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Research Article

Hemispheric Peculiarities of Cerebrolysin Effects on the Brain Functional State in Patients with Atherothrombotic Ischemic Stroke

Victor V Kuznetsov*, Valentyn N Bulchak and Svitlana Kuznetsova

Chebotarev Institute of Gerontology of the National Academy of Medical Sciences (NAMS Ukraine)

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***Corresponding author**

Victor V Kuznetsov, Chebotarev Institute of Gerontology of the National Academy of Medical Sciences (NAMS Ukraine), Email: ig@geront.kiev.ua

Keywords Cerebrolysin; Atherothrombotic; Cerebral hemodynamic; Angioneurology

Abbreviations BFV: Blood Flow Velocity; DBF: Diastolic Blood Flow; EEG: Electroencephalography; CCA: Communis Carotid Artery; ICA: Internal Carotid Artery; MCA: Medial Cerebral Artery; PCA: Posterior Cerebral Artery; Pi: Pulsator Index; Ri: Vascular Wall Resistance Index; VA: Vertebral Artery; BA: Basilar Artery

Abstract

Purpose: Complex analysis of the effect of Cerebrolysin (intravenous infusion of 10 ml for 10 days) on the hemodynamic and bioelectrical activity of the brain.

Methods: Total 25 elderly patients who developed post-atherothrombotic ischemic stroke (nearly one year after acute period) were included into study. Their electroencephalogram was recorded on the 16-channel electroencephalograph 110 Neurofax EEG (NichonKogden). An ultrasonic duplex scanning of head and neck vessels was done on the device APPLIO 600 (Toshiba).

Results and Discussion: Due to Cerebrolysin treatment we observed the statistical increase of Linear Systolic Blood Flow (LSBF) rate in some brain vessels Besides, we have observed positive reorganization of bioelectric brain activity, decrease in delta and theta power in separate areas of both hemispheres and alpha rhythm power in all areas of the right/left hemispheres against a background of increased alpha rhythm frequency.

Cerebrolysin harmonized inter-systemic interrelations between the power of separate rhythms of brain bioelectric activity and cerebral hemodynamic (LSBF).

Conclusion: Thus Cerebrolysin effects on the brain bioelectric activity are more harmonious in the patients with left- versus right-sided stroke localization that apparently determines the hemispheric peculiarities of recovery processes.

Introduction

Stroke is the one of the topical problems of modern angioneurology in view of increased incapacitation due to stroke [1-3]. The incapacitation rate reaches 3.2 per 1000 population and occupies the first place among all causes of primary incapacitation. Of 80% of the stroke-affected patients, 10% become severely disabled who constantly need outside assistance, 55% are unsatisfied with their life quality and only 15% of the survivors can return to their former activity [1-4].

In accordance with the Helsinborg Declaration 2006 on European stroke strategies, the post-stroke rehabilitation aimed to ensure by the year 2015 the independency in daily living for more than 70% of patients with a 3-month history of stroke. Unfortunately this Declaration had not been realized [3]. The main tasks of rehabilitation include: recovery of lost functions, prophylaxis of post-stroke exacerbations, psychic and social rehabilitation. At the same time the processes of recovery and compensation of disturbed functions occur at the expense of morphologic-functional and biochemical reorganization of the Central Nervous System (CNS) [5]. It has been found that neuro plasticity is a key link in the system of recovery processes [5]. Neuro plasticity is realized at the molecular, synaptic and neuronal levels [5-7]. The state of cerebral hemodynamic and bioelectrical activity of the brain produces a significant influence on the plasticity processes [5-8]. A number of authors showed that changes of cerebral hemodynamic in the stroke-affected patients show as a decrease of linear blood flow velocity and an increase of peripheral resistance of the carotid and vertebra-basilar vessel [9-12]. More marked hypo perfusion is observed in the arteries in the ischemia area.

Furthermore, the mechanisms of cerebral homeostasis auto regulation are disturbed at ischemic stroke [2,10,12,13]. The severity of cerebral blood flow disturbances correlates with the pronouncement of neurologic deficit and ischemia injury size [9,10,12,13].

Owing to the joint efforts of basic neurosciences and clinical neurology, the scientists found a cascade of the pathological-biochemical processes at ischemia and developed effective ways of brain protection. By now the time sequence of the ischemia-conditioned molecular-genetic and functional biochemical disturbances has been established. Energy deficit, glutamate excitotoxicity, calcium homeostasis disorders, lactate acidosis, oxidant stress, local inflammation and apoptosis

are the main links of ischemic cascade which is formed during acute stroke. Some manifestations of this cascade are characteristic for post-stroke recovery period [8].

