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Investigating the Brain Development in Newborns by Information-Based Analysis of Electroencephalography (EEG) Signal

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In this paper, we employ the information theory to analyze the development of brain as the newborn ages. We compute the Shannon entropy of Electroencephalography (EEG) signal during sleep for 10 groups of newborns who are aged 36 weeks to 45 weeks (first to the last group). Based on the obtained results, EEG signals for newborns in 36 weeks have the lowest information content, whereas EEG signals for newborns in 45 weeks show the greatest information content. Therefore, we concluded that the information content of EEG signal increases as the age of newborn increases. Th result of statistical analysis demonstrated that the influence of increment of age of newborn on the variations of informant content of their EEG signals was significant.

Keywords: Brain development; electroencephalography (EEG) signal; information content; Shannon entropy.

1. Introduction

Analysis of the brain development is one of the interesting topics in neuroscience among scientists. As known, human brain is formed quickly and therefore, reacts differently during human ageing. For example, children show different reactions compared to adults, when they are exposed to the same stimuli. Electroencephalography (EEG) signal as the feature of brain activity has been analyzed widely to investigate the variations of brain activity in different conditions. Therefore, analysis of the variations of EEG signal can also help us to decode the brain development in newborns.

By referring to the literature, it can be seen that the analysis of variation of newborns' brain activity after birth has attracted the attention of several scientists. For this purpose, they employed different imaging techniques to record the brain activity, and accordingly analyzed the recorded data using different analysis methods. The reported studies that analyzed Magnetic resonance (MR) images of the developing newborn brain using automatic segmentation [1] evaluated diffusion tensor images (DTI) of white and gray matters of the brain in fetal, newborn and pediatric brains using structure assignment and reconstruction [2], investigated brain development during the first year of life by analysis of MR images using finite strain theory [3], and analyzed the abnormal brain development in newborns with congenital heart disease by applying statistical analysis on MR and DTI images [4], are worthy to be mentioned.

The reviewing of literature shows that a great number of investigations have focused on analysis of EEG signal to decode the variations in the brain activity among different ages. Takahashi *et al.* [5] compared the variations of complexity of EEG signal in healthy elderly and healthy young subjects during pre- and post-photic stimulation (PS) conditions. Based on the obtained results, no significant difference was found between the groups for pre-PS condition. However, a significant change in the complexity of EEG signal was found for post-PS condition only in young subjects. Holthausen *et al.* [6] characterized the changes in the frequency distribution of EEG signal using Fourier transformation in order to investigate brain changes for newborns. The results showed that during the 35th and 41st week of Conceptional Age (CA), the Beta frequency contribution is reduced and, accordingly, the Delta band contribution is increased. Lee *et al.* [7] investigated the variations of EEG signal in the wake and sleep for adults and children using approximate entropy (ApEn). The result of their analysis showed that adults had significantly larger ApEn values than children during wakefulness. In a recent investigation [8], we applied fractal analysis to investigate the variations of complexity of EEG signal for newborns. The results showed that by increasing the age of newborns, the complexity of EEG signal increases.

Between all studies that analyzed brain activity among different ages, no study has considered how brain maturity is reflected on the information content of EEG signal. It should be noted that due to the complex, non-stationary and nonlinear structure of EEG signal, utilizing nonlinear analysis techniques such as entropy is more appropriate. Considering the wide application of different types of entropy such as approximate entropy [9, 10], Shannon entropy [11, 12], fuzzy entropy [13, 14], sample entropy [15, 16], permutation entropy [17, 18] and multiscale entropy [19, 20] in analysis of EEG signal in different conditions in this study, we apply Shannon entropy to do information-based analysis on the brain development of newborns in different ages.

In the following, first, the method of analysis will be discussed. After that, we talk about the used data and the analysis steps. The results of our analysis will be presented thereafter. Finally, we will bring the discussion and also talk about the future works.

2. Method

In this research, we would like to evaluate how the structure of EEG signal varies across different ages. Therefore, we benefit from Shannon entropy as the indicator of information content, where its greater values show greater embedded information in EEG signal, and more mature the newborn brain. In other words, we want to examine how the information content of EEG signal changes as the age of newborn increases.

