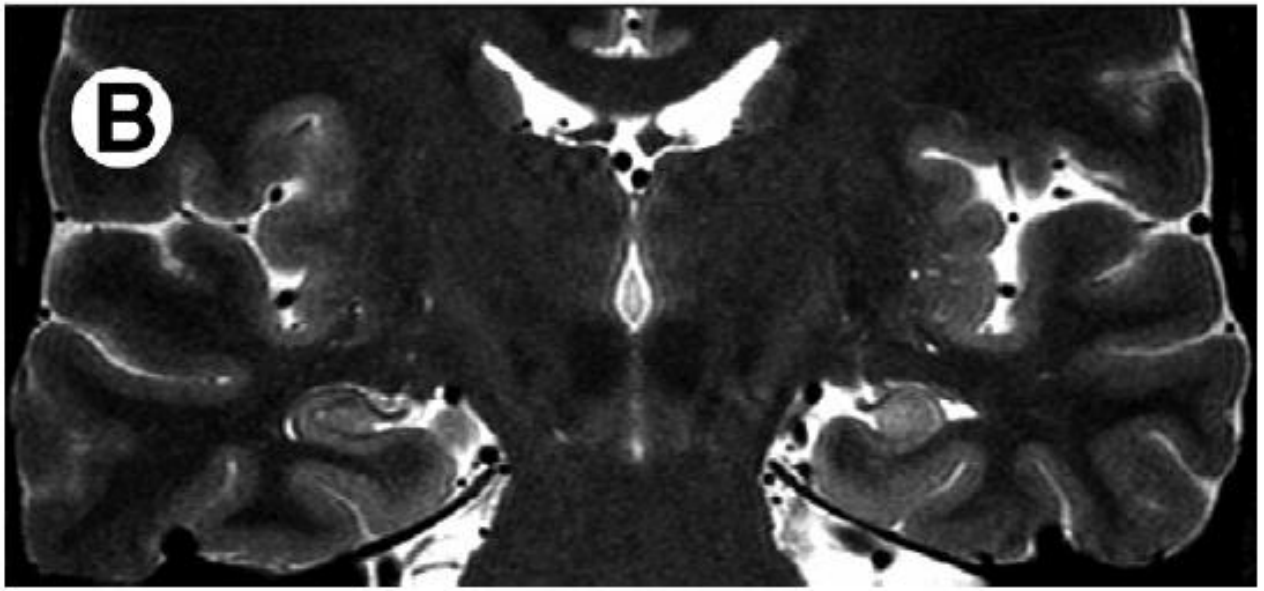

Gyrus dentatus
Sulcus hippocampalis
CA2
CA3
CA4
CA1
Subiculum


Optic tracts
Fimbria
Fimbriodentate sulcus ->
CA3
CA4
CA2
Dentate gyrus
CA1
Hippocampal sulcus ->
Subiculum
Parahippocampal gyrus

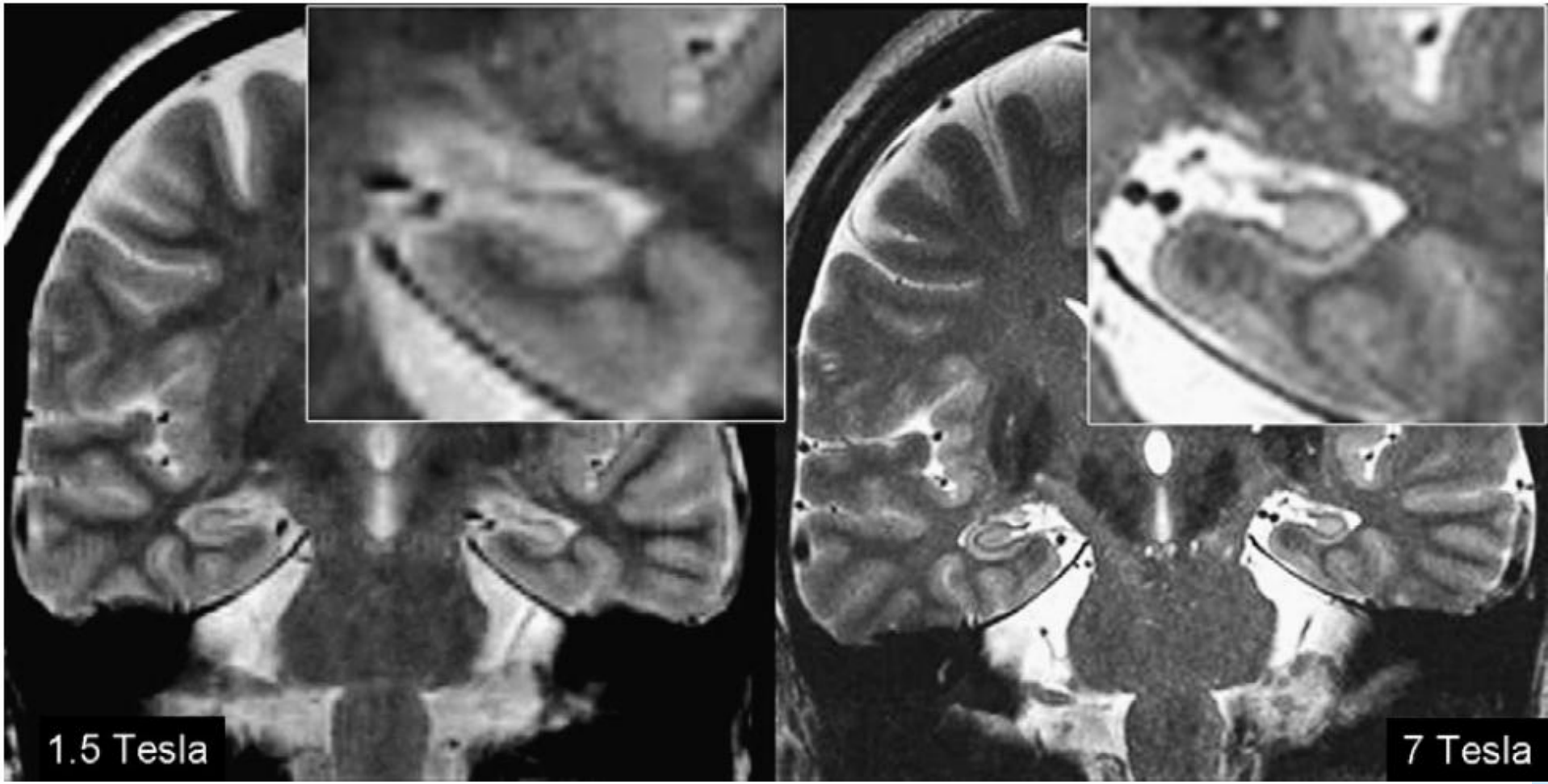
1.5 T



3.0 T

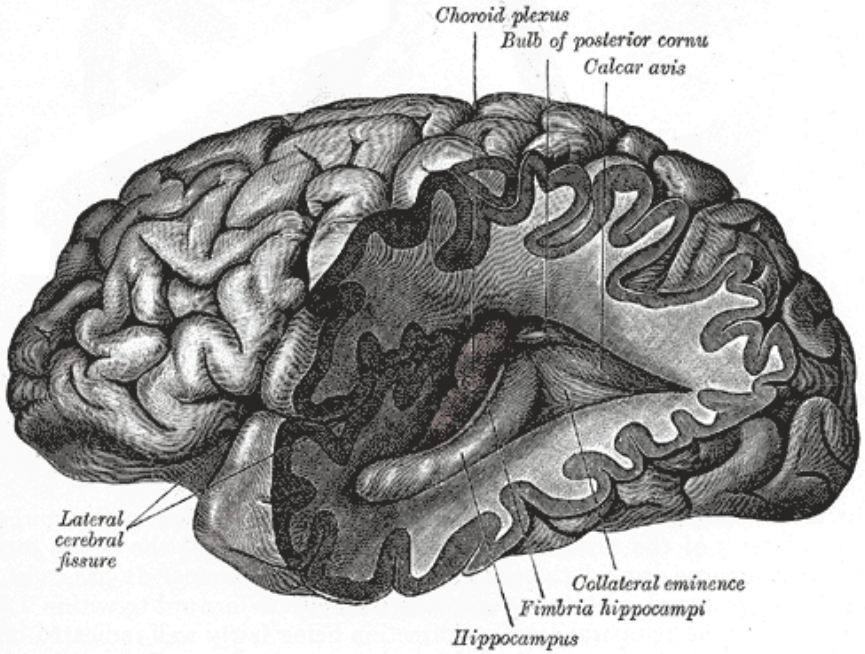


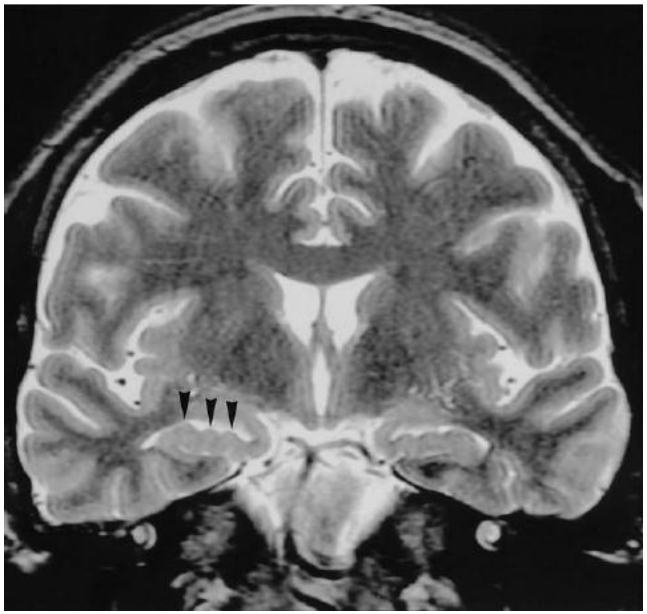
Left mesial temporal sclerosis (MTS), barely visible on 1.5 T (A) and clearly visible on 3 T.



L MTS at 1.5 and 7 T

Academic Radiology, Vol 17, No 4, April 2010





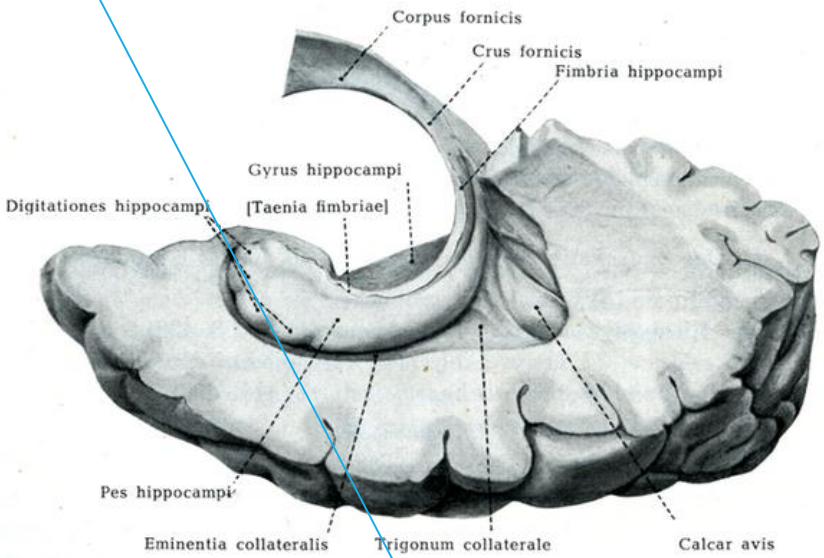
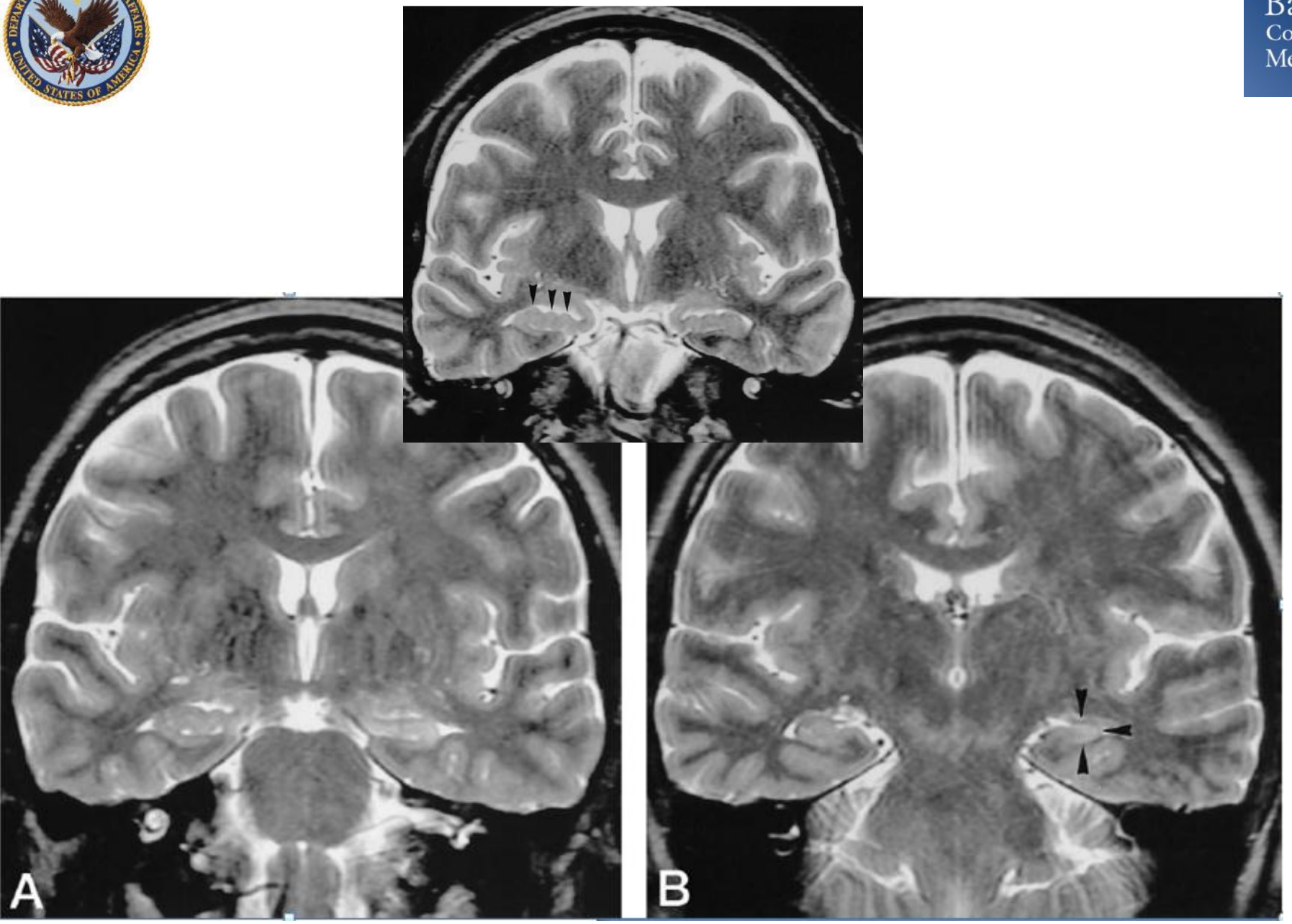


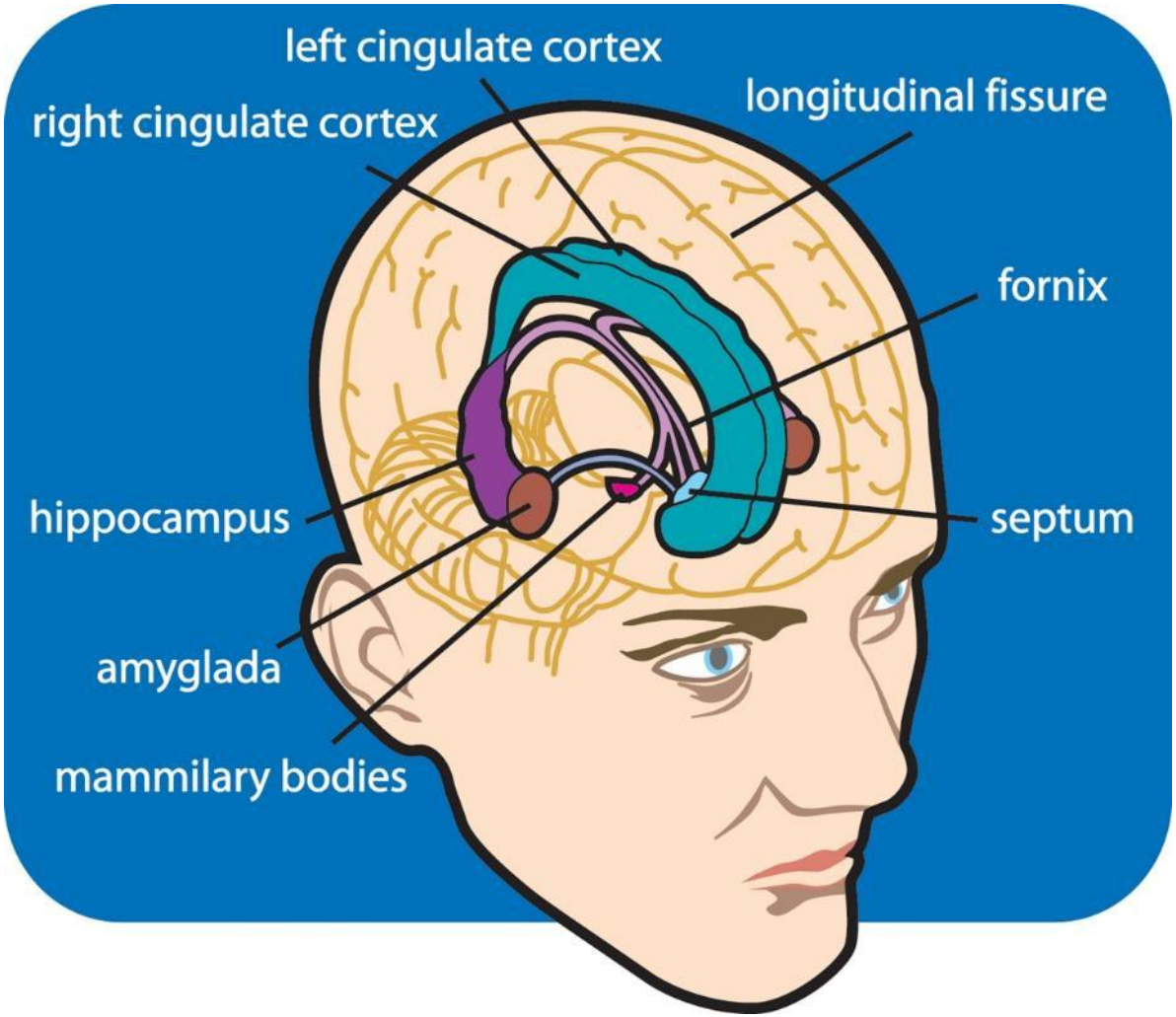
Abb. 423. *Unterhorn und Hinterhorn des Seitenventrikels. Fornix und Pes Hippocampi.*
(Fr. Kopsch praep.; L. Krause del.)

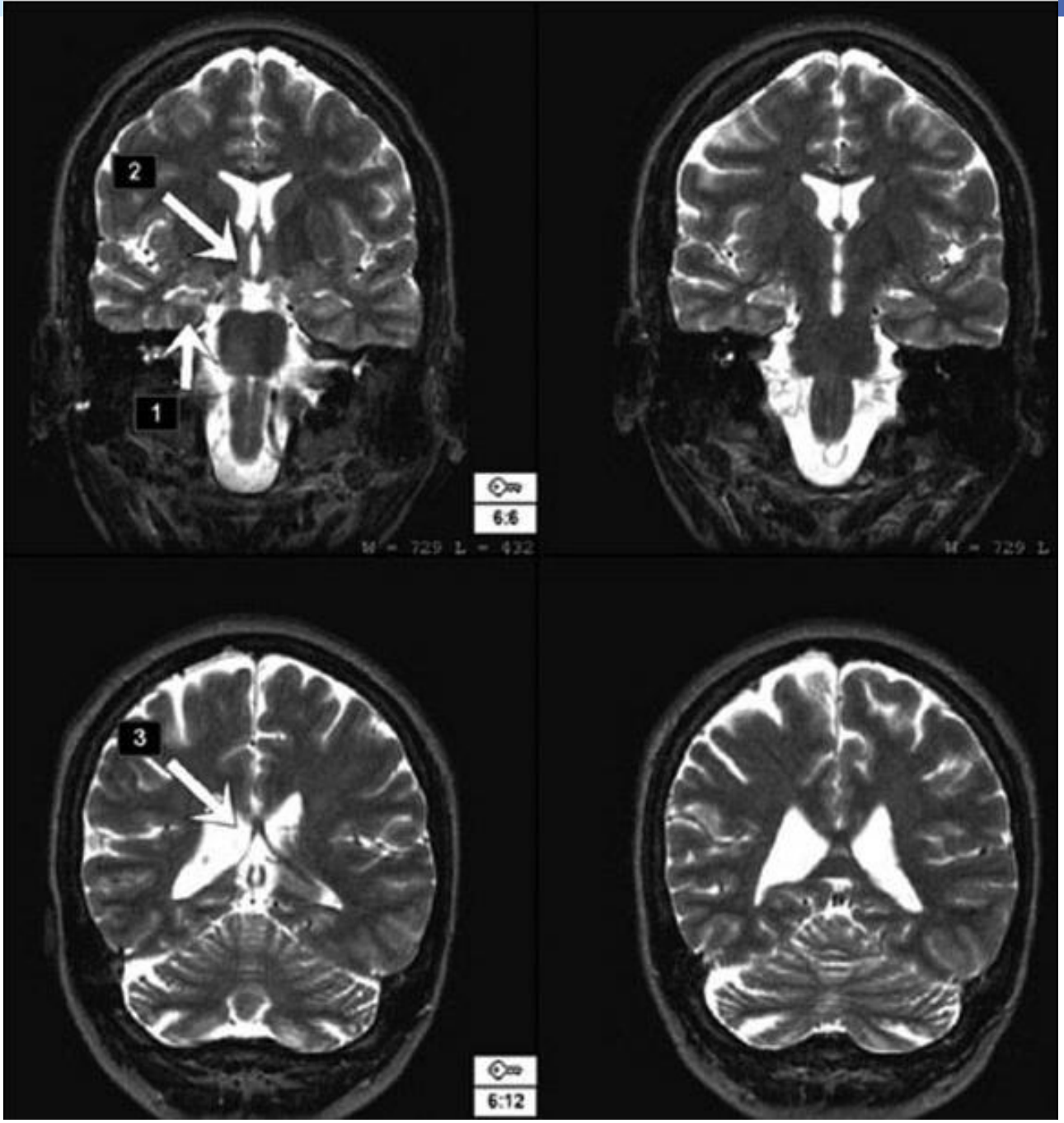
Loss of Digitations of the Hippocampal Head on High-Resolution Fast Spin-Echo MR: A Sign of Mesial Temporal Sclerosis
Oppenheim et al. AJNR Am J Neuroradiol 19:457–463



Loss of Digitations of the Hippocampal Head on High-Resolution Fast Spin-Echo MR: A Sign of Mesial Temporal Sclerosis
Oppenheim et al. AJNR Am J Neuroradiol 19:457–463

LIMBIC SYSTEM AND HIPPOCAMPUS





Hippocampal atrophy (1) with secondary atrophy of mamillary body (2) and fornix (3)


Reader - [7/3
File Edit View Navigate Protocol Format Tools Workspace Window Help
Phase1_Haneef(2)
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176 secs
Review Video
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Fp1-F7
F7-T7
T7-P7
P7-O1
Fp2-F8
F8-T8
T8-P8
P8-O2
Cz-C3
C3-T7
T7-TA1
TA1-TA2
TA2-T8
T8-C4
C4-Cz
Fp1-F3
F3-C3
C3-P3
P3-O1
Fp2-F4
F4-C4
C4-P4
P4-O2
EKG1-EKG2
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Blink
Awake
Talking
Drowsy
Clench F
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Seizure
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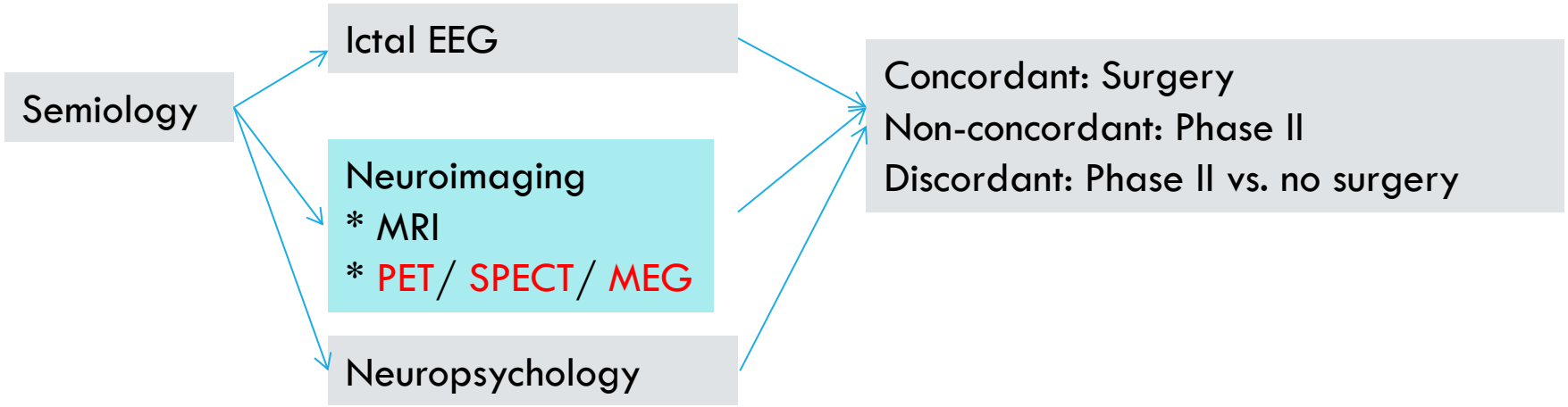
THE CLINICAL PROBLEM



