Temporal Lobe Epilepsy (TLE)

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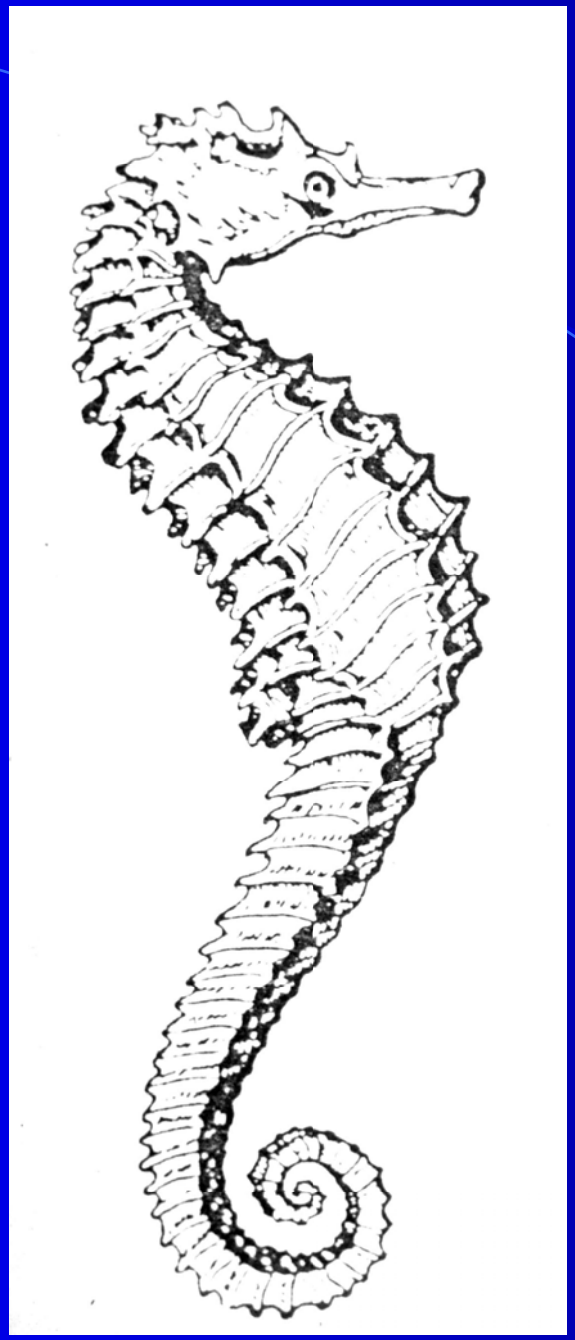
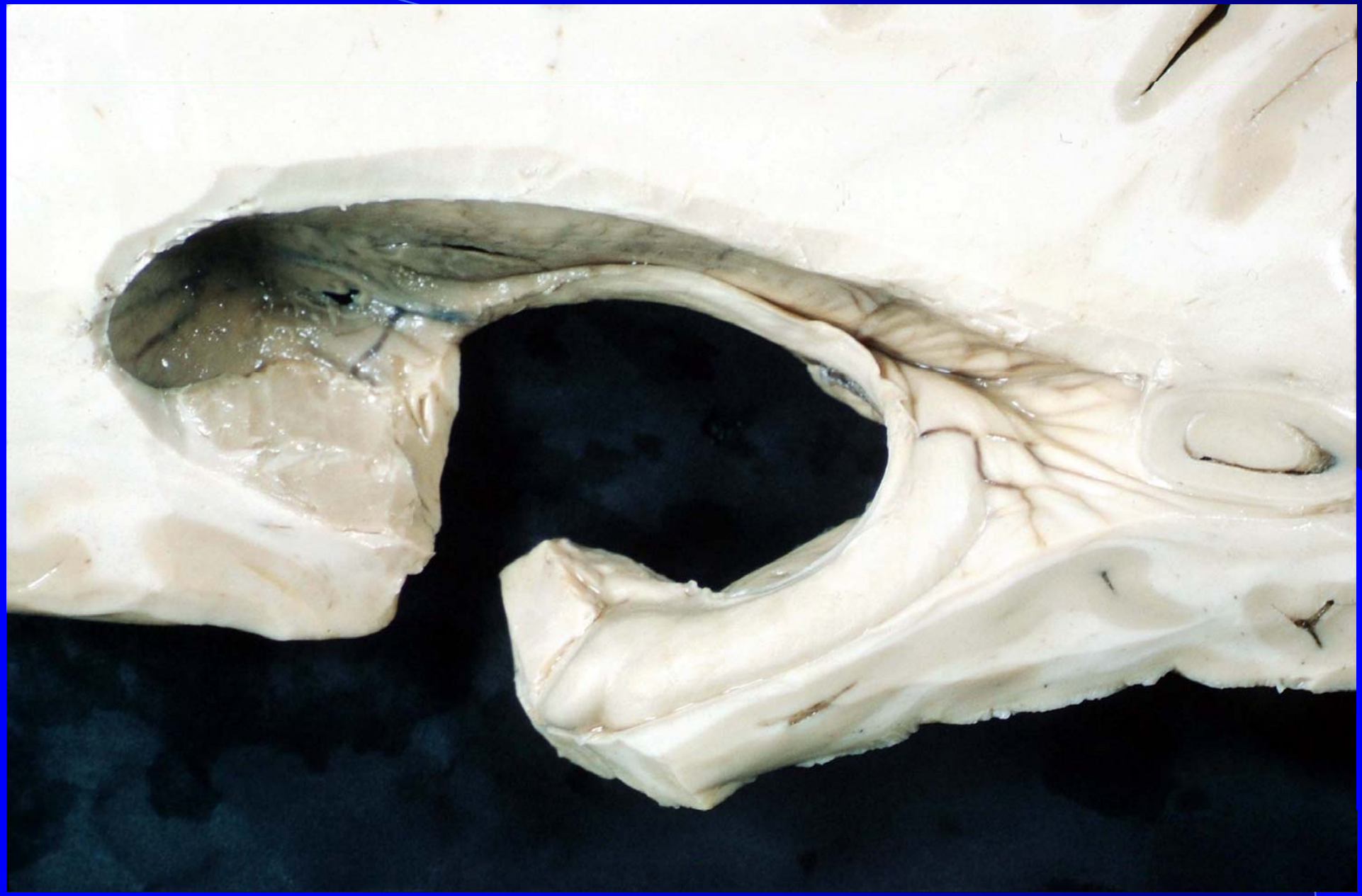
TEMPORAL LOBE EPILEPSY:
Definitions and Epidemiology I

- Medial Temporal Lobe Epilepsy (MTLE): Seizures originating in or primarily involving medial temporal lobe structures (i.e., hippocampus and amygdala)
- Lateral Temporal Lobe Epilepsy (LTLE): Seizures originating elsewhere in the temporal lobe (i.e., in the temporal lobe neocortex)
- Benign (?) Familial Temporal Lobe Epilepsy

TEMPORAL LOBE EPILEPSY:
Definitions and Epidemiology II

- Most common chronic epileptic disorder
  - Prevalence: 40% of patients with epilepsy have complex partial seizures (CPS) (Gastaut)
  - Prevalence: 55% of adults with epilepsy have complex partial seizures (Wieser)

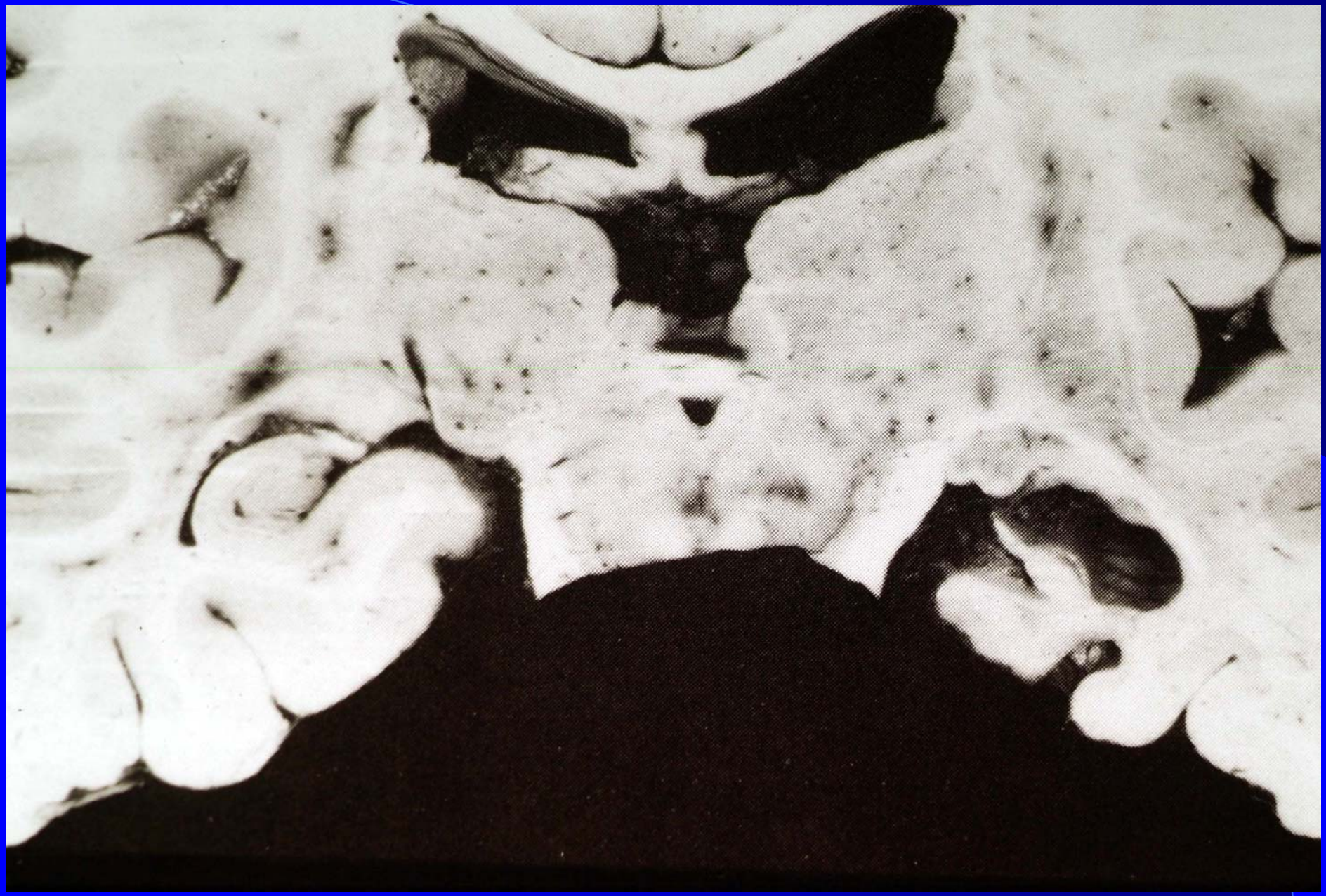




ETIOLOGY I

Most common lesion is Hippocampal Sclerosis (60-75%)

- Neuronal cell loss and gliosis in CA1, CA3, CA4 with occasional wider involvement (CA2, DG, PHG, AM)
- Symmetry of lesions
  - 80% bilateral and asymmetric
  - 10% bilateral and symmetric
  - 10% unilateral only
- Approximately 50% (40-80%) of patients with hippocampal sclerosis experienced a prolonged febrile convulsion(s) between the ages of 6 months and 6 years
- ? Cause or consequence of seizures?

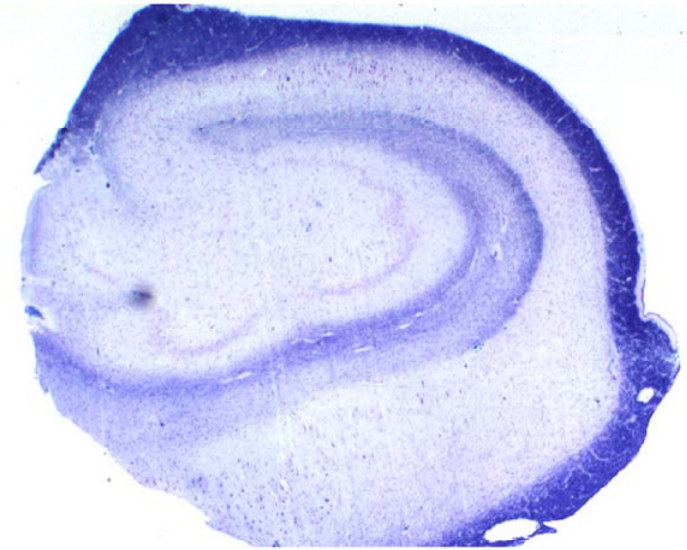



HIPPOCAMPUS
DENT. GYRUS
SUBICULUM
PARA-
HIPP.
GYRUS

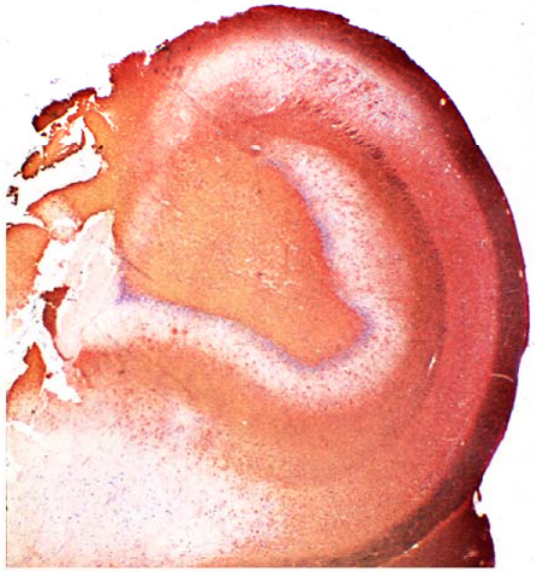
NORMAL HIPPOCAMPUS

HIPPOCAMPAL SCLEROSIS

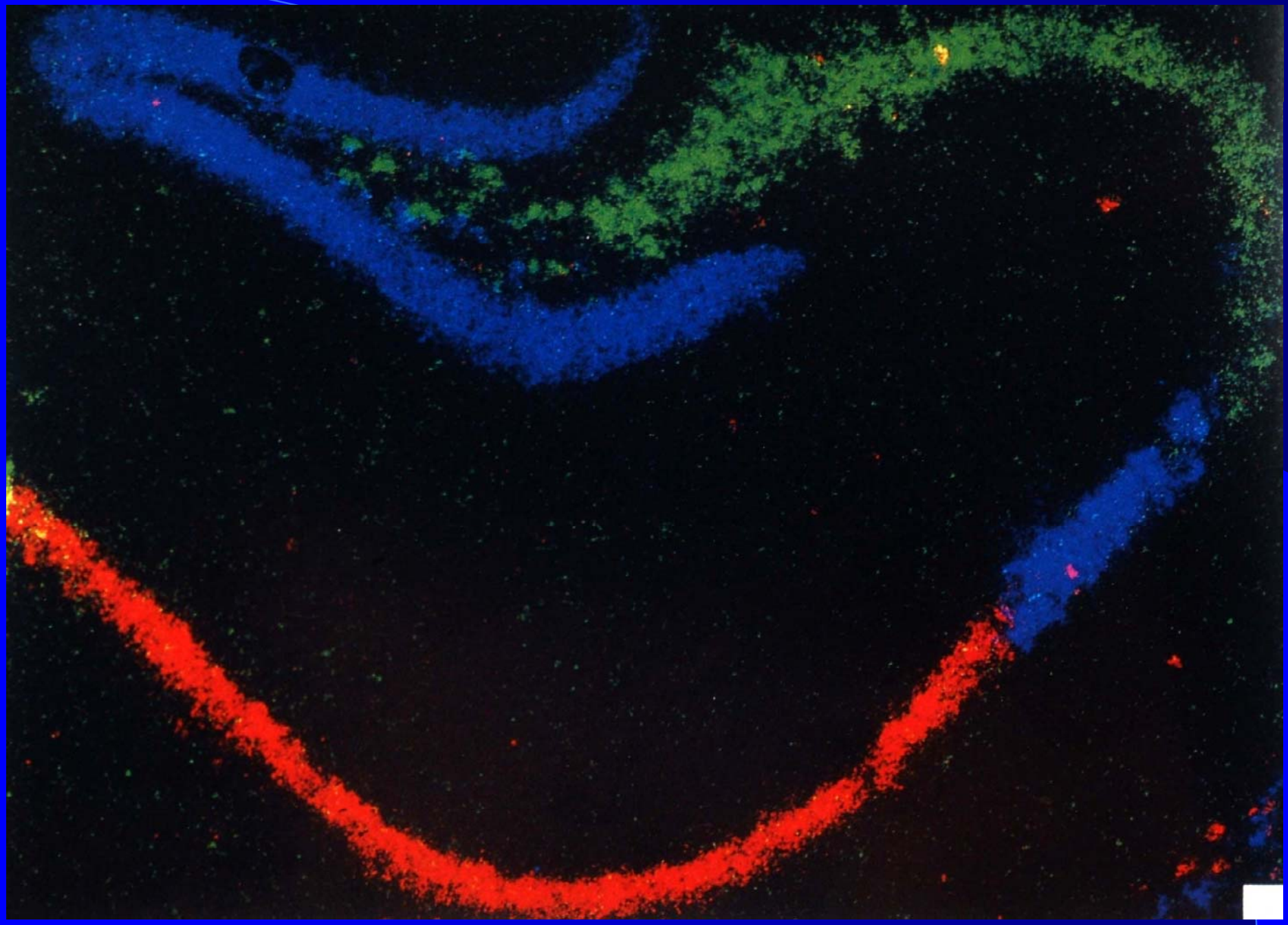
CV/LFB STAIN



GFAP STAIN



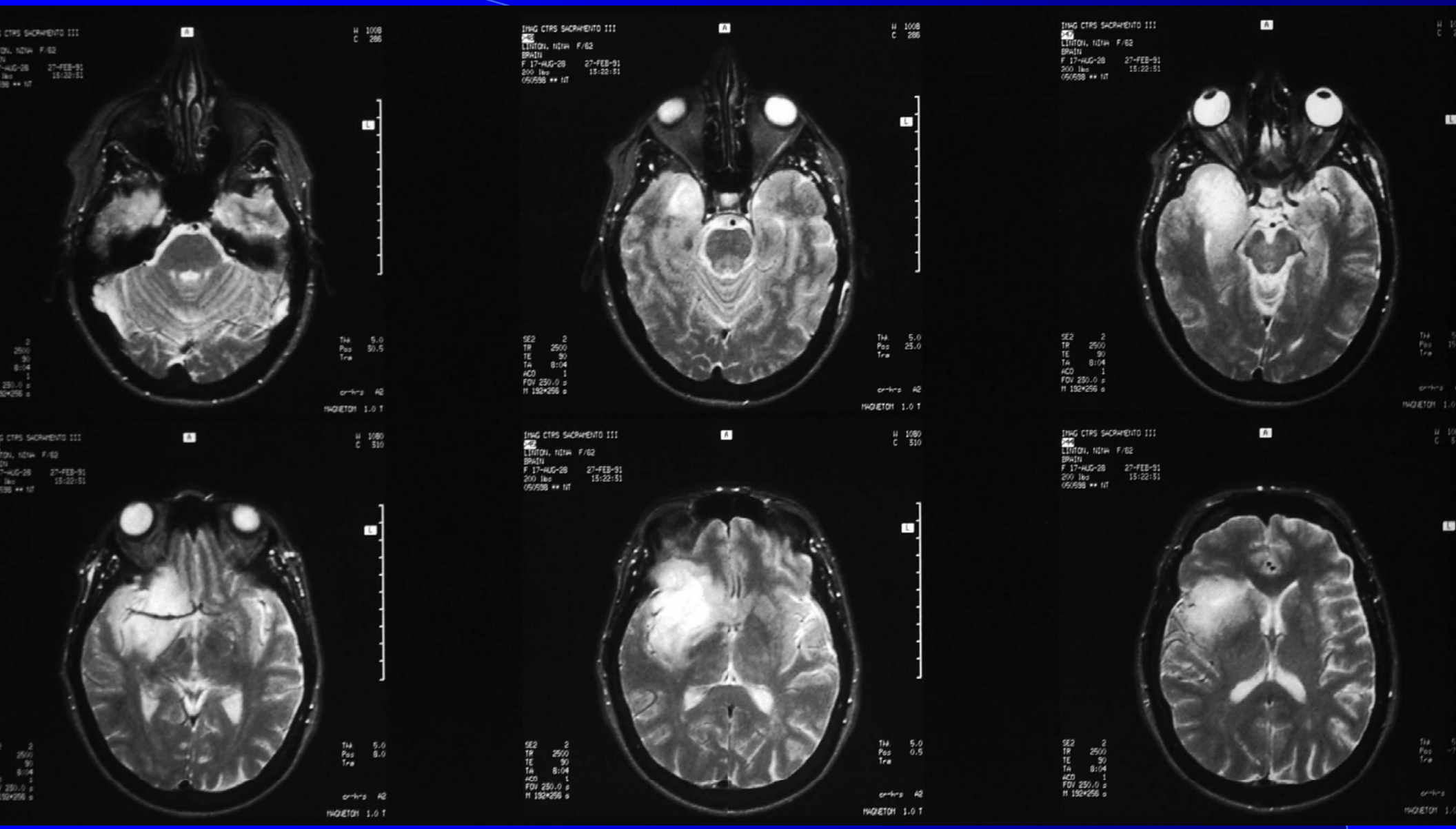
Watson C. Expert Rev Neurotherapeutics 2003;3:821-828.




