New Era of Epilepsy Surgery

understanding of the epileptic networks

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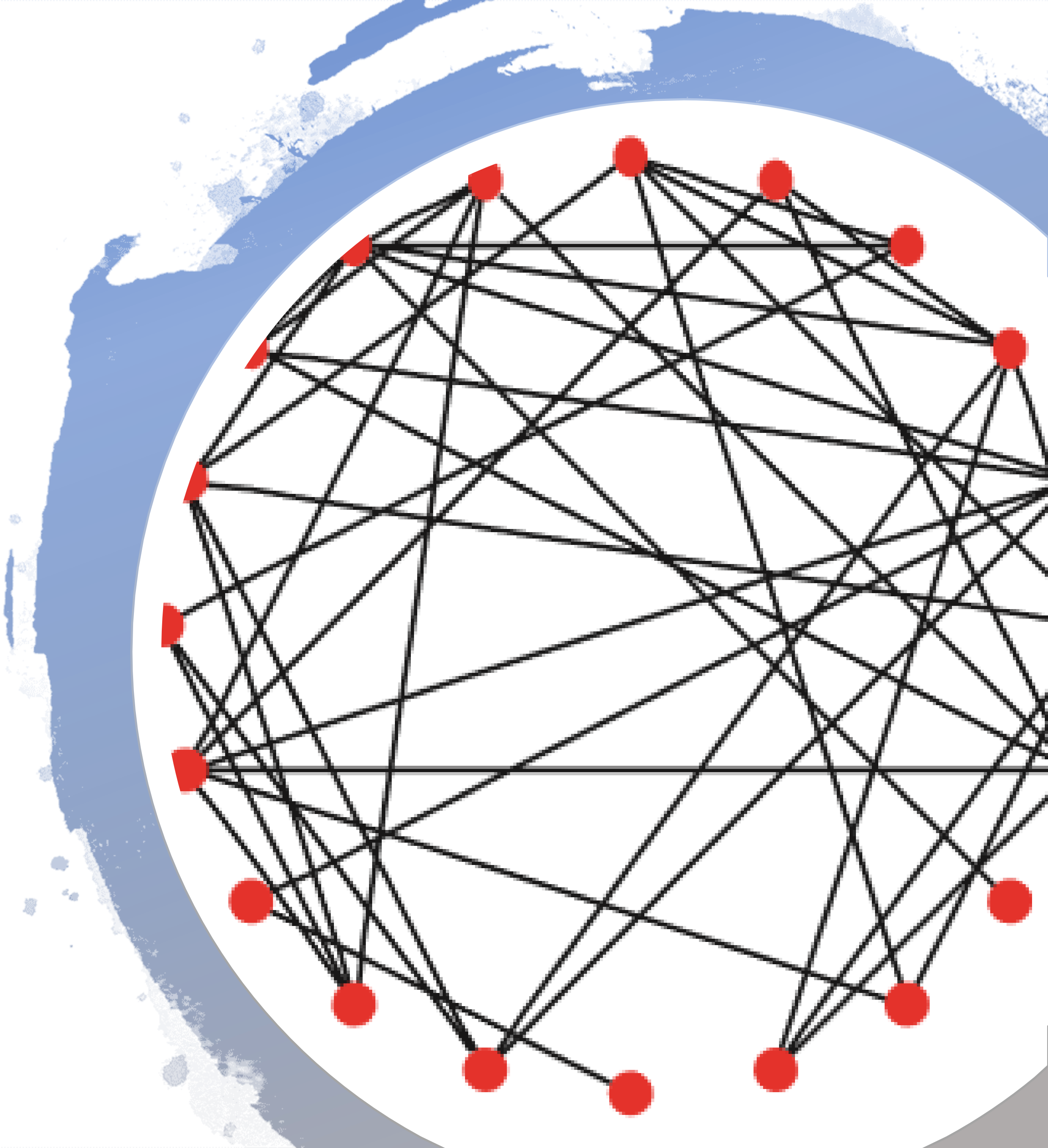
Outline

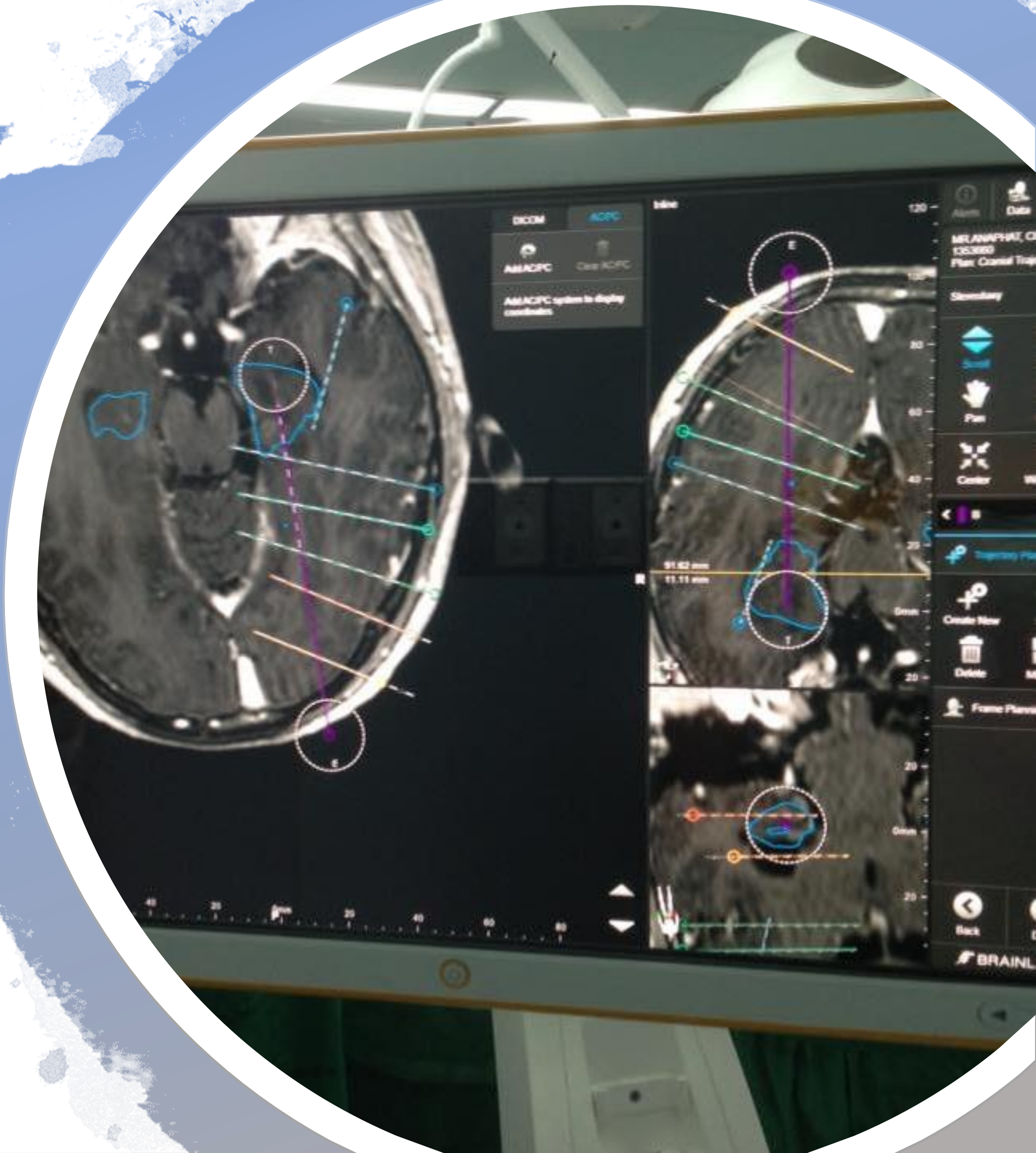
- The evolving of the epilepsy surgery and the concept of epileptogenic zone (EZ)
- SEEG and Epileptogenic networks
- Correlating semiology with SEEG signal analysis: connectivity



Epilepsy surgery

- Treatment option for **medically refractory seizure**

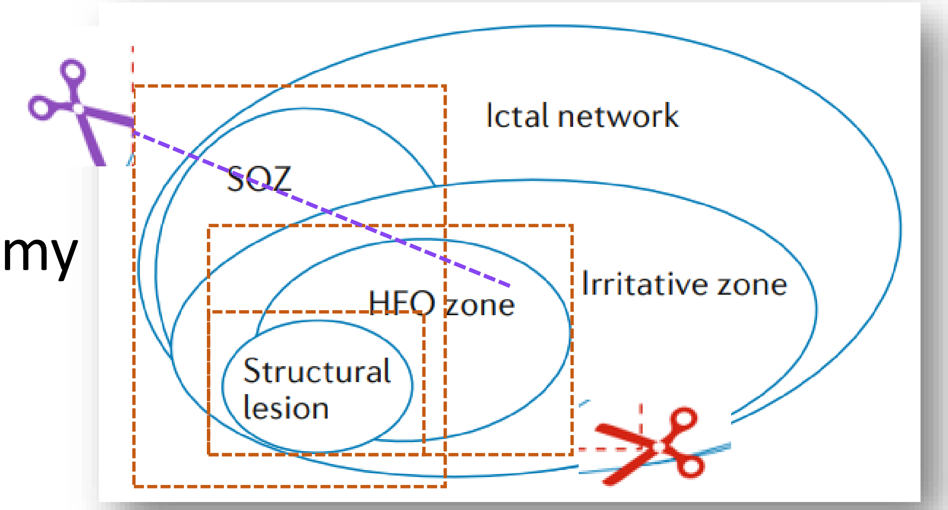
- **Surgically remediable syndrome**
  - Mesial temporal lobe epilepsy
  - Well circumscribed lesional partial epilepsy
  - Hemispheric epilepsy syndrome
  - Epilepsies in infants and young children due to large or diffuse lesions limited to one hemisphere



Epilepsy surgery

Resective surgery

- Lesionectomy
- Selective amygdalohippocampectomy
- Corticectomy
- Lobectomy
- Multilobar resection

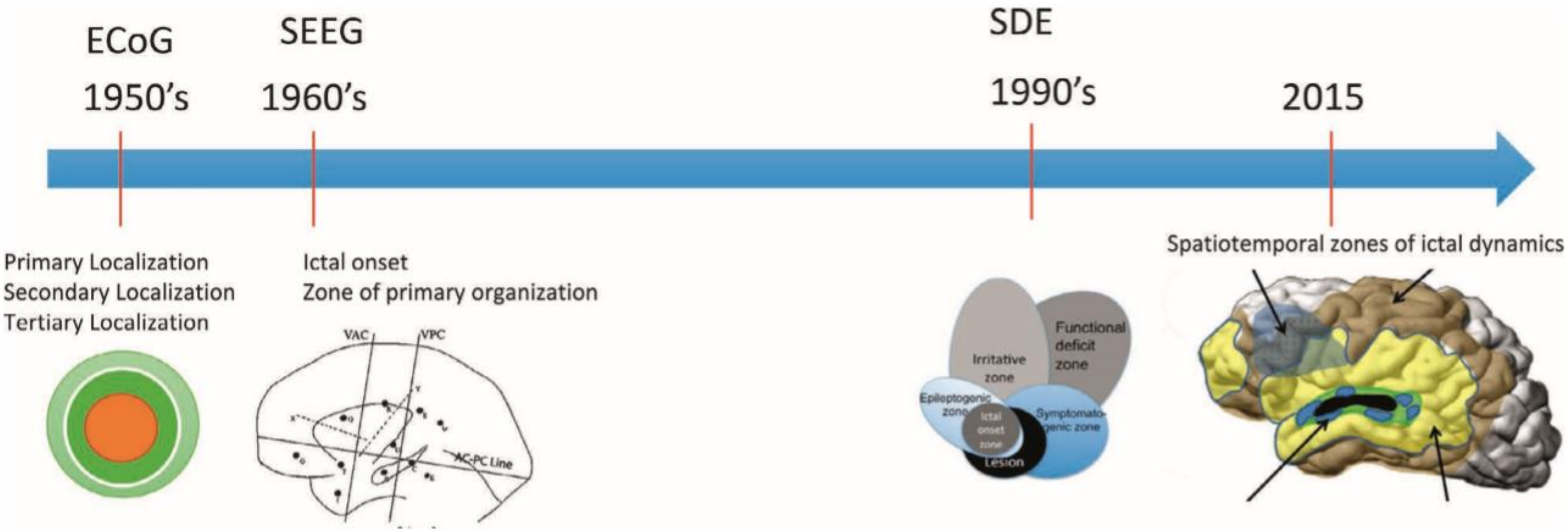


Epileptogenic Zone

Palliative Surgery

- Corpus Callosotomy
- Multiple Subpial Transections
- Vagus Nerve Stimulator

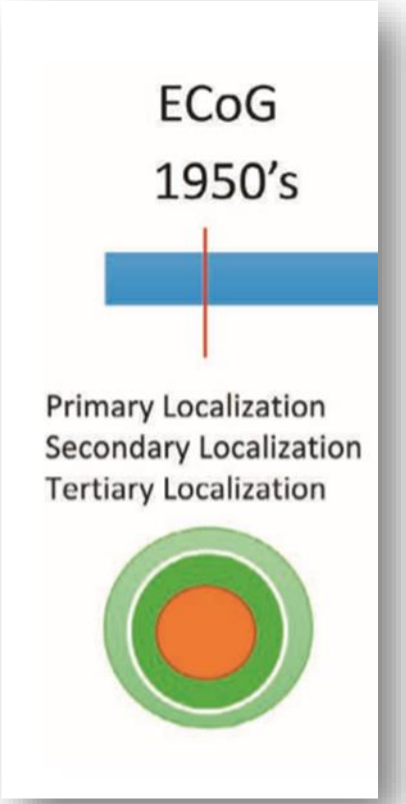
The evolving representations of the epileptogenic zone (EZ)



Lara Jehi, Epilepsy currents 2018

The evolving representations of the epileptogenic zone (EZ)

Rasmussen's Localization Concepts



Concept	Definition	Contemporary Tool Used to Define It
Primary localizing diagnosis	Estimate of where in the brain the seizure starts	EEG ictal recordings
Secondary localization	Extent and localization of the cortex that is recruited into abnormal discharging activity in a clinical seizure	Seizure spread in intracranial chronic recording
Tertiary localization	How much of the total potentially epileptogenic area must be excised to produce a satisfactory long-term reduction of the patients' seizure tendency	Limited capability to define

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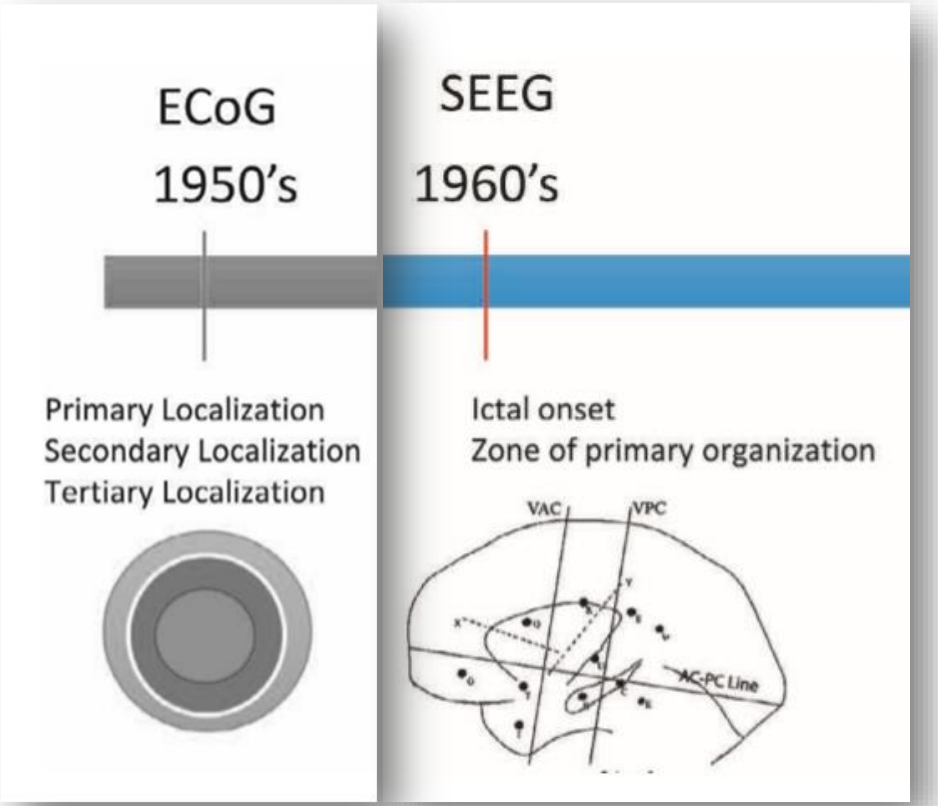
The evolving representations of the epileptogenic zone (EZ)



- In 1965, Talairach and Bancaud highlighted the inadequacy of the epileptogenic lesion definition given **"a certain number of unsatisfactory surgical results"**
- "Epileptogenic zone" (EZ) to reflect **"the site of the beginning of the epileptic seizures and of their primary organization"**
- Developed SEEG
- "Anatomo-electro-clinical" methodology

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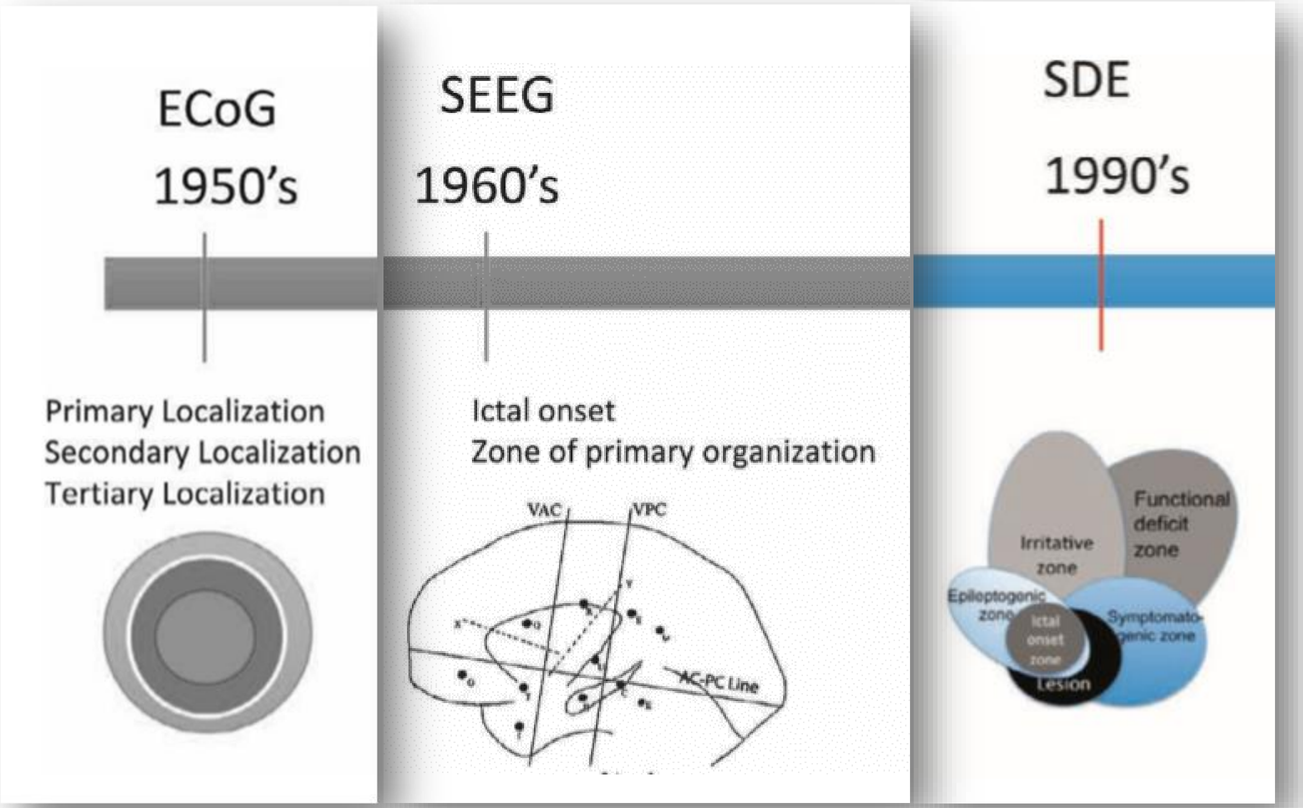
The evolving representations of the epileptogenic zone (EZ)



- In 1993, Luders et al. defined the EZ as "the area of cortex that is necessary and sufficient for initiating seizures and whose removal (or disconnection) is necessary for complete abolition of seizures"

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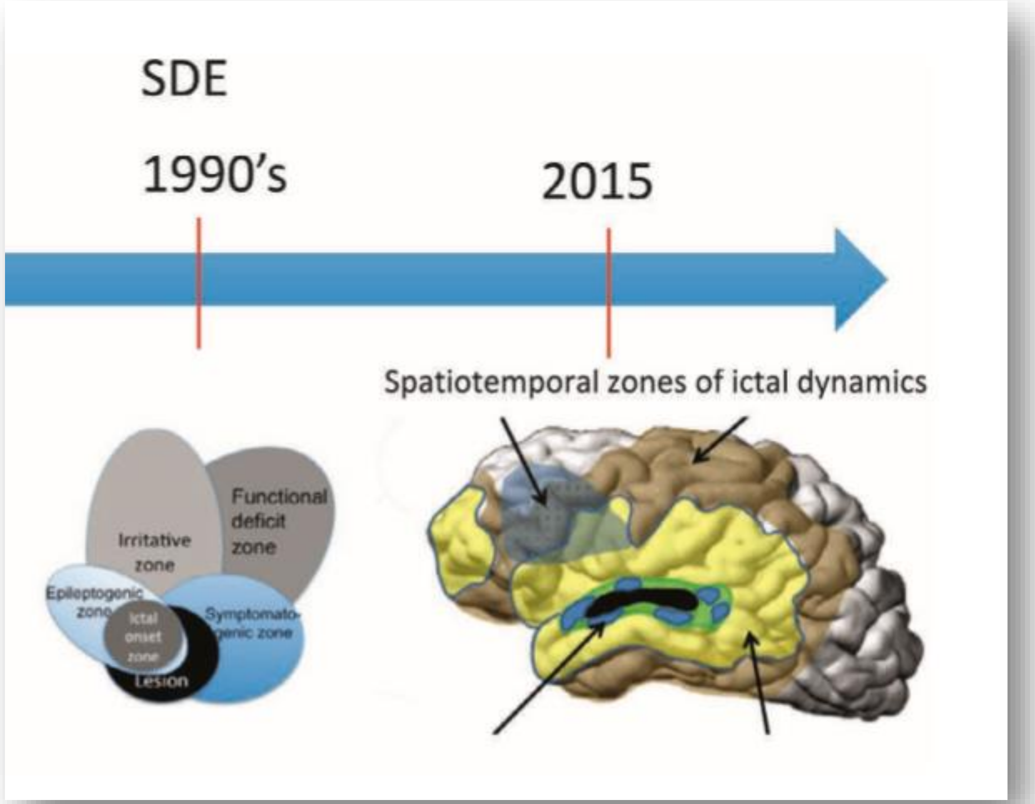
The evolving representations of the epileptogenic zone (EZ)



