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Algorithm for detecting epileptiform EEG activity in delayed cerebral ischemia

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Abstract: **An algorithm for automatic detection of epileptiform activity in EEG monitoring data with delayed ischemia after hemorrhage in the subarachnoid space of the brain is proposed and described. The algorithm is based on the formalization of the visual characteristics of epileptiform activity in the form of a peak-wave discharge pattern and analysis of the mutual correlation of multichannel EEG signals with the selected pattern. Fragments of epileptiform activity in each pair of bipolar electrodes were determined from three conditions according to the description of peak-wave discharges of epileptiform activity: 1) the value of positive mutual correlation at the peak of the correlation function should be greater than 0.4; 2) a positive peak of mutual correlation should be followed by a peak with a negative correlation; 3) the width of the peak of negative mutual correlation at half-altitude should be at least 2 times greater than that of the previous positive peak of positive mutual correlation. As with the visual detection of epileptiform activity, the neurophysiologist selected simultaneous peak-wave discharges in several bipolar electrodes. The results of testing the algorithm on an hour-long EEG recording of a patient with delayed ischemia are presented. Fragments with epileptiform activity during the hour under review were identified 17 in the right hemisphereand 2 in the left. Interhemispheric asymmetry is caused by a right-sided aneurysm in patient. The operating time of the algorithm on a modern personal computer is no more than 5 minutes to process 16 bipolar signals, so it can be used to calculate the hourly amount of epileptiform activity in almost real time of the manifestation of this indicator of delayed ischemia after aneurysmal subarachnoid hemorrhage.**

Keywords: **electroencephalogram, long-term monitoring, epileptiform activity, mutual correlation function, delayed cerebral ischemia**

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Contents

1. INTRODUCTION

Delayed cerebral ischemia usually occurs 4 to 14 days after the onset of a non-traumatic or traumatic hemorrhage in the subarachnoid space of the brain. The objectives of conservative treatment of patients with subarachnoid hemorrhage (SAH) are stabilization of the patient's condition, prevention of recurrence of SAH, prevention and treatment of vascular spasm and delayed cerebral ischemia. Intensive treatment is carried out in the conditions of monitoring the main indicators characterizing the state of the cerebrovascular system and vital functions. After admission of a patient with suspected non-traumatic or traumatic SAH to the intensive care unit of a neurosurgical hospital, a detailed neurological examination, an assessment of the severity of the condition, computer tomography (CT scan) and magnetic resonance imaging (MRI studies), transcranial and extracranial Doppler ultrasonography to assess the severity of angiospasm, electroencephalography to assess the severity of changes in the bioelectrical activity of the brain are performed.

Clinical neurological examination is the "gold standard" for diagnosing delayed cerebral ischemia, but it requires good speech contact with the patient, which is impossible in the case of severe SAH, accompanied by depression of wakefulness before coma. Neuroimaging methods, which include CT and MRI, remain the "gold standard" of instrumental diagnosis of delayed ischemia, but their main drawback is the need to transport the patient to the tomograph, which makes it impossible to use them in the monitoring mode.

Electroencephalography (EEG) records the bioelectrical activity of the brain, so any change in its functional state is immediately reflected in the indicators of the curves. Changes in EEG are directly related to volumetric blood flow [1]. Signs (indicators) of cerebral ischemia are manifested on the EEG in real time, which makes this method indispensable for intraoperative monitoring during operations on the brachiocephalic arteries, and in the intensive care unit for early diagnosis of delayed cerebral ischemia after SAH.

If brain damage due to hemorrhage has led to depression of wakefulness before coma and clinical neurological examination is difficult, and CT requires transportation of the patient to the device, continuous EEG monitoring becomes the main way to diagnose and predict the development of delayed cerebral ischemia. An alternative approach is Doppler ultrasonography monitoring. This method allows you to accurately diagnose vasospasm, but the very fact of narrowing the vessel does not always lead to cerebral ischemia, and the technical feature of ultrasound measurement of blood flow velocity allows you to determine it only at one small point

not exceeding a few millimeters, while the spasm can be localized elsewhere.

