



4° CORSO RESIDENZIALE
EEG e POTENZIALI EVOCATI
22 – 27 NOVEMBRE 2021

Pattern EEG intercrici

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Martedì, 23 novembre

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Schema

1. Definizione di intercritico:

- Tentativo di definizione
- Applicazioni alla pratica clinica
- Ruolo patofisiologico
- Conclusioni

2. Pattern intercritici epilettiformi

- Definizione IFCN

3. Semeiologia EEG dei pattern intercritici

- ACNS 2021
- RHYTHMIC AND PERIODIC PATTERNS (RPPs)



Tentativo di definizione Pattern EEG intercritici

1. Def. temporale? tra le crisi?
2. Sono piccole crisi?
3. Generano alterazioni della funzionalità corticale?
4. Che rapporto hanno con le crisi? Favorente?

Definizione

Pattern EEG intercritici: tra le crisi

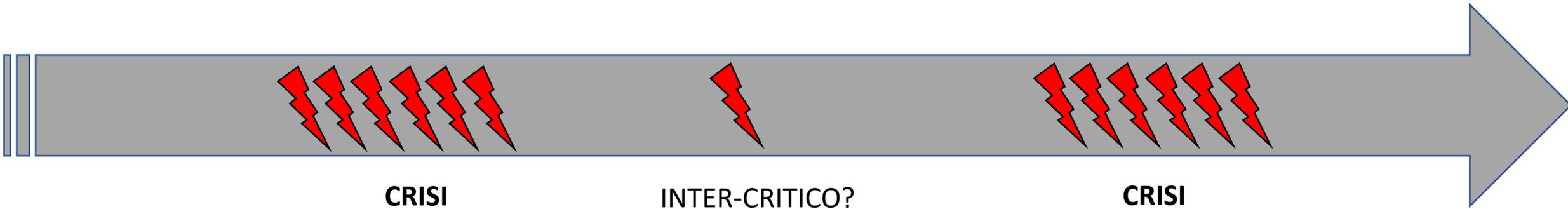
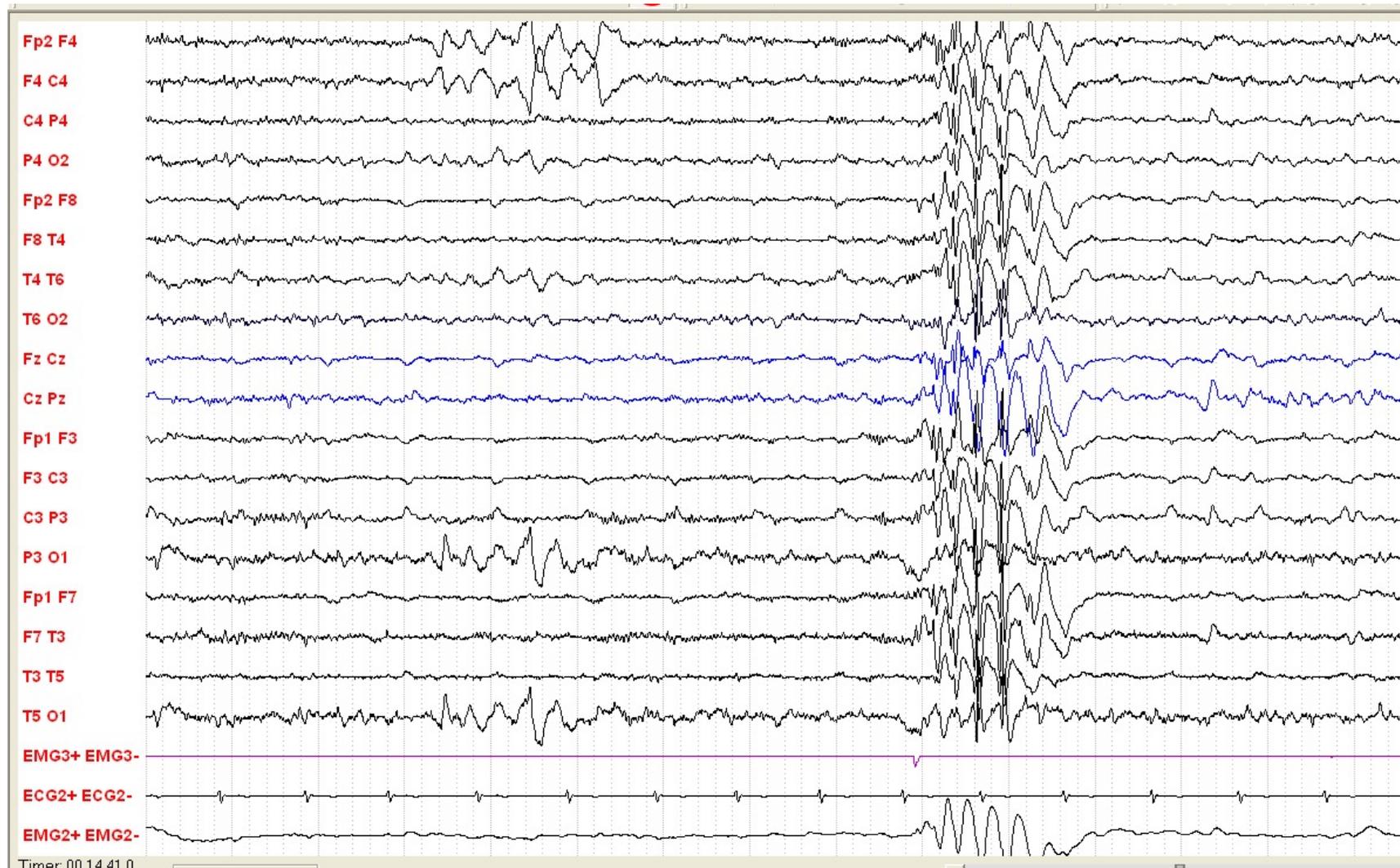


Table 1. Conceptual definition of seizure and epilepsy – 2005 report

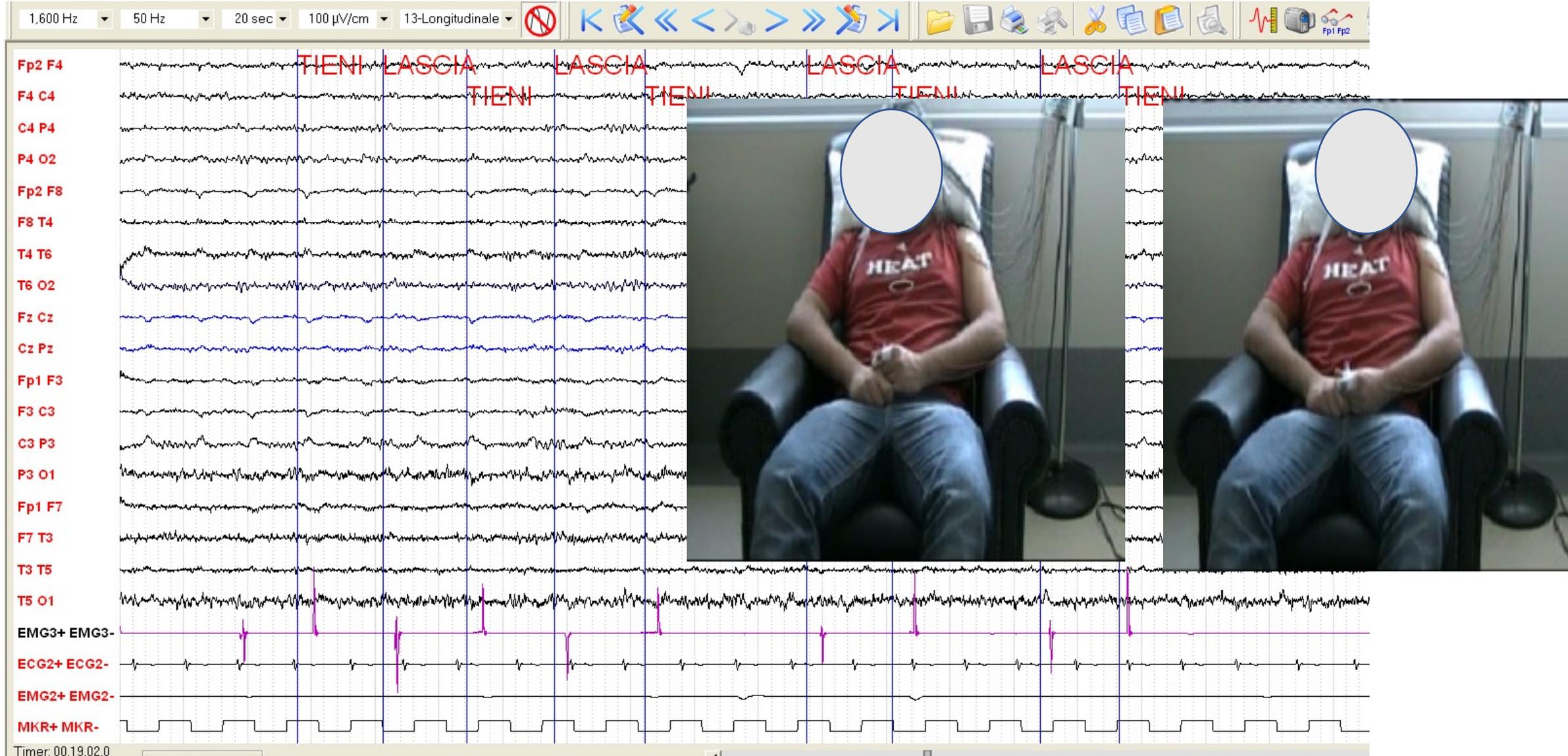
An epileptic seizure is a transient occurrence of signs and/or symptoms due to abnormal excessive or synchronous neuronal activity in the brain.

Epilepsy is a disorder of the brain characterized by an enduring predisposition to generate epileptic seizures, and by the neurobiologic, cognitive, psychological, and social consequences of this condition. The definition of epilepsy requires the occurrence of at least one epileptic seizure.

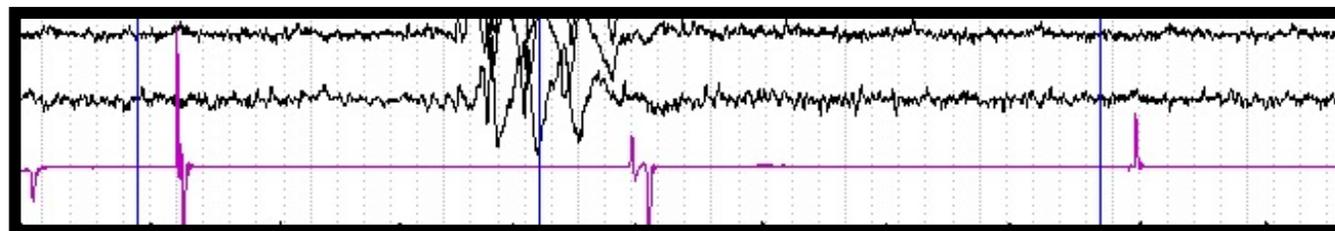
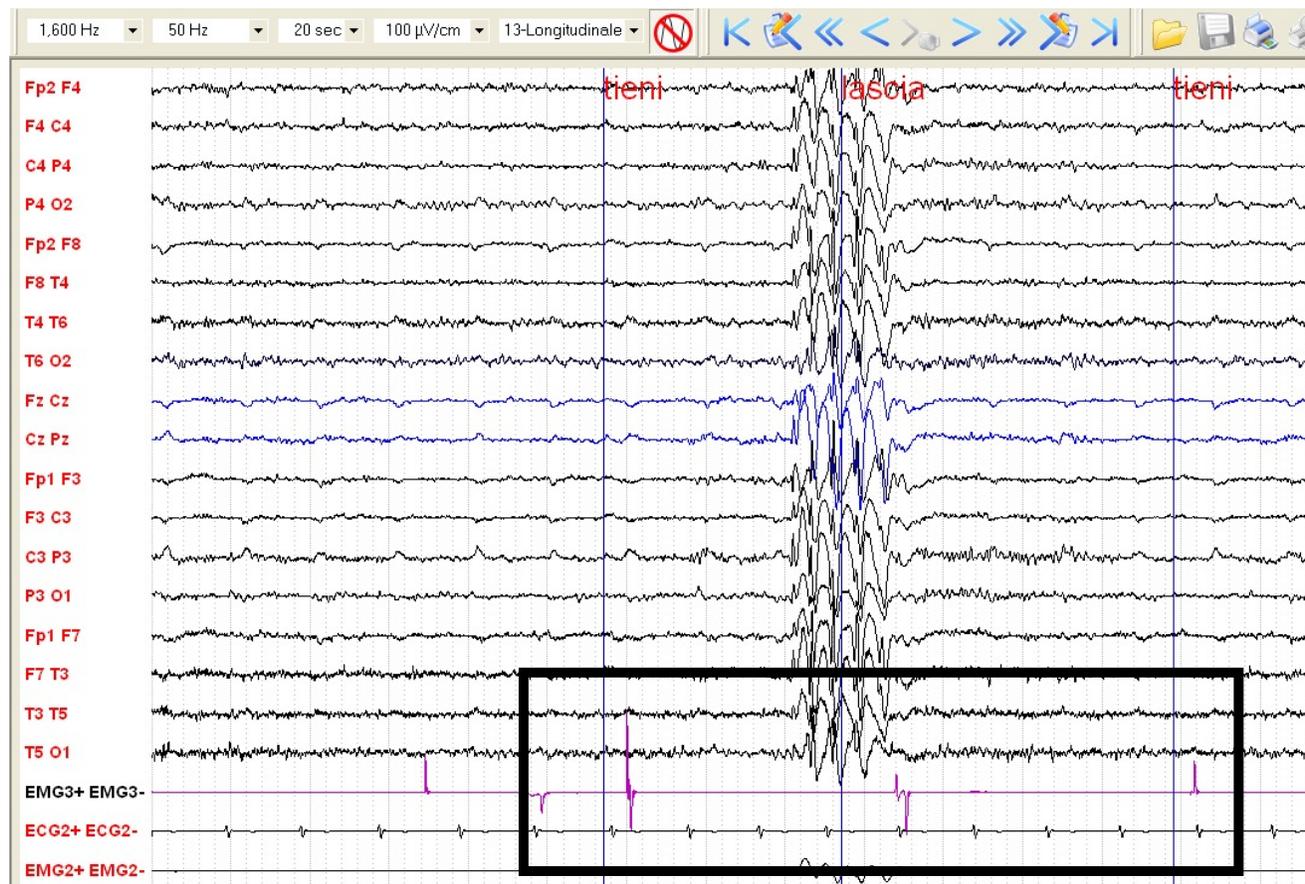
Attività epilettiforme: ictale? Interictale?



TEST LATENZE DI RISPOSTA



LATENZA AUMENTATA

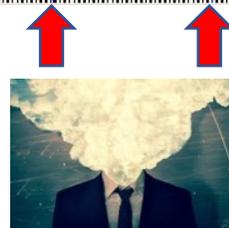


121 msec

612 msec

98msec

LATENZA AUMENTATA SLI



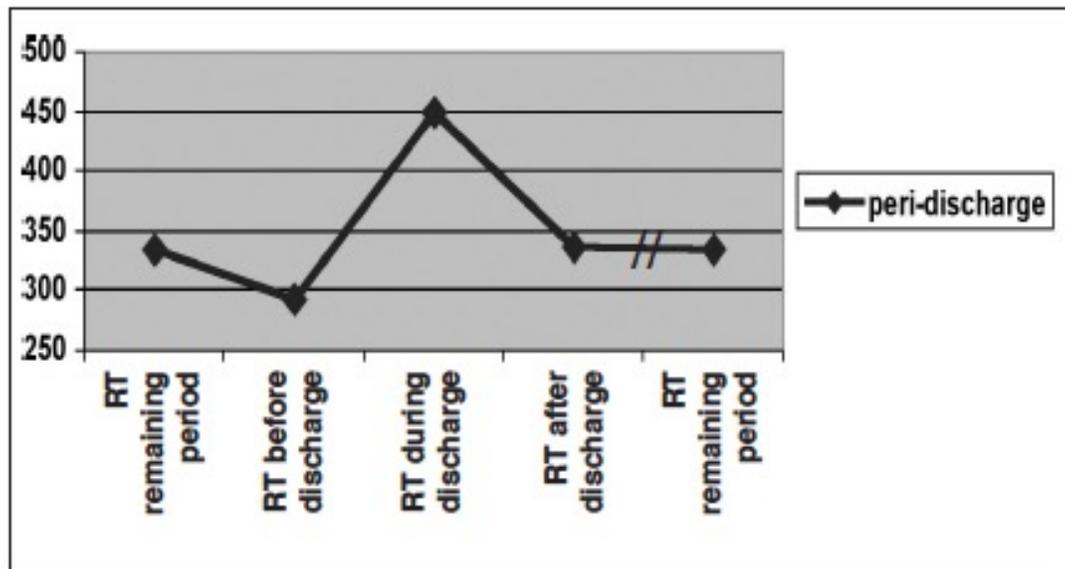


Figure 2 - Reaction times for the period with discharge versus remaining periods.

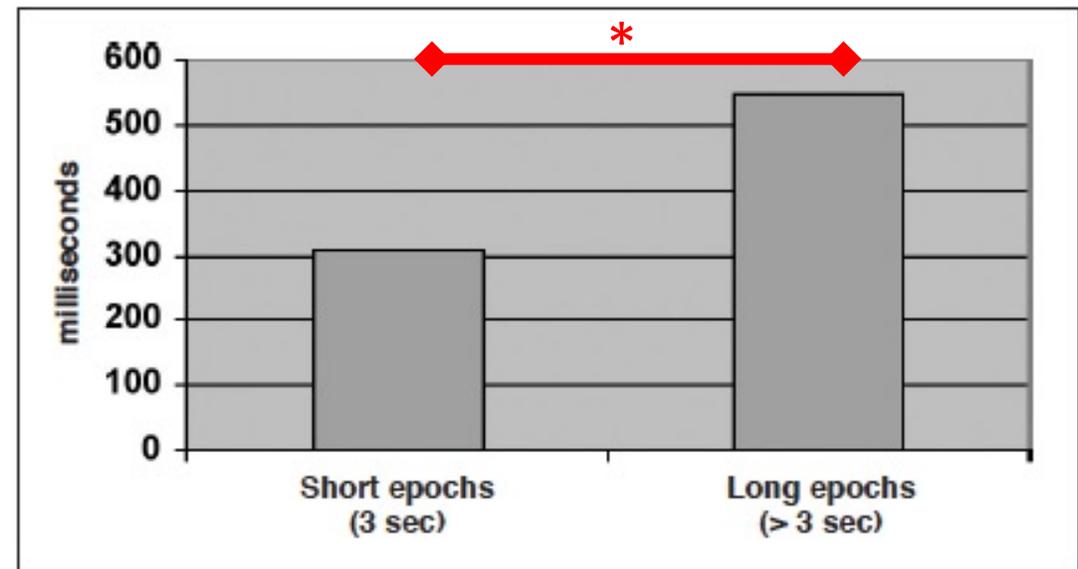
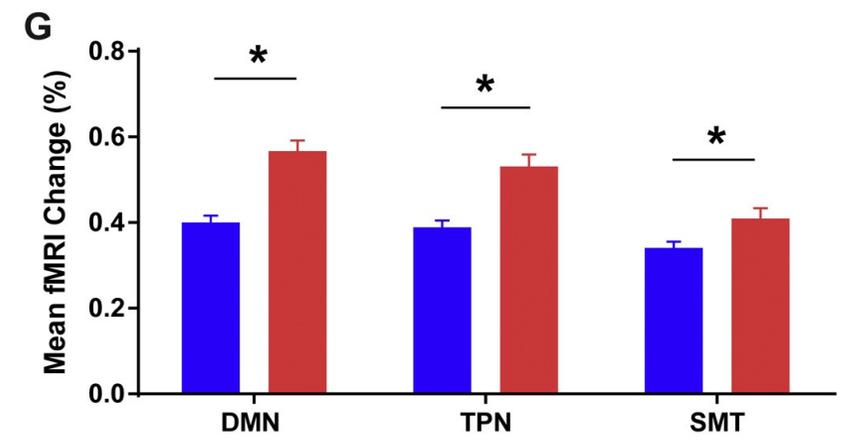
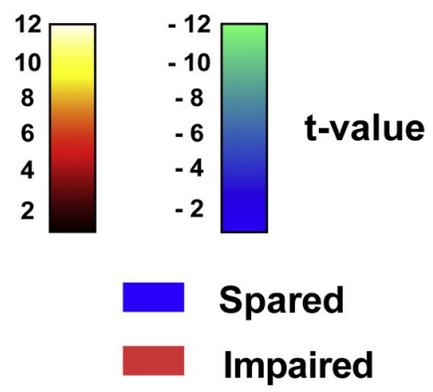
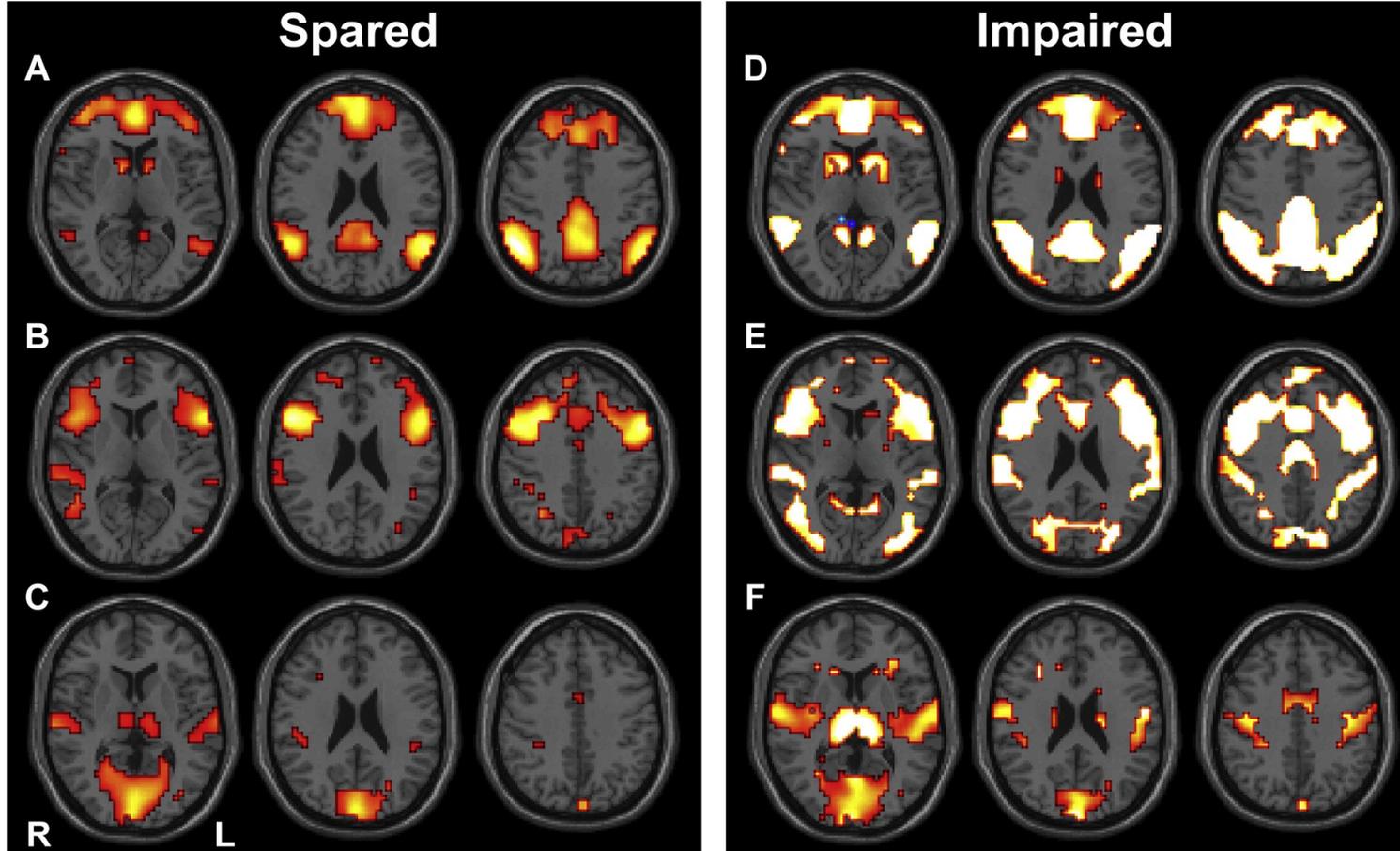


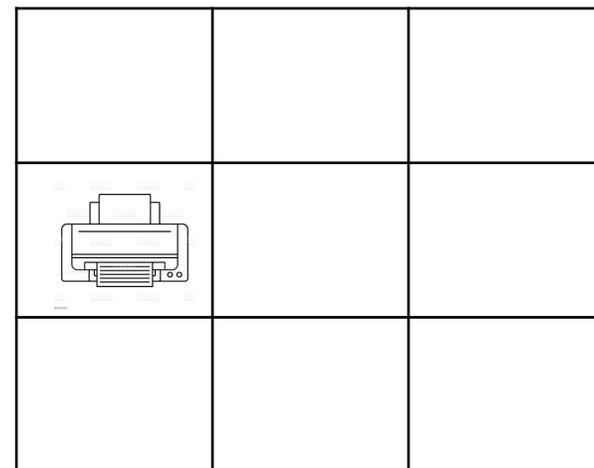
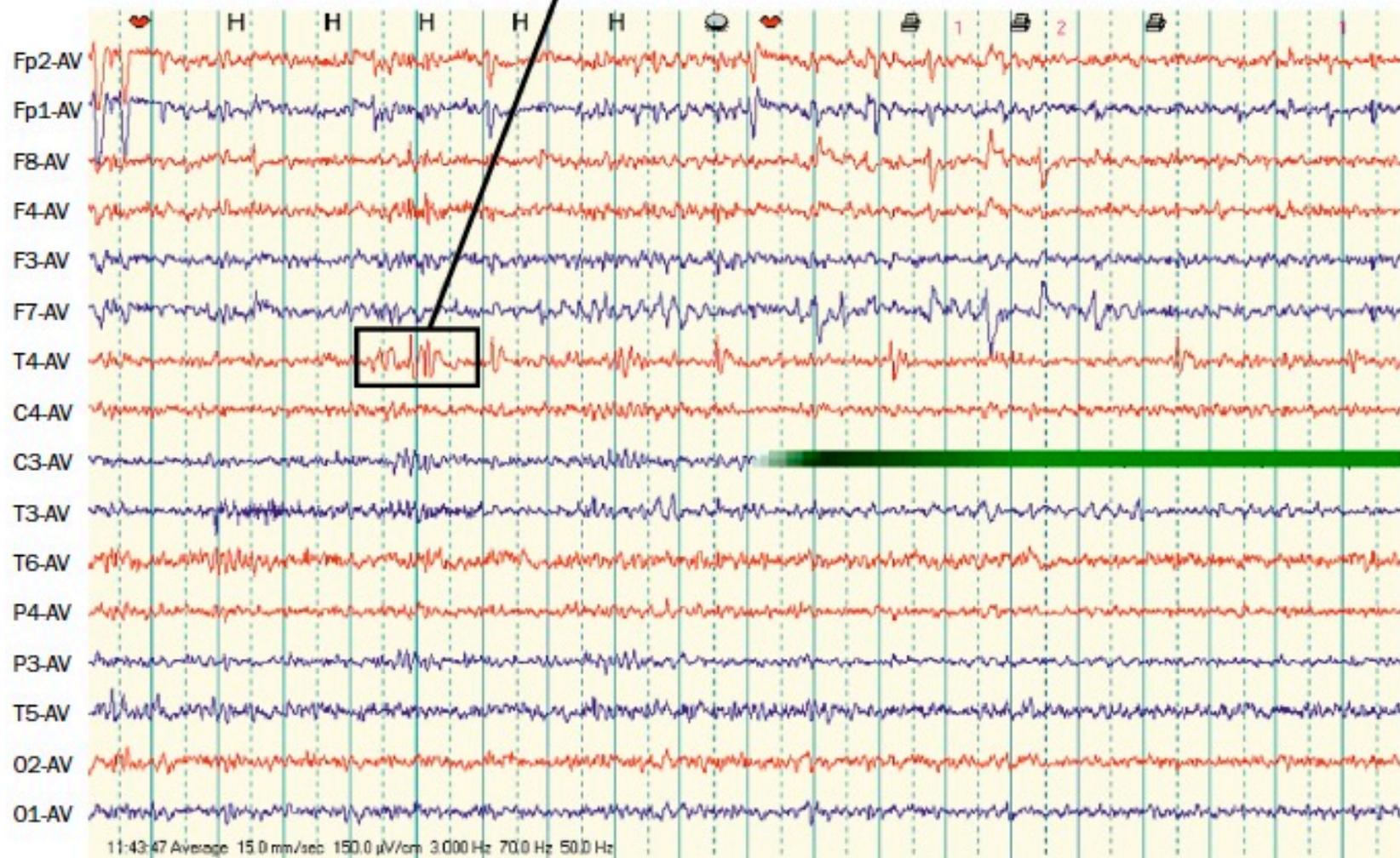
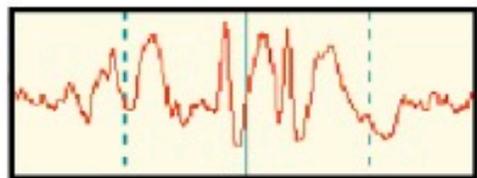
Figure 3 - Effect on reaction time of duration of discharge during the period of discharge.

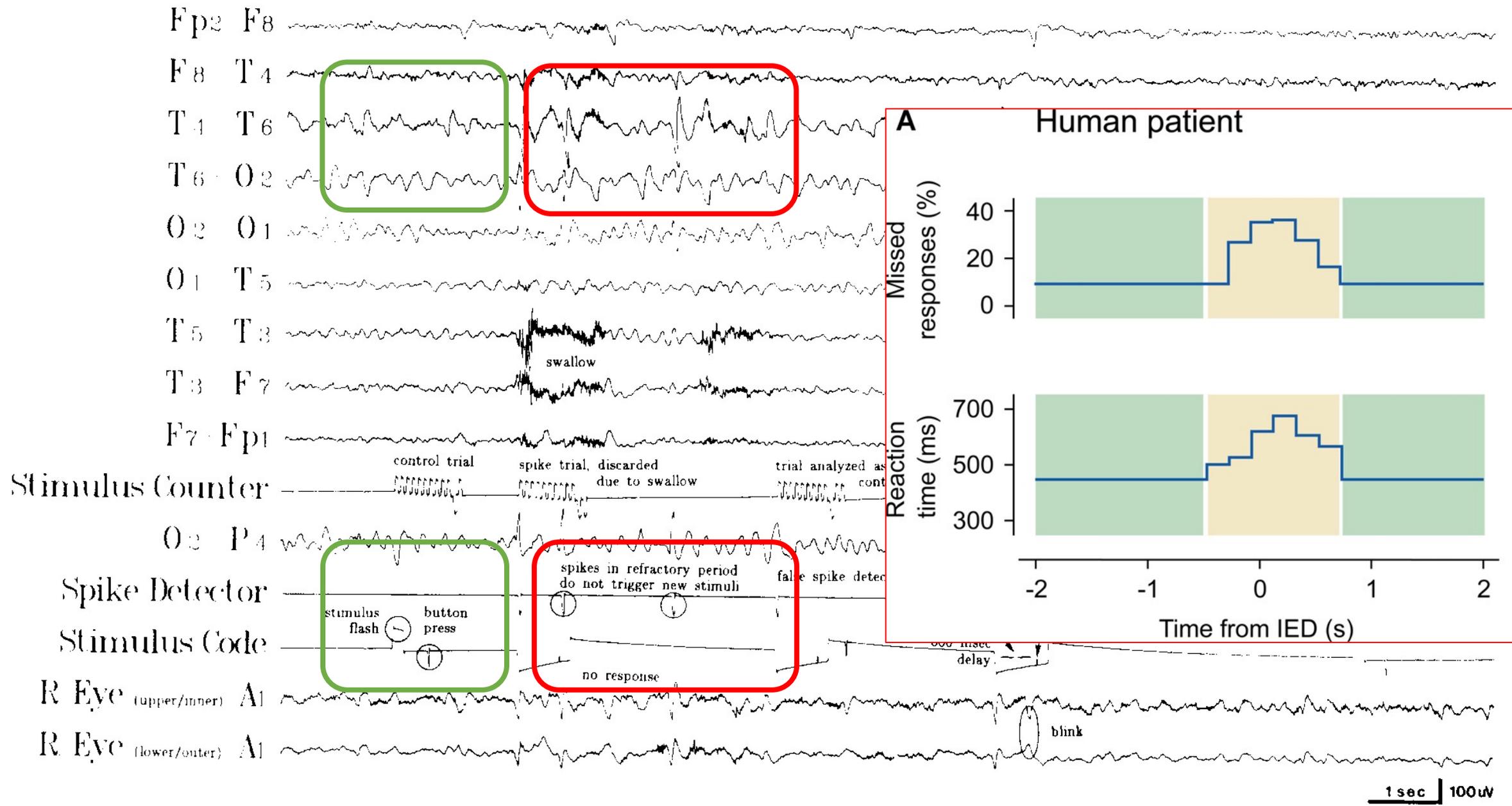
Table III - Post-hoc T-test analysis of period with and period after discharge versus other periods.

