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РАСПРЕДЕЛЕНИЕ ФИЗИОЛОГИЧЕСКИХ РЕСУРСОВ И ЭФФЕКТИВНОСТЬ ЦЕЛЕНАПРАВЛЕННОЙ ДЕЯТЕЛЬНОСТИ У БОЛЬНЫХ ЭПИЛЕПСИЕЙ

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Цель. Изучение распределения физиологических ресурсов при целенаправленной деятельности у пациентов с эпилепсией. ***Материалы и методы.*** Обследовано 70 здоровых лиц и 160 пациентов с эпилепсией. У исследуемых моделировалась целенаправленная деятельность с определением её результативности при помощи теста Шульте-Горбова. В динамике моделируемой деятельности оценивались показатели электроэнцефалограммы и вариабельности сердечного ритма; в исходном состоянии (предшествующем тесту Шульте-Горбова) определялись характеристики зрительных вызванных потенциалов, когнитивных потенциалов P300, условно-негативного отклонения. Осуществлялось исследование взаимоотношений показателей электроэнцефалографии и характеристик вариабельности сердечного ритма методом корреляционного анализа с использованием рангового коэффициента корреляции Спирмена; проводился сравнительный анализ характеристик вариабельности сердечного ритма и характеристик внешнего дыхания, а также прогнозирование результативности поведения у пациентов с эпилепсией методом логит-регрессионного анализа. ***Результаты.*** Установлено преобладание структурно-метаболических форм эпилепсии в группе пациентов с низкой результативностью деятельности. В низкорезультативной группе пациентов с эпилепсией выявлена большая сопряжённость физиологических показателей и высокий уровень характеристик, отражающих активацию стресс-реализующих систем. Для эффективного распределения пациентов с эпилепсией на группы с различной результативностью потребовалось включение в модель логит-регресии характеристик зрительного вызванного потенциала, когнитивного потенциала P300 и условного негативного отклонения, что отражает роль афферентных и ассоциативных механизмов в решении данной задачи. Увеличение физиологической «стоимости» и снижение результативности деятельности в группе больных эпилепсией уменьшает её эффективность, что связано с преобладанием структурных форм заболевания. ***Заключение.*** Предполагается роль эпилептогенных зон головного мозга у пациентов с эпилепсией не только в снижении результативности деятельности, но и в избыточной мобилизации физиологических ресурсов и увеличении физиологической стоимости деятельности, что уменьшает её эффективность.

Ключевые слова: *эпилепсия, логистический анализ, эффективность деятельности, распределение ресурсов.*

DISTRIBUTION OF PHYSIOLOGICAL RESOURCES AND EFFECTIVITY OF PURPOSEFUL ACTIVITY OF PATIENTS WITH EPILEPSY

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Aim*:* to study distribution of physiological resources in purposeful activity of patients with epilepsy. ***Materials and Methods.*** 70 Healthy individuals and 160 patients with epilepsy were ex-

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amined. In the examined individuals purposeful activity was modeled with evaluation of its effectiveness using Schulte-Gorbov test. In the dynamics of the modeled activity, parameters of electroencephalogram, variability of heart rhythm were evaluated; in the initial condition (before Schulte-Gorbov test) parameters of evoked visual potentials, P300cognitive potentials and of a conditionally-negative deviation were estimated. Interrelations between parameters of electroencephalography and of variability of heart rhythm were studied using correlation analysis with Spearman rank correlation coefficient; the comparative analysis of variability of heart rhythm and characteristics of respiratory function was performed, and effectiveness of behavior of patients with epilepsy was predicted using logit-regression analysis. ***Results.*** Predomination of structural-metabolic forms of epilepsy was found in the group of patients with low effectiveness of the activity. The low-effective group of patients with epilepsy showed a higher correlation of physiological parameters and a high level of characteristics refecting activation of stress-realizing systems. For effective distribution of patients with epilepsy into groups with different effectiveness of behavior, it was necessary to include characteristics of visual evoked potential, P300 cognitive potential and conditionally-negative deviation into logit-regression model, that reflects the role of afferent and association mechanisms in this task. Increase in physiological «cost» and reduction in the effectiveness of activity in the group of patients with epilepsy is associated with prevalence of structural forms of epilepsy. ***Conclusion.*** Epileptogenic zones in patients with epilepsy are supposed to play a role not only in reduction of effectiveness of activity, but also in excessive mobilization of physiological resources and in increase in physiological cost of activity, that diminishes its effectiveness.