EEG monitoring is the only method by which continuous round-the-clock monitoring of the functional state of the brain of a patient with SAH in the intensive care unit can be carried out to diagnose and predict the development of delayed cerebral ischemia. In combination with periodic studies using neuroimaging methods, it allows for early detection and prediction of the development of delayed ischemia, which makes it possible to begin intensive treatment and stop its development. In principle, long-term monitoring of EEG in real time of the manifestation of indicators makes it possible to diagnose and predict the development of delayed ischemia and evaluate its dynamics even before its heart attack develops, and further evaluate restoration of cerebral perfusion even before clinical improvement [2-4].

Existing EEG monitoring systems provide real-time recording of EEG in the disk memory in the presence of instrumental artifacts and artifacts of the patient's vital activity and at the same time display multi-channel EEG on the monitor for visual observation and analysis by the doctor. To highlight time intervals with artifacts caused by the patient's vital activity and the care of his medical staff, it is advisable to analyze video recordings synchronous with EEG.

Usually, the analysis of the results of long-term video-EEG monitoring is carried out retrospectively offline by viewing multichannel EEG and video fragments. The methodology for EEG analysis of delayed ischemia is traditionally based on visual analysis of curves, with the allocation of artifact-free recording areas and analysis of its background structure, single special graphic patterns, spectral energy in a certain time interval (usually 1 hour) in various frequency ranges alpha (8-13 Hz), beta (14-40 Hz), theta (4-8 Hz), delta (0.5-3 Hz), and their ratio in the delta/alpha and (delta + theta)/(alpha + beta) ranges, possessing specificity in relation to various clinical conditions. This analysis is an extremely time-consuming and time-consuming work of highly qualified neurophysiologists and, in addition, the objectivity of such a diagnosis varies significantly between individual specialists. Given the required 10–14-day duration of monitoring in patients with SAH, the use of the generally accepted analysis of graph elements visually by EEG in offline mode is almost impossible and does not allow for prompt medical decision-making in case of unfavorable development of delayed ischemia.

Therefore, for the widespread use of quantitative EEG (qEEG), it is necessary to develop an automated system for detecting indicators of delayed ischemia as a result of subarachnoid hemorrhage, which makes it possible to detect, classify and predict indicators of delayed ischemia in real time [3]. In addition, due to the artifacts of the patient's vital activity and his service by medical personnel, the automated calculation of EEG diagnostic parameters without a priori selection of data segments without artifacts or manual review by trained neurophysiologists is an unsolved problem of automatic algorithms for detecting delayed ischemia.

Numerous studies have made it possible to identify EEG patterns, which are sometimes called "malignant" in the literature, since they are characteristic of an unfavorable prognosis of survival and restoration of consciousness [2-4]. These include sustained suppression of the amplitude of background activity below 10 μV, disruption of the continuity of EEG curve oscillations with the development of the flash-suppression pattern, registration of generalized periodic discharges with the same interval between digits and monomorphic graphic patterns, etc. The main diagnostic and prognostic indicators of delayed ischemia in EEG monitoring are (1) focal and regional slowing, index decrease, and cessation of rapid activity; (2) a decrease in the variability of the EEG power averaged over the frequency range and leads separately in the left and right hemispheres of the alpha rhythm power; (3) a decrease in the ratio of the average power of alpha/delta rhythms; (4) epileptiform graphic patterns, including sporadic epileptiform discharges, lateralized rhythmic delta activity, lateralized periodic discharges, or generalized periodic discharges. Lateralized periodic discharges are sharp oscillations, such as spikes and sharp waves, that occur more or less periodically [5]. Recent studies of epileptiform anomalies have demonstrated their diagnostic and prognostic potential in monitoring delayed ischemia after SAH [3,4].

