Real-time automated detection of clonic seizures in newborns

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Highlights

- In an attempt to overcome challenges in neonatal seizure recognition, automated detection systems have been developed.
- Here we describe a new algorithm for real-time, low-cost clonic neonatal seizures detection based on differential average luminance signal analysis.
- Encouraging sensitivity, specificity and discriminatory power suggest its wider use as a screening tool.

Abstract

Objective: The aim of this study is to apply a real-time algorithm for clonic neonatal seizures detection, based on a low complexity image processing approach extracting the differential average luminance from videotaped body movements.

Methods: 23 video-EEGs from 12 patients containing 78 electrographically confirmed neonatal seizures of clonic type were reviewed and all movements were divided into noise, random movements, clonic seizures or other seizure types. Six video-EEGs from 5 newborns without seizures were also reviewed. Videos were then separately analyzed using either single, double or triple windows (these latter with 50% overlap) each of a 10 s duration.

Results: With a decision threshold set at 0.5, we obtained a sensitivity of 71% (corresponding specificity: 69%) with double-window processing for clonic seizures diagnosis. The discriminatory power, indicated by the Area Under the Curve (AUC), is higher with two interlaced windows (AUC = 0.796) than with single (AUC = 0.788) or triple-window (AUC = 0.728). Among subjects without neonatal seizures, our algorithm showed a specificity of 91% with double-window processing.

Conclusions: Our algorithm reliably detects neonatal clonic seizures and differentiates them from either noise, random movements and other seizure types.

Significance: It could represent a low-cost, low complexity, real-time automated screening tool for clonic neonatal seizures.

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1. Introduction

Seizures are the most common symptom of acute neurological disease in newborns (Volpe, 2001). The incidence rate, as reported in population-based studies, corresponds to 2.6 per 1000 live births, increasing to 11.1% for preterm neonates and to 13.5% for infants with a birth weight lower than 2500 g (Ronen et al., 1999). Therefore,
This may represent a common neurological sign in the neonatal intensive care unit (NICU) and, furthermore, could carry an increased risk of long-term morbidity (Mizrahi and Clancy, 2000).

Thus, neonatal seizures have to be promptly and accurately recognized in order to establish timely treatments. Although the traditional method of diagnosis is based on Video-ElectroEncephaloGraphic (v-EEG) monitoring, EEG interpretation is a time-consuming technique requiring specialised skills, not always readily available in the neonatal intensive care setting (Ntonfo et al., 2012). Therefore, automatic and real-time diagnostic equipment able to reliably recognize neonatal seizures would be of significant value (Kilbride et al., 2009; Shah et al., 2012; Alegre and Urrestarazu, 2011). Automatic detection of seizures by analysing EEG abnormalities has been considered (Deburchgrave et al., 2008; Cherian et al., 2011). Alternatively, the movements of the newborn's body could be acquired through a video camera and the corresponding video signal properly processed, with the aim to detect the newborn's "unusual" movements (Ntonfo et al., 2012). The acquisition of the motion strength (through image processing techniques) has been proposed as an expedient to detect the presence of neonatal seizures (Kilbride et al., 2009). To achieve this objective, clonic seizures were detected by analysing relevant motion trajectory features for gesture recognition (Karayiannis et al., 2006a,b,c).

In this paper, we rely on the low complexity image processing-based approach to the detection of clonic neonatal seizures proposed in (Ntonfo et al., 2012). This method consists of the extraction of an average differential luminance signal from acquired videos, where the average is carried out over all pixels of the difference between consecutive frames. Therefore, as periodic body movements lead to periodic average luminance signals, seizure detection reduces to periodicity detection. This low-complexity algorithm naturally leads to the implementation of low-cost camera-based diagnostic apparels to assist clinical practice (Kouamou et al., 2011, Ntonfo et al., 2012).

The aim of this study is to apply in a clinical setting a new real-time algorithm (Ntonfo et al., 2012) for clonic neonatal seizures detection, based on a low complexity image processing approach extracting the differential average luminance from videotaped body movements.

