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complex diseases
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Epilepsies (ERN EpiCARE)

Bambino Gesù
OSPEDALE PEDIATRICO



Manifestazioni ed EEG nel bambino

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CORSO VIDEO EEG LICE
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Outline

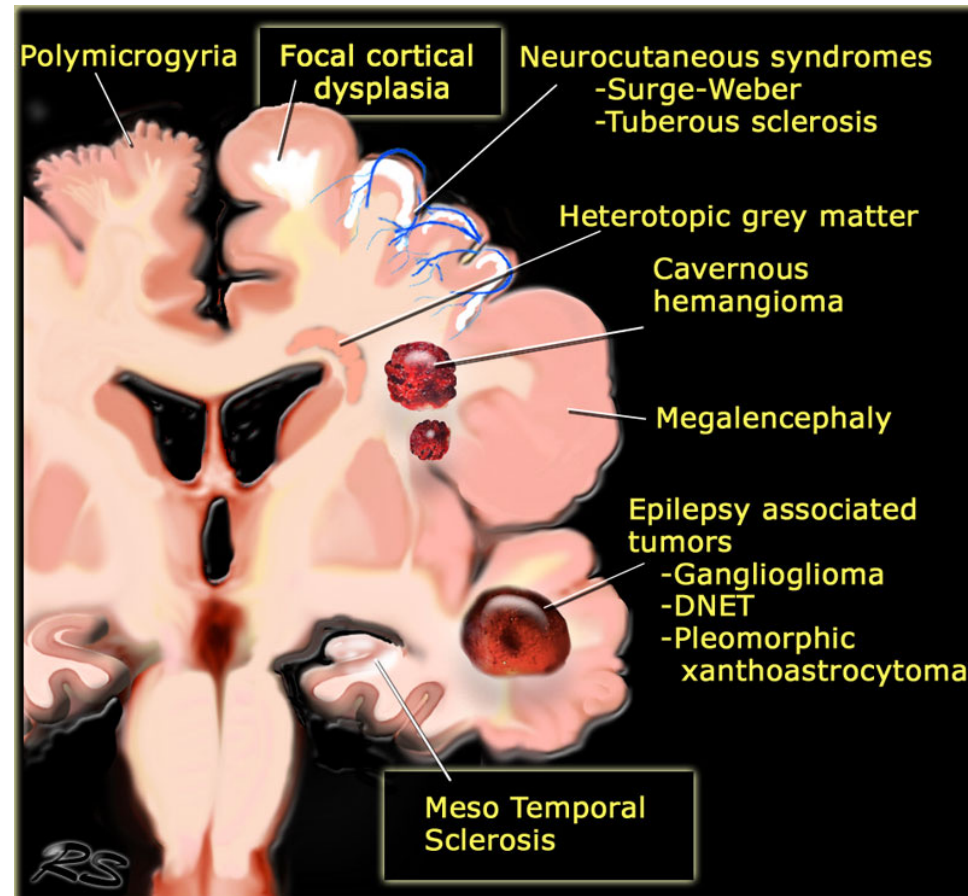
- Introduction
- Seizure semiology and EEG features
- Lateral and mesial
- Definition of elementary motor signs and gestural motor behavior
- Differential diagnosis
- Examples
- Conclusions

Introduction

- Frontal seizures might be difficult to classify
- Several eloquent areas
- Multiple connections with distant brain areas
- Differences if the involved areas is lateral or mesial, anterior/posterior
- Differential diagnosis with non-epileptic events

Etiologies

- Brain tumors
- Focal cortical dysplasia
- Vascular malformation
- Genetic causes
- Other
 - Gliosis (head trauma)
 - Post-inflammatory scars
 - Birth trauma



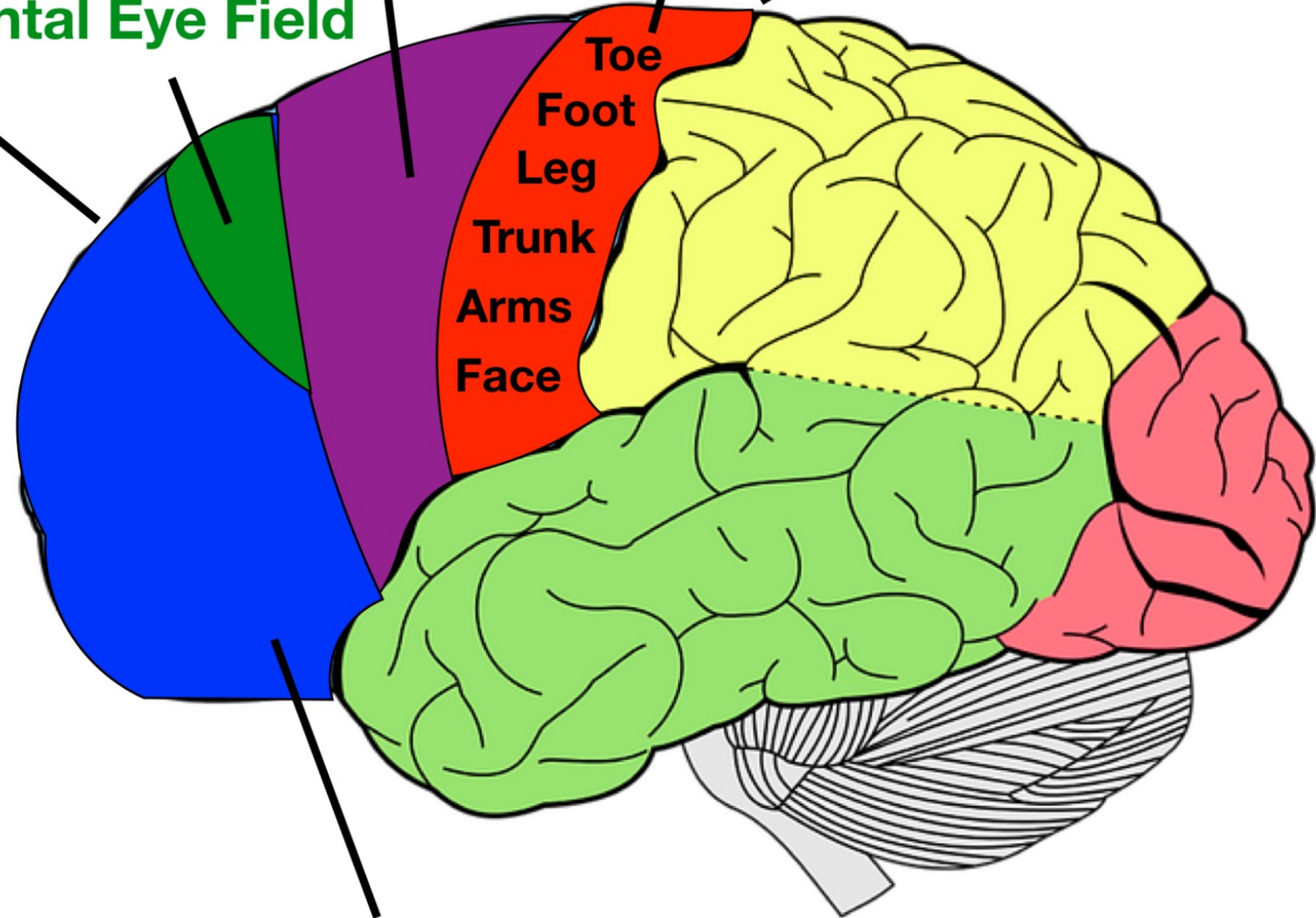
Frontal

Premotor/Supplementary Motor Cortex
Primary Motor Cortex
Central Sulcus

Frontal Eye Field

Toe
Foot
Leg
Trunk
Arms
Face

Prefrontal Cortex



Functional Areas

- **Primary Motor Cortex**
 - Voluntary Muscle Mvt.
- **Premotor/S.M.C (MAC)**
 - Planning/Coordination of Movement
- **Frontal Eye Field**
 - Voluntary Rapid Eye Mvt.
- **Prefrontal Cortex**
 - Executive Functions, Behavior, Personality

EEG features

Dorso-lateral

- Frequently bilateral abnormalities
- Multilobar
- Generalized
- Focal cortical spreading
- Muscle artifact
- Repetitive epileptiform activity

Mesial Frontal

- Inaccessibility of mesial frontal/orbitofrontal
- Rapid propagation
- Non-lateralizing epileptiform activity
- Focal interictal spikes midline/slowing
- Bilateral asynchronous discharges
- Paroxysmal fast activity/electrodecremental



Frequency and lateralizing value of some seizures symptoms and signs in lateral frontal lobe epilepsy

Symptom	Frequency in patients with lateral FLE	Lateralizing value (positive predictive value)
Postictal headache	41–53%	None (in contrast to temporal lobe epilepsy)
Unilateral tonic posturing	37–48%	Contralateral (67–100%)
Vocalization	37–77%	Probably none (contradictory data)
Postictal paresis	27–37%	Contralateral (100%)
Unilateral clonic seizure	23–37%	Contralateral (83–100%)
Head-version	22–60%	Contralateral (66–100%)
Complete loss of consciousness	19%	Nondominant
Focal somato-sensory auras	16–31%	Contralateral (100%)
Unilateral automatisms	16%	Ipsilateral (67%)
Hypermotor seizures	11–38%	None
Nonforced head-turning	11–31%	None
Postictal nose rubbing	10–37%	None
Unilateral dystonic posturing	0–21%	Contralateral (100%)

