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# SEIZURE DETECTION WITH AUTOMATED EEG ANALYSIS: A VALIDATION STUDY FOCUSING ON PERIODIC PATTERNS

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## Highlights

- Automated EEG interpretation is increasingly used in ICU recordings, where periodic discharges are relatively common.
- This study shows that the overall performance of automated EEG interpretation is good.
- However, the presence of periodic discharges seems to reduce its reliability


## Abstract

**Objective:** To evaluate an automated seizure detection (ASD) algorithm in EEGs with periodic and other challenging patterns.

**Methods:** Selected EEGs recorded in patients over 1 year were classified into four groups: A. Periodic lateralized epileptiform discharges (PLEDs) with intermixed electrical seizures. B. PLEDs without seizures. C. Electrical seizures and no PLEDs. D. No PLEDs or seizures. Recordings were analyzed by the Persyst P12 software, and compared to the raw EEG, interpreted by two experienced neurophysiologists; Positive percent agreement (PPA) and false-positive rates/hour (FPR) were calculated.

**Results:** We assessed 98 recordings (Group A= 21 patients; B= 29, C= 17, D= 31). Total duration was 82.7 hours (median: 1 hour); containing 268 seizures. The software detected 204 (=76.1%) seizures; all ictal events were captured in 29/38 (76.3%) patients; in only in 3 (7.7%) no seizures were detected. Median PPA was 100% (range 0-100; interquartile range 50-100), and the median FPR 0/h (range 0-75.8; interquartile range 0-4.5); however, lower performances were seen in the groups containing periodic discharges.

**Conclusion:** This analysis provides data regarding the yield of the ASD in a particularly difficult subset of EEG recordings, showing that periodic discharges may bias the results.

**Significance:** Ongoing refinements in this technique might enhance its utility and lead to a more extensive application.

## INTRODUCTION

Electroencephalography (EEG) represents a standard examination of brain function in patients living with epilepsy, and it is also increasingly used in subjects with acute consciousness impairment in an intensive care setting, where seizures may occur in 8-34% of patients, mostly with subclinical presentations (Privitera et al., 1994, DeLorenzo et al., 1998, Towne et al., 2000, Scheuer, 2002, Claassen et al., 2004). In both clinical situations, long-term EEG monitoring allows continuous surveillance of the cerebral activity, but it implies a thorough and time-consuming interpretation by trained neurophysiologists. Over the last few decades, automatic methods have been developed to highlight significant electrographic events, providing insight into the EEG trends, reducing evaluation time and potentially increasing patient security by alerting medical staff sooner concerning the presence of seizures. Seizure detection algorithms are available in commercial software packages, based on the analysis of rhythmic patterns with a certain waveform morphology, distribution, and evolution over time, until a threshold is achieved. Nevertheless, a major problem is the inter-patient (and, at times, intra-patient) variability of ictal patterns, ranging from quasi rhythmic or periodic discharges, over high frequency activities variation or abrupt phase changes, to more irregular groups of epileptiform transients (Gotman, 1990, Furbass et al., 2012).

Despite the increasing implementation of these automated systems and the previous literature regarding the sensitivity or specificity rates to detect seizures (Gotman, 1982, 1990, Pauri et al., 1992, Gabor, 1998, Wilson et al., 2004, Saab and Gotman, 2005, Wilson, 2005, Meier et al., 2008, Kelly et al., 2010, Hartmann et al., 2011), the application of these algorithms to patients with particular challenging EEG records has received little attention to date. Our study was conducted to address this aspect.

## METHODS

### *Study population*

Routine and long-term EEG recordings, acquired using 23 scalp electrodes placed according to the international 10-20 system in adults and children over 1 year of age, were used for this analysis. All studies were recorded on a digital system (Viasys Neurocare, Madison, WI, USA), for standard evaluations (with intermittent photic

stimulation and hyperventilation in certain cases), or in the in-patient clinics including the Intensive Care Unit (ICU), between January 2012 and March 2013.

Recordings were retrospectively selected for this study according to their features, and classified into the following groups:

A. Periodic lateralized epileptiform discharges (PLEDs, synonymous with lateralized periodic discharges (Hirsch et al., 2013)) or periodic epileptiform discharges (PEDs, synonymous with generalized periodic discharges (Hirsch et al., 2013)) with intermixed electrical seizures, defined as acceleration of their frequency over at least 2 Hz within a few seconds and/or progressive change in field and morphology, of more than 1 second of duration (**Figure 1**).

B. Monotonous PLEDs/PEDs with no seizures (first control group).

C. Electrical seizures without PLEDs/PEDs, defined as any variation of the background amplitude, together with an acceleration of frequency over 4 Hz (Hirsch et al., 2013) or a spike-and wave pattern below 4 Hz consistent with typical seizures associated with idiopathic (genetic) generalized epilepsy, and/or progressive change in field and morphology, regardless of duration.

D. No PLEDs/PEDs nor seizures (second control group), in recordings suggestive of changes in vigilance states, containing considerable artifacts, or epileptiform-looking variants of normality suggesting seizures to an untrained reader, such as prolonged runs of rhythmic mid-temporal discharges, or wicket spikes.

*Persyst 12 seizure detection description*

This algorithm (version 2013.06.25), is designed to evaluate the scalp EEG signal for changes in background activity exhibiting rhythmicity, evolution in amplitude and/or frequency, and asymmetry, and produce outputs concerning electrographic seizure activity. The algorithm is built by combining the output of many small artificial neural networks (few input and hidden nodes), each of which were trained to recognize a particular feature, e.g. frequency evolution. Uncertainty is propagated through each level of the processing, resulting in a single “is-seizure” output (0-1) per each one-second epoch. Two outputs of the algorithm are available: the identification of discrete

electrographic seizure events with a minimum duration of 11 seconds, which we used for this analysis, and a seizure probability curve that displays the probability that any one-second epoch would be marked as “seizure”. The algorithm was trained on a set of varied EEG recordings containing seizures identified by human experts, drawn from Epilepsy Monitoring Unit, Intensive Care Unit, and ambulatory settings. Non-seizure records were also utilized in training the detection algorithm; these contained a broad sampling of EEG patterns and states, including records from the ICU. There was no algorithm training to specifically or systematically attempt to identify and differentiate certain types of patterns, like lateralized or generalized periodic discharges, or gray area ICU patterns that fall into the ictal-interictal continuum (where expert electroencephalographers might have legitimate disagreements in interpretation).