In general, Shannon entropy is formulated as [21, 22]

$$H = -\sum_{i} p_i \log p_i, \tag{1}$$

where p_i shows the probability of the message (EEG signal in this research) having the value of v_i. It should be noted that i is distributed across different values of the message.

Therefore, in order to evaluate the variations of EEG signal as newborn age, we analyze the information content of EEG signal across different groups.

2.1. *Database and analysis*

In this work, we use the EEG signals that were recorded and prepared at the University of Jena and are available in [23] as open-access database. This database includes the recorded EEG signals from 1110 newborns that are categorized within 10 age groups, namely, 36 to 45 weeks. It should be noted that the data have been collected during sleep, in clinical condition. Each group has different number of subjects. Forty four-weeks group includes the minimum number of subjects (102 subjects), and five groups include the maximum number of subjects (112 subjects). Jakaite and Schetinin collected the EEG signals of each neonate from C3-T3 and C4-T4 channels of device with the frequency of 100 Hz. The duration of recorded EEG signal was different in case of different neonates. The minimum duration was 38.29 min that leads to 229,798 data points, and the maximum duration was 7.82 h that leads to 2,815,567 data points. They also filtered the EEG signal in the frequency band of 0.1–30 Hz [24]. This filter removes slow drifts with frequencies below 0.1 Hz and noise along with high-frequency interference above 30 Hz [24]. In fact, based on the literature [25, 26] the frequency range associated with sleep stages occurs in 0.5 Hz to 30 Hz. Figure 1 shows the samples of filtered EEG signal for 36 to 45 weeks newborns. As can be seen in this figure, we cannot visually recognize the differences between these signals, and therefore, we will do the information-based analysis in order to decode their variations. In fact, the analysis of the variations of EEG signal enables us to talk about brain development in newborns.

In this research, we proceeded with the computation of Shannon entropy using "wentropy" command in MATLAB. This command calculates the Shannon entropy of EEG signal based on Eq. (1). Here, it should be noted that since each age-group contains different number of subjects, in order to have precise

