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DOI 10.25789/YMJ.2022.78.05

УДК 616.31-08-039.71

INFLUENCE OF WATER INFUSION OF THE HERB PULMONARIA OBSCURA DUM. ON THE BIOELECTRIC ACTIVITY OF THE BRAIN IN WAG/RIJ FEMALE RATS

The article presents the results of a study of the bioelectrical activity of the neocortex under conditions of oral administration of an aqueous extract of the herb Lungwort (*Pulmonaria obscura* Dum.) to female rats of the WAG/Rij line. During the experiment, the animals at the same time were orally administered an aqueous infusion of the herb at the rate of 1,5 g per 200 ml of water. The results of the study showed a statistically significant ($p<0,05$) decrease in the power of the theta rhythm (6,95±0,72%) and high-frequency beta rhythm (1,83±0,56%) by the end of the first week of the experiment in the anterior areas of the brain, the delta rhythm (64,25±4,95%) and theta rhythm (21,28±5,43%) also significantly ($p<0,05$) decrease in the posterior lobe of the brain. Thus, changes in the theta rhythm and high frequency beta rhythm in the frontal lobe of the neocortex of female rats may be associated with a decrease in excitability, anxiety, and fear. The data of our work demonstrated the stimulating effect of *Pulmonaria obscura* Dum. on the brain of female rats of the WAG/Rij line, manifested by activity on the electroencephalogram.

Keywords: absence epilepsy, Pulmonaria obscura Dum, electroencephalogram, rats of the WAG/Rij line, herbal medicine.

Introduction. Medicinal plants and herbal preparations of plant origin, despite the weaker pharmacological activity, in some cases, for example, in chronic diseases, can be much more effective than their synthetic or chemical counterparts. The advantage of preparations from medicinal plants, in comparison with synthetic agents, is that they act in a complex way, they are easier to tolerate and are tolerant for the metabolic system of the human body, the overall therapeutic effect of exposure consists of the sum of multiple actions of all substances of the plant both on individual organs and on the functional systems of the body as a whole [1, 5].

Plants of the genus *Pulmonaria* include about 70 species, they are widespread in many regions of Russia, have a good raw material base and are used in folk medicine for the treatment of diseases of the upper respiratory tract, gastrointestinal tract, and hematopoietic system [1, 15, 17, 22, 26]. Lungworts are mainly used in folk medicine, they are practically not used in official medicine, due to the insufficiently studied chemical composition. According to the literature, the pharmacological activity of some species of lungwort (*Pulmonaria officinalis* L., *Pulmonaria obscura* Dum., *Pulmonaria mollis* Wulf ex Hornem) has been established - anti-inflammatory, enveloping, emollient, expectorant, analgesic, wound healing, antiseptic, having a positive effect on the urinary system, processes hematopoiesis, regulation of the activity of the endocrine glands, a number of authors point to the use of lungwort infusions in the treatment of nervous diseases [3, 11, 16, 21, 23].

Of particular interest is the use of medicinal plants in epilepsy, since this neurological disease is one of the most common in the world. Epilepsy is complicated by the fact that it can begin at any age, however, approximately 70% of debuts occur in childhood and adolescence. Various synthetic drugs are used to treat epilepsy, however, despite the severity of the therapeutic effect, they have serious side effects [29]. Therefore, an urgent task is to study the possibility of using herbal remedies in the treatment of this neurological disease, since they can be used for a long time, be effective and safe [28].

In the literature available to us, we have not seen scientific works devoted to the influence of plants of the genus lungwort on electroencephalographic indicators of the functional state of the brain in epilepsy. In this regard, the aim of the work was to study the bioelectrical activity of the brain of rats with a genetic predisposition to absence epilepsy under conditions of oral administration of an

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aqueous infusion of the herb *Pulmonaria obscura* Dum.

Materials and research methods. The experiments were carried out on sexually mature female WAG/Rij rats (n=10, m=115-135 g) at the age of six months. The genetic line of WAG/Rij rats is a model of human absence epilepsy [28]. The females were kept in the vivarium of the Department of Physiology and General Biology of the Bashkir State University, where a constant temperature (20-22 °C) and humidity were maintained. The experimental part of the work was carried out in accordance with the international principles of the Helsinki Declaration on the Humane Treatment of Animals (2000).