*Algorithm Interpretation*

Each recording was analyzed using the automated seizure detection (ASD) function, which presents on the screen as a red mark above a given threshold, being considered as a binary variable for practical purposes. We also inspected the color-coded rhythmicity and fast Fourier transformed (FFT) power spectrograms (both averaged for each hemisphere), in order to determine the presence of patterns suggestive of electrographic seizures. These analyses were always assessed using the artifact reduction device, on a time scale between 30 min and 1 h. The visual interpretation of the corresponding whole raw recording represented the gold standard comparator; all analyses were the result of agreement between two experienced neurophysiologists (ASM, AOR).

*Data analysis*

On the whole dataset, we calculated the percentage of seizures detected (either with the ASD only, or using also the spectrograms), as well as the rate of patients with seizures in whom at least one event was detected by the software. False negatives (FN) were defined as expert-marked seizures on raw recordings, not detected by any automated method. Expert-marked seizures that were also detected by the automated software

represented true positives (TP). Positive percentage agreement (PPA), a term preferred rather than “sensitivity” to describe the comparison of a new test to a non-reference standard, was calculated for each record individually, regarding both automated approaches: TP was divided by the sum of TP and FN for each patient, and described with a median (given the assumed non-normal distributions) for each group, and in order to reduce any biasing by individual patients having many seizures.

False positive (FP) detections were defined as any event identified by the ASD as a seizure, but not corresponding to any expert-marked seizure. The false positive rate (FPR), corresponding to FP divided by recording time, was described using the median of each individual FPRs across a given group; to complement this approach we also calculated FPR using the sum of individual FP divided by the whole recording time by group.

## RESULTS

We analyzed 98 recordings: 21 patients in Group A (with 170 seizures), 29 in group B, 17 in group C (with 98 seizures), and 31 in group D; globally, these recordings contained 268 seizures (groups A and C). In group A, the median number of seizures per recording was 4 (range 1-50); in group C the median was 3 (range 1-18). The total duration of all recordings was 82.7 hours, and the median recording time 1 hour (range: 20 minutes to 19 hours).

Regarding the clinical characteristics of the patient population, median age was 57 [range: 3-88] years and 48 (49%) were women. The presumed etiology was structural-metabolic in 66 (67.3%), genetic in 7 (7.1%), and unknown in 25 patients (25.5%) (Berg et al., 2010).

**Table 1** gives the overview of the results. Overall, the software detected 204/268 (=76.1%) of seizures. All ictal events were captured in 76.3% of patients and 92.3% patients with seizures had at least one event detected. Mean detection rate per subject was 90.5% (median 100%, range 0-100; interquartile range 50-100). The 64 “undetected seizures” corresponded to subtle ictal patterns without clear evolution in frequency or amplitude in 30 (46.9%), short events (duration less than 10 seconds, **Figure 2**) in 21 (32.8%), fast rhythms in 8 (12.5%) and to seizures masked by muscular artifacts in 5

(7.8%) cases. Considering the two groups presenting seizures (A and C), applying both detection methods (ASD function and spectrogram), all ictal events were captured in 29 out of 38 (76.3%) patients, whereas only in three subjects (7.7%) no seizures at all were detected. The median PPA in Group A (PLEDs plus intermixed seizures), was 75%; while in Group C (seizures only) was 100%, regardless of the methods.

Eighty false positive events were identified by the detector, overall. Across the entire dataset (82.7 hours), this gives an FPR of 0.97/h; if two extreme outliers in group B were removed (with a very high FPR, see **Figure3**; these events occurred in EEGs showing monotonous, prolonged GPEDs in both), the falsely detected events dropped to 20, with an FPR of 0.24/h. Of note, the median FPR across all recordings was 0 (range 0-75.8; interquartile range 0-4.5). False-positive detections were concentrated in groups A and B, both with periodic patterns, often due to artifacts (**Figure 4**), or prolonged GPEDs. FPR calculated by adding all false positive events across each group, divided by the total recording time of the group, are somewhat higher.

Finally, the combination of the ASD function and the spectrogram analysis increased the FPR, particularly in group B. In the control group (D), no FPs were detected using only the ASD function.

## DISCUSSION

In this study, the Persyst P12 software was evaluated in terms of PPA and FPR in a particularly difficult group of EEG patterns, including patients with periodic patterns (Group B), and with epileptiform-looking variants of normality or artifacts suggestive of ictal events (Group D). This software detected 76.1% of all seizures. The medians show high PPA and low FPR overall, but with lower performances in patients having periodic patterns, intermixed or not with seizures.

A variety of quantitative EEG analyses and display techniques have been proposed to ease EEG interpretation. Review of quantitative displays usually quickly reveals an irregular structure, abrupt phase changes or distortions, appearance or increasing of focal slowing, generalized suppression, loss of faster frequencies, or increasing or decreasing EEG variability, suggesting an ictal event. However, the distinction between

seizures from artifact-related changes, variants of normality or repetitive epileptiform elements may remain very challenging.

