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ALGORITHM FOR AUTOMATIC DETECTION OF SPORADIC EPILEPTIFORM DISCHARGES IN THE EARLY STAGE OF DEVELOPMENT OF DELAYED CEREBRAL ISCHEMIA

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Abstract. An algorithm for automatic detection of delayed cerebral ischemia index during electroencephalographic monitoring of a patient after subarachnoid hemorrhage – dynamics of sporadic epileptiform discharges, has been developed. The algorithm is based on the analysis of the cross-correlation function of the electroencephalogram with a selected sample of epileptiform spike-wave discharge. The synchronization of channels located throughout the head was studied. The number of hourly epileptiform discharges was calculated both separately for the hemispheres – the left and the right, and for the zones of the brain - frontal, parietal and central. As a result of applying the algorithm, peak-wave discharges per hour clusters exceeding the threshold value and related in time are identified. The algorithm was applied to 14 control patients and 10 patients diagnosed with delayed cerebral ischemia. Sensitivity, accuracy, and selectivity of algorithm is equal to 90%, 83%, and 79% respectively.

Key words: electroencephalography, epileptiform discharges, correlation function, delayed cerebral ischemia.

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Introduction

The most common methods of instrumental diagnostics of delayed cerebral ischemia (DCI) after subarachnoid hemorrhage (SAH) are neuroimaging methods – computed tomography and magnetic resonance imaging (CT and MRI). Tomographic methods are performed for a short period of time and are not applicable for long-term monitoring of patients. To assess the risk of DCI, it is important to use an easily mastered portable device that can record data for several hours or more. In medical practice, such a device is an electroencephalograph (EEG). It provides a non-invasive, continuous assessment of brain activity in real time and requires a relatively short review time compared to raw EEG assessment. It is used as a screening tool to specifically include patients with high-risk EEG characteristics in clinical trials testing new treatments to mitigate and prevent DCI [1, 2]. Verification of EEG examination in clinical practice is carried out by means of additional CT or MRI examination.

In recent years, publications have increasingly appeared on the results of studies on the significance of diagnostic and prognostic indicators of EEG monitoring. Retrospective studies [2, 3] have shown the possibility of differentiating patients and control subjects on the 5th day after the start of EEG monitoring of the development of DCI. Based on the results of studies of patients with SAH, a new marker of DCI has been proposed – the hourly number of epileptiform discharges (ED), which correlates with an increased risk of developing DCI.

Previously, the authors developed an algorithm for automatic detection of epileptiform activity in long-term video-EEG monitoring signals for patients suffering from epilepsy. Both EEG data and video were processed [4].

This paper describes an algorithm for automatic detection of sporadic ED per hour. It is based on the analysis of channels synchronization. Both synchronization between the channels of each hemisphere separately and between the channels located throughout the head were considered. As a result of applying the algorithm, clusters of hourly peak-wave discharges exceeding the threshold value and related in time are identified, which will help the attending physician assess the risk in the early stage of development of DCI. Comparison of ED distributions per hour with the results of clinical neurological examination will help to decide on repeat CT examination to establish the diagnosis of DCI.

1. Data and Preprocessing

We study the long-term data (several days) EEG monitoring of patients after the operation to block the SAH. After that, the patient underwent CT examination, and if cerebral ischemia was determined, then EEG examinations were not performed in such patients. EEG registration was performed in bipolar montage of 16 channels with a sampling frequency of 250 Hz according to the 10-20 scheme: Fp1-F7, F7-T3, T3-T5, T5-O1, Fp1-F3, F3-C3, C3-P3, P3-O1, Fp2-F4, F4-C4, C4-P4, T5-O1, P4-O2, Fp2-F8, F8-T4, T4-T6, T6-O2. Even leads correspond to the right hemisphere, odd ones – to the left.

In differential montage there is no common electrode. With this method of recording data, it is easier for the doctor to track local changes occurring in the brain. This type of montage is mainly used in monitoring studies.

The article examines data from 24 patients observed in the intensive care unit after surgery. In 10 patients, DCI was diagnosed, and in 14 patients DCI did not develop after surgery. The diagnosis was confirmed by CT examination.

Pre-processing was performed for each pair of leads. Power-line noise at frequencies multiple of 50 Hz was removed from the data. The signal was analyzed in the frequency band from 0.5 to 70 Hz, for this purpose an 8th order Butterworth filter was used in the forward and reverse direction in the selected frequency band. The linear trend was also removed from the signal.