Period	T-value	p-value
Period with discharge vs period before discharge	-2.47	p=.02*
Period with discharge vs period after discharge	1.998	p=.05*
Period with discharge vs remaining period	1.943	p=.06
Period before discharge vs period after discharge	-1.918	p=.06
Period before discharge vs remaining period	-2.445	p=.02*
Period after discharge vs remaining period	.155	p=.88



Test sulle punte focali compito di memoria spaziale a breve termine





Punte interictali: periodismo e inibizione corticale

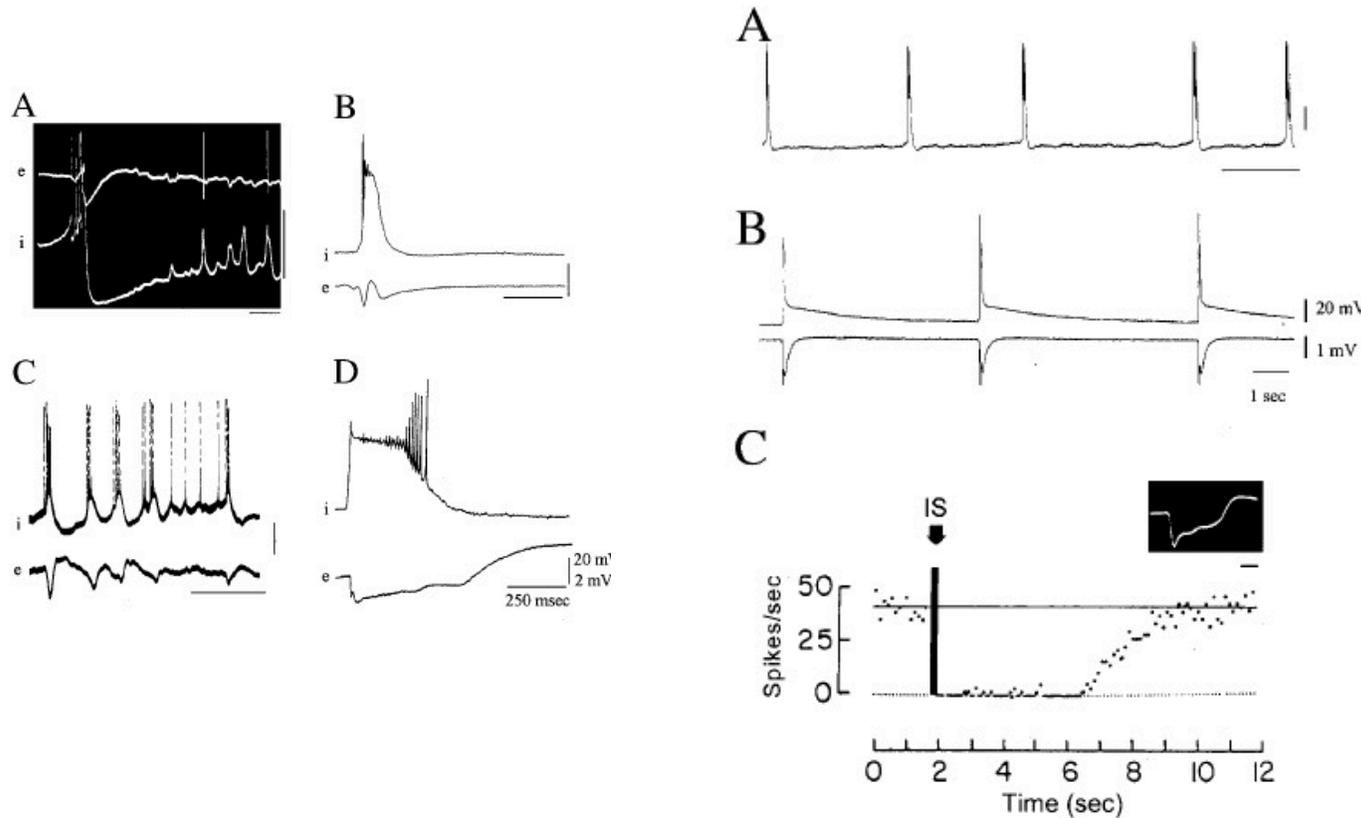


Fig. 10. Interictal spikes (ISs) in experimental models recur periodically. Intracellular bursting activity of principal neurons recorded in vitro in association with ISs shows a periodicity in the calcium-free model (A) From Valiante et al. (1995); reproduced by permission of the Society for Neuroscience, and in the bicuculline model. (B) From de Curtis et al. (1998); reproduced by permission of the Society for Neuroscience, de Curtis et al., *J. Neurosci.* In B, the correlation between intracellular PDSs and the extracellularly recorded ISs is

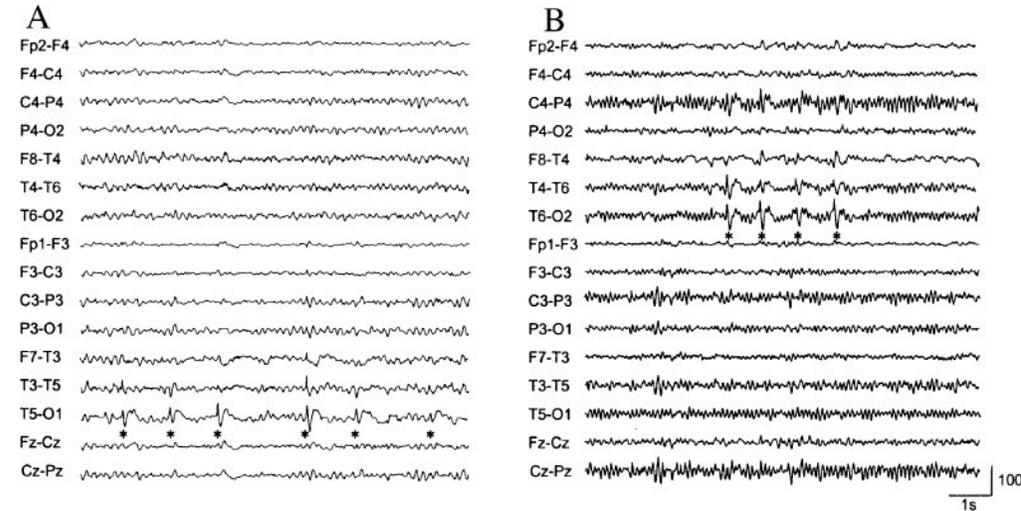


Fig. 11. Periodic interictal spikes in human focal epilepsy. (A). Temporo-occipital interictal spikes (ISs) in focal epilepsy secondary to a low grade left temporal glioma. (B) Periodic temporal ISs in a benign idiopathic epilepsy of childhood (from Avanzini et al., 2000; reproduced by permission of Verduci, Editor s.r.l.).

Punte interictali: relazione con le crisi

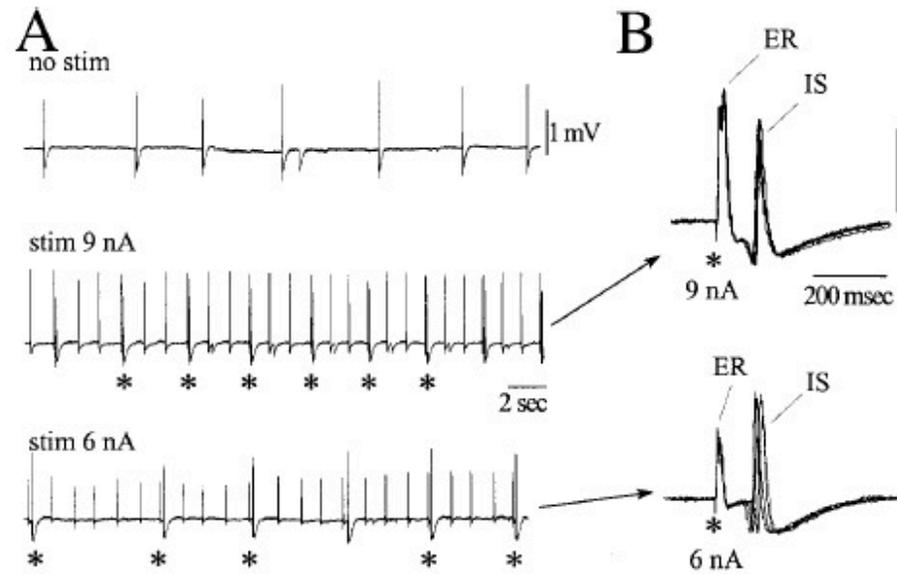
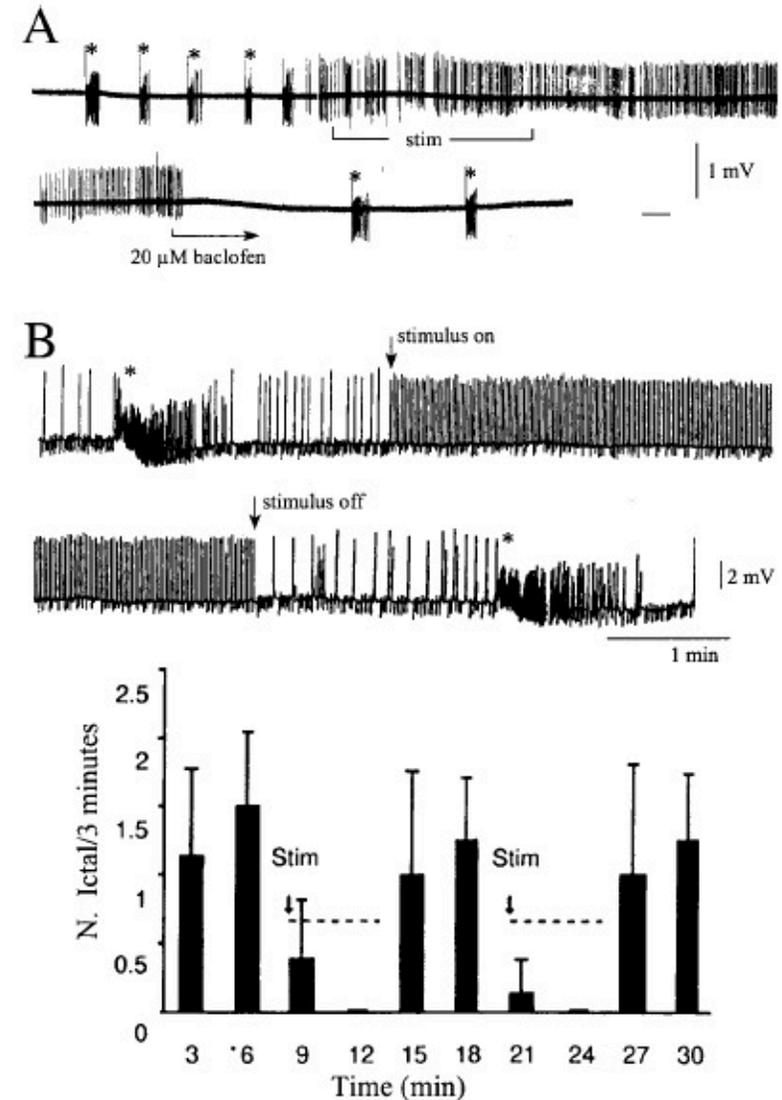
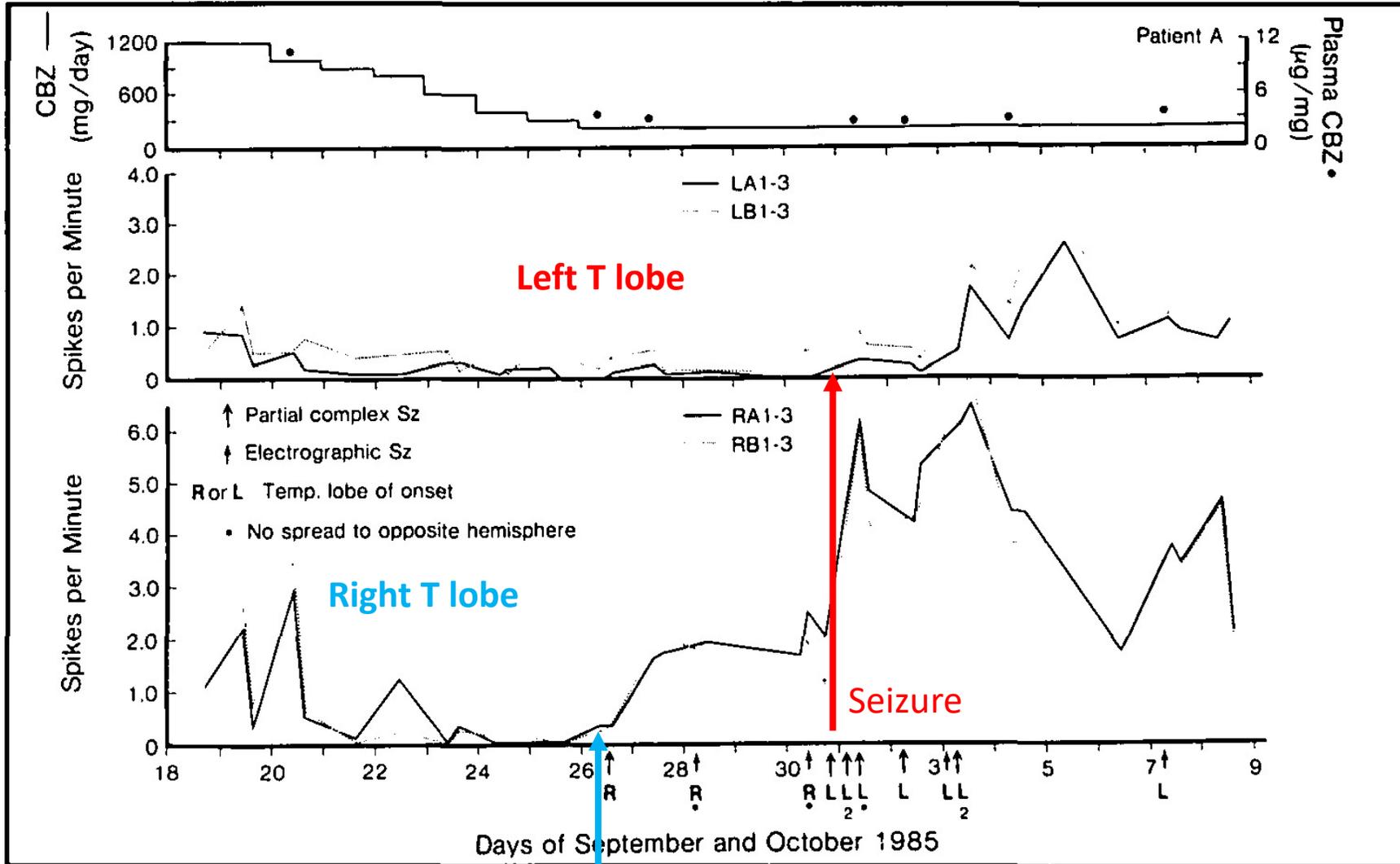


Fig. 13. An increased threshold to afferent synaptic activation is demonstrated during the interictal spikes (ISs) recorded in the isolated brain preparation after local penicillin application. Spontaneous periodic spiking is shown in the upper trace in A. In the middle trace IS were activated every 3 s during stimuli of 9 nA at 1 Hz delivered on the lateral olfactory tract, suggesting that the cortex is inhibited for about 3 s after the discharge of a IS (see details in B). When the stimulus intensity was reduced to 6 nA IS (lower trace) were recruited in the late inter-IS period (see details in B). In (B), lateral olfactory tract-evoked responses (ER) and stimulus evoked ISs marked by the asterisk in A were superimposed. A slight jittering of the IS after the response evoked by 6 nA LOT stimulation was observed.



Relationships Between Interictal Spiking and Seizures: Human and Experimental Evidence

Jean Gotman



Seizure

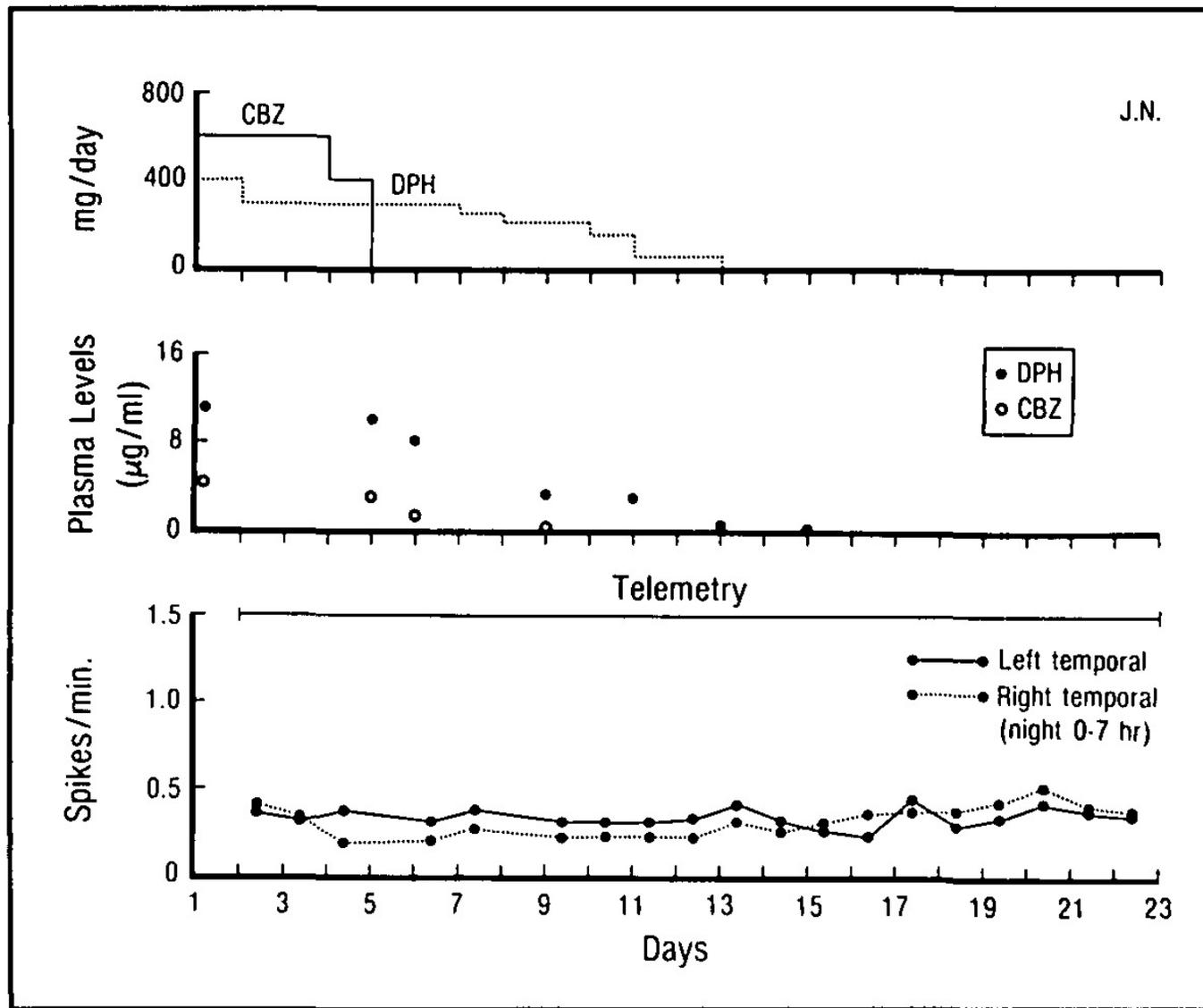
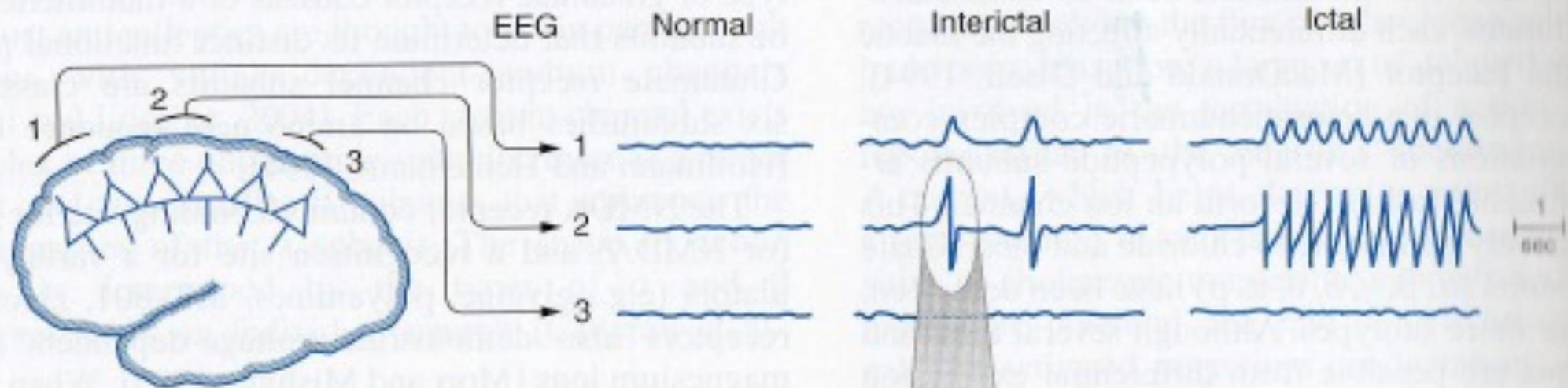
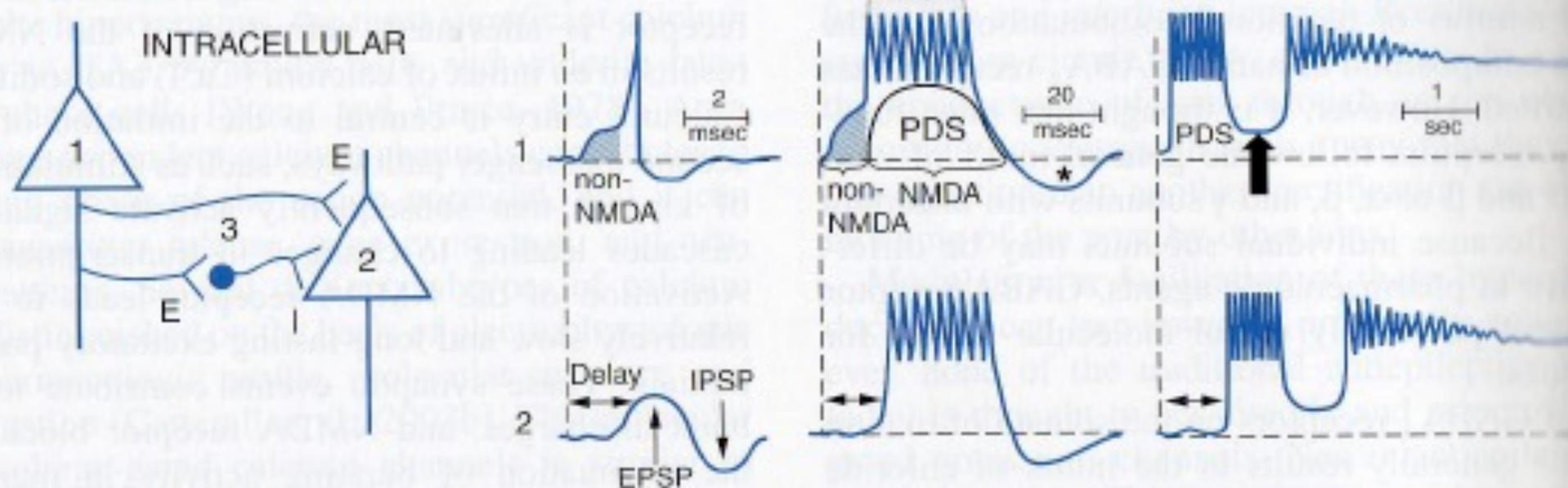


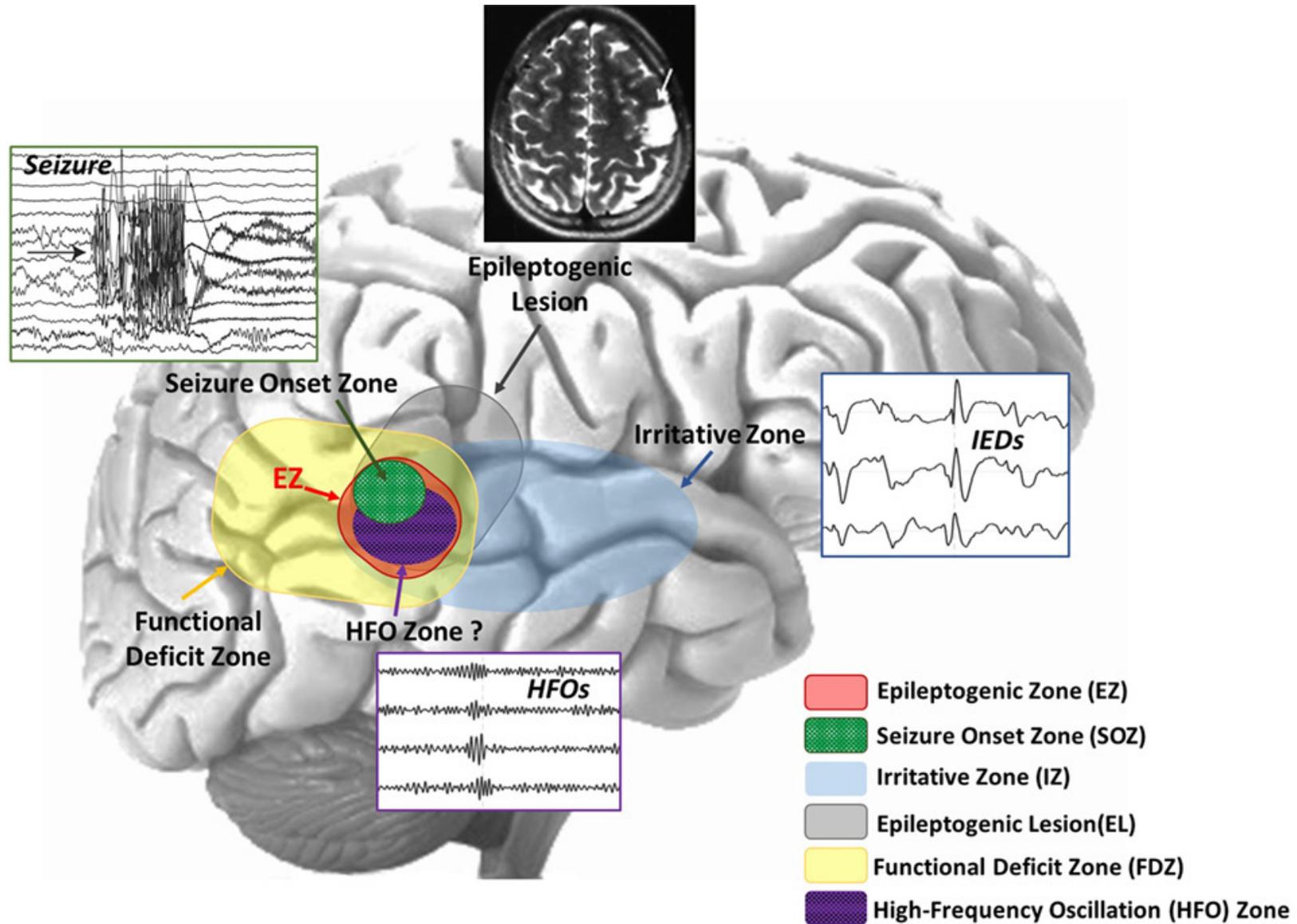
Figure 2 — Upper graph is medication dosage. Middle graph represents plasma levels and lower graph shows spiking rate in a patient with intracerebral electrodes. As antiepileptic medication decreases from “therapeutic” levels to zero, there is no change in interictal activity. Note that no seizure took place (from reference 2).

