Deep Convolutional Neural Network and Reverse Biorthogonal Wavelet Scalograms for Automatic Identification of High Frequency Micro-Scale Spike Transients in the Post-Hypoxic-Ischemic EEG

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***Abstract*—Diagnosis of hypoxic-ischemic encephalopathy (HIE) is currently limited and prognostic biological markers are required for early identification of at risk infants at birth. Using pre-clinical data from our fetal sheep models, we have shown that micro-scale EEG patterns, such as high-frequency spikes and sharp waves, evolve superimposed on a significantly suppressed background during the early hours of recovery (0-6 h), after an HI insult. In particular, we have demonstrated that the number of micro-scale gamma spike transients peaks within the first 2-2.5 hours of the insult and automatically quantified sharp waves in this period are predictive of neural outcome. This period of time is optimal for the initiation of neuroprotection treatments such as therapeutic hypothermia, which has a limited window of opportunity for implementation of 6 h or less after an HI insult. Clinically, it is hard to determine when an insult has started and thus the window of opportunity for treatment. Thus, reliable automatic algorithms that could accurately identify EEG patterns that denote the phase of injury is a valuable clinical tool. We have previously developed successful machine-learning strategies for the identification of HI micro-scale EEG patterns in a preterm fetal sheep model of HI. This paper employs, for the first time, reverse biorthogonal Wavelet-Scalograms (WS) as the inputs to a 17-layer deep-trained convolutional neural network (CNN) for the precise identification of high-frequency micro-scale spike transients that occur in the 80-120Hz gamma band during first 2 h period of an HI insult. The rbio-WS-CNN classifier robustly identified spike transients with an exceptionally high-performance of 99.82%.**

Clinical relevance—**The suggested classifier would effectively identify and quantify EEG patterns of a similar morphology in preterm newborns during recovery from an HI-insult.**

I. Introduction

Perinatal hypoxia-ischemic encephalopathy (HIE), due to an HI event at or around the time of birth, substantially evolves over time and causes significant grey and white matter injury leading to life-long impaired neurodevelopment and function [1, 2]. Our pre-clinical experiments in fetal sheep models demonstrate that a severe HI event is immediately followed by a latent phase of recovery of cerebral oxidative metabolism of around 6-8 hours similar to that seen in human newborns, before a secondary period of failure of oxidative metabolism characterized by the appearance of high-amplitude seizures emerge in the EEG [2]. The latent phase is characterized by the bulk appearance of evolving micro-scale epileptiform transients, such as high-frequency spike transients (Fig.1) and sharp waves, that are expressed on a significantly suppressed background EEG (see Fig.2 of [3]) [2, 3]. Further, we have shown that the timing and number of these events is predictive of neural outcome [4] and clinical HI EEG transients are shown to be associated with adverse outcomes [5]. Many neuroprotection therapies, such as therapeutic hypothermia may be optimally applied when started during the latent phase when cerebral oxidative metabolism is relatively stable [1, 6]. However, unlike the pre-clinical studies in animals, clinically we do not always know when an insult has started or may have occurred before birth, and thus the phase of injury [1, 6]. To improve utilization of treatments requires that we develop prognostic and diagnostic biomarkers which allow us to determine phases of injury.

We have previously developed automated algorithms for the identification of spikes [3, 7, 8] and sharp waves [4, 9-11] using reverse biorthogonal wavelets and fuzzy classifiers. We have shown in our preterm fetal sheep model that the number of automatically quantified spike transients (80-120Hz gamma-band) peak around 2-2.5 hours of the latent phase of HI recovery. Our research demonstrates that bulk transient expression is 2-4 hours, falling thereafter before the beginning of high-amplitude seizures at around 6-7 h post-insult [3, 12].

Clinically, bursts of high-frequency oscillations (HFO: >80Hz) are also shown to be the early signatures of later epileptic seizures [13]. Recently, we developed a reliable deep CNN classifier, fed with Gaussian wavelet scalogram images of EEG segments for accurate identification of sharp waves in the post-HI EEG of preterm sheep models [14].

