Seizure detection with automated EEG analysis: A validation study focusing on periodic patterns

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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 old 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 h (median: 1 h); 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.

1. 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 fre-
quency activities variation or abrupt phase changes, to more irreg-
ular groups of epileptiform transients (Gotman, 1990; Furbass 
et al., 2012).

Despite the increasing implementation of these automated sys-
tems and the previous literature regarding the sensitivity or spec-
ificity 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.

2. Methods

2.1. 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 (Visays 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 accord-
ing to their features, and classified into the following groups:

A. Periodic lateralized epileptiform discharges (PLEDs, synonym-
ous with lateralized periodic discharges (Hirsch et al., 2013)) or periodic epileptiform discharges (PEDs, synonym-
ous with generalized periodic discharges (Hirsch et al., 2013)) with intermixed electrical seizures, defined as accel-
eration of their frequency over at least 2 Hz within a few sec-
onds and/or progressive change in field and morphology, of 
more than 1 s of duration (Fig. 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, contain-
ing 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.

2.2. 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 asym-
metry, 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. fre-
quency 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 “sei-
zure”. The algorithm was trained on a set of varied EEG recordings 
containing seizures identified by human experts, drawn from Epi-
lepsy Monitoring Unit, Intensive Care Unit, and ambulatory set-
ings. Non-seizure records were also utilized in training the 
detection algorithm; these contained a broad sampling of EEG pat-
terns and states, including records from the ICU. There was no 
algorithm training to specifically or systematically attempt to iden-
tify 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 electroencepha-
lographers might have legitimate disagreements in interpretation).

2.3. 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 vari-
able for practical purposes. We also inspected the color-coded 
rhythmicity and fast Fourier transformed (FFT) power spectro-
grams (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 inter-
pretation of the corresponding whole raw recording represented 
the gold standard comparator; all analyses were the result of 
agreement between two experienced neurophysiologists (ASM, 
AOR).

2.4. Data analysis

On the whole dataset, we calculated the percentage of seizures 
detected (either with the ASD only, or using also the spectro-
grams), 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 
termed 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 distribu-
tions) for each group, and in order to reduce any biasing by individ-
ual patients having many seizures. False positive (FP) detections were defined as any event identi-
ﬁed 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.

3. 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
Fig. 1. (A, B): two consecutive screenshots of a patient with pseudo-periodic discharges on the left posterior region, evolving to a semi-rhythmic activity over the left temporal region. Longitudinal bipolar montage (right over left), 30 mm/sec, 10 μV/mm.
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 hour, and the median recording time 1 hour (range: 20 minutes – 19 h).

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. 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 s, Fig. 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 spectrograms), 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 h), this gives an FPR of 0.97/h; if two extreme outliers in group B were removed (with a very high FPR, see Fig. 3; these events occurred in EEGs showing monotonous, prolonged GPEs 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 (Fig. 4), or prolonged GPEs. 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.

### 4. 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

Fig. 3. (A, B): Graphs showing A (upper panel): positive percentage agreement (PPA) using only the automated seizure detection (ASD) function, and B (lower panel): false positive rates (FPR) by case for the ASD function.
Fig. 4. (A, B): A seizure is “incorrectly” marked on the automated detection (vertical bar, bottom screen), while the raw EEG trace seems to show essentially artifacts. B: After activation of the artifact reduction function, no seizure is indeed observed (same position as Fig. 3A).
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 s, operating as an on-line seizure detection (Saab and Gotman, 2005).

The overall detection sensitivity of IdentiEvent 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 patients in the epilepsy monitoring units or EEG laboratories, and assessed very little data concerning seizures recorded in ICU settings. When the IdentiEvent 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 Persyt 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 s), subtle diffuse electrodecrements, without any obvious evolution (Fig. 2). Conversely, false detections corresponded to muscle artifacts or electrode failures, or to prolonged GPEs. 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.

References


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