The followings are registered during recovery: brain hypoperfusion, neurometabolic, neuroimmunotrophic and regenerative changes. There occurs a morphofunctional rearrangement of the neuroergic systems [10,14]. Close interrelations of initial and remote consequences of ischemia as well as commonness of their mechanisms determine the demand for neurotrophic therapy and neuroprotection in the patients at both, acute and recovery post-stroke periods [5,6,15,16].

Along with rehabilitation measures, some authors use the neuroprotective drugs possessing action on separate links of ischemic cascade [16]. Cerebrolysin is one of them. Its efficacy has been proved not only in the 65-year experience of usage but also in the results of 76 clinical (30 of them double blind) investigations [17].

Cerebrolysin is a complex drug containing low-molecular peptides of the brain of young pigs with average molecular weight 3000 daltons, free amino acids, vitamins B1 and B12, tocopherol, folic acid and microelements [18,19]. This drug contains several neuropeptides (CNTF, GDNF, IGF-2 and IGF-1) possessing properties of natural growth factors [20,21].

Cerebrolysin is a neuropeptide preparation with neuroprotecting and neurotrophic action. Its pleyotropic effects are seen at many stages of the pathogenetic chain of ischemic cascade [22]. Its neuroprotecting action during ischemia is primarily realized via antioxidant and antiapoptic effects [17,23-27]. Cerebrolysin considerably widens the zone of hemato-encephalic barrier permeability for glucose, increasing its concentration in the brain tissue [28]. Direct stimulation influences of Cerebrolysin were registered on anaerobic energetic metabolism and decrease of lactate level [29].

Cerebrolysin produces a marked neuroimmune trophic effect thereby reducing development of inflammatory phenomena in the tissue and preventing death of neuronal structures [30]. Neurotrophic action of Cerebrolysin was demonstrated by Y. Tatebayashi in the experiments increase of the number of newly formed nerve cells in the gear gyrus dentatus [31].

Using the embolic stroke model, C. Zhang et al. demonstrated the capacity of cerebrolysin to stimulate neurogenesis [32].

There are now a large number of clinical investigations devoted to the study of the effects of various Cerebrolysin doses (10, 15, 30 and 50 ml) on acute course and recovery of the stroke [17,19,33-44]. According to the MMSE scale, the Cerebrolysin-treated patients have higher indices of cognitive functions and much higher coefficient according to the NIHHS stroke scale. The recovery of muscle strength, sensitivity and psychic state is speedier. Z. Huffner conducted a long-term observation over the patients injected with Cerebrolysin during acute stroke period and found more active recovery by such indices as Barthel index, scale of Clinical General Impression (CGI) and physical estimation of hemiplegia [19].

The prospective evaluation of the efficacy of recovery (according to the Canadian neurological scale, the Barthel index and scale of clinical general impression (CGI) conducted 3 months after cerebrolysin treatment evidenced about improvement of social contacts and physical working ability especially in the patients with left-hemispheric stroke [35]. More effective Cerebrolysin influence on regressing of neurological deficit in the patients with left-hemispheric stroke was also found by Herrschaft H et al. [40]. With right-sided stroke, the statistical improvement was found only in food intake and self-servicing ability [19]. G.S. Barolin and S. Koppi [33] analyzed effectiveness of large cerebrolysin doses (50 ml/day) in the patients with ischemic stroke at acute and early recovery periods and also pointed to the hemispheric peculiarities of its action. In the patients with left-hemispheric stroke Cerebrolysin more markedly improved recovery of the motor and speech functions and promoted activation of daily living. In the right-sided stroke patients it influenced predominantly on the cognitive processes [33].

The results of double-blind investigation conducted by D.F. Muresanu are in favor of Cerebrolysin effectivness during acute period of stroke [42]. The Cerebrolysin-treated patients had statistically higher recovery of sensitivity and cognitive functions (according to the MMSE scale).

According to the results of the multi central investigation of 20.0 ml Cerebrolysin efficacy in complex treatment of ischemic stroke in acute period, additional therapy with Cerebrolysin is effective in terms of more rapid and complete recovery of the motor, speech and all functions of daily living [41].

