Encefalopatie Epilettiche “tardive”

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“IV Corso RESIDENZIALE:
EEG e POTENZIALI EVOCATI”

Roma 24/11/21

Outlines

- Definition of Epileptic Encephalopathy
- Developmental versus Epileptic Encephalopathy
- Ictal and interictal EEG patterns
- Syndromic classification
- Example of Developmental Encephalopathy

Epileptic encephalopathy - Definitions

- "Condition in which the **epileptiform abnormalities** are believed to contribute to progressive disturbance in cerebral function."
  (Engel, 2001)

- "Evidence suggests or supports the notion that there is an **epilepsy-dependent** neurodevelopmental or neurodegenerative **process** involved in the evolution of the syndrome (as opposed to an underlying metabolic, degenerative, or encephalitic process),"

  (Engel, 2006)

- Epileptic encephalopathy embodies the notion that the epileptic activity itself may contribute to severe cognitive and behavioral impairments **above and beyond what might be expected from the underlying pathology alone** (e.g., cortical malformation), and that these can worsen over time.

- …..and…. may potentially occur in association with **any form of epilepsy**.
  (Berg et al. 2010)

- .. the term epileptic encephalopathy refers to conditions characterized by epilepsy associated with psychomotor impairment, the latter being ***potentially reversible*** once epileptic activity is controlled

Prof Ingrid Scheffer chairs the ILAE Task Force on the Classification of the Epilepsies.

"Developmental and epileptic encephalopathies"

- *Developmental encephalopathy* where there is just developmental impairment without frequent epileptic activity associated with regression or further slowing of development;
- *Epileptic encephalopathy* where there is no preexisting developmental delay and the genetic mutation is not thought to cause slowing in its own right;
- *Developmental and epileptic encephalopathy* where both factors play a role
- Where a genetic mutation is identified, the well recognized developmental and epileptic encephalopathies can be called by their gene name together with the word "encephalopathy" : *KCNK2 Encephalopathy*.

Scheffer et al., 2017

ILAE Proposal for Revised Terminology for Organization of Seizures and Epilepsies 2010

Electroclinical Syndromes and Other Epilepsies Grouped by Specificity of Diagnosis

Electroclinical syndromes

One example of how syndromes can be organized: Arranged by typical age at onset*

Neonatal period
- -Benign neonatal seizures^
- -Benign familial neonatal epilepsy (BFNE)
- -Ohtahara syndrome
- -Early Myoclonic encephalopathy (EME)

Infancy
- -Febrile seizures^, Febrile seizures plus (FS+)
- -Benign infantile epilepsy
- -Benign familial infantile epilepsy (BFIE)
- -West syndrome
- -Dravet syndrome
- -Myoclonic epilepsy in infancy (MEI)
- -Myoclonic encephalopathy in nonprogressive disorders
- -Epilepsy of infancy with migrating focal seizures

Childhood
- -Febrile seizures^, Febrile seizures plus (FS+)
- -Early onset childhood occipital epilepsy (Panayiotopoulos syndrome)
- -Epilepsy with myoclonic atonic (previously astatic) seizures
- -Childhood absence epilepsy (CAE)
- -Benign epilepsy with centrotemporal spikes (BECTS)
- -Autosomal dominant nocturnal frontal lobe epilepsy (ADNFLE)
- -Late onset childhood occipital epilepsy (Gastaut type)
- -Epilepsy with myoclonic absences
- -Lennox-Gastaut syndrome (LGS)
- -Epileptic encephalopathy with continuous spike-and-wave during sleep (CSWS)+
- -Landau-Kleffner syndrome (LKS)

Adolescence – Adult
- -Juvenile absence epilepsy (JAE)
- -Juvenile myoclonic epilepsy (JME)
- -Epilepsy with generalized tonic-clonic seizures alone
- -Autosomal dominant epilepsy with auditory features (ADEAF)
- -Other familial temporal lobe epilepsies

Variable age at onset
- -Familial focal epilepsy with variable foci (childhood to adult)
- -Progressive myoclonus epilepsies (PME)
- -Reflex epilepsies

Distinctive constellations/surgical syndromes

Distinctive constellations/Surgical syndromes
- -Mesial temporal lobe epilepsy with hippocampal sclerosis (MTLE with HS)
- -Rasmussen syndrome
- -Gelastic seizures with hypothalamic hamartoma
- -Hemiconvulsion-hemiplegia-epilepsy

Nonsyndromic epilepsies**

Epilepsies attributed to and organized by structural-metabolic causes
- -Malformations of cortical development (hemimegalencephaly, heterotopias, etc.)
- -Neurocutaneous syndromes (tuberous sclerosis complex, Sturge-Weber, etc.)
- -Tumor, infection, trauma, angioma, antenatal and perinatal insults, stroke, etc

Epilepsies of unknown cause

* The arrangement of eletroclinical syndromes does not reflect etiology,
^ Not traditionally diagnosed as epilepsy
+ Sometimes referred to as Electrical Status Epilepticus during Slow Sleep (ESES)
** Forms of epilepsies not meeting criteria for specific syndromes or constellations

This Proposal is a work in progress.....
We welcome your thoughts on this proposal. Please visit our Classification Discussion Group at: http://community.ilae-epilepsy.org/home/ to login and register your comments.

West syndrome
Lennox-Gastaut syndrome
Continuous Spike-Waves during slow-wave Sleep (CSWS)

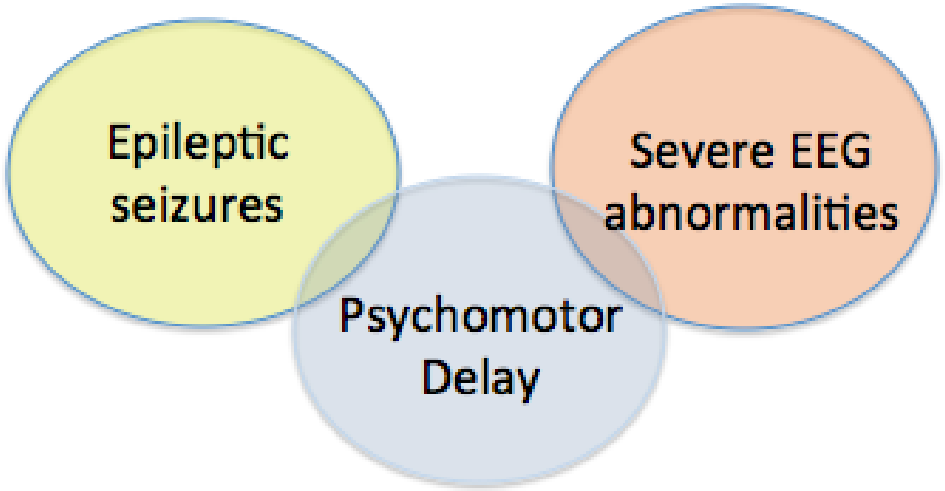
> "**Epileptic activity itself** contributes to severe cognitive and behavioural impairment above and beyond that expected from the underlying pathology and that these can worsen over time." **(Berg et al., 2010)**

> "Condition in which the **epileptiform abnormalities** are believed to contribute to progressive disturbance in cerebral function." **(Engel, 2001)**

- Etiologies are variable.
- Peculiar evolution of epilepsy towards a syndrome specific electro-clinical picture.
- Quantifiable cognitive and motor regression, characterized by an evident worsening of the neuropsychological profile when compared to pre-onset neurodevelopmental phenotype.
- Variable evolution, ranging from complete remission to very severe conditions, such as drug resistant epilepsy and severe mental retardation.

- "Condition in which the **epileptiform abnormalities** are believed to contribute to progressive disturbance in cerebral function." **(Engel, 2001)**

Epileptic Encephalopathies



ETIOLOGIES

- Brain malformations
- Chromosomal or genetic abnormalities
- Neurocutaneous diseases
- Hypoxic ischemic injuries
- Postnatal causes (vascular or infectious insults)

THERAPEUTIC GOALS

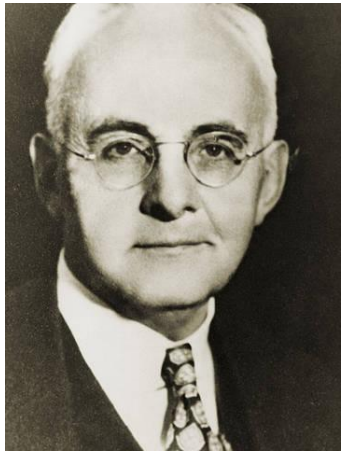
1- Seizures control

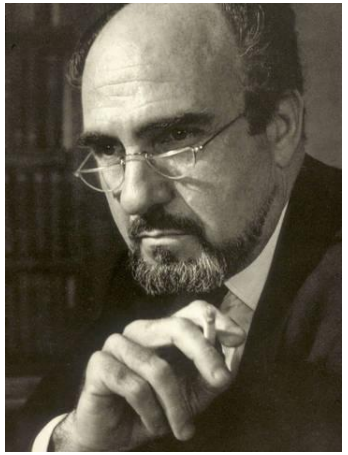
2- Decrease or resolution of EEG abnormalities

3- Developmental outcome

The Lennox Gastaut Syndrome dilemma

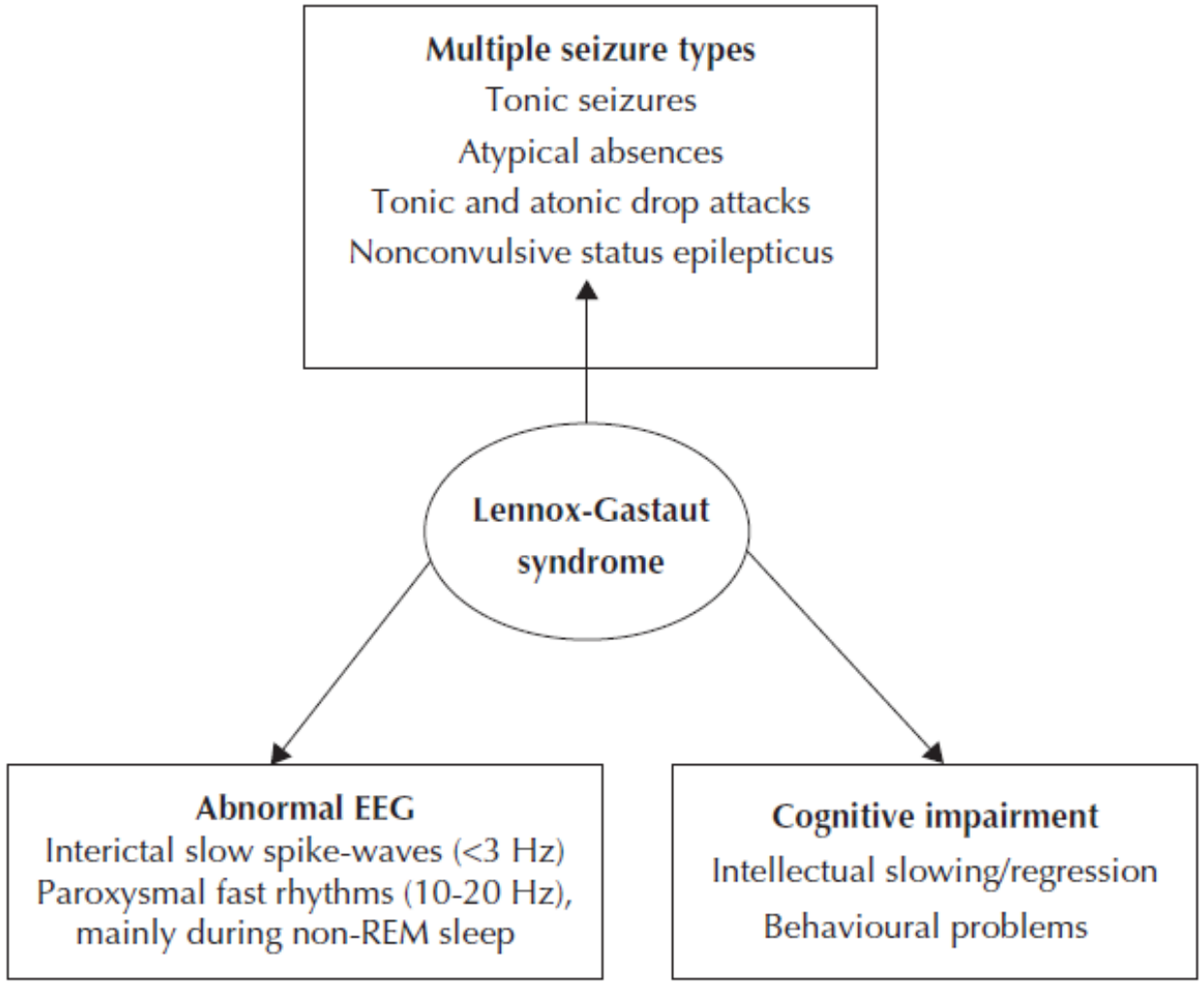
- LGS is one of the most complex epileptic disorders to manage, both for the general or pediatric neurologist and for specialists in epilepsy
- There is no biological marker of LGS available as yet and the many causes that are associated with the syndrome complicate the assessment of the disorder and the treatment protocols for trials
- There is a need for further trials and new drugs for the early treatment of LGS to be unanimously accepted by the epilepsy community.





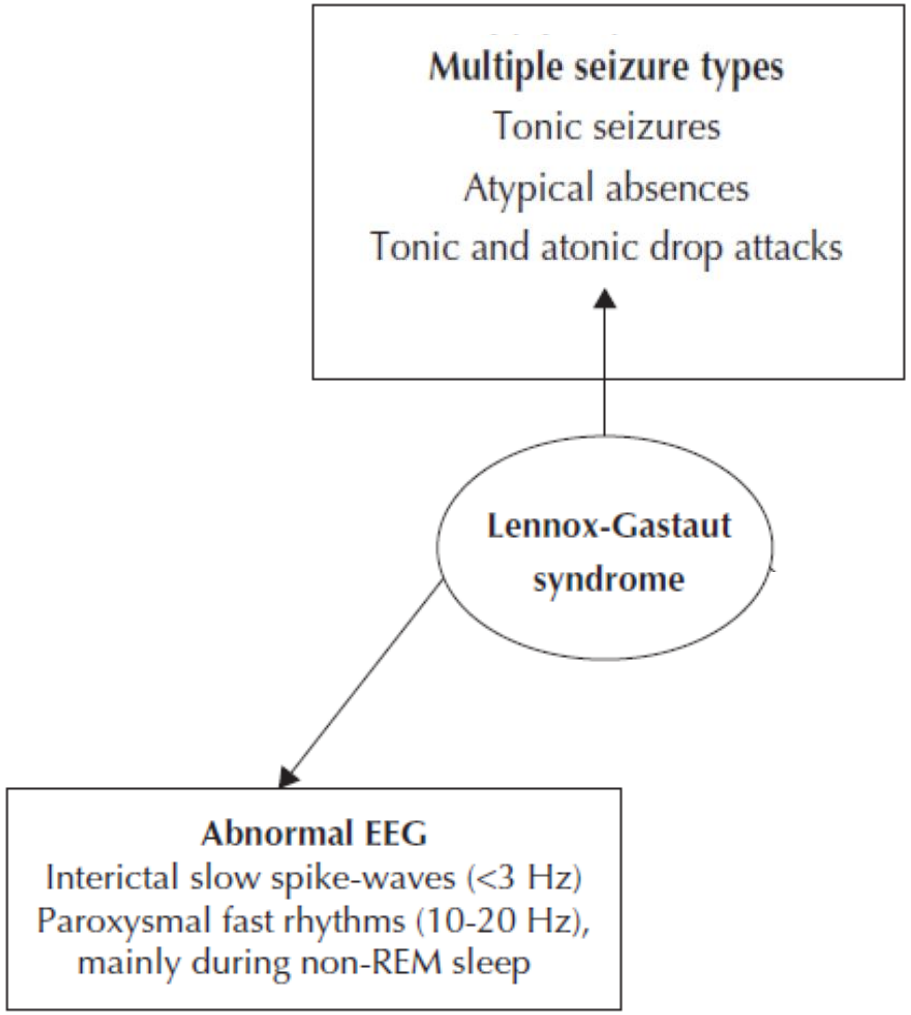
Characteristic Triad of Features in LGS

(Arzimanoglou, et.al. Epileptic Disord 2011; 13 (Suppl. 1): S3-S13)



Key criteria in LGS

(Cross JH, et.al. Frontiers in Neurology 2017; 8 (Article 505: 1-18)



Lennox-Gastaut Syndrome: Epidemiology and Etiology

- 1-10% of childhood epilepsies
- 7% of children with ID (55% LGS IQ <50)
- Prevalence: 4% of childhood epilepsies – incidence in new onset epilepsy : 0,6% *(Trevathan et al, 1997; Camfield et al, 1996)*
- Onset: 2-8yrs (most commonly 3-5yrs); very rare late onset (Down's syndrome)
- Persist through adolescence and on into adulthood
- Males have 5.3 relative risk vs female
- *De Novo* : 10% (?)
- Prior West Syndrome: 30 - 65%
- Preceding history other than West syndrome: 70 - 80%