Keywords*: epilepsy, logistic models, effectiveness of activity, distribution of resources.*

Physiological cost of behavior in integrative physiology is included into determination of the effectiveness of activity [1,2]. Effectiveness of activity is a basic concept of systemic analysis in physiology and pathology and is determined as a ratio of the result of activity to its physiological cost. In pathology the term «effectiveness of activity» is closely connected with concepts of deficit of the useful adaptive result of behavior [3], of probabilistic organization of the environmental events and reinforcement, insufficient informational about different stages of behavior, modeling of functional systems in the conditions of probabilistically determined environment and of emotional stress [4]. Here, reduction in the effectiveness of the activity may be a key factor provoking manifestation of pathological processes. Of importance is a problem of effectiveness of activity in neurological disorders, in particular, in epilepsy, which is associated with a possibility of analysis of the given disease both from the point of view of pathological systems including functionally heterogeneous structures of the nervous system united by permanent and temporary connections [5], and from the point of view of systemic physiology that associates development of epileptic seizures with functioning of physiological neuronal ensembles [6].

Aim of work: identification of peculiarities of distribution of physiological resources and of physiological cost of the activity of patients with epilepsy and of their association with clinical characteristics of the disease.

In accordance with the stated aim the following tasks were set:

1) to identify differences in the efficiency of the modeled activity in groups of patients with epilepsy in comparison with control group of practically healthy individuals;

2) to determine peculiarities of intrasystemic relationships in the studied groups;

3) to assess peculiarities of the autonomic regulation in the studied groups;

4) to determine physiological predictors of the efficiency of the activity in groups of patients with epilepsy using method of logistic regression analysis;

5) to identify differences in the physiological cost and to assess effectiveness of the activity in groups of patients with epilepsy.

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Materials and Methods

The study was conducted on the base of Ryazan State Medical University in 2012-2017. Seventy healthy individuals were examined (control group – 40 males and 30 females with average age 33.0±0.55 years) and 160 patients with epilepsy with equal gender distribution with average age 35.1±1.1 years. The group of patients with epilepsy included patients with genetic epilepsy (n=10), with structural epilepsy (n=90) and with probably symptomatic (of unspecified etiology/ cryptogenic) epilepsy out of remission (n=60) [7]. From the study there were excluded patients with pathology of respiratory and cardiovascular systems, pregnant females. From the control group there were excluded individuals with indications to the past paroxysmal disorders and with pathological alterations in the electroencephalogram (EEG). The study was approved by the local ethical committee of the university, the participants signed informed consent.

For modeling of functional load and parametrization of efficiency of the activity, Schulte-Gorbov test was used. EEG was recorded on computer electroencephalograph Neuron-spectrum-3 (Russia) in the monopolar commutation in 19 leads (with ear electrodes as reference electrodes). There were performed spectral analysis of EEG (determination of the power and frequency of theta-, alpha-, beta-1 and beta-2 oscillations), examination of cross-correlation function (determination of cross-correlation coefficients and of the mean frequency of function) [8].

Heart rate variability (HRV) was studied using Varicard 2.51 device and ISCIM 6.0 program (all – Russia), EEG was recorded in I standard lead. Statistical analysis of HRV included determination of standard error of normal to normal R-R intervals (SDNN), stress-index (SI), power of oscillations in high-, low- and very low-frequency ranges and of the total power (HF, LF, VLF, TP) [9]. Characteristics of respiration were studied on spirometabolographic complex Fitmate Med (Italy) and on ultrasound capnograph CP-01 Elamed (Russia). The following parameters were determined: the average value of lung ventilation (ventilation – Ve), respiratory rate (RR), level of oxygen, energy expenditure, partial pressure of carbon dioxide on expiration.

