Automated EEG-Based Detection of Seizures in Newborn Babies

Andriy Temko

Neonatal Brain Research Group,
Department of Electrical and Electronic Engineering,
University College Cork,
Ireland
Outline

- Background on neonatal seizures
- Newborn EEG
- Database collection
- Automated neonatal seizure detector
Neonatal Seizures

Seizure is a sign of central nervous system dysfunction.

- Are relatively common.
- Are harmful to the developing brain.
- Are difficult to diagnose.
- Are difficult to treat.
Incidence of Neonatal Seizures

- 1.8-3.5 per 1000 live births (higher in babies with low birthweight and <38 wks GA) - clinical diagnosis
- Occur early in life - 87% within first 48 hrs

Lanska MJ et al. Neurology 1995
Lanska MJ et al. Neuroepidemiology 1996
Ronen GM et al. J Pediatr 1999
Scher MS et al. Pediatrics 1993
Why Treat Seizures?

Harmful to the developing brain

Wasterlain CG et al. Epilepsia 1997
Holmes GL. Neurology 2002

“Cells that fire together, wire together”

Poor prognosis

- 20 to 40% of term babies
- 90% of preterm babies

Scher, et al 1993 Pediatrics, vol. 91, 128-134
Tekgul et al. 2006 Pediatrics, vol. 117, 1270-1280
Neonatal Seizure Treatment

- Neuroprotection
  - Total body cooling
- Drug treatment
  - AED (Anti Epileptic Drugs)

Rennie, J.M., Hagmann, C.F., Robertson, N.J.
Neonatal Cerebral Investigation, Cambridge University Press.

Piglet model
University College London

Janet Rennie
Nicola Robertson
Neonatal Seizures: Risk Factors (I)

- Abnormal CTG in labour
- Depressed Apgar score (<5 at 5 min)
- Need for resuscitation at birth
- Low foetal scalp or cord pH
- Prolonged membrane rupture
- Maternal pyrexia in labour or postpartum
- Maternal drug abuse
- Instrumental deliveries/Emergency caesarean section
- Neonatal pyrexia
- Abnormal neonatal neurological behaviour; poor feeding
- Family history of neonatal seizures
- Prematurity/Small for gestational age

Neonatal Seizures
Risk Factors (II)

25-30% of high-risk babies will develop seizures

Rennie JM, Hagmann CF, Robertson NJ
Neonatal Cerebral Investigation 2008
Connell JA et al. Arch Dis Child 1989
Neonatal Seizures (III)

- Clinical only (psychological, not neurological, not real seizures)
- Electro-clinical (visible in EEG and there are physical manifestations)
- Electrographic only (visible in EEG only)
Diagnostic Approaches

- Clinical diagnosis
- Amplitude integrated EEG (aEEG)
- Conventional EEG
Clinical Manifestation
Clinical Vs EEG diagnosis

- 526 EEG documented seizures
- 34% electro-clinical on video review
- Misdiagnosis common
- Poor inter-observer agreement

Malone et al. Epilepsia 2009
Is aEEG reliable?

- Simple device - easy to use
- One channel of compressed and filtered EEG
- Misses focal, short duration (<1 min), and low amplitude seizures
- Should not be used for diagnosing neonatal seizures

Rennie JM et al. Arch Dis Child 2004

Sensitivity - 38%
Specificity - 92%
Diagnostic Approaches

- Clinical diagnosis
- Amplitude integrated EEG
- Conventional EEG - "gold standard"
What is EEG?

- When large groups of neurons excited together a relatively large ionic current flows (principally Na⁺, K⁺, Cl⁻ ions)
- Berger in 1929 amplified this ionic potential from human cortex, by placing electrodes on the scalp
Montage and Electrodes

- Silver-silver chloride electrodes
- 10/20 international electrode placement system modified for newborn babies (F3, F4, C3, C4, Cz, T3, T4, O1, O2)
Why EEG?

- Anytime, anywhere
- EEG 0.001 - 0.002 sec temporal resolution (fMRI 1 - 3 sec)
- Information on timing of brain injury
- Accurate early diagnosis of neonatal encephalopathy
- Monitoring of treatment
- Prediction of outcome

The best available tool for diagnosing neonatal seizures

Other Measurements

Video recording

EEG channels

One channel ECG

Respiration

Arterial blood pressure

Oxygen saturation
EEG:
• Seizure detection rate ~100%
• Monitoring of seizure treatment
• Long-term prognosis

EEG interpretation:
• Requires special expertise
• Not widely available
• Not available 24/7

Automated seizure detection using computerised analysis of EEG - “Holy grail” in neonatal EEG research
Objective