Lennox-Gastaut Syndrome: Epidemiology and Etiology

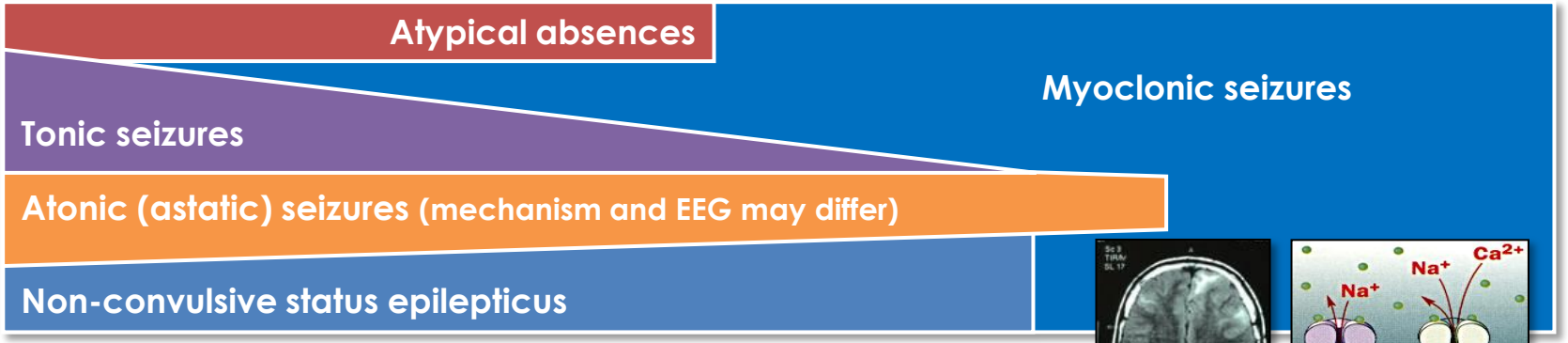
- Cryptogenic 33%
- Symptomatic 66%:
- - Brain malformation (LIS1, DCX,GPR56)
- - Infection
- - Tumor
- - TSC (TSC1, TSC2)
- - HHE
- - Gene mutations

Gene	Association
SCN1A	GEFS+/Dravet syndrome/other phenotypes
SLC2A1	GLUT1-deficiency syndrome
STXBP1	Infantile spasms/West syndrome, Lennox–Gastaut syndrome
DNM1	Infantile spasms/West syndrome, Lennox–Gastaut syndrome
GABRB3	Infantile spasms/West syndrome, Lennox–Gastaut syndrome

Cross et al. Frontiers in Neurology | www.frontiersin.org
September 2017 | Volume 8 | Article 505

(CHD2 – FOXG1)

Lennox-Gastaut syndrome (1)

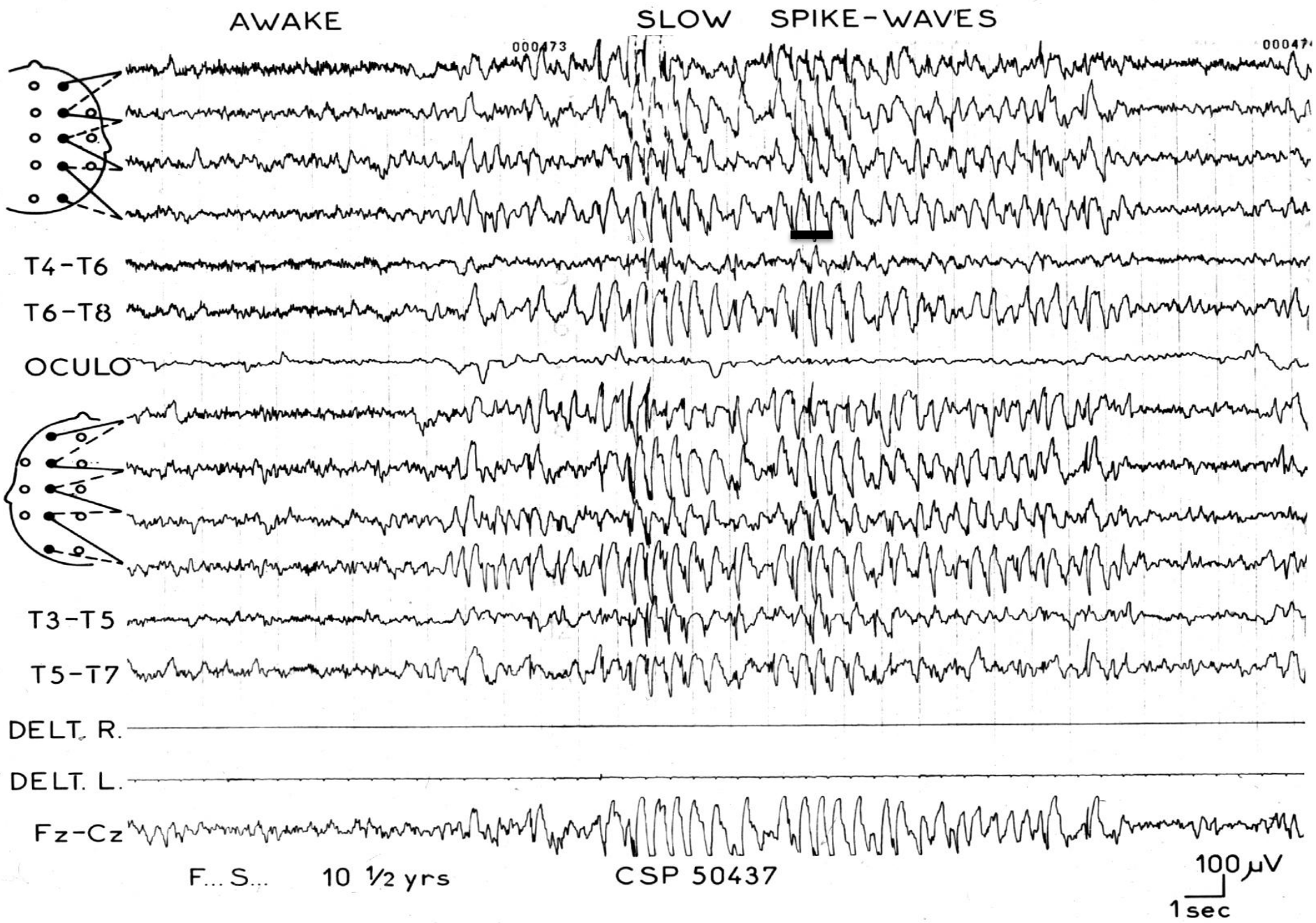


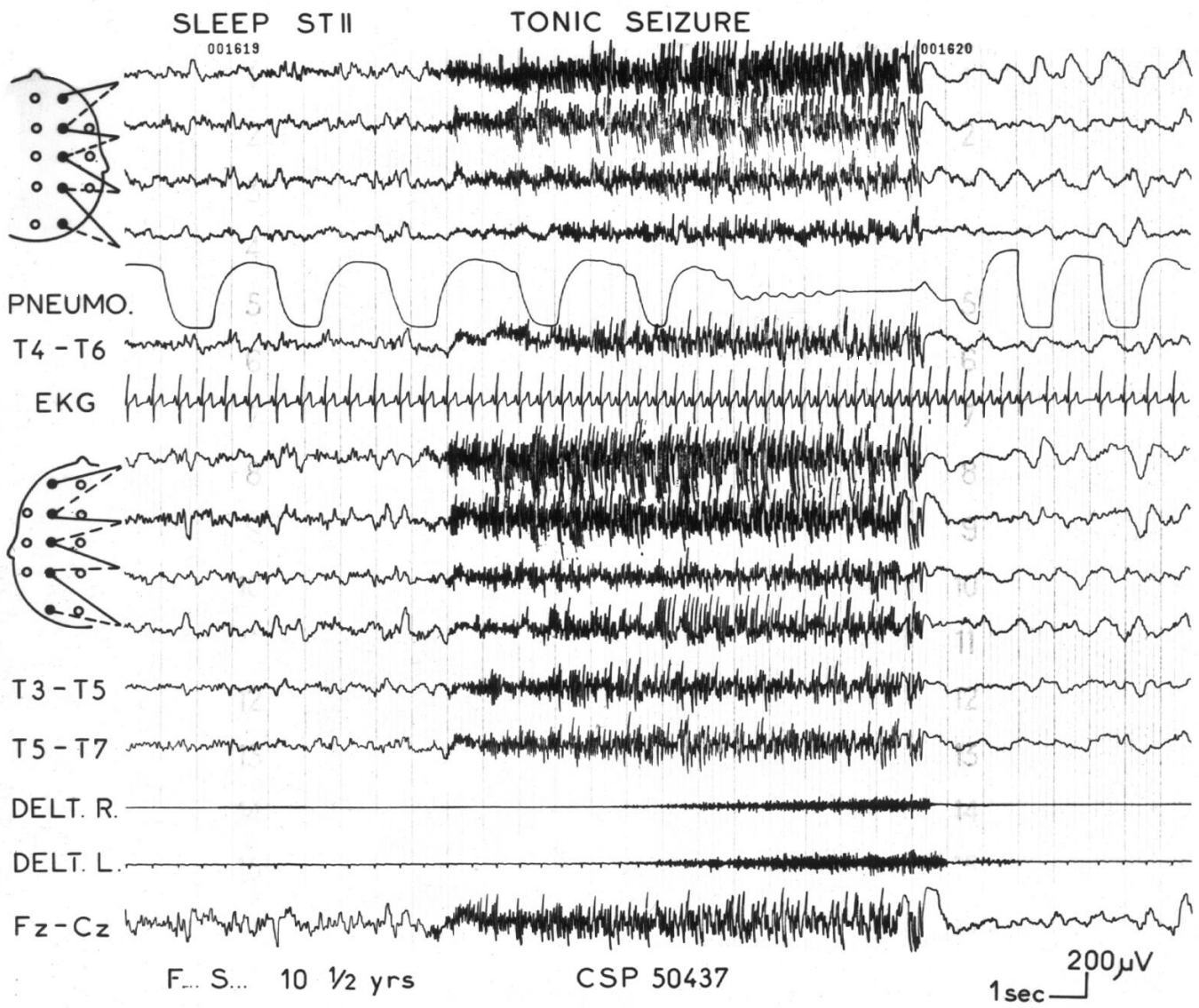
- By definition
  - Multiple types of seizures and various etiologies[1]
  - Cognitive and behavioral **deterioration**[2]
  - Frequent seizures; resistant to available AEDs[1]

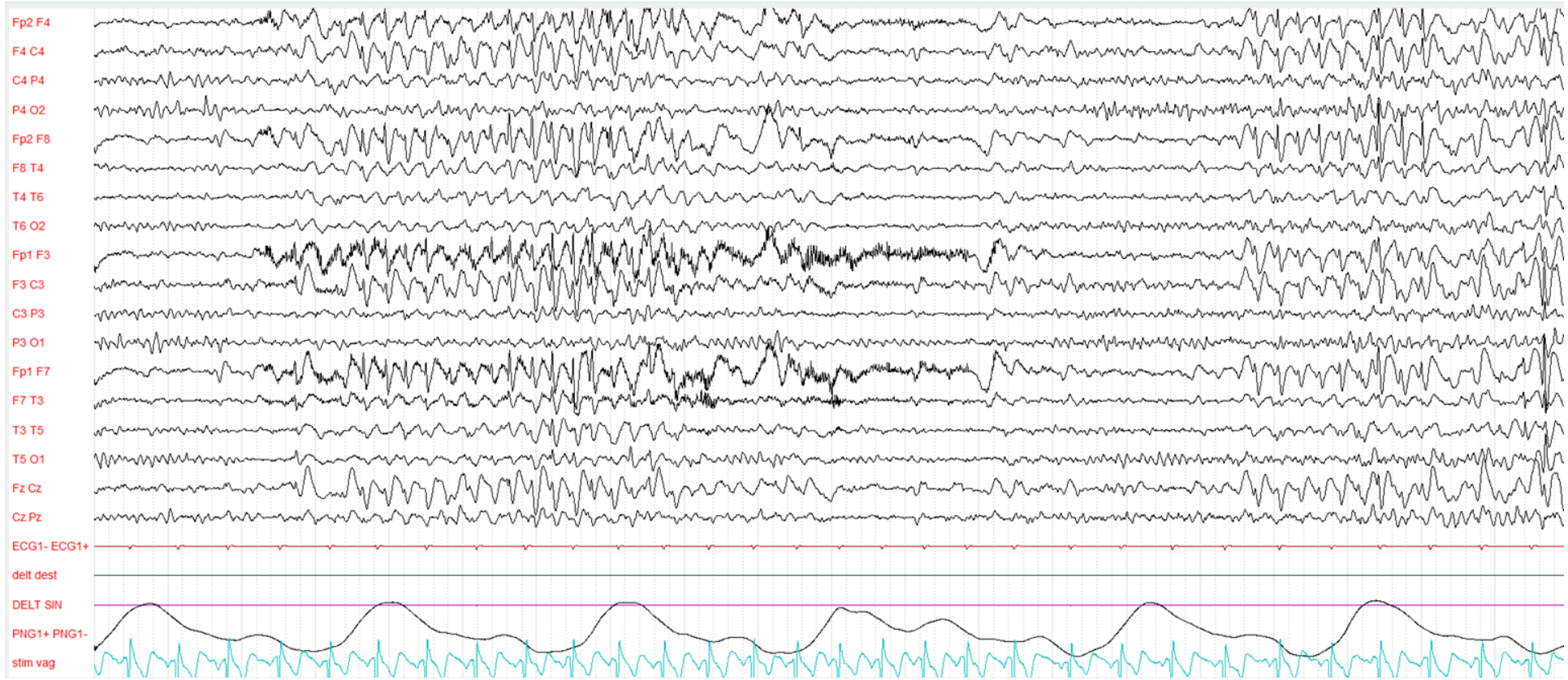
Speaker's own schematic (unpublished information)

1. Arzimanoglou A, et al. Lancet Neurol 2009;8:82–93
2. Guerrini R, et al. Epileptic encephalopathies. Oxford Textbook of Epilepsy and Epileptic Seizures. 2013:177

AED, antiepileptic drug; EEG, electroencephalogram


AWAKE
SLOW SPIKE-WAVES
000473
00047
T4-T6
T6-T8
OCULO
T3-T5
T5-T7
DELT. R.
DELT. L.
Fz-Cz
F... S... 10 ½ yrs
CSP 50437
100 µV
1 sec


SLEEP ST II
TONIC SEIZURE
001619
001620
PNEUMO.
T4 - T6
EKG
T3 - T5
T5 - T7
DELT. R.
DELT. L.
Fz - Cz
F... S... 10 ½ yrs
CSP 50437
200µV
1sec


