35th Annual International Conference of the IEEE EMBS
Osaka, Japan, 3 - 7 July, 2013

Absence Seizure Epilepsy Detection using linear and nonlinear EEG analysis methods

Vangelis Sakkalis, Giorgos Giannakakis, Christina Farmaki, Abdou Mousas, Matthew Pediaditis, *Member IEEE*, Pelagia Vorgia, and Manolis Tsiknakis, *Member, IEEE*

***Abstract*—In this study, we investigated three measures capable of detecting absence seizures with increased sensitivity based on different underlying assumptions. Namely, an information-based method known as Approximate Entropy, a nonlinear alternative (Order Index), and a linear variance analysis approach. The results on the long-term EEG data suggest increased accuracy in absence seizure detection achieving sensitivity as high as 97.33% with no further application of any sophisticated classification scheme.**

I. Introduction

EPILEPSY is the second (next to stroke) most common neurological disorder affecting approximately 1% of the world' s population. Among the different kind of seizures, absence or petit mal seizures are brief, generalized epileptic seizures of sudden onset and termination, characterized by generalized spike-and-slow wave discharges leading to consciousness impairment. Clinical manifestation includes interruption of ongoing activities, a blank stare, possibly a brief upward rotation of the eyes, speech slowing or interruption, walking interruption, etc. The attack lasts from a few seconds to half a minute, and evaporates as rapidly as it commenced. Electroencephalography (EEG) still remains the main diagnostic modality for absence seizures, even if it is often combined with MRI mostly to rule out false diagnosis related to brain tumor or stroke. When findings in the EEG are dubious, the neurologist needs to assess the clinical image through synchronized Video-EEG monitoring. Recently the automatic analysis of the video from recorded seizures has been reported in order to quantify the clinical image and propose video-based seizure detection methods [1]. However, visual seizure detection of long-term EEG is a very tedious and time-consuming that has not yet reached the reliability point to allow clinical translation. On the contrary, automated analysis of epileptic EEG signals, especially during the last couple of decades, has been proved very efficient in facilitating epilepsy diagnosis and long-term EEG seizure detection.

Manuscript received April 15, 2013.

V. Sakkalis, G. Giannakakis, C. Farmaki, A. Mousas, M. Pediaditis and M. Tsiknakis are with the Institute of Computer Science, Foundation for Research and Technology, Heraklion 71110, Greece (e-mail: {sakkalis; ggian; xfarmakh; mped; tsiknaki}@ics.forth.gr).

M. Tsiknakis is also with the Department of Applied Informatics and Multimedia, Technological Educational Institute of Crete.

P. Vorgia is with University of Crete, Department of Mother and Child Health, Faculty of Medicine, Greece (e-mail: lvorgia@med.uoc.gr).

In this direction, numerous methodologies addressing childhood epilepsy have been proposed assessing nonparametric and parametric techniques, such as wavelets and ARMA techniques [2], as well as multivariate linear and nonlinear approaches [3]. Although those studies accomplish very promising results they are not addressing in particular the absence seizure syndrome and fail to achieve optimal results. In this work, we focus on absence seizures and test various detection algorithms, in order to select the most promising ones based on their performance in terms of accuracy, sensitivity, specificity and applicability in the clinical practice. The algorithms tested include bivariate synchronization measures: Phase Locking, Nonlinear Interdependence and Cross-Correlation [3], and univariate measures: Approximate Entropy (*ApEn*) [4], Ordinal Pattern Analysis-Order Index (*OI*) [5] and Multiscale Variance Analysis (*MVA*). Out of these approaches we further investigate *ApEn*, *OI* and *MVA*, since they were found to perform best. The first reflects an information-based measure, the second a nonlinear one and the latter a linear alternative. All presented measures are based on different underlying assumptions discussed in section IV.