Network Epilepsy: 2000s to Present
"SEEG/Depth Recordings"

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Contents lists available at ScienceDirect

Journal of Clinical Neuroscience

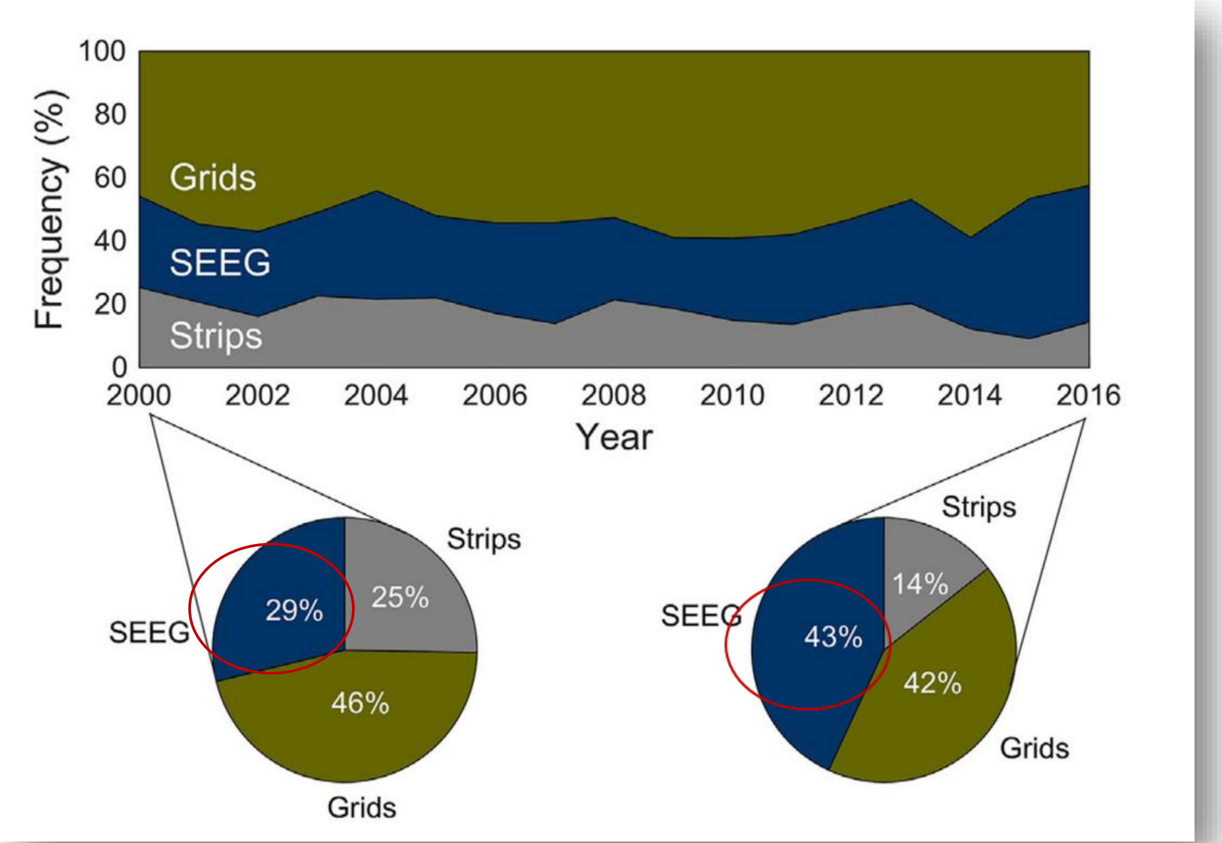
journal homepage: www.elsevier.com/locate/jocn

Clinical commentary

Increased nationwide use of stereoencephalography for intracranial epilepsy electroencephalography recordings

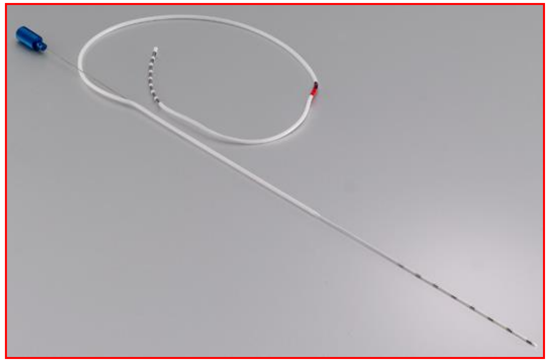
Hussam Abou-Al-Shaar[a], Andrea A. Brock[a], Bornali Kundu[a], Dario J. Englot[b], John D. Rolston[a,*]

[a] Department of Neurosurgery, Clinical Neurosciences Center, University of Utah, Salt Lake City, UT, United States
[b] Department of Neurosurgery, Vanderbilt University, Nashville, TN, United States

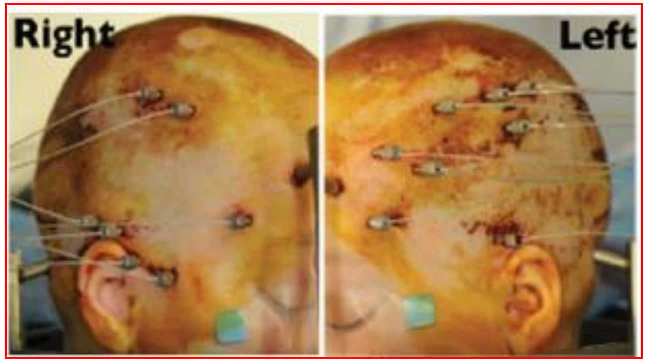


- In 2016, SEEG became the most frequently performed intracranial monitoring procedure in the Medicare population, increasing from **28.8% of total cases in 2000 to 43.1% in 2016 (*p = 0.02*).**
- The factors driving these changes are unknown

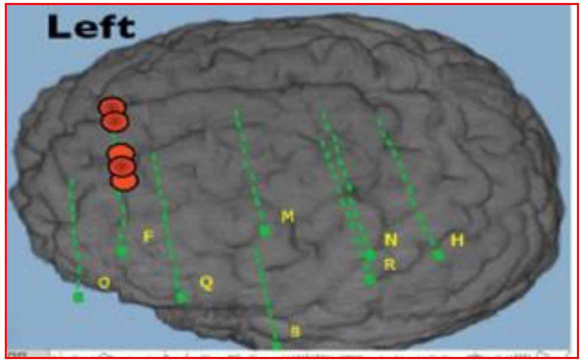
What is Stereoelectroencephalography (SEEG)?



Three-dimensional exploration of the brain using depth electrodes



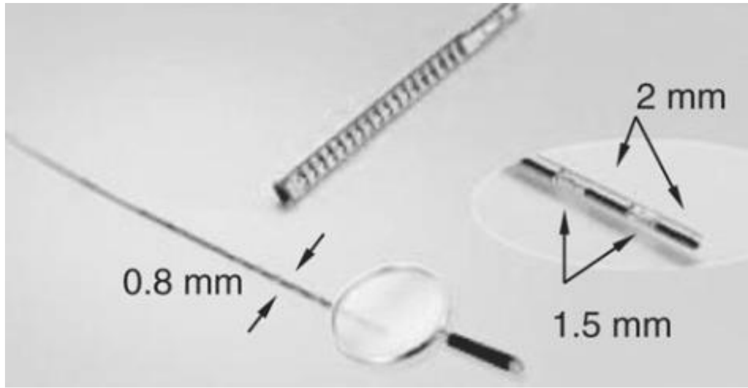
Implant of cerebral structures with the precision of stereotactic methodology



Very precise sampling and

easier to reach deep areas of cortex

SEEG ≠ Depth electrodes

- Size 

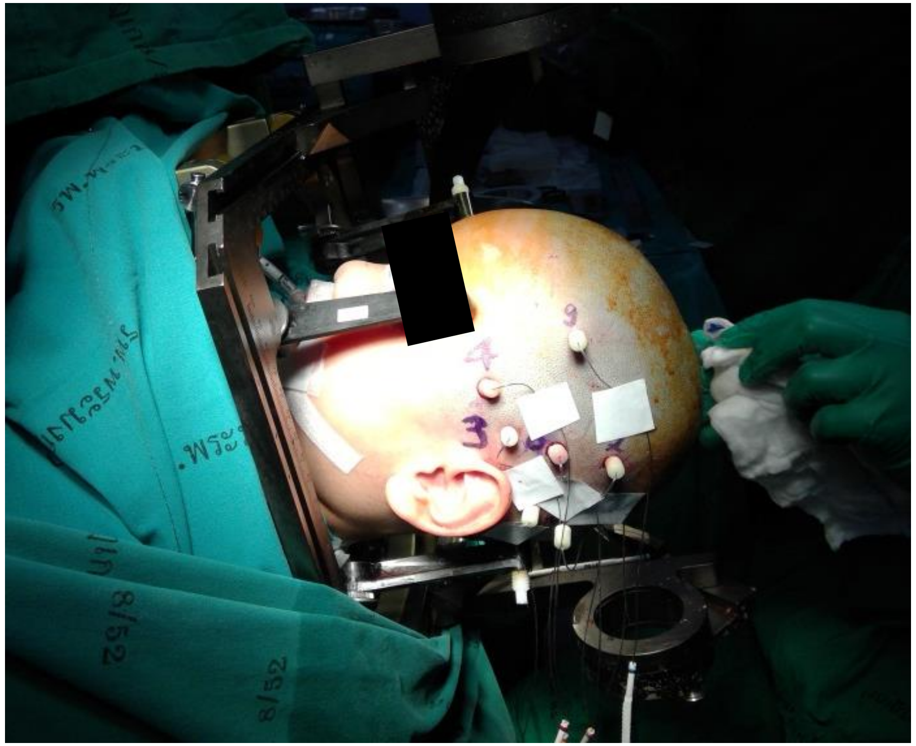
(30% smaller than depth)

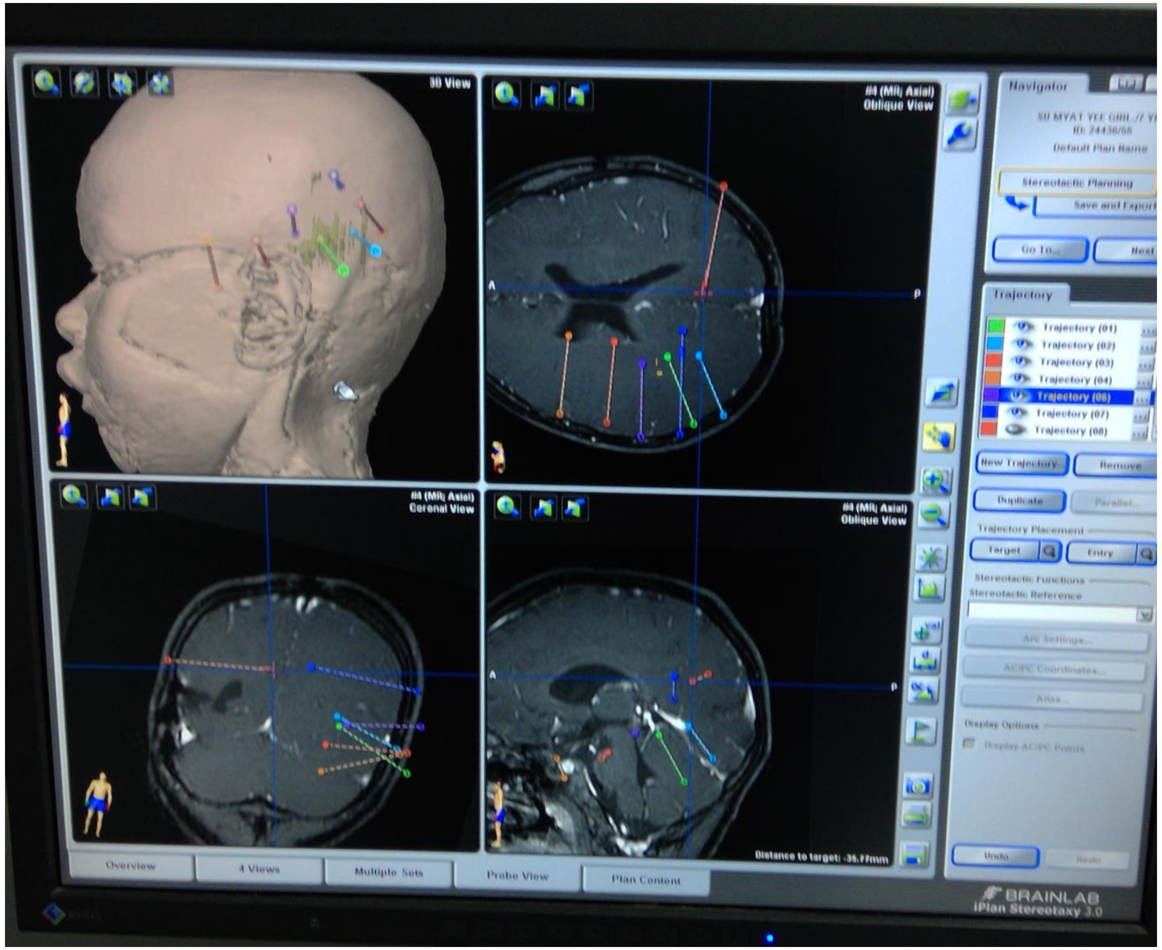
- Anatomo-Electro-Clinical correlations

- **Brain connectivity/Epileptic network**

The most important characteristic of SEEG

It enables precise recordings from *deep cortical* and subcortical structures, *multiple* noncontiguous lobes, as well as *bilateral explorations* while avoiding the need for large craniotomies

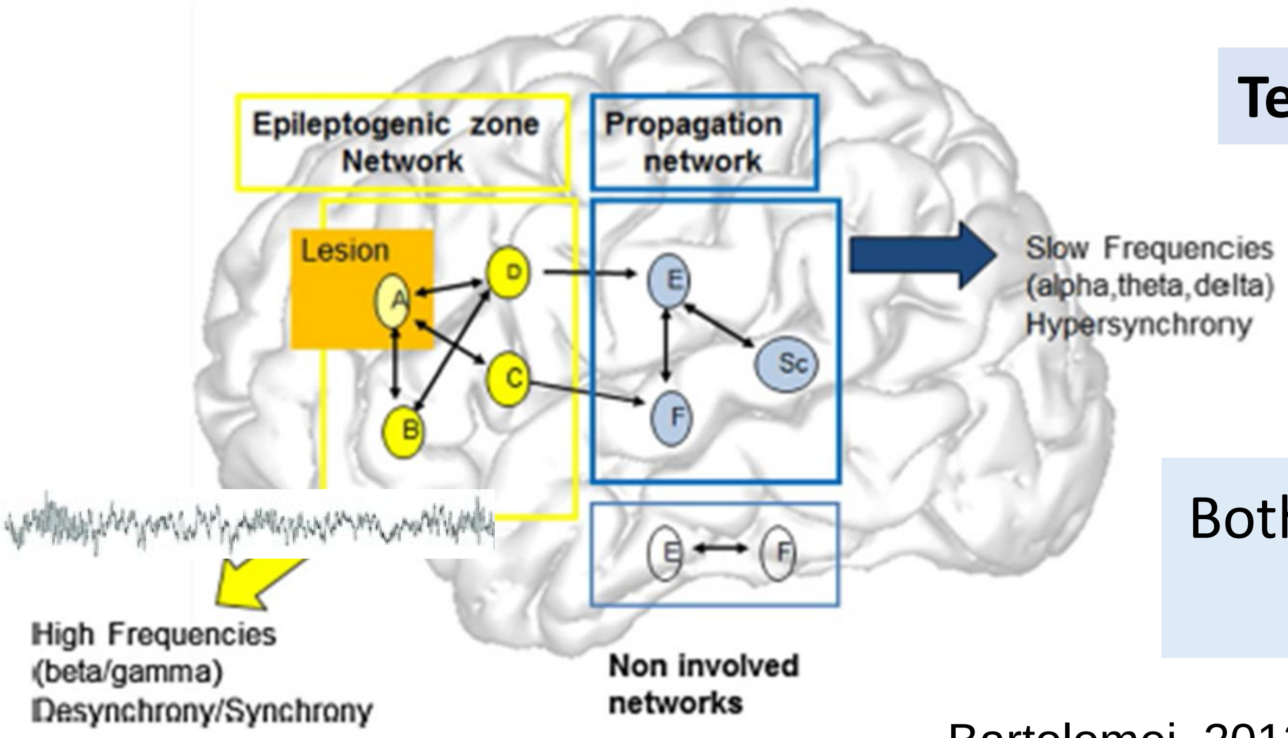




Early observations from SEEG
Anticipated concept of **Epileptic networks**

Epileptogenic zone (EZ)= region of primary organization of ictal discharge (Bancaud 1965)

Dynamic **spatiotemporal** characteristics



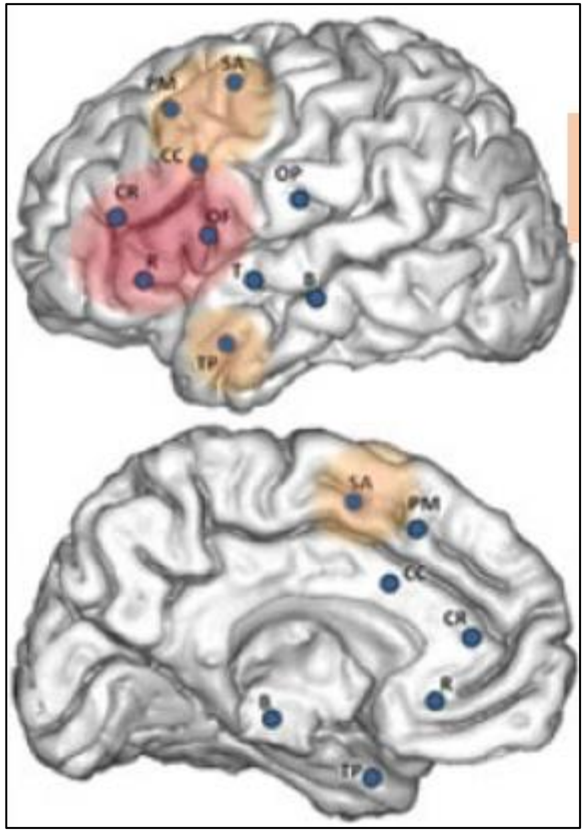
Temporal: EEG **frequency** and synchronization

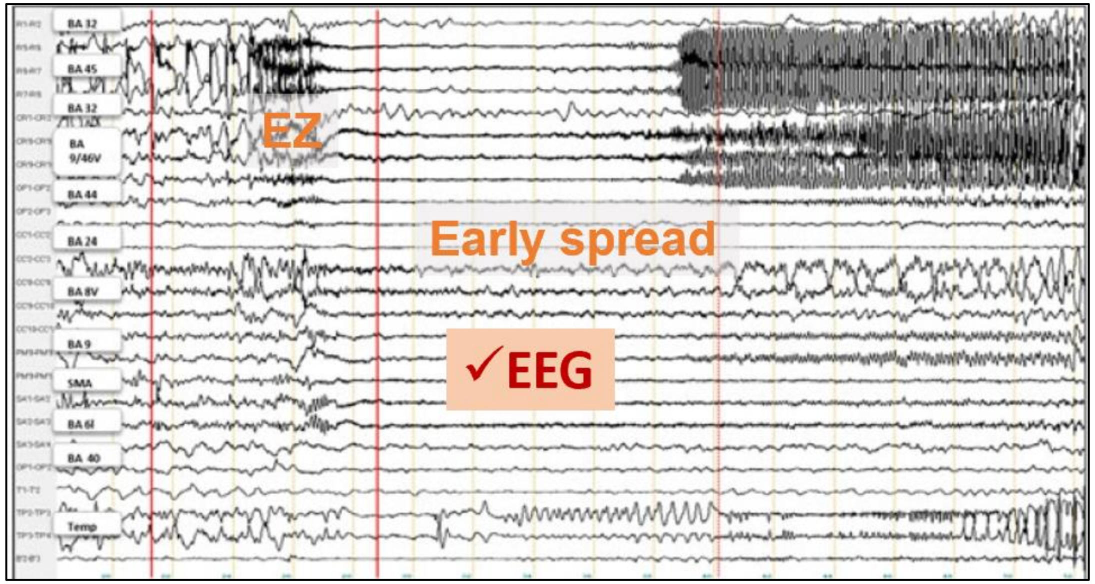
Spatial: localization of epileptic activity within a set of connected structures

Both **Spatial** and **temporal** features of seizure Influence **semiological** output