Fp2 F4
F4 C4
C4 P4
P4 O2
Fp2 F8
F8 T4
T4 T6
T6 O2
Fp1 F3
F3 C3
C3 P3
P3 O1
Fp1 F7
F7 T3
T3 T5
T5 O1
Fz Cz
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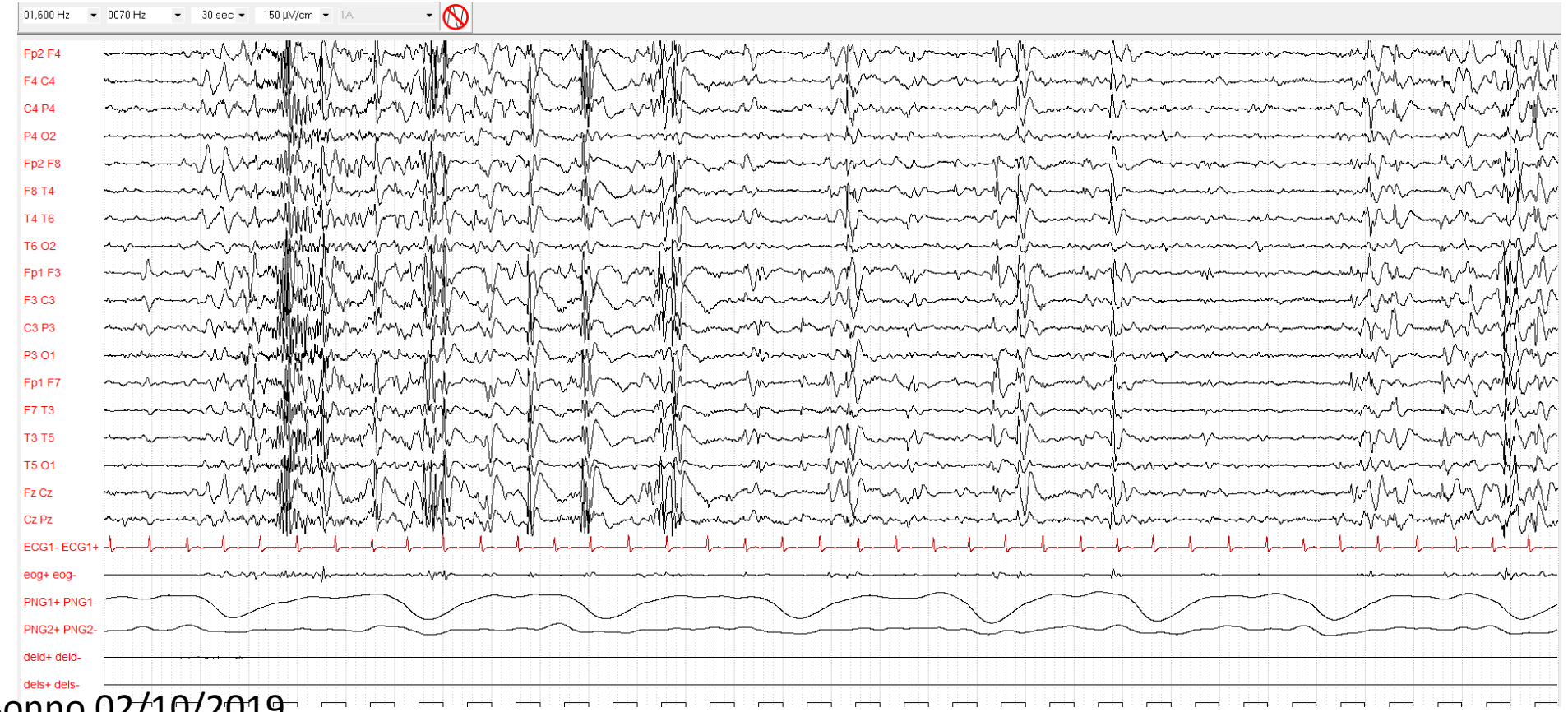
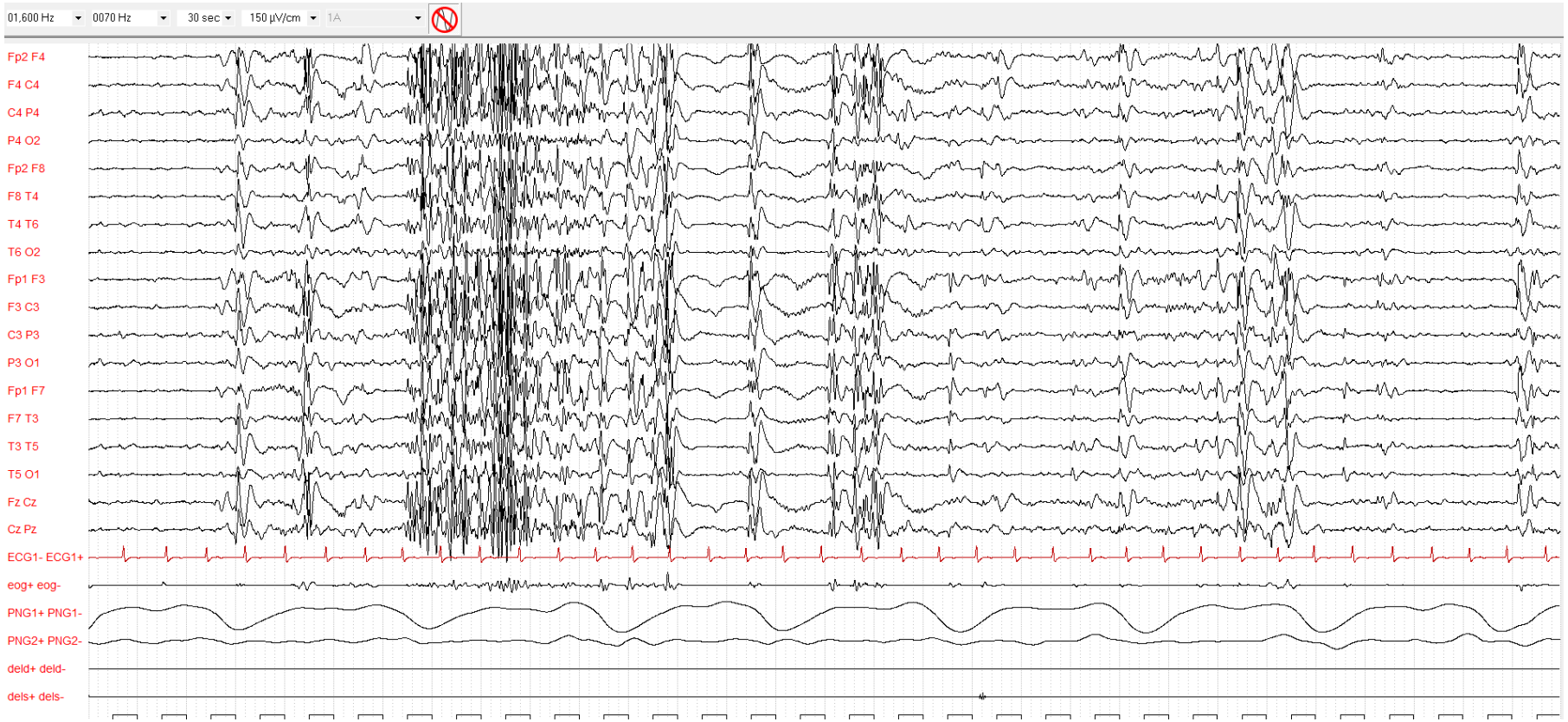
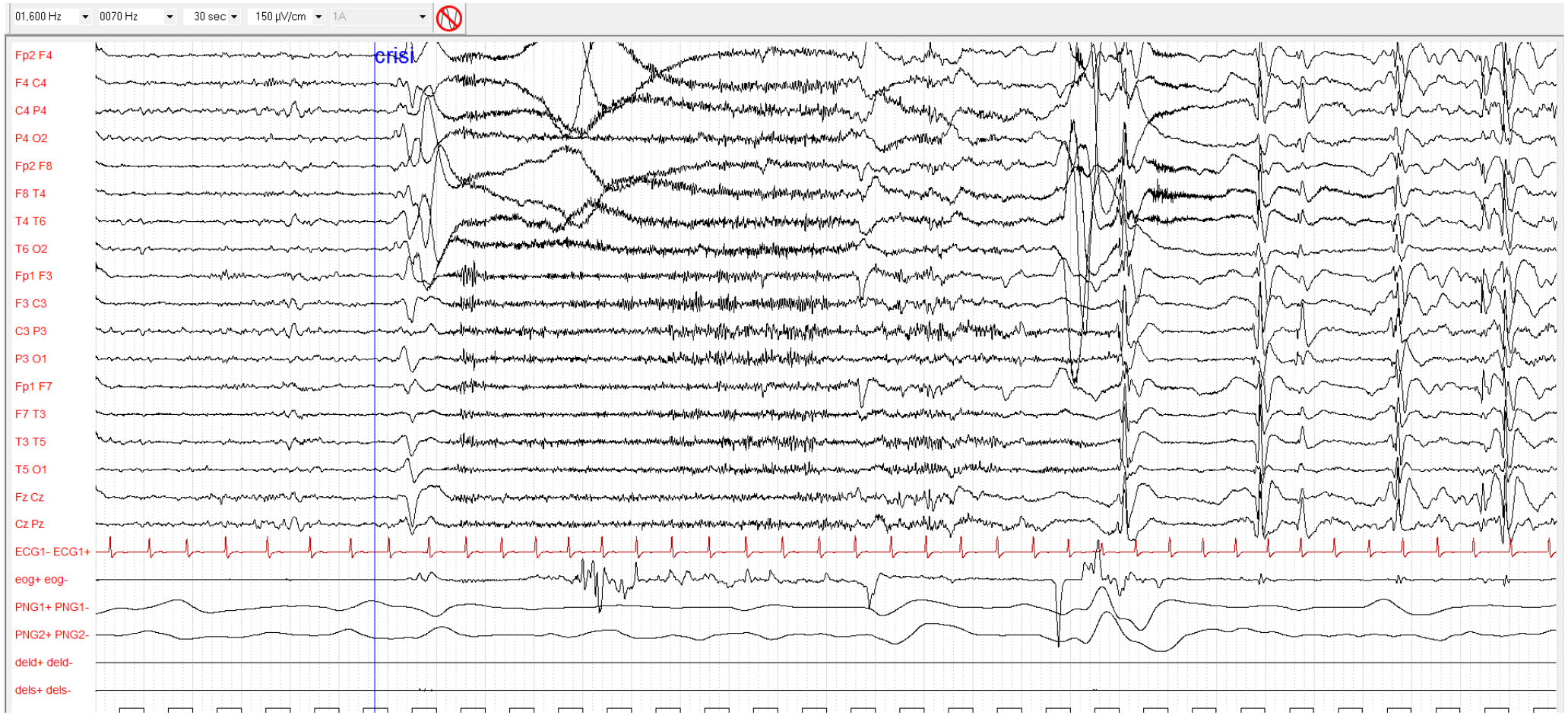
ECG1- ECG1+
delt dest
DELT SIN
PNG1+ PNG1-
stim vag



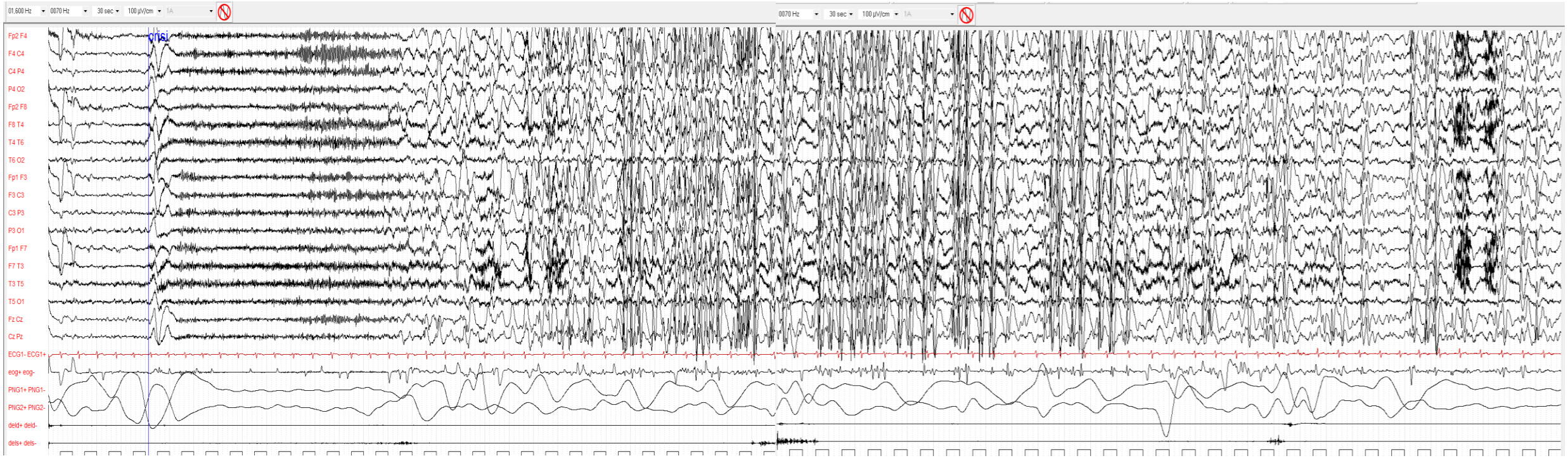
Sonno 02/10/2019



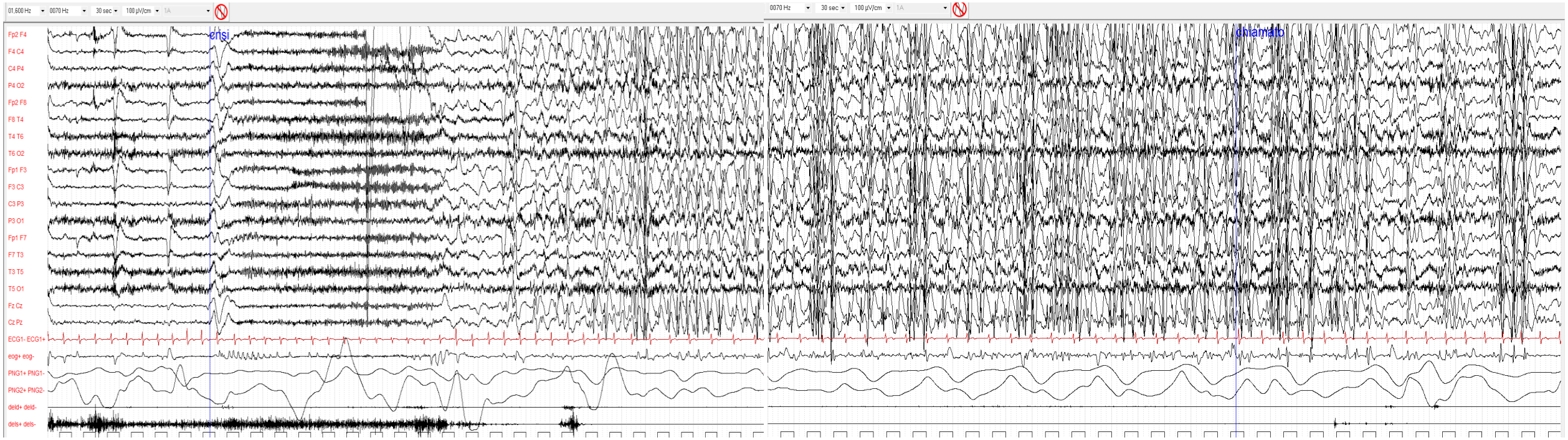
Sonno 02/10/2019



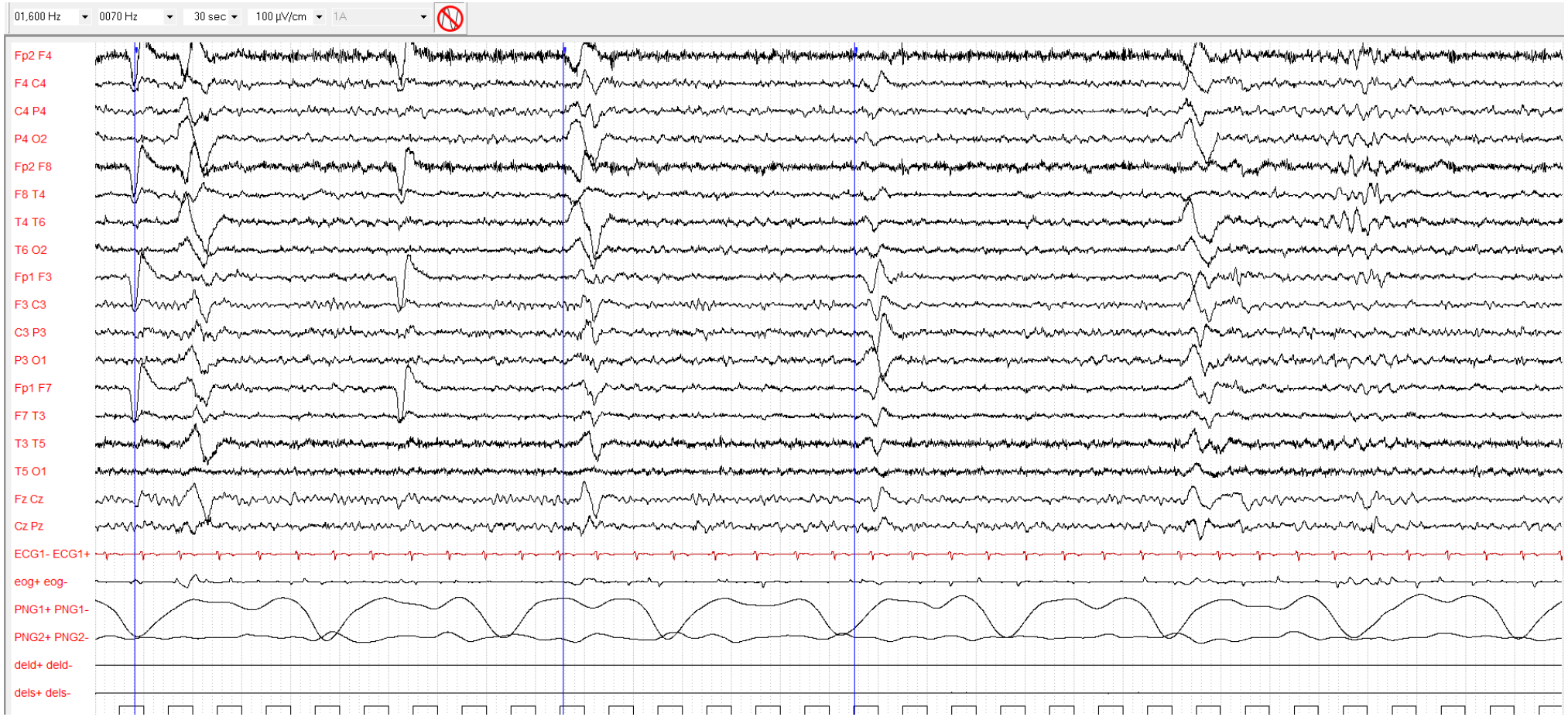
Crisi in sonno del 02/10/2019



Crisi 01/10/2019



Crisi 01/10/2019



Veglia 01/10/2019

Epilepsy with continuous spikes and waves during slow sleep

- Focal seizures, negative myoclonus and drop attacks
- ESES in NREM sleep
- Lesional and non-lesional cases
- Cognitive decline, attention deficit, behavioral problems
- Spike-Wave Index (SWI): 85-50%

