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A method to evaluate the functional state of the human brain after acute in-hospital stroke

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ABSTRACT

Acute in-hospital stroke is a severe complication of the early recovery period after cardiovascular surgery with a probability of up to 15%. Unfortunately, in-time diagnostic neuroimaging (computed tomography and magnetic resonance imaging) in cases of severe brain damages is considerably hindered increasing the risk of an adverse outcome.

The aim of the study was to develop a method to evaluate the functional state of the human brain in patients with severe in-hospital stroke measuring parameters of electrical activity in the central nervous system.

Materials and methods. The sample was composed of 20 anonymous archived electroencephalograms obtained from volunteers with no neurological disorders, 10 records of patients without neurological symptoms during general anesthesia, 17 records of patients with out-of-hospital strokes obtained from the UCLH Stroke EIT Dataset, and 18 records from patients with acute in-hospital stroke during neuromonitoring in the early postoperative recovery period. A new integral coefficient of the functional state was introduced, and an algorithm to calculate the proposed measure of the functional activity of the central nervous system was developed and implemented.

Results. The proposed method to evaluate the functional state of the human brain was applied to analyze neurophysiological records obtained from people with different activity of the nervous system: from resting state to deep coma. It was shown that the integral coefficient naturally reflects the functional state of the human brain and can be used for early detection of brain dysfunction and damages caused by cerebral hemodynamic impairment.

Conclusion. The introduced integral criterion to evaluate the functional state of the human brain can be used for long-term postoperative monitoring in cardiac patients who underwent surgical treatment.

Keywords: acute in-hospital stroke, electroencephalogram, functional state

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Способ оценки функционального состояния головного мозга при острых внутрибольничных нарушениях мозгового кровообращения

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РЕЗЮМЕ

Внутрибольничные нарушения мозгового кровообращения у пациентов кардиохирургического профиля являются тяжелым осложнением в раннем послеоперационном периоде с вероятностью появления до 15%. При развитии тяжелого поражения головного мозга проведение нейровизуализирующих диагностических исследований (компьютерной и магнитно-резонансной томографии) затруднено, что повышает вероятность неблагоприятного исхода.

Цель исследования заключается в разработке способа оценки функционального состояния головного мозга у пациентов с тяжелым течением внутрибольничного инсульта на основе неинвазивных измерений электрической активности центральной нервной системы.

Материалы и методы. Выборка составлена из 20 анонимизированных архивных записей электроэнцефалограммы добровольцев без неврологических нарушений, 10 записей пациентов без неврологических нарушений во время наркоза, 17 записей пациентов из банка данных UCLH Stroke Dataset с внебольничными инсультами и 18 записей, полученных в процессе нейрофизиологического мониторинга пациентов с тяжелым инсультом в раннем послеоперационном периоде. Для оценки функционального состояния разработан и реализован алгоритм вычисления интегрального показателя функционального состояния, характеризующего уровень функциональной активности центральной нервной системы.

Результаты. Предложенный способ оценки функционального состояния головного мозга был применен для анализа нейрофизиологических сигналов, полученных у людей с разной степенью активности нервной системы, от спокойного бодрствования до глубокой комы. Показано, что вычисляемый коэффициент закономерно отражает функциональное состояние головного мозга и может быть использован, в том числе, для раннего обнаружения нарушений, обусловленных церебральной гемодинамической недостаточностью при развитии острого инсульта.

Заключение. Интегральный критерий функционального состояния головного мозга может быть использован для длительного наблюдения за состоянием пациентов кардиохирургического профиля в ранний послеоперационный период.

Конфликт интересов. Авторы декларируют отсутствие явных и потенциальных конфликтов интересов, связанных с публикацией настоящей статьи.

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Ключевые слова: острый внутрибольничный инсульт, электроэнцефалограмма, функциональное состояние

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INTRODUCTION

Acute in-hospital stroke is a frequent adverse event in the early recovery period after cardiac surgery with a probability of up to 15% [1]. In the meantime, timely diagnosis of in-hospital stroke can be complicated particularly in coma patients. According to the study [1], in most cases, ischemic stroke is diagnosed within 3–6 hours from its onset. Taking into account a high risk of stroke within 3–7 days after cardiac surgery, neuromonitoring could be considered as a useful tool to detect early signs of cerebral hemodynamic impairment in the postoperative period [2]. Unfortunately, electrical activity of the human brain (electroencephalogram, EEG) is a complex noise-like signal characterized by low specificity in relation to causes of brain dysfunctions [3].