In [6], the results of a retrospective study of the values of the hourly number of epileptiform discharges, determined visually, were published to predict the development of delayed ischemia after SAH. Using visual offline analysis of EEG graphic patterns using the Persyst EEG Analysis Support System (https://www.persyst.com/), it was found that in many patients with SAH, the hourly number of epileptiform discharges per hour increases during the first 3 to 10 days after cerebral hemorrhage, the main risk period for delayed ischemia. In patients with developing delayed ischemia, hourly epiactivity for 3.5–6 days is significantly higher after SAH compared to those who do not develop ischemia (area under the ROC curve AUC = 0.72).

Finally, individual trends in the dynamics of epileptiform discharges over time, assessed using a group analysis of the trajectory of hourly load – the number of epileptiform discharges per hour, also help to stratify the risk of delayed ischemia. Similar results were obtained in studies of rats with pharmacological provoking of mild, moderate, and severe stroke [7]. The maximum AUC within 5 days after SAH is 0.61, and within 10 days it is 0.68. These are the results showed that the hourly number of epileptiform discharges is a useful parameter for identifying individuals at higher risk of developing delayed cerebral ischemia after SAH. These studies were performed by neurophysiologists retrospectively "manually" using the analysis of diagnostic parameters offline, using, as a rule, the Persyst EEG Analysis Support System (https://www.persyst.com). Fragments of multichannel ones lasting 5–15 seconds were analyzed. Such an analysis, firstly, is extremely time-consuming, secondly, it depends on the qualifications of neurologists [8] and, thirdly, in principle, changes in the hourly number of epileptiform discharges cannot be applied in real time. As a result, a 2022

review [3] on the diagnosis of delayed cerebral ischemia concluded that it was necessary to develop algorithms for the automatic detection of indicators of delayed cerebral ischemia after SAH.

This article proposes and describes an algorithm for automatic detection of time fragments of EEG with epileptiform activity, based on the analysis of the functions of cross correlation of EEG with a characteristic fragment of epileptiform activity and the results of its testing on clinical EEG data – monitoring of a patient after SAH.

2. ALGORITHM FOR DETECTING EPILEPTIFORM ACTIVITY

In **Fig. 1** shows the layout of the electrodes in accordance with the international standard 10–20%. For long-term EEG monitoring, bipolar mounting (differential recording scheme) Fp1-F7, F7-T3, T3-T5, T5-O1, Fp1-F3, F3-C3, C3-P3, P3-O1 – left hemisphere and Fp2-F4, F4-C4, C4-P4, T5-O1, P4-O2, Fp2-F8, F8-T4, T4-T6, T6-O2 – right hemisphere are used. Bipolar EEG recording is used to reduce trends and other artifacts. The signal is recorded at a sampling rate of 250 Hz. Signal filtering was carried out in the Matlab programming environment using filters: notch (iirnotch function) at a frequency of 50 Hz, 8th order Butterworth bandpass filter (butter function) in the frequency range 0.5-70 Hz, removal of the linear trend (detrend function).

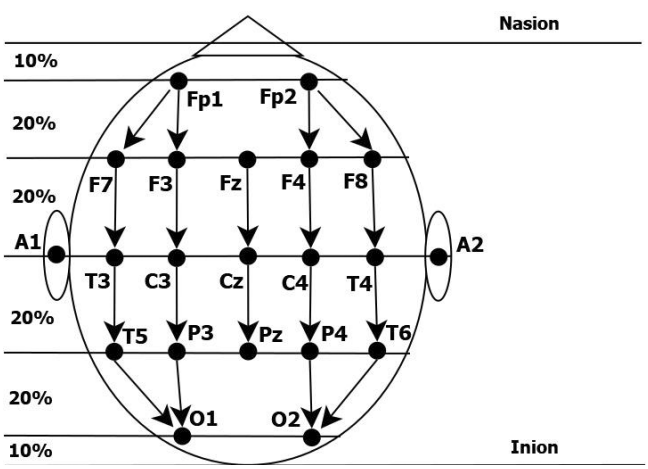

Fig. 1. *Arrangement of EEG electrodes on the scalp in accordance with the international scheme of 10-20%. Even electrodes are on the right hemisphere, odd electrodes are on the left, A1 and A2 are reference electrodes. The arrows indicate pairs of electrodes in bipolar EEG recording.*