Effects of Cerebrolysin on the dynamic of brain injury size were explored in the randomized placebo-controllable investigation of N.A. Shamalov et al. in which 47 patients were injected Cerebrolysin in the dose of 50 ml or placebo during first 12 hours after stroke onset. Therapy was continued for 10 consecutive days. The dynamic of morphometric picture of injured brain site showed speedier regress of infarction volume by 28th day in the Cerebrolysin-treated group [45].

Essential results were received based on the post-hoc analysis of the data of the international double-blind placebo-controllable investigation of Cerebrolysin acute stroke treatment (CASTA) investigation. In the subgroup of critically-ill patients (NIHSS>12) the lethality against Cerebrolysin treatment made 10% (20% in control). The rehabilitation process was essentially quickened – the difference of values based on the NIHSS scale made less than 3 scores after 90 days [39].

Cerebrolysin plus recombinant tissue-Plasminogen Activator are save full for treatment of acute ischemic stroke, judging by the fact that significantly more patients have demonstrated a favorable response to such drug combination in treated group of patients as compared to placebo group (National Institutes of Health Stroke Scale) [36].

Muresanu D.F. and coauthors demonstrated the beneficial effect of Cerebrolysin on post-stroke recovery during early rehabilitation [44].

The most recent E-COMPASS is a clinical trial designed as a multicenter, randomized, double-blind, placebo-controlled, parallel-group study. This study enrolled 75 sub-acute stroke patients with unilateral motor dysfunction. Primary objective was to demonstrate the efficacy of porcine brain peptide in improving motor recovery measured by the improvement ratio of Fugl-Meyer assessment.

Standard rehabilitation therapy with Cerebrolysin in subacute stroke improved corticospinal tract plasticity in the patients with severe motor impairment. Motor system plasticity is usually assessed by diffusion tensor and resting functional magnetic resonance imaging [34].

More studies on the action of the neuropeptides (Cerebrolysin) on brain functioning at stroke would be necessary to better evaluate the effects of Cerebrolysin in modern neurosciences and clinical practice.

Purpose

In this light we decided to study Cerebrolysin influence on the cerebral circulation and bioelectrical activity of the brain in post-stroke patients during their recovery.

Patients and Methods

Our study included 25 elderly patients (average age 61.3 ± 2.4 years) with post-atherothrombotic ischemic stroke (nearly one year after acute period) were included into study.

Using our own program, 10 ml Cerebrolysin was i.v. injected by drops during 10 days. Before and ten days after drug administration, we assessed the clinical-neurological status, daily living activities (using Barthel index) and performed ultrasound doplerography of head and neck vessels, EEG. Ultrasound dopplerography was done on scanner APPLIO 400, Toshiba. Also, the linear systolic blood flow (LSBF) and diastolic blood flow velocity (sm/sec) resistance (Ri) and pulsator (Pi) indexes were measured. The EEG was recorded on the 16-channel electroencephalograph 110 Neurofax (Nichon Kohden).

Brain bioelectrical activity was assessed with computerized EEG spectral analysis and topographic brain mapping. EEG recordings were recording in resting conditions and with eyes closed by using 19 scalp electrodes, located according to the international 10-20 system. EEG was visually inspected and free-artifact epochs. Spectral analysis was performed with a Fast Fourier Transform using. The following frequency bands were studied: delta (O.5-4 Hz), theta (4-8 Hz), alpha (8-12 Hz) and beta (12-16 Hz). Band pass filter were set at 1.5-30 Hz; amplifier sensitivity was 200 μV.

Statistics

Statistical analysis was carried out with SPSS for Window Release 6. The nonparametric Wilcoxon test was used to compare paired data obtained before and after time/treatment for each measure. The correlations of qEEG power, EEG frequency parameters and BFV were evaluated with the Pearson's linear correlation test. Results are presented as mean ± SE. Probability values lower than 0.05 were considered significant.

Results and Discussion

Under effect of Cerebrolysin there was improvement of cerebral circulation in the stroke affected patients. This hemodynamic effect was more pronounced at left-hemispheric stroke localization (Figure 1, Tables 1 and 2). With left-sided stroke there was a statistically significant increase of the BFV in the extra and intracranial vessels of the carotid and vertebra-basilar basins in the injured and intact hemispheres.