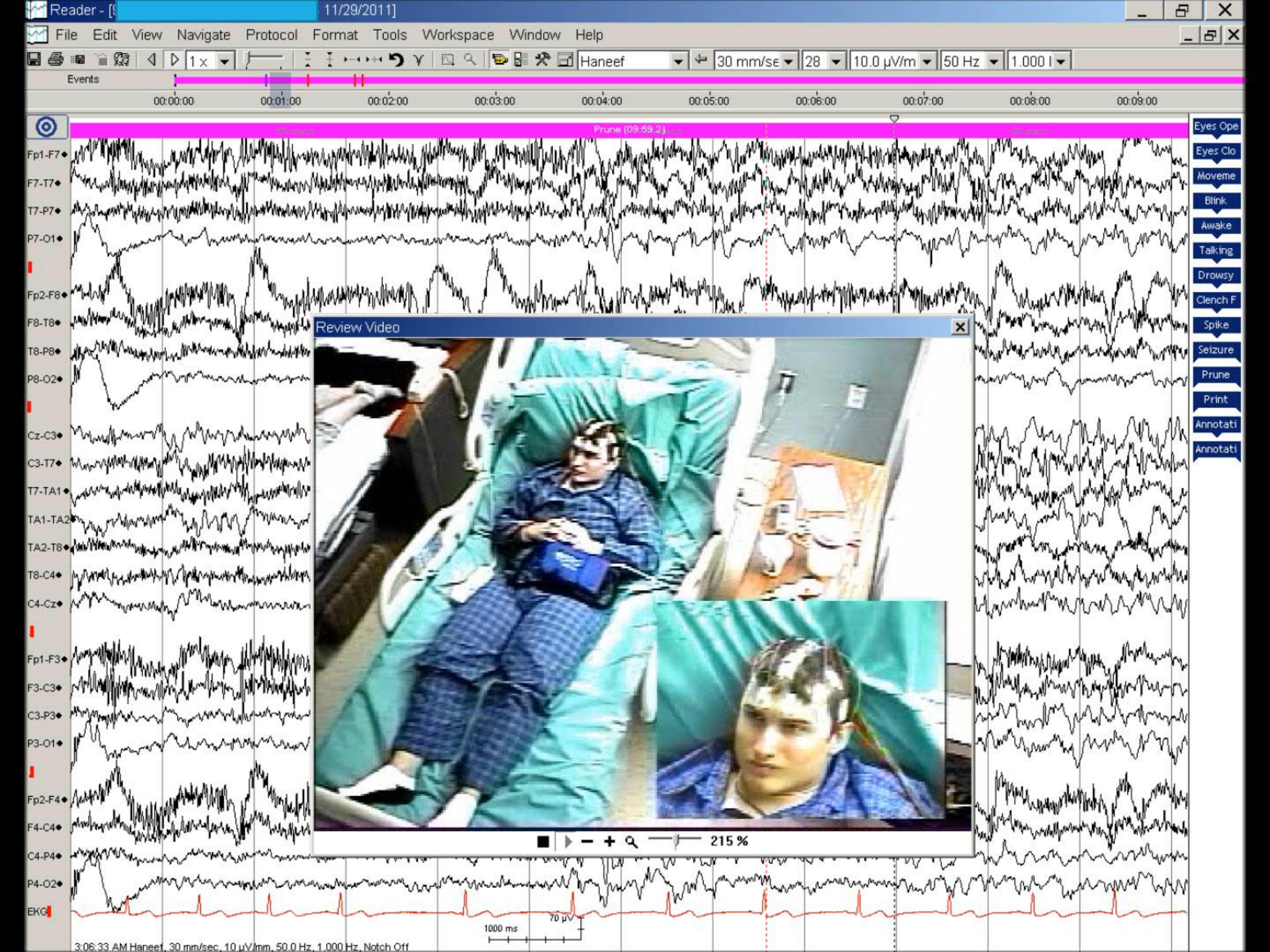
Baylor College of Medicine

PET

CASE

17-year-old male presenting with seizures

- starting as ‘shock like sensation over whole body’ and occasional right hand ‘clawing’ followed by GTCS.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Haneef
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F7-T7
T7-P7
P7-O1
Fp2-F8
F8-T8
T8-P8
P8-O2
Cz-C3
C3-T7
T7-TA1
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T8-C4
C4-Cz
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F3-C3
C3-P3
P3-O1
Fp2-F4
F4-C4
C4-P4
P4-O2
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1000 ms
70 µV
Eyes Ope
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Blink
Awake
Talking
Drowsy
Clench F
Spike
Seizure
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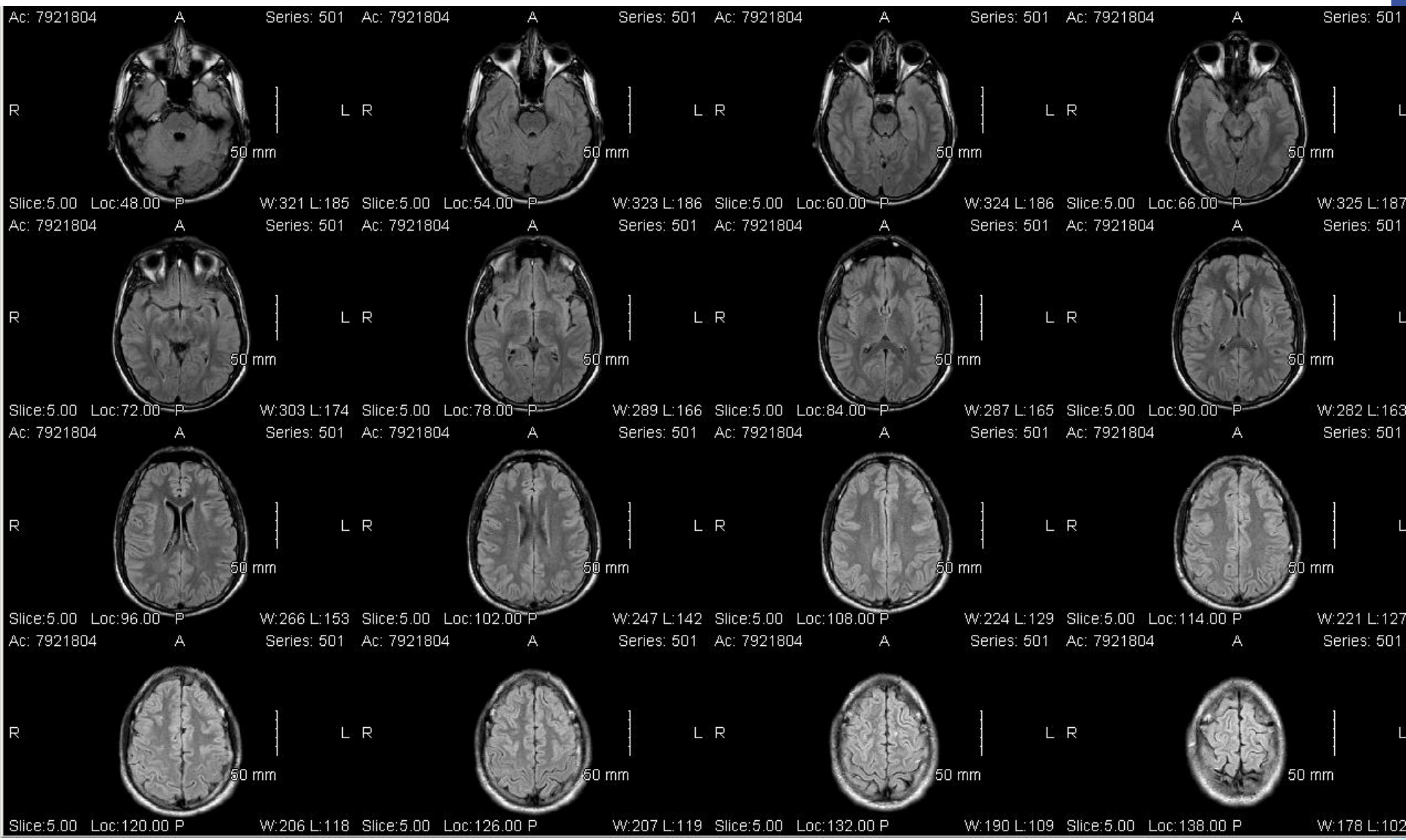
3:06:33 AM Haneef, 30 mm/sec, 10 µV/mm, 50.0 Hz, 1.000 Hz, Notch Off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Slice:5.00 Loc:66.00 P W:325 L:187
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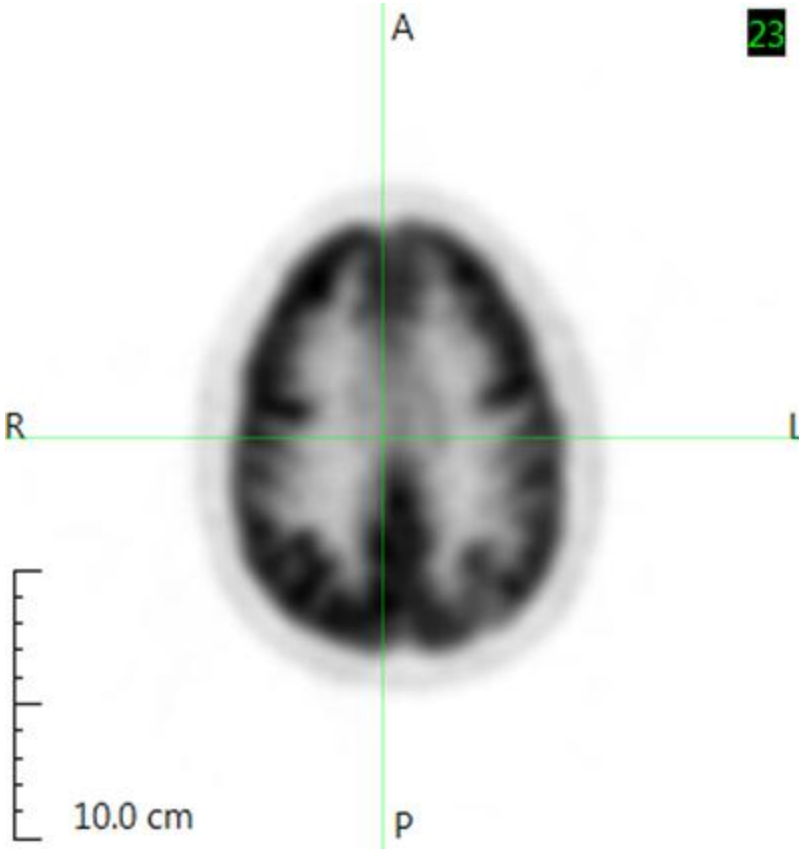
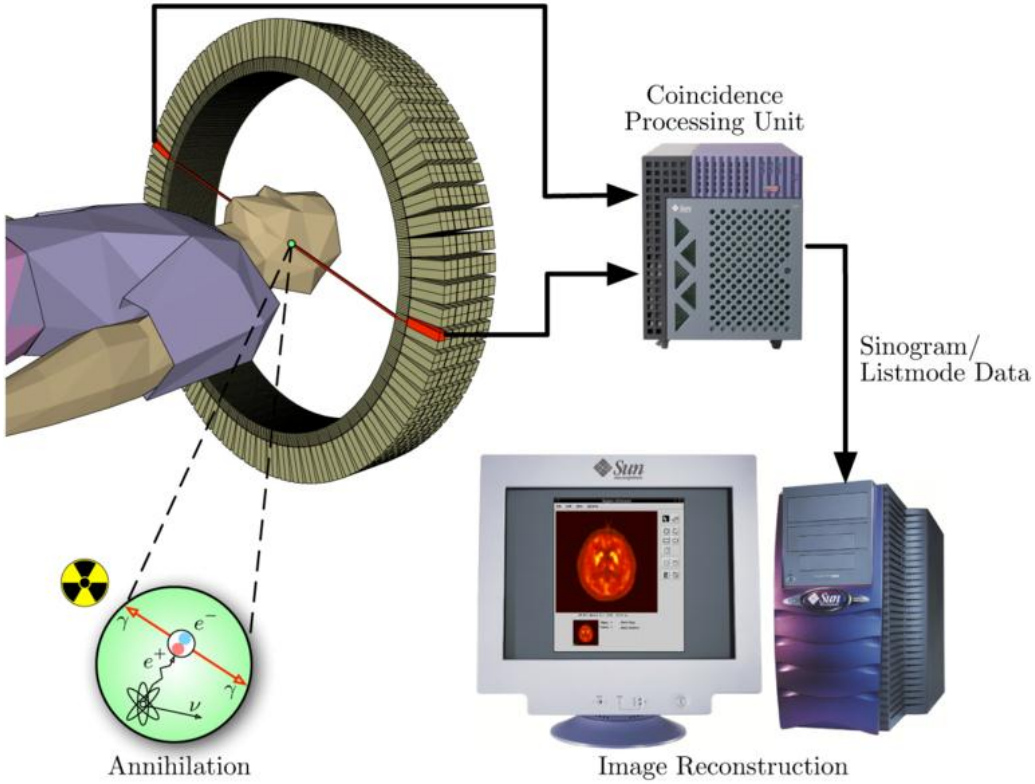

A
23
R
L
10.0 cm
P

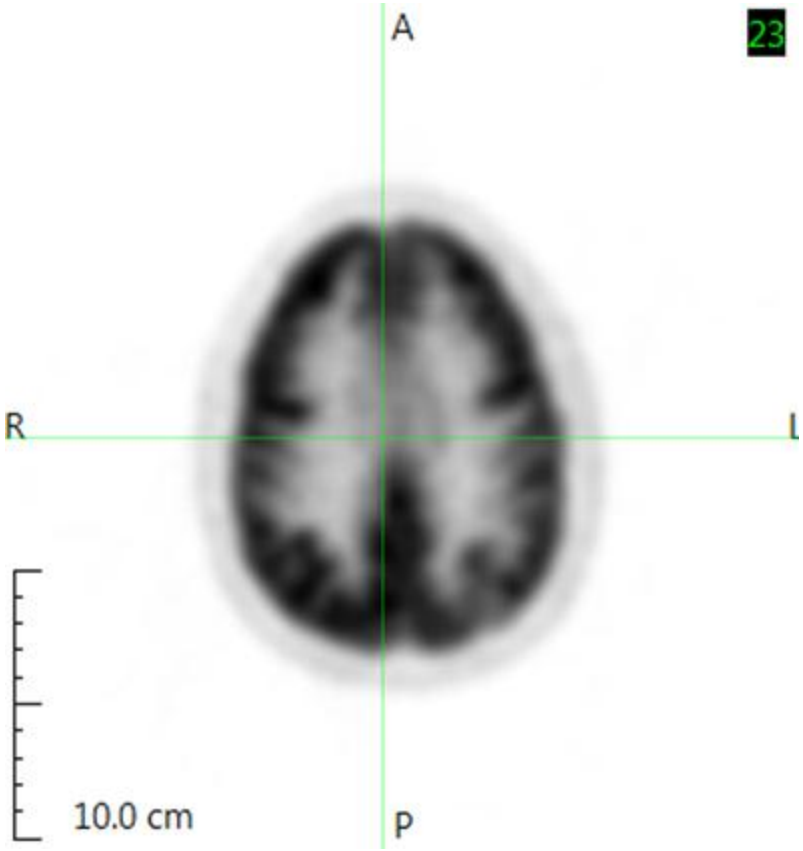
PET (POSITRON EMISSION TOMOGRAPHY)

late **1950s**: Concept of PET by David Kuhl

1961: Prototype by James Robertson (the 'head shrinker).



Radionuclide tracer (^{18}FDG) injected → positrons → strikes nearby electron (annihilating both) → gamma rays → sensed by detectors.


A
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R
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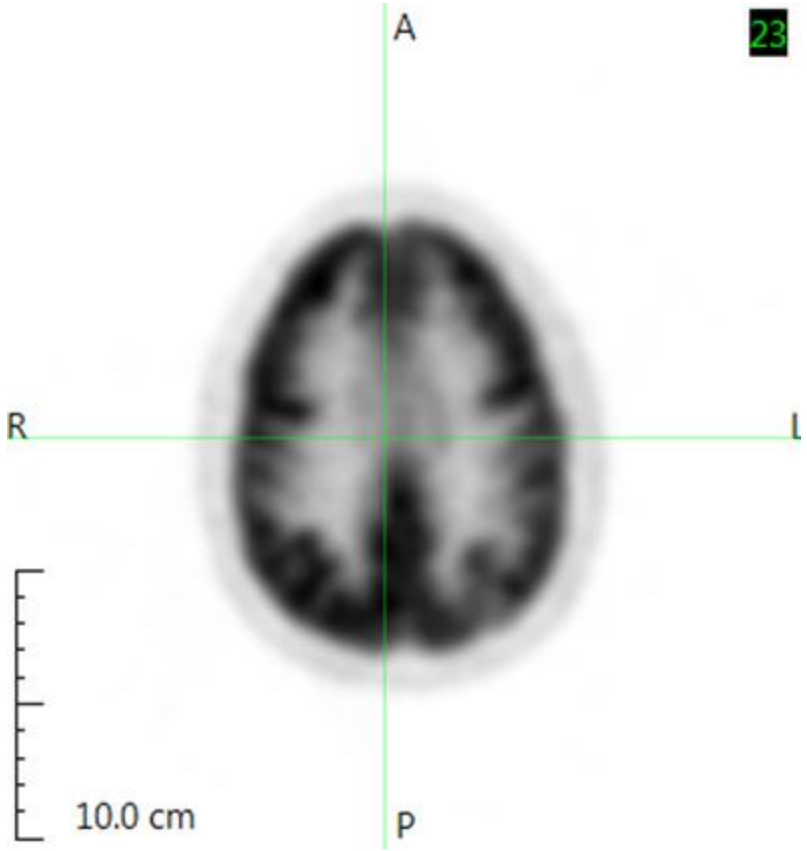
10.0 cm
P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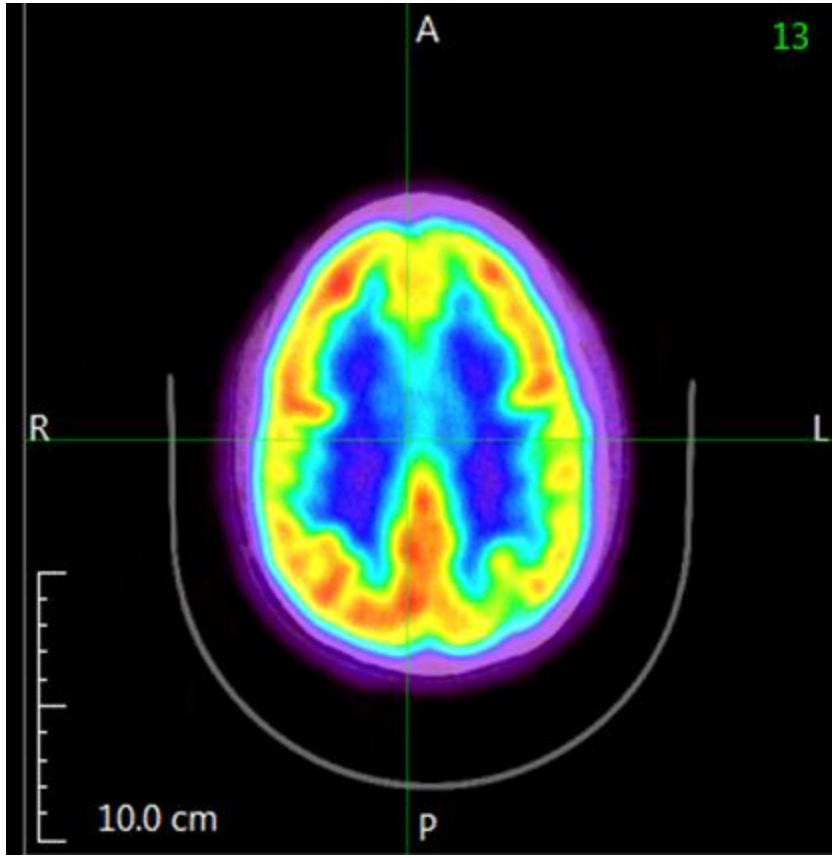
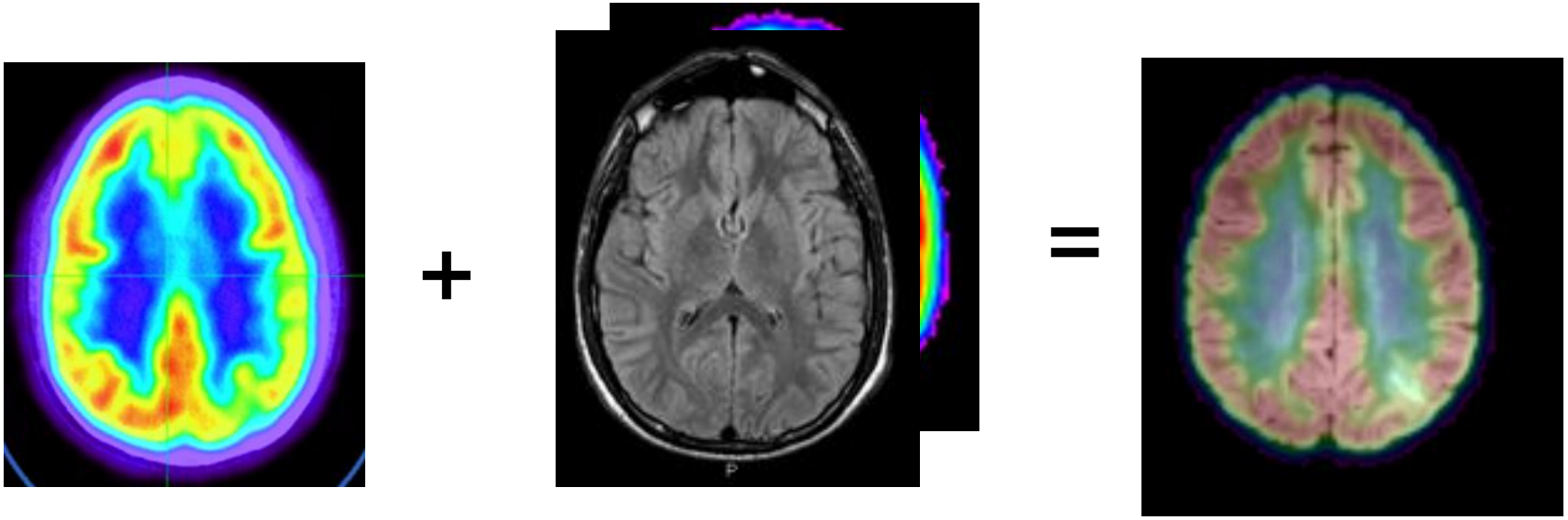
10.0 cm
P


A
13
R
L
10.0 cm
P

CO-REGISTRATION



PCOM: PET Co-registered to MRI

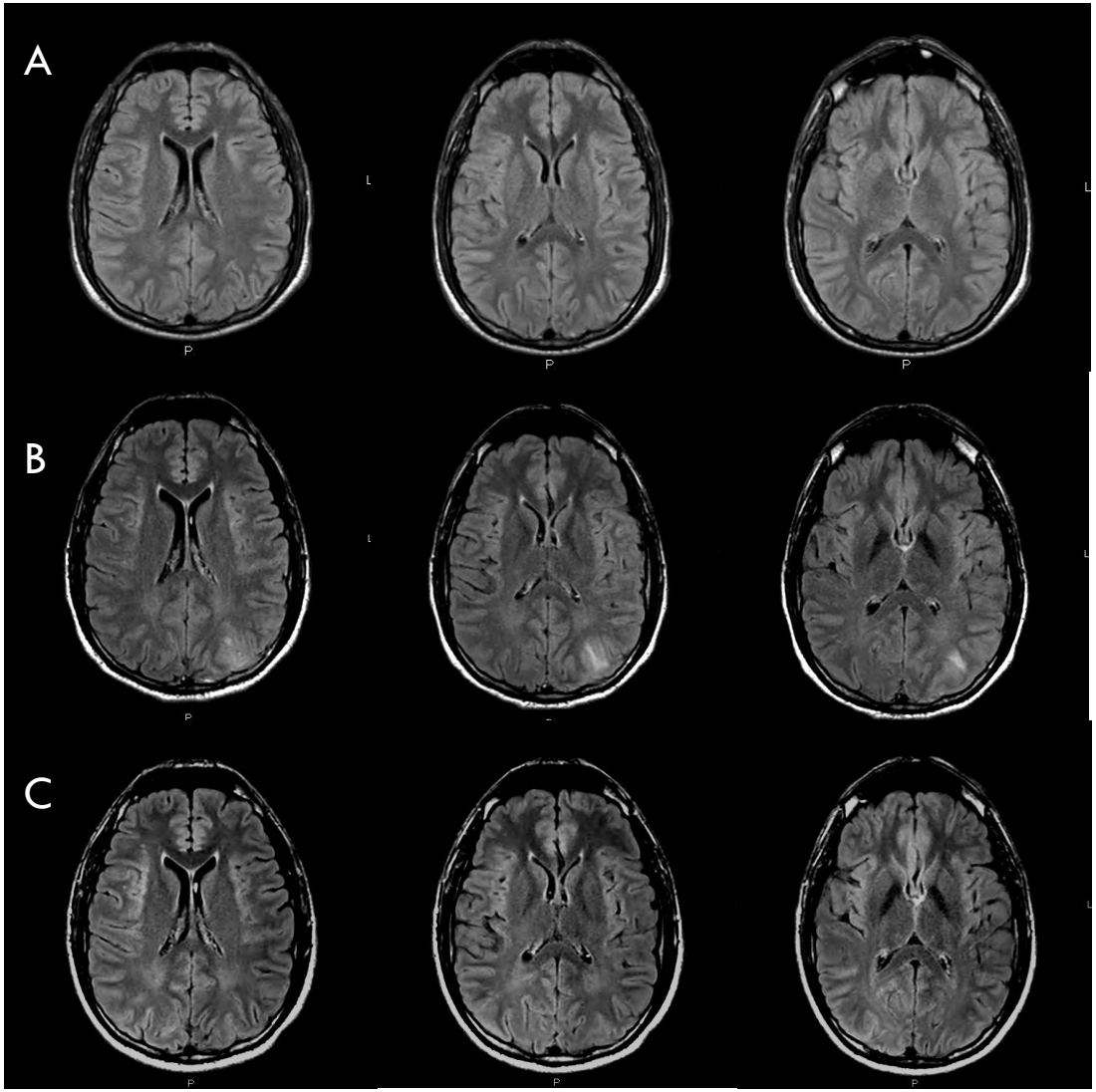
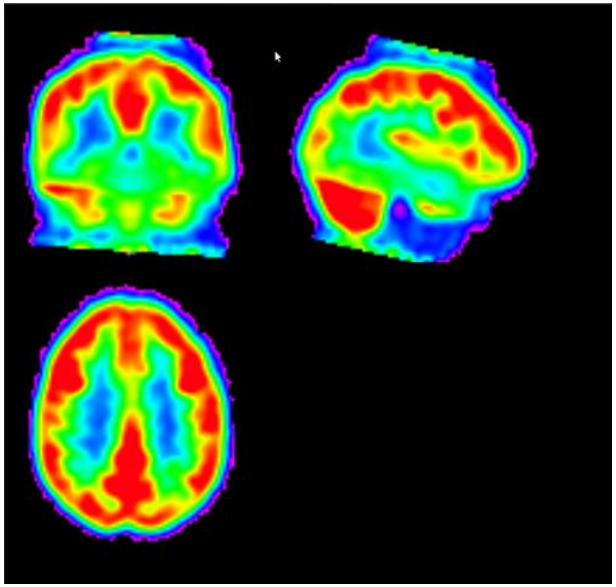
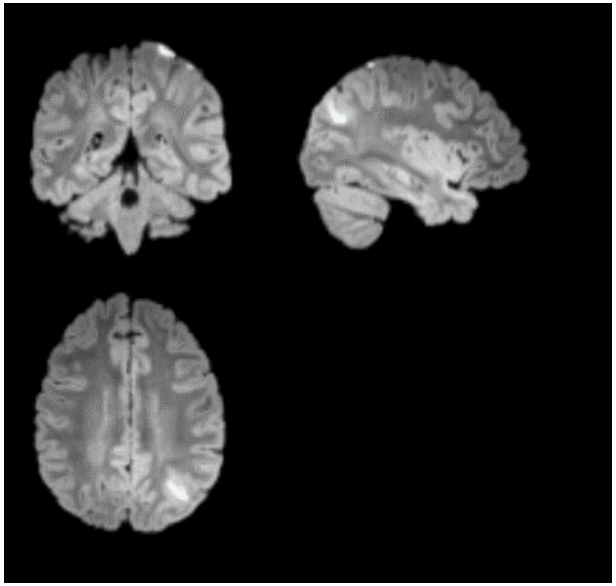
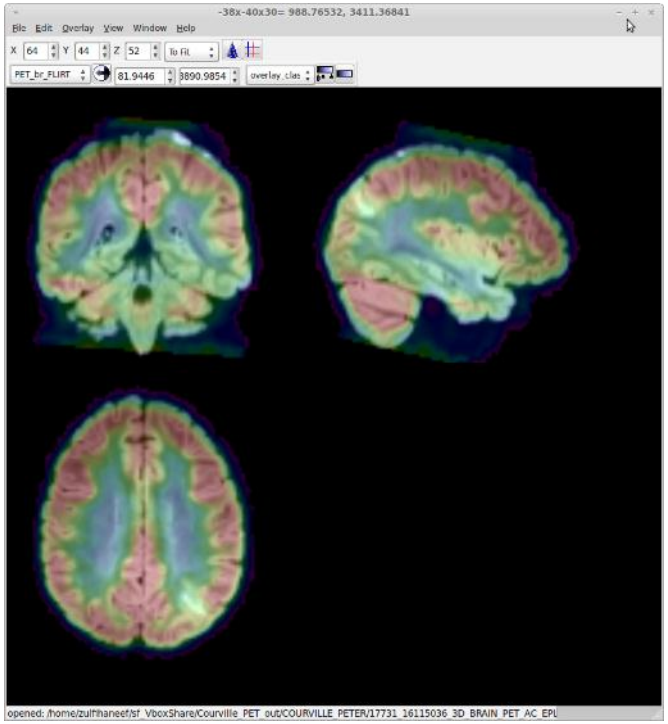


Image courtesy: Shirish Satpute



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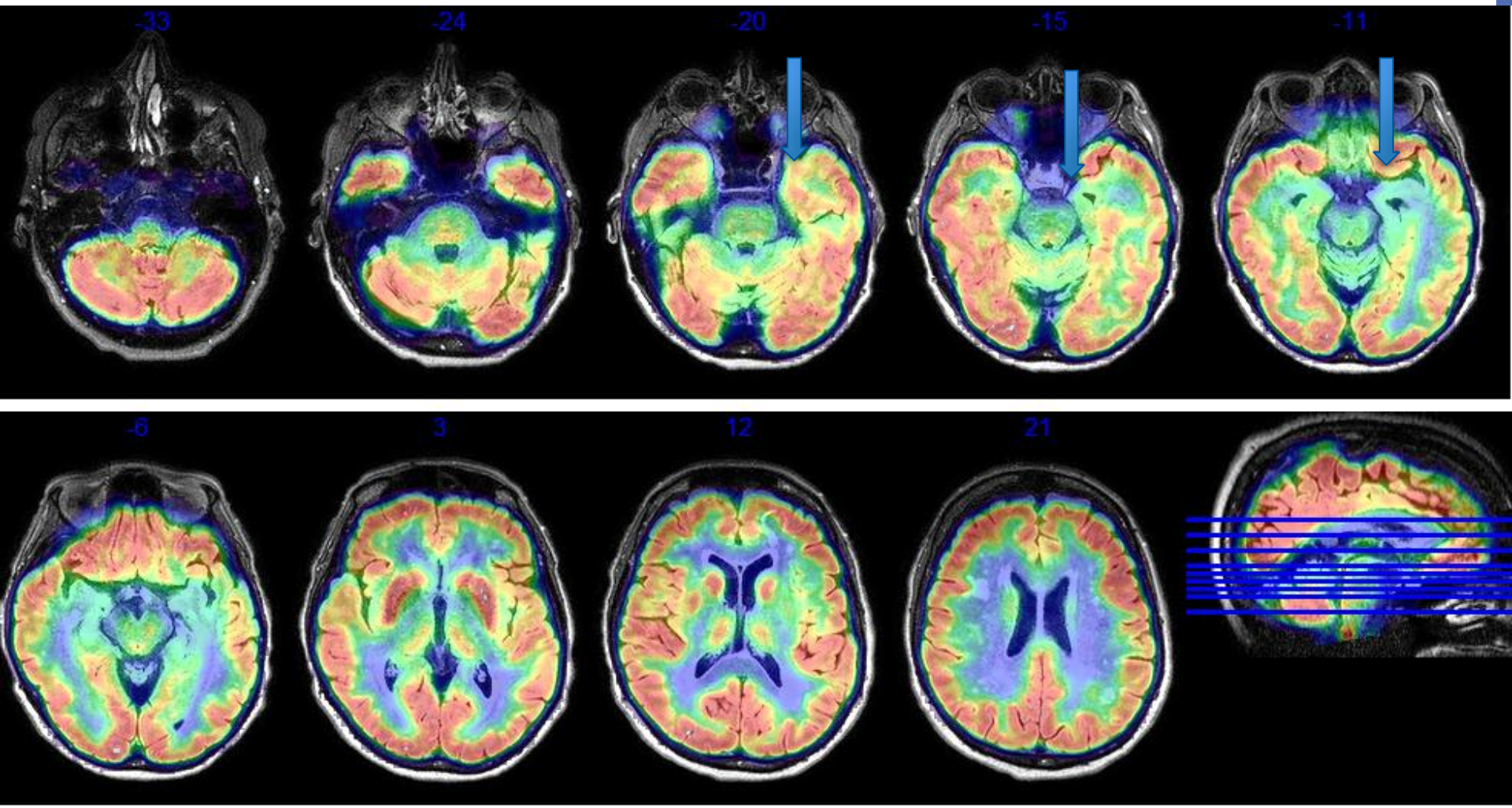
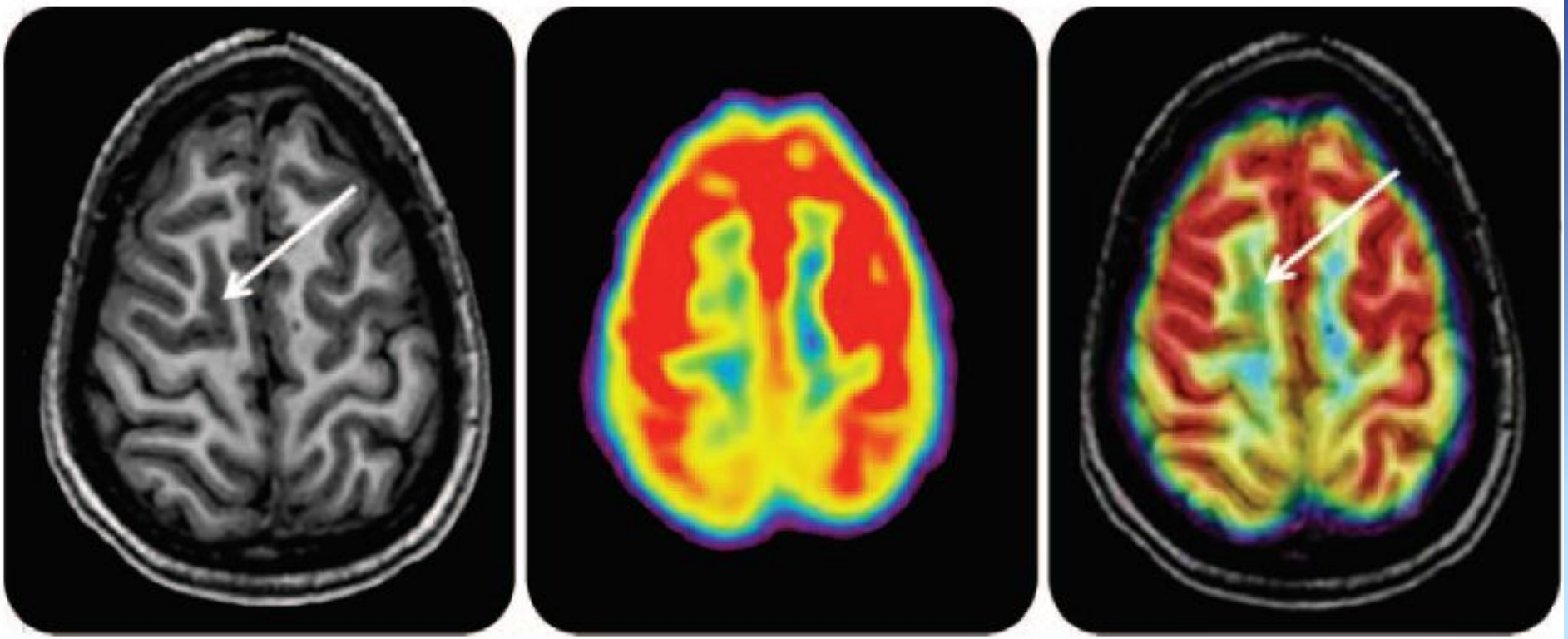
AXIAL PET-MRI FUSION





PET-MRI coregistration

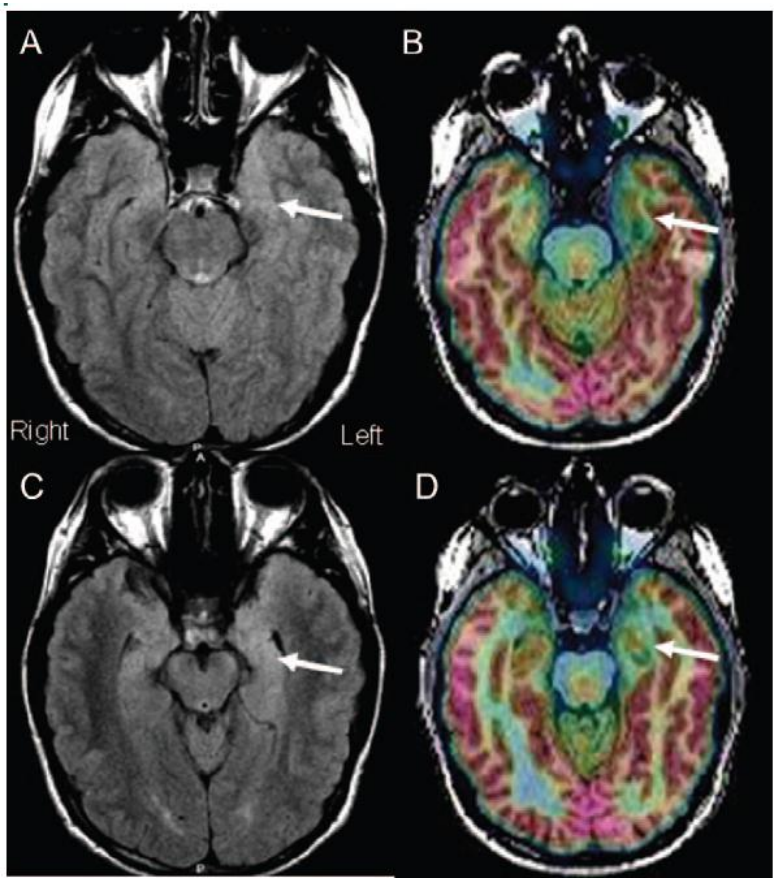
FDG-PET improves surgical outcome in negative MRI Taylor-type focal cortical dysplasias: *Chassoux et al, Neurology 2010*

PET

- In plane resolution of **2-3 mm**
- **Ictal PET:** Logistically difficult due to short $t_{1/2}$ of ^{18}FDG **(110 minutes)**. Also, long duration of glucose uptake (several minutes) makes ictal studies a complicated mix of inter-ictal, ictal and post-ictal states
- Sensitivity for MTLE: 80-90%. Correctly lateralizes in 80% cases with a normal MRI (Won 1999).