A
Brain



B
Neuronal network







Tentativo di definizione Pattern EEG intercritici

CONCLUSIONI

1. Def. temporale? tra le crisi?
 1. Sì
2. Sono crisi?
 1. No
3. Generano alterazioni della funzionalità corticale?
 1. Sì
4. Che rapporto hanno con le crisi? Favorente?
 1. Non esattamente

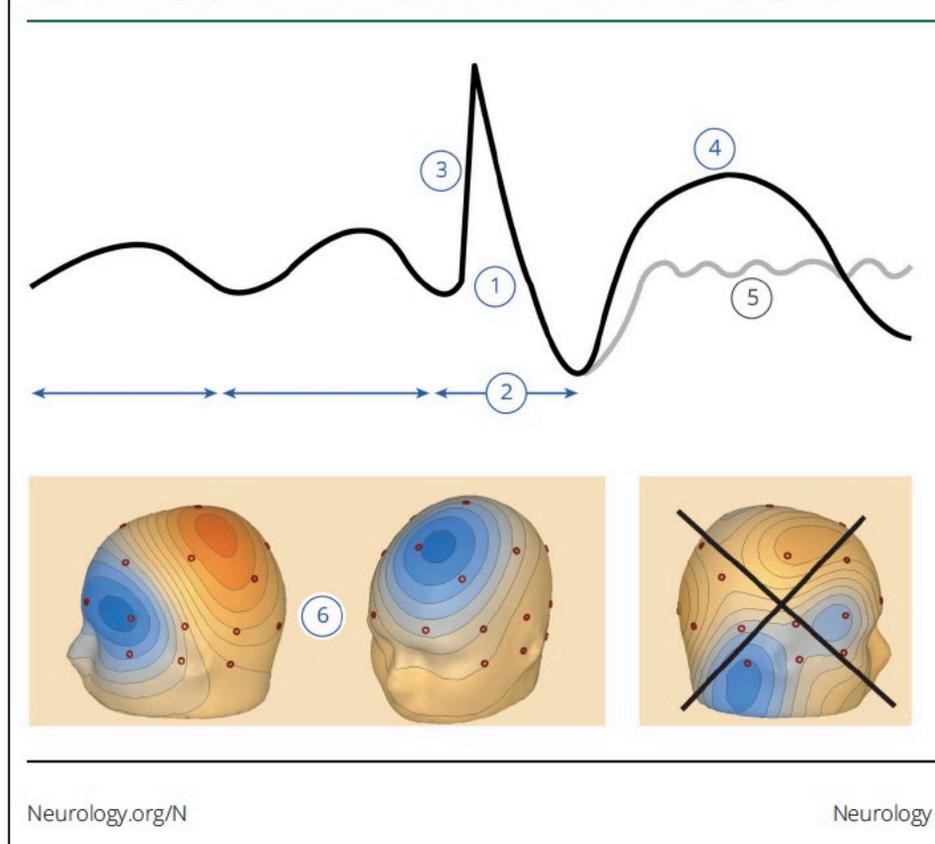
2. Pattern intercritici epilettiformi

- Epileptiform pattern:

Describes transients distinguishable from background activity with a characteristic morphology typically, but neither exclusively nor invariably, found in interictal EEGs of people with epilepsy. Epileptiform patterns have to fulfill at least 4 of the following 6 criteria:

1. Di- or tri-phasic waves with sharp or spiky morphology (i.e. pointed peak).
2. Different wave-duration than the ongoing background activity, either shorter or longer.
3. Asymmetry of the waveform: a sharply rising ascending phase and a more slowly decaying descending phase, or vice versa.
4. The transient is followed by an associated slow after-wave.
5. The background activity surrounding epileptiform discharges is disrupted by the presence of the epileptiform discharges.
6. Voltage map with distribution of the negative and positive potentials suggesting a source in the brain corresponding to a radial, oblique, or tangential orientation of the source

Figure 1 Infographic summarizing the 6 IFCN criteria for identifying IEDs



ACNS GUIDELINE

**American Clinical Neurophysiology Society's Standardized
Critical Care EEG Terminology: 2021 Version**

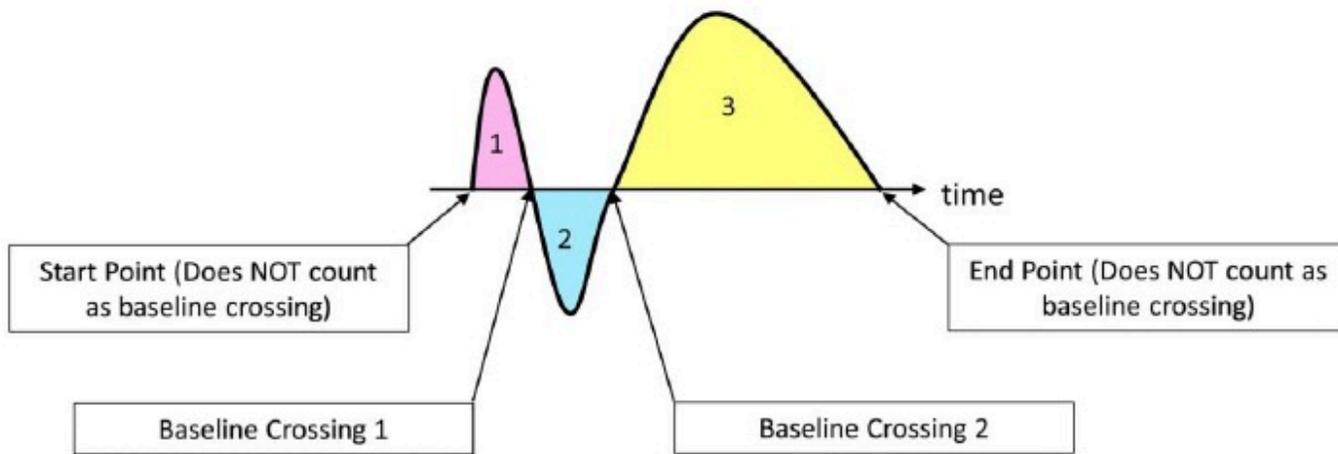
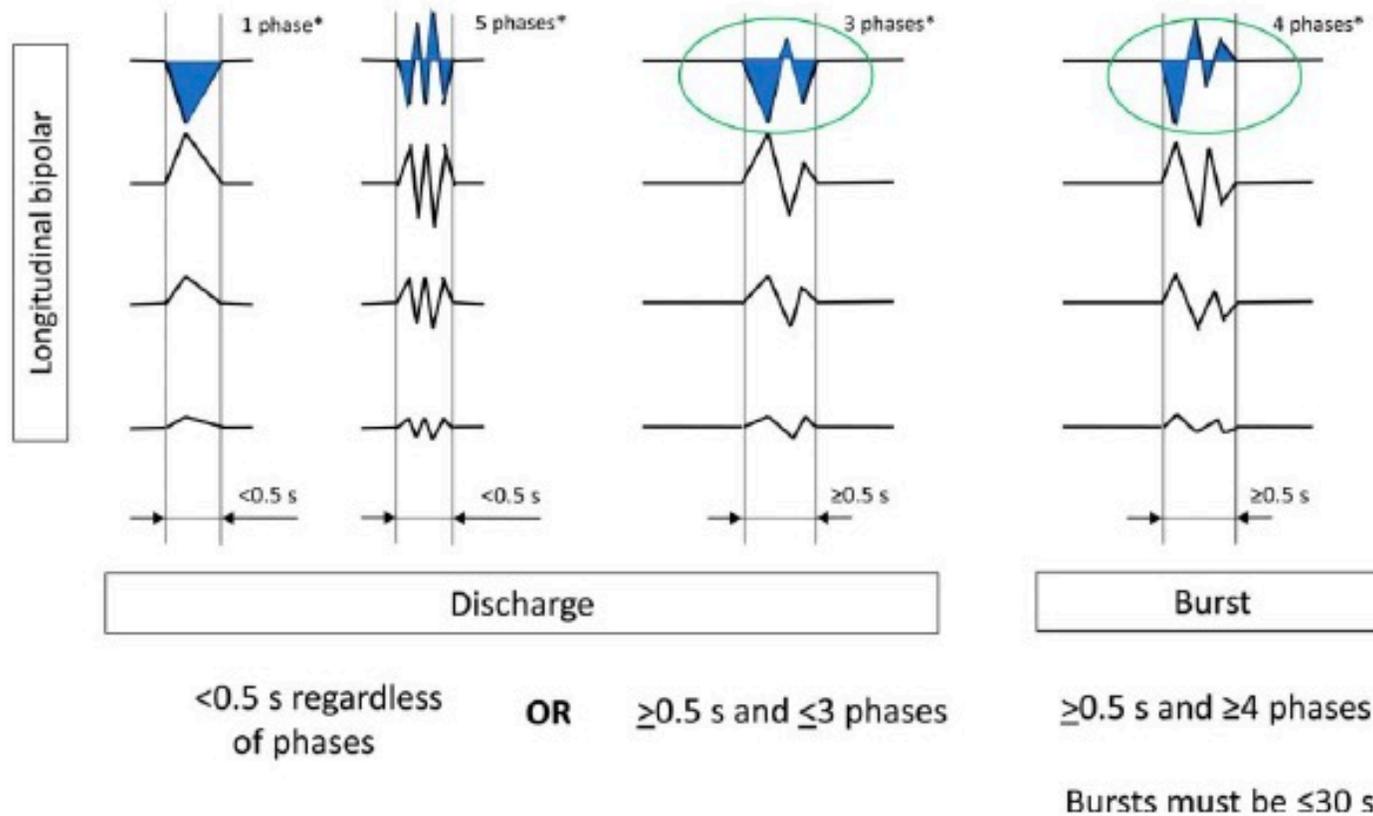


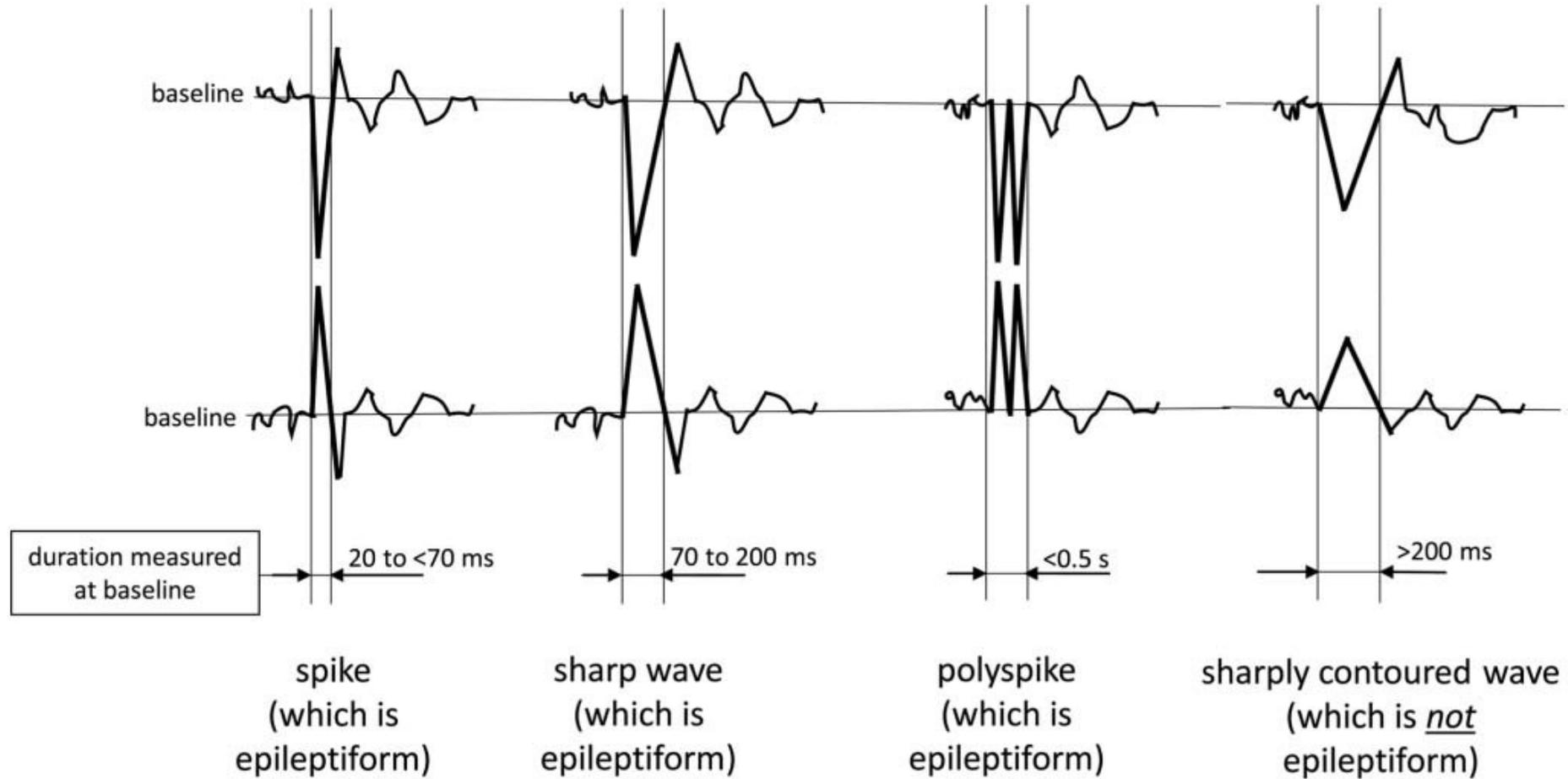
FIG. 23. The Number of Phases. Number of Phases = 1 + number of baseline crossings of the typical discharge. In this case there are a total of 2 baseline crossings, therefore the number of phases is $1 + 2 = 3$ phases. A phase is the part of the signal above or below the imaginary baseline. In this case, phase 1 (pink) is above, phase 2 (blue) is below, and phase 3 (yellow) is above again.

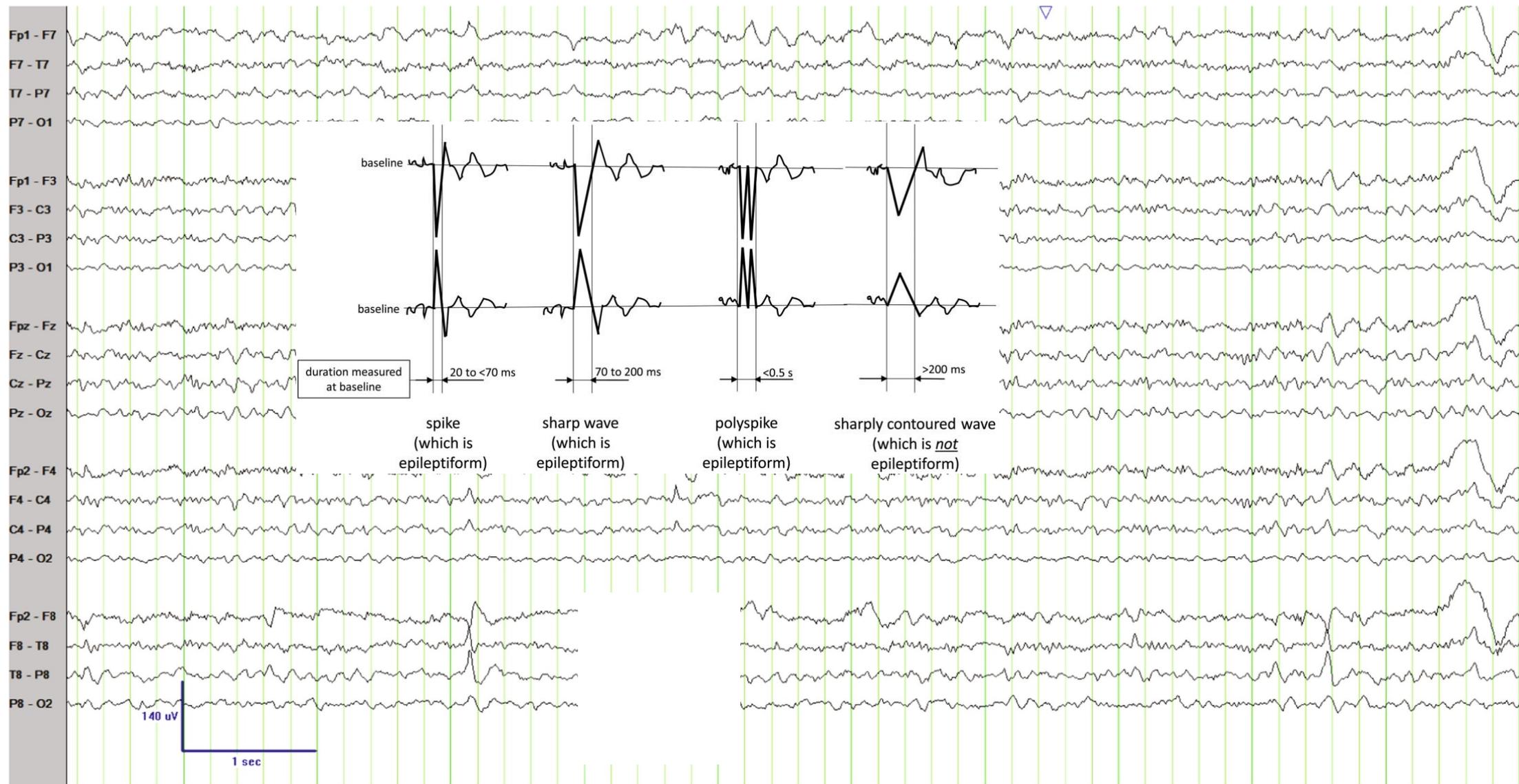
Discharge vs Burst (scarica vs raffica?)

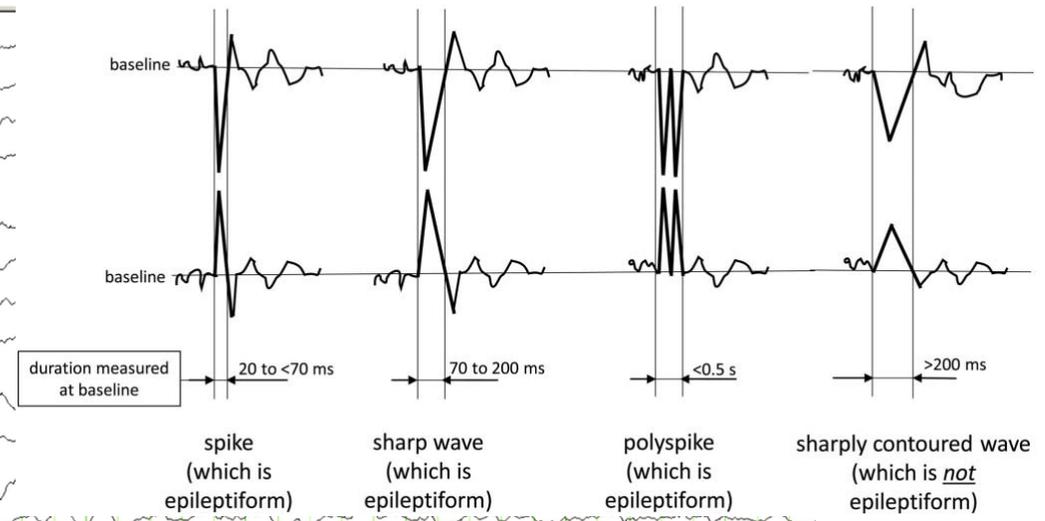
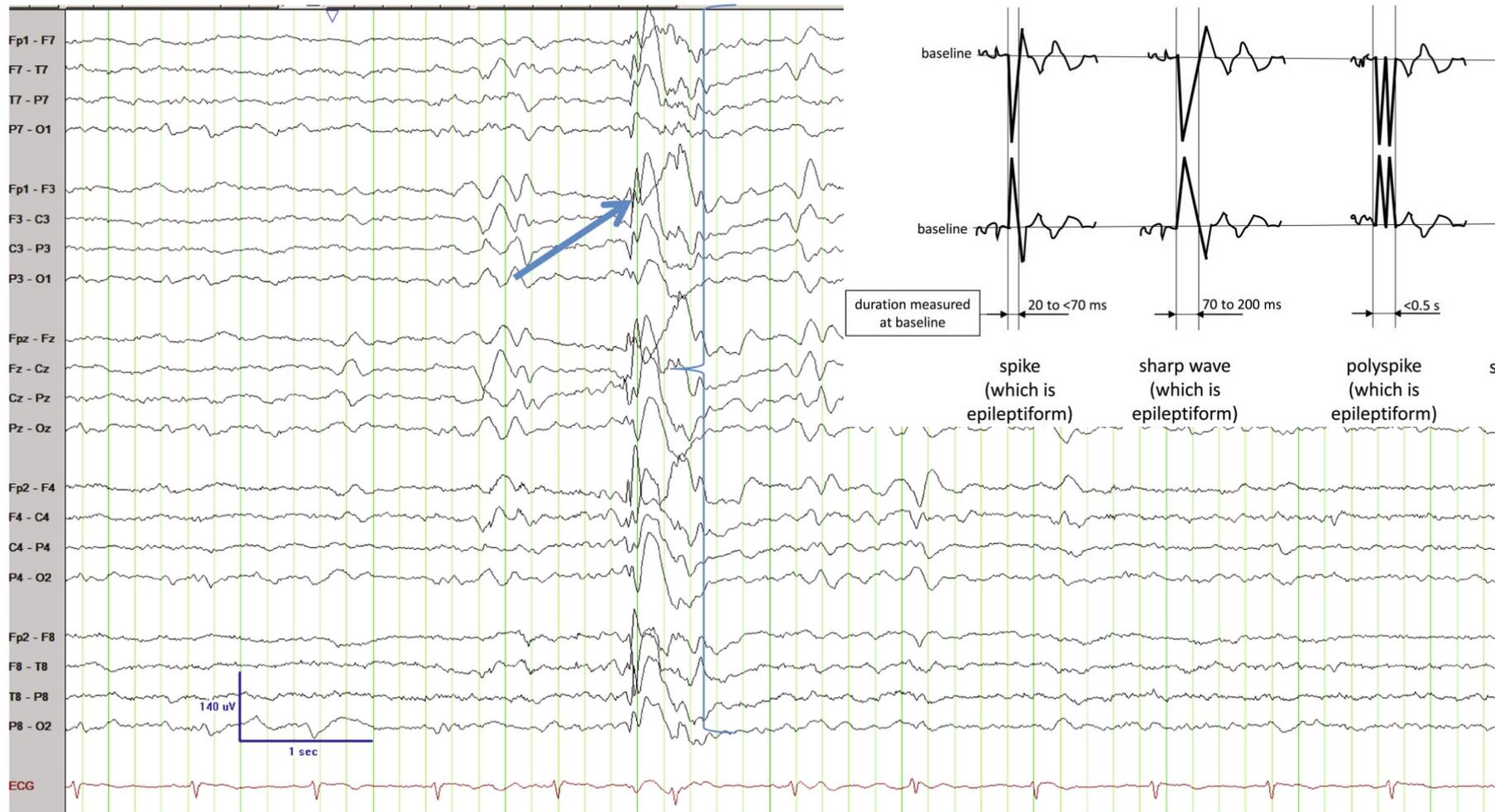


*Phase: an area under the curve on one side of the baseline

Sporadic Epileptiform discharges

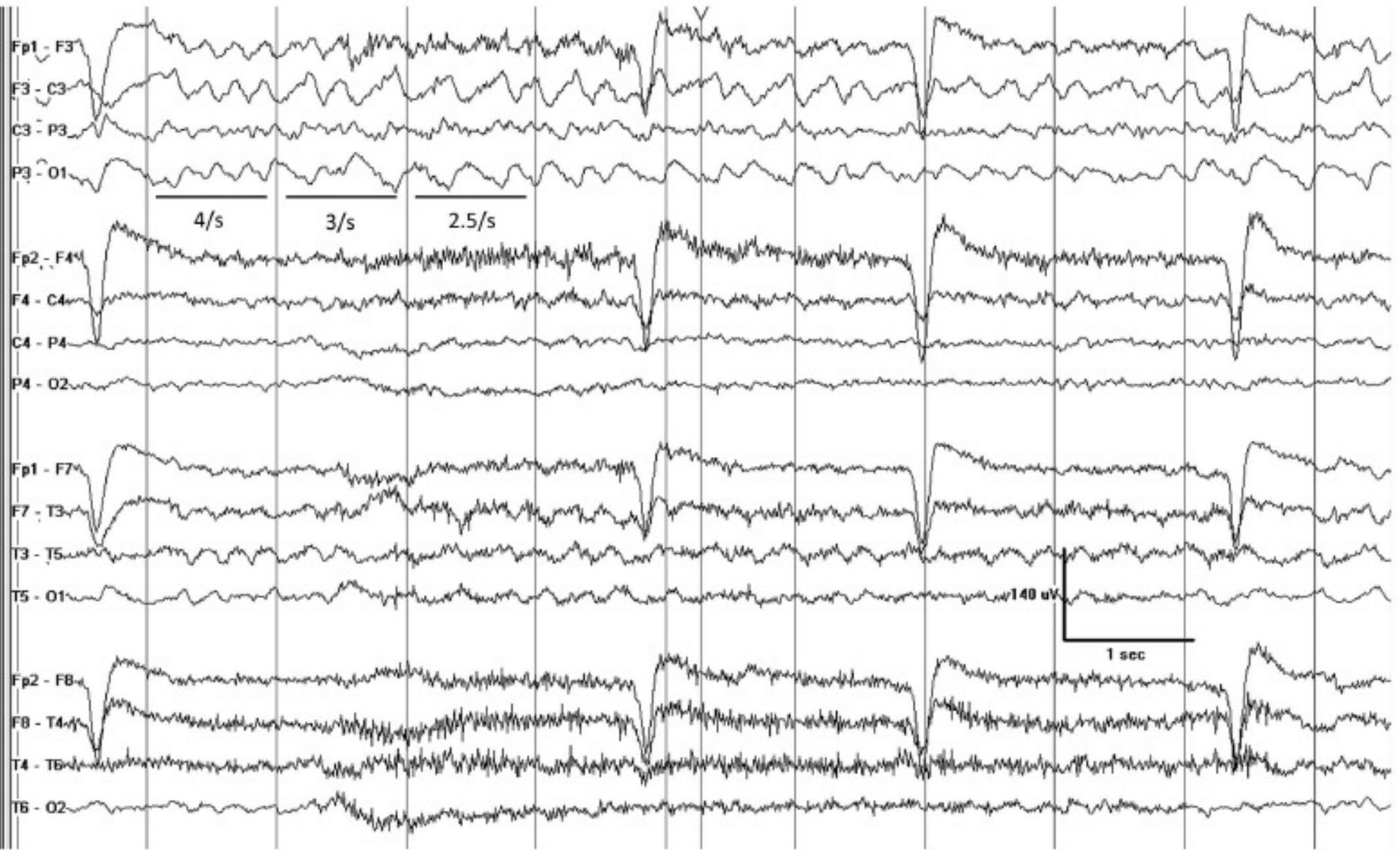






RHYTHMIC AND PERIODIC PATTERNS (RPPs)





American Clinical Neurophysiology Society's Standardized
Critical Care EEG Terminology: 2021 Version

Main term 1	Main term 2	Plus (+) Modifier
<p>G <i>Generalized</i> - Optional : Specify frontally, midline or occipitally predominant</p>	<p>PD <i>Periodic Discharges</i></p>	<p>No +</p>
<p>L <i>Lateralized</i> - Optional: Specify unilateral or bilateral asymmetric - Optional: Specify lobe(s) most involved or hemispheric</p>	<p>RDA <i>Rhythmic Delta Activity</i></p>	<p>+F <i>Superimposed fast activity – applies to PD or RDA only</i></p>
<p>BI <i>Bilateral Independent</i> - Optional: Specify symmetric or asymmetric - Optional: Specify lobe(s) most involved or hemispheric</p>	<p>SW <i>Rhythmic Spike and Wave</i> OR <i>Rhythmic Sharp and Slow Wave</i> OR <i>Rhythmic Polyspike and Wave</i></p>	<p>+R <i>Superimposed rhythmic activity – applies to PD only</i></p>
<p>Mf <i>Multifocal</i> - Optional: Specify symmetric or asymmetric - Optional: Specify lobe(s) most involved or hemispheric</p>		<p>+S <i>Superimposed sharp waves or spikes, or sharply contoured - applies to RDA only</i></p>
		<p>+FR <i>If both subtypes apply – applies to PD only</i></p>
		<p>+FS <i>If both subtypes apply – applies to RDA only</i></p>

MAIN TERM 2

Periodic Discharges (PD) → at least 6 cycles of discharges with a uniform morphology & duration with a quantifiable and regular or near regular inter-discharge interval

Discharges are waveforms with ≤ 3 phases or any waveform lasting ≤ 0.5 seconds regardless of number of phases.

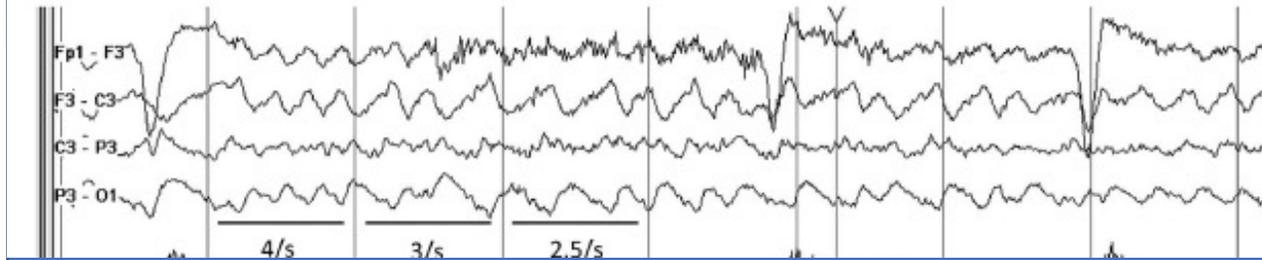
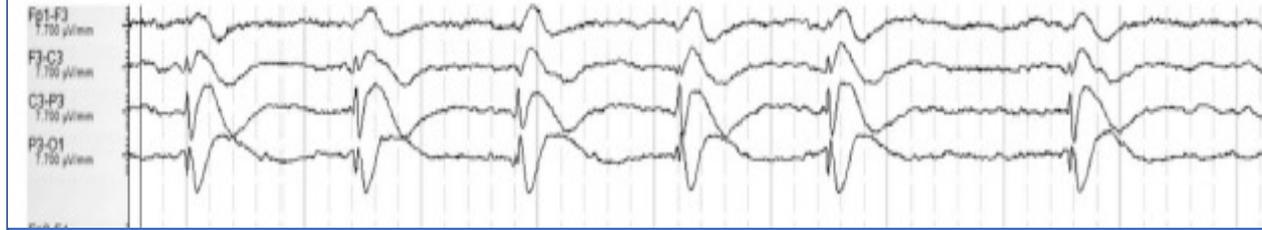
The recurrence of discharges in PD have to occur at regular or near regular intervals (i.e., the period must vary by $< 50\%$ from one cycle to the next cycle in the majority of cycle pairs).

Rhythmic Delta Activity (RDA) → at least 6 cycles of a waveform $\leq 4\text{Hz}$ with uniform morphology and duration without an interval

Similarly to PD, the duration of one cycle of an RDA must vary by $< 50\%$ from one cycle to the next cycle in the majority of cycle pairs.

! *If a pattern meets criteria for PD and RDA simultaneously, reader should interpret as PD+R rather than RDA+S.*

Spike-and-wave or Sharp-and-wave (SW) → polyspike, spike or sharp wave followed by a slow wave in a consistent, regularly repeating and alternating pattern; no interval between SW complexes



Main term 2

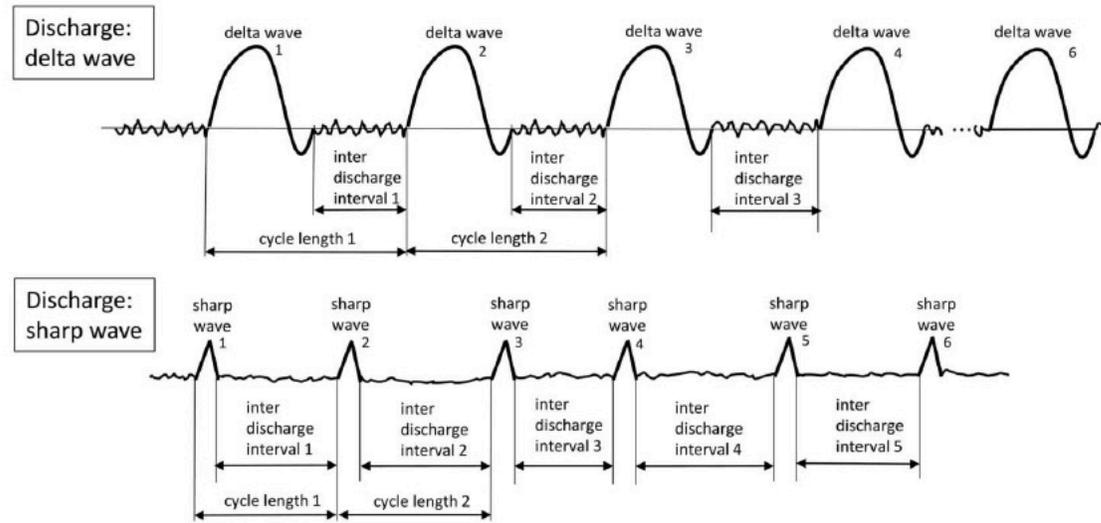


FIG. 20. Periodic Discharges (PDs).
1. Repetition of a waveform with relatively uniform morphology and duration, 2. with a clearly discernable interdischarge interval between consecutive waveforms, and 3. recurrence of the waveform at nearly regular intervals: having a cycle length (i.e., period) varying by $<50\%$ from one cycle to the next in the majority ($>50\%$) of cycle pairs. A pattern can qualify as rhythmic or periodic if and only if it continues for at least 6 cycles (e.g. 1 Hz for 6 seconds, or 3 Hz for 2 seconds).

Main term 2

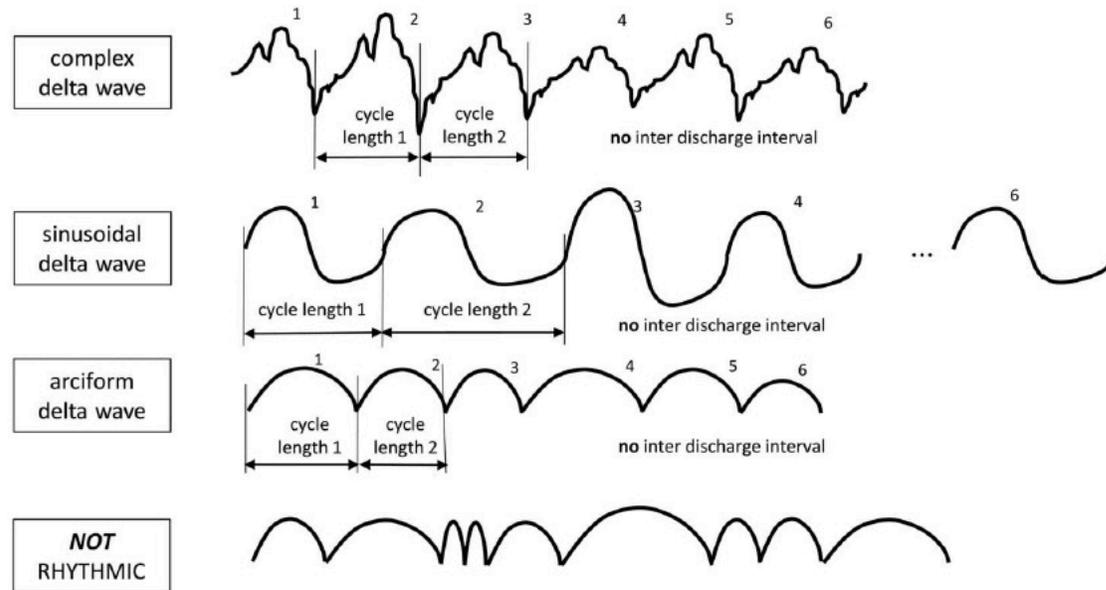


FIG. 21. Rhythmic Delta Activity (RDA).
1. Repetition of a waveform with relatively uniform morphology and duration and 2. without an interval between consecutive waveforms. 3. The duration of one cycle (i.e., the period) of the rhythmic pattern should vary by <50% from the duration of the subsequent cycle for the majority (>50%) of cycle pairs to qualify as rhythmic. A pattern can qualify as rhythmic or periodic if and only if it continues for at least 6 cycles (e.g. 1 Hz for 6 seconds, or 3 Hz for 2 seconds).