According to the published reviews, the diagnostic and prognostic potential of EEG strictly depends on EEG markers of stroke and qualification of a neurophysiologist. These facts along with complicated clinical interpretations and time-consuming neurophysiological studies (especially continuous round-the-clock neuromonitoring) may be the main reason for EEG not becoming a routine monitoring procedure in the early postoperative period.

Recently, a broadband system for multifrequency electrical impedance tomography (EIT) has been considered as a promising method for early stroke detection [4]. The EIT inherently features three-dimensional imaging options that makes it partly comparable with computed tomography (CT) and magnetic resonance imaging (MRI). Unfortunately, EIT has very low spatial resolution, preventing direct visualization of the damaged brain tissues, therefore, it cannot be used in clinical applications.

The study [5] suggests some EEG biomarkers which are highly reproducible in stroke patients. However, measuring these parameters implies active patient’s participation, which is impossible in the early postoperative period. The alternative approach is based on mapping and evaluation of coherence of the cortical electrical activity in a resting state [6]. The authors showed that the proposed method is suitable for evaluating long-term brain function recovery, but is not as effective in continuous post-surgery monitoring.

Many formal EEG-based estimators of the functional state of the human brain rely on calculated frequencies and power of the dominant brain rhythms. In the study [7], many formal EEG parameters are used as independent variables to build partial regression models showing a relationship between the power of the dominant brain rhythms and NIHSS scores. Although the models demonstrated good performance, their practical usability is questionable because they require 256-channel EEG records.

A large number of publications focus on the attempt to use EEG-based methods for monitoring the depth of anesthesia (for example, bispectral index, entropy, information complexity of EEG, etc.) as a tool to monitor the functional state of the human brain in stroke patients. Although sensitivity, specificity, and information value of the known EEG-based methods still have to be confirmed, their relevance for continuous monitoring of the brain function in the early postoperative period is beyond doubt [8].

The aim of the study was to develop a method to evaluate the functional state of the brain in cardiac surgical patients with acute in-hospital stroke in the early postoperative period.

MATERIALS AND METHODS

Anonymized archived EEG records were obtained from Siberian State Medical University (20 records, healthy subjects with no neurological disorders), Cancer Research Institute of Tomsk National Research Medical Center (NRMC) (10 patients without neurological disorders during general anesthesia), 17 records from the UCLH Stroke EIT Dataset with out-of-hospital strokes [9], and 18 records from Cardiology Research Institute of Tomsk NRMC from cardiac surgical patients with acute stroke in the early postoperative period. All records were converted to the unified format: sampling rate 250 Hz, amplitude resolution 0.25 uV, frequency range from 0 to 100 Hz. The preprocessing included high-pass filter with the time constant of 0.16 sec and low-pass filter with the cut-off frequency of 100 Hz.

EEG signals were recorded using the Encephalan 131 EEG machine (Medicom, Russia, Taganrog), Neuron – Spectrum (Neurosoft, Russia, Ivanovo), and Biosemi Active Two system (Biosemi, the Netherlands, Amsterdam). All the EEG machines had comparable technical parameters. Electrode montage schemes were also identical and corresponded to the international 10 – 20 system. After preliminary calculations, it was found that the necessary and sufficient number of channels to evaluate an integral coefficient of the functional state of the brain was 8, including O1-A1, P1-A1, C1-A1, F3-A1, O2-A2, P2-A2, C2-A2, F4-A4. The raw signals were remounted according to the monopolar montage scheme with ipsilateral ear electrodes.

Statistical analysis and signal processing were performed using free version of integrated development environment RStudio [10] with Signal and edfReader packages. The significance level of 0.05 was adopted.

RESULTS

To evaluate the functional state of the human brain, we proposed a new dimensionless index λ varying from 0 to 100 %, where 0 corresponded to zero electrical activity (brain death) and 100 % – to active state.

The algorithm to calculate λ includes the following steps.

Preprocessing of the multichannel EEG: removing baseline drift, components with frequencies above 100 Hz, and power line interference (50 Hz).

Independent component analysis (ICA) of the multichannel EEG:

$$Si(C_{1i},C_2) = ICA(EEG,ch_i,ch_{ref},$$

where S_i is signal decomposition; component C_{1i} contains mainly EEG from channel *i*; C_2 represents artefacts with amplitude well above the typical EEG voltage. These artefacts are caused by electrical activity of the heart, eye movement, electrode dislocation, and muscle contraction.

Independent components are calculated based on paired channels with one channel always being the reference one (A1 or A2 for left and right hemisphere, respectively). This approach effectively removes artefacts common for both channels and, as a result, reduces uncertainty of bispectral parameters.