Maximal increase of the LBFV was characteristic of the Medial Cerebral Artery (MCA) of the injured and intact hemispheres. There was also a statistically significant decrease of the peripheral resistance in separate vessels of the carotid basin. With right-sided stroke localization there was a statistically significant increase, the LBFV was increased in the right internal carotid and vertebral arteries, in both MCA and PCA, as well as in the basilar artery. There was a tendency to the decrease of peripheral resistance in separate vessels of the carotid basin. The degree of BFV rise in the patients with left-sided stroke localization was higher than in the patients with right-sided stroke (Tables 1 and 2).

Thus, Cerebrolysin improves cerebral hemodynamic in the ischemic stroke patients that was indicated by increased BFV along the vessels of carotid and vertebra-basilar system. In the patients with left-hemispheric stroke localization the rise of BFV is registered in the extra- and intracranial vessels of the injured and intact hemispheres, whereas in the patients with right-sided stroke it takes place in the extracranial vessels only in the injured hemisphere and in the intracranial vessels of both hemispheres.

Cerebrolysin induces the reorganization of the bioelectric activity in the post-stroke patients depending on hemispheric stroke localization (Figure 2).

The θ-rhythm power can be seen in almost all areas of the injured hemisphere as well as in the occipital and frontal areas of the intact hemisphere. It is noteworthy that under Cerebrolysin influence the α1-rhythm power decreases in all areas of both hemispheres while the α2-rhythm power increases in the parietal and temporal areas of the damaged hemisphere and in the frontal areas of the intact hemisphere. In the injured and intact hemispheres, the β1-rhythm power increases only in the frontal areas.

After Cerebrolysin treatment the α-rhythm frequency increases in both hemispheres: in all brain areas of the damaged hemisphere and in the frontal, central and occipital areas of the intact hemisphere, evidencing for the desynchronizing effect of Cerebrolysin in the patients with left-sided stroke localization (Table 1).

Table 1: The dynamic of BFV in the patients with left-hemispheric ischemic stroke before and after Cerebrolysin, cm/s.

Vessels	Hemisphere	Before treatment	After treatment
CCA	Injured	65.2 ± 1.45	64.02 ± 1.23
CCA	Intact	79.2 ± 1.93	82.32 ± 1.89
ICA	Injured	55.6 ± 1.32	61.03 ± 1.32*
ICA	Intact	63.9 ± 1.77	68.89 ± 1.84
VA	Injured	36.4 ± 0.89	40.98 ± 0.6*
VA	Intact	43.6 ± 1.81	45.61 ± 1.04
ACA	Injured	76.70 ± 1.78	80.05 ± 2.09
ACA	Intact	74.00 ± 2.14	75.30 ± 1.57
MCA	Injured	83.0 ± 1.53	90.33 ± 1.65*
MCA	Intact	82.0 ± 2.88	94.93 ± 1.71*
PCA	Injured	40.3 ± 1.32	49.91 ± 0.53*
PCA	Intact	47.1 ± 0.66	51.05 ± 0.65*
BA		46.8 ± 1.25	52.96 ± 1.26*

Note: *the statistically significant differences (p<0.05).

Table 2: The dynamic of BFV velocity in the patients with left-hemispheric ischemic stroke before and after Cerebrolysin treatment, cm/s.

Vessels	Hemisphere	Before treatment	After treatment
CCA	Intact	66.29 ± 1.79	66.14 ± 1.83
CCA	Injured	72,36 ± 1,21	65.30 ± 0.98
ICA	Intact	50.51 ± 1.07	59.74 ± 1.21*
ICA	Injured	58.13 ± 0.96	63.00 ± 1.07*
VA	Intact	29.43 ± 1.78	35.33 ± 0.82*
VA	Injured	37.34 ± 1.17	42.69 ± 0.99*
ACA	Intact	62.60 ± 1.87	66.00 ± 2.21
ACA	Injured	63.30 ± 1.54	64.00 ± 1.75
MCA	Intact	76.21 ± 1.64	91.04 ± 2.13*
MCA	Injured	62.90 ± 1.22	79.64 ± 1.99*
PCA	Intact	43.00 ± 0.45	50.85 ± 1.55*
PCA	Injured	46.40 ± 0.45	51.12 ± 0.64*
BA		45.36 ± 1.61	53.14 ± 1.51*

Note: *the statistically significant differences (p<0.05).

