A High Performing EEG Approach for the Automated Scoring of the Sleep Stages of Neonates

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An important step in the improvement of neurological care in infants is the appraisal of their brain dynamics since the understanding of their normal/abnormal neurological functionality is limited. For that reason, it is extremely important to use scalp EEG for the daily monitoring of brain activity as an assistive technology designed to improve neurological care in neonatal units (Bonifacio et al., 2011; Glass et al., 2011).

There is a number of studies that clearly demonstrate advances in the assessment of EEG activity through the refinement of various computational models used in brain activity monitoring of infants (Iyer et al., 2015a, 2015b; O'Toole et al., 2016). These analytic algorithms can be further improved by automatic epoching of EEG activity supported by the discriminative features between vigilance states (Palmu et al., 2013; Piryatinska et al., 2009; Räsänen et al., 2013).

Even though the ontogenesis of sleep stages is a very active area of research, the outcomes are controversial. Clinicians have established clear and visually distinguishable EEG patterns for both active and quiet sleep stages in neonates as young as thirty weeks post-menstrual age (André et al., 2010). A fluctuating amplitude-based EEG pattern has been detected and neurophysiologically linked to vigilance state cycling (Klebermass et al., 2011; Natalucci et al., 2013; Reynolds et al., 2014; Stevenson et al., 2014). These fluctuating EEG patterns were the prodromal stage of sleep stage cycling (Kidokoro et al., 2012, Thorenson et al., 2010). However, amplitude-based EEG sleep scoring is highly subjective and requires a clinician with specialized training. Additionally, non-automatic visual scoring of EEG epochs is sensitive to the introduction of artefacts.

To eliminate the human factor from sleep stage scoring of EEG activity based on visual inspection, a more robust and reliable automatic algorithm is needed. Apart from the fact that manual sleep scoring is prone to error, it is time-consuming to train someone and time-consuming to manually score hundreds of EEG recordings lasting an average of 7-8 hours (for a review see Aboalayon et al., 2016). A high performing automatic sleep stage scoring (ASSC) of neonatal EEG recordings is missing from the literature. An objective, computerized ASSC would be an important assistive tool for clinicians in neonatal intensive care units (Glass et al., 2011).

Many algorithmic solutions have been proposed for automatic sleep stage scoring. In one of the very first attempts, Accardo et al. estimated fractal dimension as an appropriate feature for ASSC (Accardo et al., 1998). However, the authors did not present any classification results and the estimation of the fractal dimension D required long EEG recordings. This drawback inhibits the development of real-time systems for the accurate study of the microstructure of human sleep in epochs of less than a minute. An old study proposed a sleep stage classification system for neonates using the Pittsburgh dataset, and it successfully classified EEG epochs in three stages (awake, quiet and active sleep) (Scher et al., 1996). The study also demonstrated differences between full-term and pre-term groups of gestational ages. The whole system was based on discriminant analysis, specifically a nonlinear technique that manipulates EEG structure as applied to every individual recording (Sinha et al.,2001). A more recent paper, focusing on structural EEG time profiles, clustered temporal patterns using an adaptive technique (Krajca et al., 2006). It used k-means for classification of these temporal patterns of sleep activity without presenting any classification performance.

Two recent studies attempted to revive automatic sleep stage scoring in neonates. Fraiwan et al. designed an algorithmic pre-processing step for ASSC in full-term and preterm neonates. They focused on entropic features derived from the Hilbert–Hough Spectrum, the Continuous Wavelet Transform and the Wigner–Ville Distribution (WVD) to estimate a single EEG channel (Fraiwan et al., 2011). They adopted artificial neural networks as the appropriate classifier for the evaluation of ASSC, surpassing an 84% classification accuracy with WVD-based features, which outperformed previously published work. A more recent study proposed the decomposition of EEG time series using the empirical mode decomposition method (EMD) (Huang et al.,1998) to decompose EEGs into basic intrinsic mode functions (IMF). The whole approach was presented with EEG recordings from 20 babies using time-frequency features such as zero-crossing, generalized zero-crossing, relative power and dynamic reconfiguration of dominant relative power within a 30 s epoch (Čić et al., 2013). Finally, applying feature extraction and Support Vector Machines (SVM), the authors achieved, on average, an 80% accuracy of sleep stage classification of daytime sleep in an externally validated dataset.

However, there are many limitations in the literature regarding ASSC in neonates. The majority of the sleep studies focused on ASSC in neonates using small datasets to validate the proposed methodologies. Additionally, these analyses are usually based on a couple of EEG channels, ignoring the most informative channels required for the best ASSC. Complementary sleep stage classifiers have only been developed for term infants (Paul et al., 2003; Piryatinska et al., 2009), but there were no classifiers available in the literature that could be used to automatically score sleep stages covering the whole neonatal age-range from early prematurity to term age.

A recent study (Koolen et al., 2017) in this issue of *Clinical Neurophysiology* succeeded in covering the aforementioned gaps in the literature regarding ASSC in neonates by proposing an algorithm that can be applied to the whole age range. They collected a high number of EEG recordings (N=231) from 67 infants ranging between 24 and 45 weeks of postmenstrual age. The duration of EEG collections was ten minutes from eight channel polysomnography (N=323). In the training set, they used both active and quiet sleep. The proposed feature extraction scheme revealed an informative set of 57 EEG features from spatio-temporal-spectrum domains. Adopting a greedy algorithm for feature selection, they reduced and ranked the features according to their contribution to the classification accuracy. Additionally, the authors explored the effect of both reducing the epoch length and the number of EEG channels.

Performance tests demonstrated that the proposed algorithm was able to classify correctly quiet and active sleep epochs with a high accuracy (85%), sensitivity (83%) and specificity (87%). Interestingly, the authors observed that the performance was stable and unaffected by reducing the epoch length or the number of EEG sensors. The inclusion of both healthy and ill patients represents a clear clinical validation and strength of the proposed algorithm.

Previous studies have attempted to classify sleep stages in neonates within narrower age ranges, focusing on either preterm (Kidokoro et al., 2012; Thoresen et al., 2010; Werth et al., 2016) or term (Paul et al., 2003; Piryatinska et al., 2009; Scher et al., 2005b, 2005c) infants. The present work (Koolen et al., 2017) overcomes and extends prior attempts by developing a classifier that performs well across a wide range of preterm development. Additionally, the authors have provided a proof of concept for clinical implementation and a novel synchronization index for the visualization of the fluctuating brain stages. It would be interesting in the near future to apply the proposed classification scheme to different sub-populations, such as severely abnormal EEG records.

Conflict of interest statement

Author declares that there is no conflict of interest.

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