

Tesis doctoral

FRONTAL LOBE EPILEPSY AND EEG:
NEUROPHYSIOLOGICAL APPROACH

Directores: Dr. Álvarez Sabin
Dr. Troels W. Kjaer

Programa de doctorado en Medicina Interna
Departamento de Medicina
Universidad Autónoma de Barcelona
2015

Beatriz García López

DISCUSSION

7. DISCUSSION

Frontal lobe epilepsy is probably the most frequent type after temporal lobe epilepsy, being 20-30% of all the partial epilepsies (Engel et al., 2007; Forcadas-Berdusan, 2002; Niedermeyer and Silva, 2005; Westmoreland, 1998). In the last years, there has been an increasing interest regarding this type of epilepsy, as we can see in the amount of frontal lobe epilepsy studies in the last decade. This might be due to the more extensive previous knowledge of other types of seizures compared to frontal lobe ones, most probably given by the fact that frontal lobe seizures are very varied clinically and their EEG recordings difficult to read, which makes them more complicated to study.

Looking at the morphology of the interictal epileptiform discharges in frontal lobe epilepsies, a variety of interictal waveforms can be seen with frontal seizures. These include spikes, sharp waves, spike followed by a slow wave, poly-spikes or poly-spike followed by a slow wave, and periodic sharp and slow wave complex (Tharp., 1972; Westmoreland, 1998). There are several studies grouping all interictal epileptiform activity without differentiating waveforms (Vadlamudi et al., 2004), which in some cases can lead to overlooking meaningful information from an EEG point of view. To complete the available information about the interictal epileptiform activity, in our analysis we explore and classify the different interictal waveforms including also the voltage and the EEG activity following the interictal epileptiform activity. In this regard, the sharp wave group was by far the most common interictal waveform in our sample, as 75 % of all the interictal epileptiform waveforms were "Sharp waves", simple or diphasic, but all of 70-200ms duration. We found that there were a relation between amplitude and waveform: The most common range of amplitude for sharp waves was between 50 and 200 μV and especially from 50 to 100 μV . We found a few cases with interictal poly-spike morphology with none of them of more than 100 μV . This is probably related to the fact that to show this fast activity, amplitude needs to be "low". Regarding the "spike" group, there were found more frequently with

amplitude of 50-100 μV , but if we look percentage at very low or high voltage, we find that for the waves of less than 50 μV almost half of them were spikes, and for voltage of more than 200 μV , 58% were spikes. With these findings we can see that there is a relation between amplitude and morphology for the IED. This could also suggest that there may be a correlation between the type of epilepsy and its EEG features and needs to be confirmed by other studies, as well as to be studied for other types of partial epilepsies.

Furthermore, this correlates with the work of other authors in generalized epilepsies, as Seneviratne et al., and Terney et al., who found a correlation between the different types of generalized epilepsies and some EEG features such as waveforms, distribution, ... They also remark the importance of differentiate focal from generalized epilepsies regarding the EEG point of view. Interestingly, the EEG features they found for generalized epilepsy differ from ours for frontal lobe partial epilepsy, being the results compatible and complementary. We completely agree with their considerations in terms of the importance of the EEG details, and the extensive graphical description provided in this study is aimed to help in the correct identification of the EEG activity in frontal lobe epilepsy.

As previously described by other authors (Bagla and Skidmore, 2011; Mosewich et al., 2000; Munari and Bancaud, 1992; Quesney et al., 1992; Westmoreland, 1998), interictal epileptiform activity can present as focal discharges, unilateral discharges over one frontal lobe, multifocal discharges over one frontal lobe, lateralized hemispheric discharges, bi-frontal symmetric or asymmetric, or widespread discharges. Regarding widespread interictal epileptiform discharges, Tükel and Jasper demonstrated that focal para-sagittal lesions may show bilateral slow wave discharges due to secondary bilateral synchrony. Given the wide EEG expression of epileptiform activity, it is important to carefully evaluate all the details of the EEG recording to avoid misinterpretation. In this aspect, we think that the technical advances with the introduction of electronic recording have made available a lot of interesting and necessary possibilities for making the interpretation of the EEG more accurate. In this context, the electroencephalographer must use several montages, with different

sensitivity and speed to get the most out of the recording depending on the individual needs.

Even though it has been previously reported by some authors that well-localized frontal foci are the exception (Quesney et al., 1992; Williamson and Spencer, 1986), we believe that current technology allows for localization of the majority of the foci despite their dispersion, as shown with this sample where 95% of the foci were given an electrode location.

We identified in our sample a category of unspecific irregular slow waves. The appearance of these unspecific waves is in agreement with the current knowledge. Some authors have described how other non epileptiform EEG abnormalities, as slow waves or rhythmical midline theta rhythm²², may give a clue to the abnormal hemisphere, appearing focal or lateralized. Those waves show a slowing or an asymmetry of activity over the two hemispheres (Westmoreland, 1998) and have been found to be an EEG correlate of dysfunction rather than an epileptogenic abnormality²³ (Beleza et al., 2009).

There is a well-known phenomenon regarding the influence of sleep, enhancing both epileptic seizures and interictal epileptiform discharges, whereas both of them are less frequent during REM sleep (Provini et al., 1999). Busek et al. have studied this phenomena finding that the activation of cholinergic neurons of the pontomesencephalic tegmentum during REM sleep produce inhibition of the thalamocortical synchronizing, which results in a suppression of interictal epileptiform discharges and seizures (Busek et al., 2010). According to these data, epileptiform discharges, facilitated by phasic activity during NREM sleep (spindles and K-complexes), reflect the synchronizing effect of the thalamocortical reverberation circuitry (Blumenfeld, 2005). The fact that these phasic events are more pronounced over the front central cortex

²² Once excluded drowsiness and mental activation

²³ This interictal rhythmical midline theta differentiates frontal from temporal lobe epilepsies, being found to be presented more commonly in the former.

could help explain the finding that frontal lobe seizures are more frequent during sleep, in contrast to the rest of the brain lobes (Crespel et al., 1998). This REM sleep-effect was also appreciated in our sample. We would like to note that in cases with a widespread interictal activity, this characteristic is a remarkable useful EEG detail, as it can be used to locate the focus.

A possible relation between pathologic antecedents and focus location has been previously studied. Frontal lobe tumours have been reported to be more epileptogenic, while traumatic lesions seem to be more frequent in anterior frontal and orbit-frontal regions (Forcadas-Berdusan, 2002). In our sample, a multi-factorial analysis was performed yielding a grouping in three clusters: tumoral and infectious cases related to prefrontal electrodes, vascular antecedents related to inferior frontal focus, and “other” antecedents related to left front-central electrode.

Moreover, we also explored a potential relation between pathological antecedents and the morphology of the interictal activity with a multi-factorial statistical analysis where all available parameters characterizing the interictal epileptiform activity (waveform, amplitude and EEG following IED activity) were included. Five clusters conform by very complex relations were obtained and we could not identify features making them immediately applicable for the clinical practice. We have not found any other study with a similar analysis.

Based on our sample, a classification of frontal lobe seizures is proposed. Previously, other authors have identified some morphological ictal patterns related to this type of epilepsy. Amberson, 1954; Bagla and Skidmore, 2011; Belezza and Pinho, 2011; Provini et al., 1999; Rasmussen, 1983; and Vadlamudi et al., 2004 mentioned that ictal discharges can be complex and quite variable. They can present as low-voltage fast activity, an incrementing or a recruiting rhythm, a rhythm at different frequencies, repetitive spikes or spikes and slow waves or focal or widespread attenuation or a

flattening of the background, arrhythmic activity and obscured²⁴. Depending on the position of the electric dipole, the seizure may be electrically silent with no apparent change evident in the EEG or very confusing for the electroencephalographer (Amberson, 1954; Bagla and Skidmore, 2011; Busek et al., 2010; Foldvary et al., 2001; Provini et al., 1999; Vadlamudi et al., 2004). This fact limits the following classification, as it obviously can be applied to seizures that are recorded on surface EEG. The classification we proposed agrees overall with the previous observations, and at the same time it adds a point of usefulness, as it gives strong and clear points to identify and classify frontal lobe seizures from an electroencephalographic point of view.

The classification proposes four types of morphological patterns at seizure onset:

- 1) Synchronized rhythm without a prominent change in amplitude
- 2) Low amplitude synchronized rhythm
- 3) Attenuation
- 4) Spike/sharp wave within a slow wave just before the synchronized rhythm

All the 51 cases with recorded seizures were easily assigned to one of the previous categories. We believe the classification is easy to remember and useful in the daily routine, we recommend its application in the daily routine of the neurophysiology departments.

The precise location of frontal lobe ictal discharges is often difficult and may be misleading (Foldvary et al., 2001; Provini et al., 1999; Westmoreland, 1998), as the EEG recordings in the sample have showed. In contrast to seizures arising from the temporal lobe, the ictal discharges are frequently more widespread and may become evident later in the course of the seizure (Westmoreland, 1998). Nevertheless it is recognised that ictal recordings are very useful in seizure localization and lateralization (Foldvary et al., 2001). We agree in that the propagation of frontal lobe seizures to

²⁴ Foldvary N. Et al. Refer to obscured seizures when there is a seizure pattern evolving from a period obscured by artefact such that precise time, pattern and distribution of onset was indiscernible.

contra-lateral frontal regions and ipsi-lateral temporal regions causes a problem with localization (Quesney et al., 1992), and the focal onset may be obscured by the rapid spread of the activity, but believe that a careful study with electronic recording can help in determining the location of onset in most of the cases.

Getting back to the morphological pattern, several authors have reported the fact that it is very stereotyped (Manford et al., 1996; Shih et al., 2009; Unnwongse et al., 2010; Zhao et al., 2010), which makes important to remember the morphological pattern at onset once a seizure has been identified. The analyses of our sample, regarding the variability of seizure morphological pattern over time for the same patient are in agreement with this finding, showing that seizures present a constant location at onset as well as the same morphological pattern²⁵. It is important to mention that the analysis of pattern variability was performed un-blinded, as we have different EEG formats (paper and electronic) and it was not operative to have more reviewers of the cases. We decided it was better to perform an un-blinded analysis rather than not doing it at all.

Some authors have studied the localizing value of ictal EEG in focal epilepsy given a known lesion. Foldvary DO et al. have studied this issue in both mesial frontal lobe epilepsy and lateral frontal lobe epilepsy with surface and invasive recording for comparing between them (Foldvary et al., 2001). They studied seizure-specific data as duration, pattern, distribution and duration of the ictal onset rhythm etc., finding that repetitive epileptiform activity²⁶ was significantly more common in lateral frontal lobe epilepsy; while generalized patterns²⁷ were significantly more common in mesial frontal lobe epilepsy (and occipital lobe epilepsy). In their study, eight patients had entirely obscured seizures, two patients had no EEG change and they did not find rhythmic temporal theta activity in patients with frontal lobe epilepsy. They also refer

²⁵As previously detailed, we allowed changes in amplitude and duration between seizures.

²⁶Understanding repetitive epileptiform activity as 3 or more discharges in sequence

²⁷defined as activity involving multiple electrodes over both cerebral hemispheres haven a less tan 2:1 amplitude predominance of one side over the other.

to a low percentage (3%) of lateral frontal seizures being mislateralized, and a 6% of the total mislocalized (Foldvary et al., 2001). Our data shows a percentage of 15% of non-localized seizures in the overall sample. The observation of a higher percentage of non-localized seizures, compared to the findings from the authors previously mentioned, is probably related to the fact that they include in their analysis seizures recorded from all brain lobes.

Similarly to our study, Vadlamudi et al. have explored the relation between the focus location and the location of seizure onset. They found that focus location at the frontal convexity tended to be associated with concordant interictal epileptiform discharges (IED), as 72 % of cases with a convexity seizure origin had concordant IED, whereas in seizures with a mesial frontal origin, concordant IED was present in only 33% of the patients. Similar findings have also been reported by other authors (Bautista et al., 1998; Vadlamudi et al., 2004) . In our sample, 79% of the cases where concordant and this percentage gets as high as 94% when excluding the eleven cases with an unspecific focus location or unspecific seizure location. This is a similar result, even though it is worth noting that they divided the sample into two main groups, mesial and lateral frontal lobe cases, while we regarded all data individualized, as the objective in our study was based on the electroencephalography data while they focused on the surgical outcome.

The high percentage of concordance (94%) obtained in our study when excluding the undefined cases might be due to less strict criteria in our classification as we tried to assign a maximal electrode position or a hemisphere regardless of its amplitude, while they considered a fixed amplitude criterion for defining the electrode location. Given the variability of amplitude at seizure onset, and even more in frontal lobe seizures, where we often see attenuation at onset complicating the assessment of an amplitude value, we preferred to give a more flexible interpretation by the reader in the assessment in electrode location of seizure onset.

Another plausible explanation is the different starting point of the two studies, as Vadlamudi et al. selected patients with a known frontal lobe lesion²⁸ studying afterwards the EEG recording, while we selected patients with frontal lobe IED in the EEG and that location was used to explore the concordance with the ictal onset location.

Worrell et al., 2002, reported a focal beta frequency in the 25,9% of patients associated with frontal convexity even though they did not find frontal ictal beta discharges to be significantly more likely to be associated with convexity location than with medial location of the frontal lesion, as had been previously linked by some authors (Bautista et al., 1998). In our sample 60% of the seizures started with beta frequencies. In our sample, the different electrode locations at seizure onset divided data into too many categories to find any consistent relation between frequencies and morphological patterns at onset and frontal locations. Nevertheless and according to Worrell et al. (2002) we found a tendency of association between F3/4 electrode position (especially left sided) and beta frequencies at onset²⁹.

In conclusion, and as mentioned by several authors, electroencephalographic ictal onset assessment still plays a major role in localization of the epileptic zone (Verma and Radtke, 2006).

Exploring the initiation of seizures, the transition from interictal spike discharge to an ictal pattern was already described in the first studies of electroencephalography. More recently, Azar et al. have studied “transition sharp wave” as a specific morphological pattern of transition interictal-ictal activity in neocortical and mesial epilepsy. They have found this pattern to be associated to neocortical epilepsy, as none of the patients with mesial epilepsy presented this pattern at onset (Azar et al., 2009). They found that 7.1 % of all patients admitted to the epilepsy monitoring unit (EMU) had this pattern at seizure onset. In our sample 11.76% of patients presented

²⁸Proved by excellent surgical outcome after frontal lobe surgery.

²⁹In fact all seizures arising from left frontcentral location started with beta frequencies.

“spike/sharp wave within a slow wave” as ictal onset morphology, which could be equivalent to their “transition sharp wave”. We have to note that Azar et al. included patients with presumed hippocampal origin, to confirm the absence of “transition sharp wave” pattern in these patients, which may lower the percentage of cases with this morphological pattern at onset in their sample. This pattern have been studied previously by Ralston and Papetheodorou who called the ictal discharge after the sharp wave the “afterdischarge” (Ralston, 1958; Ralston and Papatheodorou, 1960). Other authors, as Geiger and Harner, discouraged the term pointing to the lack of an obligatory relationship between the sharp discharge and the subsequent rhythmic activity (Geiger and Harner, 1978). More recently Ebersole and Pacia included an ictal onset pattern by “runs of periodic sharp waves preceding rhythmic activity”. The most recent studies propose that the transition sharp wave acts as a trigger to the ictal discharge, being sufficient but no necessary to initiate seizures (Azar et al., 2009).

The seizures are characterized by a rhythmic activity that progressively increases in amplitude and decreases in frequency and may develop into a self-sustaining focal epileptic discharge with the capacity to spread across the cortex, precipitating a focal seizure , or triggering a generalized seizure (Broughton and Gastaut, 1972; Geiger and Harner, 1978; Gloor et al., 1961; RALSTON, 1958). Looking at the frequency at seizure onset, it is well known that the frequency of discharge may vary from 1 to 30/second. Geiger et al described a transformation from an interictal pattern to a sustained rhythmic pattern in 90 % of the studied seizures, with beta frequencies in more than the 50% of the seizures (Geiger and Harner, 1978). In agreement with these authors, in our sample beta frequencies at onset have been by far the most frequent observed at seizure onset in frontal lobe seizures, with the 58.9% of seizures. This finding complements the current knowledge of frontal lobe seizures, as they included several types of seizures, with only 10/41 cases of frontal origin³⁰.

Some authors have searched for a relation between location of seizure onset and the morphological seizure pattern, dividing cases in mesial frontal and lateral frontal

³⁰In their study “obvious focal clinical seizure activity or well-demarcated focal ictal EEG associated with complex clinical seizures” regardless of its origin were included.

(Foldvary et al., 2001), but we have not found studies that correlate electrode location with morphological pattern at onset³¹. A potential relation between the morphological patterns at onset and its electrode location was explored in this study but no statistical relation found, which might be due to the dispersion of data. In our sample “spike/sharp wave within a slow wave” was easily detected but very difficult to link to a location, as the maxima expression was very widespread. In most of the cases of the sample, and specifically in all cases with this pattern, it was necessary to change several settings to assign a location both for the IED and seizures. Regarding the rest of the morphological patterns, we found that seizures arising from prefrontal electrodes did not present with “attenuation” pattern at onset, and at the same time, “attenuation” pattern was the most commonly seen in the seizures with “unspecific” location of onset.

Regarding the pathologic antecedents, some authors have found cryptogenic cases to be up to the 37% of the cases while others, as Vadlamudi et al., described most of the patients with symptomatic epilepsy aetiology, 72% versus 28% (Vadlamudi et al., 2004). These differences may be due to the different selection procedures used in the different studies. In our sample we have found 88% of symptomatic cases.

³¹ In temporal lobe epilepsy, Ebersole et al. have found a relationship between the morphological pattern at seizure onset and the location of onset (Ebersole and Pacia, 1996).

CONCLUSIONS

8. CONCLUSIONS

1. Isolated sharp waves, both with simple and diphasic morphology are the most frequent waveforms in the expression of frontal lobe IED, especially with a voltage of 50-100 μ V.
2. Spikes usually appear isolated as interictal epileptiform discharges, with a voltage of less than 50 μ V.
3. Beta frequency band was the most common observed frequency at seizure onset, with a progressive slowing of frequencies during the seizure.
4. We propose the following morphological classification of seizure onset for the daily routine in the EEG identification of frontal lobe seizures:
 - a. Synchronized rhythm without a prominent change in amplitude
 - b. Low amplitude synchronized rhythm
 - c. Attenuation
 - d. Spike/sharp wave on a slow wave just before the synchronized rhythm
5. The most common morphological pattern at seizure onset was the synchronized rhythm without a change in amplitude, followed by a low amplitude synchronized rhythm
6. The morphological seizure pattern remains the same over time within patients.
7. The location of interictal activity predicts the location of seizure onset.

8. We found some relation between pathologic antecedents and location of interictal activity, with the following clusters of associations:
 - a. "Infectious" and "tumoral" cases with left front central focus
 - b. "Vascular", "traumatic" and "without interest" cases with left inferior frontal focus
 - c. "Other" antecedents and left front-central focus (F3).

9. We found some relation between the morphology of the interictal activity and pathologic antecedent, with the following clusters of associations:
 - a. "Without antecedents of interest" and "tumoral" cases with "Isolated" "sharp waves" of "50-100 μ V"
 - b. "Traumatic" cases and "isolated" "spikes" of "less than 50 μ V"
 - c. "Infectious" cases and "sharp waves", with amplitudes of "50-100 μ V" and being the most common group with a "irregular slow wave" after the epileptic waveform
 - d. "Vascular" cases with "spikes", and with "slow wave" and "irregular slow wave" after the epileptic waveform.
 - e. "Diphasic sharp waves" as interictal waveform with two range of voltages: 100-200 μ V and more than 200 μ V; Those waves had a "slow returning to the base line" or, less frequently a "slow wave" after the epileptic waveform

These conclusions complement the main EEG characteristics that we have observed during the study of the EEG recordings of all the frontal lobe epilepsy cases.

Frontal lobe seizures are frequently short, with duration of seconds, and sometimes appear grouped in clusters, within the same recording. Clinically they present extremely varied semiology, sometimes including all kind of clinical manifestations, with or without consciousness impairment and sometimes with secondary generalization.

Trying to locate the IED it will be necessary to look for epochs in which the activity presents less active, due to the fact that when it is more active, the IED usually appears very widespread and very expressive, especially in both frontal lobes. This, combined with the utilization of different available montages, increase the possibility of locating the focus and correct diagnose the cases. The referential montage is especially useful for locating the IED, once we are used to the fact that the electronegativity of the focus is contribution to the men, which affects all channels in it second component, the "reference".

Many times the ictal expression of the electrical activity in frontal lobe seizure is subtle and difficult to interpret. Another piece of information that helps in identifying ictal EEG activity are polygraphy changes, as many frontal seizures have vegetative manifestations, with tachycardia, bradycardia and/or breathing irregularity.

Post-ictal activity should be taken into account: After the ictal activity in frontal lobe seizures we can usually observe a frontal slowing, with immediate recovery of alpha rhythm in posterior regions.

CONCLUSIONES

1. Las ondas agudas, tanto de morfología simple como difásica, son el grafoelemento más frecuente en la expresión de la actividad intercrítica en epilepsia del lóbulo frontal, especialmente con voltaje de 50-100 μ V
2. Cuando la actividad intercrítica se manifiesta en forma de “puntas”, éstas aparecen generalmente aisladas, con un voltaje menor de 50 μ V.
3. La banda de frecuencias beta fue la más comúnmente observada al inicio crítico, con un enlentecimiento progresivo de las frecuencias durante la crisis.
4. Proponemos la utilización en la práctica diaria de clasificación morfológica propuesta para identificar las crisis frontales.
 - a. Ritmo reclutante sin cambio de amplitud
 - b. Ritmo reclutante fijo y de baja amplitud
 - c. Atenuación
 - d. Punta/onda aguda sobre onda lenta justo antes del ritmo reclutante
5. El patrón morfológico más frecuente al inicio crítico fue un ritmo reclutante sin cambio en su amplitud, siendo el segundo patrón más frecuente el ritmo reclutante con marcada disminución de amplitud.
6. El patrón morfológico de las crisis se mantiene a lo largo del tiempo para un mismo paciente
7. La localización del foco determina la localización del inicio de las crisis

8. Hemos encontrado una relación compleja entre los antecedentes patológicos y la localización de la actividad intercrítica, con clusters de asociaciones:
 - a. Entre casos con antecedentes “infeccioso” y “tumoral” y localización del foco en región fontocentral izquierda.
 - b. Entre antecedentes “vascular”, “traumático” y “sin interés” y localización frontal inferior izquierda del foco.

9. Hemos encontrado una relación compleja entre la morfología de la actividad intercrítica y el antecedente patológico, con clusters de asociaciones:
 - a. Entre casos “sin antecedentes de interés” y “tumorales” con “ondas agudas”, “aisladas”, de “50-100 μ V”
 - b. Entre casos “traumáticos” y “puntas” “aisladas” de “menos de 50 μ V”
 - c. Entre casos “infecciosos” y “ondas agudas” con amplitudes de “50-100 μ V”, siendo el subgrupo más común aquel con “onda lenta irregular” después del grafoelemento irritativo.
 - d. Entre casos “vasculares” con “puntas”, seguidas de “onda lenta” u “onda lenta irregular” tras el grafoelemento paroxístico.
 - e. Entre el grafoelemento de “onda aguda difásica” y dos rangos de voltaje: 100-200 μ V and y más de 200 μ V; Este grafoelemento se siguió en el EEG de una “vuelta lenta a la línea de base” o, menos frecuentemente, de “onda lenta”.

Estas conclusiones complementan a las características electroencefalográficas que hemos observado durante el estudio de los registro EEG de todos los casos de epilepsia del lóbulo frontal:

Las crisis frontales son frecuentemente cortas, con una duración de segundos, y algunas veces se agrupan en clusters, en el mismo registro. Clínicamente presentan una semiología muy variada, incluyendo todo tipo de manifestaciones clínicas, con o sin alteración del nivel de conciencia y a veces con generalización secundaria.

Para intentar localizar la actividad intercrítica será necesario buscar épocas en las que la actividad se presente menos activa ya que cuando está más activa, la actividad intercrítica aparece generalmente con gran difusión y muy expresiva, especialmente en ambos lóbulos frontales. Esto, combinado con la utilización de los diferentes montajes que tenemos disponibles, aumentan la posibilidad de localizar el foco y diagnosticar correctamente los casos. El montaje referencial es especialmente útil para localizar la actividad epiléptica, una vez estemos acostumbrados al hecho de que la electronegatividad del foco está contribuyendo a la media, lo que afecta a todos los canales en su segundo componente, la "referencia".

Muchas veces la expresión de la actividad eléctrica de las crisis frontales es sutil y difícil de interpretar. Otro dato que puede ayudar a valorar el carácter ictal de una actividad electroencefalográfica son los cambios en la poligrafía, ya que muchas crisis frontales tienen manifestaciones vegetativas, con taquicardia, bradicardia y/o irregularidad respiratoria.

De igual manera la actividad post-crítica debe tenerse en cuenta: tras la actividad crítica en las crisis frontales suele observarse una lenificación frontal, con recuperación inmediata del ritmo alfa en regiones posteriores.

BIBLIOGRAPHY

9. BIBLIOGRAPHY

Amberson, W.R., 1954. *Epilepsy and the Functional Anatomy of the Human Brain*. Wilder Penfield and Herbert Jasper. Little, Brown, Boston, 1954. 896 pp. *Science* 119, 645–646. doi:10.1126/science.119.3097.645r a

Azar, N.J., Lagrange, A.H., Abou-Khalil, B.W., 2009. Transitional sharp waves at ictal onset—a neocortical ictal pattern. *Clin. Neurophysiol. Off. J. Int. Fed. Clin. Neurophysiol.* 120, 665–672. doi:10.1016/j.clinph.2009.01.010

Bagla, R., Skidmore, C.T., 2011. Frontal lobe seizures. *The Neurologist* 17, 125–135. doi:10.1097/NRL.0b013e31821733db

Bauer, G., Dobesberger, J., Bauer, R., Embacher, N., Benke, T., Unterberger, I., Walser, G., Luef, G., Trinka, E., 2006. Prefrontal disturbances as the sole manifestation of simple partial nonconvulsive status epilepticus. *Epilepsy Behav.* EB 8, 331–335. doi:10.1016/j.yebeh.2005.10.008

Bautista, R.E., Spencer, D.D., Spencer, S.S., 1998. EEG findings in frontal lobe epilepsies. *Neurology* 50, 1765–1771.

Beleza, P., Bilgin, O., Noachtar, S., 2009. Interictal rhythmical midline theta differentiates frontal from temporal lobe epilepsies. *Epilepsia* 50, 550–555. doi:10.1111/j.1528-1167.2008.01780.x

Beleza, P., Pinho, J., 2011. Frontal lobe epilepsy. *J. Clin. Neurosci. Off. J. Neurosurg. Soc. Australas.* 18, 593–600. doi:10.1016/j.jocn.2010.08.018

Blumenfeld, H., 2005. Cellular and network mechanisms of spike-wave seizures. *Epilepsia* 46 Suppl 9, 21–33. doi:10.1111/j.1528-1167.2005.00311.x

Blume, W.T., Oliver, L.M., 1996. Noninvasive electroencephalography in supplementary sensorimotor region epilepsy. *Adv. Neurol.* 70, 309–317.

Broughton, R.J., Gastaut, H., 1972. *Epileptic Seizures: Clinical and Electrographic*

Features, Diagnosis and Treatment. C. C. Thomas.

Busek, P., Buskova, J., Nevsimalova, S., 2010. Interictal epileptiform discharges and phasic phenomena of REM sleep. *Epileptic Disord. Int. Epilepsy J. Videotape* 12, 217–221. doi:10.1684/epd.2010.0319

Chang, C.N., Ojemann, L.M., Ojemann, G.A., Lettich, E., 1991. Seizures of fronto-orbital origin: a proven case. *Epilepsia* 32, 487–491.

Crespel, A., Baldy-Moulinier, M., Coubes, P., 1998. The relationship between sleep and epilepsy in frontal and temporal lobe epilepsies: practical and physiopathologic considerations. *Epilepsia* 39, 150–157.

Ebersole, J.S., Pacia, S.V., 1996. Localization of temporal lobe foci by ictal EEG patterns. *Epilepsia* 37, 386–399.

Engel, J., Pedley, T.A., Aicardi, J., Dichter, M.A., Moshé, S., Perucca, E., Trimble, M., 2007. *Epilepsy: A Comprehensive Textbook, Second, Plus Integrated Content Website*. ed. Lippincott Williams & Wilkins.

Foldvary, N., Klem, G., Hammel, J., Bingaman, W., Najm, I., Lüders, H., 2001. The localizing value of ictal EEG in focal epilepsy. *Neurology* 57, 2022–2028.

Forcadas-Berdusan, M.I., 2002. [Problems of diagnosis and treatment in frontal epilepsies]. *Rev. Neurol.* 35 Suppl 1, S42–46.

Geiger, L.R., Harner, R.N., 1978. EEG patterns at the time of focal seizure onset. *Arch. Neurol.* 35, 276–286.

Gloor, P., Vera, C.L., Sperti, L., Ray, S.N., 1961. Investigations on the Mechanism of Epileptic Discharge in the Hippocampus. *Epilepsia* 2, 42–62. doi:10.1111/j.1528-1167.1961.tb06246.x

Goldensohn, E.S., Zablow, L., Stein, B., 1970. Interrelationships of form and latency of spike discharge from small regions of human cortex. *Electroencephalogr. Clin. Neurophysiol.* 29, 321–322.

Jobst, B.C., Williamson, P.D., 2005. Frontal lobe seizures. *Psychiatr. Clin. North Am.* 28, 635–651, 648–649. doi:10.1016/j.psc.2005.05.012

Manford, M., Fish, D.R., Shorvon, S.D., 1996. An analysis of clinical seizure patterns and their localizing value in frontal and temporal lobe epilepsies. *Brain J. Neurol.* 119 (Pt 1), 17–40.

Mosewich, R.K., So, E.L., O'Brien, T.J., Cascino, G.D., Sharbrough, F.W., Marsh, W.R., Meyer, F.B., Jack, C.R., O'Brien, P.C., 2000. Factors predictive of the outcome of frontal lobe epilepsy surgery. *Epilepsia* 41, 843–849.

Munari, C., Bancaud, J., 1992. Electroclinical symptomatology of partial seizures of orbital frontal origin. *Adv. Neurol.* 57, 257–265.

Niedermeyer, E., Silva, F.H.L. da, 2005. *Electroencephalography: Basic Principles, Clinical Applications, and Related Fields.* Lippincott Williams & Wilkins.

Pedley, T.A., Tharp, B.R., Herman, K., 1981. Clinical and electroencephalographic characteristics of midline parasagittal foci. *Ann. Neurol.* 9, 142–149. doi:10.1002/ana.410090207

Provini, F., Plazzi, G., Tinuper, P., Vandi, S., Lugaresi, E., Montagna, P., 1999. Nocturnal frontal lobe epilepsy. A clinical and polygraphic overview of 100 consecutive cases. *Brain J. Neurol.* 122 (Pt 6), 1017–1031.

Quesney, L.F., Constain, M., Rasmussen, T., Stefan, H., Olivier, A., 1992. How large are frontal lobe epileptogenic zones? EEG, ECoG, and SEEG evidence. *Adv. Neurol.* 57, 311–323.

RALSTON, B.L., 1958. The mechanism of transition of interictal spiking foci into ictal seizure discharges. *Electroencephalogr. Clin. Neurophysiol.* 10, 217–232.

Ralston, B.L., Papatheodorou, C.A., 1960. The mechanism of transition of interictal spiking foci into ictal seizure discharges. Part II. Observations in man. *Electroencephalogr. Clin. Neurophysiol.* 12, 297–304.

Rasmussen, T., 1983. Characteristics of a pure culture of frontal lobe epilepsy. *Epilepsia* 24, 482–493.

Shih, J.J., LeslieMazwi, T., Falcao, G., Van Gerpen, J., 2009. Directed aggressive behavior in frontal lobe epilepsy: a video-EEG and ictal spect case study. *Neurology* 73, 1804–1806. doi:10.1212/WNL.0b013e3181c2933f

Tharp., B.R., 1972. Orbital Frontal Seizures. An Unique Electroencephalographic and Clinical Syndrome. *Epilepsia* 13, 627–642. doi:10.1111/j.1528-1157.1972.tb04398.x

Unnwongse, K., Wehner, T., Bingaman, W., Foldvary-Schaefer, N., 2010. Gelastic seizures and the anteromesial frontal lobe: a case report and review of intracranial EEG recording and electrocortical stimulation case studies. *Epilepsia* 51, 2195–2198. doi:10.1111/j.1528-1167.2010.02548.x

Vadlamudi, L., So, E.L., Worrell, G.A., Mosewich, R.K., Cascino, G.D., Meyer, F.B., Lesnick, T.G., 2004. Factors underlying scalp-EEG interictal epileptiform discharges in intractable frontal lobe epilepsy. *Epileptic Disord. Int. Epilepsy J. Videotape* 6, 89–95.