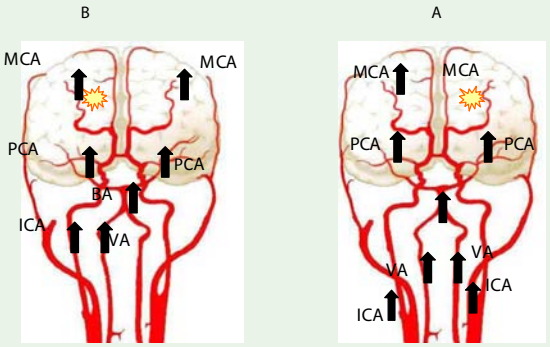

Figure 1: Mosaic of Cerebrolysin effect on the BFV in the patients with atherothrombotic ischemic stroke in the right (B) and left (A) hemispheres.

Changes in the bioelectrical activity of the brain developing owing to Cerebrolysin treatment in the patients with right-hemispheric stroke localization are characterized by the increased power in the range of slow rhythms, especially in the δ-rhythm range. Thus the capacity of δ-rhythm in the frontal, occipital and temporal areas of both hemispheres as well as in the injured hemisphere of the central area, the θ-rhythm power in the central and occipital areas of the injured hemisphere increases against background of some decrease of the power in the temporal area of intact hemisphere.

The intersystemic correlations between cerebral hemodynamic and bioelectric activity of the brain play a key role in the formation of functional-biochemical compensatory mechanisms in the post-stroke patients. Stroke disturbs these correlations. Thus in the patients with right-hemispheric stroke the frequency of α-rhythm correlates

Table 3: Dynamic of α-rhythm frequency before and after Cerebrolysin treatment in the stroke-affected patients, with a consideration of ischemia localization, Hz.

Brain areas	Hemisphere	Before		After	
		Patients with left-sided stroke	Patients with right-sided stroke	Patients with left-sided stroke	Patients with right-sided stroke
Frontal	Injured	8.35 ± 0.96	9.0 ± 0.16	9.33 ± 0.15	8.59 ± 0.13*
	Intact	8.79 ± 0.06	9.3 ± 0.14	9.62 ± 0.13*	9.10 ± 0.13
	Injured	8.35 ± 0.09	9.3 ± 0.16	9.13 ± 0.15*	8.76 ± 0.12
	Intact	9.08 ± 0,07	9.8 ± 0.18	9.87 ± 0.13*	9.40 ± 0.10*
	Injured	8.79 ± 0.13	9.6 ± 0.16	9.86 ± 0.19*	8.76 ± 0.12
	Intact	9.08 ± 0.59	9.7 ± 0.13	9.96 ± 0.13*	9.47 ± 0.16
Central	Injured	8.64 ± 0.18	9.4 ± 0.13	9.28 ± 0.16*	8.98 ± 0.12*
	Intact	9.43 ± 0.82	9.8 ± 0.12	10.11 ± 1.01*	9.40 ± 0.08*
	Injured	8.50 ± 0.17	9.4 ± 0.14	9.18 ± 0,12*	9.07 ± 0,12
	Intact	9.52 ± 0.75	10.0 ± 0.14	9.96 ± 0.86	9.63 ± 0.14*
Occipital	Injured	8.50 ± 0.12	9.6 ± 0.13	8.98 ± 0.15*	9.12 ± 011*
	Intact	9.57 ± 0.06	10.1 ± 0.16	10.01 ± 0.11*	9.96 ± 0.12
Temporal	Injured	8.45 ± 0.12	9.7 ± 0.15	9.33 ± 0.13*	9.10 ± 0.11
	Intact	9.72 ± 0.95	10.2 ± 0.16	10.40 ± 0.19	9.99 ± 0.14
	Injured	8.54 ± 0.12	9.5 ± 0.12	9.13 ± 0.13	9.26 ± 0.13
	Intact	9.67 ± 0.78	10.3 ± 0,14	10.40 ± 1.18	9.85 ± 0.12

Note: *The differences between the indices before and after Cerebrolysin treatment are statistically significant (p<0.05).