2. Detection of Epileptiform Activity

For detection of ED, we used the analysis of the cross-correlation function of EEG signals with an EEG graph element pre-selected by an expert physician – a peak-wave discharge with a sharp peak of large amplitude and a subsequent slow positive wave. The height of the selected peak is about 100 mkV, half-width is 90 mS.

Naturally, all ED cannot be identical to the standard, so it is necessary to determine the conditions by which an ED can be recognized. Let's introduce the following notations: A is amplitude; R – correlation function; σ – half-width; p-peak; w – wave. The following conditions of ED detection were formed:

1) $A_p > 40$ mkV;
2) $R_p > 0$ and $R_w < 0$;
3) $R_p > 0.4$;
4) $\sigma_p \leq 100$ mS;
5) $\sigma_w > \sigma_p$;
6) In the 40 mS interval at least in 2 channels should be synchronized spikes.

We considered two options for channels synchronization: for the channels of each hemisphere separately and for all channels simultaneously. To detect ED in one of the hemispheres, synchronization was used across the hemispheres, and when determining the occurrence of ED in certain areas of the brain - frontal, central and parietal - channel synchronization was calculated for the entire head.

As in [5], the following electrodes division into brain zones were used: anterior cerebral artery – Fp1-F7, Fp1-F3, Fp2-F8, Fp2-F4, middle cerebral artery – F7-T3, T3-T5, F3-C3, C3-P3, F8-T4, T4-T6, F4-C4, C4-P4, and posterior cerebral artery – T5-O1, P3-O1, T6-O2, P4-O2.

In the works [2, 3] it was shown that the index of the DCI is an increase in the hourly number of ED over a long period of time (more than 3 hours). Analysis of the dynamics of hourly ED shows that the fluctuation spread in each patient is in a different range. Patients with ischemia show a similar distribution of ED per hour with values less than 20. This can be considered as some activity that is present in both DCI patients and control patients.

We varied the threshold of ED/hour - 10, 15 and 20 ED/hour, below which the data were discarded. When using threshold values of 10 and 15 ED/hour, no changes were found in the sensitivity and specificity of the algorithm, while at a threshold of 20 ED/hour, the specificity of the algorithm increased, but sensitivity and selectivity decreased. Therefore, a threshold of 15 will be used to remove background activity from consideration.

After identifying ED above the threshold value, the time intervals in which they were observed were determined. A binary sequence of 0 and 1 was formed, where 0 corresponded to an hour without ED and 1 to an hour with ED. Dilation and erosion operations were applied to this sequence to combine continuous time intervals in which ED above the threshold were present. As a result, the time interval of ED existence was determined, possibly with breaks of 1-2 hours.

The criterion for inclusion in the group of patients with DCI was the presence of an ED cluster lasting more than 6 hours. In the case of a sufficiently long-time interval, according to the physician's assessment, the patient undergoes an additional CT scan to verify DCI.

Let us give examples of the distribution of hourly ED in different zones of the head, calculated for a patient diagnosed with DCI in the left hemisphere. Fig. 1 shows the distribution of hourly ED in the left hemisphere. Blue shows the number of ED per hour, black squares highlight the hours in which there were many numbers of ED, white squares indicate the hours in which there were no ED. Black and white squares were obtained after applying the dilation and erosion algorithms.

Figure 1 shows epileptic activity of varying durations. Before the 20-hour mark, ED can be observed, which lasts only one hour. Such epileptic activity cannot serve as an indicator of the development of DCI. Beyond the 20-hour mark we see the opposite, long periods of time in which ED occurs. Let's consider the selected cluster of epileptic activity located between 20 and 40 hours. In this cluster ED is observed for several hours in a row, then there are hours where ED is absent and then it appears again. Such fragments, between which there is an absence of ED for about 2 hours, were combined using a dilation algorithm. Clusters lasting longer than 6 hours were used as an indicator of the occurrence of DCI. There are 4 such clusters on the graph: between the 20 and 40 hours, between the 40 and 70 hours, between the 70 and 90 hours, and after the 100 hour and until the end of the recording.

