UDC 616-001.34: 616.8: 616.1: 612.017.1
DOI: 10.21668/health.risk/2025.1.12.eng

Read online

Research article

NEUROANTIBODIES AS RISK MARKERS FOR THE DEVELOPMENT OF AUTOIMMUNE PROCESSES IN CASE OF VIBRATION DISEASE

N.P. Chistova, G.M. Bodienkova, E.V. Boklazhenko

East-Siberian Institute of Medical and Ecological Research, 3, 12a microdistrict, Angarsk, 665827, Russian Federation

The aim of the study was to identify the features of changes in the content of neuroantibodies reflecting the risk of developing autoimmune processes in patients with hand-arm vibration syndrome (HAVS), complicated and uncomplicated arterial hypertension (AH).

A retrospective study was conducted in a sample of men aged 40 to 60 years with a diagnosed hand-arm vibration syndrome caused by local vibration and in a group comparable per sex and age, including people who worked in conditions that excluded contact with occupational physical factors. Groups of patients with HAVS, complicated and uncomplicated AH have been identified. The levels of autoantibodies to specialized structures of nervous tissue and neurotransmitters were determined in all the examined participants using the ELI-N-Test ("Immunculus", Moscow).

The study revealed an increase in the levels of neuronal AT (MBP, S-100, GFAP, NF-200, V-Ca-channel, Glu-R, DA-R, M-OR, B-end) in patients with HAVS, both burdened and uncomplicated hypertension, relative to the comparison group. At the same time, the levels of AT to the opiate M-OR receptors in people with HAVS who were not burdened with hypertension were statistically significantly higher than in patients with comorbid pathology ($p = 0.04$). Discriminant analysis showed that individuals with HAVS burdened with hypertension were characterized by a decrease in the levels of AT to gamma-aminobutyric acid receptors ($F = 8.5$, $p = 0.001$) and to the myelin basic protein ($F = 13.7$, $p = 0.001$) in comparison with patients with HAVS without hypertension. The neuron-neuron interaction disorder in patients with AH was manifested by a mismatch of correlations between the levels of autoantibodies to S-100 protein and myelin basic protein ($R = 0.29$, $p > 0.05$), voltage-dependent Ca-channel ($R = 0.41$, $p > 0.05$), dopamine receptors ($R = 0.42$, $p > 0.05$), serotonin ($R = 0.33$, $p > 0.05$) and opiates ($R = 0.32$, $p > 0.05$).

Thus, increased levels of neuronal AT (MBP, S-100, GFAP, NF-200, V- Ca-channel, Glu-R, DA-R, M-OR, B-end) in patients with HAVS, both burdened and uncomplicated hypertension, are markers reflecting the risk of developing autoimmune processes upon exposure to vibration. The reported lower levels of AT to the GABA receptor and the myelin basic protein in patients with HAVS burdened with hypertension, when compared with those with HAVS without hypertension, are apparently due to the peculiarities of the clinical course of the disease and the formation of immune tolerance to these proteins. The obtained results can be used in carrying out diagnostic, preventive and therapeutic measures for people with HAVS, including in the presence of comorbid pathology.

Keywords: *occupational stress, hand-arm vibration syndrome, arterial hypertension, immune system, nervous system, autoantibodies, gamma-aminobutyric acid (GABA), myelin basic protein, opiate receptors.*

Nadezhda P. Chistova – Candidate of Medical Sciences, Junior Researcher at the Laboratory of Immunobiochemical and Molecular Genetic Research in Hygiene (e-mail: immun11@yandex.ru; tel.: +7 (395) 558-69-10 (ext. 1411); ORCID: http://orcid.org/0000-0002-1206-6379).

Galina M. Bodienkova – Doctor of Medical Sciences, Professor, Head of the Laboratory of Immunobiochemical and Molecular Genetic Research in Hygiene (e-mail: immun11@yandex.ru; tel.: +7 (395) 558-69-10 (ext. 1411); ORCID: http://orcid.org/0000-0003-0428-3063).

Elena V. Boklazhenko – Candidate of Medical Sciences, Senior Researcher at the Laboratory of Immunobiochemical and Molecular Genetic Research in Hygiene (e-mail: immun11@yandex.ru; tel.: +7 (395) 558-69-10 (ext. 1411); ORCID: http://orcid.org/0000-0002-2025-8303).