Bartolomei, 2013

Anatomical — **Electrical** — **Clinical**

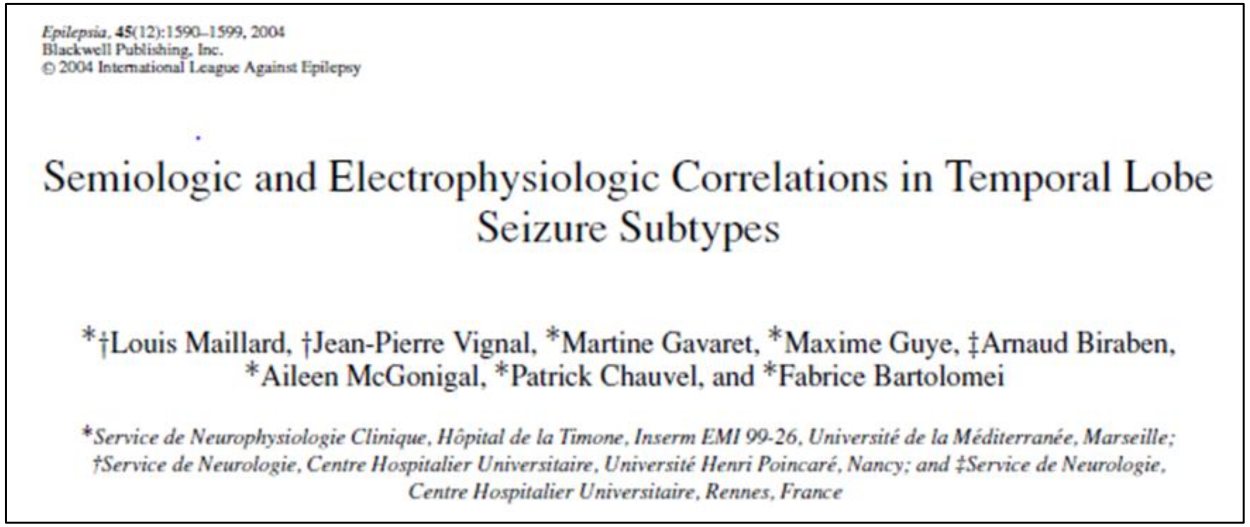




Anatomo-Electro-Clinical (AEC) correlations

Bonini F, et al. Epilepsia 2014

Temporal lobe epilepsy

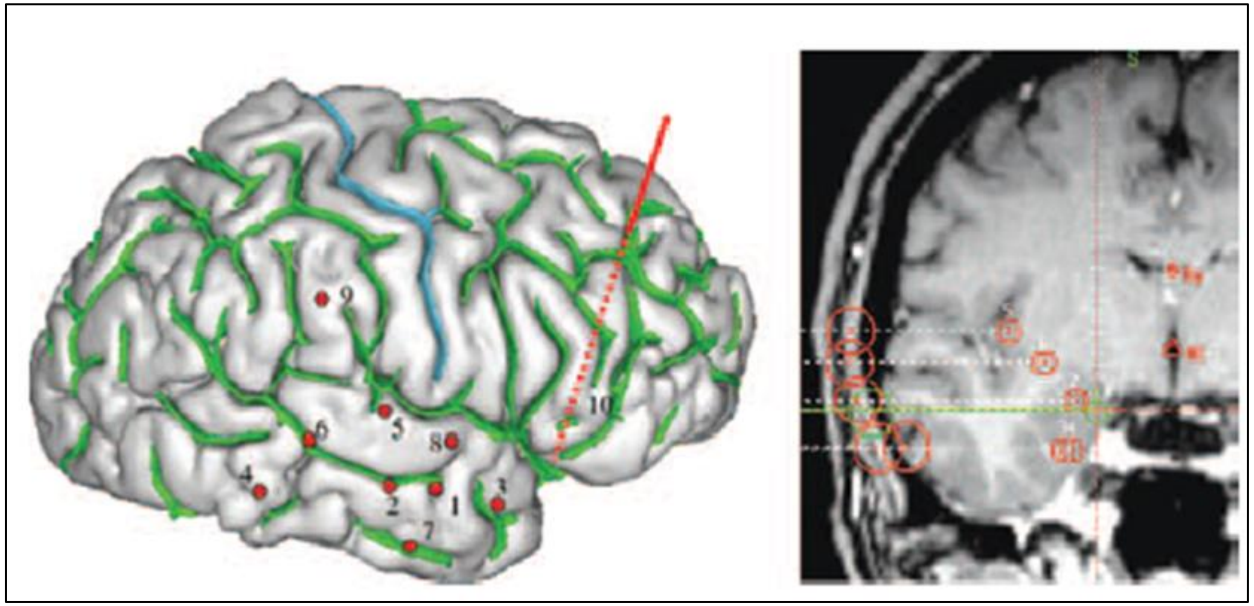


Epilepsia, 45(12):1590–1599, 2004
Blackwell Publishing, Inc.

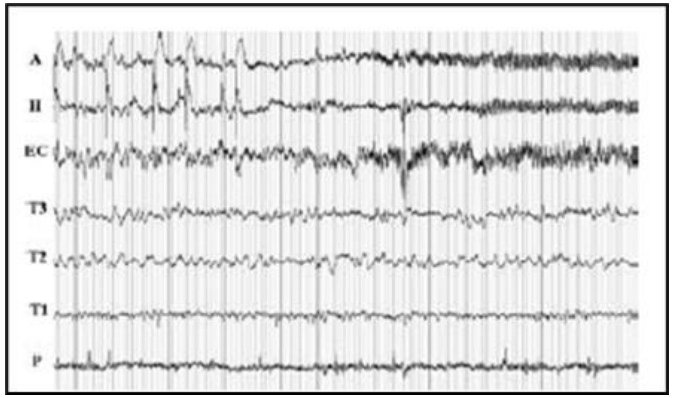
Semiologic and Electrophysiologic Correlations in Temporal Lobe Seizure Subtypes

*†Louis Maillard, †Jean-Pierre Vignal, *Martine Gavaret, *Maxime Guye, ‡Arnaud Biraben, *Aileen McGonigal, *Patrick Chauvel, and *Fabrice Bartolomei

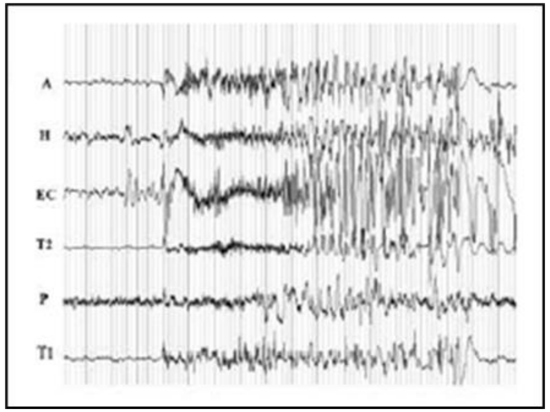
**Service de Neurophysiologie Clinique, Hôpital de la Timone, Inserm EMI 99-26, Université de la Méditerranée, Marseille; †Service de Neurologie, Centre Hospitalier Universitaire, Université Henri Poincaré, Nancy; and ‡Service de Neurologie, Centre Hospitalier Universitaire, Rennes, France*



SEEG studies with detailed semiological analysis have Allowed characterization of temporal lobe subtypes



1) Medial subtype



2) Medial-Lateral subtype

3) Lateral subtype

TABLE 4. *Distribution of the early ictal signs according to the electrophysiologic subtypes*

Early ictal features	Medial 24 (%)	Medial–Lateral 18 (%)	Lateral 13 (%)	Degree of significance
Initial loss of contact	0	7 (38.9)	7 (53.8)	$p < 0.0001$[a]
Early oroalimentary automatisms	6 (25)	10 (55.6)	1 (7.7)	$p = 0.015$[a]
Early vocalizations (groaning, howling, moaning)	3 (12.5)	7 (38.9)	1 (7.7)	$p = 0.048$[a]
Early verbal automatisms	0	5 (27.8)	0	$p = 0.028$[a]
Early upper-limb elementary automatisms	8 (33.3)	7 (38.9)	1 (7.7)	$p = 0.13$
Early upper-limb tonic posturing	2 (8.3)	0	1 (7.7)	$p = 0.45$
Early head and/or eyes deviation	3 (12.5)	4 (22.2)	3 (23.1)	$p = 0.67$

[a]Significant.

TABLE 5. *Distribution of the late ictal signs according to the electrophysiologic subtypes*

Late ictal features	Medial 24 (%)	Medial–Lateral 18 (%)	Lateral 13 (%)	Degree of significance
Late oroalimentary automatisms	14 (58.3)	4 (22.2)	2 (15.4)	$p = 0.012$[a]
Late upper-limb elementary automatisms	14 (58.3)	7 (38.9)	2 (15.4)	$p = 0.039$[a]
Late vocalization	5 (20.8)	0	2 (15.4)	$p = 0.12$
Late verbal automatisms	3 (12.5)	2 (11.1)	0	$p = 0.40$
Late upper-limb tonic posturing	6 (25)	5 (27.8)	1 (7.7)	$p = 0.41$
Late head and/or eyes deviation	8 (33.3)	6 (33.3)	3 (23.1)	$p = 0.86$
Late dysphasia	6 (25)	3 (16.7)	0	$p = 0.14$

[a]Significant.

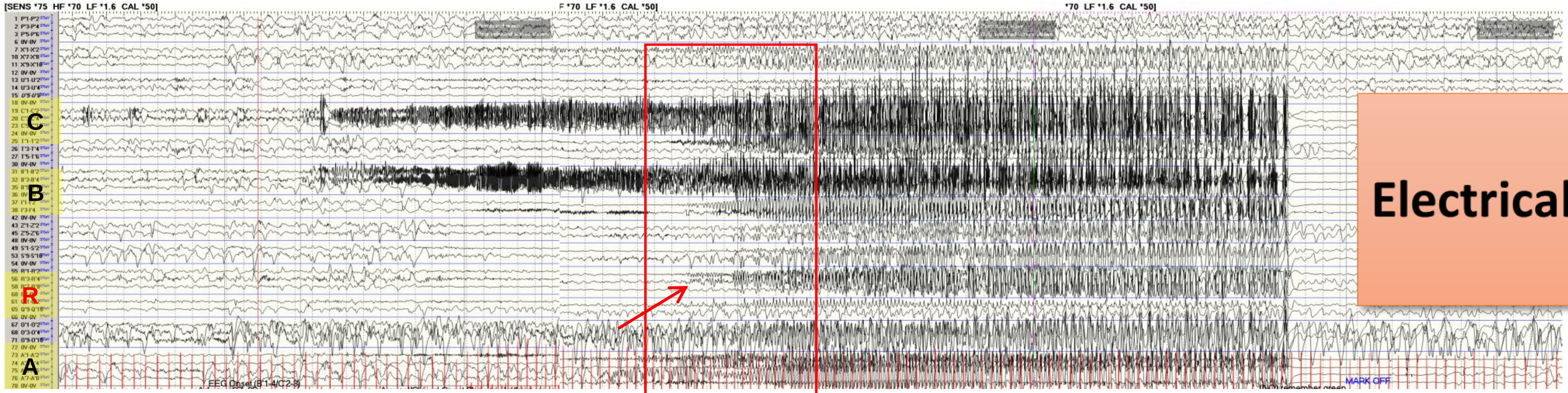
Clinical

Segment 1: Motionless

Segment 2:Chewing

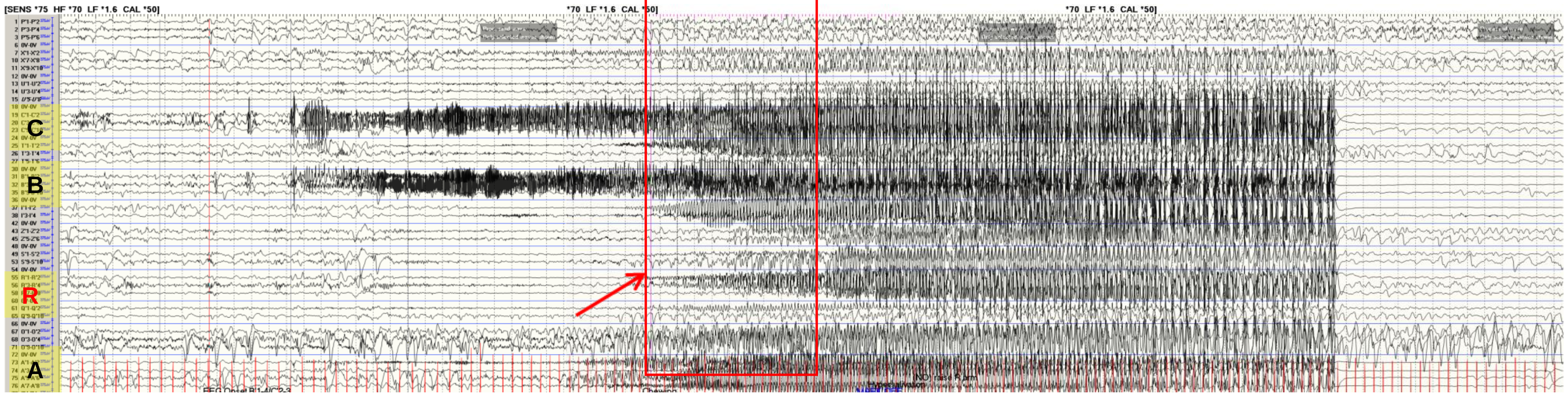
Segment 3: Rt.face/arm tonic->clonic

SZ#8

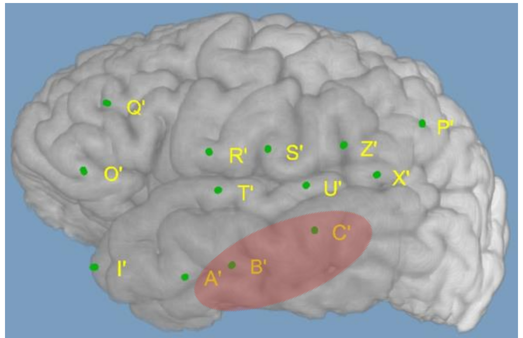


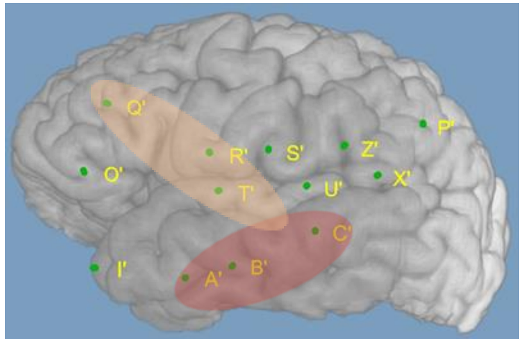
Electrical

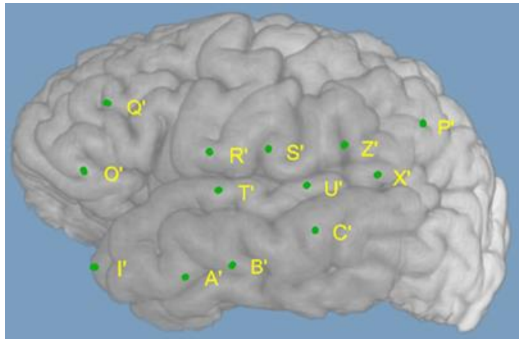
SZ#9



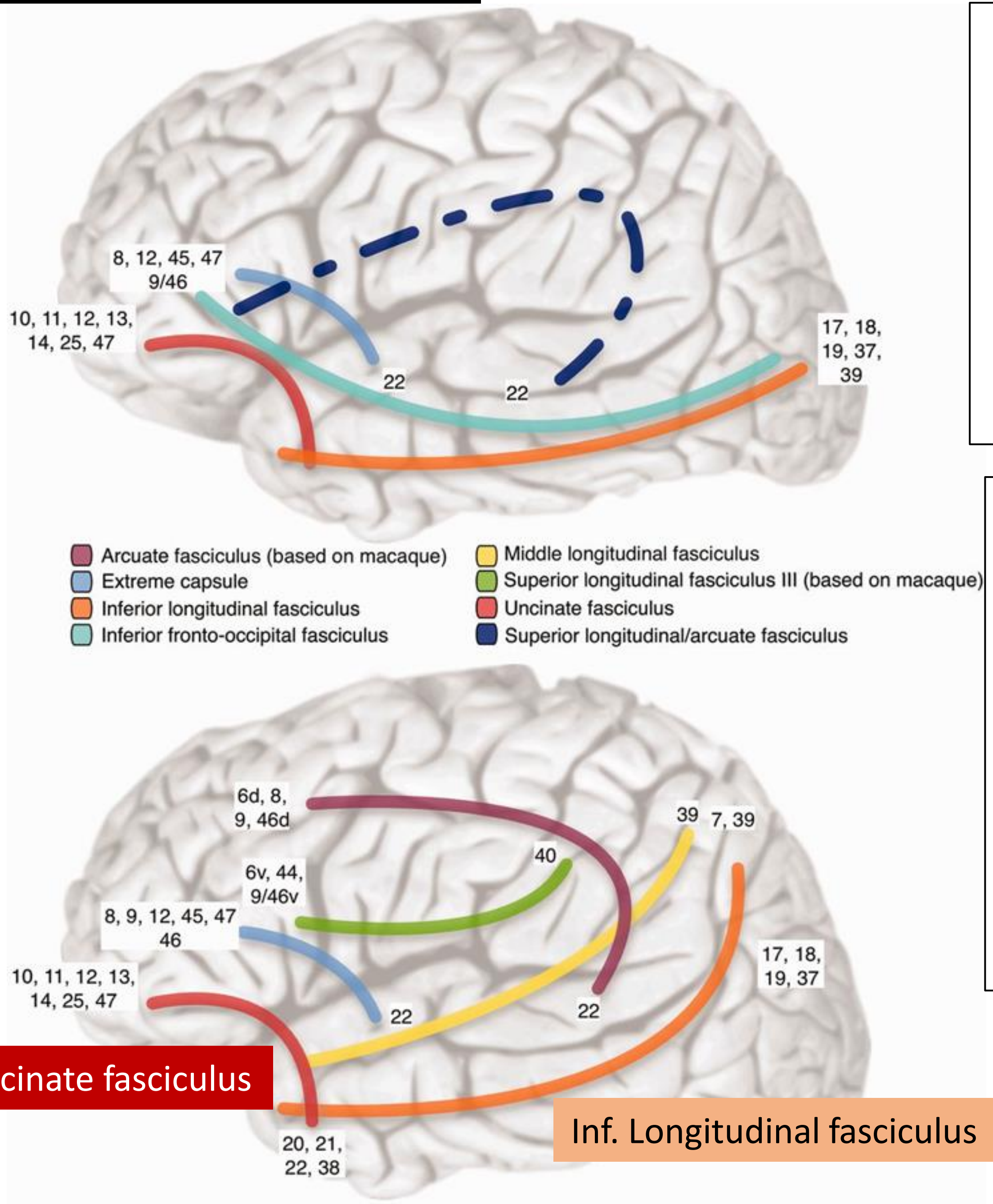
Anatomical







Temporal lobe connection



doi:10.1093/brain/awm108 *Brain* (2007), **130**, 1957–1967

Ictal clinical and scalp-EEG findings differentiating temporal lobe epilepsies from temporal 'plus' epilepsies

C. Barba,[1,2] G. Barbati,[3] L. Minotti,[4] D. Hoffmann[5] and P. Kahane[4]

[1]Pediatric Neurology Unit, Children's Hospital "A. Meyer", Florence, Italy, [2]Post-Coma Unit, Santa Lucia Foundation, Rome, Italy, [3]AFaR-Center of Medical Statistics and IT, Fatebenefratelli Hospital, Rome, Italy, [4]Neurology Department & INSERM U704, Grenoble and [5]Neurosurgery Department, University Hospital, Grenoble, France

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Brain Advance Access published December 22, 2015

doi:10.1093/brain/awv372 BRAIN 2015: Page 1 of 8 | 1

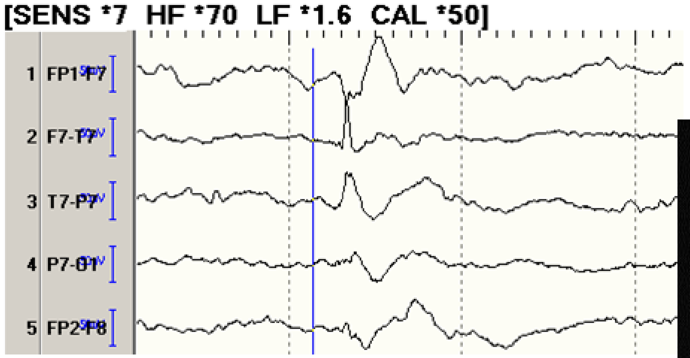
BRAIN
A JOURNAL OF NEUROLOGY

Temporal plus epilepsy is a major determinant of temporal lobe surgery failures

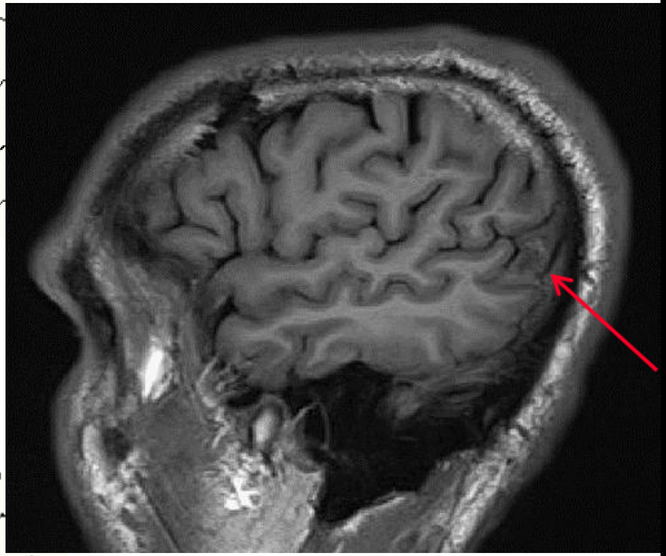
Carmen Barba,[1] Sylvain Rheims,[2,3,4] Lorella Minotti,[5] Marc Guénot,[6] Dominique Hoffmann,[7] Stephan Chabardès,[7] Jean Isnard,[2] Philippe Kahane[5,8] and Philippe Ryvlin[3,4,9]