II. Methods

A. Data acquisition and analysis

The EEG signals used in this work arise from 8 patients with epilepsy, 4 males and 4 females, aged between 2 and 10 years. Surface EEG was recorded from all patients during routine long-term Video-EEG monitoring sessions at the University General Hospital of Heraklion. Informed consent for usage of the EEG for research purposes was obtained from the patient's parents. A neurologist expert identified epileptic seizures and all of them were classified as absence-like generalized seizures. EEG signals were recorded from 21 electrodes of the 10/20 International montage that were placed as follows: Fp1, Fp2, F7, F3, Fz, F4, F8, T3, C3, Cz, C4, T4, T5, P3, Pz, P4, T6, A1, A2, O1, O2. Subjects were grounded with an electrode located between Fp1 and Fp2 on the subject's forehead. 75 artifact-free segments, containing seizures, were used in the analysis [7], and 73 segments of normal seizure-free segments of 5s were selected in order to check the method's power in detecting false positives.

B. Approximate Entropy (ApEn)

ApEn was introduced as a quantification of regularity in

sequences and time series data, initially motivated by applications to relatively short, noisy data sets [4]. Approximate entropy represents the predictability of future values in a time series on the basis of previous values, with larger values corresponding to more complexity or irregularity in the data. Given N data points from a time series $X(n)=\{x(n)\}=\{x(1), x(2),., x(N)\}$, the *ApEn* value is calculated through the following steps:

1. The vector sequences $X_v(1), X_v(2),..., X_v(N-m+1)$, are formed defined by $X_v(i)=\{x(i), x(i+1)..., x(i+m-1)\}$, which represent m consecutive values, commencing with the i^{th} point.

2. The distance between $X_v(i)$ and $X_v(j)$ is calculated, defined by

$$d\left[X_v(i), X_v(j)\right] = \max_{1\le k\le m}\left\{\left|x(i+k-1)-x(j+k-1)\right|\right\} \quad (1)$$

3. For each $X_v(i)$ the number $N_i^m(r)$ of vectors is calculated

$$d\left[X_v(i), X_v(j)\right] \le r \quad (2)$$

with r representing the noise filter level.

Then, we estimate the parameters C_i^m as,

$$C_i^m(r) = \frac{N_i^m(r)}{N-m+1} \quad (3)$$

4. We define $\phi^m(r)$ as the mean value of the parameters C_i^m:

$$\phi^m(r) = \frac{\sum_{i=1}^{N-m+1} \ln C_i^m(r)}{N-m+1} \quad (4)$$

5. *ApEn(m,r,N)* is calculated using $\phi^m(r)$ and $\phi^{m+1}(r)$ as follows:

$$ApEn\left(m,r,N\right) = \phi^m(r) - \phi^{m+1}(r) \quad (5)$$

ApEn measures the logarithmic likelihood that runs of patterns that are close (within r) for m contiguous observations remain close (within the same tolerance width) on subsequent incremental comparisons.

Various parameters are involved in the calculation of *ApEn* that can alter the results. Except embedding dimension (m), noise filter level (r), and data length (N), there is the decision whether the standard deviation used in noise filter level would be calculated from the original data series or from the individual selected EEG segments. In addition, the number of consecutive samples with *ApEn* values below a threshold, in order for a segment to be characterized as a seizure, is of paramount importance, as well as the threshold value itself. Even though these parameters are critical in calculating *ApEn*, there is no specific methodology for their optimal determination. Most of research works related to *ApEn* use the parameters described in [4] as a rule of thumb. However, as signals of different sources and pathologies can have quite different properties, these parameters should be determined, based on each specific use.

C. Order Index (OI)

The order index is a measure that can quantify the degree of order of a non-stationary time series, which makes it suitable for the analysis of the inherently non-stationary EEG signals. It can be calculated through an ordinal time series analysis, which was first proposed by Bandt and Pompe [8]. According to this approach, given a scalar time series $x_1, x_2, \mathrm{K}, x_N$ an embedding procedure forms a vector $X_t = [x_t, x_{t+\tau}, \mathrm{K}, x_{t+(m-1)\tau}]$, with the embedding dimension m and the time lag τ. Then, X_t is rearranged in an increasing order: $[x_{t+(j_1-1)\tau} \le x_{t+(j_2-1)\tau} \mathrm{K} \le x_{t+(j_m-1)\tau}]$. For m different numbers, there will be $m!$ possible permutations π, or also called ordinal patterns. If $C(\pi)$ is the number of occurrences of π, the relative frequency of each ordinal pattern π is calculated by $p(\pi) = C(\pi)/(N-(m-1)\tau)$, which can be re-sorted in descending order, thus yielding the rank-frequency distribution $p(\pi_R)$.