As stated in the State Report published by Rospotrebnadzor in 2023, hand-arm vibration syndrome (HAVS) accounted for 45.3 % of all cases in patients with pathologies caused by physical exposures[1]. Recently, the research community has taken greater interest in comorbidities, which complicate the clinical course of occupational diseases, arterial hypertension (AH) in particular, since the disease is established in 47–52 % patients with HAVS [1]. The number of adult people with AH has grown from 650 to 1.28 billion people over the last 30 years [2].

Bearing in mind that the immune system is among the first to react to environmental exposures, occupational vibration included, it is still relevant to search for informative markers associated with elevated risks of developing autoimmune processes in patients with HAVS. The hand-arm vibration syndrome has been established to typically involve changes in levels of autoantibodies to nerve tissue proteins such as myelin basic protein (MBP), S-100 protein, neurofilament protein-200 (NF-200), glial fibrillary acidic protein (GFAP), and neurotransmitter receptors [3]. As regards AH, some available literature data report elevated levels of antibodies to MBP and S-100 protein in patients with chronic cerebral ischemia caused by hypertension [4]. At the same time, we have not managed to find a sufficient number of studies that focus on functional disorders accompanied with changed levels of neuronal antibodies and report risks of developing autoimmune processes in people with HAVS burdened with AH.

It should be noted that antibodies to neuroantigens of the brain structures penetrate the blood through the blood-brain barrier (BBB). Their growing levels are evidence of damage to nerve tissues and greater BBB permeability [5]. Antibody (AB) production is a physiological mechanism aimed at homeostasis maintenance. In total, changes in AB levels can indirectly describe the state of the immune system [6], which, according to literature data, is actively involved in AH pathogenesis. However, its role in AH development still remains ambiguous. Thus, IL-17A produced by T-helpers and IFN-γ stimulate the renin-angiotensin-aldosterone system thereby causing elevated blood pressure. Cell death in the peritubular capillaries occurs due to dendritic cells activating CD8+ T-lymphocytes, which may lead to the development of renal hypertension [7].

Comorbidities aggravate the main disease considerably, promote changes in its clinical manifestations and cause fatal complications [8]. Despite a wide range of clinical diagnostic procedures, certain difficulties still occur in identifying such comorbidity as AH including its resistant forms [9]. However, it seems promising to use up-to-date statistical methods including discriminant analysis, which makes it possible to reveal informative indicators and develop mathematical formulas for AH prediction and diagnosis.

Given all the above stated, **the aim** of this study was to identify the features of changes in the content of neuroantibodies reflecting the risk of developing autoimmune processes in patients with hand-arm vibration syndrome (HAVS), complicated and uncomplicated with arterial hypertension (AH).

Materials and methods. A retrospective clinical study was conducted in a sample of 40 men aged 40 to 60 years with diagnosed HAVS caused by local vibration; they all were treated in the clinic of the East-Siberian Institute of Medical and Ecological Research. The first group was made of patients with HAVS not burdened with AH; the second one, patients with HAVS burdened with stage 1 or stage 2 arterial hypertension. The exclusion criteria were acute communicable diseases at the examination moment,

[1] Razdel 1.2.2. Analiz sostoyaniya zdorov'ya rabotayushchego naseleniya i professional'noi zabolevaemosti [Item 1.2.2. Analysis of the employable population's health and occupational morbidity]. In: *O sostoyanii sanitarno-epidemiologicheskogo blagopoluchiya naseleniya v Rossiiskoi Federatsii v 2023 g.: Gosudarstvennyi doklad [On Sanitary-epidemiological welfare of the population in the Russian Federation in 2023: State Report]*. Moscow, Federal Service for Surveillance over Consumer Rights Protection and Human Wellbeing, 2023, pp. 158–160 (in Russian).

exacerbated chronic diseases, coronary heart disease, cancer, autoimmune diseases as well as occupational diseases caused by chemical exposures. No patients with diabetes mellitus were included since the disease creates much higher risks of cardiovascular complications and damage to the nervous system thereby exerting substantial influence on the results. The reference group was made of 30 men comparable per age, who worked in conditions that excluded contact with occupational physical or chemical factors. All patients provided their written informed consent to participate in the study. The study was approved by a local ethics committee.

The patients provided their blood samples, which were taken into vacutainers with a clot activator. The vacutainers were then centrifuged for 15 minutes at 2000 rpm. Serum aliquots were put into Eppendorf tubes 1.5 ml volume, frozen and kept at -70 °C. Serum levels of the neuroantibodies (to neurofilament protein-200 (NF-200), glial fibrillary acidic protein (GFAP), S-100 protein, myelin basic protein (MBP), voltage-gated Ca-channel (V-gat. Ca-channel), glutamate receptors (Glu-R), dopamine receptors (DA-R), GABA - receptors (GABA-R), serotonin receptors (Ser-R), cholinoreceptors (Chol-R), M-opiate receptors (M-OR), B-endorphin (B-end)) were identified by using ELI-N-test systems (Immunkulus, Moscow) at the wave 450 long on a ELx800 microplate reader (BioTek, USA).