Since the automatic EEG detection system described by Hjorth more than forty years ago (Hjorth, 1970), different algorithms have been tested regarding their yield in identifying epileptic seizures, and their results show a wide variability, which relates not only to the properties inherent to each software, but also to the types of EEG that were used for the validations. The “older” generation (Gotman, 1982, 1990, Pauri et al., 1992) showed results in terms of sensitivity from 0.43 to 0.64, with FPR up to 3.3/h for Monitor 3.0 (Pauri et al., 1992). With software such as CNet and Monitor 8.0c, sensitivities of 0.93 and 0.74, and FPR of 1.4/ h and 3.0/h, respectively, were reported (Gabor, 1998). Otherwise, the Reveal system demonstrated a sensitivity between 0.74 and 0.8, with an FPR of 0.1–0.2/h only (Wilson et al., 2004). Using a neural network method for automatic and incremental learning applied to a patient-specific seizure detection (probabilistic neural network), a sensitivity of 0.89 and a FPR of 0.56/h were obtained in a small group of epilepsy monitoring and intensive care unit patients (Wilson, 2005). With the Stellate Harmonie system, the sensitivity was 0.76 and the FPR 0.34/h, with a median detection delay of 10 seconds, operating as an on-line seizure detection (Saab and Gotman, 2005). The overall detection sensitivity of IdentEvent in epilepsy monitoring unit patients was 0.80 with a very low FPR of 0.09/h (Kelly et al., 2010). Detection of seizures with the EpiScan has proved to achieve an overall sensitivity ranging from 0.73 to 0.83, with a FPR of 0.30/h (Hartmann et al., 2011, Furbass et al., 2012). Finally, with a multimorphologic ictal-pattern recognition system, the average correct detection rate was higher than 96%, with a mean false alarm rate of 0.25/h (Meier et al., 2008). It is of note that most of the studies of automated seizure detection algorithms were conducted primarily using recordings obtained on epilepsy patients in the epilepsy monitoring units or EEG laboratories, and assessed very little data concerning seizures recorded in ICU settings. When the IdentEvent and Reveal algorithms were used to assess a small number (N=11) of ICU recordings containing seizures, their detection sensitivities fell to 10.1% and 12.9%, respectively (Sackellares et al., 2011).

As compared to the aforementioned data, in the present study, including a large percentage of ICU patients with complex EEG patterns, we found a lower PPA and higher FPR in the subgroups with periodic patterns; this is probably related to the

selection of recordings with particularly challenging EEGs. The Persyst 12 seizure detection algorithm functions as a general purpose seizure detector, and was not specifically designed to address ICU EEG patterns that can sometimes possess features bordering on electrographic ictal activity without clearly being seizures. Nevertheless, the characteristics of the detector showed good performances overall. The majority of missed seizures presented with a short duration (below 10 seconds), or subtle diffuse electrodecrements, without any obvious evolution (**Figure 2**). Conversely, false detections corresponded to muscle artifacts or electrode failures, or to prolonged GPEDs. It is important to underscore that overall only less than 8% of patients having at least one seizure did not get any detected.

This study has some limitations; first, the assessment between the two methods was not blinded. Second, the definition seizures, especially in patients having additional PLEDs (group A) did not rely on robust evidence-based criteria, but was somewhat subjective, integrating also the clinical situation, as it is common in clinical practice; for example, a patient with focal periodic discharges over the dominant temporal lobe and an intermixed acceleration-deceleration of the electrogenesis is generally regarded to be in status epilepticus and deserves a consequent treatment (Sutter and Kaplan, 2012). Third, the evaluation of spectrograms includes some subjectivity, as opposed to the ASD function. Finally, we analyzed a selected group of EEGs, therefore generalizability is not implicit.

In view of these results and the above mentioned literature, current computer-assisted EEG interpretation techniques may be considered an important help for the human observer (Scheuer, 2002). However, some limitations should be outlined: in the presence of periodic patterns, false negative and false positive results may become more frequent; conversely, the use of the rhythmicity and power spectrograms in addition to the ASD increases the PPA, but also the FPR. It appears therefore important that EEG automated detections, especially in long-term monitoring, should be critically assessed for each specific patient, particularly at the beginning of the recording (Hartmann et al., 2011). Nevertheless, it is likely that ongoing refinements in seizure detection algorithms and EEG trending software will enhance their utility and lead to even more extensive applications.

This analysis provides data regarding the performance of an automated seizure detection algorithm in a difficult subset of EEG recordings, particularly including periodic patterns. This may help clinicians in the application of automated EEG algorithms, and provide developers with valuable data for possible improvements.

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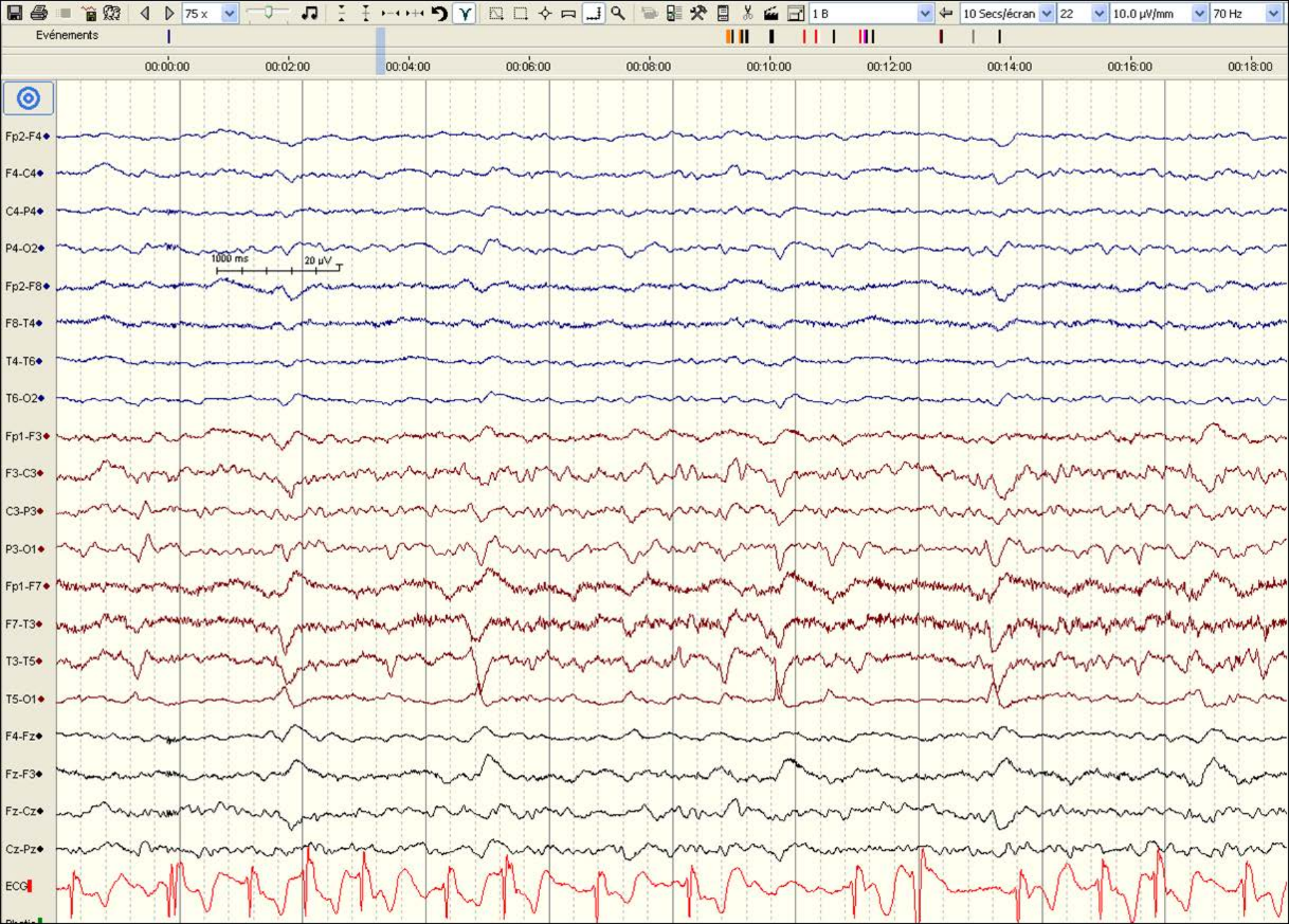
**TABLES:**