The experimental group of female rats was orally administered 1 ml of an aqueous infusion of *Pulmonaria obscura* Dum. prepared at the rate of 1.5 g of crushed dry lungwort herb per 200 ml of water daily for 21 days. The electrical activity of the brain was recorded at the end of the first, second, and third weeks of the experiment at the same time from the frontal and parietal regions of the rat neocortex using needle electrodes on a Neuron-Spectrum-1 electroencephalograph (Russia).

The obtained data were processed using the STATISTICA v.12 software package (Stat Soft Inc., USA) using the nonparametric Mann-Whitney U test. Differences were considered statistically significant at p<0,05.

Research results and discussion. Since electroencephalography is a method of recording electrical potentials, it is characterized by such a concept as frequency. EEG activity, which is a wave of approximately the same constant frequency, is called a rhythm. The following main EEG rhythms are distinguished: delta rhythm (0,5-3 Hz), theta rhythm (4-6 Hz), alpha rhythm (8-13 Hz), low-frequency beta rhythm (13-18 Hz) and high-frequency beta rhythm (18-32 Hz) [10]. Highly informative in epilepsy are alpha, beta and theta rhythms. Sinusoidal activity in the range of these rhythms is a characteristic feature of seizures occurring during epilepsy [2, 14, 21].

The study of the background EEG from both lobes of the neocortex of the control group of female rats (before the introduction of the herbal decoction) revealed the theta rhythm to be predominant; by the end of the first week of the experiment, the delta rhythm became the dominant rhythm. On the 14th day of taking the herb *Pulmonaria obscura* Dum. in females, a pronounced transition of the theta rhythm to the delta rhythm was noted, and on the 3rd week of the experiment, the theta rhythm prevailed on the EEG (Fig. 1).

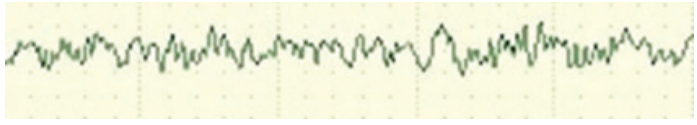
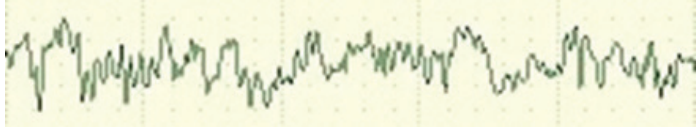
Days of definition	EEG of females
Control group (before applying *Pulmonaria obscura* Dum.)	
7th day	
14th day	
21st day	

Fig. 1. Dominant rhythms during EEG recording in female WAG/Rij rats before and after taking an aqueous infusion of the herb Pulmonaria obscura Dum.
Scale: 10 μV/mm. Development: 25 mm/s.

The study of the bioelectrical activity of the brain from the frontal region showed a significant decrease in the average power of theta rhythm (6,95±0,72%) and high frequency beta rhythm by the end of the first week of the experiment (1,83±0,56%). We associate the obtained results with a possible decrease in excitability, anxiety, and fear [9, 19, 29]. By the 21st day of the experiment, we revealed a generalized increase in the spectral power of theta- (19,20±3,75%) and beta-rhythm of high frequencies (3,23±0,46%), as well as a decrease in the delta rhythm (66 ,48±3,55%) compared with the data obtained on the 7th day of the introduction of the herb infusion. The positive effect of the water infusion of lungwort observed by us from the second week of administration is possibly associated with an increase in the theta rhythm, since the generation of theta rhythm is caused by the hippocampus, and its mossy cells regulate the course of epileptic seizures [27] (Table).

Changes in the frequency power function of electrical activity from the parietal region of the cerebral cortex have specific features. So, on the 7th day of the introduction of lungwort infusion (in comparison with the control group), we found a significant decrease in the power of the high-frequency beta rhythm in females (1,97±0,37% and 3,75±0,49%, respectively) and a statistically significant increase in the delta rhythm (76,74±3,11%). And by the 21st day of oral administration of lungwort, we found a significant increase in the beta rhythm of high frequencies (3,68±0,63%), which indicates an increase in the level of brain activation [8, 24]. In addition, by the end of the experiment, the delta rhythm (64,25±4,95%) and theta rhythm (21,28±5,43%) were statistically significantly reduced compared to the data obtained on the 7th day of the study. Most likely, the revealed results testify to the effective action of *Pulmonaria obscura* Dum. due to the high content of saponins, flavonoids and rosmarinic acid in it. Our data are consistent with the data obtained by Budantsev A.L. and Lesiovskaya E.E. (2012) [4], Polukhina T.S. and Nurgalieva G. B. (2017) [20] (Table).

