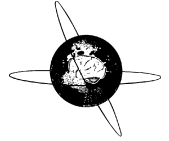




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## Grading hypoxic–ischemic encephalopathy severity in neonatal EEG using GMM supervectors and the support vector machine

Rehan Ahmed <sup>a,b,\*</sup>, Andriy Temko <sup>a,b</sup>, William Marnane <sup>a,b</sup>, Gordon Lightbody <sup>a,b</sup>, Geraldine Boylan <sup>a,c</sup>

<sup>a</sup> Neonatal Brain Research Group, Irish Centre for Fetal and Neonatal Translational Research (INFANT), Ireland

<sup>b</sup> Department of Electrical and Electronics Engineering, University College Cork, Ireland

<sup>c</sup> Department of Pediatrics and Child Health, University College Cork, Ireland

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## HIGHLIGHTS

- An automated system for grading hypoxic–ischemic encephalopathy (HIE) severity using EEG is presented.
- The classification approach is based on long-term statistical model based features.
- The proposed system could act as a decision support system to assist health care professionals in NICUs.

## ABSTRACT

**Objective:** This work presents a novel automated system to classify the severity of hypoxic–ischemic encephalopathy (HIE) in neonates using EEG.

**Methods:** A cross disciplinary method is applied that uses the sequences of short-term features of EEG to grade an hour long recording. Novel post-processing techniques are proposed based on majority voting and probabilistic methods. The proposed system is validated with one-hour-long EEG recordings from 54 full term neonates.

**Results:** An overall accuracy of 87% is achieved. The developed grading system has improved both the accuracy and the confidence/quality of the produced decision. With a new label ‘unknown’ assigned to the recordings with lower confidence levels an accuracy of 96% is attained.

**Conclusion:** The statistical long-term model based features extracted from the sequences of short-term features has improved the overall accuracy of grading the HIE injury in neonatal EEG.

**Significance:** The proposed automated HIE grading system can provide significant assistance to health-care professionals in assessing the severity of HIE. This represents a practical and user friendly implementation which acts as a decision support system in the clinical environment. Its integration with other EEG analysis algorithms may improve neonatal neurocritical care.

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### 1. Introduction

Hypoxic-ischemic encephalopathy (HIE) is a common cause of neonatal death and long-term neurological disability with reported incidences of 3–5 per 1000 births (Volpe, 2008). Perinatal asphyxia occurs when there is a lack of oxygen (hypoxia) and decreased blood supply (ischemia) to the neonatal brain around the time of birth (Berger and Garnier, 1999). If this is prolonged, hypoxic

ischemic encephalopathy develops. The long-term outcome of HIE depends on the severity of the initial HIE insult. Mild encephalopathy may have a normal outcome, 20–40% of neonates with moderate encephalopathy can have an abnormal outcome and severe encephalopathy generally leads to neurological disability or death (Gray et al., 1993) in the majority of neonates. The results of several international trials has shown that early induced hypothermia is beneficial in HIE, improving survival and reducing neurological disability (Azzopardi et al., 2009). The treatment involves cooling the infant to a body temperature of between 32–34 °C for 72 h without interruption. Therapeutic hypothermia has now become a standard of care for moderate and severe HIE.

\* Corresponding author at: Neonatal Brain Research Group, Irish Centre for Fetal and Neonatal Translational Research (INFANT), Ireland. Tel.: +353 21 490 3156.

E-mail address: [rehan@eleceng.ucc.ie](mailto:rehan@eleceng.ucc.ie) (R. Ahmed).

However to be effective, it must be commenced within 6 h of delivery. In this narrow window of time the population of neonates who would benefit from treatment (those with moderate or severe encephalopathy) must be accurately identified.

The ability to recognize and diagnose those who would benefit from therapeutic hypothermia is not always straightforward. Current neonatal practice relies on the initial assessment of the infant's clinical state and other clinical markers to grade the severity of encephalopathy following delivery. Our group has previously shown that these markers are not helpful in differentiating between grades of encephalopathy, and do not vary between mild, moderate or severe grades (Murray et al., 2006). In addition sedative drugs can confound clinical assessment. EEG monitoring on the other hand which can be used immediately after birth, can objectively grade the severity of the EEG and can monitor the evolution of the encephalopathy.

In clinical practice, the EEG is visually analyzed to grade the severity of HIE. Mostly, the HIE is classified into four main grades (Murray et al., 2009) as shown in Fig. 1. Some of the main features inspected are the inter-burst-interval (IBI), sleep-wake cycling, amplitude and the discontinuity of the background EEG (Boylan et al., 2008). However, grading HIE using the EEG requires the presence of a highly qualified neurophysiologist. This expertise is not widely available particularly around the clock in a typical busy Neonatal Intensive Care Unit (NICU), and hence an automated system for grading HIE could be of great help for medical staff.