Bispectral analysis of the component C_{1i} was followed by calculation of Gaussianity and linearity of the signal based on the Hinich method [11], as well as bicoherence and spectral power in the frequency range from 0.5 to 47 Hz. Fast Fourier transform with length $n = 512$ and Hamming window *w(n)* was used to build the bispectrum. The bispectrum was calculated for each component C_1 independently.

Test for signal normality and linearity was performed according to the procedure given in [6]. The proposed integral index of the functional state λ will be calculated if the signal passes both the normality and linearity tests:

$$Sp(f,l) = FFT_n\big(w(n)\cdot C_1(l+n+m)\big);\, l \in (1, M-n-m)$$

$$B1 = \sum_{f1=0.5}^{8}\sum_{f2=0.5}^{8}\big(Sp(f1)Sp(f2)Sp^*(f1+f2)\big)^2$$

$$B2 = \sum_{f1=0.5}^{47}\sum_{f2=0.5}^{47}\big(Sp(f1)Sp(f2)Sp^*(f1+f2)\big)^2$$

$$\beta = \begin{cases} \|C_1\|, & \|C_1\| < 1 \\ 1, & \|C_1\| \geq 1 \end{cases}$$

$$\lambda = 100\cdot(1-\sqrt{\frac{B1}{B2}})\cdot\beta$$

where *Sp* is Fourier transform of the component *C1*; *f1*, *f2* are frequency ranges; *B1* is the total power of the low-frequency bispectral components; *B2* is the total bispectral power in the range from 0.5 to 47 Hz; β is correction coefficient; λ is integral index of the functional state.

Steps 3 and 4 are repeated after moving the window by *m* samples, *m* should be chosen from 32, 64, 128, 256 as a a trade-off between computational complexity and required temporal resolution of λ.

The frequency ranges were selected using commonly agreed neurophysiological bands: 8 Hz corresponds to the lower limit of alpha activity, and the upper limit of 47 Hz allows for effective removal of power line interference (50 Hz).

The proposed integral index of the functional state of the brain was calculated using archived EEG data obtained from healthy subjects in an active state and during normal sleep, from patients undergoing surgery, and from coma patients with acute in-hospital stroke (Figure). The solid line is an average value of λ for previous 30 sec, the confidence intervals were calculated for $\alpha = 0.05$ and $n = 30$.

It could be noticed (Fig. *b, c*), that the λ index reflects the functional state of the human brain with uncertainty of no more than 10 % throughout the recording intervals. This fact confirms that the proposed index follows the functional state of the human brain within physiological variations.

Not only does the average value of λ index decrease as patient's brain functions degrade, but also the confidence intervals dramatically expand (Fig. *d, f*). It could be indirect evidence that functional degradation of the brain manifests through gradual deceleration of dominant rhythms in parallel with disturbances in cortical interactions.

These results are in good agreement with the published clinical and neurophysiological findings [1]. The authors [1] showed that the key markers characterizing the severity of condition in stroke patients include typical neurological symptoms, *a*) λ index in an active state