Verma, A., Radtke, R., 2006. EEG of partial seizures. *J. Clin. Neurophysiol. Off. Publ. Am. Electroencephalogr. Soc.* 23, 333–339. doi:10.1097/01.wnp.0000228497.89734.7a

Westmoreland, B.F., 1998. The EEG findings in extratemporal seizures. *Epilepsia* 39 Suppl 4, S1–8.

Williamson, P.D., Spencer, S.S., 1986. Clinical and EEG features of complex partial seizures of extratemporal origin. *Epilepsia* 27 Suppl 2, S46–63.

Worrell, G.A., So, E.L., Kazemi, J., O'Brien, T.J., Mosewich, R.K., Cascino, G.D., Meyer, F.B., Marsh, W.R., 2002. Focal ictal beta discharge on scalp EEG predicts excellent outcome of frontal lobe epilepsy surgery. *Epilepsia* 43, 277–282.

Zhao, J., Afra, P., Adamolekun, B., 2010. Partial epilepsy presenting as focal atonic seizure: a case report. *Seizure J. Br. Epilepsy Assoc.* 19, 326–329. doi:10.1016/j.seizure.2010.04.014

EEG GRAPHICAL APPENDIX

10. EEG GRAPHICAL APPENDIX

Some of the most representative cases are showed and commented. We have selected them among the cases with recorded seizures.

Out of the graphical study of all the frontal lobe cases I would like to stress some characteristics, which are of interest in the clinical practice:

Frontal lobe seizures are frequently short, with duration of seconds, and sometimes appear grouped in clusters, within the same recording. Clinically they present extremely varied semiology, sometimes including all kind of clinical manifestations, with or without consciousness impairment and sometimes with secondary generalization.

Trying to locate the IED it will be necessary to look for epochs in which the activity presents less active, due to the fact that when it is more active, the IED usually appears very widespread and very expressive, especially in both frontal lobes. This, combined with the utilization of different available montages, increase the possibility of locating the focus and correct diagnose the cases. The referential montage is especially useful for locating the IED, once we are used to the fact that the electronegativity of the focus is contribution to the mean, which affects all channels in it second component, the "reference".

Many times the ictal expression of the electrical activity in frontal lobe seizure is subtle and difficult to interpret. Another piece of information that helps in identifying ictal EEG activity are polygraphy changes, as many frontal seizures have vegetative manifestations, with tachycardia, bradycardia and/or breathing irregularity.

Post-ictal activity should be taken into account: After the ictal activity in frontal lobe seizures we can usually observe a frontal slowing, with immediate recovery of alpha rhythm in posterior regions.

J.B.M.

J.B.M.

J.B.M.

Patient who was born in 1971 and started having seizures at the age of 5 years old. He had an infection CNS antecedent, with MRI showing left frontal atrophy. During the seizures the patient seats suddenly on the bed, he opens his eyes and does not answer in a few seconds. Sometimes he performs some motor activity such as taking off some electrodes, or raises his arms or legs.

EEG characteristics:

The IED has its maximal expression over inferior frontal region, with sharp waves up to 100 μ V and spikes of less than 50 μ V followed by irregular slow waves.

In a referential montage (Fig.1) the IED is easier to locate than using a bipolar montage (Fig.2).

Seizures start with a synchronized rhythm arising from left frontal regions with almost immediate diffusion from F7/F3. There is quite EMG artifact, except in front central regions (less artifacted) (Fig.3,4,5,6).

J.B.M.

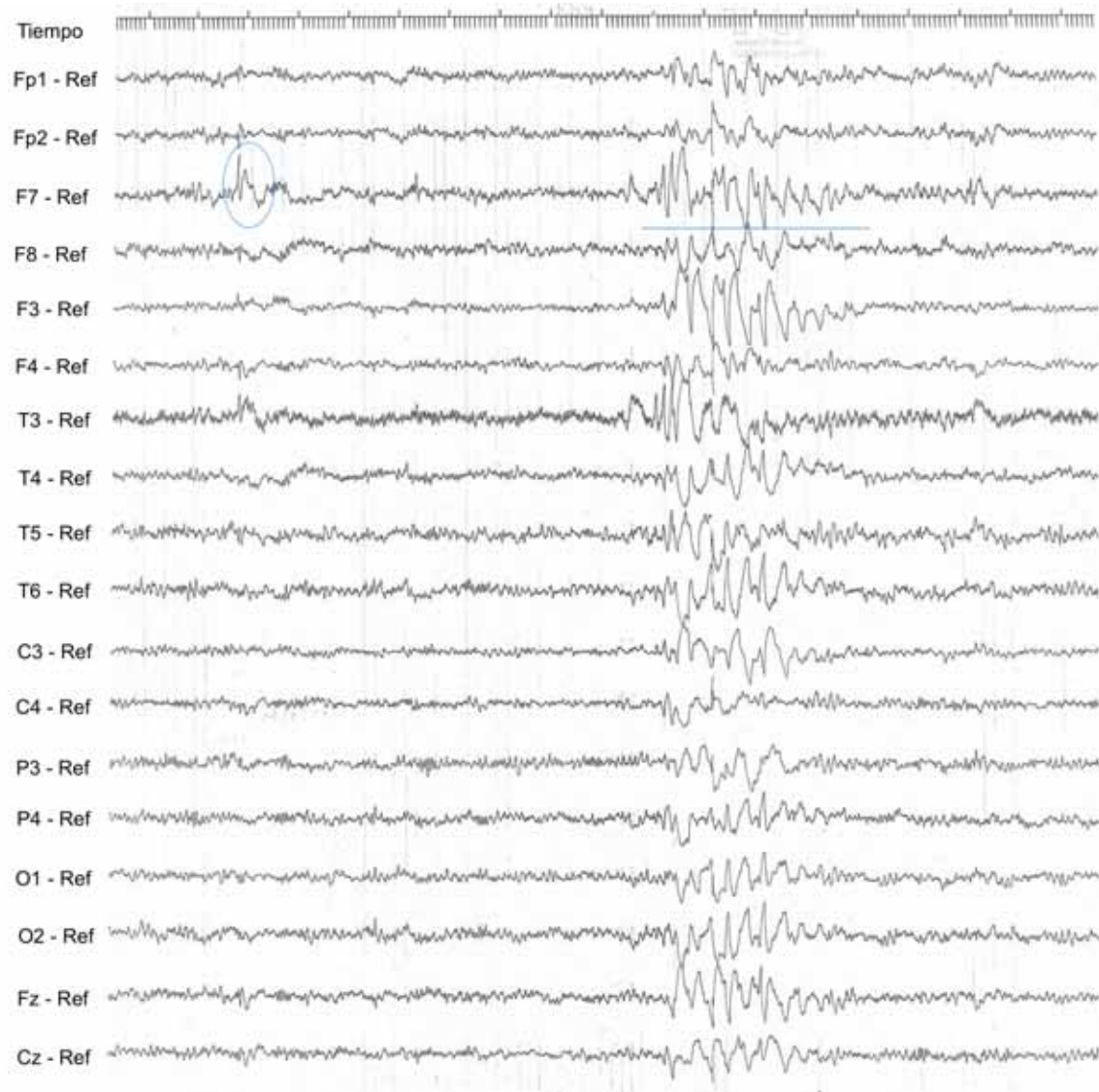


Fig. 1 Referential montage. Maximal expression of IED on left inferior frontal region, F7, and diffusion to F3, Fz, T3. We should take into account that this activity, affecting to the “reference” of the montage (the mean activity of all electrodes) causes a contrary deflection in most of the channels, especially T4, T6, P4, O1 and O2. This “referential montage effect” is crucial to understand the recordings.

J.B.M.

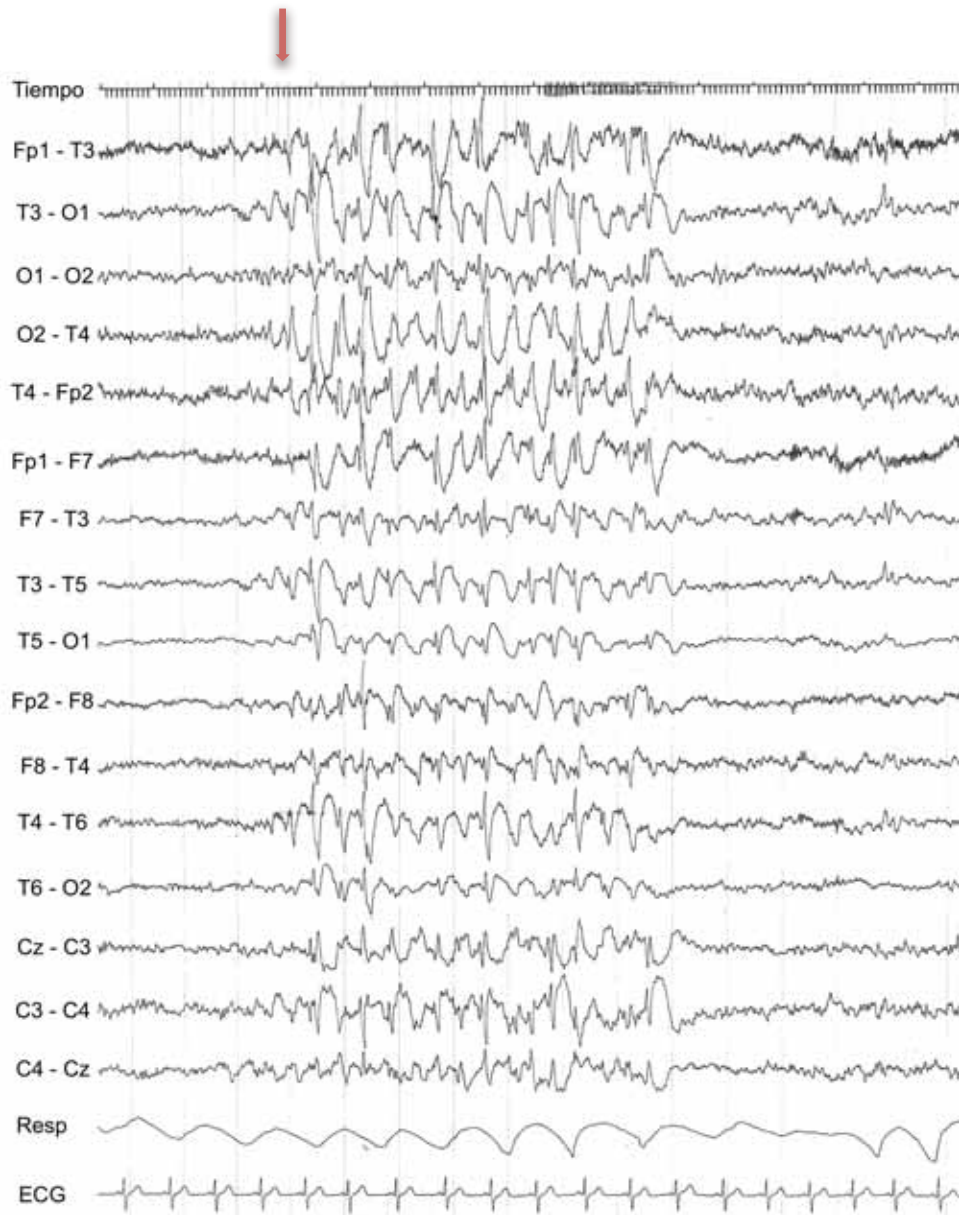


Fig. 2 Bipolar montage. Sensitivity of 100 μ V/cm. With these settings it is very complicated to locate the IED.

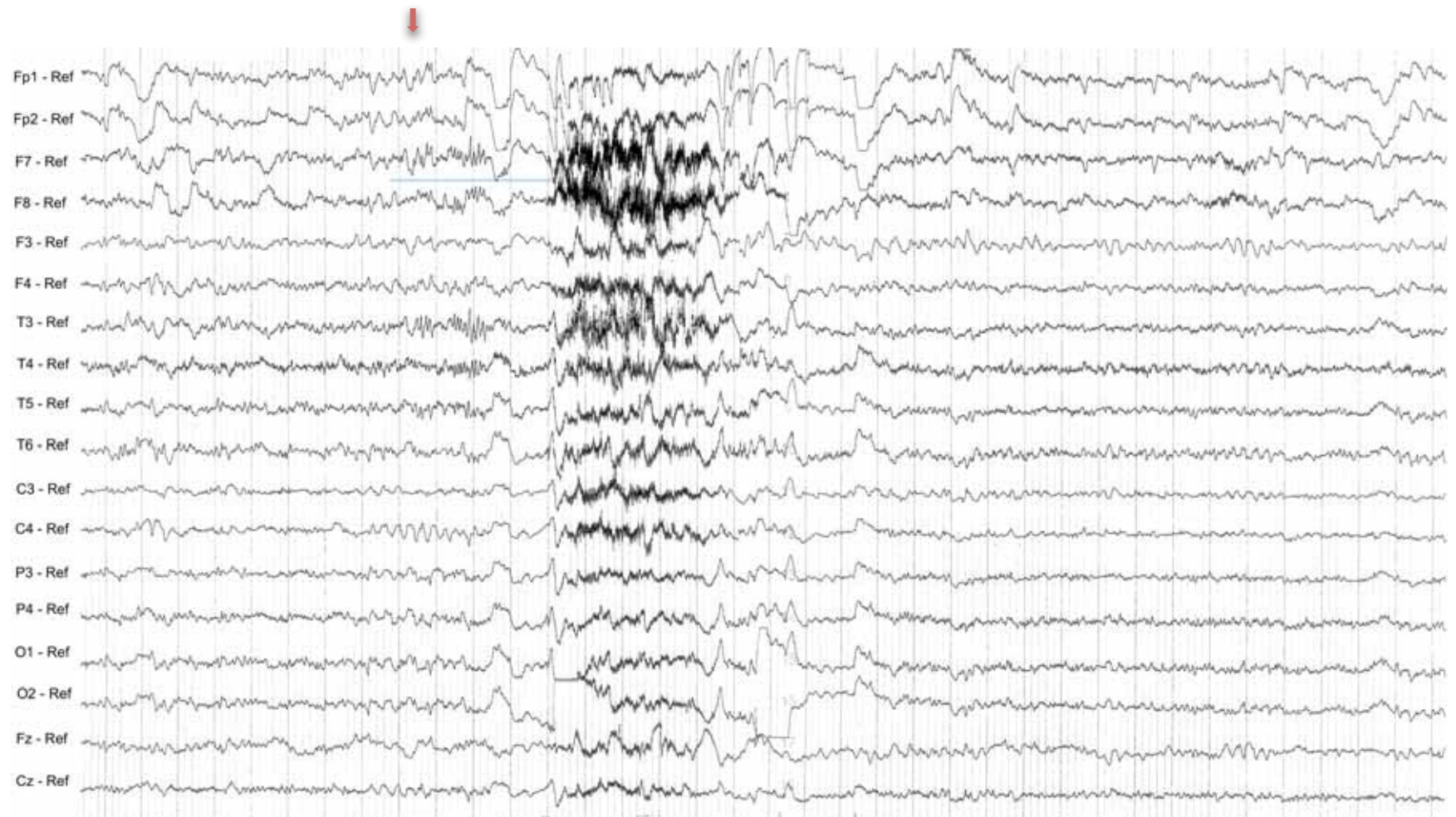


Fig 3 Referential montage. 100 μ V/cm. Left frontal synchronized rhythm as transition, with maximal expression on F7> T3, F8 with a global marked attenuation afterwards at seizure onset. Less EMG artifact in left front central electrode. Clinically during the seizures the patient seats suddenly on the bed, he opens his eyes and does not answer in a few seconds. Sometimes he performs some motor activity such as taking off some electrodes, or raises his arms or legs.

J.B.M.

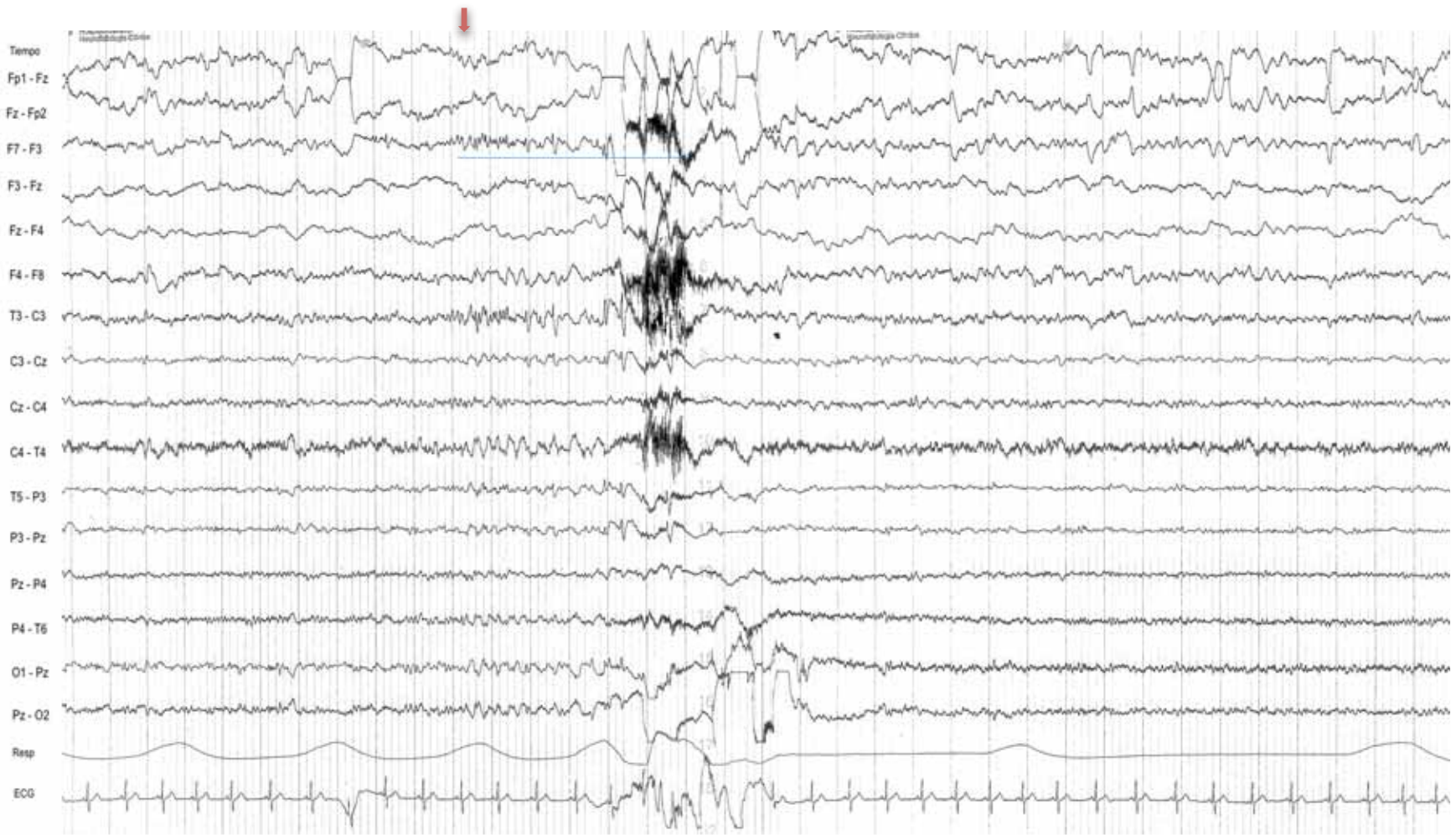


Fig 4 Collage. Seizure in a bipolar transversal montage. Sensitivity of 100 $\mu\text{V}/\text{cm}$. Attenuation with synchronized rhythm at seizure onset with maximal expression on F7, F3, Fp1. We can see changes in the polygraphy, with irregular breathing and afterwards a change in the normal breathing frequency, as well as a slowing in the EKG frequency just at seizure onset.

J.B.M.

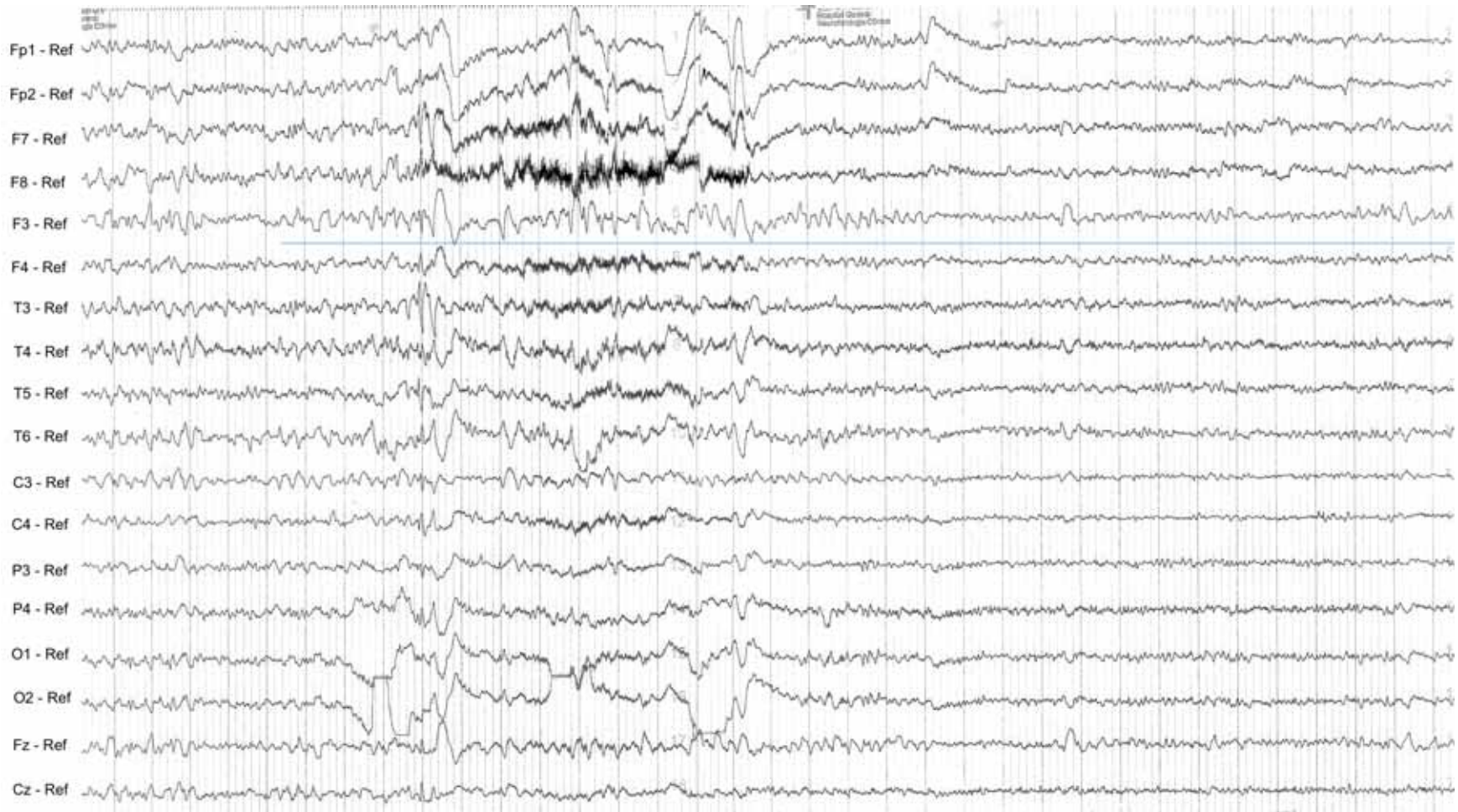


Fig 5 Seizure in a referential montage. Low amplitude synchronized rhythm just at seizure onset and progressive slowing of frequencies, with increasing amplitude.

Less EMG artifact in F3. Seizure ending with subtle post-ictal slowing.

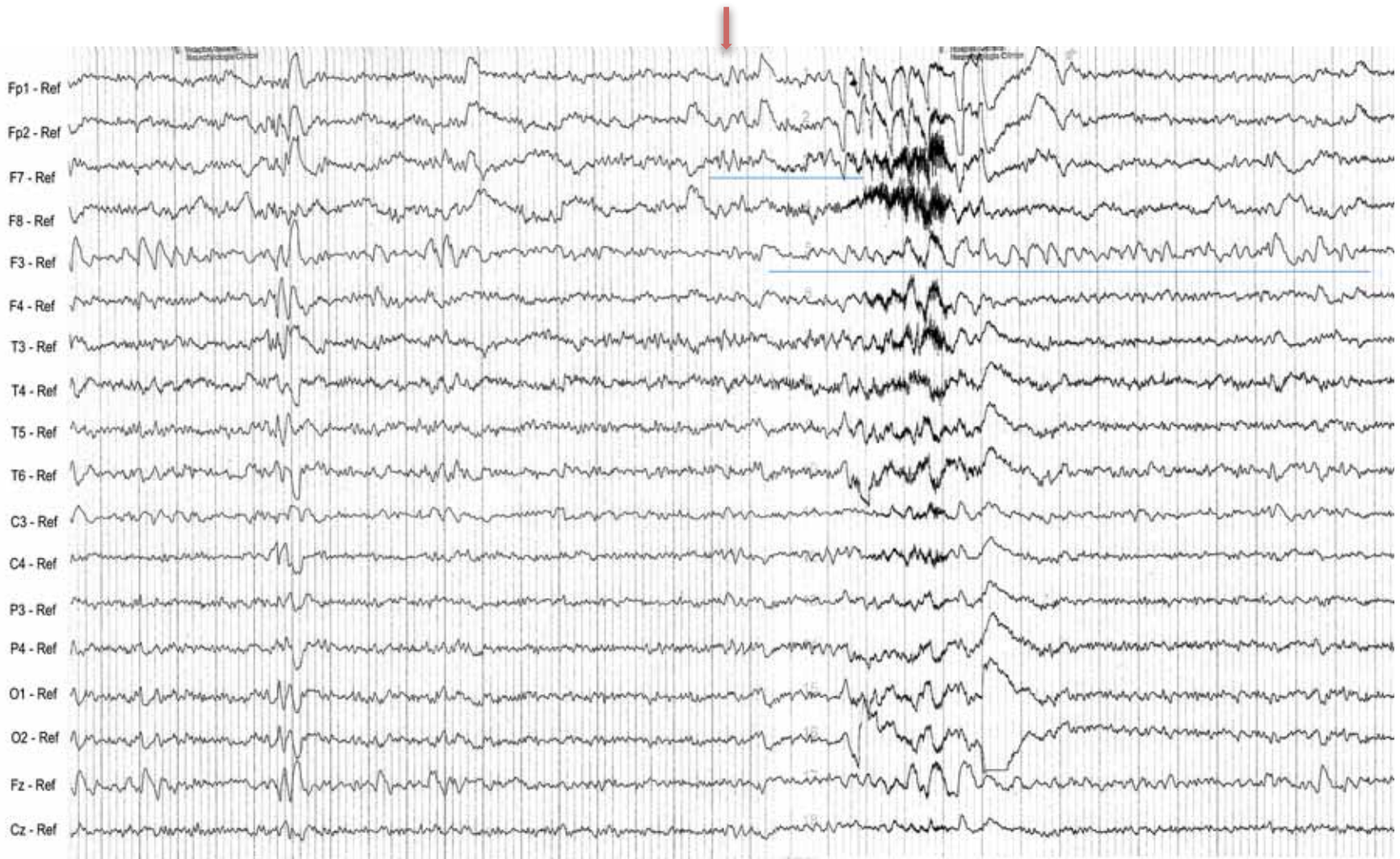


Fig 6 Seizure in referential montage preceded by IED in left frontal areas, with maximal expression in F7, F3. Attenuation with synchronized rhythm at seizure onset with maximal expression in F7 and irregular waves with maximal expression in F3.

P.V.V.

P.V.V.

P.V.V.

Patient with a generalized epilepsy that started having partial seizures at the age of 24 years old, after a craniotomy for performing a ventriculography.

Clinically, she had seizures with different intensities. In the longest episodes (around 10 seconds) she deviates both legs towards the right, to recover its original position after the seizure. There is not clear consciousness impairment and she hears a word said during the seizure and she says that she is not aware of any change, but just after the seizure she refers to have had a “distraction”.

EEG characteristics:

She presents a very active focus on right frontal region, with maximal expression in F4. It presents very widespread, so it was necessary to change several settings, as montage, sensitivity and speed to locate the focus and the location of seizure onset. Seizures start with “spike/sharp wave within a slow wave” just before the synchronized rhythm at seizure onset, detail that can be appreciated in some of the figures, with maximal expression in F4 and projected over both frontal regions.

P.V.V.

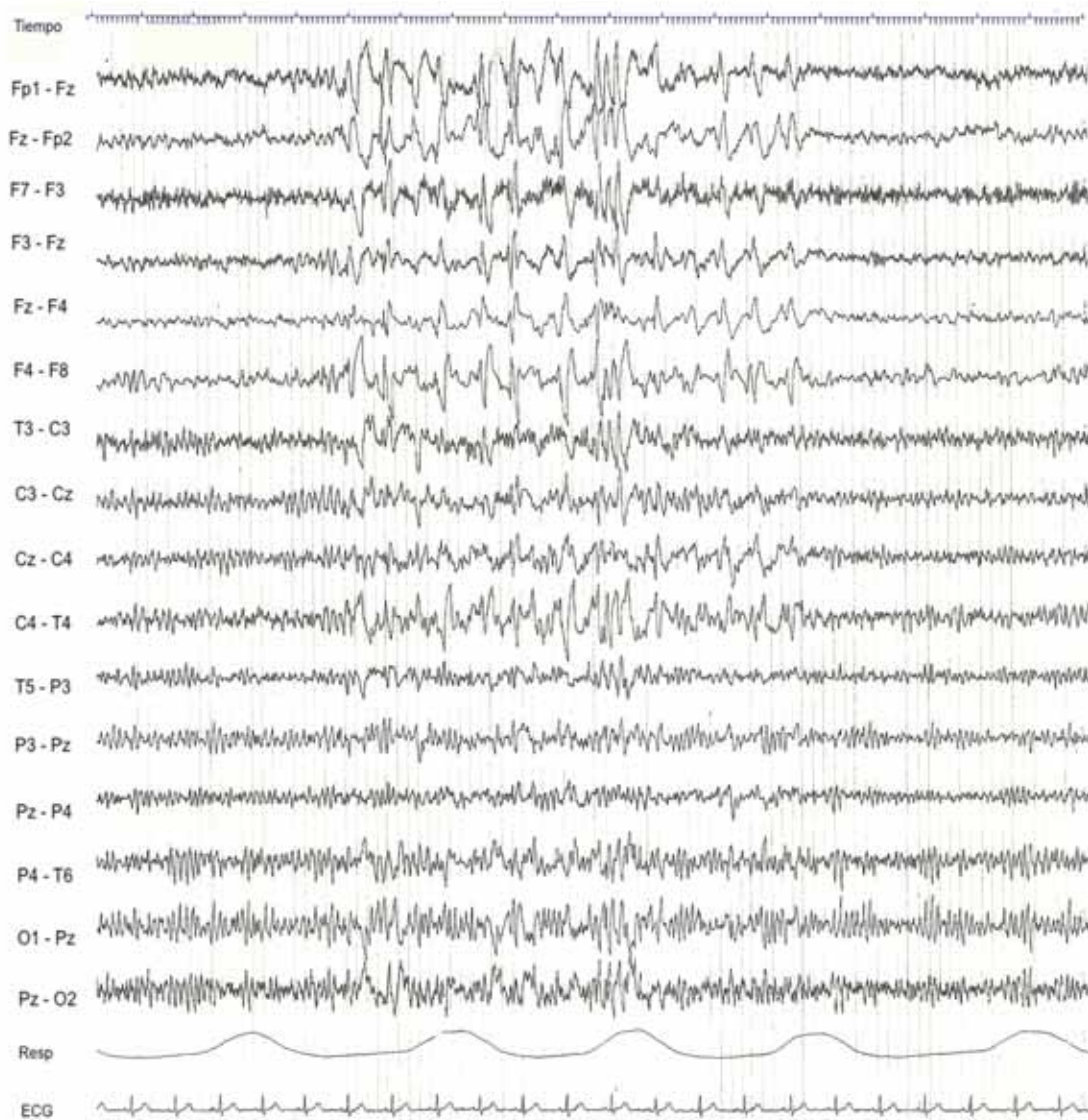


Fig. 1 Bipolar transversal montage. 100 μ V/cm. IED more expressive in Fz, F7, F3, F4. Different settings are needed to better locate the activity.

