33rd Annual International Conference of the IEEE EMBS
Boston, Massachusetts USA, August 30 - September 3, 2011

Spike Detection in the Preterm Fetal Sheep EEG using Haar Wavelet Analysis

Anita C. Walbran, *Student Member IEEE,* Charles P. Unsworth, *Member IEEE,* Alistair J. Gunn, and Laura Bennet

***Abstract*—Perinatal hypoxia is a significant cause of brain injury in preterm infants. Neuroprotective treatments have proven beneficial when commenced within 6-8 hours post hypoxic-ischemic insult. However, as the exact time of injury is unknown, there are no current means to determine which infants are in the treatment phase of the evolving injury. Recent studies suggest epileptiform transients in the first 6-8 hours are predictive of outcome. To quantify this further an automated means of transient identification is required. In this paper we describe a method using Haar wavelets to detect spikes in the preterm fetal sheep EEG after asphyxia *in utero*. The method exhibits good sensitivity and selectivity over 3 specific time periods and demonstrates the feasibility of using wavelets for spike detection in fetal sheep.**

I. Introduction

HYPOXIA before or during birth plays a key role in the development of brain injury in preterm infants [1]. During recovery from an hypoxic insult, a latent recovery phase lasting up to 6-8 hours post-insult provides a narrow window during which neuroprotective treatments must be initiated for maximum efficacy [2]. Currently, however, there are no biomarkers which define the latent phase [3].

Electroencephalography (EEG) is easily measureable and has utility in defining the evolution of injury. Amplitude suppression and high amplitude seizures are predictive of outcome after hypoxia, but only after the window of opportunity for treatment has passed [2, 3]. Recent studies suggest that more subtle features of the EEG during the latent phase may be predictive of outcome [3]. These features are epileptiform transients - typically low amplitude, high frequency (<400 ms) events such as spikes, sharp waves and slow waves that may occur in isolation, in multiples or as complexes [3]. Neonatal monitoring leaves clinicians with vast amounts of data to review and quantify, highlighting the need for signal analysis to be automated.

Wavelet analysis is suited to the detection of epileptiform transients because it allows flexible time-frequency resolution. Wavelets decompose a signal into scales where each scale covers a different frequency range, thereby enabling transients to be separated from the rest of the data. Several approaches have been presented in the literature for the detection of epileptiform transients using various wavelet families [4-6]. In this study we employ the Haar wavelet. The Haar wavelet has previously been used for ocular artifact de-noising [7, 8] and the separation of background activity and transient phenomena in EEG signals [9]. Quiroga et al. used a Haar wavelet decomposition as a precursor to superparamagnetic clustering for the detection of spikes [10].

The aim of this study was to develop a simple and robust method, requiring minimal user intervention, to assess spike activity in a preterm fetal sheep model after asphyxia *in utero* at 3 specific time periods within the latent phase.

II. Methods

A. Data acquisition

All procedures were approved by the Animal Ethics Committee of The University of Auckland. One singleton Romney/Suffolk sheep fetus of 98 days gestation (term = 147 days [11]) was instrumented under general anesthesia using sterile techniques. A catheter was inserted in the fetal brachial artery to allow blood sampling. Two pairs of EEG electrodes (Cooner Wire Co., USA) were secured on the dura over the parasagittal parietal cortex. A reference electrode was sewn over the occiput. An inflatable silicone occluder (In Vivo Metric, USA) was placed around the umbilical cord prior to returning the fetus to the uterus. During post-surgical recovery the ewe was housed with companion sheep, fed ad libitum and given daily intravenous antiobiotics (600 mg Benzylpencillin Sodium; 80 mg Gentamicin). Fetal arterial blood samples were taken daily to monitor fetal health and perform blood gas analysis.

At 103 days gestation (~27-30 weeks human brain maturation [12]) fetal asphyxia was induced by complete umbilical cord occlusion for 25 min. Fetal blood was sampled before, during and after asphyxia for blood gas analysis (Ciba-Corning Diagnostics 845 Blood Gas Analyzer/Co-oximeter, USA). The left and right fetal EEG signals were channelled through individual unity-gain head-

Manuscript received March 25, 2011. This work was supported by a Top Achiever Doctoral Scholarship from the Tertiary Education Commission, New Zealand, the Auckland Medical Research Foundation and the Health Research Council, New Zealand.