Mathematical and statistical data analysis was performed with IBM SPSS Statistics 26 and STATISTICA 10 software packages. The sample was checked for normality of the distribution by using the Shapiro – Wilk test. The patients' age and work records were given as simple mean and its error; all the remaining results, as median, upper and lower quartiles. The non-parametric Mann – Whitney test was used for quantitative comparisons in the analyzed groups depending on AH presence. Intergroup differences were deemed significant at $p < 0.05$. In Spearman's correlation analysis, correlation coefficients were considered significant at $p < 0.05$. The last stage involved conducting stepwise discriminant analysis to identify and substantiate the most informative indicators. Independent variables were represented by level of serum antibodies from the IgG class to nerve tissue antigens (NF-200, GFAP, S-100, MBP, V-gated Ca-channel, Glu-R, DA-R, GABA-R, Ser-R, Chol-R, M-OR, B-end); dependent ones, being in a group with diagnosed HAVS either burdened or not burdened with AH.

Results and discussion. Occupational vibration is known to be a stressor [10]. Significant AH risk factors include age older than 55 and occupational stress. Given that, the first stage in our study involved distributing the examined patients per their work records under vibration exposure and an age when HAVS was diagnosed in them. The analysis revealed them to be comparable in the analyzed groups (Table 1).

Table 1

Age and work records of the examined patients ($M \pm m$)

Indicator, units	Group HAVS without AH $n = 20$	Group HAVS with AH $n = 20$
Age, years	49.8 ± 1.5	49.2 ± 1.3
Work records, years	17.5 ± 1.3	18.4 ± 1.5

Note: differences are significant at $p < 0.05$.

Recently, antibodies to specific nerve tissue structures have been considered new generation markers in some neurological disorders[2]. Bearing this in mind, it seemed interesting to examine levels of neuroantibodies in blood serum of the patients with HAVS (Table 2).

[2] Poletaev A.B. Novye podkhody v rannem vyyavlenii patologicheskikh izmenenii v organizme cheloveka (immunokhimicheskii skrining kak osnova strategii perekhoda ot lechebnoi k preventivnoi meditsine) [New approaches in early detection of pathological changes in the human body (immune-chemical screening as the basis for transition from treatment to prevention)]: methodical guide for clinicians. Moscow, Immunculus Publ., 2011, pp. 64 (in Russian).

Table 2

Levels of neuroantibodies in the examined patients with HAVS, *Med (Q25; Q75)*

Indicator, units	Group HAVS without AH $n = 20$	Group HAVS with AH $n = 20$	Reference group
MBP, arbitrary units	0.272 (0.156; 0.457)^	0.183 (0.156; 0.404) ^	0.140 (0.118; 0.181)
GABA-R, arbitrary units	0.345 (0.150; 0.513)^	0.185 (0.148; 0.527)	0.177 (0.128; 0.252)
S-100, arbitrary units	0.538 (0.306; 0.643)^	0.424 (0.302; 0.610)^	0.228 (0.168;0.292)
GFAP, arbitrary units	0.471 (0.252; 0.586)^	0.325 (0.230; 0.581)^	0.282 (0.171; 0.364)
NF-200, arbitrary units	0.386 (0.253; 0.604)^	0.299 (0.239; 0.617)^	0.194 (0.158;0.258)
V-gat. Ca-channel, arbitrary units	0.315 (0.158; 0.591)^	0.213 (0.158; 0.573)^	0.152 (0.118; 0.197)
Chol-R, arbitrary units	0.289 (0.141; 0.589)^	0.178 (0.142; 0.589)	0.175 (0.128; 0.217)
Glu-R, arbitrary units	0.310 (0.194; 0.560)^	0.222 (0.184; 0.537)^	0.185 (0.150; 0.228)
DA-R, arbitrary units	0.295 (0.175; 0.482)^	0.205 (0.171; 0.456)^	0.179 (0.147; 0.254)
Ser-R, arbitrary units	0.417 (0.179; 0.576)^	0.236 (0.179; 0.577)	0.238 (0.188; 0.311)
M-OR, arbitrary units	0.308 (0.202; 0.451)^	0.241 (0.193; 0.408)*^	0.151 (0.122; 0.179)
B-end, arbitrary units	0.328 (0.182; 0.480)^	0.196 (0.168; 0.470)^	0.146 (0.118; 0.189)

Note: differences are significant at $p < 0.05$; * means significant differences between the Groups HAVS with AH and without AH; ^ means significant differences between the Groups HAVS without AH and the reference group, HAVS with AH and the reference group.