TAKE A NUMBER
1

ETIOLOGY II

- Neoplasms and hamartomas - 20%
- Scars from trauma (4%), infection (2-4%), infarction - 8-10%
- Cortical dysplasia, heterotopias, cysts, etc. - 2-5%
- Vascular malformations - 2-5%
- Dual pathology - 10-15%
- No apparent lesion - 15%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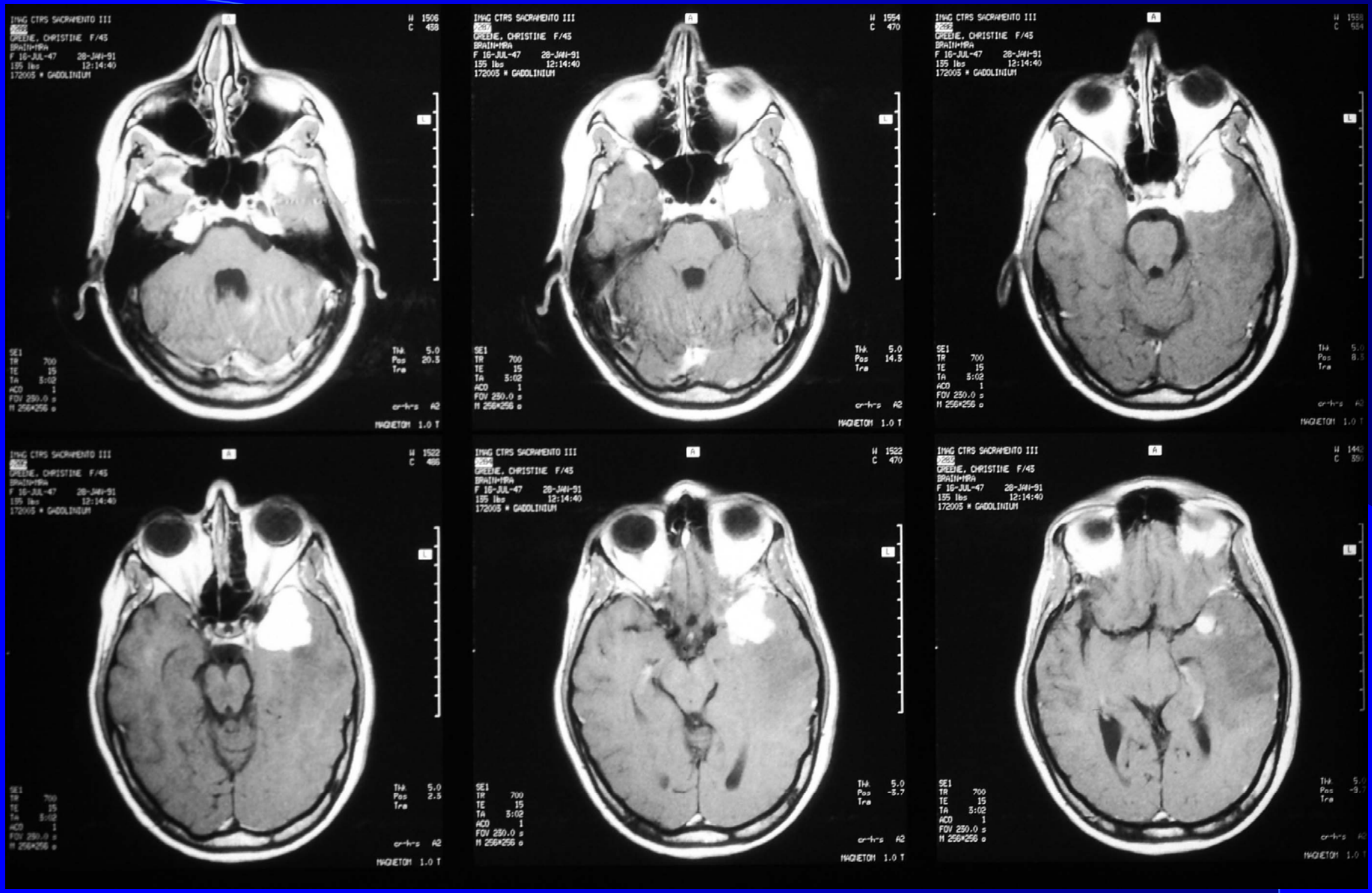
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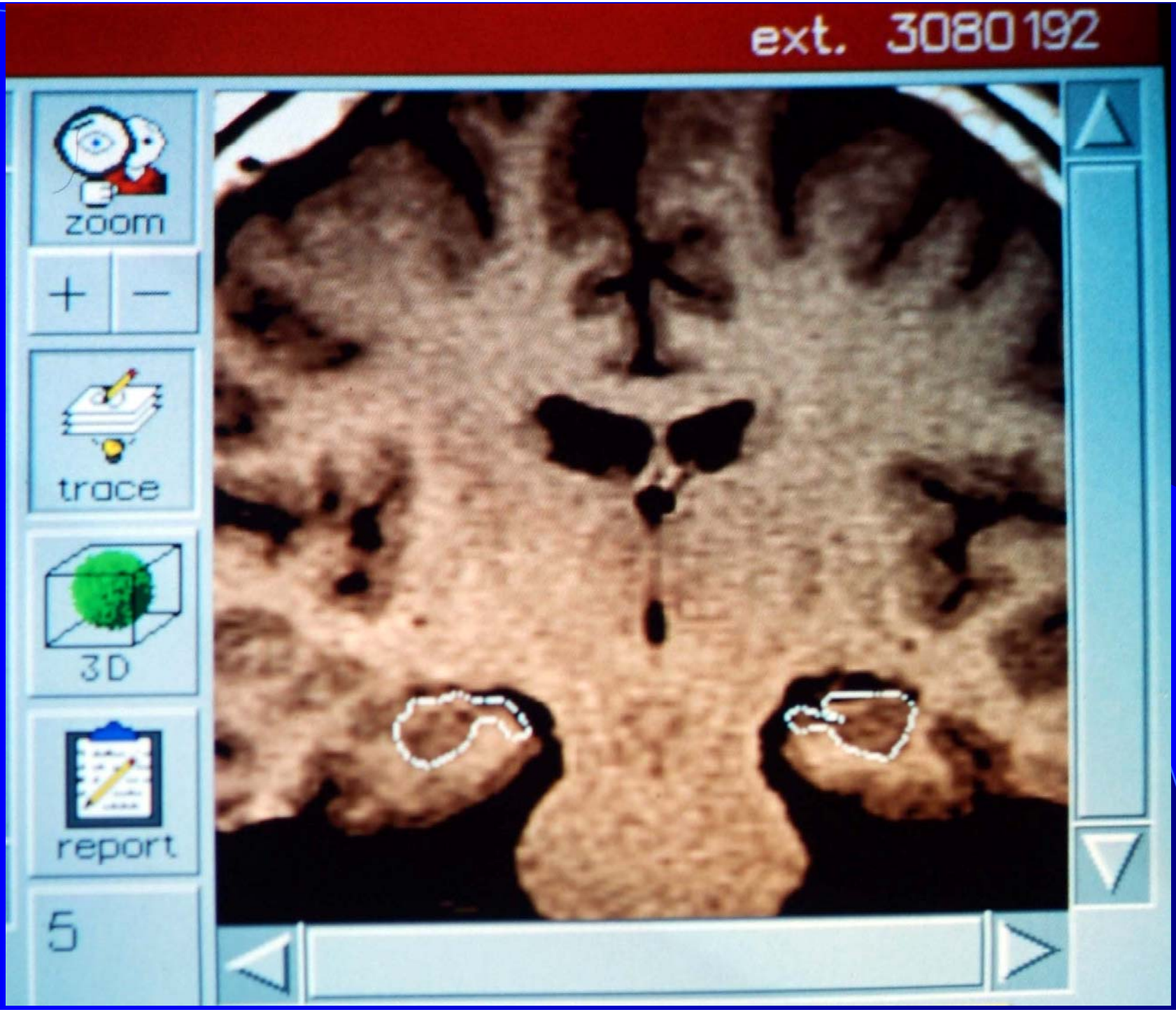
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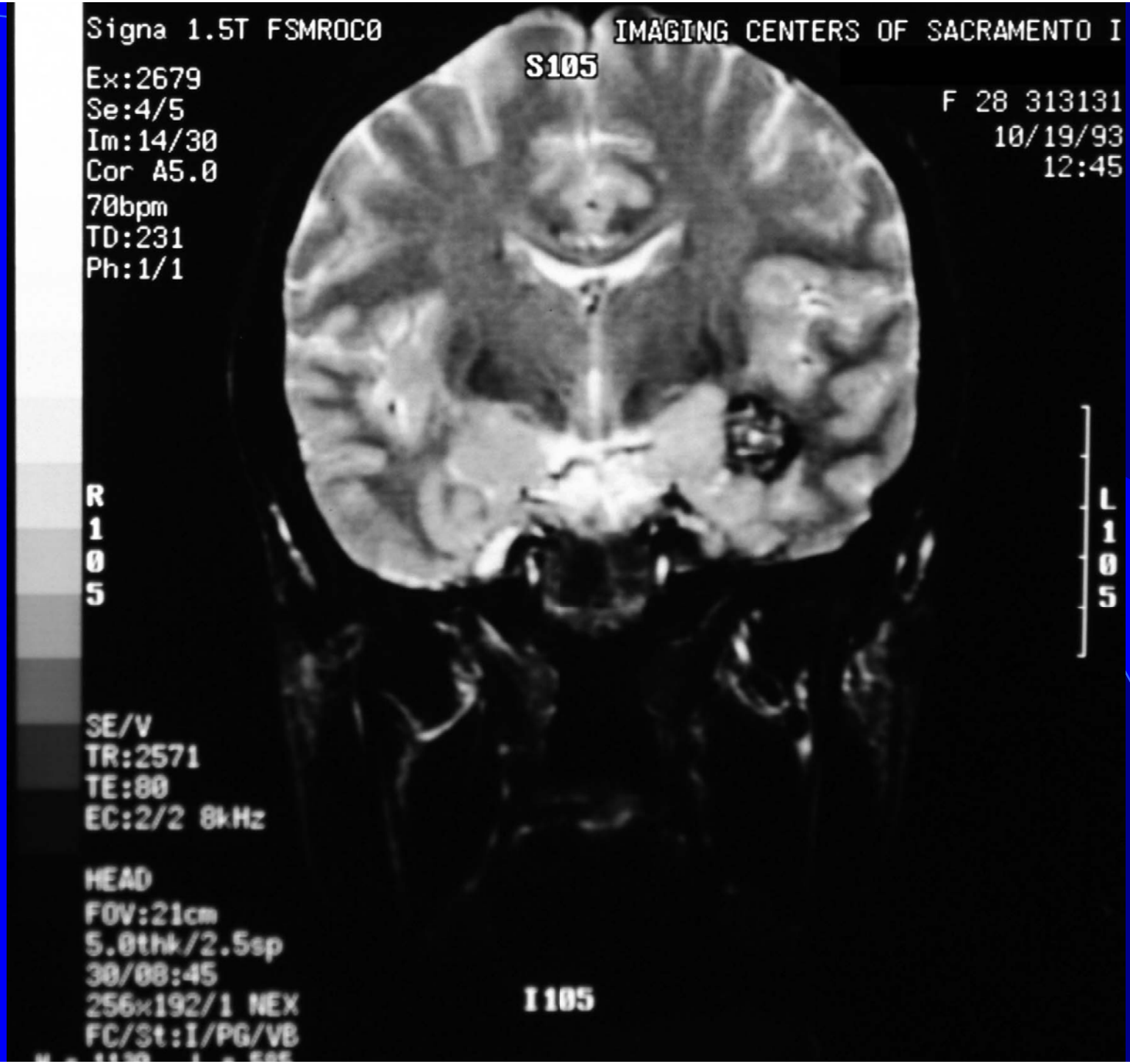
Signa 1.5T FSMROC0
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Se:4/5
Im:14/30
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70bpm
TD:231
Ph:1/1
F 28 313131
10/19/93
12:45
R
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5
L
1
0
5
SE/V
TR:2571
TE:80
EC:2/2 0kHz
HEAD
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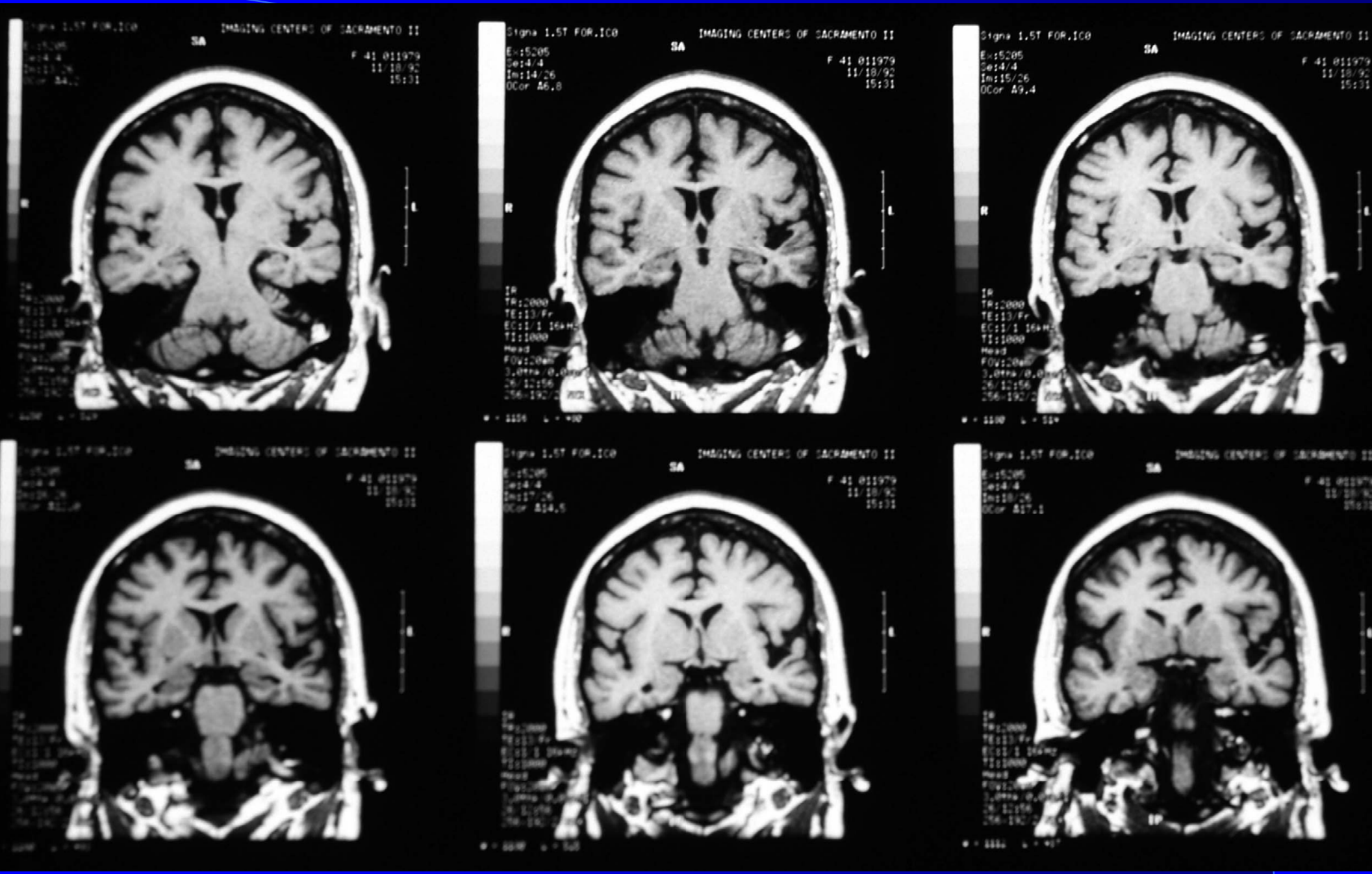
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SA
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11/10/92
15:31

DIFFERENTIAL DIAGNOSIS

- Benign epilepsy of childhood with centrotemporal spikes (BECTS, rolandic epilepsy)
- Absence seizures
  - Simple absences: vs CPS with impaired consciousness only
  - Atypical absences: vs CPS with automatisms
- Complex partial seizures from extratemporal sites
  - Frontal
  - Parietal
  - Occipital
- Migraine, Psychoses, Dissociative states, Pseudoseizures

CLINICAL FEATURES: I

- Age of onset - usually childhood, but any age is possible
- Early risk factors
  - Birth asphyxia or trauma
  - Head injury
  - CNS infection
  - Prolonged febrile convulsions
- Precipitating or triggering factors
  - Sleep deprivation
  - Stress
  - Sleep/drowsiness
  - Menstruation

CLINICAL FEATURES: II

- Seizure types
  - Simple partial seizures (SPS) (aura)
  - Complex partial seizures (CPS)
  - SPS evolving into CPS
  - Secondarily generalized tonic-clonic seizures (GTCS)
  - “Temporal lobe syncope”

SIMPLE PARTIAL SEIZURES:

Sensory Symptoms

(Consciousness Preserved)

- Olfactory - medial temporal, orbitofrontal
- Gustatory - medial temporal, insula, peri-insular
- Vertigo - lateral temporal, parietal
- Auditory - lateral temporal
- Visual - occipital, temporo-occipital

SIMPLE PARTIAL SEIZURES:
Autonomic Symptoms

- Rising epigastric sensation, other GI symptoms
- Tachycardia, arrhythmia
- Goose pimples
- Sweating
- Pallor
- Flushing
- Pupillary changes
- Incontinence
- Genital or sexual symptoms

SIMPLE PARTIAL SEIZURES:
Psychic Symptoms

- Deja vu
- Jamais vu, Depersonalization, Unreality
- Dreamy state
- Forced thinking
- Illusions/hallucinations (experiential phenomena)
  - Visual (micropsia, macropsia, change in shapes)
  - Complex cognitive states
- Emotional
  - Fear or other emotions
- Vocalization/verbalization

COMPLEX PARTIAL SEIZURES:
Mechanisms
(Consciousness Impaired)

- Impaired consciousness implies bilateral medial temporal ictal activity or unilateral ictal activity with damage to opposite side
- Ictal activity may originate in frontal, lateral temporal, parietal, or occipital lobes and propagate to medial temporal structures

COMPLEX PARTIAL SEIZURES:
Clinical Features: I

- Motionless stare or behavioral arrest with impaired awareness and responsiveness
- Automatisms: involuntary, automatic motor behaviors
  - Lip smacking, chewing, swallowing, licking, tooth-grinding
  - Picking, scratching, dressing, undressing, rearranging objects
  - Walking, running, wandering
  - Vocalization, verbalization
  - Facial expressions (emotional)
  - Masturbation, pelvic thrusting
  - Flailing, bicycling movements, spitting
  - Reactive actions or movements

COMPLEX PARTIAL SEIZURES:
Clinical Features: II

- Other motor signs
  - Early, non-forced, ipsilateral head turning
  - Contralateral, usually upper limb, tonic or dystonic posturing
  - Ipsilateral, usually upper limb, automatisms
  - Late, forced, contralateral head and eye deviation (often at the beginning of a secondarily GTCS)
  - Contralateral ictal paresis
  - Ictal vomiting
  - Ipsilateral eye blinking

COMPLEX PARTIAL SEIZURES:
Postictal Symptoms

- Confusion, disorientation
- Retrograde amnesia for the seizure and the aura
- Anterograde amnesia
- Language dysfunction (dominant temporal lobe onset)
- Contralateral postictal paresis
- Reactive automatisms - including striking out at threats or attempts at restraint

SECONDARILY GENERALIZED TONIC-CLONIC SEIZURES

- Can evolve from either SPS or CPS
- Not always a “typical” GTCS
- Can begin so rapidly that the initial partial onset is not noted by the patient or observer
- Prognosis is worse if secondarily GTCS occur frequently

NEUROLOGICAL EXAMINATION

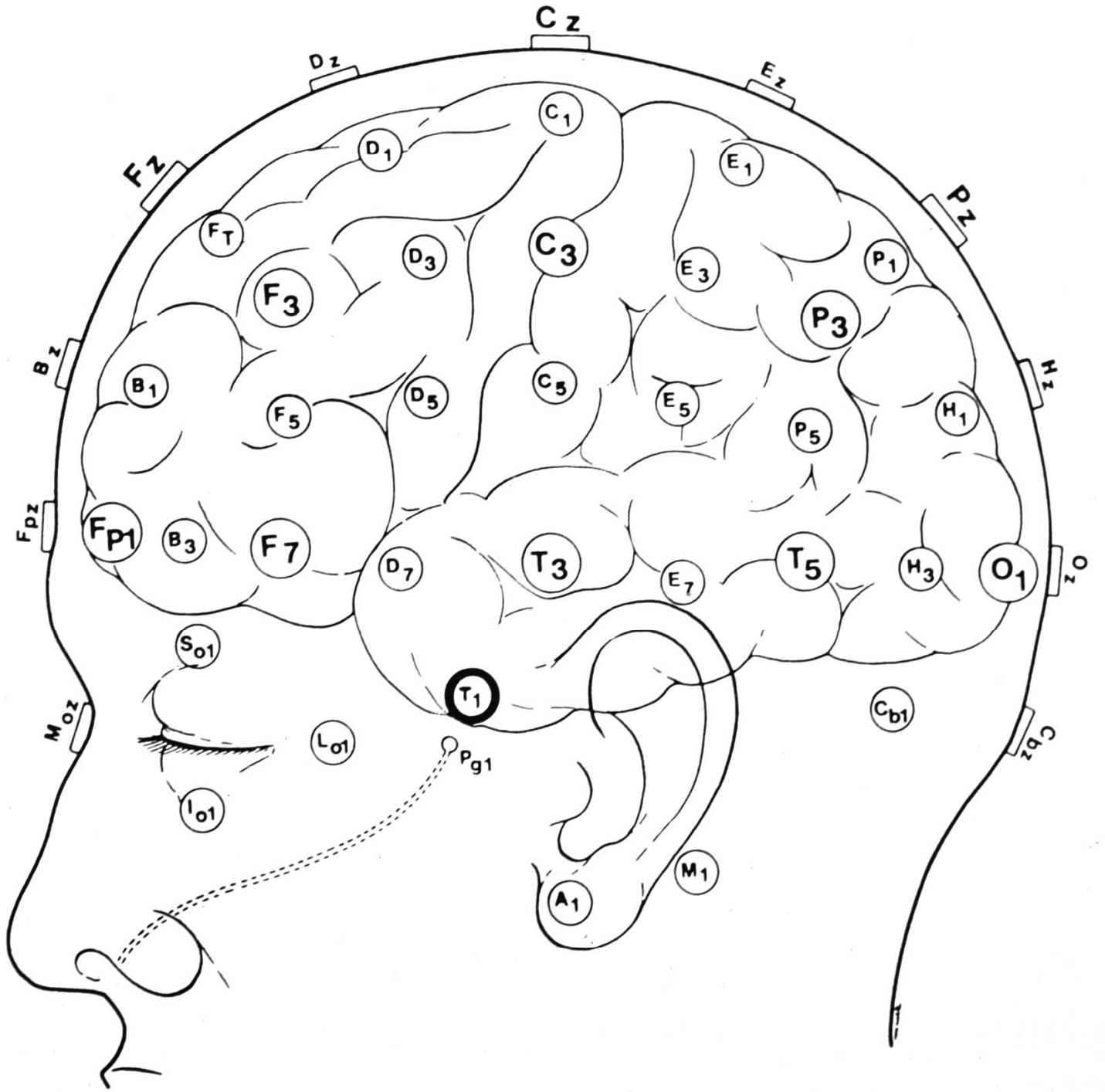
- Normal, except for decreased short term memory
- There is some evidence that repeated CPS may lead to progressive functional changes with more refractory seizures and increasing memory loss

