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Automatic Characterization of Dynamics in Absence Epilepsy

Katrine N.H. Petersen*, Trine N. Nielsen*, Troels W. Kjaer†, Carsten E. Thomsen‡ and Helge B.D. Sorensen*
*Technical University of Denmark, Department of Electrical Engineering, Denmark
†Department of Clinical Neurophysiology, Copenhagen University Hospital Rigshospitalet, Denmark
‡Department of Odontology, University of Copenhagen, Denmark

***Abstract*—Dynamics of the spike-wave paroxysms in Childhood Absence Epilepsy (CAE) are automatically characterized using novel approaches. Features are extracted from scalograms formed by Continuous Wavelet Transform (CWT). Detection algorithms are designed to identify an estimate of the temporal development of frequencies in the paroxysms. A database of 106 paroxysms from 26 patients was analyzed. The database is large compared to other known studies in the field of dynamics in CAE. CWT is more efficient than the widely used Fourier transform due to CWTs ability to recognize smaller discontinuities and variations. The use of scalograms and the detection algorithms result in a potentially usable clinical tool for dividing CAE patients into subsets. Differences between the grouped paroxysms may turn out to be useful from a clinical perspective as a prognostic indicator or when adjusting drug treatment.**

I. Introduction

Childhood absence epilepsy (CAE) is a very common disorder, easily recognized due to its characteristic 3 Hz spike-wave discharges observed in the electroencephalography (EEG). Children who suffer from CAE may experience up to several hundred seizures a day. Hence difficulties with concentration, problems with accomplishment of tasks, and limitations in social life can be experienced by the children. The treatment of CAE is often long-term and the patients may be prescribed different types of medicine over time to become seizure free [1]. Suboptimal treatment of patients is a consequence of this long duration and different types of medicine which makes it an interesting subject to study.

EEG is an integral part of the diagnosis of CAE. Analysis of the EEG improves understanding of the spike-wave complexes and a faster diagnosis and optimal treatment may be achieved. A more detailed description of the dynamic development of the fundamental frequency in the paroxysms is subject for investigation. From this, an automatic characterization of the paroxysms can be made along with an identification of subsets of patients. The dynamic development in the paroxysms has been investigated using CWT. CWT has only been used for analyzing and extracting the fundamental frequency in absence epilepsy in few studies [2]. The same decreasing tendency in the fundamental frequency is observed and the advantages of using wavelet transformation and scalograms, instead of Short Time Fourier Transform (STFT) and spectrograms, are widely recognized. Similar research from other studies have been performed on smaller databases and no relationship between scalogram appearance and medical treatment has been investigated before this study. Also, no verification of method by artificial paroxysms have been performed and documented. In this study, it has been possible to try two different mother wavelets on a relatively large database and a relationship between appearance and medical treatment has been investigated.

II. Materials and methods

A. Clinical Data

The study included sEEG-recordings from patients diagnosed with CAE. The data are from Copenhagen University Hospital Rigshospitalet and collected from 8 May 2000 to 30 June 2010. Cadwell Easy II was used to record the data. Data have been sampled at 200 Hz and filtered by an analog bandpass filter with cut-off frequencies at 0.53 Hz and 70 Hz. All analyzed signals are from EEG channel F7-FP1 based on [3].The onset and termination of paroxsysms are marked by board certified clinical neurophysiologist Troels W. Kjaer.

The database contains recordings from 26 patients with a total of 106 paroxysms with duration greater than 4 seconds. Thirteen of these paroxysms are excluded from the analysis of the dynamics characterization, because the patient suffered from disorders changing the characteristic spike-wave complexes. The 13 paroxysms are not excluded from the clinical hypothesis because the scalogram appearance matched the subset criteria. Before analyzing the data in the aspect of the spike-wave complexes, filtration by an FIR equiripple bandpass filter with cut-off frequencies at 2 Hz and 7 Hz was performed. This would exclude most of the high frequencies not relevant for the fundamental frequencies of the complexes, such as the high frequency content of the spikes. The analyzed database of patient paroxysms is larger than seen in other known studies [2] [7] [6].