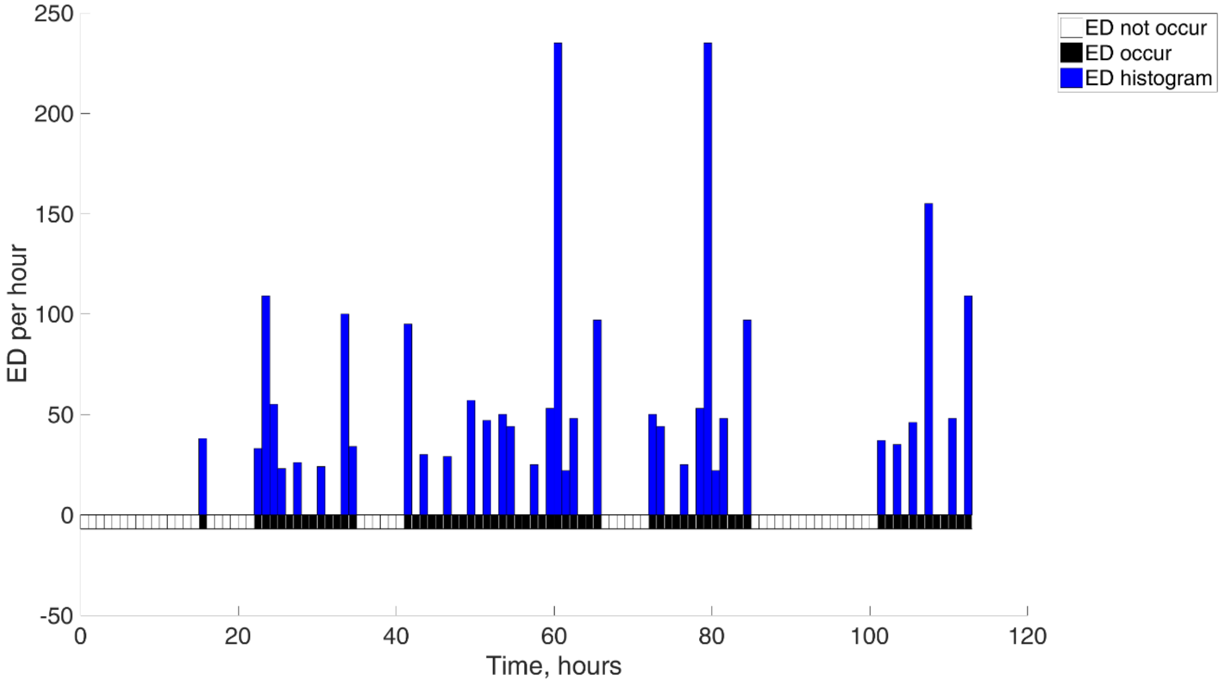

Fig. 1. Distribution of ED per hour in the left hemisphere of patient with DCI diagnosed in the left hemisphere. Blue indicates the number of ED. Black shows the time interval in which there was an ED, white shows intervals without ED.

Let us give an example of the hourly distribution of ED in the right hemisphere of the same patient with diagnosed ischemia in the left hemisphere (Fig. 2).