Comparison with the reference group established a significant increase in AB levels (to MBP, S-100, GFAP, NF-200, V-gat. Ca-channel, Glu-R, DA-R, M-OR, B-end) in both HAVS groups regardless of AH presence. We compared AB levels depending on the present comorbidity and established that the patients with HAVS not burdened with AH has significantly higher levels of autoantibodies to M-opiate receptors ($p = 0.04$), against those with HAVS burdened with AH. Levels of AB to GABA-R, Chol-R, and Ser-R were equal to those identified in the reference group in both HAVS groups with and without AH.

The correlation analysis revealed that people with HAVS combined with AH had weaker and insignificant correlations between levels of AB to S-100 protein and MBP ($R = 0.29$, $p > 0.05$), V-gated Ca-channel ($R = 0.41$, $p > 0.05$), dopamine receptors ($R = 0.42$, $p > 0.05$), serotonin receptors ($R = 0.33$, $p > 0.05$) and opiate receptors ($R = 0.32$, $p > 0.05$) (Table 3) whereas levels of all antibodies correlated with each other in the HAVS group without AH and the reference group (Tables 4 and 5).

Next, the discriminant analysis was performed to substantiate new diagnostic markers. It revealed several most significant informative signs of HAVS burdened with AH including lower levels of AB to receptors of gamma-aminobutyric acid ($F_{incl} = 8.5$, $p = 0.001$) and myelin basic protein ($F_{incl} = 13.7$, $p = 0.001$) against HAVS without AH (Table 6). Diagnostic coefficients F_1 (included in the HAVS group without AH) and F_2 (included in the HAVS group burdened with AH) were calculated per the following formulas:

$$F_1 = -3.938 + 25.067 \cdot \text{AB} - \text{MBP} - 9.6 \cdot \text{Ab} - \text{GABA}$$

$$F_2 = -2.058 + 5.317 \cdot \text{AB} - \text{MBP} + 3.838 \cdot \text{Ab} - \text{GABA}$$

Table 3

Correlations between neuroantibodies in patients with hand-arm vibration syndrome burdened with arterial hypertension

	S100	GFAP	MBP	NF-200	V-gat	Chol-R	Glu-R	GABA-R	DA-R	Ser-R	M-OR	B-end
S100	1.00	0.75	**0.29**	0.55	**0.41**	0.63	0.54	0.50	**0.42**	**0.33**	**0.32**	0.45
GFAP	0.75	1.00	0.65	0.76	0.67	0.85	0.74	0.81	0.72	0.66	0.59	0.68
MBP	0.29	0.65	1.00	0.76	0.93	0.84	0.84	0.90	0.94	0.94	0.84	0.78
NF-200	0.55	0.76	0.76	1.00	0.80	0.93	0.88	0.89	0.76	0.80	0.78	0.85
V-gat	0.41	0.67	0.93	0.80	1.00	0.89	0.88	0.90	0.92	0.97	0.86	0.90
Chol-R	0.63	0.85	0.84	0.93	0.89	1.00	0.92	0.96	0.87	0.89	0.82	0.89
Glu-R	0.54	0.74	0.84	0.88	0.88	0.92	1.00	0.91	0.82	0.86	0.76	0.82
GABA	0.50	0.81	0.90	0.89	0.90	0.96	0.91	1.00	0.91	0.93	0.88	0.90
DA-R	0.42	0.72	0.94	0.76	0.92	0.87	0.82	0.91	1.00	0.92	0.82	0.78
Ser-R	0.33	0.66	0.94	0.80	0.97	0.89	0.86	0.93	0.92	1.00	0.89	0.90
M-OR	0.32	0.59	0.84	0.78	0.86	0.82	0.76	0.88	0.82	0.89	1.00	0.88
B-end	0.45	0.68	0.78	0.85	0.90	0.89	0.82	0.90	0.78	0.90	0.88	1.00

Note: significance taken at $p < 0.05$ except S-100 and MBP, V-gat. Ca channel, DA-R, Ser-R, M-OP.