B. Continuous Wavelet Transform

CWT is in this research used for analysis of the dynamics of the frequencies in the paroxysms and to create scalograms. The frequencies are estimates of the true frequencies. CWT transforms a discrete biomedical signal $s(n)$ and is defined by:

$$W_{a,b} = \frac{1}{\sqrt{|a|}} \cdot \sum_n s(n)\psi(\frac{n-b}{a}) \quad (1)$$

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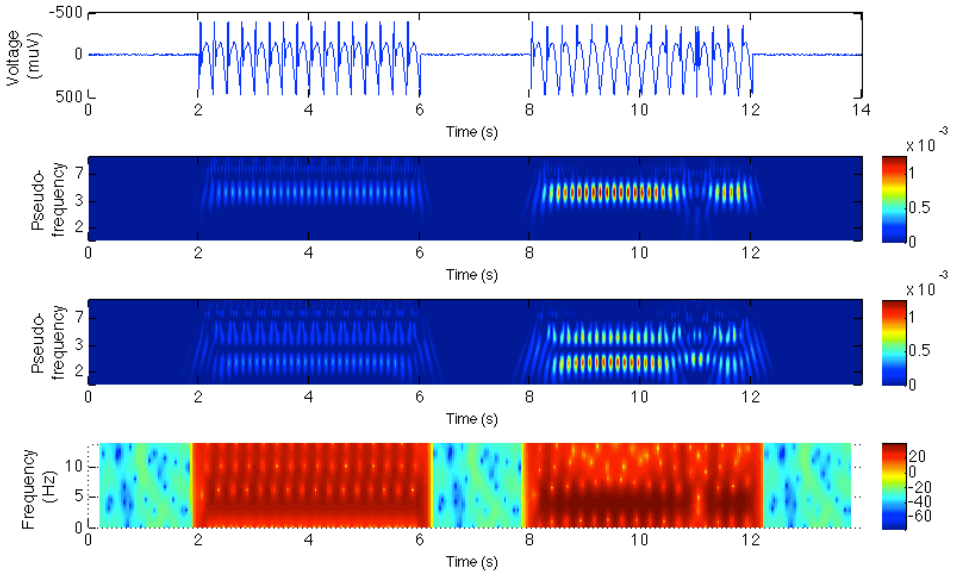

Fig. 1. *Top left:* Artificial paroxysm with fundamental frequencies of 4 Hz for spike-wave complexes, 3 Hz for wave component, and a 16.6 Hz spike component. *Top right:* Artificial paroxysm with wandering spike component in the spike-wave complexes. *Middle:* Scalograms corresponding to the artificial paroxysms made with the Morlet and modified Morlet wavelet, respectively. *Bottom:* Spectrograms corresponding to the artificial paroxysms with a window length of 1.28 sec and an overlap of 90 %. Please notice the nonlinear y-axis due to (4).

where $W_{a,b}$ is the wavelet coefficient, a is the scaling parameter, b is the time-shift parameter, and ψ is the mother wavelet.

1) Mother Wavelets: The mother wavelets used for the CWT in this study is the Morlet wavelet and the modified Morlet wavelet, defined by [2]:

$$\psi(x) = e^{\frac{x^2}{2}} \cdot cos(5x) \tag{2}$$

and

$$\psi(x) = x \cdot e^{\frac{x^2}{2}} \cdot cos(5x) \tag{3}$$

respectively, where x is the variable describing the position and scale of the wavelet. The modified Morlet was developed and described in [2]. These mother wavelets have a similar morphology compared to the spike-wave complex which makes them appealing to use.

C. Scalograms and algorithms

The scalograms are based on the wavelet coefficient and are a visualization of the time-scale relationship of a signal. When calculating the scalograms, an estimation of frequencies from the scales is used. The estimated frequencies are denoted pseudo-frequencies. The relationship between the scales and the pseudo-frequencies is given by [4]:

$$F_a = \frac{F_c \cdot F_s}{a} \tag{4}$$

where a is the scale, F_s is the sampling frequency, F_c is the center frequency of the wavelet, and F_a is the pseudo-frequency. Further on the term frequency will be used for the pseudo-frequency.

The scalogram is a representation of the percentage energy for each calculated coefficient. This percentage energy is visualized by color intensity in the scalograms. An estimate of the dynamics of the fundamental frequency can be found by the use of the two algorithms designed by the authors in [5].

The detection algorithm in relation to the Morlet mother wavelet tracks the fundamental frequency by locating maximum in each sample, extracts the peaks, and then converts the relating scales to frequency. For the modified Morlet, the two highest valued peaks in each sample is detected. The minimum between these maxima in each sample are found and only the ones at the same time instances as the maxima are saved and defined as the fundamental frequency. Outliers are removed based on the standard deviation (std) for both algorithms. If std $<$ 0.5 Hz, data points larger than a factor of $\pm$ 3·std from the mean is removed. If 0.5 Hz $\leq$ std $<$ 0.9 Hz, $\pm$ 1.2·std is removed, and if std $\geq$ 0.9 Hz, $\pm$ std is removed.

Furthermore, artificial paroxysms have been generated, and estimation of the frequencies is carried out using spectrograms as well as scalograms. This is done to compare the use of STFT to the use of CWT, and to support verification of the method.