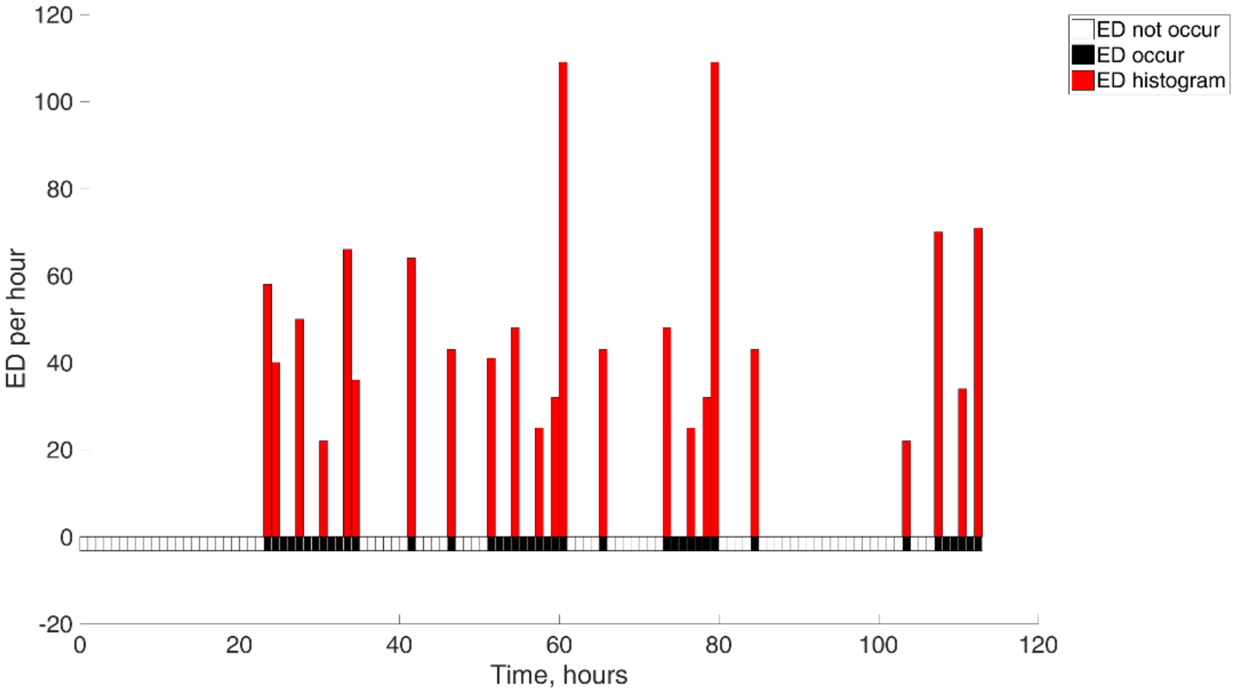

Fig. 2. Distribution of ED per hour in the right hemisphere of patient with DCI diagnosed in the left hemisphere. Red indicates the number of ED. Black shows the time interval in which there was an ED, white shows intervals without ED.

In the right hemisphere, the number of hourly ED is significantly reduced. If in the left hemisphere up to 250 ED per hour were observed, then in the right hemisphere it is almost 2 times less - up to 120 ED per hour. It is also clear that the graph is scattered: clusters of shorter duration have emerged compared to the left hemisphere, and there are more single ED columns per hour.

Let us construct graphs of the distribution of hourly ED in the left hemisphere for the same patient, but in three zones of the head: frontal (Fig. 3), central (Fig. 4) and parietal (Fig. 5).

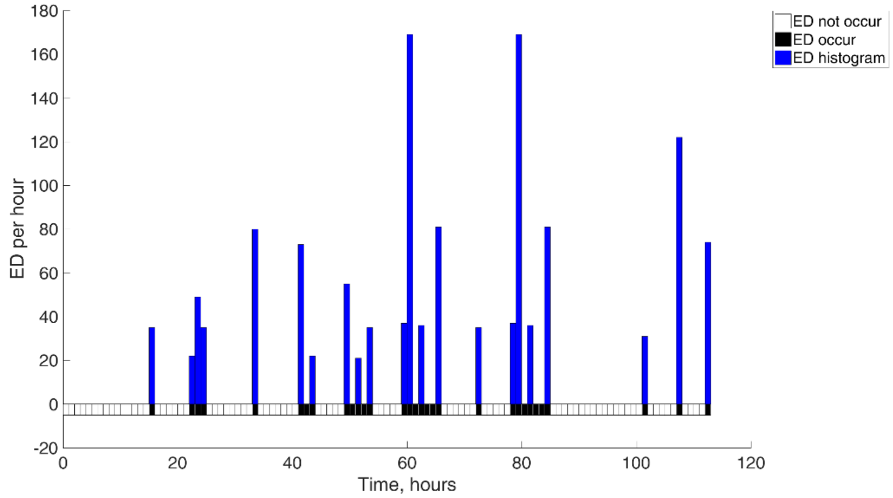

Fig. 3. Distribution of ED per hour in frontal zone in the left hemisphere of patient with DCI diagnosed in the left hemisphere. Blue indicates the number of ED. Black shows the time interval in which there was an ED, white shows intervals without ED.