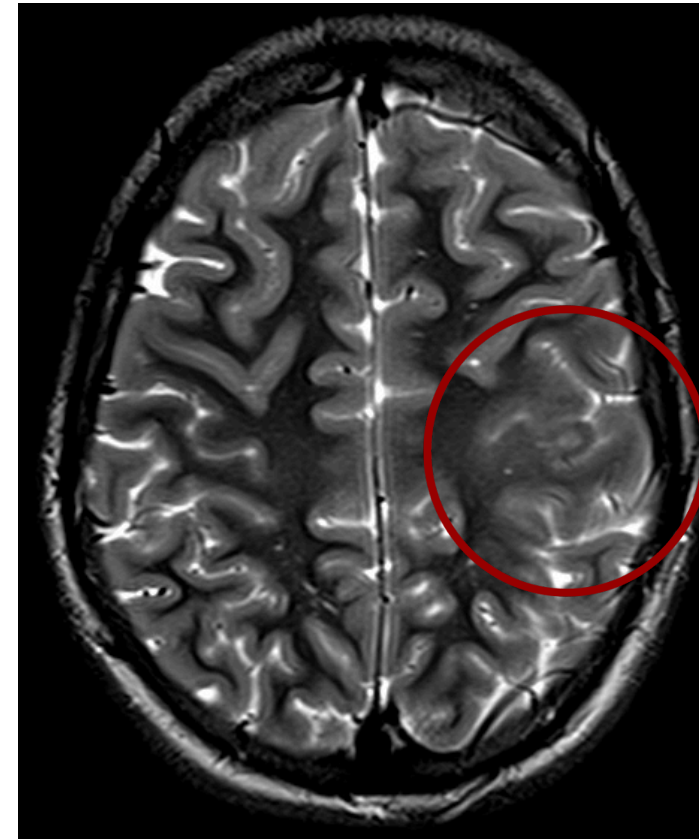
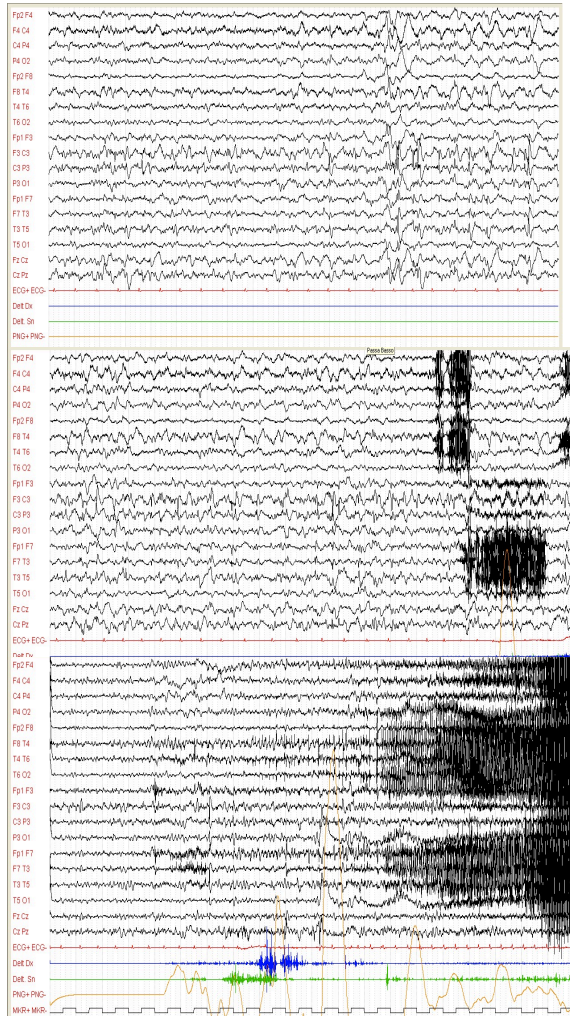
Luders, 2010

General features

- High seizure frequency (clusters and SE)
- Short duration
- Frequent bilateral tonic-clonic
- Post-ictal headache

In *children* with FLE, the immature cortex architecture might influence seizure semiology; the lack of automatisms and secondary generalization has been attributed to this feature

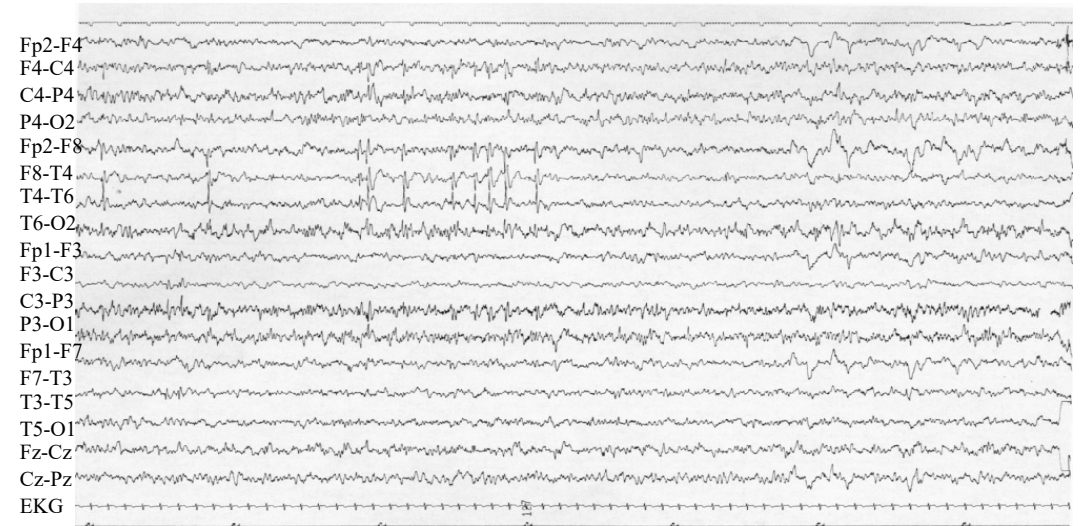
Seizures highly suggest the site: semeiology indicate the primary involvement of eloquent areas (1)



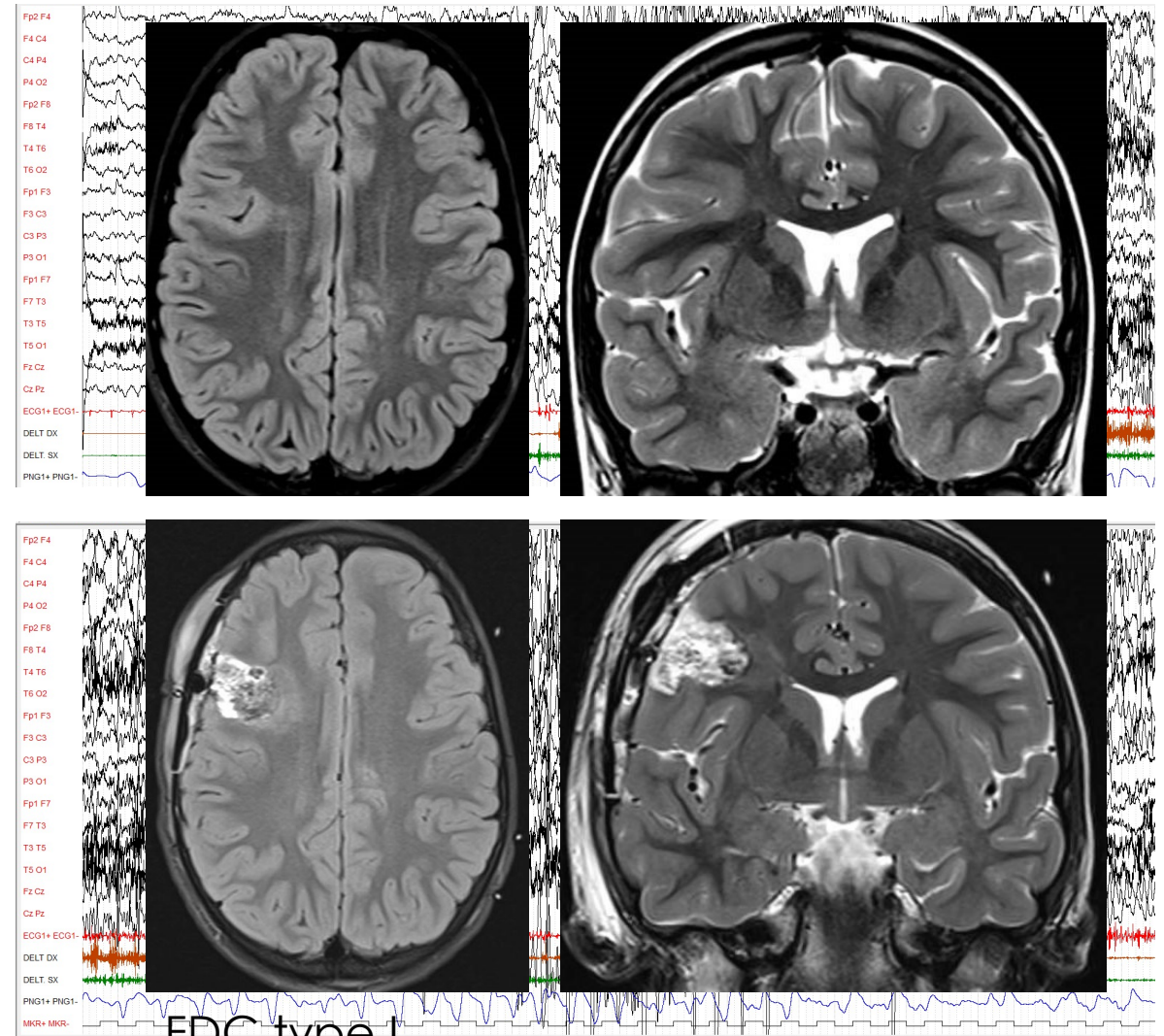
- We can indicate to the neuroradiologist where to search for



Seizures highly suggest the site: semeiology indicate the primary involvement of eloquent areas (2)



Seizures highly suggest the site: semeiology indicate the primary involvement of eloquent areas (3)



