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## PATHOGENETIC ROLE OF CHANGES IN THE TYPE OF BLOOD CIRCULATION IN THE DYNAMICS OF BRAIN VASCULAR DISORDERS

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Features of the heart rate variability at patients with acute disorder of cerebral circulation depending on the type of hemodynamics were studied in acute period of disease and in a condition of relative functional rest. Surveyed men and women (121 patients, 30-55 years old) were divided into 3 groups according to the type of hemodynamics that was defined at the first day of their disease: the groups of patients with hyper-, hypo- and normodynamic types of hemodynamics were selected. The integral rheography of the body was carried out again on the 7th day of hospitalization of the patients. And according to the received data all examined individuals were divided into subgroups. The evaluation of indicators of the heart rate variability at patients during acute period of disease showed the significant increase of activity of the sympathetic link of regulation among people with hyperdynamic type of hemodynamics: the indices of tension and vegetative balance also as the standard deviation of NN intervals (SDNN) were rather law. The same patients examined on the 7<sup>th</sup> day of their disease demonstrated the reduction of the indices of tension and vegetative balance and the increase of the mean square difference between the duration of adjacent R-R intervals (RMSSD). These changes were regarded as gradual weakening of the sympathetic influences on cardio-vascular system in stabilization period. At examination of patients in a week from the moment of their hospitalization transformation of the type of hemodynamics was revealed among many of the surveyed. The indices of tension and vegetative balance were the lowest among patients with acute disorder of cerebral circulation and initially hyperdynamic type of hemodynamics and newly formed hypodynamic type of blood circulation. While patients with acute disorder of cerebral circulation and constantly hyperdynamic type of blood circulation showed the maximal tension in operation of the regulatory systems.

**Keywords:** stress; adaptation; type of hemodynamics; acute violation of cerebral circulation; heart rate variability; autonomic regulation.

# ПАТОГЕНЕТИЧЕСКАЯ РОЛЬ ИЗМЕНЕНИЯ ТИПА КРОВООБРАЩЕНИЯ В ДИНАМИКЕ МОЗГОВЫХ СОСУДИСТЫХ КАТАСТРОФ

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Изучены особенности вариабельности сердечного ритма (ВСР) у пациентов с острым нарушением мозгового кровообращения (ОНМК) в зависимости от типа гемодинамики в 1-е сутки развития заболевания и на 7-й день после сосудистой катастрофы. Обследуемые (121 пациент, мужчины и женщины, от 30 до 55 лет) при поступлении в стационар были разделены на 3 группы: пациенты с ОНМК и гипердинамическим типом кровообращения, с ОНМК и нормодинамическим типом кровообращения и с ОНМК и гиподинамическим типом гемодинамики. На 7-й день от начала заболевания всем пациентам была повторно проведена интегральная реография тела и в зависимости от вновь сформированного типа гемодинамики пациенты каждой группы были разделены на подгруппы: в каждой группе были выделены исследуемые с гипердинамическим, гиподинамическим и нормодинамическим типами кровообращения. Оценка показателей ВСР в 1-е сутки нахождения пациента в стационаре выявила существенное повышение активности симпатического звена регуляции у больных с ОНМК и гипердинамическим типом кровообращения: низкие значения стандартного отклонения NN-интервалов (SDNN), индекса напряжения регуляторных систем (ИН) и индекса вегетативного равновесия (ИВР). На 7-й день пребывания в стационаре пациенты с ОНМК и гипердинамическим типом кровообращения характеризовались повышением показателей среднеквадратичного различия между длительностью соседних R-R-интервалов (RMSSD) и снижением ИН и ИВР. При обследовании паци-

ентов через неделю от момента госпитализации у многих из них было обнаружено изменение типа гемодинамики. У пациентов с ОНМК и исходно гипердинамическим типом кровообращения ИВР и ИН были ниже, чем у пациентов с вновь сформированным гиподинамическим типом гемодинамики. Установлено, что у пациентов с ОНМК и стабильно гипердинамическим типом гемодинамики (и в 1-е сутки, и на 7-е сутки) наблюдается максимальная напряженность работы регуляторных систем.

**Ключевые слова:** стресс; адаптация; типы гемодинамики; острое нарушение мозгового кровообращения; вариабельность сердечного ритма; вегетативная регуляция.

