


**About authors:**

Kurushina Olga Viktorovna, MD, PhD, Head of the department of neurology, neurosurgery with the course of medical genetics, with the course of neurology, manual therapy, reflexotherapy. tel.: +7(8442)361354; e-mail: ovkurushina@mail.ru

Barulin Alexander Evgenievich, MD, PhD, Professor, head of the course of neurology, manual therapy, reflexotherapy. tel.: +7(8442)361354; e-mail: barulin23@mail.ru

Karpov Sergey Mikhailovich, MD, PhD, Professor, head of the Department of Neurology, Neurosurgery and Medical Genetics; tel.: +79054101523; e-mail: karpov25@rambler.ru

© Schetinin V., Jakaite L., 2017

UDC 616.71-018.44-002.2-089.844

DOI – https://doi.org/10.14300/mnnc.2017.12076

**ISSN – 2073-8137**

**IMPORTANCE OF EEG FEATURES IN ACTIVE AND QUIET SLEEP FOR ASSESSMENT OF NEWBORN BRAIN MATURATION AT NEONATAL CENTRES**

**Schetinin V., Jakaite L.**

**University of Bedfordshire, United Kingdom**

**АНАЛИЗ ЗНАЧИМОСТИ ЭЭГ В БЫСТРОЙ И МЕДЛЕННОЙ ФАЗАХ СНА ДЛЯ ОЦЕНКИ РАЗВИТИЯ МОЗГА НОВОРОЖДЕННЫХ В НЕОНАТАЛЬНЫХ ЦЕНТРАХ**

**В. Щетинин, Л. Якайте**

**Университет Бедфордшира, Великобритания**

Newborn brain development can be analysed and interpreted by EEG-experts scoring maturity-related features in sleep electroencephalogram (EEG). These features widely vary during the sleep hours, and their importance can be different in quiet and active sleep stages. The level of muscle and electrode artefacts during the active sleep stage is higher than that in the quiet stage that could reduce the importance of features extracted from the active stage. In this paper, we use Bayesian methodology of averaging over Decision Tree (DT) models to assess the newborn brain maturity and explore importance of EEG features extracted from the quiet and active sleep stages. The use of DT models enables to find the EEG features which are most important for the brain maturity assessment. The method has been verified on EEG data recorded from 995 patients of neonatal centres under a project of the University of Jena (Germany) in 2004. The research has been supported by the Leverhulme Trust (UK), and anonymised EEG recordings have been made available for public research under support of the University of Bedfordshire (UK).

**Keywords:** newborn electroencephalogram, feature importance, sleep stages, Bayesian classification, decision trees

Для решения задач оценки развития мозга новорожденных эксперты неонatalных центров в Европе и Северной Америке используют электроэнцефалограммы (ЭЭГ), записанные во время сна новорожденных, для последующего распознавания и анализа прогностических признаков. Эти признаки, однако, варьируют в течение сна, в то время как их параметры различаются в медленной и быстрой стадиях сна. Уровни мускульных
Newborn’s brain development can be assessed by experts observing the maturity-related patterns in sleep electroencephalograms (EEG) [1, 2]. Clinical experts use these patterns to estimate a newborn’s physiological age [3], although these patterns widely vary during sleep hours and between patients so that the analysis becomes difficult and laborious. For assisting experts in the interpretation, automatic analysis of the maturity-related patterns has been proposed and shown promising [2, 4, 12].

Typically, sleep EEG is recorded during a few hours and comprises one or more cycles of the active sleep (AS) and quiet sleep (QS) stages. These cycles or stages are recognizable in sleep EEG, and the EEG features extracted from these stages make different contribution to the maturity assessment [5].

The sleep stages are recognizable in newborn EEG since approximately 30 weeks post-conception. At this age, the QS is recognized as a pattern with high voltage bursts of delta, theta and alpha activity interrupted by periods with very low voltage. In contrast, the AS pattern is recognized as a longer period of uninterrupted medium-voltage theta and delta activity. The cyclic variations in the voltage and frequency corresponding to the sleep stages become more distinguishable with the brain maturation. For full-term newborns, the AS pattern is characterized by low-to-moderate voltage activity in theta, alpha and beta bands, whereas the QS pattern is often characterized by a high voltage delta activity [2, 5, 6].

