An autonomous real-time single-channel detection of absence seizures in WAG/Rij rats

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Abstract. This paper presents a real-time, completely automated and patient independent algorithm for detection of absence seizures in WAG/Rij rats as a valid animal model of human absence epilepsy. Single-channel EEG recordings containing totally 488 seizures from 8 WAG/Rij rats were analyzed using the real-time SWD detection algorithm. The proposed algorithms based on the variation of wavelet power to the background power in two specific frequency bands whose spectral power are highly correlated with SWDs. The wavelet powers of two specific frequency bands are calculated with a pattern-adapted mother wavelet and compared with an adaptive ratio of background power of each frequency band. The results indicate used algorithm is able to detect the whole 488 seizures within less than 1 s with sensitivity of 100%. The average precision for 1200, 1400 and 1600 point of window size was 95.2%, 98.3% and 99.17%, respectively. The present algorithm, with its high sensitivity and specificity, could be used for further studies of absence seizures in humans and rats and could be implemented as real-time system for closed loop deep brain stimulation systems.

Key words: Absence epilepsy — EEG — WAG/Rij rats — Wavelet analyses — Pattern-adapted wavelet

Introduction

Absence seizures are generalized non-convulsive seizures most common in childhood. These types of seizures that are also referred to as petit mal seizures, have two essential components: clinically, disorder in consciousness (absence); Electroencephalography (EEG), presence of Spike and Wave Discharges (SWDs) in EEG signals. Duration of absence seizure varies from a few seconds to half a minute and some epileptic patients may experience up to hundreds of attacks in a day (Crunelli and Leresche 2002). Knowing the number of seizures and duration of each seizure is a key factor to evaluate the efficacy of a drug or other interventional therapy in order to treat seizure disorders. Generally, visual detection on absence seizures is less practical due to their brief duration, high frequency of occurrence and subtle clinical manifestations (Xanthopoulos et al. 2009). So development of an algorithm that is able to automatically detect these types of seizures with an acceptable accuracy is an effective support to epileptic patients. Unfortunately, 30% of epilepsy patients cannot be treated appropriately by any available therapies such as antiepileptic drugs or surgery. In such cases, a real-time system that capable of detecting seizures onset and their instant suppressing can take epilepsy under control. Genetic animal models with "spontaneous, episodic, paroxysmal and recurrent" seizures are needed to study the basic mechanisms of human absence epilepsies since genetic factors play the most important role in the research towards the generalized epilepsy syndromes (Löscher 1984). We have used WAG/Rij rats as a mostly accepted animal model of human absence epilepsy. They share many clinical and electroencephalographic characteristics with human absence seizures (Löscher 1984; Van Luijtelaar and Coenen 1986). In animals with absence seizures, SWDs usually have a mean frequency of 7–8 Hz. Moreover, using Fourier transform, it

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has been revealed that the frequency of SWDs is 10–11 Hz at the onset and 7–8 Hz at the end of spike and wave discharges (Drinkenburg et al. 1993). In recent years, various methods have been applied to detect absence seizures in both human and animal subjects. The time-frequency domain approaches are the most appropriate method to analyze non-stationary signals such as EEG and electrocardiography (ECG) (Van Hese et al. 2003; Xanthopoulos et al. 2009; Ovchinnikov et al. 2010).

In the majority of the reported methods for detection of epileptic seizures, researchers used patient-specific methods. These methods have higher performance compared to generic methods due to consistency of seizure and non-seizure EEG characteristics of each patient and their great heterogeneity across patients of the same type of epilepsy. However, generic methods with high sensitivity and accuracy are easier and faster to apply and more appropriate for clinical usage. There are very few studies on generic detection of absence seizures. We propose a real-time generic seizure detection method based on the power spectra of Continues Wavelet Transform (CWT) with pattern-adapted mother wavelet in two specific frequency bands that is capable to detect the onset and offset of seizures in WAG/Rij rats. In this generic method, the performance of the algorithm does not depend on the individual properties of EEG signals of each rat and the parameters of the algorithm are set in advance.