P.V.V.

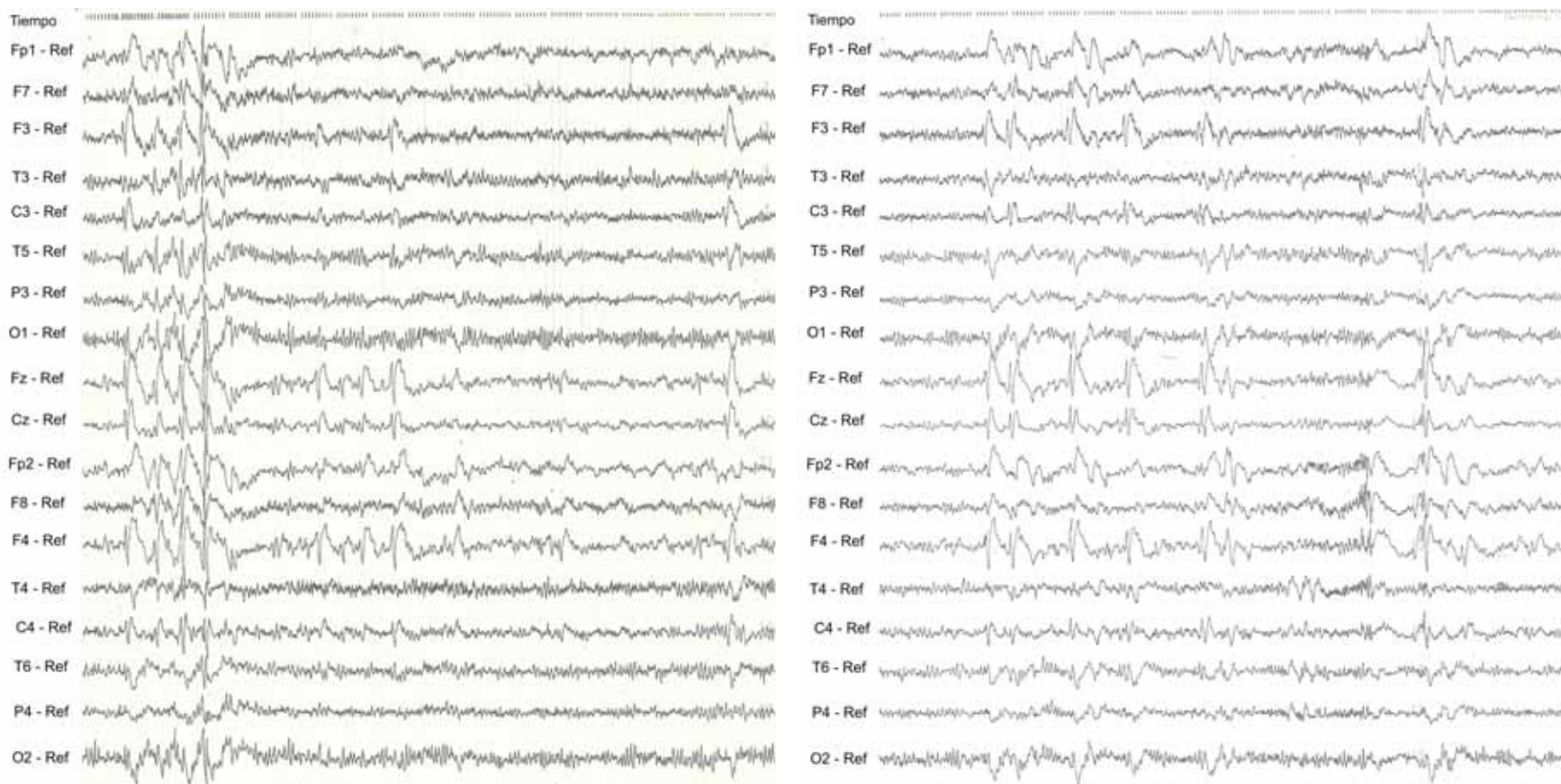


Fig. 2.1, 2.2. When the IED appears so widespread, we should wait and look for an epoch where the IED appear less active, because then it will appear more located. In this case, we can see the focus more and less active, and much more located in right front-central regions, with maximal expression in F4 and Fz, especially in 2.2.

P.V.V.

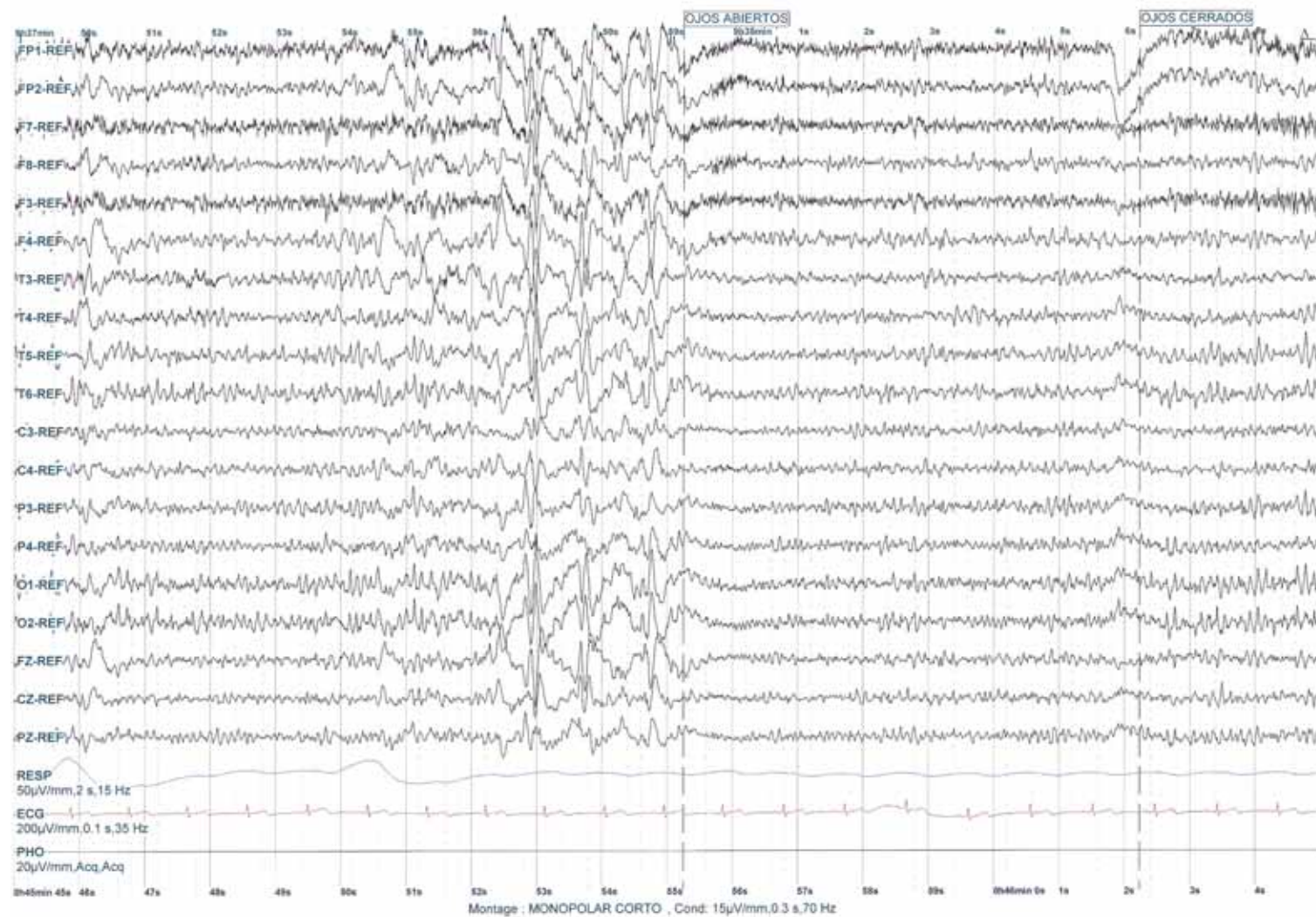


Fig. 3 Referential montage. Reactivity to eyes opening. Sometimes you can see reactivity to different alert states, which does not exclude the epileptic nature of the activity, as somnolence and superficial sleep usually activate paroxistic activity. In fact we recorded an epileptic seizure in this recording.

P.V.V.

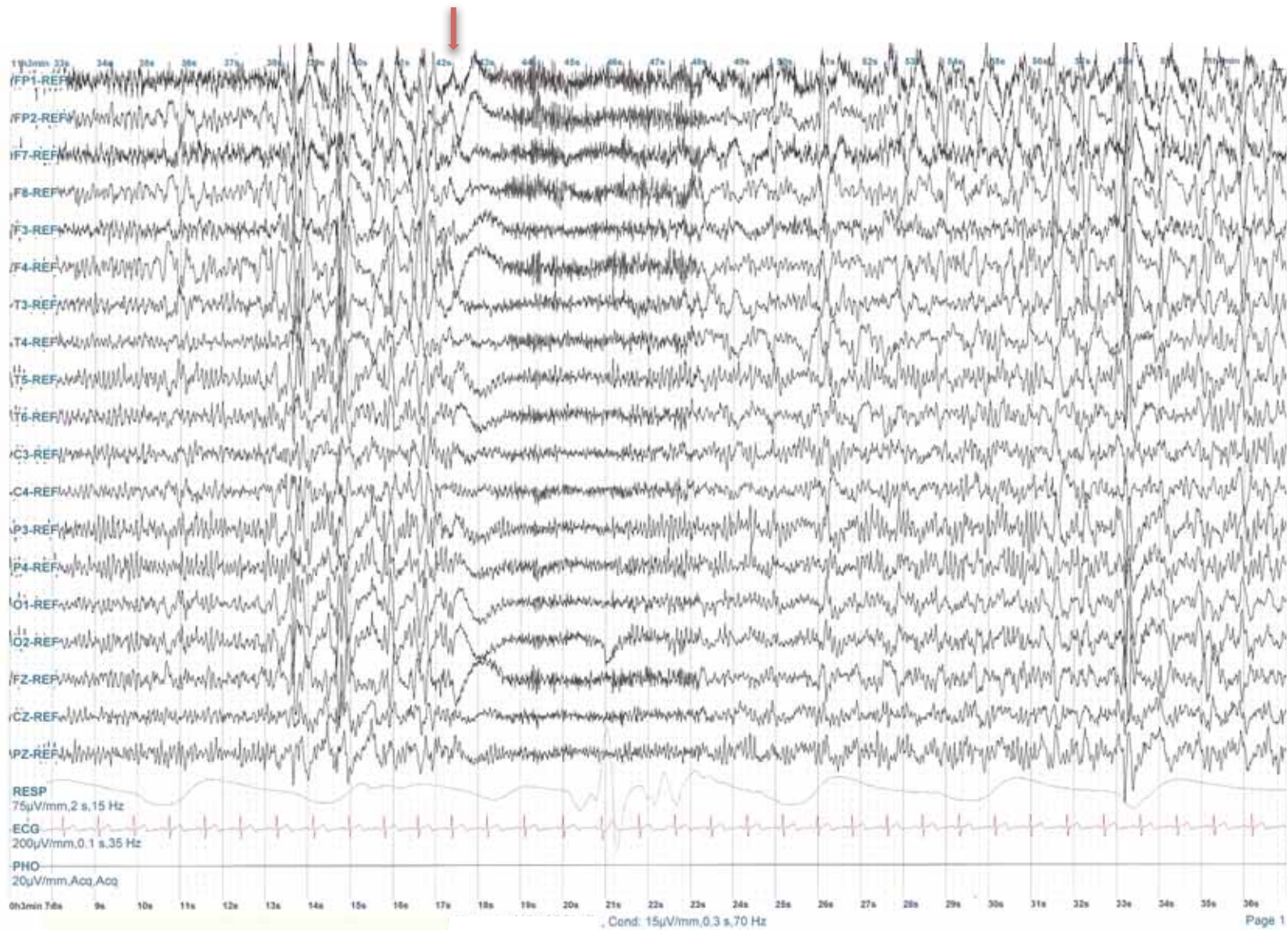


Fig. 4 Referential montage. Seizure with spike/sharp wave within a slow wave just before the synchronized rhythm at seizure onset with maximal expression in F4 >Fp2. The ictal activity is followed by diphasic spikes followed by slow wave and afterwards a slowing predominantly in right frontal regions, with maximal expression in F4, where there appears some sharp waves and spikes followed by irregular slow wave. We must pay attention to subtle changes in both EKG rhythm and breathing: we can see a light slowing of EKG frequency and irregular breathing during the seizure.

P.V.V.

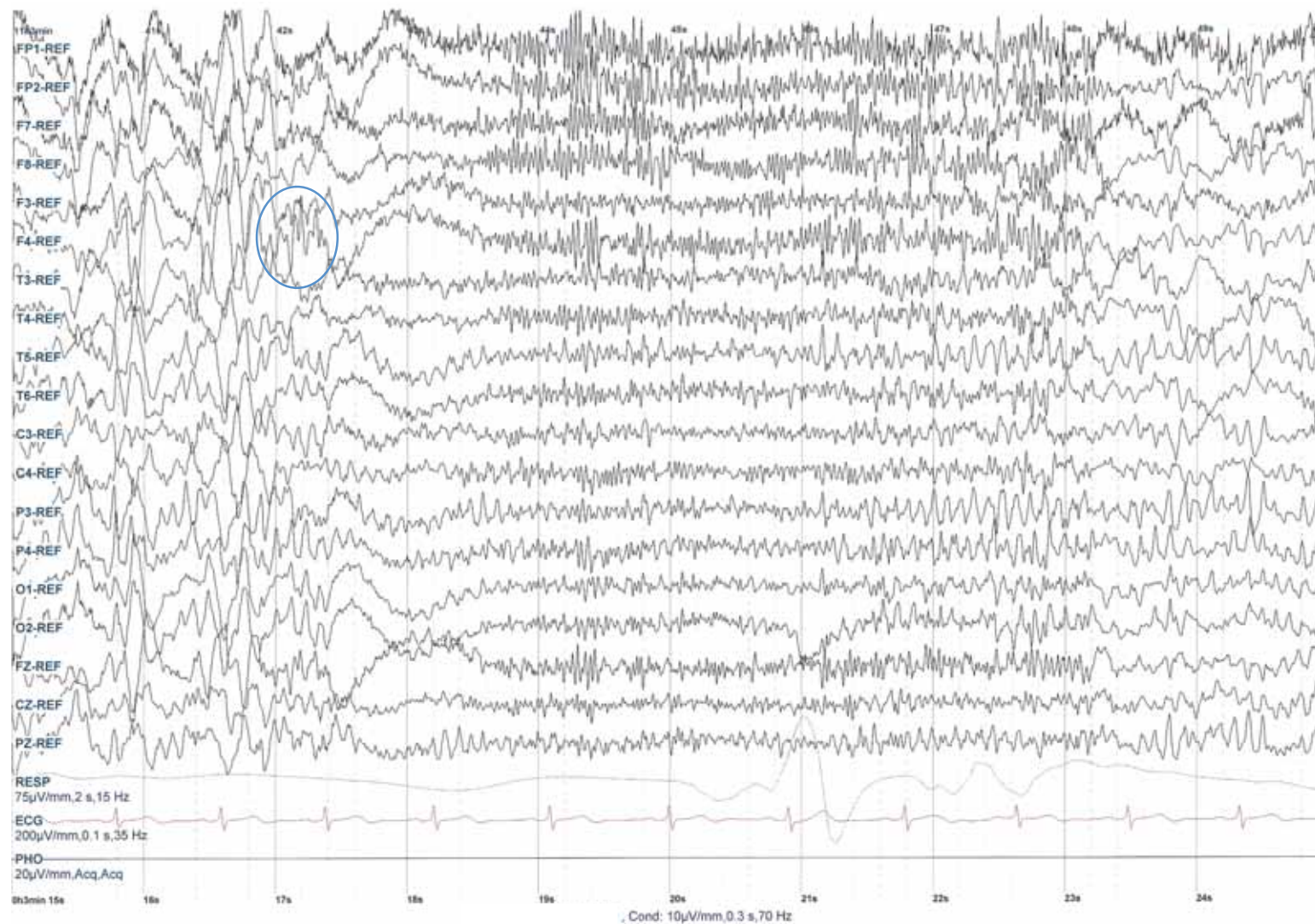


Fig. 5 Same seizure and montage, with different speed (10s/page;10µV/mm). Attenuation and synchronized rhythm with maximal expression in both F4, F8 and also very expressive in both Fp1, Fp2, Fz, F7 F3. Breathing irregularity and EKG frequency (less evident in this configuration of 10 s/page)

P.V.V.



Fig. 6 Full seizure view, with the on-going EEG activity. Poligraphy changes during the seizure become more evident. When the IED is less active we can see a right predominance, with maximal expression in front-central region, F4 and diffusion to F8 and Fp2. Clinically she deviates both legs towards the right, to recover its original position after the seizure. There is not clear consciousness impairment and she hears a word we said to her during the seizure and at that moment she said that she was not aware of any change, but just after the seizure she refers to have had a “distraction”.

M.G.O.

M.G.O.

M.G.O.

Patient with nocturnal frontal lobe epilepsy, with seizures almost all nights, with up to 20 episodes recorded in a PSG per night, with none pathologic antecedent, who started having seizures at the age of 18 years old. No MRI available.

Clinically during the seizures he gyrus the trunk towards the left side while moving both arms and legs with clenched fists, from sleep, awaking him.

EEG characteristics:

Electroencephalography recordings showed left frontal focus, with maximal expression in left front-central region, F3, mainly consisting of isolated sharp waves of 100-200 μ V and seizures during sleep with synchronized rhythm without attenuation at onset, at 13 Hz of frequency and very short duration.

M.G.O.



Fig. 1 Bipolar standard, 10 μ V/mm. Awake state, basal activity. Normal.

M.G.O.

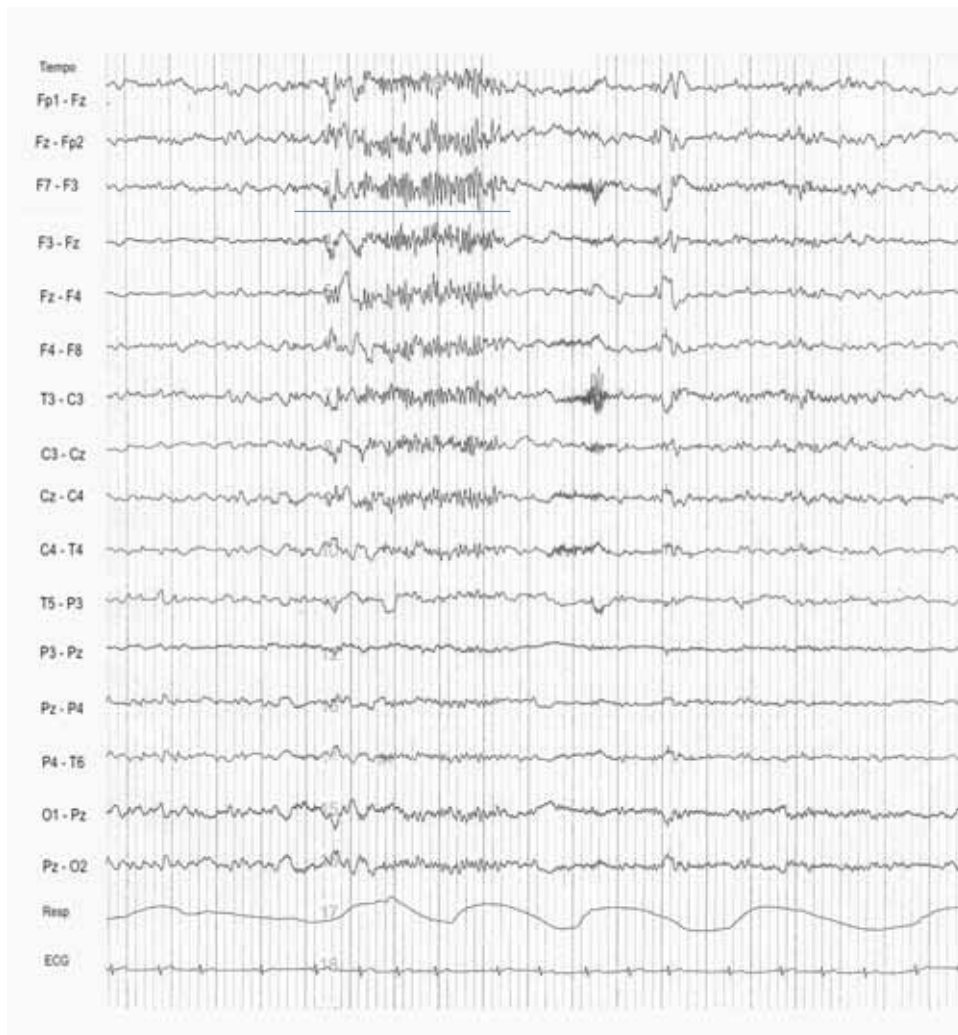


Fig. 2 Bipolar transversal montage. Seizure arising from sleep activity, with synchronized rhythm at 13 Hz with left predominance, with maximal expression in F7, F3, and also expressive in Fp1, Fp2, Fz, Cz, C3. Poligraphy changes with increasing EKG frequency and breathing irregularity during the brief seizure.

M.G.O.

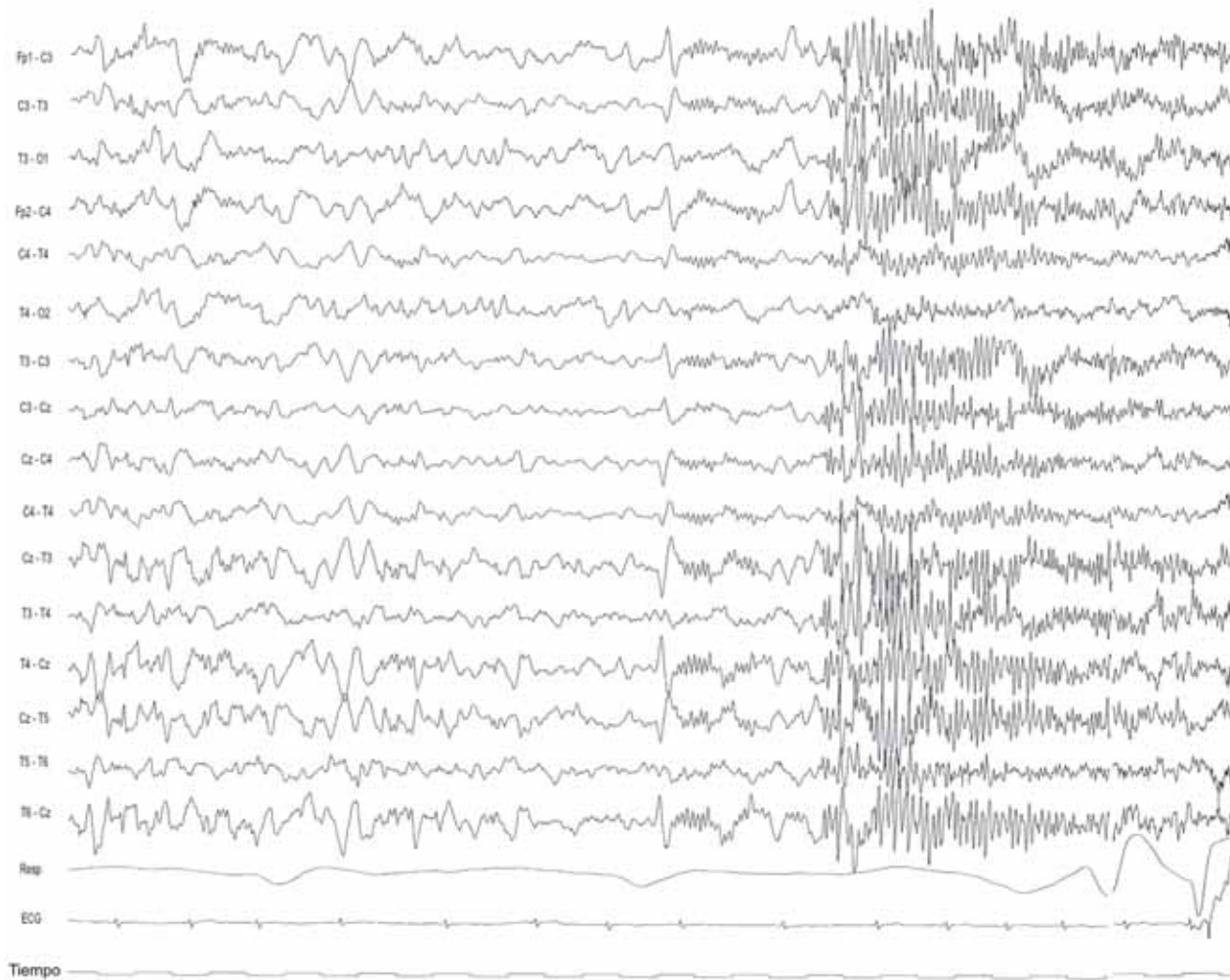


Fig. 3 Standard bipolar montage. Sleep activity, with a vertex sharp wave and spindle in central regions. Afterwards we can see high amplitude synchronized rhythm with maximal expression in both prefrontal regions Fp1, Fp2 and left hemisphere dominance, comparing channels C3-T3, T3 -O1 with C4-T4 and T4-O2 respectively. Increased EKG frequency and breathing irregularity just after seizure onset.

M.G.O.

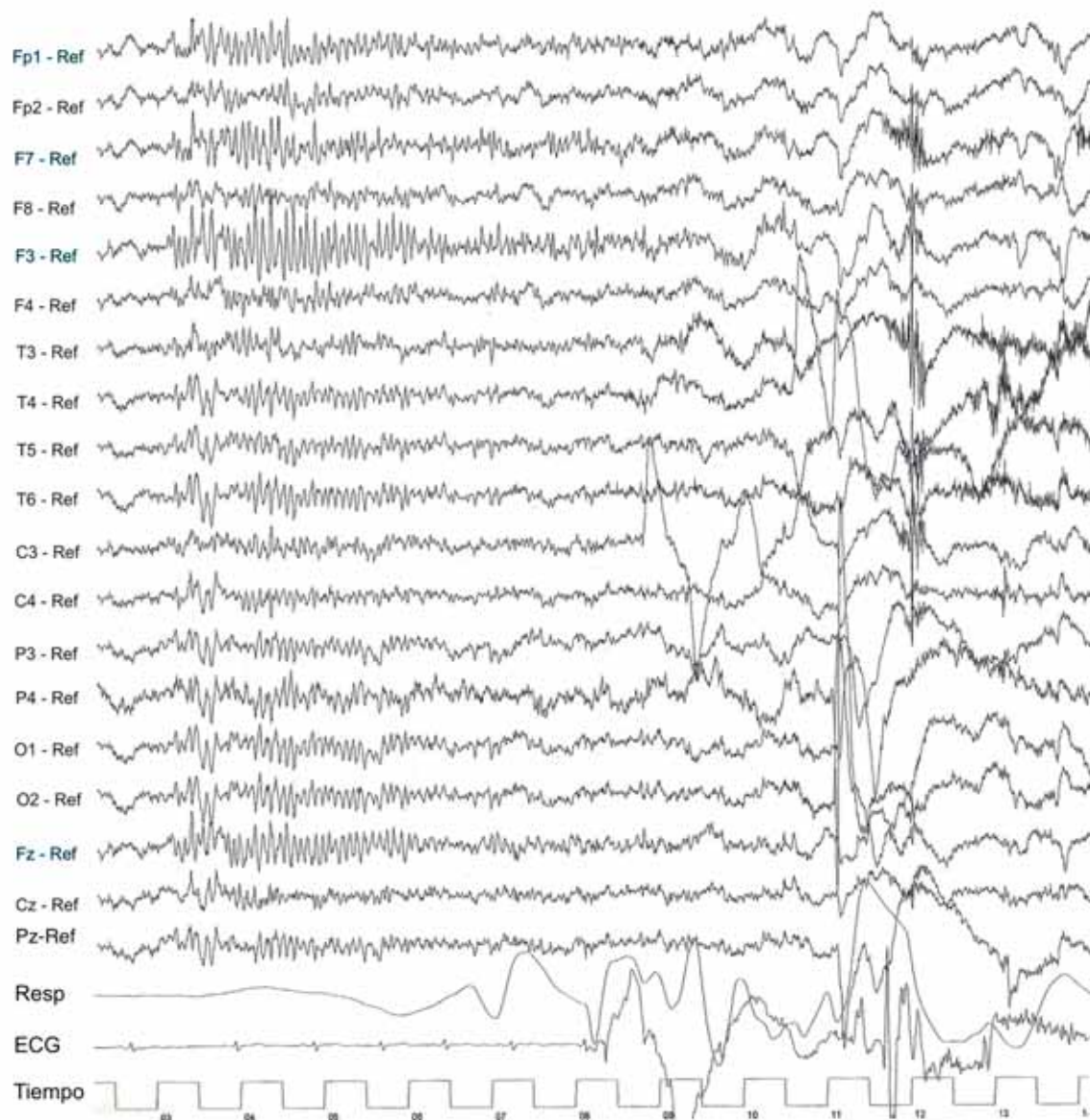


Fig. 4 Referential montage that helps a lot in locating the ictal activity, arising with synchronized rhythm with maximal expression in F3, followed by F7, Fp1 and Fz, and less expressive but still evident in right frontal regions, without attenuation at onset. It is remarkable the short duration of the seizure. Evident breathing irregularity and EKG frequency change.

M.G.O.

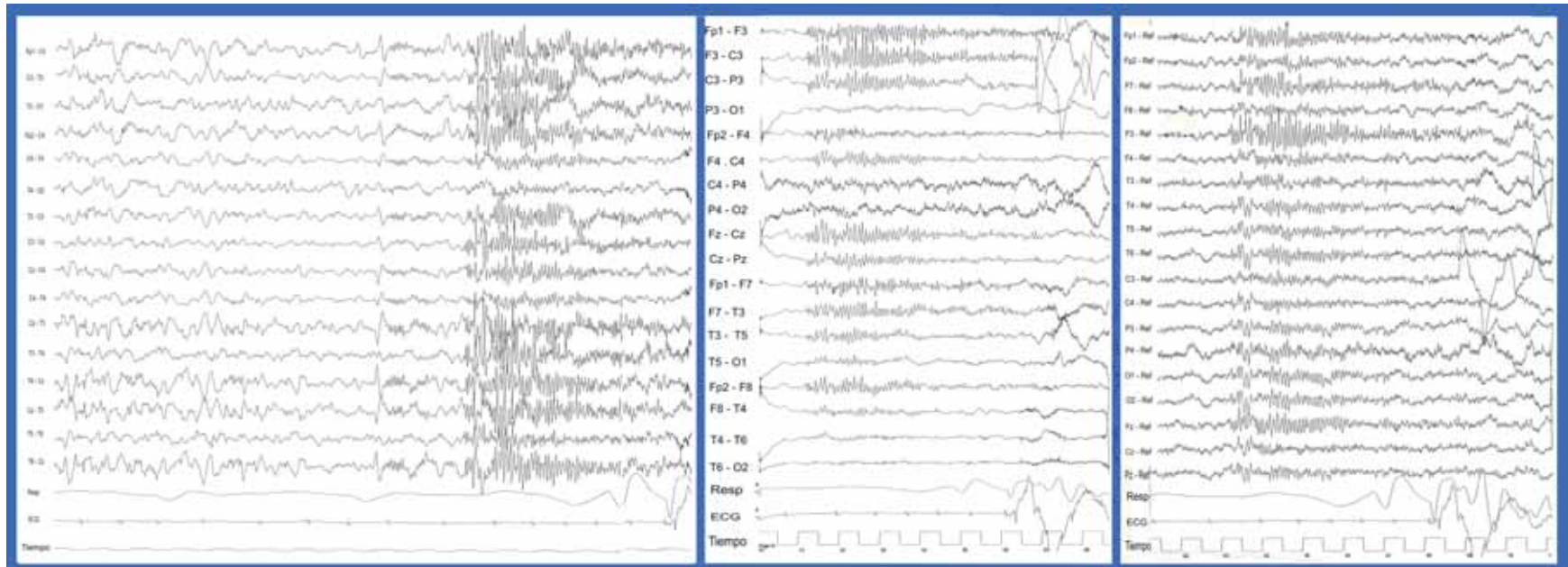


Fig. 5 Mosaic image comparing ictal activity in different montages: standard bipolar, longitudinal and referential. Maximal expression of the synchronized rhythm in F3, and also evident in F7, Fz, Fp1, Fp2, F8 regions. Clinically seizures awake the patient; He gyrus the trunk towards the left side while moving both arms and legs with clenched fists.