**Table 1.** Results regarding the positive percent agreement (PPA) and false positive ratio (FPR) per hour in each group and in the whole studied cohort. PPA 1: Median PPA using only the automated seizure detection (ASD) function. PPA 2: Median PPA including ASD function and spectrograms. FPR 1 (per hour): Median false positive rate using the ASD function only. FPR 2 (per hour): Median false positive rate through both methods. FPR* relates to the sum of false positive across each groups, divided by the total recording time in the group. Results are formulated in terms of median (range), interquartile range (IQR), except in the last column.

| | PPA 1<br>Median (Range)<br>IQR | PPA 2<br>Median (Range)<br>IQR | FPR 1<br>Median (Range)<br>IQR | FPR 2<br>Median (Range)<br>IQR | FPR* |
|---|---|---|---|---|---|
| Group A<br>(Periodic patterns and seizures) | 75 (0-100)<br>4.8-100 | 75 (0-100)<br>50-100 | 0 (0-6.1)<br>0-0 | 0 (0-17.1)<br>0-0 | 0.76 |
| Group B<br>(periodic patterns only) | | | 0 (0-27.0)<br>0-0 | 6.06 (0-75.8)<br>3-9.09 | 4.28 |
| Group C<br>(seizures only) | 100 (0-100)<br>13.33-100 | 100 (0-100)<br>50-100 | 0 (0-6.1)<br>0-0 | 0 (0-28.3)<br>0-3 | 0.06 |
| Group D<br>(no seizures, no periodic patterns) | | | 0 (0-0)<br>0-0 | 0 (0-9.1)<br>0-2.9 | 0.0 |
| Total | 100 (0-100)<br>5.9-100 | 100 (0-100)<br>50-100 | 0 (0-27.0)<br>0-0 | 0 (0-75.8)<br>0-4.5 | 0.97 |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C4-P4
P4-O2
Fp2-F8
F8-T4