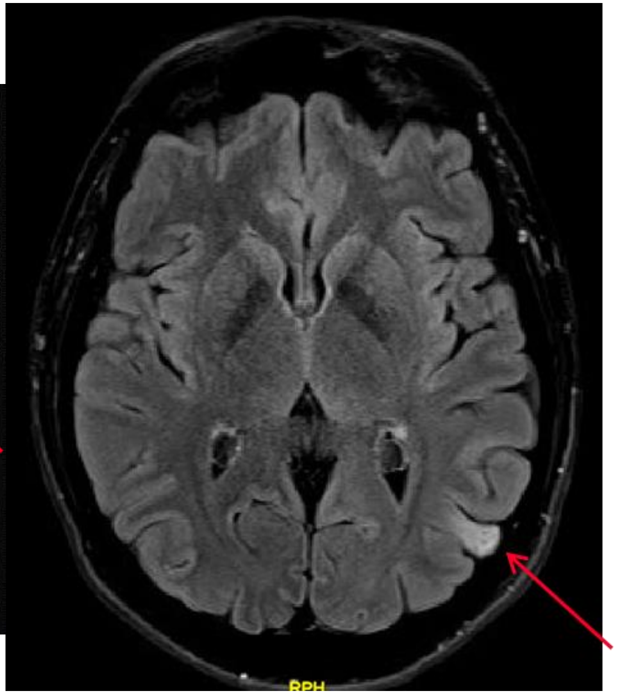
Recognition of TLE subtypes helps exploration strategy and impact on surgical outcome

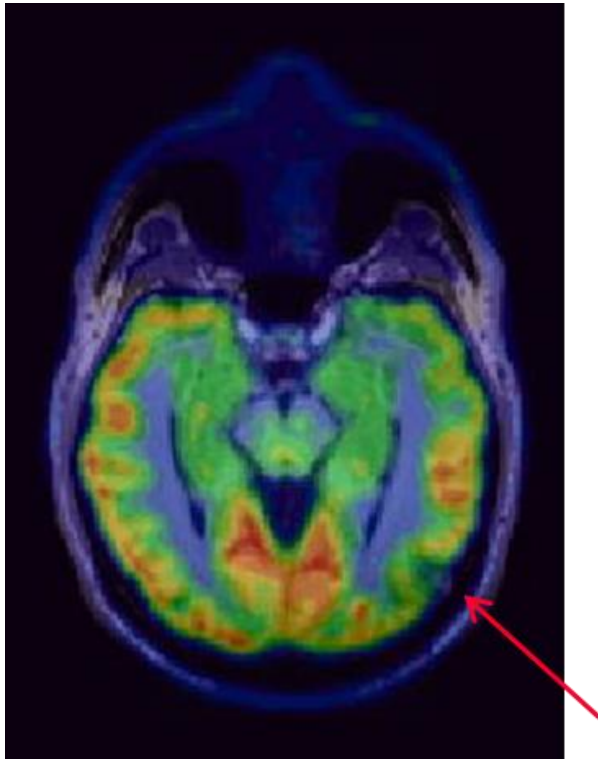
Case a 31-year-old with intractable epilepsy, RH
Seizure onset: 14 years
Seizure: focal impaired awareness

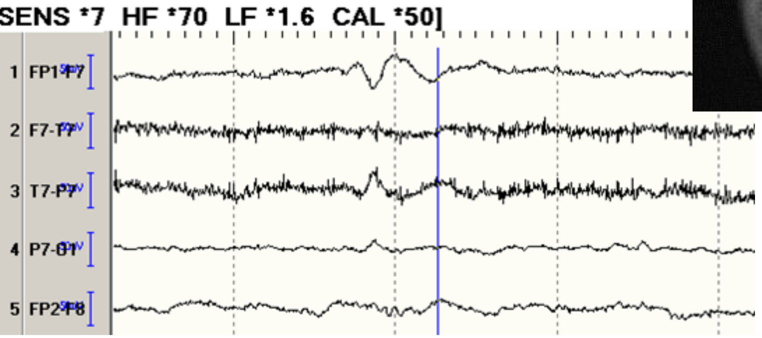


Scalp EEG
Interictal: F7/T7





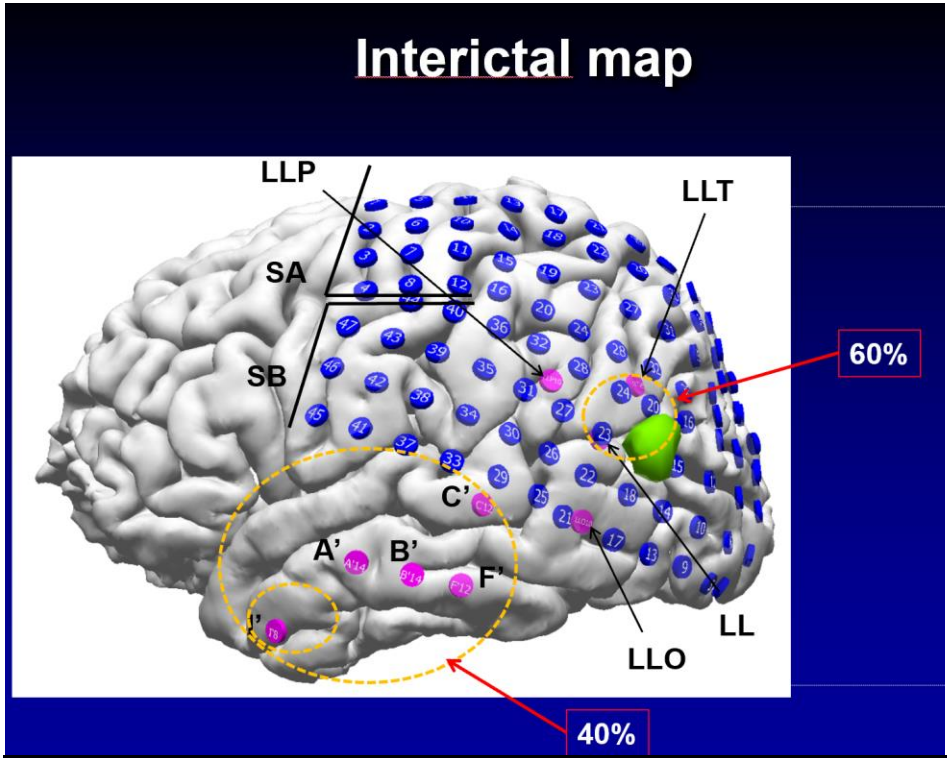


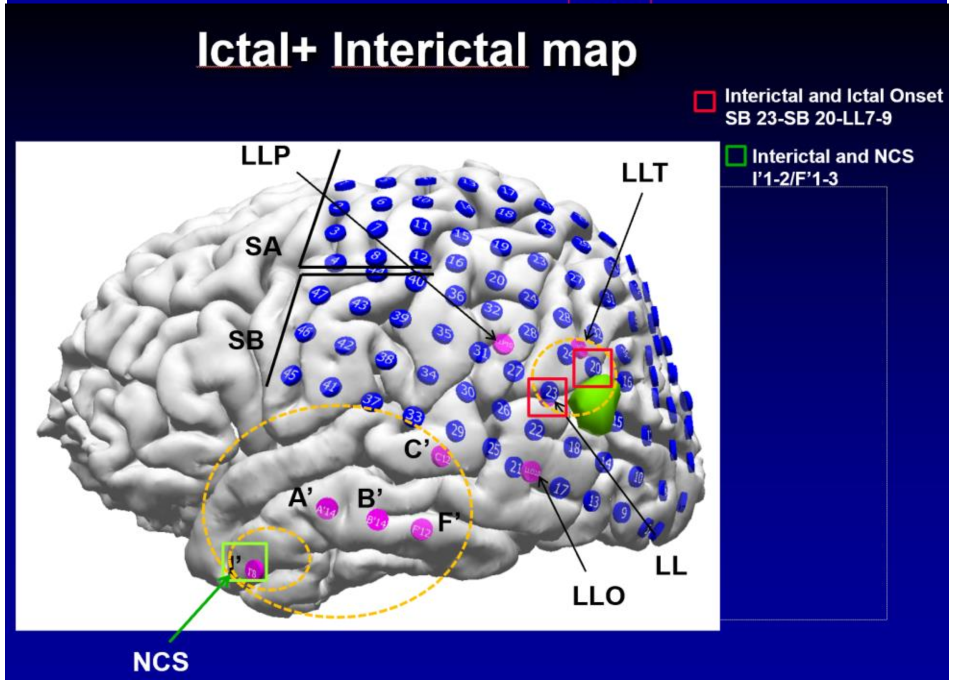


Scalp EEG
Interictal: T7/P7

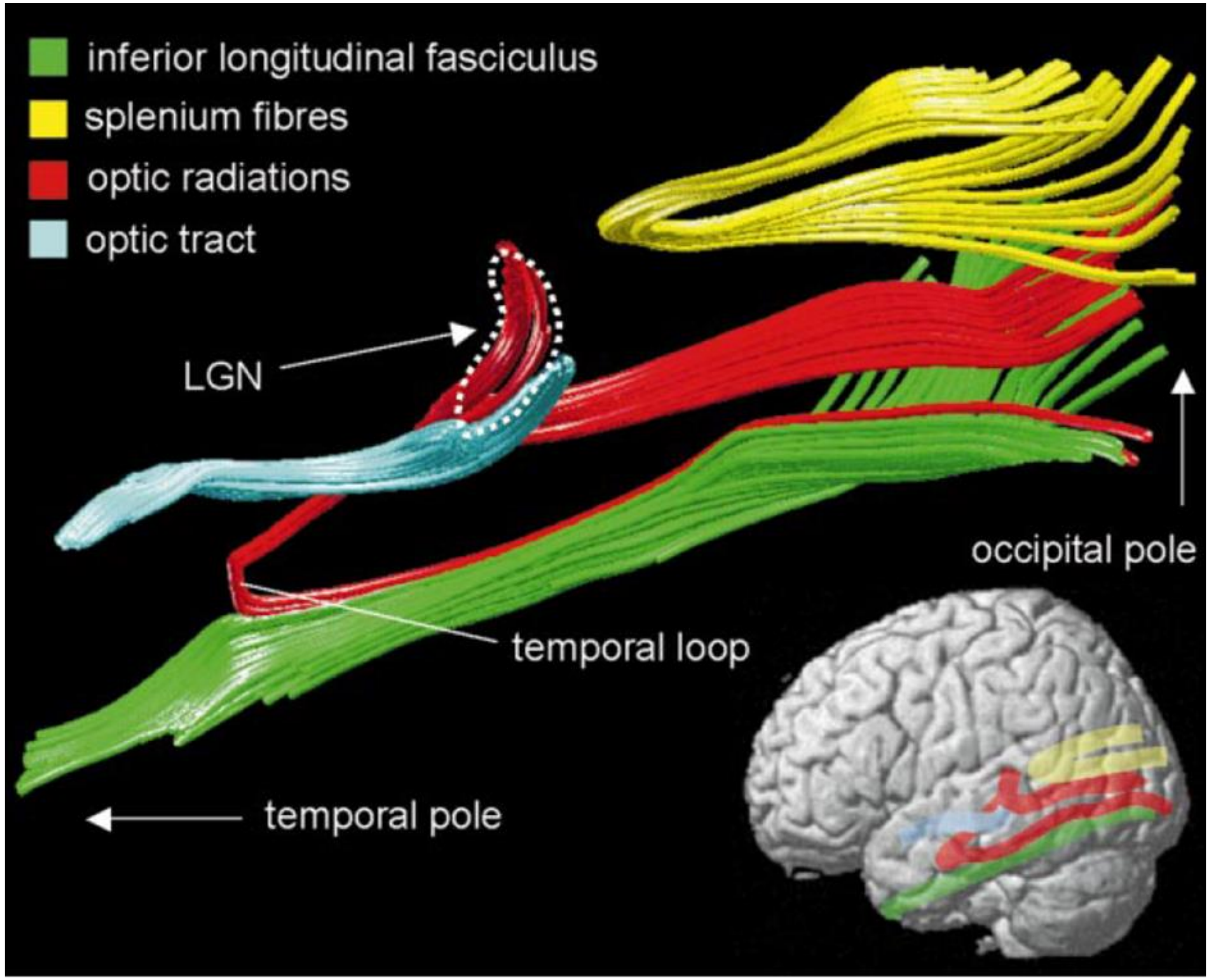
MRI: suspected DNET at
dorsal left middle temporal gyrus
at the temporal occipital junction

PET scan
SEVERE HYPOMETABOLISM IN THE
LEFT LATERAL T-O JUNCTION





Case a 31-year-old with intractable epilepsy, RH
Seizure onset: 14 years
Seizure: focal impaired awareness

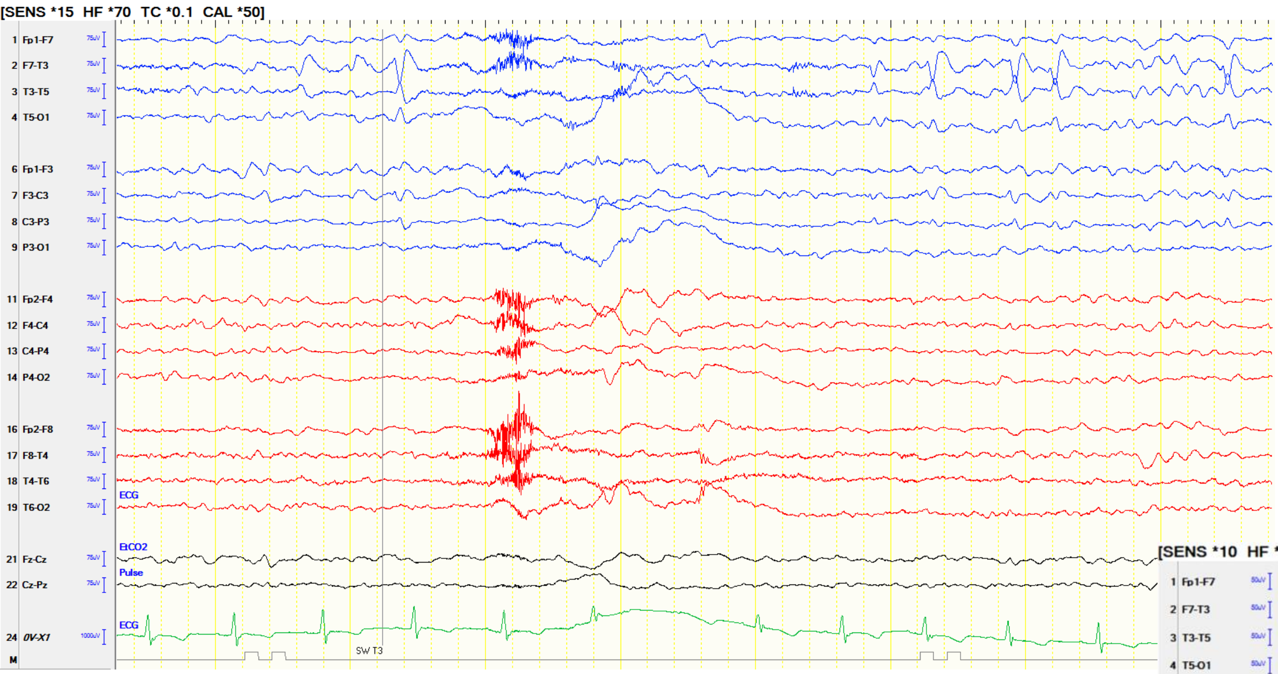


Case a 9-year-old boy with intractable epilepsy

- ชักครั้งแรก อายุ 3 ปี
- ลักษณะชัก : ผู้ป่วยจะดูสับสน ขยับตัว มือขยับไปมา เรียกไม่รู้สึกตัว เป็นนาน 10-15 นาที
- MRI brain: unremarkable
- EEG:
  - Interictal: T3, F7, Fp1, Fz
  - Ictal: 1. F7, T3
    2. Fp1, F3

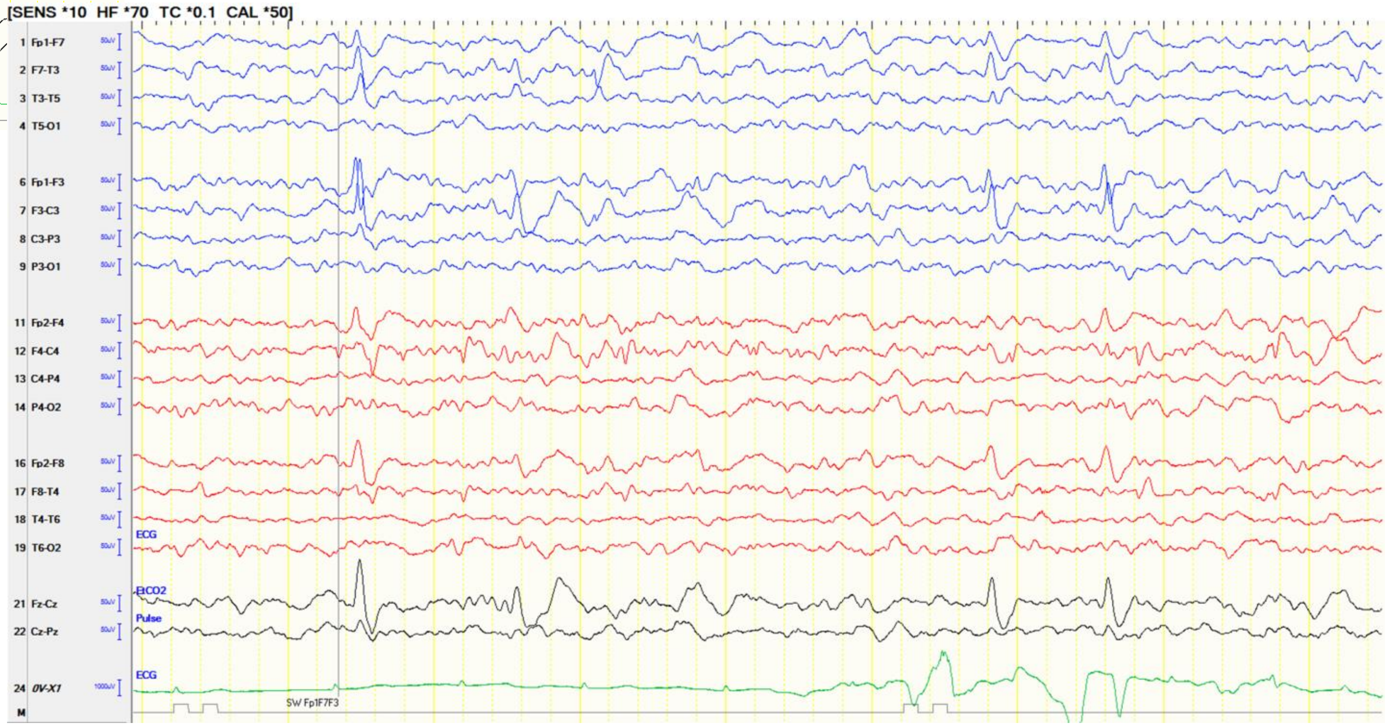
- video

SW T3

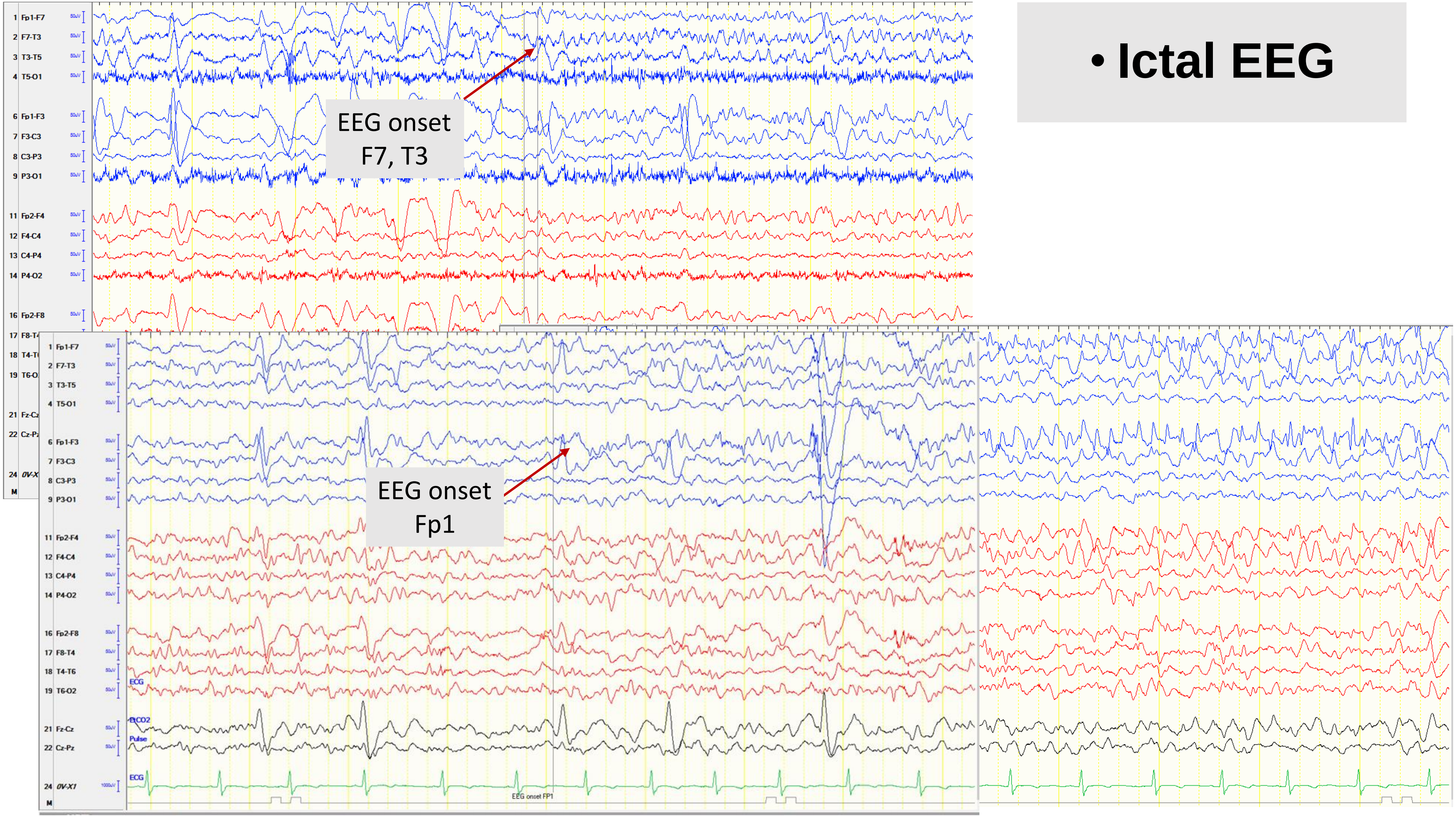


- **Interictal EEG**

SW Fp1/ Fz



- **Ictal EEG**


EEG onset
F7, T3
EEG onset
Fp1
1 Fp1-F7
2 F7-T3
3 T3-T5
4 T5-O1
6 Fp1-F3
7 F3-C3
8 C3-P3
9 P3-O1
11 Fp2-F4
12 F4-C4
13 C4-P4
14 P4-O2
16 Fp2-F8
17 F8-T4
18 T4-T6
19 T6-O2
21 Fz-Cz
22 Cz-Pz
24 0V-X1
ECG
EtCO2
Pulse
ECG
EEG onset FP1