In **Fig. 2** shows an example of a 5-second fragment of a bipolar EEG of a patient with delayed ischemia after SAH in the frontal part of the right hemisphere, recorded on 10/14/2022.

From Fig. 2 shows that the characteristic features of the graph element of epileptiform activity (see, for example, recording in a pair of channels C4-P4) is the presence of a high-amplitude (100 μV) acute negative peak with a duration of 90 msec at a half-altitude and a wave following it with a duration of more than 2 times. To detect a fragment of epileptiform activity, we used the analysis of the cross correlation of the function (Matlab xcorr function) of EEG recording in each pair of bipolar electrodes with a negative peak sample, which was chosen as a negative EEG peak in a pair of C4-P4 electrodes in a time interval of about 3.5 seconds. The green dots indicate the maximum and zero correlation values.

In **Fig. 3** shows the function of cross correlation of the bipolar signal of the EEG fragment shown in Fig. 2, with selected sample. A fragment of epileptiform activity is highlighted in red, which was determined from three conditions according to the description

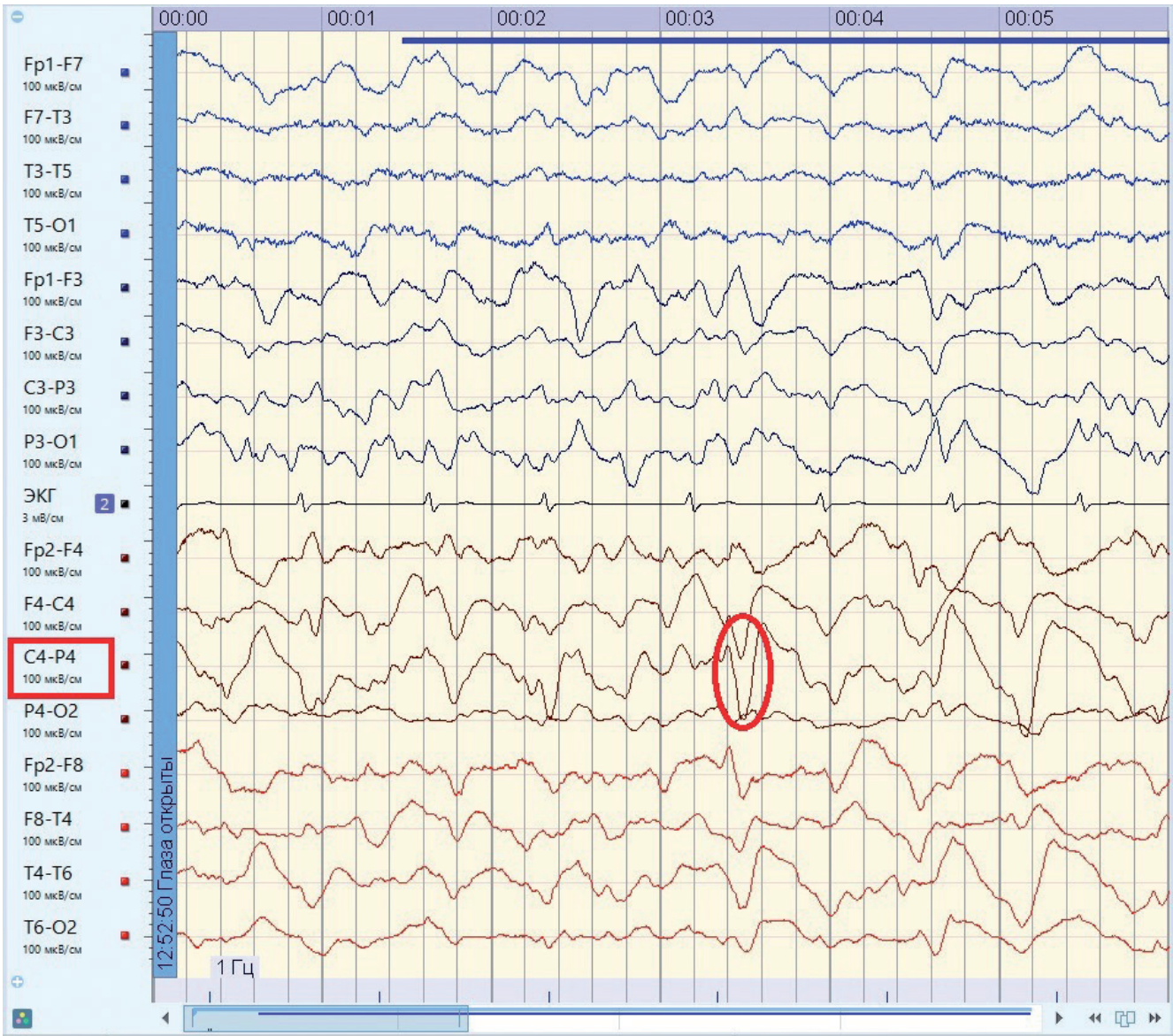

Fig. 2. *A 5-second fragment of an EEG recording with epileptiform activity indicated by a red circle.*

of peak-wave discharges of epileptiform activity:

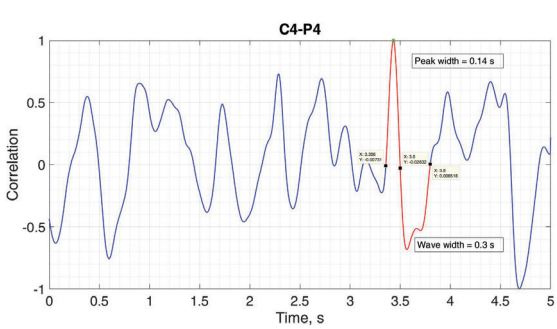