Materials and Methods

Animal

Eight adult male WAG/Rij rats with 250 g mean body weight and 6–8 months old were enrolled in this study. They were purchased from Shefa Neuroscience Research Center in Tehran, Iran. The animals were cared under laboratory condition (temperature 22°C, light/dark 12/12 hours) cycle and unlimited access to food and water). Before surgery, the rats were housed in small groups at single cage, but after surgery they were housed separately. We worked on the animal ethics of Tabriz University of medical sciences.

Surgery

The rats were anaesthetized with injection of ketamine (60 mg/kg, *i.p.*) and xylazine (20 mg/kg, *i.p.*) (Gorji et al. 2011). Two cortical monopolar stainless steel electrodes were implanted in the frontal (Coordinates: AP: 0.22 mm, L: 0.24 mm) and occipital cortex (Coordinates: AP: −11.04 mm, L: 4 mm) for EEG recording using a stereotaxic instrument and Paxinos and Watson atlas (Paxinos and Watson 2006). The coordinates were taken with bregma zero-zero and skull

flat position. The frontal electrode was for recording and the occipital one was used as ground. The electrodes were wire stainless steel (WPI, 0.05" bare, 0.08" coated) and fixed in the socket with dental cement and the socket was fixed to the skull.

Recording

One week after the surgery, the animals were located in a Faraday cage in freely moving condition for signals recording. The head sockets of rat were connected to flexible and shielded copper cables for EEG recording. Prior to signal recording, we let rats to adapt with environment for 30 minutes. The signals were amplified by a DAM 80 AC amplifier (WPI Inc., USA) and filtered by a 50 Hz Notch filter. Then, the signals were digitized by a Powerlab instrument running the Chart software (ver. 05, AD Instrument, Australia) with a sampling rate of 1 kHz, and finally saved in the lab chart formatted data. The animals were free to move in an isolated chamber and only restricted by attached cables. In these rats, SWDs occurs mainly during quiet awakeness and drowsiness but rarely during rapid eye movement (REM) sleep or active wakefulness (Kostopoulos 2009).

Analysis

One-channel EEG data was analyzed over a window of a certain width with 50% overlapping between windows. The wavelet power of the both frequency bands were calculated and compared with a ratio of the background power for each window.

CWT is provided by equation (1):

$$C(b,s) = \int_{-\infty}^{+\infty} x(t)\Psi^{*}_{s,b}(t)\,dt \tag{1}$$

$$\Psi_{s,b}(t) = \frac{1}{\sqrt{s}}\Psi_{0}\left(\frac{t-b}{s}\right) \tag{2}$$

where x (t) is the signal to be analyzed. Ψ^{*}(t) is the complex conjugation of the wavelet or the basis function Ψ(t) represented by equation (2).

The mother wavelet used to generate all the basic functions is designed based on some desired characteristics associated with that function. The translation parameter *b* relates to the location of the wavelet function as it is shifted through the signal. Thus, it corresponds to the time information in the Wavelet Transform. The parameter *s* relates to the stretching or compressing of the wavelet function and corresponds to frequency information. The mother wavelet is a normalized function with an average of zero and limited energy (Mallat 1999).

Seizure detection

Developing a valid wavelet based on a desired pattern allows exploiting the advantages of matched filtering in the framework of the CWT. Since, the EEG signals of epileptic seizure epochs contain a superposition of dilated and translated versions of SWD patterns, these patterns and the values of the scale-position pairs should be identified. Hector Mesa (2005) has illustrated the capability of the pattern adapted wavelet procedure to detect the epileptic spikes in EEG signals. We have constructed a pattern adapted wavelet approximating form spike and wave discharges using one of the available methods in Matlab Wavelet toolbox. Pattern adapted wavelet was constructed based on the method proposed by Mesa and the constructing procedure has been given in the Matlab as an example entitled "Epileptic Spikes in EEG Signals- Constructing Adapted Wavelets from a Single EEG Channel". The constructed mother wavelet fulfills the requirements for wavelet bases (e.g., continuity, zero mean amplitude, and finite or near finite duration). This wavelet is real and appropriate for CWT. We used wavelets without FIR filter and scale function. The predefined families of such wavelets include Morlet and Mexican hat. Moreover, the detection algorithm based on complex Morlet wavelet resulted in precise detection of seizures in EEG of WAG/Rij rats (Sitnikova et al. 2009; Ovchinnikov et al. 2010).