Phase I noninvasive evaluation

Lesion

MRI/VBM
PET
Neurological exam
Neuropsychology

Ictal data

Video-EEG
Ictal SPECT
Ictal and post-ictal
Neurologic and
neuropsychologic
examination

Interictal Data

Video-EEG
High density EEG
MEG
PET

Phase I noninvasive evaluation

Lesion

MRI-nonlesional

Neurological exam-normal

Neuropsychology

Ictal data

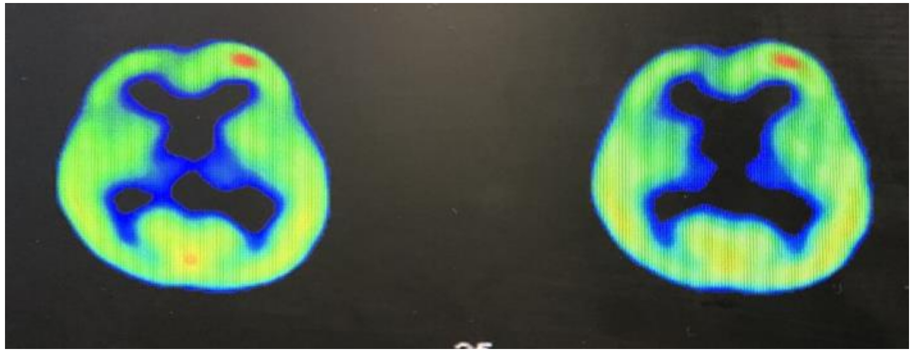
Video-EEG-

2 Ictal onset

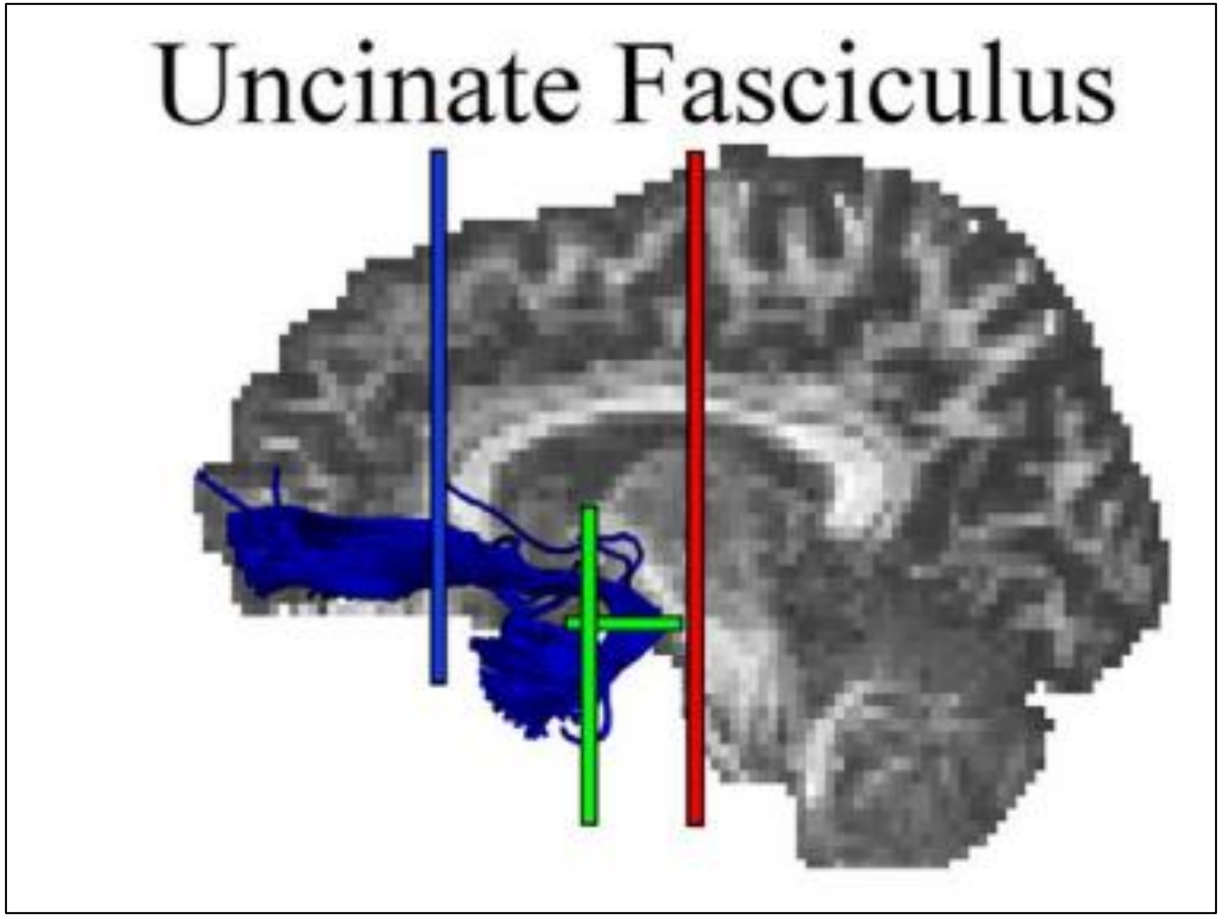
1.F7,T3

2. F3

Ictal SPECT-Left frontal



Frontotemporal network



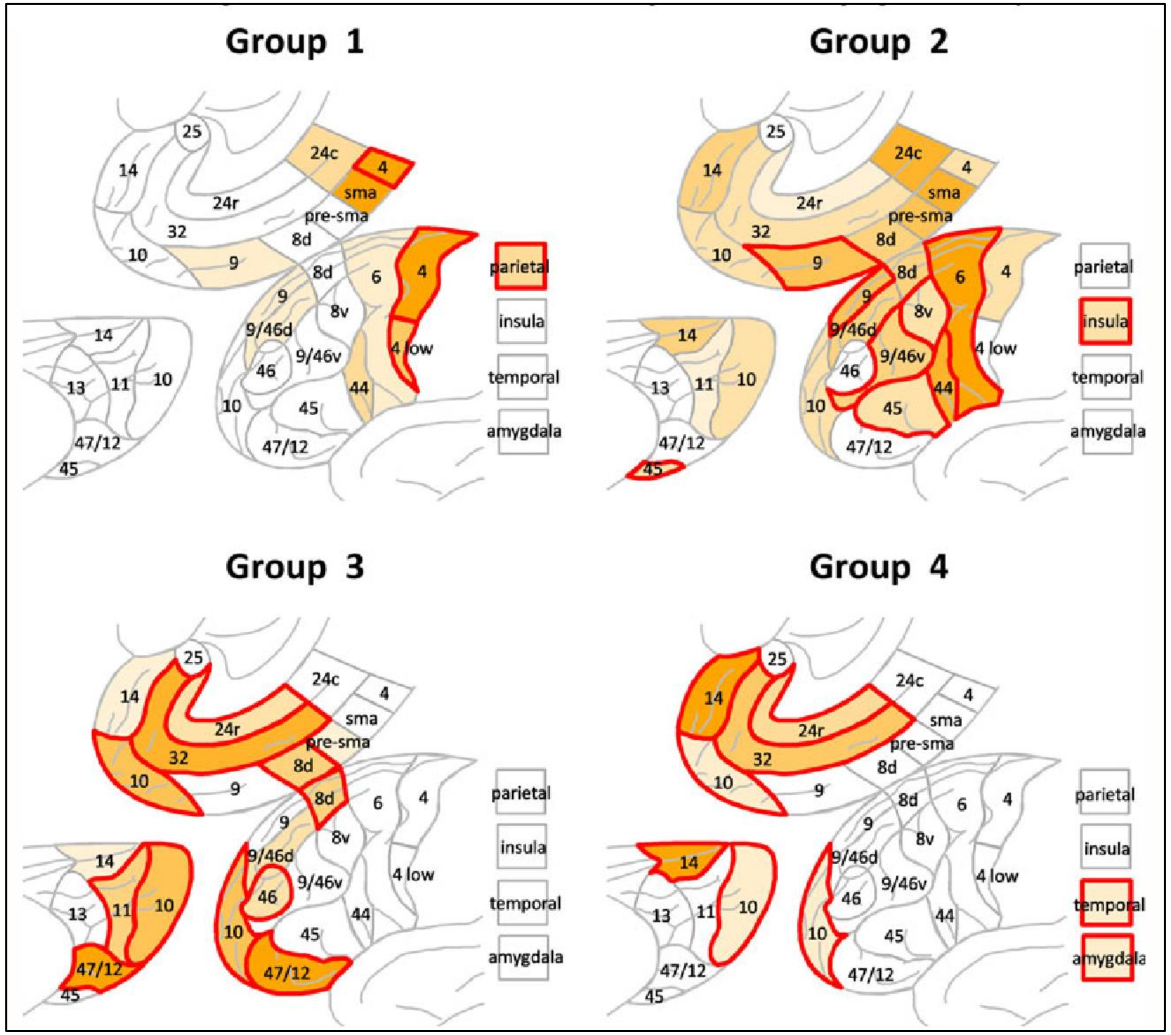
Frontal vs. Temporal?

Frontal lobe seizures: From clinical semiology to localization

*†[1]Francesca Bonini, *†‡[1]Aileen McGonigal, *†‡Agnès Trébuchon, *†‡Martine Gavaret, *†‡Fabrice Bartolomei, *†§Bernard Giusiano, and *†‡Patrick Chauvel

Epilepsia, 55(2):264–277, 2014
doi: 10.1111/epi.12490

Group 1
Elementary motor signs
With no gestural behaviour

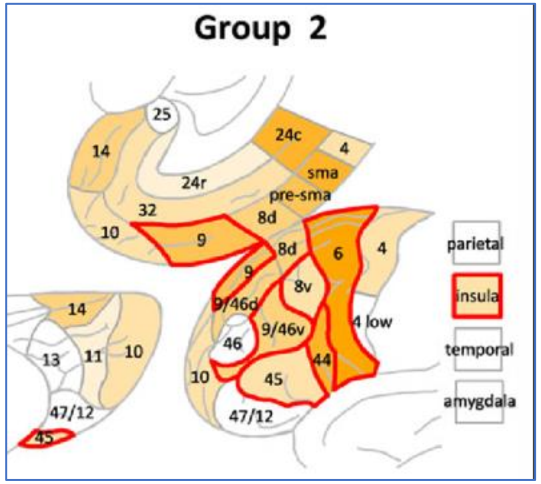


Group 2
Association of elementary motor signs and
Proximal gestural motor Beh; non-integrated appearance

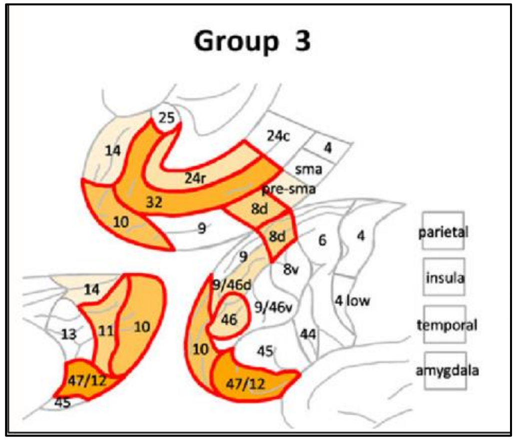
Group 3
Distal stereotypies,
Integrated appearance,
No elementary signs

Group 4
Fear-related behaviour,
no elementary motor signs

Video

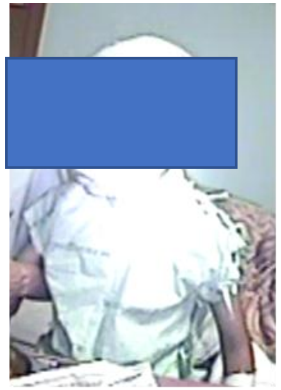


Group 2
Association of elementary motor signs and Proximal gestural motor Beh; non-integrated appearance



Group 3
Distal stereotypies, Integrated appearance, No elementary signs


Proximal stereotypies

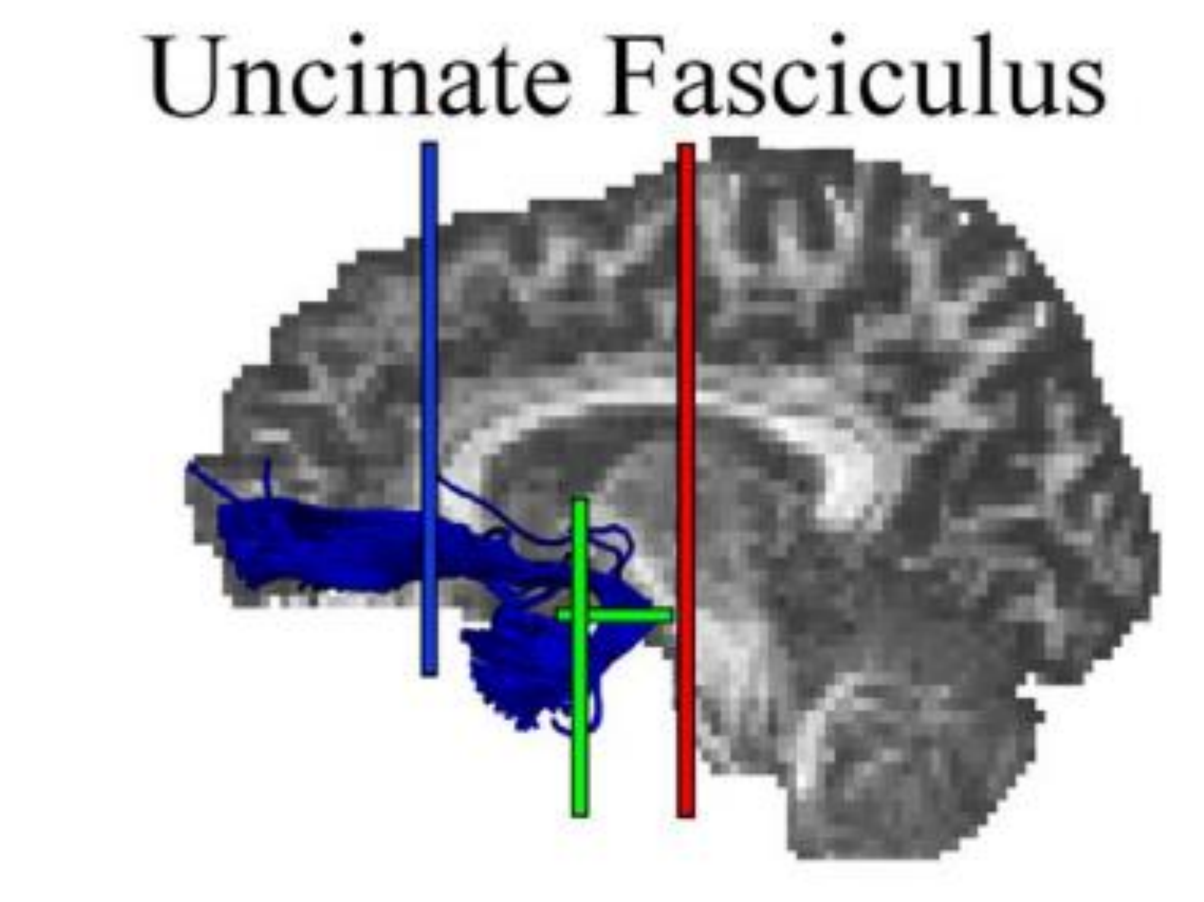

No facial expression


distal stereotypies

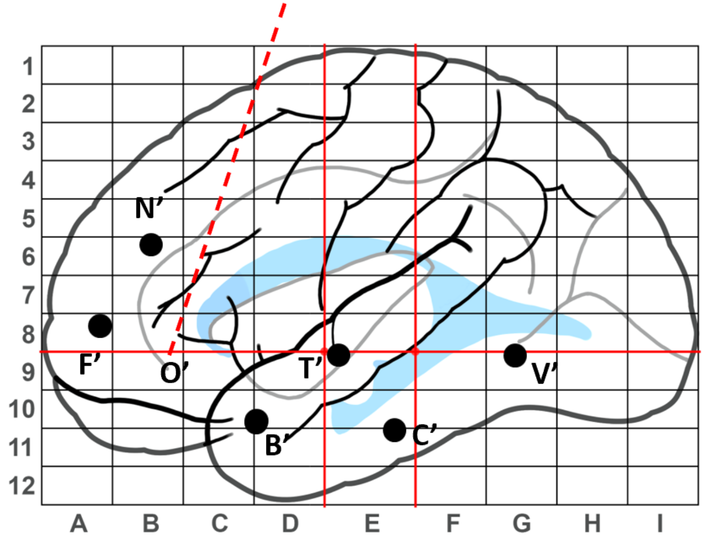

R leg stereotypies

Frontotemporal network

Knowing epileptic network helps



SEEG map



F'- Frontopolar
N'- MFG – Ant. Cingulate
O' - Orbitofrontal
B' – Head of hippo/temporal pole
T' – STG-Ant. Insula
C' - Inferior temporal gyrus- PHG

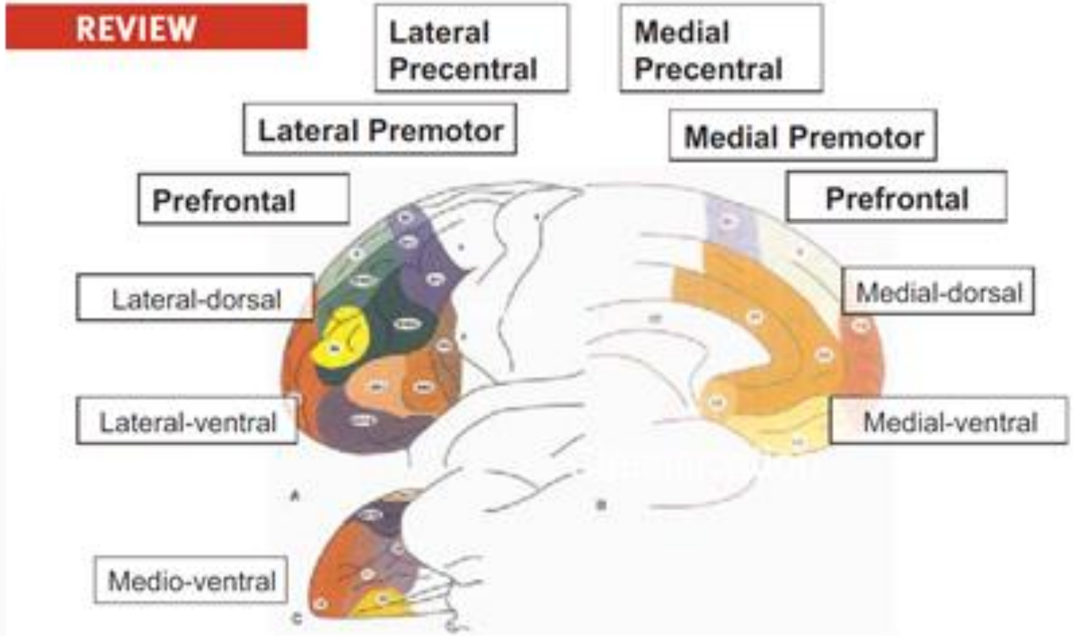
V' – Posterior temporal

Hypothesis: frontotemporal network

Progression

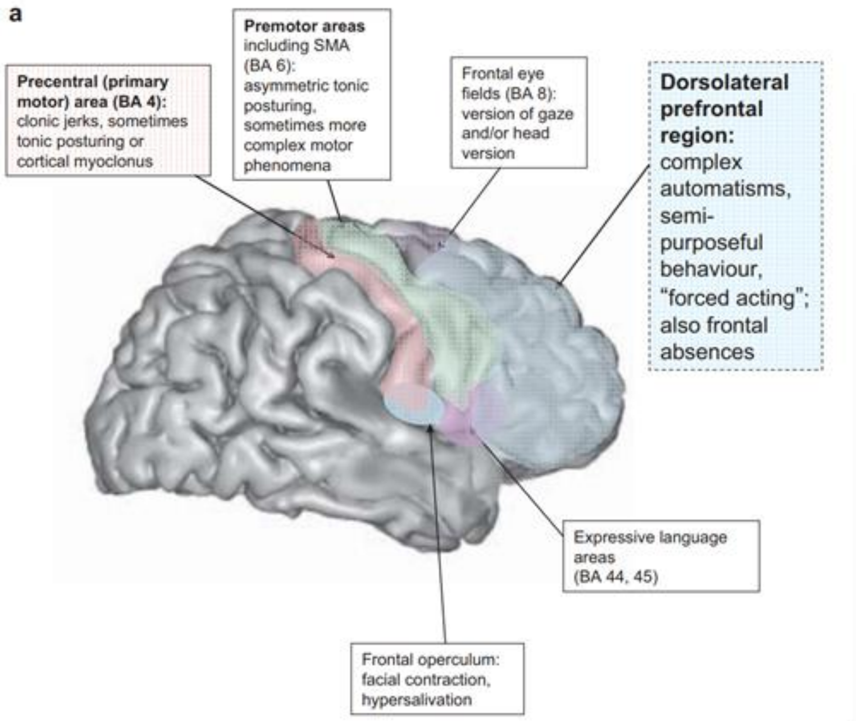
- Surgery: resection of the left frontal pole (involve O’)
- Pathology: FCD type IIa
- Seizure outcome: Engel I (seizure free since surgery)
- Improvement of development