2. Methods

This study was conducted on video-EEG recordings collected in the neonatal seizures database elaborated by the Child Neuropsychiatry Unit of the Neuroscience Department at Parma University. This database collects all neonatal seizures of newborns consecutively admitted to the NICU of Parma University-Hospital between June 2001 and August 2012. In our Unit all newborns at high risk of seizures, on the basis of predisposing factors (such as birth asphyxia, sepsis, meningitis, metabolic disorders, malformations, intraventricular hemorrhage, or periventricular leucomalacia or cranial ultrasounds) or presenting clinical signs suggestive of seizures, routinely receive serial video-EEGs during the neonatal period.

During data collection, neonatal seizures were defined according to Volpe's classification, modified by Lombroso, as subtle, clonic, tonic, and myoclonic and had to be associated with EEG changes. Polygraphic v-EEGs were obtained at the bedside in the NICU. Depending on the infants' head size, 21 or 10 cerebral electrodes were applied according to the 10–20 International System, and electrocardiogram, lateral eye movements, chin electromyography activity, and abdominal respiration were the other physiologic variables most frequently monitored, with a technician present throughout the recording. The recordings continued until a complete cycle of wakefulness, quiet and active sleep were obtained or, when the state changes were not clearly distinguishable, for at least 60 min. EEG ictal discharges were selected according to the following criteria: (1) clear beginning and end, (2) lasting more than 10 s, and (3) evolution in frequency and morphology. All behavioural changes and specific clinical correlates were noted. Clinical seizures without v-EEG correlates were not considered. Clonic seizures were selected through v-EEG analysis, by expert medical personnel. Each video recording has the following characteristics: (a) video sample frequency: 25 frames/s; (b) video resolution: 320 × 240 pixels.

We initially identified 58 patients having experienced neonatal seizures and being monitored with at least one v-EEG. As 44 of them had more than one v-EEG, the total number of reviewed v-EEGs was 208, with a mean number of v-EEGs/patient of 3586 (range: 1–16). Eighty-three v-EEGs had to be rejected as non-ictal (seizures had been detected in previous EEGs, either with or without concomitant video monitoring) and five EEGs had no video (either partially damaged, or having the patient almost completely covered or hidden from the camera), whereas 24 v-EEG recordings belonging to 18 patients had to be excluded due to the presence of only electrographic seizures.

Whenever more than one seizure type was present, only for the aims of this study, we classified the video according to the most prevalent seizure type observed.

For the purposes of the present study, according to the semeiological classification (Lombroso, 1996) of neonatal seizures, we selected for further evaluation only videos containing clonic seizures as the single predominant seizure type, due to previous observations (Karayiannis, 2005a, 2006a, b, c) where they seemed to be the seizure type with the most clearly identifiable motor pattern. This allowed us to finally identify 23 videos from 12 patients containing 78 seizures of clonic type, for a total video length of 18:03:48 (mean video duration 00:47:07, range 00:02:42–01:06:40), total seizure duration of 00:46:56 (mean seizure duration of 00:00:36, range 00:00:04–00:03:18) suitable for further analysis carried out by means of the video signal processing algorithm already published (Ntonfo et al., 2012). In particular, the approach proposed (Ntonfo et al., 2012) is the core processing algorithm of a software tool which takes a video at its input and analyses it offline. The 23 videos were entirely reviewed and movements were labelled as either:

- clonic;
- other seizure types;
- noise (whenever changes in the room lightning, staff manoeuvres/movements in front of the camera or around the baby disturbed the recording), in order to exclude these latter from analysis.

From visual inspection 502 noise events for a total length of 04:44:08 (mean 00:00:34, range 00:00:01–00:33:32) and 668 motor events representing either neonatal seizures of non-clonic type or other active body movements for an overall duration of 04:15:22 (having rounded up 7 myoclonic events lasting less than 1 s each, mean duration 00:00:23, range 00:00:01–00:07:28) were also recognised. Of these latter, 201 represented clinical seizures of non-clonic type, corresponding to a total duration of 02:18:20, and a mean duration of 00:00:41 (ranging from a minimum of 00:00:10 by definition and maximum duration of 00:07:13). The remaining 467 motor events represented either random movements or brief ictal events, for example myoclonic jerks, of less than 10 s duration, for an overall length of 01:57:02, mean duration 00:00:15, range from 00:00:01 to 00:07:28.