Main term 2

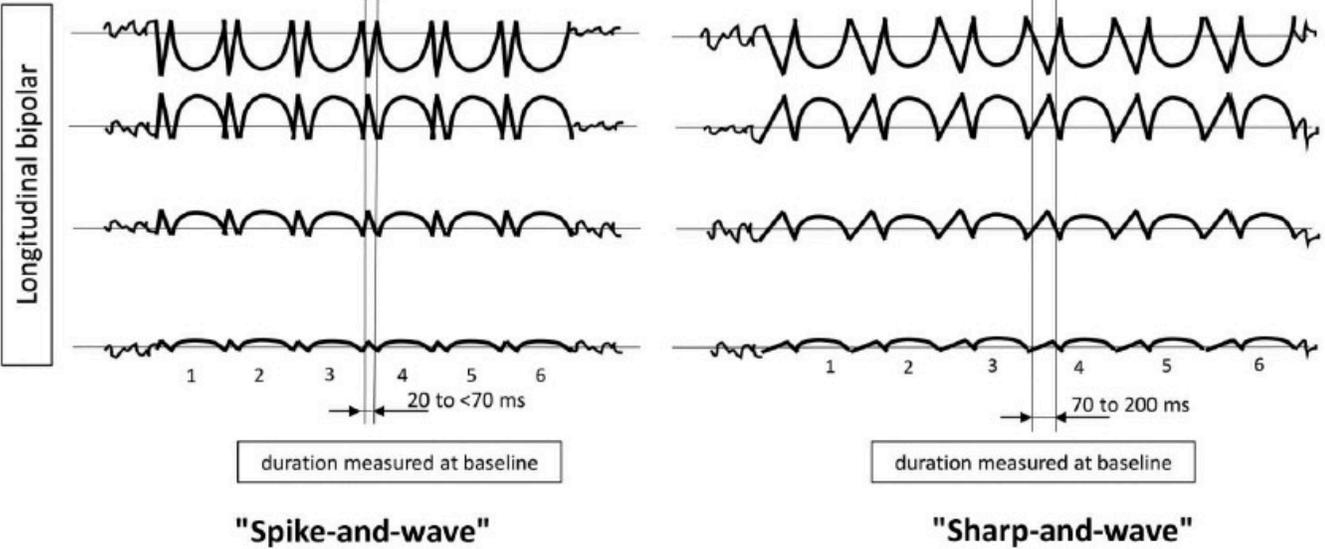


FIG. 22. "Spike-and-wave" or "Sharp-and-wave" (SW). Spike-and-wave or Sharp-and-wave (SW): Polyspike, spike, or sharp wave consistently followed by a slow wave in a regularly repeating and alternating pattern (spike-wave-spike-wave-spike-wave), with a consistent relationship between the spike (or polyspike or sharp wave) component and the slow wave for at least 6 cycles; and with no interval between one spike-wave complex and the next (if there is an interval, this would qualify as PDs, where each discharge is a spike-and-wave).

Main term 1

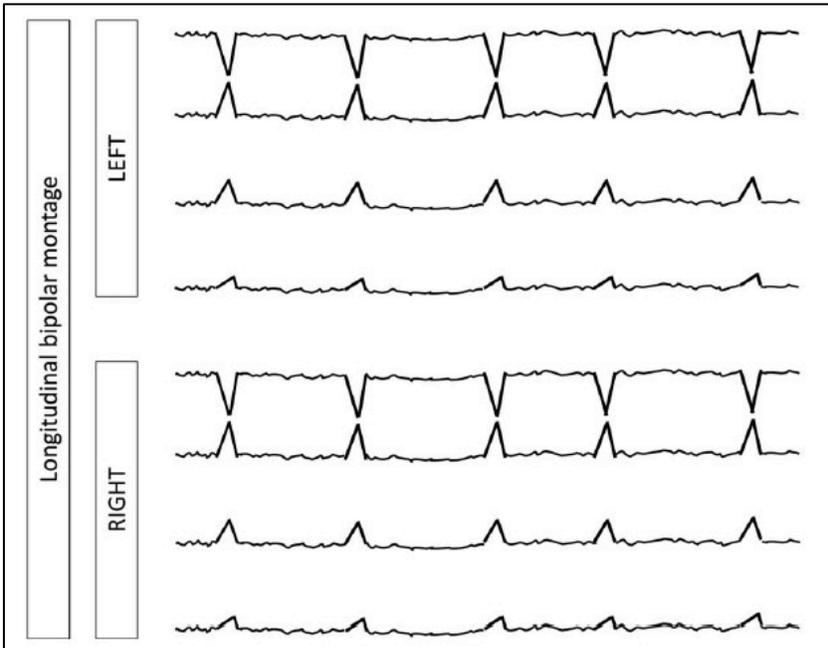


FIG. 13. Generalized Periodic Discharges (GPDs). Generalized: Bilateral synchronous and symmetric periodic discharges. In this case, the pattern is “frontally predominant.”

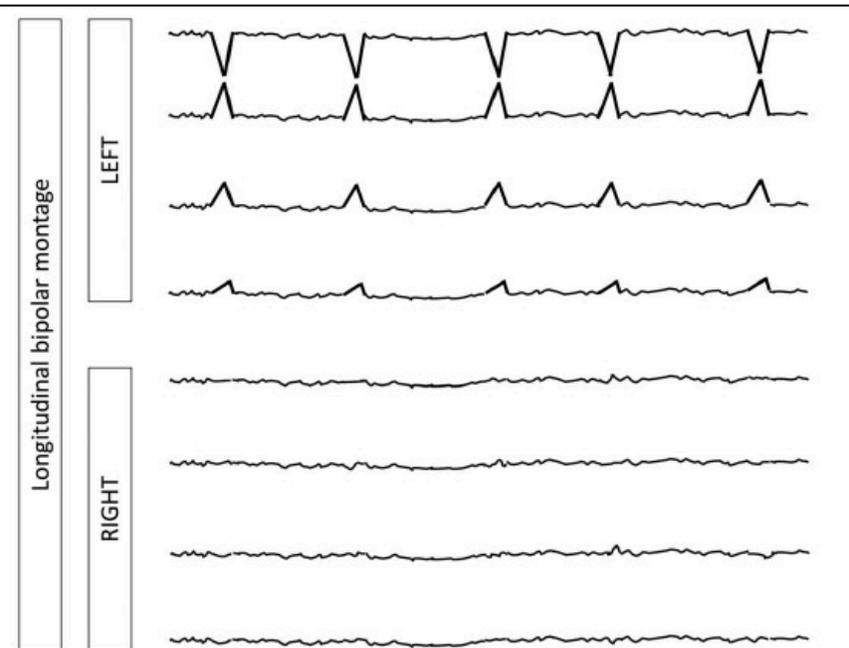


FIG. 14. Lateralized Periodic Discharges (LPDs, unilateral). Unilateral: Periodic discharges only seen in one hemisphere (in this case left).

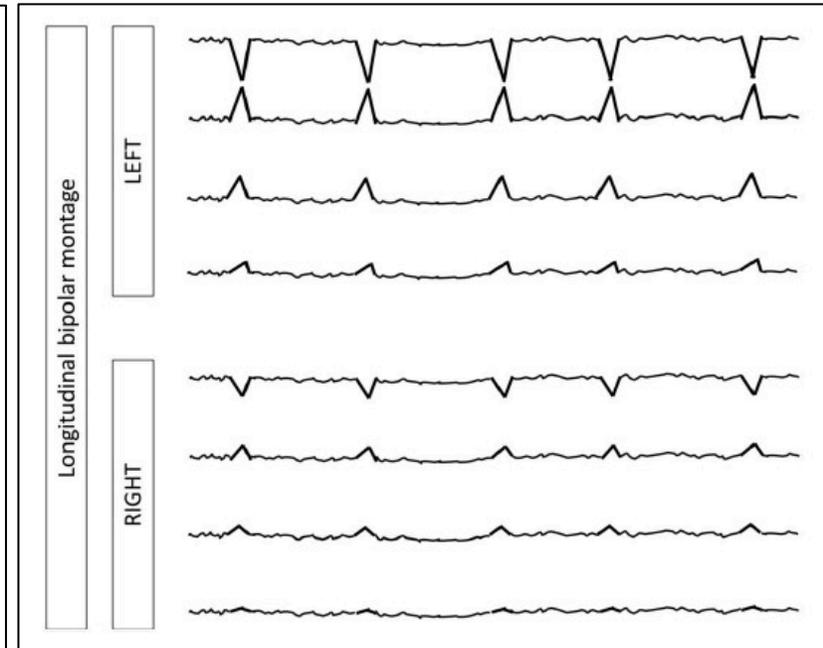


FIG. 15. Lateralized Periodic Discharges (LPDs, bilateral asymmetric). Bilateral asymmetric: Periodic discharges seen bilaterally but clearly and consistently (>80% of the time) higher amplitude over one hemisphere (in this case left).

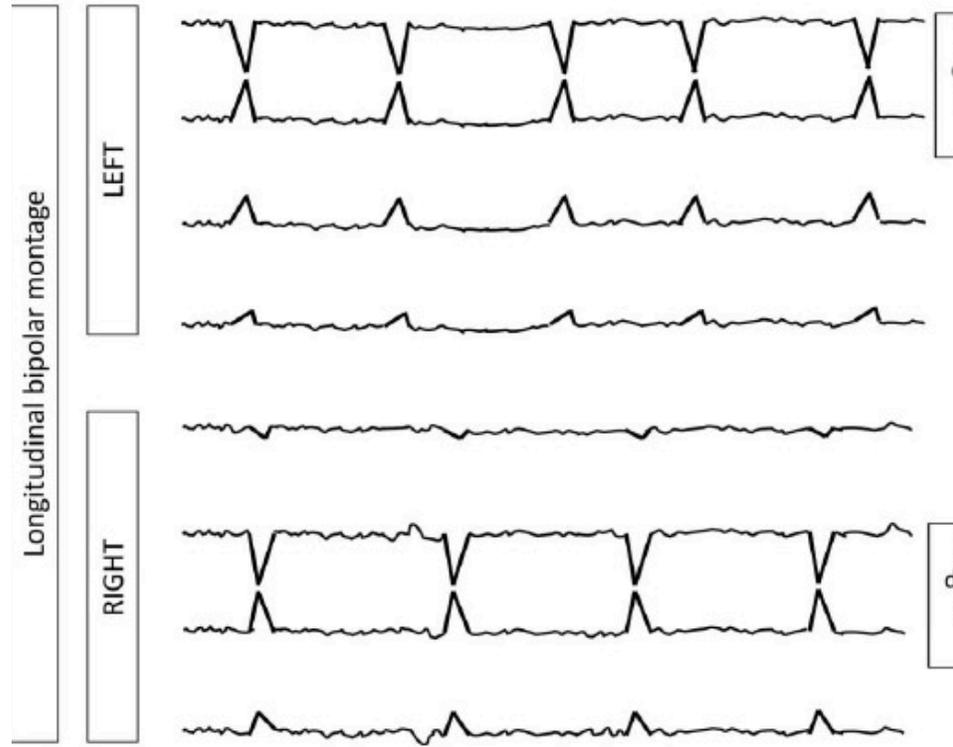


FIG. 17. Bilateral Independent Periodic Discharges (BIPDs). BIPDs, lateralized patterns occur in each hemisphere asynchronously and at different frequencies.

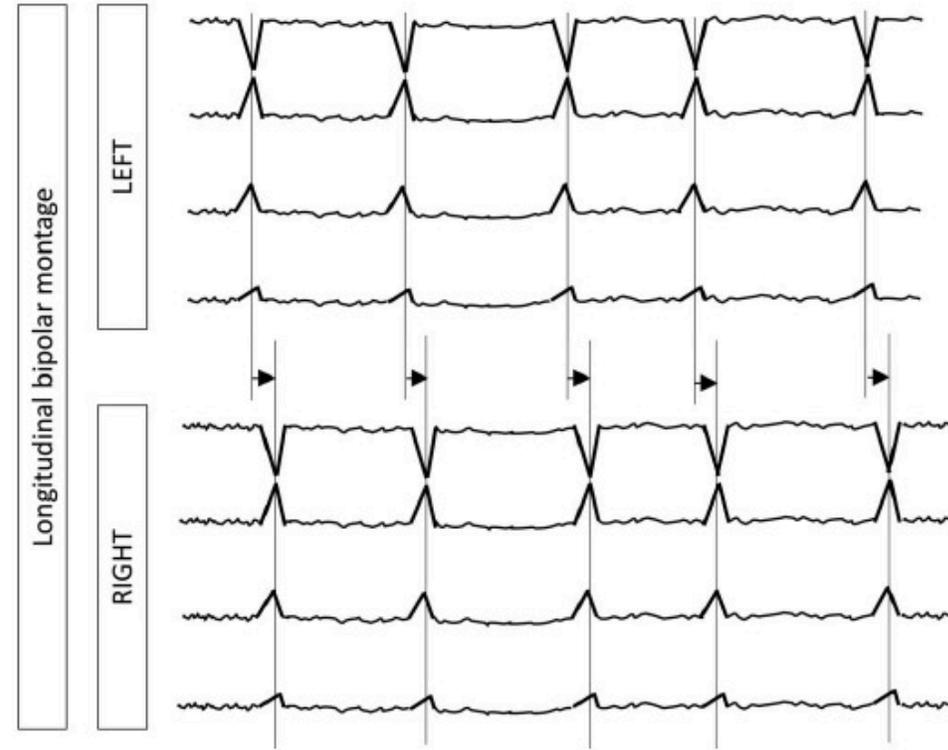


FIG. 16. Lateralized Periodic Discharges (LPDs, bilateral asynchronous). Bilateral asynchronous: Periodic discharges seen bilaterally but clearly and consistently (>80% of the time) earlier on one side (in this case left). These are not Bilateral Independent (BI) because the latency between hemispheres is fixed (i.e., they are not independent populations).



19. Multifocal Periodic Discharges (MfPDs). In MfPDs, periodic discharges occur in three independent locations simultaneously with at least one in each hemisphere. If all three locations occurred within a single hemisphere this would remain a focal discharge.

18. Unilateral Independent Periodic Discharges (UIPDs). In UIPDs, periodic discharges occur in two independent locations simultaneously with both populations within a single hemisphere (this case left).

Major modifiers										Minor modifiers		
Prevalence	Duration	Frequency	Phases ¹	Sharpness ²	Absolute Amplitude	Relative Amplitude ³	Polarity ²	Stimulus Induced	Evolution ⁴	Onset	Triphasic ⁵	Lag
Continuous ≥90%	Very long ≥1h	≥4/s	>3	Spiky <70ms	High ≥200μV	>2	Negative	SI <i>Stimulus Induced</i>	Evolving	Sudden ≤3s	Yes	A-P <i>Anterior-Posterior</i>
		3.5/s	3									
Abundant 50-89%	Long 5-59min	3/s	2	Sharp 70-200ms	Medium 50-199μV	≤2	Positive	Sp <i>Spontaneous only</i>	Fluctuating	Gradual >3s	No	P-A <i>Posterior-Anterior</i>
		2.5/s	1									
Frequent 10-49%	Intermediate duration 1-4.9min	2/s	1	Sharply contoured >200ms	Low 20-49μV		Dipole	Unk <i>Unknown</i>	Static			No
		1.5/s										
Occasional 1-9%	Brief 10-59s	1/s		Blunt >200ms	Very low <20μV		Unclear					
		0.5/s										
Rare <1%	Very brief <10s	<0.5/s										

- NOTE 1: Applies to PD and and SW only, including the slow wave of the SW complex
- NOTE 2: Applies to the predominant phase of PD and the spike or sharp component of SW only
- NOTE 3: Applies to PD only
- NOTE 4: Refers to frequency, location or morphology
- NOTE 5: Applies to PD or SW only

Evoluzione

EVOLUTIVO

1



2



3



FLUTTUANTE

1



2



3



2



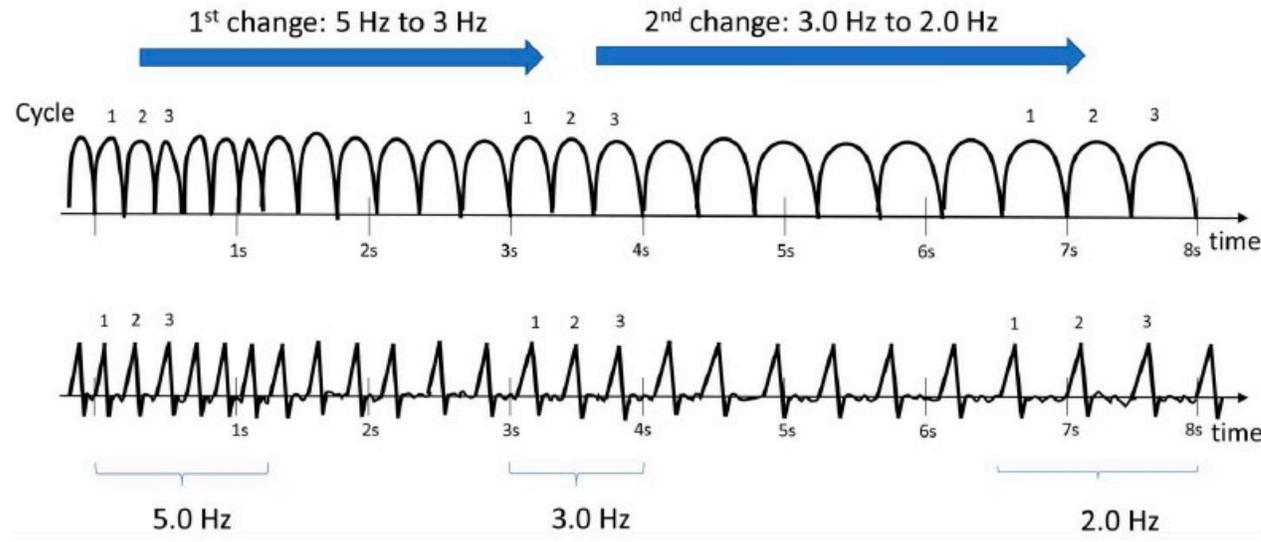


FIG. 24. Evolution of frequency. At least 2 unequivocal, sequential changes in frequency; defined as at least 2 consecutive changes in the same direction by at least 0.5 Hz. To qualify as present, a single frequency must persist for at least 3 cycles. The criteria for evolution must be reached without the evolving feature (frequency) remaining unchanged for 5 or more continuous minutes.

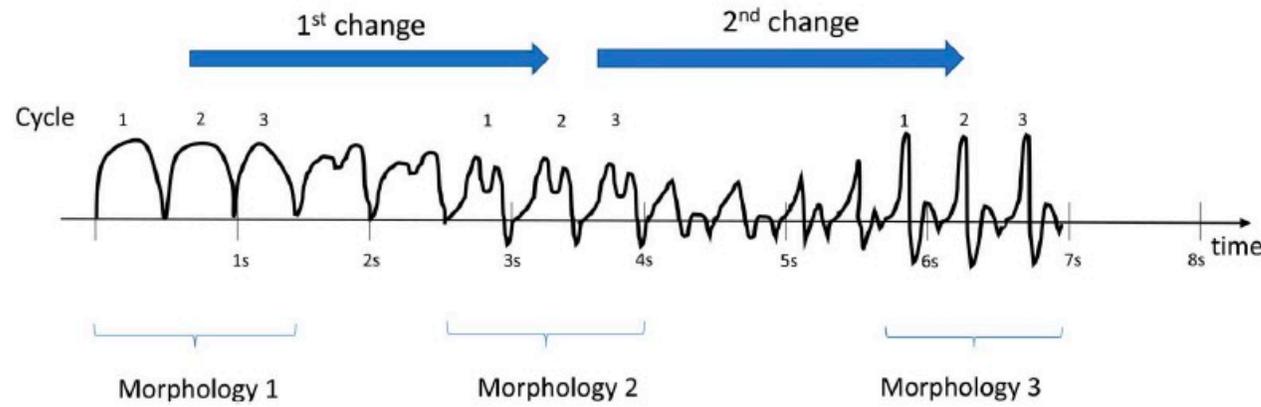


FIG. 25. Evolution of morphology. At least 2 consecutive changes to a novel morphology. Each different morphology or each morphology plus its transitional forms must last at least 3 cycles.

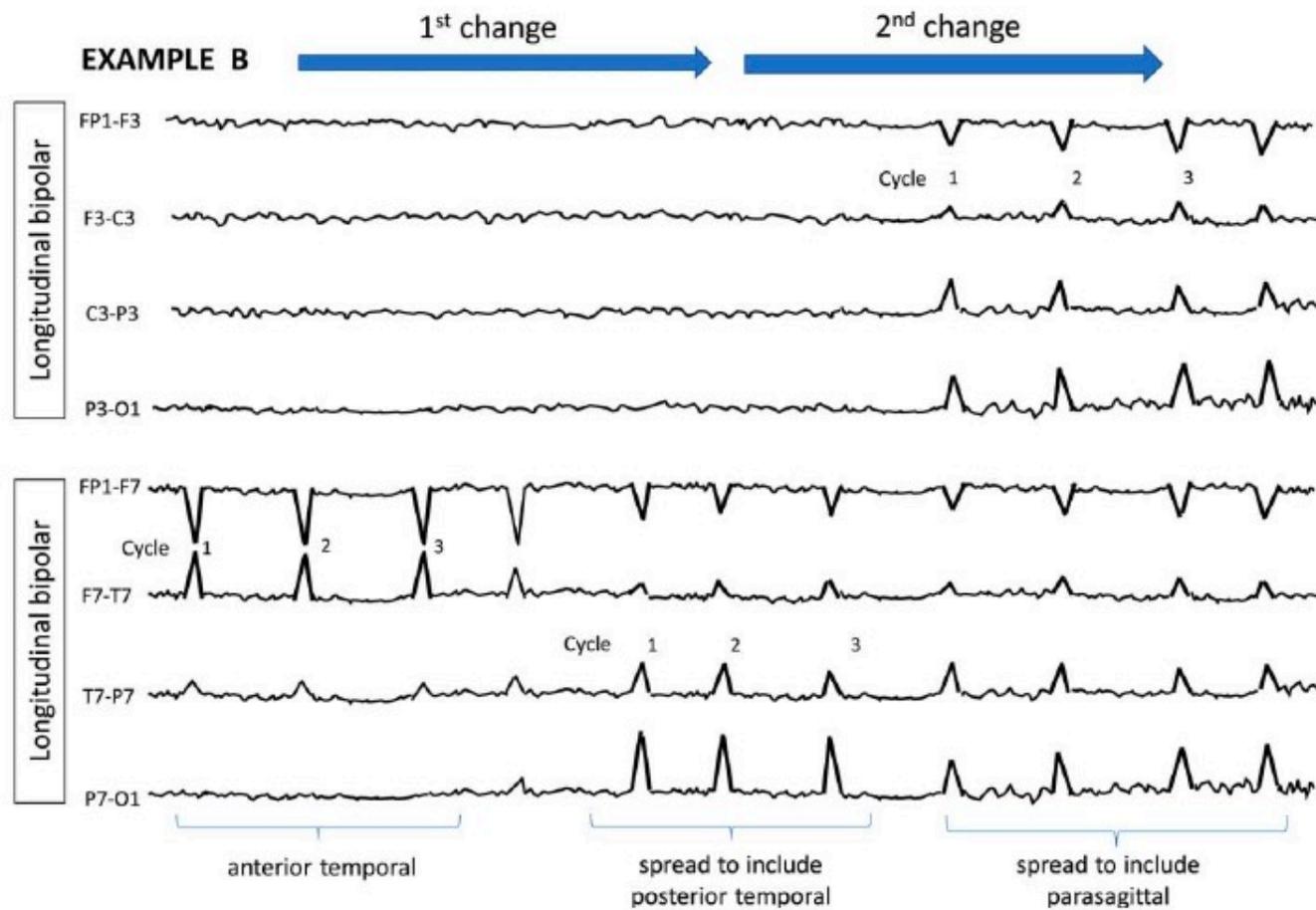


FIG. 26. Evolution of location. Defined as sequentially spreading into or sequentially out of at least two different standard 10–20 electrode locations. To qualify as present, a single location must persist for at least 3 cycles.

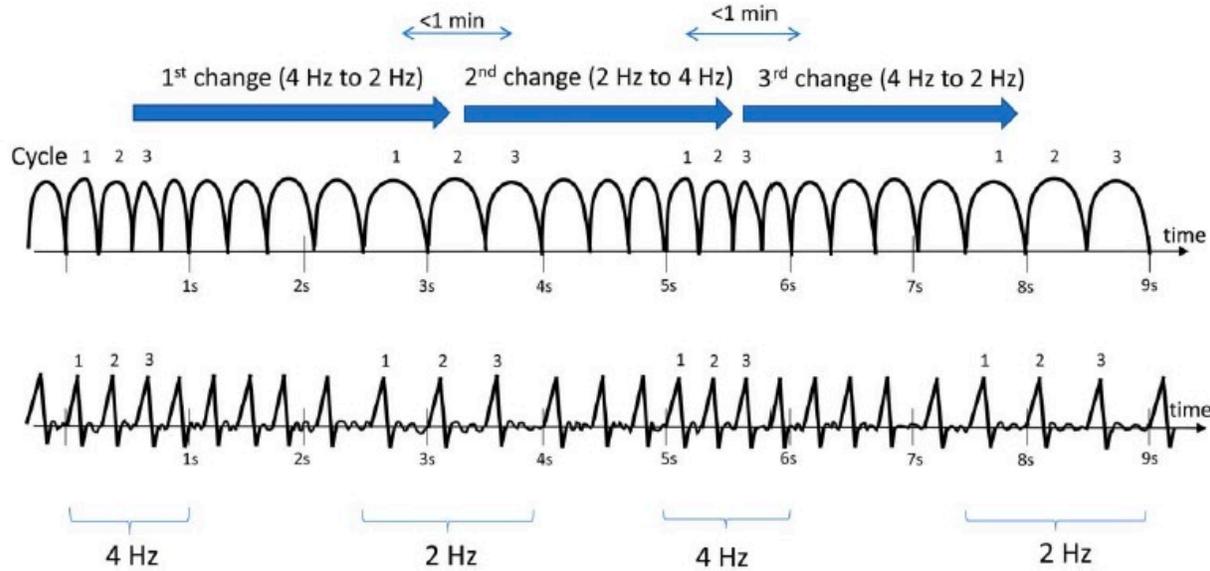


FIG. 27. Fluctuating frequency. ≥ 3 changes, not more than one minute apart, in frequency (by at least 0.5 Hz), but *not qualifying as evolving*. This includes patterns fluctuating from 1 to 1.5 to 1 to 1.5 Hz. To qualify as present, a single frequency must persist at least 3 cycles (e.g. 1 Hz for 3 seconds, or 3 Hz for 1 seconds).

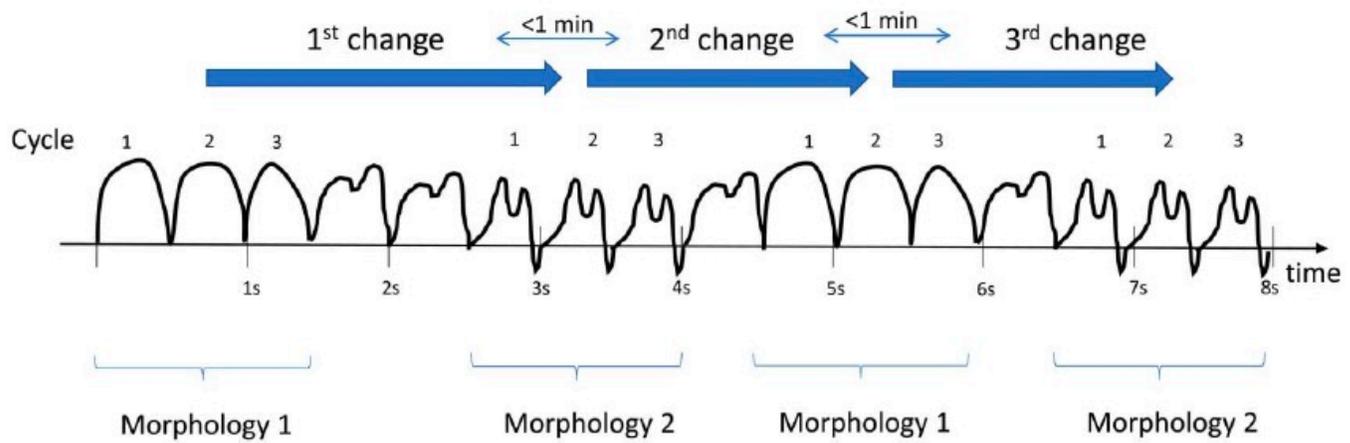


FIG. 28. Fluctuating morphology. ≥ 3 changes, not more than one minute apart, in morphology, but *not qualifying as evolving*. This includes patterns alternating between 2 morphologies repeatedly. To qualify as present, a single morphology must persist at least 3 cycles.

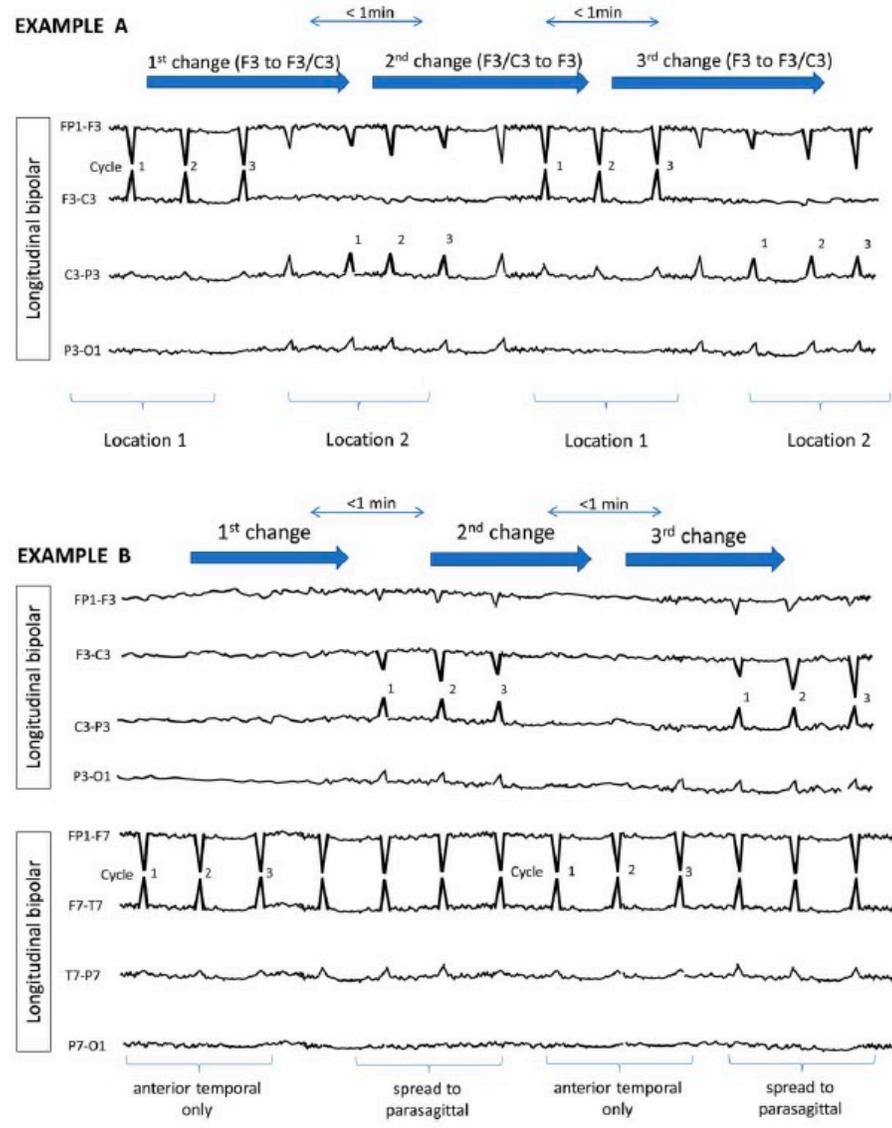


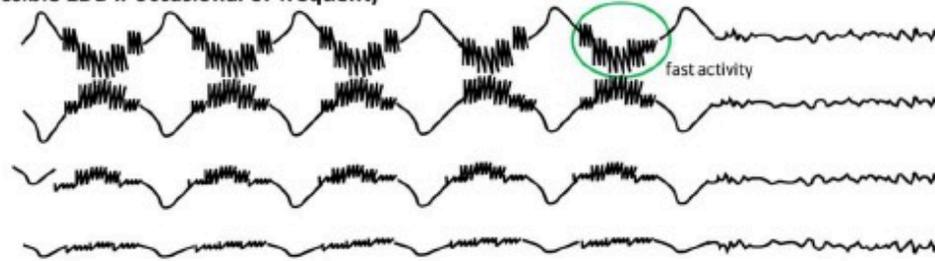
FIG. 29. Fluctuating location. ≥ 3 changes, not more than one minute apart, in location (by at least 1 standard inter-electrode distance), but *not qualifying as evolving*. This includes patterns spreading in and out of a single electrode repeatedly. To qualify as present, a single location must persist at least 3 cycles.