FDG-PET/MRI COREGISTRATION IMPROVES DETECTION OF CORTICAL DYSPLASIA (CD)

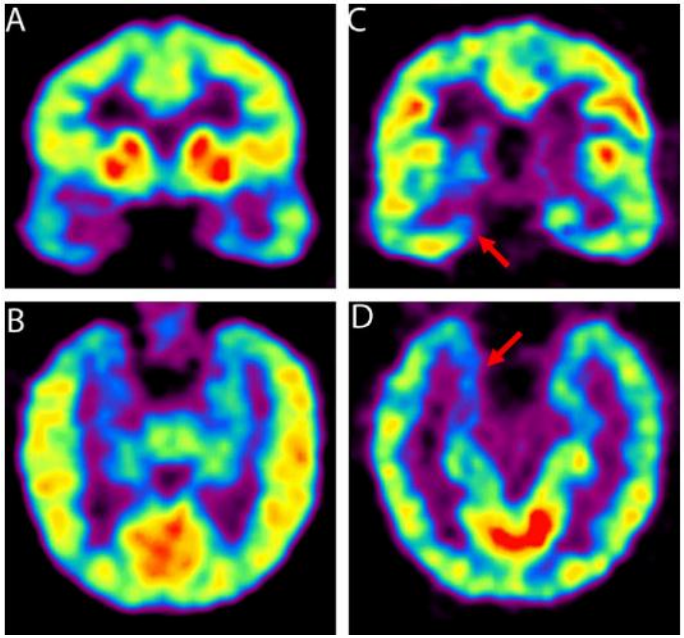
- CD is difficult to treat as MRI may be normal.
- With PET/MRI co-registration, more CD was detected, and fewer cases required intracranial electrodes.
- Type I CD
  - Abnormal outside MRI in 15%
  - Abnormal MRI in 60% by epilepsy neuroradiologist
  - Abnormal FDG-PET scans in 70%
- Colored images improve diagnostic accuracy



FDG-PET/MRI coregistration improves detection of cortical dysplasia in patients with epilepsy. ***Neurology 2008***

N. Salamon, MD, J. Kung, BA, S.J. Shaw, MD, J. Koo, MD, S. Koh, MD, J.Y. Wu, MD, J.T. Lerner, MD, R. Sankar, MD, PhD, W.D. Shields, MD, J. Engel, Jr., MD, PhD, I. Fried, MD, PhD, H. Miyata, MD, PhD, W.H. Yong, MD, H.V. Vinters, MD, G.W. Mathern, MD

NEURO-RECEPTOR PET



- [11C]flumazenil (FMZ):
  - Lower GABA receptor binding in epileptic focus,
  - distinguishes patients with frequent seizures.
  - More accurate for extra-TLE?
  - Short $t_{1/2}$ (20 min) hampers clinical use
- Serotonin receptors (5-HT1A): [18F]MPPF
  - Serotonin widely distributed in limbic structures and thought to inhibit seizures
  - Reduced ipsi-lesional binding to hippocampus, temporal pole, insula and temporal neocortex.
- a-[11C]methyl-Ltryptophan (a-MTrp)
  - Useful for Tuberous sclerosis
- opioid-based ligands has shown some promise
  - delta-selective opioid receptor ligand [11C]methylnaltrindole also showed increased receptor availability in the epileptogenic temporal lobe
- Dopamine receptor ([18F]Fallypride)
  - Dopaminergic system may be part of the endogenous anticonvulsant mechanism
  - D2/D3-receptor binding was reduced at the pole and the lateral aspects of the epileptogenic temporal lobe,
  - no change in hippocampal binding although all patients had hippocampal atrophy

SPECT/ SISCOM

CASE

42 year old man with seizures since age 13.

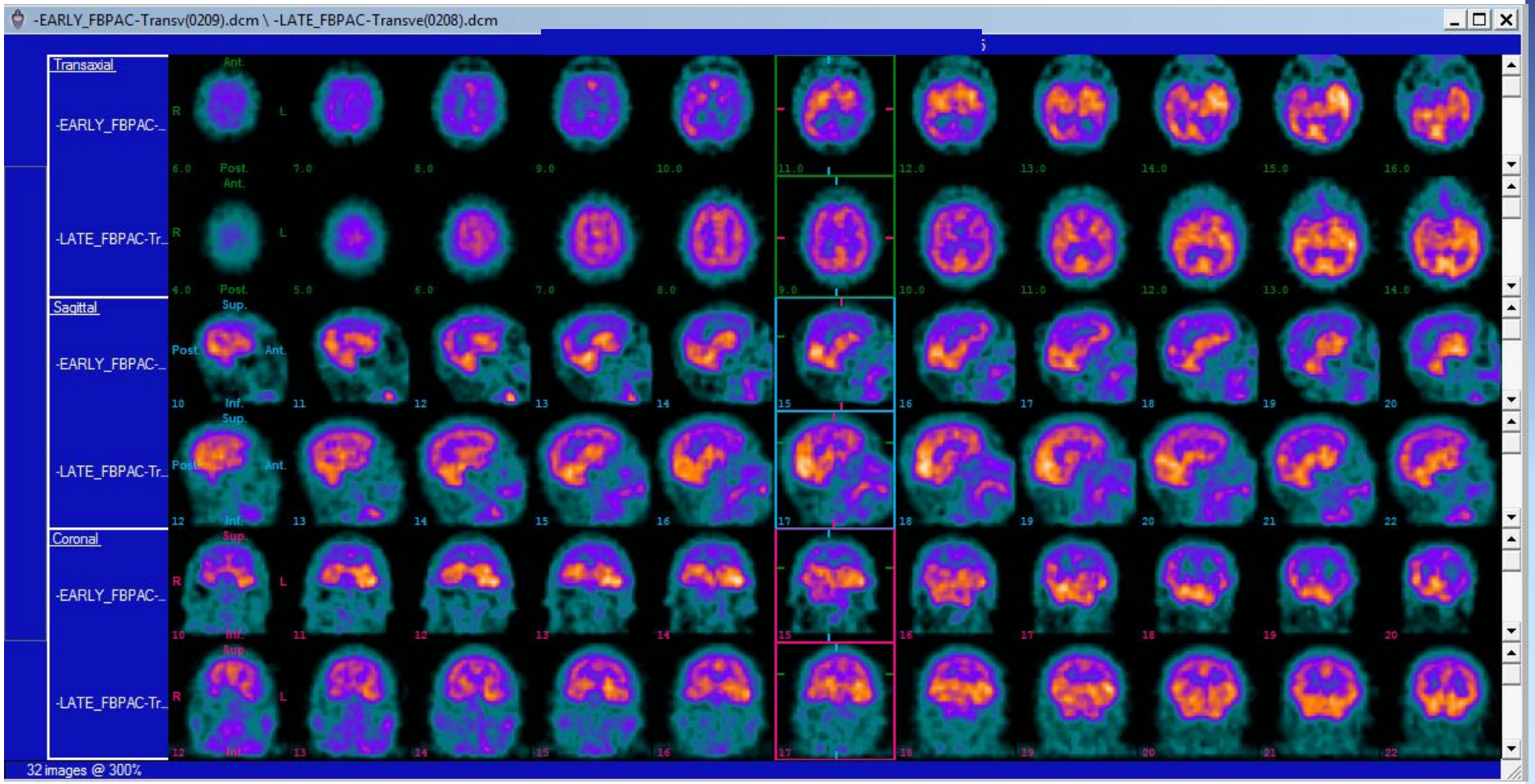
- Aura: feeling unwell with chest discomfort.
- Seizures: Behavioral arrest, automatisms with L hand with secondary generalization.

Failed AED and considered for surgery.

EEG: Left temporal sharps > right temporal.

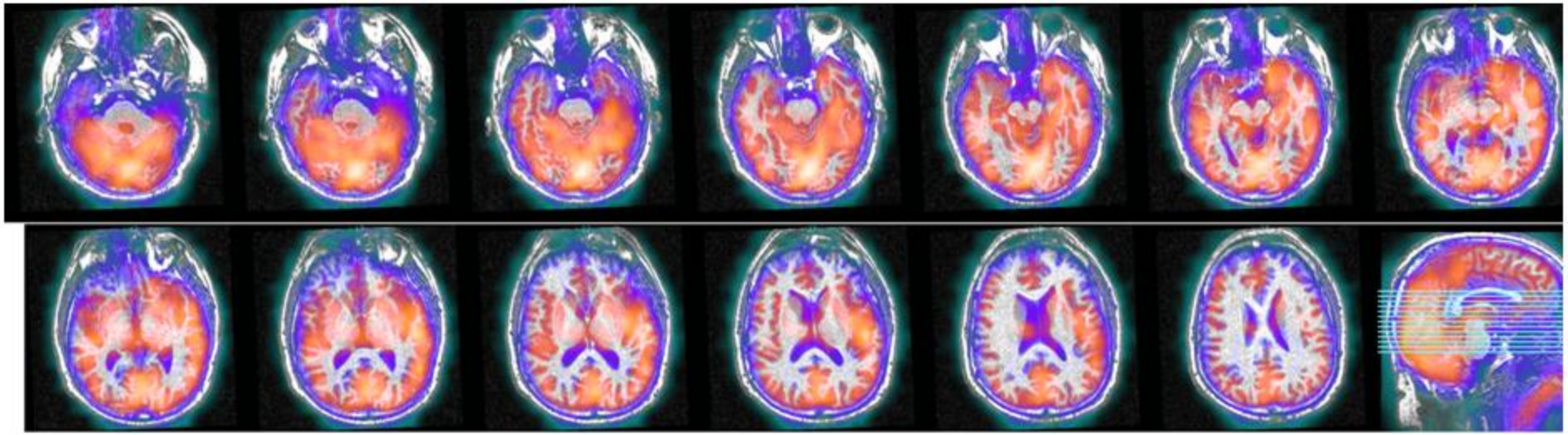
Unclear seizure onset, appears left temporo-parietal

MRI/ PET: Non-lateralized

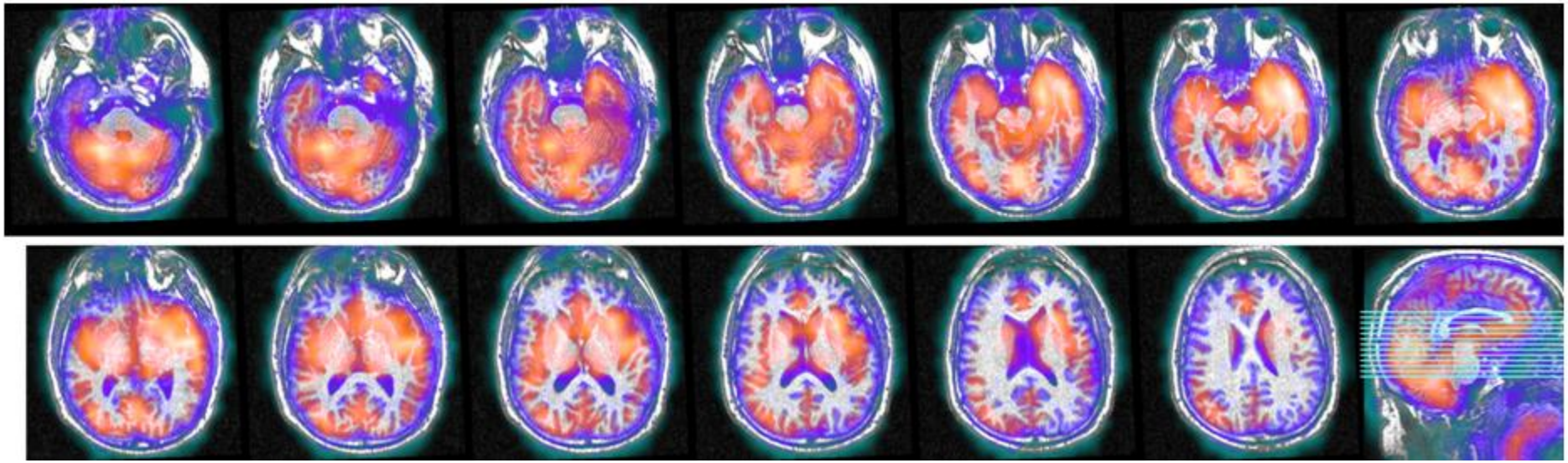

-EARLY_FBPAC-Transv(0209).dcm \ -LATE_FBPAC-Transve(0208).dcm
Transaxial
-EARLY_FBPAC-...
-LATE_FBPAC-Tr...
Sagittal
-EARLY_FBPAC-...
-LATE_FBPAC-Tr...
Coronal
-EARLY_FBPAC-...
-LATE_FBPAC-Tr...
32 images @ 300%

Ictal SPECT

INTER-ICTAL SPECT CO-REGISTERED TO MRI



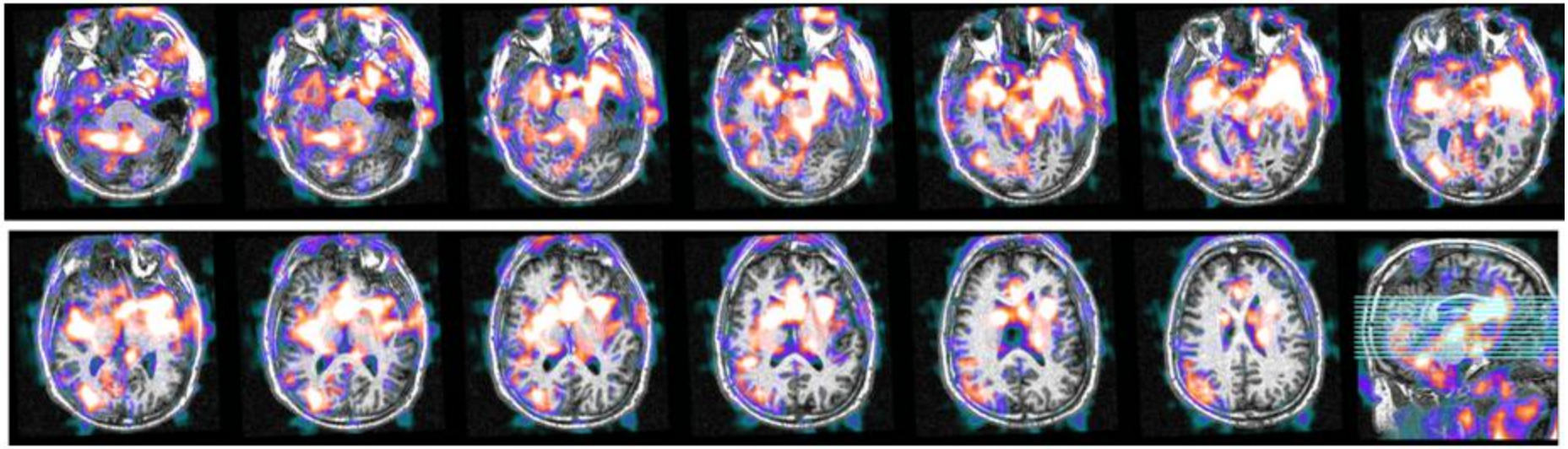
ICTAL SPECT CO-REGISTERED TO MRI



ICTAL-INTERICTAL_SUBTRACTION

SISCOM:

SUBTRACTION ICTAL SPECT CO-REGISTERED TO MRI



SPECT:
SINGLE PHOTON EMISSION COMPUTED TOMOGRAPHY

- Ictal study, ideally injected within 30-45 seconds of ictal onset
- Delay in injection of radio-ligand (>45 sec from seizure onset) can cause
  - a) more involvement of propagation pathways (these pathways not needed to be resected)
  - b) post-ictal switch phenomenon which can result in false localization/ lateralization.
- $t_{1/2}$ of 6 hours. Need to use tracer within this time.
- iodine-123- and technetium-99m-labeled ligands are available

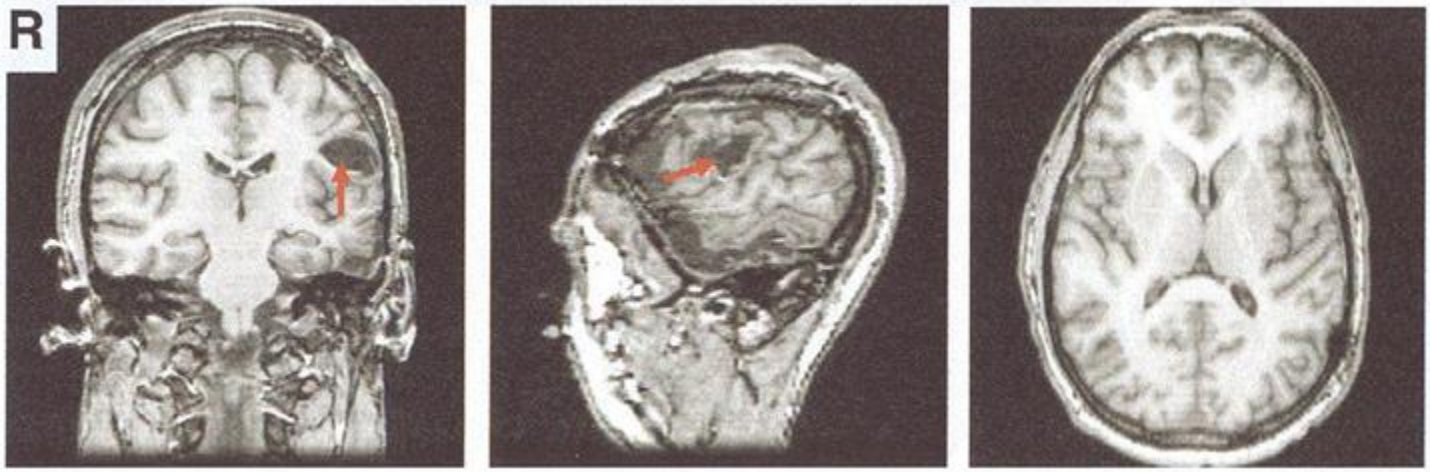
MEG/ MSI

CASE

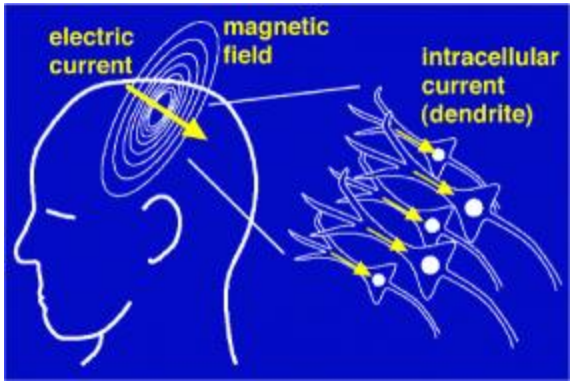
22 y/o RH man with post-trauma epilepsy following fall from 2 stories through skylight on to concrete, sustaining right parietal skull fracture extending to temporal fossa and left F-P subdural / left T-P intraparenchymal bleeds.

Seizures

- Aura of right-sided sensory changes (arm), right side of head
- Difficulty speaking, then weird feeling in back of throat, moving up neck
- Progress to stiffening and shaking of right arm, head version to the right and then generalization.
- Auras occur 3-4 times per week.



MEG: MAGENTO-ENCEPHALO-GRAM

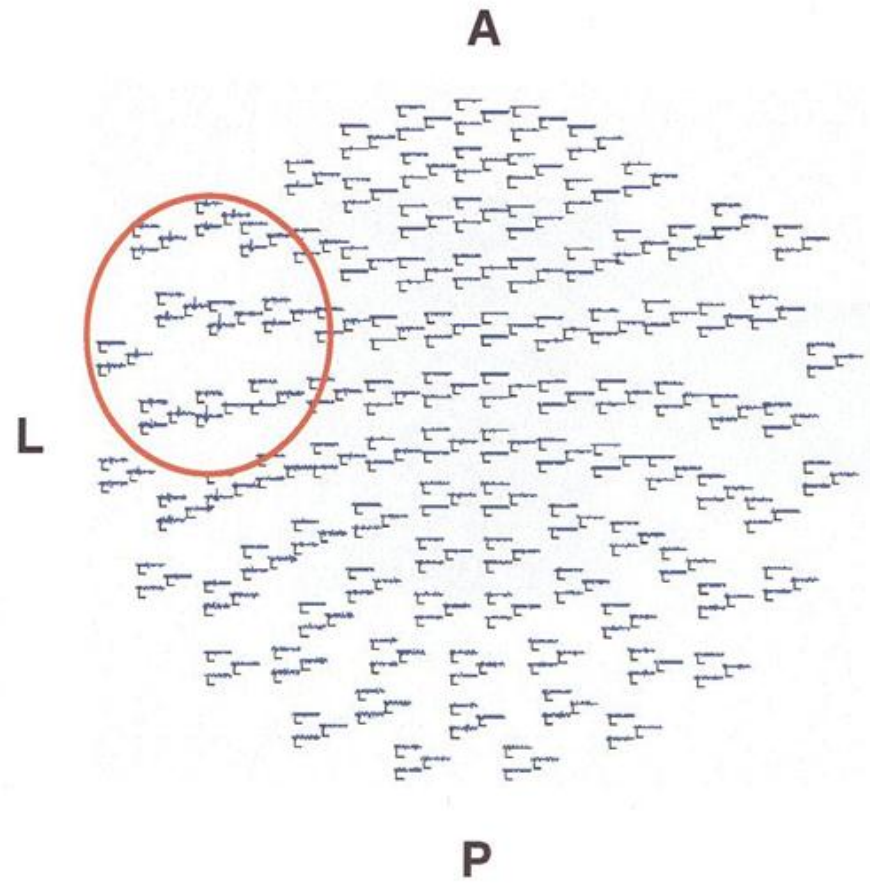


- Cortical activity: 10 fT (10^{-15})
- Alpha rhythm: 10^{3} fT
- Earth: 50 x 10^{3} nT (10^{-9})
- MRI: 1.5-3 T

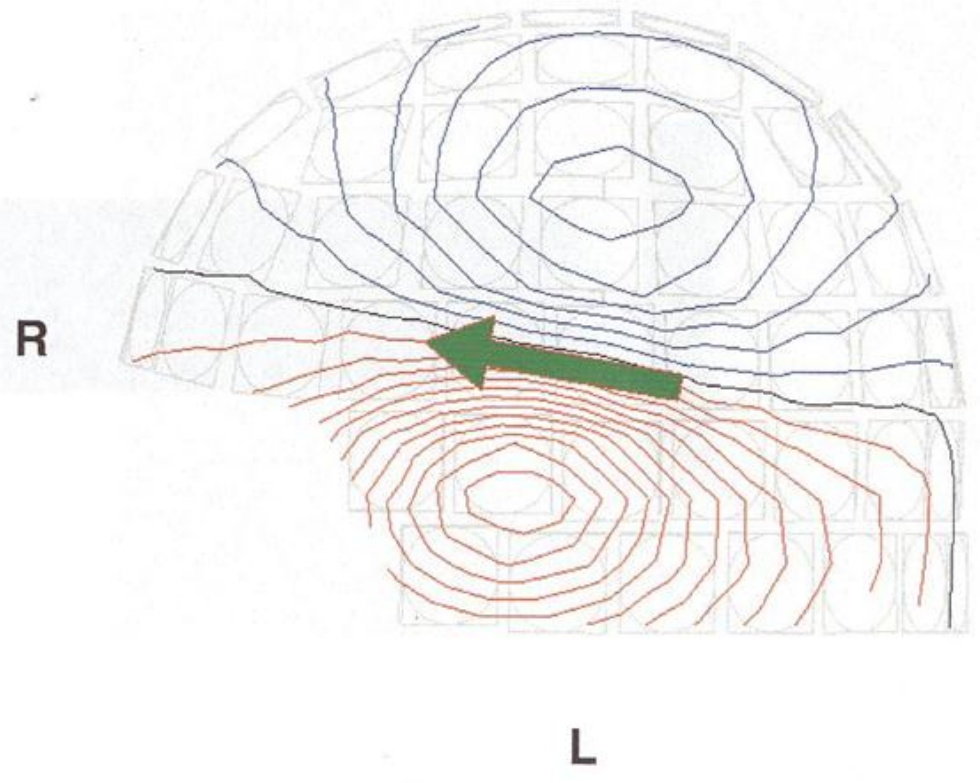
1964: Extremely sensitive magnetometers based on superconducting loops developed in Ford Labs (Robert **Jaklevic**): SQUID (superconducting quantum interference devices) detectors

1968: David **Cohen** (U. Illinois) measures MEG signals

1980s: Multiple sensor arrays (about 300) made by MEG manufacturers.



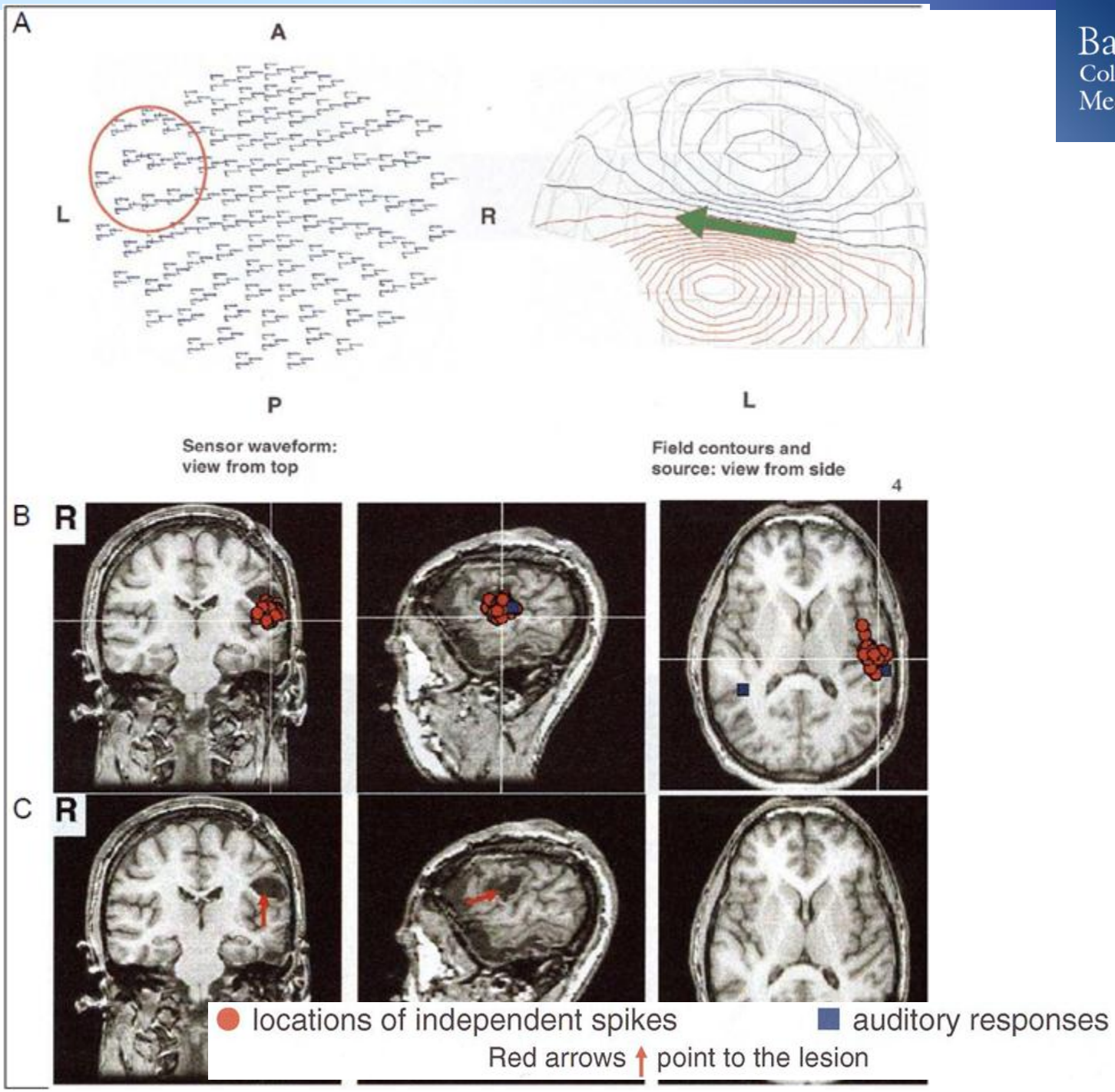
Sensor waveform:
view from top



Field contours and
source: view from side

Baylor College of Medicine

MEG + MRI =
MSI (MAGNETIC SOURCE IMAGING)

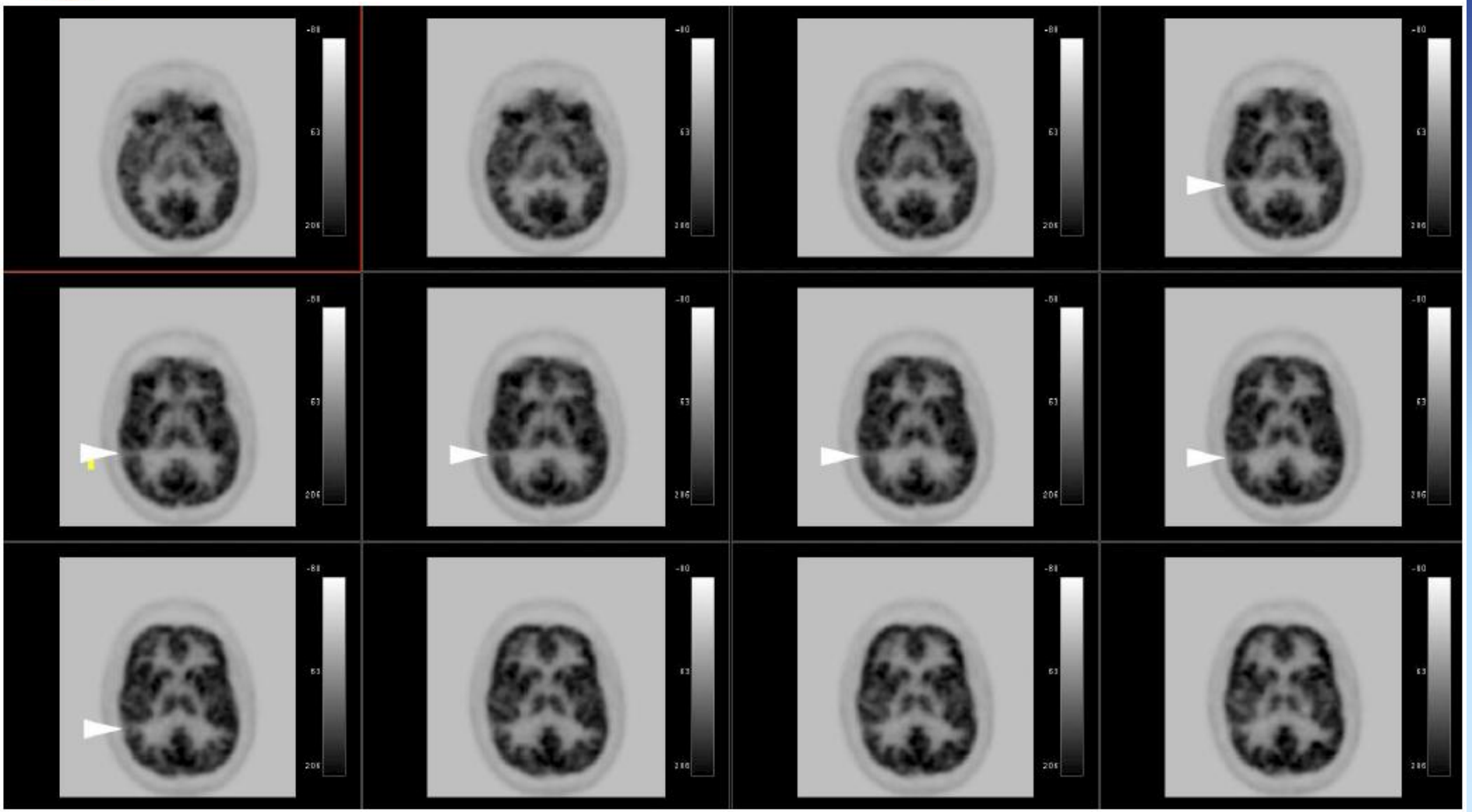


MEG/ MSI

MEG	EEG
Magnetic signals	Electrical signals
Skull/ scalp is “magnetically tranparent”	Skull/ scalp attenuates EEG signals
Purer cortical signal detection (Better for cortical sources)	Mix of superficial and deeper signals (Better for deeper sources)

CASE:
MULTI-MODAL IMAGING (MEG/ SPECT/ PET)

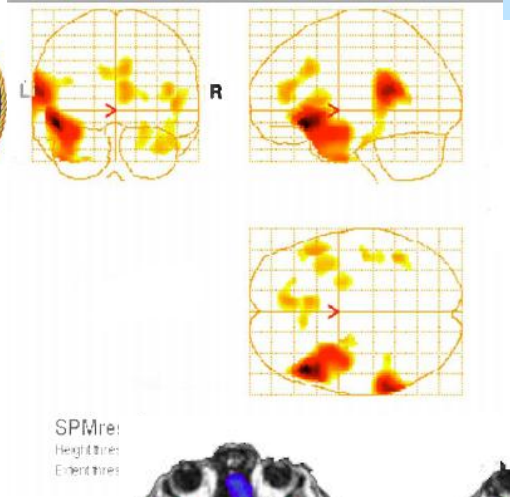
17-y/o with intractable epilepsy and normal EEG & MRI.