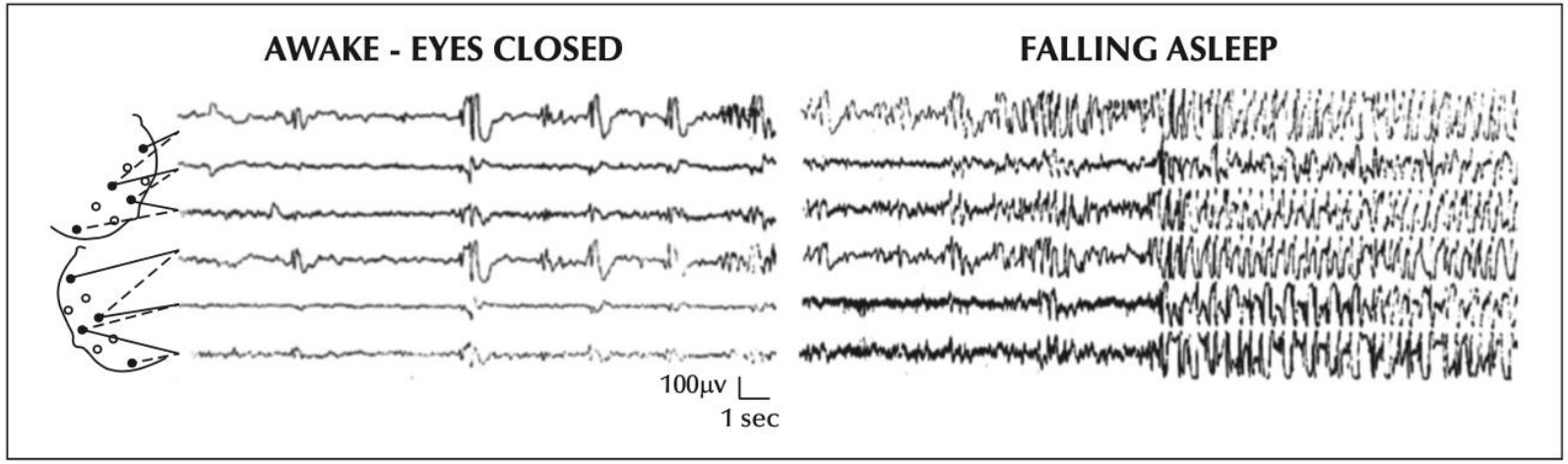
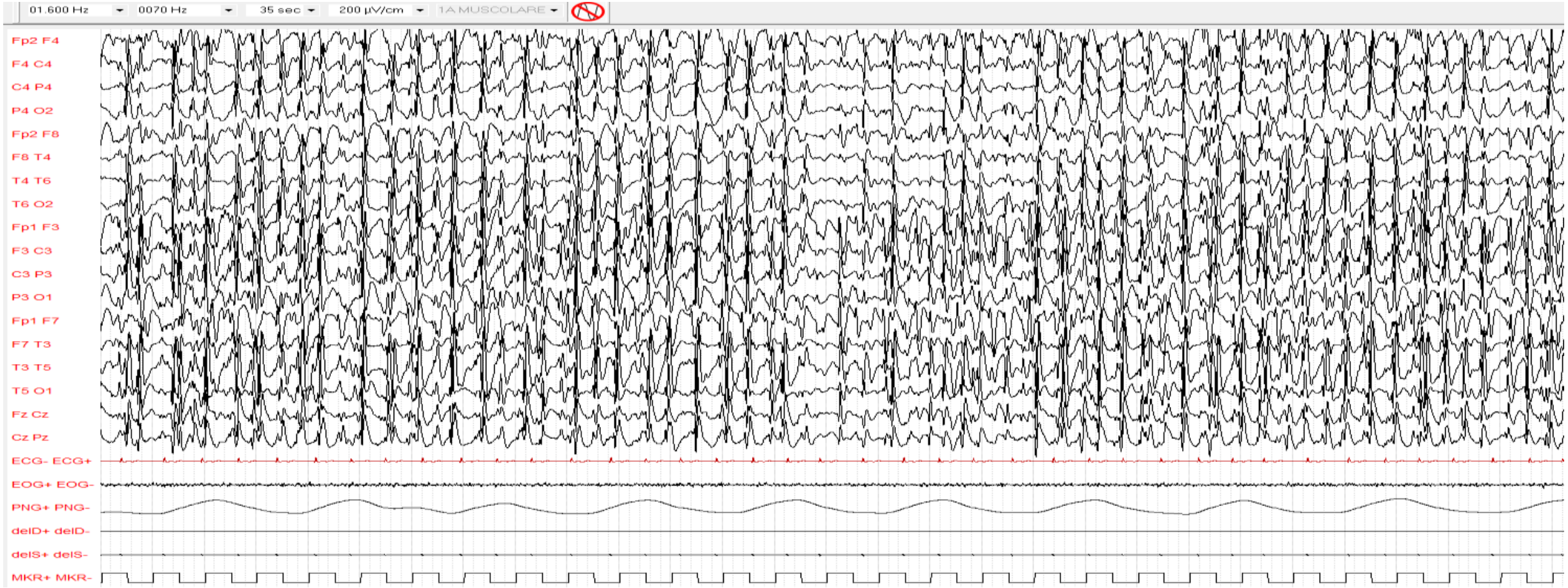
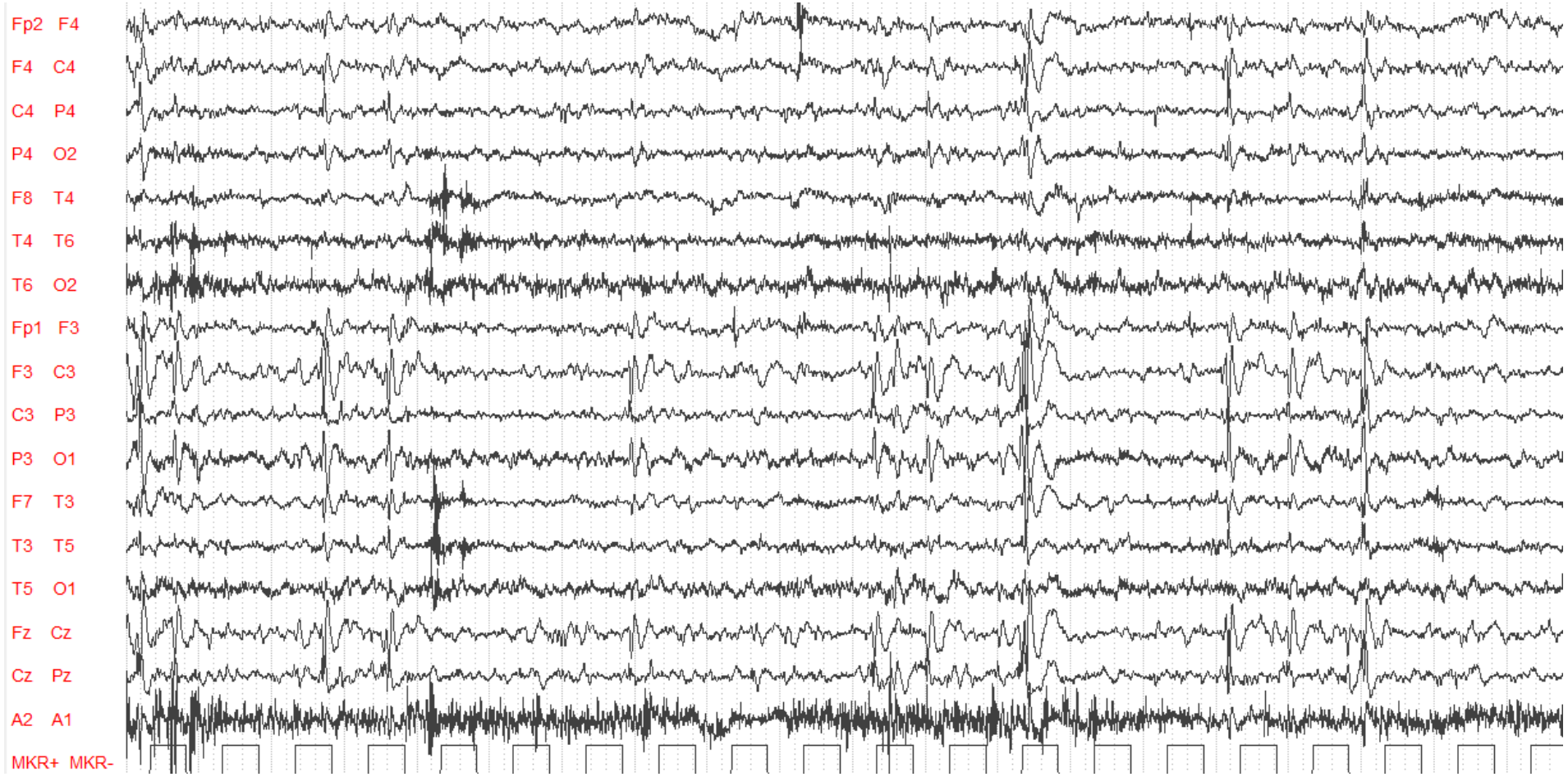


Figure 1. EEG tracing of an eight-year-old boy showing the transition from wakefulness to sleep and the appearance of continuous spike-and-wave discharge upon falling asleep (modified from the original report by Patry *et al.*, 1971).

Ne.Ma. Esiti emorragia cerebale neonatale idrocefalo derivato, crisi, disturbo apprendimento



Centro-temporal spikes are the hallmark of Rolandic Epilepsy



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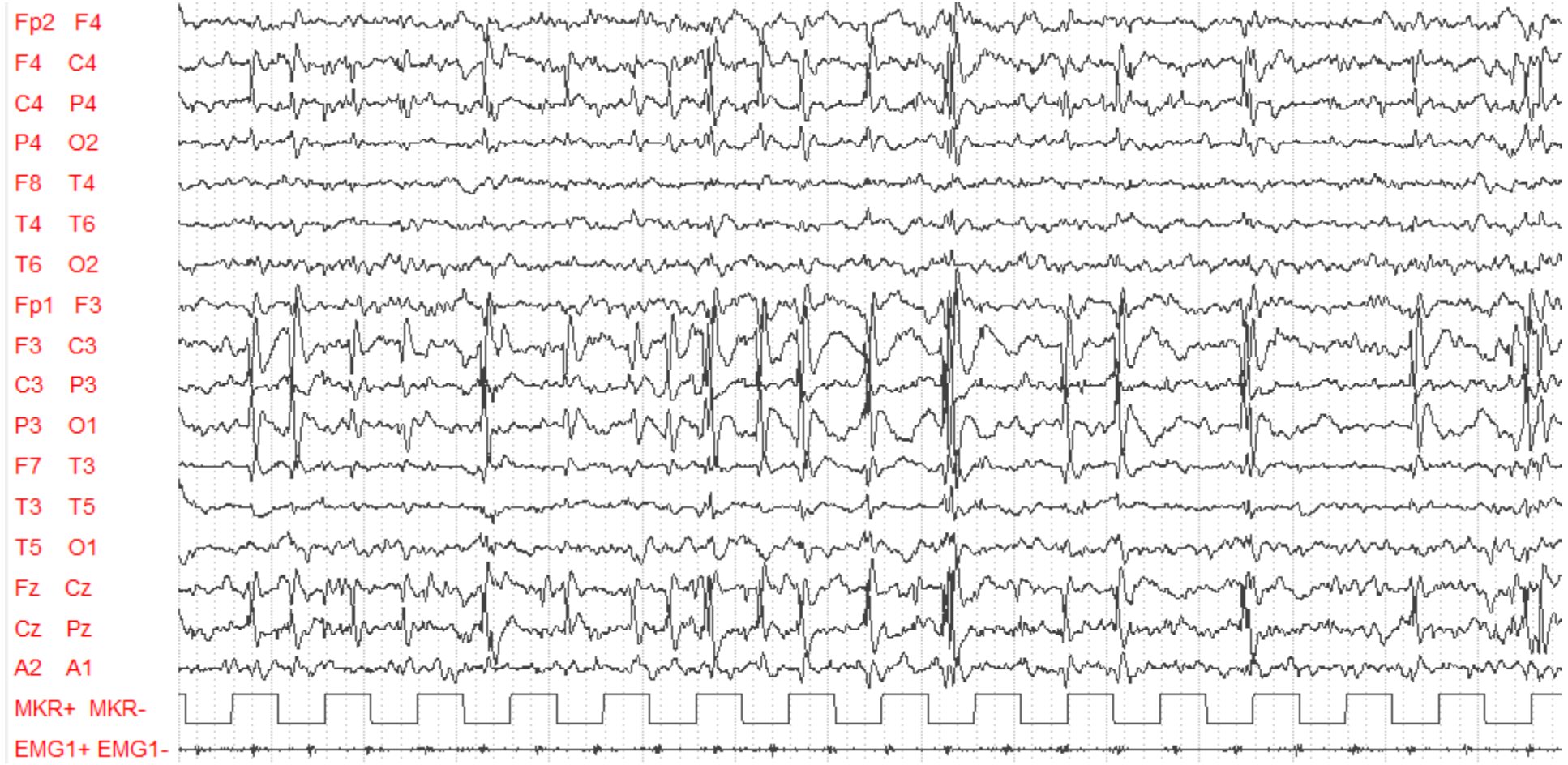


Atypical forms of BECTS

(Aicardi and Chevrie, 1982)

- **Atypical seizure characteristics**: earlier age of onset, day-time only seizures, postictal Todd's paresis, prolonged seizures or Status Epilepticus
- **Atypical EEG findings:** atypical spike morphology and location, absence-like spike and wave discharges, abnormal background activity, ESES.
- **Poor neuropsychological outcomes**.

The prevalence of atypical presentations and comorbidities of benign childhood epilepsy with centrotemporal spikes

*Eliel Tovia, †Hadassa Goldberg-Stern, ‡Bruria Ben Zeev, §Eli Heyman, ¶Nathan Watemberg, *Aviva Fattal-Valevski, and *Uri Kramer

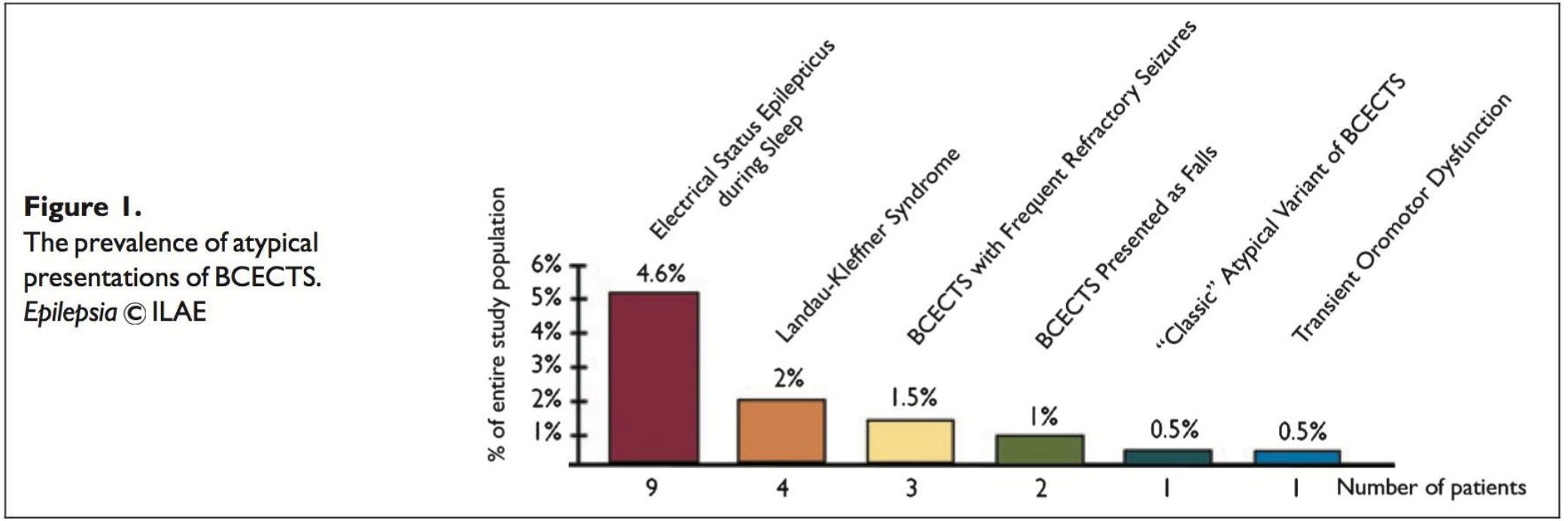
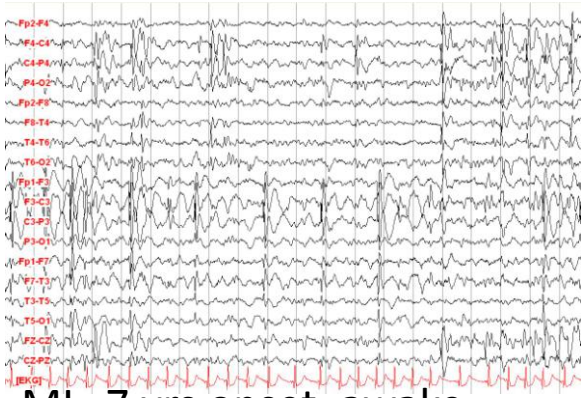
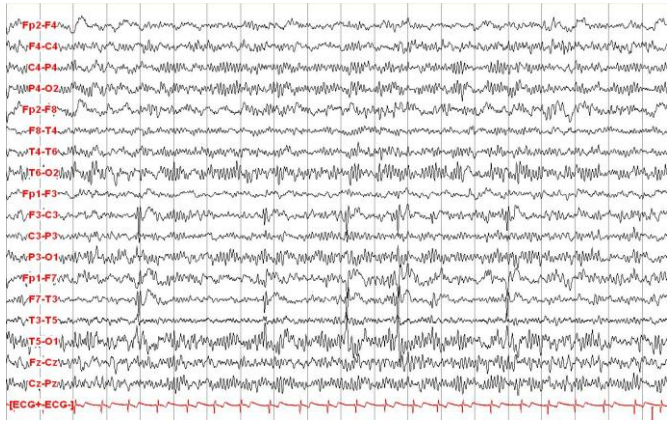


Figure 1.
The prevalence of atypical presentations of BCECTS.
Epilepsia © ILAE

Epilepsia, 52(8):1483–1488, 2011



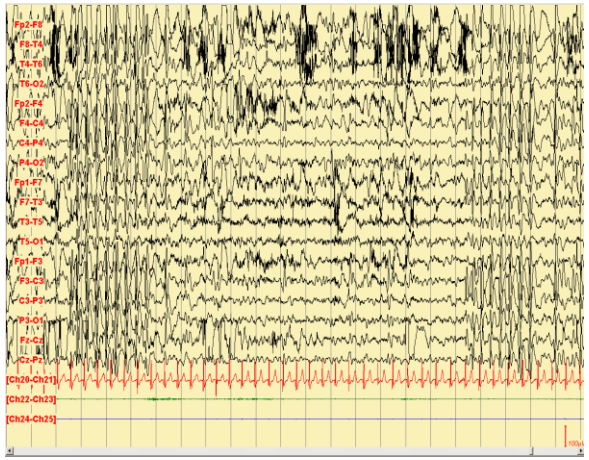
ML, 7 yrs onset, awake



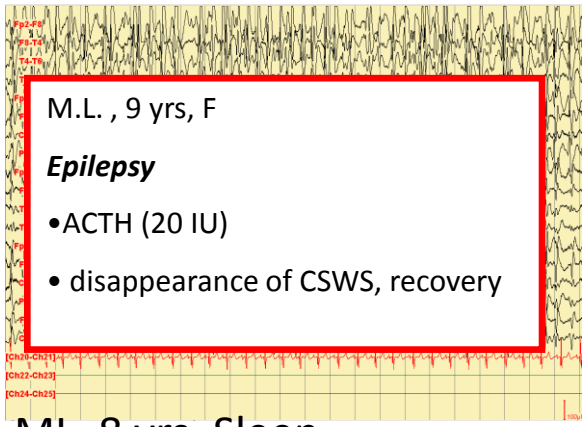
ML, 9 yrs outcome

Epilepsy

- Onset of rolandic seizures
- After 6 months new focal motor seizures without impairment of counsciousness
- Drop attacks and abcences
- Cognitive and attention deficits
- CLB and LEV ineffective
- Video-EEG: multiple myoclonic seizures, CSWS