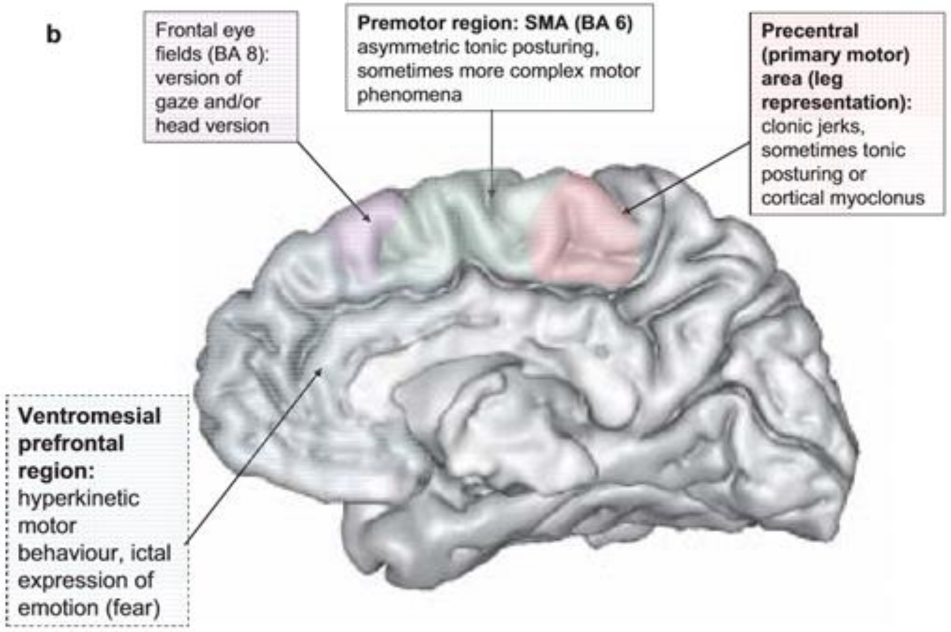
REVIEW



Frontal lobe epilepsy: seizure semiology and presurgical evaluation

Dr Aileen McGonigal[†] and Professor Patrick Chauvel[*]
[*]Director of Neurophysiology and Neuropsychology and [†]Clinical Research Fellow in Epileptology, Service de Neurophysiologie Clinique, Hôpital de la Timone and Laboratoire de Neurophysiologie et Neuropsychologie, INSERM EMI9926, Faculté de Médecine, Marseille, France;
Email: aileenmcg@hotmail.com
Practical Neurology, 2004, 4, 260–273

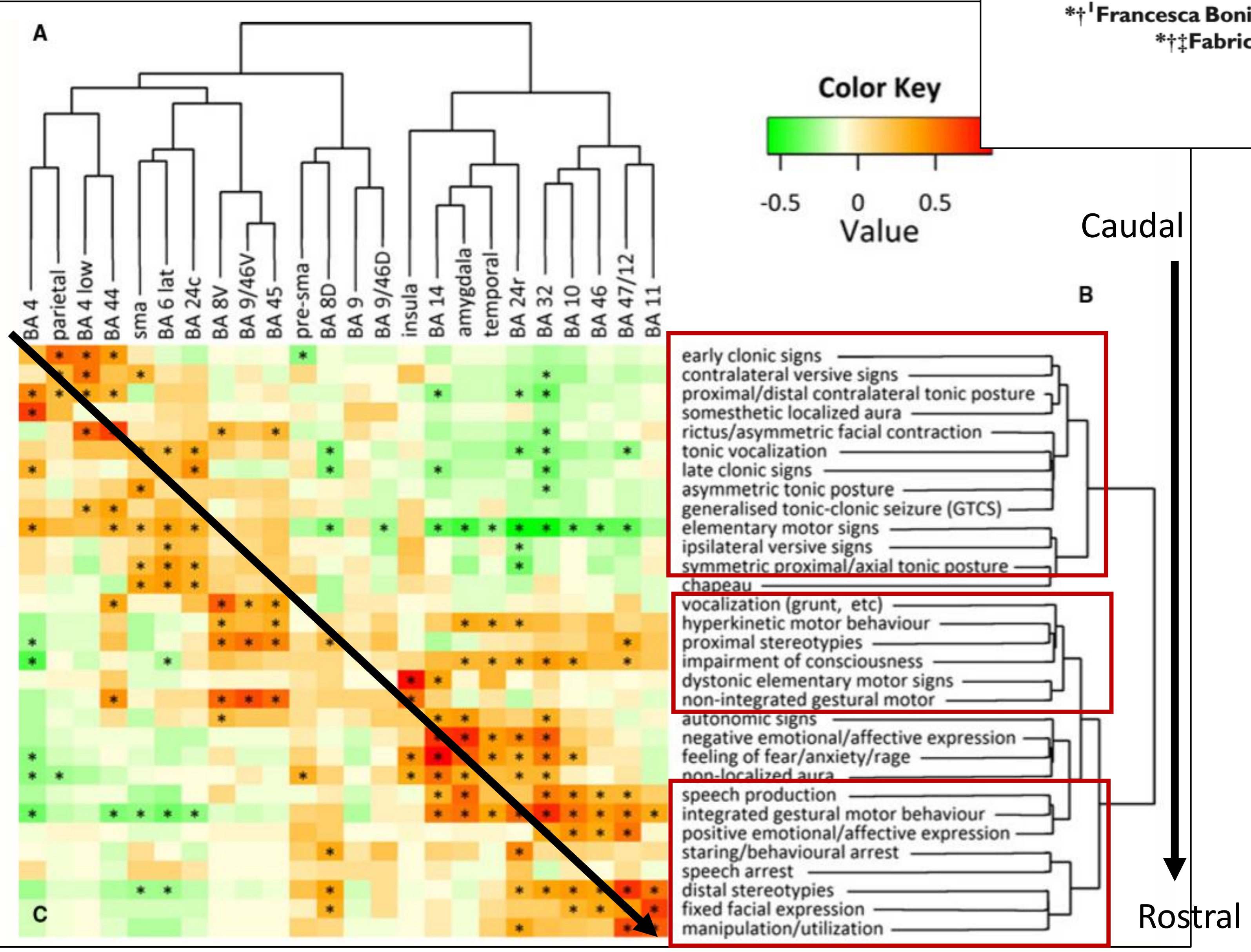




Frontal lobe seizures: From clinical semiology to localization

*†[1]Francesca Bonini, *†‡[1]Aileen McGonigal, *†‡Agnès Trébuchon, *†‡Martine Gavaret, *†‡Fabrice Bartolomei, *†§Bernard Giusiano, and *†‡Patrick Chauvel

Epilepsia, 55(2):264–277, 2014
doi: 10.1111/epi.12490



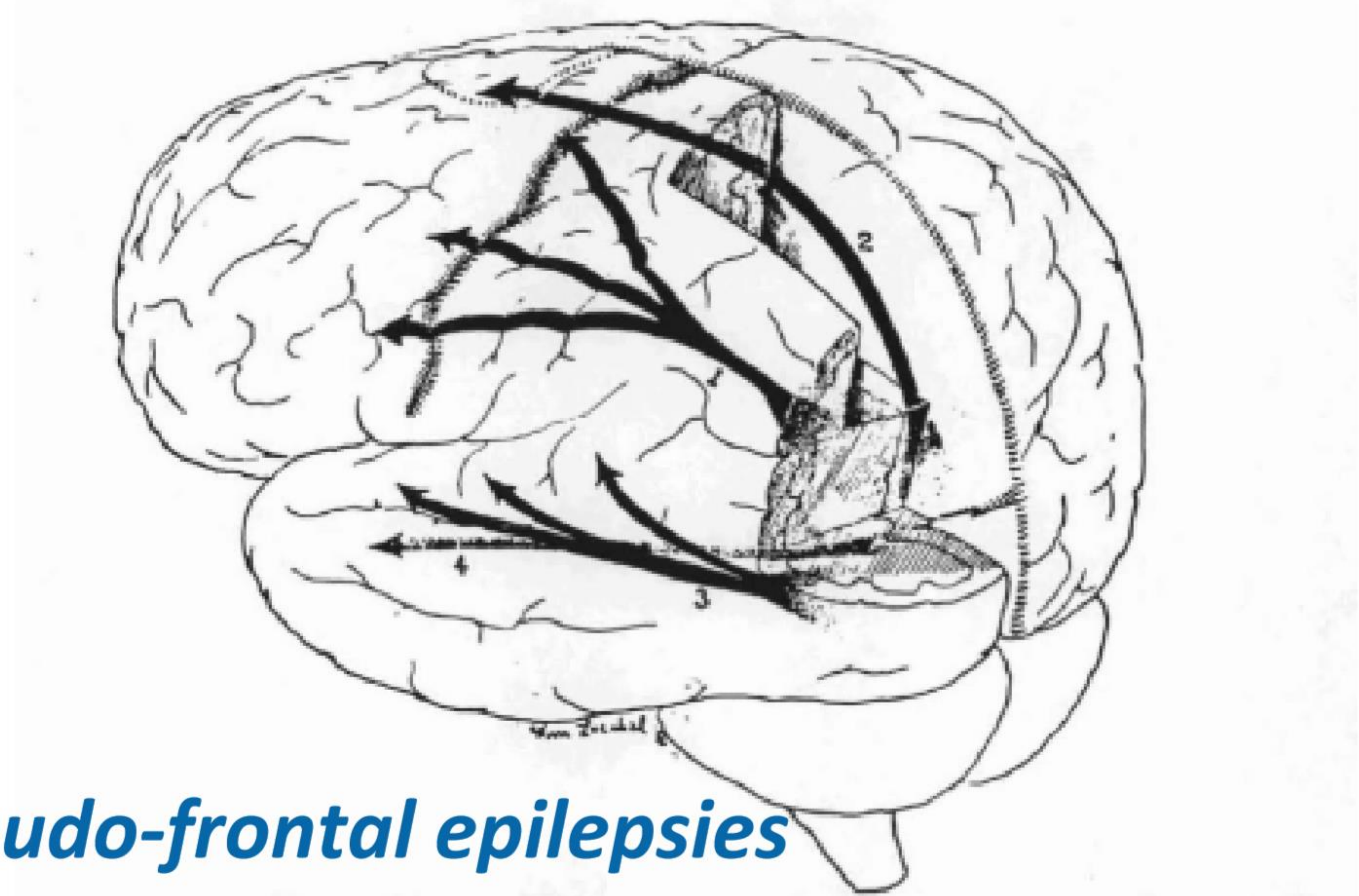
Even complex motor semiologies showed correlation with **cortical organization**

Elementary motor signs

Proximal movements “unnaturalistic” Pattern +/- tonic signs

Complex “naturalistic” pattern Distal movements, emotion

Parietal lobe epilepsy: “*frontal pattern*”



pseudo-frontal epilepsies

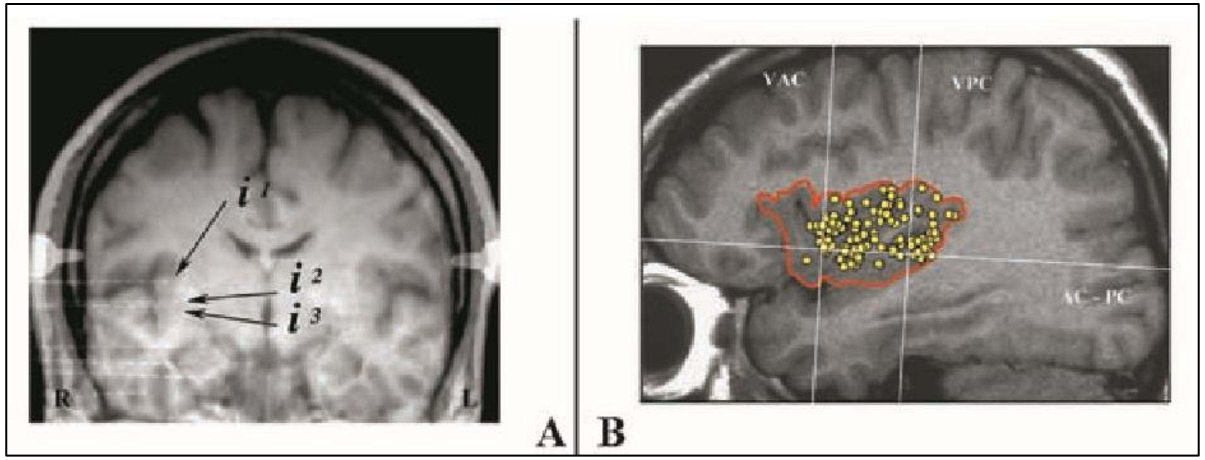
Patterns of spread from occipital lobe seizure origin. (From Ajmone-Marsan and Ralston, 1957, with permission.)

Epilepsia, **45**(9):1079–1090, 2004
Blackwell Publishing, Inc.

Clinical Manifestations of Insular Lobe Seizures: A Stereo-electroencephalographic Study

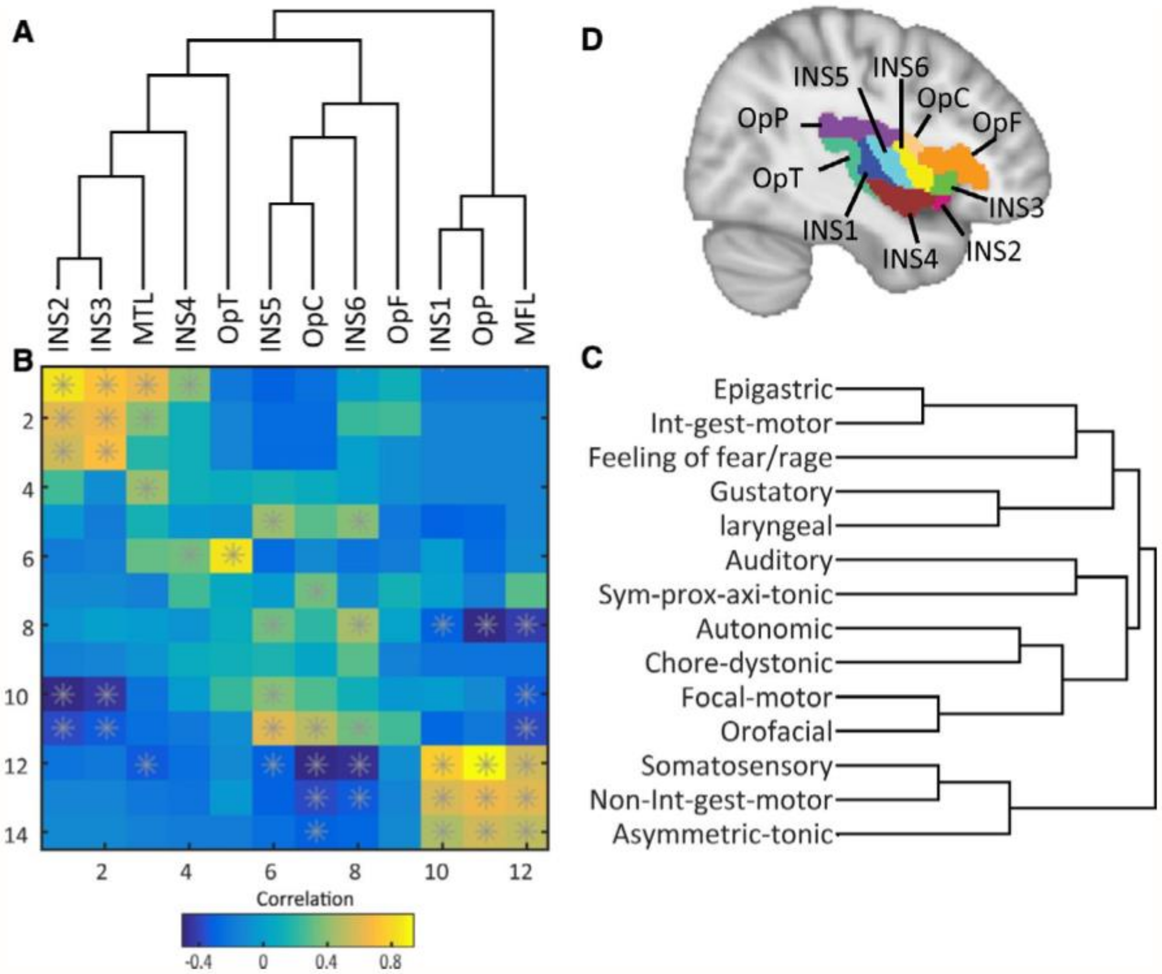
*Jean Isnard, †Marc Guénot, †Marc Sindou, and *François Mauguière

**Functional Neurology and Epileptology Department and †Functional Neurosurgery Department, Neurological Hospital, Lyon, France*



This ictal sequence occurred in full consciousness, beginning with a sensation of **laryngeal constriction**
Laryngeal discomfort or throat tightening associated with **unpleasant paresthesias or sensations of warmth affecting the perioral region** or large somatic territories, followed by **focal somatomotor** manifestations

Semiologic subgroups based on insular connectional **architecture** rather than gyral anatomy



EPILEPSIA APRIL 2020

DOI: 10.1111/epi.16501

Semiologic subgroups of insulo-opercular seizures based on connectional architecture atlas

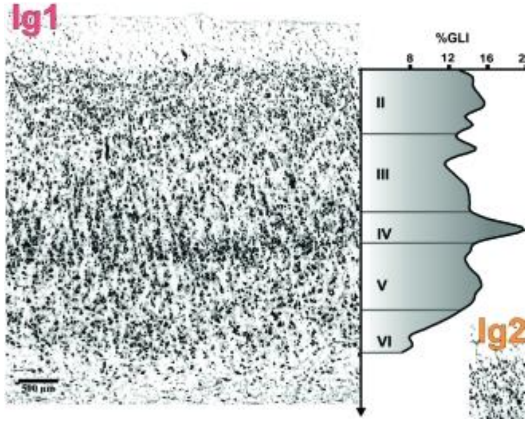
Haixiang Wang[1], Aileen McGonigal[2,3], Kai Zhang[4], Qiang Guo[5], Bingqing Zhang[1], Xiu Wang[5], Xiao Wang[6], Jiuluan Lin[1], Xiancheng Song[1], Qian Feng[1], Siyu Wang[1], Mengyang Wang[6], Xiaoqiu Shao[7], Xiaoyan Liu[8], Liang Wang[9,10], Wenjing Zhou[1]

<u>Methods</u>: Retrospectively collected a large series of 37 patients with insuloopercular seizures explored by SEEG

<u>Result:</u>

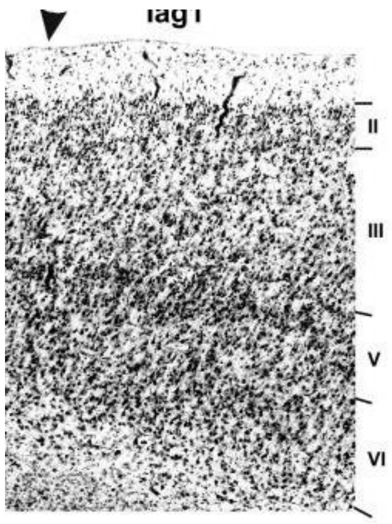
- Group 1 -epigastric sensation and/or integrated gestural motor behaviors with or without feelings of fear or rage
- Group 2 - auditory sensations and symmetric proximal/axial tonic signs
- Group 3 were orofacial and laryngeal signs
- Group 4 were somatosensory signs followed by nonintegrated gestural motor behaviors and/or asymmetric tonic signs

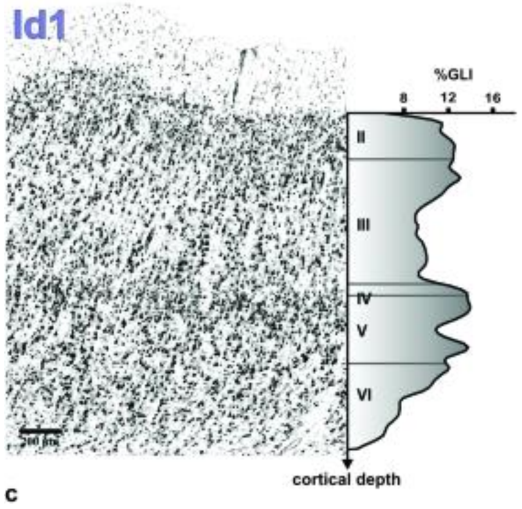
Insula connections based on probable cytoarchtectural areas