E.T.R.

E.T.R.

E.T.R.

Patient without any pathologic antecedent who starts with seizures at 8 years old, during sleep. Orientated as generalized epilepsy continues with seizures at night, secondary generalized, without pharmacologic control of the seizures. Normal MRI. At 18 years old is recorded in our department, asked for a second opinion due to the lack of control of seizures. Clinically seizures were partial complex, with different degrees of clinical manifestations regarding its intensity, from a slight blink to a gyrus of the head to the right, being unable to repeat any word.

EEG characteristics:

We recorded burst of low amplitude synchronized rhythm of 50h 100 μ V and sharp waves followed by a slow wave of 50h 100 μ V. The fast aspect of paroxysm and front central location may have confused the first recording, as well as the fact that seizures occurred during sleep. Other confusing factor is the wide spreading of the focus activity that makes the activity very present in both left and right front central electrodes, as the generalized epilepsies do.

In this case it was very important to change settings while reading the recordings, as well as the recording of sleep. We recorded daytime sleep, with very frequent short seizures. A polysomnographic study was performed, without finding slow phases (phase 3NREM) and very fragmented sleep with a lot of partial seizures of left front central origin and with REM epochs without interictal epileptiform activity (fig. 5).

Seizures present with synchronized rhythm without attenuation and left front central predominance; we explored consciousness during the seizures, by telling her a word and asking her for repeating it, without success.

E.T.R.

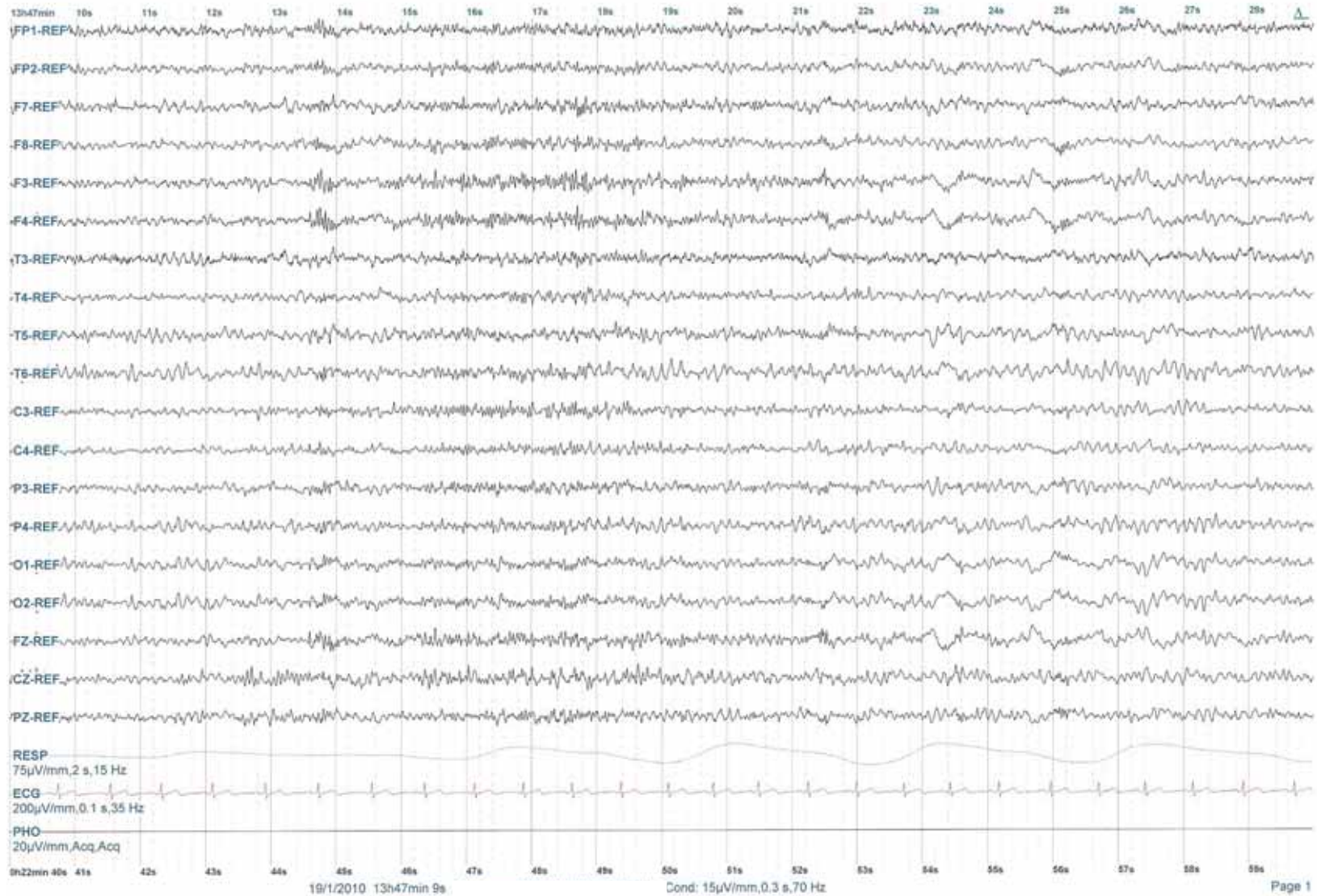


Fig. 1 Referential montage. Burst of synchronized rhythm with maximal expression in F4, also evident in both Fp1 and Fp2, F3, and Fz. Afterwards there are irregular slow waves in both frontal regions, with maximal expression in F4, Fz, F3. Increasing EKG frequency and change in breathing polygraph. Ictal activity presents with different intensity, from milder clinically and electrically, to more evident both clinically and electrically, as part of its nature.

E.T.R.

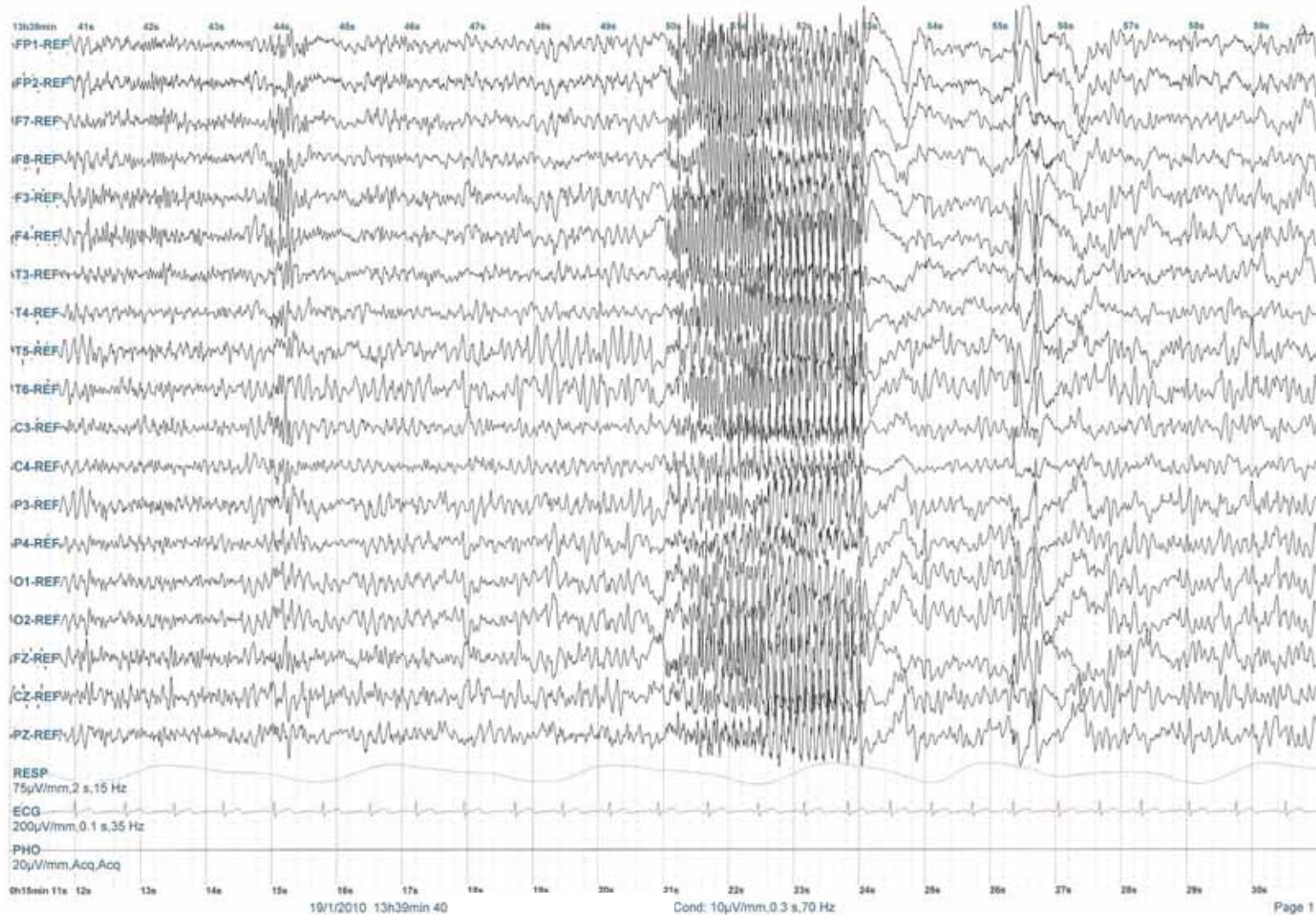


Fig. 2 Referential montage, with a short seizure consisted on high amplitude synchronized rhythm at around 20 Hz with very fast diffusion. Sensitivity of 10µV/mm. The only clinical manifestation is a gyrus of the head towards the right and sometimes the only clinical manifestation is impaired consciousness, being unable to repeat words said to her during the seizures. Before the most evident seizure we can see a brief tentative of a seizure starting, with a very brief burst of synchronized rhythm of 400 ms. duration approximately with maximal expression in F3, being evident in both F7, Fp1, Fp2, Fz, F4, and F8 as well.

E.T.R.

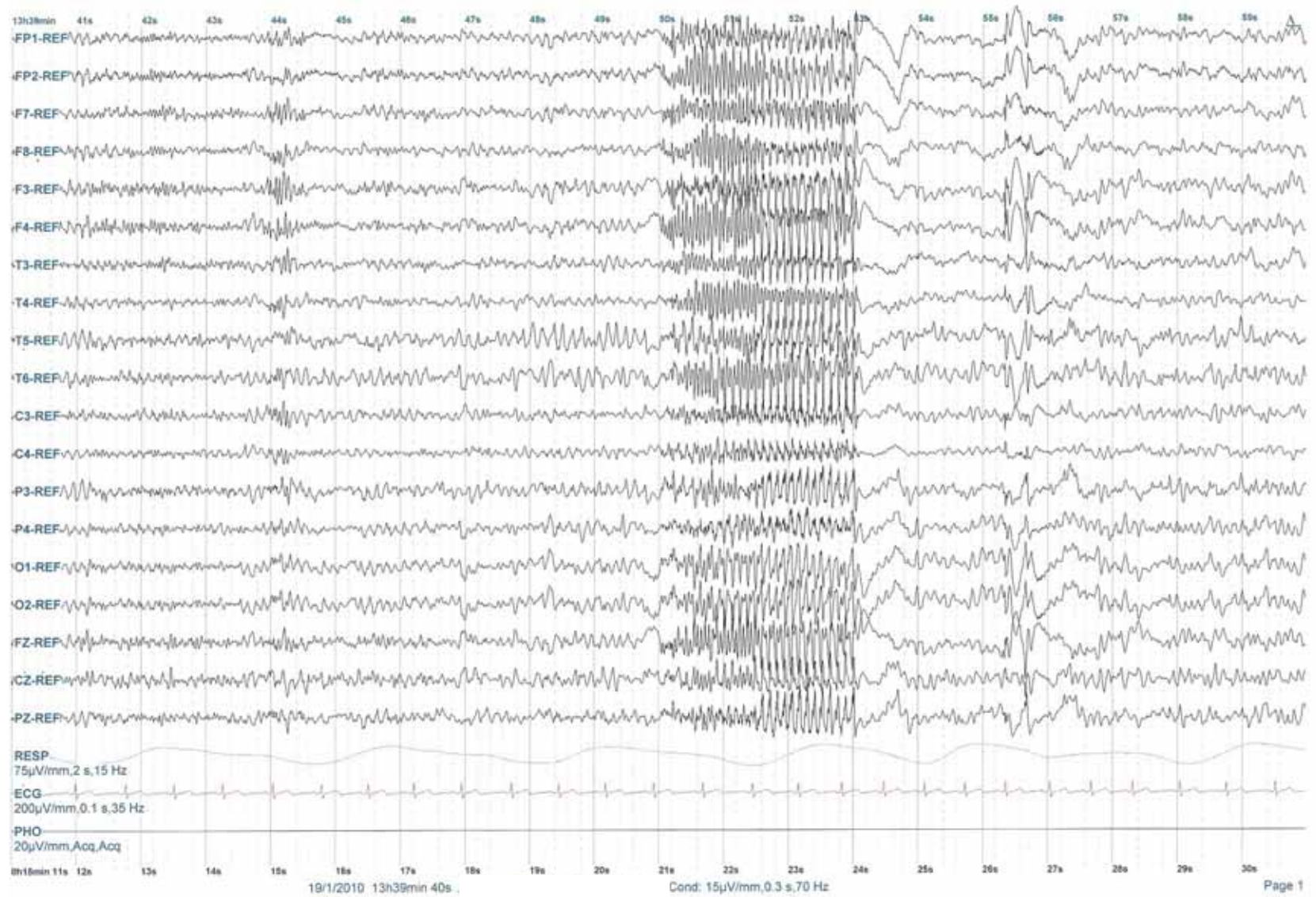


Fig. 3 Same epoch with decreased sensitivity to 15µV/mm. We can change sensitivity to better look at the detail of the EEG activity. After seizure ending we can see IED of sharp wave followed by slow wave in both prefrontal and front-central regions, with maximal expression in front-central regions and slight more amplitude in F3.

E.T.R.

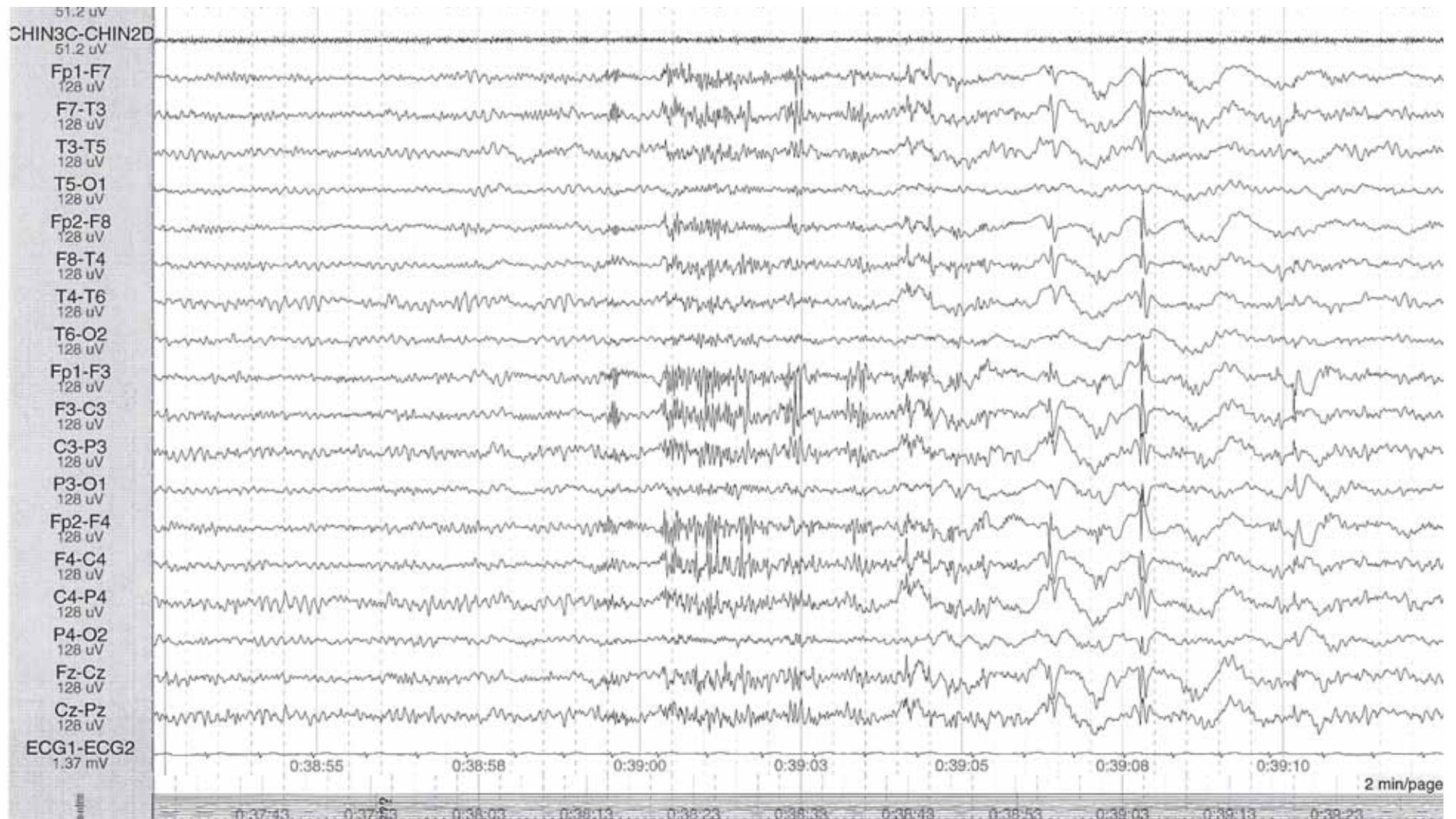


Fig. 4 Polysomnographic study. Awake stated. Similar finding to day-time sleep, with multiple short seizure activity consisting of synchronized rhythm and afterwards IED with maximal expression in F3, F7.

E.T.R.

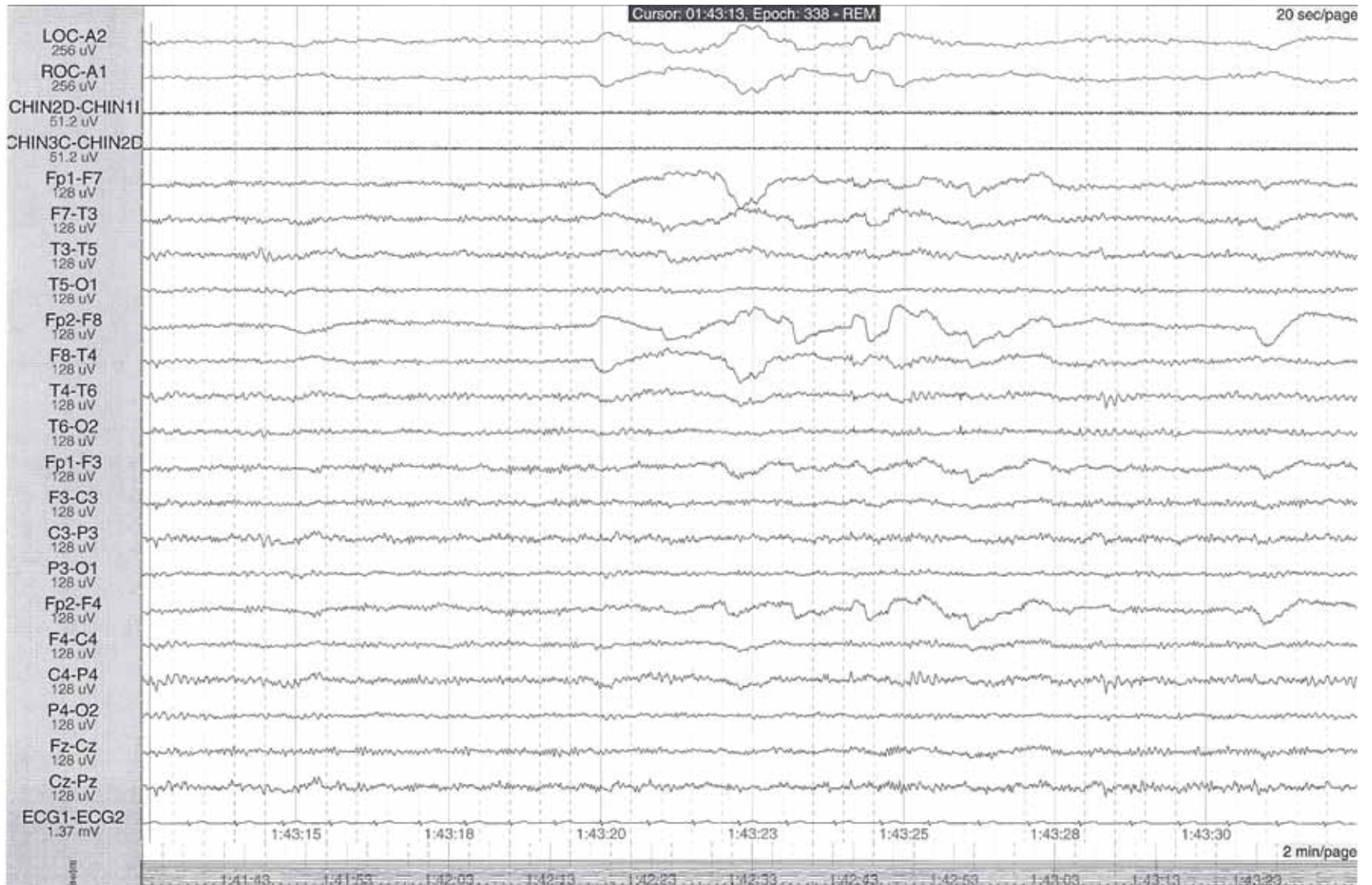


Fig. 5 Polysomnographic study. REM sleep without paroxistic activity with rapid eye movements.

S.R.S.

S.R.S.

S.R.S.

Patient without any known pathologic antecedent, who started having seizures at the age of 6 years old. Normal TC and MRI.

Clinically she presented simple partial seizures, without secondary generalization. They consisted of aphasia and down tonic deviation of both oral commissures and eye movements. After the seizure she refers that she is aware of her eyes moving but not of the mouth contraction. She frequently had clusters of several seizures; Two clusters of three seizures each appeared in one of the recordings.

EEG characteristics:

The IED is located in left frontal regions, mainly F7 >F3, as the following graphic shows in the different montages. The main interictal waveform was isolated spikes and sharp waves of less than 50 μ V. Seizures appeared in clusters, of very short duration (around 10 seconds), and they start with a low amplitude synchronized rhythm over left frontal regions with maximal expression in left inferior frontal region, F7, with starting frequencies at around 17 Hz.

S.R.S.

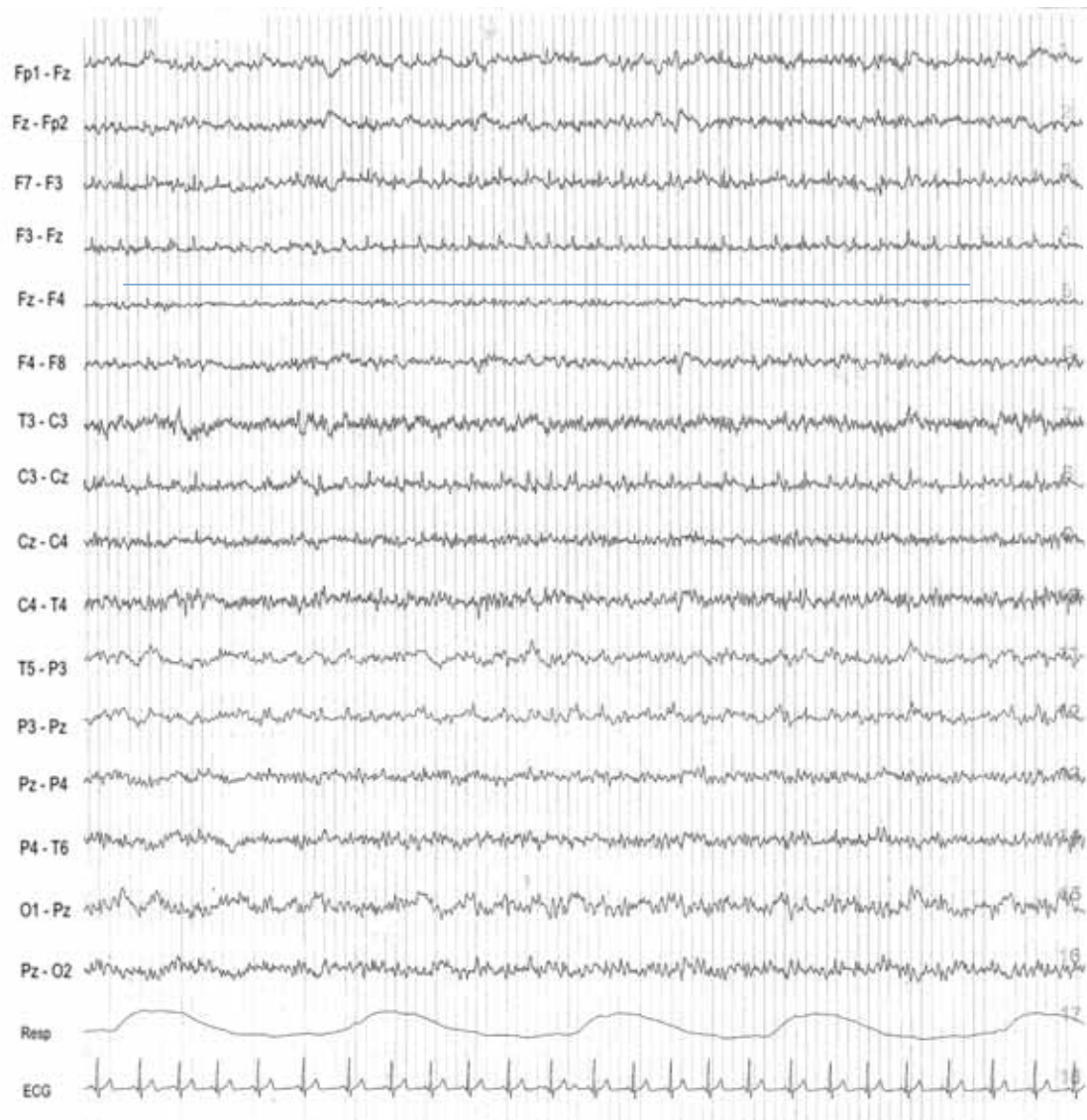


Fig. 1 Bipolar transversal montage. $10\mu\text{V}/\text{mm}$. Isolated and repetitive low voltage spikes in left frontal regions, with maximal expression in F3, also evident in F7, Cz. It could be thought that this activity might correspond to the "QRS" complex of the EKG, but looking carefully, we realize that the frequency is not the same.

S.R.S.

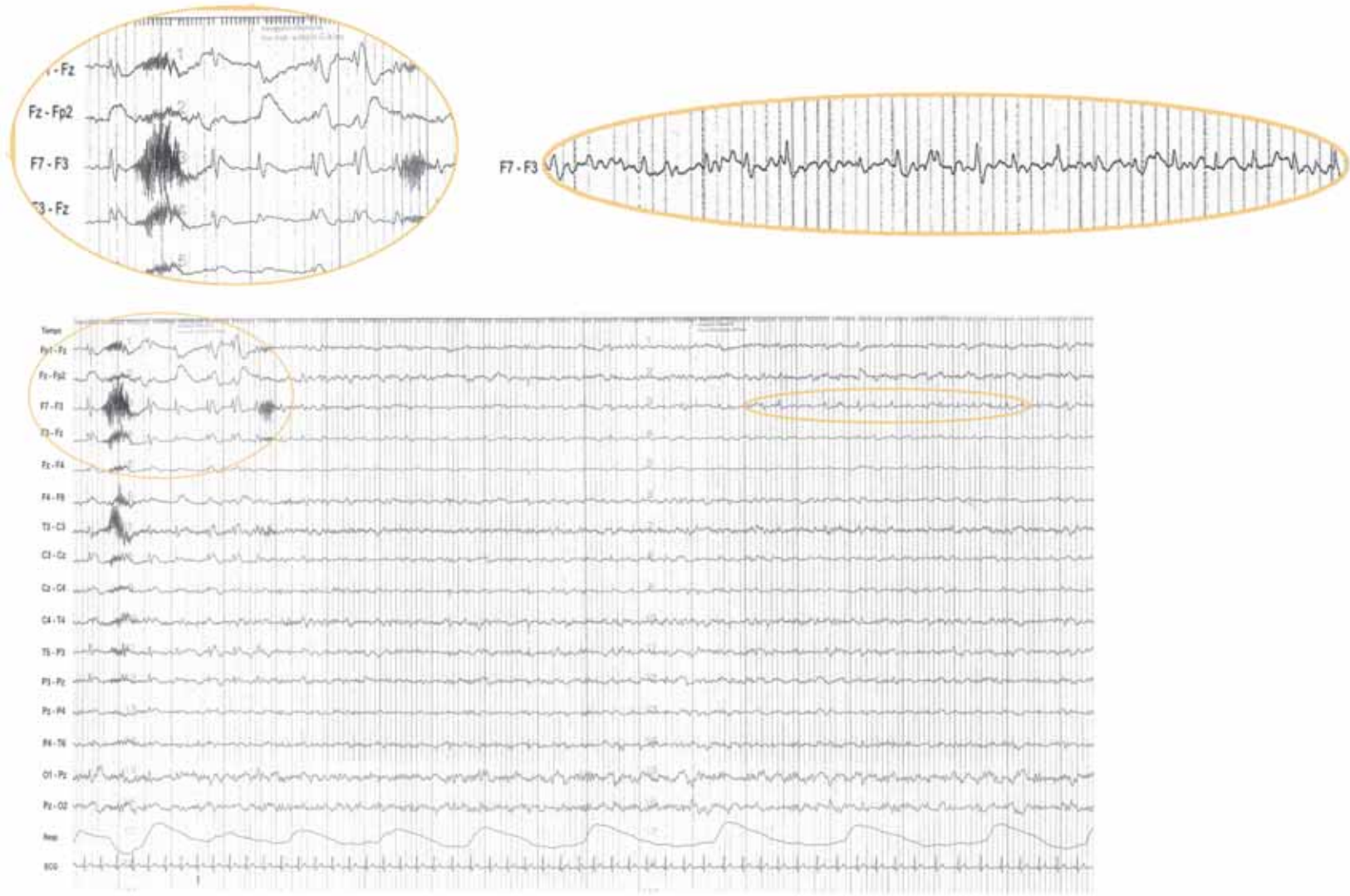


Fig. 2 Bipolar transversal montage. IED with maximal expression in left inferior frontal region, F7 and diffusion to Fp1 and F3 regions.

S.R.S.