Figure 1 illustrates the pattern adapted mother wavelet constructed from the spike and wave discharges of the EEG signals recorded from the WAG/Rij rats. We have calculated the CWT of the EEG signals using the pattern adapted wavelet and complex Morlet wavelet (Cmor) for specific frequency bands. We compared seizure detection performance of the adapted wavelet to the complex Morlet wavelet. For early detection of seizures, among all the scales usually used in the decomposition of EEG signal, we are interested in the frequency band in which the onset of SWDs activity appears (~10–11 Hz). By focusing on this low frequency range, the high frequency artifacts are neglected. Moreover, the spectral analysis of EEG signal demonstrated that some high frequency components (30–80 Hz) also appear in the EEG during SWDs. Therefore, the other artifacts such as movement artifacts and normal physiological state changes (e.g. sleep episodes) are ignored by considering this high frequency band. Sleep episodes are characterized by high-voltage synchronized activity and often accompanied by sleep spindles (7–14 Hz) (Sitnikova et al. 2009). The wavelet power in the mentioned frequency ranges in each window was calculated and the spectrogram of SWDs is depicted in Figure 2 where these two frequency bands are also shown. The sum of the calculated wavelet power in each individual frequency gives the absolute wavelet power over the whole frequency range. The absolute wavelet power for the both frequency bands were calculated in each window and compared with a ratio $(R(i))$ of the background power of each frequency range. When the values of absolute wavelet power in both frequency bands are greater than the ratio times of background power, a seizure was detected. The background power for each frequency range, $BP(i)$, was estimated as the mean of absolute wavelet powers in a non-epileptic region. The
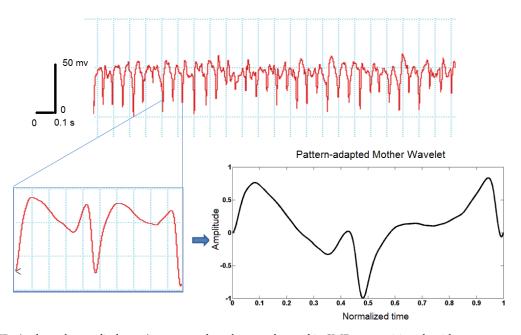

Figure 1. SWDs (spike and wave discharges) pattern and mother wavelet used in SWDs recognition algorithm.
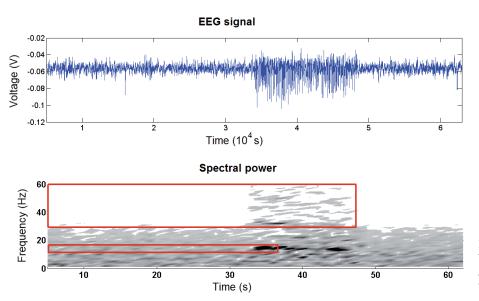
EEG signal

Spectral power

Figure 2. Two specific frequency bands used for seizure detection and changes of wavelet power in these bands.

value of background power for each frequency band was updated in each window for normal EEGs and this value was retained for seizure epochs. Figure 3 depicts the mechanism of seizure detection in the two frequency bands.

Firstly, the value of R(i) was determined for each animal individually and the results of pattern-adapted-based and Cmor-based seizure detection algorithms were compared. After finding the best mother wavelet, we improved the algorithm by automatic calculation of detection ratio. The value of the R(i) was varied during seizure and normal epochs for

accurate determination of seizure onset and offset. Then, the algorithm automatically identifies its incorrect detections with calculating the duration of last seizure and adjusting the value of R(i) for more precise detection in the next epochs.