A. C. Walbran is with the Department of Engineering Science, The University of Auckland, Auckland 1010, New Zealand. (phone: +64-9-373-7599 ext 87061; fax: +69-9-373-7468; e-mail: a.walbran@auckland.ac.nz).

C. P. Unsworth is a Senior Lecturer at the Department of Engineering Science, The University of Auckland. Auckland 1010, New Zealand. (e-mail: c.unsworth@auckland.ac.nz).

L. Bennet is a Professor in the Department of Physiology, Faculty of Medical and Health Sciences, The University of Auckland, Private Bag 92019, Auckland, New Zealand (email:l.bennet@auckland.ac.nz).

A. J. Gunn is a Professor in the Department of Physiology, Faculty of Medical and Health Sciences, The University of Auckland, Private Bag 92019, Auckland, New Zealand (email: aj.gunn@auckland.ac.nz).

stages for reduction of noise by selective signal amplification (×10,000). Low-pass filtering with a sixth-order low-pass Butterworth anti-aliasing filter, with the -3 dB point set to a cut-off frequency of 50 Hz, was performed. The fetal EEG was recorded for 8 hours post-asphyxia and digitised at a frequency of 64Hz.

B. Epoch Analysis

In this analysis, spike activity was determined in 10 min bins during 3 specific time periods during the latent phase; 0.5 hour (h), 3.0 h and 6.2 h. These time points were chosen to determine spike activity during 1) the early-latent phase, where there is profound EEG amplitude suppression and cerebral hypoperfusion [1], 2) the mid-latent phase, the beginning of progressive metabolic deterioration and where maximal transient activity has been observed previously [1, 13], and 3) the late-latent recovery phase, where transient activity decreases just prior to the onset of large amplitude seizures, beyond which treatment is no longer effective [1].

C. Waveform analysis

All spikes of the left EEG during the 3 latent time periods were manually identified by the authors. A spike was defined as having a sharp outline and duration of less than 70 ms, corresponding to frequencies greater than 14.3 Hz, typically superimposed on a suppressed EEG background [14]. Spike amplitude was defined to be greater than 20 μV.

D. Wavelet theory

Wavelet analysis is a time-frequency based method useful for processing non-stationary signals whose constituent frequencies vary with time. The main advantage of wavelet analysis over techniques such as the short time Fourier transform is that it can provide optimal resolution in both time and frequency [10, 15]. The wavelet transform (WT) maps a signal from a time-based representation to a representation based on discrete scales m and discrete times n. The WT is defined as the convolution of a signal $x(t)$ with dilated and translated versions of a mother wavelet $\psi_{m,n}(t)$,

$$T_{m,n} = < x(t), \psi_{m,n}(t) > . \quad (1)$$

By calculating the transform at various scales and locations we obtain a multiresolution decomposition of the signal whereby the signal has been separated into detail and approximation coefficients. Due to the redundancy of the procedure, power-of-two logarithmic scaling of dilation and translation steps is often used; this is known as the dyadic grid arrangement [15]. The shape of the wavelet function should reflect the type of feature to be isolated in the signal. The Haar wavelet is suited to time series with sharp jumps or steps so is useful for isolating peaks or discontinuities [4]. Additionally, it has compact support and is orthogonal so allows spikes to be represented with few coefficients and without a priori assumptions regarding the shapes of the spikes [10]. For these reasons, the WT is implemented using the Haar wavelet in this study.

The Haar mother wavelet is given by,

$$\psi(t) = \begin{cases} 1 & 0 \le t < 1/2 \\ -1 & 1/2 \le t < 1 \\ 0 & elsewhere \end{cases} \quad (2)$$

A signal can be decomposed into approximation (S) and detail (T) coefficients using (3) and (4) [15].

$$S_{m+1,n} = \frac{1}{\sqrt{2}}\left[S_{m,2n} + S_{m,2n+1}\right] \quad (3)$$

$$T_{m+1,n} = \frac{1}{\sqrt{2}}\left[S_{m,2n} - S_{m,2n+1}\right] \quad (4)$$

The approximation coefficients give a coarse signal representation [10] while the detail coefficients retain the dropped components [5]. By analysing the signal detail at the appropriate scale it is possible to detect spikes. The signal detail approximation at each scale m can be obtained by,

$$d_m(t) = \sum_{n=0}^{2^{M-m}-1} T_{m,n}\psi_{m,n}(t) \quad (5)$$

where M is the number of scales for a full decomposition and the scaling wavelet function is given by (6), representing scaled and translated versions of the mother wavelet.

$$\psi_{m,n}(t) = 2^{-m/2}\psi(2^{-m}t - n) \quad (6)$$

E. Haar wavelet signal decomposition

We use a Haar wavelet analysis to detect EEG spikes. Our data has a sampling rate of 64 Hz so assuming optimal sampling at the Nyquist frequency was performed our frequency range is 0-32 Hz. A full signal decomposition was performed and the frequency sub-bands for the first 4 decomposition levels are given in Table I.