T4-T6
T6-O2
Fp1-F3
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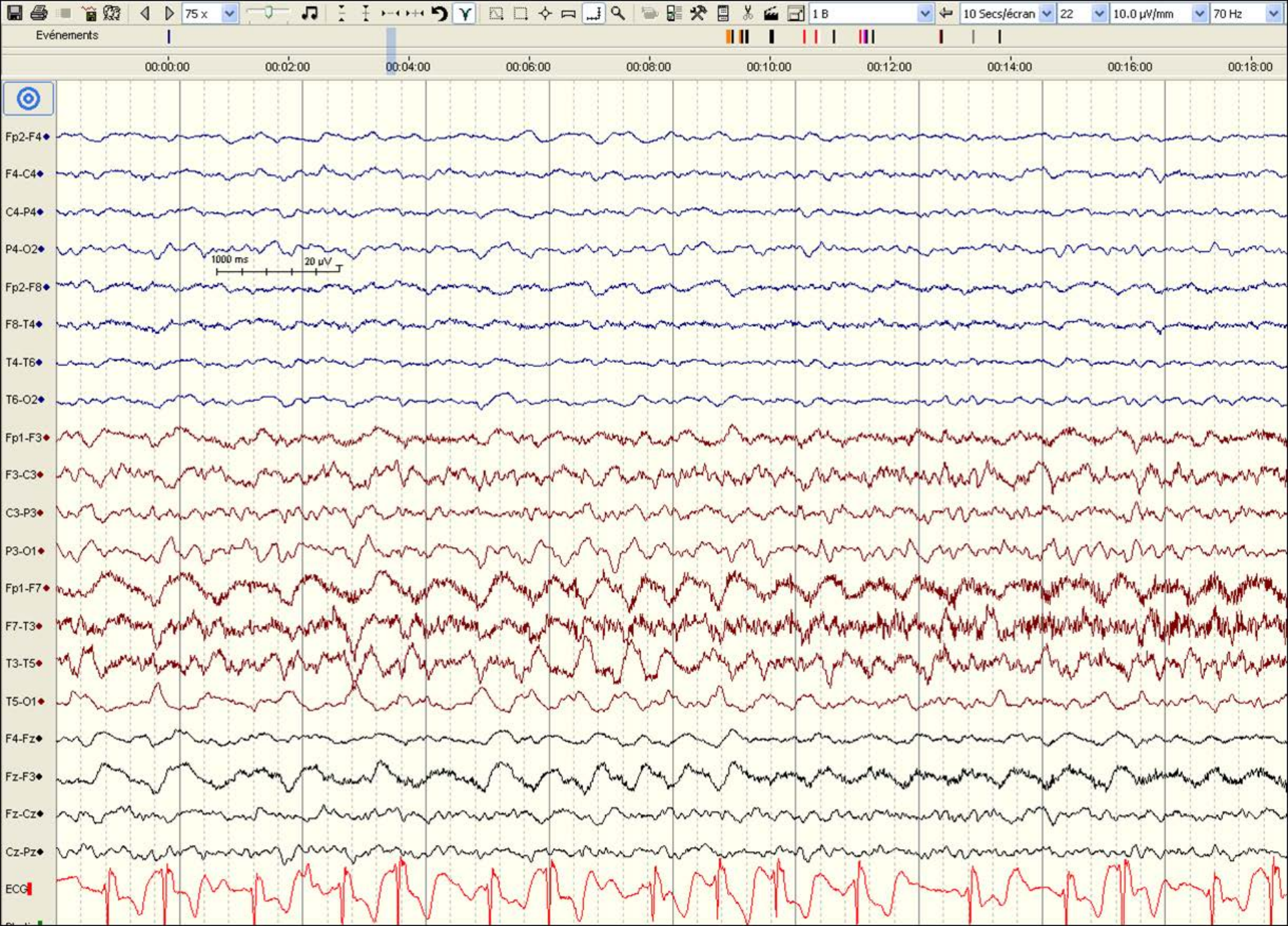
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F4-C4
C4-P4
P4-O2
1000 ms
20 µV
Fp2-F8
F8-T4
T4-T6
T6-O2
Fp1-F3
F3-C3
C3-P3
P3-O1
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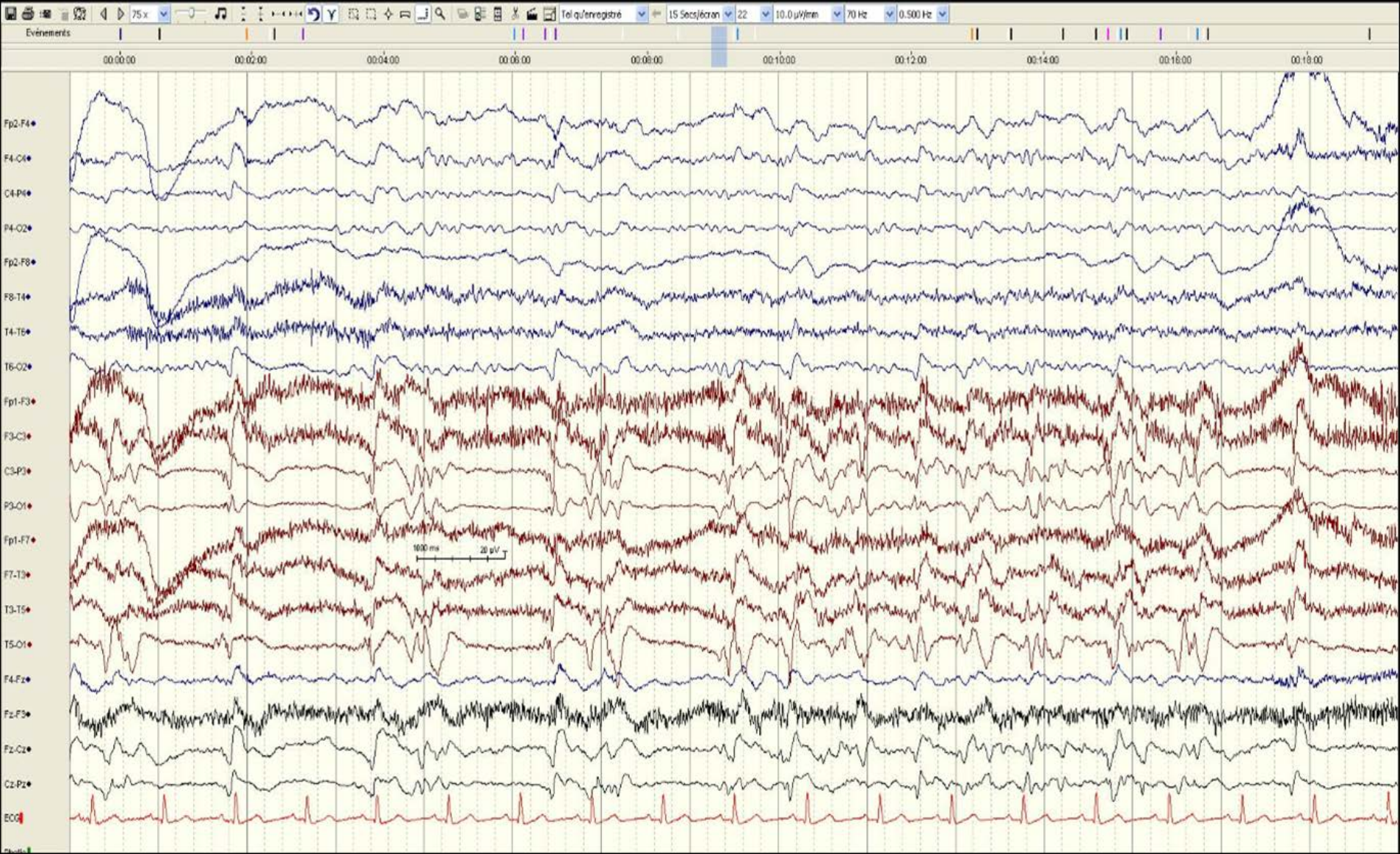
Cz-Pz
ECG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P3-O1
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Cz-Pz
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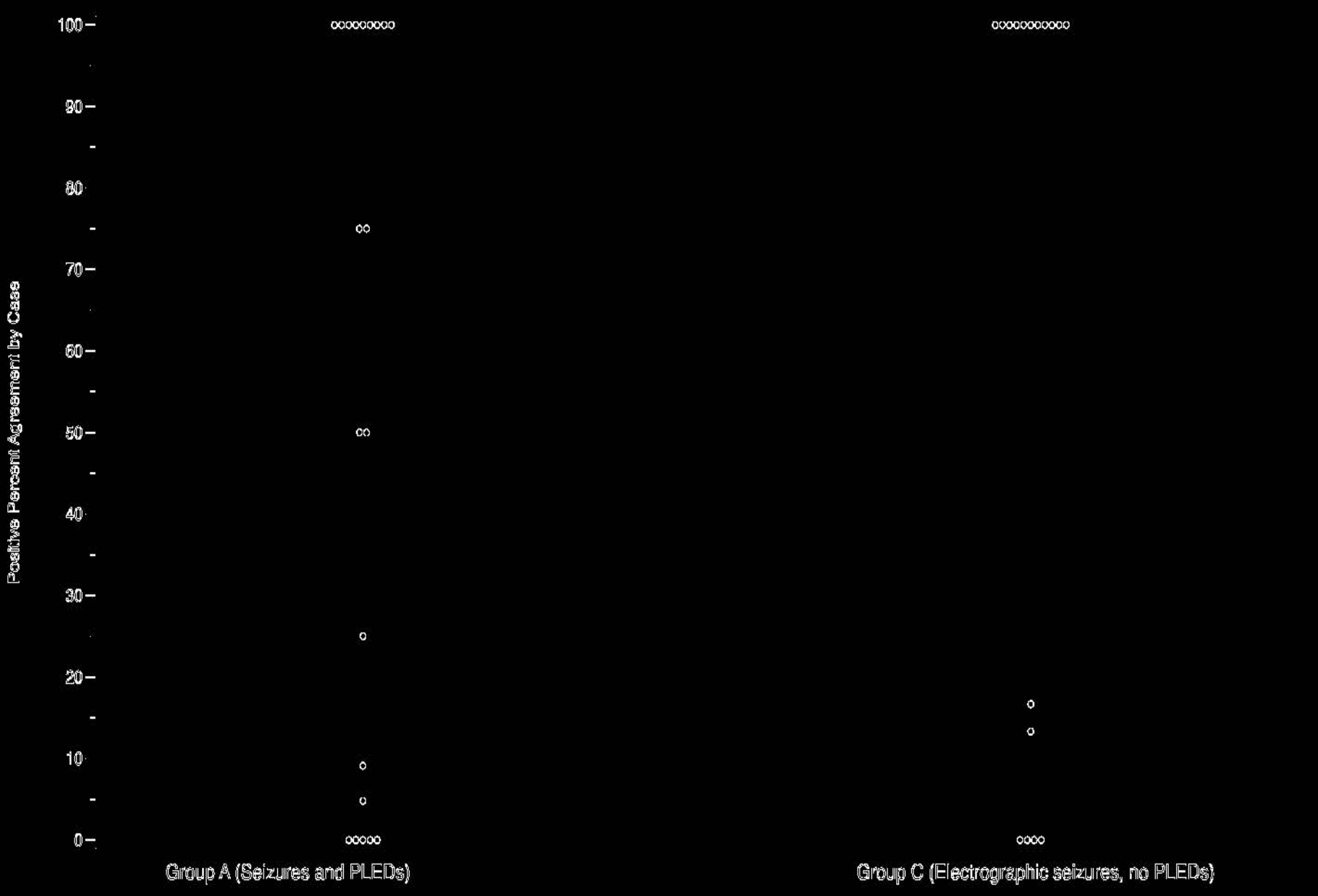
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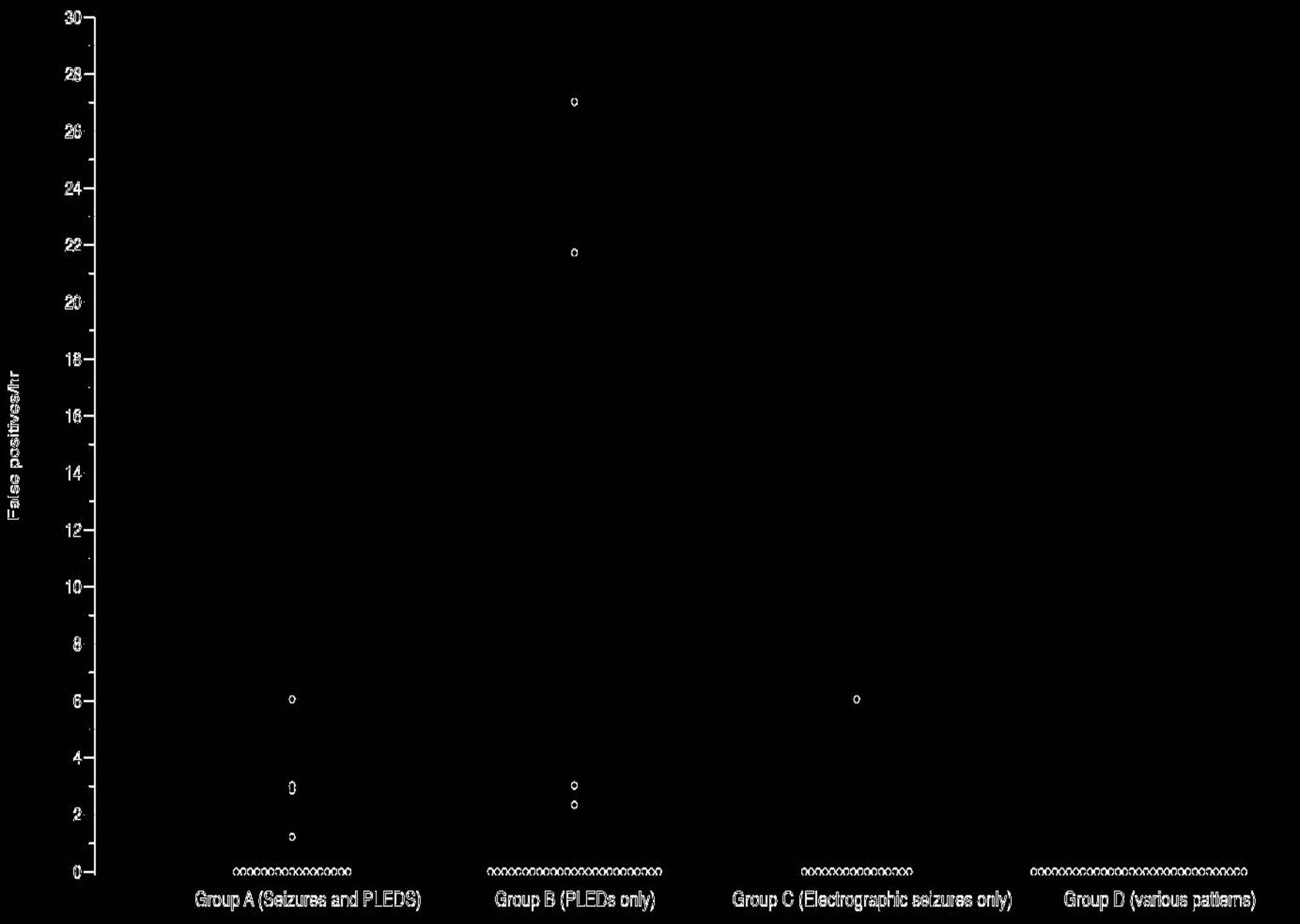
Group A (Seizures and PLEDs)
Group C (Electrographic seizures, no PLEDs)