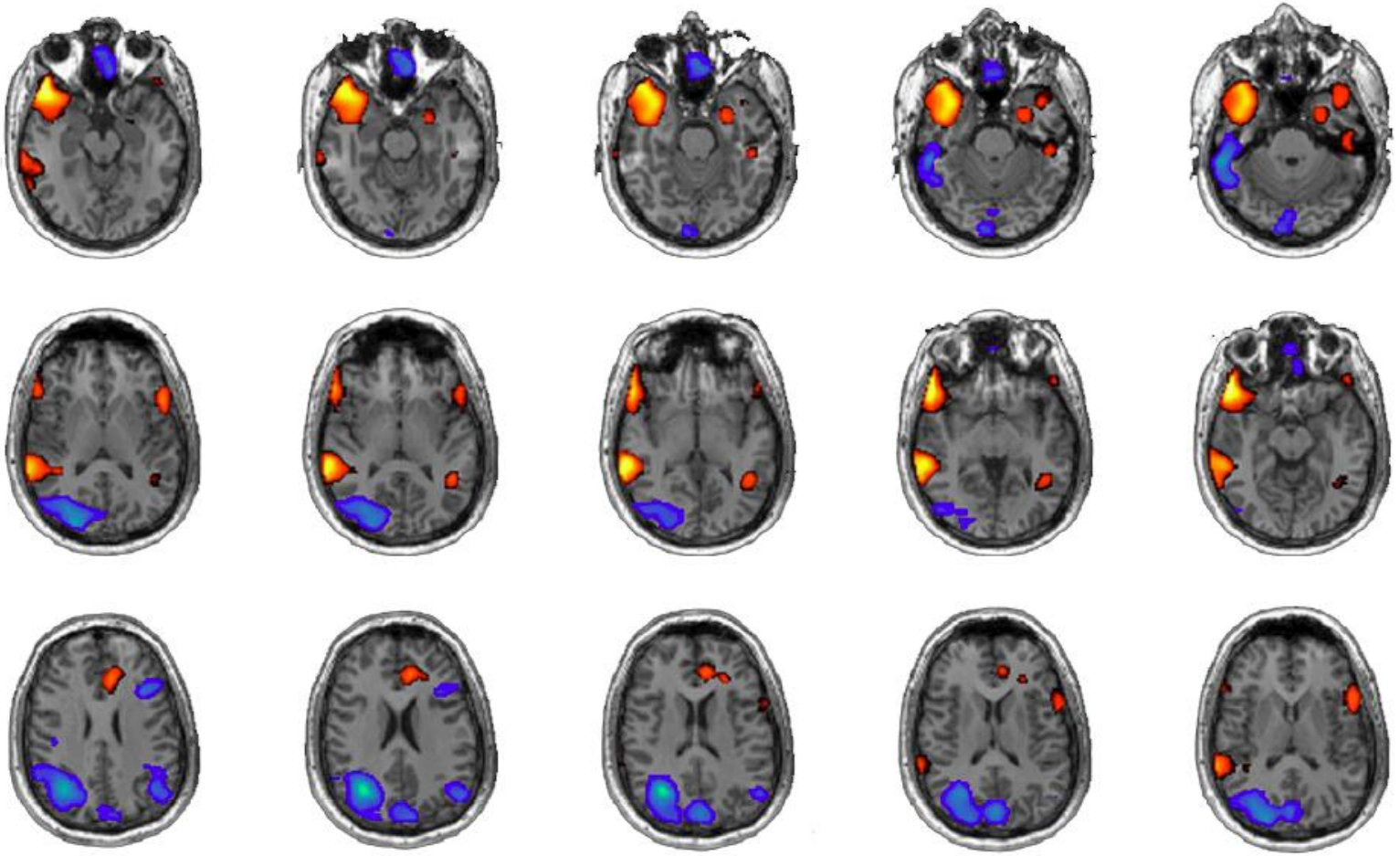


PET shows relative focal hypometabolism in the right lateral temporal (white arrows).

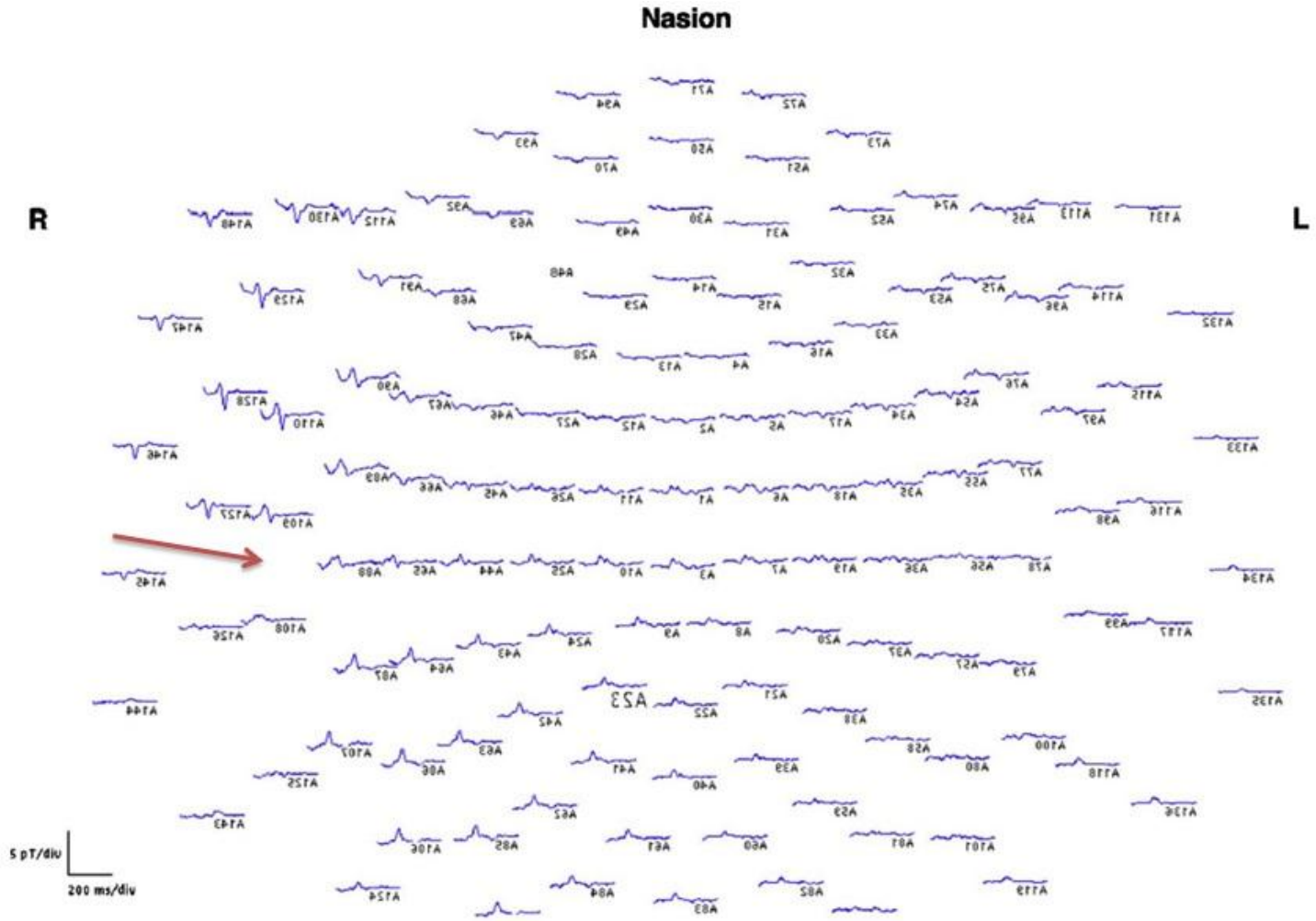
The role of FDG-PET, ictal SPECT, and MEG in the epilepsy surgery evaluation.
Knowlton, Epilepsy & Behavior 8 (2006)

SISCOM





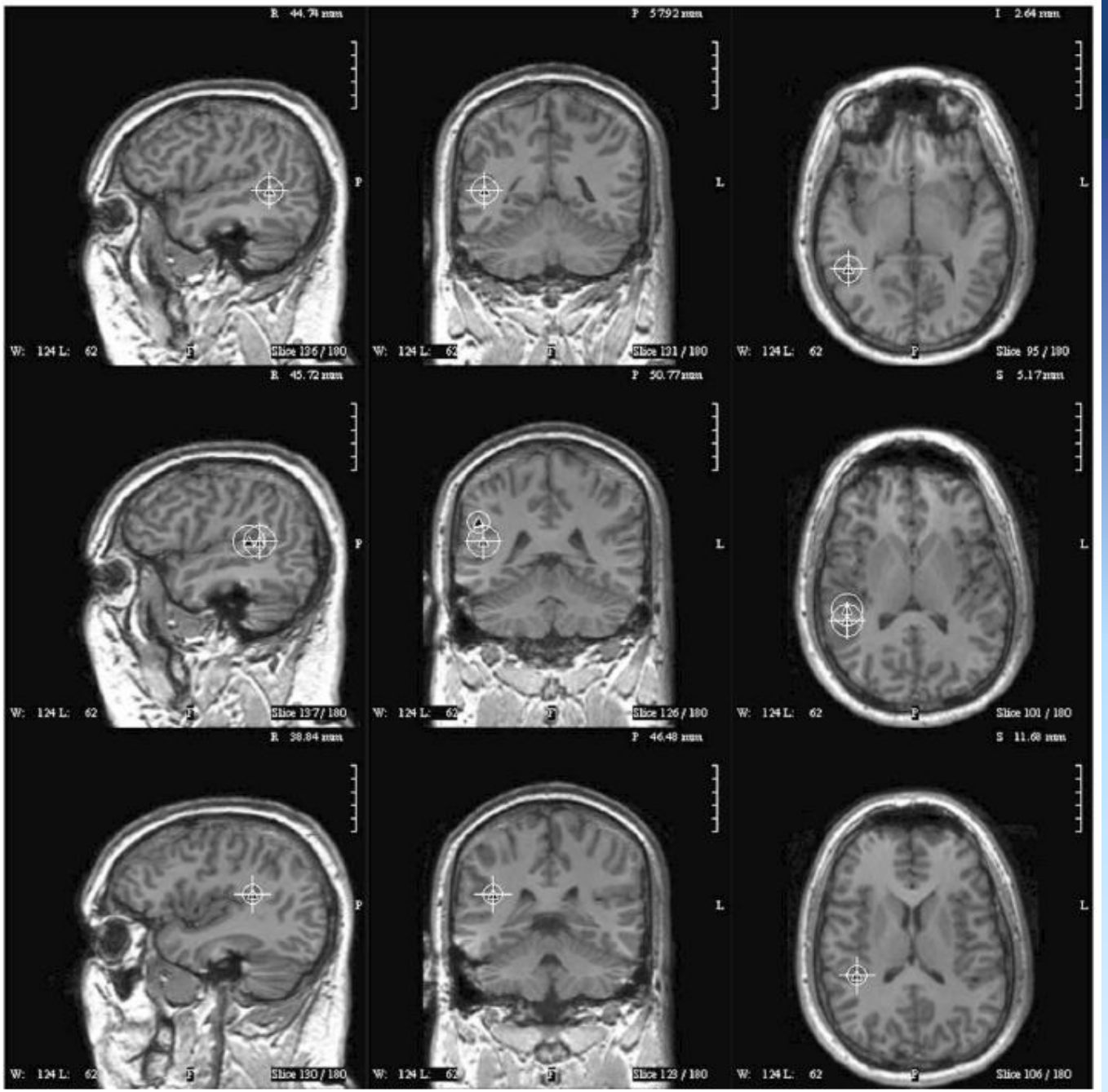
The role of FDG-PET, ictal SPECT, and MEG in the epilepsy surgery evaluation.
Knowlton, Epilepsy & Behavior 8 (2006)



MEG: 148 magnetometers show sharp wave over the lateral right hemisphere.

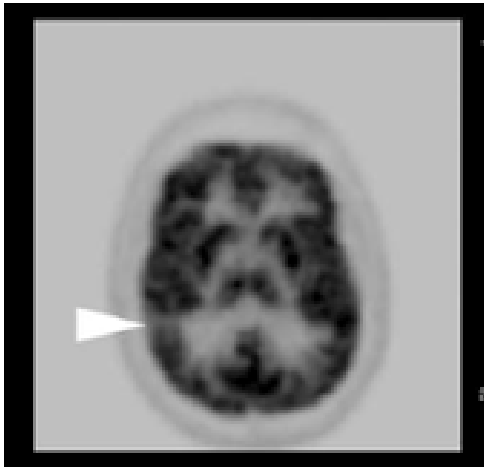
The role of FDG-PET, ictal SPECT, and MEG in the epilepsy surgery evaluation.
Knowlton, Epilepsy & Behavior 8 (2006)

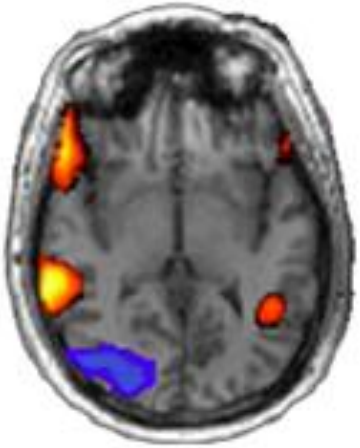
MEG + MRI =
MSI (MAGNETIC SOURCE IMAGING)

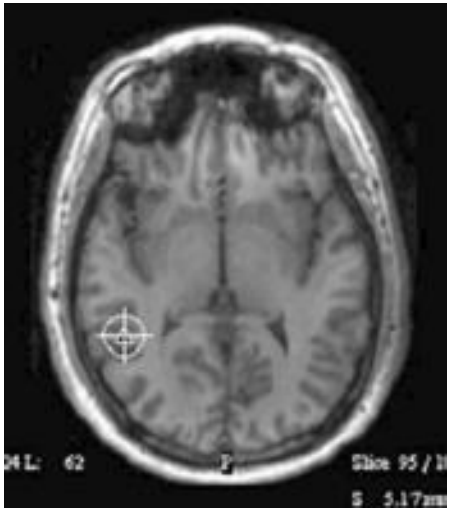


The role of FDG-PET, ictal SPECT, and MEG in the epilepsy surgery evaluation.
Knowlton, Epilepsy & Behavior 8 (2006)

MULTI-MODAL IMAGING







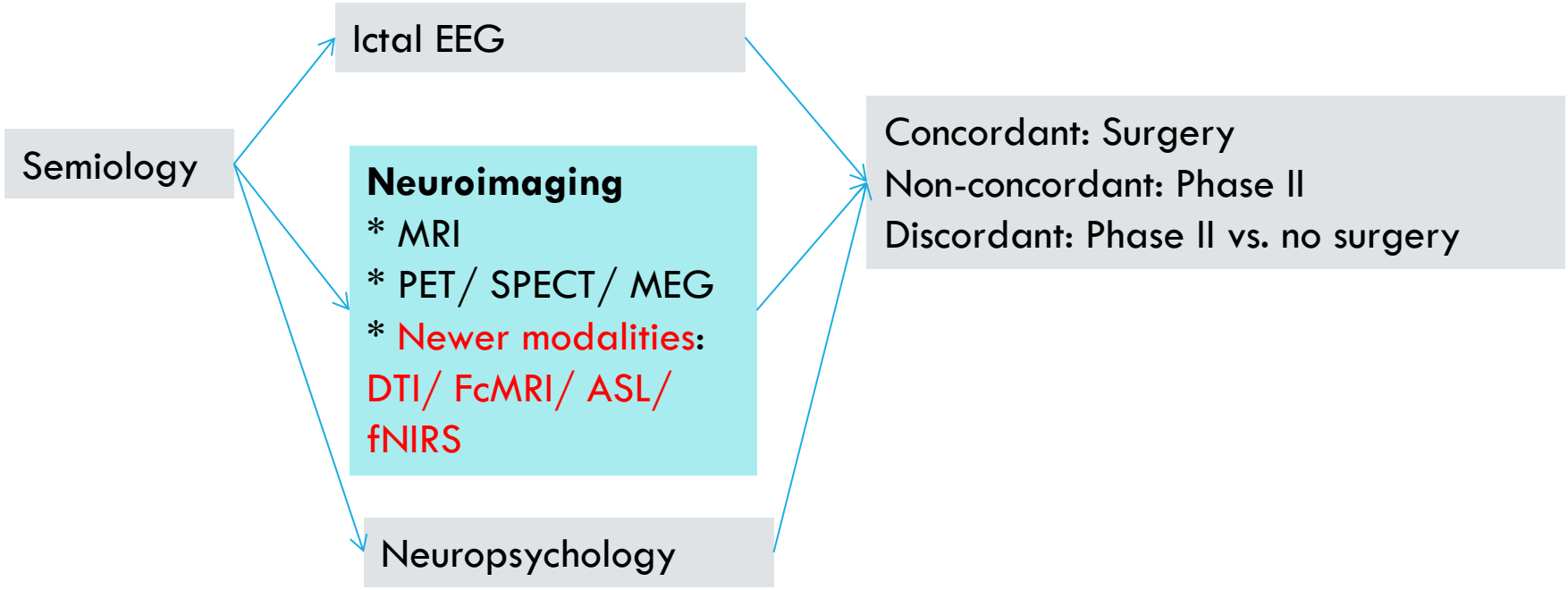
The role of FDG-PET, ictal SPECT, and MEG in the epilepsy surgery evaluation.
Knowlton, Epilepsy & Behavior 8 (2006)
A systematic review on MEG and its use in the presurgical evaluation of localization-related epilepsy:
M. Laua, D. Yama, J.G. Burneoa, b,

UTILITY OF MULTI-MODAL IMAGING IN EPILEPSY SURGERY

	Sensitivity	Specificity
Interictal SPECT	70%	36%
Ictal SPECT (30 s injection)	90%	77%
Interictal PET	84%	86%
MEG	84%	52%

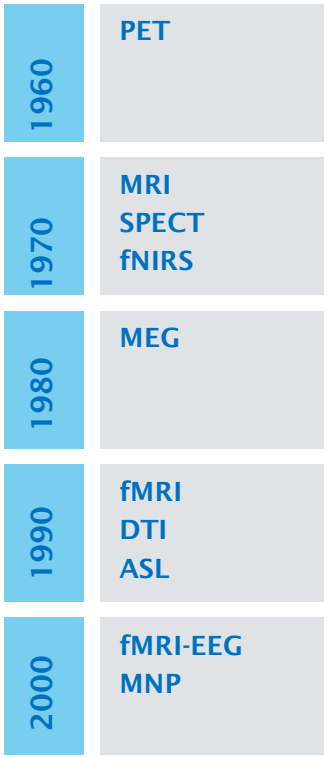
NEWER MODALITIES: DTI/ FCMRI/ ASL/ FNIRS

THE CLINICAL APPROACH



NEURO-IMAGING

1. MRI
2. PET & Co-registration
3. SPECT
4. MEG/ MSI
5. fMRI
6. fMRI-EEG
7. DTI
8. fcMRI
9. fNIRS
10. ASL



FMRI

CASE

26 y/o Chinese woman with seizures since age 10 months.

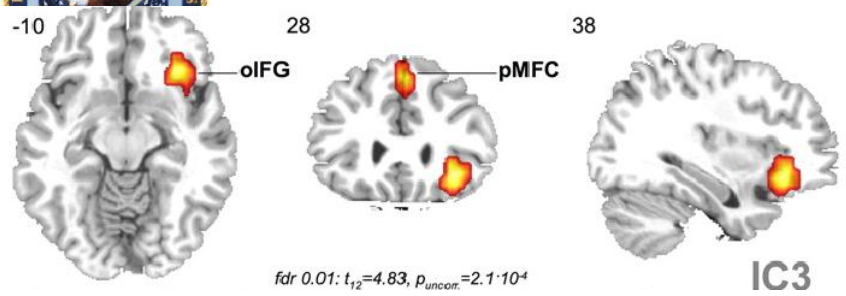
- Aura: Uncomfortable, "weird feeling“
- Ictus: Impaired awareness, staring, oral automatisms, and right arm dystonia.

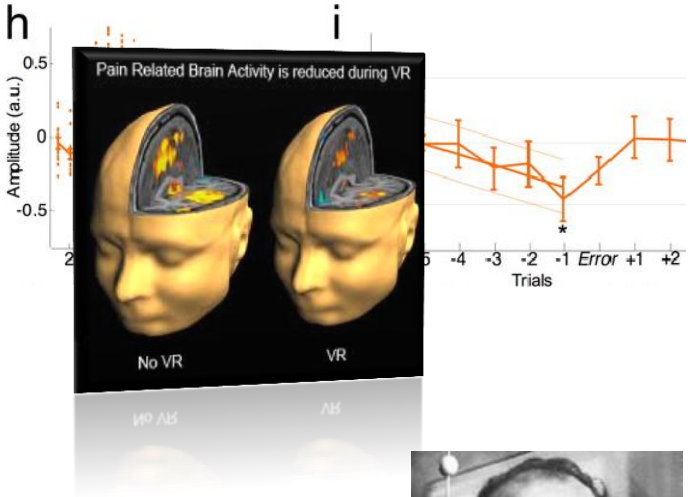
PMH of febrile seizures.

MRI: Left Mesial Temporal Sclerosis (MTS)

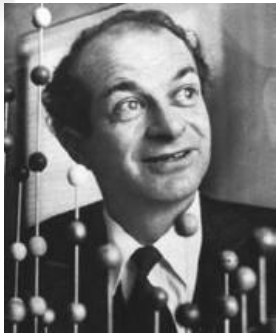
EEG: Left sided seizures,

Planned L Anterior Temporal Lobectomy: concern for language





fMRI (functional MRI)

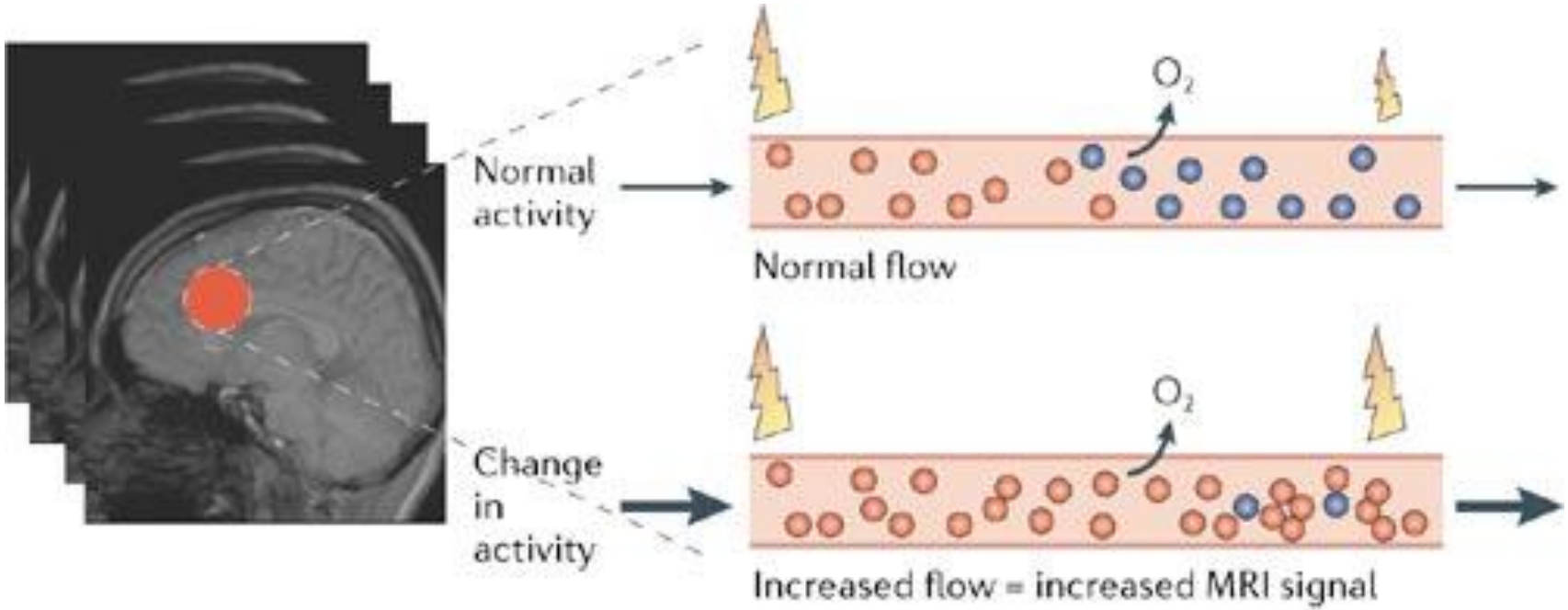


1936: Linus **Pauling** and Charles **Coryell** show that O2 rich blood (Hb) was weakly repelled by magnetic fields, while O2 depleted blood (dHb) was attracted to a magnetic field.

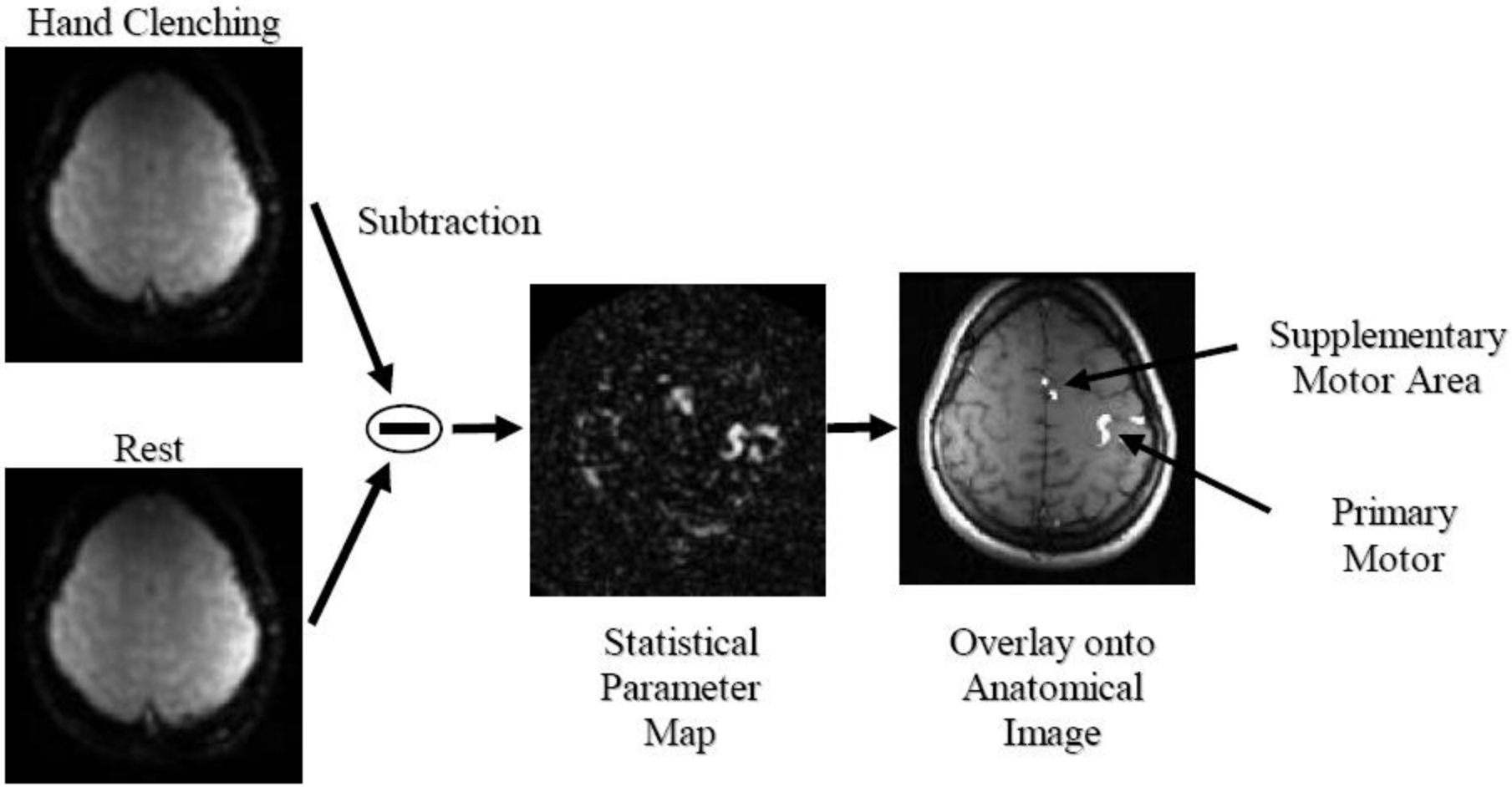
1990: Ogawa (AT&T Bell labs) uses the concept of BOLD contrast to propose fMRI.

- Oxygenated Hb is diamagnetic and deoxygenated Hb is paramagnetic.
- Paramagnetic **deoxy-Hb** distorts the static magnetic field, causing more rapid phase dispersal and decay of MR decay parameter, (**shorter T2**).