PERSONALITY TRAITS
("Temporal lobe personality")

- Aggressive
- Passive
- Emotional
- Humorless, sober
- Hypermoral
- Religiosity
- Circumstantial
- Hypergraphic
- Hyposexual
- Psychiatric symptoms (Depression, Psychosis)

DIAGNOSTIC STUDIES:
Interictal EEG

- Unilateral or independent bilateral spikes, spike and wave complexes, sharp waves, slow waves
- Abnormalities are best seen with basal electrodes
  - Pg1, Pg2
  - A1, A2
  - T1, T2
  - Zg1, Zg2
  - Sp1, Sp2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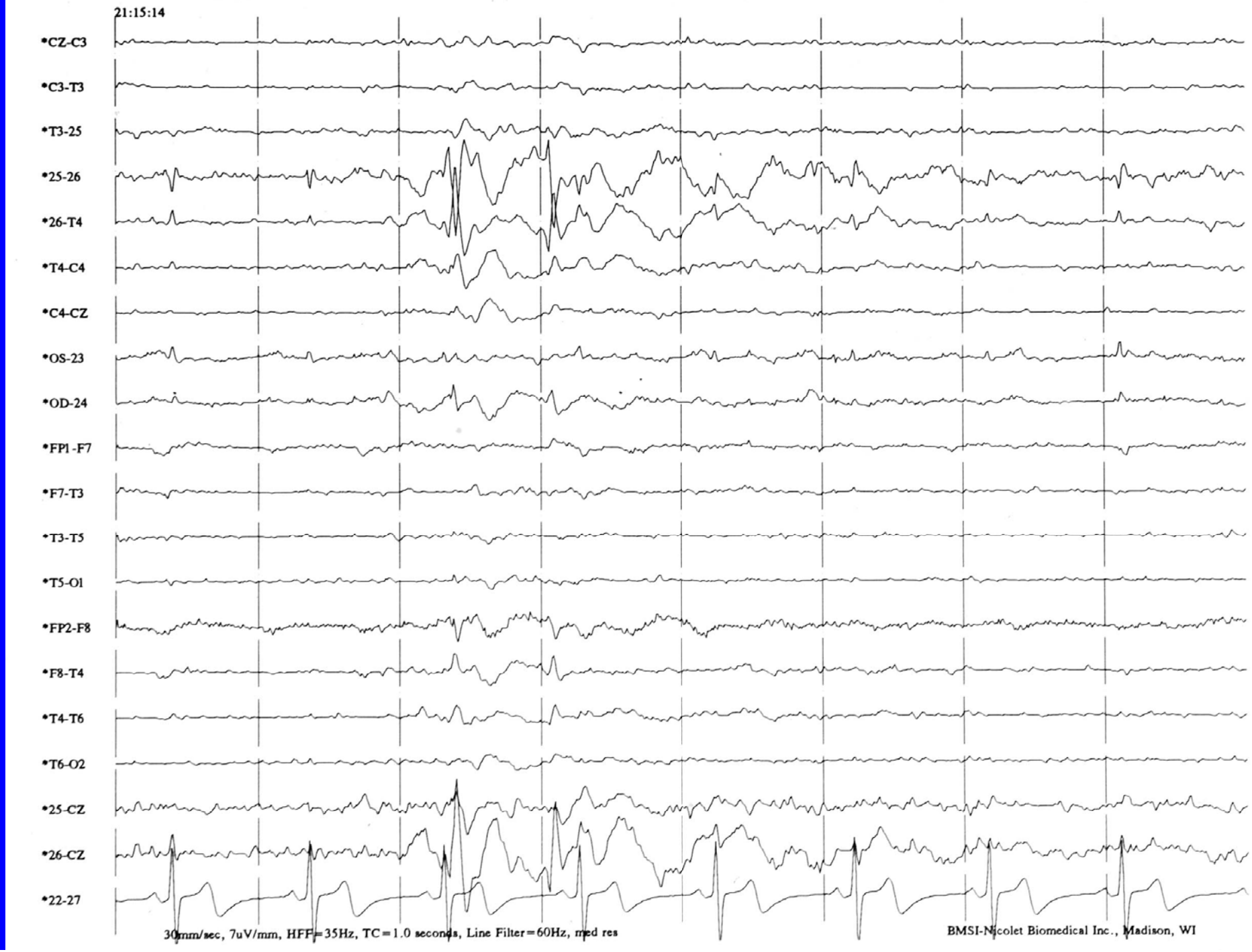
Io1
M1
A1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*C3-T3
*T3-25
*25-26
*26-T4
*T4-C4
*C4-CZ
*OS-23
*OD-24
*FP1-F7
*F7-T3
*T3-T5
*T5-O1
*FP2-F8
*F8-T4
*T4-T6
*T6-O2
*25-CZ
*26-CZ
*22-27
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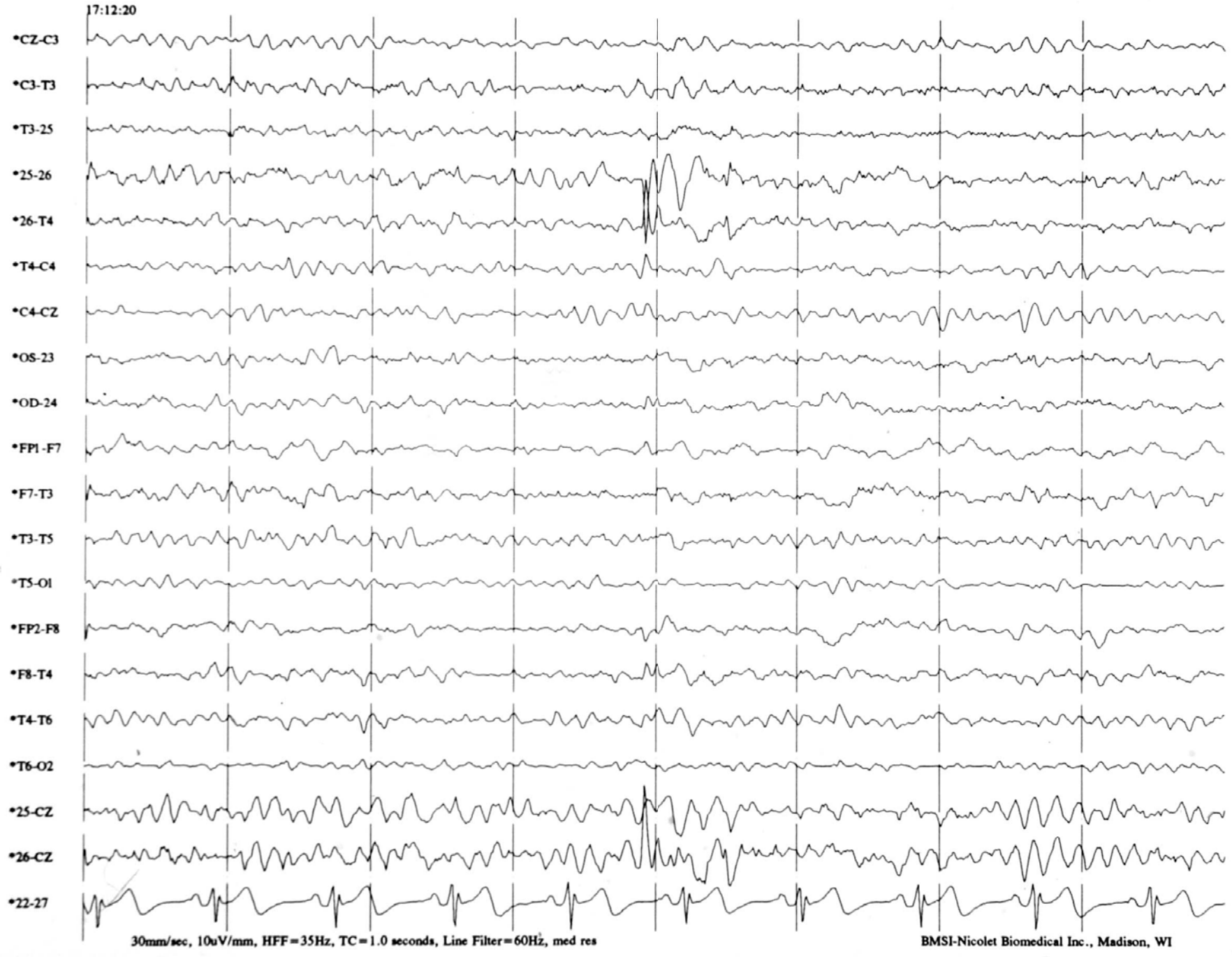
BMSI-Nicolet Biomedical Inc., Madison, WI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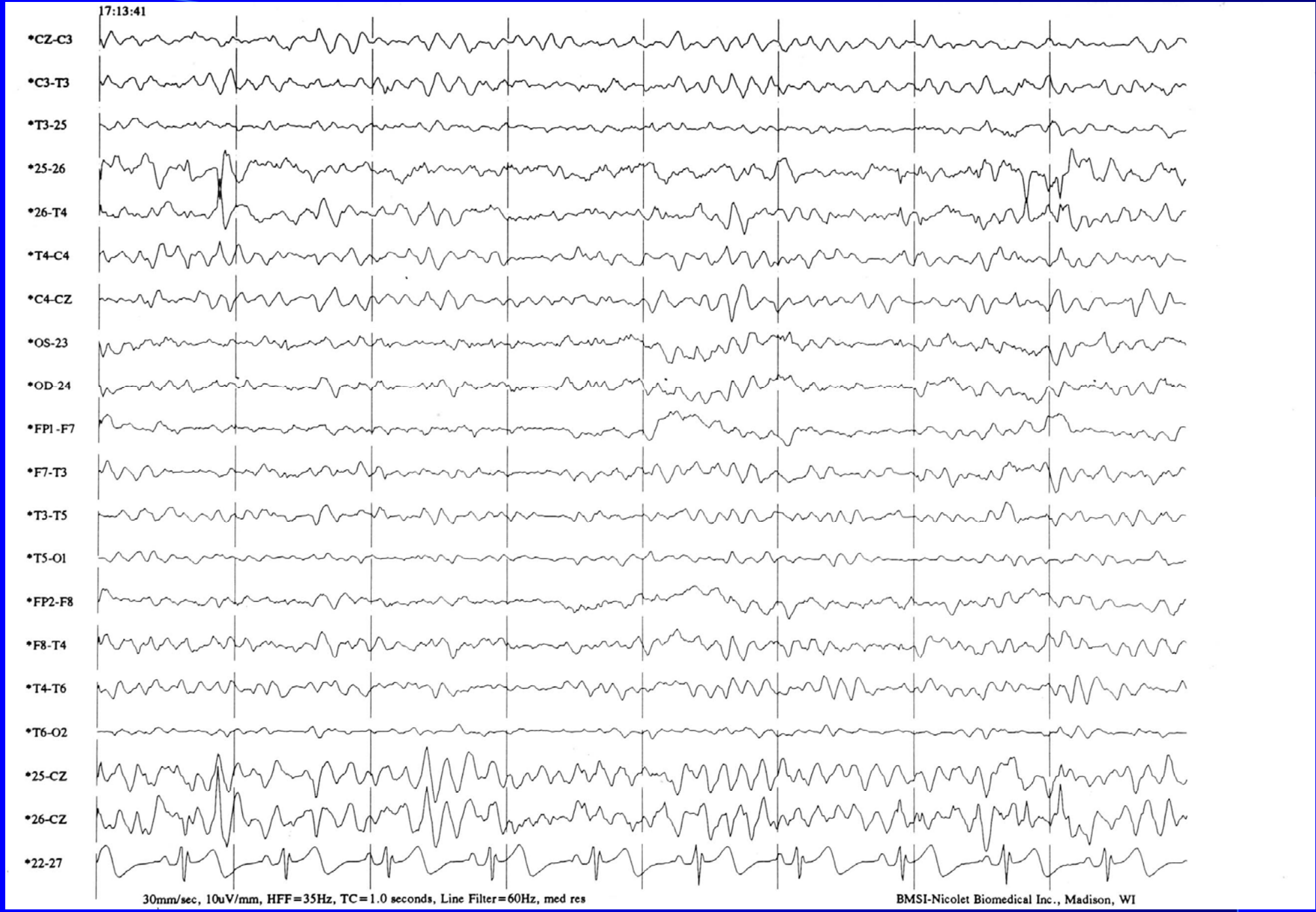
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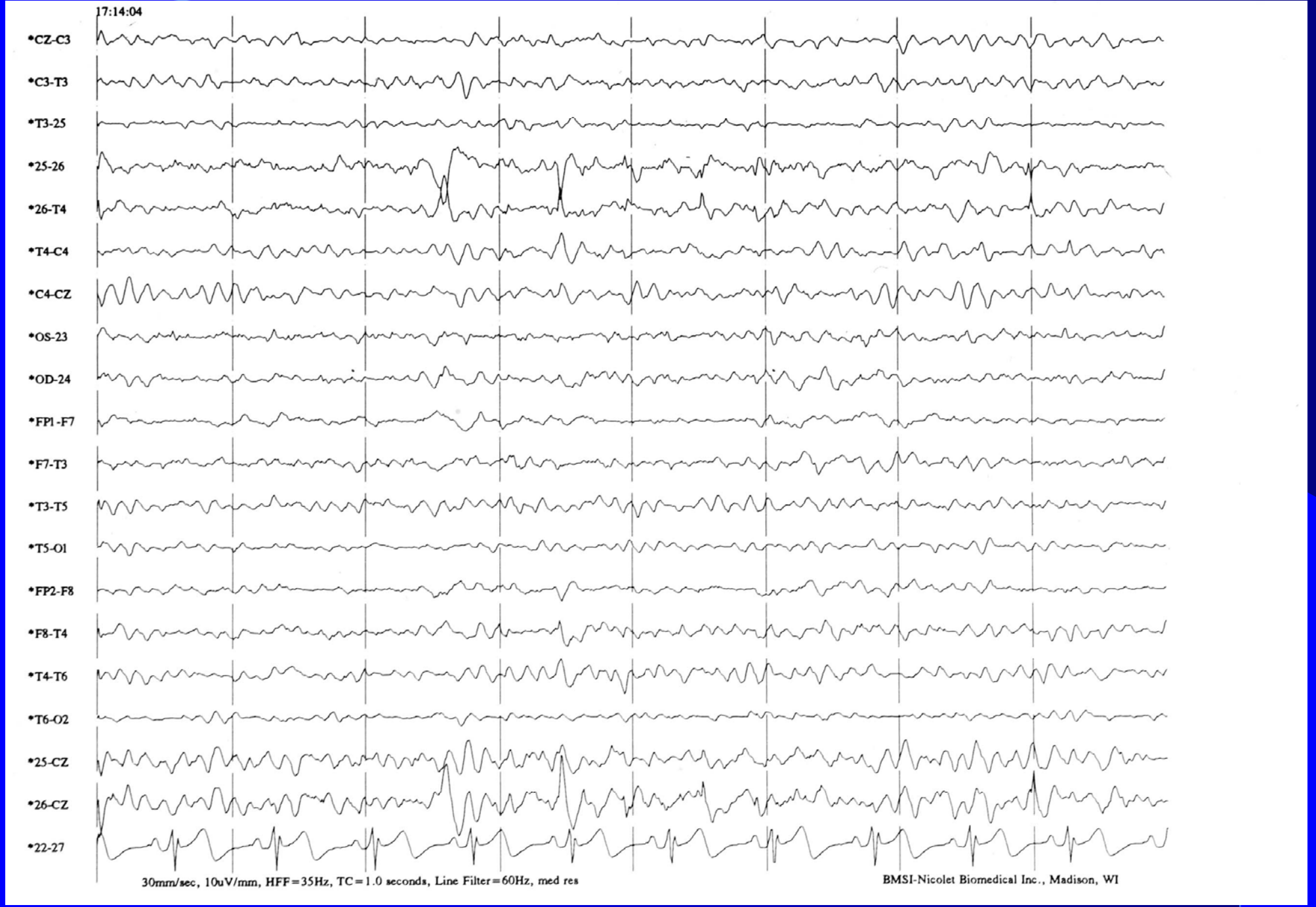
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*FP1-F7
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*T3-T5
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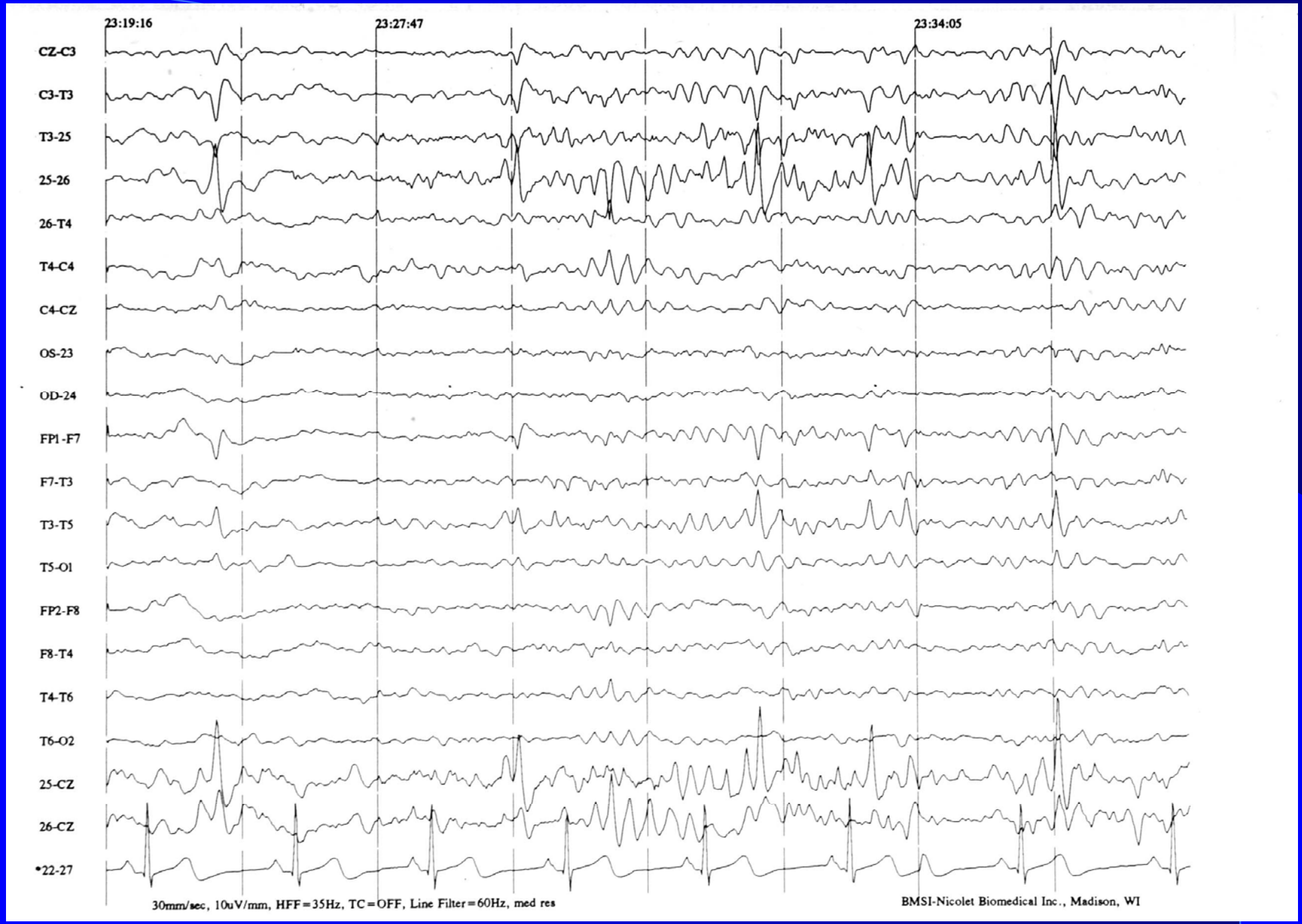
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23:27:47
23:34:05
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C3-T3
T3-25
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26-T4
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C4-CZ
OS-23
OD-24
FP1-F7
F7-T3
T3-T5
T5-O1
FP2-F8
F8-T4
T4-T6
T6-O2
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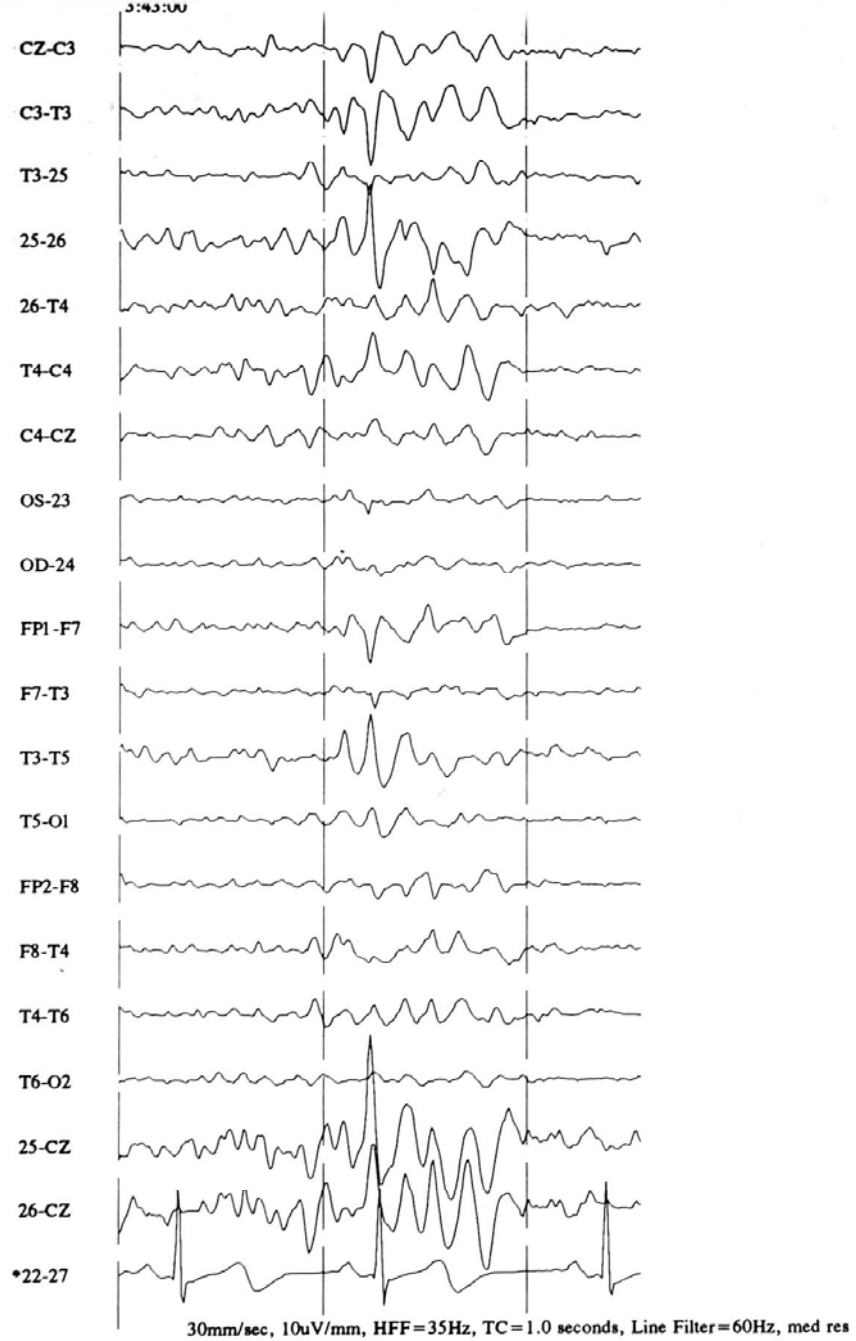