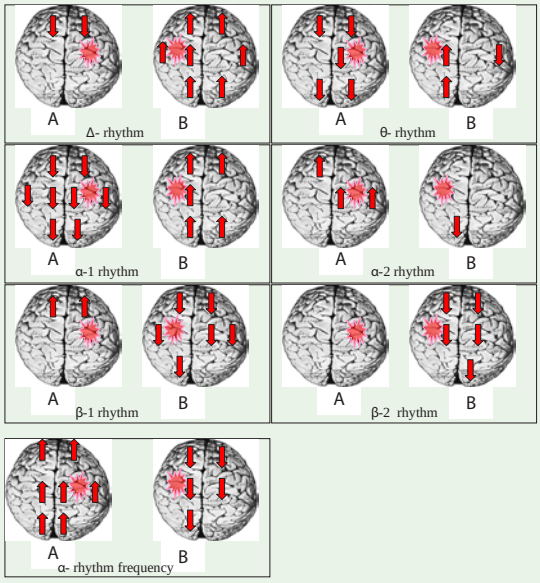

Figure 2: Direction of the changes in the main EEG rhythms power and α-rhythm frequency under Cerebrolysin effect in the left (A) and right (B) hemispheres.

positively with the BFV in the right CCA and negatively with the BFV in the right VA and BA arteries (total number of correlations - 3) (Figure 3).

In the patients with left-sided stroke the correlations appear to be more sophisticated: the α-rhythm frequency correlates positively with the BFV in the right VA and MCA and with the left ICA against a background of negative correlation with the BFV in the right and left CCA (total number of correlations – 11) (Figure 4).

In the patients with right-hemispheric stroke Cerebrolysin enhances positive correlations of the BFV with the frequency of α-rhythm predominantly in the injured hemisphere (Figure 3). Thus the BFV in the right CCA correlates with α-rhythm frequency in the right and left temporal, central and frontal areas and with the BFV in the left VA with α-rhythm frequency in the left frontal, central and temporal areas of the right hemisphere (total number of correlations – 10).

In the patients with left-hemispheric stroke, the frequency of α- rhythm in the temporal area of the Cerebrolysin-treated patients positively correlates with the BFV in the left and right ICA. In the

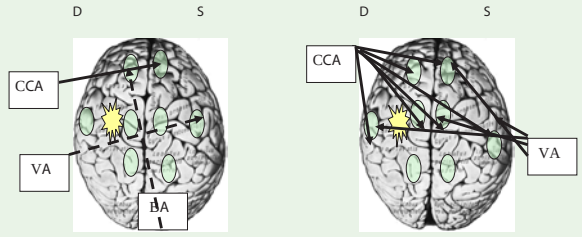

Figure 3: Correlations between BFV in the extra- and intracranial vessels and α-rhythm frequency in the right hemisphere before and after Cerebrolysin treatment.

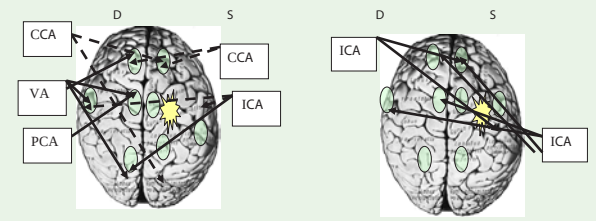

Figure 4: Correlations between BFV in the extra- and intracranial vessels and α-rhythm frequency before and after Cerebrolysin treatment.

intact hemisphere the α-rhythm frequency in the temporal, central and frontal areas correlates with the BFV in the left ICA (total number of correlations - 6).

Thus, Cerebrolysin harmonizes interrelations between the frequency of the main EEG rhythm (α-rhythm) and blood flow velocity in the extracranial vessels (CCA, ICA, VA).

Results finished

The results obtained by us clearly demonstrate Cerebrolysin effects on the EEG parameters, cerebral circulation and interrelations between the frequency of the main EEG rhythm (α-rhythm) and blood flow velocity.

Discussion

Hemispheric peculiarities of Cerebrolysin effect were also described by A.B. Gekht [37]. Furthermore, intensive regress of neurologic disorders (degree of paresis, muscle tone, speech, coordination and motor function) after Cerebrolysin treatment (10.0 ml, for three weeks) was observed in the patients with left-sided ischemia localization. The type of EEG reorganization is characterized with decreased power in the range of δ-, θ- and β- rhythms in the injured hemisphere and reduced inter-hemispheric asymmetry. In the patients with right-sided stroke there was a statistically significant increase of the δ- and θ- rhythm power against absence of any essential changes in other bioelectric activity indices. In view of the fact that similar inter-hemispheric patterns of the EEG hemodynamic were accompanied by improvement of clinical and other neurophysiologic parameters, the authors assume that this type of EEG changes in the patients with right- and left-hemispheric stroke is the special form of brain bioelectric activity rearrangement induced by neurotrophic and neuro-regulatory action of Cerebrolysin [37].