Current ideas on the mechanisms of acute cerebrovascular accident (ACVA) are closely linked to the concept of emotional stress, which is considered as one of the most significant risk factors for the development of vascular pathology, especially in young people [2, 8]. In cases of cerebral hemodynamics disorder, over-tension and regulation failure occur at both central and peripheral levels, as well as discoordination of stress-implementing and stress-limiting systems that leads to damage development [3, 6]. The severity of the vegetative component of stress response in ACVA development is of great importance in the course of the disease, which enables the use of assessing heart rate variability (HRV) to predict the risks of possible complications and adverse outcomes [7]. Thus, the risk of ischemic brain damage is known to be higher in patients with low activity of the parasympathetic segment of the autonomic nervous system [1, 5].

The characteristics of systemic hemodynamics as a reflection of the central influences on the effector systems of the body should also be taken into account when assessing the severity of damage in ACVA development, making predictions for the patient and development of preventive measures aimed at prevention of this disease [4]. However, the relationship between the mechanisms of hemodynamics, the aspects of its regulation in the acute and subacute periods of vascular disorders, and the nature of brain damage in patients with cerebrovascular accident is not fully understood.

This study aimed to establish the dynamics of changes in the type of blood circulation in ACVA development and to determine its role in damage formation

We examined 121 patients aged 30 to 55 years (31.8% of women, 68.2% of men). Body integral rheography (BIRG) was performed using a complex of cardiorespiratory system and tissue hydration KM-AR01-Diamant, and HRV was evaluated using the CardioKit software package (Gosstandart certificate of the Russian Federation No. 2335 and certificate of the Ministry of Health of the Russian Federation No. ROSS RU IM02.AO3991). Patients were examined at day 1 after ACVA and day 7 after hospitalization. Statistical data processing

was performed using parametric (Student's t-test) and nonparametric (Wilcoxon-White, Shapiro-Wilk) methods.

Upon admission to the hospital, all patients were divided into 3 groups according to the type of hemodynamics, namely, 76 ACVA patients with hyperdynamic circulation, 28 patients with normodynamic circulation, and 17 patients with hypodynamic circulation.

Assessment of HRV indices revealed a significant increase in activity of the sympathetic regulation link among ACVA patients with hyperdynamic circulation, as evidenced by a 50% decrease in the standard deviation of NN intervals (SDNN) compared with standardized general population indicators. The values of the mean-square difference between the duration of adjacent R-R intervals (RMSSD) in this group of patients were below normal and did not exceed 16 (11; 35) ms (Figure 1). In ACVA patients with normo- and hypodynamic circulation, RMSSD did not exceed normal values and was equal to an average of 20 ms. In the group of patients with hypodynamic type of blood circulation, SDNN was significantly higher than in groups with hyper- and normodynamic circulation at 41 (16; 82) ms, which suggests intensification of the parasympathetic regulation link, resulting in a hypodynamic circulation.

The activation of the sympathetic regulatory link in ACVA patients with hyperdynamic circulation was confirmed by high values of the strain index (SI) of regulatory systems and the autonomic balance index (ABI) of 286.5 (153.5; 532) and 431.5 (228; 805) c. u., respectively. Among ACVA patients with hypodynamic circulation, these indicators were lower than in other study groups (ABI was 262 [84; 776] c. u., and SI was 154 [87; 554] c. u.) (Figure 2).

Analysis of HRV data in ACVA patients, obtained at day 7 after a vascular accident, revealed an increase in SDNN and RMSSD values (by 33% and 31%, respectively) and a decrease in SI (by 15%) and ABI (by 18%) in ACVA patients with hyperdynamic circulation. High values of these indicators in such patients during hospitalization and the decrease in the above indices at day 7 of hospitalization indicate a pronounced activity of the sym-

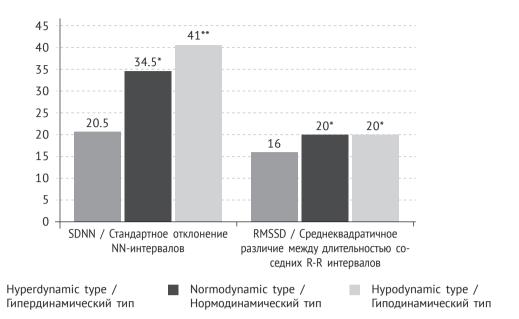


Fig. 1. Indicators of SDNN and RMSSD in patients with acute cerebrovascular accidents and different types of haemodynamics in the first days after vascular catastrophe. \* - reliably when comparing indicators of the groups of hyperdynamic and normodynamic types of blood circulation, p < 0.05; \*\* - reliably when comparing indicators of the groups of hyperdynamic and hypodynamic types of blood circulation, p < 0.05