After analyzing the background EEG recording, we were able to determine the presence of visual phenomena "Epileptiform activity" (Fig. 2) and complexes "acute wave - slow wave" (Fig. 3), which are signs of the presence of absences in the experimental animal model. During the experiment, a decrease in the number of these phenomena is noted, which confirms the positive effect of the use of an aqueous infusion of the herb *Pulmonaria obscura* Dum.

The results of the statistical evaluation of the spectral characteristics of the electroencephalogram from the neocortex of female WAG/Rij rats before and after 7. 14. 21 days of taking an aqueous infusion of lungwort obscure

Experiment day	The share of the neocortex	Delta rhythm.%	Theta rhythm.%	Alpha rhythm.%	Low-frequency beta rhythm.%	High-frequency beta rhythm.%
Control group (determination before application of *Pulmonaria obscura* Dum.)	Frontal	72.75±4.12[1]	13.03±2.89[2]	6.98±0.80	3.63±0.29	3.33±0.27[5]
	Parietal	67.08±4.43[7]	17.33±3.16	7.53±0.59	4.10±0.35	3.75±0.49[10]
7th day	Frontal	76.55±2.00	6.95±0.72[2.3]	6.88±1.27	3.50±0.71	1.83±0.56[5.6]
	Parietal	76.74±3.11[7.8]	11.71±2.81[9]	6.74±1.79	2.78±0.78	1.97±0.37[10.11.12]
14th day	Frontal	74.63±5.11	10.03±3.05[4]	7.68±1.81	4.35±1.24	3.13±0.78
	Parietal	70.00±5.66	14.25±3.74	8.25±1.82	4.00±0.64	3.30±0.50[11]
21st day	Frontal	66.48±3.55[1]	19.20±3.75[3.4]	7.38±1.67	3.50±0.52	3.23±0.46[6]
	Parietal	64.25±4.95[8]	21.28±5.43[9]	6.88±1.03	3.73±0.14	3.68±0.63[12]

Note: 1 - statistically significant differences ($p < 0.05$) on the 7th and 21st days of the study; 2 - the values are reliable ($p < 0.05$) when comparing the control group and on the 7th day of the experiment; 3 - statistically significant differences ($p < 0.05$) on the 7th and 21st days; 4 - reliable values ($p < 0.05$) on the 14th and 21st days; 5 - statistically significant differences ($p < 0.05$) of the control group and on the 7th day of the experiment; 6 - the values are reliable ($p < 0.05$) on the 7th and 21st days; 7 - statistically significant differences ($p < 0.05$) of the control group and on the 7th day of the experiment; 8 - the values are reliable ($p < 0.05$) on the 7th and 21st days; 9 - the values are reliable ($p < 0.05$) on the 7th and 21st days; 10 - the values are reliable ($p < 0.05$) when comparing the rhythm frequencies of females in the control group and on the 7th day of the introduction of lungwort; 11 - statistically significant differences ($p < 0.05$) on the 7th and 14th days; 12 - the values are reliable ($p < 0.05$) on the 7th and 21st days of the study.

Earlier studies of the antiepileptic effect of plant materials showed that intragastric administration of total extracts from Mongolian astragalus (Astragalus mongholicus Bunge) at a dose of 1250 mg/kg revealed a significant effect on the EEG of rats: the intensity of the theta rhythm (stress rhythm) decreased - the effect manifested itself as in the sensorimotor in the cortex and in the hippocampus, it was detected in 30-45 minutes, reaching a maximum in 60-90 minutes after administration. Restoration of the initial bioelectrical activity was observed 120–180 min after administration [7]. Comparing the results obtained by Zhalsray Aldarmaa on the study of Mongolian Astragalus with our data, we can conclude that both Mongolian Astragalus and Lungwort have a positive effect on the central nervous system, due to changes in the theta-rhythm power indicators.