ML, 8 yrs, Myoclonic Seizure



M.L. , 9 yrs, F

Epilepsy

- ACTH (20 IU)
- disappearance of CSWS, recovery

ML, 8 yrs, Sleep

Rolandic Epilepsy

Clinical spectrum and medical treatment of children with electrical status epilepticus in sleep (ESES)

*Uri Kramer, *Liora Sagi, †Hadassa Goldberg-Stern, ‡Nathanel Zelnik, §Andreea Nissenkorn, and §Bruria Ben-Zeev

30 pts
Arypical BECTS. 11 pts
Symptomatic 19 pts
Efficacy of AEDS < 41%
Efficacy of steroids 65%

Cognitive deterioration : 17 (57%)
Regression in attention, speech, communication: 13 (43%)

Permanent cognitive deficit (IQ decline): **14 (46%)**
Significant correlation: **duration of ESES**

Epilepsia, 50(6):1517–1524, 2009

Clinical spectrum and medical treatment of children with electrical status epilepticus in sleep (ESES)

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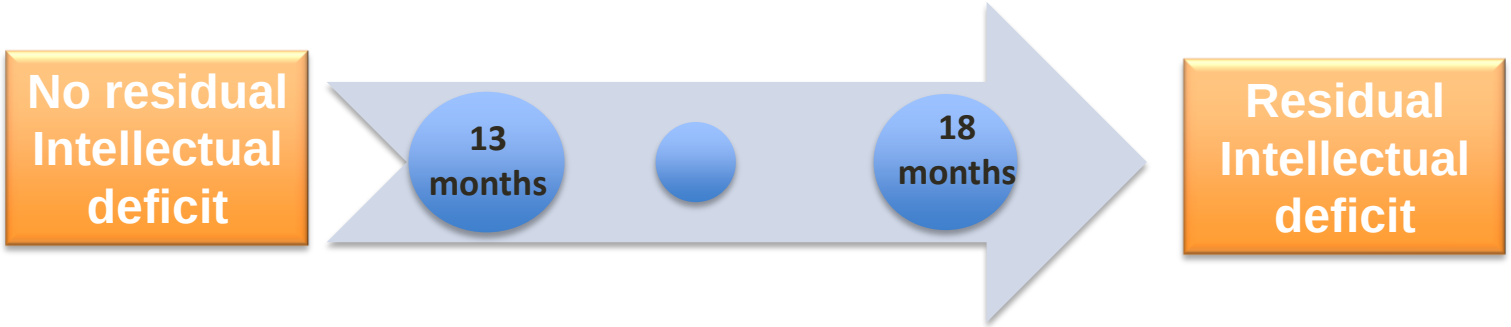
ESES Duration



The duration of ESES range 2–60 months

with **no significant**

difference between the different etiologies

N=30

Epilepsia, 50(6):1517–1524, 2009

A qualitative awake EEG score for the diagnosis of continuous spike and waves during sleep (CSWS) syndrome in self-limited focal epilepsy (SFE): A case-control study

Alec Aeby [a,*], Roberto Santalucia [a,b], Audrey Van Hecke [a], Andrea Nebbioso [c], Justine Vermeiren [a], Nicolas Deconinck [a], Xavier De Tiège [d], Patrick Van Bogaert [e,f]

Purpose: To determine whether awake EEG criteria can differentiate epileptic encephalopathy with continuous spike and waves during sleep (EE-CSWS) at the time of cognitive regression from typical, self-limited focal epilepsy (SFE).

Methods: This retrospective case-control study was based on the analysis of awake EEGs and included 15 patients with EE-CSWS and 15 age-matched and sex-matched patients with typical SFE. The EEGs were anonymised and scored by four independent readers. The following qualitative and quantitative EEG indices were analysed: slow-wave index (SLWI), spike-wave index (SWI), spike-wave frequency (SWF), long spike-wave clusters (CLSW) and EEG score (between grades 0 and 4). Sensitivity and specificity were assessed using receiver operating characteristic (ROC) curves and their reproducibility with a kappa test.

Results: Based on a highly sensitive cut-off, EE-CSWS patients were 8.4 times more likely than those with SFE to have an SLWI $> 6\%$, 15 times more likely to have an SWI $> 10\ \%$ and six times more likely to have a CLSW of ≥ 1 s. There was substantial agreement between readers (with kappa values of 0.64, 0.69 and 0.67). EE-CSWS patients were 13 times more likely to have an SWF of $> 11\ \%$ and 149 times more likely to have an EEG score of ≥ 3 than typical SFE patients. Agreement about these ratings was almost perfect (kappa 0.91 and 0.86).

Conclusion: An EEG score of ≥ 3 on a 20-min awake EEG differentiates typical SFE from EE-CSWS at the time of cognitive regression, with good reliability across readers with different levels of expertise.

Seizure: European Journal of Epilepsy 84 (2021) 34–39

GRIN2A mutations in acquired epileptic aphasia and related childhood focal epilepsies and encephalopathies with speech and language dysfunction

Lesca G. et al. 2013

nature genetics

Epileptic encephalopathies are severe brain disorders with the epileptic component contributing to the worsening of cognitive and behavioral manifestations[1]. Acquired epileptic aphasia (Landau-Kleffner syndrome, LKS)[2] and continuous spike and waves during slow-wave sleep syndrome (CSWSS)[3] represent rare and closely related childhood focal epileptic encephalopathies of unknown etiology[4,5]. They show electroclinical overlap with rolandic epilepsy (the most frequent childhood focal epilepsy) and can be viewed as different clinical expressions of a single pathological entity situated at the crossroads of epileptic, speech, language, cognitive and behavioral disorders[6–10]. Here we demonstrate that about 20% of cases of LKS, CSWSS and electroclinically atypical rolandic epilepsy[11–13] often associated with speech impairment can have a genetic origin sustained by *de novo* or inherited mutations in the *GRIN2A* gene (encoding the *N*-methyl-D-aspartate (NMDA) glutamate receptor α2 subunit, GluN2A). The identification of *GRIN2A* as a major gene for these epileptic encephalopathies provides crucial insights into the underlying pathophysiology.

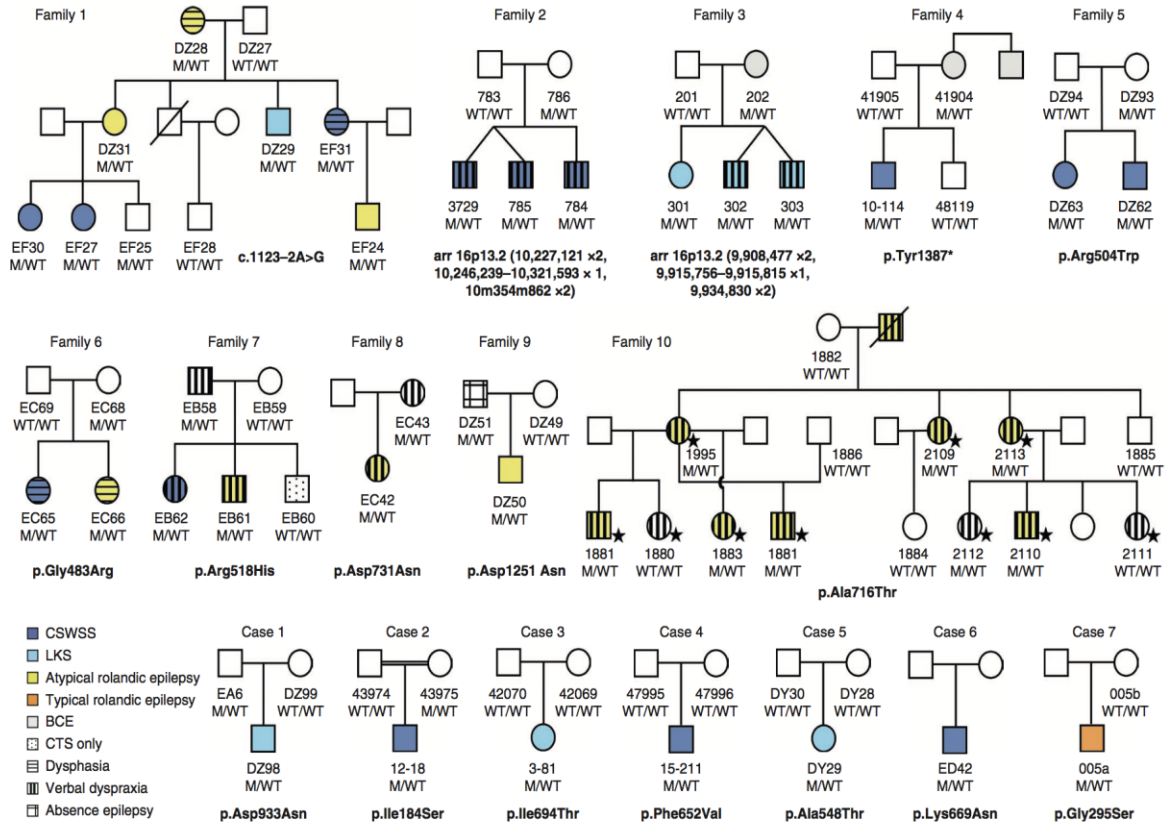


Figure 1 Inherited and *de novo* *GRIN2A* mutations in individuals and families with variable association of LKS, CSWSS, atypical rolandic epilepsy and speech impairment. CSWSS, continuous spike and wave during slow-wave sleep syndrome; LKS, Landau-Kleffner syndrome; BCE, benign childhood epilepsy; CTS, centrotemporal spikes; WT, wild-type *GRIN2A* allele; M, mutant *GRIN2A* allele; arr, array-CGH. Patient numbers are indicated under the symbols of individuals from whom DNA was available. Empty symbols represent unaffected individuals. In family 1, subject EF24 experienced his first rolandic seizures at age 22 months in the course of this study. In family 10, black stars indicate the subjects who inherited the previously reported p.Asn327Ser SRPX2 alteration; in this family, all affected individuals had intellectual deficiency of variable degree[17].

Electrical status epilepticus in sleep: The role of thalamus in etiopathogenesis

Huseyin Kilic [a,*], Kubra Yilmaz [a], Parvana Asgarova [b], Osman Kizilkilic [b], Gokçe Hale Hatay [c], Esin Ozturk-Isik [c], Cengiz Yalcinkaya [d], Sema Saltik [a]

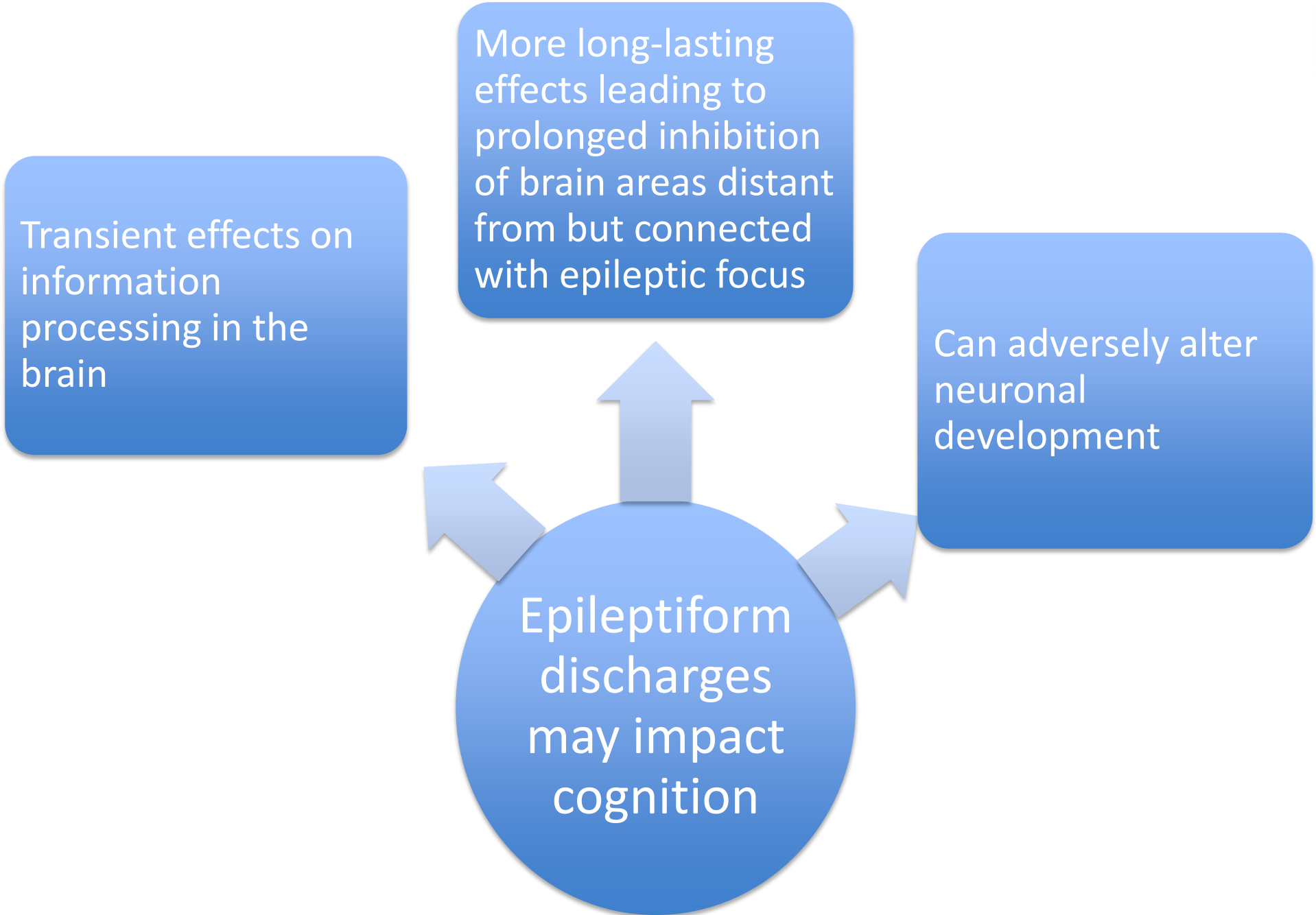
Purpose: In patients diagnosed with epilepsy, decreased ratio of N-acetyl aspartate to creatine (NAA/Cr) measured in magnetic resonance spectroscopy (MRS) has been accepted as a sign of neuronal cell loss or dysfunction. In this study, we aimed to determine whether a similar neuronal cell loss is present in a group of encephalopathy with electrical status epilepticus in sleep (ESES) patients

Methods: We performed this case-control study at a tertiary pediatric neurology center with patients with ESES. Inclusion criteria for the patient group were as follows: 1) a spike-wave index of at least 50%, 2) acquired neuropsychological regression, 3) normal cranial MRI. Eventually, a total of 21 patients with ESES and 17 control subjects were enrolled in the study. MRI of all control subjects was also within normal limits. 3D Slicer program was used for the analysis of thalamic and brain volumes. LCModel spectral fitting software was used to analyze single-voxel MRS data from the right and left thalamus of the subjects.

Results: The mean age was 8.0 ± 1.88 years and 8.3 ± 1.70 years in ESES patients and the control subjects. After correcting for the main potential confounders (age and gender) with a linear regression model, NAA/Creatine ratio of the right thalamus was significantly lower in the ESES patient group compared to the healthy control group ($p = 0.026$). Likewise, the left thalamus NAA/Cr ratio was significantly lower in the ESES patient group than the healthy control group ($p = 0.007$). After correcting for age and gender, right thalamic volume was not statistically significantly smaller in ESES patients than in healthy controls ($p = 0.337$), but left thalamic volume was smaller in ESES patients than in healthy controls ($p = 0.024$).

Conclusion: In ESES patients, the NAA/Creatine ratio, which is an indicator of neuronal cell loss or dysfunction in the right and left thalamus, which appears regular on MRI, was found to be significantly lower than the healthy control group. This metabolic-induced thalamic dysfunction, which was reported for the first time up to date, may play a role in ESES epileptogenesis.

Seizure: European Journal of Epilepsy 93 (2021) 44–50


More long-lasting effects leading to prolonged inhibition of brain areas distant from but connected with epileptic focus
Transient effects on information processing in the brain
Can adversely alter neuronal development
Epileptiform discharges may impact cognition

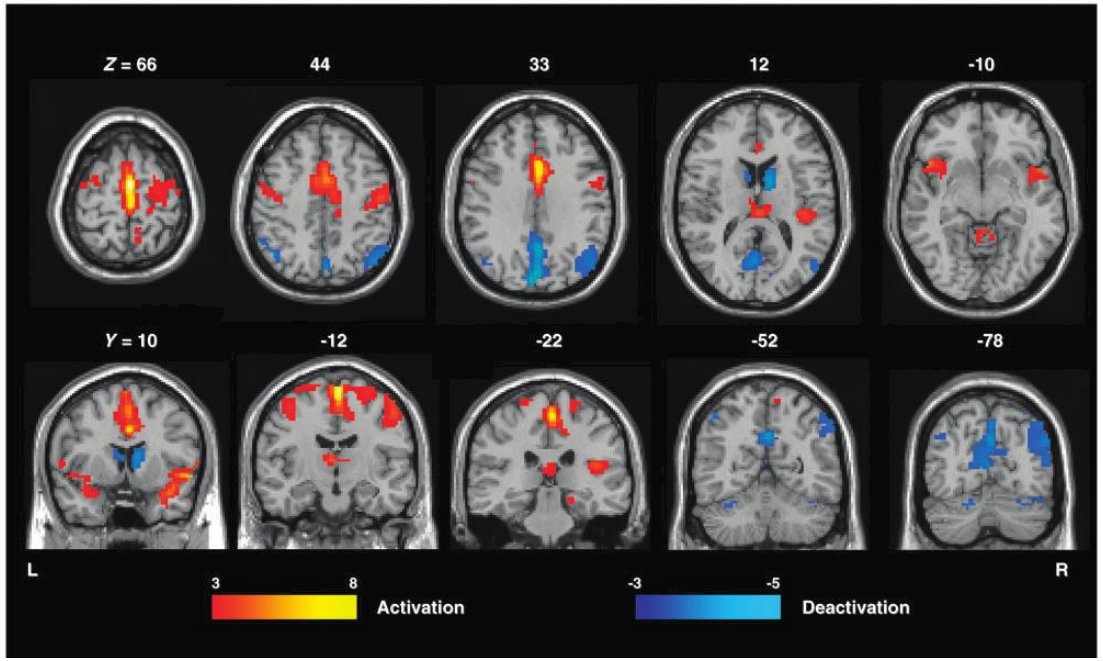
doi:10.1093/brain/awq183 Brain 2010: 133; 2798–2813 | 2798

BRAIN
A JOURNAL OF NEUROLOGY

Neuronal networks in children with continuous spikes and waves during slow sleep

Michael Siniatchkin,[1] Kristina Groening,[1] Jan Moehring,[1] Friederike Moeller,[1] Rainer Boor,[2] Verena Brodbeck,[3] Christoph M. Michel,[3] Roman Rodionov,[4] Louis Lemieux[4] and Ulrich Stephani[1]

- The spike-related deactivations were found in structures of the default mode network (precuneus, parietal cortex and medial frontal cortex)in all patients and in caudate nucleus in four.