Granular insula, well developed layer IV

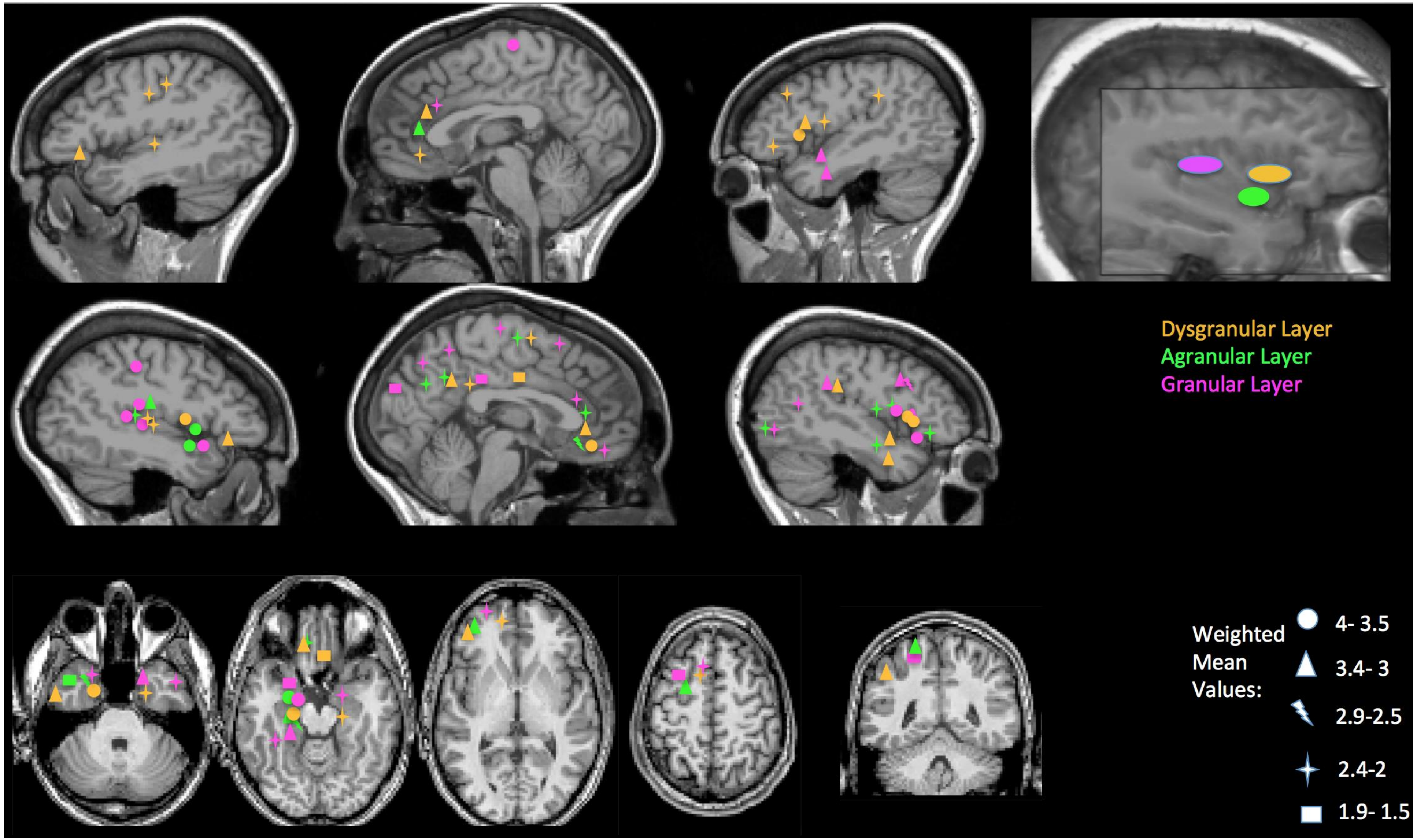
Agranular insula, loss of layer IV



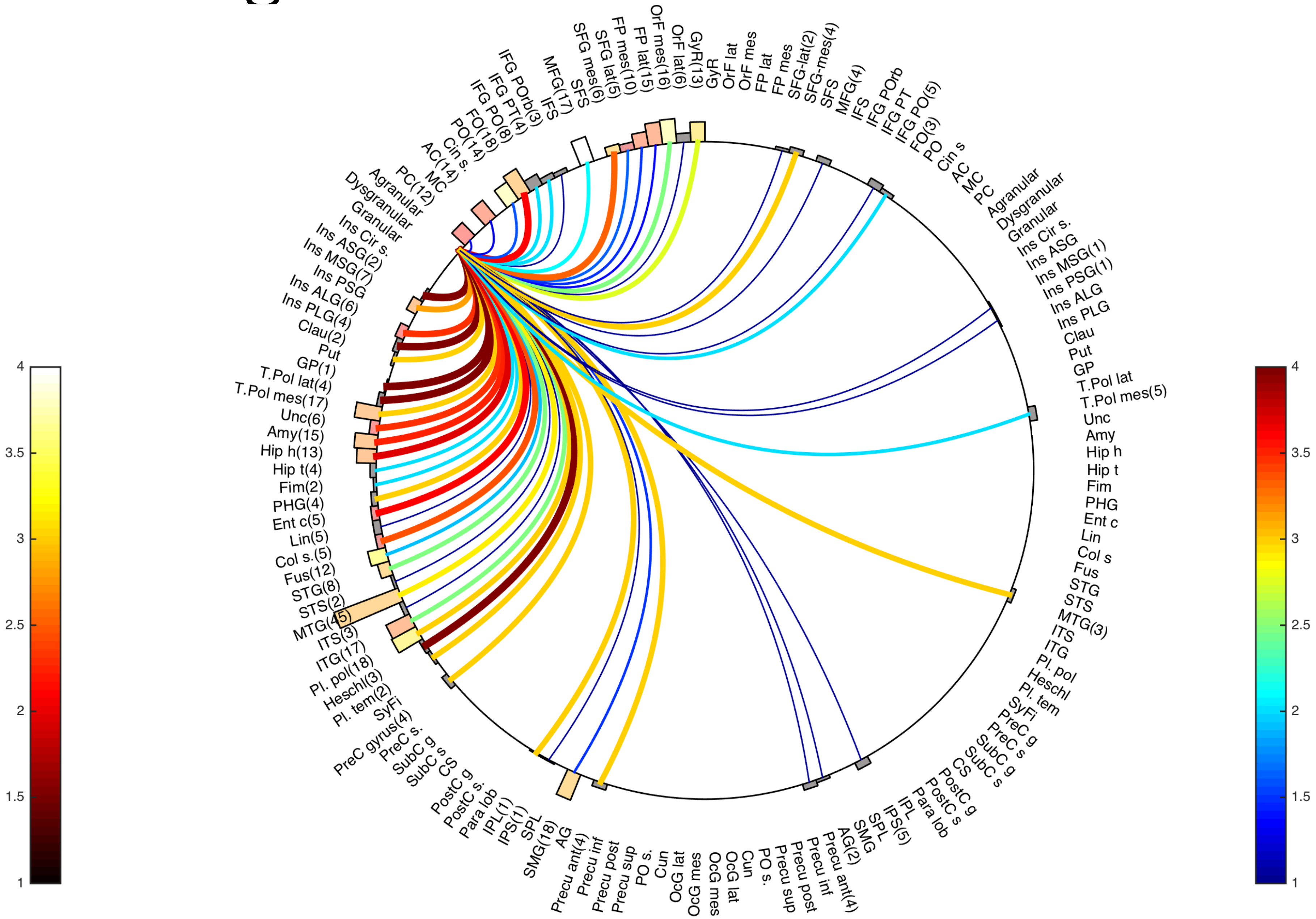


Dysgranular insula, disorganized layer IV

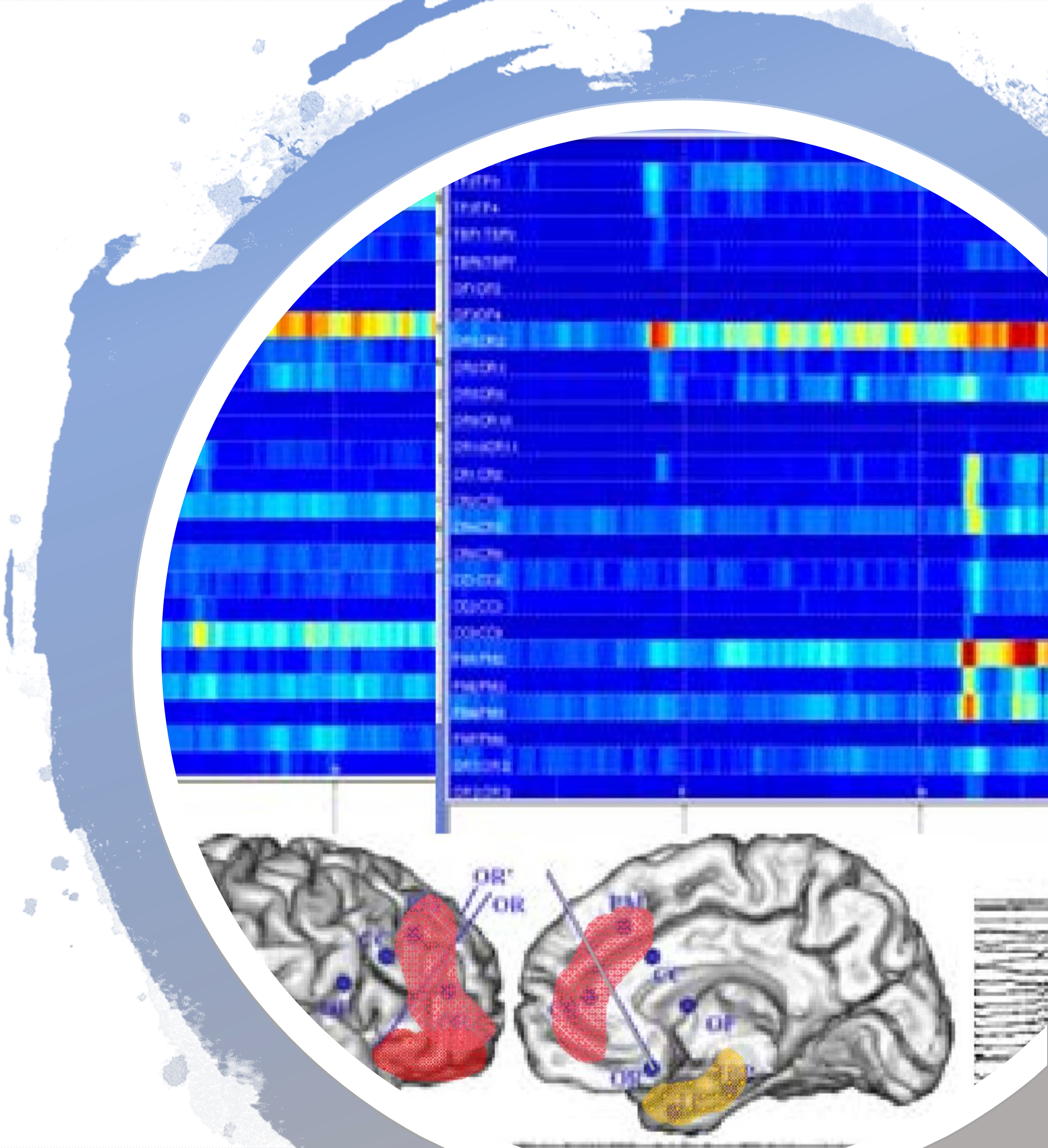
Cytoarchitecture and Probabilistic Maps of the Human Posterior Insular Cortex
Florian Kurth,1,2 Simon B. Eickhoff,14 Axel Schleicher,1 Lars Hoemke,2 Karl Zilles,13 and Katrin Amunts24


Dysgranular Layer
Agranular Layer
Granular Layer
Weighted Mean Values:
4- 3.5
3.4- 3
2.9-2.5
2.4-2
1.9- 1.5

Left Agranular



Correlating semiology with SEEG signal analysis: connectivity



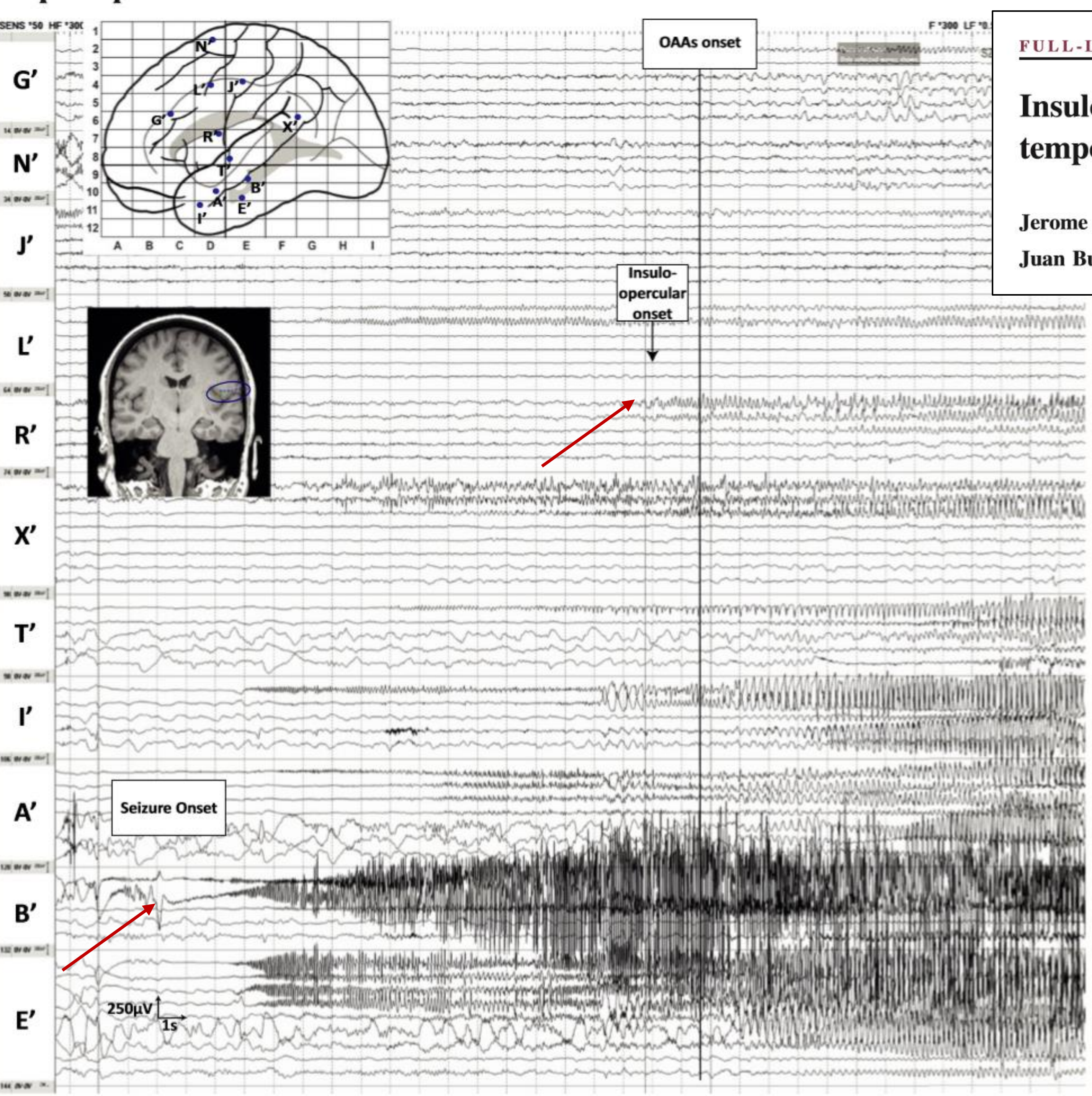
Semiology and Epileptic Networks

Aileen McGonigal, MD, PhD[a,b]

Table 2
Examples of studies examining semiology in conjunction with signal analysis of stereoelectroencephalography

Investigators, Year	Semiological Pattern	Epilepsy Localization	Main Anatomic Structures	Signal Analysis	Change in Network Synchrony
Bartolomei et al,[51] 2002	Humming	Temporal lobe	STG, prefrontal cortex	Rhythmic discharge over STG (6 or 15 Hz). Increased coherence between STG and prefrontal cortex	Increased
Bartolomei et al,[52] 2005	Fear behavior	Prefrontal cortex	Ventromesial orbitofrontal cortex, anterior cingulate, amygdala (limbic system)	Sudden loss of synchrony between orbitofrontal cortex and amygdala at seizure onset/clinical onset	Decreased
Arthuis et al,[53] 2009	Impaired consciousness	Temporal lobe	Temporal structures, parietal lobe, thalamus	Excessive synchrony; ie, functional coupling, between temporal and extratemporal structures, notably parietal cortex and thalamus	Increased
Bartolomei et al,[54] 2012	Déjà vu	Mesial temporal lobe	Rhinal cortices, hippocampus	Increased high-frequency EEG signal correlation between mesial temporal structures in seizures producing déjà vu	Increased
Lambert et al,[55] 2012	Impaired consciousness	Parietal lobe	Superior and inferior parietal lobules, precuneus, parietal operculum, supplementary motor area	Increased synchrony was associated with progressively greater degrees of altered responsiveness. A statistically significant nonlinear relationship was found between h2 values and degree of alteration of consciousness, suggesting a threshold effect	Increased
Aupy et al,[56] 2018	Oroalimentary automatisms	Temporal lobe	Medial basal temporal lobe, opercular cortex	Increased coherence occurred between mediobasal temporal structures and insulo-opercular cortex before onset of rhythmic chewing movements	Increased

Neurosurg Clin N Am 31 (2020) 373–385



FULL-LENGTH ORIGINAL RESEARCH

Epilepsia

Insulo-opercular cortex generates oroalimentary automatisms in temporal seizures

Jerome Aupy[1,2,3] | Ika Noviawaty[1,4] | Balu Krishnan[1] | Piradee Suwankpakdee[1,5] | Juan Bulacio[1] | Jorge Gonzalez-Martinez[1] | Imad Najm[1] | Patrick Chauvel[1]

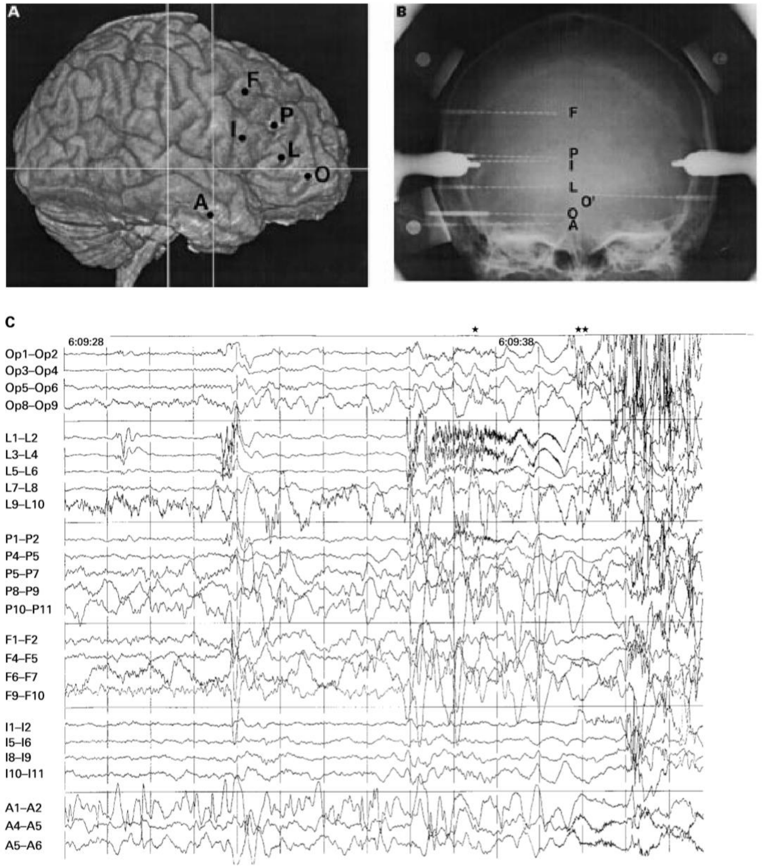
- In seizures with medial temporal onset, oroalimentary automatism occurrence depends on ictal discharge propagation to ***operculo-insular areas***
- Rhythmically synchronized activity at ***theta frequency*** between amygdala-hippocampus and operculo-insular cortex underlies the emergence of oroalimentary automatisms in temporal seizures

Analyze semiology in order
Early signs more reliable

J Neurol Neurosurg Psychiatry 2001;**70**:186–191

Fear as the main feature of epileptic seizures

A Biraben, D Taussig, P Thomas, C Even, J P Vignal, J M Scarabin, P Chauvel

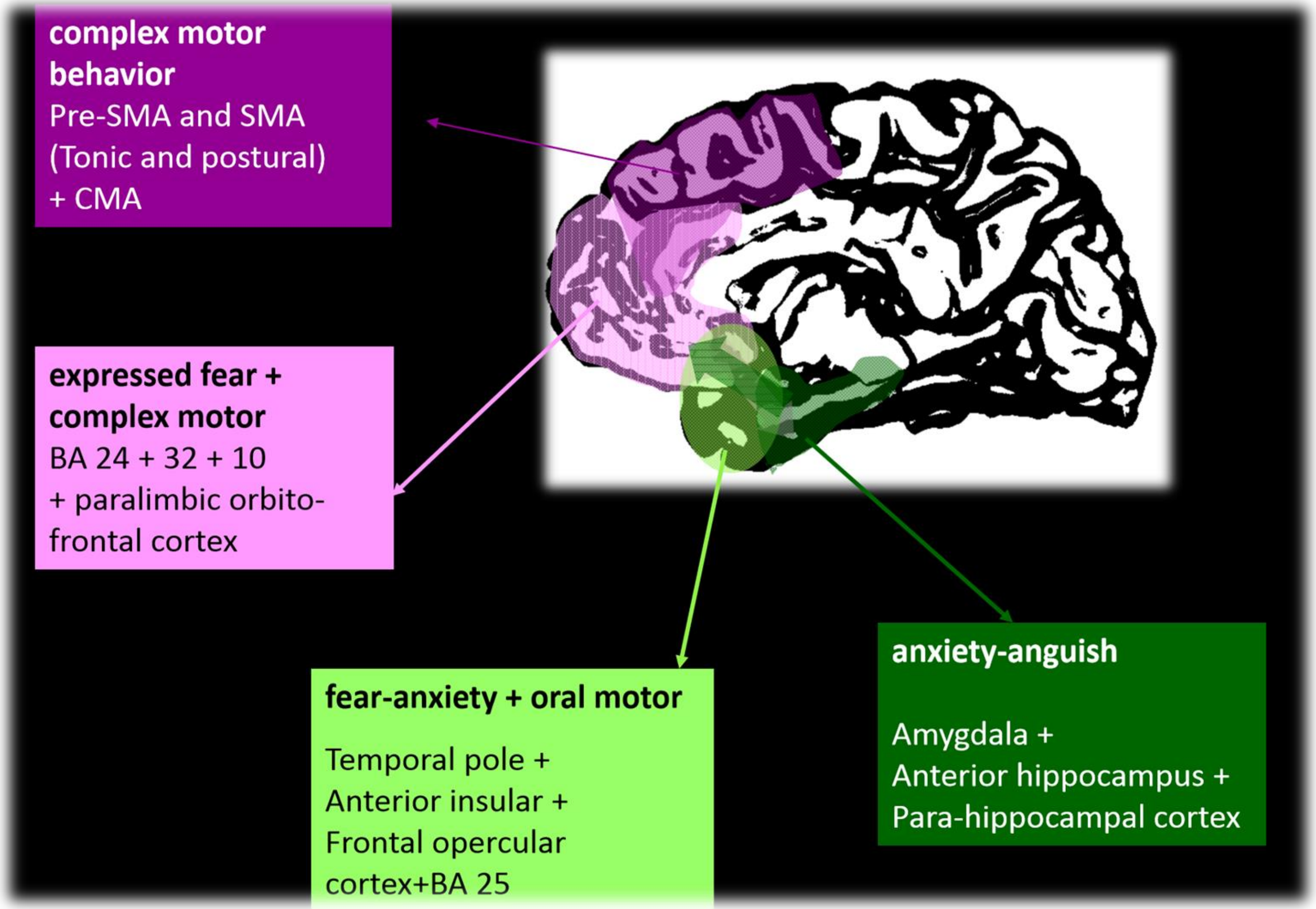


This limbic network involve
- Orbitoprefrontal
- Anterior cingulate
- Temporal limbic cortices