FMRI BOLD SIGNAL



- Blood flow : ↑ ↑ ↑
- O2 utilization : ↑
- Blood oxygen level : ↑ ↑
- Deoxy Hgb level : ↓ ↓


Hand Clenching
Subtraction
Rest
Statistical Parameter Map
Overlay onto Anatomical Image
Supplementary Motor Area
Primary Motor

Object Naming Task

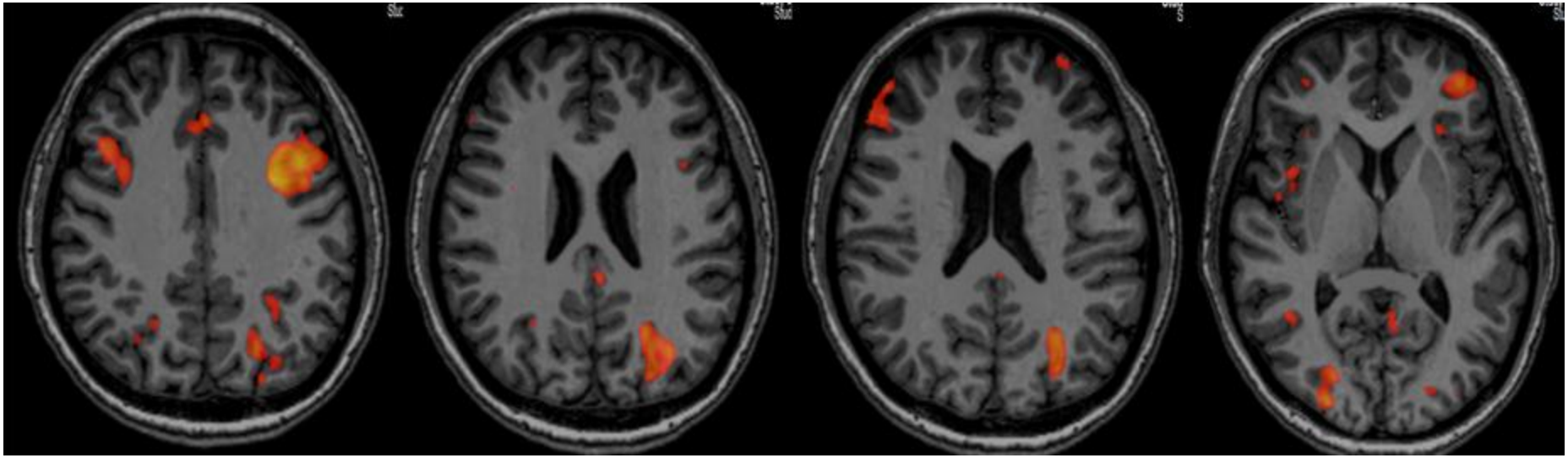
Rest and relax when you see: ⊕

Try to relax and do nothing. Do not say to yourself the name of the object on the screen.

When you see the picture of an object like:

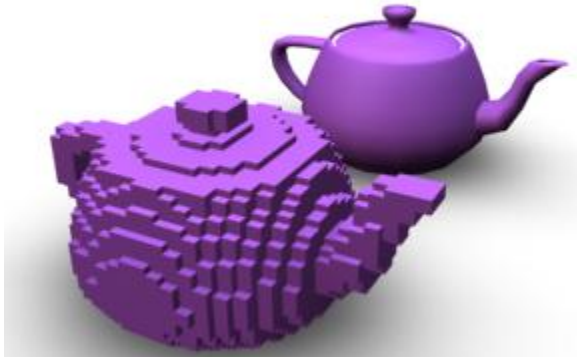
Think at the name of the object

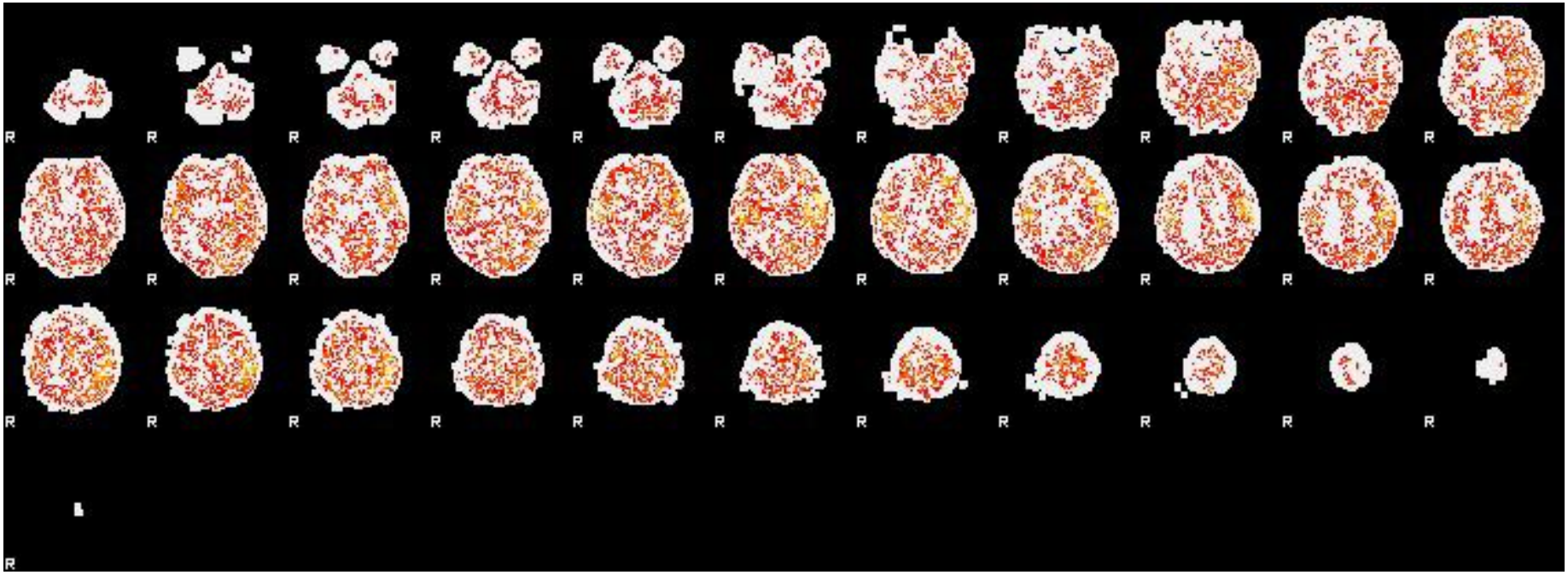
Try to keep still.



VOXEL

- The smallest 3-D unit of a volume
- Analogous to a pixel in a digital image (voxel= volume pixel)
- Typically 2-3 mm^3 for BOLD
- 50 000 voxels in brain





Epilepsia, 54(2), 314–322, 2013
doi: 10.1111/epi.12068

FULL-LENGTH ORIGINAL RESEARCH

Language lateralization by fMRI and Wada testing in 229 patients with epilepsy: Rates and predictors of discordance

Julie K. Janecek, Sara J. Swanson, David S. Sabsevitz, Thomas A. Hammeke, Manoj Raghavan, Megan E. Rozman, and Jeffrey R. Binder

Department of Neurology and the Comprehensive Epilepsy Center, Medical College of Wisconsin, Milwaukee, Wisconsin, U.S.A.

SUMMARY

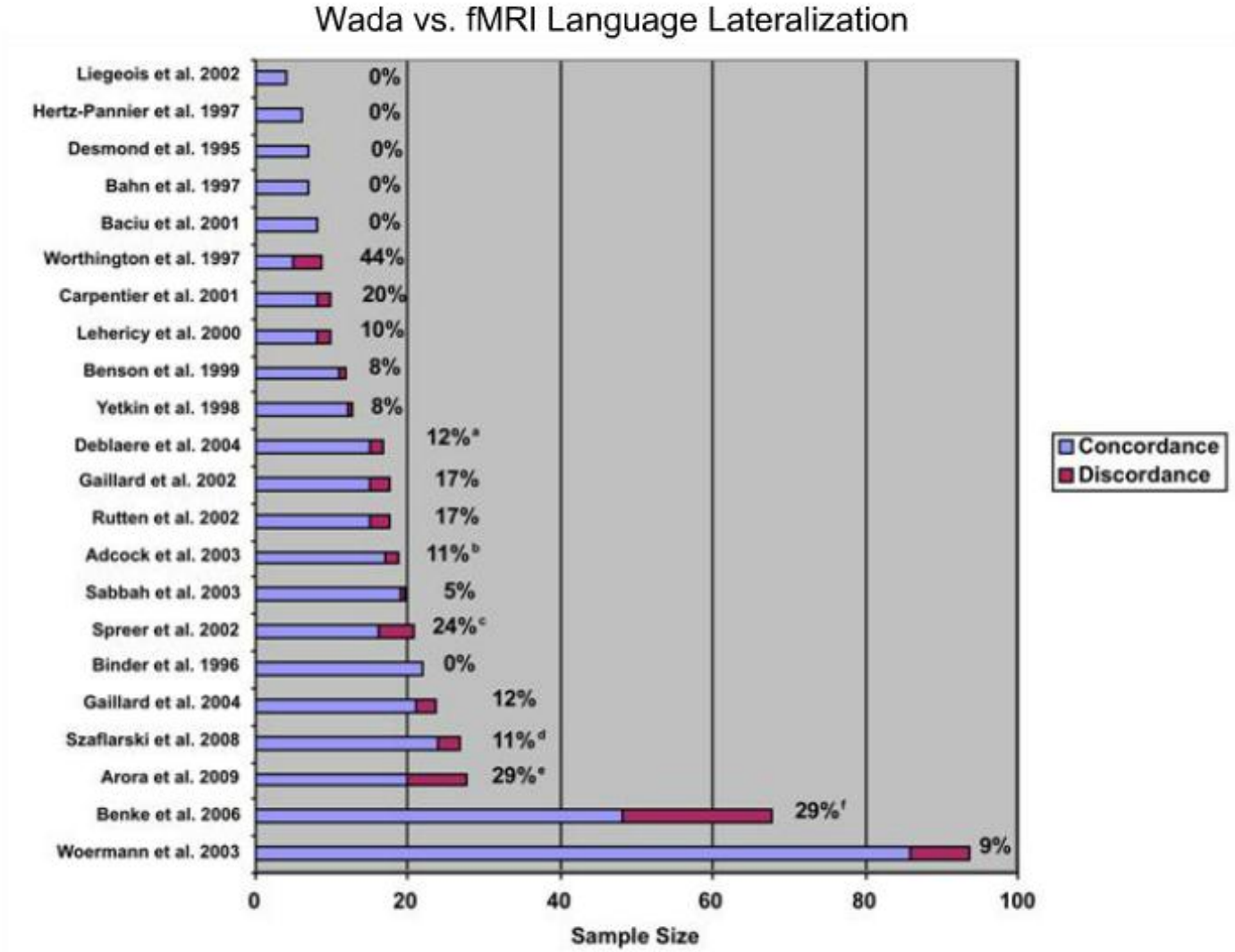
Purpose: To more definitively characterize Wada/functional magnetic resonance imaging (fMRI) language dominance discordance rates with the largest sample of patients with epilepsy to date, and to examine demographic, clinical, and methodologic predictors of discordance.

Methods: Two hundred twenty-nine patients with epilepsy underwent both a standardized Wada test and a semantic decision fMRI language protocol in a prospective research study. Language laterality indices were computed for each test using automated and double-blind methods, and Wada/fMRI discordance rates were calculated using objective criteria for discordance. Regression analyses were used to explore a range of variables that might predict discordance, including subject variables, Wada quality indices, and fMRI quality indices.

Key Findings: Discordant results were observed in 14% of patients. Discordance was highest among those categorized by either test as having bilateral language. In a multivariate model, the only factor that predicted discordance was the degree of atypical language dominance on fMRI.

Significance: fMRI language lateralization is generally concordant with Wada testing. The degree of rightward shift of language dominance on fMRI testing is strongly correlated with Wada/fMRI discordance, suggesting that fMRI may be more sensitive than Wada to right hemisphere language processing, although the clinical significance of this increased sensitivity is unknown. The relative accuracy of fMRI versus Wada testing for predicting postsurgical language outcome in discordant cases remains a topic for future research.

KEY WORDS: Epilepsy, Language lateralization, fMRI, Wada.


Wada vs. fMRI Language Lateralization
Liegeois et al. 2002
Hertz-Pannier et al. 1997
Desmond et al. 1995
Bahn et al. 1997
Baciu et al. 2001
Worthington et al. 1997
Carpentier et al. 2001
Lehericy et al. 2000
Benson et al. 1999
Yetkin et al. 1998
Deblaere et al. 2004
Gaillard et al. 2002
Rutten et al. 2002
Adcock et al. 2003
Sabbah et al. 2003
Spreer et al. 2002
Binder et al. 1996
Gaillard et al. 2004
Szaflarski et al. 2008
Arora et al. 2009
Benke et al. 2006
Woermann et al. 2003
0%
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20%
10%
8%
8%
12%a
17%
17%
11%b
5%
24%c
0%
12%
11%d
29%e
29%f
9%
0
20
40
60
80
100
Sample Size
Concordance
Discordance

MEMORY FMRI

SLEH – controls vs. patients - Memory

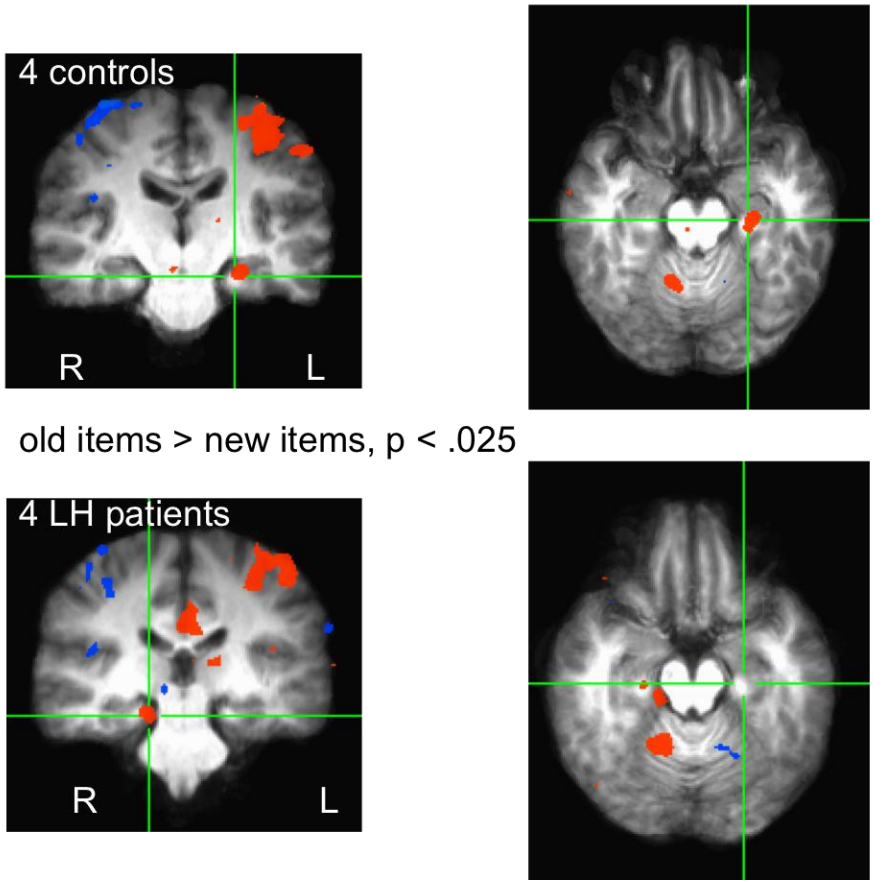


Image courtesy: Cris A. Hamilton

Baylor College of Medicine

FMRI-EEG

CASE

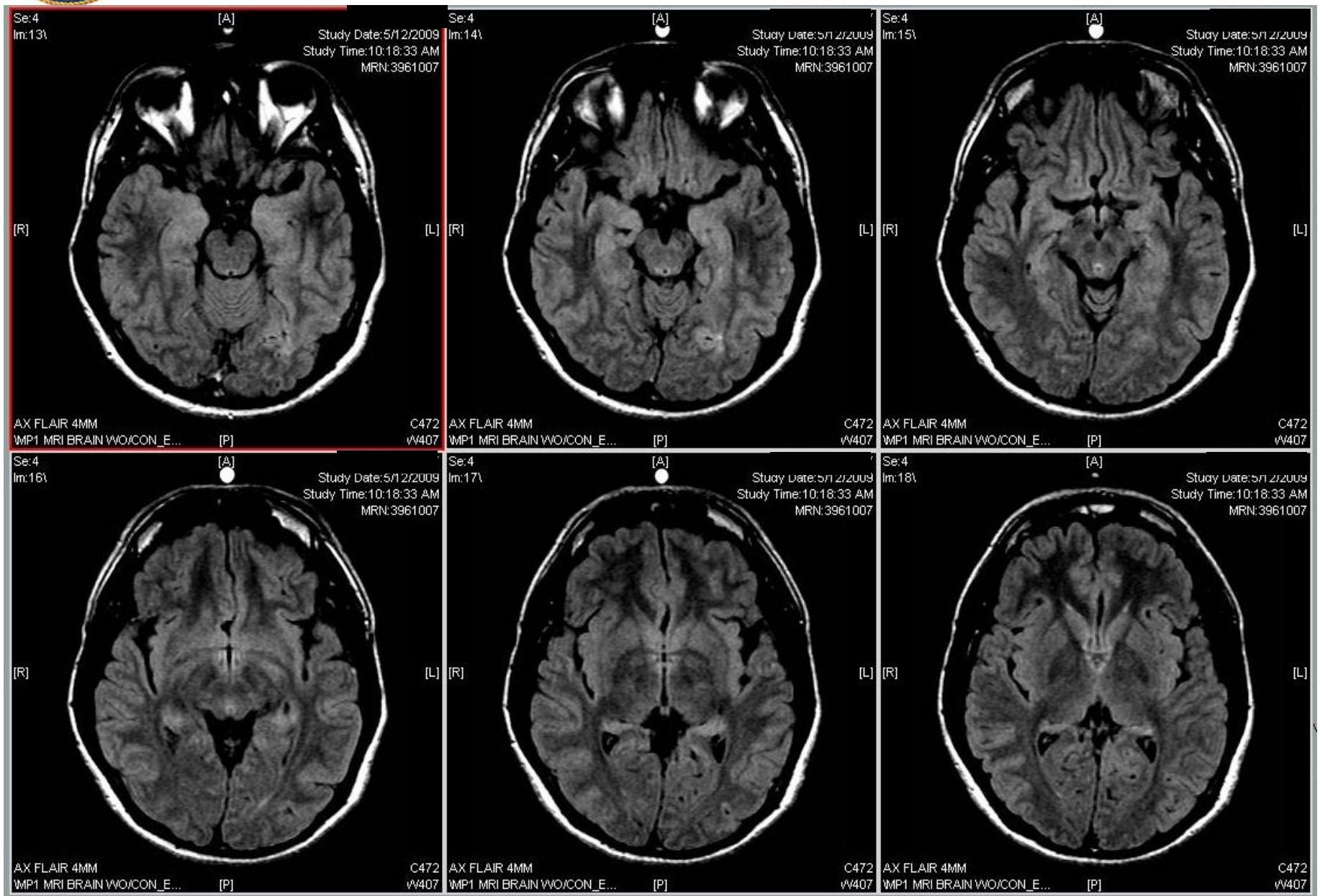
23 y/o man with intractable complex partial seizures

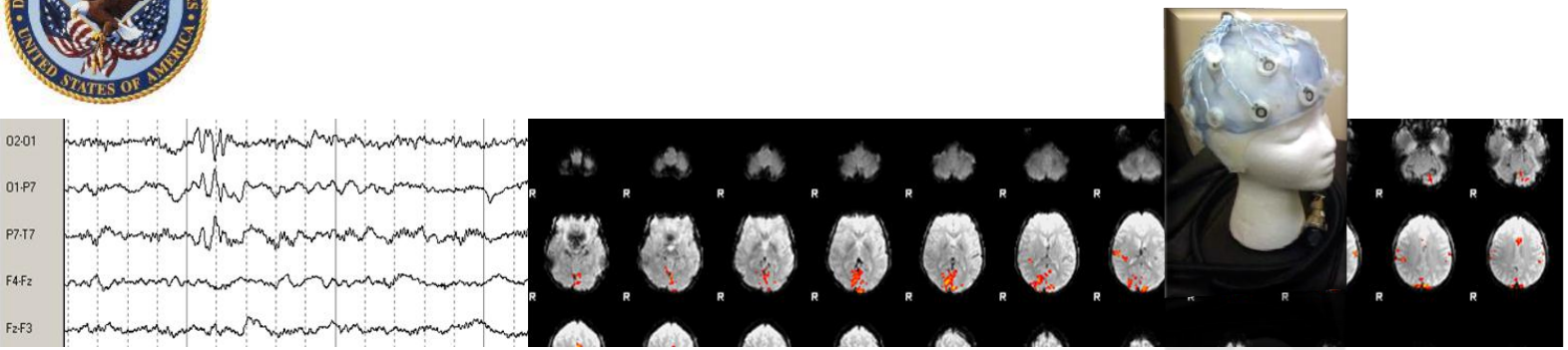
Aura: a very bright light in bilateral visual fields and "foggy vision." At the same time, he also "hears something" similar to somebody talking, but not very clearly.

Ictus: His sister states that at this time, he might talk "gibberish" and would have a smile/ grin over his face. There will be loss of contact for about 20 seconds.

Has had 3 GTCS in his life

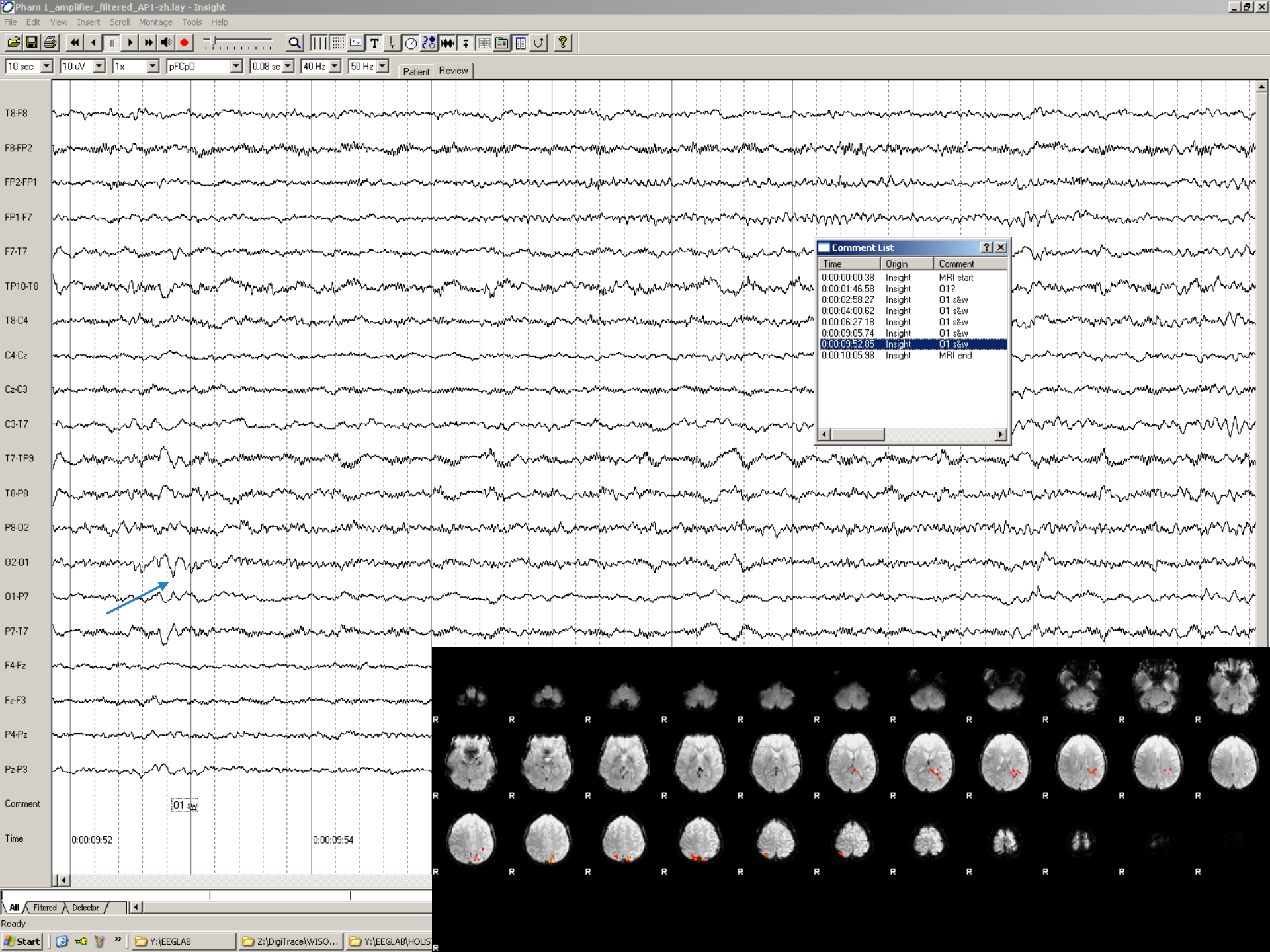
PATIENT WITH CPS





EEG-fMRI

1992: John Ives, Steve Warach and Franz Schmitt performed the first EEG recording within an MRI (Siemens 1.5 T; Beth Israel Hospital, Boston)


Pham 1_amplifier_filtered_AP1-zh.lay - Insight
File Edit View Insert Scroll Montage Tools Help
10 sec
10 uV
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pFCp0
0.08 se
40 Hz
50 Hz
Patient
Review
T8-F8
F8-FP2
FP2-FP1
FP1-F7
F7-T7
TP10-T8
T8-C4
C4-Cz
Cz-C3
C3-T7
T7-TP9
T8-P8
P8-O2
O2-O1
O1-P7
P7-T7
F4-Fz
Fz-F3
P4-Pz
Pz-P3
Comment
O1 sw
Time
0:00:09:52
0:00:09:54
Comment List
Time Origin Comment
0:00:00:00.38 Insight MRI start
0:00:01:46.58 Insight O1?
0:00:02:58.27 Insight O1 s&w
0:00:04:00.62 Insight O1 s&w
0:00:06:27.18 Insight O1 s&w
0:00:09:05.74 Insight O1 s&w
0:00:09:52.85 Insight O1 s&w
0:00:10:05.98 Insight MRI end
All
Filtered
Detector
Ready
Start
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Z:\DigiTrace\WISO...
Y:\EEGLAB\HOUST

Pham 1_amplifier_filtered_AP1-zh.lay - Insight

File Edit View Insert Scroll Montage Tools Help

10 sec | 10 uV | 1x | pFCp0 | 0.16 se | 50 Hz | 60 Hz | Patient | Review

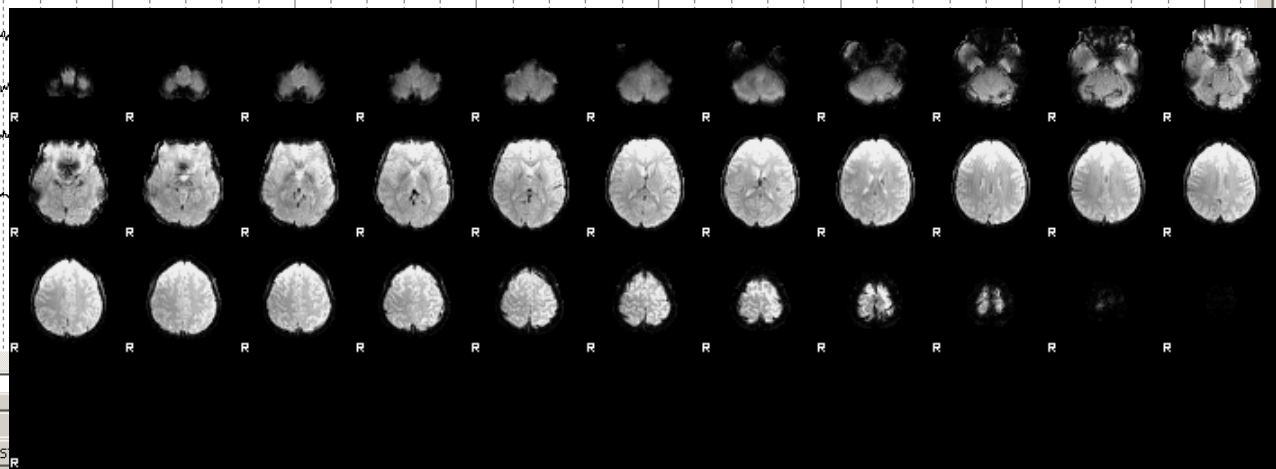
T8-F8
F8-FP2
FP2-FP1
FP1-F7
F7-T7
TP10-T8
T8-C4
C4-Cz
Cz-C3
C3-T7
T7-TP9
T8-P8
P8-O2
O2-O1
O1-P7
P7-T7
F4-Fz
Fz-F3
P4-Pz
Pz-P3
Comment
Time

O1 sw

0:00:02:58
0:00:03:00

Comment List

Time	Origin	Comment
0:00:00:00.38	Insight	MRI start
0:00:01:46.58	Insight	O1?
0:00:02:58.27	Insight	O1 s&w
0:00:04:00.62	Insight	O1 s&w
0:00:06:27.18	Insight	O1 s&w
0:00:09:05.74	Insight	O1 s&w
0:00:09:52.85	Insight	O1 s&w
0:00:10:05.98	Insight	MRI end



All | Filtered | Detector

Ready

Start | Y:\EEGLAB | Z:\DigiTrace\WISO... | Y:\EEGLAB\HOUST

Pham 1_amplifier_filtered_AP1-zh.lay - Insight

File Edit View Insert Scroll Montage Tools Help

10 sec | 10 uV | 1x | pFCp0 | 0.08 se | 40 Hz | 50 Hz | Patient | Review

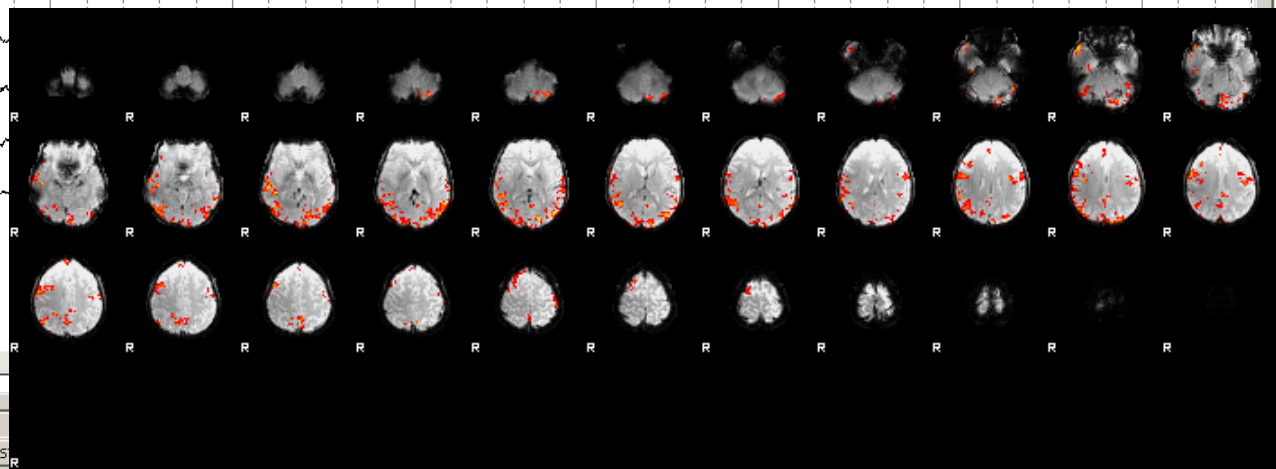
T8-F8
F8-FP2
FP2-FP1
FP1-F7
F7-T7
TP10-T8
T8-C4
C4-Cz
Cz-C3
C3-T7
T7-TP9
T8-P8
P8-O2
O2-O1
O1-P7
P7-T7
F4-Fz
Fz-F3
P4-Pz
Pz-P3
Comment
Time

O1 sw

0:00:04:00
0:00:04:02

Comment List

Time	Origin	Comment
0:00:00:00.38	Insight	MRI start
0:00:01:46.58	Insight	O1?
0:00:02:58.27	Insight	O1 s&w
0:00:04:00.62	Insight	O1 s&w
0:00:06:27.18	Insight	O1 s&w
0:00:09:05.74	Insight	O1 s&w
0:00:09:52.85	Insight	O1 s&w
0:00:10:05.98	Insight	MRI end