ACNS Standardized Critical Care EEG Terminology: 2012 version Reference Chart

Main term 1	Main term 2	Plus (+) Modifier
<p>G <i>Generalized</i> - Optional : Specify frontally, midline or occipitally predominant</p>	<p>PD <i>Periodic Discharges</i></p>	<p>No +</p>
<p>L <i>Lateralized</i> - Optional: Specify unilateral or bilateral asymmetric - Optional: Specify lobe(s) most involved or hemispheric</p>	<p>RDA <i>Rhythmic Delta Activity</i></p>	<p>+F <i>Superimposed fast activity – applies to PD or RDA only</i></p>
<p>BI <i>Bilateral Independent</i> - Optional: Specify symmetric or asymmetric - Optional: Specify lobe(s) most involved or hemispheric</p>	<p>SW <i>Rhythmic Spike and Wave</i> OR <i>Rhythmic Sharp and Slow Wave</i> OR <i>Rhythmic Polyspike and Wave</i></p>	<p>+R <i>Superimposed rhythmic activity – applies to PD only</i></p>
<p>Mf <i>Multifocal</i> - Optional: Specify symmetric or asymmetric - Optional: Specify lobe(s) most involved or hemispheric</p>		<p>+S <i>Superimposed sharp waves or spikes, or sharply contoured - applies to RDA only</i></p>
		<p>+FR <i>If both subtypes apply – applies to PD only</i></p>
		<p>+FS <i>If both subtypes apply – applies to RDA only</i></p>

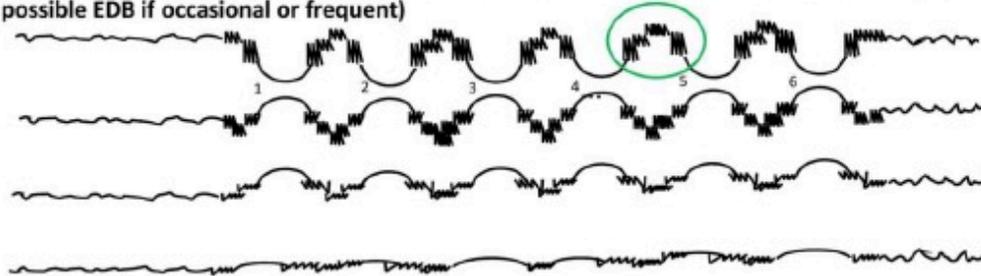
Longitudinal bipolar

EXAMPLE A: RDA+F (also qualifies as definite EDB if the RDA is abundant or continuous, or possible EDB if occasional or frequent)



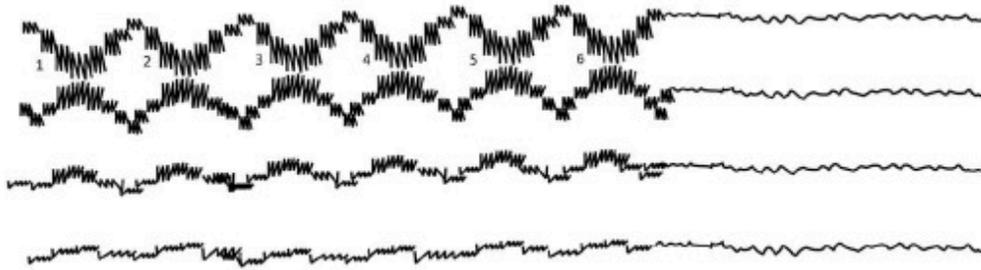
Longitudinal bipolar

EXAMPLE B: RDA+F (also qualifies as definite EDB if the RDA is abundant or continuous, or possible EDB if occasional or frequent)



Longitudinal bipolar

EXAMPLE C: RDA+F (also qualifies as possible EDB if the RDA is abundant or continuous)



Longitudinal bipolar

EXAMPLE D: RDA (**NOT** +F, as fast activity is part of the background and present even when the pattern is not; **NOT** EDB since not RDA+F or periodic delta bushes)

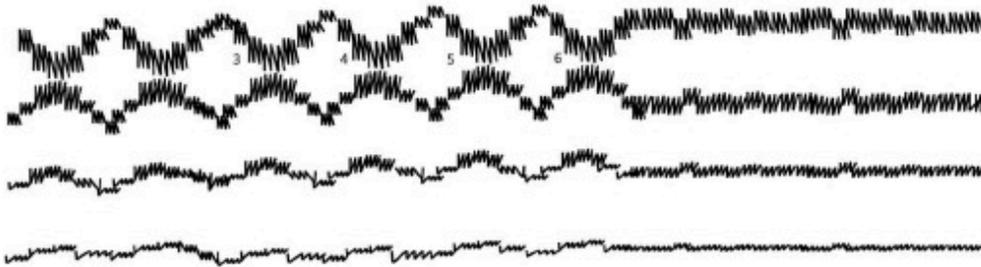


FIG. 31. Rhythmic Delta Activity PLUS fast activity (RDA+F). If a pattern qualifying as RDA or PDs has associated continuous fast frequencies (theta or faster), this can and should be coded as +F if the fast activity is not present in the background activity when the RDA or PDs is not present.  fast activity cycling with the rhythmic delta and having a stereotyped relationship to the delta wave. EDB = Extreme Delta Brush.

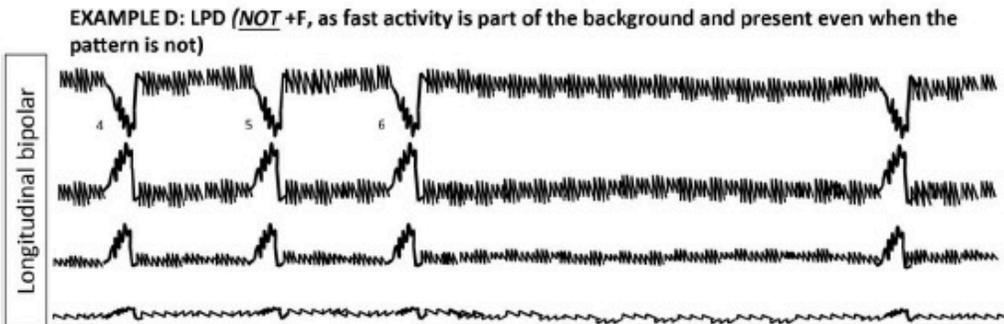
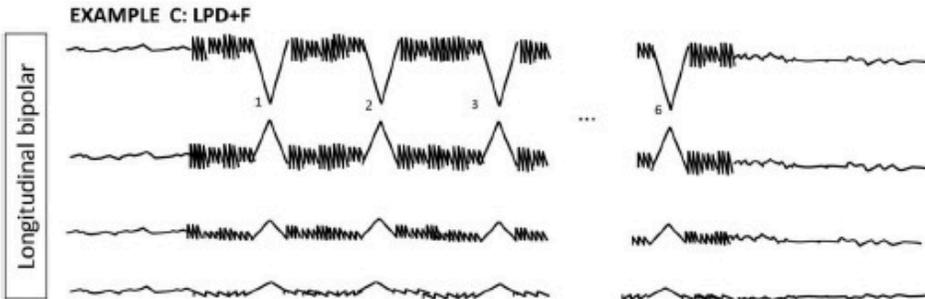
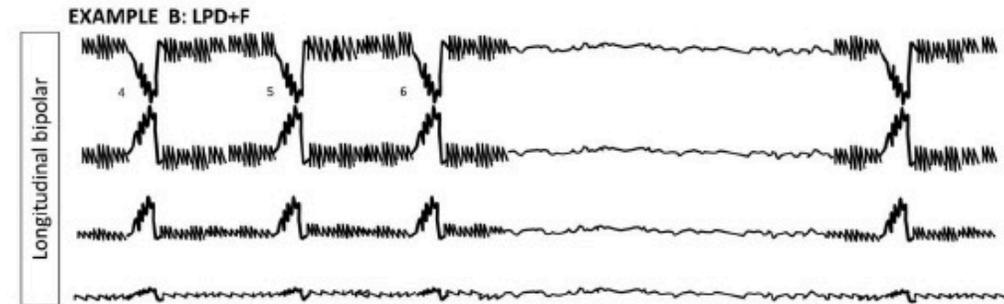
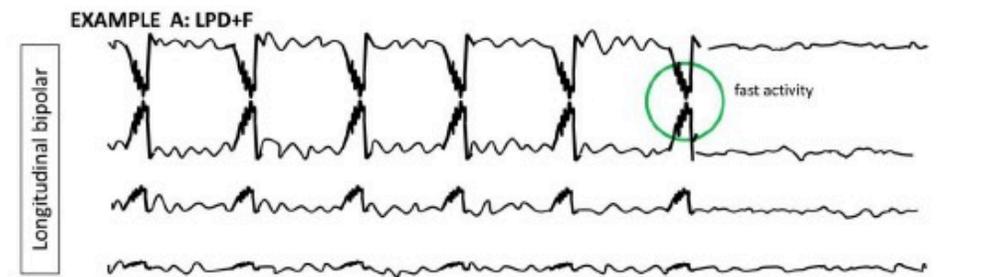


FIG. 30. Lateralized Periodic Discharges PLUS *fast* activity (LPDs+F). Code as +F if the fast activity is part of the RDA or PDs pattern and not simply part of the background activity. ○fast activity cycling with the periodic discharge.

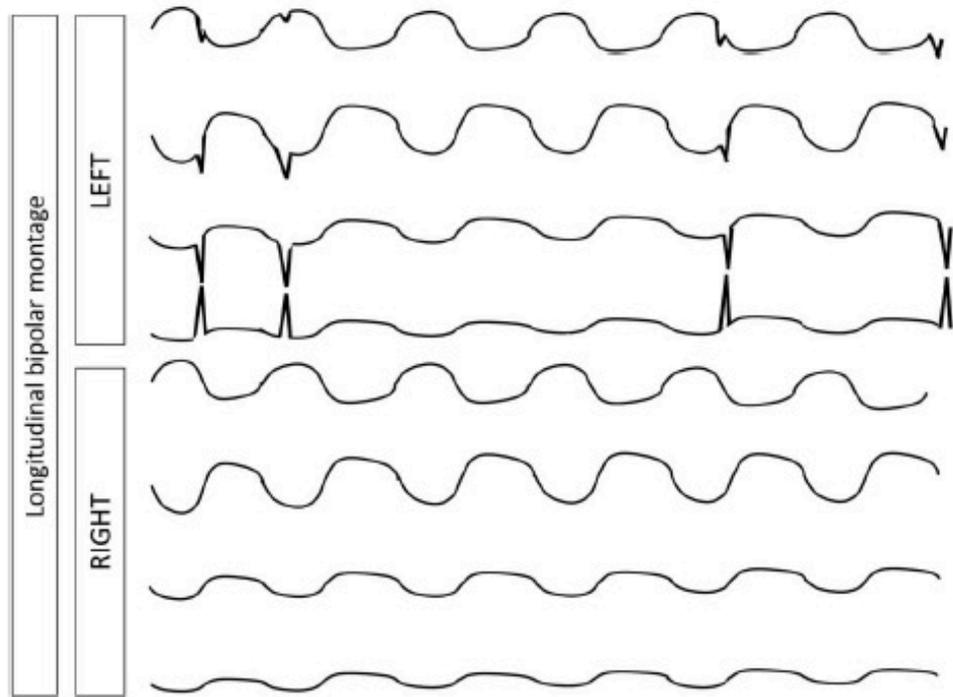


FIG. 33. Generalized Rhythmic Delta Activity PLUS Spikes (GRDA+S). Generalized rhythmic delta activity with associated spikes in one hemisphere only (RDA on one side and synchronous RDA +S on the other) would still qualify as GRDA+S.

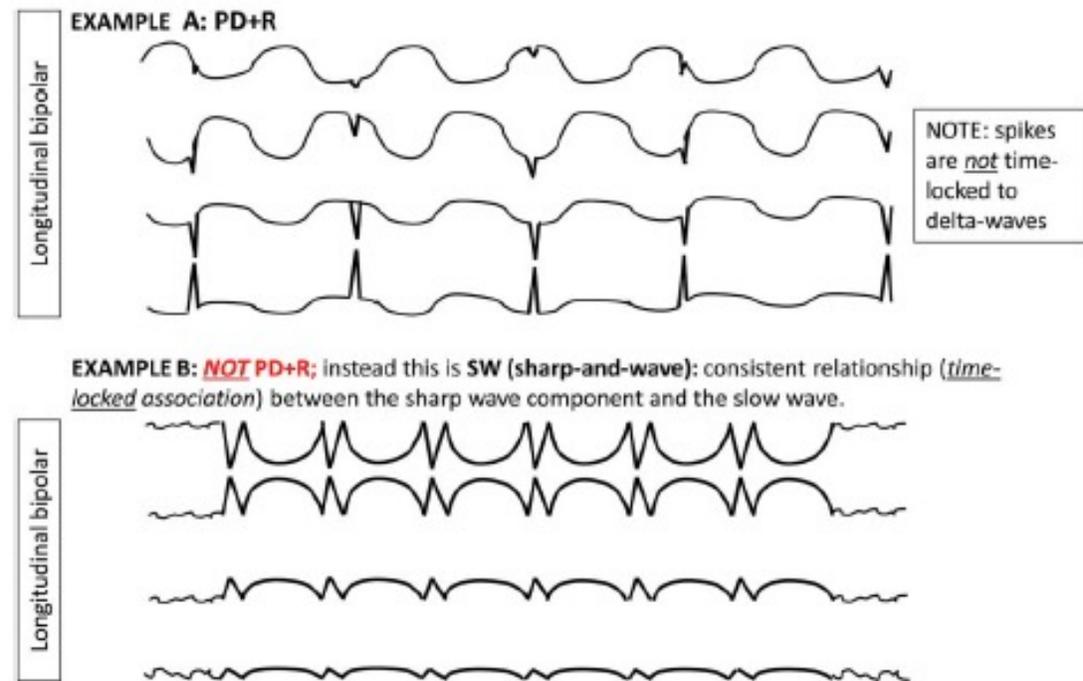
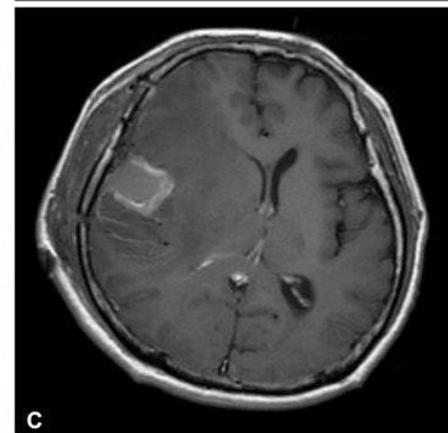
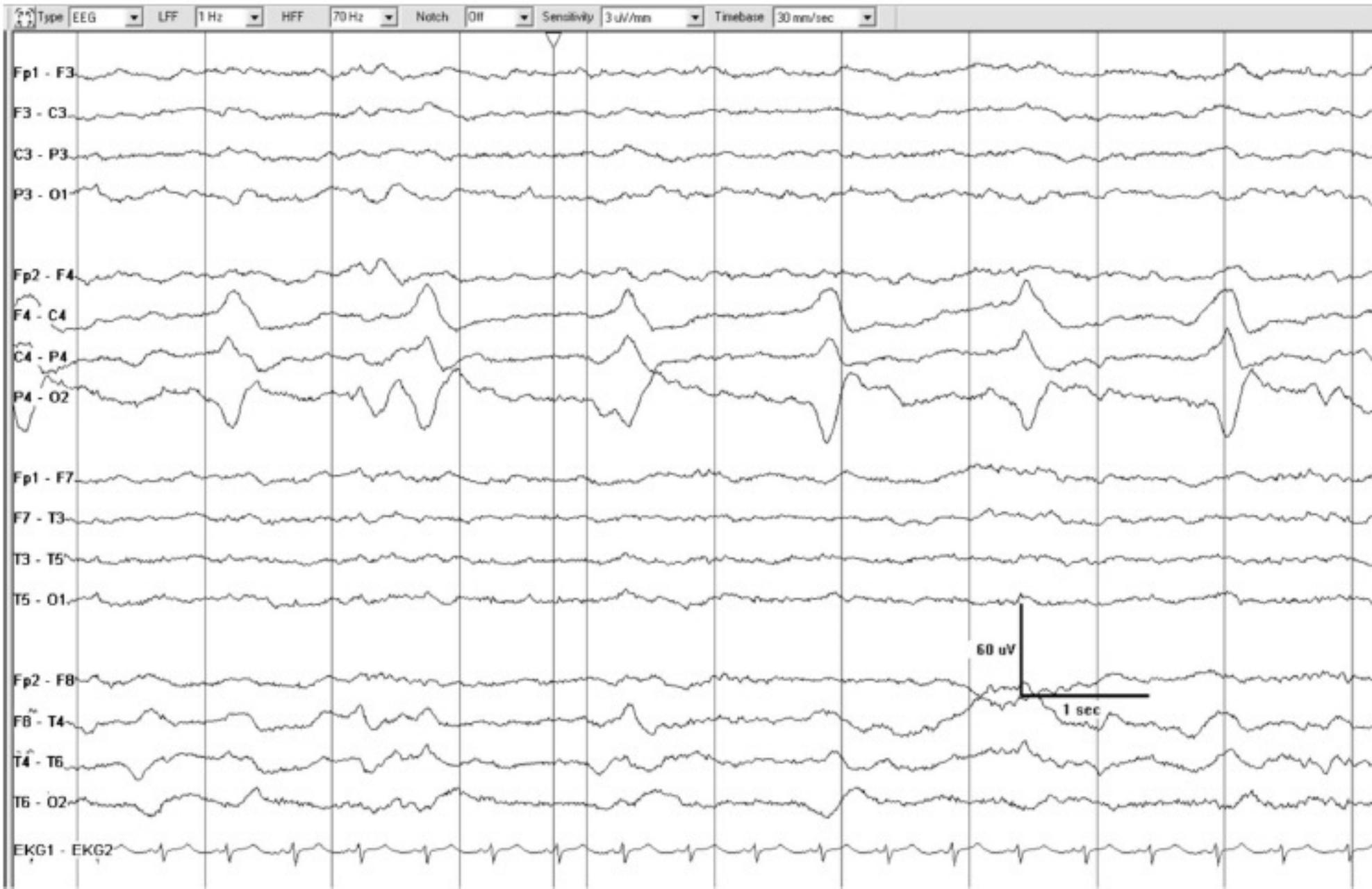


FIG. 32. Periodic Discharges PLUS RDA (PDs+R). RDA occurring at the same time as PDs but *without* time-locked association with the PDs would qualify as PDs+R.

TABLE 1. New Terms for Older Terms

OLD Term		NEW Term
Triphasic waves, most of record	=	continuous 2/s GPDs (with triphasic morphology)
PLEDs	=	LPDs
BIPLEDs	=	BIPDs
GPEDs/PEDs	=	GPDs
FIRDA	=	Occasional frontally predominant brief 2/s GRDA (if 1-10% of record)
PLEDS+	=	LPDs+
SIRPIDs* w/ focal evolving RDA	=	SI-Evolving LRDA
Lateralized seizure, delta frequency	=	Evolving LRDA
Semirhythmic delta	=	Quasi-RDA

*SIRPIDs = stimulus-induced rhythmic, periodic or ictal discharges.



Lateralized periodic discharge (LPD)

- They consist of lateralized complexes, usually 1-2 Hz, often as sharp waves or spikes which may be followed by a slow wave
- LPDs are indicative of an **acute non-specific brain dysfunction** or unilateral brain lesion, usually destructive, and they are most often present in cases of cerebral infarction.
- LPDs are usually recorded on the area adjacent to infarction, which is partially affected by the disease process and is able to generate electrical activity (Chong et al., 2005; Brenner 2004).
- Some authors emphasized the importance of associated metabolic disturbances.
- LPDs have frequently been associated with acute cerebral injury secondary to:
 - **vascular events** (Chatrian et al., 1964a; Markand and Daly, 1971; Schwartz et al., 1973; De La Paz and Brenner, 1981;
 - **viral infections** (Schwartz et al. 1973),
 - **cerebral tumors** (Schwartz et al., 1973; Erkulvrawatr, 1977; Walsh and Brenner, 1987)

LPD: ictal or interictal

- LPDs tend to be **transient** and **resolve spontaneously within 2 to 3 weeks**, the discharges tend to decrease in amplitude, the repetition rate decreases and then the discharges cease.
 - Usually seen in the acute state (usually < 24 hrs after onset of illness)
 - 50% of LPD disappear after several days
 - 90% of LPD disappear within 4 weeks
- Chronic LPDs have been reported in chronic epilepsy or old static lesions, especially related to recent seizures, alcohol withdrawal or chronic toxic-metabolic disturbances.
- The major controversy about LPD is whether they are **ictal, interictal or a postictal (?)**.
- **Increased focal glucose metabolism** has been demonstrated associated with LPDs, reinforcing their probable epileptogenic nature²⁷. Although they indicate an ictal pattern in some cases, LPDs are usually considered an interictal change or an unstable ictal-interictal continuum^{2,3}.
- LPDs are usually associated with obtundation in 95% of patients, **focal seizures and focal neurological signs may occur in 80%**, and ***epilepsia partialis continua* in 30%** of the patients^{14,23}.
- **Clinical seizures** or *status epilepticus* were seen during the course of illness in 126 (**90%**) patients in a study performed by Snodgrass et al.
- The prevalence of LPDs in routine EEG laboratories ranges from 0.1% to 1%^{13-15,30}.

LPD: ictal or interictal

Markedly Increased Mesiotemporal Lobe Metabolism in a Case with PLEDs: Further Evidence that PLEDs are a Manifestation of Partial Status Epilepticus

Adrian Handforth, Jung Tung Cheng, *Mark A. Mandelkern, and David M. Treiman

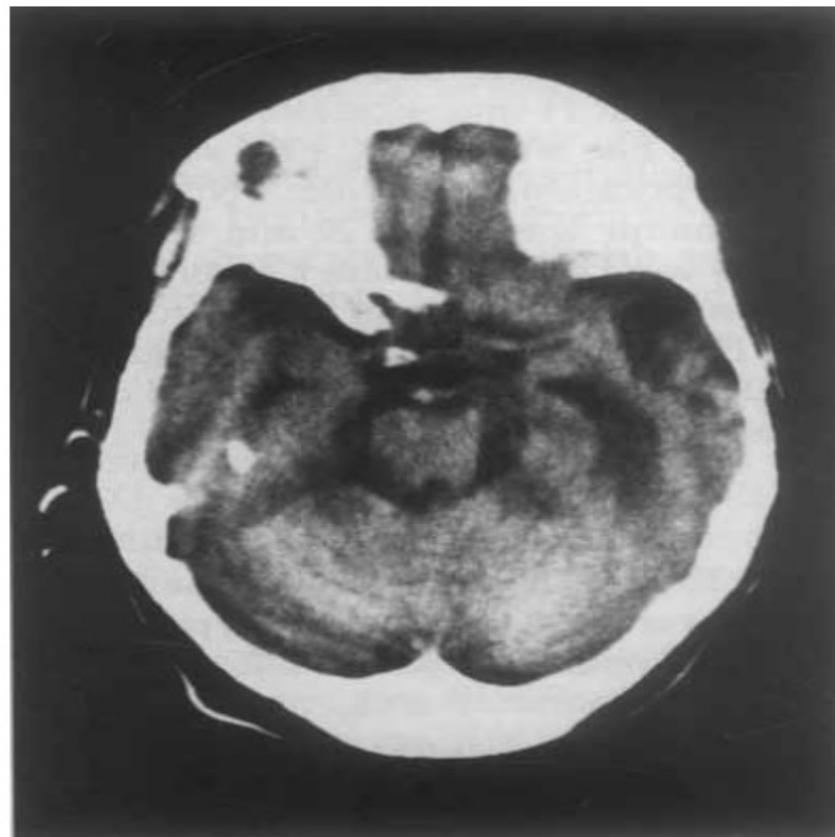
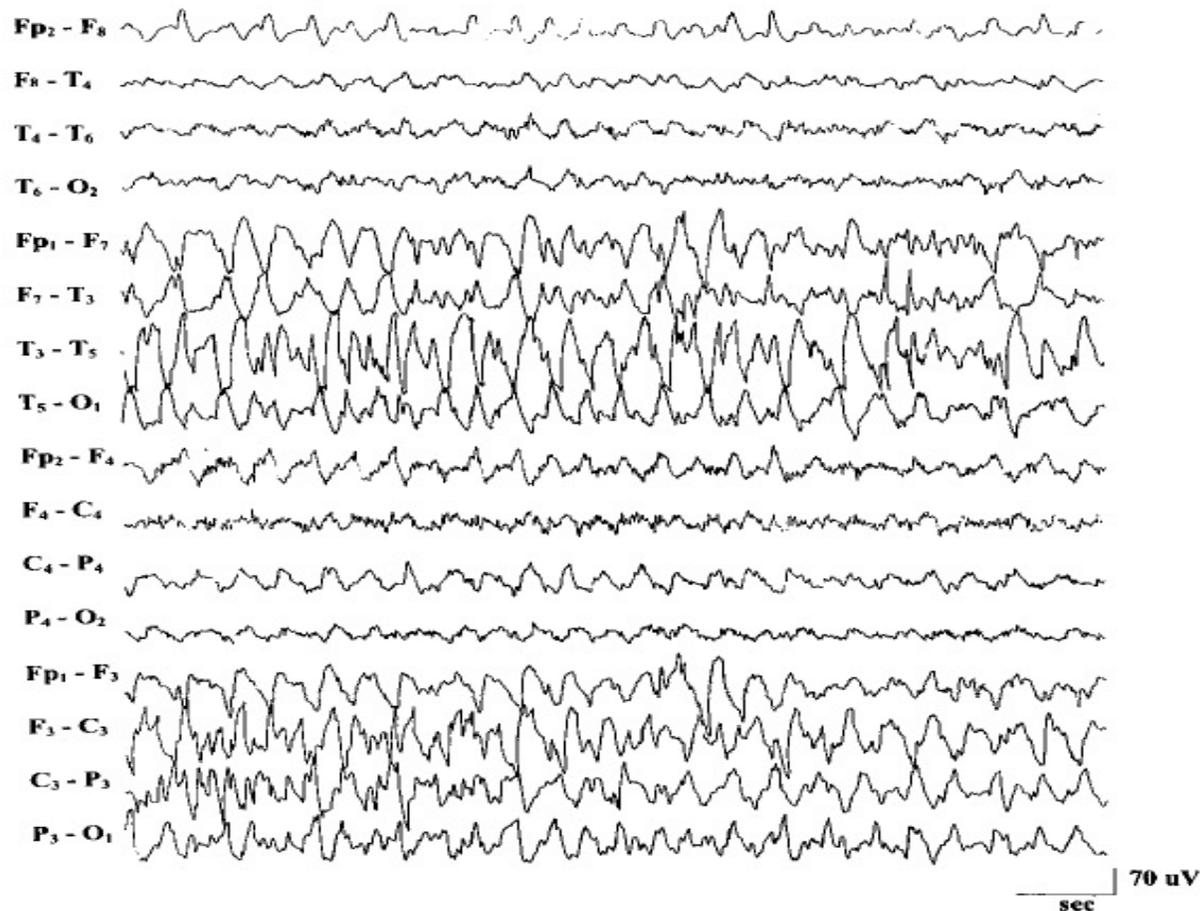


FIG.1. EEG on day 1, on presentation with generalized convulsive status epilepticus, shows predominantly left-sided seizure activity. Computed tomography scan on day 2 showed an old lesion in left temporal lobe secondary to intracerebral hemorrhage 5 years before the patient's presentation.