Some of the early studies used to assess the EEG grade of HIE focused on developing quantitative features. The goal of such studies was to identify, using statistical tests of significance, the key features that can either help to distinguish different grades of HIE or predict the outcome of HIE injury at a later age. Various methods were used to analyze these features such as linear regression analysis or classification trees (Ambalavanan et al., 2006; Korotchikova et al., 2011).

Automatic grading of HIE-EEG is a relatively new area. The main motivation for developing an automated HIE grading system is to assist cotside care-givers in interpreting the neonatal EEG. As can be seen in Fig. 1 the HIE-EEG exhibits various patterns, some of which may be similar across HIE grades; however it is the inter-pattern variability or the way such patterns occur over the whole EEG recording which helps to characterize its grade. Thus,

grading the background EEG requires an amount of data that is large enough to capture the slower time scale components that discriminate between the HIE grades.

In a study by Stevenson et al. (2013), the EEG was first segmented into 64 s epochs. A non-linear amplitude modulated signal model was assumed to describe the EEG over this duration. Using time–frequency analysis, the EEG signal was decomposed into its amplitude modulated and instantaneous frequency components. Basic statistics (mean, standard deviation, skewness and kurtosis) of these components over the 64 s window were used as the key features to characterize the EEG. A multiclass linear discriminant classifier was then used to assign a severity grade.

In a more recent study, Matic et al. proposed a tensor-based approach in which continuous EEG was first adaptively segmented and short-term quantized features were extracted (Matic et al., 2014). These features were then subsequently used to create a 3D model of a specific grade referred as the tensor. Features extracted from this model were then fed to a multiclass classifier for classification.

The work presented in this study takes a different approach. First a set of short-term features are extracted from 8 s EEG epochs on which stationarity can be assumed. The sequence of short-term feature vectors is used to extract statistical model based long-term features. A multi-class classifier based on the support vector machine (SVM) is then used to exploit this information and classify these sequences into one of the four grades. Fig. 2 shows an overview of this process. This approach combines a generative statistical modeling technique known as the Gaussian mixture model (GMM) with the discriminative SVM and is known as the *supervector* approach (Campbell et al., 2006). This method has previously shown promising results in many pattern recognition areas where similarly a decision has to be made over a long data segment and where the statistical feature distribution within a segment is more important than the sequentiality of the data (Hu et al., 2007; You et al., 2009; Zhuang et al., 2010).

The paper is organized as follows: Section 2 describes the dataset, the GMM and supervector kernel concept, followed by an overview of the complete system. Results are presented in Section 3 and are discussed in Section 4 with the conclusion drawn in Section 5.

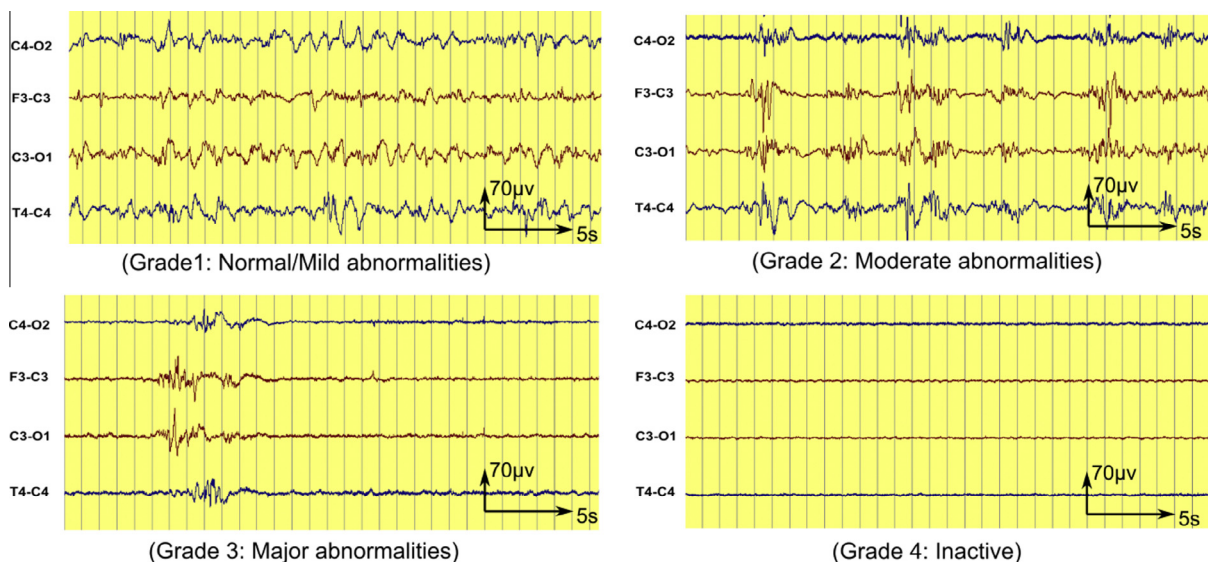


Fig. 1. Clear examples of EEG showing different grades of HIE.

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