False positives/hr
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26
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8
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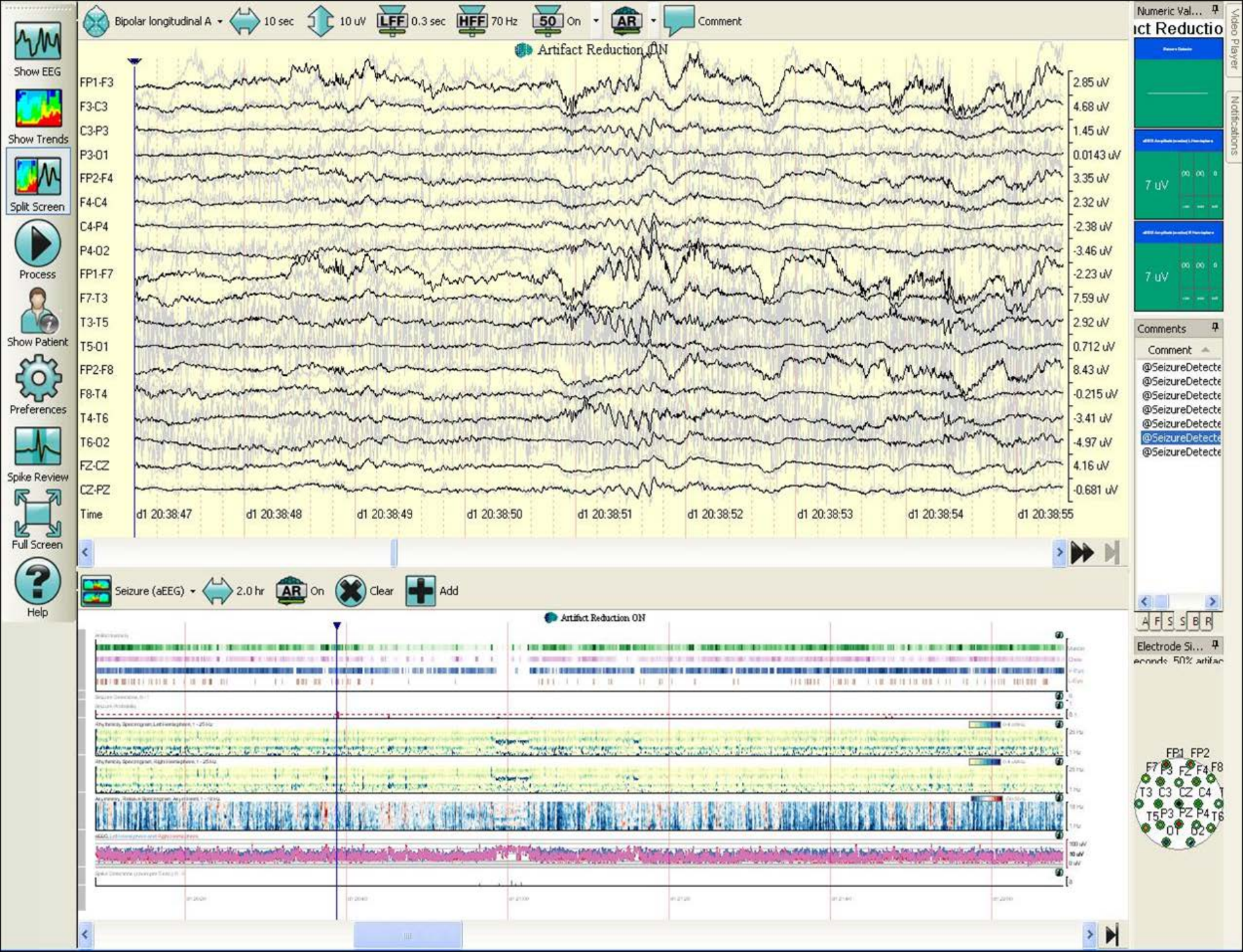
Group A (Seizures and PLEDS)
Group B (PLEDs only)
Group C (Electrographic seizures only)
Group D (various patterns)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P3-O1
FP2-F4
F4-C4
C4-P4
P4-O2
FP1-F7
F7-T3
T3-T5
T5-O1
FP2-F8
F8-T4
T4-T6
T6-O2
FZ-CZ
CZ-PZ
Time
d1 20:38:47
d1 20:38:48
d1 20:38:49
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d1 20:38:51
d1 20:38:52
d1 20:38:53
d1 20:38:54
d1 20:38:55
2.85 uV
4.68 uV
1.45 uV
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3.35 uV
2.32 uV
-2.38 uV
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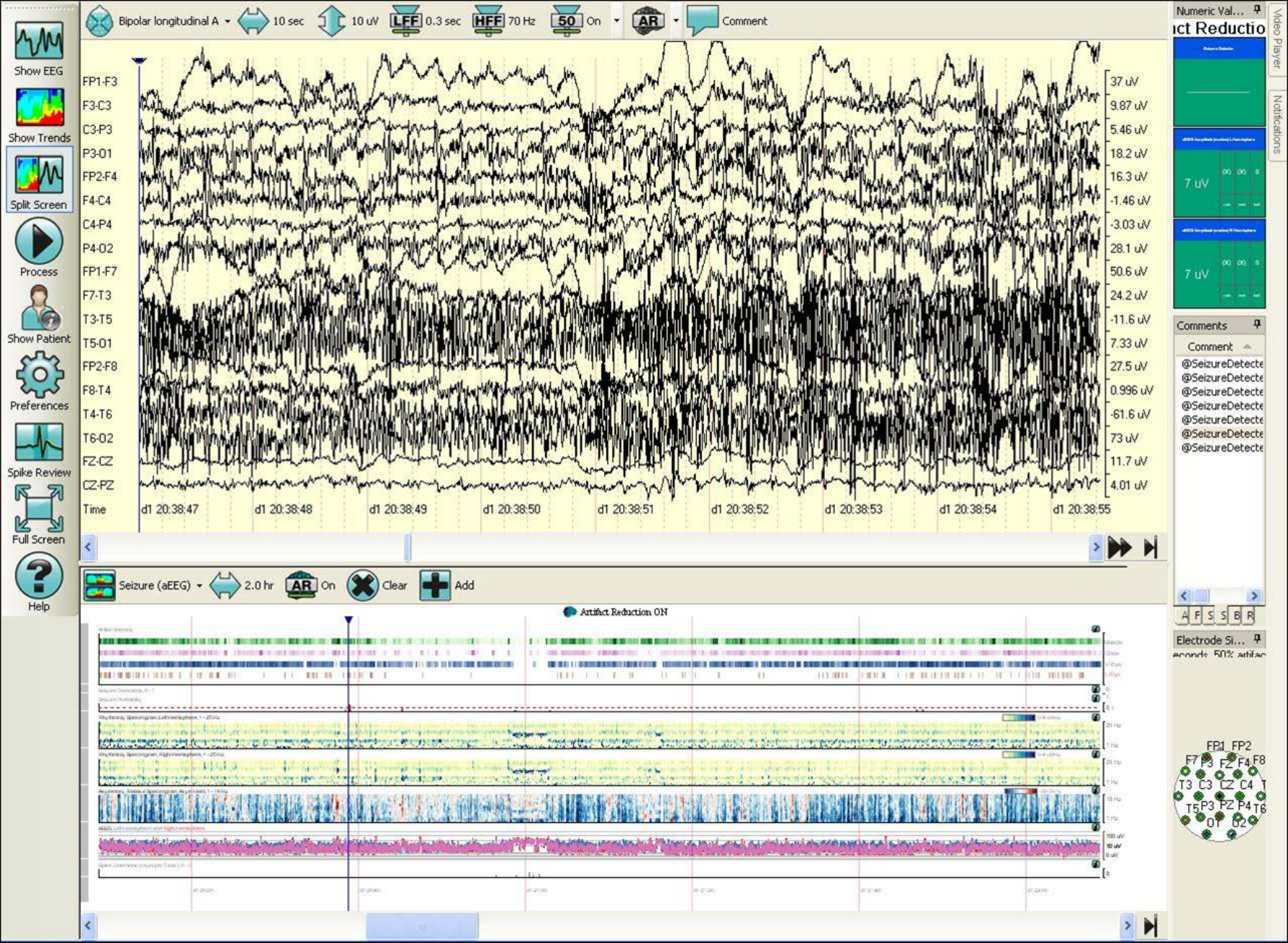
7.59 uV
2.92 uV
0.712 uV
8.43 uV
-0.215 uV
-3.41 uV
-4.97 uV
4.16 uV
-0.681 uV
Show EEG
Show Trends
Split Screen
Process
Show Patient
Preferences
Spike Review
Full Screen
Help
Seizure (aEEG)
2.0 hr
AR On
Clear
Add
Artifact Reduction ON
Numeric Val...
ict Reductio
7 uV
7 uV
Comments
Comment
@SeizureDetecte
@SeizureDetecte
@SeizureDetecte
@SeizureDetecte
@SeizureDetecte
@SeizureDetecte
@SeizureDetecte
A F S S B R
Electrode Si...
FP1 FP2
F7 F3 FZ F4 F8
T3 C3 CZ C4
T5 P3 PZ P4 T6
O1 O2
Video Player
Notifications