Table 4

Correlations between neuroantibodies in patients with hand-arm vibration syndrome without arterial hypertension (R)

	S100	GFAP	MBP	NF-200	V-gat	Chol-R	Glu-R	GABA-R	DA-R	Ser-R	M-OR	B-end
S100	1.00	0.94	0.88	0.90	0.92	0.92	0.89	0.88	0.88	0.93	0.89	0.91
GFAP	0.94	1.00	0.94	0.88	0.92	0.94	0.87	0.87	0.93	0.95	0.89	0.92
MBP	0.88	0.94	1.00	0.91	0.97	0.97	0.89	0.89	0.99	0.94	0.96	0.94
NF-200	0.90	0.88	0.91	1.00	0.97	0.96	0.83	0.90	0.92	0.95	0.94	0.91
V-gat	0.92	0.92	0.97	0.97	1.00	0.99	0.87	0.89	0.96	0.95	0.95	0.92
Chol-R	0.92	0.94	0.97	0.96	0.99	1.00	0.85	0.91	0.97	0.97	0.95	0.95
Glu-R	0.89	0.87	0.89	0.83	0.87	0.85	1.00	0.86	0.91	0.86	0.91	0.84
GABA	0.88	0.87	0.89	0.90	0.89	0.91	0.86	1.00	0.92	0.96	0.95	0.94
DA-R	0.88	0.93	0.99	0.92	0.96	0.97	0.91	0.92	1.00	0.94	0.97	0.94
Ser-R	0.93	0.95	0.94	0.95	0.95	0.97	0.86	0.96	0.94	1.00	0.96	0.97
M-OR	0.89	0.89	0.96	0.94	0.95	0.95	0.91	0.95	0.97	0.96	1.00	0.95
B-end	0.91	0.92	0.94	0.91	0.92	0.95	0.84	0.94	0.94	0.97	0.95	1.00

Note: significance taken at $p < 0.05$.

Table 5

Correlations between neuroantibodies in the reference group (R)

	S100	GFAP	MBP	NF-200	V-gat	Chol-R	Glu-R	GABA-R	DA-R	Ser-R	M-OR	B-end
S100	1.00	0.72	0.47	0.70	0.51	0.46	0.52	0.68	0.60	0.76	0.60	0.66
GFAP	0.72	1.00	0.67	0.74	0.74	0.63	0.69	0.63	0.57	0.65	0.62	0.78
MBP	0.47	0.67	1.00	0.62	0.85	0.44	0.57	0.47	0.45	0.60	0.38	0.68
NF-200	0.70	0.74	0.62	1.00	0.71	0.45	0.62	0.65	0.59	0.69	0.63	0.75
V-gat	0.51	0.74	0.85	0.71	1.00	0.52	0.63	0.55	0.50	0.59	0.44	0.69
Chol-R	0.46	0.63	0.44	0.45	0.52	1.00	0.77	0.66	0.75	0.53	0.29	0.57
Glu-R	0.52	0.69	0.57	0.62	0.63	0.77	1.00	0.80	0.84	0.66	0.51	0.64
GABA	0.68	0.63	0.47	0.65	0.55	0.66	0.80	1.00	0.92	0.82	0.49	0.67
DA-R	0.60	0.57	0.45	0.59	0.50	0.75	0.84	0.92	1.00	0.73	0.54	0.64
Ser-R	0.76	0.65	0.60	0.69	0.59	0.53	0.66	0.82	0.73	1.00	0.45	0.67
M-OR	0.60	0.62	0.38	0.63	0.44	0.29	0.51	0.49	0.54	0.45	1.00	0.68
B-end	0.66	0.78	0.68	0.75	0.69	0.57	0.64	0.67	0.64	0.67	0.68	1.00

Note: significance taken at $p < 0.05$.

Table 6

Informative indicators obtained by the discriminant analysis in the groups of the examined patients with HAVS both burdened and not burdened with arterial hypertension

Indicators	*F*-inclusions	Wilkes' lambda	Degree of freedom 1	Degree of freedom 2	*p*
Autoantibodies to GABA receptors, arb. units	8.454	0.865	2	1	0.001
Autoantibodies to MBP, arb. units	13.706	0.986	1	1	0.001

Note: *p* is the level at which differences are significant.

Validity of the proposed formulas was tested using a training sample: correct identification equaled 85 % in HAVS patients with AH (20 people) and 75 % in HAVS patients without AH (20 people).

It is worth noting that these results were obtained for relatively small groups. In further research, when new patients are included into training samples, it seems quite feasible to obtain an authentic mathematical model for assessing risks of autoimmune processes in people with HAVS both burdened and not burdened with AH.