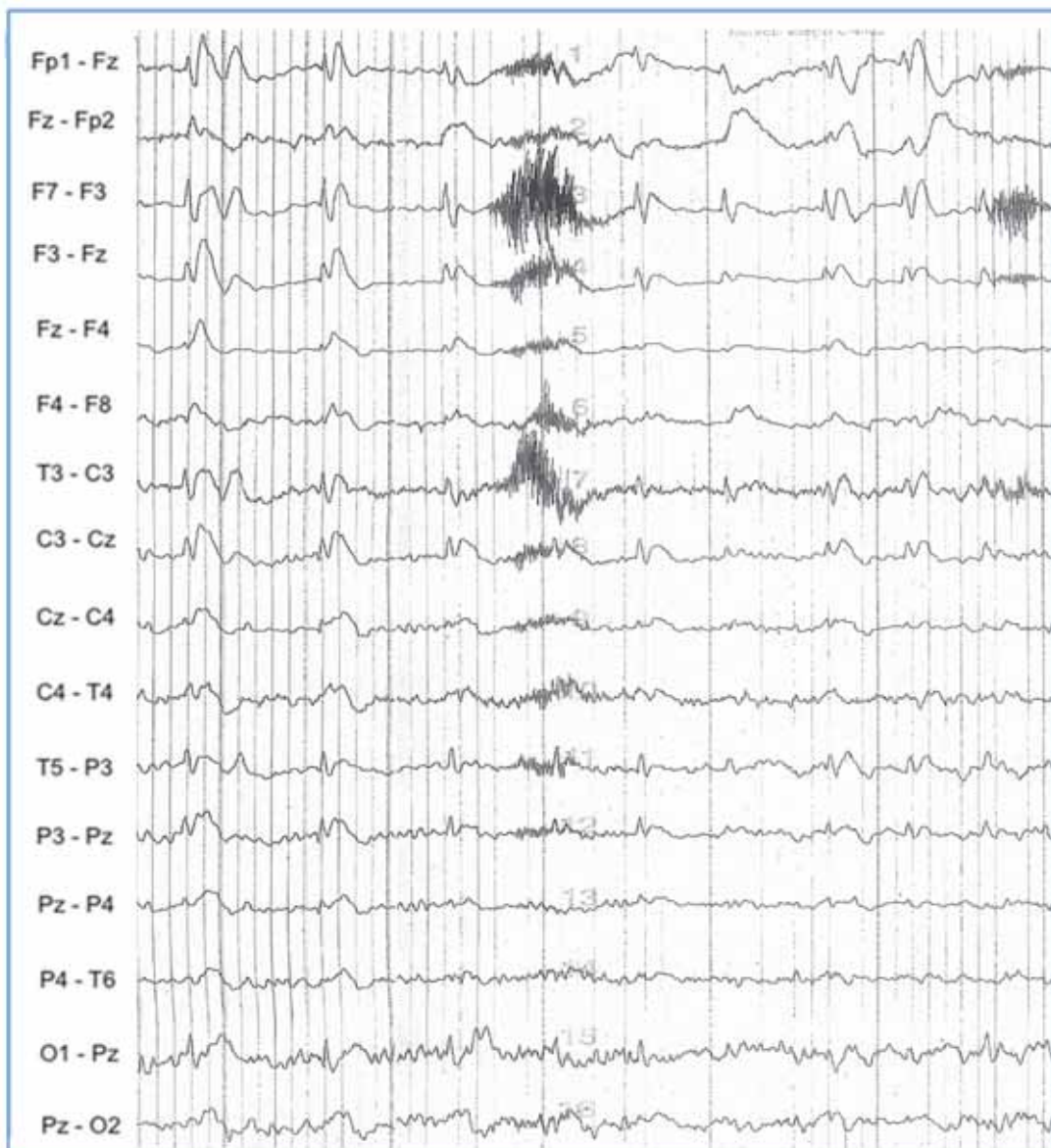


Fig. 3 Bipolar transversal montage. Amplified view of the left frontal interictal epileptiform activity, with maximal expression in F7 and diffusion to Fp1, F3, T3, O1.

S.R.S.



Fig. 4 Bipolar triangular montage. Cluster of seizures arising with a low amplitude synchronized rhythm left inferior frontal areas, F7, that arises blocking irregular slow waves and ending with a high amplitude slow wave. Slight increase in EKG frequency during the seizure. Afterwards, the focal IED becomes more evident, with a diphasic spike followed by a slow wave of higher voltage and diffusion. The patient refers block of language and eye movements with tonic deviation to the left.

S.R.S.



Fig. 5 Detailed view of seizure onset, with attenuation and low amplitude synchronized rhythm with maximal expression in left inferior frontal region (F7) and front-central region (F3).

S.G.N.

S.G.N.

S.G.N.

Patient with seizures since he was one year old with scarce pharmacologic control. He did not present any pathologic antecedent. At the age of 5 years old he started having partial seizures with secondary generalization. Normal TAC and MRI. He used to have clusters of seizures, with 1 to 3 seizures per week.

Clinically, he presents different manifestations regarding the intensity of the seizures. He opens his eyes and seat on the bed with automatism, impaired consciousness, tachycardia, face blushing and urine incontinence. He recovers consciousness very quickly after seizure but remains bradipsychic during post-ictal slowing.

EEG characteristics:

He presents a well organized basal activity.

High voltage spikes followed by a slow wave mainly constitute the IED, with maximal expression in left inferior frontal region, F7, with diffusion to both pre-frontal areas, Fp1, Fp2, mid line frontal, Fz, and front-central regions, F3, F4. Seizures are preceded by diphasic spike paroxysm with maximal expression in Fp1, F7, F3, and start with attenuation and low amplitude synchronized rhythm arising from left pre-frontal and inferior frontal Fp1, F7 followed by a marked postictal slowing over frontal regions with left predominance, with mixed spikes and poly-spikes.

S.G.N.

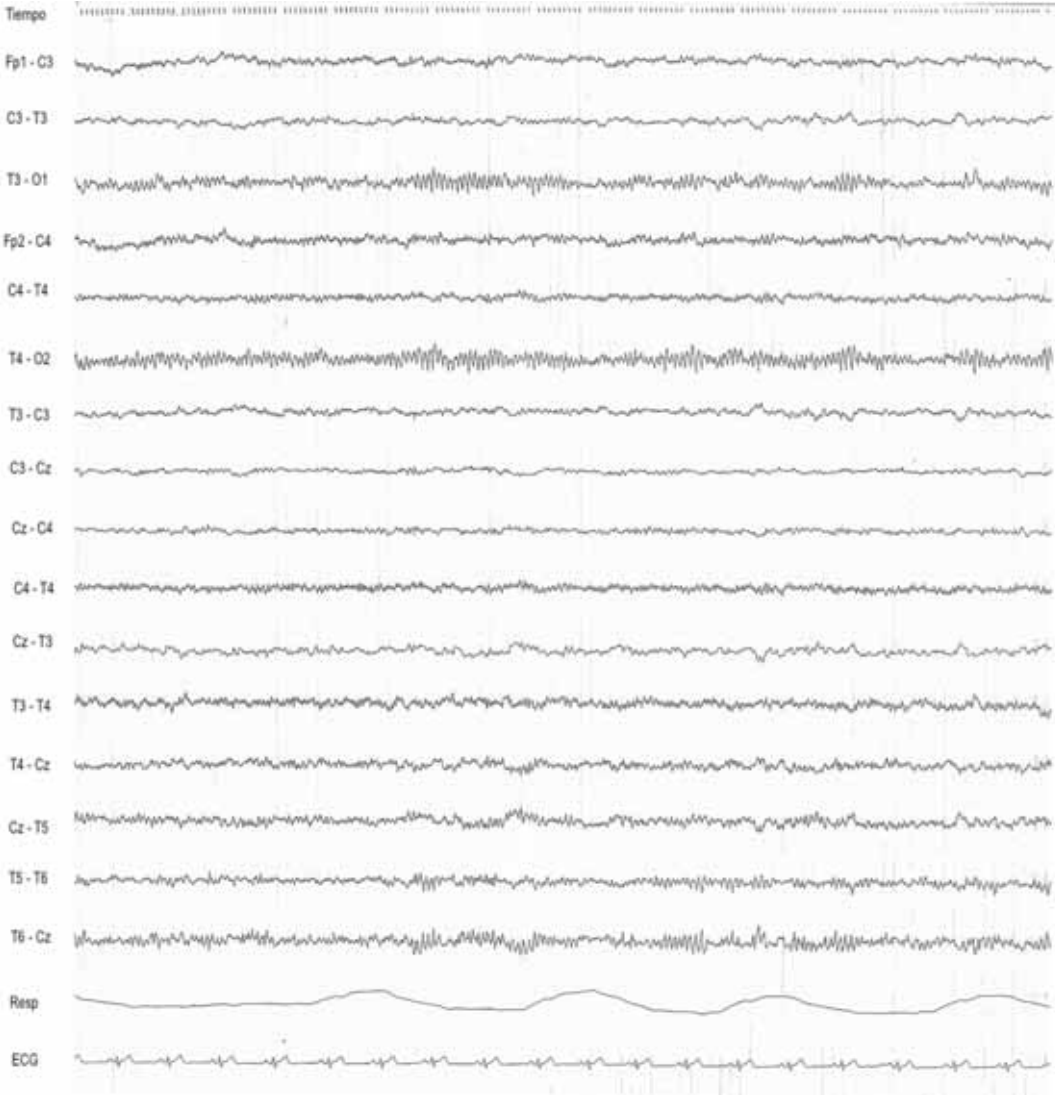


Fig. 1 Standard bipolar montage. Well organized basal activity. Normal

S.G.N.

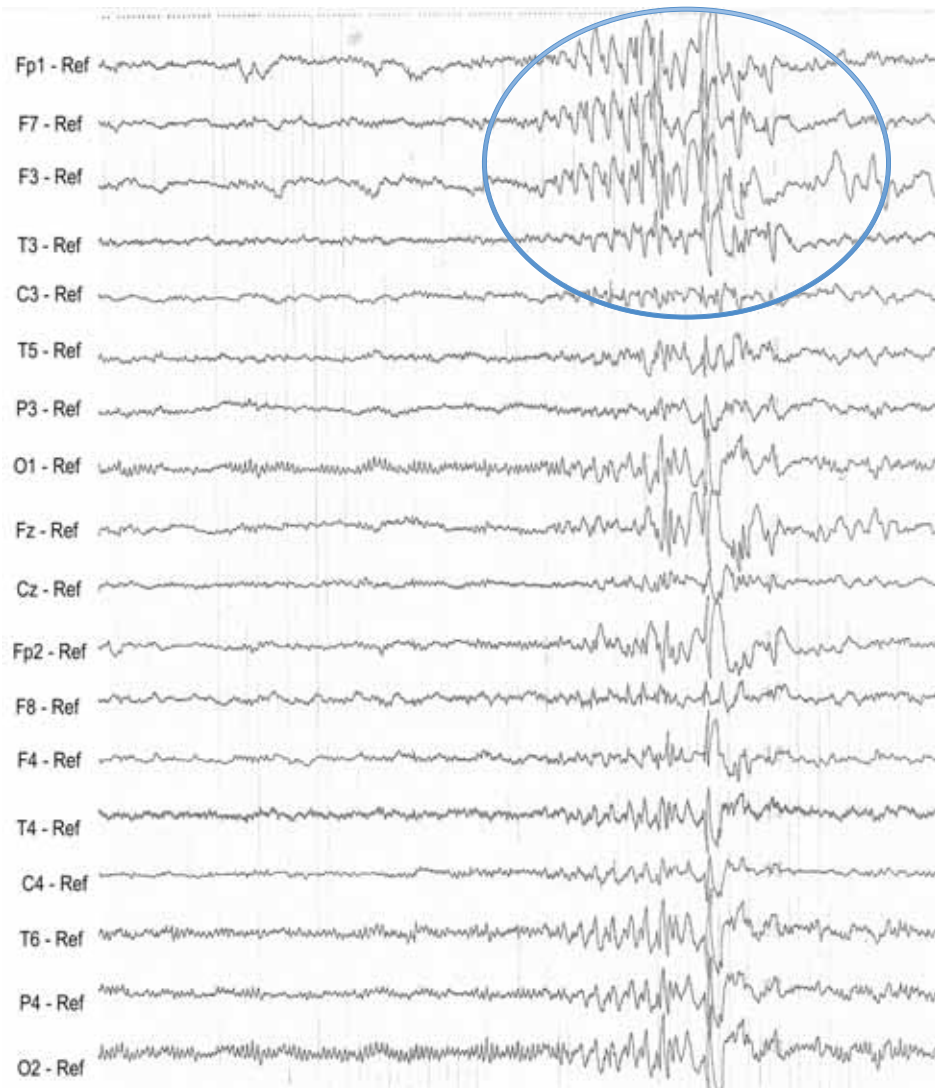


Fig. 2 Referential montage. High amplitude spikes followed by a slow wave with maximal expression in left frontal regions F3, F7, Fp1 and diffusion especially to Fz, Fp2. Reference of the montage affected by the electronegativity of the IED (opposite waveforms evident in most of the channels).

S.G.N.

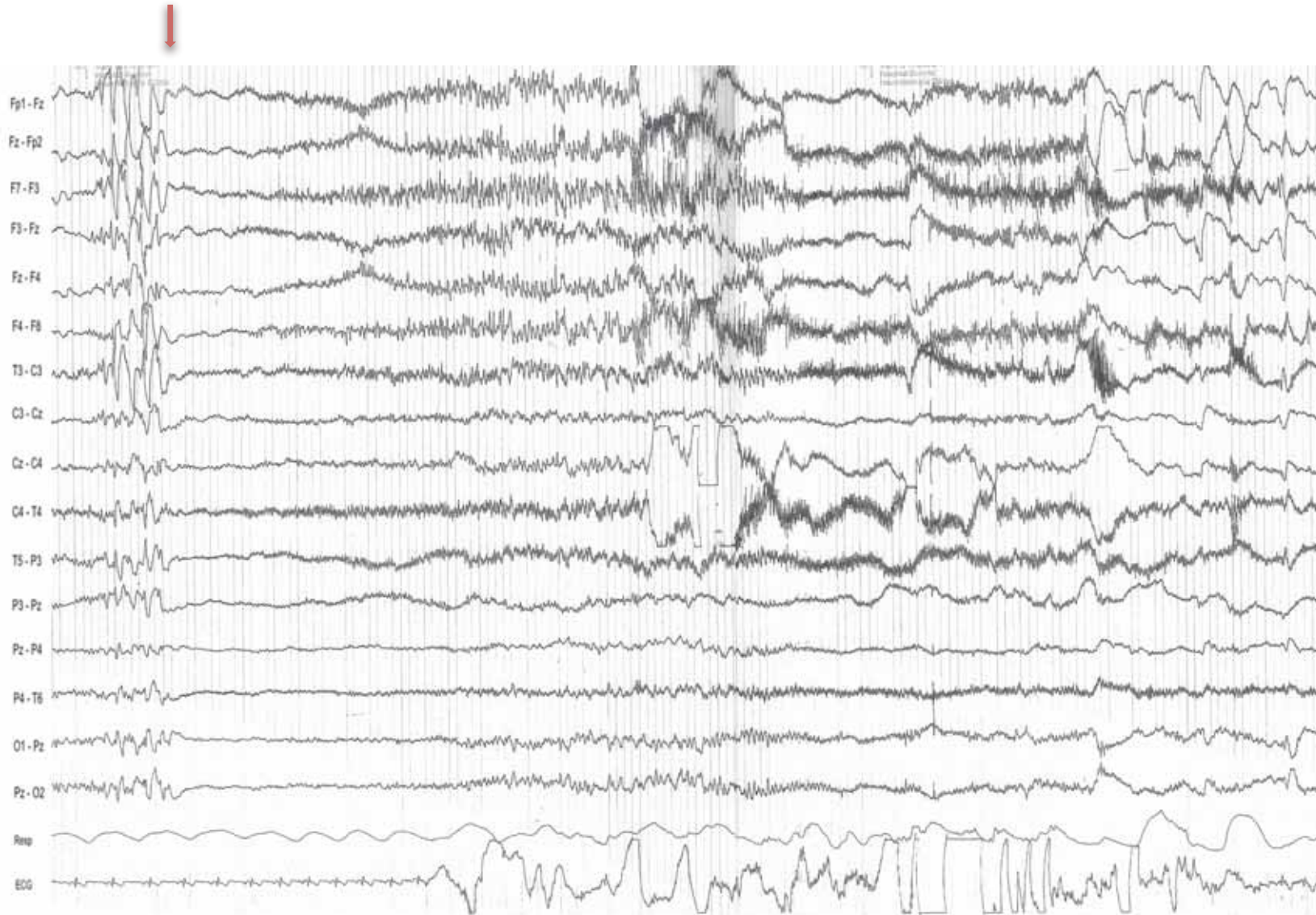


Fig. 3 Transversal montage. Seizure activity is preceded by diphasic spike paroxysm with maximal expression over left frontal regions, especially Fp1, F7, F3. Seizure starts with attenuation and low amplitude synchronized rhythm at onset, with increasing amplitude and expression in both frontal regions, with maximal expression in Fp1, F7 and F3 regions. Poligraphy changes in breathing rhythm and slight tachycardia during the seizure.

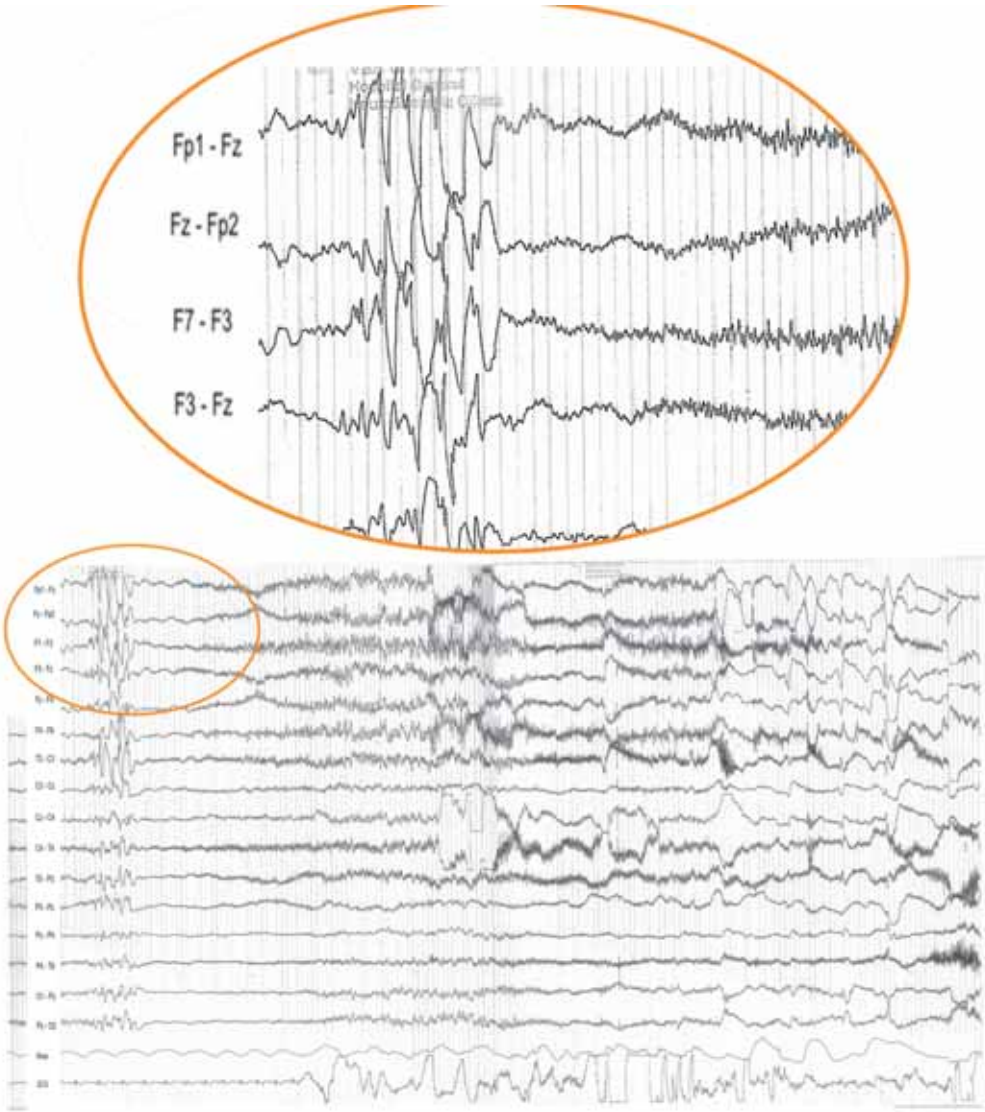


Fig. 4 Transversal montage. Detailed view of seizure onset, with the arising synchronized rhythm, with maximal expression in Fp1, F7 and F3.

S.G.N.

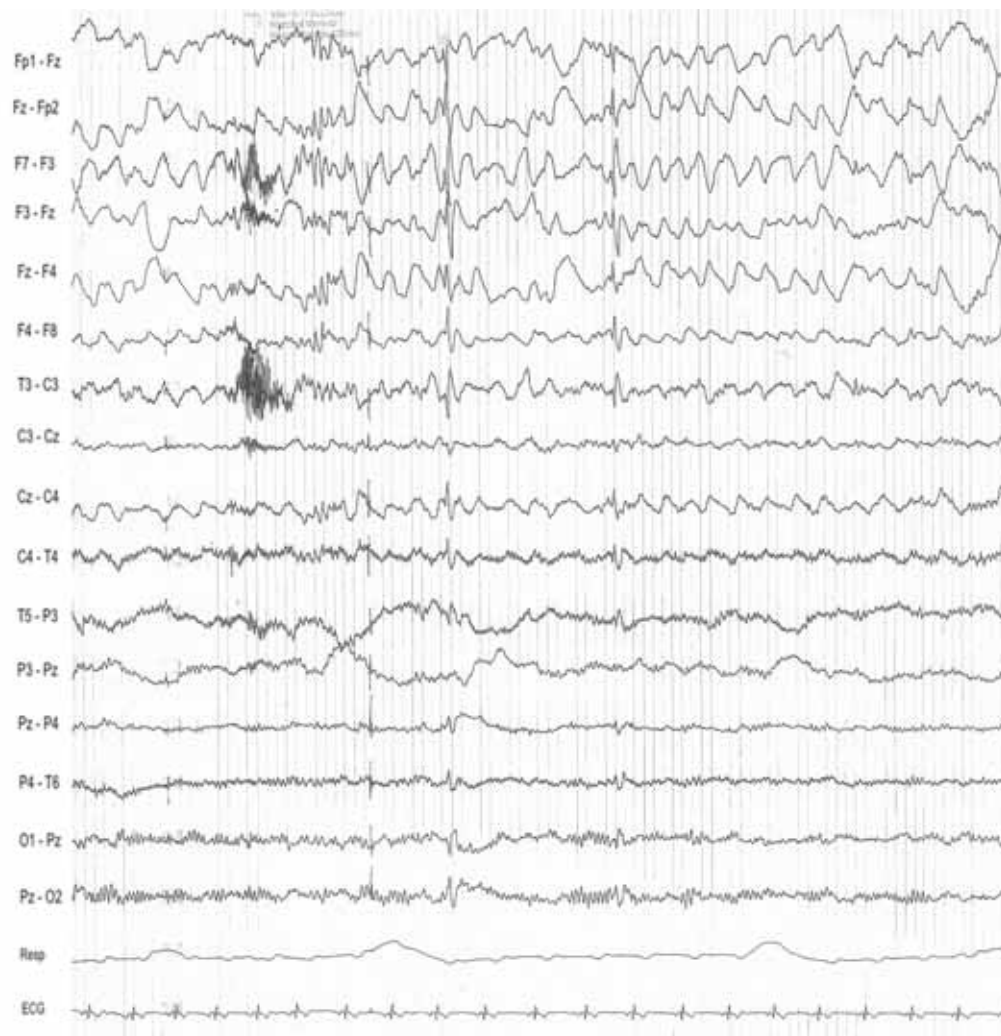


Fig. 5 Transversal montage. After the seizure there were a marked slowing over frontal region, during 17 minutes with left predominance. Meanwhile the patient was brady-psychic.

P.R.T.

P.T.R.

P.R.T.

Patient without any antecedent of interest who started having seizures at 5 years old. He presented abdominal sepsis, when he was referred to the department due to episodes with for extremities clonic movements. We recorded a partial seizure, without any clinical evident manifestation associated.

EEG characteristics:

IED was mainly constituted by isolated low voltage sharp waves, very well located in right inferior frontal region. Seizures arise from that region with a synchronized rhythm without an amplitude change at onset at around 12-13 Hz, with up to 8 minutes of duration.

The referential montage helps in locating the activity, which acquires maximal expression in right inferior frontal, F8, and fast diffusion especially to Fp2, F4 and T4 regions.

P.R.T.

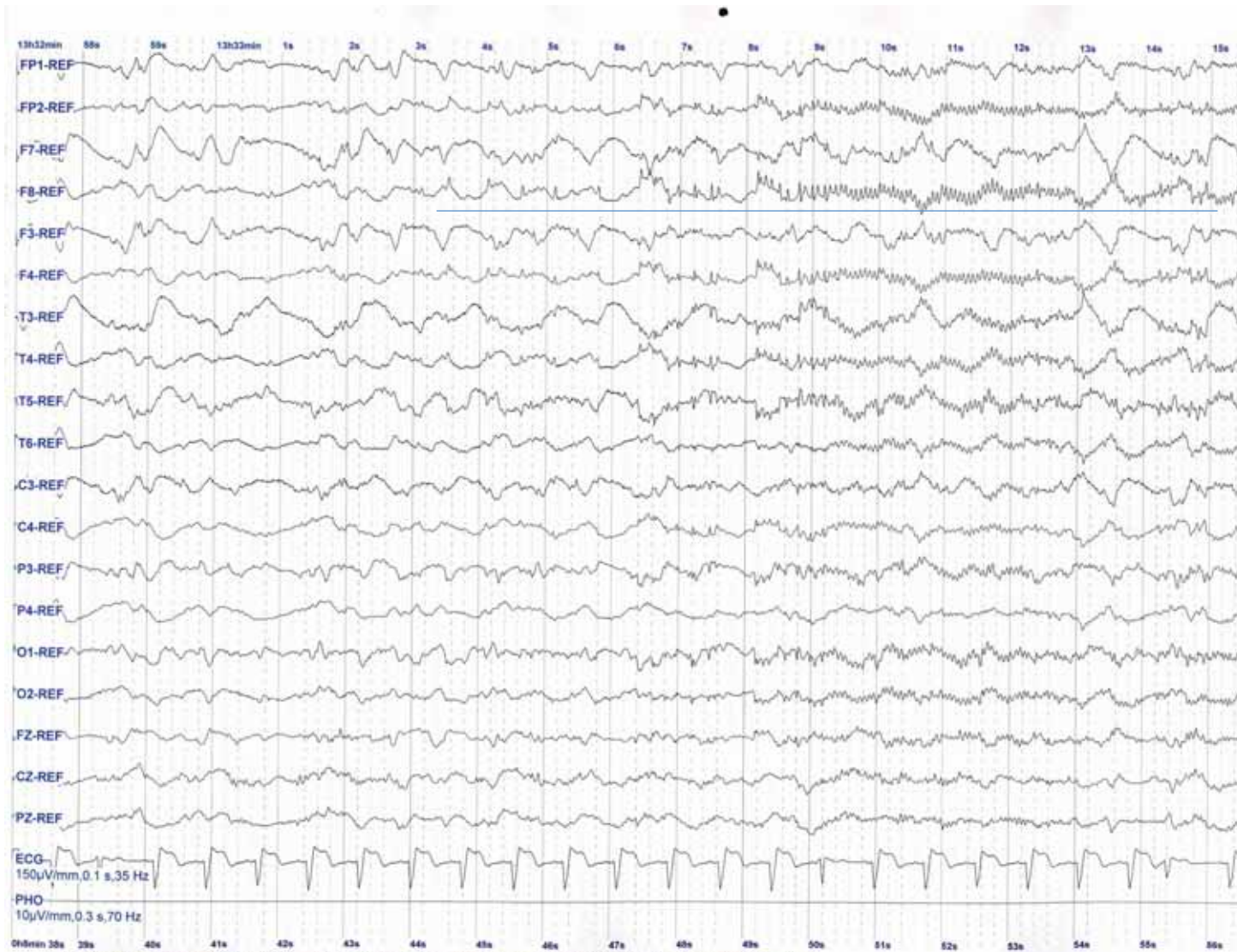


Fig. 1 Referential montage. Right frontal interictal isolated low voltage spikes with maximal expression in F8 and seizure onset with fast diffusion to Fp2, F4, T4. The referential montage makes that the electro-negativity in right frontal regions affects the reference, being responsible for the opposite waveforms in the rest of channels.

P.R.T.

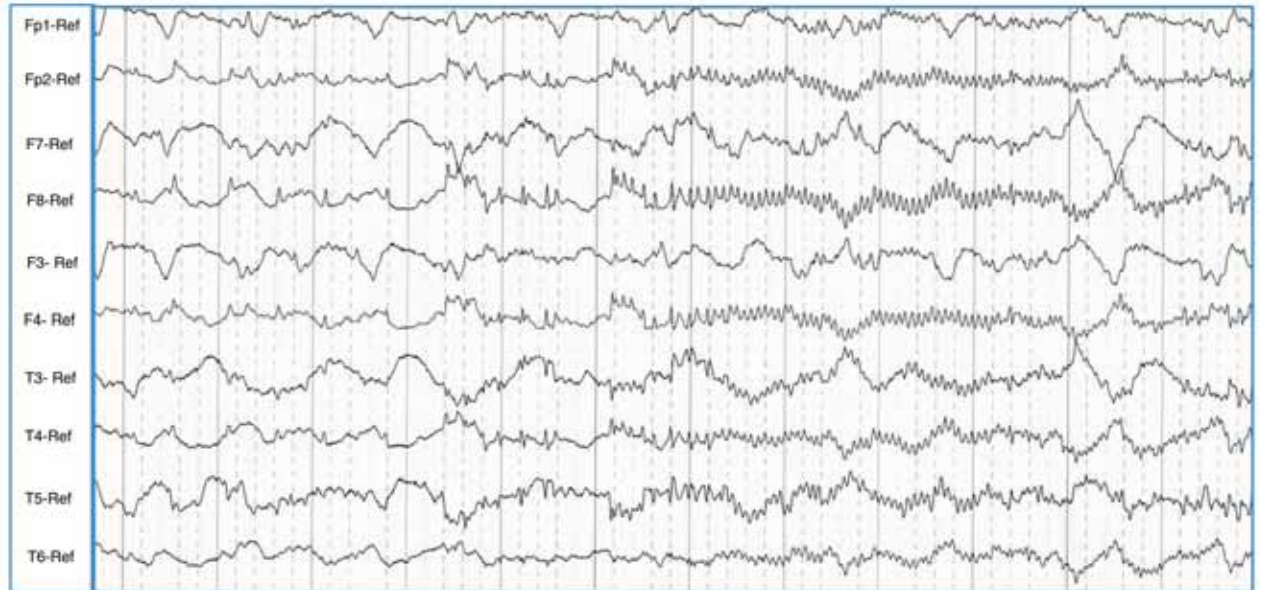
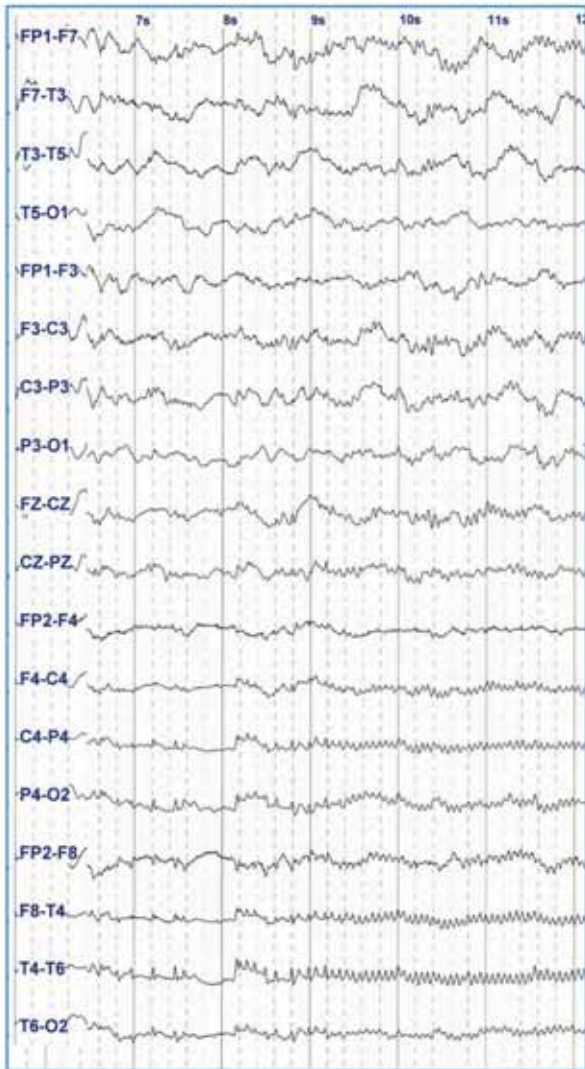


Fig. 2 Comparative view of ictal activity in a longitudinal bipolar montage and referential one. The referential montage locates much better the epileptiform activity, with maximal expression in F8 and diffusion to F4, Fp2, T4.

P.R.T.