- To develop an automated seizure detection algorithm for implementation in Neonatal Intensive Care Unit - strong collaboration between clinicians and biomedical engineers
Identify seizure and non-seizure epochs of EEG.
Class Definition

• **Seizure**
  - Any rhythmic activity is suspicious
  - Focal origin with spread
  - Evolves in amplitude and morphology
  - “Sudden, repetitive, evolving, stereotyped waveforms that have a definite beginning, middle and end…”
  - Minimum duration 10 sec

• **Nonseizure**
  - coloured stochastic process contaminated by other deterministic EEG patterns

Clancy and Legido, 1987
Newborn EEG

Signals from the EEG exhibit

- Nonlinearity
  - mapping
  - dynamics

- Nonstationarity
  - short – seconds (bursts, transients)
  - medium – minutes to hours (sleep states)
  - long – years (interconnectivity)

Roessgen, 1997,
Celka & Colditz, 2002,
Boashash & Mesbah, 2003,
Rankine et al., 2007
Newborn EEG (I)

- Background
- White Gaussian noise
- System
- Modulations
- Trace alternant
- Trace discontinu
- Seizure
- Spikes/transients
- Delta waves/brushes
- Abnormal
- Noise/artifact
- Electrical
- Physiological
- Biological

Newborn EEG
Newborn EEG (II)

Modelling
- nonlinear, non-stationary models best simulate EEG

A Nonstationary Model of Newborn EEG, L. Rankine, N. Stevenson, M. Mesbah, B. Boashash
Challenges

- Human computer is difficult to replicate
- Neonatal seizures (unlike infants and adults) demonstrate high inter and intra individual variability
  - Various seizure morphologies
- They evolve both temporally and spatially
- Low SNR/SBR
  - Can be of relatively low amplitude
  - Influenced by background EEG activity
  - Artefacts are common and impact on detection
- Rarity of seizure in a recording
Evolving Seizure
Right Side Focal Seizure
Spatial Evolution
Low Amplitude Seizure
Artefacts

Biological

- Spontaneous respiration
- Excessive sweating

Non-biological

- Rocking a cot
- Mechanical ventilation
Newborn EEG Database

- Neurologically Compromised Babies
  - Term
  - Preterm
- Healthy Babies
Early approach - within 6 hrs after birth

Parental consent

I. Korotchikova, G. B. Boylan, E. M. Dempsey, C. A. Ryan, “Presence of both parents during consent process in non-therapeutic neonatal research increases positive response”, submitted to Archives of Disease in Childhood

Minimal handling

“Disturbing a sick neonate in any way may cause his condition to deteriorate, usually by making him hypoxic”

Robertson 1993
Preparation (II)

- Measuring head
- Scalp preparation with gel
- Application of electrodes using conductive paste
- Securing electrodes with medical tape and soft net
Recruitment Criteria For Sick Babies

2 or more of the following:

- Evidence of foetal distress
- Initial pH < 7.1
- Apgar score < 6 @ 5 min
- Resuscitation at birth
- Abnormal neurology or seizures
Recruitment Criteria For Healthy Babies

- Gestation > 37 weeks
- Normal foetal heart rate prior to delivery
- No requirement for resuscitation following delivery
- Apgar scores of > 8 at 5 mins
- Normal cord pH (>7.1)
- Normal neurological examination (Amiel Tison assessment)
Database Statistics

- Healthy term babies - 86
- HIE babies - 66
  - 17 with electrographic seizures
    - 267.9 hrs of EEG recording in total (mean duration - 15.76 hrs per baby)
    - 705 seizure events

The big advantage over many studies
- Size
- Etiology
- Data quality
- Follow-up info
Automated Seizure Detection

EEG

- Preprocessing: Filtering, re-sampling, artefact removal, segmentation
- Feature extraction: 55 features. Frequency (envelope), model-based (AR), structural (entropy), time-domain (ZCR,E), etc
- Classification: SVM
- Postprocessing: Seizure or nonseizure

Smoothing and thresholding
Preprocessing

- Independent Component Analysis
  - multiple sensor processing
- Re-sampling
  - 32Hz
  - band pass filter (improved performance)
- Segmentation
  - 8 second epoch
  - 50% overlap
Feature Extraction (I)

55 feature set (proven to be useful for the task in many studies)

- Time domain
  - Amplitude and moments
  - AR model residuals
  - Hjorth parameters (complexity, activity, mobility)

- Frequency
  - peak identification
  - frequency band energy
  - Wavelet energy

- Structural & Information based
  - Shannon entropy, spectral entropy, fractal dimension
Feature Extraction (II)

- aEEG
- Spectral edge frequency
- Total power
- Spectrogram
- Spectral entropy
- Band power
Classification

The output of systems is a probability of the seizure!
- Different confidence levels – different decisions
- Flexibility for clinical needs (unlike rule-based methods)
Post-processing