The QS and AS patterns were found significantly different in terms of voltage, powers in the delta and theta bands, as well as in terms of the number and length of pseudo-stationary segments [7].

Such a feature as the dimensional complexity of neonatal EEG has been explored and shown to be significantly higher during the AS [8]. An attempt to discriminate the sleep stages by using a set of 88 statistical features representing the voltage, frequency and cepstral coefficients has been described in [9]. Another approach has been undertaken by segmenting newborn EEG into pseudo-stationary intervals which are then clustered by the mean frequency and voltage. It has been shown that the EEG intervals from the QS and AS stages were assigned to different clusters [10]. Another study has shown that the importance of features extracted from the QS and AS stages was different. Particularly, the powers in theta and beta bands were most informative during the AS, whereas the alpha band was prevalent during the QS [11]. A recent study [18] showed that important maturational features related to synchrony of EEG activity can be extracted from QS stage.

The above findings inspired us to explore the importance of EEG features extracted from the QS and AS stages for the assessment. In this research we use the methodology of Bayesian averaging over classification models, in particular, over decision tree (DT) models [13, 14]. These models are widely used in practice due to their explanatory ability. The use of DT models has been also shown promising for estimating EEG feature importance [15, 17]. The Bayesian averaging enables estimation of the full predictive posterior probability distribution that is required for accurate estimation of uncertainty in assessments.

Aim of the investigation: Development of a new method for reliable evaluation of brain maturity in newborns at risk of developmental pathologies for EEG experts of neonatal centres

Material and Methods. In our experiments we used 952 EEG obtained in different clinics from newborns of age from 36 to 45 weeks of post-conception. Each of the 10 age groups has been made including around 100 recordings. The recordings were made with the C3-T3 and C4-T4 electrodes with a sampling rate 100 Hz. The electrodes were positioned according to the standard 10-20 electrode system.

Newborn sleep EEG are weak signals with average amplitude around 50 µV. During sleep hours EEGs are contaminated by noise and artifacts, so that there is the need of cleaning EEG data. Before processing, EEGs are normally rectified to make all amplitudes positive.

The variability of an EEG recorded during sleep hours of a newborn is quite high and can additionally affect the accuracy of recognition of age-related patterns in EEG. We found that the Mean-to-Deviation Ratio (MDR), defined as $m/s$, was around 1.0, where $m$ and $s$ are the mean and standard deviation of rectified EEG amplitudes.

The common artifacts, such as muscle, cardiac, eye blinking, breathing, and electrode movement, can be labeled by an expert and then removed from EEG data. In our EEG data, the rate of labeled artifacts widely ranged from 0.01 to 0.5, and the average rate of artifacts was around 0.1.

The EEGs were recorded in a number of clinics, and artifacts were labeled by different EEG experts. Consequently, we could not expect that the EEG artifacts were labeled consistently and so decided to remove from the EEG data only amplitude artifacts. We defined these artifacts as EEG samples with abnormally high amplitudes. Such artifacts can be automatically detected by using the standard method of adaptive thresholding [16].

The idea of this method is based on the observation that the probability of abnormal EEG samples is distinctly smaller than that of normal samples. For stationary signals, the abnormality of samples can be adequately estimated in terms of their amplitudes. However, EEG are non-stationary signals, and abnormalities should be estimated within a window sliding over the EEG recording. The standard deviation over samples in a window has been shown providing more accurate estimates of the abnormality than the mean over sample amplitudes as
its value is more sensitive to the non-stationarity of EEG [16].

In our implementation, a window of length $W$ is moved over an EEG of length $N$, and the deviation $d_i$ over samples in the window is counted for its central sample $j=W+1, \ldots, N-W$. The probability distribution over $d_i$ is estimated in order to find the most frequent value $d_i$, as well as the maximal deviation $d_{\text{max}}$. Consequently, we expect that the normal EEG samples appear most frequently with the deviation $d_i$ and the abnormal samples appear with a higher deviation. This allows us to count probability $q_i$ that the $i$-th sample with deviation $d_i$ is an artifact:

$$q_i = \frac{d_i - d_i^*}{d_{\text{max}}}$$

Given an acceptable probability of artifacts in the window, $q_0$, we can then label a sample as an artifact if its deviation exceeds the threshold $d_0$:

$$d_0 = d_i^* (d_{\text{max}} - d_i^*) q_0$$

The above technique is based on finding a reasonable trade-off between the accuracy of artifact detection and the amount of normal EEG samples being removed. In our experiments, we found that such a trade-off is achieved with a sliding window of 10-s duration and $q_0=0.225$.