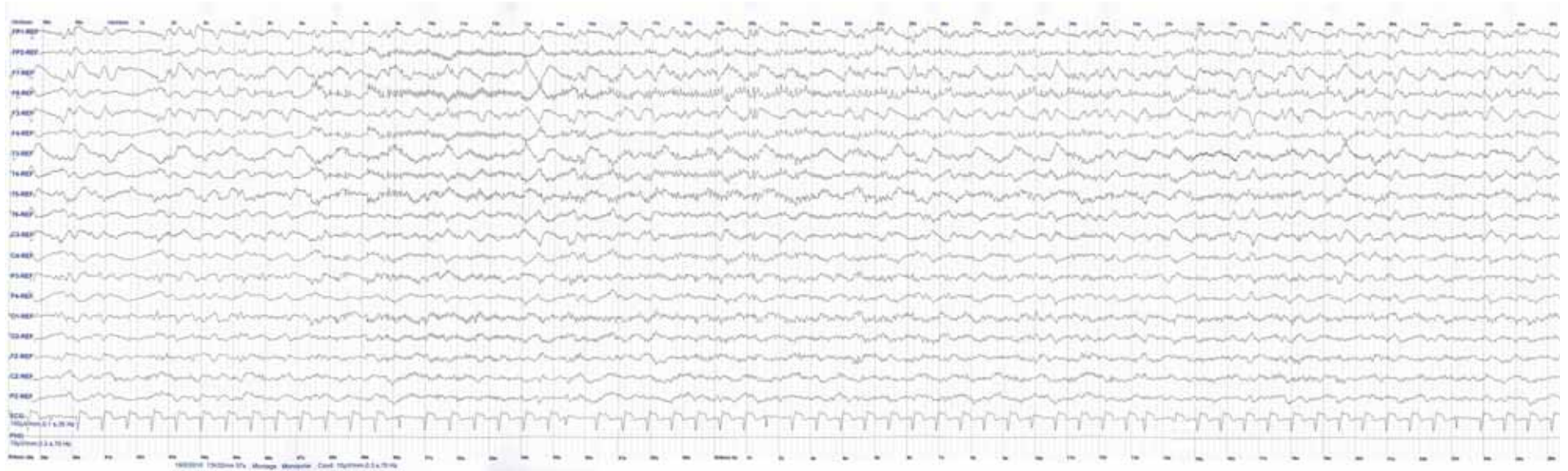


Fig. 3 Referential montage. Full seizure collage view, with a synchronized rhythm arising from F8 and fast diffusion to Fp2, F4, T4. Ictal activity lasted up to 8 minutes, with different degrees of intensity, in terms of grade of synchronicity of the activity showed.

T.O.R.

T.O.R.

T.O.R.

Patient with infectious antecedent with brain abscess who underwent surgery and started having seizures at 36 years old. She had seizures with scarce pharmacologic control, and at least two epileptic status.

Clinically she presents an oculi-cephalic deviation towards the left, facial clonic movements (blinking, chin) then she raises her left extended arm with clenched fist and afterwards clonic movements with the right arm in flexion with clenched fist. Sometimes there is also a tonic extension of left leg. Just after the seizure she recovers consciousness immediately and she is able of moving right arm but not left arm (Todd paralysis).

EEG characteristics:

Right frontal slowing is seen. Ictal onset is characterised by a low amplitude synchronized rhythm arising from right pre-frontal region, Fp2, which increases progressively in amplitude.

T.O.R.

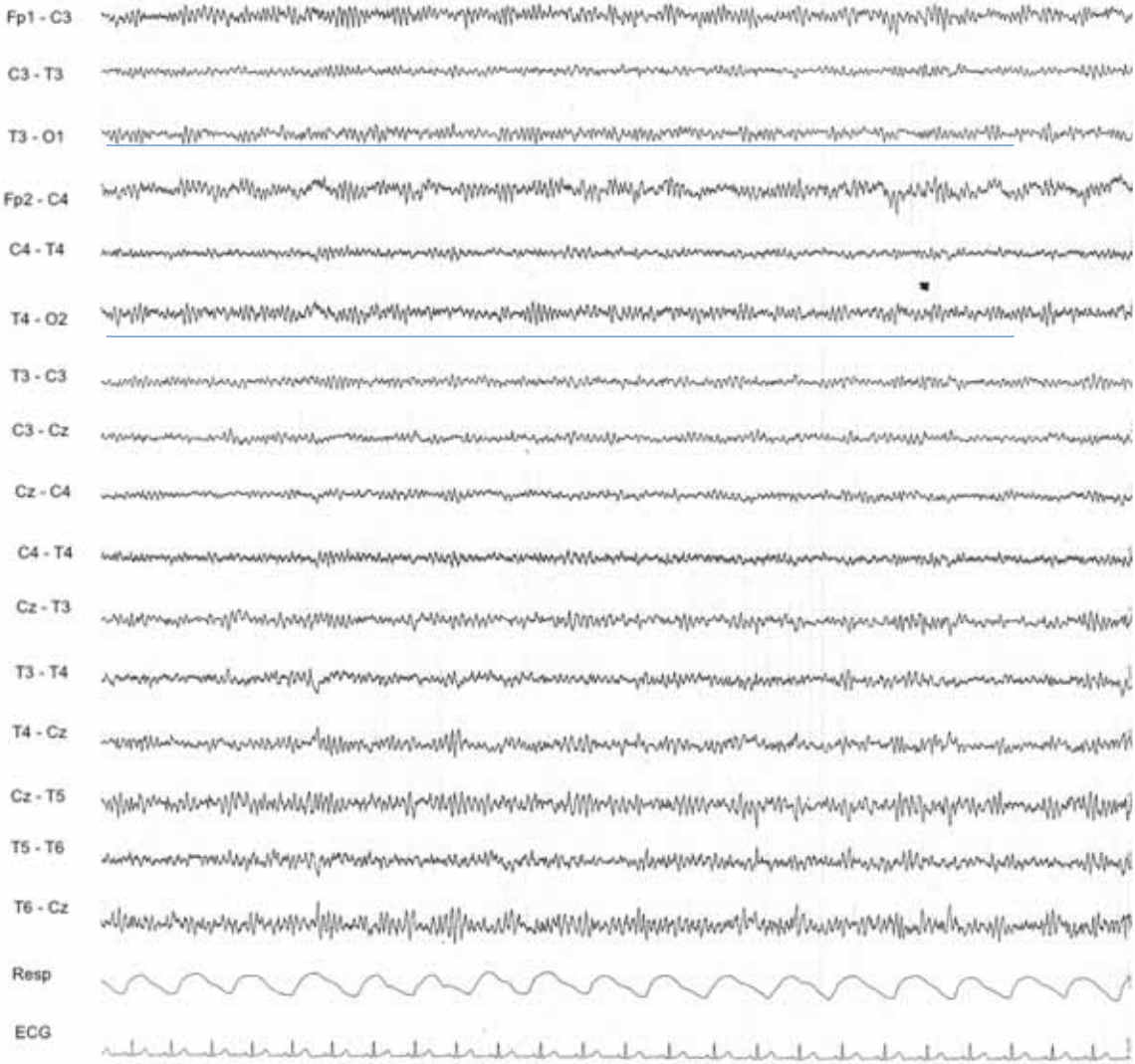


Fig. 1 Standard bipolar montage. Awake and well organized basal activity without interictal epileptiform discharges. Normal

T.O.R.

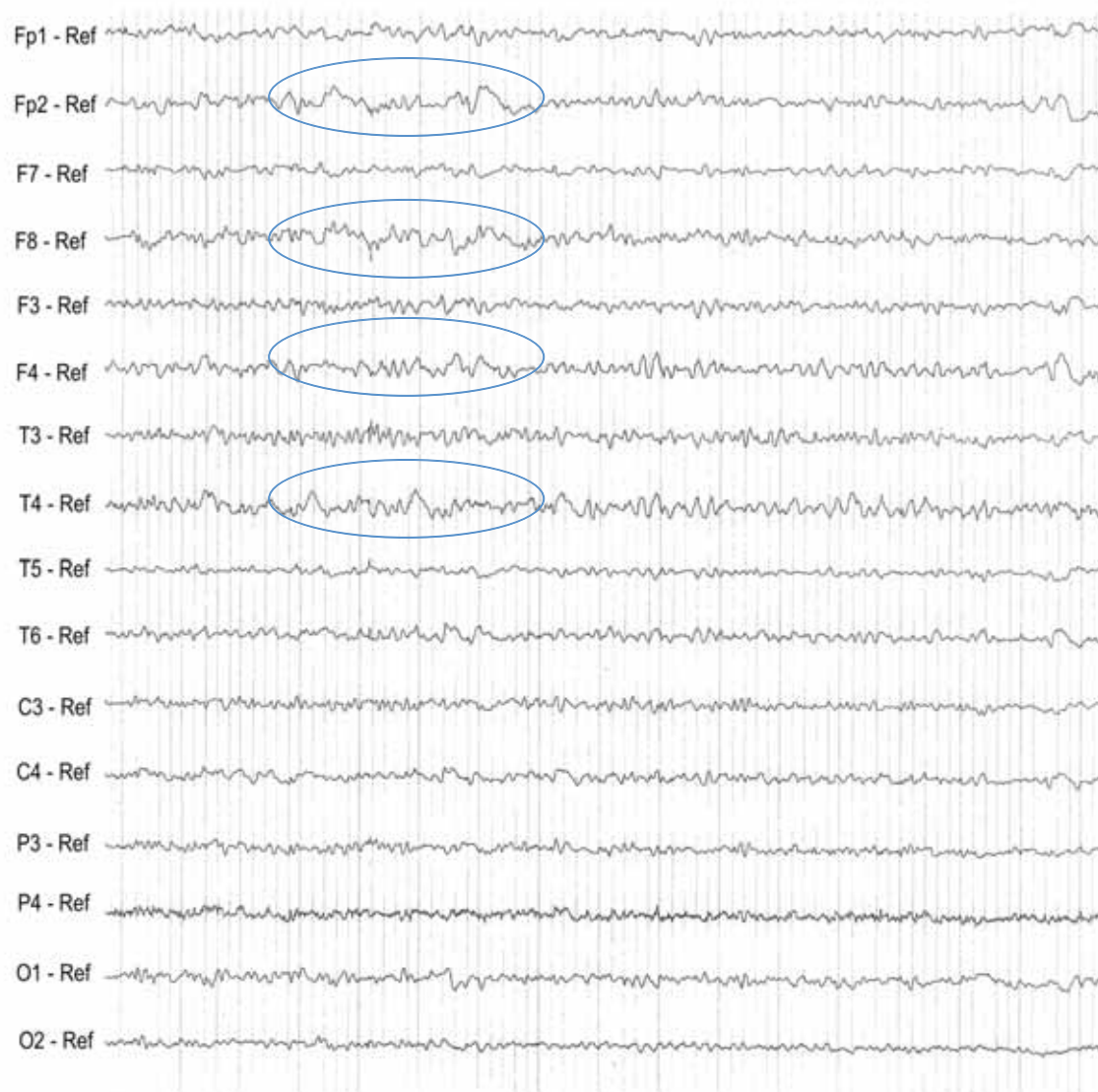


Fig. 2 Unspecific right sided irregular slow waves, in Fp2, F8, F4 and T4 regions.

T.O.R.

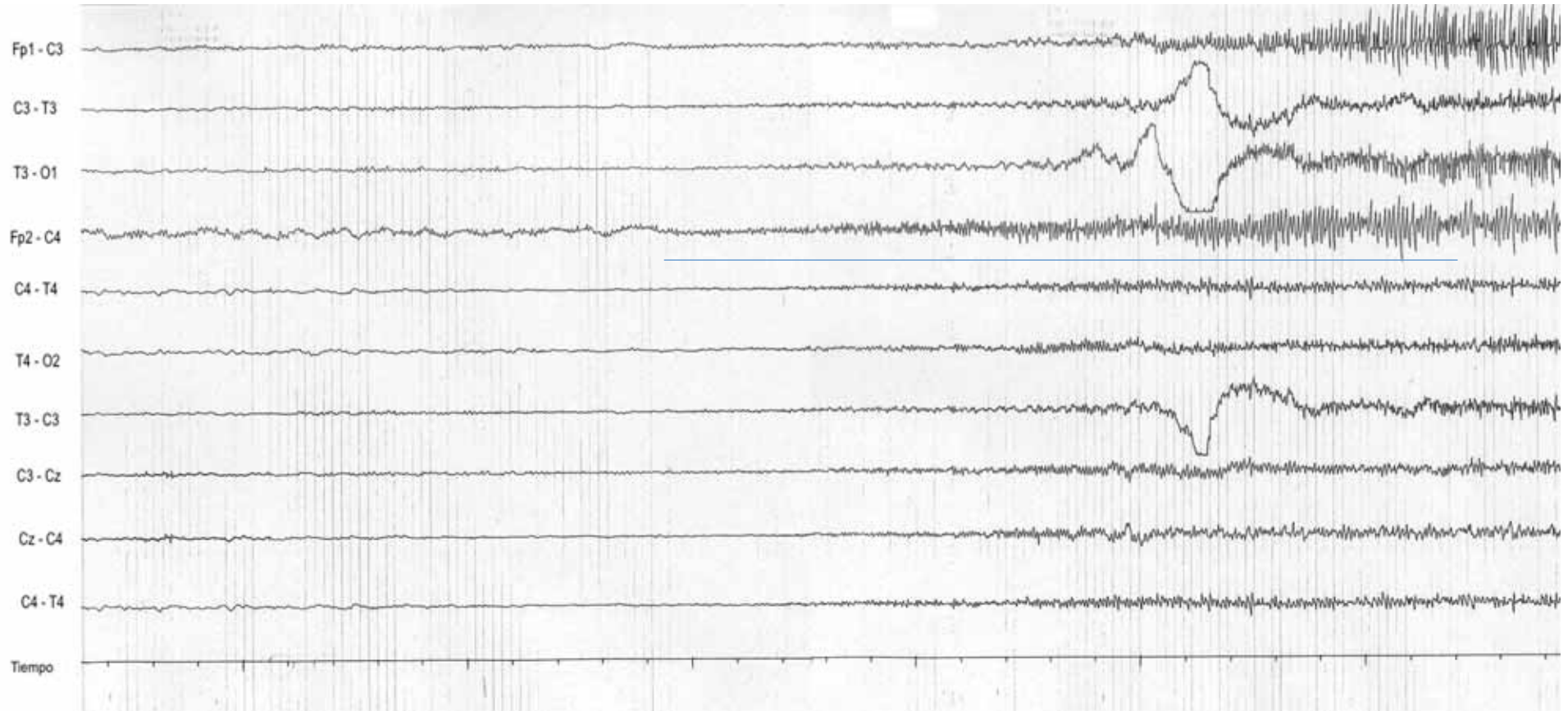


Fig. 3 Standard bipolar montage. Seizure onset from right prefrontal region. The blue line highlights the block of the slow waves in right pre-frontal region, Fp2, with progressive increasing amplitude and diffusion. Clinically she presents an oculi-cephalic deviation towards the left, facial clonic movements (blinking, chin), then she raises her left extended arm with clenched fist and afterwards clonic movements with the right arm in flexion with clenched fist. Sometimes there is also a tonic extension of left leg. Just after the seizure she recovers consciousness immediately and she is able of moving right arm but not left arm (Todd paralysis).

T.O.R.



Fig. 4 Standard bipolar montage. On-going seizure and ending.

M.V.S.L.

M.V.S.L.

M.V.S.L.

Patient who had perinatal complications due to torn umbilical cord with normal development. She started having seizures at 16 years old.

Normal MRI. Clinically the manifestations of seizures varied from impaired consciousness for a few seconds to a head deviation towards the left, moving both arms extended, sometimes with episode retrograde amnesia, regarding the intensity of the ictal activity, regarding on the intensity of the ictal activity.

EEG characteristics:

EEG recordings show a focus with bilateral expression with both frontal expression and maximal expression variable in right inferior frontal, F8, and left front central electrode, F3 probably to a near mid-line focus in origin. We can see very high amplitude (more than 200 μ V) sharp waves with a slow returning to the base-line with maximal expression in left front-central region, F3.

Seizures present preceded by a spike/sharp wave within a slow wave with left side predominance, and a synchronized rhythm afterwards, but with such a fast widespread added to the bilateral expression of the IED it is difficult to assign a definite origin.

M.V.S.L.

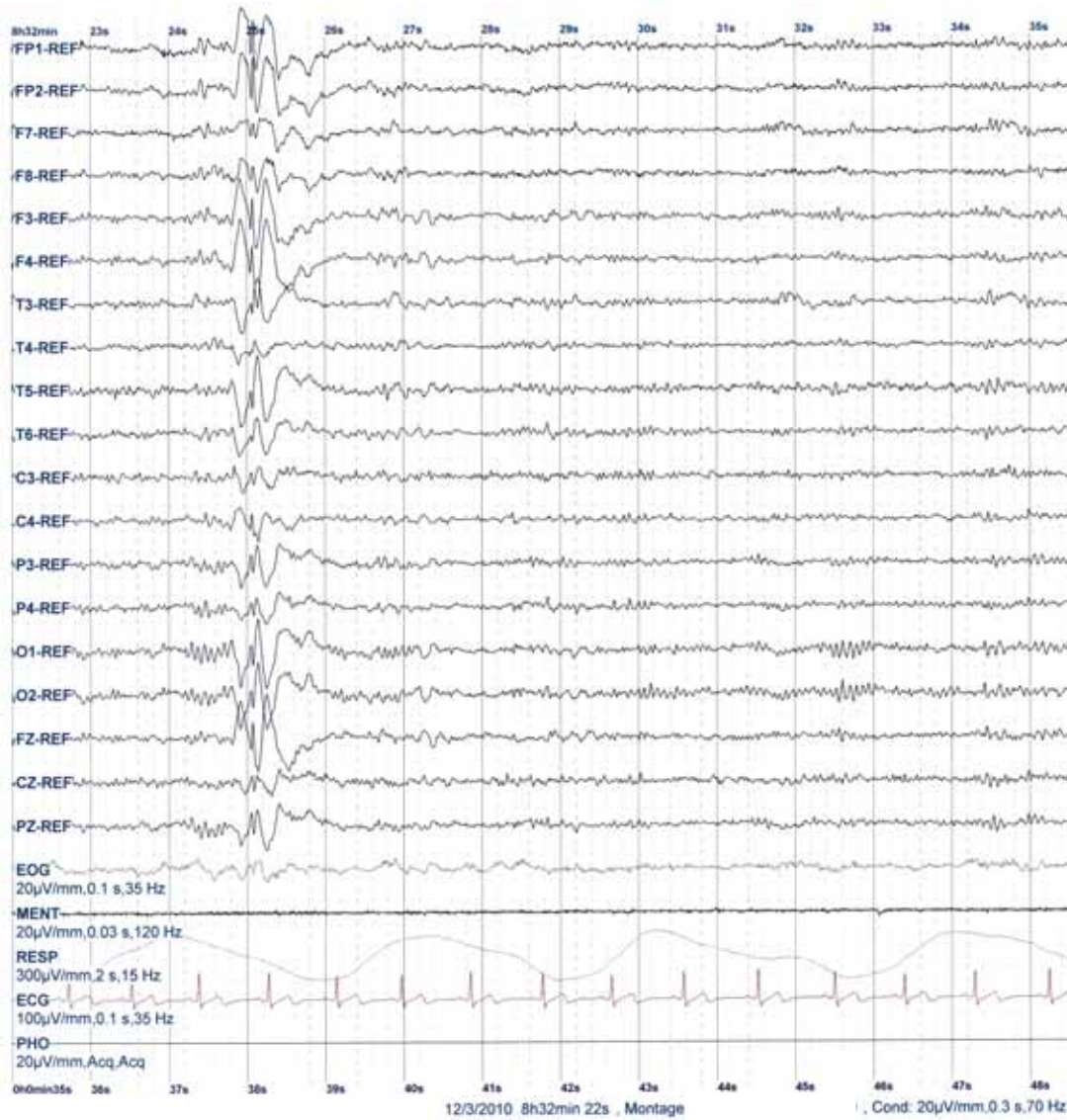


Fig. 1 Referential montage. Paroxysmic activity of sharp wave followed by a slow wave with maximal expression in both pre-frontal and front-central regions (F3, Fp1, Fz, F4, Fp2).

M.V.S.L.



Fig. 2 Referential montage. Usual sensitivity of 10 µV/mm. With such a high amplitude it is necessary to change settings, to look into the paroxysms for analyse their morphology and location in detail and look for less active epochs.

M.V.S.L.



Fig. 3 Referential montage. Same epoch with sensitivity of 20 µV/mm to try to assign a maximal expression of the activity, that appears very widespread. We can see the focus with bilateral expression, with diphasic sharp waves and a slow returning to the base-line. Its maximal expression is usually in left front-central regions, F3, also evident especially in Fz, F4 but sometimes it is in inferior frontal region, F8, and diffusion to F4, Fp1 and Fp1. The important detail for considering it one focus is that it appears synchronous.



Fig. 4 Referential montage. Very active, widespread and even rhythmic interictal activity. We can see the foci previously shown. We need to look into this kind of waveforms carefully, as we have already commented, due to the fact that the electronegativity of the focus is responsible for the contrary deflection of the waves in the channels that do not present this electronegativity.

M.V.S.L.

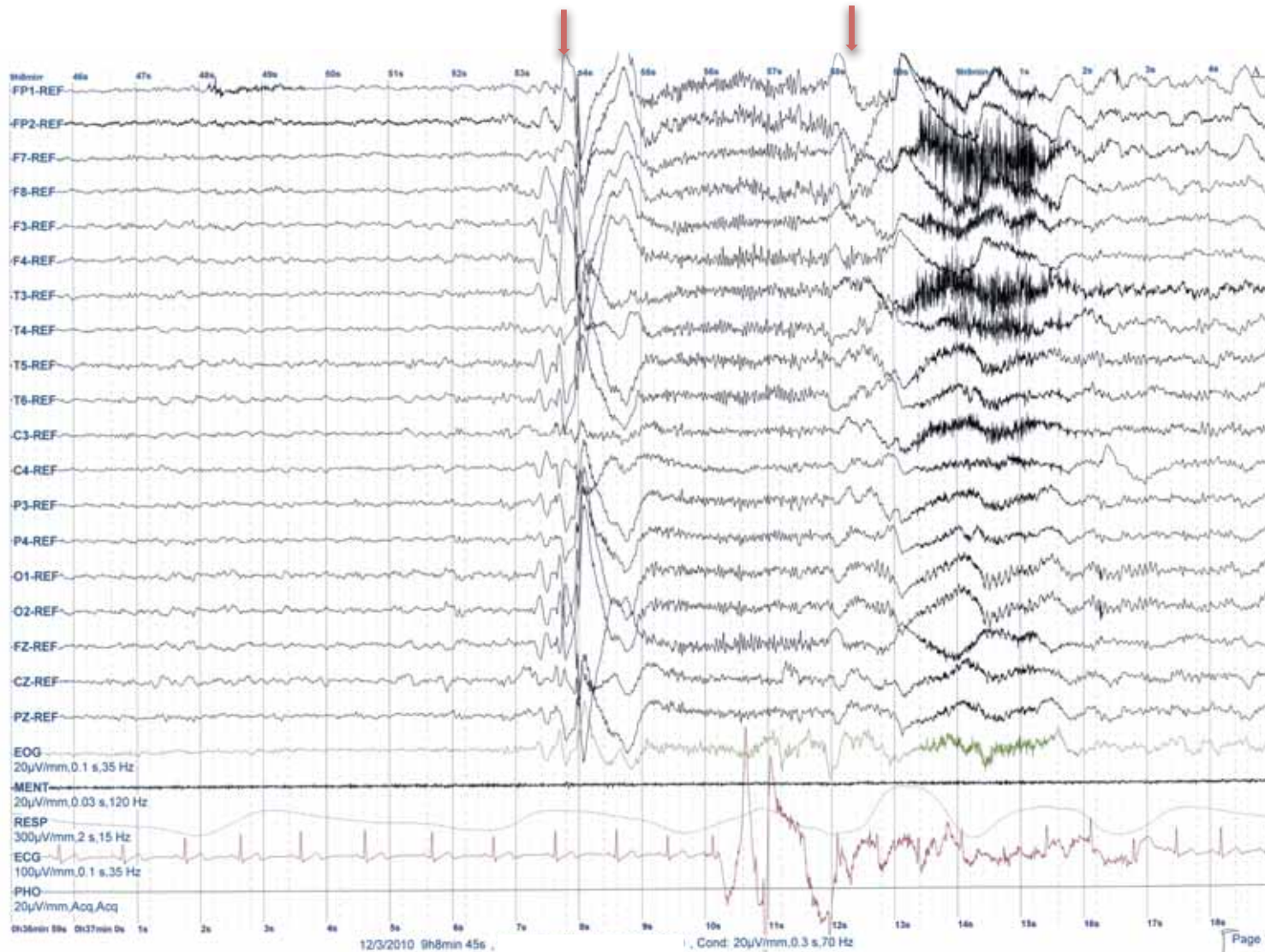


Fig. 5 Referential montage. Ictal activity is preceded by a spike/sharp wave within a slow wave arising afterwards low voltage synchronized rhythm at around 21 Hz without a clear maximal region of origin. Short duration of seizure and immediate alpha rhythm after seizure in both occipital regions with a prominent slowing in frontal regions. A red arrow marks the onset and seizure ending. Polyrhythmic changes are evident from seizure onset (irregular breathing and tachycardia).

M.V.S.L.



Fig. 6 Referential montage. Immediate postictal slowing in both frontal regions and interictal discharges with maximal expression in left front-central electrode (F3)

M.V.S.L.

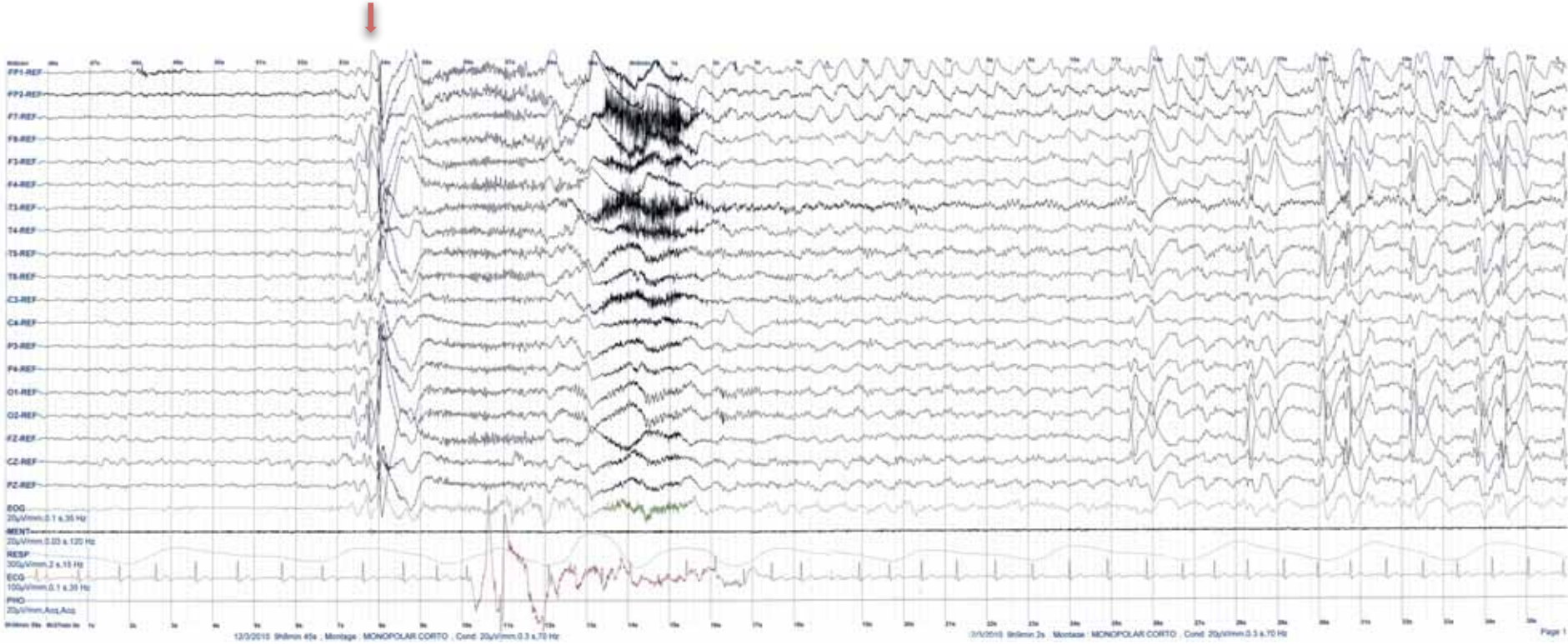


Fig. 7 Collage for a full view of ictal and post-ictal activity, made of both of the previous figures (fig. 5 and fig.6)

J.M.P.

J.M.P.

J.M.P.

Patient that started with seizure at the age of four years old, without a known pathologic antecedent and normal MRI.

Clinically he sudden extends his four extremities, with blushing face and a tendency of head and sight deviation towards his right.

EEG characteristics:

IED with maximal expression in right inferior frontal electrode, F8. Seizures consists of a block of all the activity with a global attenuation of voltages and a low voltage synchronized rhythm more expressive in front-central regions, without a clear lateralization and masked by EMG activity. We can see apnea in the breathing band and there seem to exist a change in EKG rhythm, with bradycardia, masked with the EMG artifact.

J.M.P.

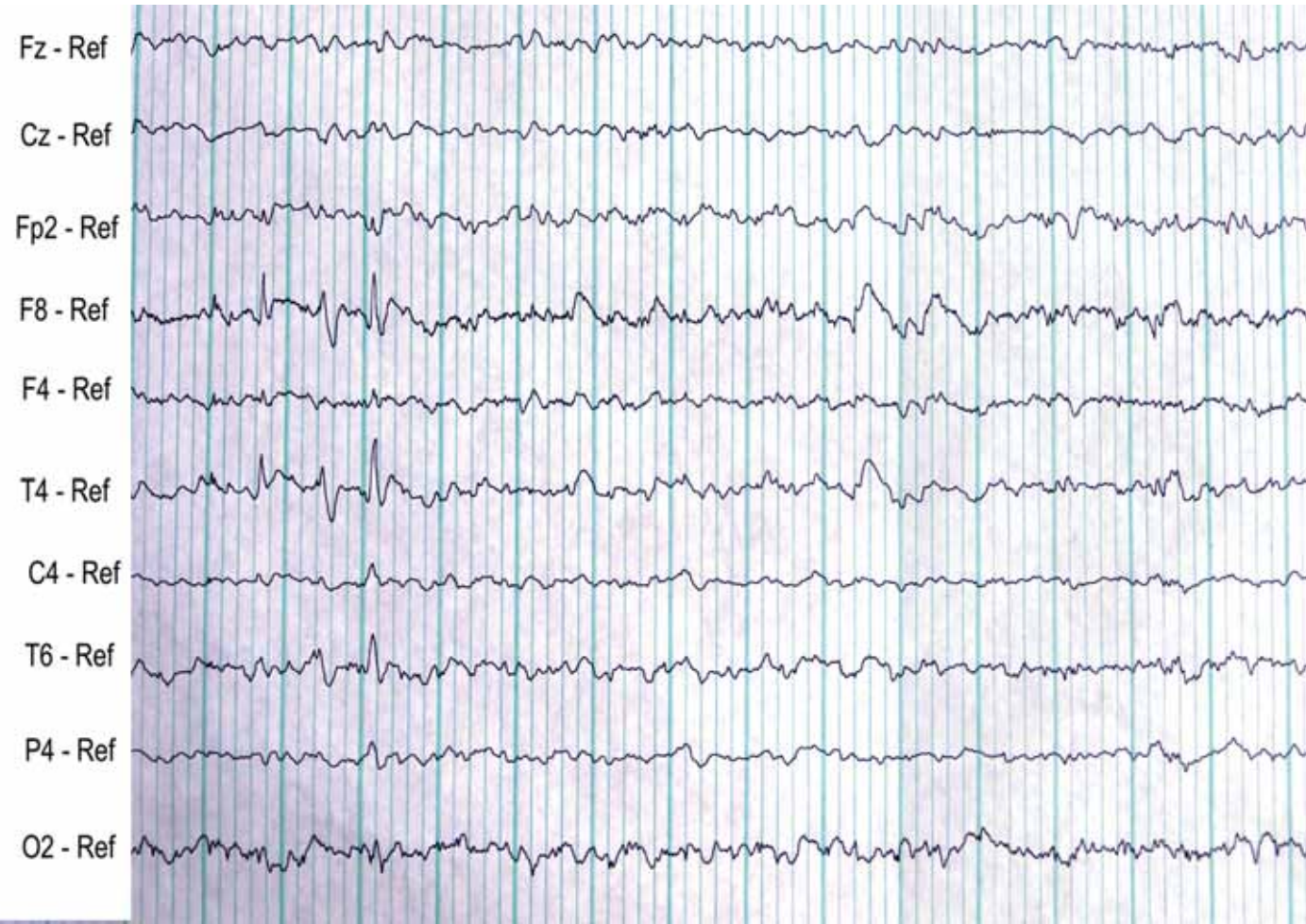


Fig. 1 Piece of recording for a detailed view of IED. Sharp waves with maximal expression in F8 , T4. Afterwards we can see irregular slow waves in the same regions, with maximal expression in F8.