At present, immunological markers, which can predict risks of various occupational diseases, HAVS included, are being investigated quite actively [3]. Humoral immunity indicators (immunoglobulins A, M, G) [11], pro-inflammatory (IL-1β, IL-2, IL-8, IL-10, IL-17, TNF-α) and anti-inflammatory (IL-4) cytokines [12] are being investigated as additional informative indicators reflecting involvement of the immune system in HAVS patients burdened with AH. However, not enough light has been shed on the role, which belongs to antibodies to specific nerve tissue structures and neuromediators relative to risks of developing autoimmune processes in patients with HAVS burdened with AH.

Natural antibodies to diverse antigenic determinants including neuron, neuroglia and receptor components are always present in the body [13]. Highly sensitive test-systems for ELISA tests allow measuring neuroantibodies in blood samples as opposed to methods, which require using only cerebrospinal fluid. An identified AB level can reflect the nerve tissue state and functioning of its components. In this study, we revealed elevated levels of neuronal antibodies (to MBP, S-100, GFAP, NF-200, V-gat. Ca-channel, Glu-R, DA-R, M-OR, B-end) in patients with HAVS both burdened and unburdened with AH against the reference group. Levels of antibodies to M-opiate receptors (M-OR) were significantly higher in HAVS patients without AH in comparison with those who had HAVS burdened with comorbidity ($p = 0.04$). Opioids are known to perform stress-limiting activity and to be a link in both urgent and long-term adaptation [14]. They reduce levels of adrenocorticotropic hormone, aldosterone, vasopressin, glucagon and cortisol and increase levels of insulin and testosterone. Elevated levels of antibodies to opioids can indicate pronounced failure to adapt to stressor vibration exposure.

In up-to-date research, vibration is shown to be a significant occupational stressor [10]. The body response to stress is known to have three stages: (1) anxiety; (2) resistance; (3) depletion[3]. All organs and systems in the human body participate in building adaptability and resistance to stress. The immune system is among the first to react to various stressor exposures. Both elevated and reduced AB levels have diagnostic significance. A titer of specific antibodies can grow in case of immune activation and decline in case of immunosuppres-

[3] Selye H. The general adaptation syndrome and the diseases of adaptation. *J. Clin. Endocrinol. Metab.*, 1946, vol. 6, pp. 117–230. DOI: 10.1210/jcem-6-2-117

sion[4]. Any shift in levels of neuroantibodies reflects staging in the development of pathological processes [6].

Strong positive correlations between all neuronal antibodies established in the reference group by correlation analysis show their adequate production by antibody-producing immune system cells in case vibration exposure is absent. The foregoing character of the established correlations was also identified in patients with HAVS not burdened with AH, which indicates unidirectional rise in AB levels in this group.

A mismatch of correlations between levels of S-100 protein and levels of some other markers was identified in the examined patients with HAVS burdened with AH. S-100 protein is responsible for intracellular and extracellular regulation of energy metabolism, cell differentiation and growth [15]. It is known to be a calcium-binding protein. A weakened correlation between levels of AB to S-100 protein and voltage-gated Ca-channel can be a sign of disrupted interaction between the compound and calcium ions and changes in synapse functioning. A weakened correlation between levels of AB to S-100 protein and dopamine, serotonin and opiate receptors may indicate developing emotional and volitional disorders [16] accompanied with changes in S-100 protein levels. A weakened correlation between levels of antibodies to S-100 protein and MBP may indicate damage to nerve tissue and a growth in the blood-brain barrier permeability [5, 17].

AH is a factor that aggravates HAVS clinical course; given that, we made an attempt to identify the most diagnostically significant indicators among all analyzed ones. The accomplished discriminant analysis established a decline in levels of antibodies to gamma-aminobutyric acid (GABA) receptor in patients with HAVS burdened with AH against those who had only HAVS. GABA is considered a key inhibition mediator in the brain. In addition, GABA drugs are known to normalize blood pressure in patients with AH [18]. The pathway of blood pressure reduction can involve inhibiting the baroreceptor by binding GABA with neuron receptors in the solitary tract of the medulla oblongata [19]. Lower levels of antibodies to myelin basic protein (MBP) in HAVS patients with AH against those with HAVS not burdened with AH may be another informative indicator. MBP is known to participate in forming the multilayer myelin sheath by creating complexes with lipids. When these structures crumble, MBP levels grow in blood and cerebrospinal fluid. Changes in levels of antibodies to MBP give evidence of the immune system response to myelin sheath destruction. As reported in previous studies, slower nerve impulse transmission along the proximal and distal axon sections identified in patients with HAVS, a decline in M-response amplitude and a longer latent period in animal experiments give evidence of active demyelination developing upon vibration exposure [20]. Several studies reported that patients with AH tended to have lower myelin contents in myelin sheaths of the brain structures [21, 22].