Рис. 1. Значения показателей SDNN и RMSSD у пациентов с острым нарушением мозгового кровообращения и разными типами кровообращения в 1-е сутки после сосудистой катастрофы. \* — достоверно при сравнении показателей группы гипер- и нормодинамического типа кровообращения, р < 0,05; \*\* — достоверно при сравнении показателей группы гипер- и гиподинамического типа кровообращения, р < 0,05

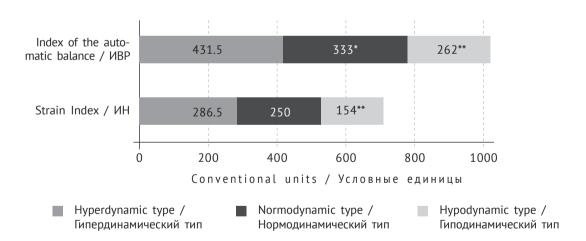


Fig. 2. Indicators of the autonomic balance and strain index in patients with acute cerebrovascular accidents and different types of haemodynamics in the first days after vascular catastrophe. \* - reliably when comparing indicators of the groups of hyperdynamic and normodynamic types of blood circulation, p < 0.05; \*\* - reliably when comparing indicators of the groups of hyperdynamic and hypodynamic types of blood circulation, p < 0.05

Рис. 2. Показатели индекса вегетативного равновесия (ИВР) и индекса напряжения регуляторных систем (ИН) у пациентов с острым нарушением мозгового кровообращения и разными его типами в 1-е сутки после сосудистой катастрофы. \* — достоверно при сравнении показателей группы гипер- и нормодинамического типов кровообращения, р < 0,05; \*\* — достоверно при сравнении показателей группы гипер- и гиподинамического типов кровообращения, р < 0,05

pathetic regulation department in the acute period and a gradual decrease in the sympathetic effects on the cardiovascular system while stabilizing the patients' condition.

In ACVA patients with normodynamic circulation, there was a slight increase in SDNN and RMSSD values and a pronounced decrease in ABI (by 22%) and SI (by 35%) compared with similar values (Table 1).

In an HRV study conducted at day 7 of hospitalization, it was found that SDNN was 35% higher in ACVA patients with hypodynamic circulation than in ACVA patients with normodynamic circulation

and more than 70% higher than in ACVA patients with hyperdynamic circulation. RMSSD values in ACVA patients with hypodynamic circulation were 2 or more times higher than RMSSD values in ACVA patients with normo- and hyperdynamic circulation. This dynamics can be regarded as a progressive increase in the activity of the parasympathetic regulatory segment in ACVA patients with hypodynamic circulation.

After 7 days of admission to the inpatient facility, all groups of ACVA patients were divided into subgroups taking into account the newly formed types of hemodynamics. Hence, out of 76 ACVA patients

 $Table\ 1\ /\ Taблицa\ 1$  Changes in HRV in patients with acute cerebrovascular accidents depending on the type of haemodynamics Изменения показателей вариабельности сердечного ритма у пациентов с острым нарушением мозгового кровообращения в зависимости от типа кровообращения