All | Filtered | Detector

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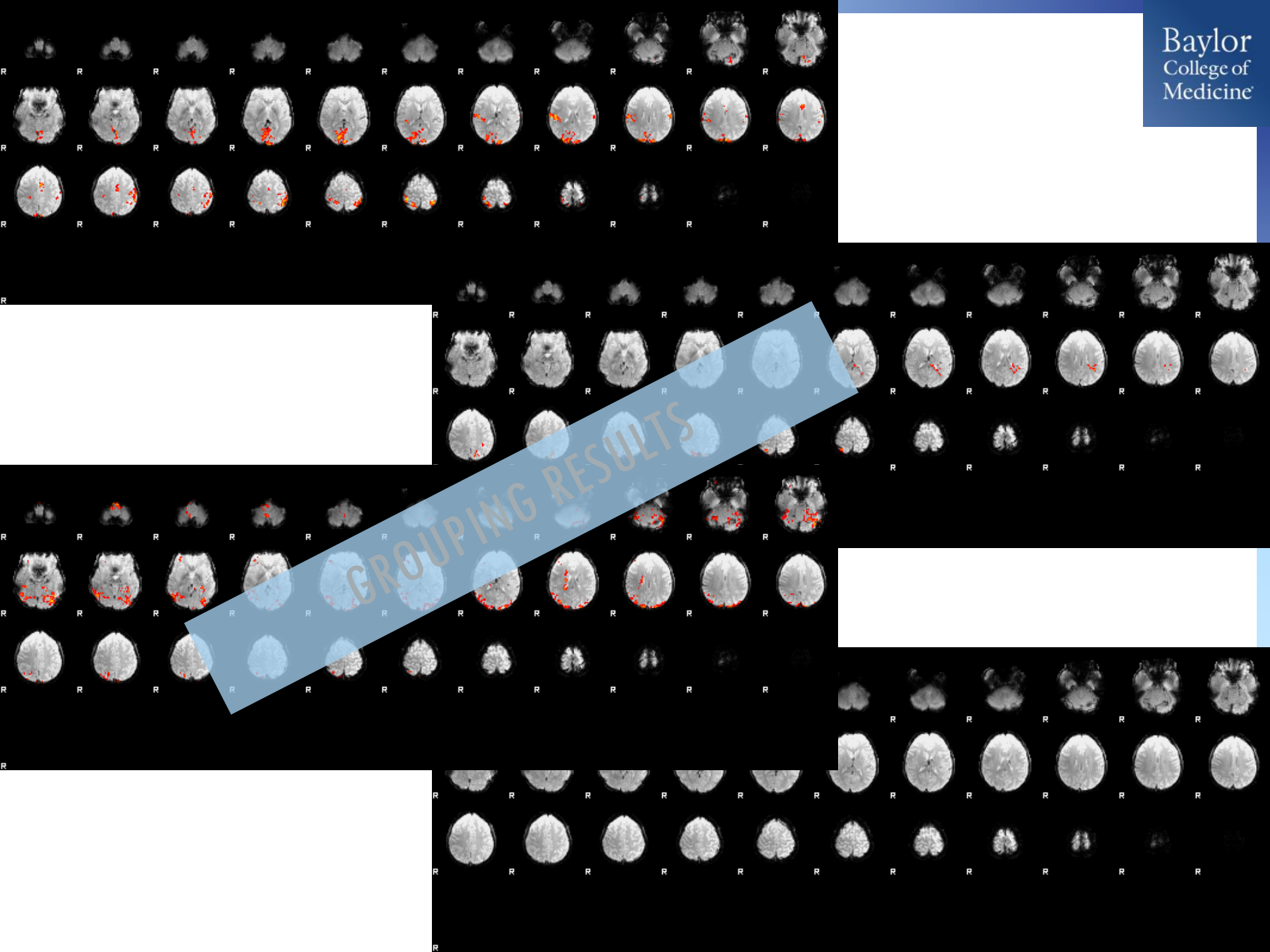
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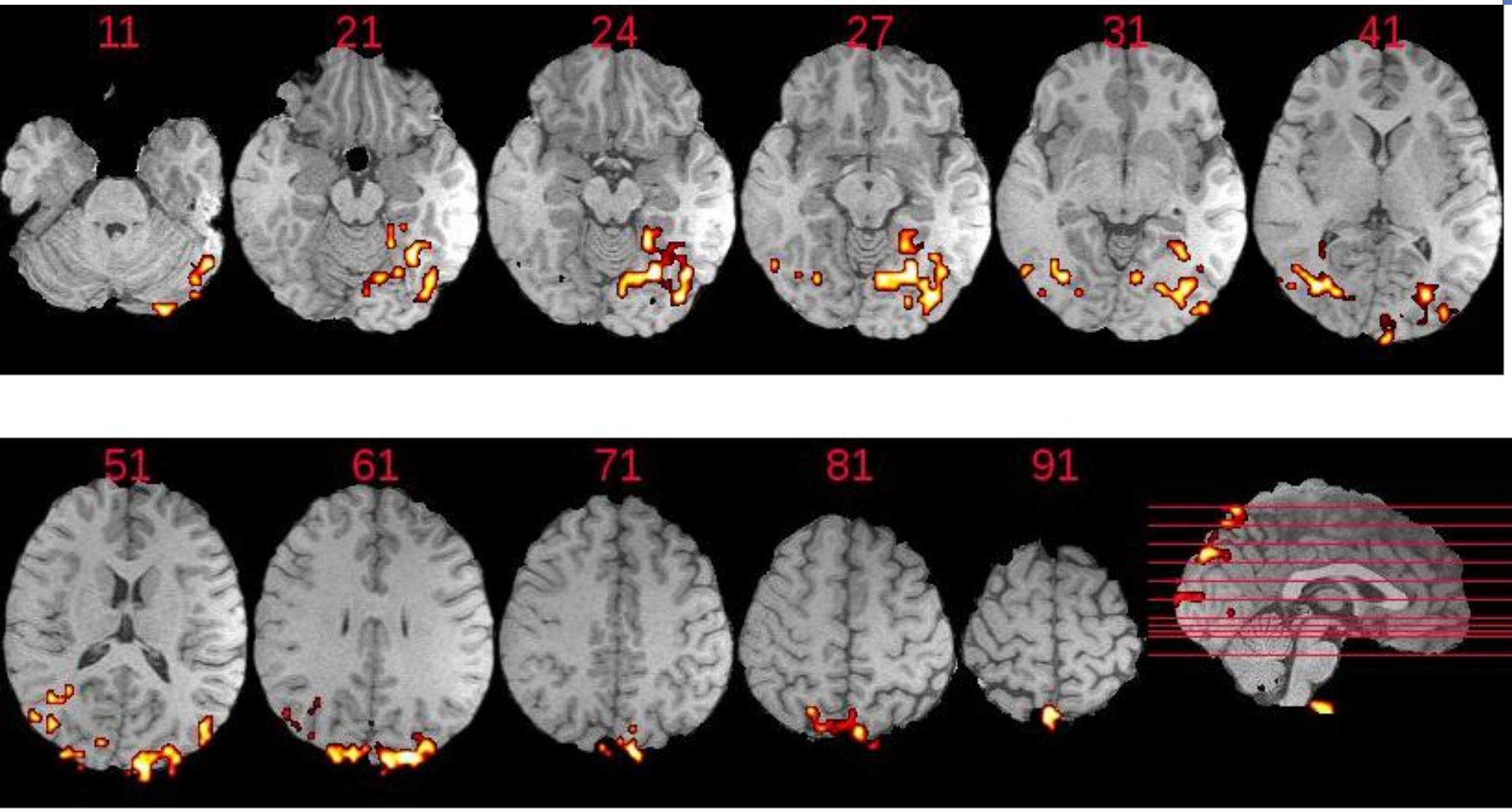
Medicine
GROUPING RESULTS

FMRI- SPIKE MODEL



PATIENT WITH CPS

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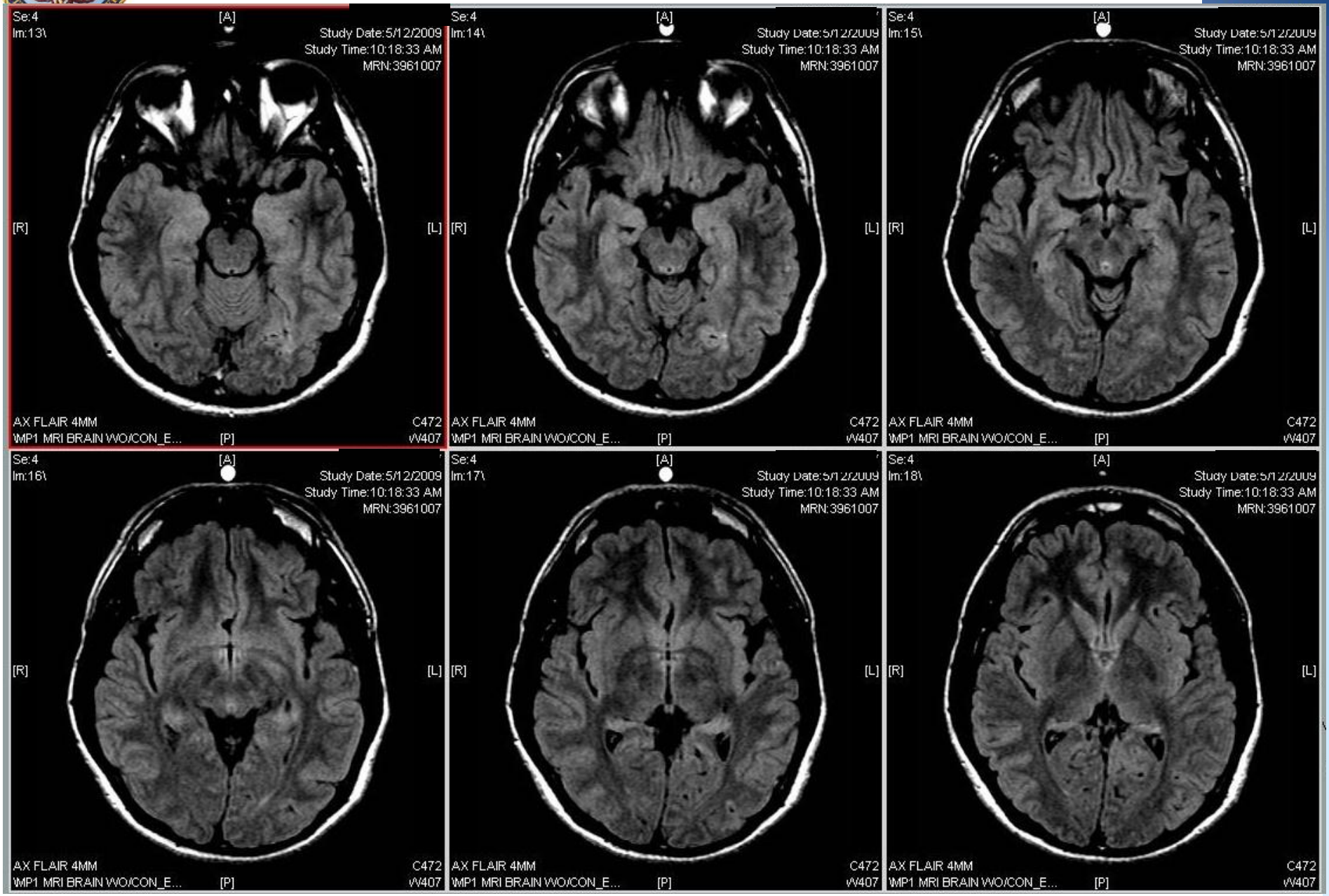


ROLE OF EEG-FMRI IN EPILEPTIC FOCUS

In 33 patients with EEG-fMRI

29 **(88%) were concordant** (BOLD showed similar information as EEG)

21 **(64%) had contributory** (BOLD provided additional information to EEG)

*Pittau, F., F. Dubeau, et al. (2012). "Contribution of EEG/fMRI to the definition of the epileptic focus." Neurology **78**(19): 1479-1487.*

DTI/ TRACTOGRAPHY

CASE :

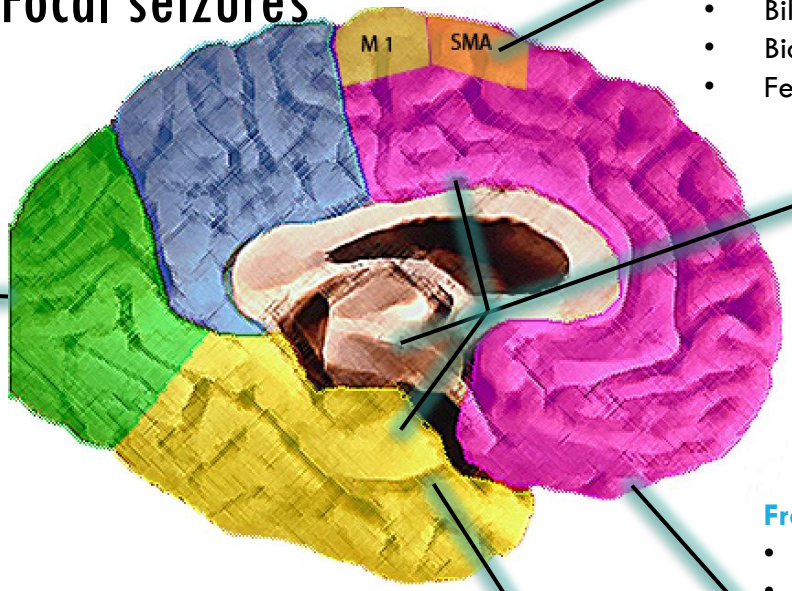
23 y/o man with intractable complex partial seizures

Aura: a very bright light in bilateral visual fields and "foggy vision." At the same time, he also "hears something" similar to somebody talking, but not very clearly.

Ictus: His sister states that at this time, he might talk "gibberish" and would have a smile/ grin over his face. There will be loss of contact for about 20 seconds.

Has had 3 GTCS in his life

SEMIOLOGY: Focal seizures



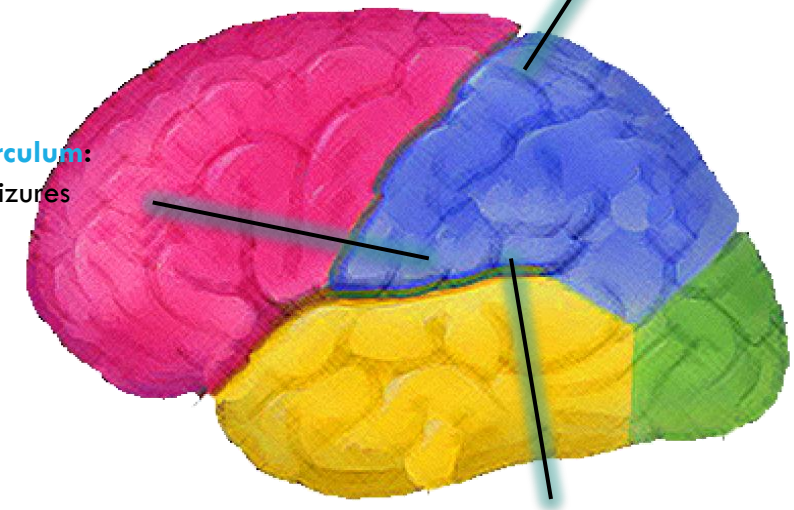
SMA
- Bilateral movements
- Bicycling
- Fencing (C/L arm extension)

Occipital seizures:
Unformed visual hallucinations/ Colors
Blindness

Gelastic (laughter)
-Hypothalamic
-mesial temporal
-frontal cingulate

Frontal Lobe Epilepsy
- Sleep onset
- Frequent
- Abrupt/ explosive
- Bicycling
- Hyperkinetic with complex postures and loud vocalizations (grunting screaming moaning)
- Brief with no post-ictal confusion

Post-central gyrus:
Sensory seizures



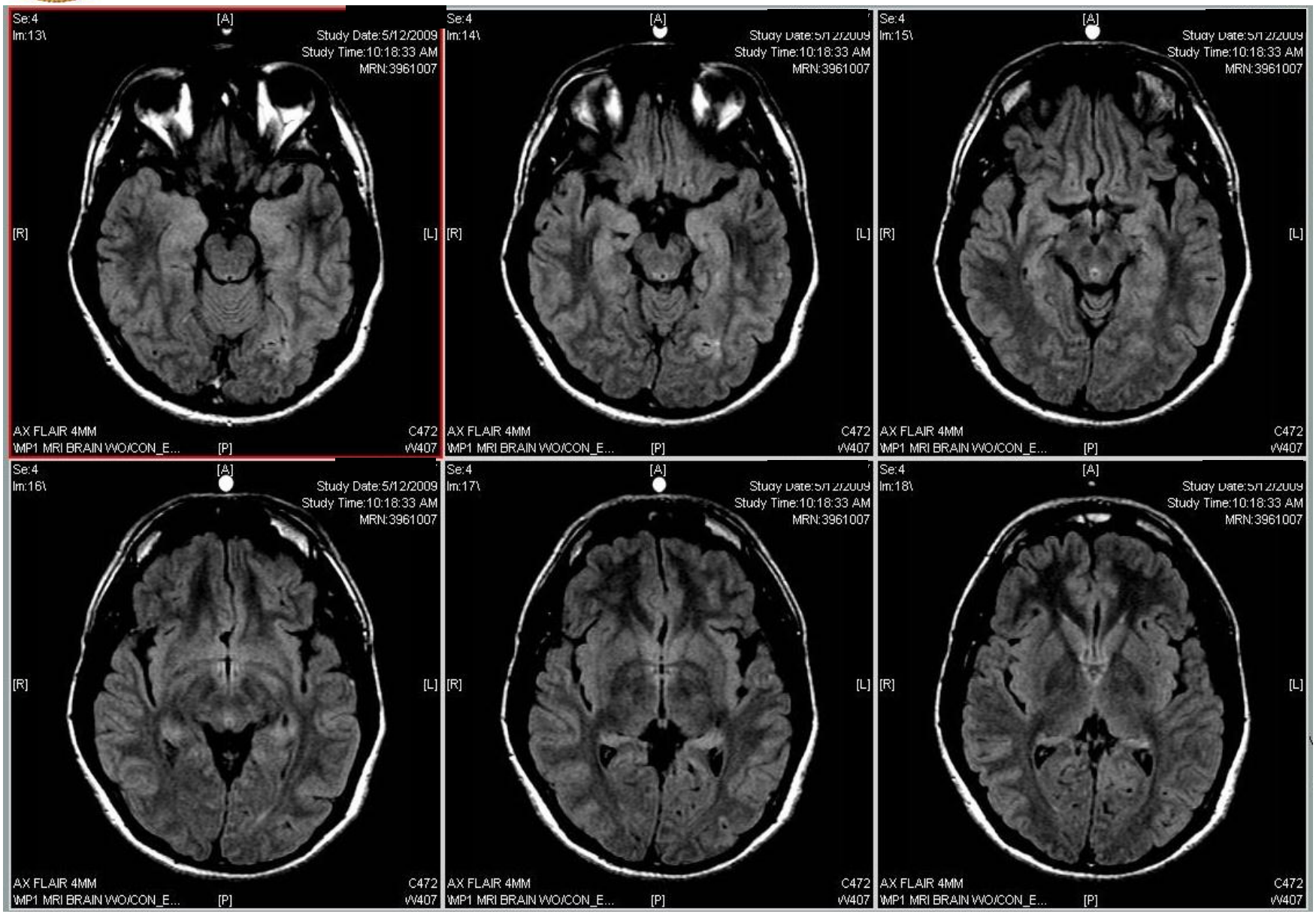
Parietal operculum:
Gustatory seizures

Temporal
•Hippocampal: oral/ manual automatism, C/L dystonia, I/L eye blinks
•Right temporal: Ictal emesis, spitting, micturition, drinking
•Left temporal: Piloerection (goosebumps)
•Sign of 4: C/L arm extension
•Post-ictal cough

Heschl's gyrus: Auditory aura (tinnitus)
Planum temporale: Vertiginous aura ("tornado epilepsy")

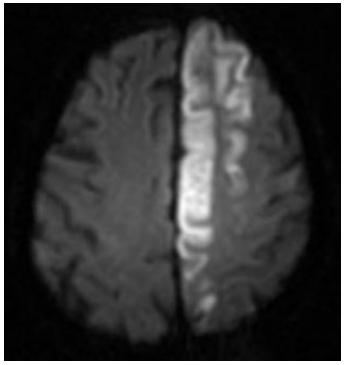
PATIENT WITH CPS

Baylor College of Medicine

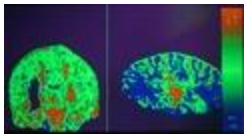


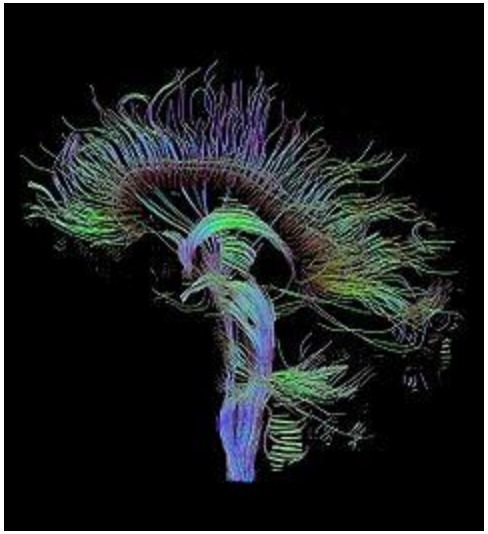
DTI: Diffusion Tensor Imaging

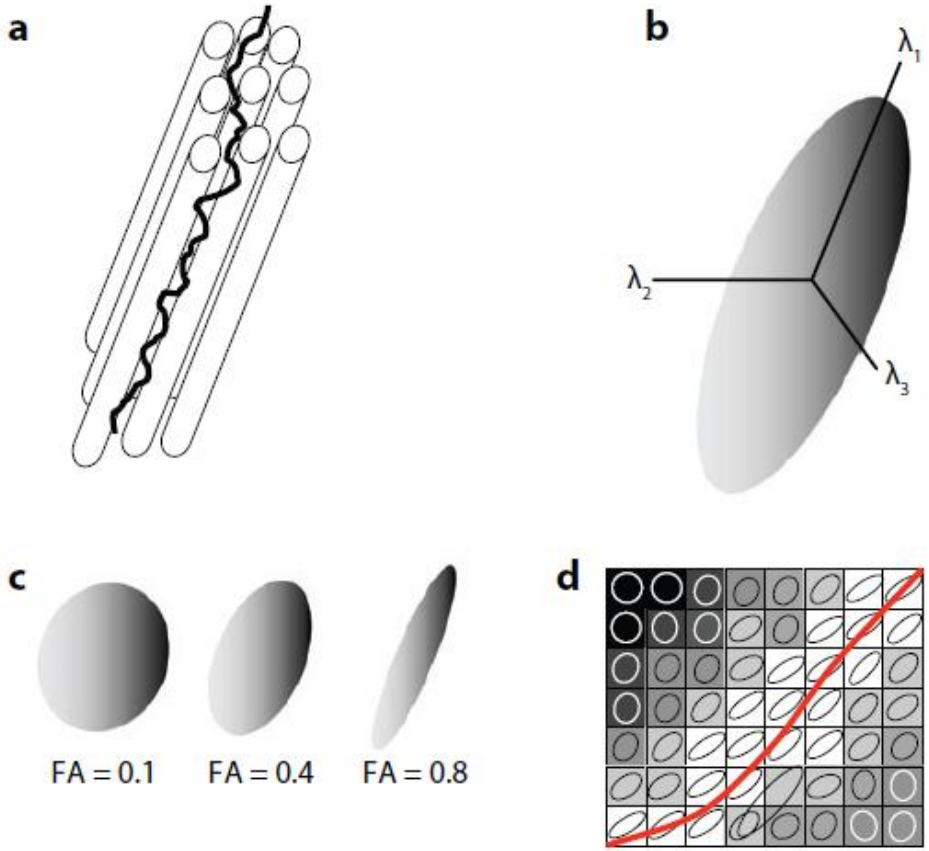
1980s: Diffusion MRI is described, allowing mapping of water diffusion in tissues.

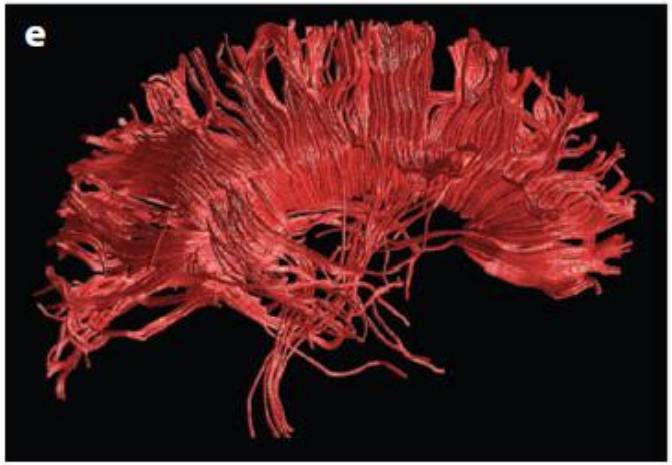


1991: first color maps of white matter fiber orientation using diffusion MRI (Douek et al)

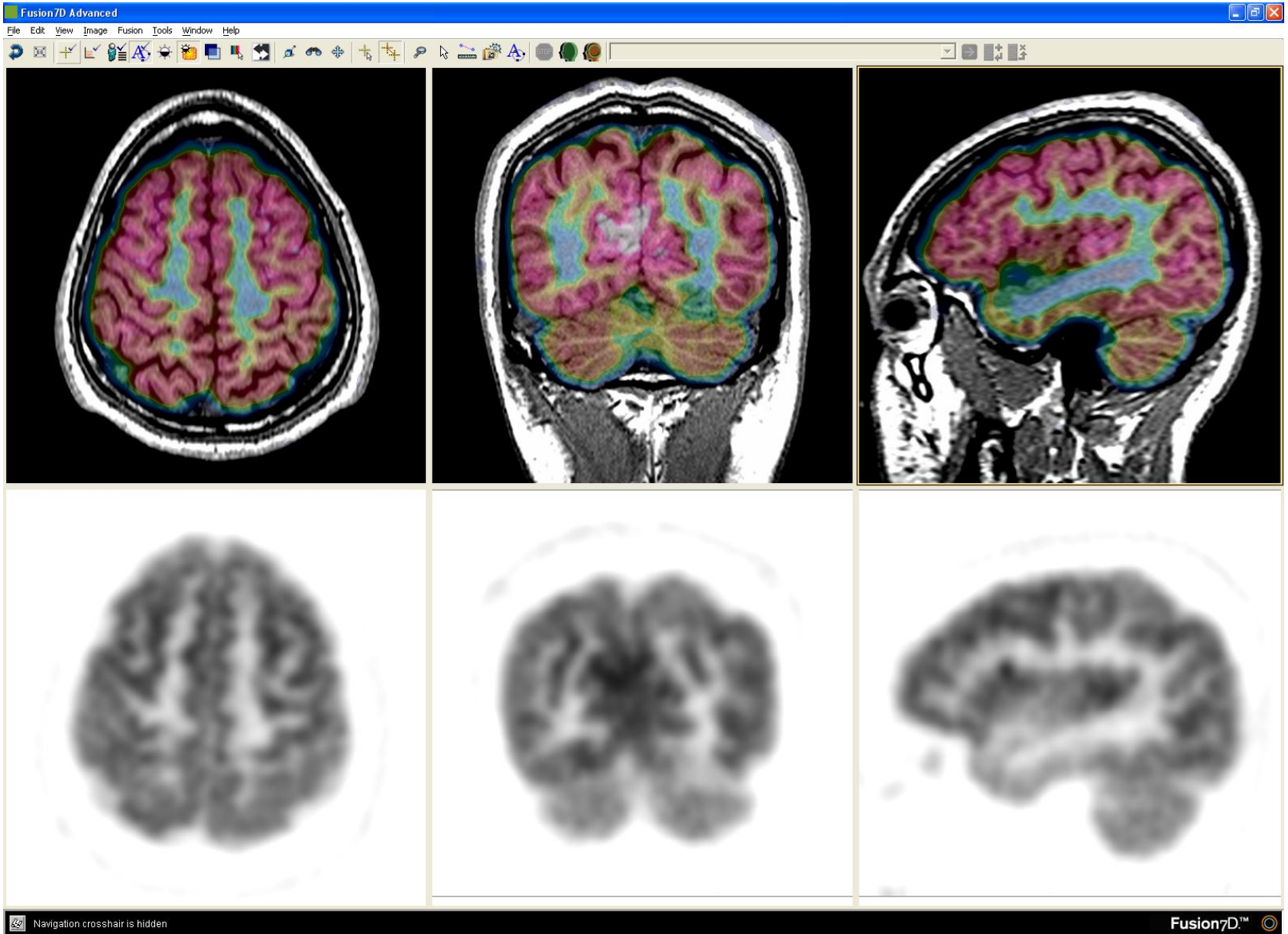








Johansen-Berg and Rushworth. **Using Diffusion Imaging to Study Human Connectional Anatomy.** Annu. Rev. Neurosci. 2009. 32:75–94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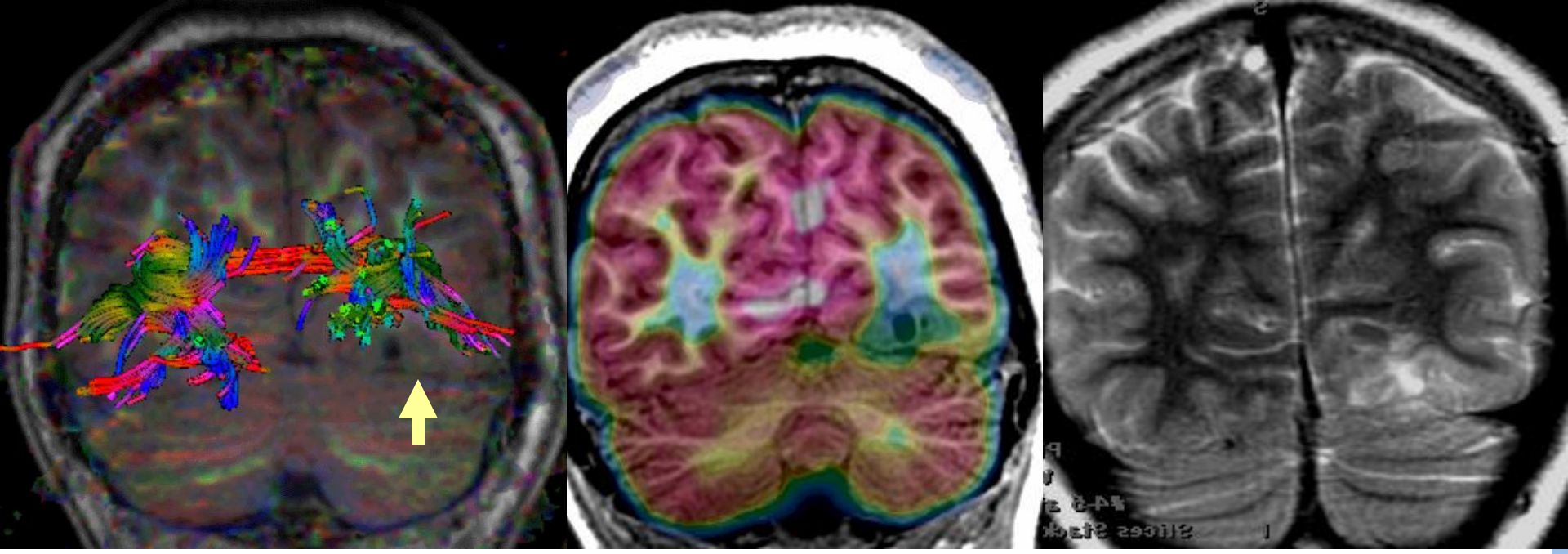
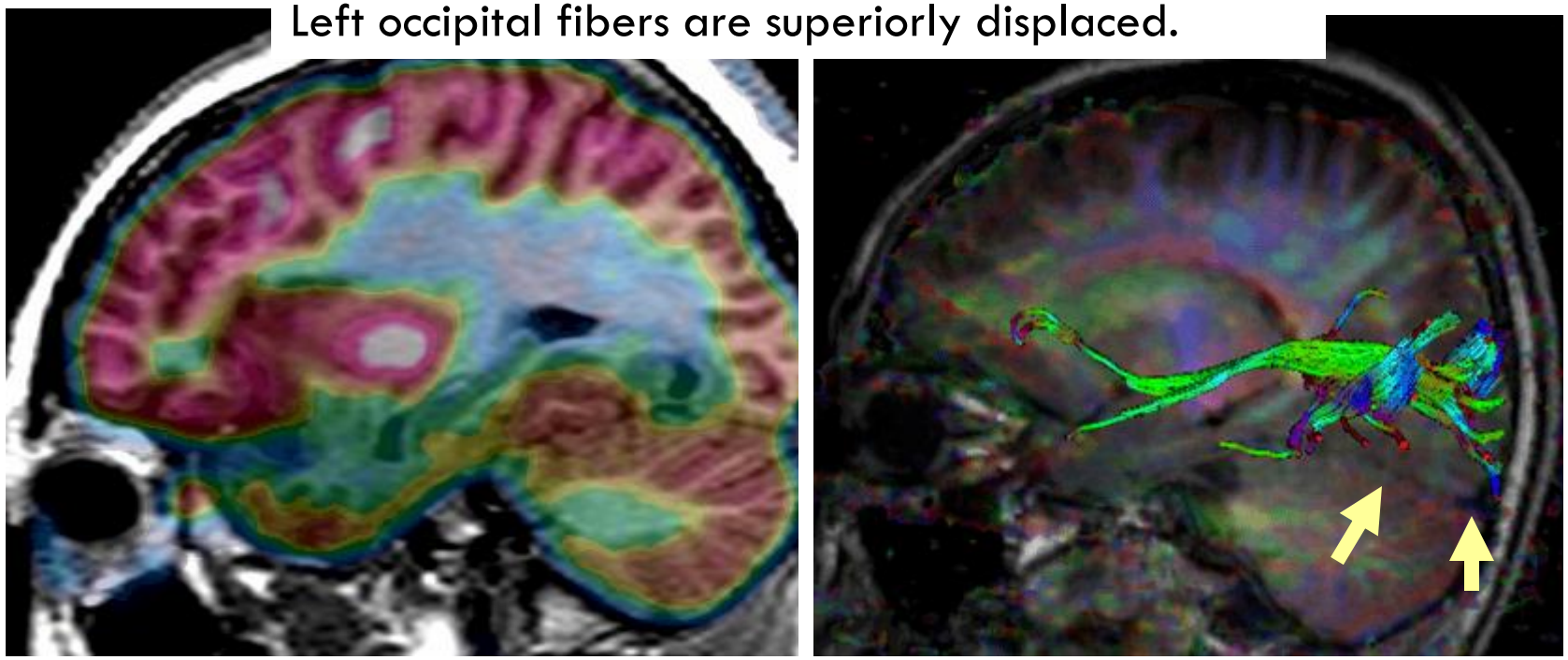
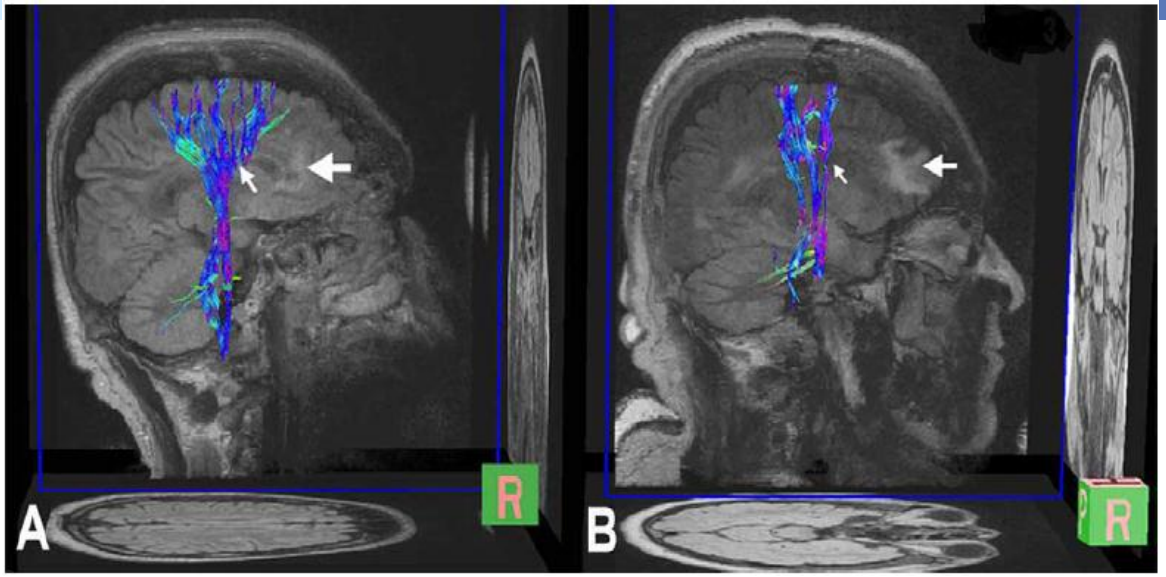
Navigation crosshair is hidden
Fusion7D.™