The whole videos were subsequently analysed using the aforementioned image processing algorithm to check for sensitivity (defined as the ratio between true positives and the sum of true positives and false negatives) (Karayiannis et al., 2005b) and spec-
ificity (defined as the ratio between true negatives and the sum of true negatives and false positives) (Kouamou et al., 2011), in correctly classifying clonic seizures with respect to spontaneous movements or other seizure types.

As described previously (Ntonfo et al., 2012), the proposed video processing algorithm has various operational conditions, depending on how consecutive frames are processed. In particular, it can operate considering: (i) the use of disjoint consecutive frame windows, where each window lasts 10 s (this operational condition is denoted as “single window”); (ii) the use of two interlaced windows, with 50% overlapping between consecutive windows; (iii) the use of three consecutive interlaced windows (with 50% overlap between consecutive pairs). For the three above-mentioned cases, specificity and sensitivity of the periodicity detection algorithm (Ntonfo et al., 2012) characterized by a “decision threshold” (a parameter between 0 and 1) which allows to discriminate the potential presence of a clonic event. The use of successive interlaced windows increases the reliability of seizure detection, as single seizures could manifest across disjoint windows and, therefore, could be missed if single windows were analysed in a disjoint fashion. In fact, even if we assume that a clonic seizure occurs when periodicity is detected across multiple (overlapped) windows, the movements of the body part affected by seizures might change across consecutive overlapping windows, making the estimated values of the movement period vary on a per-window basis (Fig. 1).

In order to quantify motion, we consider a generic video signal composed of a sequence of frames sampled with period T, where a frame at discrete time i is an array of matrices of M x N pixels containing red, green, and blue (RGB) values. The corresponding grey-scale matrix is the luminance of the considered frame. As an illustrative example of a grey-scale frame sequence, a few video frames relative to the recording of a newborn affected by clonic seizures, which manifest themselves as movements of the legs, are shown in Fig. 2, first line. The grey-scale frames have then to be properly filtered so that the output frame sequence is representative of the moving parts of the infant body. In this study, we use a simple differential filtering method: an output frame is given by the difference of two consecutive frames. The resulting output video signal, (Fig. 2, second line), is still a grey-scale video signal in which the movement parts are highlighted. As one can see, each pixel has a luminance value that varies in a grey scale, typically with 256 (0–255) grey levels.

Considering all M x N pixels, a relatively long monitoring time would generate a huge quantity of data to process. In order to limit complexity, we move from a large range of 256 possible values of luminance for a pixel to a binary scale. To this end, it is very important to choose the quantization threshold value above which the brightness of a pixel will be mapped into a “1” (which corresponds to the maximum luminance value of 255). An appropriate choice of the quantization threshold minimizes the conversion error and contributes also to the reduction of the effects of other spurious readings that occur even in the absence of movement. The resulting sequence after binary-scale conversion is shown in Fig. 2, third line. After conversion to the binary scale, there may still be many pixels that are highlighted (converted to “1” in the binary scale) even if they do not correspond to moving body parts. Therefore, they act as noise for the detection of the body movements. In order to reduce the remaining nuisance, we use one of the fundamental operations in morphological image processing: erosion. In erosion, every object pixel that is touching a background pixel, for example the object border, is changed into a background pixel. This opera-

![Fig. 1. On the left: Single window-based processing with partial window overlap. (a) First window. (b) Second window. (c) Third window. On the right: Multiple window-based processing, with groups of three interlaced windows. (a) First group. (b) Second group. (c) Third group.](image-url)
tion is helpful to eliminate irrelevant details from the image and is based on a kernel, such as a square of \( m \times m \) pixels. After erosion, some noisy (i.e., bright and isolated) pixels may still exist but their number is negligible with respect to the number of pixels of the moving parts. The degree of erosion can be adjusted by choosing the value of \( m \) or the number of times the frame is processed. Obviously, erosion leads to the loss of a part of the signal which is, however, negligible. The resulting image sequence, after the sequence in Fig. 2 (third line) undergoes a single erosion process with \( m = 3 \) (Fig. 2, fourth line).