	Type of haemodynamics / Тип кровообращения						
Index / Показатель	hyperdynamic / гипердинамический (n = 76)		normodynamic / нормодинамический $(n=28)$		hypodynamic / гиподинамический (n = 17)		
	1 <sup>st</sup> day / 1-й день	7 <sup>th</sup> day / 7-й день	1 <sup>st</sup> day / 1-й день	7 <sup>th</sup> day / 7-й день	1 <sup>st</sup> day / 1-й день	7 <sup>th</sup> day / 7-й день	
SDNN, ms/mc	21 [13; 51]	28 [19; 49]	35 [19; 77]	36 [21; 42]	41 [16; 82]	48 [43; 86]	
p	0.29		0.070		0.91		
RMSSD, ms / мс	16 [11; 35]	21 [14; 38]	20 [14; 51]	24 [16; 36]	20 [10; 40]	47 [26; 51]	
p	0.11		0.66		0.74		
Index of the autonomic balance, conventional units / ИВР, у. е.	459 [130; 974]	295 [173; 681]	333 [97; 793]	262 [176; 703]	262 [84; 776]	174 [66; 212]	
p	0.013		0.92		0.26		
Index of the autonomic rhythm, conventional units / BIIP, y. e.	9.63 [4.56; 19.42]	7.52 [4.66; 11.92]	8.28 [2.82; 14.80]	5.92 [4.13; 10.85]	5.95 [2.93; 18.80]	5.25 [2.24; 6.04]	
p	<0.001		0.35		0.15		
Indicator of adequacy of regulation processes, conventional units / ΠΑΠΡ, y. e.	87 [52; 111]	85 [50; 108]	78 [40; 92]	64 [48; 93]	60 [47; 95]	45 [37; 77]	
p	0.87		0.60		0.48		
Strain index, conventional units / UH, y. e.	330 [82; 722]	229 [97; 457]	211 [47; 521]	163 [102; 429]	154 [53; 554]	102 [36; 152]	
p	0.0066		0.58		0.28		
Indicator of the activity of regulatory systems, conventional units / $\Pi APC$ , y. e.	7 [5; 0]	5 [3; 6]	6 [5; 0]	4 [2; 5]	5 [4; 0]	4 [2; 5]	
p	< 0.001		< 0.001		0.0035		

Note. p — significance of differences in comparison of indicators in patients on the 1st and  $7^{th}$  day when performing the Wilcoxon test (for related samples). Примечание: p — значимость различий при сравнении показателей у пациентов на 1-й и 7-й день при выполнении теста Вилкоксона (для связанных выборок). ИВР — индекс вегетативного равновесия, ВПР — вегетативный показатель ритма, ПАПР — показатель адекватности процессов регуляции, ИН — индекс напряжения, ПАРС — показатель активности регуляторных систем.

Table 2 / Таблица 2

Number of patients with acute cerebrovascular accidents in the  $1^{st}$  and  $7^{th}$  days of the study Количество пациентов с острым нарушением мозгового кровообращения и разными типами кровообращения в 1-e и 7-e сутки исследования

Type of haemodynamics on the 1st day of study / Тип кровообращения	Type of haer Тип в	General result / Обший итог			
в 1-й день	hyperdynamic / гипердинамический				
Hyperdynamic / Гипердинамический	50	11	15	76	
Normodynamic / Нормодинамический	4	19	5	28	
Hypodynamic / Гиподинамический	2	2	13	17	
General result / Общий итог	56	32	33	121	

Table 3 / Таблица 3

Changes in HRV in patients with acute cerebrovascular accidents and initially hyperdynamic type of haemodynamics depending on the newly formed (on the  $7^{th}$  day) type of blood circulation  $Me[Q_1; Q_2]$ 

Изменение показателей вариабельности сердечного ритма у пациентов с острым нарушением мозгового кровообращения и изначально гипердинамическим типом гемодинамики в зависимости от вновь сформированного на 7-е сутки от начала заболевания типа кровообращения Me [Q,; Q,]

Type of haemo	-	Day / Сутки	SDNN, ms/mc	RMSSD, ms / мс	Index of the autonomic balance, conventional units / ИВР, у. е.	Strain index, conventional units / ИН, y. e.
Initially hyperdyn		1 <sup>st</sup> day /	20.5	16	431.5	286.5
Исходно гиперди		1-е сутки	[13; 51]	[11; 35]	[228; 805]	[153.5; 532]
The newly formed types /	hyper- /	7 <sup>th</sup> day /	41.18	27.98	493.2	335.58
	гипер-	7-е сутки	[28.17; 54.18]	[21.30; 34.65]	[382.4; 603.9]	[251.57;419.58]
Вновь сформированные типы	normo- /	7 <sup>th</sup> day /	41.72	31.63	485.09	302.9
	нормо-	7-е сутки	[23.45; 59.99]	[12.55; 50.71]	[202.84; 767.33]	[124.4; 481.32]
кровообраще-	hypo- /	7 <sup>th</sup> day /	43.57	29.64	344.71	211.5
ния	гипо-	7-е сутки	[31.95; 55.19]	[21.88; 37.4]	[205.27; 84.15]*	[121.75; 301.24]*

*Note.* \* The relative significance of differences in inter-group comparison in groups with the newly formed types of haemodynamics, p < 0.05. *Примечание.* \* Относительная достоверность различий при межгрупповом сравнении в группах с вновь сформированными типами кровообращения, p < 0.05, ИВР — индекс вегетативного равновесия, ИН — индекс напряжения.

with hyperdynamic circulation at day 1 after a vascular accident, only 50 patients had the same type of hemodynamics a week later. The type of blood circulation changed to normodynamic in 11 patients and hypodynamic in 15 patients.