Results

The results of pattern-adapted-based and Cmor-based seizure detection algorithms for a window size of 1400 ms

Wavelet power spectrum for f = 30:80

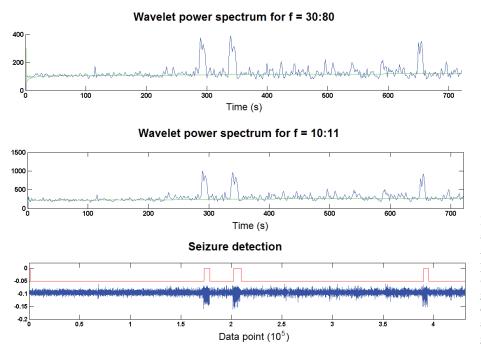**Wavelet power spectrum for f = 10:11**

Seizure detection

Figure 3. EEG signals and detected seizure events by our algorithm. **A.** Wavelet power and background power for frequency range of 30–80 Hz. **B.** Wavelet power and background power for frequency range of 10–11 Hz. **C.** EEG signals of rat 1 and seizures realm detected by algorithm.
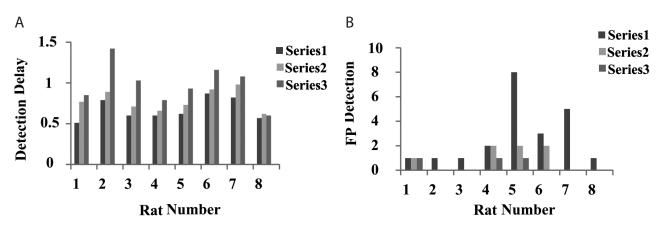
A

B

Figure 4. Results of seizure detection algorithm for three sizes of window (Series1, Series2 and Series3 indicate the result of size of 1200, 1400 and 1600 ms, respectively). **A.** Average of time required to detect seizure of each rat. **B.** Number of False Positive Detection for each rat.

are given in Table 1 and 2 for 6 rats, respectively. We have compared the performance of each detection algorithm *versus* visual scoring.

In these tables, False Negative (FN) is the number of seizures not detected by seizure detection algorithm. False Positive (FP) is the number of events recognized as seizure in a wrong way and True Positive (TP) is the number of seizures detected correctly by seizure detection algorithm. Sensitivity and precision are also calculated as follows (Altman and Bland 1994; Fawcett 2006):

Precision = TP/(FP + TP) *100
Sensitivity = TP/(FN + TP) *100

The results of Cmor-based detection algorithm were the same as the ones obtained by Ovchinnikov et al. (2010). This comparison has demonstrated that the pattern-adapted-based algorithm has more precision and sensitivity than

Cmor-based detection algorithm. So, we have used the pattern adapted mother wavelet to increase sensitivity and precision of the detection algorithm.

In the last pattern-adapted-based detection algorithm, the value of R(i) was automatically adapted in real-time manner. In this algorithm, we have reduced the number of characteristics that may have impact on algorithm performance such as individual properties in the amplitude of background EEG and the individual threshold value. Therefore, the speed of detection as well as its sensitivity and precision are only depended on the size of window. Since detection of all seizures is crucial, we have tested this algorithm for three lengths of window in which the algorithm has the highest sensitivity. The sensitivity of these sizes of window was 100% and the number of false positive detections and detection delay values were compared. Figure 4 shows the histogram of the false positive detections and detection delay values of the all eight rats for window size of 1200, 1400, and 1600 ms.

Table 1. Results of pattern-adapted-based seizure detection algorithm with individual ratio of background power

Rat Number	FN	TP	FP	Sensitivity (%)	Precision (%)
1	0	24	1	100	96
2	0	78	1	100	98.7
3	0	22	1	100	95.65
4	0	69	1	100	98.6
5	0	84	0	100	100
6	0	47	1	100	97.9
Average	0	54	0.83	100	97.8

FN, False Negative (the number of seizures not detected by seizure detection algorithm); TP, True Positive (number of seizures detected correctly by seizure detection algorithm); FP, False Positive (the number of events recognized as seizure in a wrong way).

Table 2. Results of Cmor-based seizure detection algorithm with individual ratio of background power

Rat Number	FN	TP	FP	Sensitivity (%)	Precision (%)
1	0	24	1	100	92.3
2	0	78	1	100	98.7
3	0	22	1	100	100
4	0	69	1	100	98.6
5	0	84	0	100	100
6	2	45	4	95.75	91.8
Average	0.33	53.67	1.16	99.29	96.9

For abbreviations see Table 1.