Show EEG
Show Trends
Split Screen
Process
Show Patient
Preferences
Spike Review
Full Screen
Help
Bipolar longitudinal A
10 sec
10 uV
LFF 0.3 sec
HFF 70 Hz
50 On
AR
Comment
FP1-F3
F3-C3
C3-P3
P3-O1
FP2-F4
F4-C4
C4-P4
P4-O2
FP1-F7
F7-T3
T3-T5
T5-O1
FP2-F8
F8-T4
T4-T6
T6-O2
FZ-CZ
CZ-PZ
Time
d1 20:38:47
d1 20:38:48
d1 20:38:49
d1 20:38:50
d1 20:38:51
d1 20:38:52
d1 20:38:53
d1 20:38:54
d1 20:38:55
37 uV
9.87 uV
5.46 uV
18.2 uV
16.3 uV
-1.46 uV
-3.03 uV
28.1 uV
50.6 uV
24.2 uV
-11.6 uV
7.33 uV
27.5 uV
0.996 uV
-61.6 uV
73 uV
11.7 uV
4.01 uV
Numeric Val...
ıct Reductio
7 uV
7 uV
Comments
Comment
@SeizureDetecte
@SeizureDetecte
@SeizureDetecte
@SeizureDetecte
@SeizureDetecte
@SeizureDetecte
@SeizureDetecte
A F S S B R
Electrode Si...
econds 50% artifac
Video Player
Notifications
Seizure (aEEG)
2.0 hr
AR On
Clear
Add
Artifact Reduction ON
FP1 FP2
F7 F3 FZ F4 F8
T3 C3 CZ C4 T
T5 P3 PZ P4 T6
O1 O2