Conclusion. Therefore, elevated levels of neuroantibodies (to MBP, S-100, GFAP, NF-200, V-gated Ca-channel, Glu-R, DA-R, M-OR, B-end) in patients with HAVS both burdened and uncomplicated with AH are markers reflecting the risk of developing autoimmune processes upon vibration exposure. Identified lower levels of antibodies to GABA and MBP receptor in patients with HAVS burdened with AH against those patients with HAVS who did not have AH are obviously caused by a specific clinical course of the disease and developing immune tolerance to the foregoing proteins. Our findings can be used in carrying out diagnostic, preventive and therapeutic measures for people with HAVS including those who have comorbid pathology.

Funding. The research was accomplished within the State Assignment.

Competing interests. The authors declare no competing interests.

[4] Poletaev A.B. Novye podkhody v rannem vyyavlenii patologicheskikh izmenenii v organizme cheloveka (immunokhimicheskii skrining kak osnova strategii perekhoda ot lechebnoi k preventivnoi meditsine) [New approaches in early detection of pathological changes in the human body (immune-chemical screening as the basis for transition from treatment to prevention)]: methodical guide for clinicians. Moscow, Immunculus Publ., 2011, pp. 64 (in Russian).

References

1. Tatarovskaya N.A. Arterial hypertension as a risk factor of vascular disorders of the patients with vibration disease. *Aspirantskie chteniya 2016. Materialy nauchno-prakticheskoi konferentsii s mezhdunarodnym uchastiem «Molodye uchenye – ot tekhnologii XXI veka k prakticheskomu zdravookhraneniyu»*, 2016, pp. 69–70 (in Russian).

2. NCD Risk Factor Collaboration. Worldwide trends in hypertension prevalence and progress in treatment and control from 1990 to 2019: a pooled analysis of 1201 population-representative studies with 104 million participants. *The Lancet*, 2021, vol. 398, no. 10304, pp. 957–980. DOI: 10.1016/S0140-6736(21)01330-1

3. Bodienkova G.M., Boklazhenko E.V. Comparative assessment of neurochemical indicators in patients with occupational pathology due to physical and chemical factors. *Neirokhimiya*, 2021, vol. 38, no. 4, pp. 385–390. DOI: 10.31857/S1027813321040026 (in Russian).

4. Usmanova D.D. The role of neurotrophic factors in the pathogenesis of chronic cerebral ischemia. *Meditsinskie novosti*, 2015, no. 9, pp. 66–67 (in Russian).

5. Odinak M.M., Tsygan N.V., Ivanov A.M., Kamilova T.A., Nikitin V.Yu., Meshkova M.E. Protein s100β – biomarker of brain injury. *Bulletin of the Russian Military Medical Academy*, 2011, no. 1 (33), pp. 210–214 (in Russian).

6. Bodienkova G.M., Boklazhenko E.V., Katamanova E.V. Clinical value of regulatory autoantibodies in development of neurointoxication with metallic mercury vapours. *Bulletin of the East Siberian Scientific Center SB RAMS*, 2012, no. 2–1 (84), pp. 20–23 (in Russian).

7. Wenzel U., Turner J.E., Krebs C., Kurts C., Harrison D.G., Ehmke H. Immune Mechanisms in Arterial Hypertension. *J. Am. Soc. Nephrol.*, 2016, vol. 27, no. 3, pp. 677–686. DOI: 10.1681/ASN.2015050562

8. Vertkin A.L., Khovasova N.O. Komorbidnost' – novaya patologiya. Tekhnologii ee profilaktiki i lecheniya [Comorbidity is a new pathology. Technologies of its prevention and treatment]. *Arkhiv" vnutrennei meditsiny*, 2013, no. 4, pp. 68–74 (in Russian).

9. Timakova A.Yu., Saydaeva M.I., Skirdenko Yu.P. Pseudoresistant arterial hypertension: causes and difficulties of diagnosis. *Nauchnoe obozrenie. Meditsinskie nauki*, 2020, no. 1, pp. 36–41 (in Russian).