Visual evoked potentials (VEP) to check board pattern were recorded on software-hardware complex Neuro-MEP (Russia) with the frequency of changing stimuli 1 per second, with active electrodes positioned in leads O1, O2, Oz; and with reference electrode in Fz. Latency of peaks N75, P100, N145 and interpeak amplitude N75P100, P100N145, N145P200 were analyzed, subelectrode impedance was below 5 kOhm. Endogenous evoked potential P300 was recorded in leads Fz, Cz, Pz with application of a relevant sound stimulus (2000 Hz pitch) and of an irrelevant sound signal (1000 Hz pitch), the response of participants was recorded in the form of pressing the button. Latency N2, P3 and amplitude P2N2, N2P3 were determined. Contingent negative variation wave (CNV) was studied with application of a warning (sound of 2000 Hz pitch) and triggering (sound of 1000 Hz pitch) stimuli. The amplitude of the wave was evaluated in leads Fz, Cz, Pz [10].

For statistical processing Statistica 10.0 program was used. Cluster analysis included k-averages procedure (distribution of participants into clusters). Descriptive statistics of the groups of studied individuals suggested description of the mean value and of 95% confidence interval. Analysis of variations (ANOVA) was conducted to identify differences between samples using F-test. In comparison of the quantity of patients in subgroups contingency tables and χ^2 criterion were used. To examine relationships between parameters, Spearman correlation coefficient was used, the relationship was considered reliable at $p<0.05$.

To create a model of classification of patients with epilepsy into clusters with different effectiveness of performing the test, logit regressive analysis was used with description of dependent variable (probability of distribution into a group), of absolute term of an equation, of regression coefficients for independent variables and of independent variables as such (predictors). As a function of

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losses, maximum likelihood method and Hook-Jeeves pattern were used; as a criterion of agreement χ^2 test and achieved p-level were used; relations of chances were determined for independent variables as a characteristics of their significance [11].

Results and Discussion

Two groups of patients with epilepsy were defined on the basis of Schulte-Gorbov test. The first group included patients with a fast choice of numbers including mistaken answers, and patients with less mistakes; group 2 included patients with opposite characteristics, in this context group 1 (n=91) was considered efficient, and group 2 (n=69) – low efficient (Table 1).

Table 1

Characteristics of Load Test in Studied Groups

Characteristics	Patients with epilepsy, group 1 (average, 95%CI)	Patients with epilepsy, group 2 (average, 95%CI)	Control (average, 95%CI)	F	p
Average interval, s	1.5 (1.4-1.7)	2.2 (2.0-2.3)	1.2 (1.0-1.3)	120	0.001
Interval after error, s	0.6 (0.3-0.7)	1.9 (1.5-2.0)	0.7 (0.5-1.0)	40	0.001
Interval before error, s	0.2 (0.1-0.3)	0.9 (0.6-1.1)	0.4 (0.3-0.5)	28	0.001
Number of errors, n	0.7 (0.5-0.9)	2.2 (1.7-2.5)	0.8 (0.6-1.0)	26	0.001

Note: CI – confidence interval

Difference of clinical characteristics of groups of patients with epilepsy in the defined groups was found: in group 2 there were reliably more patients with structural epilepsy (43%) in comparison with group 1 (74%, χ^2=9.8, p=0.002).

Relationships of parameters of ECG and HRV in the studied groups in the form of correlation pleiades are given below in graphic models. The following designations are used: 1, 2, 3 – characteristics of spectral power of frequency components of EEG in the left frontal and occipital leads; 4, 5, 6 – frequency parameters of EEG in the left frontal and occipital leads; 7, 8, 9, 10 – correlation of EEG in F3-F4, O1-O2, F3-C3, P3-O1 leads; 11, 12, 13, 14 – frequency of cross-correlation function of F3-F4, O1-O2, F3-C3, P3-O1; 15, 16, 17, 18, 19 – parameters of HRV: VLF, LF, HF, SDNN, SI; solid lines showed positive, dotted lines showed negative correlation relationships. From the pictures paired correlation were excluded, that were the same in all groups, in particular, correlations of parameters of statistical analysis of the dynamic set of R-R intervals and spectral characteristics of HRV.