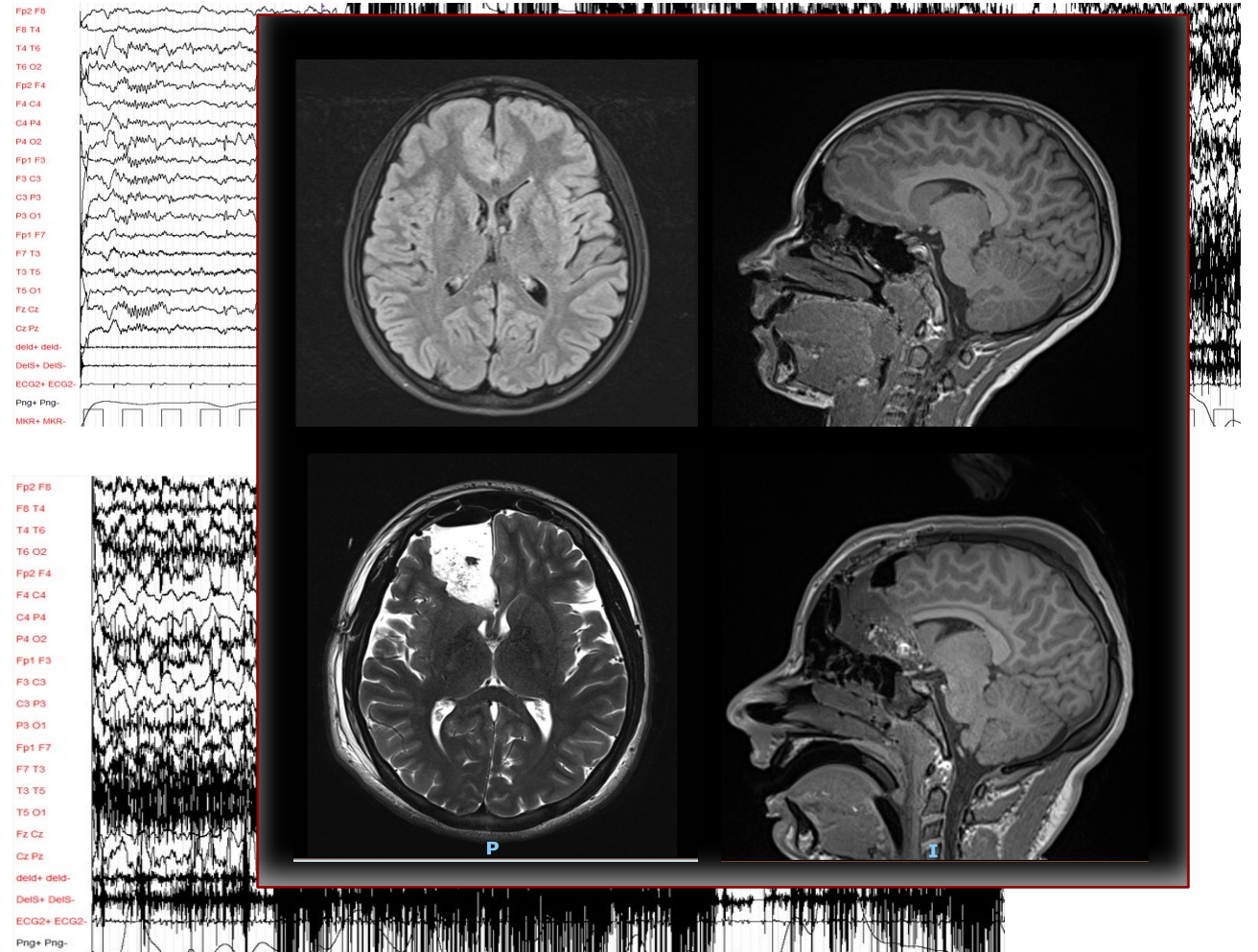
FDC type I

Seizure's symptoms and signs in mesial frontal lobe epilepsy

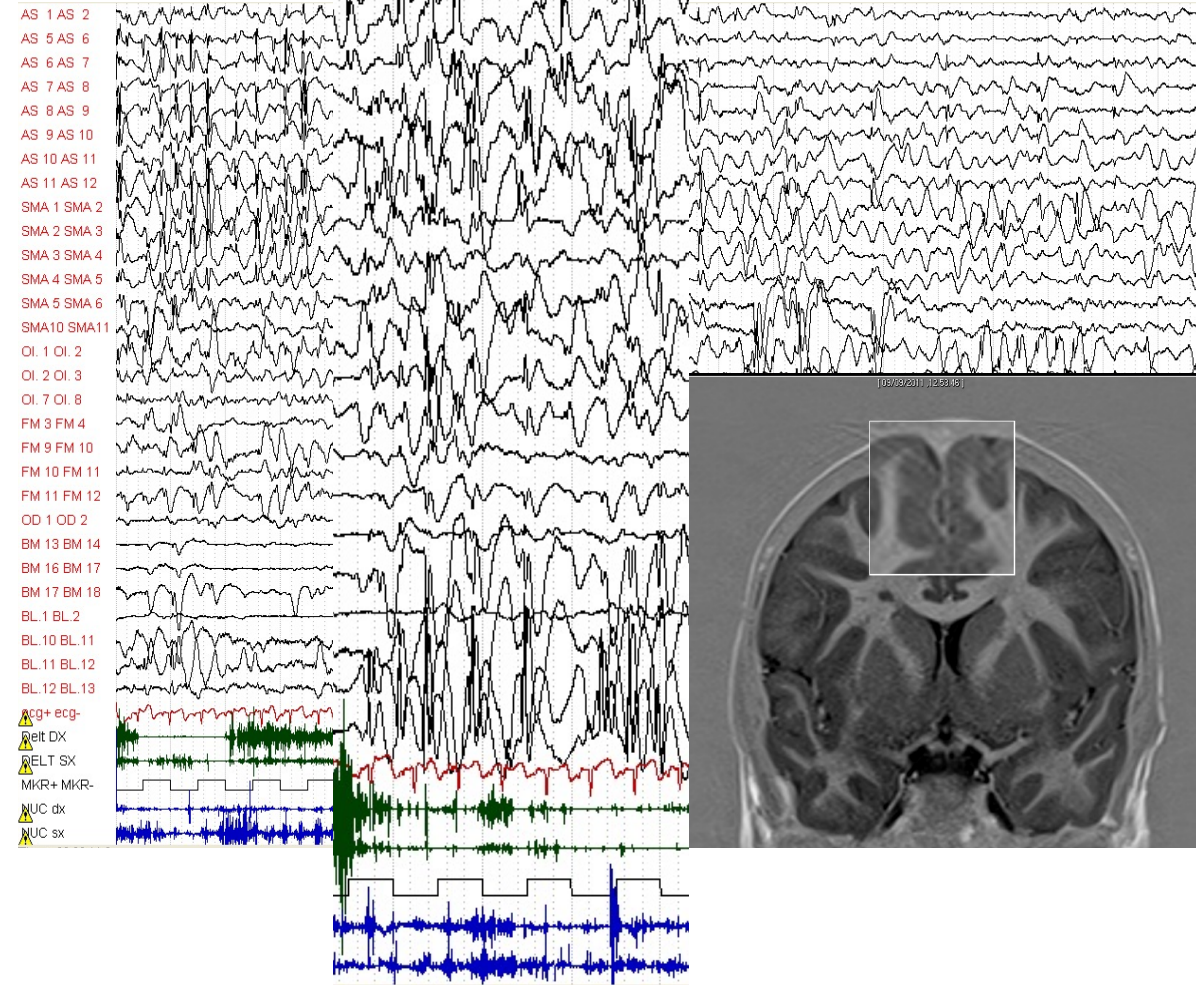
- Bilateral asymmetric tonic seizures
 - Abrupt onset of tonic posturing
 - 4 limbs might be involved
 - Incoordinate movements
 - Consciousness might be preserved
- Hypermotor seizures
- Frontal lobe absences
- Negative myoclonus

Bilateral asymmetric tonic seizures

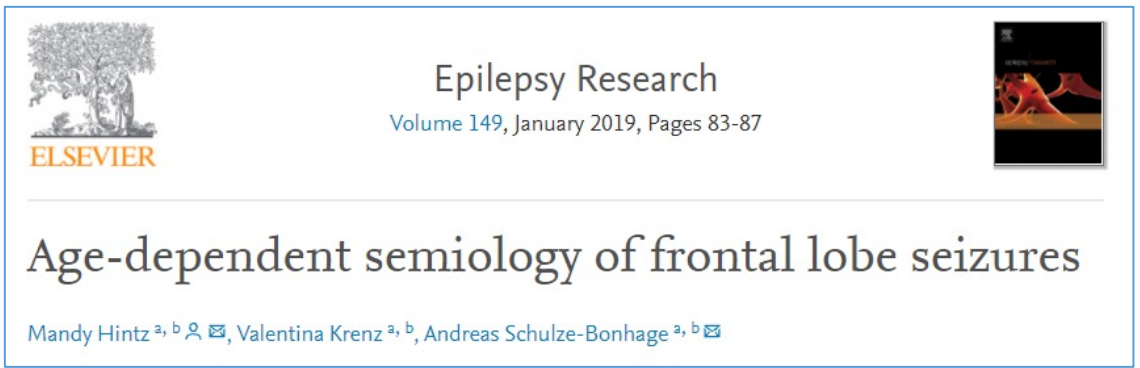
Hypermotor seizures (mesial pre-frontal)



Negative myoclonus in symptomatic focal seizures



➔ Few studies focused on pediatric semiology in FLE



122 patients, diagnosed with frontal lobe epilepsy
Onset of epilepsy ranged between 0 and 56 years

Myoclonic components as most frequent manifestations in children

Clonic features and hypermotor components without significant age-dependent changes