- Smoothing by moving average filter applied over probabilities
- “Or” multi-channel fusion
- “Collar” to compensate the difficulties for detection of pre-seizure and post-seizure parts
Metrics

Epoch-based metrics
- Sensitivity = % Seizure epochs correctly classified
- Specificity = % Non-seizure epochs correctly classified
- ROC curve = Plot of all sensitivity and specificity pairs

Event-based metrics
- GDR = % seizures detected
- FD/h = Mean number of false detections per hour
Results

Epoch-based metrics

Event-based metrics

Performance of SVM-based Seizure Detection System

Temko et al., 2009

ROC curve

Sensitivity

Specificity

Temko et al., 2009

ROC 96.3%

Aarabi et al., 2007

Liu., 1992

Navakatikyan et al., 2006

Greene et al., 2008

ROC 81%

Good Detection Rate

False Detection per Hour (FD/h)

Temko et al., 2009

Navakatikyan et al., 2006

Mitra et al., 2009

Gotman et al., 1997

Temko et al, An SVM based system for neonatal ..., EMBC'09

Temko et al, Performance measurements for neonatal seizure..., submitted

Clinical Neurophysiology 2010
Clinical Interface

- Presenting the results of the algorithm to the clinician
  - no examples of automated diagnosis (decision making)
  - medico-legal issues
- Let the clinician do the post-processing
  - must provide a level of confidence to clinician
Neonatal Seizure Detection
Video Demos

Offline program

Online Viasys NicOne™
integrated

Temko et al., UK patent office application 2009
Offline Demo

Seizure File Analysis

- Load .edf File
- Load Model File
- Analyze File
- Cancel

Options:
- Clinical Settings
  - 0.7
- Engineering Settings
  - 0.74
  - 0.5
  - Mean Variance
  - Moving Average
Online Demo
Analysis of Errors

Most frequent sources of false detections produced by the SVM-based seizure detection system @ 1 FD/h.

Detection of seizures of different duration by the SVM-based seizure detection system @ 1FD/h.

Temko et al, Neonatal Seizure Detection..., submitted Clinical Neurophysiology 2010,
Other Relevant Research

• Validation on healthy babies
  Temko et al., Validation of the SVM-based..., Biostec 2010, Valencia

• Build a GMM based neonatal seizure detector
  Thomas, Temko, et al., Gaussian mixture models for classification..., submitted to Physiological Measurements, 2010

• Introduce a new metric for clinicians to accompany the event based metrics
  Temko et al, Performance measurements for neonatal seizure..., submitted to Clinical Neurophysiology 2010

• Performed a study on usefulness of ECG for neonatal seizure detection
  Doyle, Temko, et al., Heart Rate Based Automatic Seizure Detection in the Newborn, submitted Medical Engineering and Physics, 2010
NEonatal seizure treatment with Medication Off-patent: evaluation of efficacy and safety of bumetanide: NEMO

- Treatment of neonatal seizures with AED (antiepileptic drug)
- European funded (FP7)
- Multicentre RCT
- 13 partners in 6 countries
- PK/PD evaluation
- EEG monitoring
- Neurodevelopmental outcome

Seizures not responding to 1st dose of PB
Seizures confirmed on EEG
Randomisation
PB plus placebo
PB plus bumetanide
Molecular Medicine Ireland Fellowship 2008

- **The BiHIvE Study - Biomarkers in Hypoxic Ischaemic Encephalopathy**
  - Collaborative study between Paediatrics & Child Health and Obstetrics & Gynaecology, UCC
  - To develop an early predictive biomarker based algorithm for HIE severity and neurodevelopmental outcome
  - Recruitment of babies with HIE, EEG and blood biomarkers
- Taugagrening
- Nervus
- Nicolet
- Cardinal health
- Carefusion
  - Vital Signs monitoring
  - Software Licences for Baby Link
  - Code Libraries for real time seizure detection
  - Technical support for Babylink
Efficient Embedded Digital Signal Processing for Mobile Digital Health

Making Medical Sensor Systems “Smart”
- Increasing the complexity of Signal Processing that can be carried out at the Sensor
- Increasing the possible number of Sensors and the collaboration between them.

Research is Application Driven and informed by Clinical Needs

Future Work

- **Clinical trials**
  - What is the best way to display the algorithms’ outputs to clinicians?
  - What effect will an automated seizure detection have on neonatal intensive care practice?

- **Improvement of the seizure detector**
  - Integration of the obtained feedback from analysis of errors
  - Inclusion of temporal evolution information for detection of seizures (previous work on HMMs in BCI)
  - Fusion of SVM and GMM (for an ROC area improvements!)
  - Increasing the robustness of detector to changes in recording environment
Thank you