In another experiment, two groups of subjects were involved: the first group took a standardized (pharmacopoeial) alcoholic extract of Rhodiola rosea (*Rhodiolae rosea* L.), the second - a tincture of (*Schizandra chinensis* (Turcz.) Baill.) in standard dosages (30 drops per 100 ml of water). After a single dose of Rhodiola rosea extract, the majority of the subjects changed (decreased compared to the initial values) in the average values of delta, beta and gamma rhythms in both hemispheres. Schisandra chinensis tincture intake did not lead to statistically significant changes in EEG rhythms; the most significant changes occurred in the theta rhythm [12]. Thus, we came to the conclusion that long-term use of *Pulmonaria obscura* Dum. has a better effect than *Schizandra chinensis* (Turcz.) Baill., but less effective than a single application of *Rhodiolae rosea* L.

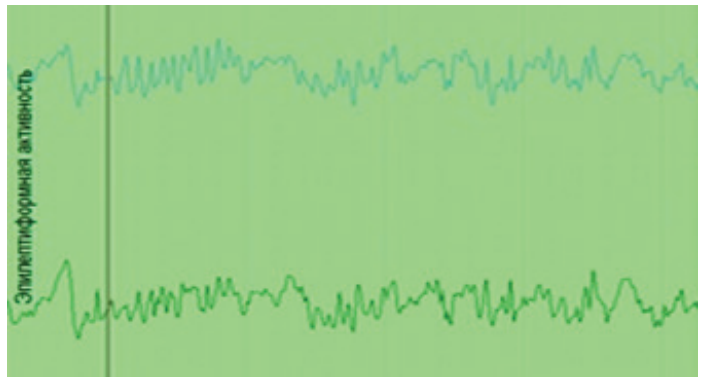


Fig. 2. Epileptiform activity. Scale: 30 μV/mm. Reamer 30 mm/s

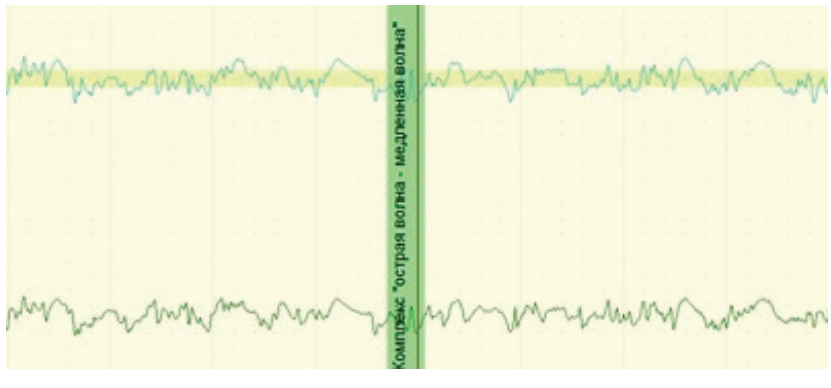


Fig. 3. Complex "acute wave - slow wave" on the electroencephalogram. Scale: 30 μV/mm. Reamer 30 mm/

Conclusion. Thus, as a result of the study, for the first time data were obtained from an electroencephalographic study of the brain of female WAG/Rij rats with oral administration of an aqueous infusion of *Pulmonaria obscura* Dum. Experimental data showed that the course of taking the water infusion of Pulmonaria obscura Dum. at a dose of 1,5 g per 200 ml of water and for a duration of

three weeks, it has a beneficial effect on the electroencephalogram of the brain of rats prone to absence epilepsy [6]. The study lasted 21 days, since the effect of phytopreparations, as a rule, manifests itself by the 3rd week of their use [25]. We assume that *Pulmonaria obscura* Dum. has a positive effect on the state of the functional activity of the brain of rats with absence epilepsy due to the content of a complex of biologically active substances (anthocyanins, flavonoids, saponins, ascorbic, rosmarinic acids, various macro- and microelements) [4, 20]. Further research in this area should be continued to substantiate the possibility of using lungwort herb in the complex therapy of patients with epilepsy.