Figure 1 shows an example of removing artifacts from a sleep EEG. The upper plot shows the raw EEG which was contaminated by artifacts visible as samples of a high amplitude. The second plot shows the labels of these artifacts, whose rate was 0.116. The third plot shows the clean EEG. We see that the MDR of the raw EEG was 0.97, and for the clean EEG it increased to 1.06 due to removal of the amplitude artifacts.

![Fig. 1. Segmentation of QS stages in EEG](image)

The background information about sleep patterns in EEG given in the Introduction inspired us to segment EEG into QS and AS sleep stages. Similarly to the above technique of detecting EEG artifacts, these sleep stages can be segmented by adaptive thresholding. Within this technique, duration of the window and threshold value are made adjustable in order to achieve the best accuracy of segmentation on EEG data labeled by an expert. Besides, the information about a minimal duration of QS stage and a maximal duration of breaks, which can happen during QS, are used to improve the segmentation accuracy.

In our experiments, a threshold was adapted to an EEG recording as follows. First, we counted the deviation of samples, $d_i, k=1, \ldots, K$, in a window sliding over an EEG recording, where $K=\text{Ent}(\frac{N-W}{L})$ is the number of windows counted in an EEG, and $L$ is the window shift step. Then we counted a probability distribution histogram, $p_i, i=1, \ldots, M$, over the deviation values $v_i$, where $M$ is the number of bins in the histogram. Namely, the probabilities $p_i$ are the portions of samples whose deviation values are between $v_i$ and $v_{i+1}$. Thus, given a probability $P_0$, we can find a bin $M_0$:

$$M_0 = \sum_{i=1}^{M} p_i \geq P_0, M_0 \leq M,$$

and then choose a corresponding deviation interval, whose center is defined as the desired threshold. In this context, probability $P_0$ is normally associated with a prior on the frequency of an event detected by the segmentation technique.

In our experiments on EEG with the labeled QS stages, we have set $P_0=0.5$ to reflect the fact that the QS intervals represent, on average, a half of an EEG recording. The best accuracy of segmentation was achieved when the maximal duration of QS break intervals was set equal to one min. The minimal duration of QS intervals was set to seven min to enable segmenting QS intervals fragmented at the beginning and at the end of an EEG recording.

The QS segmentation of an EEG is illustrated in Figure 1. The upper plot shows the EEG as the solid line. The dashed line in this plot shows the detected QS stages. The second plot shows the amplitude artifacts which were detected during the QS stages. The third plot shows the EEG cleaned from the artifacts. The lower plot illustrates the process of thresholding detection of QS stages in the clean EEG. The dashed line in the third plot shows the result of QS detection. As the segmentation is made on the clean EEG, finally we extend the duration of sleep stages to the artifacts removed from the raw EEG. The resultant QS labels are shown in the upper plot as the dashed line.

The upper plot shows that the QS stages have been properly segmented despite the high level of artifacts shown to be detected in the second plot. The window duration $W$ and shift $L$ were set to 30 s and 1.5 s, respectively.

The labeled QS and AS intervals were used for extracting EEG features for classification of brain maturity within the methodology of Bayesian averaging over DT models. The details of implementation of the Bayesian method can be found in [17].

**Results and Discussion.** After cleaning and segmentation, the EEG data were represented by 9 features, namely the spectral powers in the six frequency bands, (1) Subdelta, (2) Delta, (3) Theta, (4) Alpha, (5) Beta, and (6) Beta2 (features 1–6), and three features of EEG discontinuity, described in [17]. The spectral powers have been computed with fast Fourier transform over 6-s epochs, which then were averaged within each band in order to represent an EEG by a six-element vector. The artifacts were detected and removed, and the sleep stages in each EEG were segmented into QS and AS intervals.