In Figure 1 the dynamics of intrasystemic relationships in the group of practically healthy individuals are given. In the background condition reliable correlations between parameters of EEG and HRV were not determined, after cognitive load two reliable correlation relationships were determined: between frequency of alpha-oscillations of EEG O1 and VLF of HRV (R=-0.264, p=0.042), and between intrahemispheric correlation P3-O1 of EEG and VLF of HRV (R=0.274, p=0.039) (Fig. 1).

In group 1 of patients with epilepsy the background condition was characterized by a high level of interrelation of physiological parameters: reliable correlations of beta-1 oscillations of EEG with LF parameter of HRV (R=-0.223, p=0.026), interhemispheric cross-correlations of EEG in frontal leads with mean-square deviation of HRV (R=0.278, p=0.012), interhemispheric cross-correlation of EEG in the occipital leads with HF parameter of HRV (R=0.347, p=0.001), cross-correlation frequency of EEG in the occipital leads with SDNN of HRV (R=-0.236, p=0.001). After cognitive load the amount of reliable correlations significantly decreased: interhemispheric correlation of EEG in O1-

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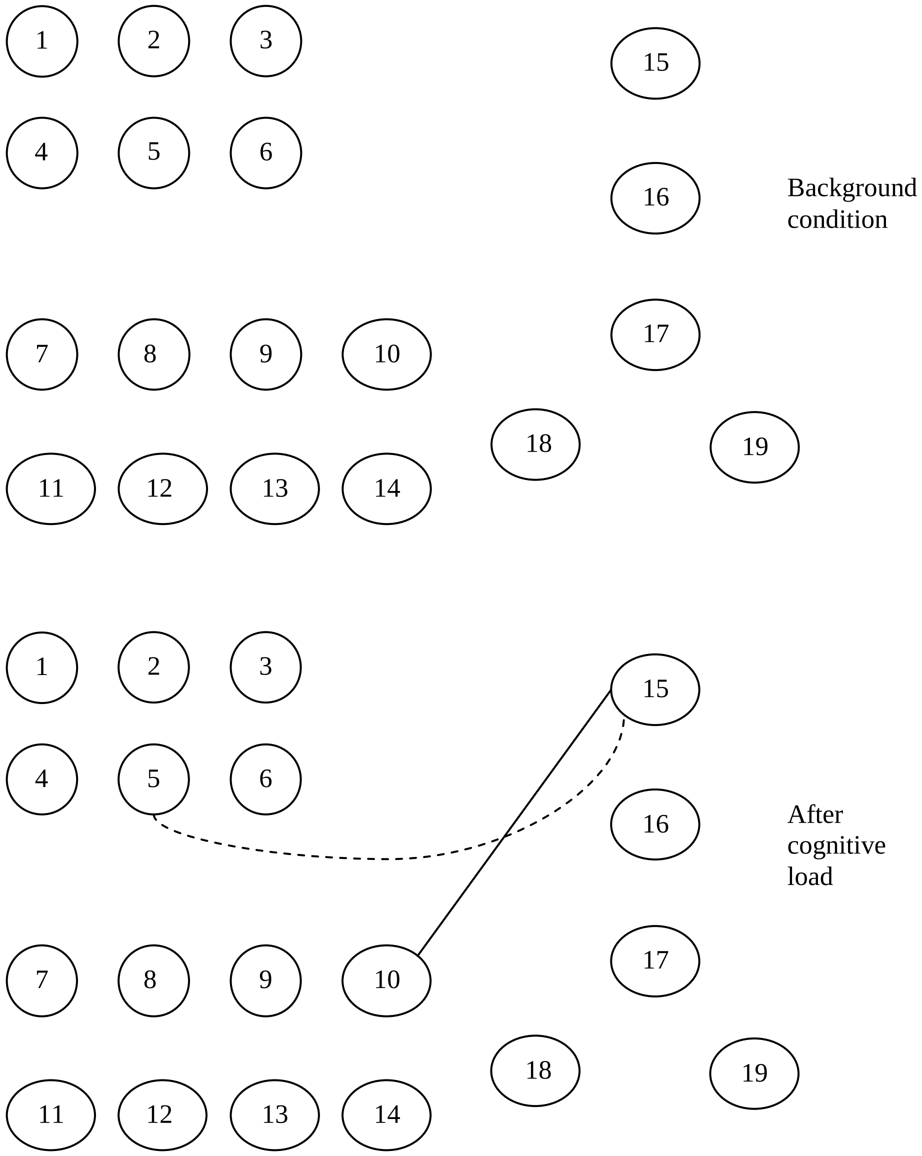