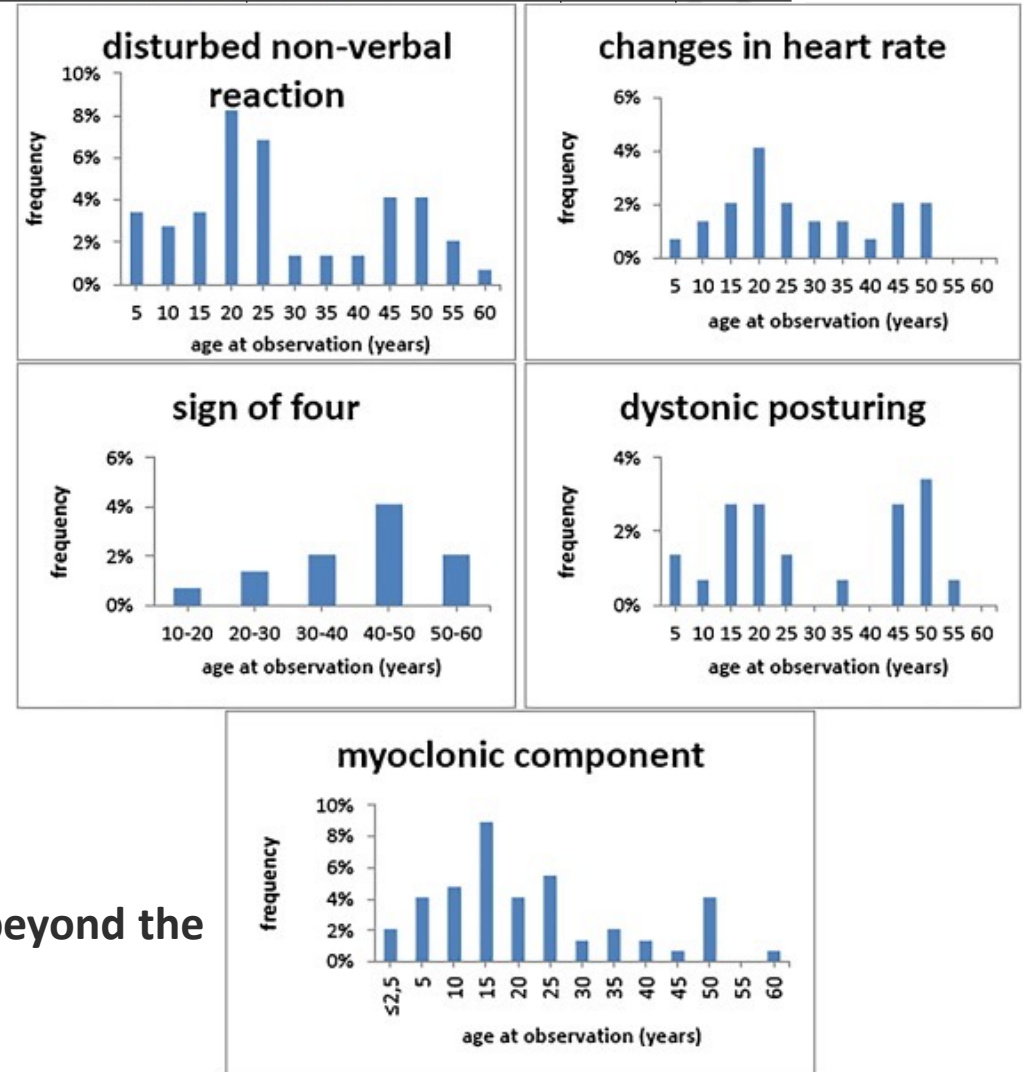
Absence of aura in patients under six years

During the first years of life:

- Signs as aura-like sensations probably underestimated due to limitations in interactions
- Verbal responsiveness less reliably assessable

Semiological signs as consequence of the connectivity within and beyond the frontal lobe and its maturation during life

etiology	n	%
focal cortical dysplasia	58	47.5
tuberous sclerosis	3	2.5
tumors	19	15.6
neurodevelopmental tumor	7	5.7
infection	3	2.5
posttraumatic	3	2.5
perinatal lesion	2	1.6
hemorrhage residual	2	1.6
cavernoma	2	1.6
focal cortical dysplasia or tumor	2	1.6
other	4	3.3
unknown	27	22.1
overall	122	100.0



A Detailed Analysis of Frontal Lobe Seizure Semiology in Children Younger Than 7 Years

*†András Fogarasi, *†József Janszky, *Eduardo Faveret, *Tom Pieper, and *Ingrid Tuxhorn

Epilepsia. 2012

14 patients with medically refractory FLE based on focal cortical dysplasia, aged 3-81 months (mean 30 months)

Frequent epileptic spasms and behavioural changes

Rare focal seizures with evolution in GTCs

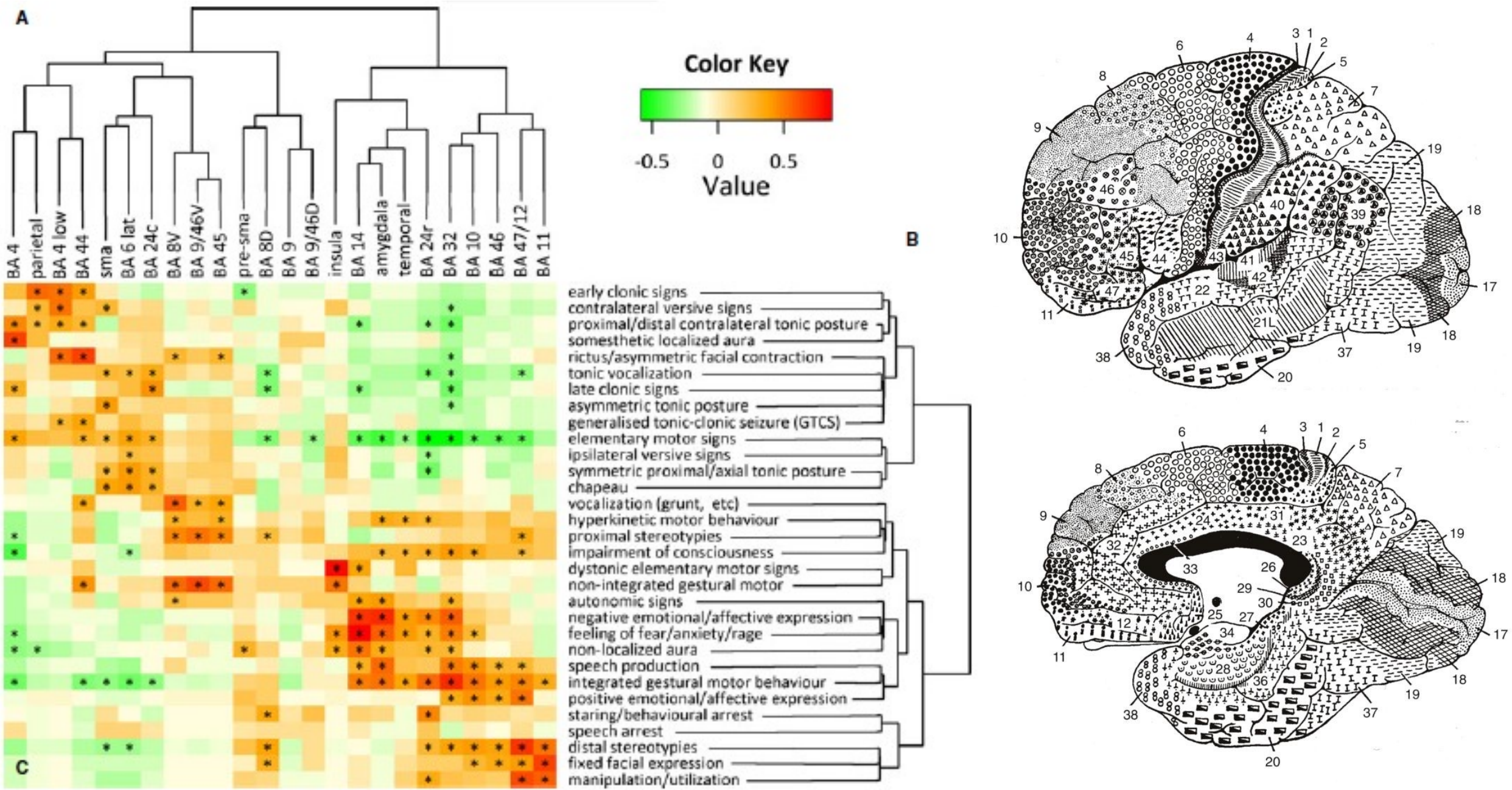
Absence of hypermotor seizures and motor automatisms

Seizure type	Frequency among patients	Frequency among seizure onsets
Tonic	9 (64%)	39 (35%)
Clonic	5 (36%)	27 (24%)
Epileptic spasm	5 (36%)	18 (16%)
Myoclonic	1 (7%)	7 (6%)
Psychomotor	2 (14%)	8 (7%)
Hypomotor	2 (14%)	6 (5%)
Unclassified motor	1 (7%)	4 (4%)
Isolated aura	1 (7%)	2 (2%)
Total	14 patients (100%) ^a	111 seizures (100%)