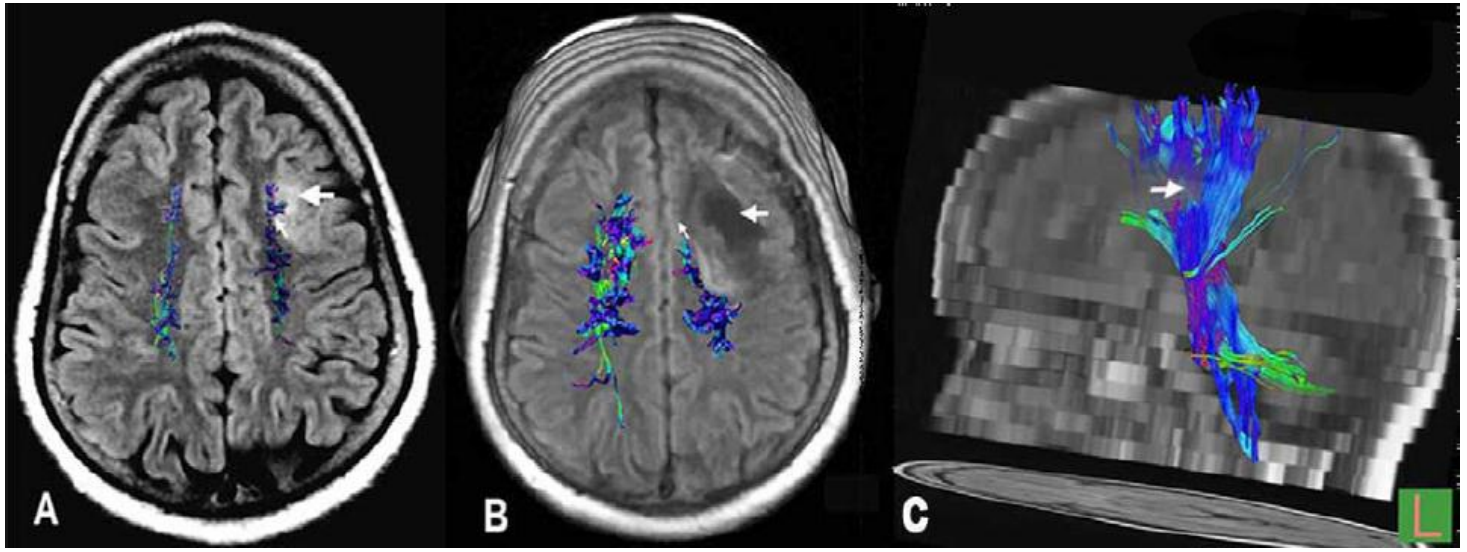


Left occipital fibers are superiorly displaced.





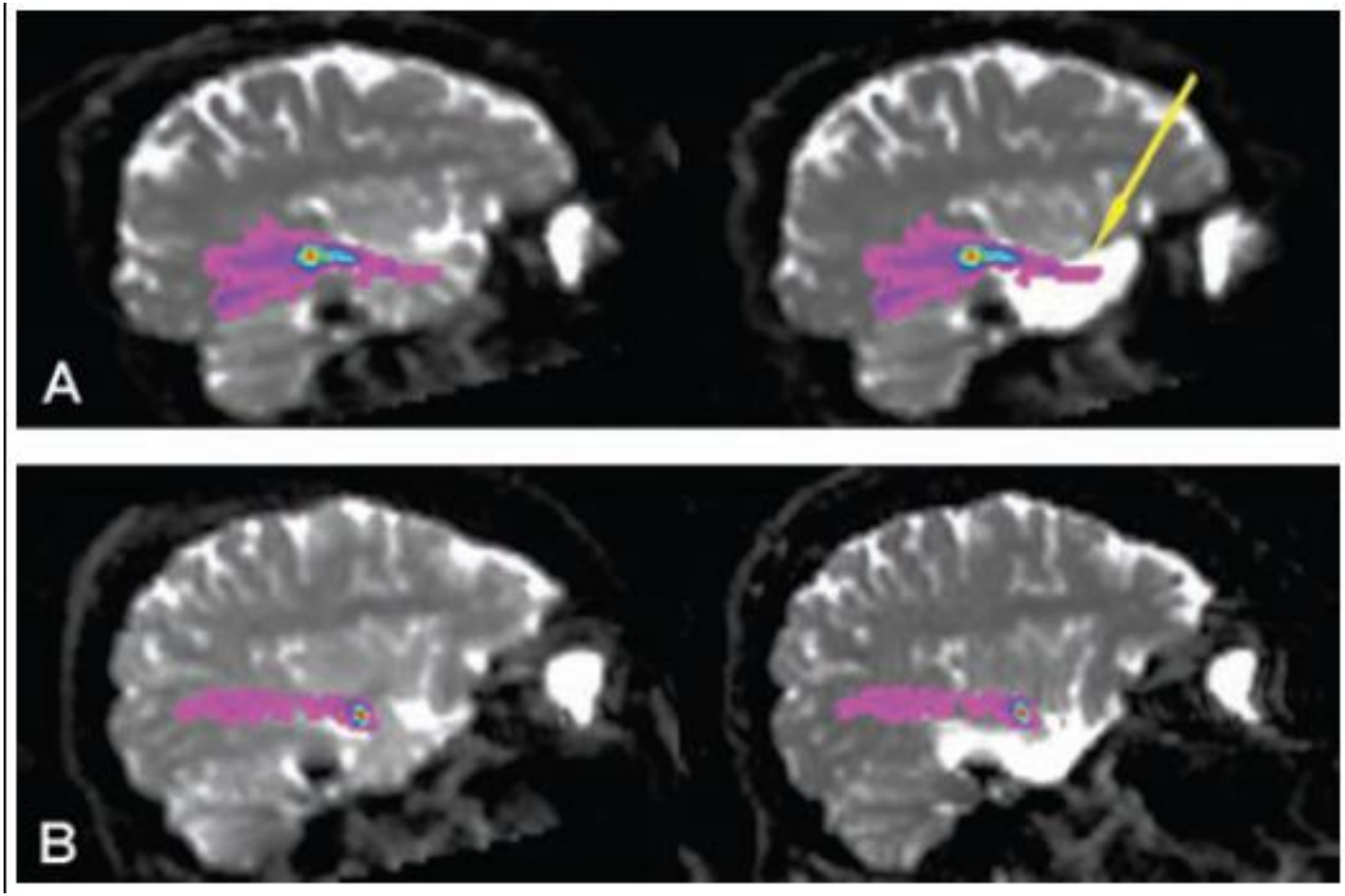
➢A distance <u>of 1 cm of eloquent tissue from proposed surgical site</u> was taken as indicative of surgical safety



Utility of diffusion tensor imaging tractography in decision making for extratemporal resective epilepsy surgery

Ashalatha Radhakrishnan, Jija S. James, Chandrasekharan Kesavadas, Bejoy Thomas, Biji Bahuleyan, Mathew Abraham, Kurupath Radhakrishnan.

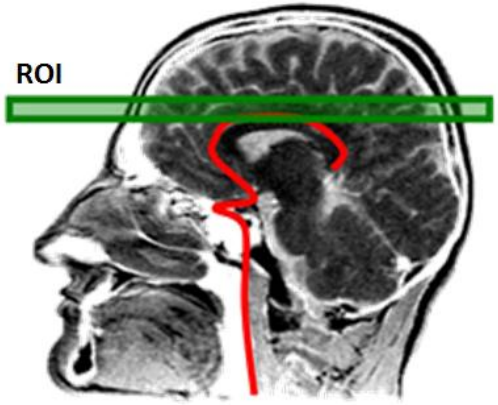
Epilepsy Research (2011) 97, 52—63



Yogarajah & Duncan. Diffusion-based MRI and Tractography in Epilepsy. Epilepsia 2009.

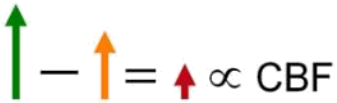
ARTERIAL SPIN LABELING

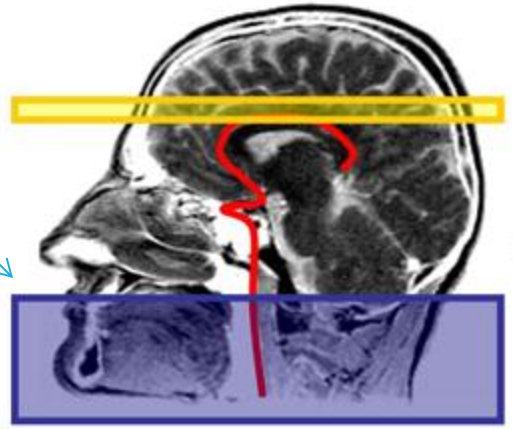
ARTERIAL SPIN LABELING (ASL)



- One method of fMRI using blood labeling

1. Baseline MRI of a ROI
2. Arterial blood magnetically tagged with 180^0 RF pulse and ROI rescanned (tagged blood has lower MR signal due to loss of phase coherence)
3. Baseline MR - Tagged image = Perfusion image

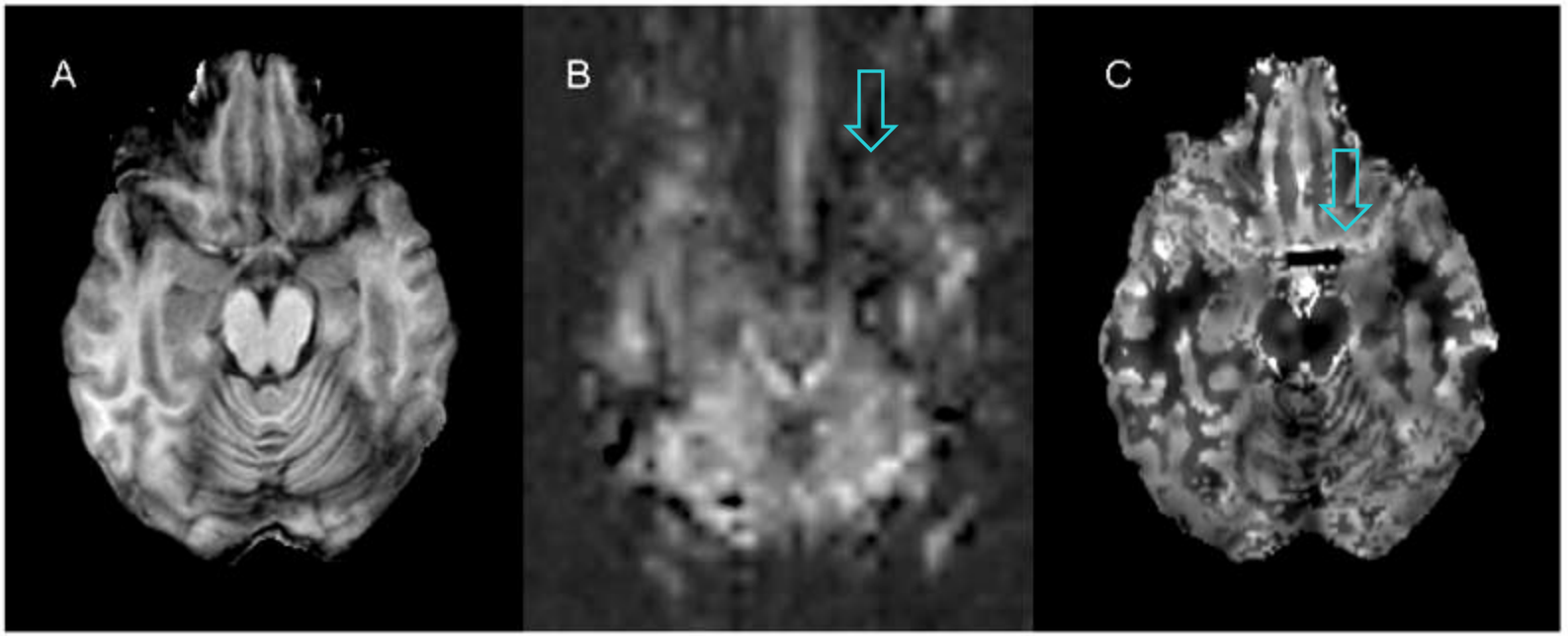




- Non-invasive and repeatable without harmful effects.
- Licensing/ post-processing issues have prevented wider clinical use
- ASL has been used to show mesial temporal hypometabolism on the side of seizures, which correlated with PET hypometabolism as well as hippocampal volume loss

***Haneef Z**, Chen DK. Functional Neuro-Imaging as a Pre-Surgical Tool in Epilepsy. Annals of Indian Academy of Neurology 2013*
***Images**: http://fmri.research.umich.edu/research/main_topics/asl.php*

ASL VS. PET IN PATIENT WITH LEFT TLE



MRI ASL PET

Lim YM, Cho YW, Shamim S, Solomon J, Birn R, Luh WM, et al. Usefulness of pulsed arterial spin labeling MR imaging in mesial temporal lobe epilepsy. Epilepsy Res. 2008;82:183-9.

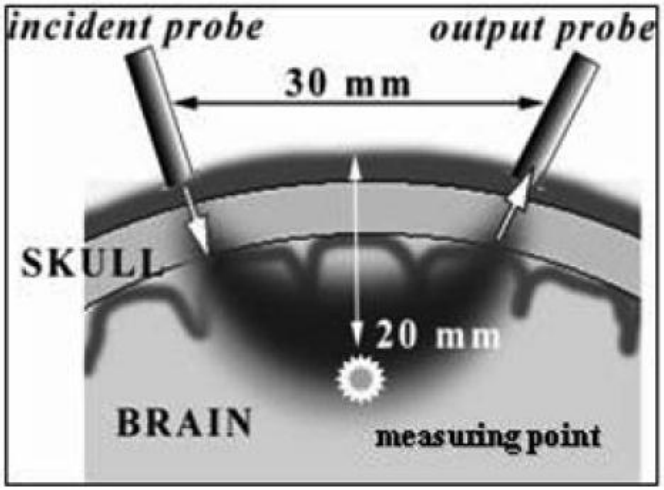
NEAR INFRA-RED SPECTROSCOPY

NEAR INFRA-RED SPECTROSCOPY (NIRS)

- Low resolution functional imaging technique first described in 1977
- Portable and easy to use with existing techniques.

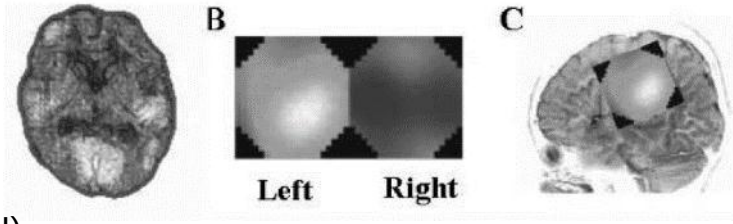
1. Transmitter probe transmits near infra-red spectrum wavelength rays
2. These pass through cranium about 2 cm deep when it is absorbed by Hb.
3. Reflected light is detected by a sensor probe
4. Strength of reflected light is inversely related to Hb concentration in brain

- Images obtained can co-registered to brain MRI to lateralize and localize



Epilepsy:

- Correctly identifies affected hemisphere during seizures (Fig 2), as corroborated by simultaneous ictal SPECT and intracranial EEG
- Detects extra-temporal & temporal lobe seizures
- Potential to be a useful addition to the pre-surgical work-up of epilepsy,
- Useful for language lateralization (additional/ alternative to Wada & fMRI)
- Disadvantage is the inability to measure changes in deeper cortex (deep sulci, insula, parasagittal mesial cortex, mesial and basal temporal lobes, infra-tentorial cortex, and the basal ganglia)



1. *Haneef Z, Chen DK. Functional Neuro-Imaging as a Pre-Surgical Tool in Epilepsy. Annals of Indian Academy of Neurology 2013*
2. *Watanabe E, Nagahori Y, Mayanagi Y. Focus diagnosis of epilepsy using near-infrared spectroscopy. Epilepsia. 2002*

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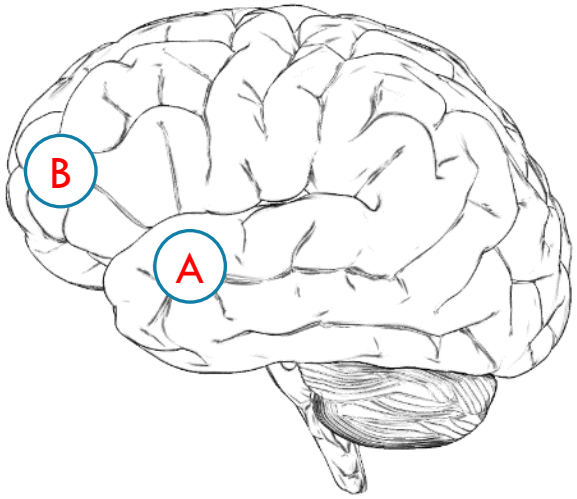
FUNCTIONAL CONNECTIVITY MRI

	Concept	Functional change	Structural change
Lesion (Localization)	Functional Specialization	Memory dysfunction (hippocampal) in TLE	hippocampal atrophy
Network	Functional Integration	Behavioral dysfunction (distributed) in TLE	widespread cortical atrophy (frontocentral, lateral temporal, dorsal parietal, mesial orbitofrontal, cingulate and thalamic)

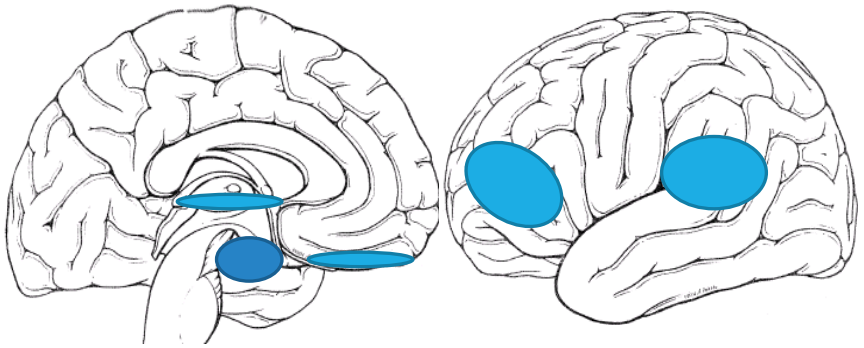


INTERICTAL DEFICITS IN TLE:
LOCALIZATION VS. NETWORK

COGNITION & BEHAVIOR IN TLE

Neuropsych findings in TLE

- Memory deficits
- Depression
- Behavioral changes/ social issues
- Psychosis
- Language deficits
- Anxiety/ aggression

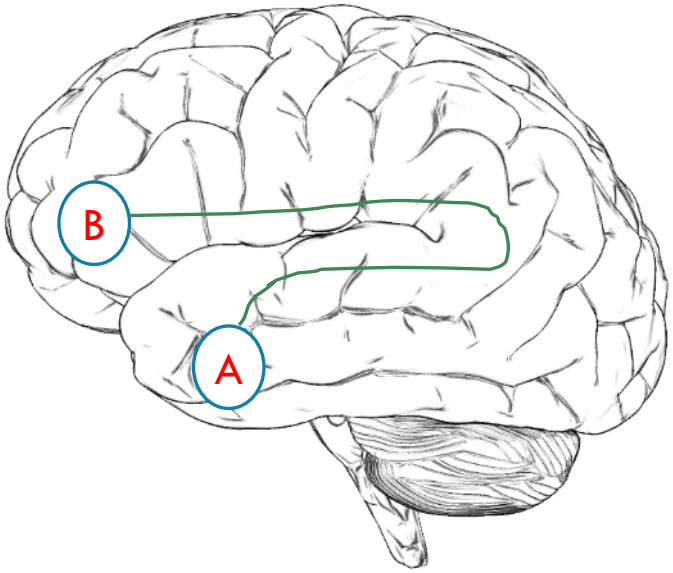


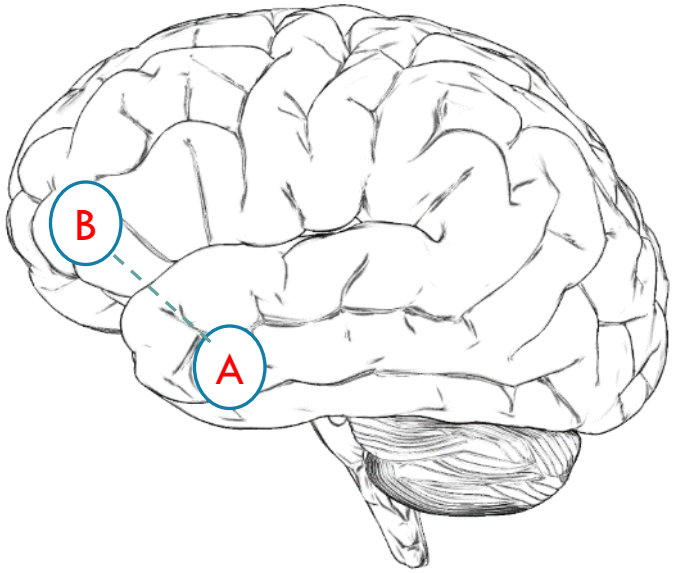
Temporal lobe personality (Geshwind syndrome)[1,2]

Circumstantiality, hypergraphia, hyposexuality, hyper-religiosity, hyper-morality, viscosity

1. Waxman SG and Geschwind N. The interictal behavior syndrome in temporal lobe epilepsy. Archives of General Psychiatry 1975; 32, 1580-1586. PMID: 1200777.
2. Bear DM and Fedio P. Quantitative analysis of interictal behavior in temporal lobe epilepsy. Archives of Neurology 1977; 34, pp 454-467. PMID: 889477.

CONNECTIVITY BETWEEN BRAIN REGIONS



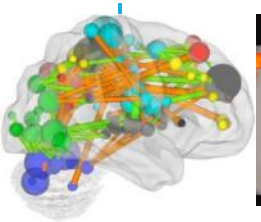


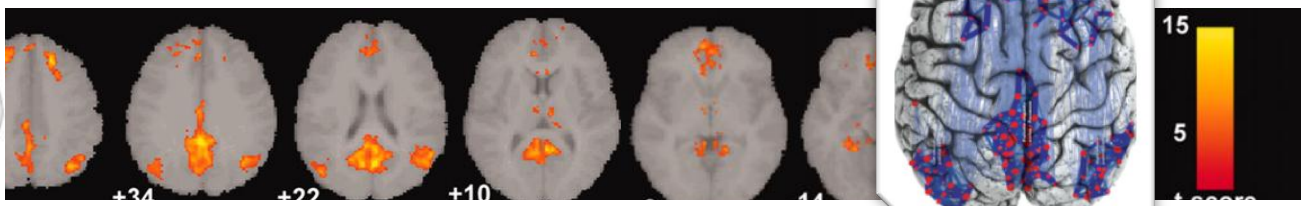
Structural Connectivity
White matter tracts

Eg. DTI

Functional Connectivity
Correlation of activity between spatially remote brain regions

Eg. fMRI, MEG, EEG





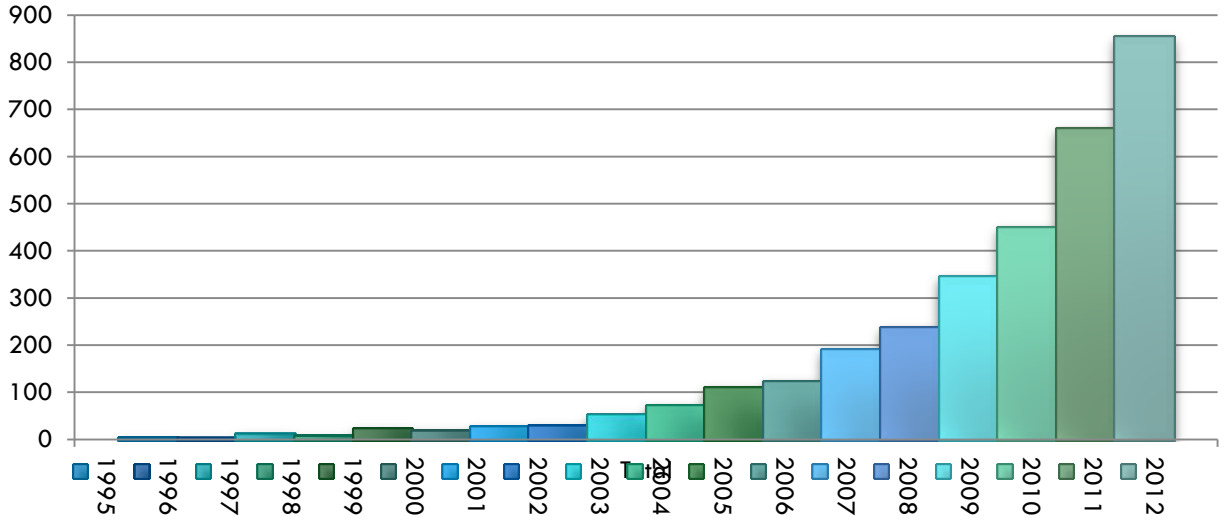
- 2000s: fMRI-EEG
- 1990s: fMRI/ DTI
- 1980s: MRI
- 1980s: MEG
- 1970s: SPECT
- 1960s : PET

fcMRI: Functional Connectivity MRI a.k.a resting state fMRI

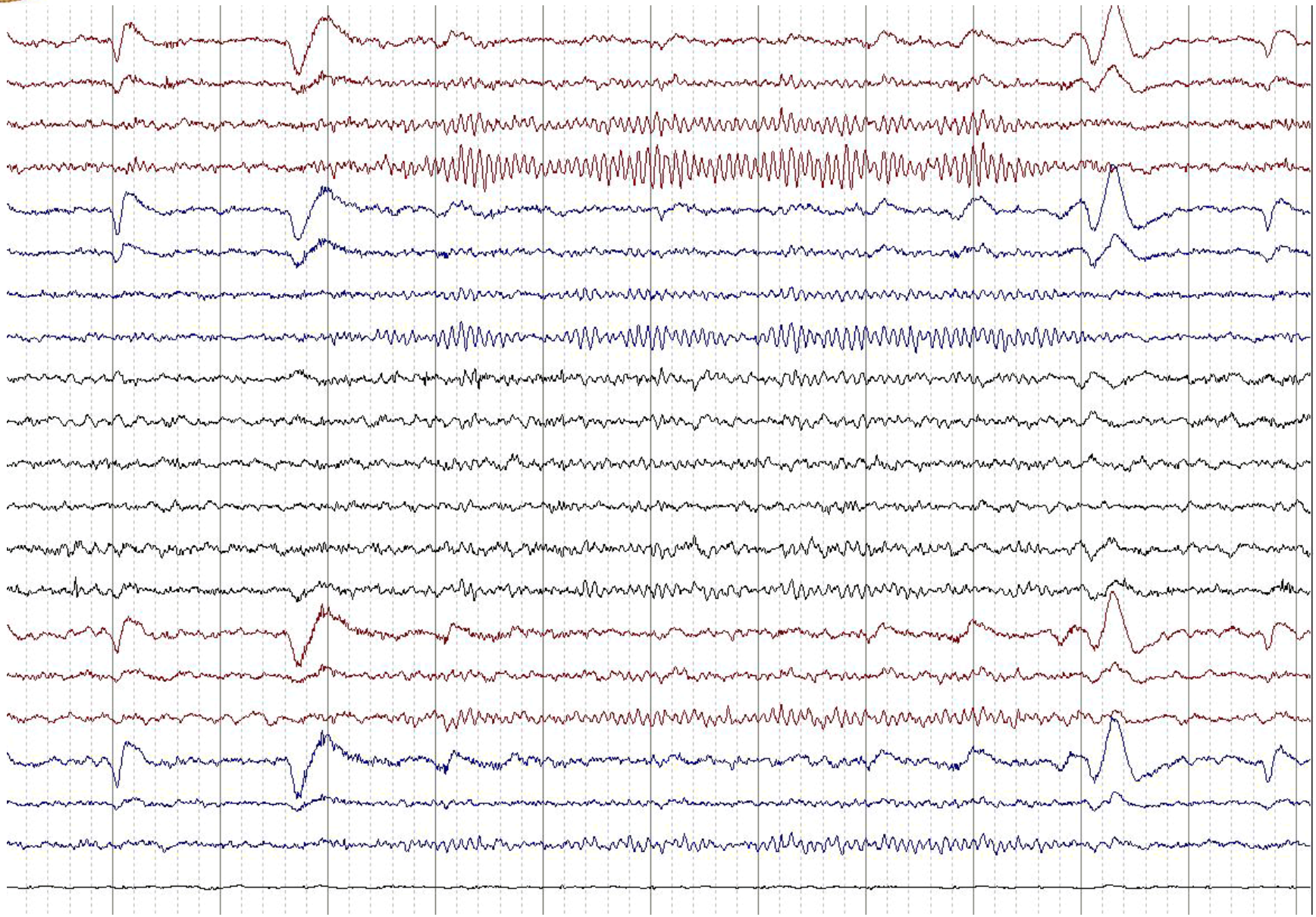
An fMRI technique that attempts to delineate functionally connected brain areas using similarity of voxel time courses.