Fig. 3. *Cross correlation of a 5-second EEG fragment with a negative EEG peak in a pair of C4-P4 electrodes in a time interval of about 3.5 sec from Fig. 2.*

1) the value of positive cross correlation at the peak of the correlation function should be greater than 0.4;

2) a positive peak of cross correlation should be followed by a peak with a negative correlation;

3) the width of the peak of negative cross correlation at half-altitude should be at least 2 times greater than that of the previous positive peak of positive cross correlation.

3. RESULTS OF PROCESSING CLINICAL EEG RECORDINGS

An hour-long EEG recording was analyzed at a 3-hour daily recording on 12.10.2023 before CT examinations in patient D., who had a ruptured aneurysm of the right internal carotid artery. On CT on 10/15/2023, a hematoma was found in the area of surgery in the right front temporoparietal region. CT scan dated 10/18/2023 diagnosed ischemia in the right temporal and occipital lobes of part of the right hemisphere. It should be noted that the EEG fragment in which the sample of epileptiform activity presented in Fig. 2 was selected was recorded on another day of EEG monitoring.

In **Fig. 4** as an example is a fragment of the EEG of patient D. in the time interval of 2 hours 45 minutes 38 seconds – 2 hours 45 minutes 41 seconds, which visually determines the epileptiform activity.