A structural analysis of the Cerebrolysin influence on the brain bioelectric activity in the patients with acute stroke was performed [46]. The investigators distinguished three types of EEG reactions and they believe that the type of EEG response to Cerebrolysin in large measure depends on the morphologic-structural changes of CNS (cortical-subcortical interactions), as the pharmacological effects of the drug are maximally realized in the damaged brain structures. Besides, the author suggests assessing optimal therapeutic dose of Cerebrolysin, considering not only neurologic disorders but also the type of EEG reaction to Cerebrolysin administration. Probably it is advisable that analysis of EEG reactions be performed with the consideration of the side of damaged hemisphere that will allow identify the mechanisms of formation of hemispheric peculiarities of Cerebrolysin action in the stroke-affected patients. Based on the available data about functional-biochemical asymmetry of the brain

and hemispheric clinic-neurologic peculiarities of stroke course, we shall discuss possible mechanisms of various types of EEG reactions to Cerebrolysin. Various functional-biochemical interrelationships between right and left hemispheres and the brainstem play a definite role in the hemispheric peculiarities of EEG reactions to Cerebrolysin. There are data showing the existence of more close interrelationships between the left hemisphere and the reticular formation, while the right hemisphere is more connected with the diencephalic and limbic structures [47,48].

The post-stroke patients show the hemisphere-dependent differences of integral indexes of the power of the rhythms characterizing a whole EEG structure. During brain activation these integral indexes are higher/ more increased in the left hemisphere. In the patients with left- versus right-sided stroke the recovery of the EEG pattern is speedier [7,49].

Stroke causes metabolism changes and reorganization of interhemispheric relationships that can also influence on the EEG reactions to various pharmacologic drugs [10].

The biochemical aspect also plays role in the formation of intrahemispheric and intersystemic interrelationships of the brain electrogenesis. Presently hemispheric asymmetry in terms of composition of many neuromediators and metabolic activity has been established. Thus the levels of N- acetylaspartate, choline and inositol are higher in the right thalamus - α-rhythm pacemaker, while the noradrenaline level is higher in the left thalamus. Biochemical asymmetry is also characteristic for the cortex as a whole. The cortex of right hemisphere contains more GABA and serotonin and the activity of enzymes (COMT-acetyltransferase and MAO) is higher [50,51], while the left hypothalamus contains more noradrenalin [52]. Considering the fact that the Cerebrolysin acts on the neurotrophic processes and neuromediatory systems and, in view of functional-biochemical brain asymmetry, there are different types of EEG reactions at with right- and left-hemispheric stroke [7].

More harmonic influence of Cerebrolysin on the bioelectric activity of the brain and cerebral hemodynamic being registered in the patients with left-sided stroke localization leads to their better post-stroke recovery.

We believe that the obtained data about hemispheric peculiarities of Cerebrolysin influence on cerebral hemodynamic and brain bioelectric activity can serve as neuro-functional basis for specialized use of the peptide bioregulators in the

Conclusions

Cerebrolysin treatment of the patients affected with ischemic stroke has shown

1. Improvement of cerebral hemodynamics in both, extra- and intracranial vessels of the carotid and vertebra-basilar basins of the injured and intact hemispheres.
2. Type of EEG structure changes is determined by hemispheric stroke localization.
3. With right-sided stroke, changes of bioelectric activity of the brain under Cerebrolysin influence are characterized by increased power in the range of δ- and α1-rhythms in two hemispheres against background of reduced power in the θ-rhythm in the injured hemisphere and some decrease of the α-rhythm power.
4. With left-sided stroke, cerebrolysin decreases the power within δ- and θ- rhythms range in both hemispheres and increases the α-rhythm frequency.
5. Cerebrolysin produces a more marked influence on the structure of brain bioelectric activity in the patients with stroke localization in the left-hemisphere that is conditioned both, by the neurobiochemic brain asymmetry and post-stroke hemispheric rearrangement of the metabolism and central hemodynamic in this category of patients.
6. Cerebrolysin harmonizes correlations/interrelations between cerebral hemodynamics and frequency spectrum of the bioelectrical activity of the brain.
7. Owing to the positive effects of Cerebrolysin on cerebral hemodynamics and brain bioelectric activity in the patients affected with ischemic stroke, we can recommend inclusion of Cerebrolysin in the complex rehabilitation program.

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