Thus we define the average luminance signal or average motion signal as the function whose value at time \( i \) is given by the number of highlighted pixels in the corresponding frame. At this point, the key idea of the proposed approach to neonatal seizure detection resides in the observation that, in the presence of clonic seizures, the characteristic periodicity of body movements appears in the average motion signal. Therefore, the problem of clonic seizure detection reduces to the detection of the presence of periodicity in the motion signal.

In Fig. 3a, the average motion signal, extracted from a video of a newborn affected by a neonatal seizure, is shown. A periodic pattern clearly emerges. For comparison, in Fig. 3a, the EEG and the electromyographic (EMG) signals corresponding to the same seizure occurrence are shown. In the latter subfigure, a periodic pattern appears as well. To make the correspondence clearer, in Fig. 3b, we also directly compare the Fp2-C4 (EEG) signal with the average motion signal. This illustrative example suggests that the proposed approach exhibits a good agreement with the predictions based on the EEG/EMG analysis. Further details have been described in a previous publication (Ntonfo et al., 2012).

The same process as above was also applied to video-EEGs of neonates not affected by neonatal seizures, used as controls. The selection was based on the following inclusion criteria: absence of both electroclinical and electrographic seizures (during the recording as well as anamnestically), normal background EEG, absence of pathological movements on video-EEG. The polygraphic video-EEGs were performed because one newborn presented perinatal asphyxia, one was reported as having episodes of apnoea, one was a preterm newborn of 31 weeks of gestational age and the last two were irritable with startle and tremor. Videos were reviewed and noise (as described above) and movements were noted by medical personnel. We considered 6 videos from 5 neonates, corresponding to a total duration of 04:34:29 (mean: 00:45:45, minimum 00:30:51, maximum 00:58:46), during which a total of 426 movements were recorded for a total duration of 01:19:02 (mean duration 00:00:11, range 00:00:01–00:02:22), whereas 99 noise events (mean duration 00:00:08, range 00:00:01–00:00:49) for an overall duration of 00:14:00 were also noted.

### 2.1. Statistical analysis

The performance of the proposed detection system is analysed considering a binary classification test, i.e., classifying the results into two groups: presence of clonic seizures in the video of the newborn (positive) and presence of random movements (negative). Therefore, the following situations may occur: clonic seizure correctly diagnosed (True Positive, TP); random movement correctly diagnosed (True Negative, TN); random movement incorrectly diagnosed as seizure (False Positive, FP); and clonic seizure incorrectly diagnosed as random movement (False Negative, FN).
Receiver operating characteristic (ROC) curves were constructed to measure the performance of our system in detecting clonic seizures.

Statistical analysis was performed using the Statistical Package for the Social Sciences (Version 17.0.1. Chicago, IL: SPSS Inc.; 2008).

### 3. Results

The considered approach, outlined above, has been tuned in order to guarantee good sensitivity and specificity values. The ROC curves obtained are shown below (Fig. 4): they express the varying ratio between TPs (sensitivity) and false alarms (1-specificity) for single, double or triple window, respectively. In particular, an optimized value of the decision threshold has been determined by means of ROC curves, more specifically, the best value of the decision threshold has been selected as the one which minimizes the distance between the corresponding (1-specificity, sensitivity) point and the optimum point (0,1) on the ROC curve. With the considered set of videos (with frame rate equal to 25 frame/s) and video processing algorithm’s window length (set to 10"), the best value of the decision threshold is 0.5. It can be observed that with all three considered algorithms the discriminatory power, indicated by the Area Under the Curve (AUC) parameter, is always higher than 0.7 (see Table 1a–c and Fig. 4). Furthermore, the best accuracy is achieved with two interlaced windows (AUC = 0.796), whereas the accuracy with the single-window (AUC = 0.788) and triple-window (AUC = 0.728) algorithms is lower.