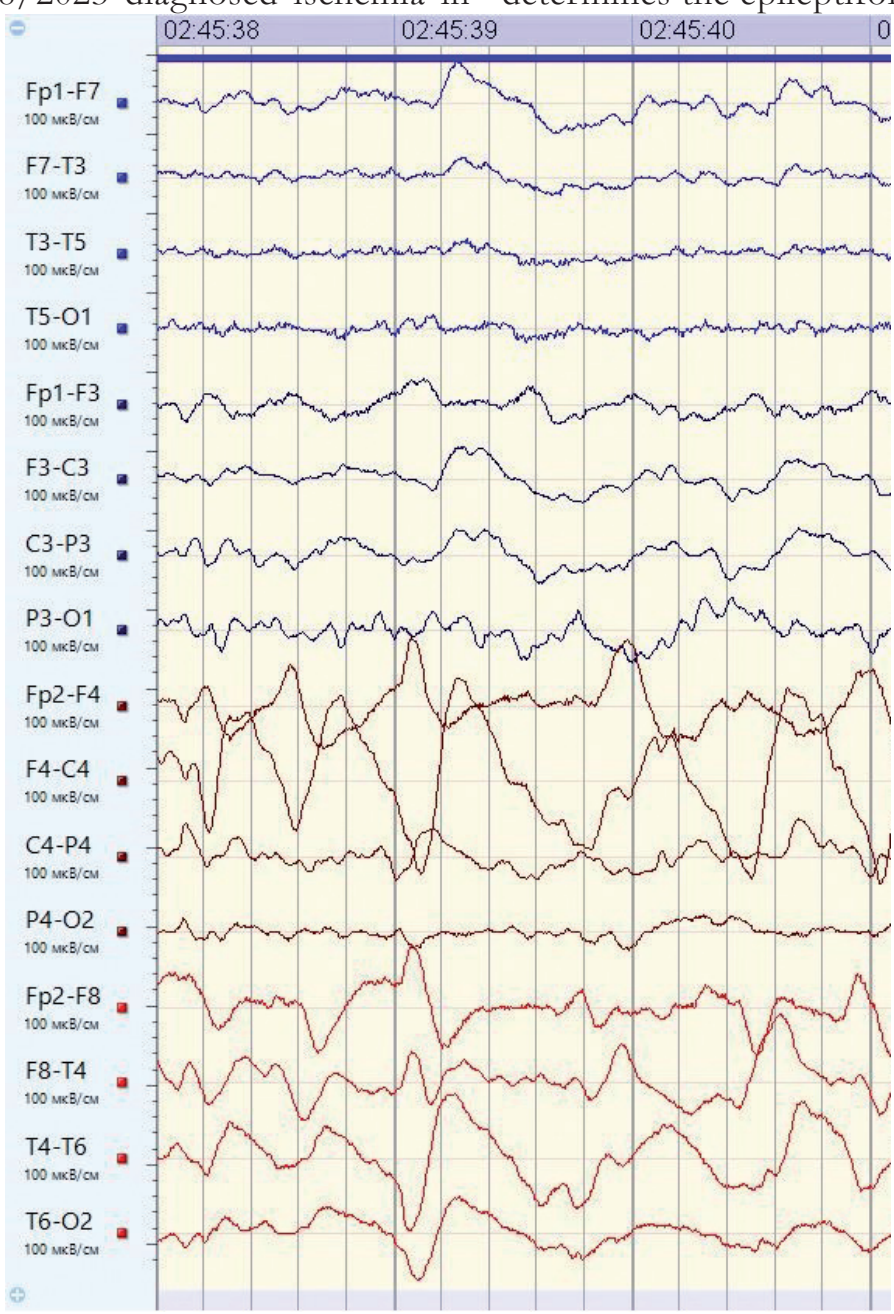

Fig. 4. *Fragment of the EEG of patient D. in the time interval 2 hours 45 minutes 38 seconds – 2 hours 45 minutes 41 seconds.*

In **Fig. 5** shows the functions of the cross correlation of the EEG with the sample described in section 2. The peaks corresponding to epileptiform activity simultaneously in 3 bipolar pairs of F4-C4, T4-T6 and T6-O2 electrodes at about 39 seconds of the fragment and the peak in one bipolar pair of F4-C4 electrodes at 41 seconds are highlighted in red.

