Automated neonatal spike train detection as part of a neonatal seizure detection system

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***Abstract*— Neonatal seizures are an important sign of central nervous system dysfunction and require immediate medical attention. In this paper a new algorithm is presented for the detection of seizures in the electroencephalogram (EEG) of neonates. In contrast to the common approach in the literature, we define two (rather than one) types of seizures. This paper presents a new algorithm for the detection of one of these seizure types, namely a spike train, in the electroencephalogram (EEG) of neonates. The sensitivity of this algorithm is 98%, the positive predictive value 86% with a false positive rate of 0.6 per hour. Preliminary results on this subset indicate a clinically usable algorithm and outperform other published methods. An algorithm for the second seizure type was also developed but will be explained in a follow-up paper.**

I. INTRODUCTION

Seizures occur in approximately 0.5% of all neonates. The causes of seizures are many and various, with 90% of all cases being attributed to biochemical imbalances within the CNS, hypoxic ischemic encephalopathy, intracranial hemorrhages and infarcts, intracranial infection and developmental (structural) anomalies [12]. The manual detection of these seizures is usually based on clinical signs in conjunction with visual assessment of the EEG. In neonates the clinical seizures are often subtle and and may be missed without constant supervision [4]. Also many seizures tend to be subclinical, detected only by EEG monitoring. Furthermore, EEG analysis requires particular skills which are not always present around the clock in the neonatal intensive care unit (NICU). This implies that many seizures are missed [9]. For these reasons an automated system that reliably detects neonatal seizures would be of significant value in the NICU.

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In the literature many seizure detection algorithms have been described. The best known methods are based on computing a running autocorrelation function [8], rhythmic discharges detection [5] and modeling and complexity analysis [3]. Others are based on the extraction of features using entropy, wavelets, frequency content, etc and then training a classifier ([6], [13], [1]) to correctly categorize these features.

In this paper we will use a different approach. Most neonatal seizure detection algorithms make no distinction between different types of seizures. We, on the contrary, defined two seizure types. The first is the spike train type (Fig. 1) , the second the oscillatory type (Fig. 2). The major difference between the two types lies in the fact that the oscillatory type is a fluent, continuous kind of seizure whereas the spike train type consists of spikes interrupted by lower voltage EEG. Different detection algorithms were developed for the two types. During analysis both algorithms run in parallel and a detection occurs if one or both of the algorithms detects a seizure. A novel approach is that the developed algorithms will mimic a human observer reading EEG. In case of a spike train a human observer looks for a repetitive pattern of very similar repeated spikes. Therefore an algorithm based on this strategy must first find these spikes and then check their repetitiveness and similarity. In this paper we will present the spike train detection. The oscillation detection will be discussed in a follow-up paper.

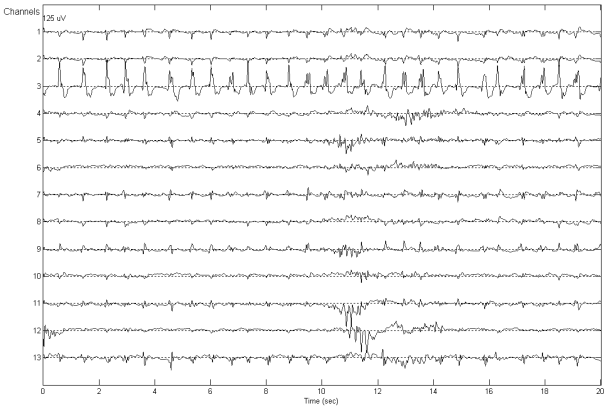

Fig. 1. Example of spike train seizure, dominant on channel 3.

II. METHODS

A. Spike train detection

According to the "human observer approach" we need to look for highly correlated, repetitive, spikelike segments of EEG. Therefore, the algorithm consists of two steps. The

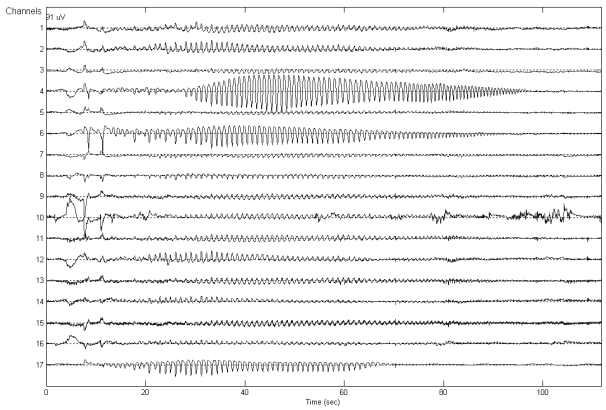

Fig. 2. Example of oscillation seizure, dominant on channel 4.