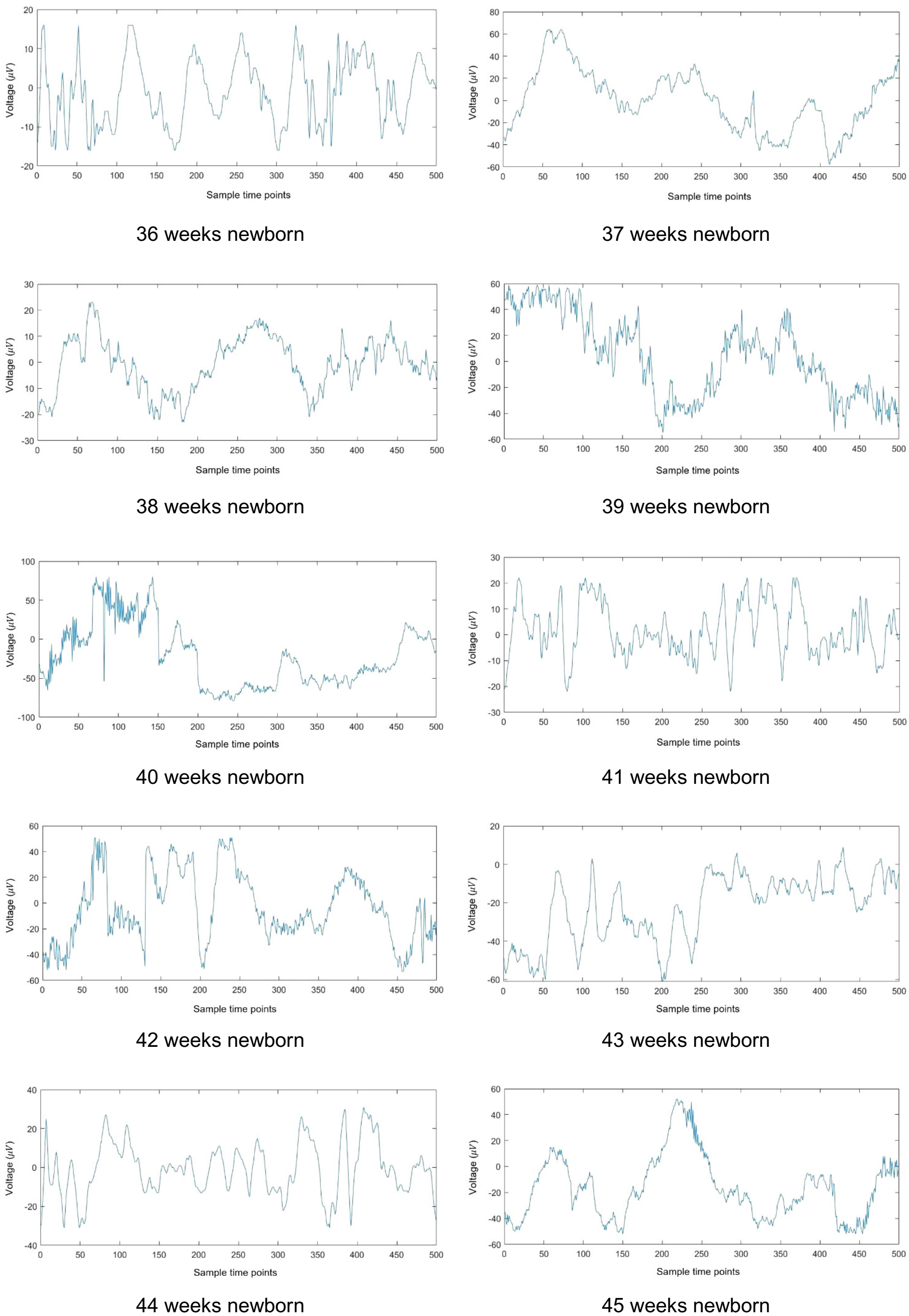

Fig. 1. Sample filtered EEG signals that recorded from 36 to 45 weeks newborns.

statistical analyses, we considered 102 subjects as the minimum number of subjects between all age-groups.

We ran ANOVA test on the calculated values of Shannon entropy in order to analyze the significance of variations of EEG signal as newborn ages. An ANOVA test is a way to find out if the results of study are significant [27]. We also performed *post-hoc* Tukey test to compare the significance of difference in Shannon entropy of EEG signal between different groups. The Tukey test is a statistical tool used to determine if the relationship between two sets of data is statistically significant [28]. In order to check the linearity of the relationship between the variations of entropy of EEG signal with the variations of age, we conducted least square regression analysis.

3. Results

The Shannon entropy of EEG signal (mean value) for different groups are provided in Fig. 2.

According to the result of analysis, Shannon entropy of EEG signals have various values in case of different age groups. As can be seen in Fig. 2, Shannon entropy of EEG signal obtained the lowest value in case of 36-weeks group. Since Shannon entropy indicates the information content of EEG signal in this research, therefore, it can be mentioned that EEG signals of subjects in 36-weeks group have the lowest information content. By looking at the alteration of Shannon entropy of EEG signal in Fig. 2, we can understand that by increasing the age of subjects, the Shannon entropy of EEG signal increases. In other words, the information content of EEG signal increases with newborns' age. As can be seen, EEG signal has the greatest information content in case of 45-weeks group.

In case of statistical analysis, since based on the result of ANOVA test, p-value $=$ 0.000 is smaller than 0.05 (significance level), therefore, the effect of variations of age on the variations of information content of EEG signal was significant. Therefore, it

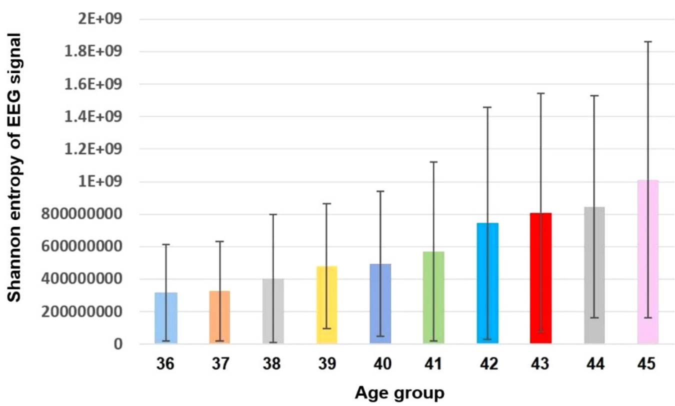

Fig. 2. The Shannon entropy of the EEG signal in case of different groups. Error bars show the standard deviations.

can be said that the information content of EEG signal increases significantly with newborns' age. The result of least square regression analysis ($y = 77374480.245455x - 2533663994.7109$) indicates the linear variations of entropy of EEG signal with the variations of age. In addition, the calculated value of R-Square (as the goodness-of-fit), 0.6135, indicates that age can explain 61.35% of the variance in the information content of EEG signal.