Out of 28 ACVA patients with normodynamic circulation admitted to the hospital, 19 patients did not change the type of hemodynamics after a week, and 5 patients formed a hyperdynamic type.

Among 17 ACVA patients with hypodynamic circulation, at day 1 after a vascular accident, 13 patients remained hypodynamic, 2 patients changed to hyperdynamic, and 2 patients changed to normodynamic (Table 2).

A repeated (day 7) examination of HRV indices in ACVA patients with hyperdynamic circulation upon admission revealed a tendency to increase in SDNN and RMSSD in all patients.

It was revealed that in ACVA patients with the initially hyperdynamic circulation, ABI was lower in patients with the newly formed hypodynamic circulation, so that it was 28% less compared with patients with the newly formed normodynamic circulation and 30% less than in patients with newly formed hyperdynamic circulation. SI was also lower (by 30%) in patients with the newly formed hypodynamic circulation (Table 3).

Among ACVA patients with normodynamic circulation at day 1 after a vascular accident, differences

Table 4 / Таблица 4

Changes in HRV in patients with acute cerebrovascular accidents and initially normodynamic type of haemodynamics depending on the newly formed (on the  $7^{th}$  day) type of blood circulation Me [O, O, O]

Изменение показателей вариабельности сердечного ритма у пациентов с острым нарушением мозгового кровообращения и изначально нормодинамическим типом гемодинамики в зависимости от вновь сформированного на 7-е сутки от начала заболевания типа кровообращения  $Me[Q_1; Q_2]$ 

J 1	modynamics / робращения	Day / Сутки	SDNN, ms/mc	RMSSD, ms / мс	Index of the autonomic balance, conventional units / UBP, y. e.	Strain index, conventional units / ИН, y. e.
Initially hyperdynamic / Исходно гипердинамичский		1 <sup>st</sup> day / 1-е сутки	34.5 [18.5; 77]	20 [14; 51]	333 [96.5; 793]	250 [62; 521]
The newly formed	hyper- / гипер-	7 <sup>th</sup> day / 7-е сутки	30.0 [20.01; 39.98]	23.25 [9.06; 37.43]	392.0 [146.8; 637.1]	239.75 [65.18; 414.31]
types / Вновь сформиро- ванные типы кровообра- щения	normo- / нормо-	7 <sup>th</sup> day / 7-е сутки	40.21 [25.75; 54.66]	29.31 [16.1; 42.52]	316.47 [218.42; 414.52]	196.10 [128.67; 263.53]
	hypo- / гипо-	7 <sup>th</sup> day / 7-е сутки	45.25 [20.07; 70.42]*	31.25 [20.34; 2.15]*	299.5 [104.89; 94.10]*	154.75 [118.32; 327.82]*

Note. \*The relative significance of differences in inter-group comparison in groups with the newly formed types of haemodynamics, p < 0.05. Примечание. \* Относительная достоверность различий при межгрупповом сравнении в группах с вновь сформированными типами кровообращения, p < 0.05.

were also found in subgroups formed according to the types of blood circulation formed at day 7 of hospitalization. Thus, patients with newly formed hypodynamic circulation were characterized by higher values of SDNN (higher by 50.8%) and RMSSD (higher by 34.3%) compared with those whose type of hemodynamics changed to hyperdynamic. Compared with these patients, the patients with newly formed hypodynamic circulation had lower ABI (23.6%) and SI (35%) (Table 4).

Changes in HRV indices at day 7 in ACVA patients with initial hypodynamic circulation were not evaluated due to the small number of patients in the newly formed groups and also due to the difficulty of statistical processing of the small sample data.

#### CONCLUSION

The most effective regulation of effector systems functioning was noted in ACVA patients with normoand hypodynamic types of blood circulation, which were constant throughout the study period. The greatest tension in the work of regulatory systems was registered in ACVA patients with hyperdynamic type of blood circulation, especially in those whose type of hemodynamics did not change during the subsequent 7 days.

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