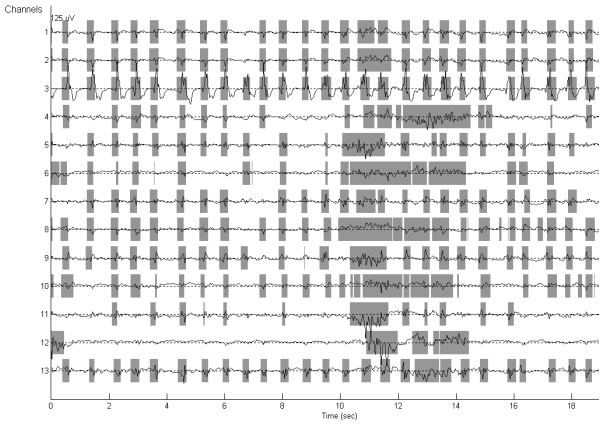

Fig. 3. Segmentation of a spike train. After segmentation only the highest energy segments of the EEG remain.

first step detects highly energetic segments in the EEG. The second step analyses the correlation between these segments.

1) Adaptive segmentation based on non-linear energy: The first step in the segmentation is the calculation of the energy of the EEG by means of a non-linear energy operator (NLEO). This operator is useful to segment the EEG in quasi-stationary segments [2] and is given by (see Appendix 1).

$$\psi_g[X_{(n)}] = X_{(n-l)}.X_{(n-p)} - X_{(n-q)}.X_{(n-s)}, \quad (1)$$
$$l + p = q + s$$

with X_n the current sample, X_{n-l} the l-th sample before sample n, etc. As parameter setting, we used l=1, p=2, q=0 and s=3 [2].

Subsequently, the root mean square (RMS) of the energy is calculated with a moving window of 50 samples and 30 samples of overlap. The resulting RMS signal is a smoothed version of the frequency-weighted energy of the signal.

Next, this signal is divided into overlapping epochs of 15 seconds. Each epoch is thresholded so that only the highest energy signals in the epoch remain. The threshold is adaptive to the signal and defined as:

$$threshold = \frac{1}{2}.std(epoch).q3(epoch) \quad (2)$$

with *std(...)* and *q3(...)* the standard deviation and 75th percentile of the *epoch*, respectively. The 75th percentile guarantees that only the highest energy parts of the signal are selected. The standard deviation adapts the threshold to the variability in the signal. This means that signals with a high variability get a higher threshold. Due to the overlap of the windows some parts of the epoch may be analysed multiple times. Identical segmentations to previous segmentations are rejected. Fig. 3 shows an example of the results from segmentation of a spike train.

Next, the spikiness of each high-energy segment is calculated. The spikiness is defined as:

$$spikiness = \frac{|q3(segment) - q1(segment)|}{|q3(background) - q1(background)|} \quad (3)$$

with *q3(...)* and *q1(...)* the 75th and 25th percentile, respectively. The background is defined as the EEG with a length of the considered spike just before and after the spike (Fig. 4). The goal of this step is to reduce the number of segments used for further analysis, by selecting only the segments surrounded by lower voltage EEG. Introduction of this step was found to lower the false positive rate of the algorithm.

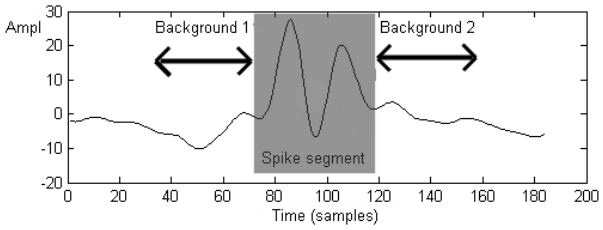

Fig. 4. Definition of the spikiness of a segment. This segment has a spikiness of 3.8.

Besides a certain spikiness, there are a few secondary constraints on the high-energy segments. The minimum length of a segment is 100ms, the maximum length is 2s and the minimum amplitude is 5 μV. These constraints are not very strong but they help to reduce the number of correlations which must be calculated in the next step and so the calculation time is reduced. They also decrease the number of false positives by preventing detection of very small signals (like noise). Those segments that meet all criteria are considered true spikes, and enter the next stage of the analysis.