With the visual detection of epileptiform activity, the neurophysiologist distinguishes simultaneous peak-wave discharges in several electrodes. To exclude the artifact genesis of discharges, taking into account the phenomenon of volumetric propagation of bioelectric activity generated by the cerebral cortex, it is advisable to allocate time fragments with simultaneous graphic elements in 2 or more closely spaced bipolar pairs of electrodes. During the hour under review, 17 such fragments were identified in the right hemisphere and 2 in the left. This interhemispheric asymmetry is due to a right-sided aneurysm in patient D.

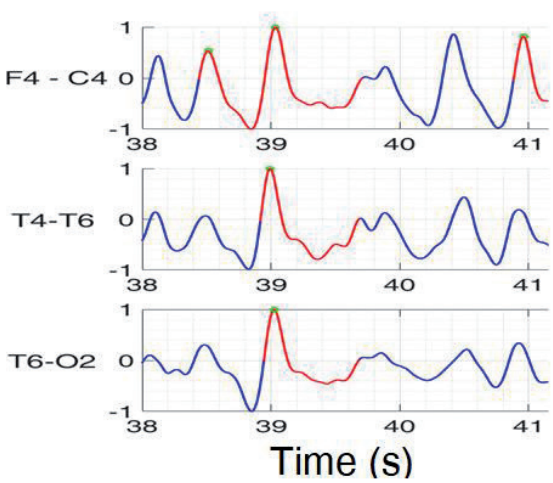

Fig. 5. *Cross correlation of EEG, peaks corresponding to epileptiform discharges are highlighted in red. On the chart, the time is indicated in seconds, the countdown starts from 2 hours 45 minutes and the 38th second.*

The operating time of the algorithm on a modern personal computer is no more than 5 minutes to process 16 bipolar signals, so it can be used to calculate the hourly amount of epileptiform activity in almost real time of the manifestation of this indicator of delayed ischemia after SAH.

4. CONCLUSION

Usefulness of quantitative EEG in detecting delayed cerebral ischemia after aneurysmal subarachnoid hemorrhage. It provides a non-invasive, continuous assessment of brain activity in real time and requires a relatively short time to determine the diagnostic indicators of delayed ischemia compared to a medical assessment of the baseline EEG. With the increasing availability of software capable of calculating these EEG functions in real time, it has great clinical potential for the timely treatment of delayed ischemia. EEG can also be used as a screening tool for patients with qEEG features to assess the high risk of inclusion in clinical trials testing new treatments to mitigate and prevent delayed ischemia. The development of a multifunctional algorithm based on all the above-mentioned functions of the EEG, including epileptiform activity, is the next step in optimizing the algorithm for predicting delayed ischemia, which can be clinically implemented. Ultimately, qEEG is a promising modality implemented in everyday practice, allowing for non-invasive real-time monitoring with global whole-brain coverage. At the same time, it has the potential advantage of cost- and time-effectiveness, especially given the future development of automated systems

that could facilitate rapid detection and early intervention in delayed ischemia.

This article describes the proposed algorithm for automatic detection of EEG epileptiform activity, based on the formalization of the description of peak-wave discharges of epileptiform activity and its visual detection by neurophysiologists. Testing of the algorithm on clinical data showed its adequacy to the neurophysiological description of epileptiform activity in delayed ischemia after hemorrhage in the subarachnoid space of the brain.

The operating time of the algorithm on a modern personal computer is no more than 5 minutes to process 16 bipolar signals, so it can be used to calculate the hourly amount of epileptiform activity in almost real time of the manifestation of this indicator of delayed ischemia after aneurysmal subarachnoid hemorrhage. Therefore, we believe that the application of the developed algorithm will solve the problem of detecting epileptiform activity and assessing its development with delayed ischemia in real time of the manifestation of this indicator.

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