Patient no./sex	Age at epilepsy onset (mo)	Age at video recording (mo)	Daily seizure frequency	Localization by 1. MRI lesion 2. PET hypometabolism 3. EEG seizure pattern	Engel class	Duration of follow-up (mo)	Seizure onset and → evolution
1/F	1	3 and 14	4 series	1. R precentral 2. R precentral 3. R precentral	I A	29	a, clonic (started with BC) b, tonic
2/F	3	6	2-4	1. R frontomesial 2. Normal 3. R precentral	III A	38	a, ES b, hypomotor (started with BC)
3/F	1	10 and 14	5-30	1. R dorsolateral 3. R frontal	I A	24	Clonic → tonic → clonic
4/F	1	10 and 26	3-40 series	1. L precentral 2. L precentral 3. L precentral 3. R centroparietal	III A	35	a, clonic b, psychomotor
5/F	2	12 and 36	4-6 series	1. R frontomesial 2. R precentral 3. R frontocentroparietal	I A	16	a, tonic → ES b, tonic → psychomotor
6/M	1	13 and 18	5-15	1. L frontal 3. L frontomesial	I A	3	Tonic
7/M	11	19	10 series	1. R precentral 1. R occipital 2. R frontotemporooccipital 3. R precentral	I A	7	Myoclonic → tonic → myoclonic
8/M	7	23	2-4	1. L dorsolateral 2. L frontal 3. L frontocentrottemporal	I A	33	a, hypomotor (started with BC) b, unclassified motor
9/M	14	26 and 57	1-4 series	1. L frontomesial 2. Normal 3. L precentral	I A	26	ES
10/F	16	30	2-5 series	1. R frontopolar 3. R frontal	I A	36	ES (started with BC)
11/F	3	59	6-8 series	1. R frontomesial 3. R frontal 3. Generalized	I A	6	a, ES b, tonic
12/M	56	68	3-35	1. L frontomesial 2. L centroparietal 3. L frontomesial	I C	92	Tonic → clonic
13/F	2	68	6	1. R frontobasal 3. R frontal	I A	27	Tonic (started with BC)
14/M	35	81	2-4	1. R frontomesial 2. R precentral 3. R frontotemporal 3. R precentral	I A	38	a, clonic b, tonic → clonic c, isolated aura

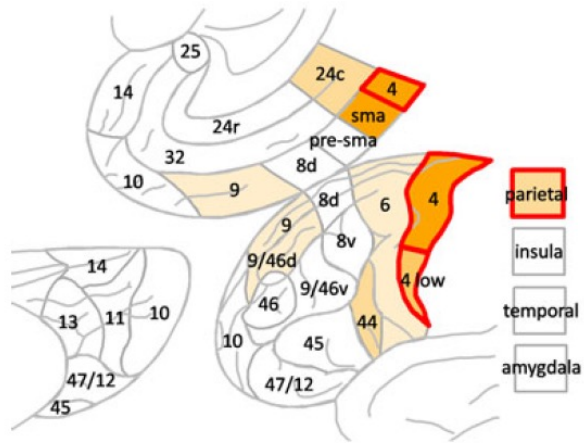
Definition of semiologic terms

- **Elementary motor signs:** clonic movements and tonic or dystonic contraction and/or posturing as well as head and/or eye version.
- **Gestural motor behavior:** the overall (quite heterogeneous) category of complex motor behaviors, readily distinguishable from elementary motor signs.
 - Stereotypies: excessive production of one type of motor act, necessarily resulting in repetition. Movements of trunk and limbs (proximal stereotypies), or of hands/feet (distal stereotypies);
 - Hyperkinetic movements: excessive amount of movement (hyperactivity) and/or excessive amplitude, speed, and acceleration.
 - Integrated gestural motor behavior: recognizable, ordered sequences of movement within the seizure (reaching, grasping, pedalling, kicking, tapping, rocking, or hitting). Facial appearance tended to be congruent with other ictal behavioral features
 - Non-integrated gestural motor behavior: disjointed or even anarchic appearance including facial expression.

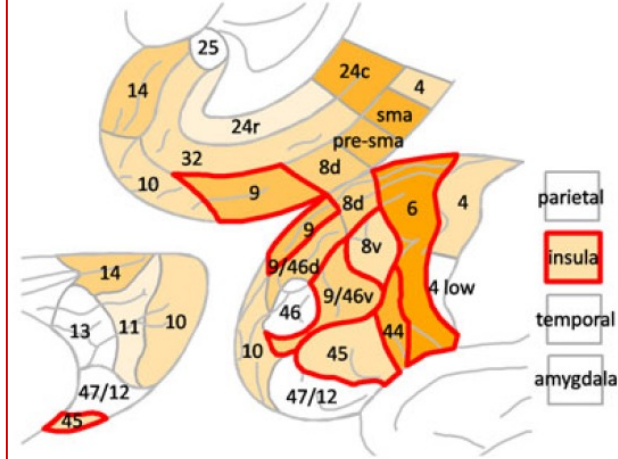


Bonini F, McGonigal A, Trébuchon A, Gavaret M, Bartolomei F, Giusiano B, Chauvel P. *Epilepsia*. 2014 Feb;55(2):264-77. doi: 10.1111/epi.12490. Epub 2013

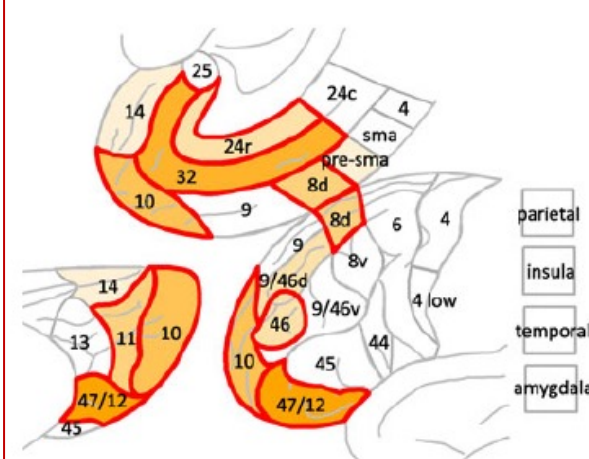
Group 1



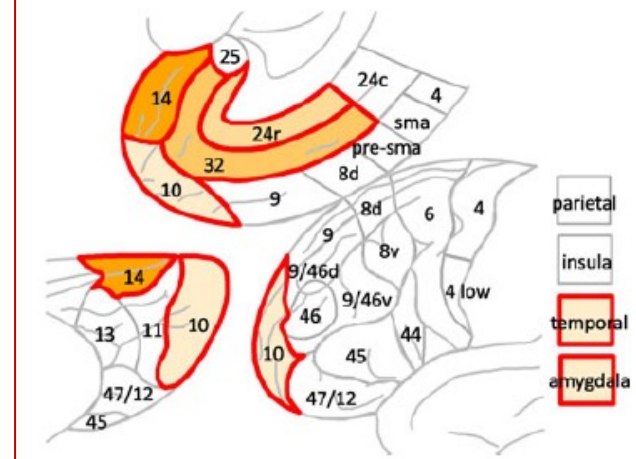
Group 2



Group 3



Group 4



- One or more motor signs
- Somesthetic localized aura and tonic vocalization
- Absence of gestural motor behavior and of emotional features
- Early spread network: significant involvement of rolandic cortex, rolandic operculum, parietal cortex; minor involvement of lateral and medial premotor cortices.
- Ictal discharge: medial and lateral premotor regions at onset

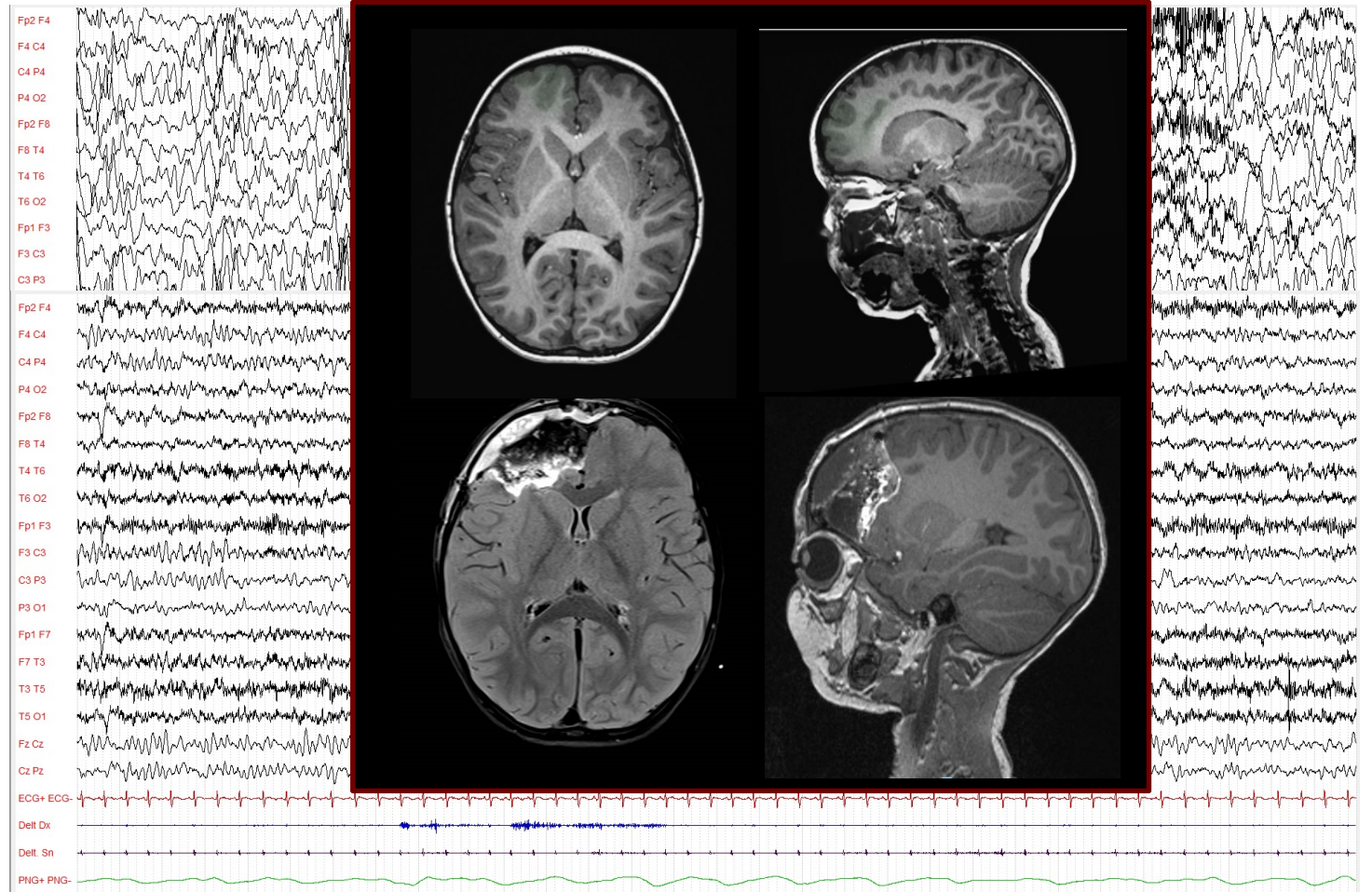
- Co-occurrence of elementary motor signs (typically symmetric axial tonic posture and facial contraction such as “chapeau de gendarme”) and nonintegrated gestural motor behavior
- Nonlocalized aura and more complex nonverbal vocalization
- Absence of integrated gestural motor behavior, distal stereotypies, early clonic signs, and fixed facial expression
- Early spread network: both premotor and lateral prefrontal regions
- Ictal discharge: both medial and lateral aspect at onset