2) Analysis of the correlation: Our human observer detects a seizure when there is a pattern of repetitive and similar spikes. Our algorithm checks similarity between signals by calculating the correlation between them. To determine if the detected spikes follow a repetitive pattern, the cross-correlations between a certain segment and all other segments present in the preceding 10 seconds of EEG are calculated. If the segments have different lengths, the shortest segment is padded with zeros to the length of the longest. A seizure is detected if the current segment has a maximum cross-correlation higher than 0.8 with a least 5 other segments in the preceding 10 seconds. These 10 seconds are then labeled as seizure activity. Fig. 5 shows 2 similarly spike segments and their cross-correlation.

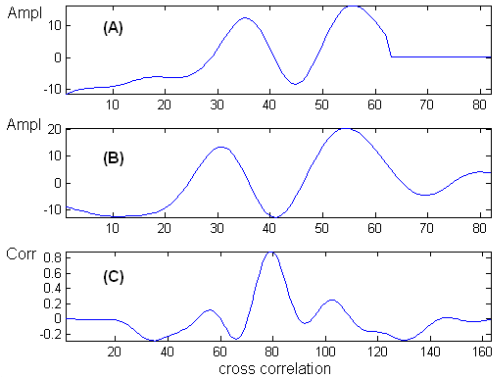

Fig. 5. (A), (B): Two segmented spikes, note the added zeros in figure (A). (C) cross-correlation of the segmented spikes. The maximum value of the cross-correlation is a good measure of similarity between two segments.

TABLE I

Results of the algorithm on 6 patients (tr: training set, te: test set).

Patiënt	*Sensitivity (%)*	*PPV (%)*	*FP/h*	*EEG duration (h)*
1 (tr)	95	81	0.29	24.4
2 (tr)	100	100	0	7.5
3 (tr)	100	86	0.4	7.5
4 (te)	95	85	1.3	7.5
5 (te)	100	78	1	7.5
6 (te)	X	X	X	7.5
mean	98	86	0.6	10.88

III. DATA

All data were recorded at the Sophia Children's Hospital (part of the University Medical Center Rotterdam, the Netherlands). The dataset consisted of long-term video-EEG monitoring of 6 full-term neonates with 13 up to 17 EEG channels according to the 10-20 system of electrode placement. The duration of the EEG was 24.4h for one neonate and 7.5h recordings for the others. Sampling frequency was 256 Hz. All EEG's where scored for seizure activity by an experienced neurologist and all showed seizures of the spike-train type. The algorithm was applied channel by channel. If it detected a seizure in 1 channel, the whole EEG at that time instance was labeled as seizure activity. No spatial information is used because most seizures start very locally and are hence only captured by one EEG channel.

IV. RESULTS

We defined a training set of 3 patients and a validation set of 3 patients. An overview of the results is given in Table 1. The first 3 patients are the training set. Figures 7 and 8 show 2 examples of a detected seizure. The highlighted segments are those which are correlated with at least 5 other segments in the preceding 10 seconds. The first highlighted segment represents the start of the detection.

Sensitivity and positive predictive value (PPV) are defined as [10]:

$$Sensitivity = (SZdet/SZtot).100 \quad (4)$$

with SZtot the number of seizures marked by the neurologist, and SZdet the number detected by our algorithm.

$$PPV = (EVsz/EVtot).100 \quad (5)$$

with EVtot and EVsz the total number of detected events and the number of detected seizures, respectively. Sometimes a single seizure is detected several times by the algorithm. In our approach all events detected by our algorithm that are part of a single seizure are considered as one EVsz detection.

Another good measure of the performance of the algorithm is the number of false positives per hour (FP/h). This measure represents an important indicator of the practical usability of the algorithm, because each FP implies that somebody in the ICU will have to check the patient unnecessarily.

In Table 1, the results of patient 6 are not shown. The entire EEG was labeled as seizure and this is due to a very pronounced ECG artefact. In this case, the algorithm detects the QRS complexes of the ECG captured by the EEG-leads (example Fig. 6). In principle, this problem can be solved again by mimicking how a human observer treats such artefacts. That is, by correlating the detected pattern with the directly measured ECG (which is usually co-registered with the EEG for this very purpose). If the time between the successive spikes is equal to the time between heartbeats, the detected pattern is most likely due to the ECG and not to seizure activity. This artefact did not occur in the training set.