- Despite aetiological heterogeneity, patients with CSWS were characterized by activation of the similar neuronal network: perisylvian region, insula and cingulate gyrus.
- The deactivations in structures of the default mode network are consistent with the concept of epileptiform activity impacting on normal brain function by inducing repetitive interruptions of neurophysiological function.

- "Condition in which the **epileptiform abnormalities** are believed to contribute to progressive disturbance in cerebral function." **(Engel, 2001)**

Epilepsia, 52(4):766–774, 2011
doi: 10.1111/j.1528-1167.2010.02948.x

FULL-LENGTH ORIGINAL RESEARCH

EEG-fMRI reveals activation of brainstem and thalamus in patients with Lennox-Gastaut syndrome

*Michael Siniatchkin, *Diana Coropceanu, *Friederike Moeller, †Rainer Boor, and *†Ulrich Stephani

*Department of Neuropediatrics, Christian-Albrechts-University, Kiel, Germany; and †Northern German Epilepsy Center, Raisdorf, Germany

Even if etiologies of Lennox-Gastaut syndrome (LGS) are diverse, the multiple causes converge into a final common pathway that results in this specific epilepsy phenotype.

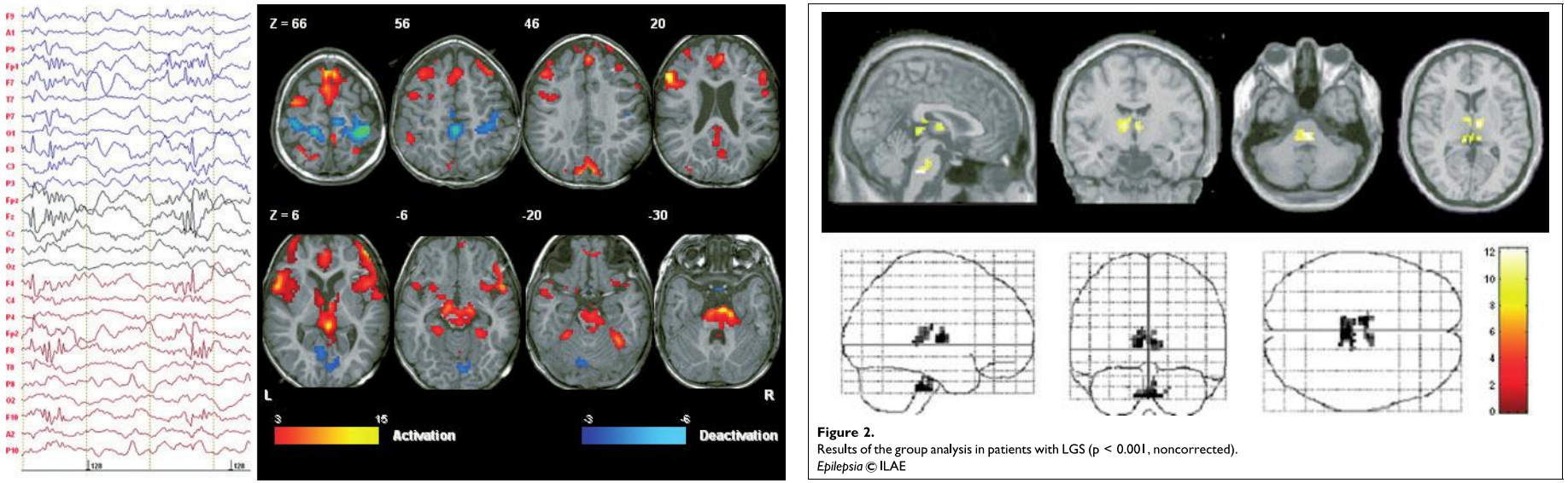


Figure 2.
Results of the group analysis in patients with LGS ($p < 0.001$, noncorrected).
Epilepsia © ILAE

Significant activation of brainstem and thalamus (especially centromedian and anterior thalamus) associated with epileptiform discharges in patients with LGS.

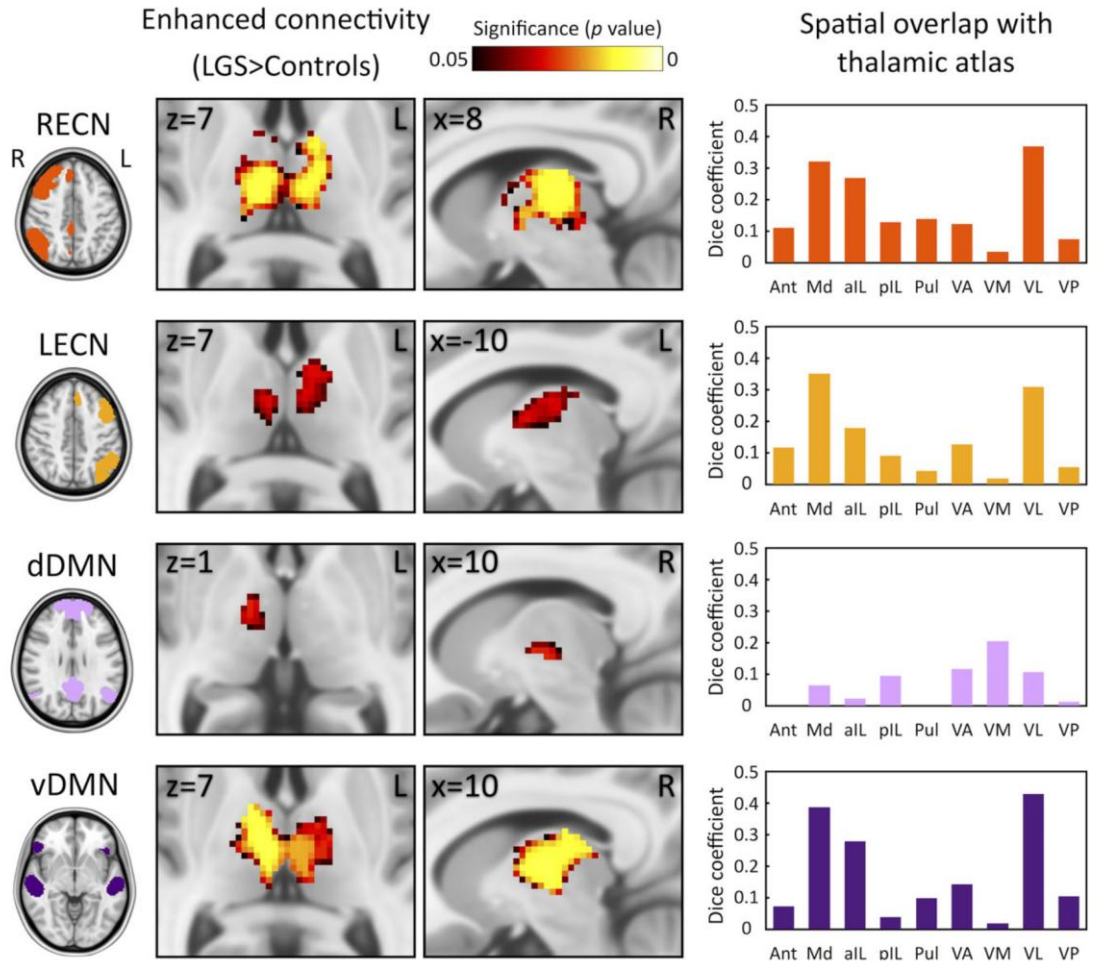
Thalamocortical functional connectivity in Lennox–Gastaut syndrome is abnormally enhanced in executive-control and default-mode networks

*†Aaron E. L. Warren, *‡David F. Abbott, *‡§Graeme D. Jackson, and *†‡§John S. Archer

Epilepsia, 58(12):2085–2097, 2017

Conclusions

Our findings identify specific thalamocortical circuits affected in LGS. Despite heterogeneous etiologies, functional connectivity is abnormally enhanced between the mediodorsal and ventrolateral thalamus, and the cortical default-mode and executive-control networks. In contrast, posterior thalamic areas, which show dominant connectivity with primary and sensory cortical networks, are less affected in LGS. Given our previous studies showing that epileptic activity in LGS disrupts the default-mode and executive-control networks,[3–6,12] we hypothesize that the mediodorsal and ventrolateral thalamus may be candidate targets for modulating abnormal network behavior underlying LGS, potentially via emerging thalamic neurostimulation therapies.

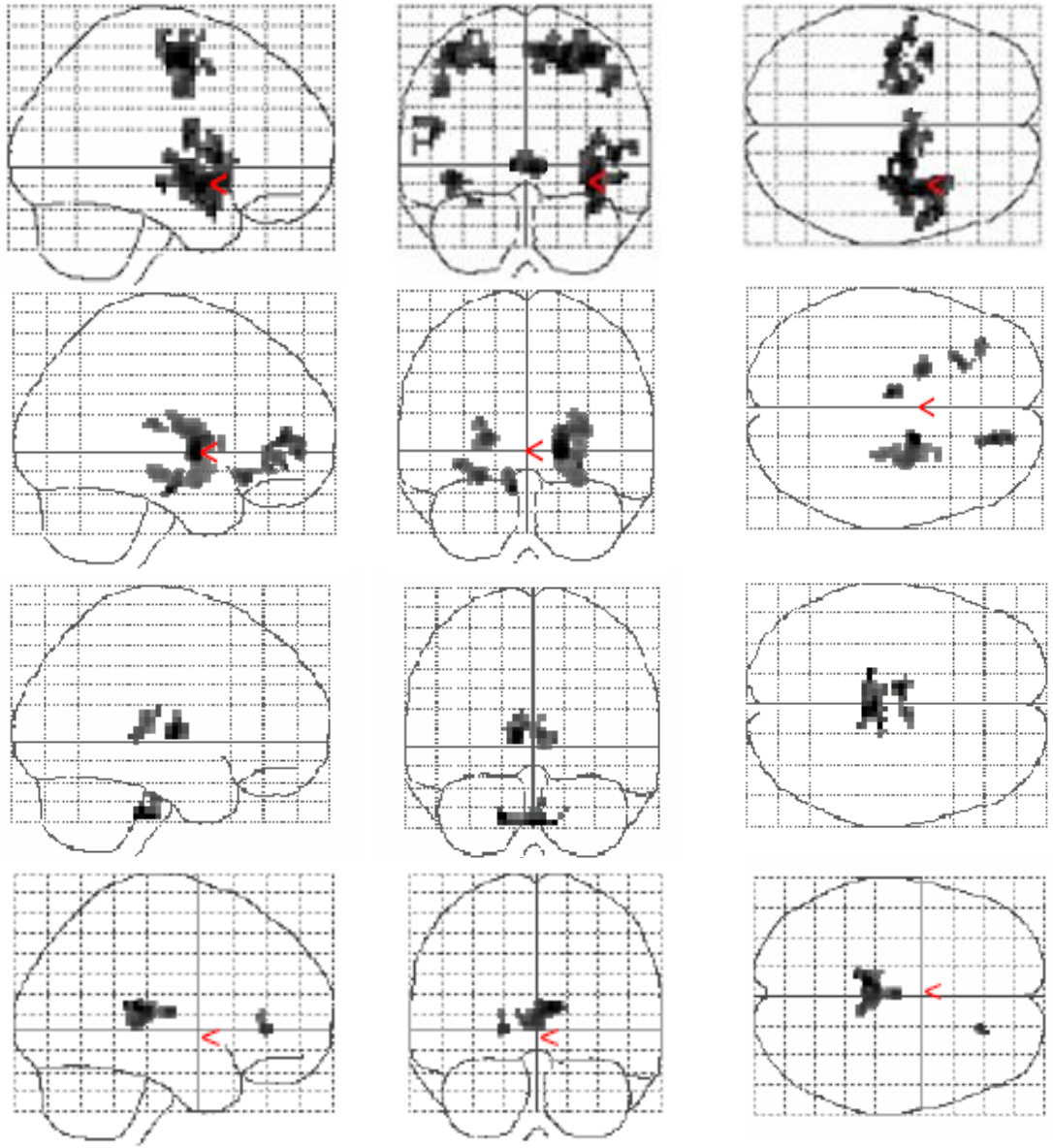


CSWS

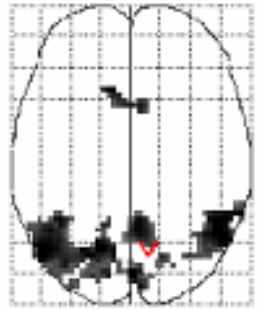
West syndrome

Lennox-Gastaut

Absence seizures



Deactivation in the Default mode network



Multiple causes may activate a syndrome specific neuronal network

Courtesy of Siniatchkin

- "Condition in which the **epileptiform abnormalities** are believed to contribute to progressive disturbance in cerebral function."
  (Engel, 2001)

Steroids in CSWS

- Prednisone or Hydrocortisone, early and prolonged ACTH or corticosteroid therapy, intravenous Methylprednisolone pulses followed by oral prednisolone.
- Improvement of language, cognition and behavior was reported in almost all patients reported and was usually accompanied by an improvement of the EEG.
- Some patients might relapse during steroids withdrawal, the risk of relapse seeming to be related to brief duration of treatment.
- This potential benefit has to be balanced with the well-known side effects of a long term steroids therapy (weight gain with Cushingoïd aspect, failure to thrive and increased risk of bone fracture).

The response to conventional AED is often incomplete and/or transitory.

Corticosteroids seem to have more long lasting effects.

Van Bogaert, 2006

Bambino Gesù
OSPEDALE PEDIATRICO

Should epileptiform discharges be treated?

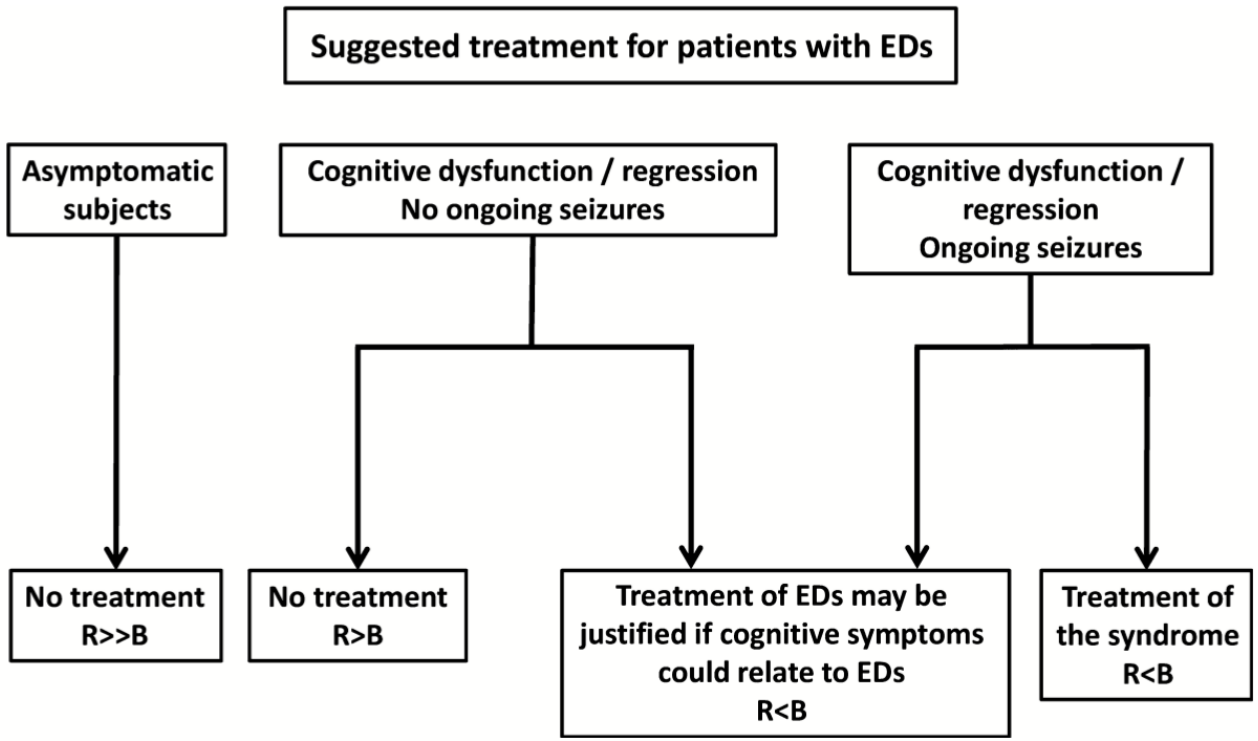
*†Iván Sánchez Fernández, †Tobias Loddenkemper, ‡Aristea S. Galanopoulou, and ‡§Solomon L. Moshé

To evaluate the impact of epileptiform discharges (EDs) that do not occur within seizure patterns – such as spikes, sharp waves or spike waves – on cognitive function and to discuss the circumstances under which treatment of EDs might be considered. Methods used in this article is "Review of the literature". EDs may disrupt short-term cognition in humans. Frequent EDs for a prolonged period can potentially impair long-term cognitive function in humans. However, there is conflicting evidence on the impact of EDs on long-term cognitive outcome because this relationship may be confounded by multiple factors such as underlying etiology, seizures, and medication effects. Limitations of existing studies include the lack of standardized ED quantification methods and of widely accepted automated spike quantification methods. Although there is no solid evidence for or against treatment of EDs, a non–evidence-based practical approach is suggested. EDs in otherwise asymptomatic individuals should not be treated because the risks of treatment probably outweigh its dubious benefits. A treatment trial for EDs may be considered when there is cognitive dysfunction or regression or neurologic symptoms that are unexplained by the underlying etiology, comorbid conditions, or seizure severity. In patients with cognitive or neurologic dysfunction with epilepsy or EDs, treatment may be warranted to control the underlying epileptic syndrome. EDs may cause cognitive or neurologic dysfunction in humans in the short term. There is conflicting evidence on the impact of EDs on long-term cognitive outcome. There is no evidence for or against treatment of asymptomatic ED.