Fig. 1. Interrelation between characteristics of EEG and VCR in healthy individuals

Note: in figures 1-3 continuous lines show direct correlations, discontinuous lines show negative correlations; designation of used parameters numbers is presented in the text

O2 – HF of HRV (R=0.272, p=0.007) was determined (Fig. 2).

In Figure 3 the dynamics of alterations of interrelations of EEG and HRV characteristics in group 2 of patients with epilepsy is given. In the background condition 4 reliable correlation interrelations were identified: interrelation between theta-oscillations frequency of EEG in the left frontal leads and VLF of HRV (R=0.316, p=0.014), between intrahemispheric cross-correlation of EEG in the frontal-central leads and HF of HRV (R=0.317, p=0.015), between intrahemispheric cross-correlation of EEG in the frontal-central leads and SDNN of HRV (R=0.304, p=0.033), between frequency of cross-correlation of EEG in the left parietal-occipital leads and SDNN of HRV (R=-0.236, p=0.001). After cognitive

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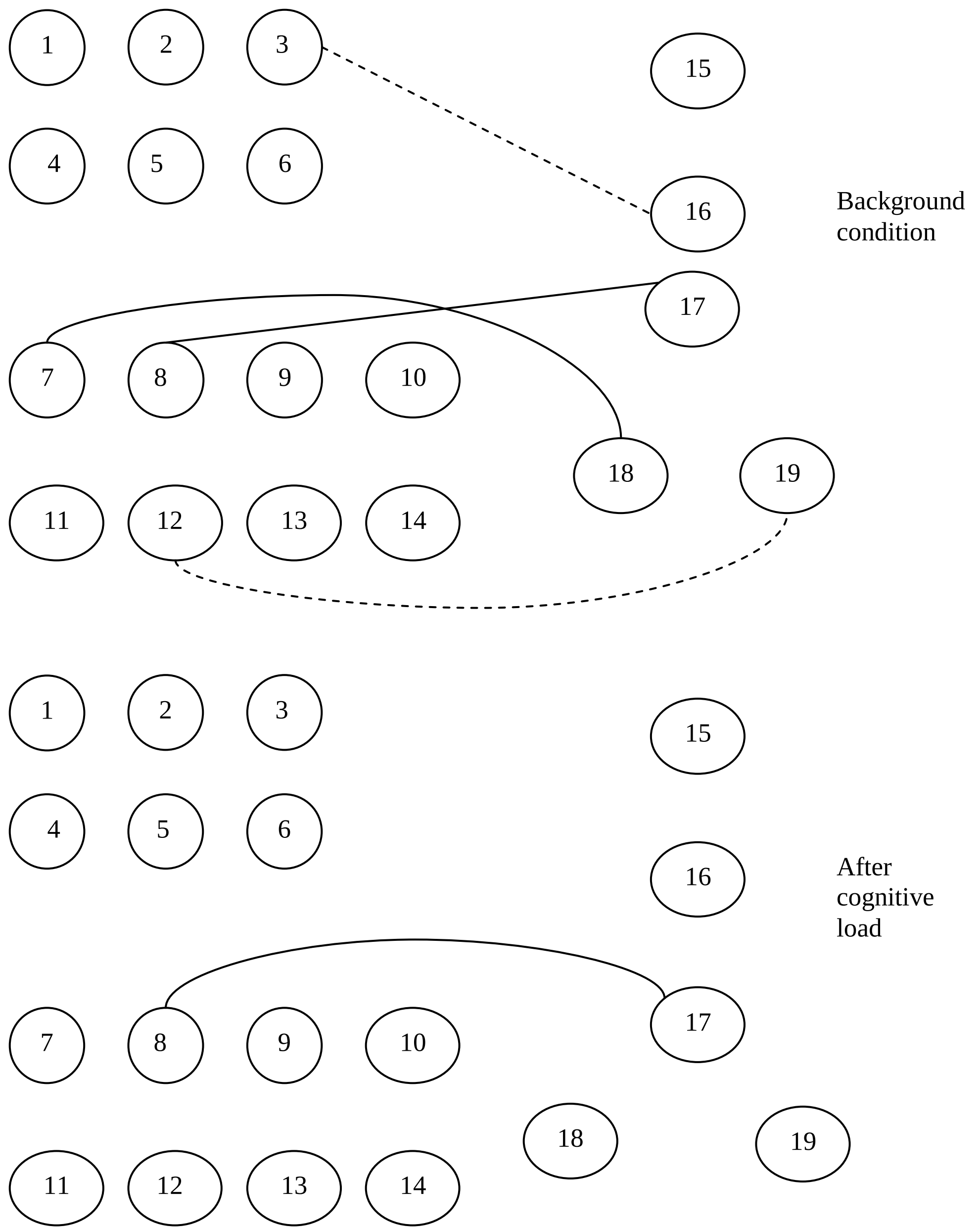