The result of pairwise comparisons between all groups showed that 23 pairwise comparisons have significant difference in their Shannon entropy, where 36-weeks group has significant difference with more groups. As Table 1 shows, 36 weeks subjects (as the youngest age group) showed significant change in the Shannon entropy of EEG signal with five age groups, namely, 41, 42, 43, 44 and 45 weeks. By looking at the other comparisons in this table, we can understand that by increasing the age of subjects in different groups, less significant difference can be found in their Shannon entropy with the groups having greater age.

Therefore, the yearly increment of newborns' age from 43 weeks does not make significant change in the information content of EEG signal compared to other weeks. In addition, significant development of the brain for newborns in 45 weeks can be understood from the significant change in the Shannon entropy of their EEG signal versus other seven groups.

In summary, we can conclude that the changes in the brain's structure (brain development in other word) can be seen by analysis of the Shannon entropy of EEG signal. The results showed that the EEG signals of subjects in 45-weeks group have the greatest information content.

4. Discussion

In this research, we evaluated the variations of EEG signal to investigate the brain development steps in newborns. We benefited from Shannon entropy as the indicator

Table 1. p-value for significant difference in the Shannon entropy of EEG signal.

Comparison	p-value	Comparison	p-value
36 versus 41 weeks	0.0436	38 versus 45 weeks	0.0000
36 versus 42 weeks	0.0000	39 versus 42 weeks	0.0324
36 versus 43 weeks	0.0000	39 versus 43 weeks	0.0016
36 versus 44 weeks	0.0000	39 versus 44 weeks	0.0002
36 versus 45 weeks	0.0000	39 versus 45 weeks	0.0000
37 versus 42 weeks	0.0000	40 versus 43 weeks	0.0031
37 versus 43 weeks	0.0000	40 versus 44 weeks	0.0004
37 versus 44 weeks	0.0000	40 versus 45 weeks	0.0000
37 versus 45 weeks	0.0000	41 versus 44 weeks	0.0206
38 versus 42 weeks	0.0000	41 versus 45 weeks	0.0000
38 versus 43 weeks	0.0000	42 versus 45 weeks	0.0289
38 versus 44 weeks	0.0000		

of information content. The results of analysis showed that the EEG signal experiences the greatest and lowest Shannon entropy in case of 45 and 36 weeks newborns. Therefore, it can be said that the information content of EEG signal increases with increase in the age of newborns. The results of statistical analysis indicated the significant effect of age increment on the information content of EEG signal.

Based on the result of statistical analysis, when the age of newborns increases over 43 weeks, no significant variation in the information content of EEG signal compared to other older groups (namely 44 and 45 weeks) can be seen. It means that the rate of development of brain between 43 weeks, 44 weeks, and 45 weeks is smaller than the earlier ages. In addition, the results showed that the development of the brain in 45 weeks causes significant change in the information content of EEG signal compared to more age groups. For instance, 30-weeks group only shows significant difference with five groups (i.e., 41, 42, 43, 44, 45 weeks old), whereas 45-weeks group shows significant difference with six groups (i.e., 37, 38, 39, 40, 41, 42 weeks old). In general, the results of analysis show the power of information theory to decode brain development in newborns.

Here, it should be noted that the result of this investigation is in line with obtained results in other studies. For instance, Ferri *et al.* [29] showed that the structure of sleep EEG in newborns is significantly different from that of adults. Corsi-Cabrera *et al.* [30] demonstrated significant week-by-week changes in sleep EEG signal in newborns. In our recent investigation [8], we applied fractal analysis in order to investigate the variations of complexity of EEG signal for newborns. The results showed that by increasing the age of newborns, the complexity of EEG signal increases. In other words, we showed that the development of brain can be evaluated by analysis of EEG signal. The results of this study also showed that the development of brain can be reflected on variations of information content of EEG signal in another example.

The conducted investigations in this study can be further developed to analyze the variations of other physiological conditions of newborns (such as heart rate, respiration) as they age.

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