TABLE I
FREQUENCY SUB-BANDS

Scale m	Approximation frequency band (Hz)	Detail frequency band (Hz)
1	0-16	16-32
2	0-8	8-16
3	0-4	4-8
4	0-2	2-4

At scale 1, the frequency components of the signal detail encompass most frequency components of spikes. Therefore, the signal detail in scale 1 is expected to be large when spikes are contained in the data. Fig. 1 shows the detail coefficients for m = 1 - 4 in a 6 s segment of data containing spikes. Large detail coefficients are observed at m = 1 and m = 2, where spikes are located in the EEG time series thus confirming the relationship between large signal detail and

spike presence. Therefore, if the detail coefficients exceed a defined threshold, we can say that a spike is likely to exist in the data. We focussed on detecting spikes in scale 1 as it best encompasses the frequency components of spikes.

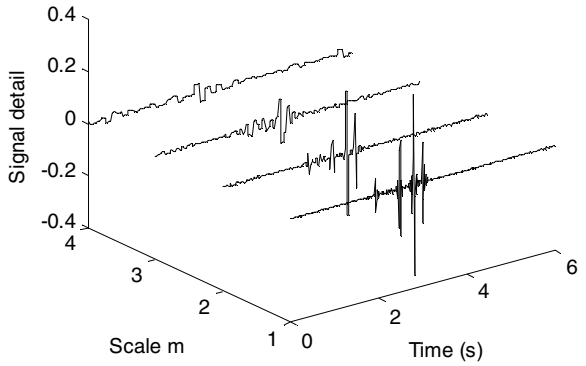

Fig. 1. Detail coefficients at scales m = 1 – 4 for the 6 s segment of EEG data in Fig. 2A. Large detail coefficients are observed where spikes are located in the time domain.

F. Haar wavelet analysis

The EEG was de-meaned and normalised and then a Haar wavelet decomposition performed for the 10 min EEG segments at the 3 specified time periods in the latent phase. A non-overlapping window of 1024 data points was employed. At scale 1 this translates to a frequency resolution of 0.125 Hz. Next, the signal detail was constructed at each scale using the scaling wavelet function. Following quick visual inspection of the scale 1 detail coefficients, a threshold was defined heuristically in order to extract the large detail coefficients corresponding to spikes in the time domain. Thresholding was performed on the raw detail coefficients, rather than absolute values, so that the coefficients corresponding to negative polarity spikes would be retained. If the absolute value of the detail coefficient exceeded the threshold, the data point number was recorded as a potential spike location. To ensure the potential detection was above the 20 μV amplitude criteria for a spike, a tight window was defined around the potential spike location and the amplitude of the detection was checked in the corresponding section of the EEG time series. If the detection did not exceed the amplitude criteria then it was removed as a potential spike detection. When moving in time along the detail coefficients array during thresholding, if a spike location was found, the increment along the array moved forward by the average spike width to prevent the same spike being detected twice. The potential spike locations detected from the analysis were then compared with the start location of the spikes manually identified by the authors.

G. Performance evaluation

Algorithm performance was evaluated in terms of sensitivity, the proportion of actual spikes correctly detected by the algorithm (7), selectivity, the proportion of algorithm detections that are actual spikes (8) [6] and overall algorithm performance, the average of sensitivity and selectivity (9),

$$Sensitivity = TP/(TP + FN) \times 100 \quad (7)$$

$$Selectivity = TP/(TP + FP) \times 100 \quad (8)$$

$$Overall\_performance = (Sensitivity + Selectivity)/2 \quad (9)$$

A true positive (TP) is a spike detected by the algorithm that was also identified by the expert, a false positive (FP) is a spike detected by the algorithm that was not identified by the expert, and a false negative (FN) is a spike identified by the expert but not detected by the algorithm.