Epilepsia, 56(10):1492–1504, 2015

Should epileptiform discharges be treated?

*†Iván Sánchez Fernández, †Tobias Loddenkemper, ‡Aristea S. Galanopoulou, and ‡§Solomon L. Moshé



Epilepsia, 56(10):1492–1504, 2015

Epilessia Mioclono-Astatica
(Epilessia con crisi mioclono-atoniche)

- Prevalenza: 1-2% delle epilessie pediatriche <9 anni
- Maschi più affetti delle femmine (3:1)
- Età di esordio: 18 e 60 mesi (1 anno e mezzo – 5 anni)
- Crisi a differente semeiologia:

  - Crisi miocloniche (100%) isolate o in serie, muscoli prossimali più coinvolti, flessione del capo rapida, o caduta

  - Crisi tonico-cloniche (75-95%)in veglia all'esordio

  - Assenze (62-89%) con riduzione del tono o mioclonie del capo

  - Crisi atoniche identificate con la video/EEG e la poligrafia, accanto alle crisi miocloniche e mioclono-atoniche

  - Crisi toniche (nel 30-95%) assiali e durante il sonno

  - Stati di Male a semeiologia minima (Minor motor status)
- Alterazione attività cerebrale di fondo

  - Delta asincrono diffuso, ampio voltaggio

  - Punte diffuse o multifocali

Bambino Gesù
OSPEDALE PEDIATRICO

Evolu

- La prognosi a lungo termine varia da completa remissione con normale sviluppo a ritardo mentale ed epilessia resistente
- Outcome favorevole è stato riportato dal 30-50% dei casi (Doose, 1992; Kaminska et al., 1999; Oguni et al., 2002

Display Settings: Abstract

Neuropediatrics. 2002 Jun;33(3):122-32.

Treatment and long-term prognosis of myoclonic-astatic epilepsy of early childhood.

Oguni H, Tanaka T, Hayashi K, Funatsuka M, Sakauchi M, Shirakawa S, Osawa M.
Department of Pediatrics, Tokyo Women's Medical University, Tokyo, Japan. hoguni@ped.twmu.ac.jp

81 pazienti con MAE
68 % dei pz remissione delle crisi
14 % ricorrenza di crisi TCG dopo un periodo di remissione
18 % farmacoresistente con ritardo mentale
minor epileptic status and nocturnal TCG
Storia familiare di epi e minor motor status
come fattori di rischio

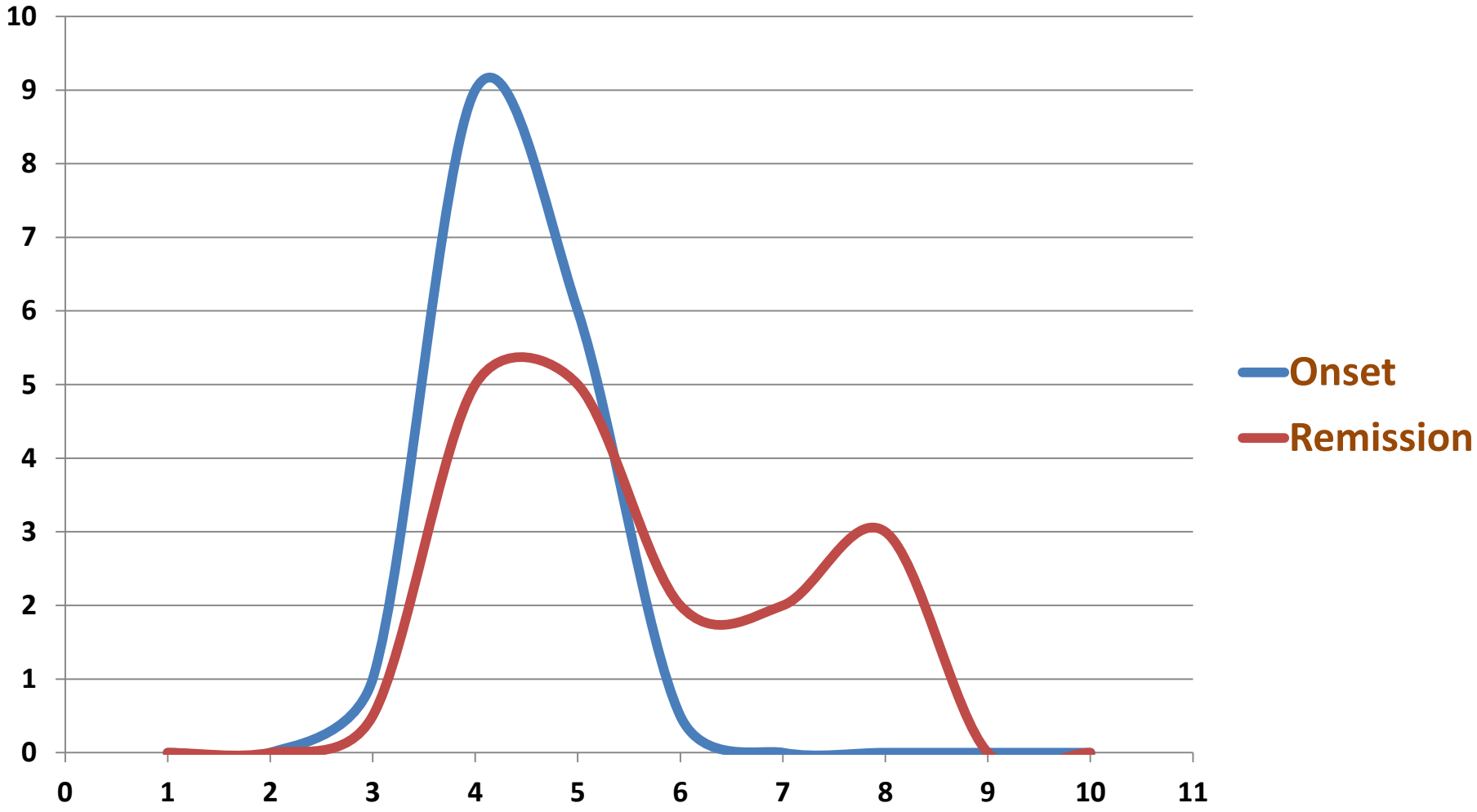
Neuropsychological Findings: Myoclonic Astatic Epilepsy (MAE) and Lennox-Gastaut Syndrome (LGS)

Melissa Filippini, Antonella Boni, Gloria Dazzani, Angelo Guerra and Giuseppe Gobbi
Child Neurology Unit, Epilepsy Center, Neuropsychological Laboratory for Children with Epilepsy, Maggiore "C. A. Pizzardi" Hospital, Bologna, Italy

Pazienti in studio 7
5 livello cognitivo normale
2 lieve ritardo mentale

23 soggetti studiati
Dopo 36 mesi 67% dei soggetti libero da crisi
43% livello cognitivo normale
52% lieve ritardo
5% ritardo moderato

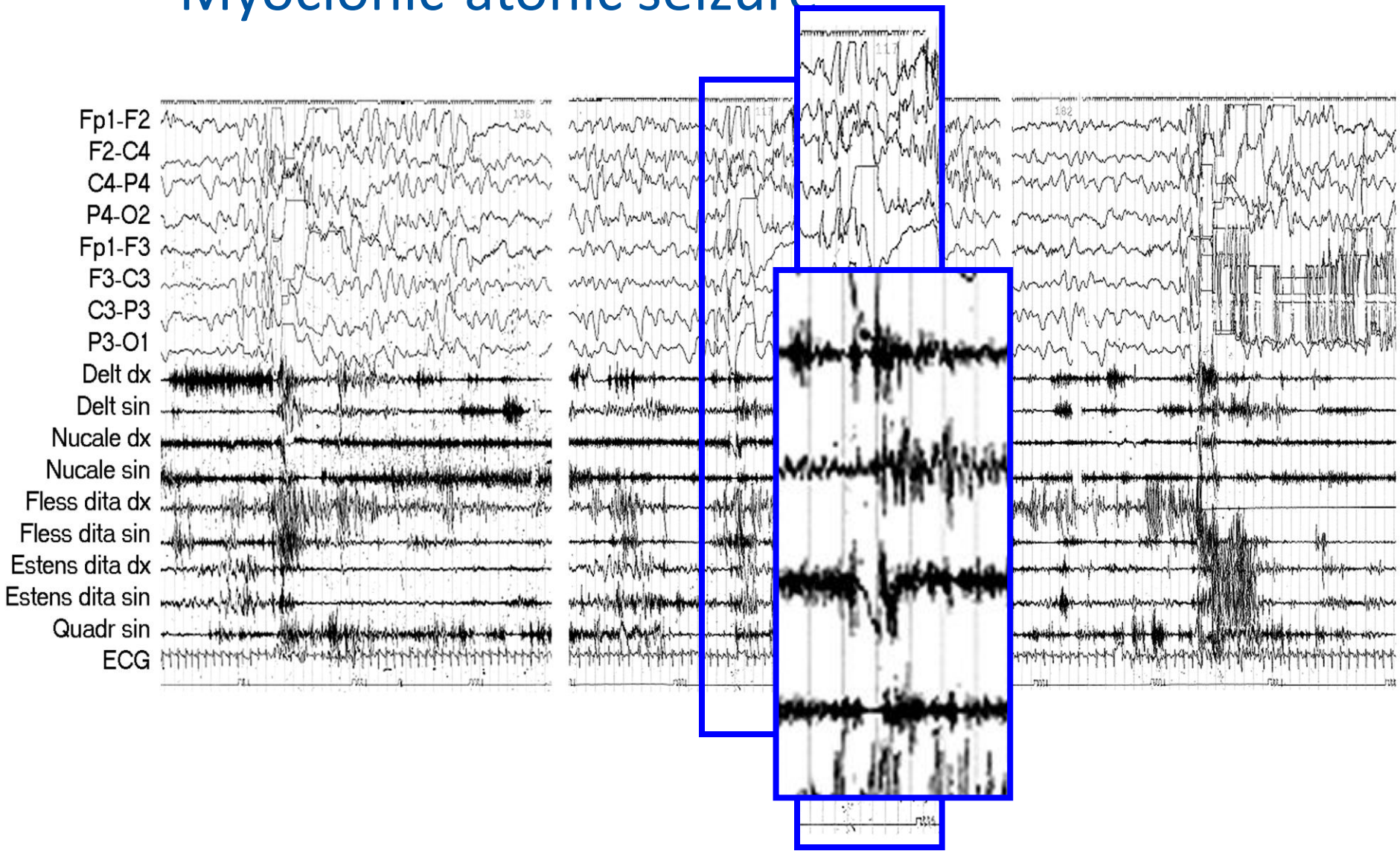
Age at onset/remission

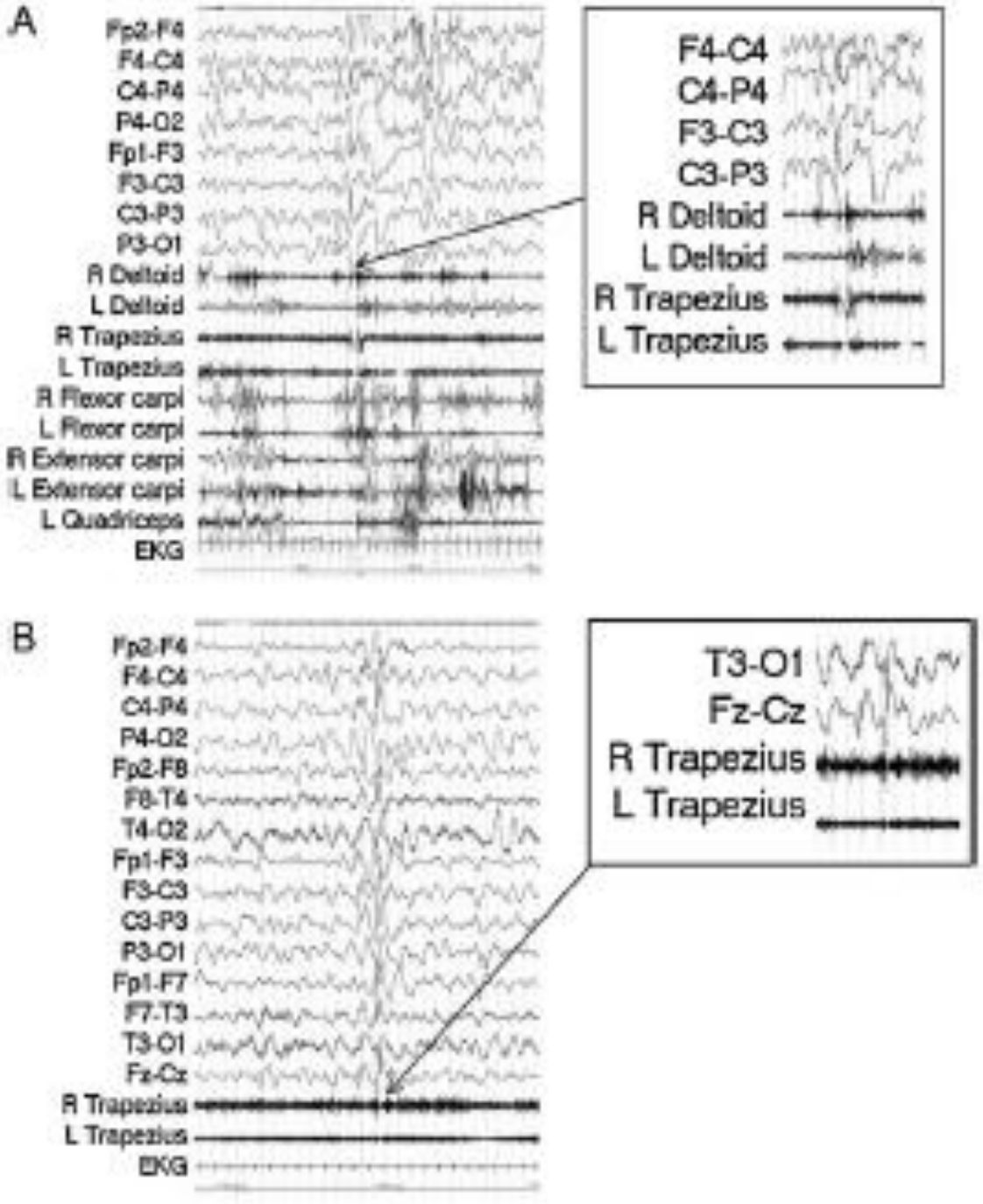


Tipo di crisi

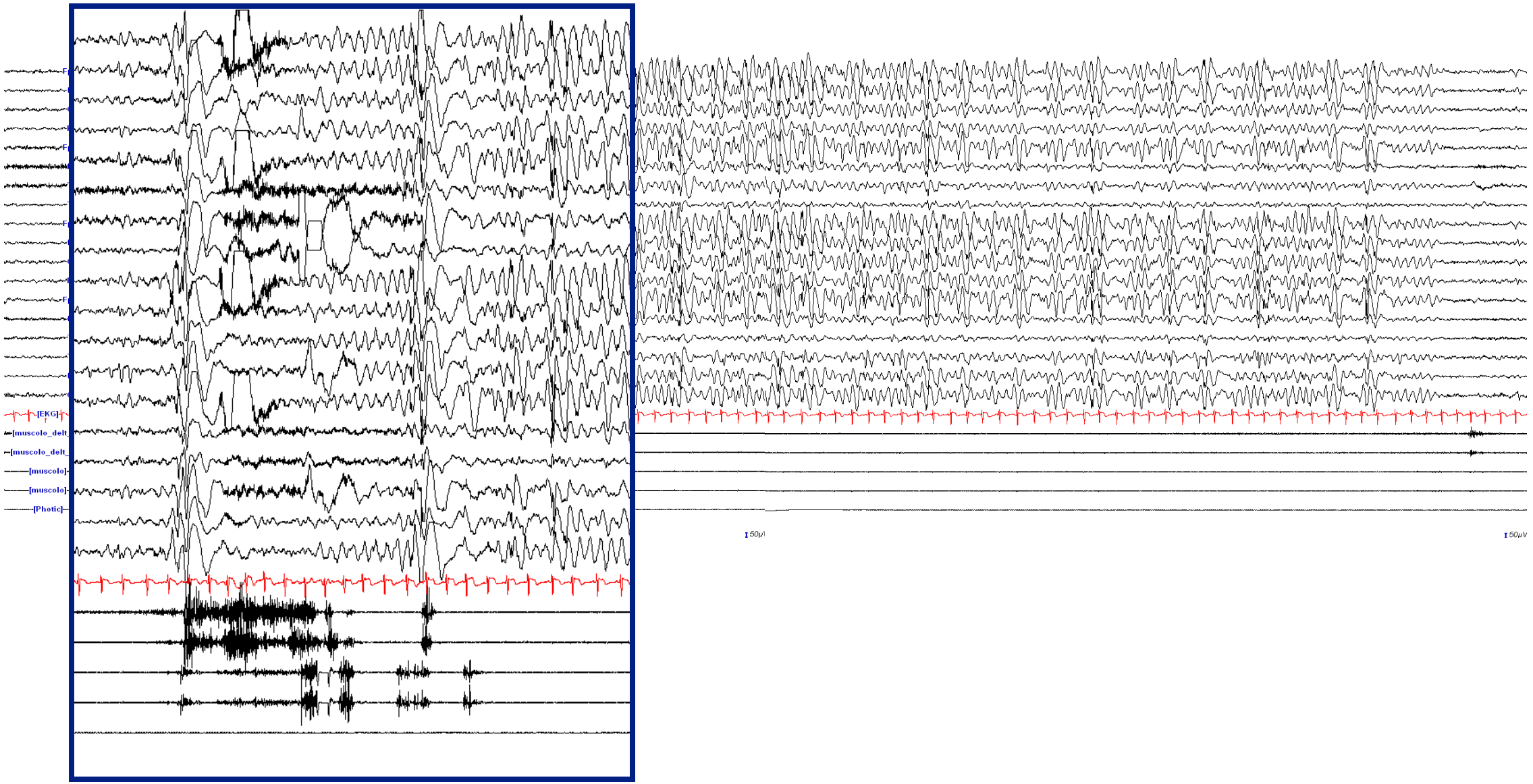
- Crisi mioclono-astatiche (100%)
- Mioclonie (64.8%)
- Crisi tonico-cloniche (76.5%)
- Assenze (82.3%) con riduzione del tono o mioclonie del capo
- Crisi atoniche (70.6%)
- Crisi toniche (35.3%)
- Minor Motor Status (11,8%)