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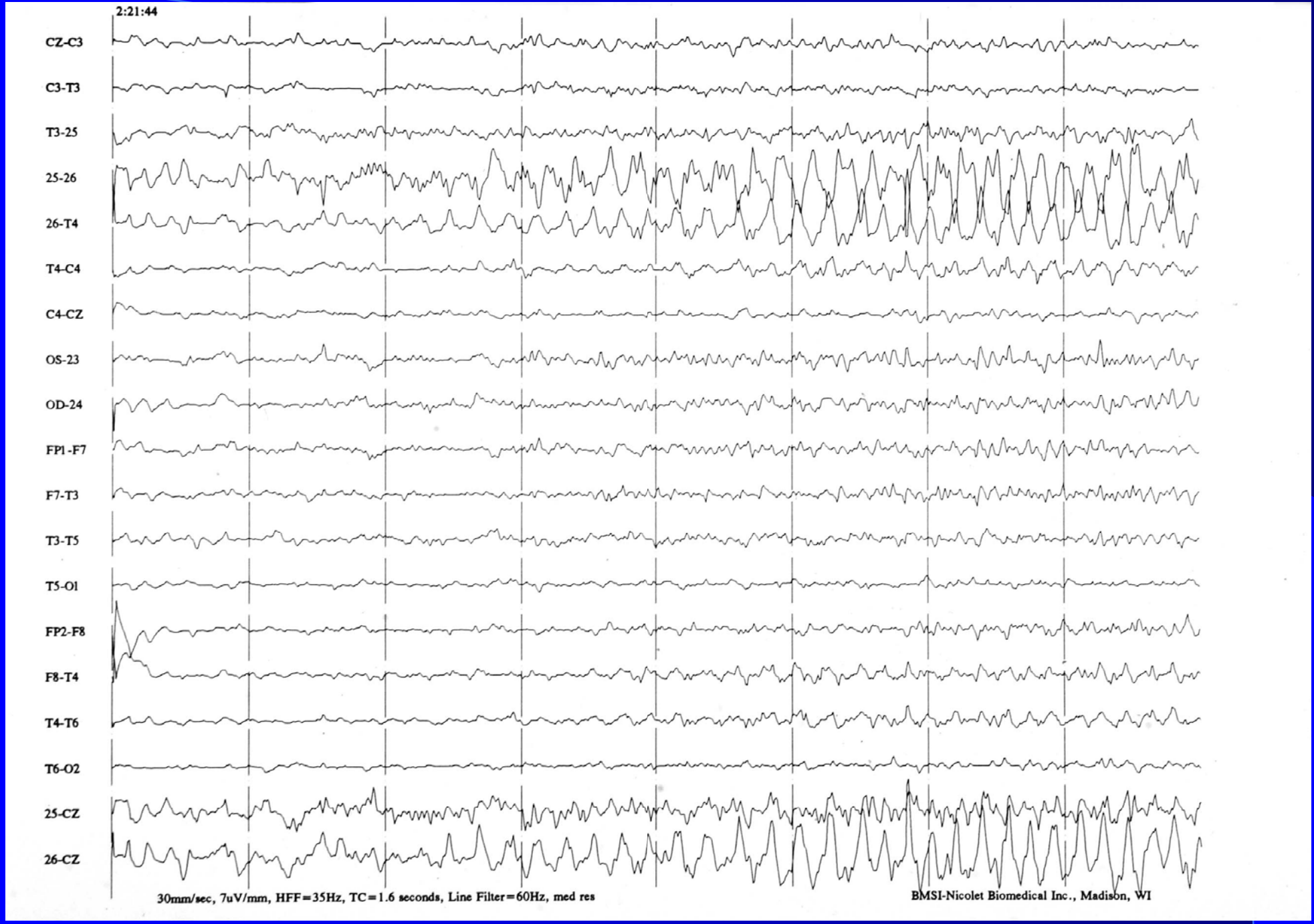
DIAGNOSTIC STUDIES:
Ictal EEG (EEG-Video Monitoring)

- Suppression of background, evolving low voltage fast activity, rhythmic 5-7 Hz sharp waves, spread ipsilaterally, spread contralaterally
- Initial focal onset: ictal activity seen in one sphenoidal electrode before spread to the lateral temporal electrodes
- Delayed focal onset: ictal activity appears in one sphenoidal electrode many seconds (<30) after a nonlocalizing onset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C3-T3
T3-25
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26-T4
T4-C4
C4-CZ
OS-23
OD-24
FP1-F7
F7-T3
T3-T5
T5-O1
FP2-F8
F8-T4
T4-T6
T6-O2
25-CZ
26-CZ
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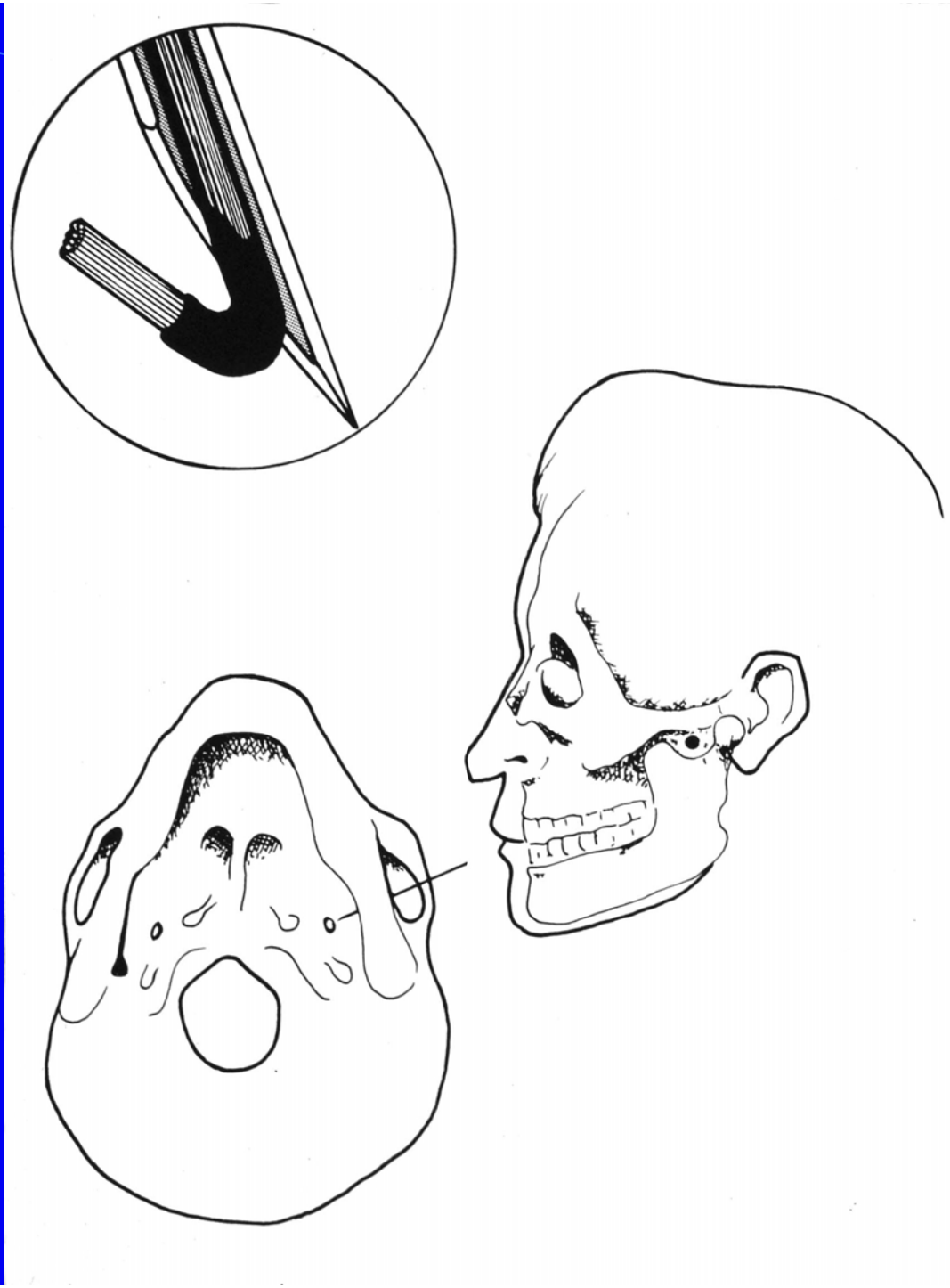
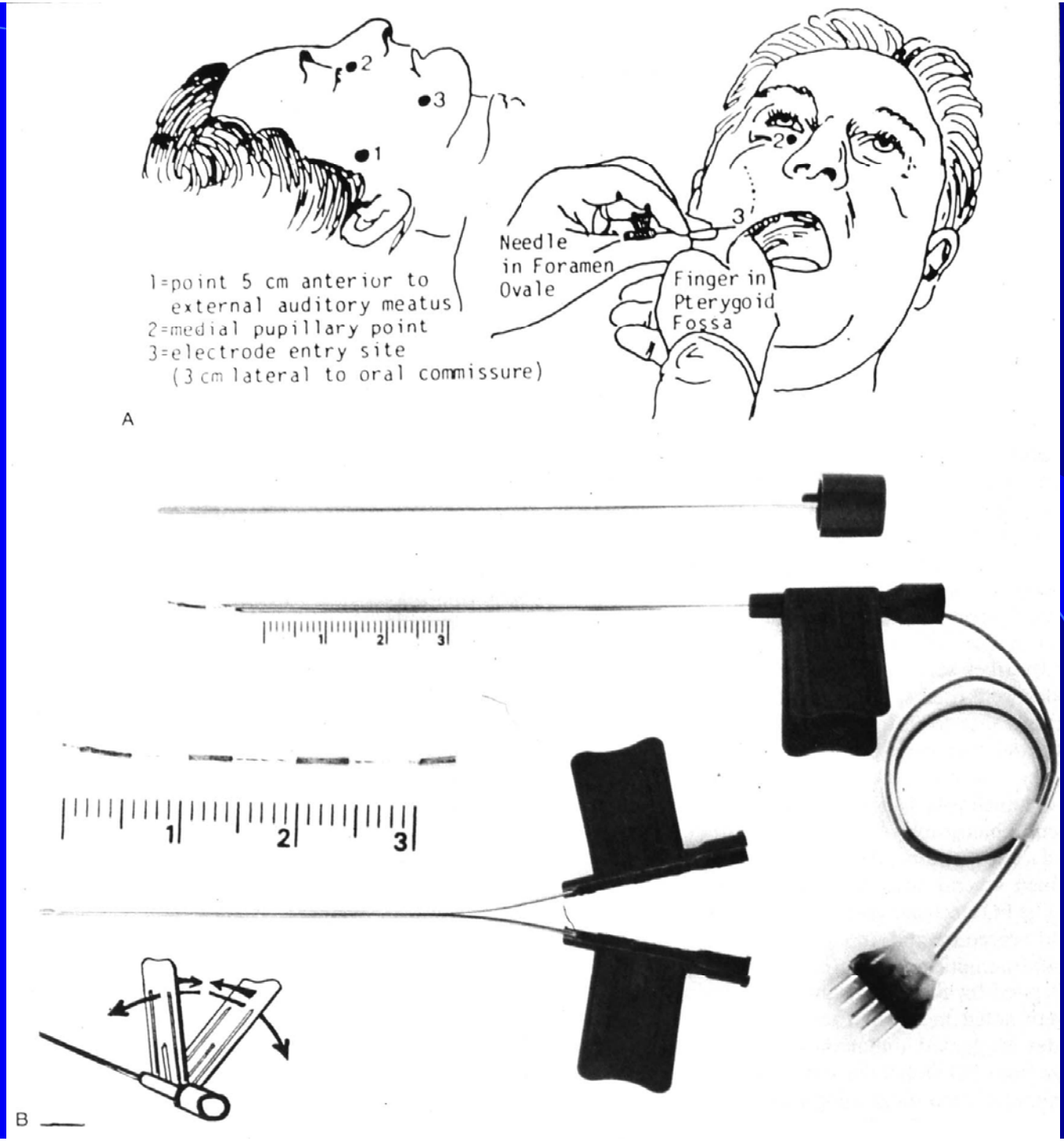
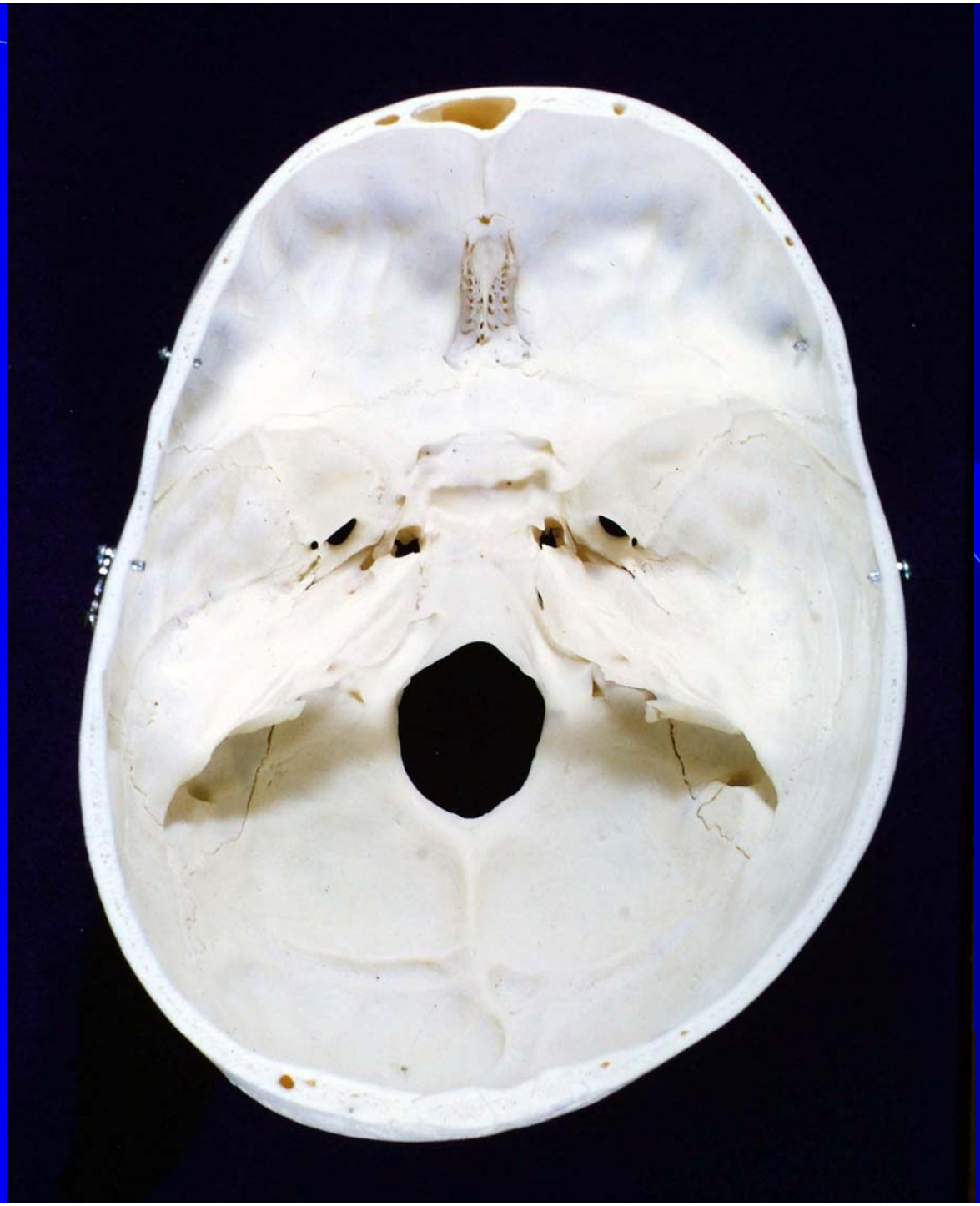
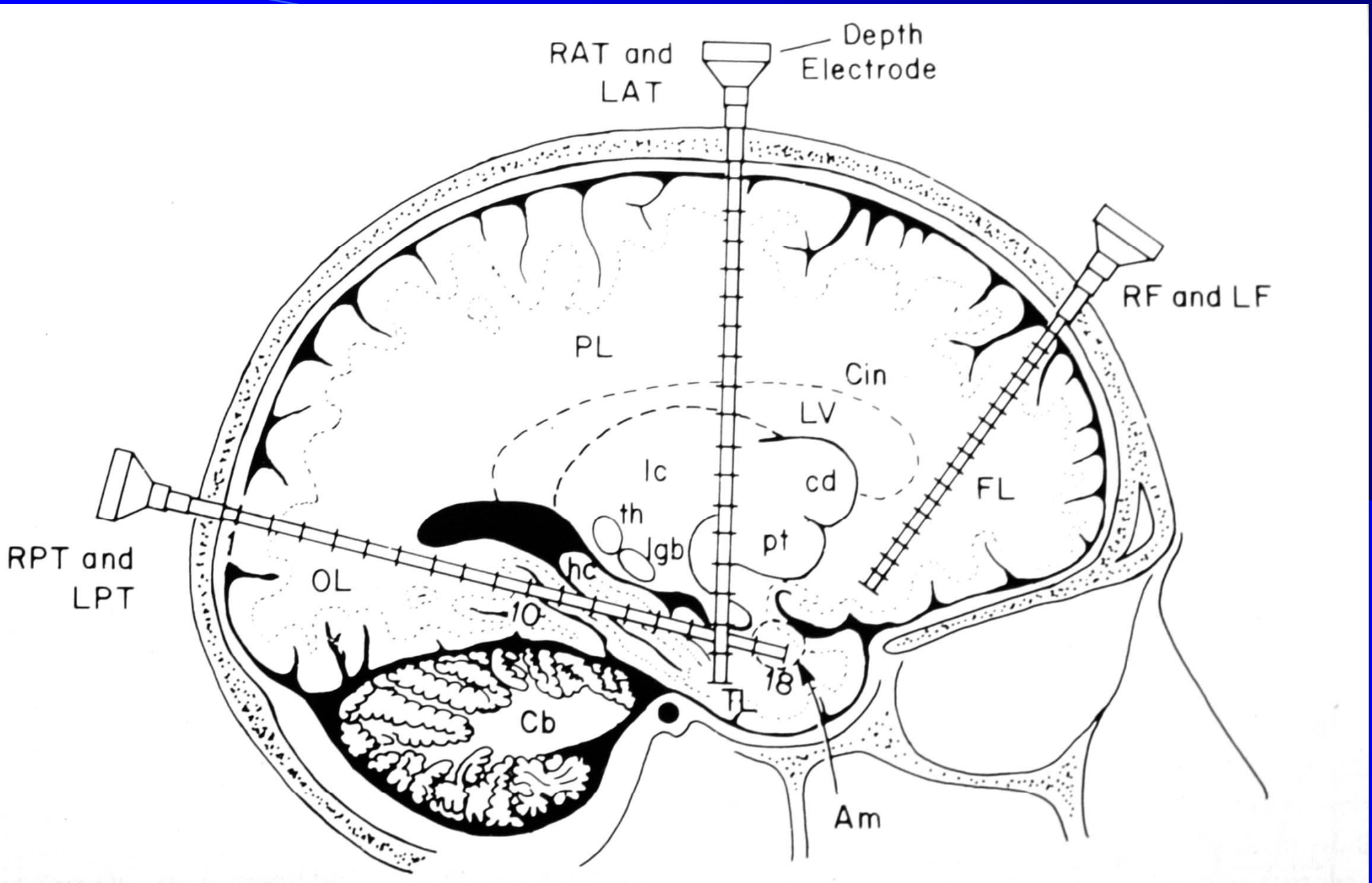
DIAGNOSTIC STUDIES:
Ictal EEG (EEG-Video Monitoring)