This paper combines, for the first time, the exceptional robustness of our WS-CNN approach, previously tested on sharp waves [14], with spectrally-rich feature maps extracted from EEG segments using reverse biorthogonal wavelets (namely, rbio2.8 basis function over a broad scale-range of 1-19) to identify high-frequency micro-scale spike transients

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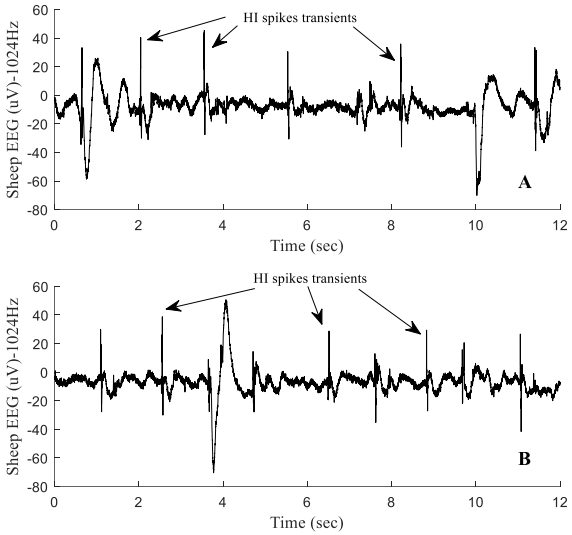

Figure 1. (A), (B): Sample EEG sections containing high frequency micro-scale HI spike transients within a 25 min hypoxic ischemic ECoG section (30-55 min post-insult) from an asphyxicated preterm fetal sheep.

in the gamma frequency band (80-120Hz) in the post-HI EEG of preterm fetal sheep. The performance of the rbio-WS-CNN classifier was be evaluated over 25 minutes signal during the most critical period of the early-latent phase (0-2 hours from HI insult). The work is an initial step further that validates the reliability of our robust WS-CNN classifier for successful classification of HI EEG transients (e.g. spikes).

II. METHODS

A. Data collection

The animal procedures in this study were approved by the Animal Ethics Committee of the University of Auckland. HI signals were collected from two preterm fetal sheep at around 0.7 gestational age (~104 days, where term is 147 days gestation). Fetal sheep brain maturation at this age is equal to a preterm human brain of age 27-30 weeks gestation [15]. The animal management and surgical procedures have been described previously [3, 16]. During the surgery, two pairs of electrodes (made of Cooner wire, Cooner Wire, Chatsworth, CA, USA) were symmetrically placed on the dura over the parasagittal parietal lobe to collect data from the left and right sides of the brain. A reference electrode was also sewn over the occiput. Data from dural placement of electrodes is referred to as the electrocorticogram (ECoG), and therefore from here we refer to data as ECoG. The HI insult was induced by 25 min occlusion of the umbilical cord as previously described [3]. The insult and recovery was monitored via cardiovascular and blood samples for oxygenation [3]. Seven hours of post-HI fetal ECoG was recorded and digitized at 1024Hz sampling rate. A sample 25 minute ECoG section within the first two hours of the HI insult (minutes 30 to 55) was chosen for transient analysis. All the HI spike transients within the chosen ECoG interval were manually annotated by an expert (HA). Clinically, an EEG event with a length of <70ms and an amplitude of >20μV is defined as a spike. However, for consistency with our previous studies [3, 7, 17], an ideal HI gamma spike was characterized as a transient with a pointed peak amplitude of >20μV and a much shorter duration (namely less than 12.5ms that is equivalent to the frequency range of >80Hz).