D. Division of scalograms for clinical hypothesis

In addition to the investigation of the dynamics of the frequencies, the scalograms have been categorized into 10 different groups based on appearance. Two out of the 10 groups were chosen based on the location of the color intensity, their similar duration, and the number of paroxysms in these groups. The two groups have further been tested for the hypothesis of a possible relationship between scalogram appearance and medical treatment.

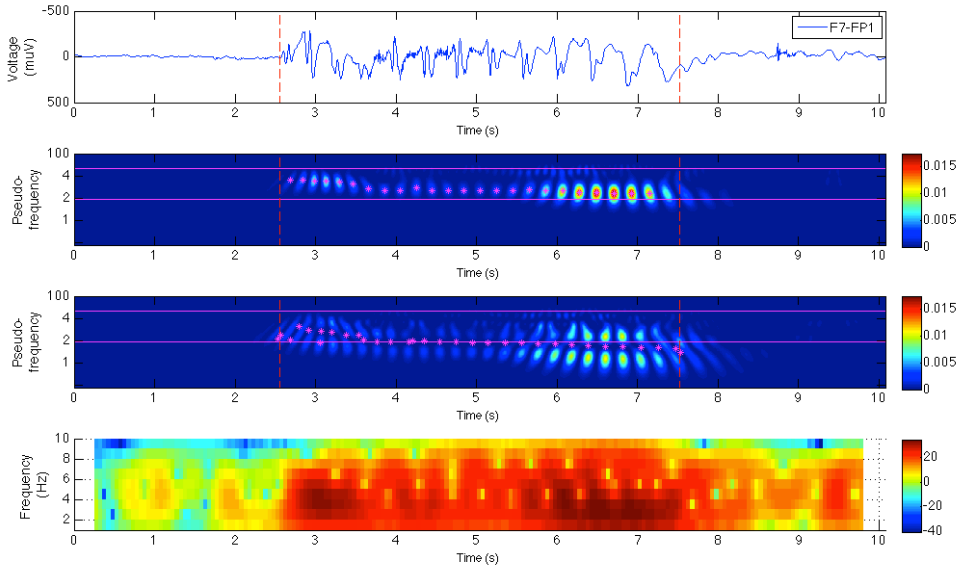

Fig. 2. *Top:* Paroxysm from database. *Middle:* Scalogram corresponding to the paroxysm using first the Morlet and secondly the modified Morlet wavelet. Detection of frequency is shown with magenta colored dots. The horizontal lines represent the 2 and 6 Hz borders. The scalogram belongs to the group with short paroxysms having high color intensity in the terminal phase. *Bottom*: Spectrogram corresponding to the paroxysm, made with a window length of 0.5 seconds and an overlap of 90 %. Please notice the nonlinear y-axis due to (4).

The two groups are defined as:

- Group HITS: Short paroxysms with high color intensity in the terminal phase of the paroxysm.
- Group HIIS: Short paroxysms with high color intensity in the initial phase of the paroxysm.

An example of a paroxysm from group HITS is presented in Fig. 2. An example of a paroxysm from group HIIS will not be visualized in this paper. After categorization of the scalograms, a database research of patient records was performed.

III. Results

A. Analysis of artificial paroxysms

Two different artificial paroxysms have been generated, one with and one without a moving spike component in the spike-wave complexes, see Fig. 1. The detection of the fundamental frequency has been performed for the artificial paroxysm without the moving spike component. The data have been filtered between 2 Hz and 7 Hz to concentrate on the frequency of spike-wave complex. The mean frequency detected using CWT, with the Morlet mother wavelet, was 4.11 Hz with a std 0.188 Hz, and for STFT, the mean was 3.80 Hz with a std $9.001 \cdot 10^{-16}$ Hz. The fundamental frequency of the artificial paroxysm is expected to be equal to the spike-wave complex frequency, being 4 Hz. The Morlet mother wavelet was chosen to be used, because the modified Morlet has an offset in frequency due to the difference in center frequency of the mother wavelets.

The spectrograms are less detailed than the scalograms [4]. The scalograms have therefore been used as foundation of the frequency detection and general analysis of the paroxysms. The fundamental frequency in the spectrograms is seen as the red band expanded from the paroxysm starts until it terminates. In the scalogram, the fundamental frequency is seen as the track along the local maxima, magenta dots in Fig. 1, which facilitate location of the dynamic changes in the scalogram directly. Generation of the artificial paroxysm and corresponding scalogram assures accurate detection of the fundamental frequency in the scalograms of the data, because a basis of comparison between real and artificial paroxysms are made. In some CAE paroxysms, polyspikes have been detected by visual inspection. To see how this translates onto a scalogram, the artificial paroxysm with moving spike is shown in Fig. 1 along with the two corresponding scalograms.