- Types of electrodes
  - Extracranial electrodes plus sphenoidal electrodes (noninvasive)
  - Extracranial electrodes plus foramen ovale electrodes (semi-invasive)
  - Depth electrodes (invasive)
  - Subdural grids and strips (invasive)




1=point 5 cm anterior to external auditory meatus
2=medial pupillary point
3=electrode entry site (3 cm lateral to oral commissure)
Needle in Foramen Ovale
Finger in Pterygoid Fossa
A
B

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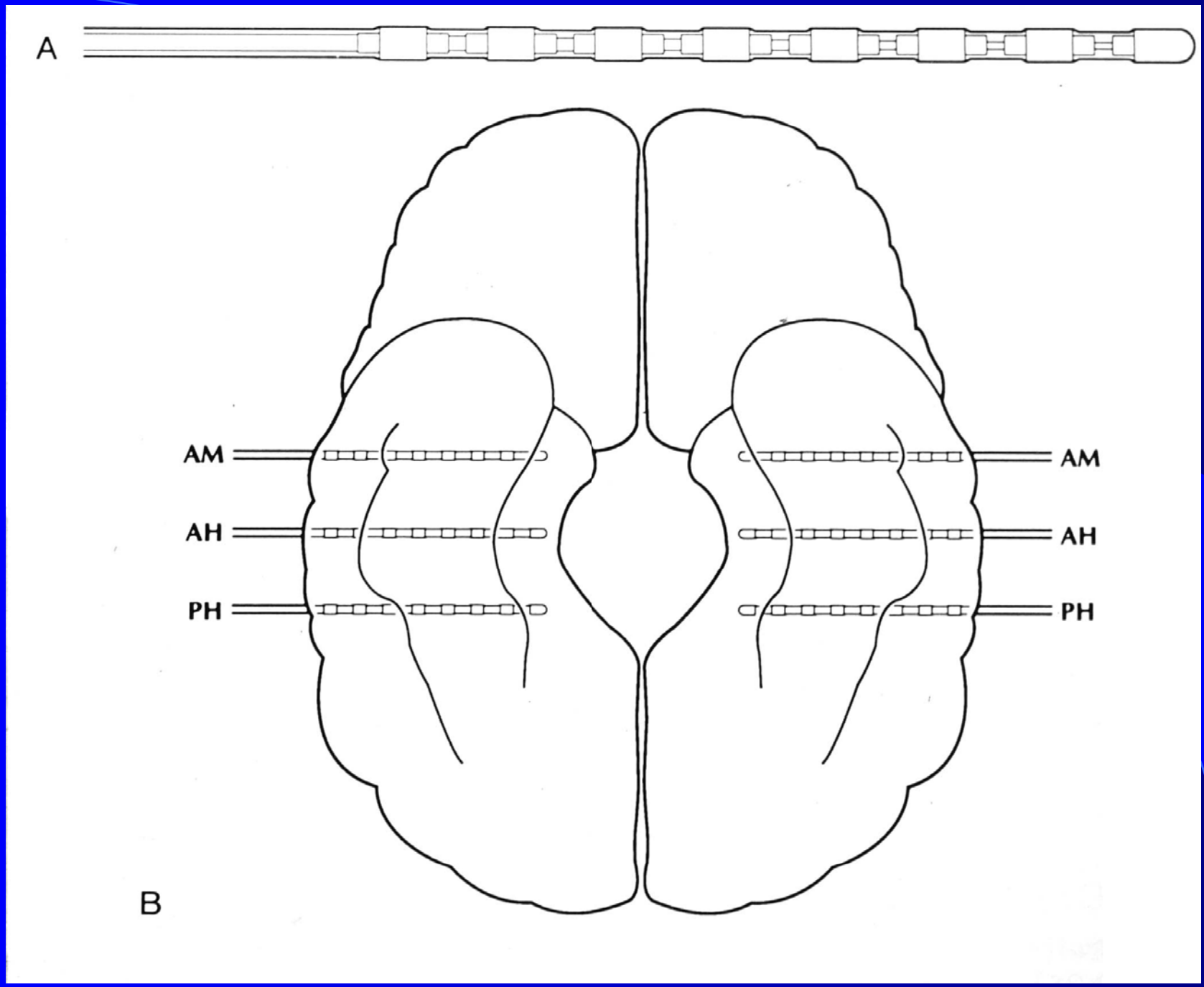
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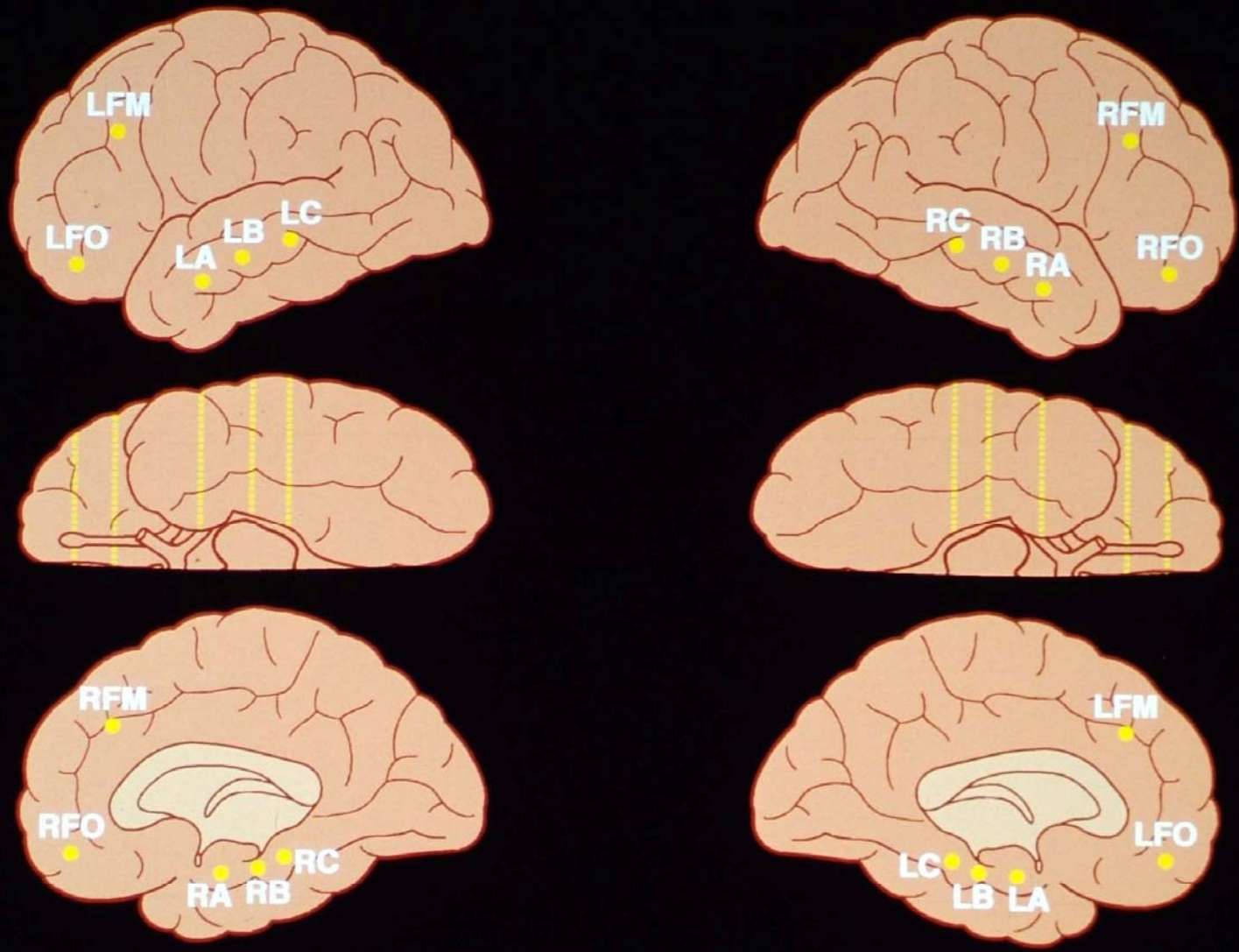
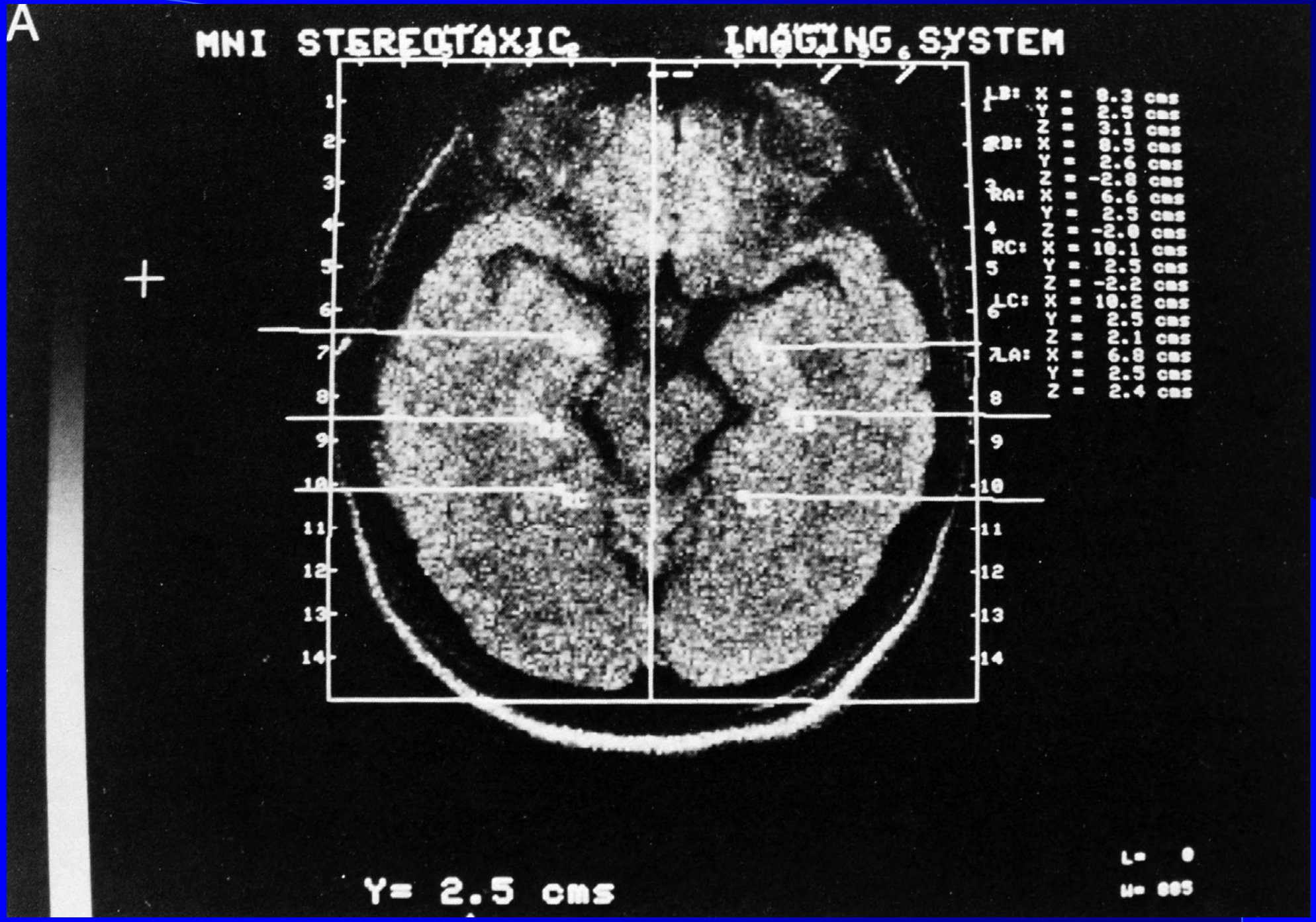
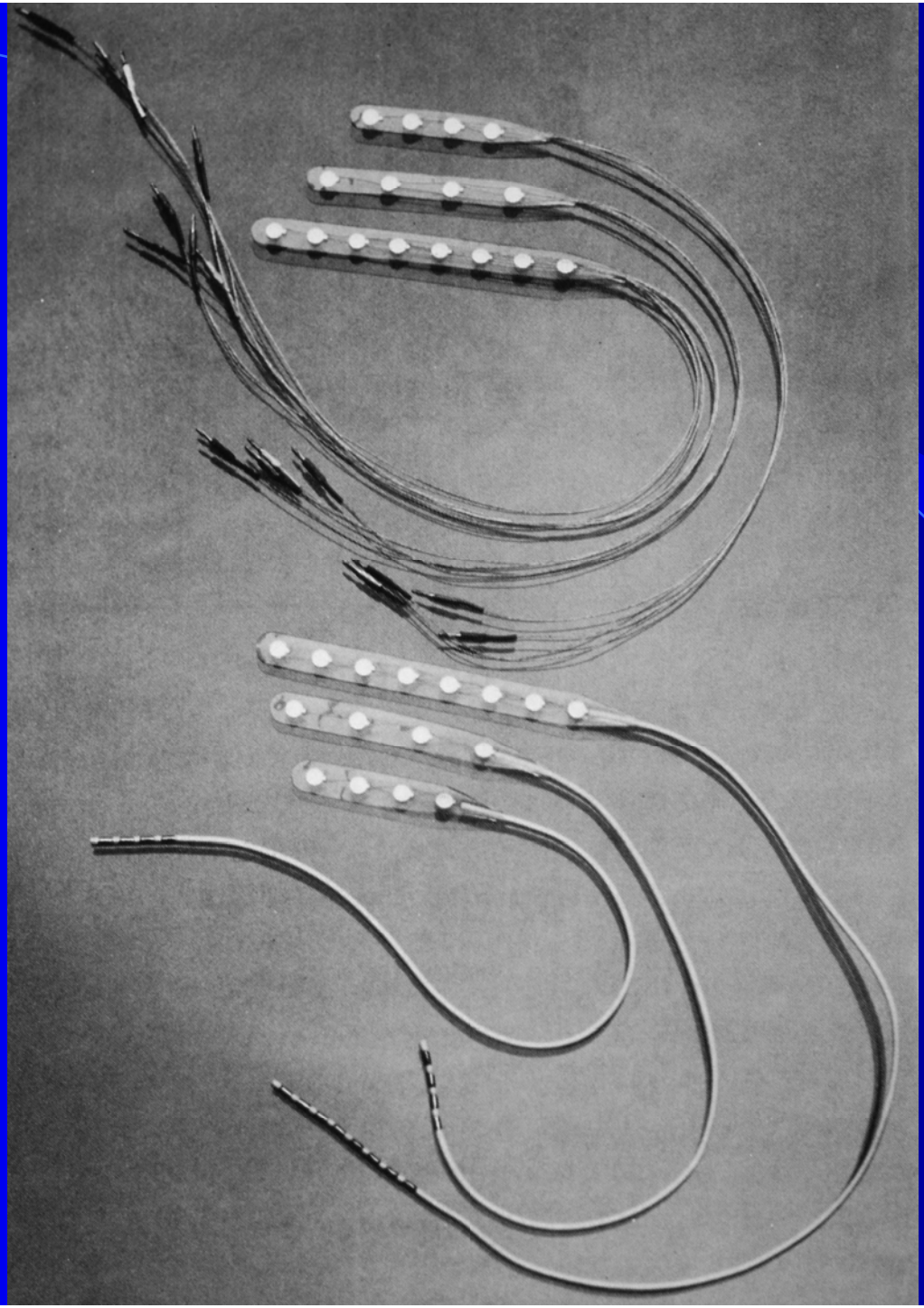
B