B. Feature extraction using Reverse Biorthogonal WT

The non-complex mother bases in the biorthogonal wavelet family such as the reverse biorthogonal wavelets offer desirable features (i.e. symmetry), that are well-matched with inherent characteristics of an ideal HI spike transient [3, 7, 18]. We have previously demonstrated that rbio2.8 mother wavelet can be used as an optimal wavelet function for the time-localization of HI spike transients when used as the transfer function in a continuous wavelet transform (CWT) [3]. Feature extraction plays a pivotal role in machine learning and signal processing, where a more detailed set of features generally leads to better accuracies. In this work, the CWTs of the zero-meaned ECoG segments, using rbio2.8 mother wavelet at scales 1-19, are initially applied to generate scalogram images of an arbitrary ECoG segment. Images stored at the resolution of 303×404 pixels. Examples of the HI spike transients within 30-55 minutes post-insult are shown in Fig 2A-D. The corresponding scalogram images of the ideal gamma spikes in Fig. 2A-D are shown in Fig 2E-H, respectively. Examples of non-spike events, as well as their corresponding scalogram images, are shown in Fig. 3A-D and Fig 3E-H, respectively. The suggested feature extraction strategy, through employing a continuous range of spectral features of an ECoG segment using rbio2.8 CWT at scales 1-19, provides robust feature maps for a successful classification, distinctively. The classifier was trained over raw noisy data for generalization.

C. The proposed deep 2D-CNN classifier

Convolutional neural networks (CNN) are one of the enhanced deep-learning structures that have been successfully applied to HI data for seizure detection in neonatal EEG [12, 19-21] and sharp wave identification in experimental data [11, 14]. This work incorporates the robustness of our 17-layers deep CNN (namely the WS-CNN classifier [14]) with spectrally-rich feature maps extracted of the ECoG segments, using rbio2.8 wavelet at scales 1-19, to identify micro-scale spike transients in HI data from a preterm fetal sheep. The proposed WS-CNN architecture has been previously described in [14]. The kernel size and stride parameters, at each layer, were set to desired values according to the convolutional computational needs (see table II in [14]). Wavelet transformed input images of size 303×404×3 were fed to the classifier and processed through seven convolutional (with rectified linear activation units (ReLU) after each convolutional layer), seven max-pool and three fully connected layers (total of 17 layers deep CNN). The output of the CNN block was then passed into a softmax and a classification layer for final designation between a spike and non-spike event and noise or artifact. The parameters of the classifier (weights and bias) were updated using a stochastic gradient descent with momentum (SGDM) strategy to minimize the loss function $E(\theta)$ considering a learning rate of α=0.01and a momentum of $\gamma = 0.09$, where θ represents the parameters vector:

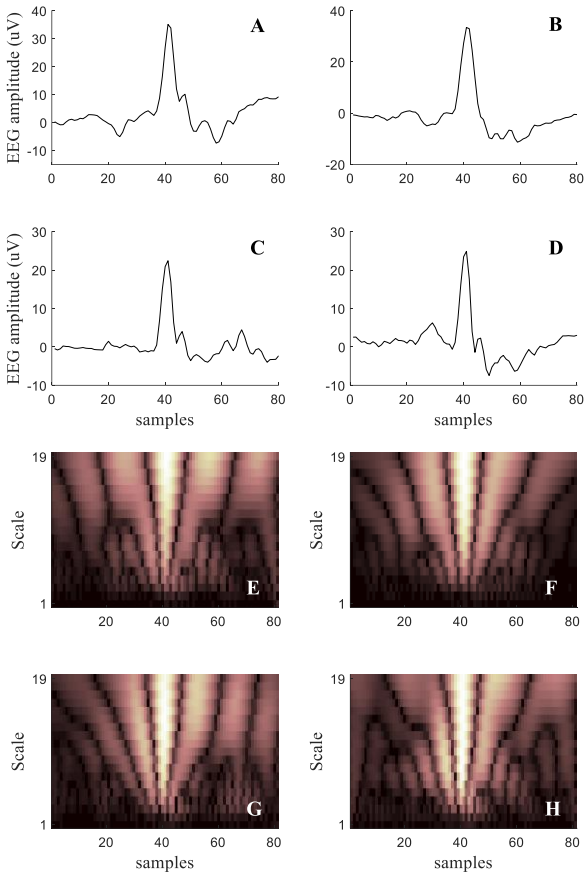

Figure 2. (A-D): Examples of high-frequency micro-scale HI spike transients within a 25 min HI ECoG segment (30-55 min post-insult) used for training of the rbio-WS-CNN. (E-H): scalograms of the corresponding spikes in (A-D), respectively, using rbio2.8 mother wavelet of scales 1-19.