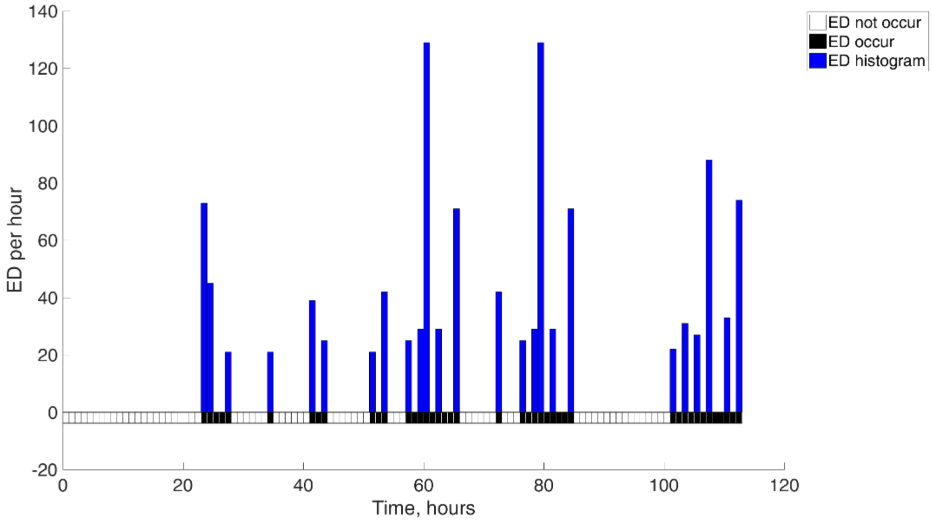

Fig. 4. Distribution of ED per hour in the central zone in the left hemisphere of patient with DCI diagnosed in the left hemisphere. Blue indicates the number of ED. Black shows the time interval in which there was an ED, white shows intervals without ED.

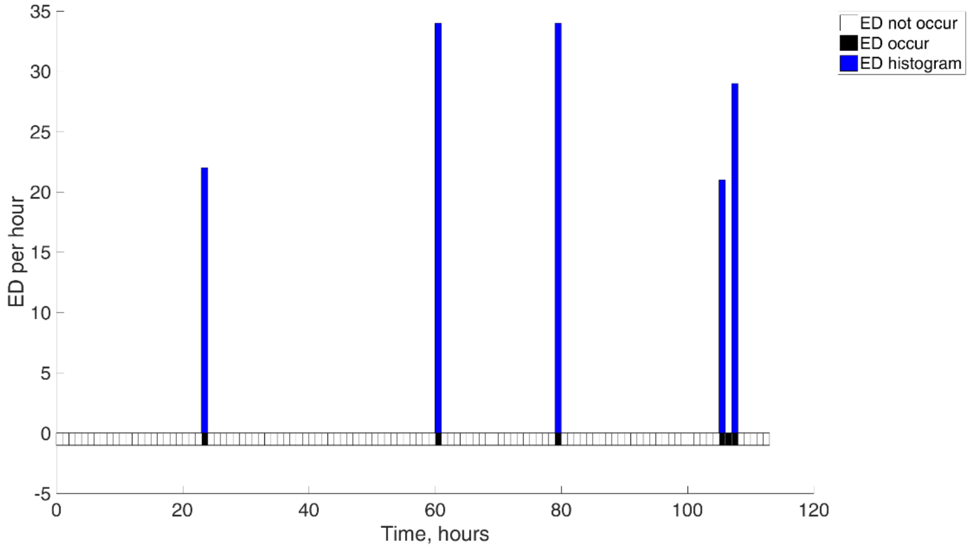

Fig.5. Distribution of ED per hour in parietal zone in the left hemisphere of patient with DCI diagnosed in the left hemisphere. Blue indicates the number of ED. Black shows the time interval in which there was an ED, white shows intervals without ED.

As you can see, the distribution of hourly discharges by brain zones differs from the distribution by hemisphere. Clusters with long duration of hourly ED are not observed in the parietal zone (Fig. 5). Hourly ED and one cluster lasting more than 3 hours are observed. In the frontal (Fig. 3) and central (Fig. 4) zones, clusters lasting more than 6 hours or more are present in almost the same zones that were found in the left hemisphere. In both zones these clusters are present in the interval between 50 and 70 hours and between 70 and 90 hours, in the central zone there is still a cluster after 100 hours. This correlates with the clinical conclusion. That is, in addition to determining in which hemisphere DCI occurred, it is possible to clarify the zones in which it is observed.