3 days after GTC status

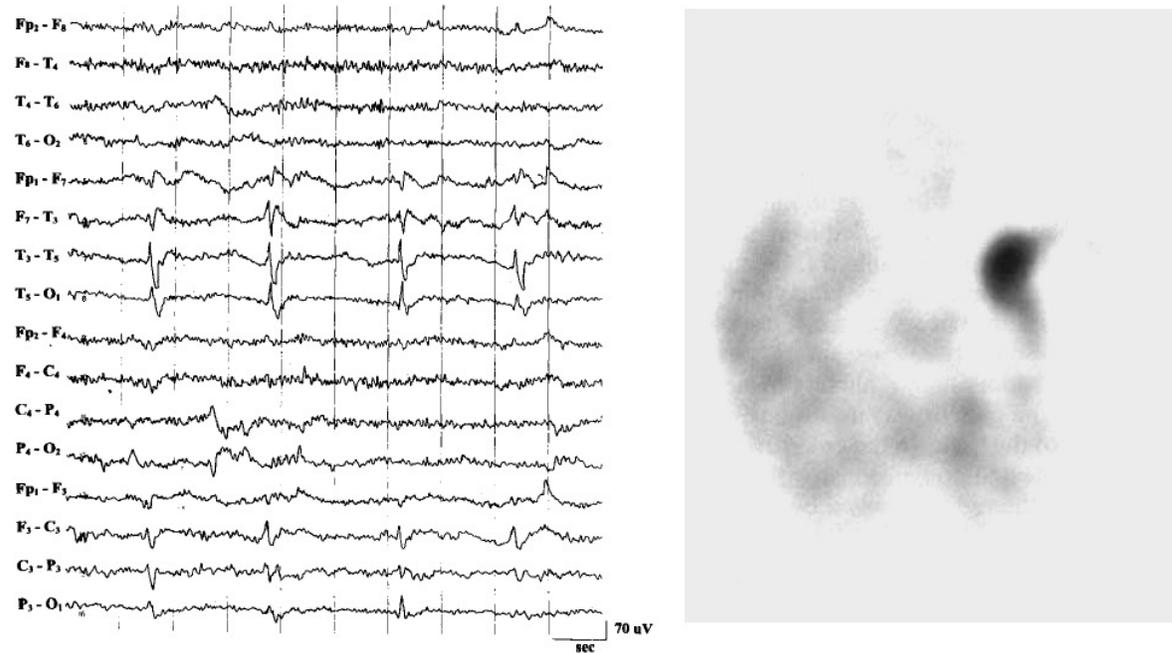


FIG. 2. EEG on day 3, after FDG-positron emission tomography (PET) scan (**right**) showed left-sided temporal-periodic lateralized epileptiform discharges (PLEDs). PLEDs were also evident on days 1 and 2 and on day 3 before the PET scan. The FDG-PET scan image was generated to display the contrast between left temporal lobe and other brain structures. Left mesiotemporal lobe showed markedly increased FDG uptake, compatible with seizure activity. Background cerebral FDG uptake was not altered except in the areas previously damaged by infarct, where uptake was reduced.

after 15 days

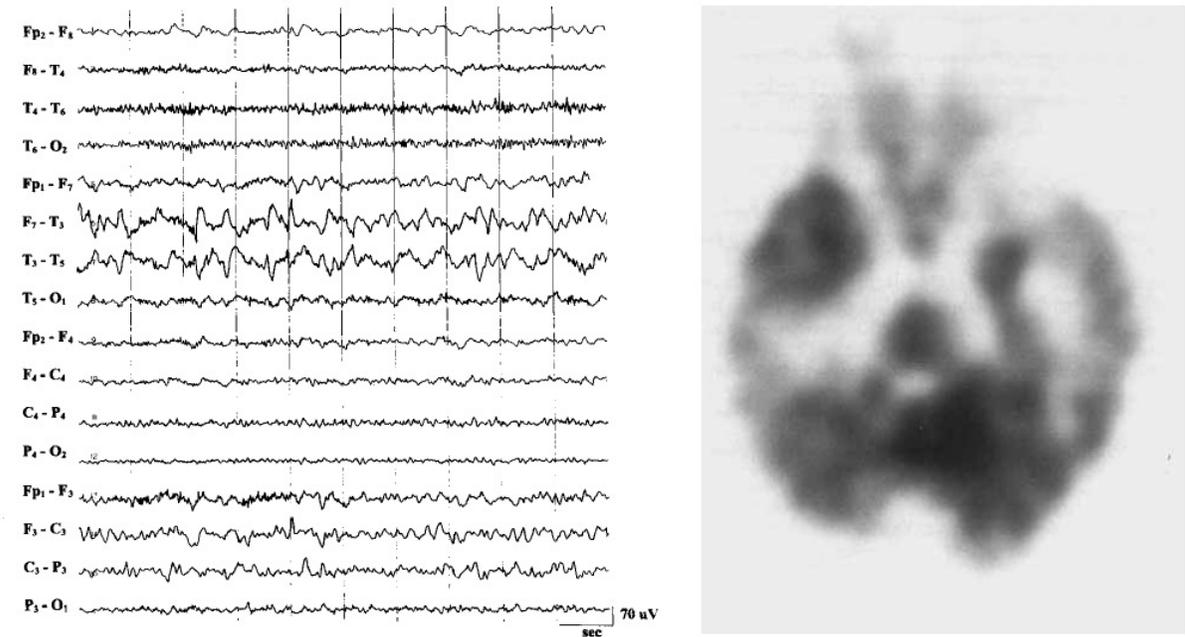
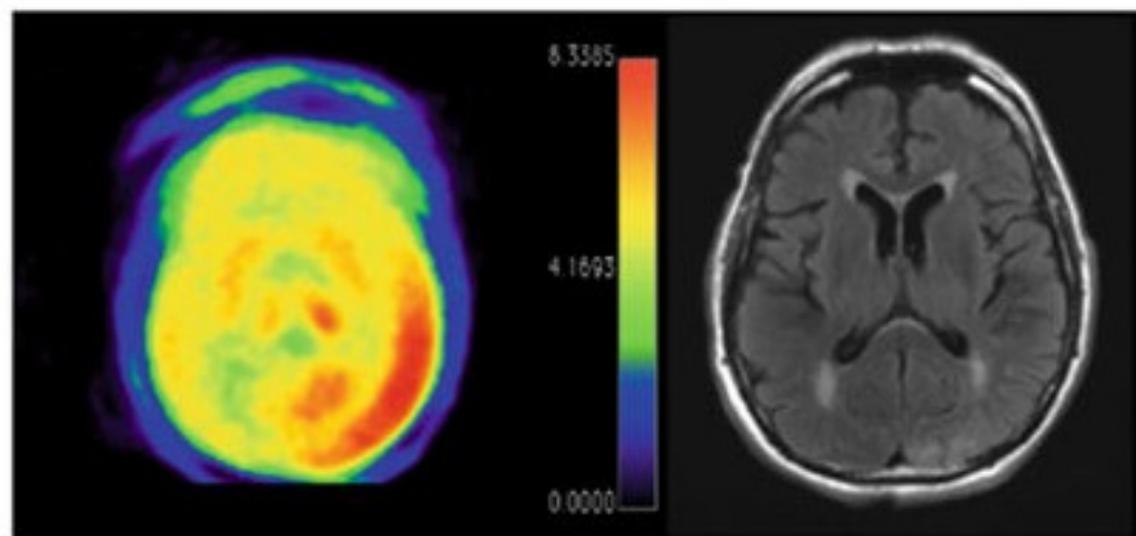
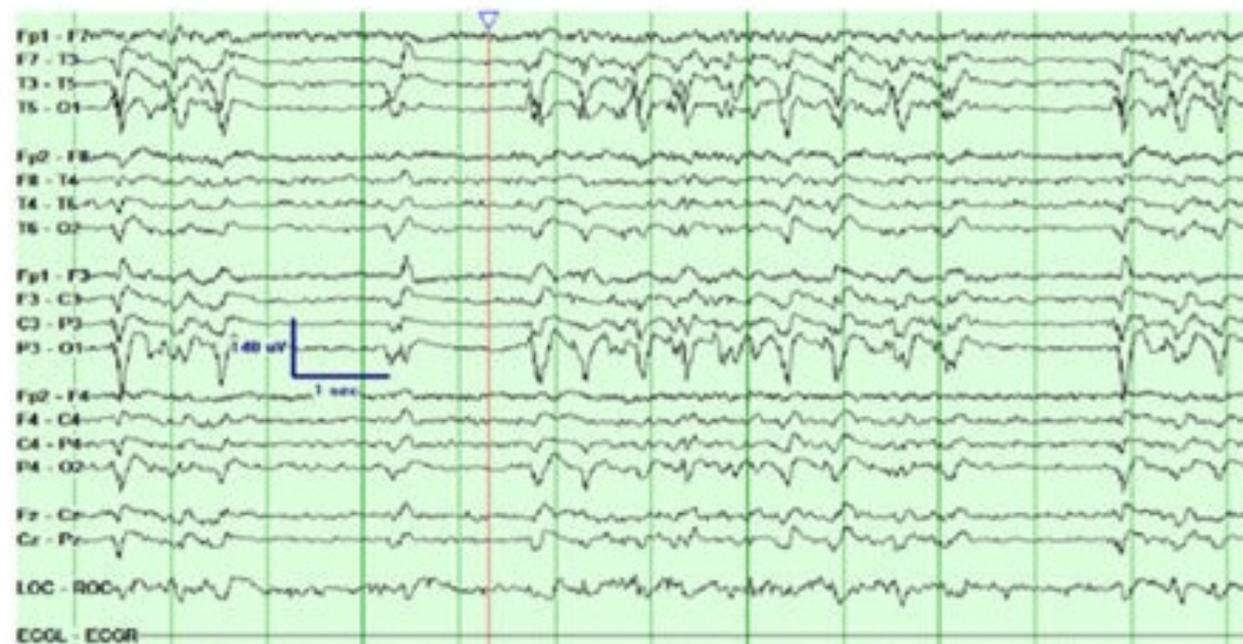


FIG. 3. EEG on day 18 showed considerable irritability, with fluctuating degrees of sharp wave activity, but nonetheless was improved from that of day 3. FDG-positron emission tomography on day 17 demonstrated that left mesiotemporal lobe, although showing glucose metabolism comparable to that of the right side and thus reduced as compared with the previous scan, still displayed more metabolism than the left laterotemporal lobe and therefore remained relatively hypermetabolic.

REGIONAL

C



Prognostic Implications of Periodic Epileptiform Discharges

Daniel San Juan Orta, MD; Keith H. Chiappa, MD; Alejandro Z. Quiroz, PhD; Daniel J. Costello, MD, MRCPI; Andrew J. Cole, MD, FRCPC

Results: We obtained complete clinical, neuroimaging, neurophysiologic, and long-term outcome data in 118 patients. In the subgroup of patients with PLEDs, absence of seizures at onset (odds ratio, 0.21 per point; 95% confidence interval, 0.04-0.97) and an acute etiology for the PLEDs (odds ratio, 0.14 per point; 95% confidence interval, 0.03-0.72) were associated with death. A nonneoplastic cause for PLEDs was associated with independent functionality (odds ratio, 0.45 per point; 95% confidence interval, 0.3-0.67).

Table 3. Neurological Examination, Seizures at Onset, and History of Epilepsy in Patients With Periodic Epileptiform Discharges

Clinical Finding	Patients, No. (%)		
	PLEDs (n=82)	BIPLEDs (n=23)	GPEDs (n=17)
Neurological examination			
Focal	60 (73.1)	10 (43.4)	3 (17.6)
Coma	14 (17.0)	11 (47.8)	12 (70.5)
Coma and focal	7 (8.6)	2 (8.6)	1 (5.8)
Normal	1 (1.2)	0	1 (5.8)
Seizures			
Acute seizure	57 (70.3)	10 (43.4)	5 (29.4)
History of epilepsy	13 (22.8)	3 (13)	2 (11.7)

Abbreviations: BIPLEDs, bilateral periodic epileptiform discharges; GPEDs, generalized periodic epileptiform discharges; PLEDs, periodic lateralized epileptiform discharges.

Table 4. Functional Capacity of Patients With Periodic Epileptiform Discharges With Follow-up of at Least 1 Year

Functional Capacity	No. (%)		
	PLEDs (n=79)	BIPLEDs (n=23)	GPEDs (n=17)
Dependent	43 (54.4)	9 (39.1)	9 (52.9)
Death	19 (24.0)	9 (39.1)	5 (29.4)
Independent	17 (21.5)	5 (21.7)	3 (17.6)

Periodic lateralized epileptiform discharges: association with seizures*

BETÜL BAYKAN, DEMET KINAY, AYŞEN GÖKYİĞİT & CANDAN GÜRSES

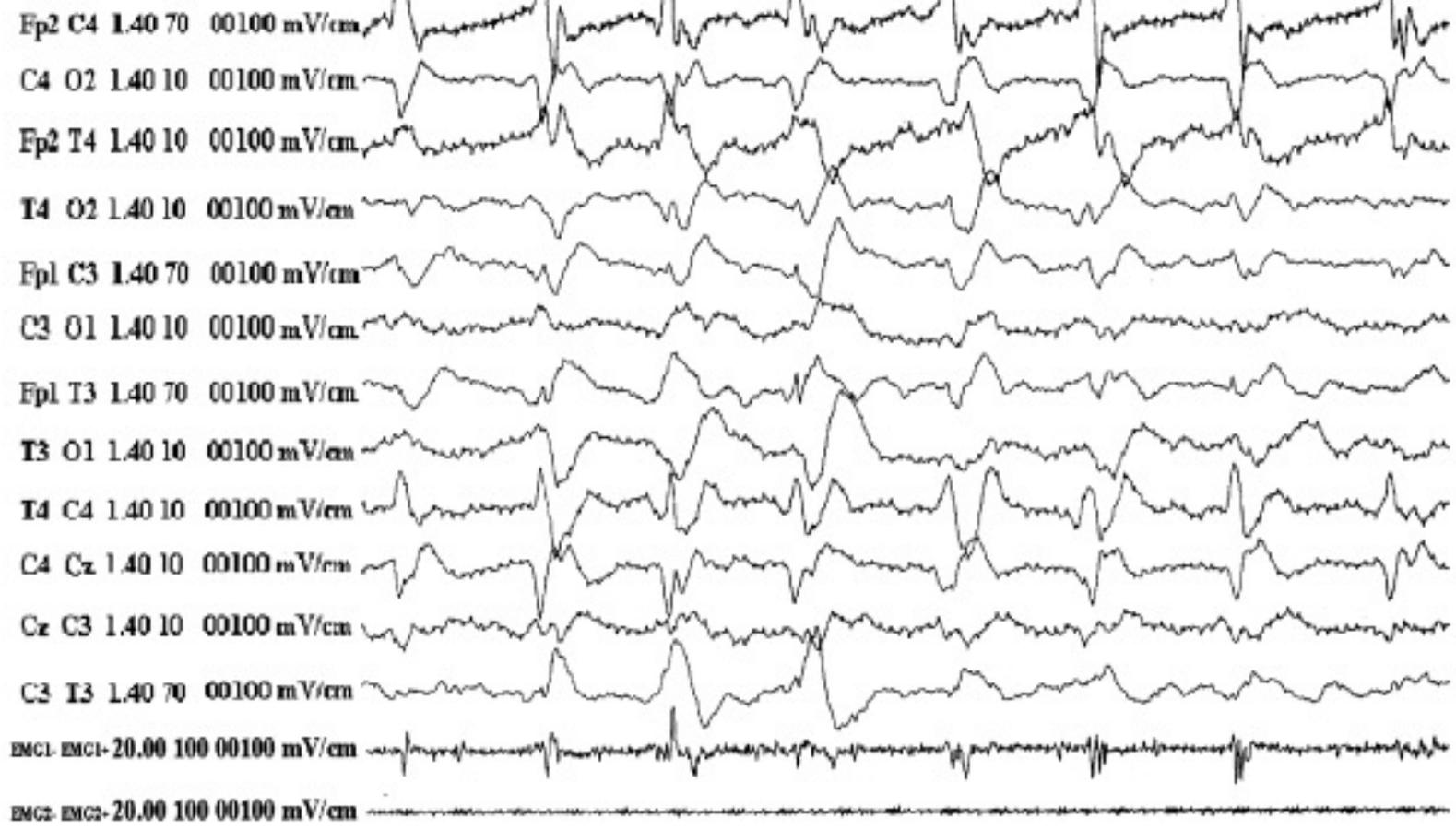
Table 1: Etiology of PLEDs.

Adults	Cases with seizures		Cases without seizures	
CNS infections		11		3
Focal encephalitis ^a	10		2	
Tuberculous meningitis	1		—	
Creutzfeldt–Jakob Disease	—		1	
Cerebrovascular Disease		11		3
Ischemic stroke	8		1	
Intracerebral hemorrhage	—		2	
Cerebral venous occlusion	1		—	
Tuberculous vasculitis	2		—	
Neoplasm		5		—
Undetermined ^b		4		—
Focal cerebral lesion of unknown etiology		2		1
Children		5		—
Progressive neurodegenerative disorders	3		—	
Undetermined ^b	2		—	

^a Two with pathologically proven herpes simplex encephalitis; 10 with probable herpes simplex encephalitis (clinically and/or MRI supported); ^b cases with cryptogenic partial epilepsy.

INPUT FILTERS REFERENCE

(-) (+) low high value



MRK dim.: 1.0 cm * 3.0 cm





Bilateral independent periodic discharges (BIPDs)

Definition

Rarer than their related cousins LPDs, may carry a **poorer prognosis**. BIPDs are asynchronous, repetitive, independent left and right hemispheric discharges, often with a sharp or spike morphology, typically ranging from 100–300 μV (Schomer and Lopes da Silva, 2011), which recur at regular intervals up to 3 per second, with a clear period between adjacent discharges (Hirsch et al., 2013)

Bilateral independent periodic discharges (BIPDs)

Prevalence

- BIPDs are far less common than LPDs; only 0.2% of unselected patients undergoing EEG have BIPDs (Fitzpatrick and Lowry, 2007).
- Etiology matters: BIPDs are seen in 9.5% of patients with CNS infection (Carrera et al., 2008), but in only 1% of patients with intracerebral hemorrhage (Treiman et al., 1990).

Etiologies

- BIPDs are usually found in settings of **acute and subacute injury**, rather than chronic conditions (San Juan Orta et al., 2009).
- The most common causes reported are infections, anoxic injury (de la Paz and Brenner, 1981), stroke, tumors (San Juan Orta et al., 2009), and metabolic disorders (Pedersen et al., 2013); more rare causes include Hashimoto's encephalitis (Fitzpatrick and Lowry, 2007) and lupus (Aye et al., 2013).

Association with seizures

- BIPDs also have **a high association with seizures**, which are reported in 43–78% of patients with BIPDs (de la Paz and Brenner, 1981; Fitzpatrick and Lowry, 2007; San Juan Orta et al., 2009);
- Patients with BIPDs often have a **poor neurologic exam**, and 48% are comatose (compared to 17% of patients with LPDs).

Bilateral independent periodic discharges (BIPDs)



Bilateral independent periodic discharges (BIPDs)

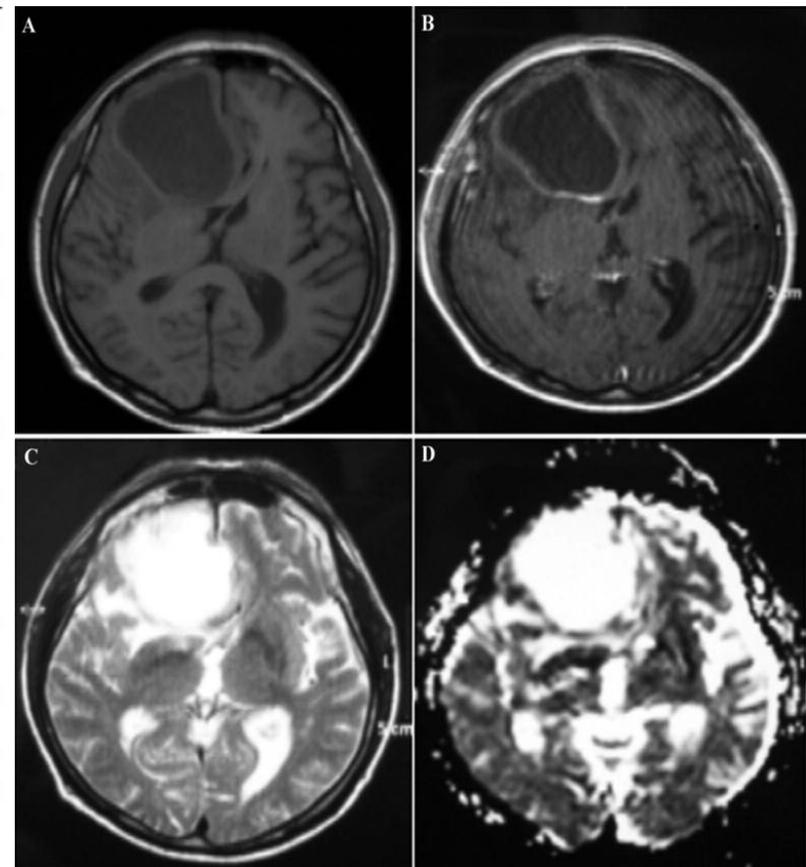
Imaging

- In one study, focal findings on imaging were less common in patients with BIPDs (25%) compared to LPDs (74%) (Pedersen et al., 2013)

Outcome:

- BIPDs have been thought of as a marker of more severe disease and as an indicator of **worse prognosis** than LPDs.
- The reported **mortality ranges from 39–100%** (Pedersen et al., 2013; San Juan Orta et al., 2009).
- The largest comparisons of BIPDs to LPDs have shown higher mortality in BIPDs. De la Paz et al. found a 61% mortality in 18 patients with BIPDs, more than twice the 29% found in the 45 patients with LPDs (de la Paz and Brenner, 1981).

Bilateral independent periodic discharges (BIPDs)



Fp1-F7
F7-A1

Fp1-F7
F7-T3
T3-T5
T5-O1

Fp1-F3
F3-C3
C3-P3
P3-O1

FZ-CZ
CZ-PZ

Fp2-F4
F4-C4
C4-P4
P4-O2

Fp2-F8
F8-T4
T4-T6
T6-O2

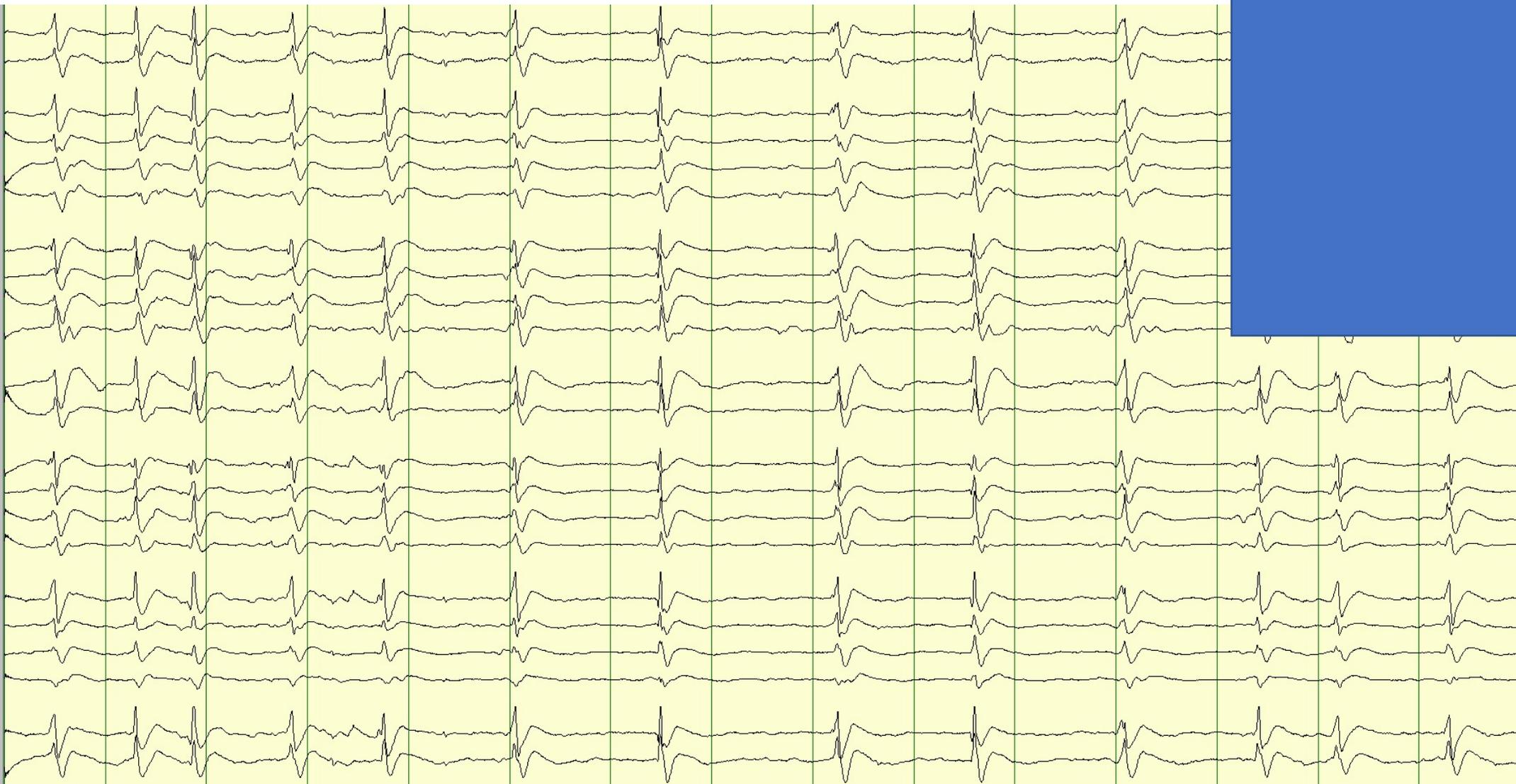
Fp2-F8
F8-A2

EKG

low filter: 1.0 Hz; high filter: 70.0 Hz; notch filter: ON; montage: double banana

1 sec

200µV



GPD (Generalized periodic discharges)

Definition

- GPDs at first appear closely related to LPDs and BiPDs;
- however, **metabolic illnesses** more commonly give rise to GPDs.
- GPDs are bilaterally synchronous, repetitive discharges (often with a sharp or spike morphology), typically with amplitudes >100 μV , repeating at regular intervals at up to 3 per second, with a clear period between adjacent discharges (Hirsch et al., 2013)

Prevalence

- A large review of 3064 patients undergoing cEEG found GPDs in 138 (4.5%) (Foreman et al., 2012); other studies have found a much lower prevalence, from 0.8–1.8% (Lee et al., 2016; Swisher et al., 2015). GPDs often coexist with LPDs.

GPD (Generalized periodic discharges)

Etiologies

- The majority of patients with GPDs have a **toxic-metabolic illness or sepsis**, and many have coexisting brain injury as well (Foreman et al., 2012; Husain et al., 1999; San Juan Orta et al., 2009; Yemisci et al., 2003).
- Patients with GPDs are usually **comatose or stuporous**, comatose 70% of the time in one study (Foreman et al., 2012; San Juan Orta et al., 2009).

Association with seizures

- The rates of seizures with GPDs are significant though not quite as high as the seizure rates of BIPDs and LPDs.
- In a case-control study of 200 patients on cEEG with GPDs and 200 without, seizures were much more prevalent in the GPD group (46%) compared to the controls (34%) (Foreman et al., 2012).
- **Higher rates of concomitant seizures are seen with higher frequencies of GPDs**; while GPDs <1.5 Hz were not significantly associated with seizures in one large multicenter study, GPDs occurring at 1.5–2 Hz had an odds ratio of 2.3 for association with seizures and of 3.3 **at high frequencies (2 Hz)** (Rodriguez Ruiz et al., 2016).

Imaging :

- Similar to the other periodic findings described, **a combination of subcortical and cortical injuries are common in GPDs** (Yemisci et al., 2003), though isolated subcortical lesions are present in 30% (San Juan Orta et al., 2009) PET is less commonly reported

Triphasic GPD (Generalized Periodic Discharge):

there are three principal phases: the main deflection being downward, representing a surface positive change. This dominant phase is usually preceded by a low-amplitude (often rounded or even absent) negative deflection and followed by a long, slow, broad slow-rising deflection, giving the entire complex a triphasic contour.

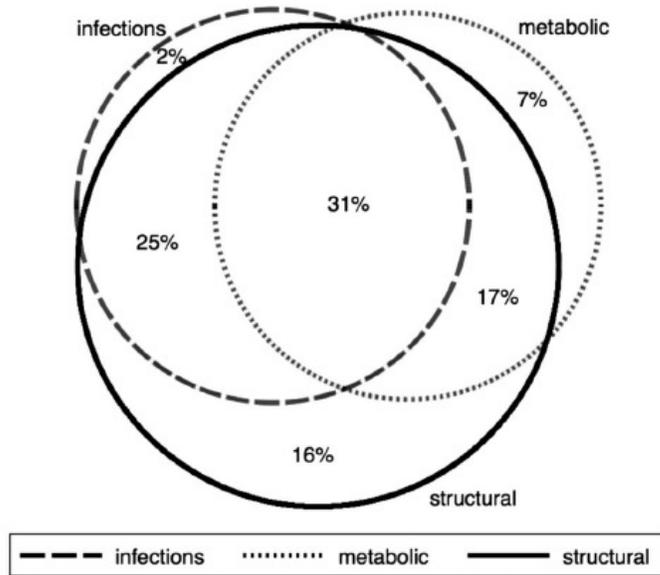


FIG. 3. Proportional distribution of infections, metabolic derangements, and structural brain abnormalities in 105 encephalopathic patients with triphasic waves. Adapted with permission from Sutter et al. (2013b).

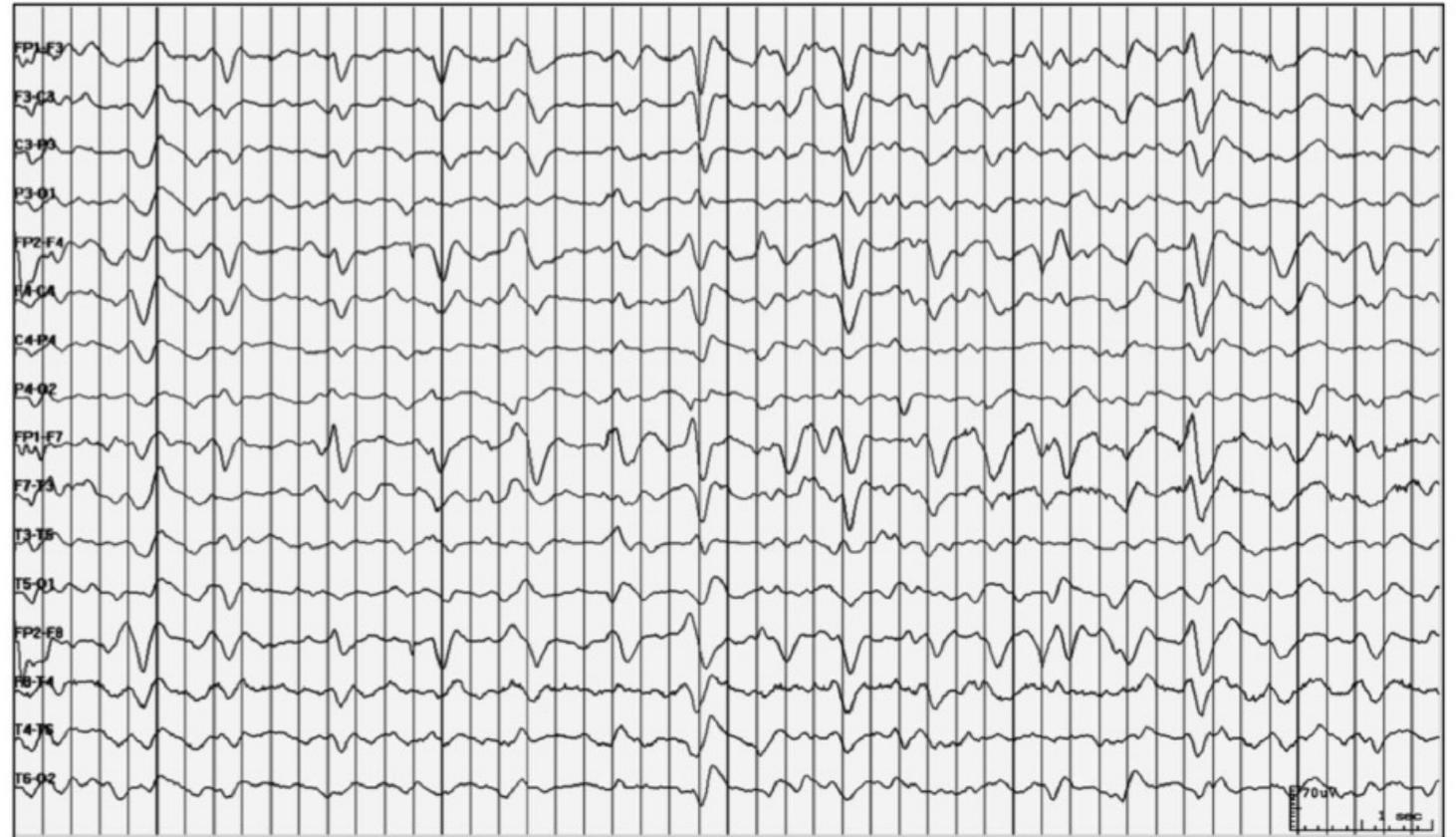


FIG. 5. Triphasic waves in acute encephalopathy. Generalized slowing of background activity with frequencies in the theta (4–8 Hz) and delta (<4 Hz) range and bilateral high-voltage (70–100 μV) triphasic waves with a frontocentral maximum and an anterior-posterior or posterior-anterior shift.