Fig. 2. Interrelation between characteristics of EEG and VCR in the efficient group of patients with epilepsy

load the structure of interrelations changed, but their number remained the same: relationships between power of theta-oscillations of EEG and LF of HRV (R=-0.266, p=0.043), between interhemispheric cross-correlation in the occipital leads of EEG and LF parameter of HRV (R=0.287, p=0.031), between intrahemispheric correlation of EEG in the left parietal-occipital leads and SDNN of HRV (R=0.270, p=0.043), between correlation frequency of EEG in P3–O1 leads and LF parameter of HRV (R=-0.279, p=0.037) were identified. In the analysis of parameters of HRV, a reliably higher SI level and reduction in variability of cardiointervals were found in patients with epilepsy.

In the background condition a reliable reduction of SDNN in group 2 of patients with epilepsy was found in comparison with group 1. Parameters of tension index in the control group moderately increased in cognitive load and then deceased, while in groups 1 and 2 of

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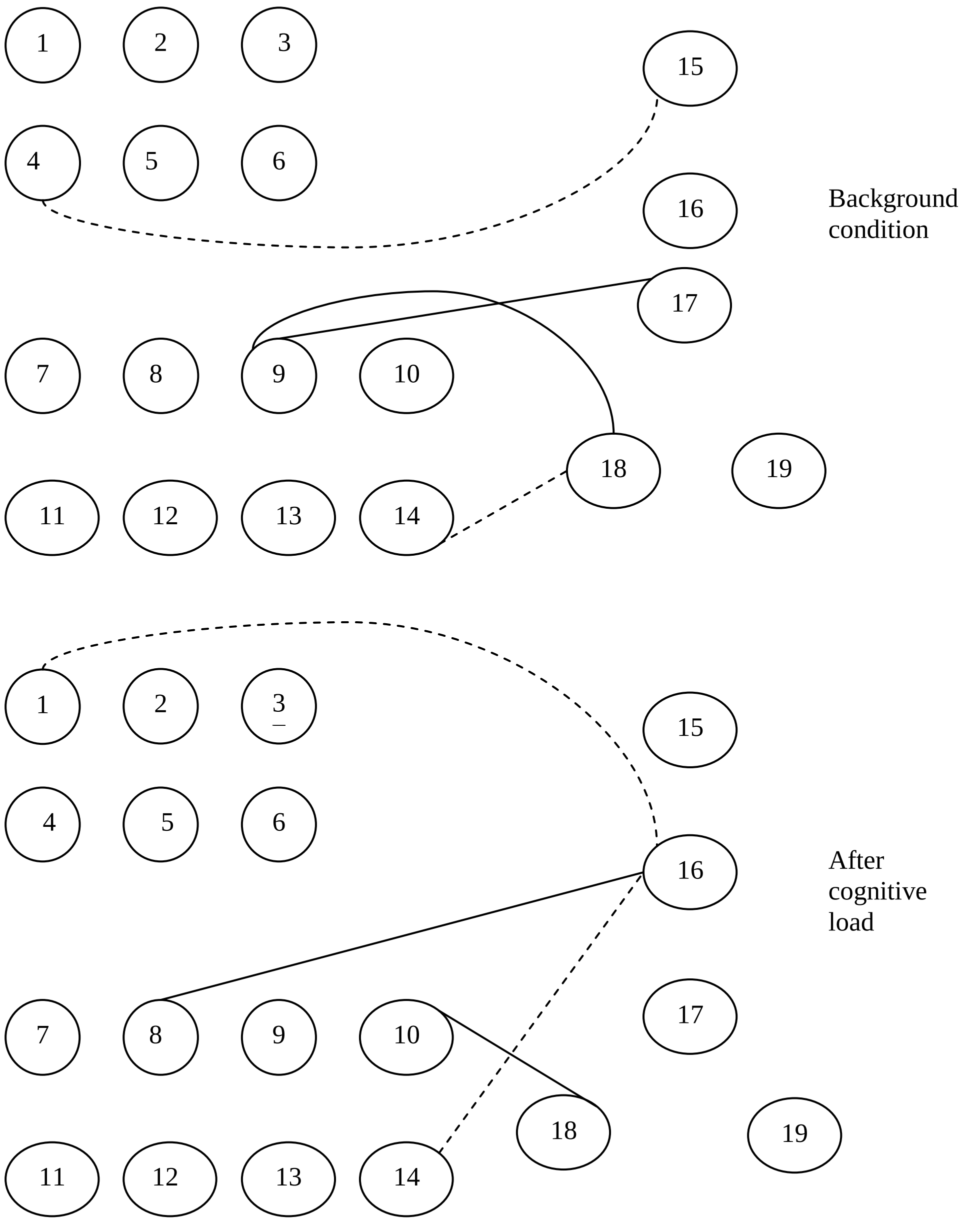

Fig. 3. Interrelation between characteristics of EEG and VCR in the low-efficient group of patients with epilepsy

patients with epilepsy the level of SI of regulatory system after cognitive load remained high (Table 2).

Parameters of respiration reflected a higher level of lung ventilation in patients with epilepsy in group 2 after cognitive load.