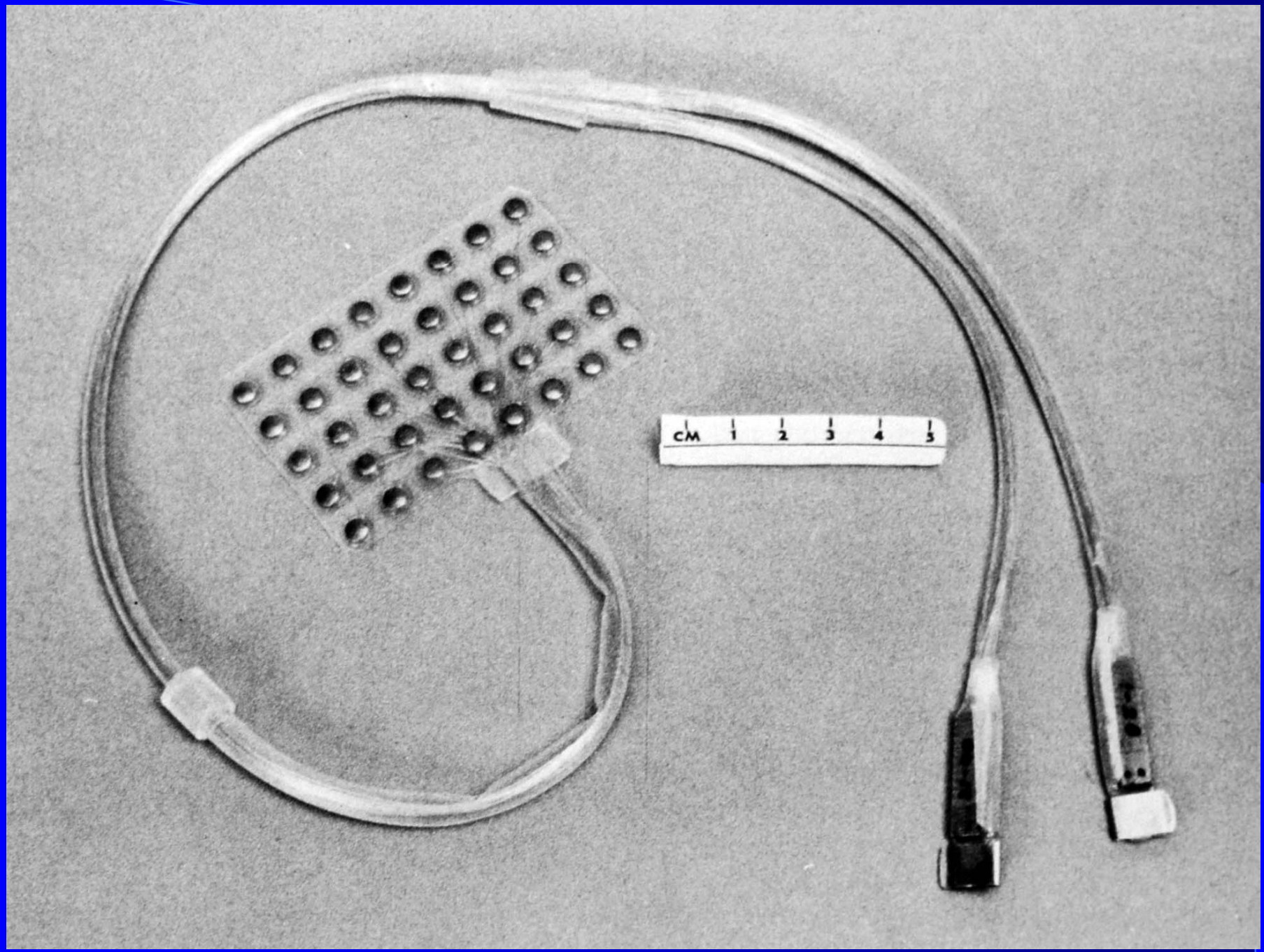
Depth Electrode Placement

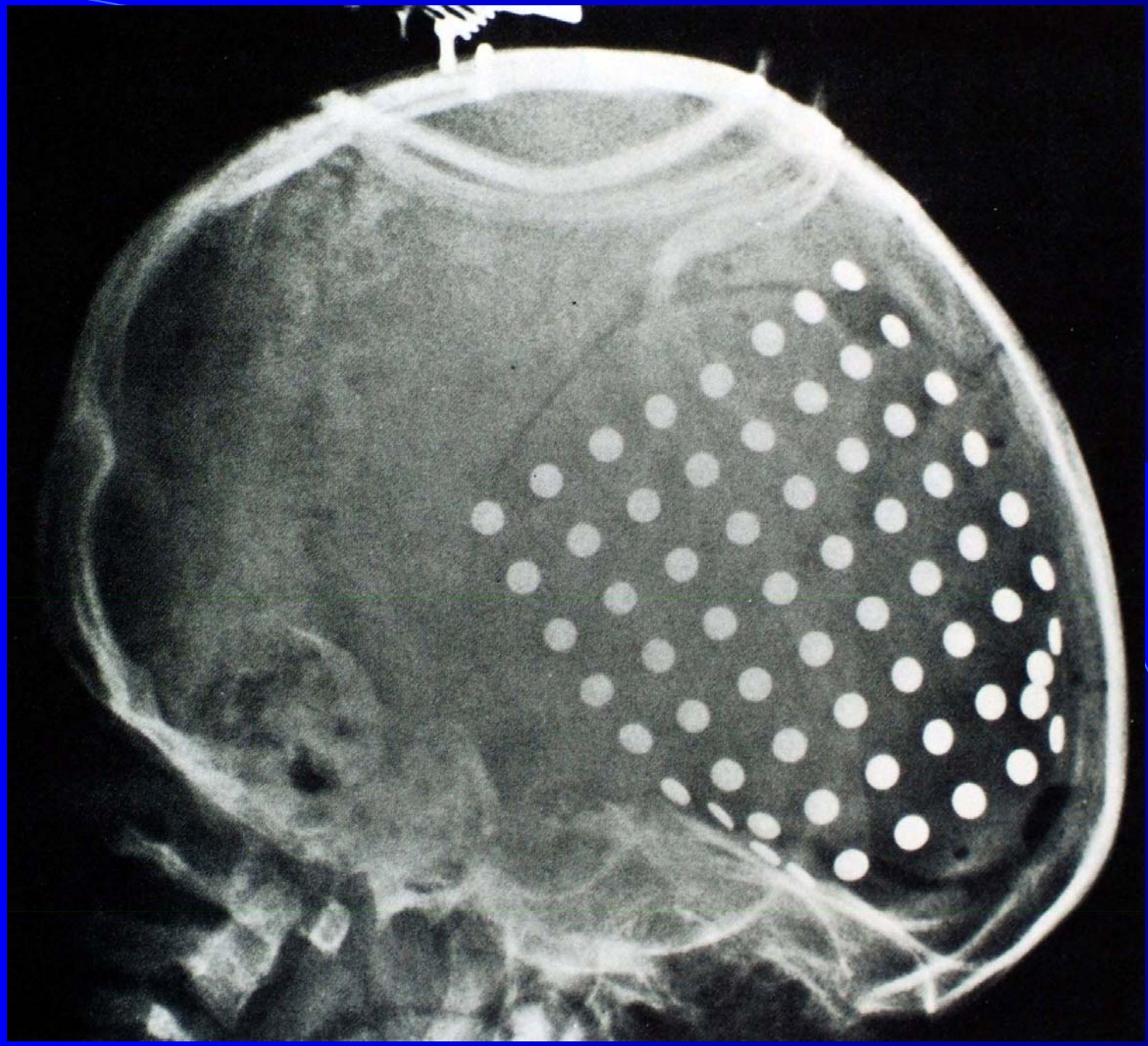


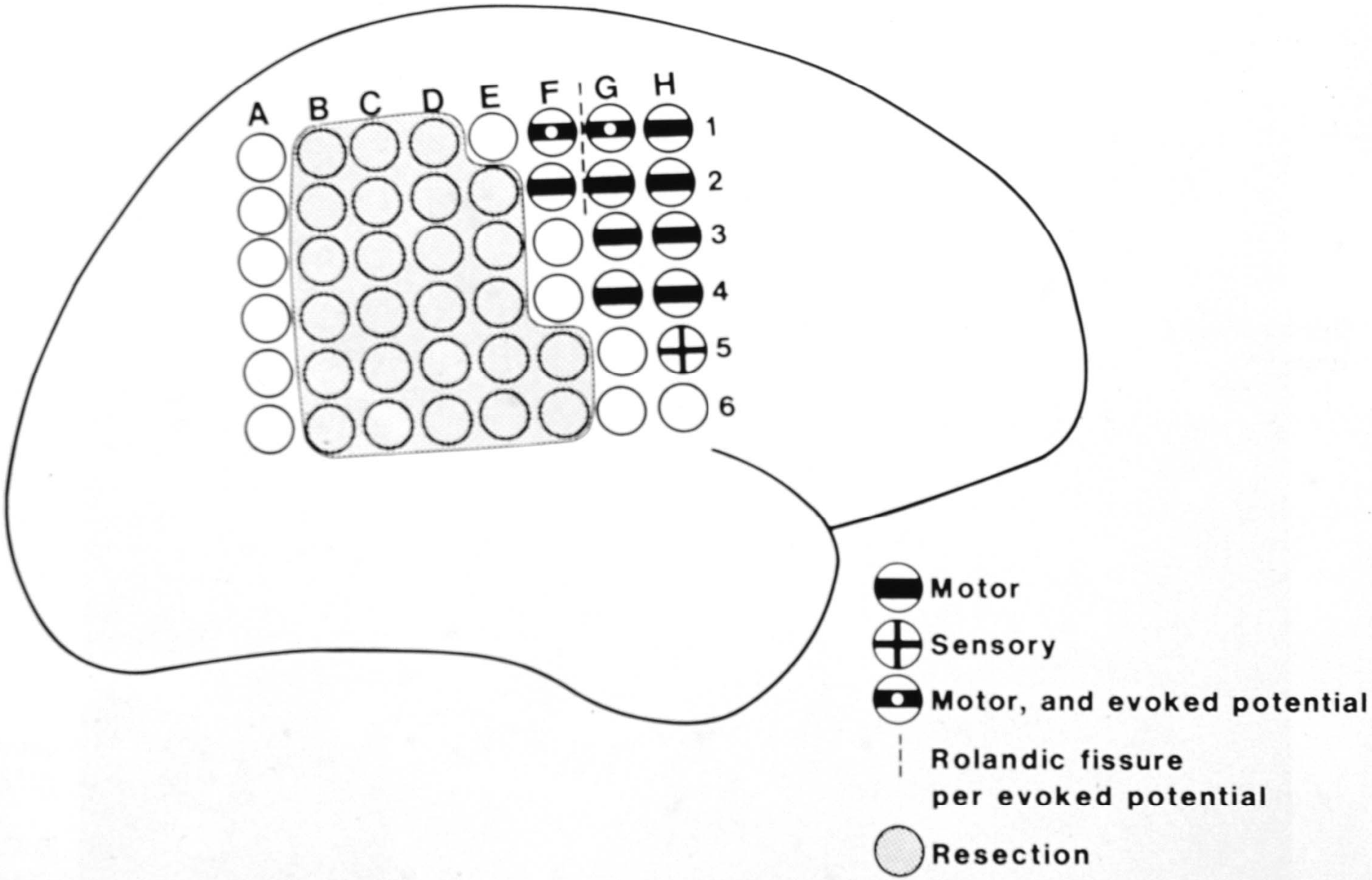
(Gloor, et al, 1982)


A
MNI STEREOTAXIC IMAGING SYSTEM
LB: X = 8.3 cms
Y = 2.5 cms
Z = 3.1 cms
RB: X = 8.5 cms
Y = 2.6 cms
Z = -2.8 cms
RA: X = 6.6 cms
Y = 2.5 cms
Z = -2.0 cms
RC: X = 10.1 cms
Y = 2.5 cms
Z = -2.2 cms
LC: X = 10.2 cms
Y = 2.5 cms
Z = 2.1 cms
LA: X = 6.8 cms
Y = 2.5 cms
Z = 2.4 cms
Y= 2.5 cms




CM 1 2 3 4 5



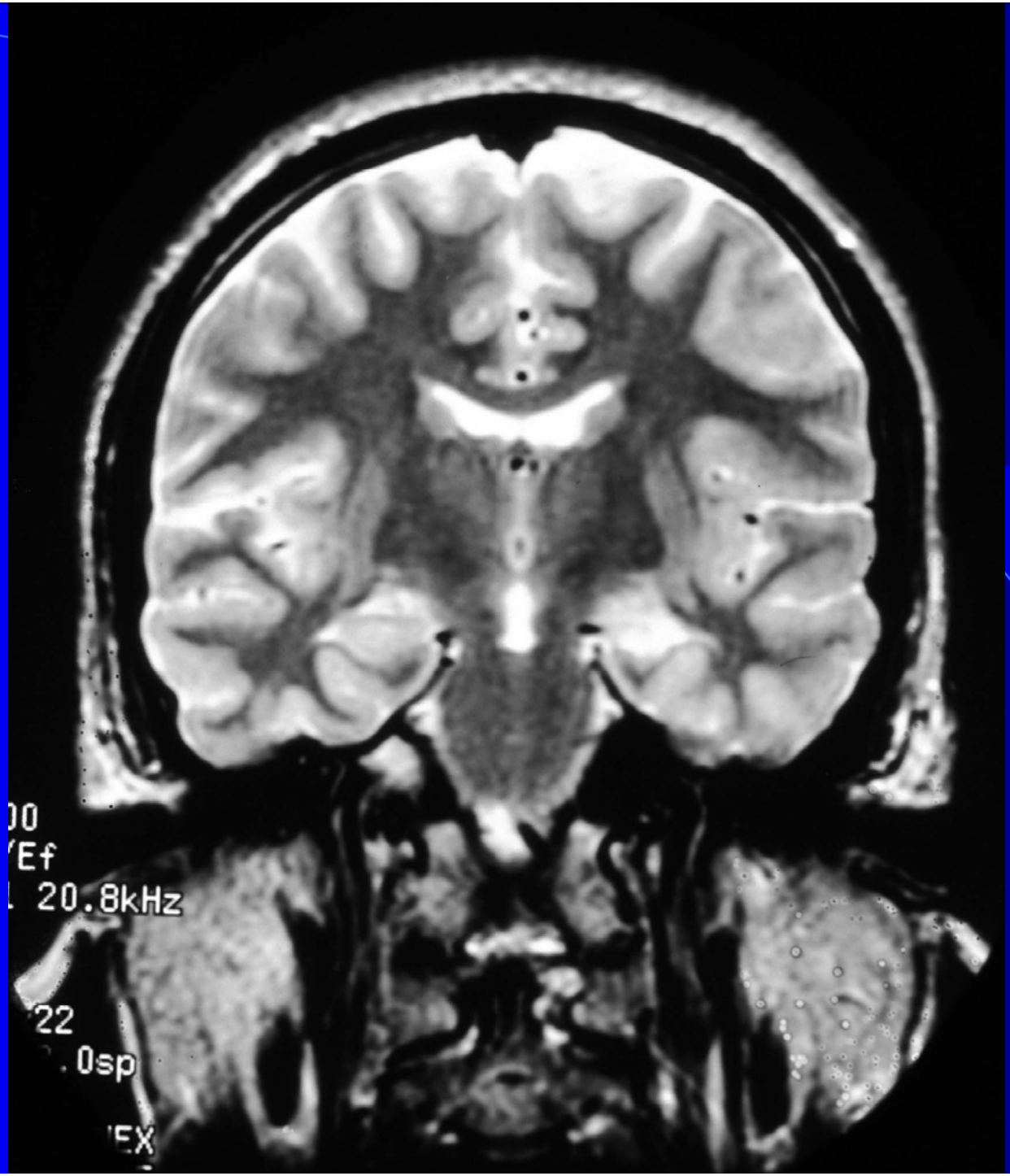

A
B
C
D
E
F
G
H
1
2
3
4
5
6
Motor
Sensory
Motor, and evoked potential
Rolandic fissure
per evoked potential
Resection

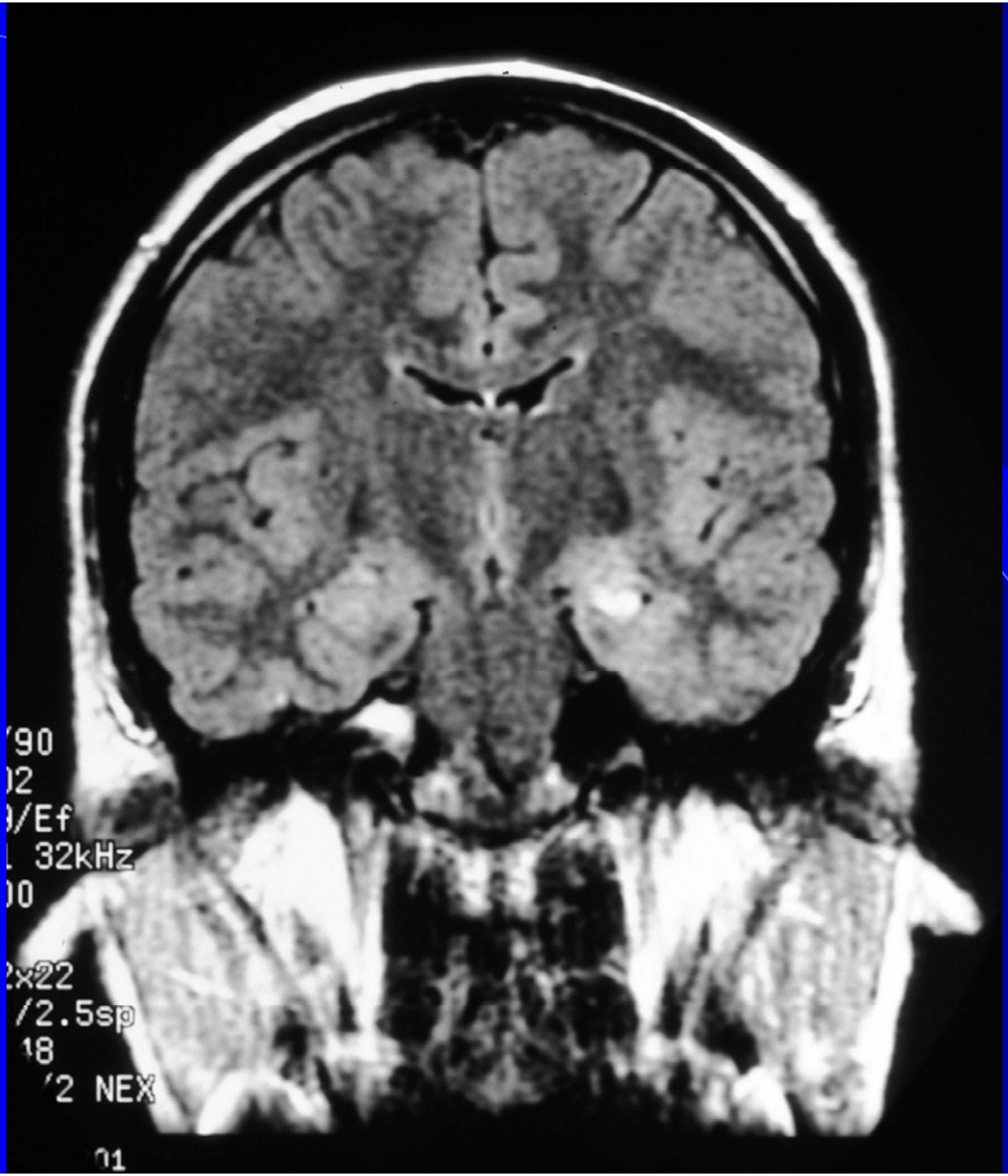
NEUROIMAGING STUDIES:
CT Scan

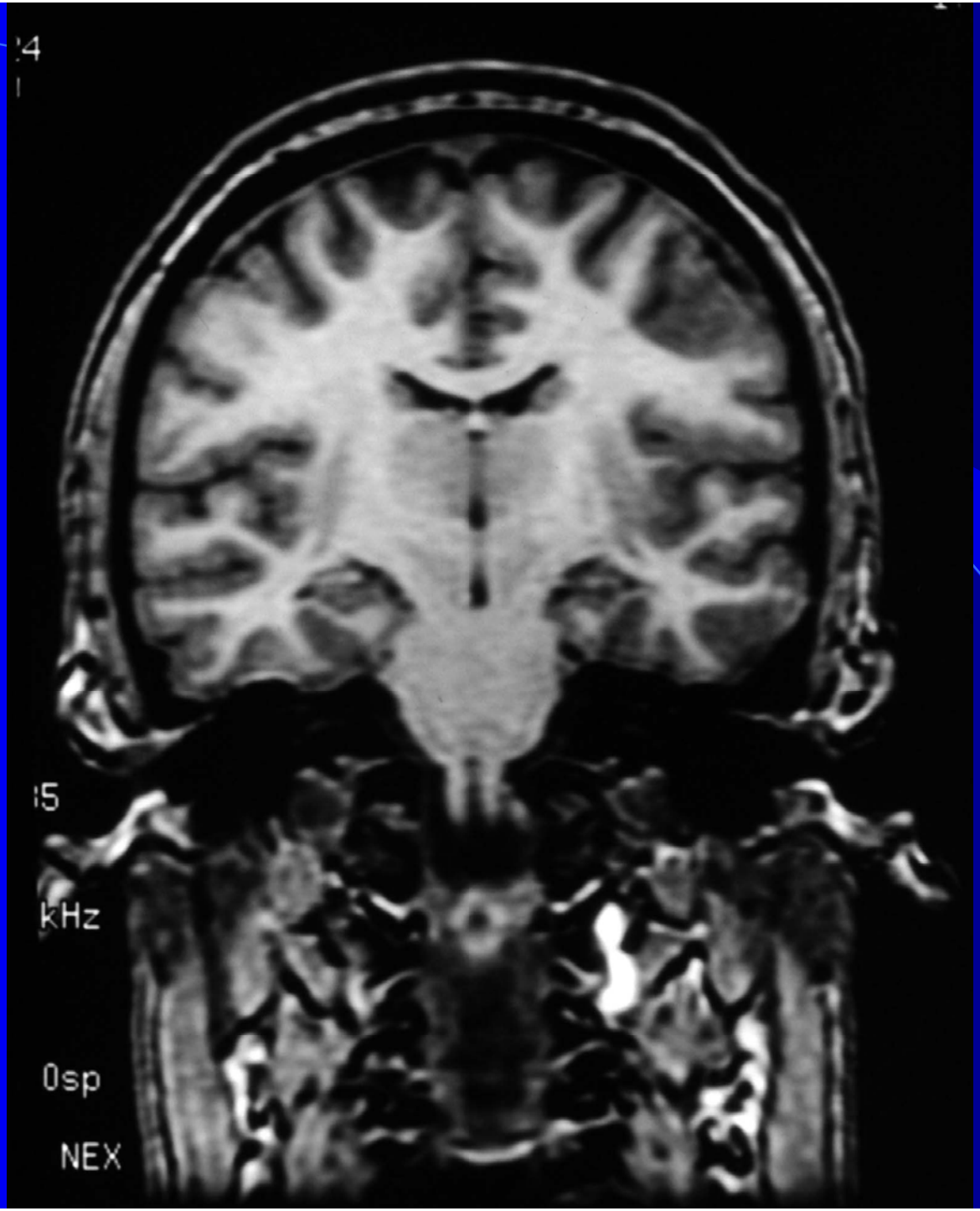
- Probably not indicated in temporal lobe epilepsy

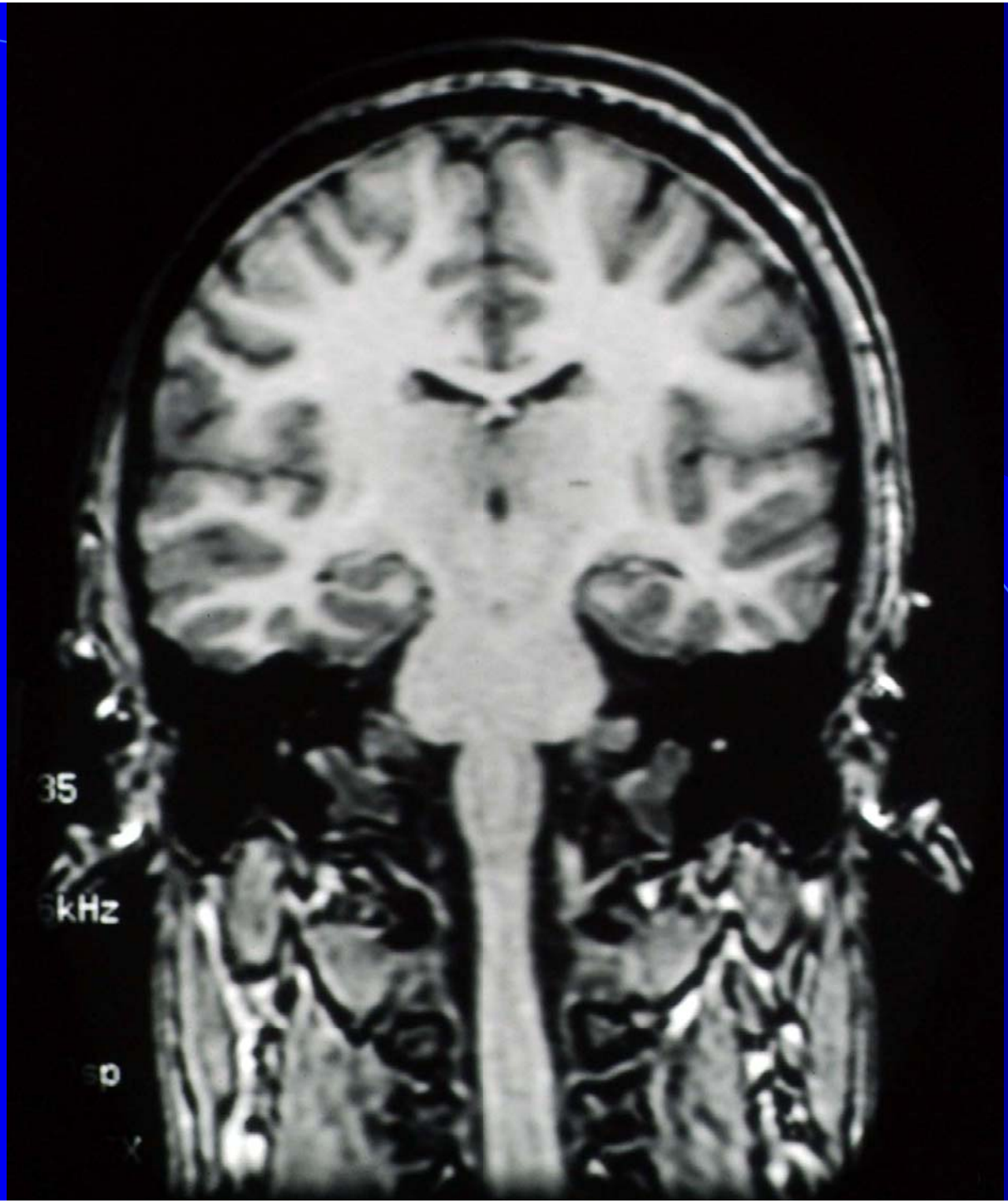
NEUROIMAGING STUDIES:
Qualitative MRI Scan

- Coronal and horizontal sections
- Increased signal intensity in hippocampus on T2, proton density, or FLAIR images
- Enlargement of the inferior horn of the lateral ventricle
- Decrease in size (atrophy) of hippocampus on T1-weighted images
- T2-weighted images are necessary for lesion detection
- 70-89% accurate in lateralizing side of seizure onset