B. Characterize dynamics of the fundamental frequency in CAE

The method tested on artificial paroxysms has been used on the database, using both mother wavelets. A tendency of decreasing fundamental frequency was detected in 80.6 % (using Morlet wavelet) of the scalograms. This corresponds to results seen in similar published studies where the frequency has been detected either with the use of STFT or wavelet transformation [2]. When comparing the two methods with different mother wavelet, an offset in frequency is seen for the method using the modified Morlet. Though the frequency values are not the same in the two methods, the overall dynamic in frequencies are the same which is tested using statistical Z-tests. The detection of the fundamental frequency in a paroxysm is shown in Fig. 2. Here the outliers have been removed. The detection of the frequency dynamics in paroxysms from the database has shown to be very effective, but some outliers are present after automatic removal and thus have to be removed by

TABLE I
MEDICAL TREATMENTS FOR CAE PATIENTS - *Percentage of total amount of paroxysm per group*

MEDICINE	HIIS	HITS
Lamotrigin (LTG)	100 %	23.8 %
Valproat (VPA)	0 %	71.4 %
Ethosuximid (ESM)	14 %	23.8 %
Total	of 7 paroxysms	of 21 paroxysms

post processing of the results.

C. Division of scalograms for clinical hypothesis

The investigation of a possible correlation between medical treatment and appearance of scalograms have led to the information listed in Table I. The medical treatments listed are the medicine that made the child seizure free after the recordings were made.

IV. DISCUSSION

One previous study, [2], use CWT and scalograms as analyzing methods for absence epilepsy as well, but not as an automatic characterizing tool, and the appearances of the scalograms have not been investigated to the same extend as it is the case with this study. The method is verified with artificial paroxysms which contributes to the novel approach used in this study compared to [2]. The larger database used in this research has made automatic categorization of groups possible, and from this, subsets of patients have been successfully identified.

A. Artificial paroxysms and scalograms

By generating artificial paroxysms with known frequencies and amplitude, it is possible to understand, interpret, and explain the appearance of the scalograms, and from this a basis of comparison to the real paroxysms is made. The detection of the fundamental frequency in the artificial paroxysm with stationary spikes using STFT and CWT resulted in almost equal mean frequencies. Although CWT had a higher std, the mean frequency obtained was closer to the ideal value of 4 Hz, compared to the use of STFT. This implies that CWT can detect more details but still capture the mean. STFT resulted in a low std possibly caused by the coarser frequency resolution seen in STFT [4]. The same observation is made when analyzing real paroxysms. For both the artificial and real paroxysms an interaction between the signal components is observed resulting in changes in the dynamics. The CWT can capture these changes which suggests that this method is better than STFT for this study.

The scalograms have shown to be more detailed than spectrograms as well. Because of the better time-frequency resolution, scalograms are more detailed than spectrograms, and in case of an automatic characterization, details are of high priority. The CWT and scalograms are therefore decided to be the preferred methods for characterizing the dynamics in the paroxysms.

Polyspikes have also been identified and recreated in an artificial paroxysm. In Fig 1 it is seen that a change in pattern happens when a polyspike occurs. This can explain why the peaks are not similar in some instances in the scalograms from the real paroxysms. This must be taken into account when visually analyzing the scalograms for the real paroxysms. The high frequency of polyspikes is not a problem in the detection due to the bandpass filtering of data.

B. Clinical hypothesis

An investigation of matching between medicine and appearance of the scalogram has been performed and the following have been observed; A tendency of correlation between the scalograms with high intensity in the beginning phase and Lamotrigin treatment has been identified. The same tendency is seen with the paroxysms, where the intensity is in the terminal phase, and treatment with Valproat, where none of the children with paroxysms, having high intensity in the beginning, were seizure free after a Valproat treatment. These tendencies have only been tested on a small database of 28 paroxysms and should be tested on a larger database.

V. CONCLUSION

The automatic characterization of the dynamics of the frequencies with the use of CWT and scalograms is a novel approach to interpret the paroxysms in CAE. The precision of CWT gives an opportunity to notice small discontinuities and variations in the signal compared to the use of STFT. This approach does what is expected, and it is a method that is highly usefull for detection of the tendencies in the paroxysms, automatically and visually. The use of scalograms has shown to be a potential tool for clinical use, interpretation, and classification of paroxysms. Also, a tendency between the location of color intensity and medical treatment is observed which raises new questions of possible interest in this field of science. If a clear parallel is drawn between the scalograms and the medical treatment, it could optimize the treatment and help improve the lives of the CAE patients.

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