b) normal sleep

c) surgery, induced anesthesia

d) stage III coma

e) stage IV coma

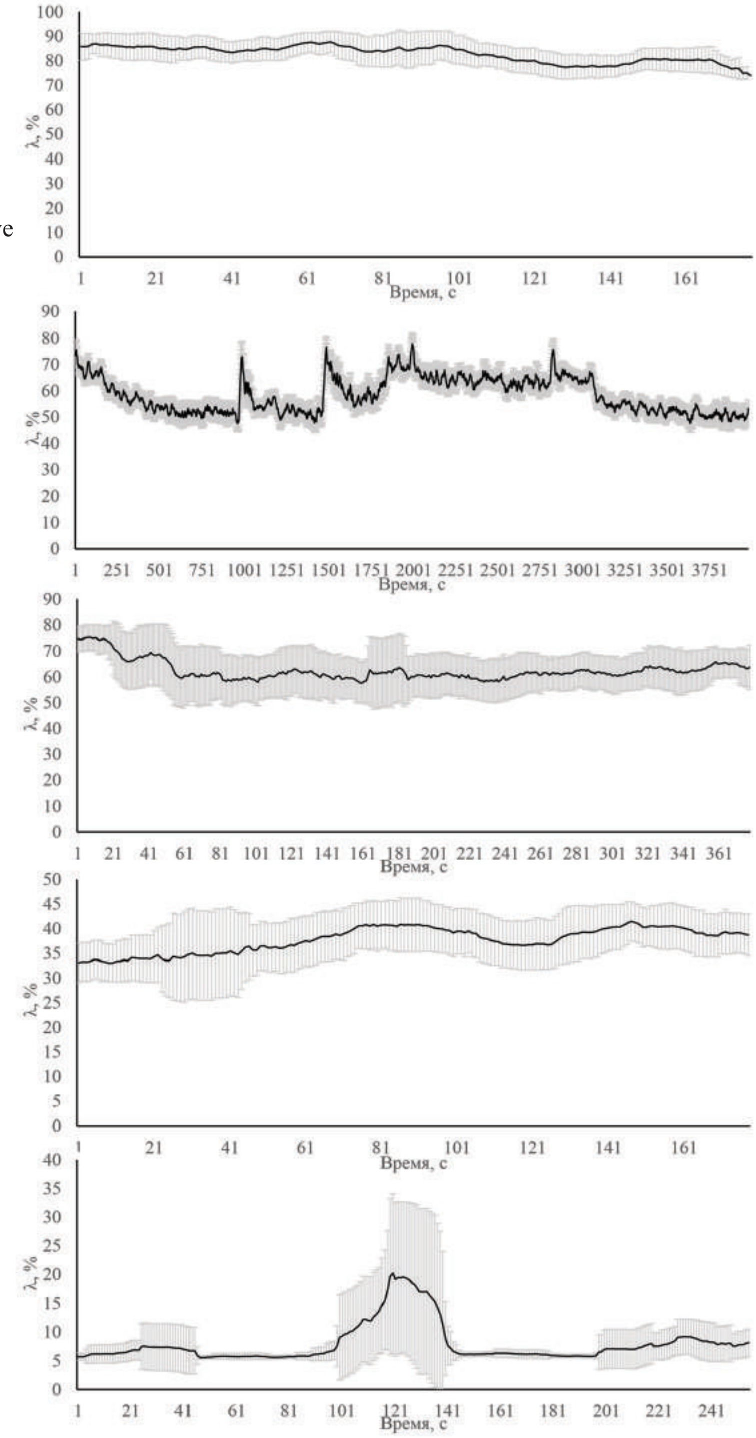

Figure. Dynamics of the integral coefficient of the functional state of the brain: *a* – in an active state; *b* – during normal sleep; *c* – during surgery with induced anesthesia; *d* – stage III coma; *f* – stage IV coma

absence of the dominant EEG rhythm on the occipital electrodes, decreasing frequency of the electrical activity, and a lack of response to external stimuli.

Certainly, the selected examples are not quite typical of clinical practice, and the real cases are definitely more complicated; however, they allow to evaluate margins of the functional state of the brain. Unfortunately, the absolute values of λ can be used to differentiate only quite distinctive functional states of the brain, but its relative variations are sensitive enough to follow individual changes.

DISCUSSION

The proposed EEG-based method for evaluating the functional state of the human brain takes into account the commonly accepted neurophysiological concepts that attribute certain changes in electrical activity to functional degradation of the brain. One of the most well-known parameters estimating the depth of anesthesia – bispectral index (BIS) – is based on the same concepts, but does not include cortical interactions. Our algorithm to calculate the λ index is different from the earlier described ones in the following:

Instead of raw EEG signals, independent components of multichannel EEG are used to calculate the λ index. This step significantly improves the reproducibility of the estimator.

Multichannel EEG must include at least 8 separate channels to reduce λ index uncertainty through spatial averaging.

The correction coefficient β was introduced to expand the dynamic range and numerical stability of the algorithm down to the lowest amplitude of EEG signals, which allows to evaluate even the most severe conditions of the brain.

The main drawback of the proposed index is low specificity with respect to the causes of brain dysfunction. As a result, it is almost impossible to diagnose the exact pathology that has caused the brain damage. One more limitation is a small size of the sample, which included only well distinguishable EEG records. Clinical ranges of the λ index can be found in expanded trails including more patients and a wider spectrum of functional states. Nevertheless, in the present form, the proposed integral index is sensitive enough to detect changes in the functional activity of the brain.

Taking into account the main features of the λ index, we would suggest two possible applications in clinical practice: control over the depth of anesthesia and continuous neurophysiological monitoring in the early postoperative period. We believe that the index will be the most effective for continuous monitoring of cardiac surgical patients in the early postoperative period.

CONCLUSION

The proposed integral index of the functional state of the human brain features some desirable properties, such as high reproducibility and clear physiological interpretation. The method is numerically stable and can deal even with very low-amplitude EEG. Sensitivity and specificity of this index in different pathologies require further expanded studies.

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