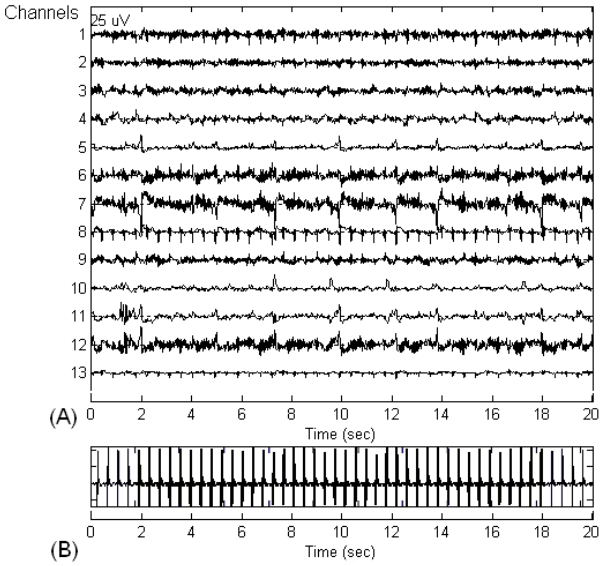

Fig. 6. (A): EEG with with strong ECG artefact (most dominant on channel 8). (B) corresponding ECG.

If we exclude patient 6 the sensitivity of the algorithm was found to be 98% with a PPV of 86% and 0.6FP/h.

V. DISCUSSION

The sensitivity of this algorithm is very good and its false positive rate is acceptable for online monitoring. The preliminary results on this subset are much better than those of other published algorithms which get a PPV ranging from

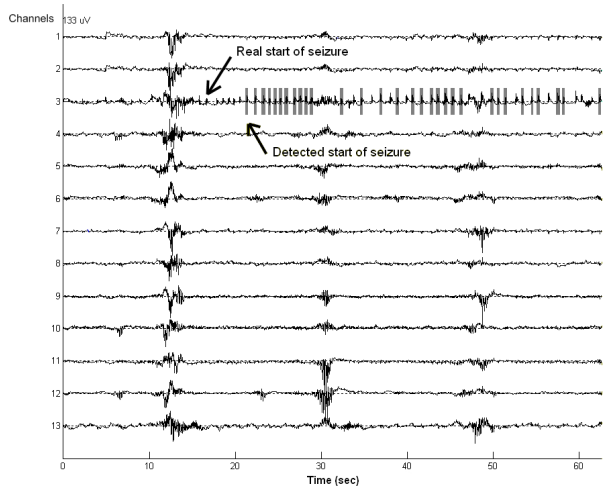

Fig. 7. Example of a detected seizure. The highlighted segments are correlated with a least 5 other previous segments present in the previous 10 seconds of EEG.

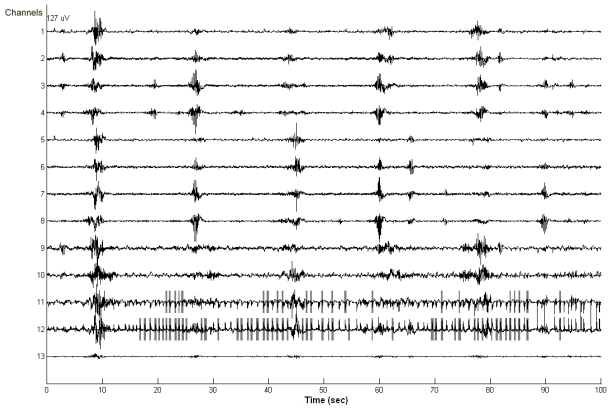

Fig. 8. Example of a detected seizure. The highlighted segments are correlated with a least 6 other previous segments present in the previous 10 seconds of EEG.

10 - 49% at a sensitivity between 73 - 98% [10]. Of course we only tested a small number of patients and more extensive tests will be needed to corroborate these results.

Our algorithm is resistent to artefacts (proven by the high PPV) because only very repetitive artefacts can be falsely detected. The strong criterion of at least 5 similar spikelike segments in 10 seconds of EEG prevents spurious detection of many artefacts (like motion/muscle artefacts), whereas it does not disturb the detection of a seizure.

However, the most important drawback of the present algorithm is that some artefacts may also consist of a repetitive spike pattern e.g. the ECG artefact. Further research is needed to separate these false detections from the true positives.