The position error was calculated to measure the error between the spike location detected by the algorithm A_i and the spike start location identified by the expert E_i for all true positive detections (10).

$$Position\_error_i = A_i - E_i \quad (10)$$

III. RESULTS

A. Blood composition measurements

Complete umbilical cord occlusion induced profound hypoxia, hypercapnia and acidosis which rapidly resolved after release of the occluder (Table II).

B. Performance evaluation

An example segment of raw left EEG from the early-latent phase is depicted in Fig. 2A with spikes identified by the authors marked with an arrow. The corresponding detail coefficients at scale 1 are shown in Fig. 2B. As expected the large detail coefficients align with the spikes in the time domain.

The authors identified 213, 88 and 73 spikes in the early-, mid- and late-latent phases respectively. Table III provides the algorithm performance in terms of sensitivity, selectivity, overall performance and position error at the optimal threshold level. The optimal threshold level was determined to be that which minimised the difference between sensitivity and selectivity.

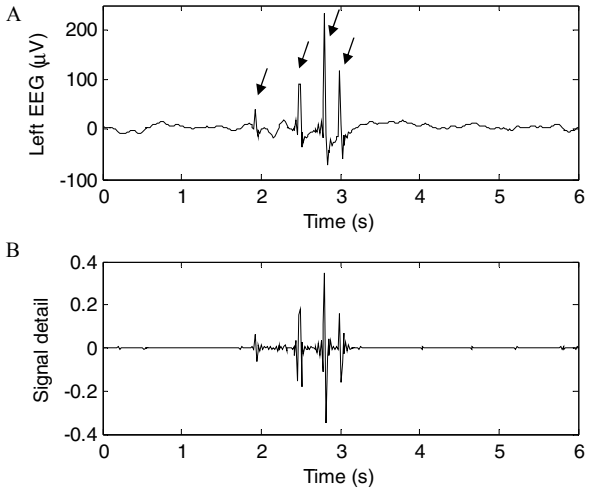

Fig. 2. A: Raw left EEG segment with spikes marked by the arrow. B: Corresponding detail coefficients from scale 1.

TABLE II
BLOOD COMPOSITION RESULTS

	Baseline	Asphyxia	30 min post	3 hour post	6 hour post
pH	7.36	6.98	7.21	7.39	7.37
$PaCO_2$ (mmHg)	45.6	152.3	48.3	44.8	45.9
PaO_2 (mmHg)	24.2	6.9	28.9	27.6	26.8

pH, partial pressure of arterial carbon dioxide ($PaCO_2$) and partial pressure of arterial oxygen (PaO_2) values 30 min before occlusion (baseline), after 20 min of occlusion (asphyxia) and 30 min, 3 and 6 hours after the end of occlusion (post).

TABLE III
ALGORITHM PERFORMANCE

	Early-latent	Mid-latent	Late-latent
Threshold	0.022	0.031	0.07
Sensitivity (%)	80.3	81.8	74.0
Selectivity (%)	79.2	82.8	71.1
Overall performance (%)	79.8	82.3	72.6
Position error (10^{th}, 90^{th} percentile)	(-1, 2)	(-1, 2)	(0, 2)

The position error is given in terms of the number of data points.

IV. Discussion

We have presented a simple and effective method for the detection of epileptiform spikes in the preterm fetal sheep EEG during the latent phase following an hypoxic insult. The method offers good sensitivity and selectivity and minimal error in detected spike locations, demonstrating the feasibility of using wavelets to detect spikes in the fetal sheep EEG hypoxic-ischemic model. Our results show that the best results in terms of sensitivity and selectivity were obtained in the following order: mid-, early- then late-latent phase. The lower performance in the late latent phase was primarily due to the increased number of sharp waves, with those around 70 ms appearing as false positives.

A limitation of the algorithm is that small amplitude spikes can be missed due to the threshold value chosen. Lowering the threshold will allow more of these small amplitude spikes to be detected therefore increasing sensitivity, however, this is at the expense of selectivity as additional false positives arise. Unlike other approaches such as [6] where only the largest amplitude spike occurring within a 3 s sampling period is detected, our method is able to detect single spikes as well as multiple spikes located very closely in time. Seldom does the algorithm miss a spike that occurs immediately after another in time.

In all three latent periods at least 80% of spikes were detected within -1 to 2 data points of the expert identified spike location demonstrating that the algorithm is able to extract spike location with high accuracy.

Although the Haar wavelet is suited to detecting sharp jumps or steps in the data [4], as are characteristic of spikes, it is likely not the best wavelet to use. Future work will include employing other mother wavelets to detect spikes. We intend to extend the analysis to include the detection of sharp waves to provide enhanced ability to determine which phase of evolving injury the brain is in. The algorithms will be applied to a larger cohort of animals and refined further as necessary.