GPDs: Triphasic waves



TABLE 4. Clinical Predispositions for TWs

<i>Without</i> white matter disease/subcortical atrophy	Hepatic encephalopathy, hyperammonemia Uremia, other marked electrolyte abnormalities Anoxia Toxins/medications (e.g., lithium, baclofen)
<i>With</i> white matter disease/subcortical or diffuse atrophy	Mild infections (e.g., urinary tract infection, upper respiratory tract infection) Lesser degrees of electrolyte imbalance, toxins

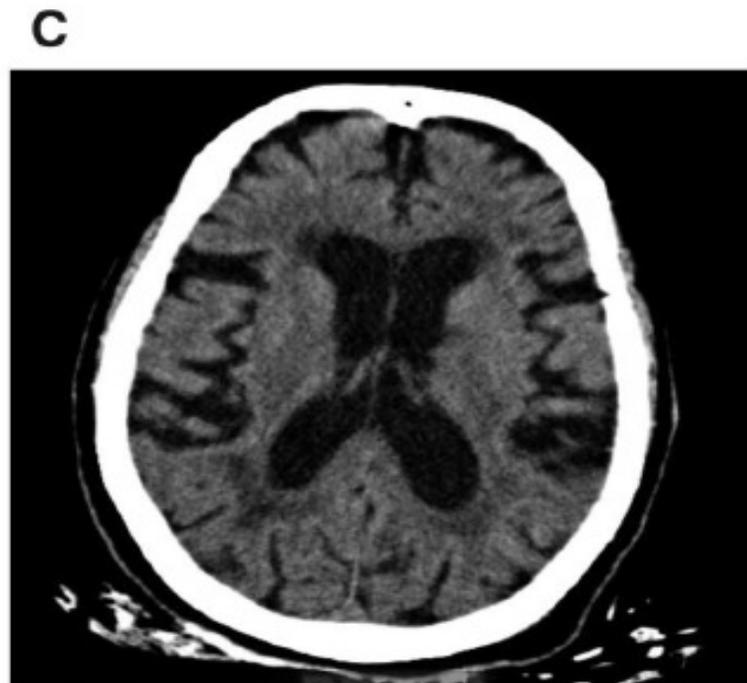
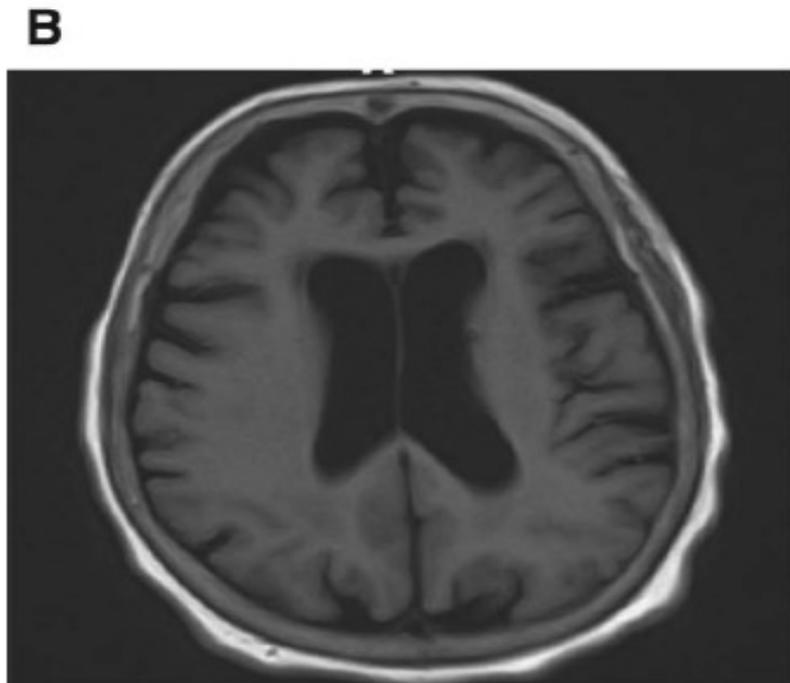


FIG. 12. A, EEG showing intermittent TWs of modest voltage, increased with arousal. B and C, The MRI (B) and head CT (C) revealing white matter disease and ventricular dilation in a patient with *normal* ammonia but with a urinary tract infection. This illustrates that even *without* high ammonia, TWs may occur with white matter disease/diffuse cerebral atrophy along with a relatively minor intercurrent urinary infection (see Table 4).



Lateralized rhythmic delta activity (LRDA)

Definition

- LRDA is a unilateral repetitive waveform, with nearly uniform duration and morphology, recurring at up to 3 Hz without a measurable inter-waveform interval (Hirsch et al., 2013). LRDA tends to occur in shorter runs (often lasting less than one minute) than do LPDs (Gaspard et al., 2013).

Prevalence

- One series found LRDA in 27/558 (4.7%) of acutely ill patients on continuous EEG monitoring (Gaspard et al., 2013); 44% associated with LPDs.

Etiologies

- The most common conditions are intracerebral and subarachnoid hemorrhages;
- stroke, tumor, traumatic brain injury, and infection (Gaspard et al., 2013).
- A high proportion (70%) of patients with LRDA have a focal abnormality on neurologic examination, concordant with the side of LRDA (Gaspard et al., 2013).

Association with seizures

- **HIGH**: Gaspard et al. (2013) found seizures in the 63% of patients with LRDA, most of which were nonconvulsive, even higher than with LPDs (57%)
- Similarly to LPDs and GPDs, faster rates of LRDA have a higher risk of associated seizures.

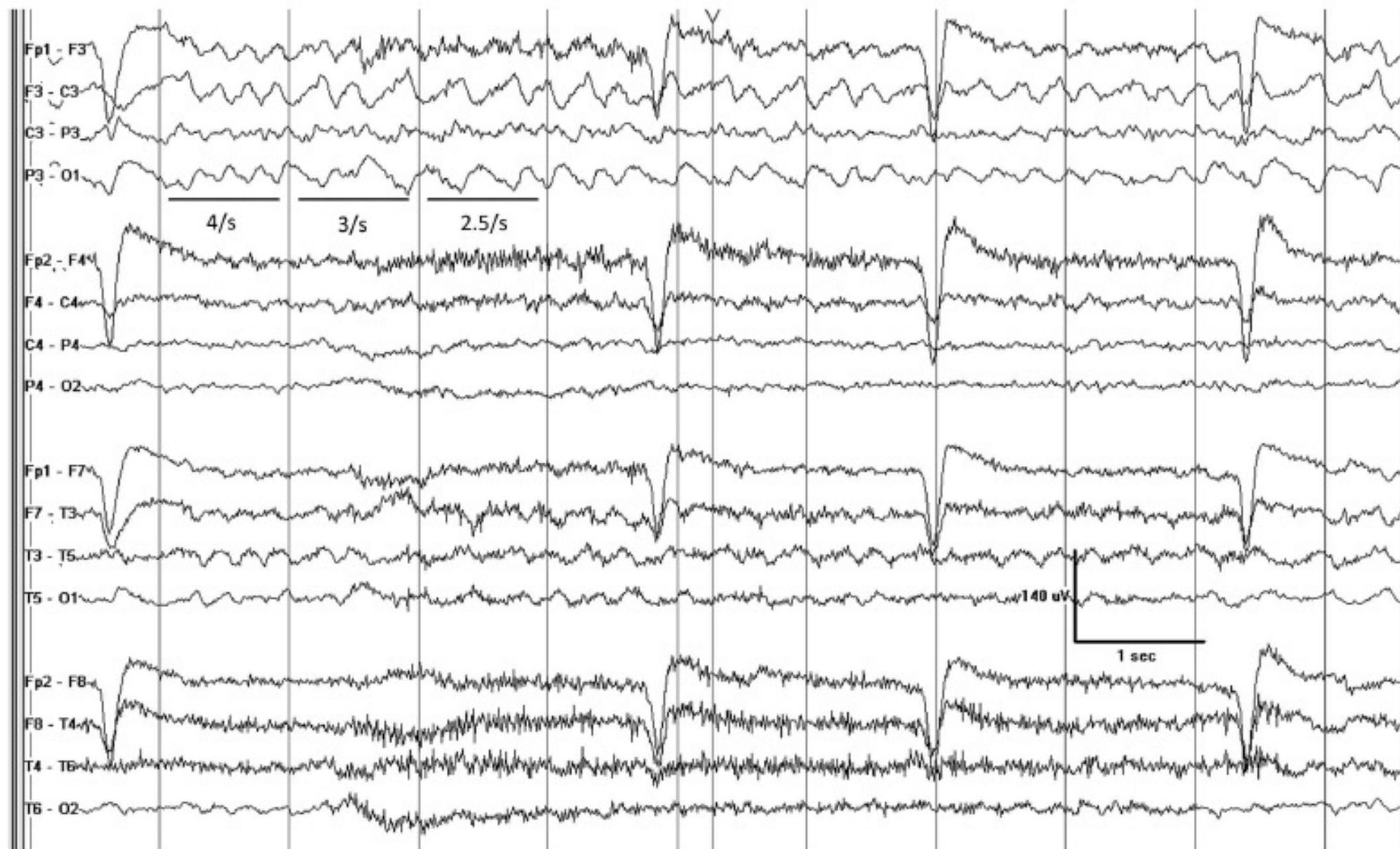
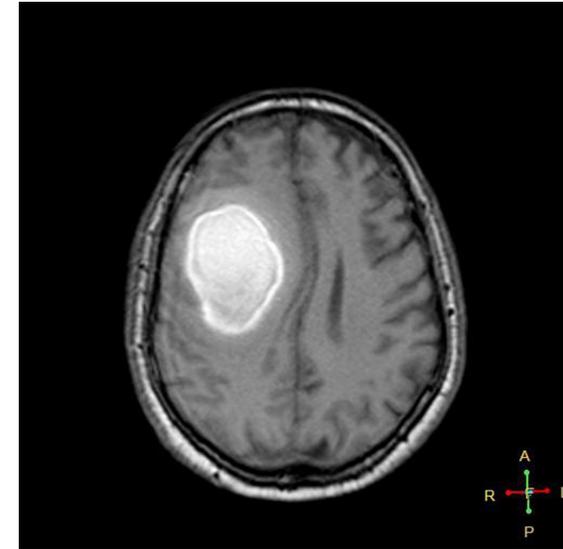
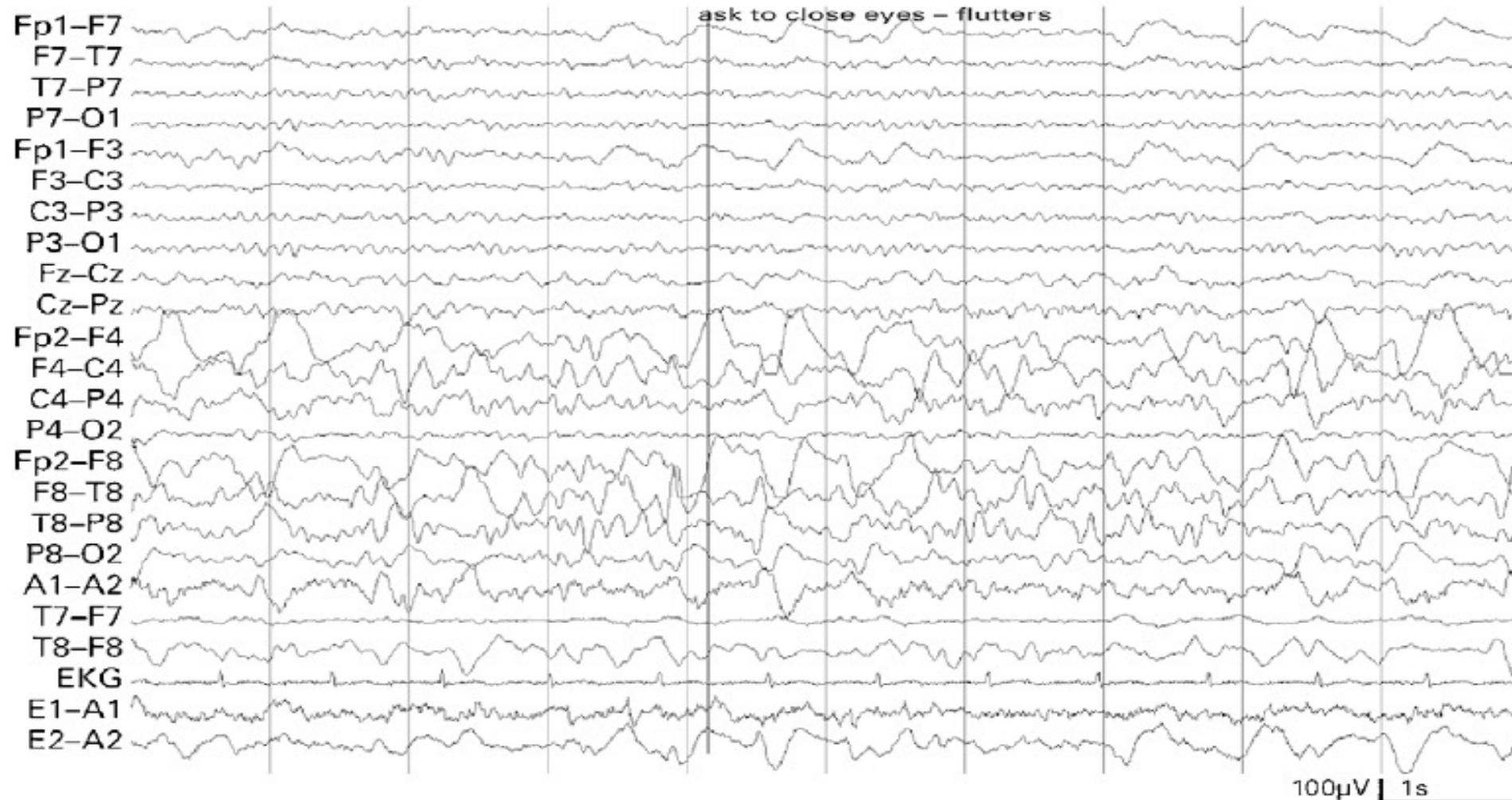


FIG. 17. Evolving LRDA: Lateralized rhythmic delta activity that evolves in frequency and morphology from a 4 per second blunt RDA to a 2.5 per second sharply contoured RDA.

Lateralized rhythmic delta activity (LRDA)

Imaging: nearly all patients with LRDA have a cortical and subcortical focal injury on the side of the rhythmic activity (Gaspard et al., 2013).



Lateralized rhythmic delta activity (LRDA): acute stroke

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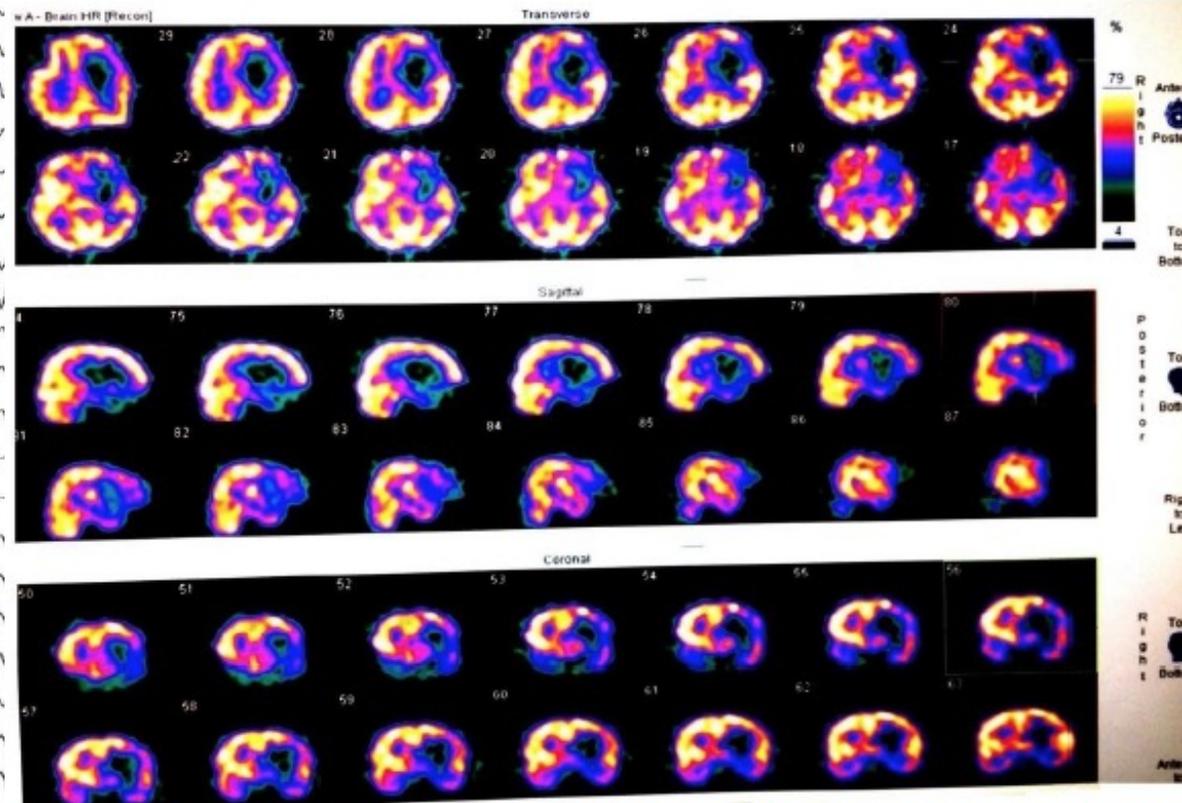
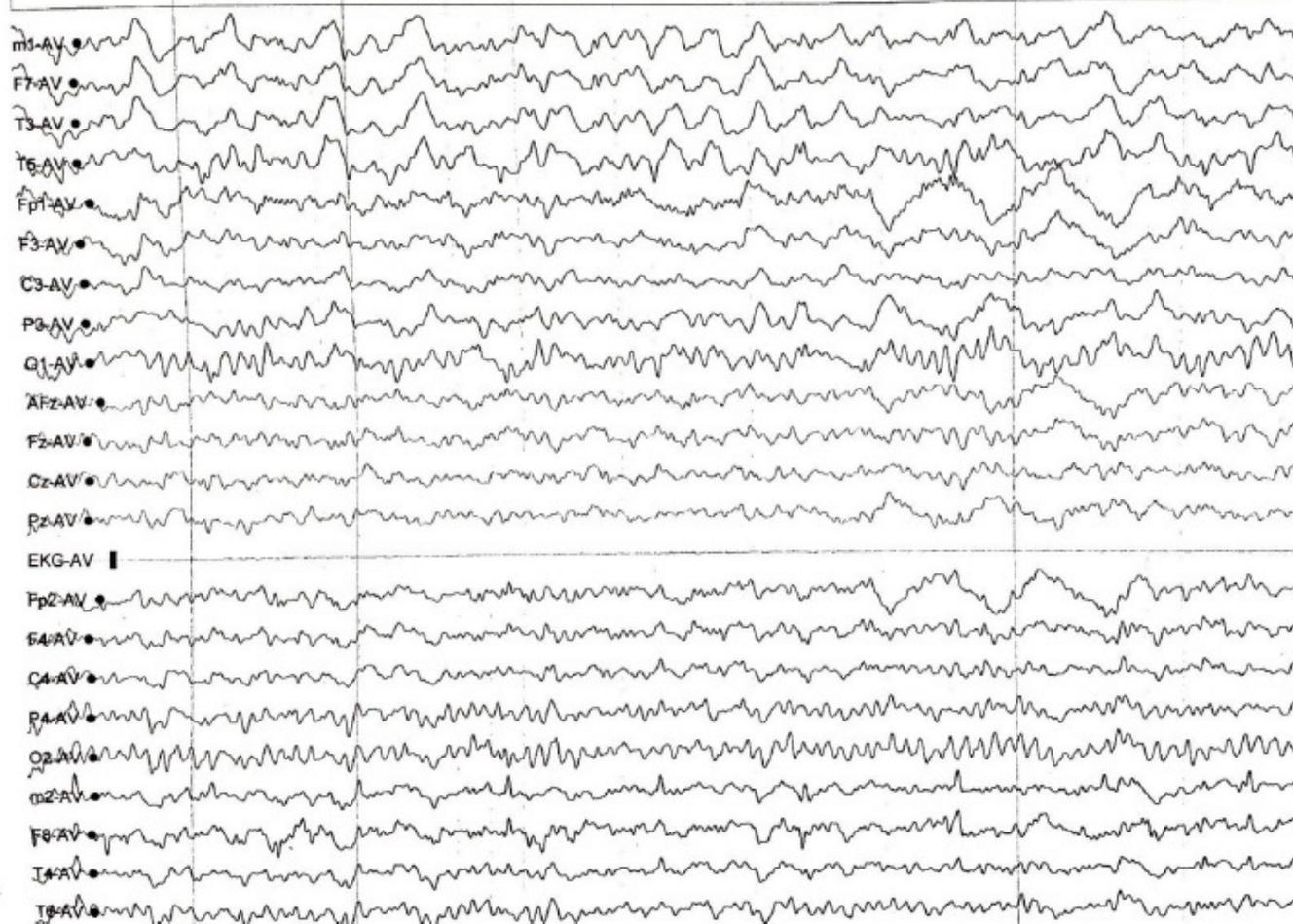
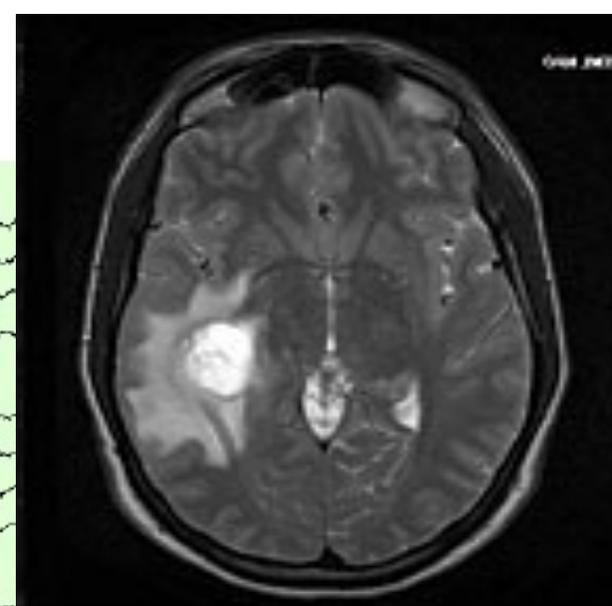
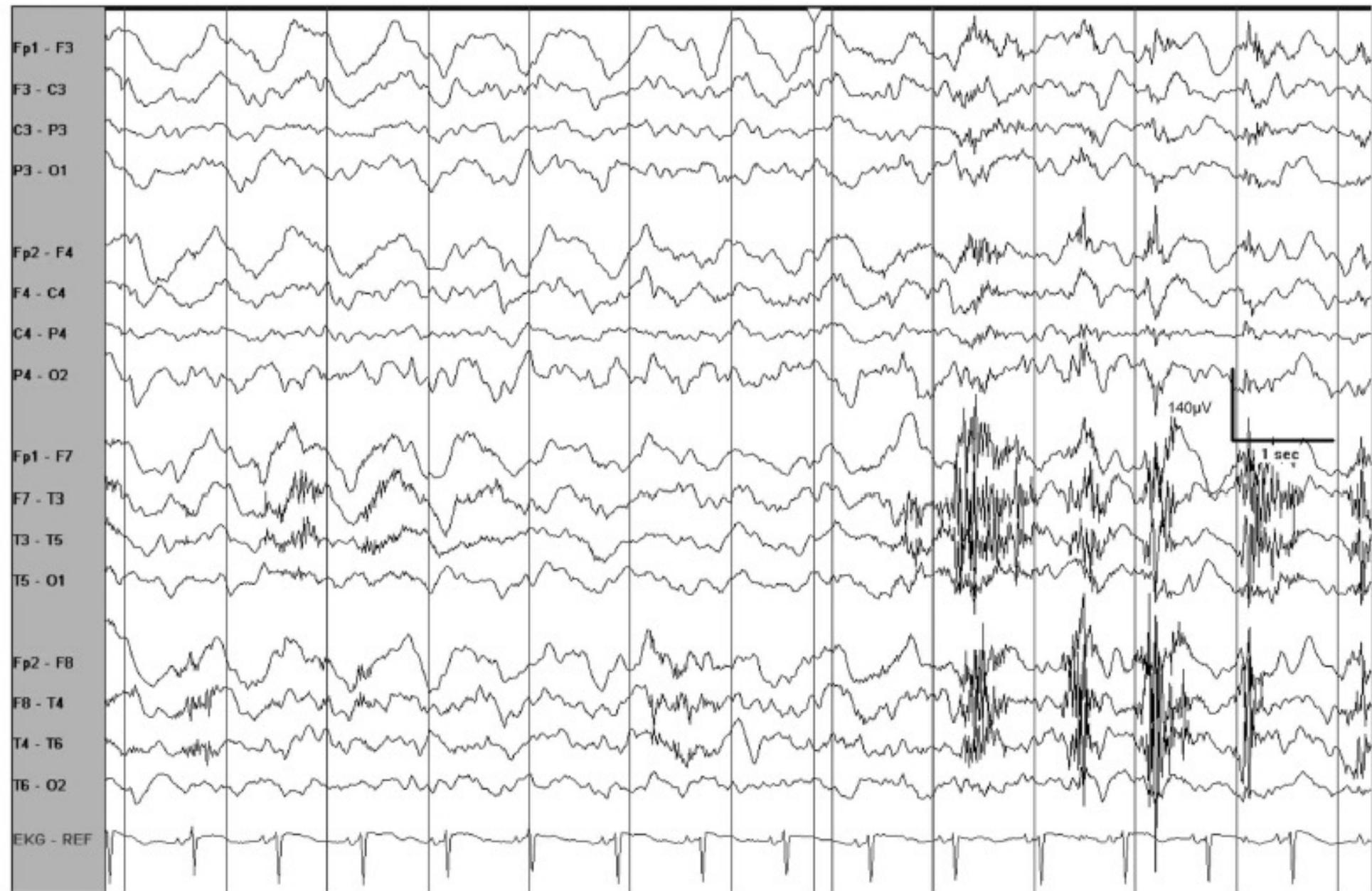


Figure 2: SPECT in a 63 years old male patient with acute Ischemic stroke shows severe Ischemia and Infarction seen in part of left temporal lobe, left frontal lobe, left parietal lobe, left insular part, left basal ganglia.

Figure 1: EEG in a 63 years old male patient with acute ischemic stroke shows low to middle amplitude slow waves visualized in the left hemisphere and are more obvious in M1, F7, T3, T5 leads.

Lateralized rhythmic delta activity (LRDA): brain metastases





Generalized rhythmic delta activity (GRDA)

Definition

- Perhaps **the most benign** inhabitant of the ictal-interictal zone, GRDA is a bilateral, bisynchronous and symmetric repetitive waveform, often >100 uV in amplitude, with nearly uniform duration and morphology recurring at up to 3 Hz (Hirsch et al., 2013)
- Prior to the ACNS guidelines 2012, the term (FIRDA) was frequently used

Prevalence

- GRDA was reported in 16.1% of patients undergoing cEEG monitoring in 4772 patients (Rodriguez Ruiz et al., 2016);

Etiologies

- In one series, the majority (55%) of patients had a **structural lesion**, while an **infectious condition, renal disease, or sedative medication were commonly associated** (Accolla et al., 2011).

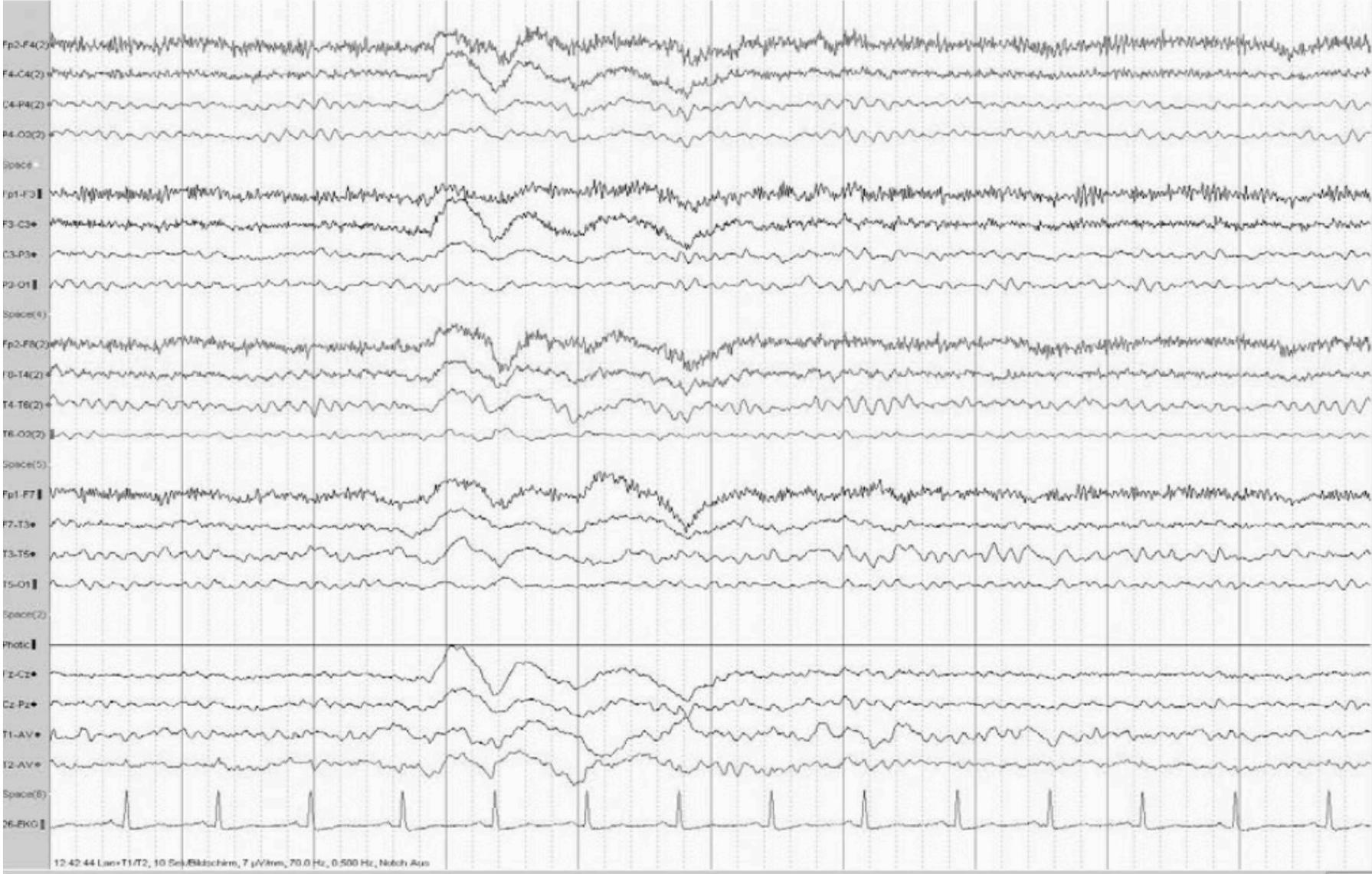
Association with seizures

- In 1513 critically ill patients with periodic or rhythmic activity found that GRDA was **NOT associated** with an increased risk of seizures (Rodriguez Ruiz et al., 2015).