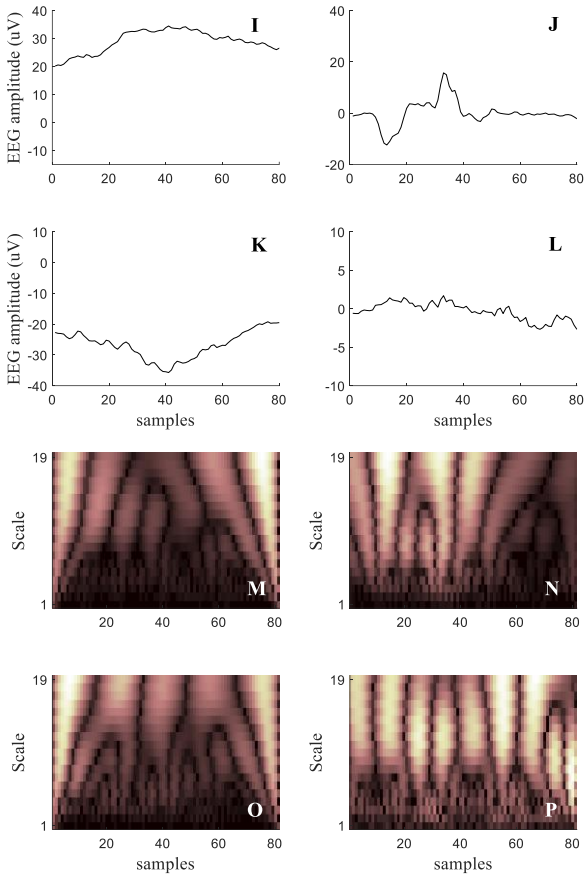

Figure 3. (A-D): Examples of none-spike segments within a 25 min hypoxic ischemic ECoG section (30-55 minutes post-insult) used for training of the Rbio-WS-CNN. (E-H): scalograms of the corresponding spikes in (A-D), respectively, using rbio2.8 mother wavelet of scales 1-19.

$$\boldsymbol{\theta}_{l+1} = \boldsymbol{\theta}_l - \boldsymbol{\alpha}\nabla E(\boldsymbol{\theta}_l) + \boldsymbol{\gamma}(\boldsymbol{\theta}_l - \boldsymbol{\theta}_{l-1}) \qquad (1)$$

The α and γ were not further tuned due to the satisfactory high performance of the classifier with the initial setup. The classifier was executed over a total of 120 epochs with a data distribution proportion of 90% for training (training 75% and validation 25%) and 10% for final testing of the net (Fig. 4). A total of 1240 manually annotated samples, including 620 spike and 620 non-spike segments, were used for training, validation, and testing of the rbio-WS-CNN. Due to working with high-frequency components (namely, gamma spike transients) in a high-resolution dataset, the validity of the method was further assessed over a second dataset, containing much higher number of non-sharp events (4424 samples). This assures that the classifier would still perform well under the influence of other high-frequency background activity, artifact and/or high-frequency noise contamination. The algorithm was developed and executed in Matlab® software on a single workstation computer:

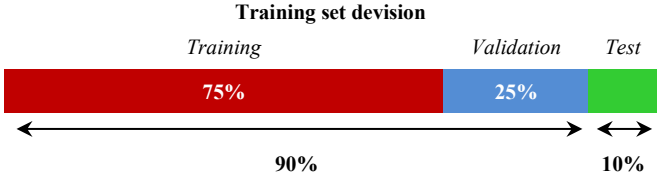

Figure 4. Allocations of the ECoG datasets for training, validation and testing of the proposed rbio-WS-CNN architecture

Intel® Core™ i7-7700 CPU 3.60GHz, 4 cores processor with 16GB RAM memory.