Acknowledgment

We would like to thank EEG technician Mark Gunning from the Department of Physiology, The University of Auckland.

References

[1] A.J. Gunn and L. Bennet, "Timing of injury in the fetus and neonate," *Current Opinion in Obstetrics and Gynecology*, vol. 20, (no. 2), pp. 175-181, 2008.

[2] M. Thoresen, "Hypothermia after Perinatal Asphyxia: Selection for Treatment and Cooling Protocol," *The Journal of Pediatrics*, vol. 158, (no. 2, Supplement 1), pp. e45-e49, 2011.

[3] L. Bennet, L. Booth, and A.J. Gunn, "Potential biomarkers for hypoxic-ischemic encephalopathy," *Seminars in Fetal and Neonatal Medicine*, vol. 15, (no. 5), pp. 253-260, 2010.

[4] C. Torrence and G.P. Compo, "A Practical Guide to Wavelet Analysis," *Bulletin of the American Meteorological Society*, vol. 79, (no. 1), pp. 61-78, 1998.

[5] F. Sartoretto and M. Ermani, "Automatic detection of epileptiform activity by single-level wavelet analysis," *Clinical Neurophysiology*, vol. 110, (no. 2), pp. 239-249, 1999.

[6] K.P. Indiradevi, E. Elias, P.S. Sathidevi, S. Dinesh Nayak, and K. Radhakrishnan, "A multi-level wavelet approach for automatic detection of epileptic spikes in the electroencephalogram," *Computers in Biology and Medicine*, vol. 38, (no. 7), pp. 805-816, 2008.

[7] P.S. Kumar, R. Arumuganathan, K. Sivakumar, and C. Vimal, "Removal of Ocular Artifacts in the EEG through Wavelet Transform without using an EOG Reference Channel," *Int. J. Open Problems Compt. Math*, vol. 1, (no. 3), pp. 188-200, 2008.

[8] S.V. Ramanan, N.V. Kalpakam, and J.S. Sahambi, "A novel wavelet based technique for detection and de-noising of ocular artifact in normal and epileptic electroencephalogram," in Communications, Circuits and Systems, 2004. ICCCAS '04. 2004 International Conference on, 2004, pp. 1027-1031 Vol.2.

[9] L. Pon, M. Sun, and R.J. Sclabassi, "Adaptive separation of background activity and transient phenomenon in epileptic EEG using mathematical morphology and wavelet transforms," in Engineering in Medicine and Biology Society, 2000. EMBS '00. 22nd Annual International Conference of the IEEE, 2000, pp. 1583-1585 vol.2.

[10] R.Q. Quiroga, Z. Nadasdy, and Y. Ben-Shaul, "Unsupervised spike detection and sorting with wavelets and superparamagnetic clustering," *Neural Comput.*, vol. 16, (no. 8), pp. 1661-1687, 2004.

[11] J.M. Dean, S.A. George, G. Wassink, A.J. Gunn, and L. Bennet, "Suppression of post-hypoxic-ischemic EEG transients with dizocilpine is associated with partial striatal protection in the preterm fetal sheep," *Neuropharmacology*, vol. 50, (no. 4), pp. 491-503, 2006.

[12] G.H. McIntosh, K.I. Baghurst, B.J. Potter, and B.S. Hetzel, "Foetal brain development in the sheep," *Neuropathology and Applied Neurobiology*, vol. 5, (no. 2), pp. 103-114, 1979.

[13] L. Bennet, J.M. Dean, G. Wassink, and A.J. Gunn, "Differential Effects of Hypothermia on Early and Late Epileptiform Events After Severe Hypoxia in Preterm Fetal Sheep," *J Neurophysiol*, vol. 97, (no. 1), pp. 572-578, January 1, 2007.

[14] M. Scher, "Neonatal seizures: an expression of fetal or neonatal brain disorders," in Fetal and Neonatal Brain Injury. Mechanisms, management and the risks of practice, D. K. Stevenson, W. E. Benitz and P. Sunshine eds. 2nd ed., Cambridge: Cambridge University Press, 2003, pp. 735-784.

[15] P.S. Addison, *The illustrated wavelet transform handbook: Introductory theory and applications in science, engineering, medicine and finance.*, New York: Taylor & Francis Group, 2002.