Biraben et al, 2001

Look for the clue of exactly localization

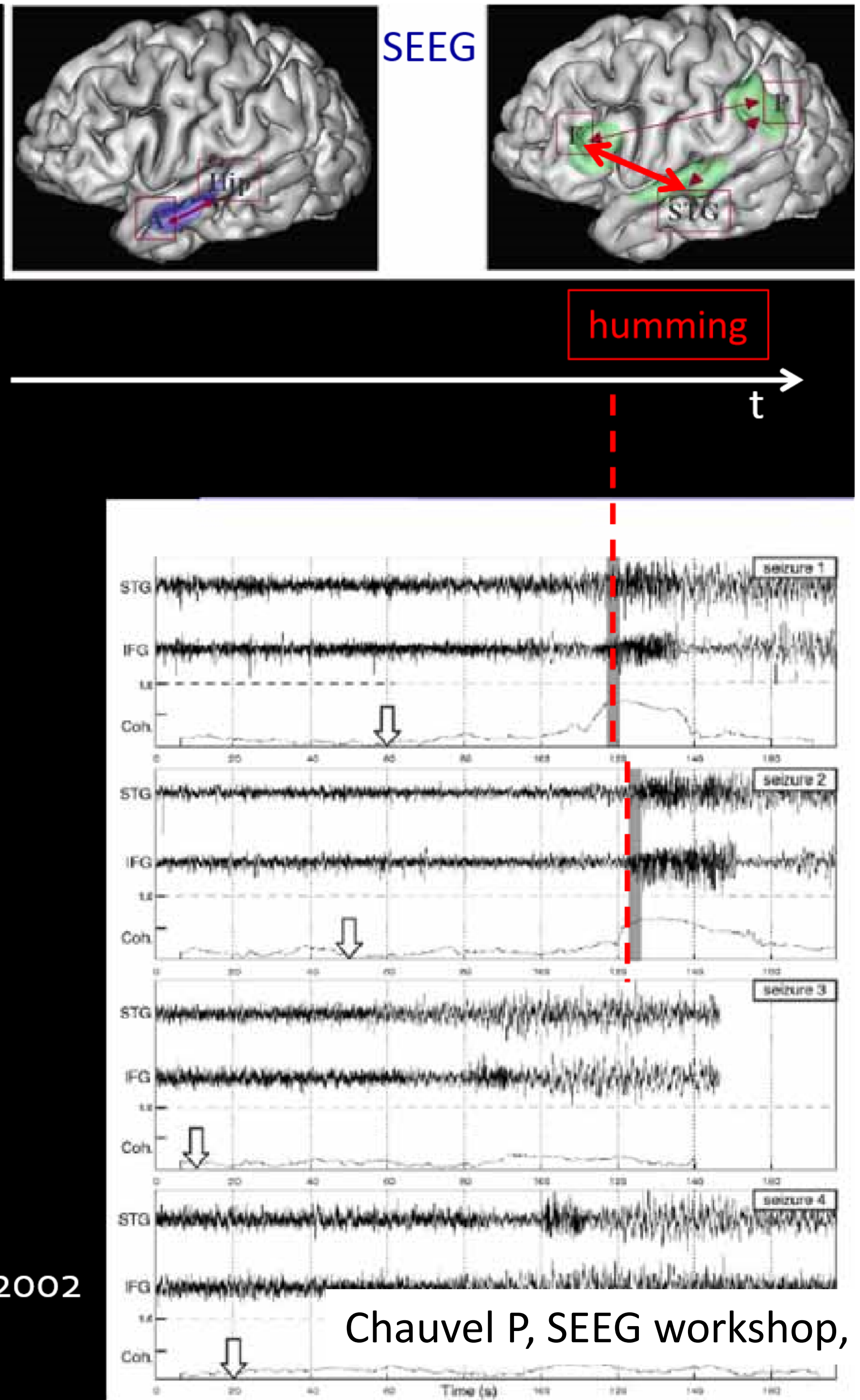
- The ictal *motor* behavior appears as an *integrated* feature within an emotional context



Chauvel P, SEEG workshop, Cleveland clinic

Ictal Humming

- MTLS onset
- Arising with spread of theta discharge
- Through a STG-IFG network activation

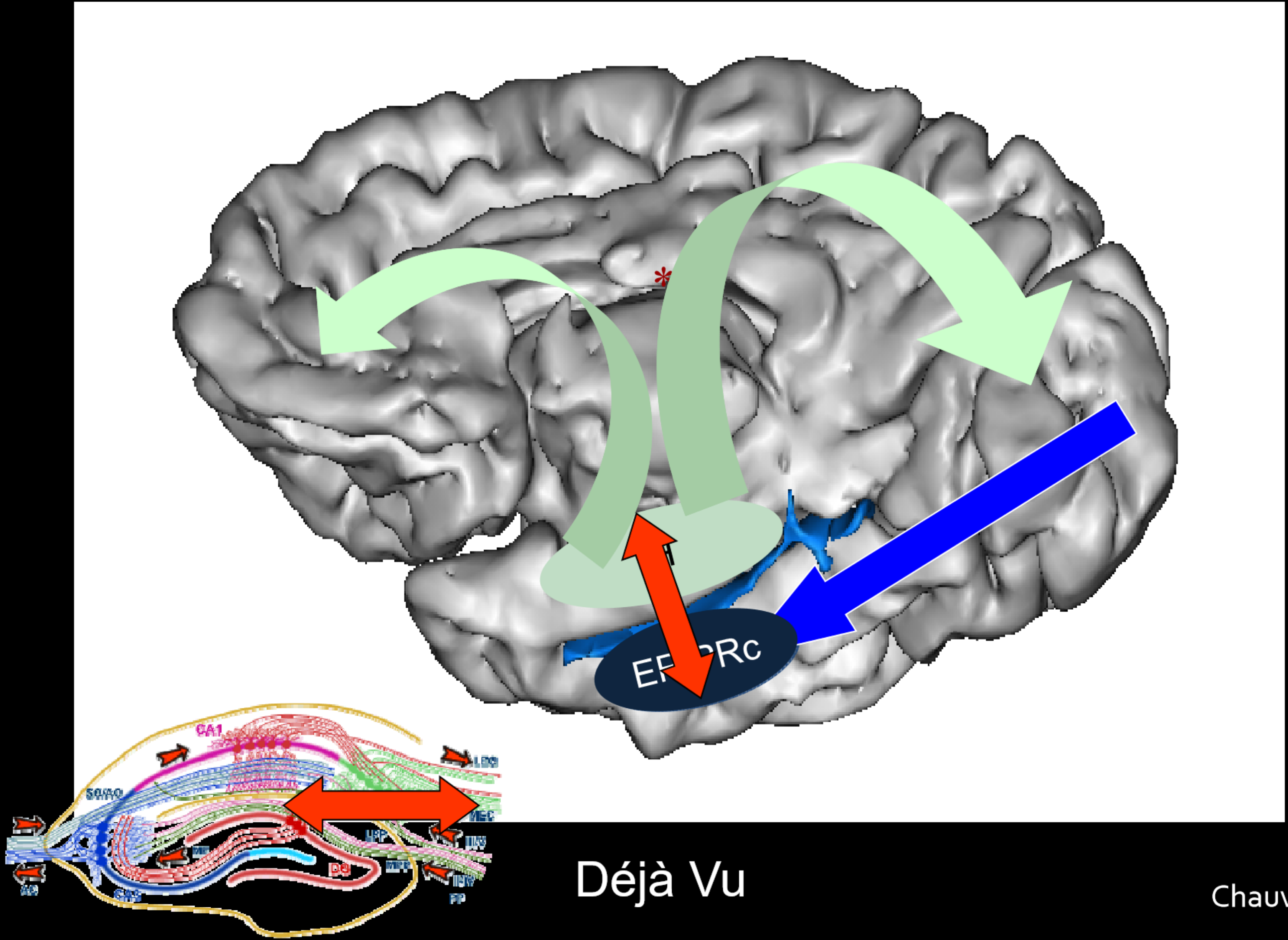


Bartolomei et al., 2002
Guedj et al., 2006

Chauvel P, SEEG workshop, Cleveland clinic

1- Ventral stream synchronizes with hippocampus

2- ER ***shifts*** the mode of cerebral processing from one of identifying external stimuli to one of ***retrieving*** internal representations

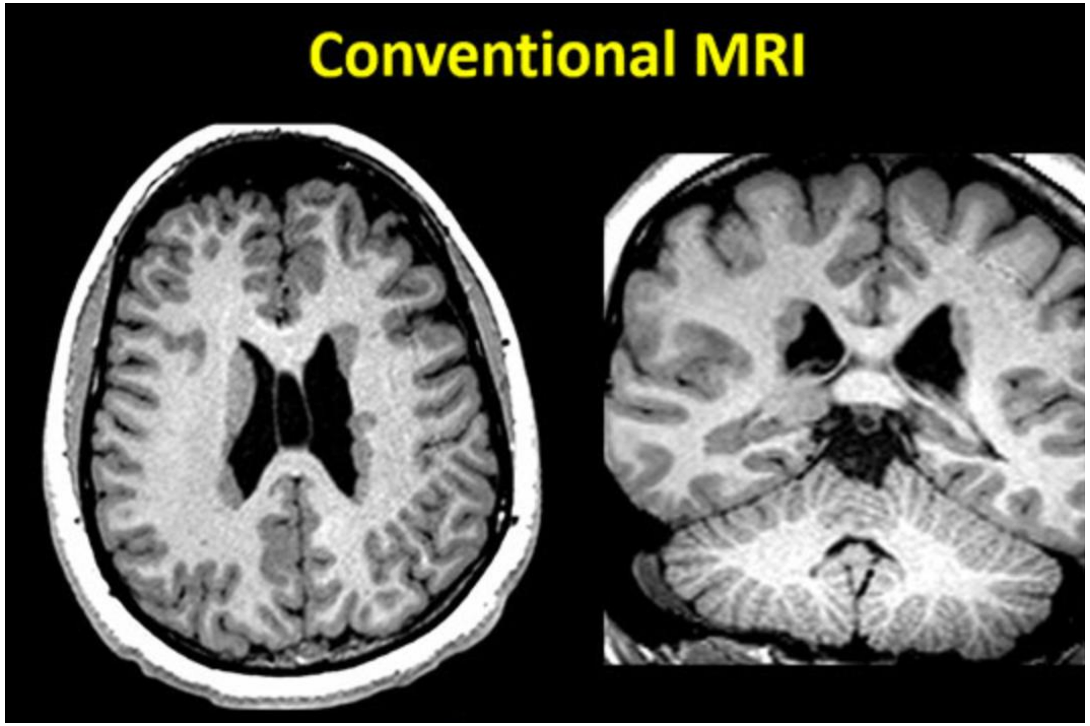


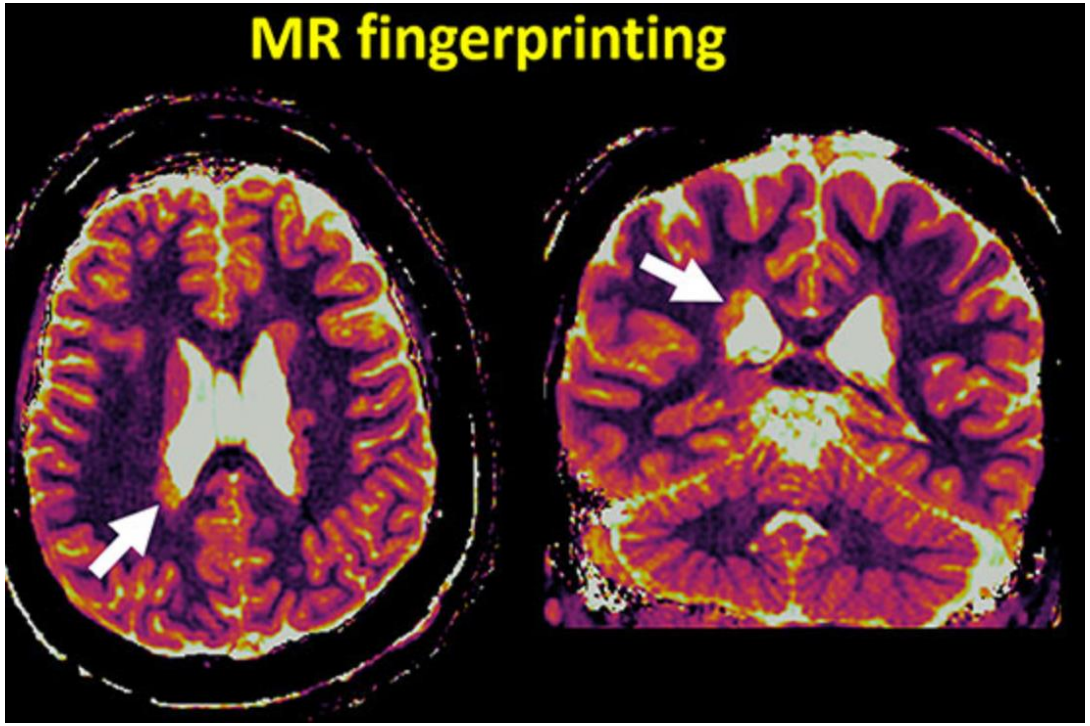
Déjà Vu

Chauvel, 2014

Future direction of Epilepsy surgery

- Maximize the yield of current methods (Multimodality integration)
- Imaging of “Epileptic lesion”





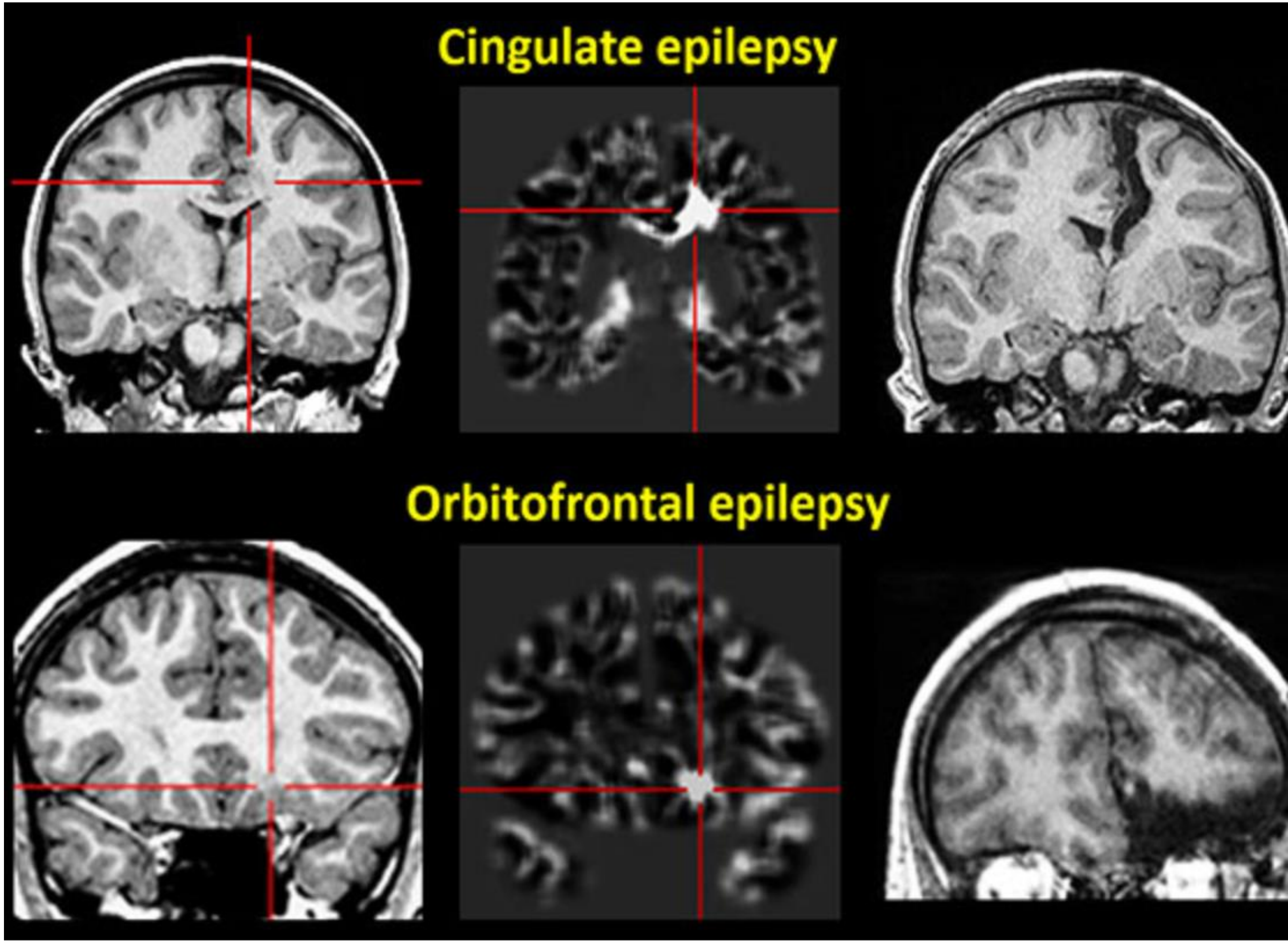
MR fingerprinting (MRF): New results with novel technique for quantitative MRI

- T1 maps from the 3D MRF scan in axial and coronal views showing the nodules at the occipital horn of the right lateral ventricle (arrows) representing significantly higher T1 values, differentiating themselves from the other nodules.
- **The nodules with the higher T1 values were later confirmed to have caused the epilepsy in this patient, who is now seizure-free after resection.**

Dr. Wang and colleagues, AES 2018

Post-processing Voxel-based morphometry (VBM)

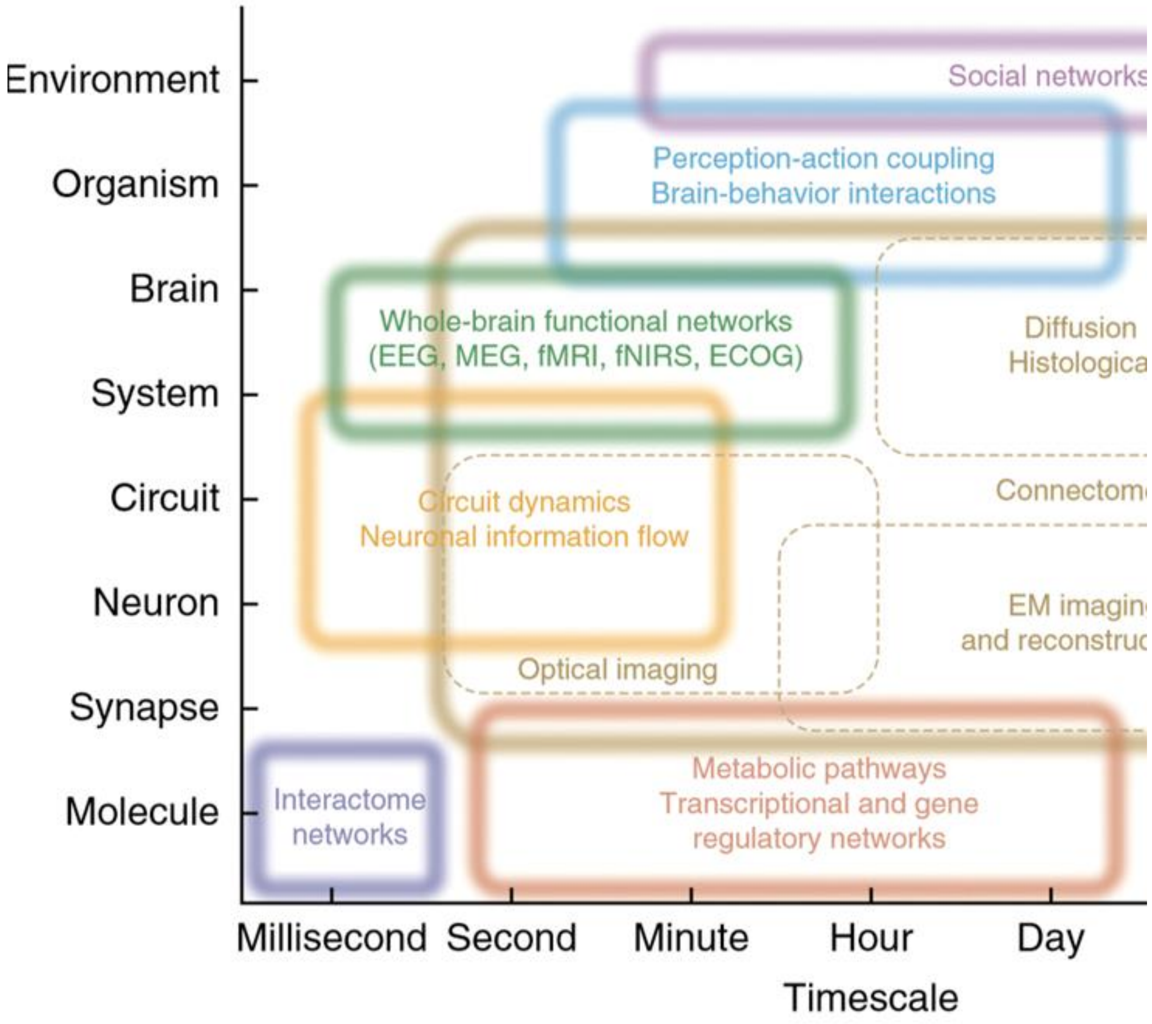
Next frontier:
MRF + post-processing
Discover epileptic lesion??



Conventional MRI T1-image   VBM   Post surgery Sz-free

Future direction of Epilepsy surgery

- Surgery of genetic epilepsy
- Post surgical preventive therapies (target based gene therapy)



nature neuroscience, March 2017

Thank you