00
Ef
20.8kHz
22
0sp
EX


/90
)2
)/Ef
32kHz
)0
2x22
/2.5sp
18
'2 NEX
01


:4
:5
kHz
0sp
NEX


35
kHz

Quantitative Volumetric MRI: Technique

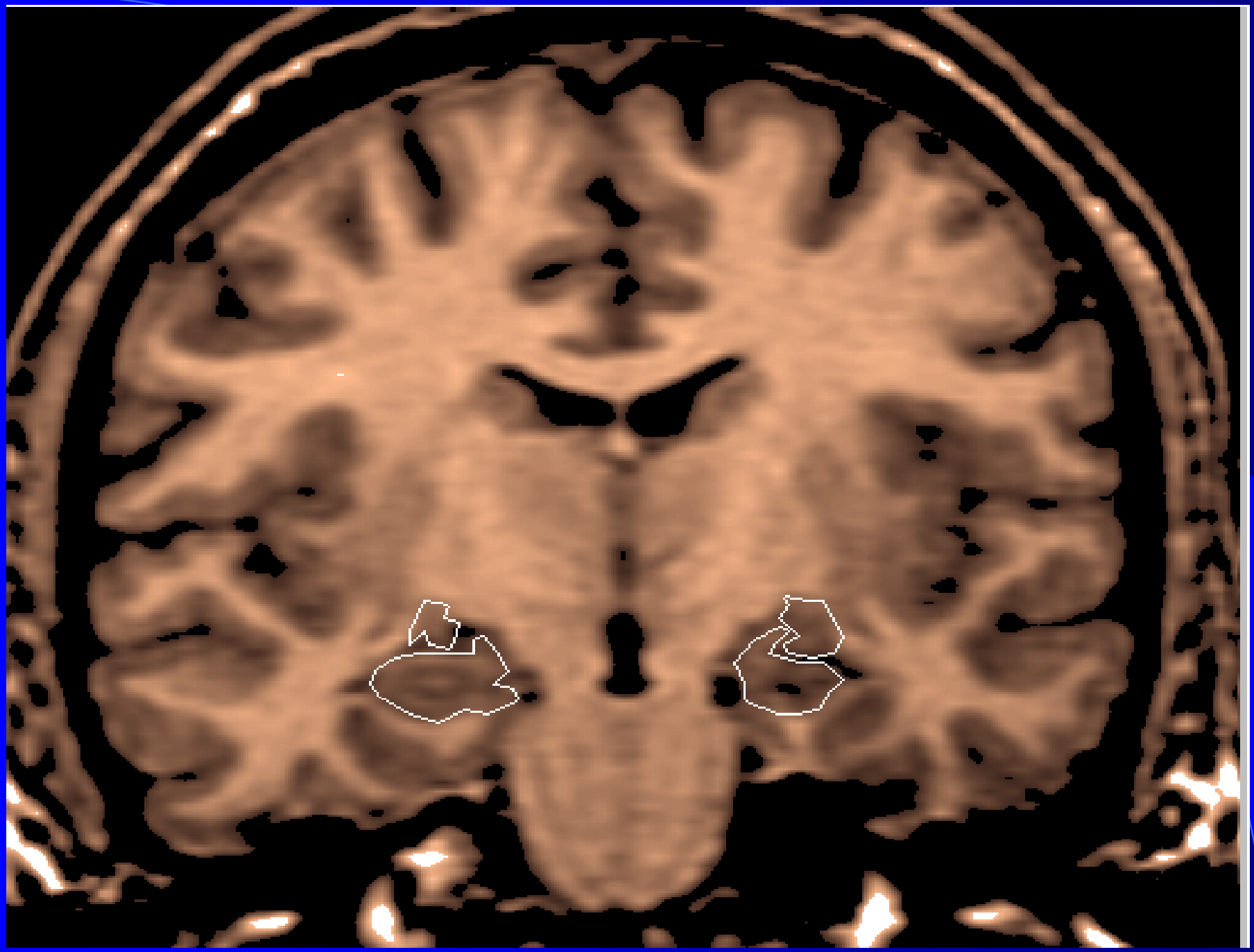
- High resolution, thin coronal sections
  - 1.5 mm, contiguous sections
  - Angled sections, perpendicular to the plane of the lateral sulcus
  - T1-weighted, inversion recovery, or gradient echo sequences
- Transfer images to computer work station
- Manually outline the hippocampus and amygdala
- Computer calculates the volumes of the HF and AM
- Compare volumes and ratios (smaller/larger) to controls

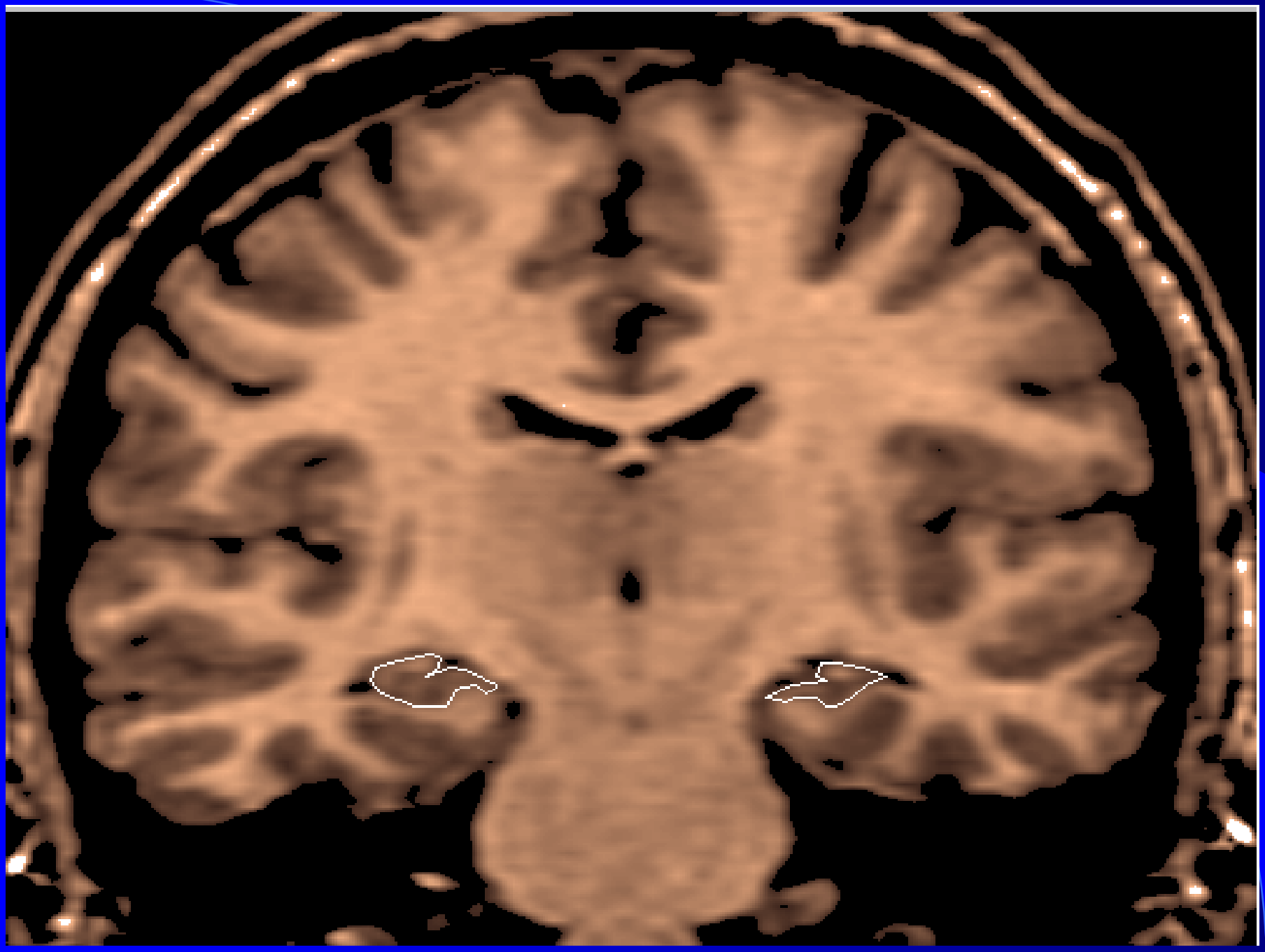
Watson et al, 1992

Quantitative Volumetric MRI: Interpretation

- Hippocampal or amygdaloid sclerosis is diagnosed if the volumes are 2 SDs smaller than the control population or the ratios are less than 0.90
- 87% accurate if HF volumes alone are used
- 93% accurate if HF and AM volumes are used
- Probably useful in patients with bilateral, independent, temporal seizure onsets

Watson et al, 1992
Cendes et al, 1993

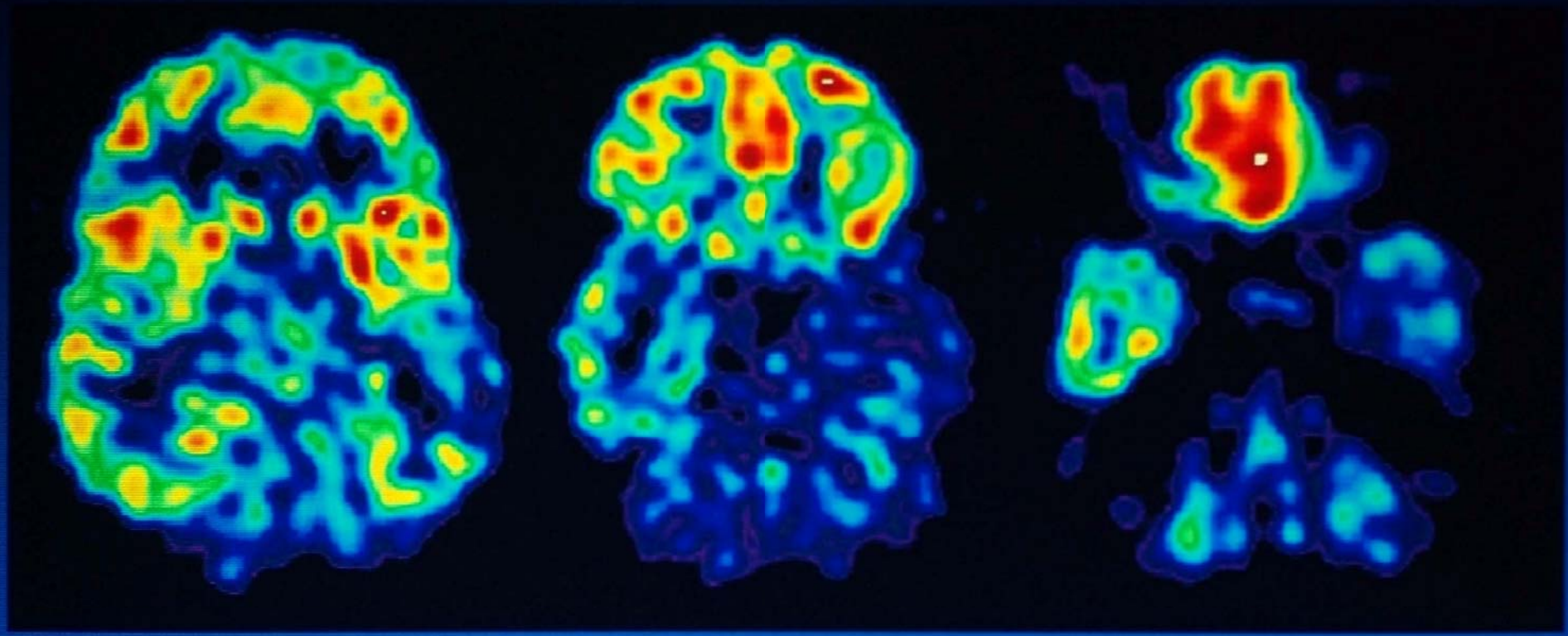




NEUROIMAGING STUDIES:
FDG-PET Scan

- Interictal hypometabolism in involved temporal lobe
- Ictal hypermetabolism in involved temporal lobe
- 80-90% accurate

TEMPORAL LOBE EPILEPSY



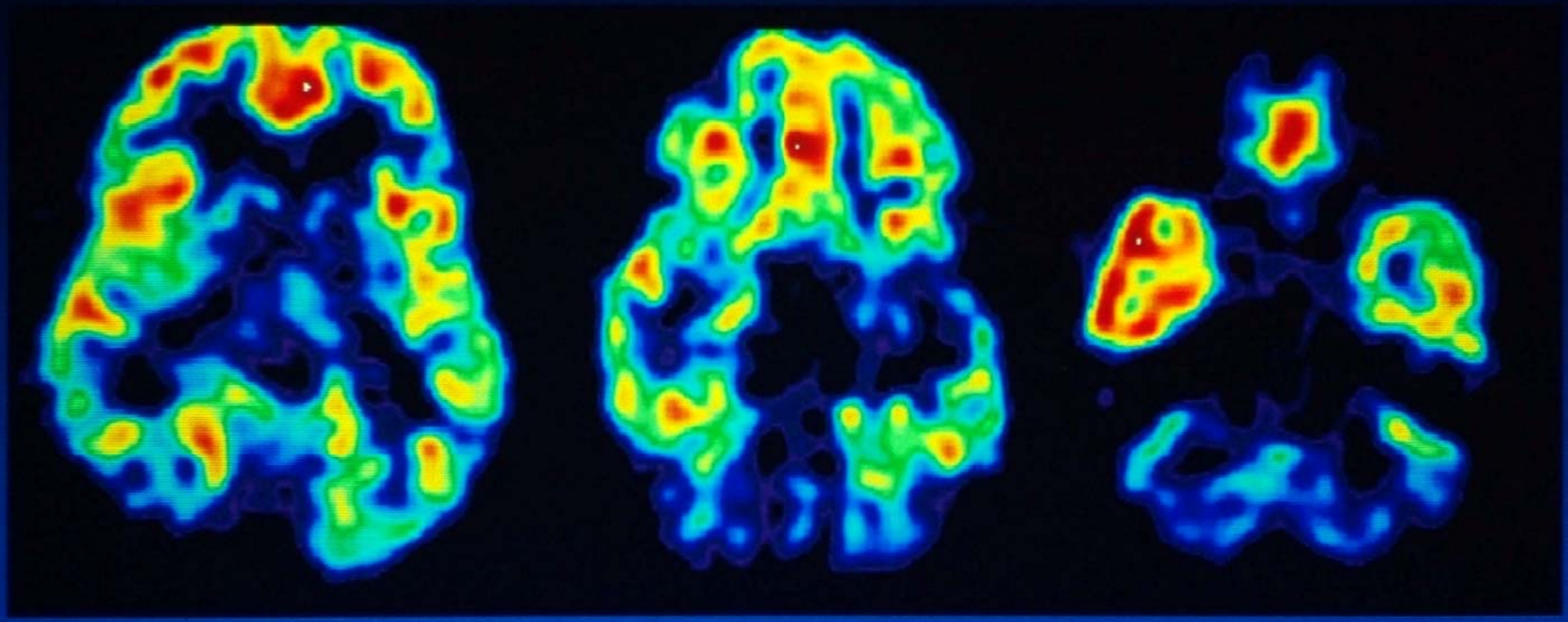
[F-18]Fluorodeoxyglucose

Children's Hospital of Michigan PET Center
Wayne State University

NEUROIMAGING STUDIES:
FMZ-PET Scan

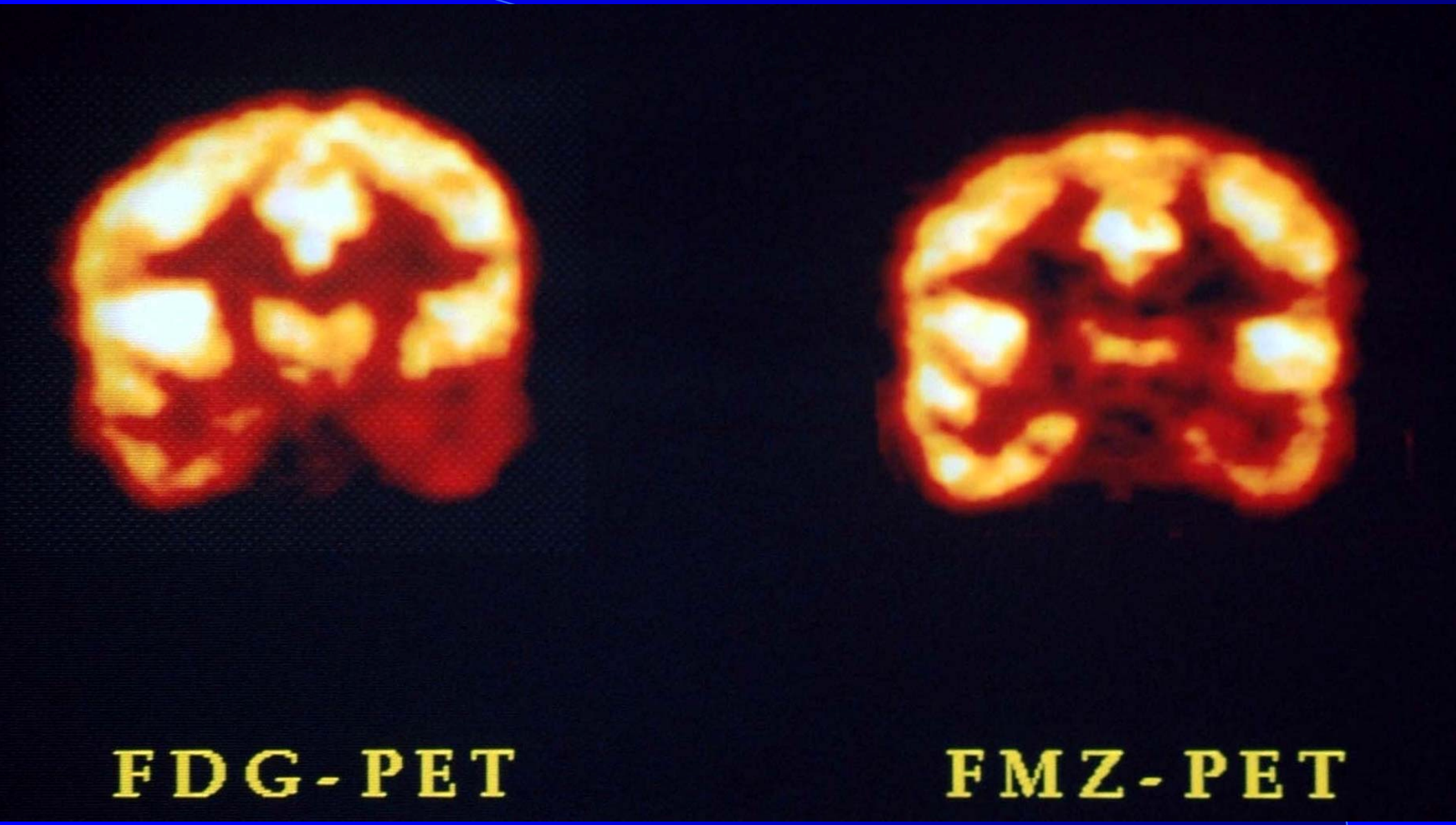
- Interictal decrease binding in involved temporal lobe
- Localizes epileptogenic region more precisely than FDG-PET scanning
- Accuracy yet to be determined

TEMPORAL LOBE EPILEPSY



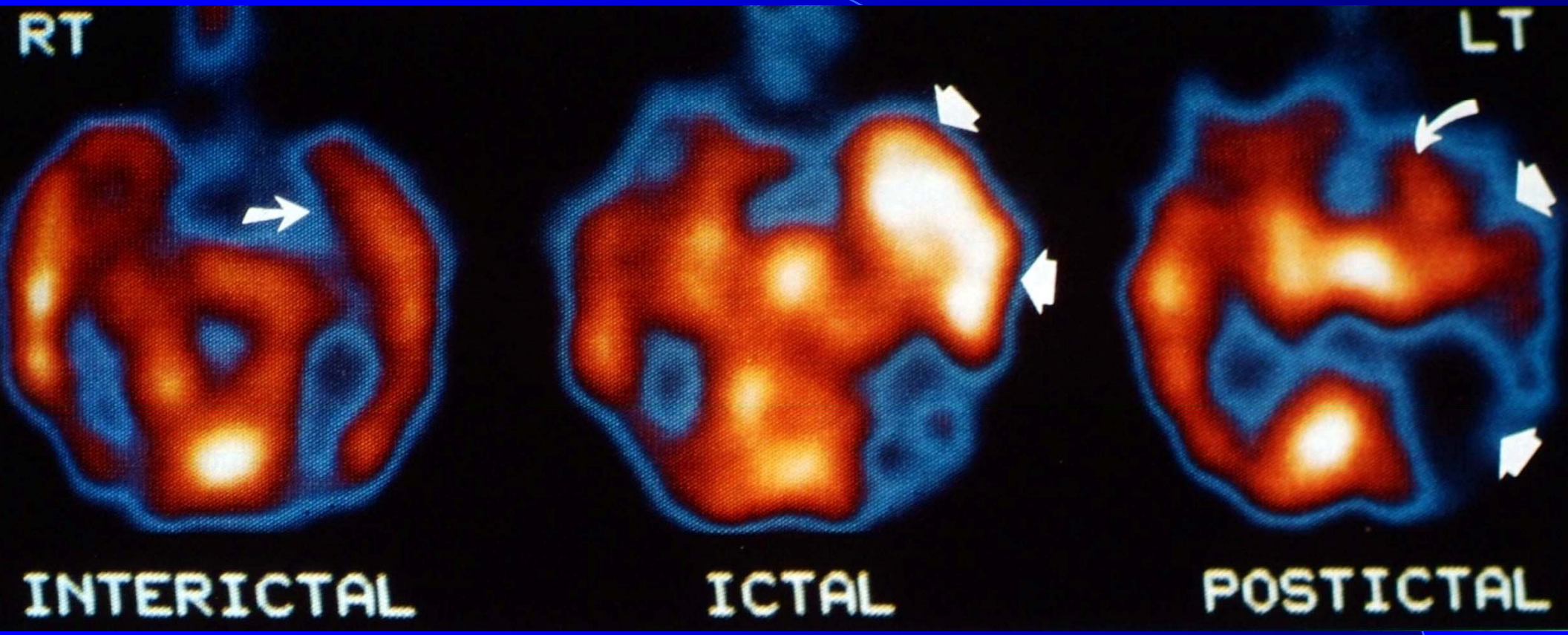
[C-11]Flumazenil

Children's Hospital of Michigan PET Center
Wayne State University


FDG-PET
FMZ-PET

NEUROIMAGING STUDIES:
HMPAO-SPECT Scan

- Interictal hypoperfusion of involved temporal lobe
- Ictal hyperperfusion of involved temporal lobe (much more helpful than interictal scan)
- 60-72% accurate