III. Results

The deep rbio-WS-CNN classifier was able to classify gamma spikes with 100% accuracy for all performance measures (including sensitivity, selectivity, precision, and overall accuracy) in the initial dataset with no false negative (missed) or false positive (wrong) detections. The reliability of the rbio-WS-CNN under potential influence of other high-frequency background activity, artifact, or noise, was further investigated using a much bigger dataset of 4486 ECoG samples containing 4424 non-spike samples. The rbio-WS-CNN classifier was able to accurately classify patterns with an overall accuracy of 99.82% (AUC: 0.999). Results from the confusion matrix and the ROC curve are shown in Table I and Fig. 5, respectively. The sensitivity, selectivity, and precision measures of the net were evaluated to be 100%, 99.82%, and 88.57%, respectively. These were measured from a total of 4478 correct classifications including 62 spikes (true positive (TP)) and 4416 none-spike hits (true negative (TN)), with only eight wrong detections (FP) and no missed spikes (FN). Due to working with high-resolution spectral features of an ECoG segment (scalogram images), the classifier was also able to correctly identify patterns with inverse polarity (upside-down spikes) in the dataset.

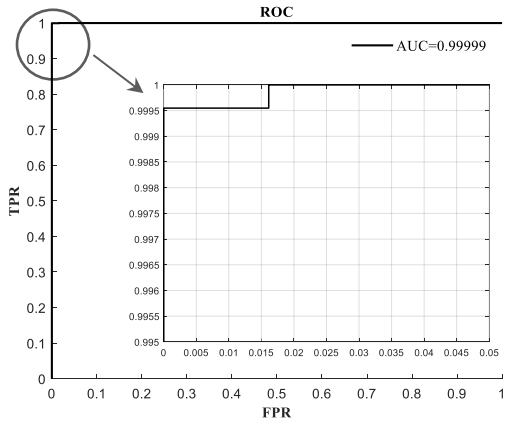

Figure 5. ROC curve and the corresponding AUC for the 17-layers rbio-WS-CNN gamma spike classifier

TABLE I. PERFORMANCE MEASURES OF THE RBIO-WS-CNN CLASSIFIER

Test data	TP hits	TN hits	FP hits	FN hits	Sen (%)	Sel (%)	Precision (%)	Accuracy (%)
10%	62	62	0	0	100	100	100	100
New Set	62	4416	8	0	100	99.82	88.57	99.82

IV. CONCLUSION

This paper employed, for the first time, reverse biorthogonal wavelet-scalograms of ECoG segments to train a 17-layer deep CNN classifier for the precise identification of high-frequency micro-scale spike transients in the post-HI recordings of preterm fetal sheep. The preliminary results confirm the reliability of the rbio-WS-CNN classifier for the post-HI identification of high-frequency micro-scale spike transients from high-frequency noise, artifact and other background activity in 1024Hz sampled recordings. The classifier was trained and tested over a 25 minute hypoxic ECoG recordings, including 4486 patterns during the first two hours of HI-insult, from an *in utero* preterm fetal sheep model. The selected ECoG section overlaps with the critical period in which the number of clinical and experimental transients have been shown to be associated with adverse outcomes. Results emphasize that the rbio2.8 CWT scalograms at scales 1-19 is a good choice for continuous spectral feature extraction from the ECoG signal, providing robust feature maps for the classifier to accurately identify gamma spikes with an overall accuracy of 99.82%. The suggested classifier is generic and could be effectively used for the identification of other EEG patterns (e.g. seizures) in clinical data from preterm newborns during recovery from HIE, including patterns that are specifically appear with a similar morphological characteristics, both in time and frequency domains. Results implicitly indicate the necessity of upgrading the current 256Hz clinical sampling rate to higher sampling rates that could also provide information in higher frequency bands (i.e. gamma).

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