1995: Bharat Biswal demonstrates the concept of fcMRI in the motor cortex of humans

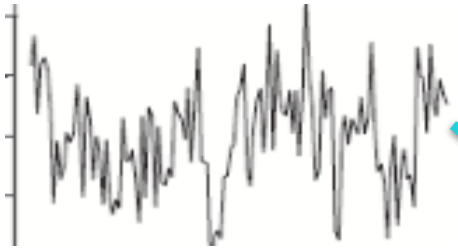
850+ publications per year by 2012.

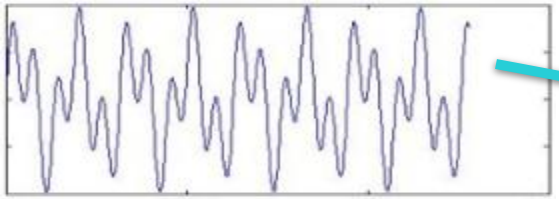


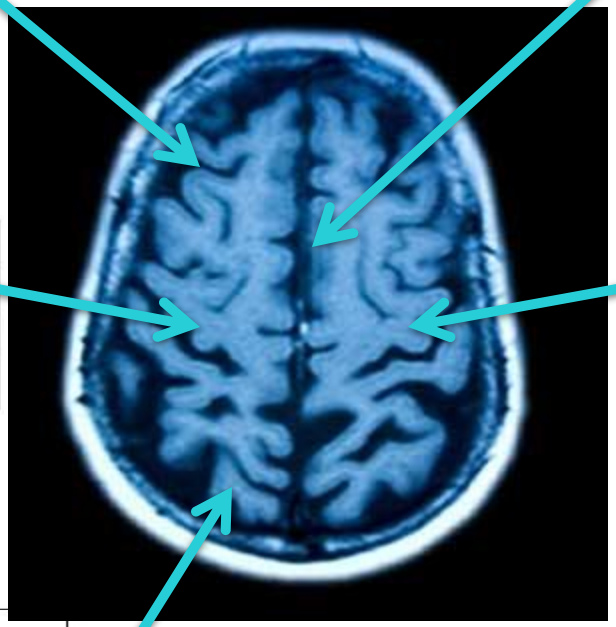
TIME SERIES

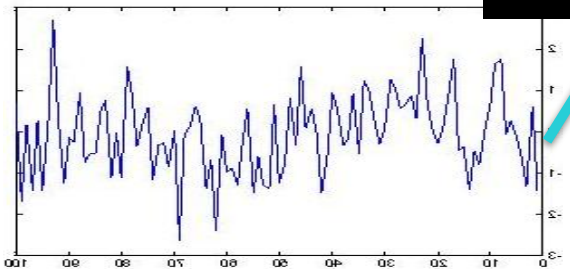


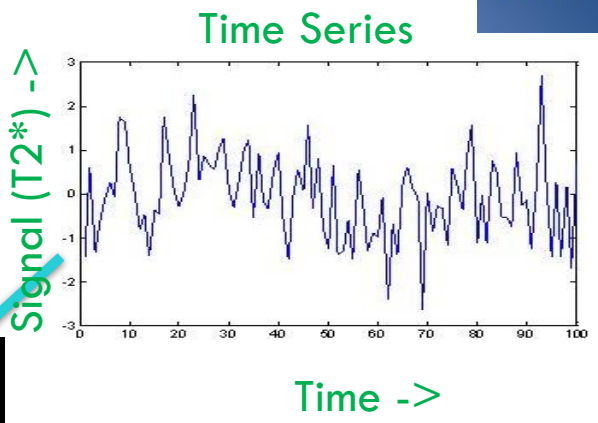
RESTING STATE FMRI VOXEL TIME SERIES

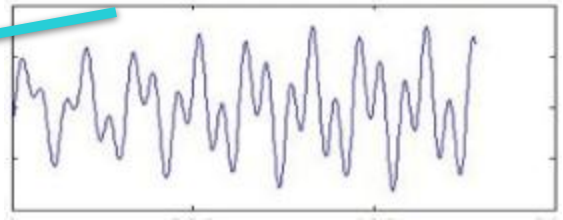






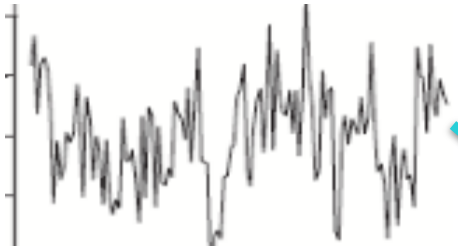


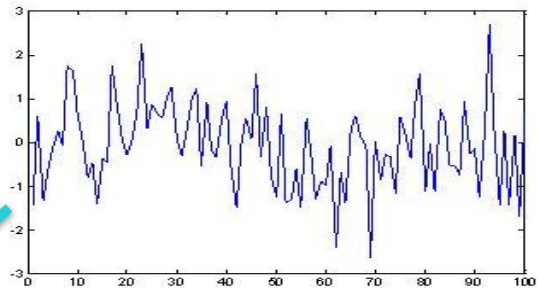


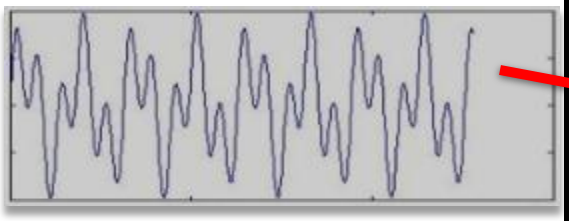


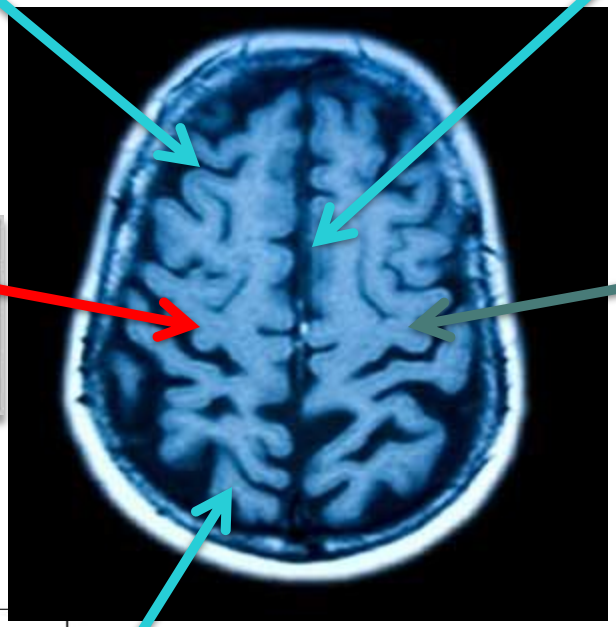
Resting state functional connectivity

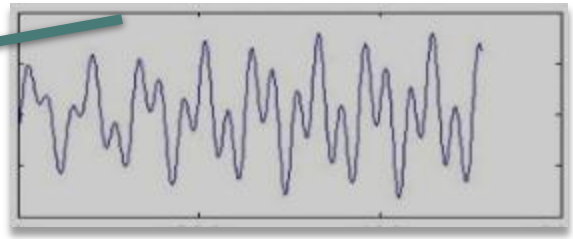
Correlations in spontaneous fluctuations (<0.1 Hz) between remote brain areas

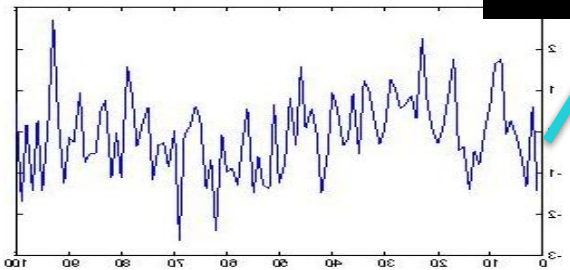












Types of FC-MRI

1. Seed Based (ROI)
2. ICA
3. Others

SEED (ROI) BASED FC

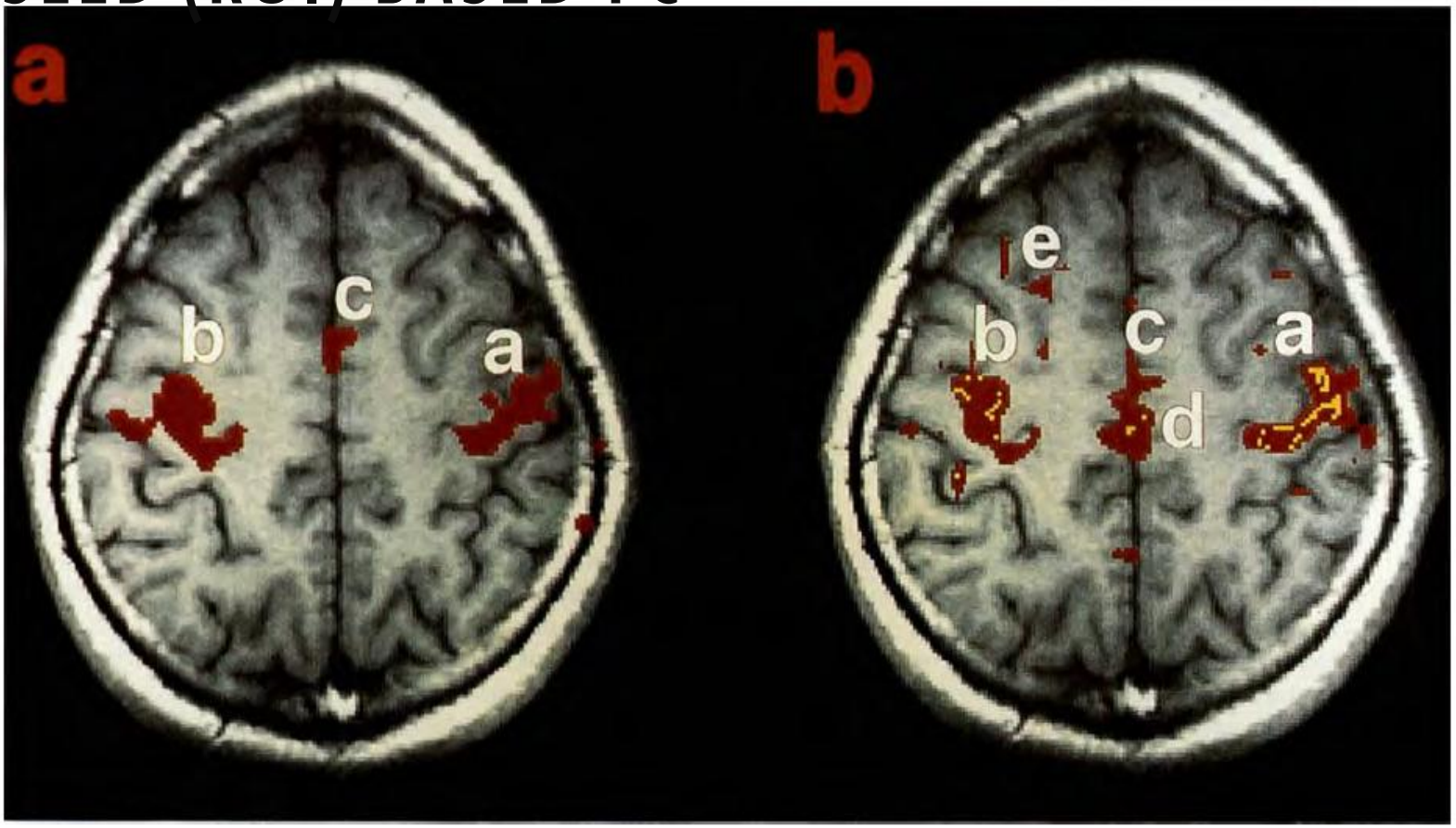


FIG. 3. (Left) FMRI task-activation response to bilateral left and right finger movement, superimposed on a GRASS anatomic image. (Right) Fluctuation response using the methods of this paper. See text for assignment of labeled regions. Red is positive correlation, and yellow is negative.

Biswal, B., Yetkin, F. Z., Haughton, V. M., & Hyde, J. S. (**1995**). Functional connectivity in the motor cortex of resting human brain using echo-planar MRI. *Magn. Reson. Med., 34, 537–41.*

- Similar results have been found in multiple other networks including
  - Visual *(Lowe et al., 1998; Cordes et al., 2000)*,
  - Auditory *(Cordes et al., 2000)*,
  - Language *(Cordes et al., 2000; Hampson et al., 2002)*,
  - Dorsal and ventral attention systems *(Fox et al., 2006a)*,
  - Corticothalamic circuits *(Zhang et al., 2008)*, and a
  - Frontal opercular network (stimulus salience) *(Seeley et al., 2007b)*.
  - Default Mode Network

COGNITION & BEHAVIOR IN TLE

Neuropsych findings in TLE

- Memory deficits
- Depression
- Behavioral changes/ social issues
- Psychosis
- Language deficits
- Anxiety/ aggression

Temporal lobe personality (Geshwind syndrome)[1,2]

Circumstantiality, hypergraphia, hyposexuality, hyper-religiosity, hyper-morality, viscosity

1. Waxman SG and Geschwind N. The interictal behavior syndrome in temporal lobe epilepsy. Archives of General Psychiatry 1975; 32, 1580-1586. PMID: 1200777.

2. Bear DM and Fedio P. Quantitative analysis of interictal behavior in temporal lobe epilepsy. Archives of Neurology 1977; 34, pp 454-467. PMID: 889477.

FCMRI IN PSYCHIATRY

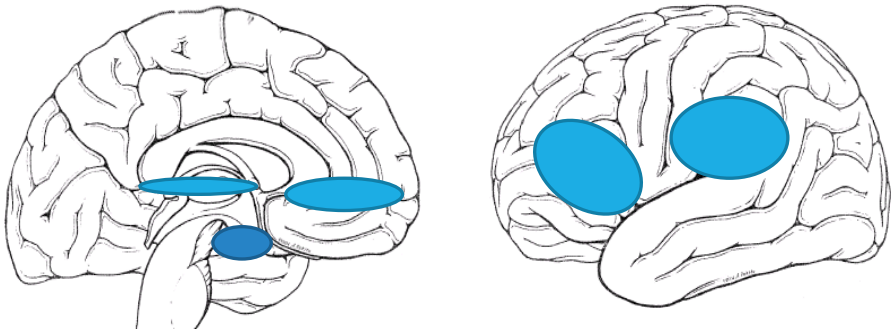
Memory deficits

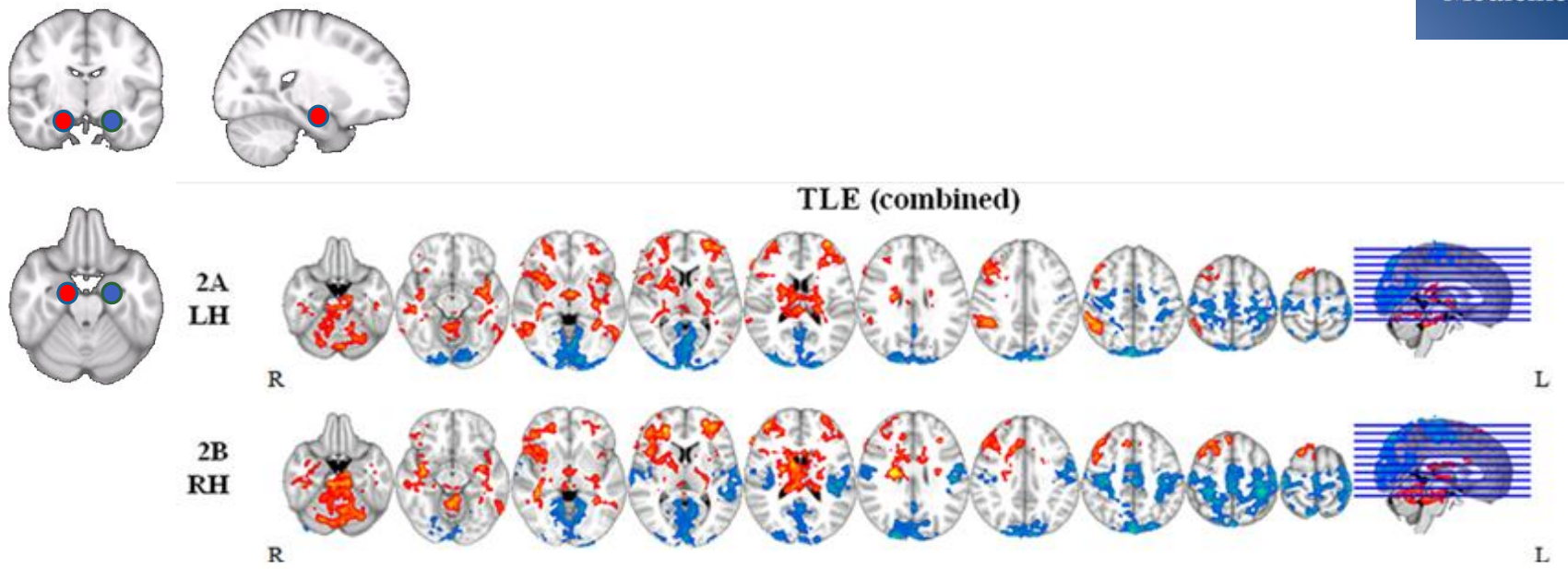
Depression:

- DMN:↑ subgenual and thalamic connectivity *(Greicius 2006)*
- DMN: ↑ L frontopolar/ L insula, ↓ L cuneus connectivity *(Wolf 2011)*

Behavioral changes/ social issues: Social cognition medial frontal

Psychosis: Increased medial frontal connectivity in Schizophrenia *(Salvador 2010)*





TLE was associated with

- ↑ **hippocampal connectivity** to key **limbic** areas (temporal lobe, insula, thalamus), **frontal** lobes, **basal ganglia, brainstem** and cerebellum
- ↓ **connectivity** to **sensorimotor** (visual, somatosensory, auditory, primary motor) and the **DMN** (precuneus).
- Left TLE had more marked connectivity changes than right TLE.

Haneef Z, Lenartowicz A, Yeh HJ, Levin HS, Engel J Jr, Stern JM.
Functional Connectivity of Hippocampal Networks in Temporal Lobe Epilepsy. Epilepsia 2013

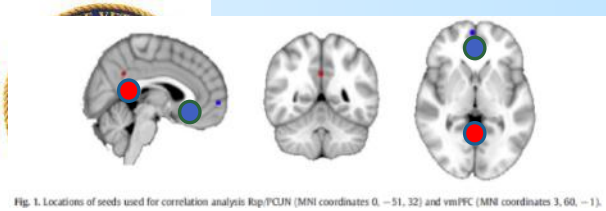


Fig. 1. Locations of seeds used for correlation analysis Rsp/PCUN (MNI coordinates 0, −51, 32) and vmPFC (MNI coordinates 3, 60, −1).

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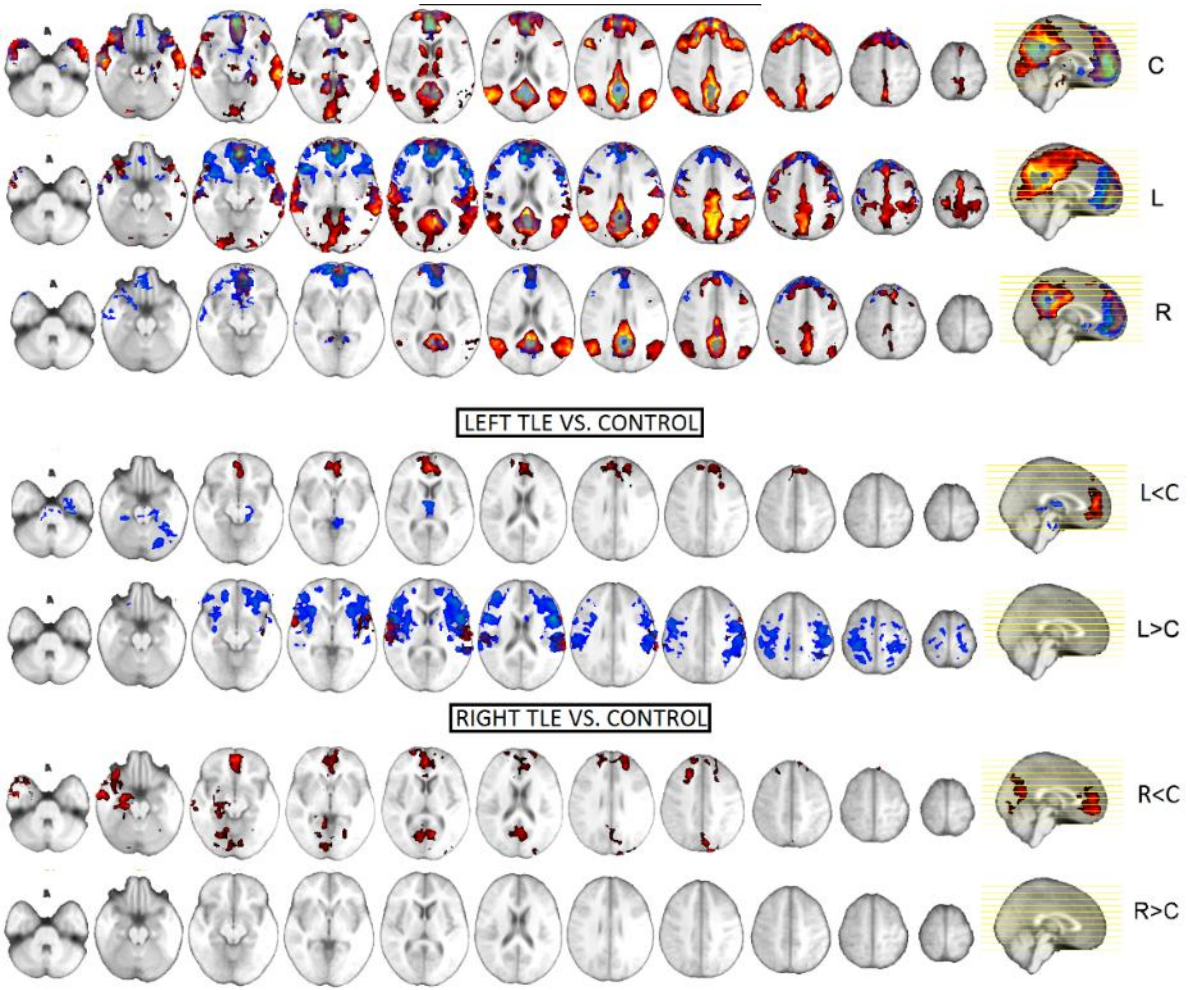
DMN seen in Controls (C), Left TLE (L) and Right TLE (R)

Posterior/
anterior DMN
Seeds

Findings
[1] TLE: ↓ connectivity between anterior & posterior DMN
[2] L TLE: ↑connectivity
[3] R TLE: ↓ connectivity



Haneef, Lenartowicz, Yeh, Engel, Stern
Effect of lateralized temporal lobe epilepsy on the default mode network. Epilepsy & Behavior 2013

Neuroimaging is a key component in the surgical workup of Epilepsy:

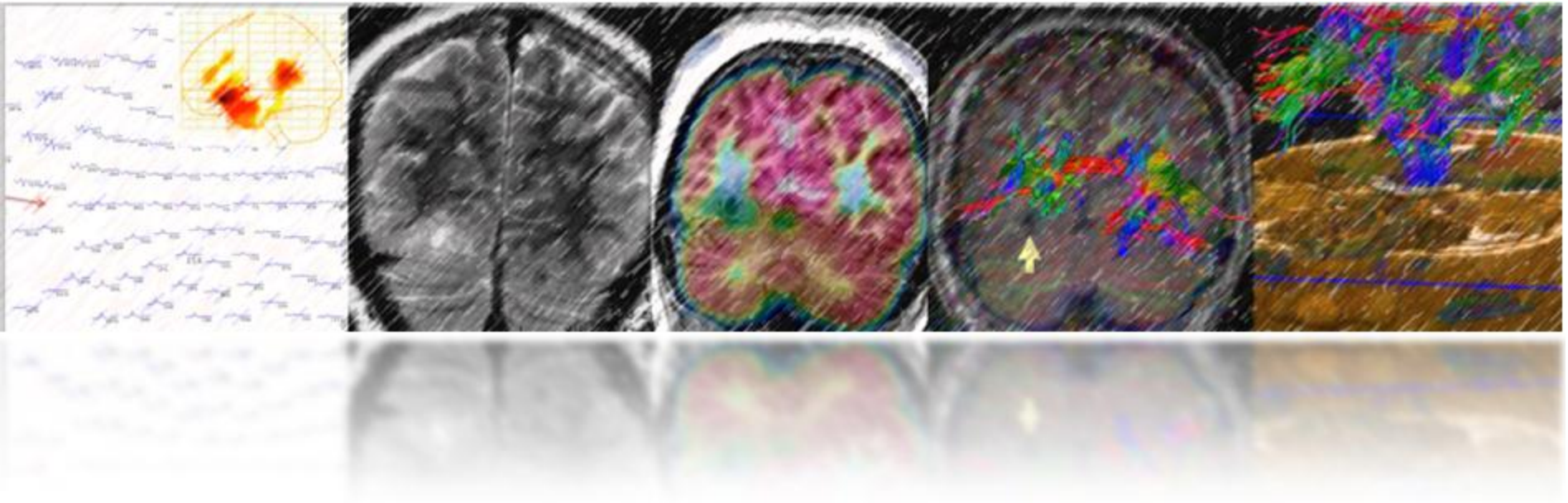
- MRI, PET, SPECT, MEG

Emerging techniques hold promise for epilepsy workup and evaluation of network level pathophysiology:

- fMRI-EEG, fcMRI/ RS-fMRI, DTI, ASL, fNIRS

Other techniques not discussed

- MR Spectroscopy (MRS), Magneto- nanoparticles, Voxel Based Morphometry (VBM)



SUMMARY

DEAD SALMON CAUTIONS AGAINST RED HERRINGS IN FMRI RESEARCH

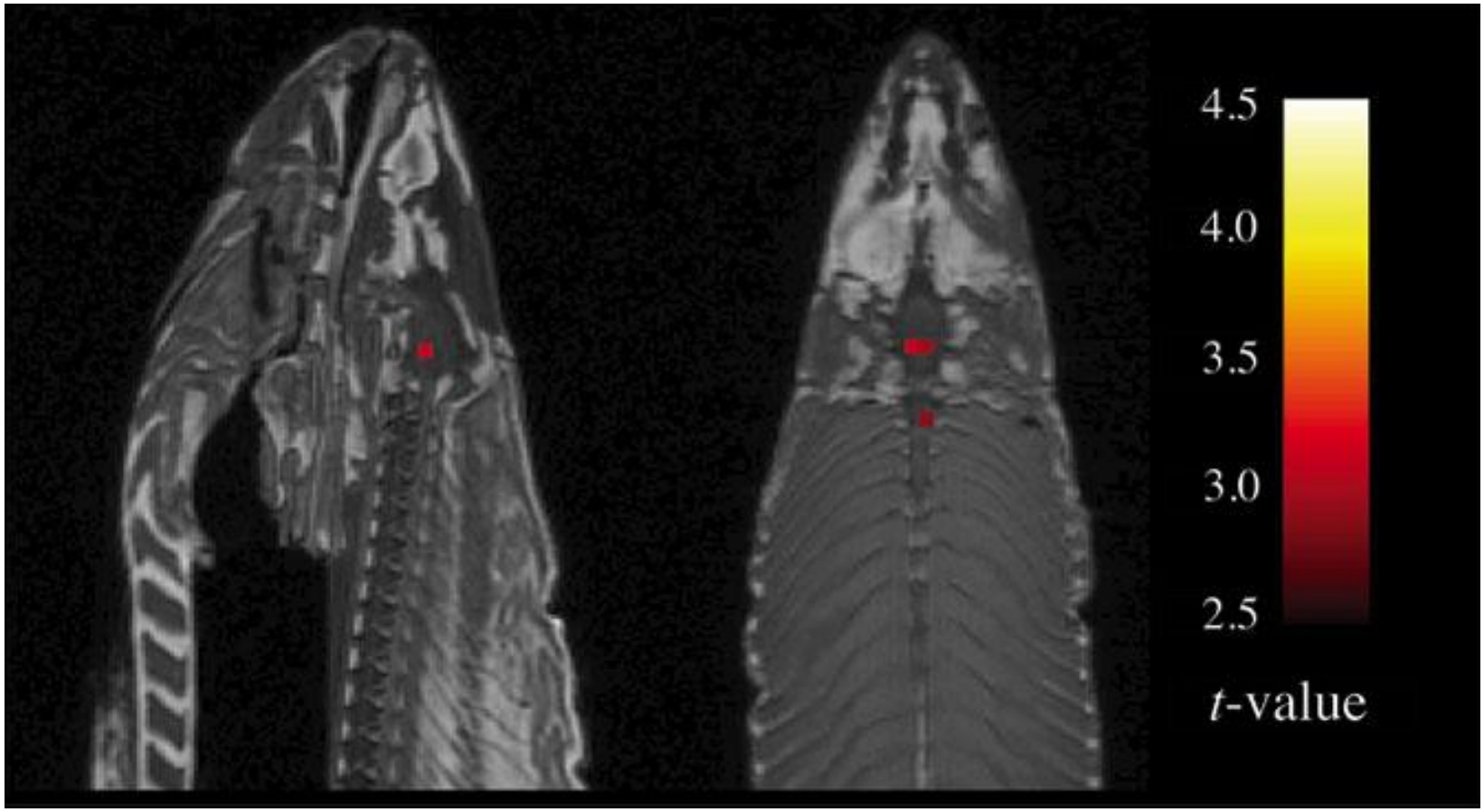
METHODS

Subject. One mature Atlantic Salmon (Salmo salar) participated in the fMRI study. The salmon was approximately 18 inches long, weighed 3.8 lbs, and was not alive at the time of scanning.

Task. The task administered to the salmon involved completing an open-ended mentalizing task. The salmon was shown a series of photographs depicting human individuals in social situations with a specified emotional valence. The salmon was asked to determine what emotion the individual in the photo must have been experiencing.

Design. Stimuli were presented in a block design with each photo presented for 10 seconds followed by 12 seconds of rest. A total of 15 photos were displayed. Total scan time was 5.5 minutes.

DEAD SALMON CAUTIONS AGAINST RED HERRINGS IN FMRI RESEARCH



ACKNOWLEDGEMENTS

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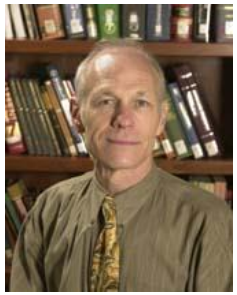
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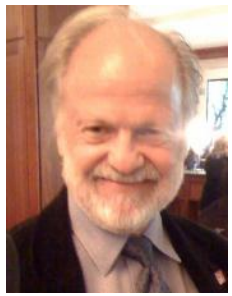
Jerome Engel Jr., MD, PhD