Ouyang *et al.* in [5] introduce a measure called order index (*OI*), which quantifies the degree of order (non-randomness) of an EEG time series. To this end, a surrogate time series can be generated by random shuffling of the original time series, thus maintaining the same distribution of the original data, while destroying their ordinal patterns. Assuming that any ordinal index has the same probability of occurrence in the shuffled data, the order index is defined:

$$OI_m = \sqrt{m!/m!-1}\sqrt{\sum_{i=1}^{m!}\left(p(\pi_{R_i}) - p_e\right)^2} \quad (6)$$

where $p(\pi_{R_i})$ represents the rank frequency of the EEG series and $p_e = \{1/N, \mathrm{K}, 1/N\}$ represents the uniform distribution. Low values of the order index indicate more noisy and random data, while higher values indicate EEG data with more regular and deterministic information.

In the current study, the order indices of short overlapping windows of the EEG recordings were calculated using Eq. (7). The embedding dimension was chosen as the minimum that satisfies the condition $N \ge (m+1)!$, in order to allow every possible ordinal pattern of this dimension to occur in a time series of length N (satisfying $m! \le N-(m-1)\tau$), as well as to avoid undersampling (satisfying $N>>m!+(m-1)\tau$) [9]. A threshold was applied to detect possible seizure activity, using the procedure described in Section II-E.

D. Multiscale Variance Index (MVI)

Statistical variance is a measure that describes how dispersed is a set of values around their arithmetic mean. While, in an EEG recording, the pre-seizure period has a relatively low variance, the onset of an absence seizure is characterized by the typical spike-and-wave pattern, which contains extremely high values. Thus, segments that contain parts of the seizure are expected to have high variance.

After segmenting the time series with a sliding window, the variance of each segment is calculated. Only those segments with variance higher than the mean of all the variances are selected. To avoid seizure-free segment selection that happens to have variance above the mean we require a certain amount of consecutive segments to have variance above the mean. In our study, this amount was set to segments corresponding to 4 sec. The first and the last segment of the longest run of consecutive above-threshold segments contain the onset and end of the seizure, respectively.

Multiscale application is achieved using the same procedure applied to the above two segments with a smaller window and sliding step. Keeping only the first segment of the run-up for the onset and the last for the end, two more segments are generated. The new segments, smaller in length due to the smaller window, are contained at the initial segments and still carry the beginning and end of the seizure. In a recursive way, one is able to zoom-in from the initially peaked segments and focus on narrower and narrower segments providing better estimates for the onset and end of the seizure. The recursion procedure terminates when the sliding step reaches the value of 1 sample length.

E. Threshold and seizure detection rule determination

Seizures are detected if they last approximately 4-10 sec. Hence, the amount of consecutive measure values needed to be below the threshold was set to samples corresponding to 4sec. Threshold can be extracted from normal and artifact free EEG periods using the Chebyshev inequality:

$$P\{|Measure(n) - \mu| \geq k\sigma\} \leq \frac{1}{k^2} \qquad (7)$$

where μ, σ are the mean value, standard deviation of the selected measure distribution and k the chosen statistical threshold. The Chebyshev inequality is applicable for any statistical distribution and is not limited only to normal distribution.

III. Results

Our study was able to identify and visualize the seizure onset period using different analysis methods. For the final evaluation, a period starting at 17000 samples before and ending at 10000 samples after the seizure was selected. To evaluate each method' s performance, sensitivity, specificity and accuracy measures were calculated and are presented in Tables I,II. Sensitivity is the percentage of seizures correctly recognized by the method, specificity represents the percentage of normal EEG segments classified correctly as seizure free, and accuracy represents the percentage of both seizure and non-seizure segments correctly classified.

A. Approximate Entropy (ApEn)

ApEn was estimated from the EEG signals in sliding overlapping windows of length of 512 samples (2 sec) and a step of 256 samples (1 sec), with m=2 and r=0.1*standard deviation of each waveform data. The threshold was set to meet the criterion of having a confidence level of 90% for the *ApEn* values. A typical variation of all measures is presented in Figure 1.