Imaging

- the underlying brain lesion (when present) is more frequently lateralized in 77% patients (Accolla et al., 2011)

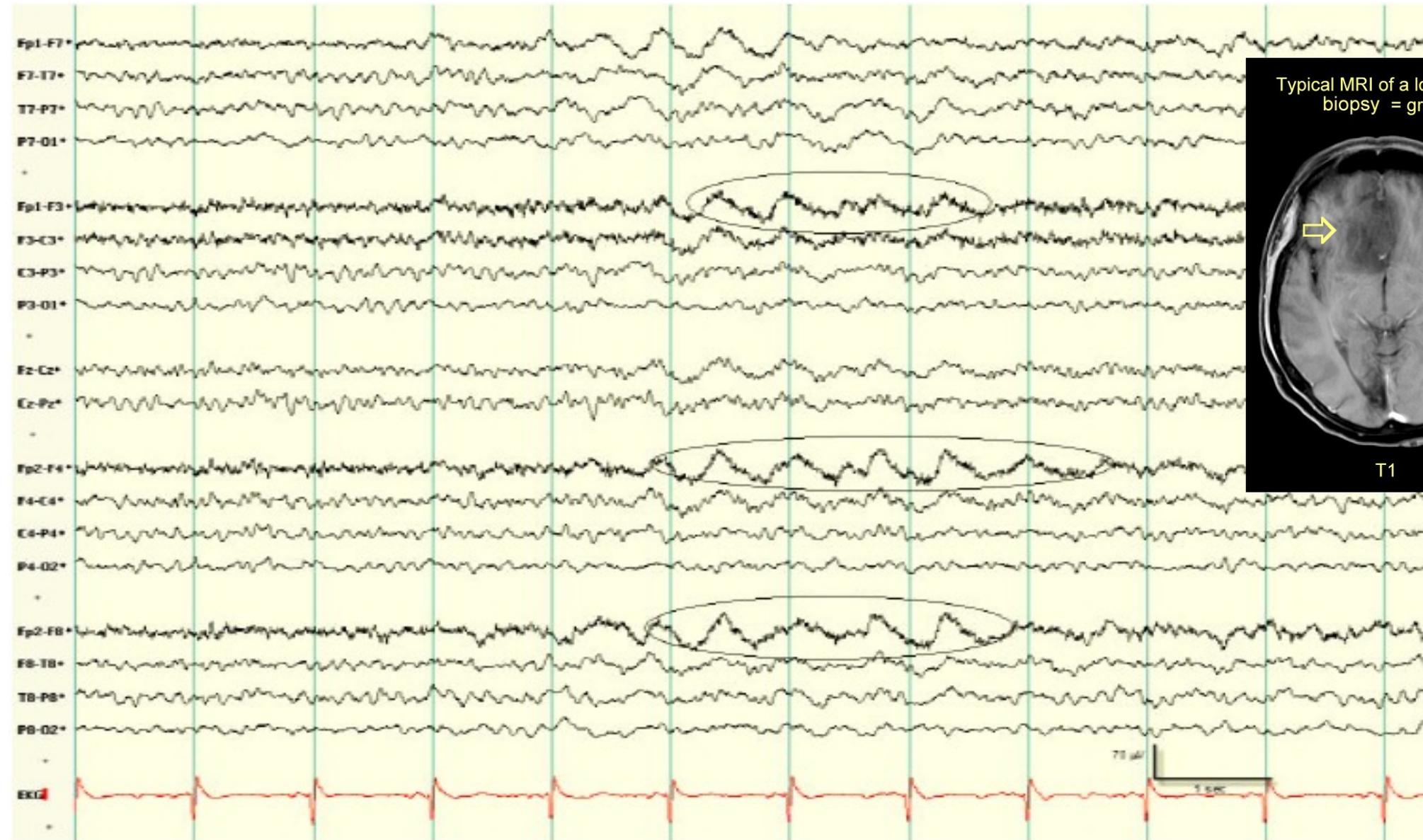
Generalized rhythmic delta activity (GRDA): TIA



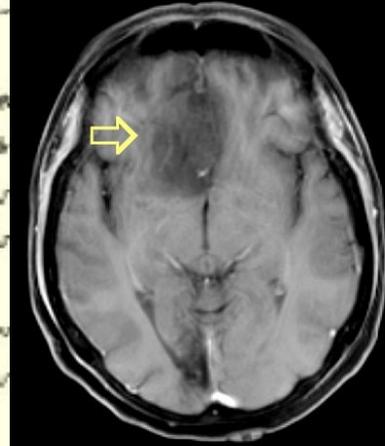
Generalized rhythmic delta activity (GRDA): chronic stroke



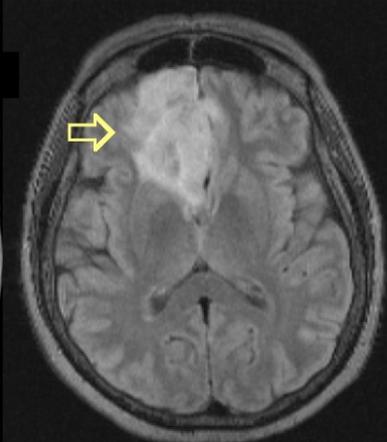
Generalized rhythmic delta activity (GRDA): glioma



Typical MRI of a low grade glioma in right frontal lobe
biopsy = grade 2 oligodendroglioma



T1



T2 or FLAIR

MONORHYTHMIC FRONTAL DELTA ACTIVITY IN THE HUMAN
ELECTROENCEPHALOGRAPH : A STUDY OF 100 CASES ¹

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London, England*

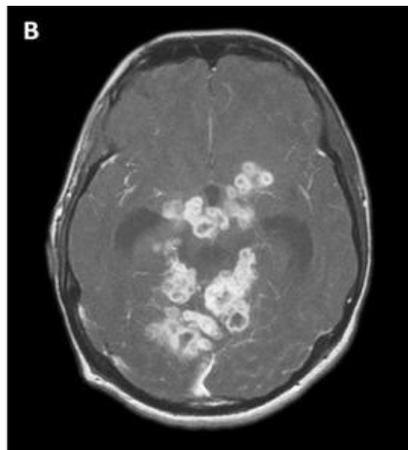
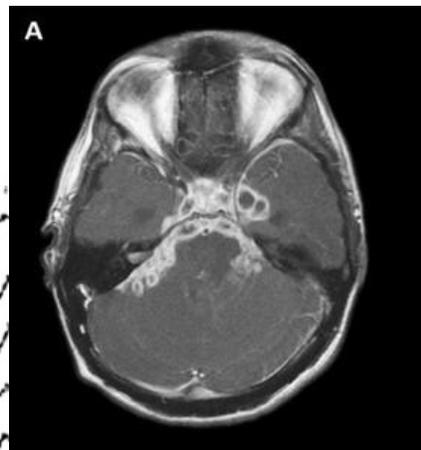
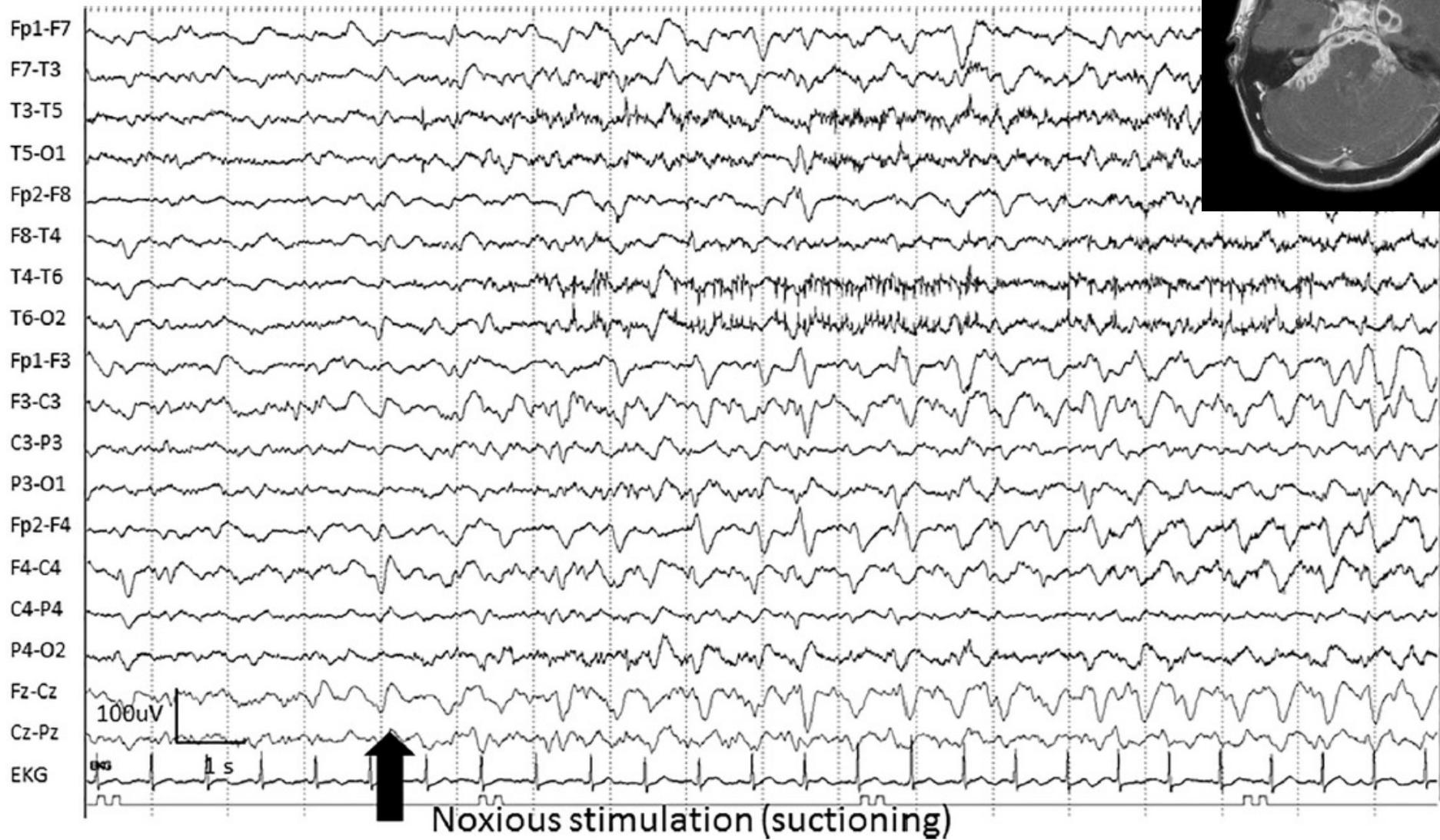
(Received for publication: October 30, 1958)

Tumours (including abscess)	43
Epilepsy (idiopathic or symptomatic of unknown etiology)	25
Psychiatric disturbances	11
"Degenerative" diseases	8
"Vascular" diseases	7
Infection (meningitis)	3
Head injury	2
Aqueduct stenosis	1
	<hr/>
Total:	100

TABLE II
Incidence of Electroencephalographic Abnormalities

Lesions	Total patients	Electroencephalograms normal		Electroencephalograms abnormal *					
		No. of patients	Per cent	Dysrhythmia		Arrhythmia		Dysrhythmia and arrhythmia	
				No. of patients	Per cent	No. of patients	Per cent	No. of patients	Per cent
Tumor of cerebellopontine angle	22	10	45	10	45	2	9	—	—
Tumor of cerebellar hemisphere	17	3	18	11	65	1	6	2	12
Tumor of midline of posterior fossa	27	5	18	13	48	4	15	5	18
Tumor of third ventricle	12	2	17	9	75	1	8	—	—
Obstructive hydrocephalus	9	1	11	5	56	1	11	2	22

* In cases of respective lesions.



Stimulus-induced rhythmic, periodic, or ictal discharges (SIRPIDs)

Definition

- A special subtype of patterns in the ictal-interictal continuum, SIRPIDs are rhythmic, periodic, or ictal-appearing patterns consistently elicited by stimulation of the patient (i.e. suctioning, noise, or physical examination of the patient) (Hirsch et al., 2004).
- The stimulus-induced nature may be indicated by adding “SI” to a following term such as SI-GPDs or SI-LRDA under the ACNS standardized terminology guidelines (Hirsch et al., 2013).

Stimulus-induced rhythmic, periodic, or ictal discharges: (SIRPIDs)

Prevalence

SIRPIDs are a relatively common phenomenon in the critically ill, found in 10–34% of patients undergoing EEG monitoring (Braksick et al., 2016; Hirsch et al., 2004; Ong et al., 2012).

Etiologies

SIRPIDs also stem from **many etiologies**, the most common being intracerebral hemorrhage, anoxic brain injury, metabolic disturbances, traumatic brain injury, and drug toxicity (Braksick et al., 2016; Hirsch et al., 2004; Van Straten et al., 2014).

Association with seizures

Most studies report a **strong** association of SIRPIDs with seizures, with 27–51% of patients found to have coexisting spontaneous seizures (Braksick et al., 2016; Hirsch et al., 2004)

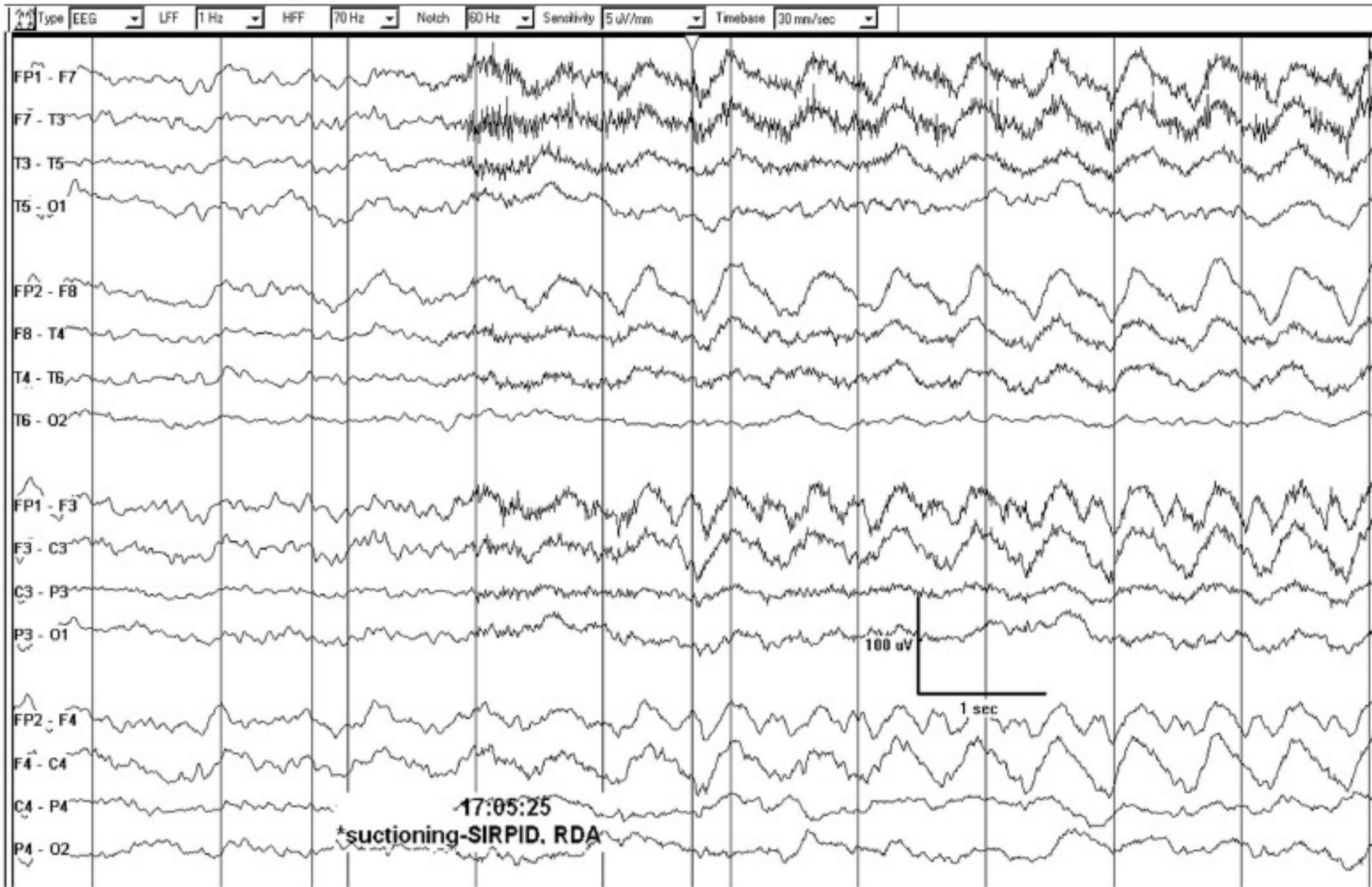
However, the largest series of patients on cEEG monitoring found no increased association of seizures in patients with stimulus-induced compared to spontaneous patterns (Rodriguez Ruiz et al., 2016).

Imaging

In the three reports of patients with SIRPIDs who received SPECT, there was **no increase in cerebral blood flow during SIRPIDs** (Smith et al., 2014; Zeiler et al., 2011).

Outcomes

Focal SIRPIDs have been associated with a poor outcome when present in patients with intracerebral hemorrhage (Claassen et al., 2007) and cardiac arrest.



Rodriguez Ruiz jama 2016

Associazione con le crisi

Table 3. Periodic/Rhythmic Patterns and Seizures With and Without Plus Modifier

Pattern	No. of Sessions Without Seizures	No. of Sessions With Seizures	Odds Ratio (95% CI) ^a	FDR-Adjusted P Value ^{a,b}	Odds Ratio Controlled for Frequency (95% CI) ^c	FDR-Adjusted P Value (Controlled for Frequency) ^{b,c}
GRDA without Plus	644 (87)	96 (13)	1.27 (0.97-1.65)	.14	1.38 (0.98-1.91)	.11
GRDA with Plus	161 (86)	26 (14)	0.86 (0.51-1.40)	.62	0.94 (0.52-1.63)	.86
GPDs without Plus ^d	461 (88)	61 (12)	1.13 (0.81-1.55)	.55	0.98 (0.68-1.38)	.92
GPDs with Plus ^d	125 (72)	49 (28)	3.00 (1.94-4.56)	<.001	2.11 (1.23-3.56)	.02
LRDA without Plus	219 (78)	62 (22)	1.93 (1.35-2.71)	.001	1.46 (0.87-2.37)	.23
LRDA with Plus	78 (60)	51 (40)	3.57 (2.25-5.63)	<.001	3.12 (1.77-5.44)	<.001
LPDs without Plus ^d	326 (64)	183 (36)	6.68 (5.30-8.42)	<.001	6.53 (5.15-8.28)	<.001
LPDs with Plus ^d	123 (42)	170 (58)	13.35 (9.99-17.89)	<.001	12.66 (9.09-17.67)	<.001
BIPDs without Plus	77 (75)	26 (25)	1.59 (0.90-2.72)	.17	1.66 (0.94-2.85)	.14
BIPDs with Plus	11 (58)	8 (42)	3.27 (0.99-10.30)	.09	3.38 (1.00-10.77)	.09

Abbreviations: BIPDs, bilateral independent periodic discharges; FDR, false discovery rate; GPDs, generalized periodic discharges; GRDA, generalized rhythmic delta activity; LPDs, lateralized periodic discharges; LRDA, lateralized rhythmic delta activity.

^a The odds ratios compare patients with patterns vs patients without patterns and are adjusted for age, sex, site, and diagnoses.

^c Odds ratios and P values were additionally adjusted for frequency to control for confounding risk.

^d The statistically significant difference for Plus vs no Plus for GPDs and LPDs was FDR-adjusted P < .001. Seizures were seen in 202 of 3427 sessions (6%) of patients with no patterns.

Table 4. Effect of Specific Frequencies on Association With Seizures

Pattern	No (%)		Odds Ratio (95% CI)	FDR-Adjusted P Value	Odds Ratio (Plus-Controlled) ^a	FDR-Adjusted P Value ^a
	Sessions Without Seizures	Sessions With Seizures				
GRDA						
<1.5 Hz	297 (87)	45 (13)	1.34 (0.91-1.93)	.20	1.47 (0.99-2.15)	.10
1.5 to 2 Hz	248 (88)	35 (12)	0.97 (0.62-1.47)	.92	1.05 (0.66-1.64)	.86
≥2 Hz	137 (84)	26 (16)	1.31 (0.78-2.12)	.38	1.44 (0.85-2.37)	.25
Not recorded	123 (88)	16 (12)	1.11 (0.59-1.96)	.79	1.18 (0.63-2.10)	.65
Any frequency	805 (87)	122 (13)	1.18 (0.93-1.50)	.26		
GPDs						
<1.5 Hz	345 (86)	55 (14)	1.35 (0.94-1.91)	.17	1.12 (0.74-1.64)	.65
1.5 to 2 Hz	65 (76)	20 (24)	2.31 (1.25-4.11)	.02	1.72 (0.86-3.29)	.19
≥ 2 Hz	54 (68)	25 (32)	3.30 (1.79-5.87)	<.001	2.30 (1.14-4.46)	.04
Not recorded	122 (92)	10 (8)	0.73 (0.34-1.41)	.47	0.68 (0.31-1.34)	.38
Any frequency	586 (84)	110 (16)	1.53 (1.17-1.99)	.005	NA	NA
LRDA						
<1.5 Hz	101 (83)	21 (17)	1.56 (0.87-2.66)	.20	1.10 (0.57-2.02)	.81
1.5 to 2 Hz	106 (76)	34 (24)	1.79 (1.08-2.89)	.05	1.36 (0.77-2.33)	.37
≥2 Hz	61 (60)	40 (40)	3.98 (2.41-6.50)	<.001	3.43 (2.03-5.70)	<.001
Not recorded	29 (62)	18 (38)	2.86 (1.36-5.89)	.02	2.28 (1.03-4.89)	.08
Any frequency	297 (72)	113 (28)	2.36 (1.78-3.13)	<.001	NA	NA
LPDs						
<1.5 Hz	325 (60)	220 (40)	7.55 (6.03-9.46)	<.001	6.20 (4.82-7.97)	<.001
1.5 to 2 Hz	58 (50)	59 (50)	10.89 (7.09-16.76)	<.001	6.42 (3.89-10.54)	<.001
≥2 Hz	20 (34)	38 (66)	16.40 (8.97-30.64)	<.001	10.60 (5.54-20.62)	<.001
Not recorded	46 (56)	36 (44)	4.93 (5.80-15.82)	<.001	8.41 (5.03-13.93)	<.001
Any frequency	449 (56)	353 (44)	8.61 (7.08-10.49)	<.001	6.53 (5.15-8.28)	<.001
BIPDs						
Any frequency	88 (72)	34 (28)	1.83 (1.12-3.03)	.04		

Abbreviations: BIPDs, bilateral independent periodic discharges; FDR, false discovery rate; GPDs, generalized periodic discharges; GRDA, generalized rhythmic delta activity; LPDs, lateralized periodic discharges; LRDA, lateralized rhythmic delta activity; NA, not applicable.

^a Odds ratios and P values were additionally adjusted for plus to control for confounding risk using FDR.

Figure. Model of Pattern Characteristics and Seizure Risk

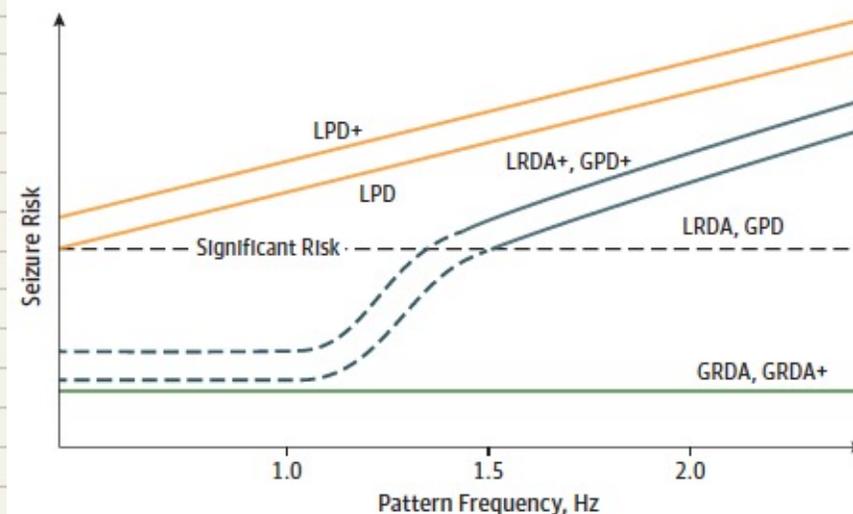
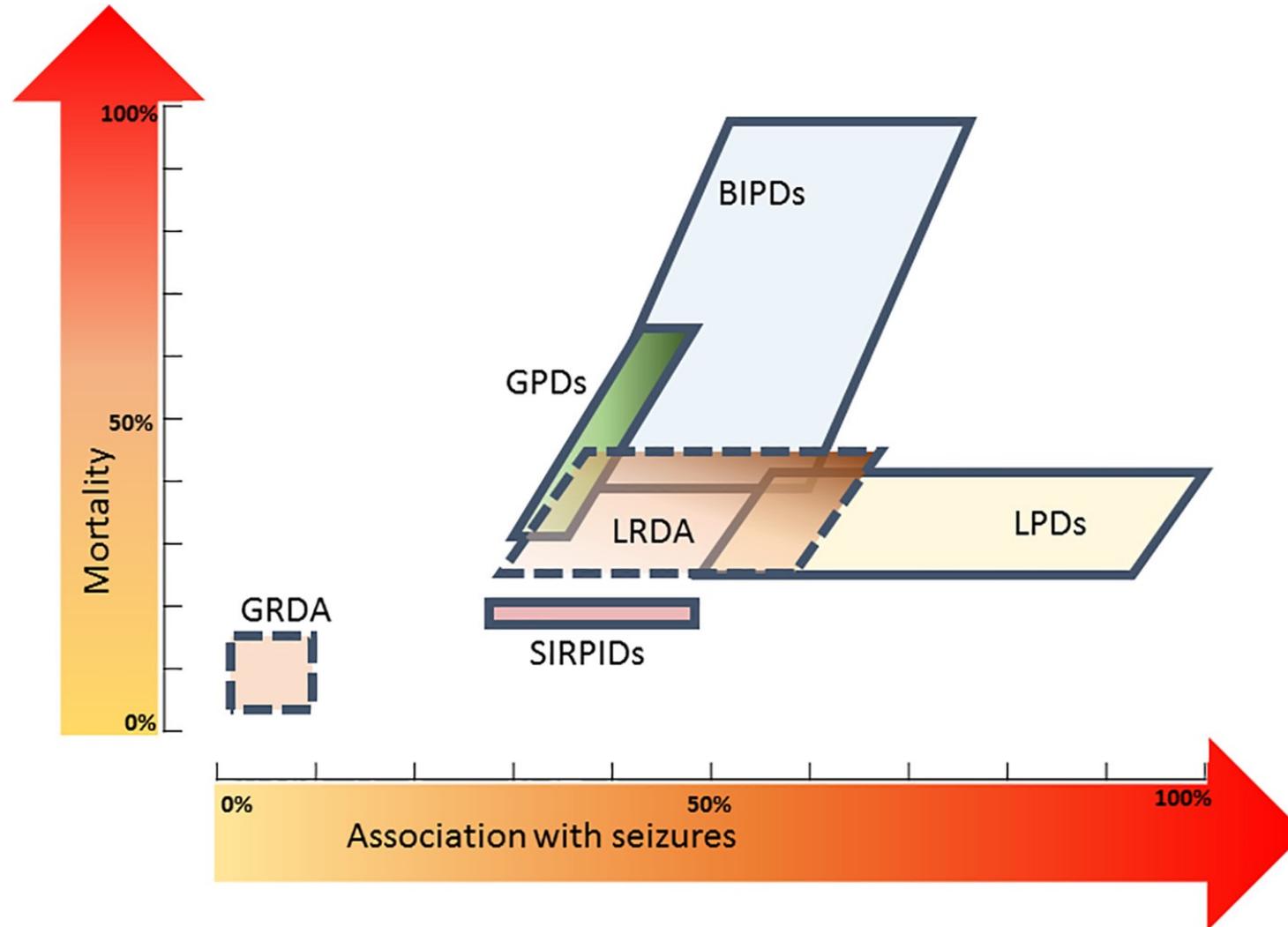


Table 1
Reported etiologies, association with seizures, and mortality of periodic and rhythmic patterns.

Feature	Common causes		Association with seizures	Mortality
Lateralized Periodic Discharges (LPDs)	Stroke Tumor Infection	Hemorrhage	50–100%	24–41%
Bilateral Independent Periodic Discharges (BIPDs)	Stroke Anoxic injury Metabolic disorders	Infection Tumors	43–78%	39–100%
Generalized Periodic Discharges (GPDs)	Metabolic Sepsis Anoxic	Stroke	29–50%	30–64%
Lateralized Rhythmic Delta Activity (LRDA)	Hemorrhage Stroke Tumor	TBI Infection	25–63%	
Generalized Rhythmic Delta Activity (GRDA)	Encephalopathy Stroke Hemorrhage	Tumor Infection Drug induced	No additional association with seizures compared to controls without GRDA	
Stimulus-Induced Rhythmic, Periodic, or Ictal Discharges (SIRPIDs)	Hemorrhage Anoxic injury Drug toxicity	Metabolic TBI	27–51% One large study found no increase in seizures when features had stimulus-induced compared to spontaneous patterns	17%

Population of the ictal-interictal zone: The significance of periodic and rhythmic activity

Emily L. Johnson, Peter W. Kaplan, 2017 Clinph practice



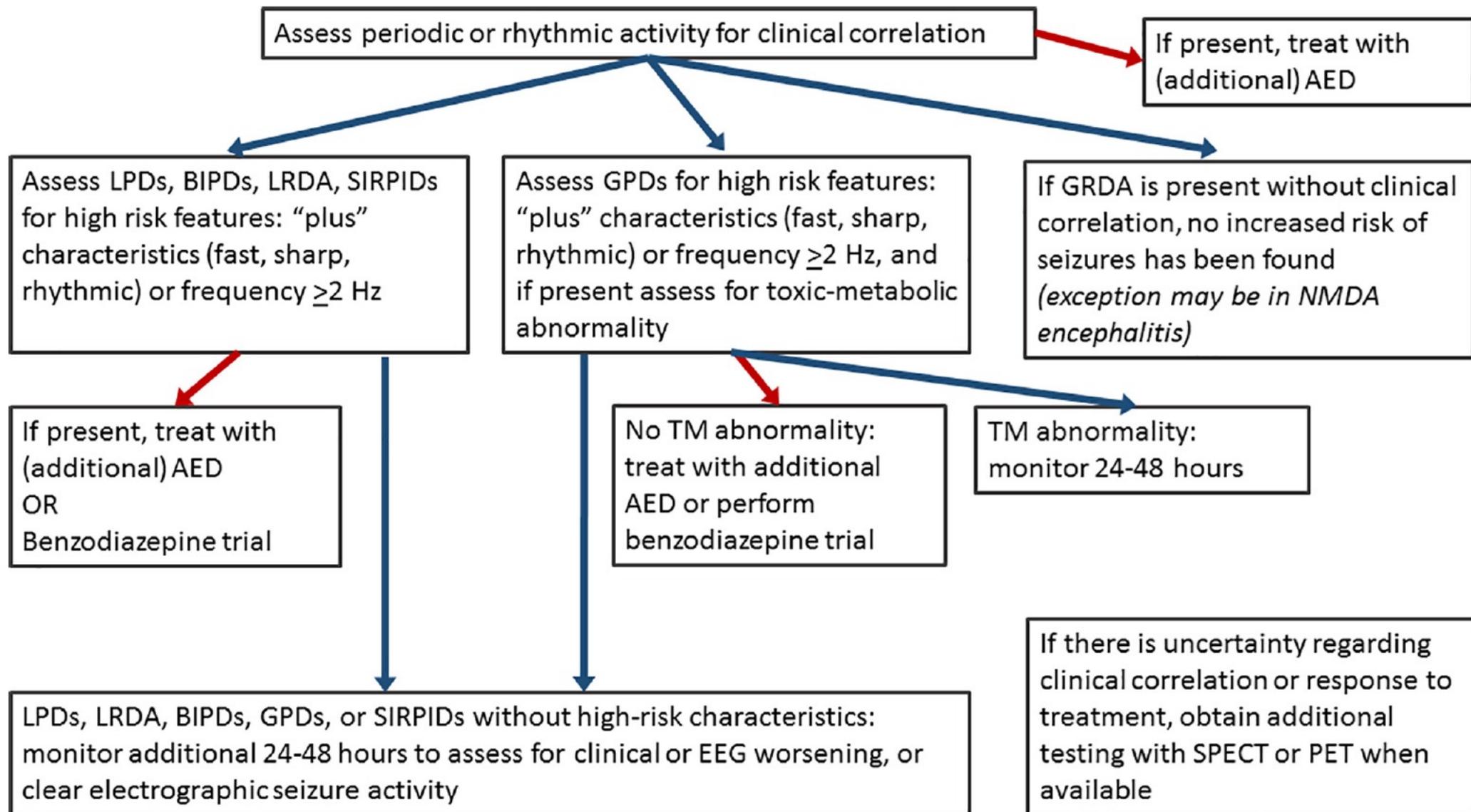


Fig. 8. Suggested algorithm for approach to patterns on the ictal-interictal continuum. AED = antiepileptic drug; LPDs = lateralized periodic discharges; BIPDs = bilateral independent periodic discharges; GPDs = generalized periodic discharges; LRDA = lateralized rhythmic delta activity; GRDA = generalized rhythmic delta activity; SIRPIDs = stimulus-induced rhythmic, periodic, or ictal discharges; TM = toxic-metabolic.

Non trattiamo l'EEG ma le crisi dei pazienti.
Il bello del gioco è cercare il correlato clinico, ma spesso non è affatto semplice.