- Integrated gestural motor behavior with distal stereotypies, fixed facial expression or positive emotional expression, proximal stereotypies and speech production
- Absence of any elementary motor signs
- Early spread network and ictal discharge: rostral prefrontal ventrolateral regions, rostral cingulate gyrus

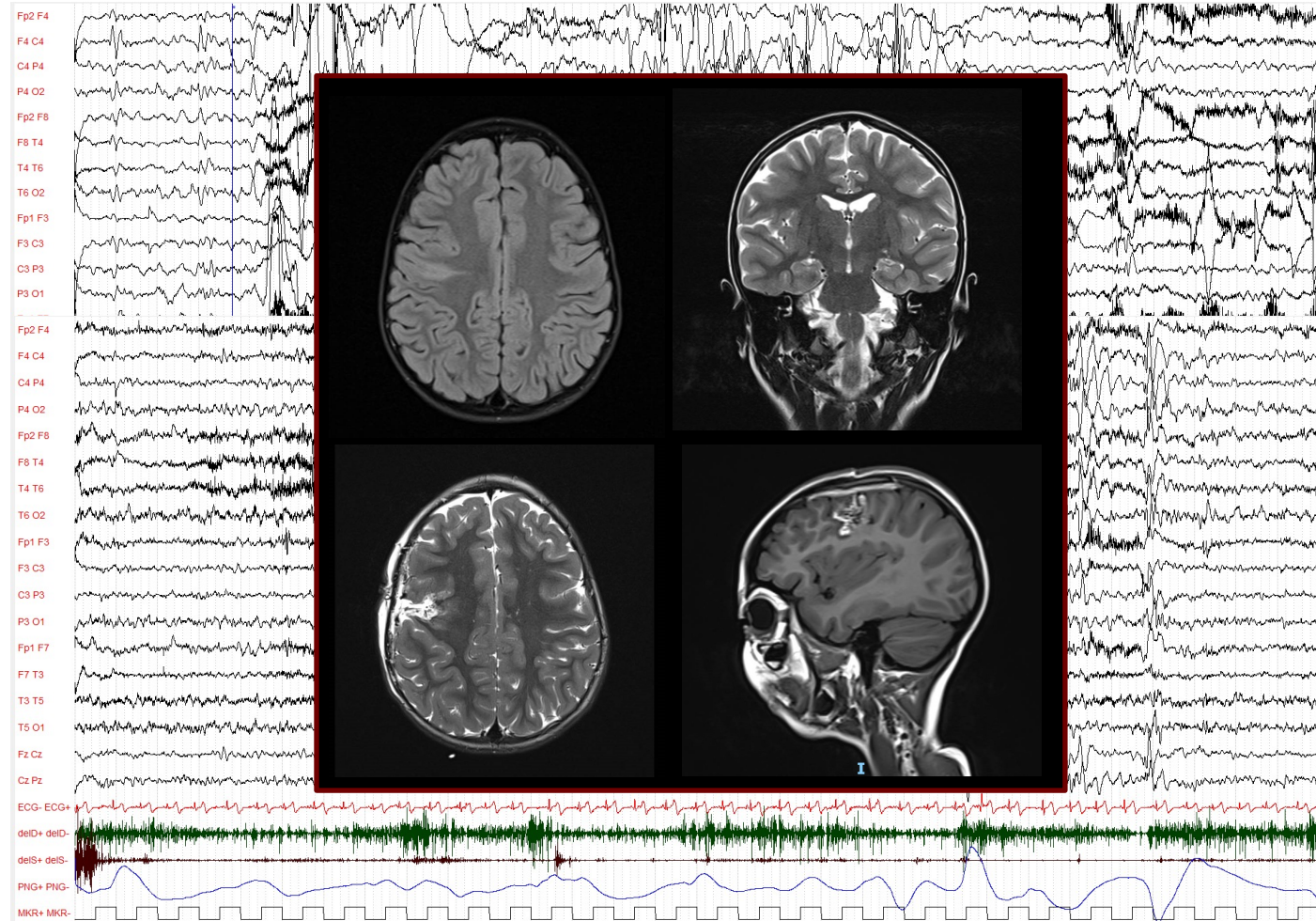
- Integrated gestural behavior of fear, sometimes hyperkinetic, with attempt to fight or to escape, frightened facial expression, sometimes screaming or swearing, and autonomic signs.
- Absence of elementary motor signs
- Early spread network and ictal discharge: orbital and medial-prefrontal network with propagation to amygdala and anterior temporal regions



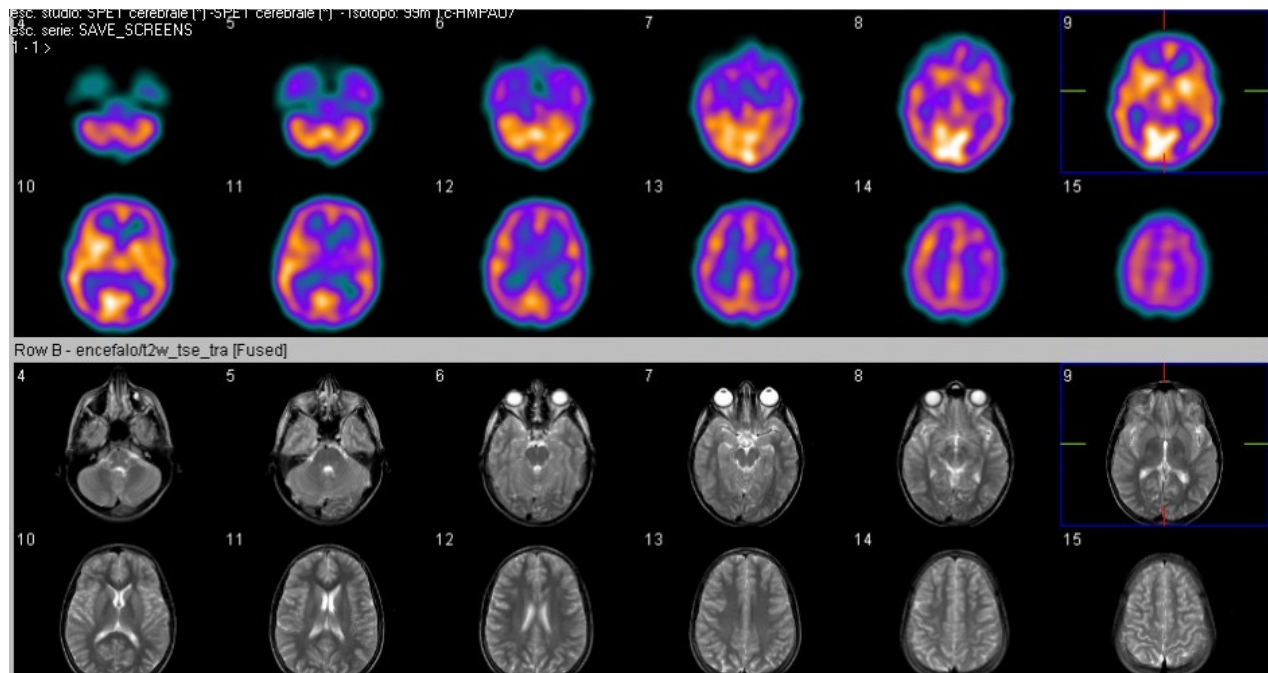
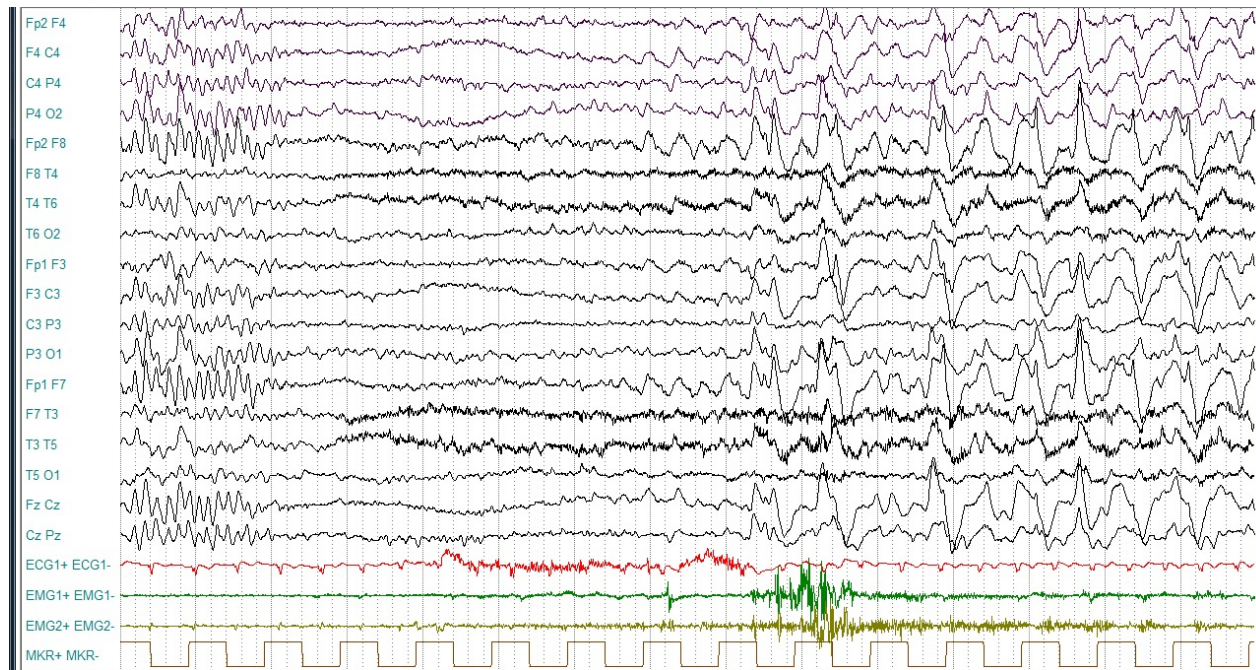
Group 1