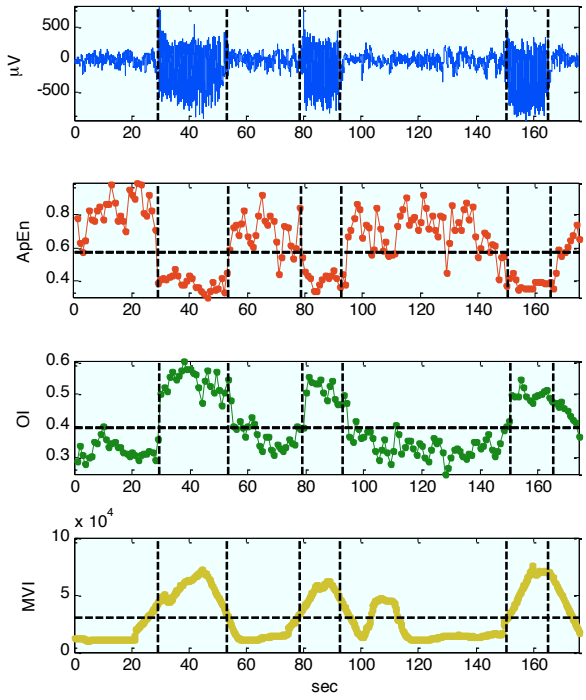

Figure 1. EEG recording at the *Cz* channel, containing seizures and corresponding variation of *ApEn, Order Index (OI)* and *Multiscale Variance Index (MVI)*. The vertical dashed lines denote the start and end of a seizure, while the horizontal dashed line represents the detection threshold.

The seizure detection rule could detect the presence/ absence of a seizure. It is observed that *ApEn* decreases during a seizure. A seizure segment presents repetitive patterns resulting in low values, whereas the normal EEG is not predictable in terms of its morphology. It can be observed that a great value of sensitivity and accuracy is achieved. Also, it is notable that all normal seizure-free EEG segments are classified correctly. *ApEn* values of epileptic EEG appeared to be significant lower than those of normal EEG (Mann-Whitney Test, $p<0.001$).

B. Order Index (OI)

OI was estimated for all the aforementioned EEG epochs for sliding overlapping windows of length of 512 samples (2 sec) and a step of 256 samples (1 sec). Consequently, the embedding dimension was chosen to be m = 4 and the order indices of each window were averaged over a short range of time lags (τ: 1- 5) to decrease fluctuations of the estimates. The statistical threshold k was chosen to be k=4.5. A seizure is detected if *OI* has a value higher than the threshold for a

number of consecutive windows corresponding to 4 seconds in length. It is obvious from the results presented in Tables I, II that *OI* can accurately detect the majority of the seizures. All the remaining seizures had shorter duration than the typical duration of 4-10s, thus failing to pass the threshold of the consecutive windows of 4s length. In addition, the algorithm achieved to correctly classify the "clean" seizure-free data segments as 'no seizure', but 10 false positives were detected in neighboring segments close to the seizures.

C. Multiscale Variance Index (MVI)

Channel selection is integrated in the algorithm. For every EEG signal the channel with the maximum variance was selected for the subsequent segmentation. The initial window was 10sec (2560 samples) in length with a sliding step of 0.25sec (64 samples). The number of consecutive segments for classifying a run-up as a seizure was set at 2x(Window Length/ Sliding Step) or 80 consecutive segments. Tables I and II summarize the performance of the algorithm. Given that a segment contains enough part of the seizure to raise its variance above mean, the ratio (Window Length/ Sliding Step) expresses the number of consecutive segments that still contains that same part. The multiplier ($\geq$1) controls the extra consecutive segments that one wishes to add at the head and tale of the run-up as the sliding window enters and exits the seizure part. Because of the relatively large initial window, the algorithm is biased towards detecting seizures longer in duration leading to lower sensitivity rates. The use of a smaller window (e.g. 2 sec), although it was found to increase the sensitivity significantly, it produced higher false positives, too.