To predict distribution of patients with epilepsy into groups with different efficiency of the activity, a method of logistic regression was used with inclusion of characteristics of visual evoked potential, of cognitive evoked potential P300 and of contingent negative variation (CNV) into regression model (Table 3).

Convergence of this model in χ^2=23.5 p=0.0006; assessment of parameters were statistically significant. The correct classification of patients to groups was 83% in group 1 and 70% in group 2.

Analysis of parameters of modeled activity in patients with epilepsy showed that

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Table 2

Dynamics of Parameters of VCR and of Characteristics of Respiration in Groups

Parameters	Patients with epilepsy, group 1 (average, 95% CI)	Patients with epilepsy, group 2 (average, 95% CI)	Control (average, 95% CI)	F	p
SDNN background, ms	35 (31-38)	29 (26-31)	50 (44-55)	21.6	0,001
SI background, conventional units	501 (401-601)	575 (378-772)	247 (174-320)	6.5	0.002
SDNN cognitive load, ms	35 (31-38)	31 (27-34)	42 (37-48)	7.8	0.001
SI cognitive load, conventional units	515 (403-626)	541 (365-717)	297 (218-375)	4.1	0.018
SDNN after load, ms	34 (31-38)	30 (26-34)	50 (44-56)	22.7	0.001
SI after load, conventional units	617 (332-903)	585 (426-744)	223 (163-283)	3.1	0.046
Ve after load, L/min	8.4 (7.9-8.7)	9.4 (8.7-9.9)	8.3 (7.9-9.1)	3.2	0.040
RR after load, per min	15.1 (14.3-15.9)	17.0 (15.8-18.0)	14.9 (13.7-15.9)	4.7	0.010