Table 1 shows the rates of artifacts removed from the QS and AS intervals as well as from the whole EEG. This rate includes EEG samples which have been detected as artifacts within the proposed segmentation technique. The artifact rates are shown with the mean and 2 standard deviation exceeds the threshold $\sigma$.

<table>
<thead>
<tr>
<th>Feature</th>
<th>Mean Artifacts (%)</th>
<th>2σ Artifacts (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>QS</td>
<td>0.972</td>
<td>0.167</td>
</tr>
<tr>
<td>AS</td>
<td>1.057</td>
<td>0.458</td>
</tr>
</tbody>
</table>

**Fig. 1. Segmentation of QS stages in EEG**
more than twice higher than that in the AS intervals. The second plot in Figure 1, which shows the labeled artifacts in the raw EEG, confirms that the artifact rate in the QS intervals is higher than that in the AS intervals.

### Artifact rates in the sleep stages

<table>
<thead>
<tr>
<th>Sleep stage</th>
<th>Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>QS</td>
<td>0.12±0.21</td>
</tr>
<tr>
<td>AS</td>
<td>0.05±0.07</td>
</tr>
<tr>
<td>QS and AS</td>
<td>0.09±0.13</td>
</tr>
</tbody>
</table>

Table 1

In the first two experiments with the Bayesian classification, we used the features extracted from the QS and AS intervals. The third experiment has been run with the features extracted from the whole, unsegmented EEG in order to compare the importance of features within the Bayesian classification.

Table 2 shows the accuracy of the Bayesian classification obtained with the above settings within a 10-fold cross validation for the features extracted from the QS and AS stages as well as from the whole EEG. The accuracy is evaluated within three intervals of weeks post-conception commonly used by the EEG experts.

### Accuracy of assessment for 10 groups within three intervals

<table>
<thead>
<tr>
<th>Sleep stage</th>
<th>Performance, % week intervals 0</th>
<th>1</th>
<th>2</th>
<th>Entropy</th>
</tr>
</thead>
<tbody>
<tr>
<td>QS</td>
<td>25.2±7.4</td>
<td>64.8±8.8</td>
<td>85.5±8.3</td>
<td>206.1±11.7</td>
</tr>
<tr>
<td>AS</td>
<td>26.7±9.9</td>
<td>60.8±10.0</td>
<td>82.5±7.1</td>
<td>210.6±11.8</td>
</tr>
<tr>
<td>Both</td>
<td>28.8±5.5</td>
<td>63.9±9.0</td>
<td>82.9±7.5</td>
<td>207.1±9.8</td>
</tr>
</tbody>
</table>

The performance is shown by the mean accuracy within 2σ standard deviation intervals. The entropy $E$ is counted over an ensemble of $K$ DT models, in order to estimate the uncertainty of the ensemble: $E = \sum_{i=1}^{K} p_i \log_2(p_i)$, where $p_i$ are the class posterior probabilities provided by the DT models.

Figure 2 shows the importance of features extracted from the QS and AS intervals. Observing the results, we see that the most important feature extracted from the AS intervals is related to the discontinuity (feature 7). In the QS intervals, the powers in the Delta, Theta and Alpha bands are also shown to be important.

### Conclusions

In this paper, we explored the importance of EEG features used for the newborn brain maturity assessment within the methodology of Bayesian averaging over decision tree (DT) models. This methodology has been shown providing the most accurate estimates of class posterior distribution, while the use of DT models has been shown capable of finding features making valuable contribution to the assessment. Based on clinical observations that the EEG features in various sleep stages are different, we assumed that there exist EEG intervals which provide the most informative features, which can be extracted from intervals of quiet sleep.

### Acknowledgments

The research is funded by the Leverhulme Trust, UK. The authors are grateful to the University of Jena, Germany, for granting the clinical EEG data for the research.

### References

The paper presents an analysis of the relationship between the duration of cholecalciferol supplementation at different doses and the 25(OH)D concentration in infants during their first year of life. We evaluated 496 infants aged 1 month to 12 months who were divided into four groups depending on the duration of vitamin D supplementation: up to 8 weeks, 8–15 weeks, 16–24 weeks, and over 24 weeks.