TABLE I
DISTRIBUTION OF CONTINGENCY TABLE

		Seizure		
		Present	Absent	Total
ApEn	Positive	**73**	14	87
	Negative	**2**	73	75
	Total	75	87	162
OI	Positive	60	**10**	70
	Negative	15	73	88
	Total	75	83	158
MVI	Positive	57	**10**	67
	Negative	18	73	91
	Total	75	83	158

TABLE II
SYSTEMS' PERFORMANCE MEASURES

	Performance Measures		
	Sensitivity	*Specificity*	*Accuracy*
ApEn	**97.33%**	83.91%	90.12%
OI	80%	**87.95%**	84.18%
MVI	76%	**87.95%**	82.28%

IV. Discussion

The results presented in this work indicate that the proposed analysis methods are able to detect absence seizures with increased certainty. Although, *ApEn* was able to achieve great discrimination power in terms of sensitivity reaching 97%, specificity was higher in *MVI* and *OI* (reaching 88% for both methods). Since the presented measures outperform each other in different performance measures, it is expected to achieve even better results if fused together by more sophisticated classifiers than just the threshold criterion. However, our approach in this work has been articulated with straightforward application of the involved algorithms.

In comparing the presented approaches with other published works related to absence seizures the sensitivity results we achieved are better than the multiple signal classification, autoregressive and periodogram methods presented in [6], achieving maximum classification accuracy of 92% (sensitivity: 90%, specificity 93.6%) applying artificial neuronal network (ANN) classifiers in 5 epileptic patients. A wavelet-based method [7] was able to reach a sensitivity of 97.2% using a support vector machine (SVM) in 19 patients diagnosed with childhood absence epilepsy. Under this prism, the presented approaches seem promising if feature fusion, sophisticated classifiers and optimal parameter sets are used. Additional studies engaging more subjects and testing the robustness of each method against artifacts and other epileptic-like brain activity is expected to enhance detection accuracy and validate these findings further.

References

[1] M. Pediaditis, M. Tsiknakis, L. Koumakis, M. Karachaliou, M. Voutoufianakis, P. Vorgia, "Vision-Based Absence Seizure Detection, " *in Proc.* 34th Annual International Conference of the IEEE EMBS, San Diego, California USA, 28 August - 1 September, 2012.

[2] V. Sakkalis, T. Cassar, M. Zervakis, K. P. Camilleri, S. G. Fabri, C. Bigan, E. Karakonstantaki, and S. Micheloyannis, "Parametric and nonparametric EEG analysis for the evaluation of EEG activity in young children with controlled epilepsy", *Comput Intell Neurosci*, 465293, 2008

[3] V. Sakkalis, C.D. Giurcaneanu, P. Xanthopoulos, M.E. Zervakis, V. Tsiaras, Y. Yang, E. Karakonstantaki, S. Micheloyannis V. Sakkalis, , "Assessment of linear and nonlinear synchronization measures for analyzing EEG in a mild epileptic paradigm", *IEEE Trans Inf Technol Biomed*, 13: 433-441, 2009

[4] S. Pincus "Approximate entropy as a measure of system complexity". Proc. Nati. Acad. Sci. USA, Vol. 88, pp. 2297-2301, March 1991.

[5] G. Ouyang, C. Dang, D. A. Richards, and X. Li, "Ordinal pattern based similarity analysis for EEG recordings", *Clin Neurophysiology*, 121:694-703, 2010

[6] A. Alkan, E. Koklukaya, A. Subasi, "Automatic seizure detection in EEG using logistic regression and artificial neural network," *Journal of Neuroscience Methods*, vol. 148, pp. 167-176, 2005.

[7] U.R. Acharya, , *et al.*, Automated diagnosis of epileptic EEG using entropies Biom. Sig. Proc. and Control, 2012, 7, pp. 401 – 408.

[8] C. Bandt, and B. Pompe, "Permutation entropy: a natural complexity measure for time series", *Phys Rev Lett*, 88:174102, 2002

[9] J. M. Amigo, S. Zambrano, and M. A. F. Sanjuan, "True and false forbidden patterns in deterministic and random dynamics", *Europhysics Lett*, 79: 50001, 2007.