Myoclonic-atonic seizure

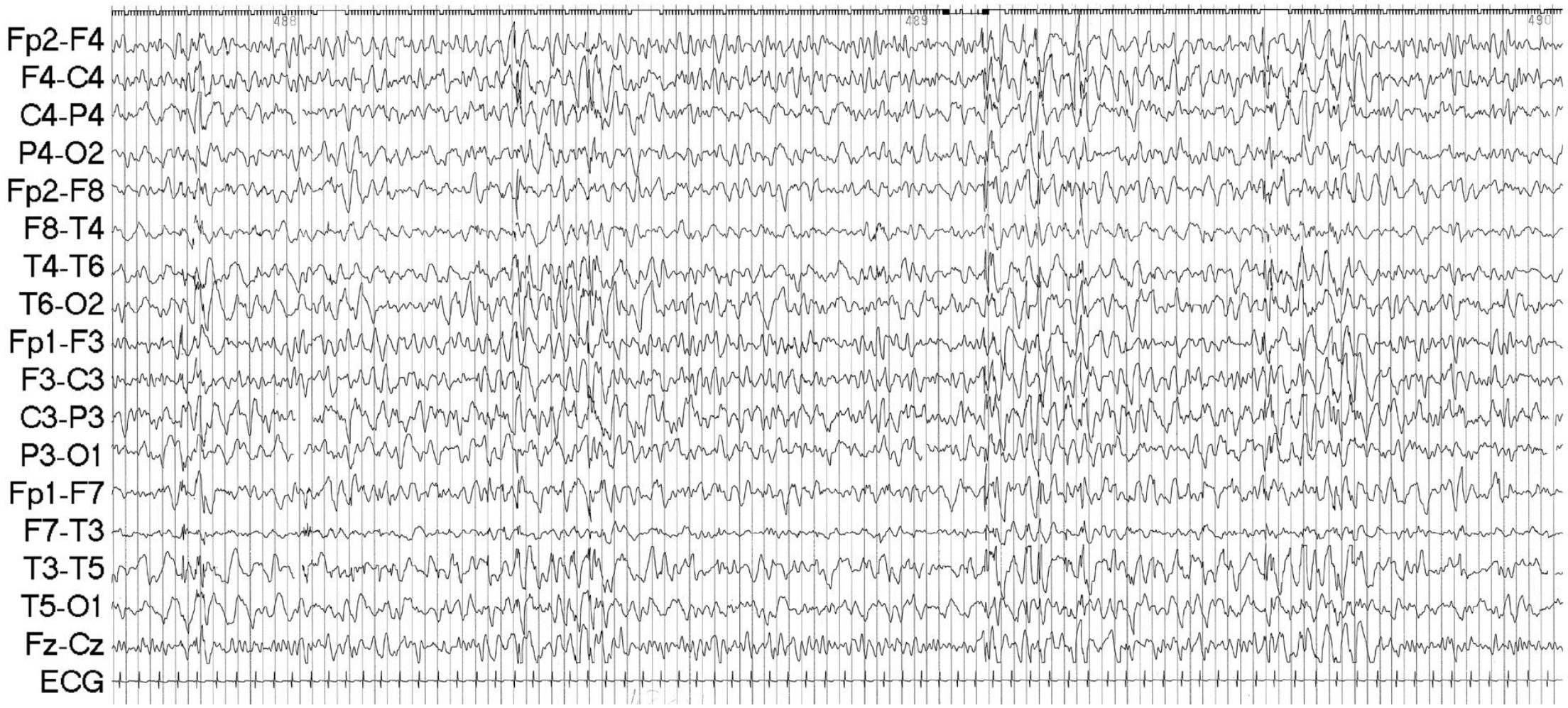



A
Fp2-F4
F4-C4
C4-P4
P4-O2
Fp1-F3
F3-C3
C3-P3
P3-O1
R Deltoid
L Deltoid
R Trapezius
L Trapezius
R Flexor carpi
L Flexor carpi
R Extensor carpi
L Extensor carpi
L Quadriceps
EKG
F4-C4
C4-P4
F3-C3
C3-P3
R Deltoid
L Deltoid
R Trapezius
L Trapezius
B
Fp2-F4
F4-C4
C4-P4
P4-O2
Fp2-F8
F8-T4
T4-O2
Fp1-F3
F3-C3
C3-P3
P3-O1
Fp1-F7
F7-T3
T3-O1
Fz-Cz
R Trapezius
L Trapezius
EKG
T3-O1
Fz-Cz
R Trapezius
L Trapezius

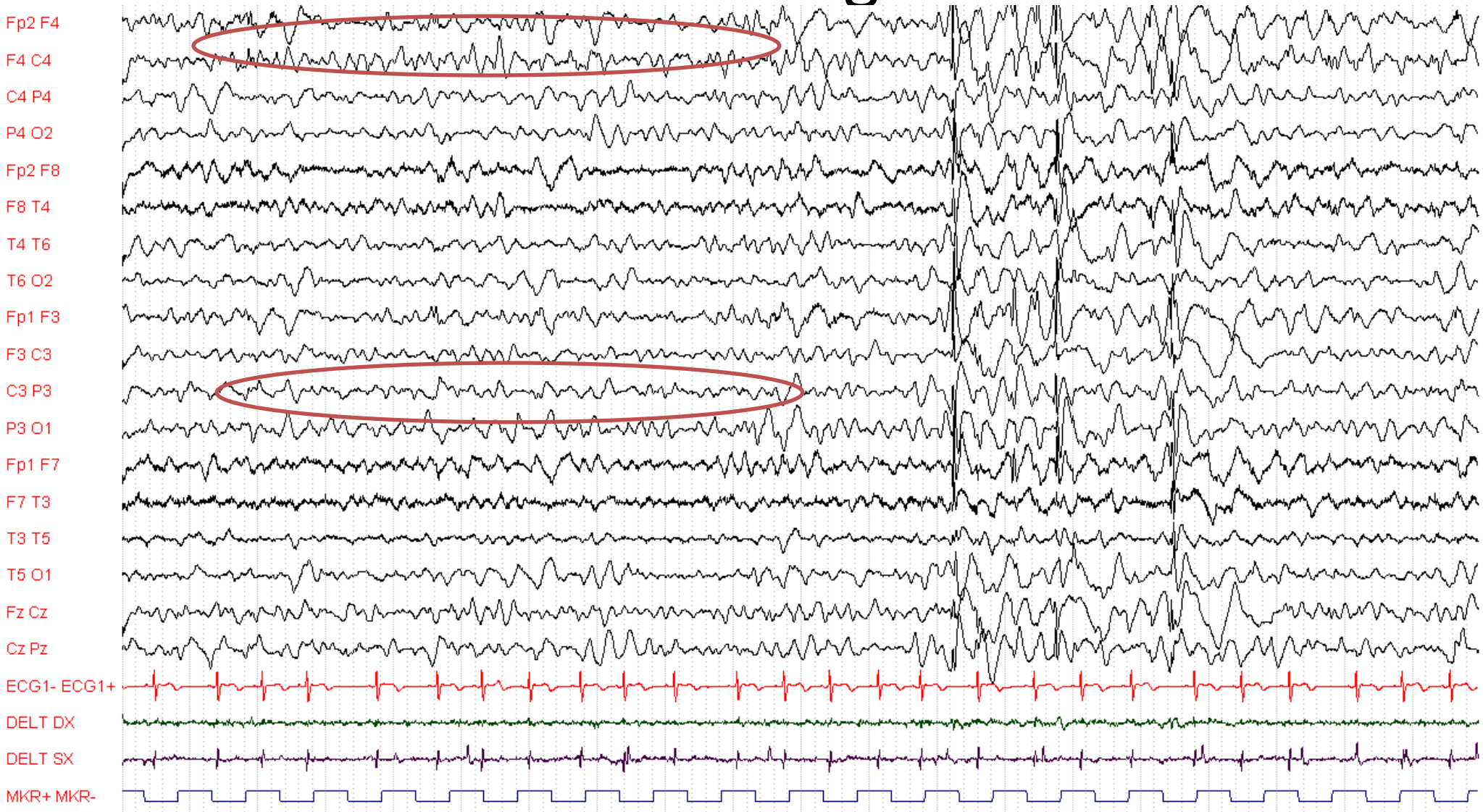
Mioclonie ed Assenza



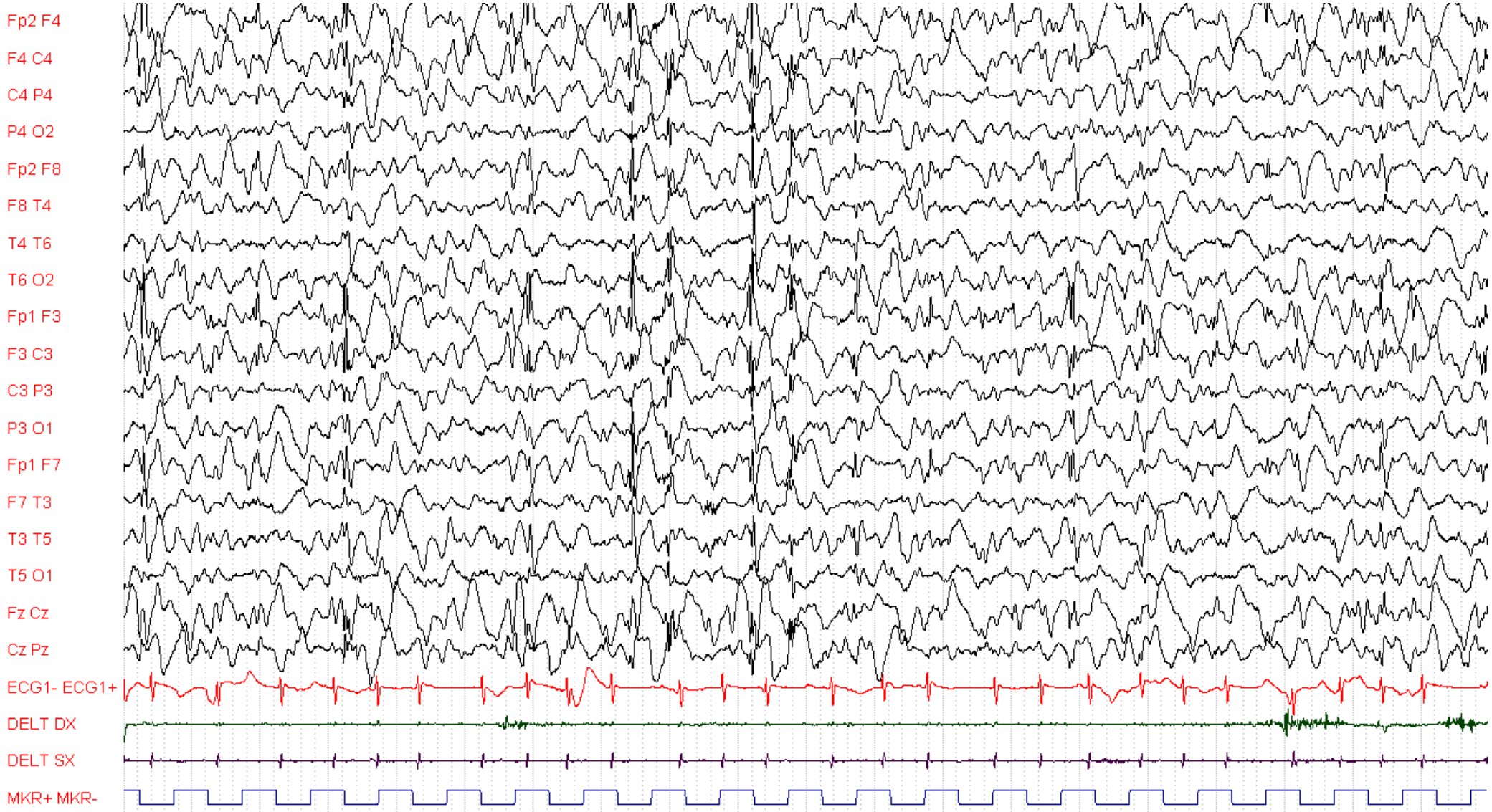
Minor Motor Status



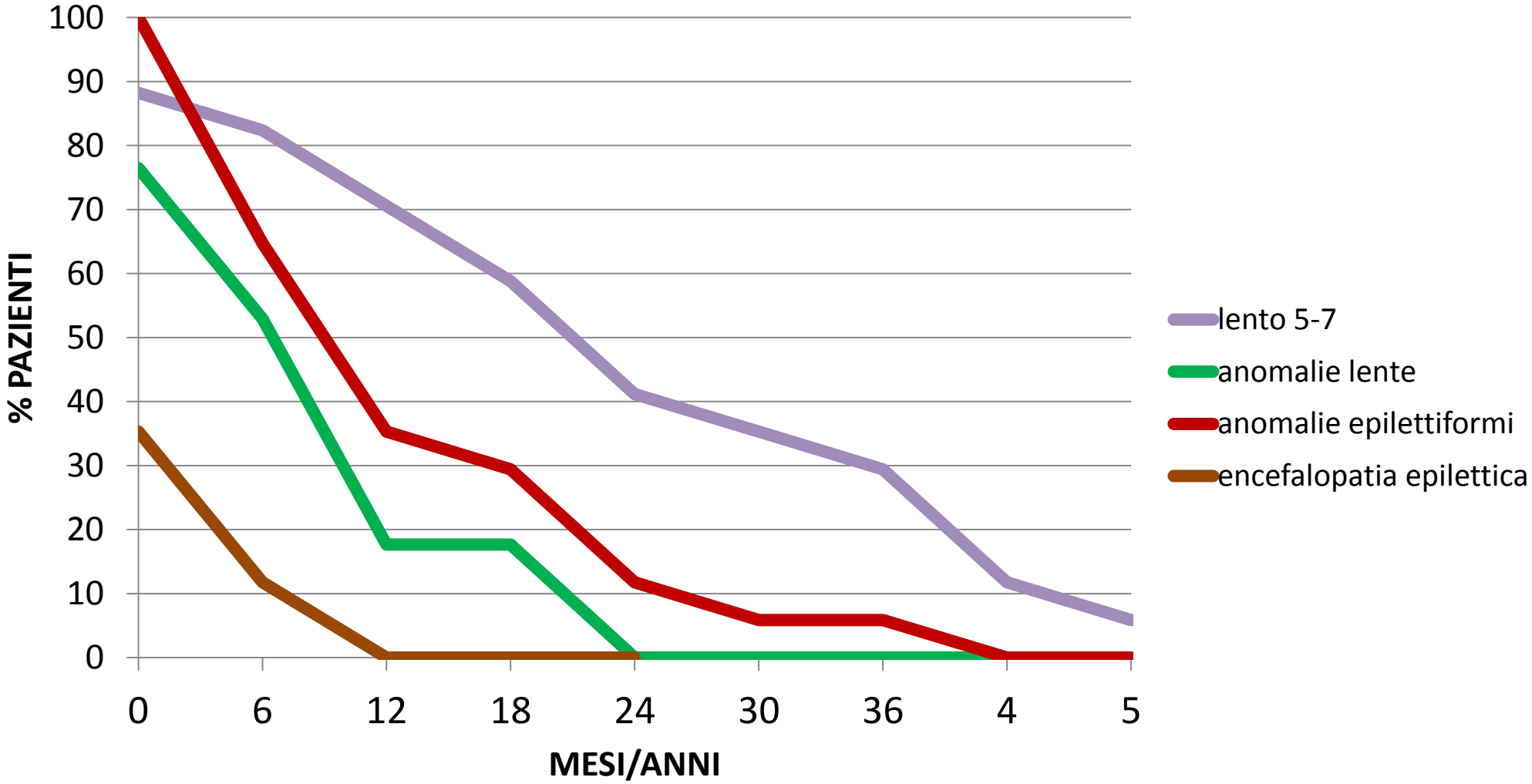
EEG veglia



Encefalopatia epilettica



Evoluzione EEG



Evoluzione EEG

- 2 pazienti con anomalie epilettiformi in sede Centro-Temporale dopo 18 e 30 mesi
- 2 pazienti con risposta foto-parossistica epilettiformi dopo 3 e 5 anni