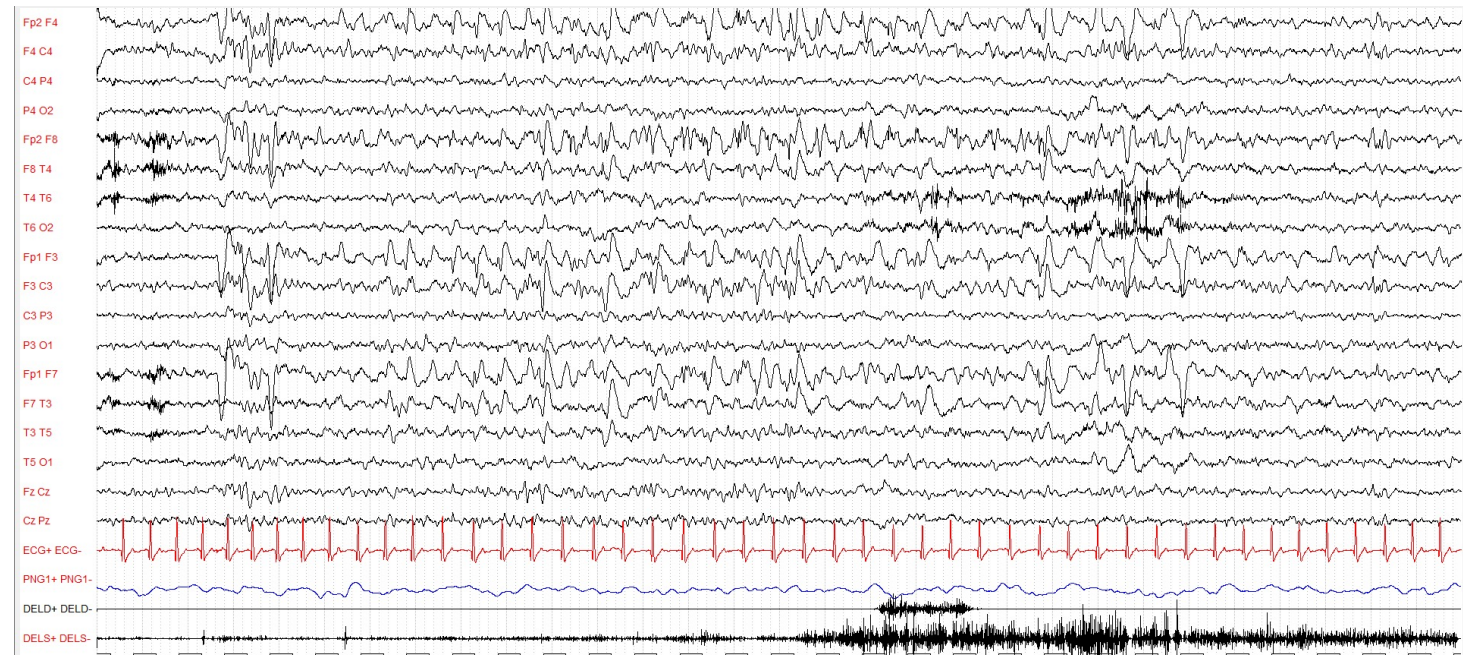
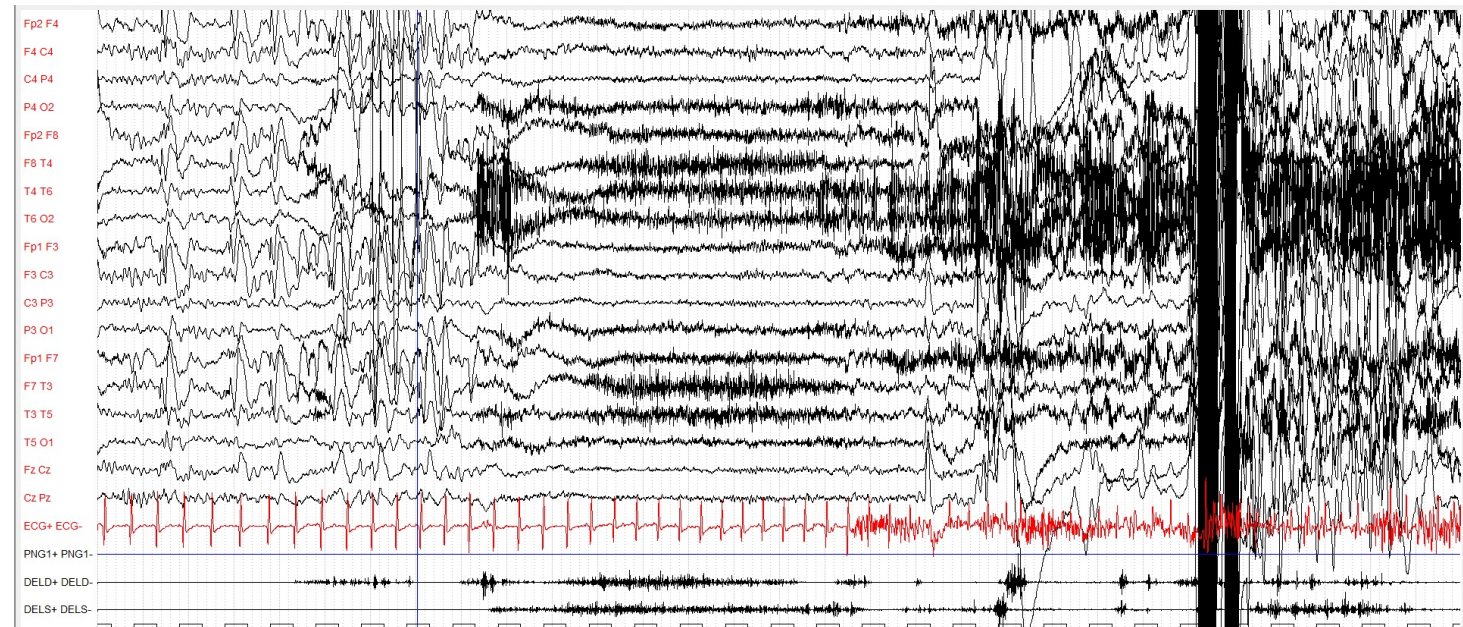
Group 2