Table 3

Characteristics of Logit-Regression Load for Classification of Patients with Epilepsy in Groups with Different Efficiency of Activity

Parameters	Regression Coefficients	χ^2	p	Odds ratio
Intercept coefficient	9.0	8.8	0.037	28
Alpha-rhythm frequency of EEG in O1	-1.0	9.0	0.022	0.71
Cross-correlation of EEG in F3-F4	-0.36	4.2	0.045	0.69
Interpeak amplitude of N75P100 VEP in Oz lead	-0.22	8.0	0.036	0.80
Interpeak amplitude of P2N2 P300 in Cz	0.04	4.3	0.044	1.04
CNV amplitude in Cz	-0.04	4.2	0.045	0.96
SDNN VCR	-0.02	4.2	0.045	0.98

differences in them were associated both with the speed of activity and with the level of selective control. Insufficient efficiency was associated with domination of patients with structural epilepsy in group 2 with existence of the respective morphophysiological basis, and also with peculiarities of integrative activity of physiological mechanisms [12].

The dynamics of intrasystemic interrelationships in the group of healthy individuals and in patients with epilepsy was evaluated in the analysis of correlations between characteristics of EEG and HRV during the test. In healthy individuals there were no reliable correlations in the background condition which indicates a low level of interrelation between physiological mechanisms and functional tension [13], which was manifested only after a cognitive load (this reflects reliable correlation relationships after performing the test). In group 1 of patients with epilepsy the functional condition before the test was characterized by a higher intrasystemic coupling in comparison with healthy individuals, coupling between parameters decreased after the functional load. Group 2 of patients with epilepsy was characterized by a high background correlation of EEG and HRV that was preserved after the load, that is, by a high intrasystemic tension reflecting a high level of physiological «costs» in realization of the activity.

A study of mechanisms of the autonomic dysfunction on the basis of data of HRV showed that maximal activation of ergotropic mechanisms as a component of stress-realizing system [14] was determined in low efficiency of activity of patients with epilepsy; this phenomenon was traced through all stages of the modeled purposeful activity. After the functional load in group 2 patients with epilepsy, a buildup of stress-index was determined. Taking into account these facts, a non-specific character of the above mentioned interrelations between EEG and HRV can be suggested that reflects neurophysiological correlates of distress.

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For classification of patients with epilepsy by efficiency of the activity it was necessary to include characteristics of exogenous evoked potentials of cognitive potentials P300 and of CNV into the model of logistic regression, which indicates the necessity of taking into account not only the level of the activity of non-specific mechanisms determining its cost, but also afferent and associative mechanisms specific of the modeled activity, in the assessment of effectiveness of the activity [15]. Classification of the tested individuals into groups was carried out with sufficient reliability.

It may be reasonable to speak about influence of epileptogenic zones on the key behavioral mechanisms of patients with epilepsy which impairs comparison of parameters of the realistic result of the activity with its information model, influences excessive mobilization of physiological resources and increases physiological cost of the activity even with reduction of its efficiency, and is associated with the reduction in the effectiveness of activity in epilepsy.

Conclusions

1. Effectiveness of the purposeful activity in patients with epilepsy is decreased both due to reduction in its efficiency, and to increase in the physiological cost.

2. High physiological cost of the modeled activity of patients with epilepsy exist in all stages of the functional load.

3. One of basic characteristics that reflects specificity of systemic organization of purposeful activity in healthy individuals and in patients with epilepsy is effectiveness of the activity.

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