In detail, our algorithm performance in discriminating between clonic events, noise or other body movements (being either different ictal phenomena or spontaneous movements) shows a maximum sensitivity of 86% with single-window processing (corresponding specificity: 63%), a sensitivity of 71% (corresponding specificity: 69%) with double-window processing and finally a sensitivity of 48% (corresponding specificity: 78%) with triple-window processing (Table 1a–c).

As long as videos from seizure-free newborns are concerned, having set the threshold at 0.5 as above, the specificity of our algorithm reaches 76% with a single-window approach, 91% with a
double-window approach and 97% with a triple window approach (Table 2a–c).

4. Discussion

Automatic detection systems have been developed to overcome limitations in neonatal seizure identification mainly linked to the difficulties in clinical recognition and the need for highly specialised expertise to correctly interpret v-EEG. Alternative strategies already used in clinical practice, for example amplitude-integrated EEG, have proven very useful but unable to completely substitute conventional v-EEG, due to various drawbacks, such as the use of a limited set of electrodes, the presence of a time-compressed trace (carrying a non-negligible risk of missing brief seizures), the presence of false positives due to artefacts and the need for formal training for correct use and interpretation, thus requiring resources which are not always available (Shah et al., 2012).
Essentially, two different kinds of answers to this relevant clinical problem have arisen from research: one based on the development of algorithms combining different types of biological signals, like electrocardiogram, respiration, reduced EEG channels (Faul et al., 2005; Greene et al., 2007) and one based on motion analysis (Karayiannis et al., 2006a, b, c). The two types of monitoring systems have different, possibly complementary, advantages and limitations.

We are presenting a new method for real-time, video recording-based clonic seizures recognition, analysing luminescence changes determined by motion patterns. The proposed approach was tested on 23 v-EEGs recorded on 12 patients and containing a total of 78 clonic seizures and 668 motor events characterized either by seizures of non-clonic type or spontaneous body movements, with three different approaches, namely with one window or two/three interlaced (with 50% overlap) windows. In all cases, each window is 10 s long. From the results shown in Table 1, it can be stated that the proposed approach with a single window processing guarantees the highest performance for the detection of pathological events, showing the highest sensitivity, 86%. This result is due to the fact that single window processing analyzes the periodicity over a short interval (i.e., a 10 s window), so that even short clonic events can be detected. Unfortunately, with single-window processing isolated almost-periodic random movements may be labelled as pathologic, thus reducing specificity, which equals 63%. On the contrary, the use of interlaced windows excludes clonic events which are too short to cover the duration of three successive overlapping windows, thus reducing the sensitivity (which lowers to 48%), but also prevents isolated almost-periodic movements to be labelled as seizures, thus increasing the specificity to 78%. From these results, it can also be observed that the type of processing (single or multiple window-based) has a strong impact on the sensitivity, whereas the specificity tends to be less affected.

AUC results are very encouraging, as they show that the performance of our algorithm in classifying motor events in neonates is accurate and worth testing in a wider population of newborns to confirm the present data. It could also be experimentally tested online together with v-EEG monitoring.

Furthermore, our algorithm performance in subjects without neonatal seizures shows positive results, with a specificity ranging from 76% when using a single-window to 97% when using a triple-window approach (Table 2), confirming that this method reliably classifies motor and environmental phenomena other than clonic seizures.

We think that this new automatic detection system shows many advantages: (i) it has a low cost, as it is based on the use of a video camera, thus encouraging a more widespread monitoring of high risk newborns in different clinical settings; (ii) it is non-invasive, as no electrodes need to be attached to the patient, thus allowing long-term monitoring and causing minimal interference with intensive care procedures or devices. Furthermore, one of the most relevant differences from previously described video-processing techniques, usually requiring long monitoring periods, is the short latency of the decision, giving the opportunity of a real-time non-EEG dependent diagnosis, with immediately available and readily interpretable information, even by non-experienced personnel, as the program will simply alert staff of the high probability of an on-going seizure.