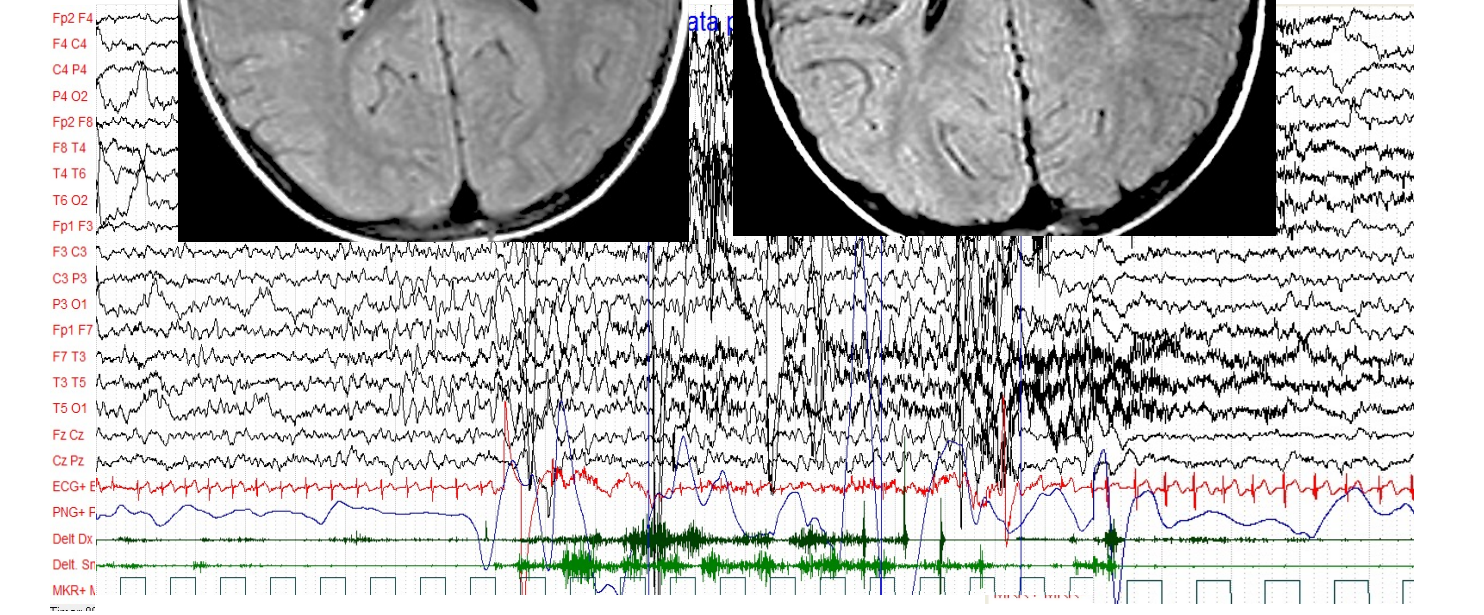
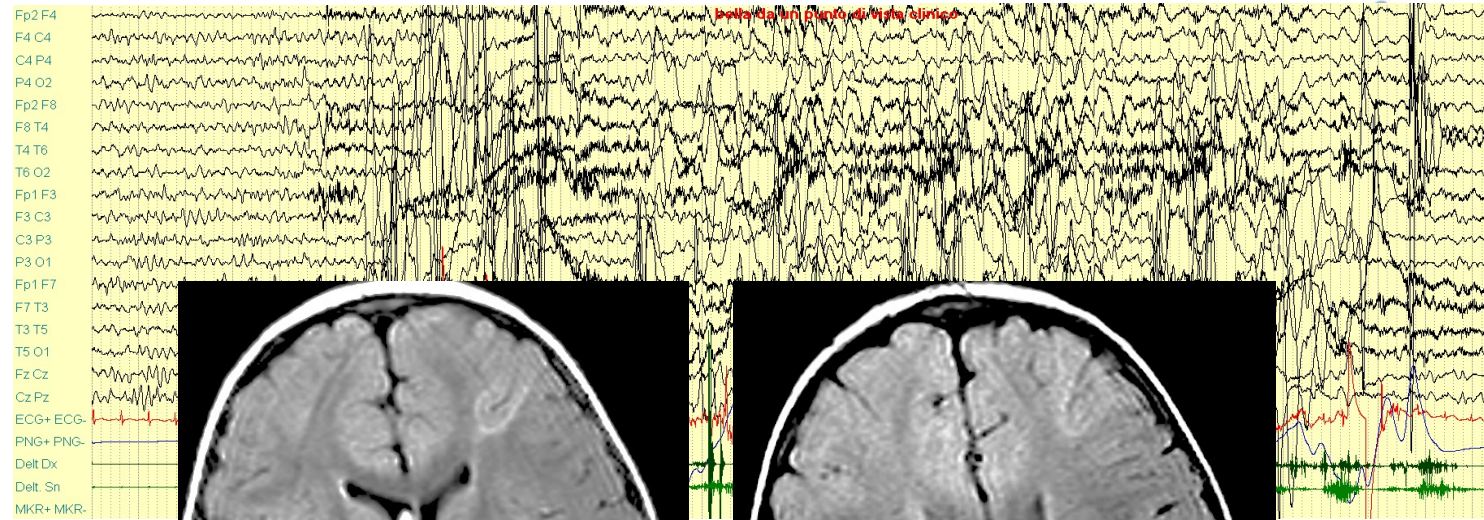


Group 3



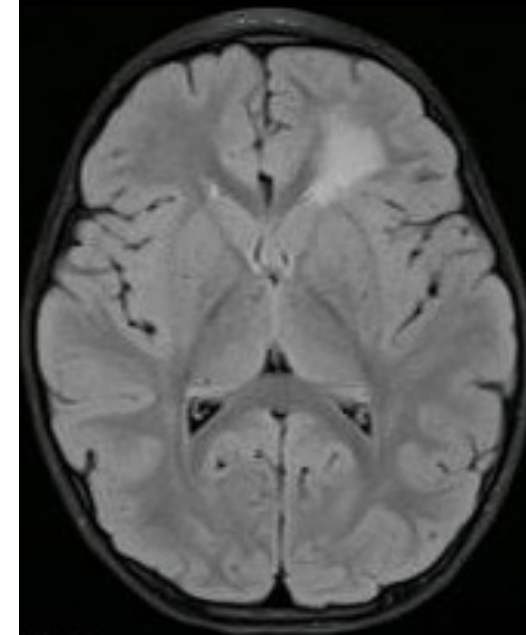
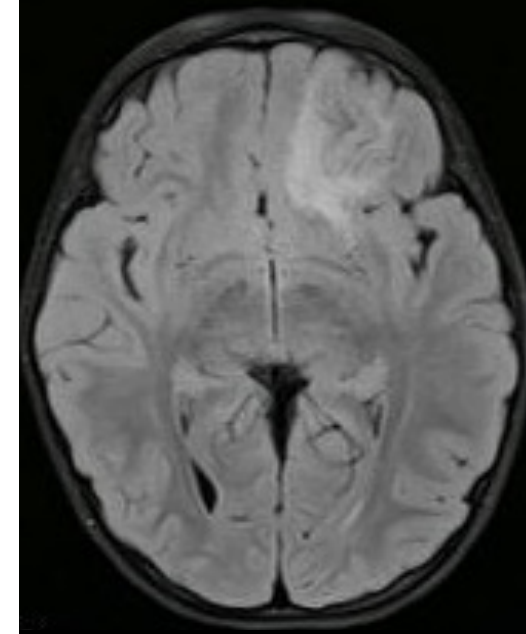
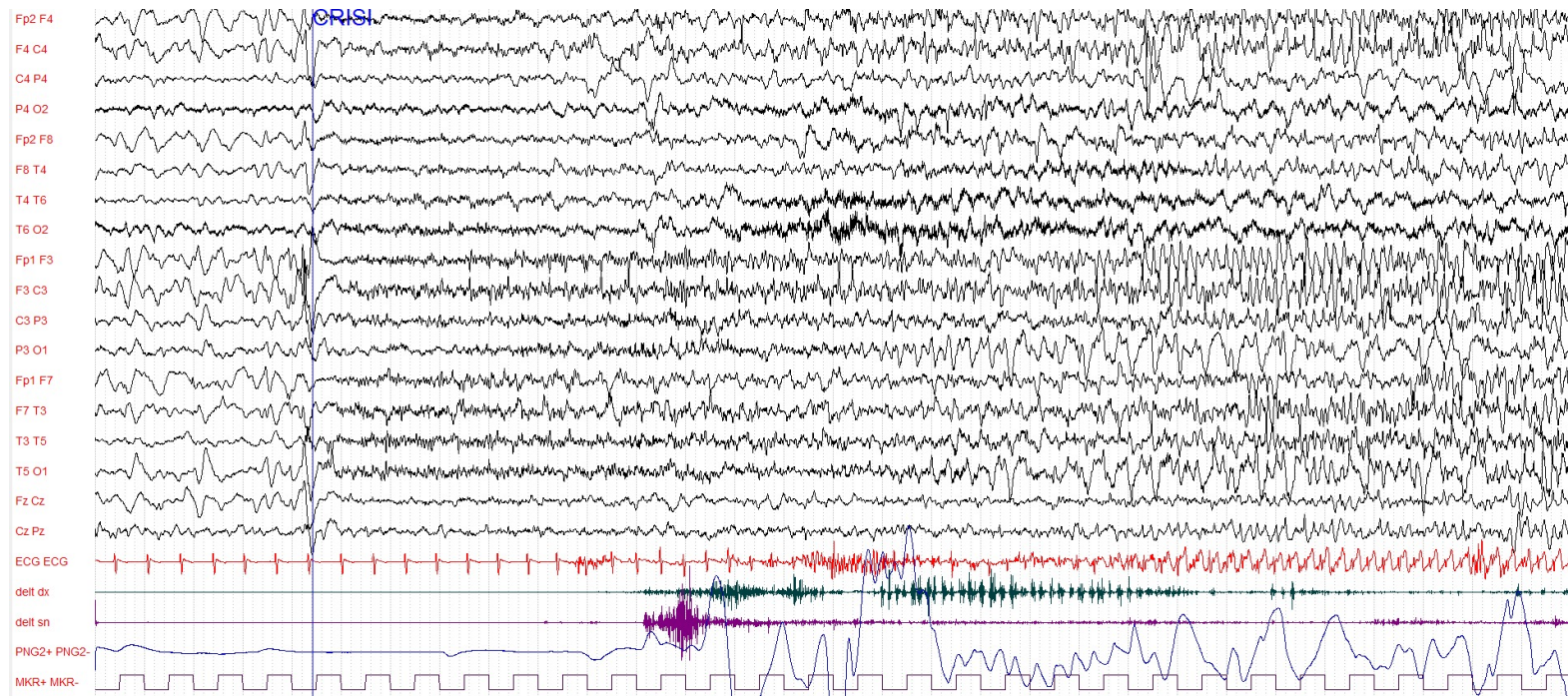
Group 4





Seizures roughly suggest the region but do not indicate the putative site of origin: the complexity of a typical semeiology





Difficulties with frontal lobe seizures

- Complex and multidirectional connectivity through distant cortico-cortical efferent pathways with rapid, widespread propagation of seizure discharges
- Seizures often with complex motor behavior, sometimes with emotional signs
- Semiologic patterns not consistently related to localization on seizure onset but to individual propagation pathways
- High reproducibility of the electroclinical pattern for a given patient's seizures but marked variation between patients
- Difficulties in characterizing electro-clinical patterns and in predicting epileptogenic zone
- Large cortex surface and regions far from EEG electrodes placed on the scalp

Conclusions (1)

- Semiologic and electrical patterns of frontal lobe seizures are difficult to characterize, and liable to be misleading in predicting localization of seizure onset
- Relation between semiologic patterns and sublobar localization remains unclear
- Marked variation exists between patients, making categorization and classification challenging
- The connectivity of frontal lobe associative areas supports spread through distant cortico-cortical pathways (multilobar and multidirectional),

Conclusions (2)

- Different etiologies without specific clinical features
- Seizure's semiology determinate by the site of onset and the regions involved in the propagation of the critical discharge
- Some deficits on executive functions, sometimes more severe after surgery
- Few studies about symptoms over time
- Few studies about specific semiology in children

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