RT
LT
INTERICTAL
ICTAL
POSTICTAL

DIAGNOSTIC STUDIES:
Neuropsychological Evaluation

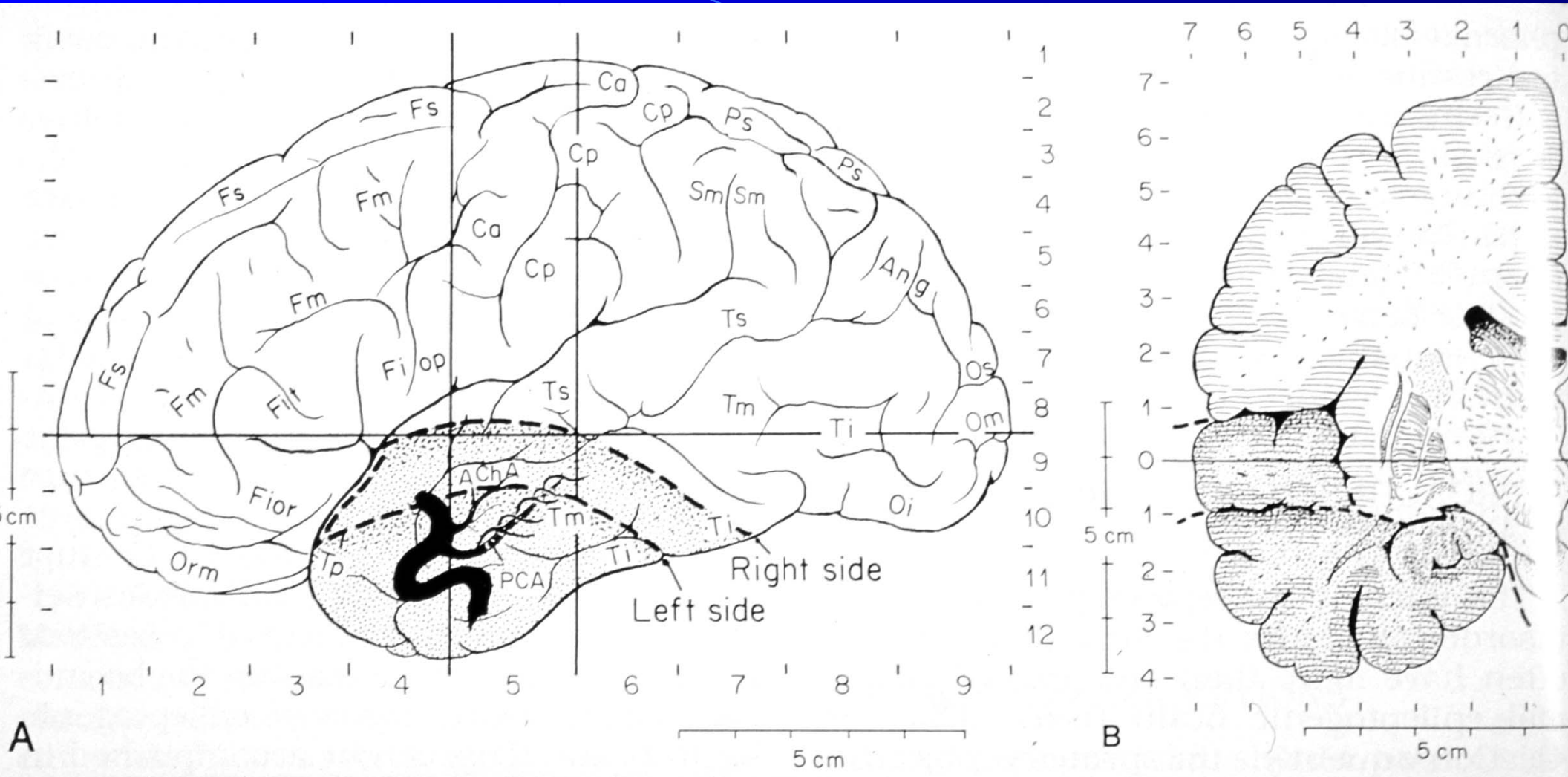
- Impaired verbal (left side) or visual-spatial (right side) memory function
- Intracarotid amytal (Wada) test
  - Same findings as above

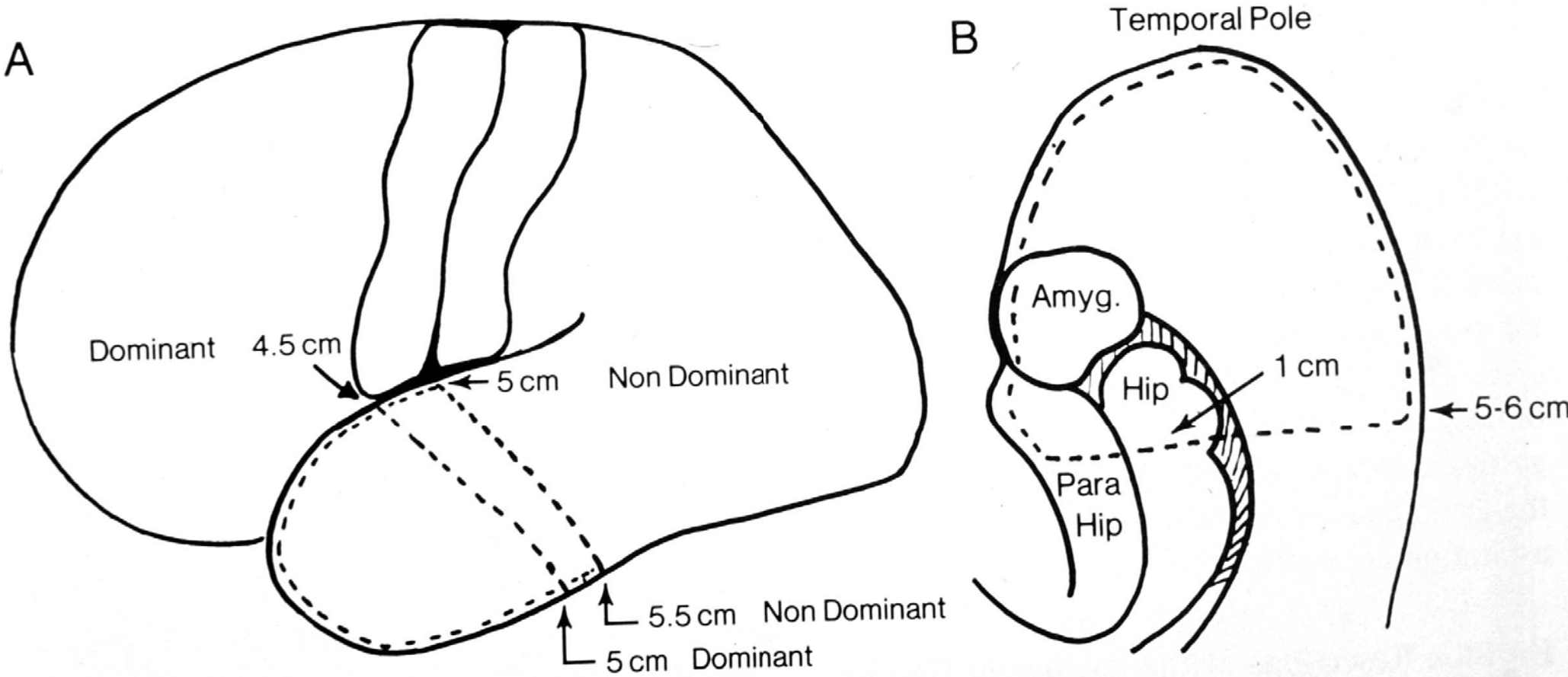
TREATMENT:
Antiepileptic Drug Therapy

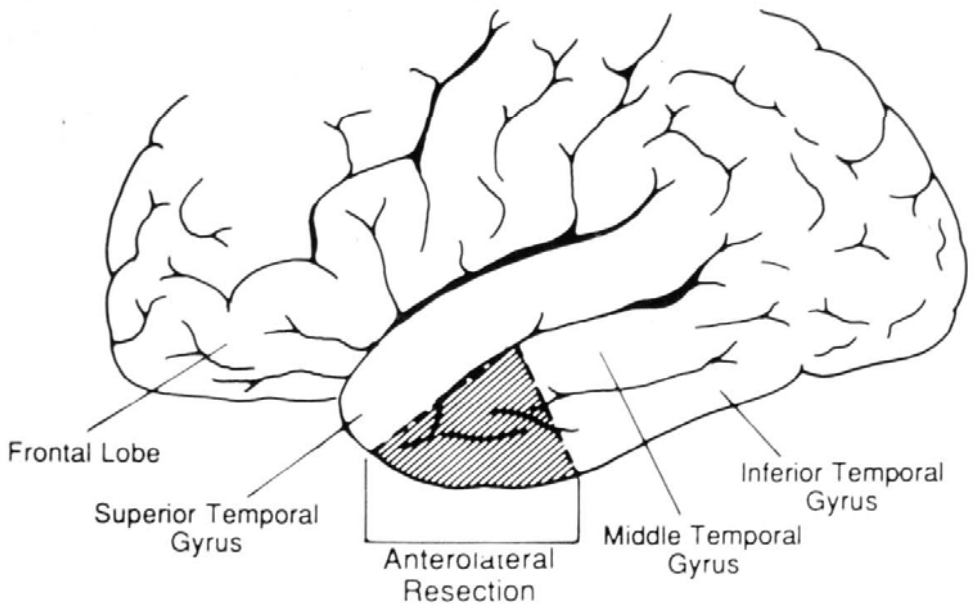
- Carbamazepine (CBZ) (Tegretol)
- Phenytoin (PHT) (Dilantin)
- Valproic acid (VPA) (Depakote)
- Primidone (PRM) (Mysoline)
- Phenobarbital (PB)
- Felbamate (FBM) (Felbatol)
- Gabapentin (GBP) (Neurontin)
- Lamotrigine (LTG) (Lamictal)
- Topiramate (TPM) (Topamax)
- Tiagabine (TGB) (Gabitril)
- Oxcarbazepine (OXC) (Trileptal)
- Levetiracetam (LEV) (Keppra)
- Zonisamide (ZNS) (Zonegran)
- Pregabalin (PGB) (Lyrica)
- Lacosamide (LCM) (Vimpat)
- Vigabatrin (VGB) (Sabril)

TREATMENT:
Surgical Treatment

- Standard anterior temporal lobectomy
  - En bloc
  - Subpial aspiration
- Modified anterior temporal lobectomy with extensive amygdalohippocampectomy
- Selective amygdalohippocampectomy
- Amygdalectomy

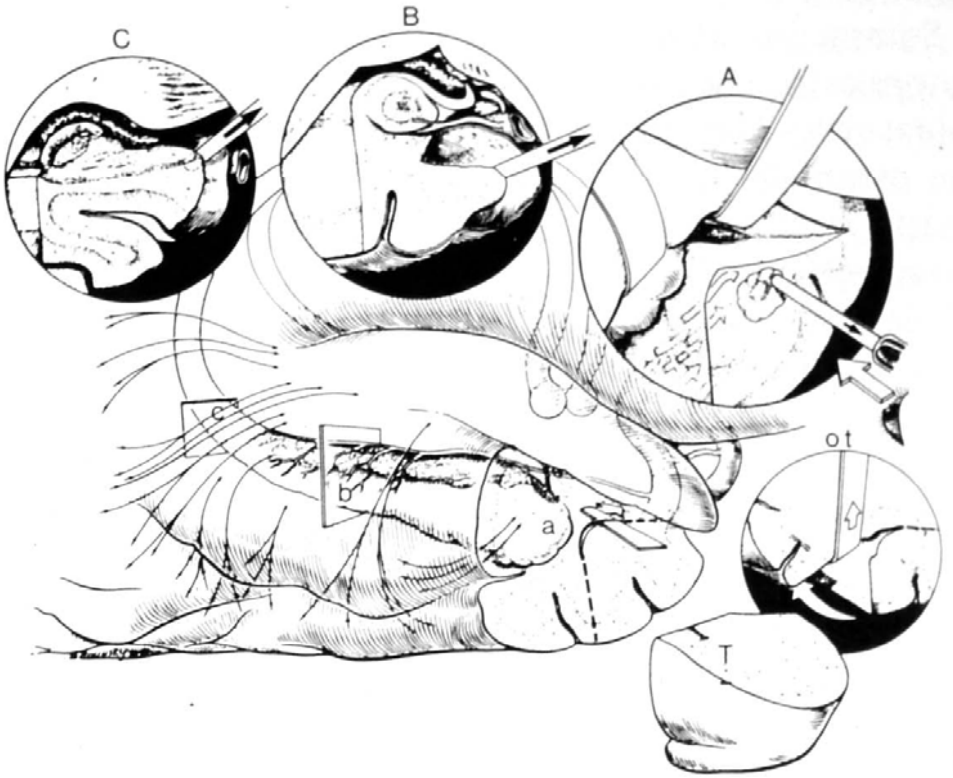

Fs
Fm
Fm
Fs
Fm
Fit
Fi op
Fior
Orm
Ca
Cp
Ca
Cp
Cp
Ps
Ps
Sm
Sm
Ang
Ts
Ts
Tm
Ti
Os
Om
Oi
AChA
Tm
Ti
Tp
PCA
Ti
Right side
Left side
5 cm
A
5 cm
B


A
Dominant
4.5 cm
5 cm
Non Dominant
5.5 cm
Non Dominant
5 cm
Dominant
B
Temporal Pole
Amyg.
Hip
1 cm
5-6 cm
Para
Hip

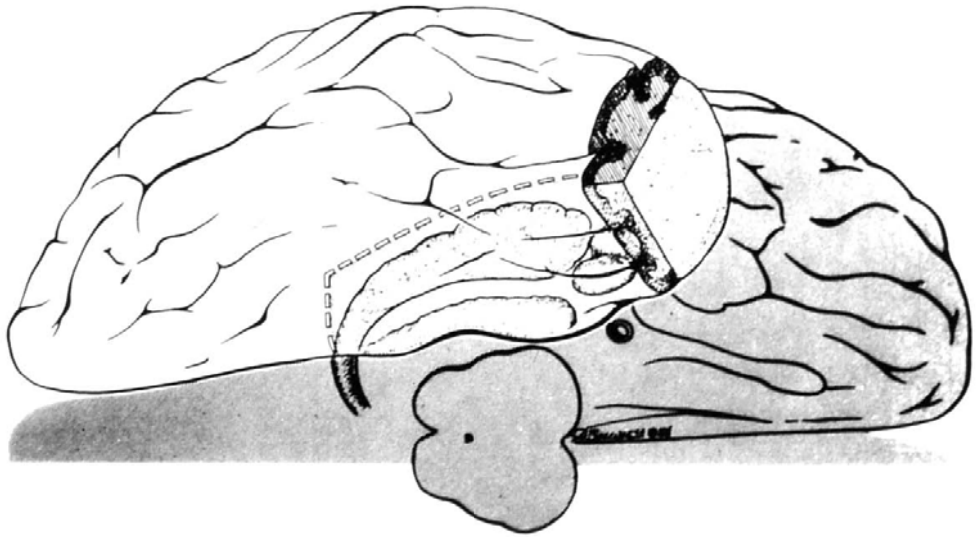


A

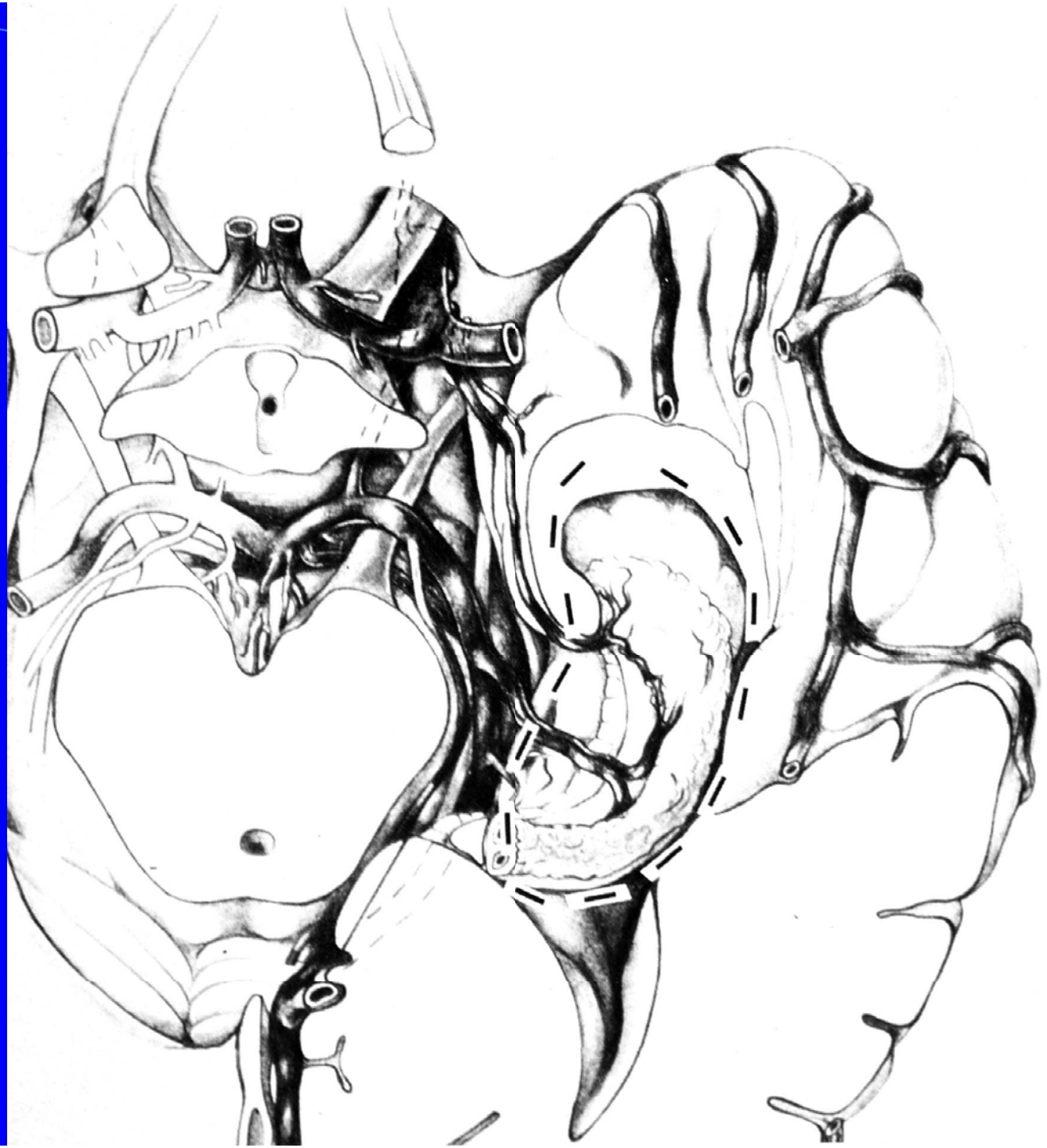
Area of temporal neocortex resected



B



C



MEDICAL CONTROL OF PARTIAL SEIZURES:
% Seizure-free for One Year

Seizure Type	VA I (118)	VA II (264)
• CPS	21%	29%
• CPS, GTCS	41%	38%
• 2ary GTCS	61%	54%

(Mattson RH, et al. *Epilepsia* **34** (Suppl 6): 50, 1993)

MEDICALLY INTRACTABLE TEMPORAL LOBE EPILEPSY: SURGICAL vs OPTIMAL MEDICAL THERAPY I

5 YEAR FOLLOW-UP

OUTCOME	SURGICAL GROUP (N=92)	MEDICAL GROUP (N=81)
• Class I (Seizure-free)	44 (48%)	3 (4%)
• Class II (1-5 seizures/yr.)	19 (21%)	2 (2%)
• Class III (> 75% reduction)	8 (9%)	13 (16%)
• Class IV (< 75% reduction)	21 (23%)	63 (78%)

(Ojemann, et al. *Epilepsia* **33** (Suppl 3): 29, 1992)

MEDICALLY INTRACTABLE TEMPORAL LOBE EPILEPSY: SURGICAL vs OPTIMAL MEDICAL THERAPY II

10 YEAR FOLLOW-UP

OUTCOME	SURGICAL GROUP (N=26)	MEDICAL GROUP (N=36)
• Class I (Seizure-free)	16 (62%)	2 (6%)
• Class II (1-5 seizures/yr.)	2 (8%)	4 (11%)
• Class III (> 75% reduction)	2 (8%)	8 (22%)
• Class IV (< 75% reduction)	6 (23%)	22 (61%)

(Ojemann, et al. *Epilepsia* **33** (Suppl 3): 29, 1992)

PROGNOSIS I

- Temporal lobe epilepsy is the most refractory type of adult epilepsy
  - Only 10 to 30% of patients are controlled (Class I and II) with antiepileptic drugs
  - Approximately 33% of patients are disabled in a psychosocial sense
  - Spontaneous remission rate may be as low as 20%
  - However, if typical TLE is present, the surgical cure rate is the best (70-90%)
- Progression of the seizure disorder may occur with time if it is not treated aggressively
  - CPS may become more frequent and more difficult to control
  - A progressive loss of short term memory may occur

PROGNOSIS II:
Predictors of Poor Outcome

- Early onset of seizures (< 2 years of age)
- Large number of seizures
- Presence of secondarily GTCS
- History of status epilepticus
- History of prolonged febrile seizures

PROGNOSIS III:
Predictors of Good Outcome

- No obvious etiology
- Family history of epilepsy
- Normal EEG
- Childhood onset (> 2 years of age)