J.M.P.

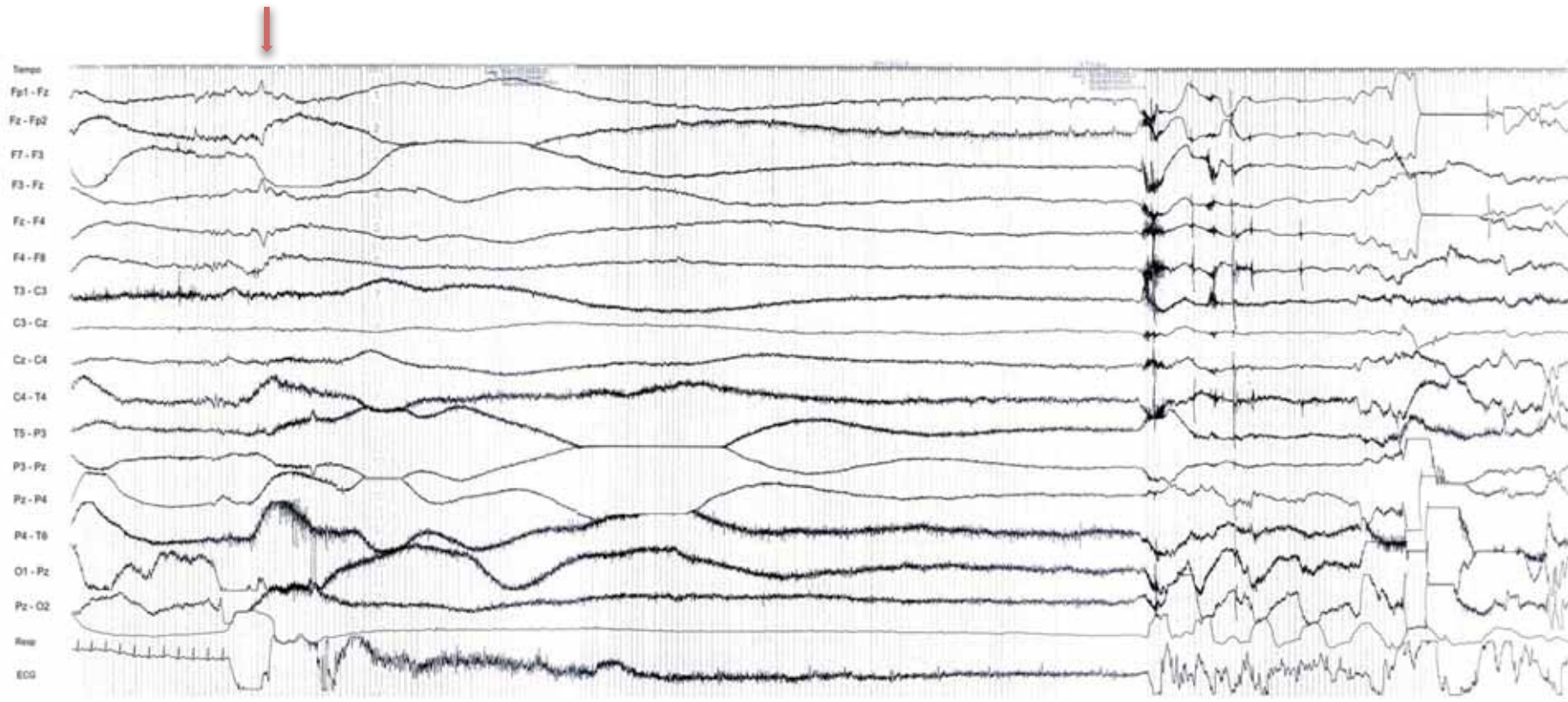


Fig. 2 Bipolar transversal montage. Global attenuation with low voltage synchronized rhythm at seizure onset with maximal expression in front-central regions, being not possible to assign a specific region as responsible for the seizure onset, due to the immediate diffusion of ictal activity, with block of the previous activity. Apnea and probably bradycardia, masked with EMG artifact.

J.L.C.

J.L.C.

J.L.C.

Patient who started with seizures at 34 years old after a C.V.A. Clinically he remained quiet with impairment of consciousness

EEG characteristics:

Interictal activity shows isolated spikes and poly-spikes of less than 50 μ V, and sharp waves of 50-100 μ V, with maximal expression in right inferior frontal and prefrontal regions (F8>Fp2). We recorded seizures starting with a synchronized rhythm without a prominent change in amplitude at 12 Hz with maximal expression in right inferior frontal region, F8.

J.L.C.

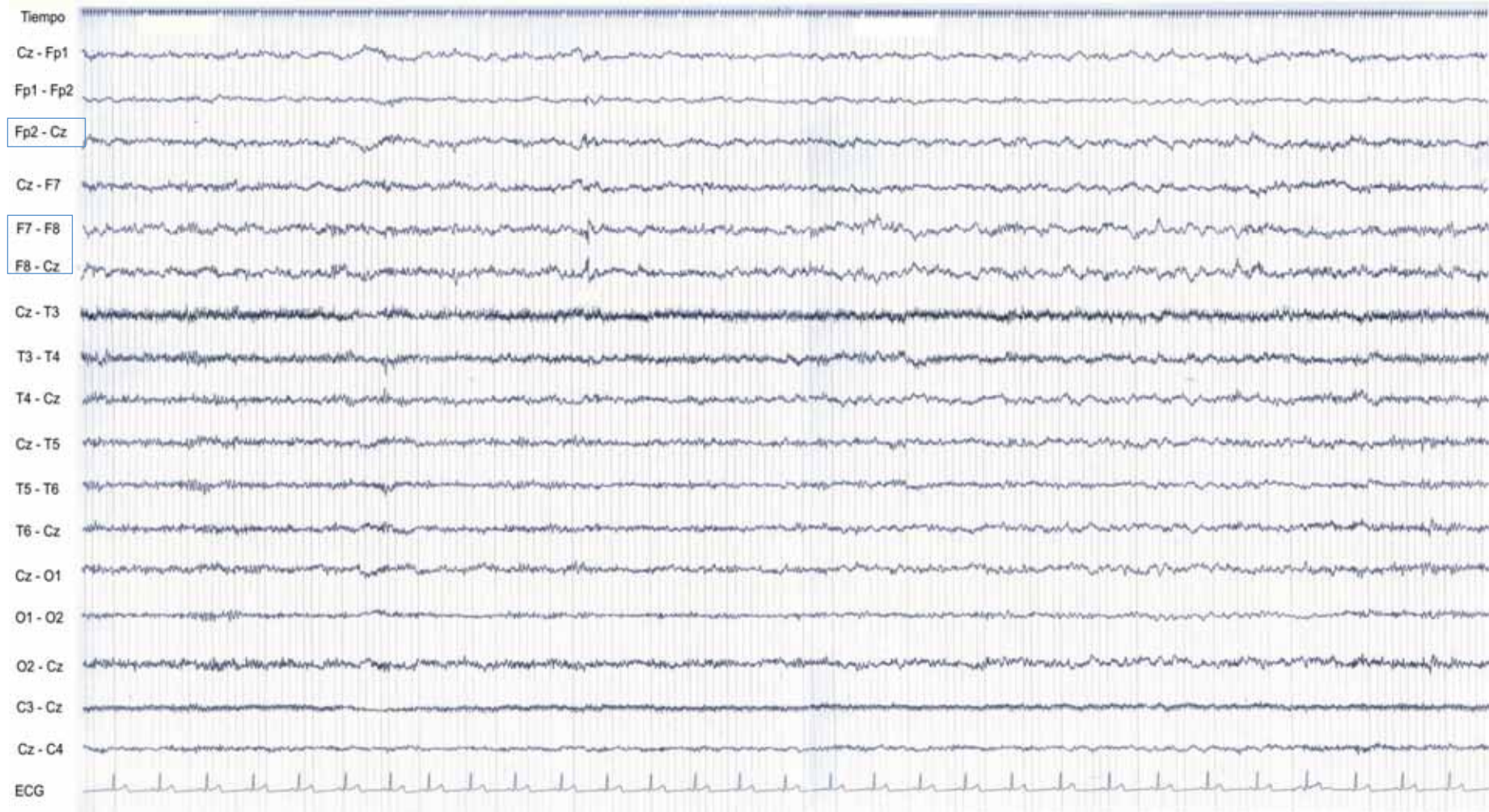


Fig 1 Bipolar triangular montage. Awake. Interictal low voltage spike in right inferior frontal (F8) and unspecific irregular slow waves with maximal expression in right frontal regions, with maximal expression in F8 and also evident in Fp2.

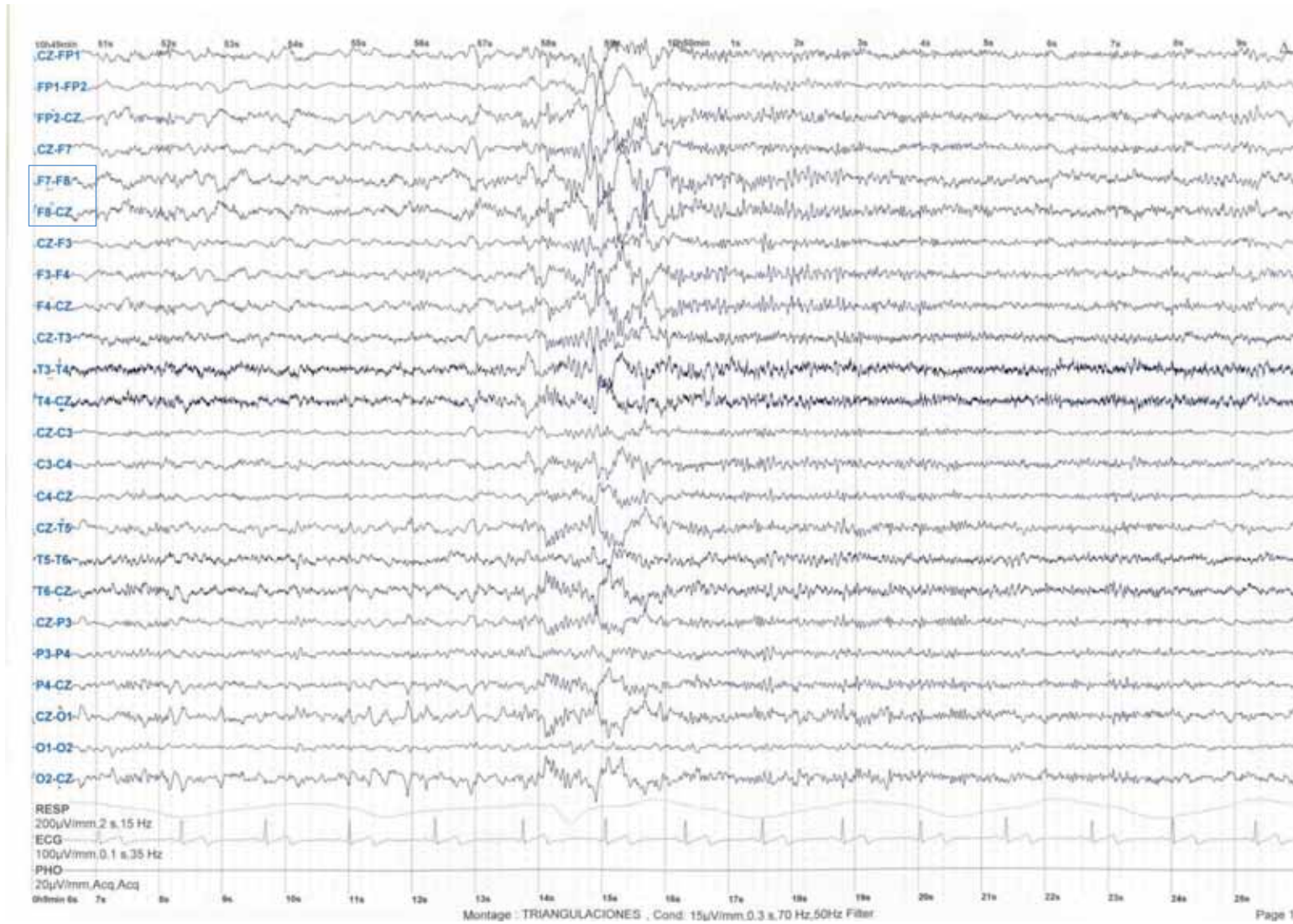


Fig 2 Transversal montage with sensitivity of 15 μ V/mm. Sleep activity, with sharp waves in vertex and spindles. Interictal activity with spikes and irregular slow waves with maximal expression in right frontal regions, maximal expression in F8, Fp4, Fp.2

J.L.C.

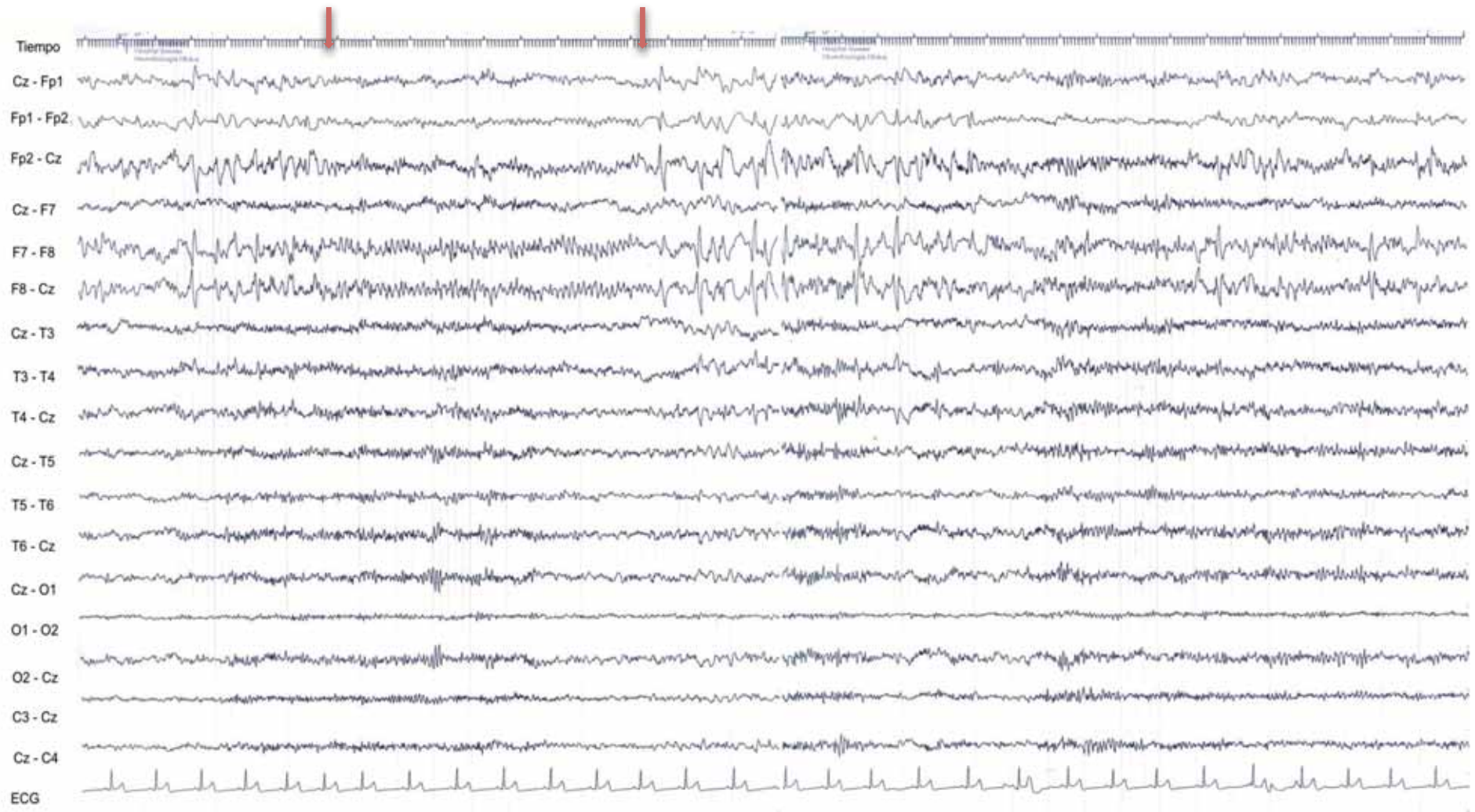


Fig 3 Transversal montage. Sensitivity of $10\mu\text{V}/\text{mm}$. Synchronized rhythm at seizure onset with maximal expression in right inferior-frontal region F8, Fp2, with slight tachycardia. Clinically he remains quiet but with impaired consciousness.

J.L.C.

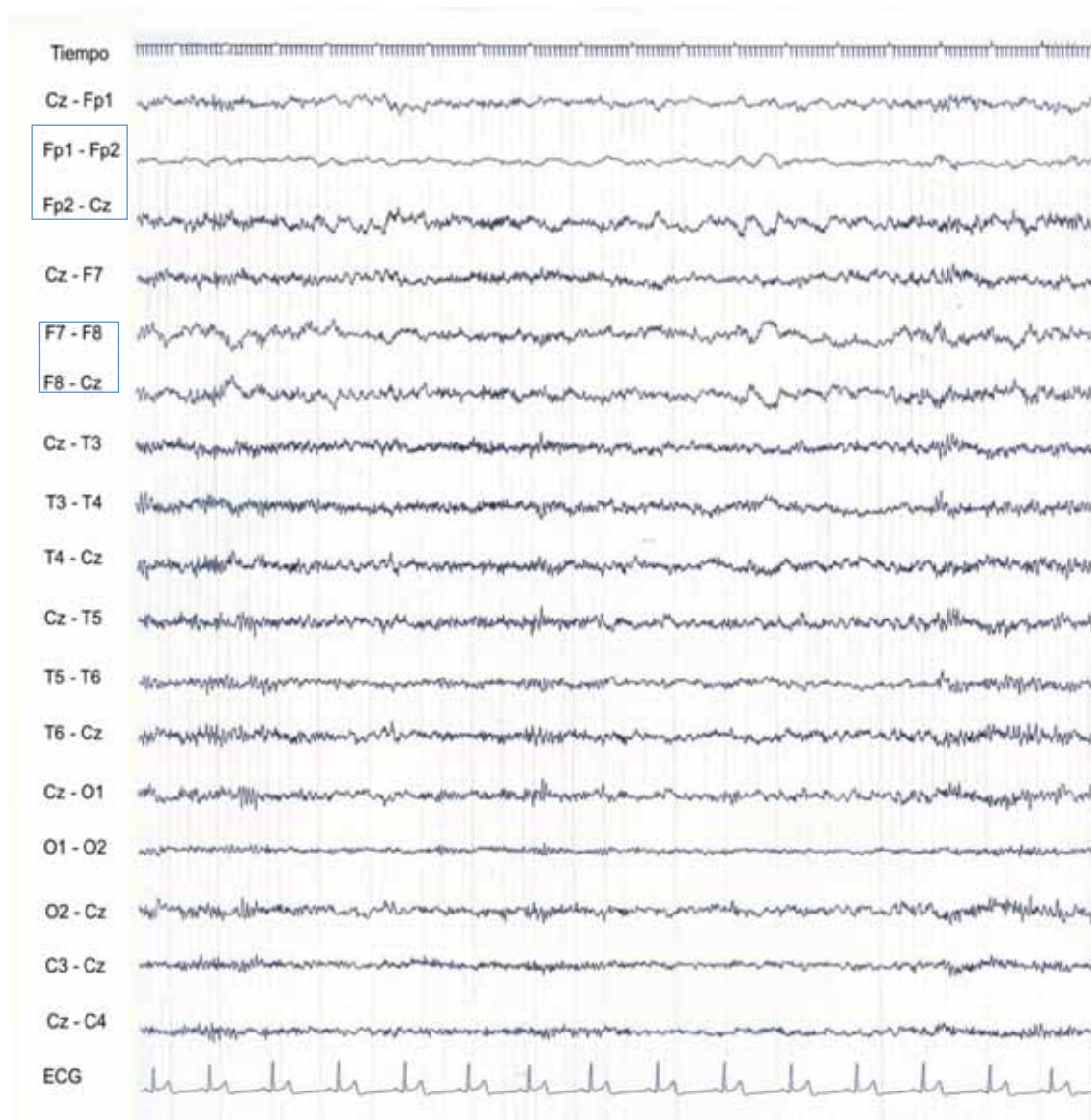


Fig 1 Triangular montage. Postictal slowing in right inferior frontal and prefrontal regions, F8, Fp2

M.J.R.C.

M.J.R.C.

M.J.R.C.

Patient without any related antecedent who started having seizures at 57 years old. Clinically says “eh”, and move right hand and afterwards the left foot with a stop while performing numerical series.

EEG characteristics:

Irregular slow waves with maximal expression in left frontal regions. Seizures are precedent by sharp waves in left frontal regions, with global attenuation afterwards and very low synchronized rhythm and progressive increasing amplitude and decreasing frequencies. Increased EKG frequency and irregular breathing observed in polygraphy channels

M.J.R.C.

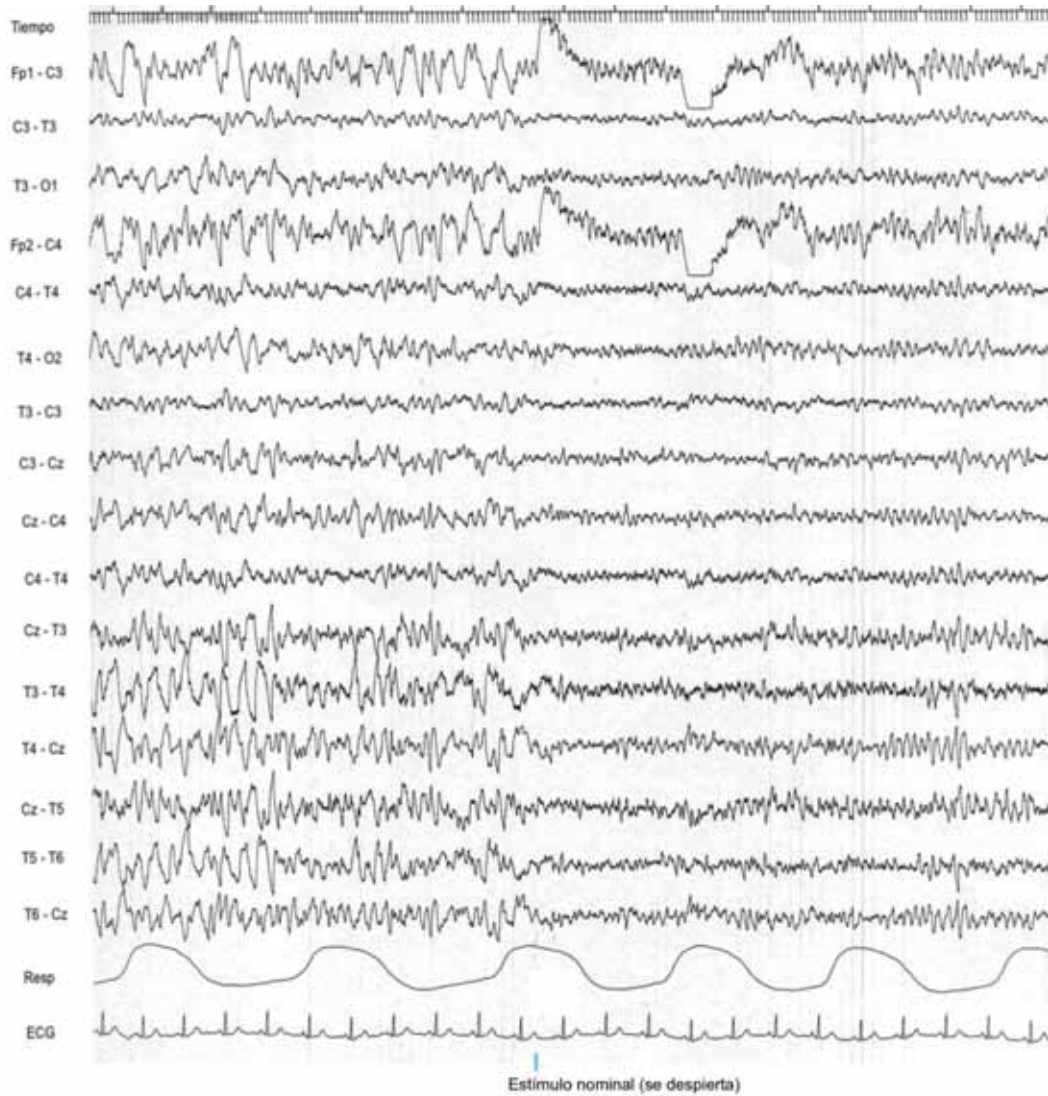


Fig 1 Awaken from superficial sleep with a nominal stimulus and basal activity normally structured.

M.J.R.C.

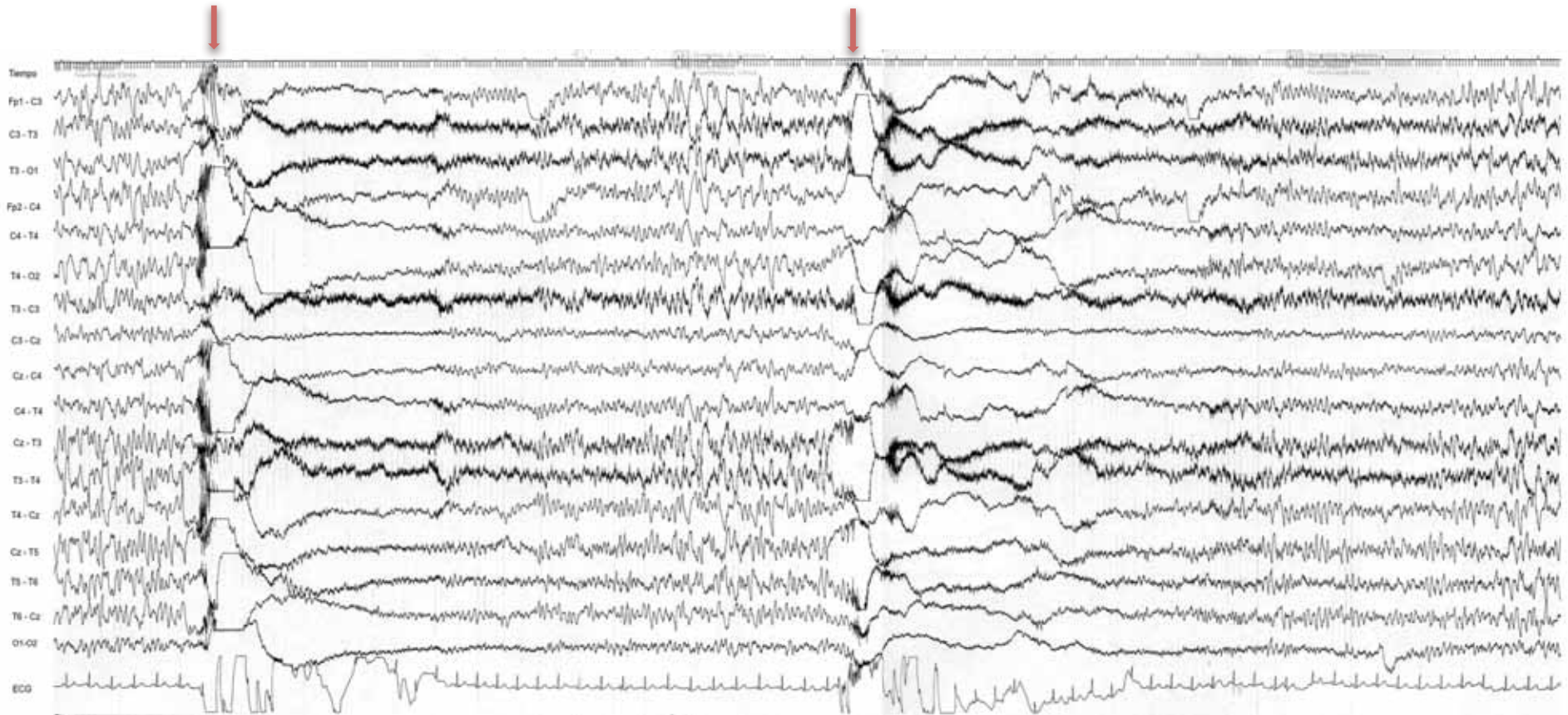


Fig .2 Standard bipolar montage. Two short seizures being the main morphological characteristic at onset a global attenuation of voltage. In some seizures (view fig. 4) it was possible to observe a left frontal predominance of sharp waves just before seizure onset, with the settings available. There is a slight tachycardia during seizures. Clinically she cannot continue making numeric series, says eh, and move right hand and afterwards the left foot.

M.J.R.C.

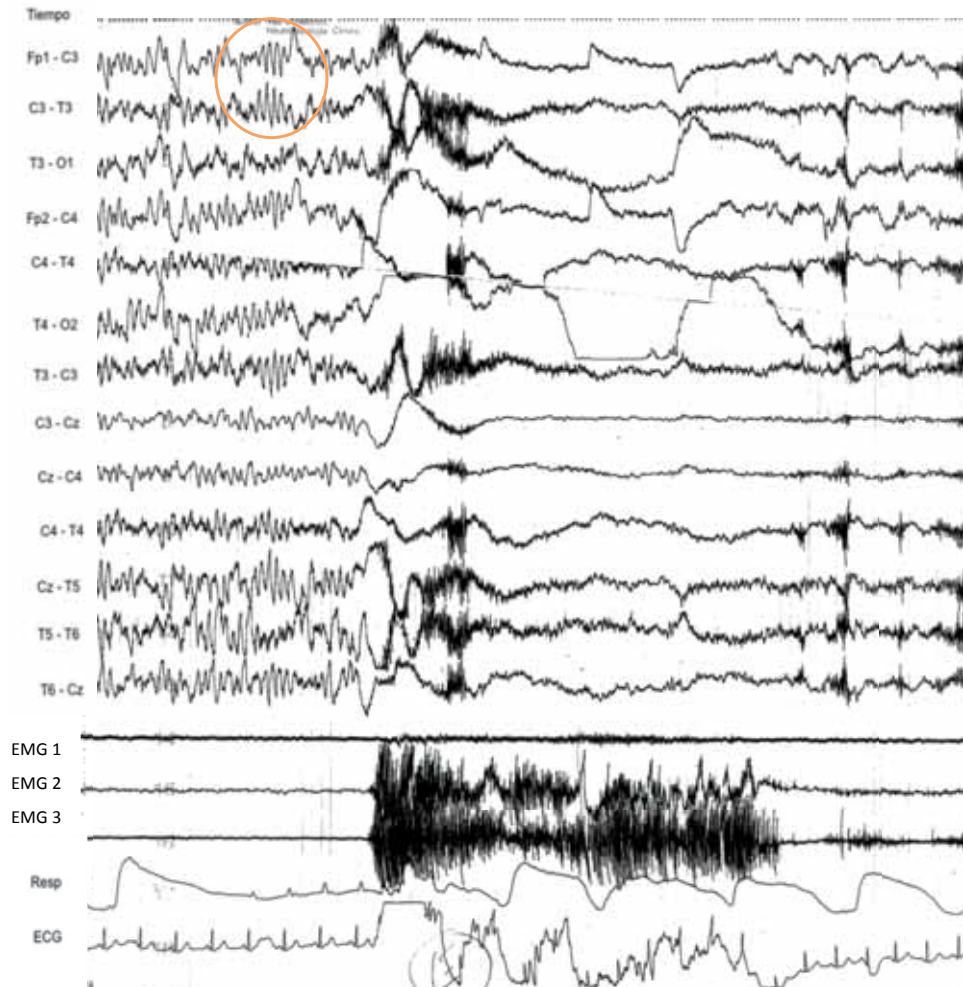


Fig.3 Bipolar standard montage. 10 μ V/mm. Sharp waves just before the attenuation at seizure onset in both pre-frontal regions and left central region (left side dominance, channels Fp1-C3 and C3-T3).

M.A.D.G.

M.A.D.G.

M.A.D.G.