Table 3. SWD detection results of 8 WAG/Rij rats for two size of window (W)

		Rat Number								Average
		1	2	3	4	5	6	7	8	
Number of visual detection		24	78	22	69	84	47	58	106	61
W = 1400	FN	0	0	0	0	0	0	0	0	0
	TP	24	78	22	69	84	47	58	106	61
	FP	1	0	0	2	2	2	0	0	0.87
	Sensitivity (%)	100	100	100	100	100	100	100	100	100
	Precision (%)	96	100	100	97.2	97.7	95.9	100	100	98.3
	Detection time after the onset (s)	0.77	0.89	0.71	0.66	0.73	0.92	0.98	0.62	0.79
W = 1600	FN	0	0	0	0	0	0	0	0	0
	TP	24	78	22	69	84	47	58	106	61
	FP	1	0	0	1	1	0	0	0	0.37
	Sensitivity (%)	100	100	100	100	100	100	100	100	100
	Precision (%)	96	100	100	98.5	98.8	100	100	100	99.17
	Detection time after the onset (s)	0.85	1.42	1.03	0.79	0.93	0.93	1.08	0.6	0.99

For abbreviations see Table 1.

As shown in these figures, the window length directly affects speed and precision of SWD detection. If a shorter window is used, it takes less time to detect SWDs, however, the probability of false detection increases. On the other hand, a wider window yields a better precision and, in change, it takes longer time to detect a seizure. It was found that the window sizes of 1400 and 1600 ms are the optimal choices (acceptable speed and highest sensitivity and precision) and provide a reasonable compromise between speed of SWD detection and number of errors. The average precision of the window size of 1200 ms is 95.2% and the seizures are detected after 0.5–0.87 s of visual detection. The results obtained from application of the final pattern adapted-based detection algorithm on the EEG signals recorded from eight different WAG/Rij rats are presented in Table 3. In this table, the sizes of window (W) are 1400 ms and 1600 ms with an overlapping of 50%.

Discussion and Conclusions

This study presents a generic algorithm that is capable of automatic real-time detection of absence epileptic seizures in WAG/Rij rats, as an animal model of human absence seizures. It was found that the proposed algorithm is able to detect SWDs with a high sensitivity and precision as seizure occurs. The algorithm uses the baseline as a reference level to avoid excessive false detections due to noise artifacts that tend to change the overall amplitude of recordings for longer periods of time. Moreover, employing the two frequencies bands whose power spectra changes are highly correlated with SWDs can reduce false detection probabilities during physiological or non-physiological artifacts. Using an adaptive ratio to handle the variability of SWDs amplitude and considering a pattern of SWDs as a mother wavelet have increased the ability of seizure detection.

Generally, very few studies have focused on real-time detection of absence seizures in rats. Only one study by Ovchinnikov et al. (2010) proposed a real-time detection algorithm for WAG/Rij rats. In their report, a real-time reliable algorithm was described for seizure detection in WAG/Rij rats. Although the reported sensitivity was 100% for real-time detection of seizures, the results of 24-h recording analysis showed some missed SWDs. Moreover, the only purpose of their algorithm was to determine the moment of onset of SWDs and the duration of seizures was not measured. Furthermore, their method was only partly automatic since it requires an individually threshold setting for each rat and the precision and sensitivity of method are critically dependent on the appropriate threshold selection.

We have used variable window size and the results of three different window sizes confirmed that accuracy and detection time can be increased by broadening the window size. Therefore, based on the desired application, a tradeoff between the precision and detection delay can be accomplished. The window size of 1600 ms has the highest precision (99.17%) and SWDs can be detected within 0.6–1.4 s after the visual determination of seizure onset. Moreover, the window size of 1400 ms also has more precision and sensitivity than the previous presented works with less than one second detection time.