The presented algorithm had no patient-specific optimization and we would like to keep it this way. However, if this algorithm is going to be implemented in an bedside monitor it should be possible to manually adjust the sensitivity and FP/h by adapting relevant thresholds. The 2 most important thresholds are the number of correlated spikes in a 10 second window (now set to 5) and the correlation value between different spikes (now set to 0.8).

VI. Appendix 1

Teager proposed a simple non-linear energy operator (NLEO) (ψ_{teager}) , given here in its discrete form [7]:

$$\psi_{teager}[X_{(n)}] = X_{(n)}^2 - X_{(n-1)}.X_{(n-2)} \tag{6}$$

with X_n the current sample, X_{n-1} the previous sample, etc. The most important property of this operator is the behaviour for a pure sinewave:

$$\psi_{teager}[A.cos(\omega_o n + \theta)] = \frac{1}{2}.A^2.\omega_o^2 \tag{7}$$

This formula indicates that the output will be proportional to the square of both the amplitude and the frequency. In this regard, the NLEO may be considered superior to other energy estimators that simply average the square of the signal and are independent of frequency. A more generalized version is given in [11] as:

$$\psi_g[X_{(n)}] = X_{(n-l)}.X_{(n-p)} - X_{(n-q)}.X_{(n-s)}, \tag{8}$$
$$l + p = q + s$$

It can be shown that for l≠p and q≠s, ψ_g is more robust to noise. If the input signal contains additive noise then the output will not contain a component reflecting the input noise. A possible selection for the parameters is l=1, p=2, q=0 and s=3 [2].

References

[1] A. Aarabi, F. Wallois, and R. Grebe. Automated neonatal seizure detection: A multistage classification system through feature selection based on relevance and redundancy analysis. *Clin. Neurophysiol.*, 117:328–340, 2006.

[2] R. Agarwal, J. Gotman, D. Flanagan, and B. Rosenblatt. Automatic eeg analysis during long-term monitoring in the icu. *Electroencephalogr. Clin. Neurophysiol.*, 107:44–58, 1998.

[3] P. Celka and P. Colditz. A computer-aided detection of eeg seizures in infants: A singularspectrum approach and performance comparison. *IEEE transactions on biomedical engineering*, 49(5):363–369, 2002.

[4] R.R. Clancy, A. Legido, and D. Lewis. Occult neonatal seizures. *Epilepsia*, 29:256–261, 1988.

[5] J. Gotman, D. Flanagan, J. Zhang, and B. Rosenblatt. Automatic seizure detection in the newborn: methods and initial evaluation. *Electroencephalogr. Clin. Neurophysiol.*, 103:356–362, 1997.

[6] B.R. Greene, G.B. Boylan, R.B. Reilly, P. de Chazal, and S. Connolly. Combination of eeg and ecg for improved automatic neonatal seizure detection. *Clin. Neurophysiol.*, 118:1348–1359, 2007.

[7] J.F. Kaiser. On a simple algorithm to calculate the energy of a signal. In *IEEE International Conference on Acoustics, Speech, and Signal Processing (ICASSP90)*, pages 381–384, Apr. 1990.

[8] A. Liu, J.S. Hahn, G.P. Heldt, and R.W. Coen. Detection of neonatal seizures through computerized eeg analysis. *Electroencephalogr. Clin. Neurophysiol.*, 82:363–369, 1992.

[9] M.C. McBride, N. Laroia, and R. Guillet. Electrographic seizures in neonates correlate with poor neurodevelopmental outcome. *Neurology*, 55:506–514, 2000.

[10] M.A. Navakatikyan, P.B. Colditz, C.J. Burke, T.E. Inder, J. Richmond, and C.E. Williams. Seizure detection algorithm for neonates based on wave-sequence analysis. *Clin. Neurophysiol.*, 117:1190–1203, 2006.

[11] E.I. Plotkin and M.N.S. Swamy. Nonlinear signal processing based on parameter invariant moving average modeling. In *Proc. CCECE '21.*, pages TM3.11.1–TM3.11.4, 1992.

[12] J.J. Volpe. *Neurology of the newborn.* PA: Saunders, 1987.

[13] P. Zarjam, M. Mesbah, and B. Boashash. An optimal feature set for seizure detection systems for newborn eeg signals. In *ISCAS (5)*, pages 33–36, 2003.