Patient without any known pathologic antecedent, who started having seizures at 16 years old. He refers having more seizures while eating. Clinically he has different types of seizures described as partial simple seizures, with dysphasia and tonic contraction of the left side of the face, tachycardia and irregular breathing. Complex partial seizure, starting as the already described simple ones with posterior consciousness impairment and tonic contraction of both arms, especially the right one and flexion of his head, blowing. He also has seizures with secondary generalization.

EEG characteristics:

The EEG recordings show a very active inferior frontal paroxysmal activity of isolated sharp waves of 100-200 μ V, with maximal expression in F7 and variable widespread of the interictal activity. We performed several EEG recordings, including a more complete EEG study, using 10/10 system for recording with double number of electrodes. This study showed a maximal expression of the IED in F7, FT7, T7 regions.

Seizures had a left dominant low amplitude synchronized rhythm at around 24 Hz being very active in several left frontal electrodes with immediate involvement of all frontal regions before the first clinical manifestations.

M.A.D.G.

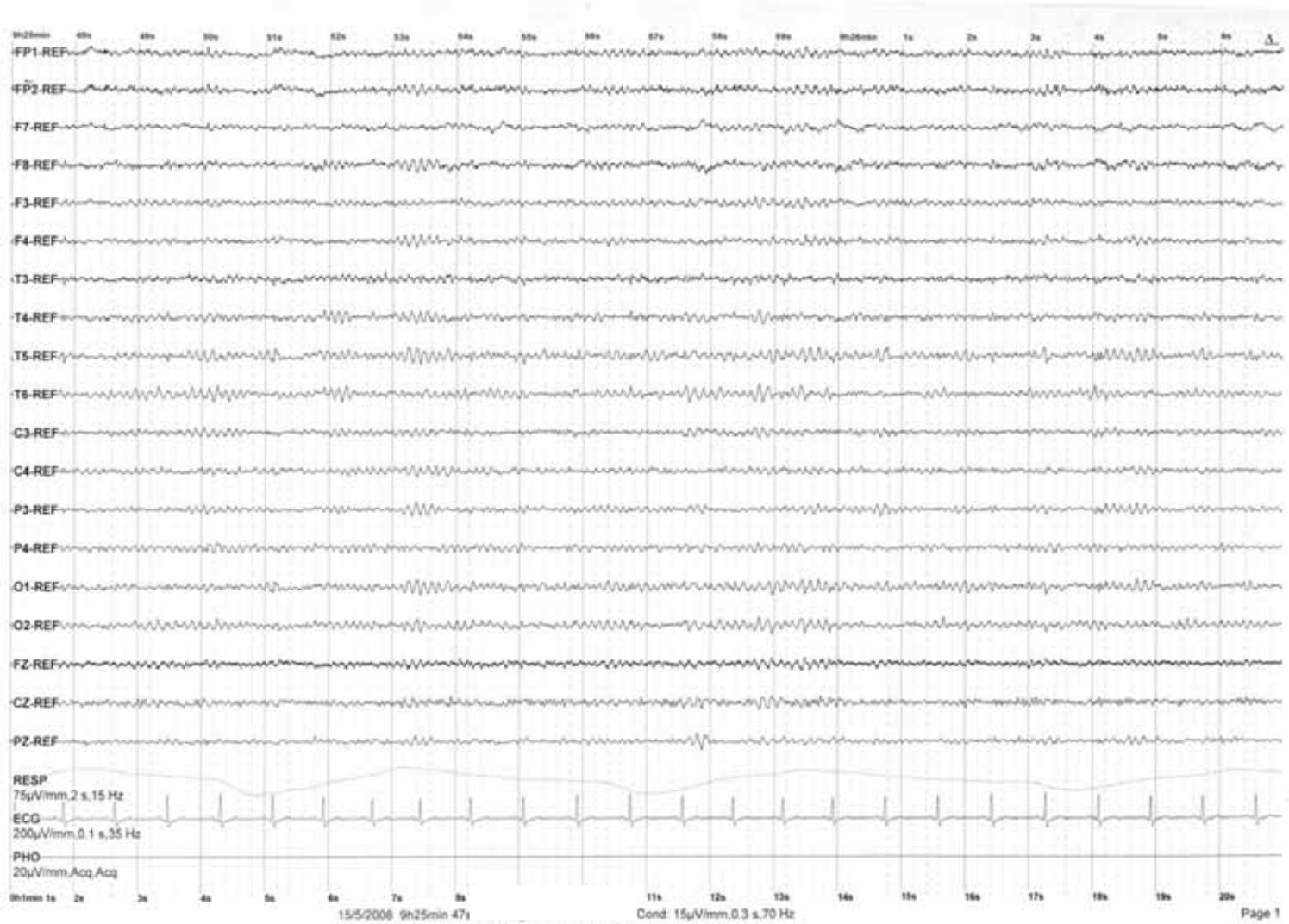


Fig. 1 Referential montage. Awake state, basal activity, normal.

M.A.D.G.



Fig. 2 Hyperventilation enhances IED with predominant expression in left frontal regions, with maximal expression in left inferior frontal, F7 and diffusion to F3, Fz, Fp1, Fp2, T3.

M.A.D.G.

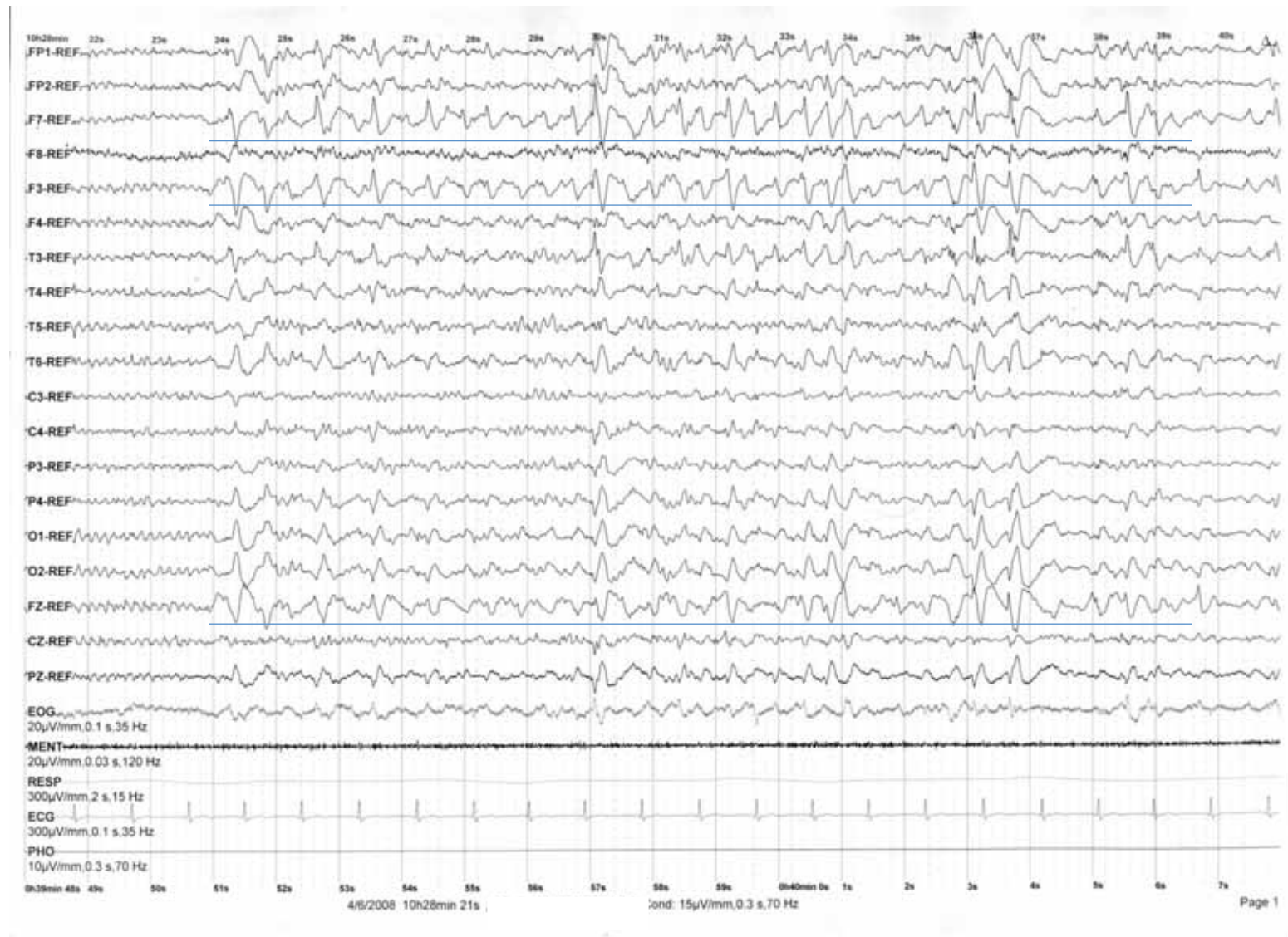


Fig. 3 Referential montage. Sharp waves of 100-200 µV with maximal expression in left inferior-frontal, left front-central midline front-central and left mid temporal regions.

M.A.D.G.

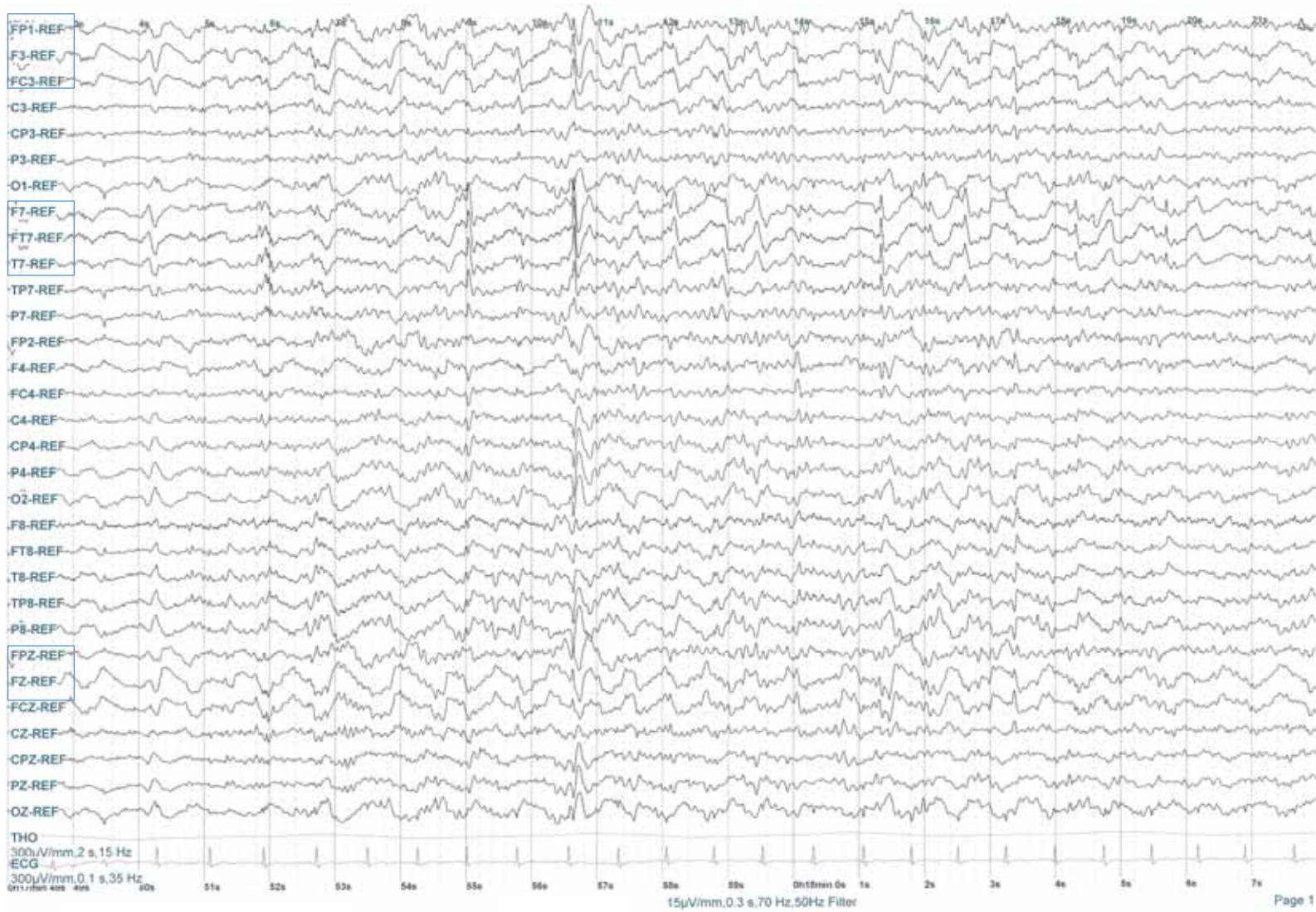


Fig. 4 Referential montage. Double electrode density (10/10 system). IED with maximal expression in FT 7 electrode and diffusion to F7, T7, Fp1, F3, Fc3, Fpz and Fz. Opposite direction of waveforms due to the referential montage effect.

M.A.D.G.

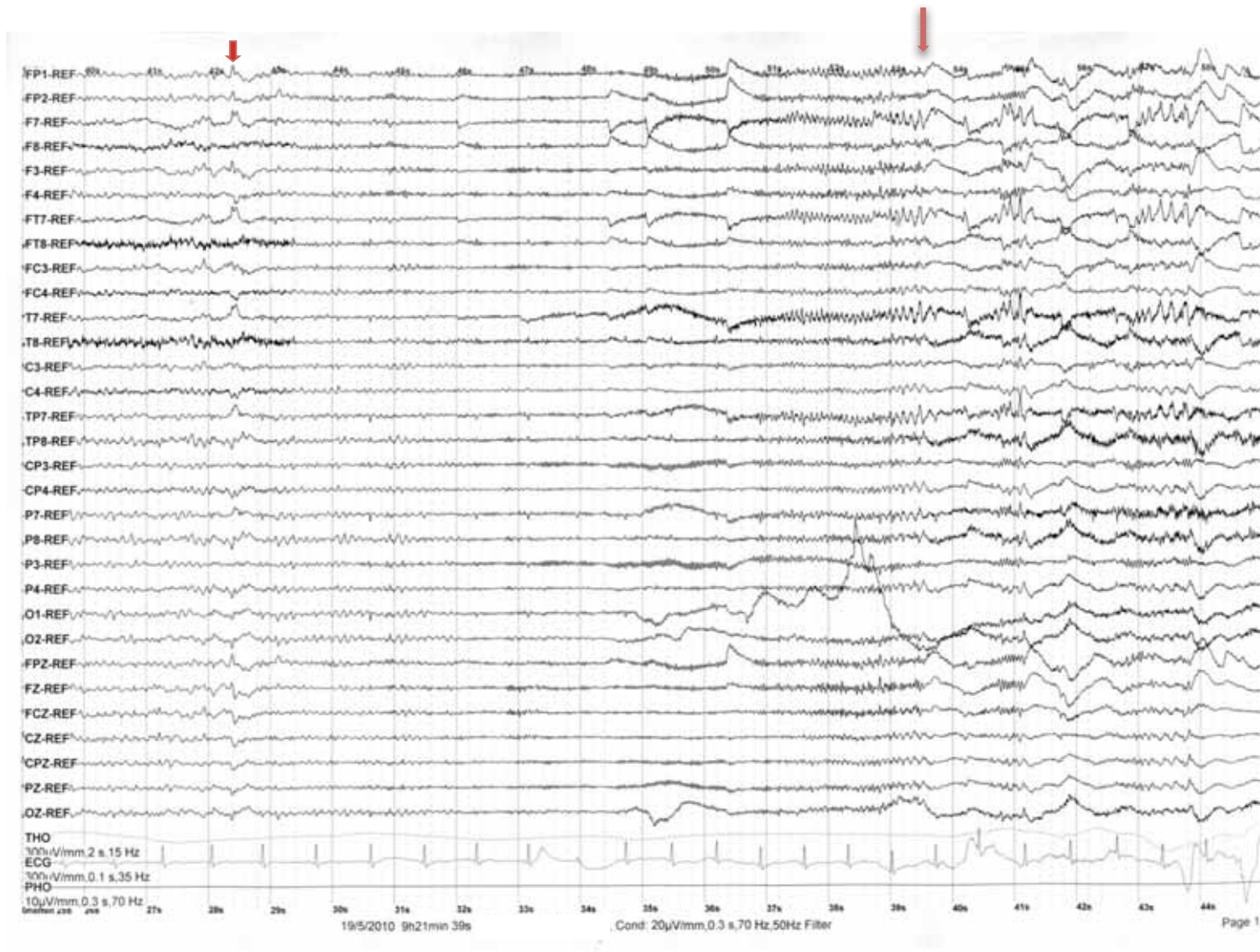


Fig. 5 Referential montage, with 10/10 system. Seizure starting with global attenuation of voltages, and afterward low amplitude synchronized rhythm being very difficult to locate at onset, and progressive left dominance of the expression in Ft7, T7, F7, Fp1.

M.A.D.G.

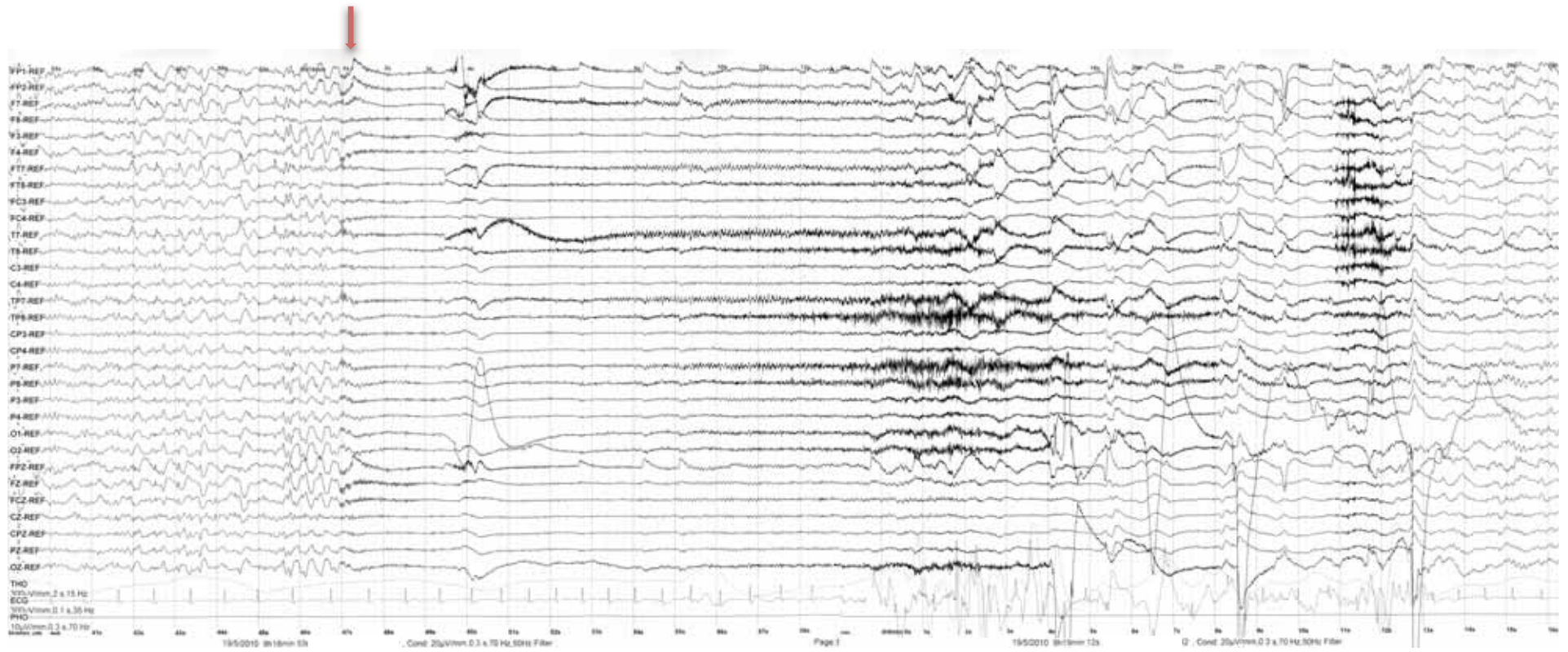


Fig. 6 Referential montage with 10/10 system. Mosaic of a full view of seizure, starting with a very low attenuation synchronized rhythm with frontal predominance, preceded by a group of left frontal sharp waves in Ft7, T7, F7 and F3. During the seizure there is a progressive slowing of frequency, from around 25 Hz at onset to slow alpha frequencies and postictal slowing.

M.A.D.G.

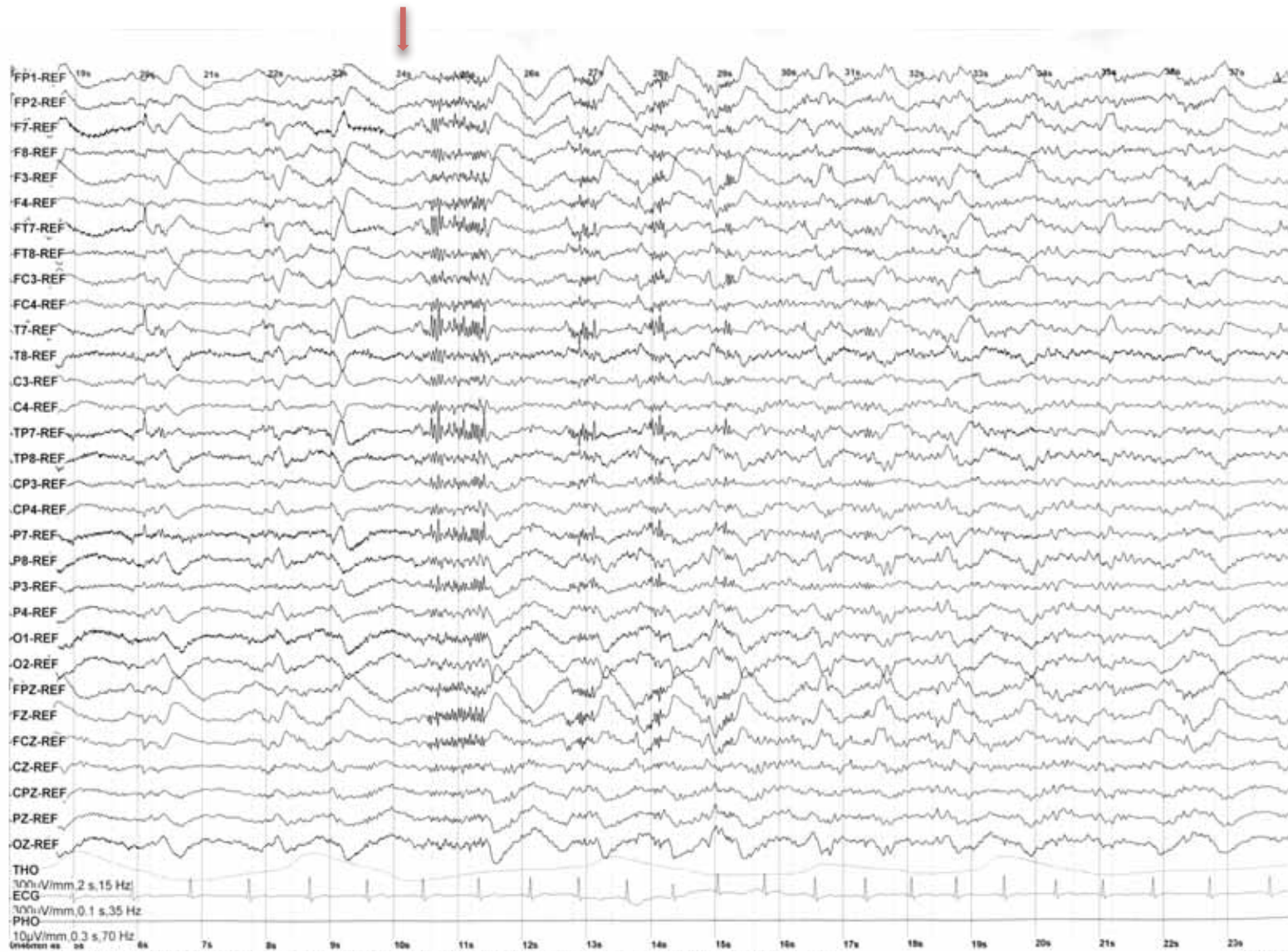


Fig. 7 Same recording. Isolated sharp waves in F7, Ft7, T7, Tp7 and after 3 seconds short global attenuation followed by synchronized rhythm with maximal expression in the same regions and very fast diffusion to next electrodes and short duration, followed by slow waves and three more burst of very brief synchronized rhythm followed by slow wave more expressive in left frontal regions: Fp1 Fp2, F3>F4, FC3, T7, F7, Fp7, Fpz and Fz.

M.A.D.G.

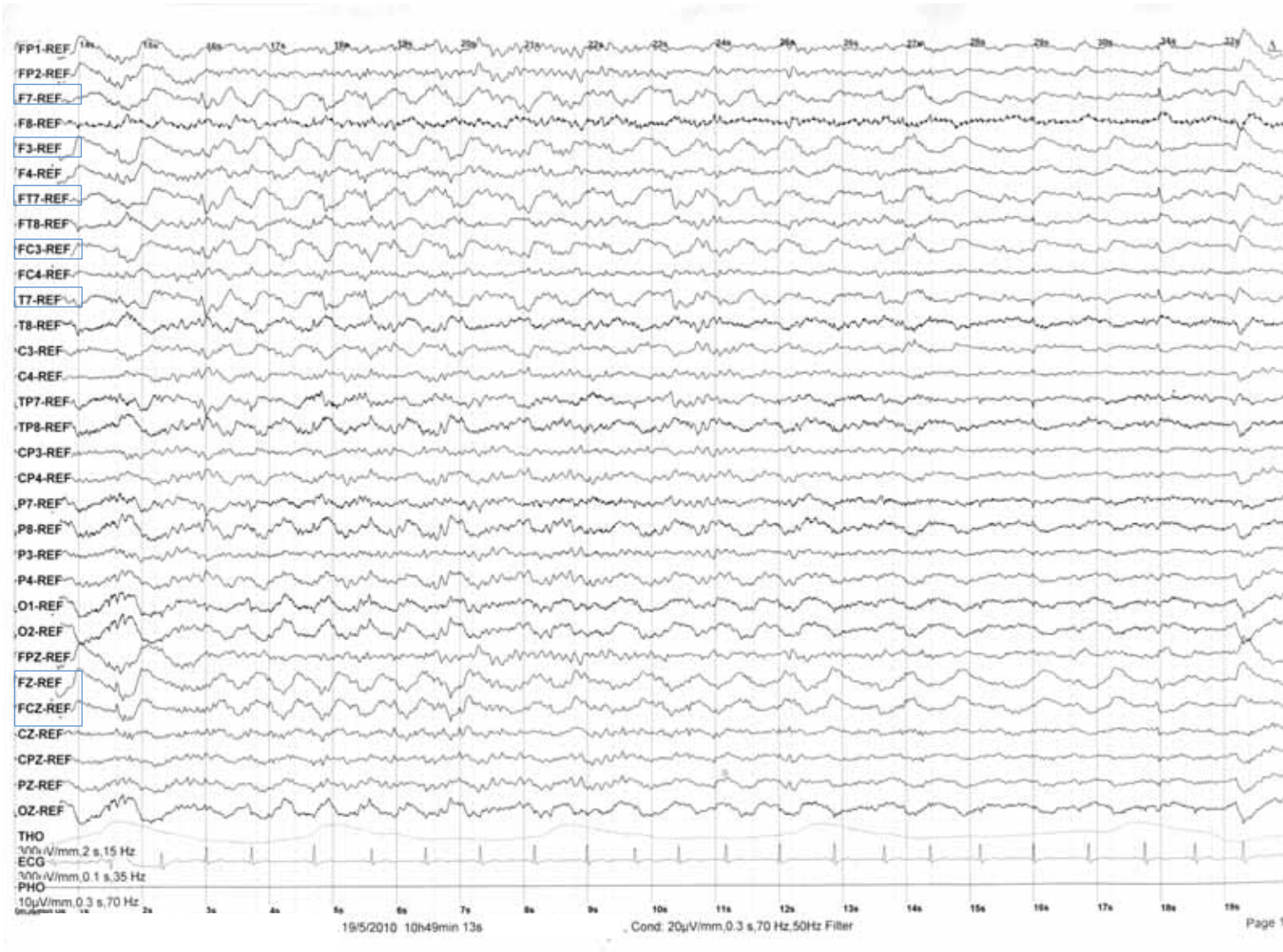


Fig. 8 Referential montage, 10/10 system. Postictal slowing with left frontal predominance of delta activity, with maximal expression in F7, F3, FT7, FC3, T7, Fz, FcZ.

M.A.D.G.

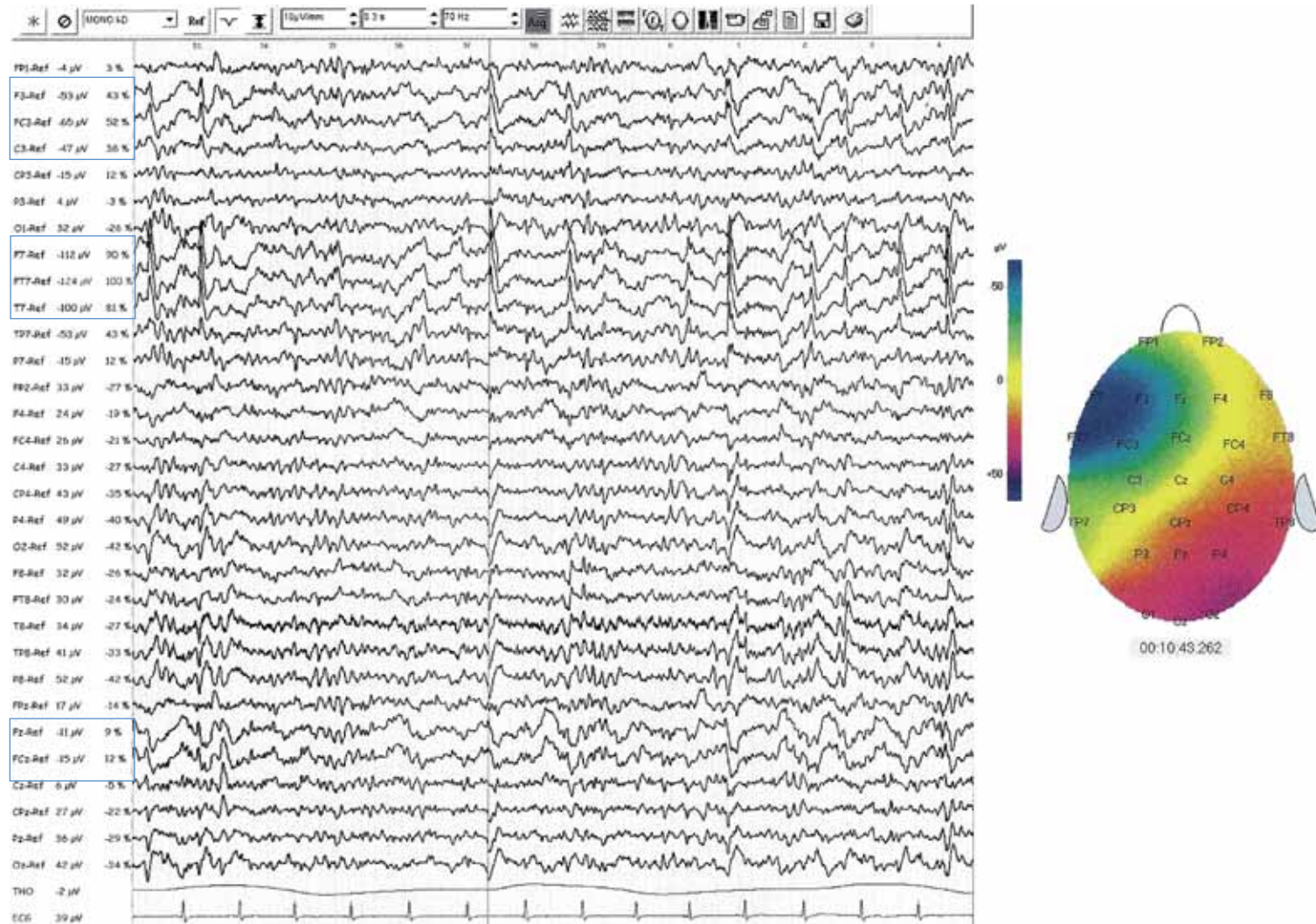


Fig. 9 Sharp waves up to -124 μV of negativity in FT7 electrode. Electronegativity is presented in blue colour in the adjacent brain map