Restrictions. During the experiment, the result of recording the interictal (interictal) background EEG was evaluated, on which it is possible to determine the beginning, end, and duration of the ictal (attack) sections of the EEG. In addition, by examining the inerictal areas, we can indicate the location of the affected areas [13, 18]. In our study, interictal activity on the baseline EEG plays a key role, as we study absence epilepsy, which is characterized by acute wave-slow wave complexes that typically last 3 to 5 seconds. In this study, the ictal areas of the electroencephalogram were rare. We attribute this to the fact that the EEG recording was not long enough (about 120 minutes).

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DIAGNOSTIC AND TREATMENT METHODS

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RESULTS OF THE STUDY OF COGNITIVE FUNCTIONS IN PATIENTS WITH BRAIN INJURY

DOI 10.25789/YMJ.2022.78.06

УДК 616-06:616.89-008.46

In the Amur Regional Psychoneurological Dispensary of the Amur Medical Academy, a controlled, open, randomized study was conducted to study cognitive functions in 20 patients with a history of traumatic brain injury (men aged 36 to 58 years, the main group). The control group consisted of 20 practically healthy volunteers. Cognitive functions were assessed using the Montreal Cognitive Assessment (MoCA-test), the Schulte Table method, and the 10-word test. The results of the study showed that in patients in the late period of traumatic brain injury, the presence of cognitive disorders is recorded in 100% of cases. Mild and moderate cognitive impairment in patients with traumatic brain injury up to 6 years is expressed by a 3-fold decrease in work efficiency relative to healthy volunteers, mental stability, short-term and long-term memory. It was concluded that it is necessary to conduct a mandatory neuropsychological examination in patients with craniocerebral injury in the long-term period in order to timely and pathogenetically substantiated pharmacological correction of post-traumatic cognitive dysfunction.

Keywords: cognitive impairment, traumatic brain injury, remote period, work efficiency, degree of development, mental stability, memory, attention, patients.

The problem of cognitive impairment in patients with traumatic brain injury remains a priority today, taking into account the statistical increase in the number of traumatic brain injuries in modern society and the sufficient development of neurorehabilitation methods to compensate for motor deficits, which leads to a less pronounced decrease in the quality of life of patients. than the presence of a defect in cognitive functions [1, 4, 16]. The works of domestic researchers show that the severity and qualitative characteristics of the consequences of various craniocerebral injuries directly depend on the severity and mechanism of injury: in 20% of cases, the consequences of a craniocerebral injury lead to disability, in 45% - to a decrease in working capacity, and only 25% patients return to their previous work [3, 6, 7, 12]. At the same time, it should be noted that in the last decade, most scientists unanimously leave the prevailing positions behind cognitive impairments that form in the late period of mild and moderate traumatic brain injury [2]. This is due to the late diagnosis of cognitive disorders, since patients with traumatic brain injury, as a rule, are represented by a contingent of young people with a high potential for compensatory abilities [9]. For a long time, this category of patients is able to almost fully perform certain work, compensating for the lack of attention and concentration by additional checking of the results of work, and memory loss - by using auxiliary techniques in the form of written recording of the necessary information or repeated verbal repetition [4]. However, the use of auxiliary techniques is an additional load on the functional reserve of the central nervous system, which leads to increased fatigue, and, ultimately, to a decrease in mental performance. That is why, during the initial visit to the doctor in the late period of mild and moderate craniocerebral injury, patients present with complaints that fall into the asthenic range (decreased performance, fatigue, decreased concentration and memory, etc.), which should focus the doctor to conduct a neuropsychological examination to assess cognitive functions, since even minimal dysfunction and mild cognitive impairment can transform into post-traumatic dementia. Moderate cognitive impairment is a decrease in cognitive abilities that goes beyond the age-related educational gender norm, which is reflected in the patient's complaints and may be noticeable to others, however, the presence of moderate cognitive impairment does not lead to significant difficulties in everyday life and is not accompanied by a change in social, household and professional activities, with the exception of the most complex activities [5]. The presence of moderate cognitive impairment in patients with a history of traumatic brain injury is an urgent problem in psychoneurology and predetermines the need for early diagnosis and adequate pathogenetically substantiated therapy in order to correct neuropsychological symptoms and maintain the habitual lifestyle of patients for the longest possible time [13].

The aim of the study was to study cognitive functions in patients in the late period of traumatic brain injury.

Material and methods. A prospective controlled open randomized study was

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