In conclusion, our seizure detection algorithm, with its high sensitivity and specificity, can be applied for further studies of spontaneous SWDs in humans and rats and can

be implemented as a real-time system for closed loop deep brain stimulation systems. All features needed for implementation of a deep brain stimulation closed loop systems (high sensitivity and precision, real-time detection of SWDs, no need to individual setting for each rats) were included. Moreover, our algorithm has adequate onset detection time for real-time seizure detection applications. Furthermore, our generic single-channel seizure detection algorithm is very appropriate to clinical use due to its auto-matching with patient-specific characteristics which reduce patient handling tasks and lower data processing rate using a single channel EEG data.

References

Altman D. G., Bland J. M. (1994): Diagnostic tests 2: Predictive values. BMJ **309,** 102
http://dx.doi.org/10.1136/bmj.309.6947.102

Crunelli V., Leresche N. (2002): Childhood absence epilepsy: genes, channels, neurons and networks. Nat. Rev. Neurosci. **3,** 371–382
http://dx.doi.org/10.1038/nrn811

Drinkenburg W., Van Luijtelaar E., Van Schaijk W., Coenen A. (1993): Aberrant transients in the EEG of epileptic rats: a spectral analytical approach. Physiol. Behav. **54,** 779–783
http://dx.doi.org/10.1016/0031-9384(93)90092-T

Fawcett T. (2006): An introduction to ROC analysis. Pattern Recognit. Lett. **27,** 861–874
http://dx.doi.org/10.1016/j.patrec.2005.10.010

Gorji A., Mittag C., Shahabi P., Seidenbecher T., Pape H.-C. (2011): Seizure-related activity of intralaminar thalamic neurons in a genetic model of absence epilepsy. Neurobiol. Dis. **43,** 266–274
http://dx.doi.org/10.1016/j.nbd.2011.03.019

Kostopoulos G. (2009): Brain mechanisms linking epilepsy to sleep. In: Encyclopedia of Basic Epilepsy Research. (Ed. P. Schwartzkroin), pp. 1327–1336, Elsevier, London

http://dx.doi.org/10.1016/B978-012373961-2.00112-0

Löscher W. (1984): Genetic animal models of epilepsy as a unique resource for the evaluation of anticonvulsant drugs. Methods Find. Exp. Clin. Pharmacol. **6,** 531–547

Mallat S. (1999): A Wavelet Tour of Signal Processing. Academic press

Mesa H. (2005): Adapted wavelets for pattern detection. In: Progress in Pattern Recognition, Image Analysis and Applications. (Eds. A. Sanfeliu and M. L. Cortes), pp. 933–944, CIARP, Havana, Cuba
http://dx.doi.org/10.1007/11578079_96

Ovchinnikov A., Lüttjohann A., Hramov A., van Luijtelaar G. (2010): An algorithm for real-time detection of spike-wave discharges in rodents. J. Neurosci. Methods **194,** 172–178
http://dx.doi.org/10.1016/j.jneumeth.2010.09.017

Paxinos G., Watson C. (2006): The Rat Brain in Stereotaxic Coordinates. Academic press

Sitnikova E., Hramov A. E., Koronovsky A. A., van Luijtelaar G. (2009): Sleep spindles and spike–wave discharges in EEG: their generic features, similarities and distinctions disclosed with Fourier transform and continuous wavelet analysis. J. Neurosci. Methods **180,** 304–316
http://dx.doi.org/10.1016/j.jneumeth.2009.04.006

Van Hese P., Martens J.-P., Boon P., Dedeurwaerdere S., Lemahieu I., Van de Walle R. (2003): Detection of spike and wave discharges in the cortical EEG of genetic absence epilepsy rats from Strasbourg. Phys. Med. Biol. **48,** 1685–1700
http://dx.doi.org/10.1088/0031-9155/48/12/302

Van Luijtelaar. E., Coenen A. (1986). Two types of electrocortical paroxysms in an inbred strain of rats. Neurosci. Lett. **70,** 393–397
http://dx.doi.org/10.1016/0304-3940(86)90586-0

Xanthopoulos P., Liu C. C., Zhang J., Miller E. R., Nair S., Uthman B. M., Kelly K., Pardalos P. M. (2009): A robust spike and wave algorithm for detecting seizures in a genetic absence seizure model Conf. Proc. IEEE Eng. Med. Biol. Soc. 2184–2187
http://dx.doi.org/10.1109/iembs.2009.5334941