For both control patients and DCI patients, hourly ED distribution graphs were calculated. These distributions were also analyzed and clusters of ED with duration of more than 6 hours were identified. Subsequently, a comparison was made between the results obtained by our algorithm and the assessment of expert clinicians.

3. Results

The paper analyzed EEG monitoring data from 24 patients after surgery, in whom cerebral ischemia was not detected by CT studies immediately after surgery. As a result, 14 patients without diagnosed DCI after SAH – control patients, and 10 patients with diagnosed DCI were considered.

We studied the dynamics of hourly numbers of sporadic ED in two options: in different hemispheres – the left and the right, and in brain zones - frontal, central and parietal. In medical practice, a conclusion about the occurrence of ischemia is made if ED occurs in large quantities over a long period of time. When evaluating the algorithm, we considered that DCI occurred if ED continued for 6 hours. Table 1 shows the values of correspondence to expert opinions when using the left and the right hemisphere analysis algorithm. The "Diagnosis" column shows the diagnosis made by the clinician; the "Quantity" column shows how many such diagnoses were made by the doctor. "True Positive" shows that the conclusion by algorithm coincides with the expert's conclusion. “False positive” means that the diagnosis made by the algorithm does not match the expert's assessment. “False negative” indicates that the algorithm has identified another diagnosis as the selected one. Example of a “False Negative”: the current diagnosis under consideration is DCI, the algorithm has identified the control as DCI.

Table 1. Statistics on patients diagnosed with DCI in the left and/or the right hemispheres and control patients without DCI.

Diagnosis	Quantity	True Positive	False Positive	False Negative
DCI in the left hemisphere	3	2	1	3
DCI in the right hemisphere	3	3	0	2
DCI in both hemisphere simultaneously	4	4	0	3
Control	14	11	3	1

Table 2. Statistics on patients diagnosed with DCI in different zones of the brain and control patients without DCI.

Diagnosis	Quantity	True Positive	False Positive	False Negative
DCI in both hemispheres simultaneously in frontal zone	**2**	**2**	**0**	**3**
DCI in the left hemisphere in frontal zone	**1**	**1**	**0**	**3**
DCI in the right hemisphere in central zone	**3**	**2**	**1**	**3**
DCI in the left hemisphere in two zones simultaneously – central and parietal	**2**	**2**	**0**	**3**
DCI in all zone simultaneously	**2**	**2**	**0**	**3**
Control	**14**	**11**	**3**	**2**

Table 1 shows that the algorithm recognized 8 patients with DCI out of 10, and 11 out of 14 control patients, 2 patients were falsely recognized as control patients, and 3 control patients were falsely recognized as DCI, thus the sensitivity is 90% and selectivity is 79%, and accuracy is 83%. Similarly, a table shows the brain zones of DCI patients (Table 2).

As you can see in this case the algorithm recognized 8 patients with DCI out of 10, and 11 out of 14 control patients, 2 patients were falsely recognized as control patients, and 3 control patients were falsely recognized as DCI.

This observation suggests that this algorithm for determining the occurrence of DCI by brain zones in different hemispheres allows us to estimate where the DCI focus is localized. Compared to the determination of ischemia by hemispheres, only the selectivity of the algorithm decreases by almost 10%.

Conclusion

An algorithm for automatic detection of sporadic epileptiform discharges per hour – an index of delayed ischemia after subarachnoid hemorrhage – was developed. The algorithm is based on the analysis of the correlation function of all pairs of EEG leads with a reference peak-wave discharge and the analysis of the dynamics of the hourly number of epileptiform discharges. The conditions for their determination are given and clusters of these discharges are detected on the second day of recording electroencephalograms.

The algorithm was used to detect delayed cerebral ischemia both in individual hemispheres and in areas of the brain - central, frontal and parietal. It has been shown that the analysis of the distribution of ED by zones can serve clinicians as an additional factor determining the localization of the DCI.

Accuracy, sensitivity and selectivity were calculated for clusters of epileptiform discharges with a minimum duration of 6 hours and a threshold of ED/hour of 15 was applied. The algorithm of analyze of ED per hour was shown to have high sensitivity, accuracy, and selectivity equal to 90%, 83%, and 79% respectively.

The developed algorithm is implemented in the MATLAB software environment. The processing time of the hourly recording of the patient's electroencephalogram is several minutes, which allows it to be used in the real-time of delayed cerebral ischemia development.

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