One of the limitations of this study is the recognition of clinical events only, so that electrographic seizures with no clinical correlate would be missed, especially in the case of administration of therapies suppressing movements (curare) or favouring electroclinical uncoupling (barbiturates, benzodiazepines). Therefore, the proposed approach is mainly conceived for early identification of high-risk newborns allowing an immediate low-cost preliminary diagnosis based on clinical aspects of neonatal seizures. It is not intended to completely replace EEG, which is still the gold-standard technique for the diagnosis of neonatal seizures. In other words, an automatic video camera-based system could be used to permanently monitor every patient in the neonatal care unit, whereas EEG would be required for a definitive diagnosis only when the system indicates, with high probability, the potential presence of seizures, encouraging a rational use of resources.

In the future, it could be either used independently from EEG or integrated into more complex automated detection systems, jointly processing EKG, Continuous Functional Monitoring (CFM), respiration and saturation signals, in order to detect both clinical and subclinical seizures, especially in some subsets of patients, like paralysed newborns.

For the time being this system has only been tested with clonic seizures, as they show the highest rhythmicity. It must be acknowledged that this seizure type represented 38.8% of all the seizures occurring in the analysed videos. Nevertheless, our algorithm has proven to correctly identify 71% of the clonic events in our cohort, confirming its potential role as an integrative tool in neonatal care monitoring. Moreover, in the future, its sensitivity and specificity in subtle or myoclonic seizures could be tested, potentially increasing the spectrum of applicability of our algorithm.

If this strategy was to be confirmed as valuable, the vast majority of electroclinical neonatal seizures in both term and preterm neonates would be covered (Scher, 1993), significantly increasing correct recognition of potential acute neurological disease in newborns. We would also like to highlight that this program has been conceived as a screening tool to alert clinical staff and correctly select patients to be monitored and timely treated.

Clonic seizures present as repetitive, rhythmic jerking of muscle groups in the face, limbs, or trunk, with slow rate of repetition, usually at 1–4 Hz (Mizrahi and Kellaway, 1987). When compared to non-epileptic repetitive abnormal movements, like clonus or tremor, they are consistently slower and more rhythmic (Mizrahi, 2012). This means that periodicity characteristics are available for correct differential diagnosis between clonic seizures and similar pathological movements by our motion analysis algorithm. It could be argued that clonic jerking is one of the most readily recognisable seizure types in the newborn, and in fact it is reported that a percentage as high as 70% of neonatal seizures recognised by trained nurse staff show a clonic pattern (Murray et al., 2008). Nevertheless, the same study demonstrated that only 65% of all neonatal seizures were identifiable on clinical grounds only, probably due to their brief duration and focal location, thus rendering under-diagnosis quite likely in the busy intensive care unit setting, as recognition by nursing/medical staff would require the presence of dedicated one-to-one staff on a 24 h basis. Furthermore, staff recognition skills can vary significantly among different institutions.

Clonic seizures recognition also carries important implications for etiologic diagnosis, as they are frequently associated with localised brain injury, mostly of vascular origin, e.g. stroke (Selton et al., 2003).

An even more relevant data outlined in the aforementioned article (Murray et al., 2008) is that electroclinical seizures correspond to only 18.8% of the total seizure burden. This means that continuous monitoring, which is a very expensive and time-consuming technique, should be used to correctly assess these infants. We therefore think that the key point is to correctly select infants for further conventional monitoring, and this is when this motion analysis technique would be most beneficial.

The observed results are very encouraging and suggest that this approach could lead to the implementation of low-cost camera-based devices to assist neonatal medical personnel for early diagnosis of neonatal seizures.
Disclosure

All the authors report no conflicts of interest or financial disclosures. The manuscript does not report results of a clinical trial. This study is not industry-sponsored.

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