10. Poterjaeva E.L., Fedina R.G., Hasnulin V.I. Industrial vibration – negative stress factor influencing men' hypophysial-suprarenal system. *Byulleten' nauchnogo soveta «Mediko-ekologicheskie problemy rabotayushchikh»*, 2007, no. 2, pp. 60–62 (in Russian).

11. Baraeva R.A., Strizhakov L.A., Borzykh Y.I. Factors of humoral immunity in the combined course of vibration disease and hypertension. *Meditsina truda i promyshlennaya ekologiya*, 2019, no. 9, pp. 558–559. DOI: 10.31089/1026-9428-2019-59-9-558-559 (in Russian).

12. Babanov S.A., Baraeva R.A., Strizhakov L.A., Moiseev S.V., Fomin V.V. The state of cytokine regulation and endothelial dysfunction in the combined course of vibration disease and arterial hypertension. *Terapevticheskii arkhiv*, 2021, vol. 93, no. 6, pp. 693–698. DOI: 10.26442/00403660.2021.06.200880 (in Russian).

13. Zaichik A.M., Poletaev A.B., Churilov L.P. Natural autoantibodies, immunological theories and preventive medicine. *Vestnik Sankt-Peterburgskogo universiteta. Meditsina*, 2013, no. 2, pp. 3–16 (in Russian).

14. Lishmanov Y.B., Maslov L.N., Naryzhnaya N.Y., Pei J., Kolar F., Zhang Y., Portnichenko A.G., Wang H. Endogenous opioid system as a mediator of acute and long-term adaptation to stress. Prospects for clinical use of opioid peptides. *Annals of the Russian Academy of Medical Sciences*, 2012, vol. 67, no. 6, pp. 73–82 (in Russian).

15. Zhukova N.V., Mavrutenkov V.V., Ushakova G.A. Neurospecific protein s100b – a universal biochemical marker of damage. Part I. General issues (history, genetics, biochemistry, physiology). *Klinicheskaya infektologiya i parazitologiya*, 2014, no. 4 (11), pp. 53–64 (in Russian).

16. Hamon M., Blier P. Monoamine neurocircuitry in depression and strategies for new treatments. *Prog. Neuropsychopharmacol. Biol. Psychiatry*, 2013, vol. 45, pp. 54–63. DOI: 10.1016/j.pnpbp.2013.04.009

17. Astakhin A.V., Evlasheva O.O., Levitan B.N. Clinical and diagnostic value of myelin basic protein and neuron specific enolase in medical practice. *Astrakhanskii meditsinskii zhurnal*, 2016, vol. 11, no. 4, pp. 9–17 (in Russian).

18. Shimada M., Hasegawa T., Nishimura C., Kan H., Kanno T., Nakamura T., Matsubayashi T. Anti-Hypertensive Effect of Gamma-Aminobutyric Acid (GABA)-Rich Chlorella on High-Normal Blood Pressure and Borderline Hypertension in Placebo-Controlled Double Blind Study. *Clin. Exp. Hypertens.*, 2009, vol. 31, no. 4, pp. 342–354. DOI: 10.1080/10641960902977908

19. Mei L., Zhang J., Mifflin S. Hypertension alters GABA receptor-mediated inhibition of neuronsin the nucleus of the solitary tract. *Am. J. Physiol. Regul. Integr. Comp. Physiol.*, 2003, vol. 285, no. 6, pp. 1276–1286. DOI: 10.1152/ajpregu.00255.2003

20. Rukavishnikov V.S., Pankov V.A., Kuleshova M.V., Katamanova E.V., Kartapol'tseva N.V., Rusanova D.V., Bodienkova G.M., Titov E.A. On theory of sensory conflict under exposure to physical factors: main principles and concepts of formation. *Meditsina truda i promyshlennaya ekologiya*, 2015, no. 4, pp. 1–6 (in Russian).

21. Laporte J.P., Faulkner M.E., Gong Z., Akhonda M.A.B.S., Ferrucci L., Egan J.M., Bouhrara M. Hypertensive Adults Exhibit Lower Myelin Content: A Multicomponent Relaxometry and Diffusion Magnetic Resonance Imaging Study. *Hypertension*, 2023, vol. 80, no. 8, pp. 1728–1738. DOI: 10.1161/HYPERTENSIONAHA.123.21012

22. Trofimova O., Latypova A., DiDomenicantonio G., Lutti A., de Lange A.-M.G., Kliegel M., Stringhini S., Marques-Vidal P. [et al.]. Topography of associations between cardiovascular risk factors and myelin loss in the ageing human brain. *Commun. Biol.*, 2023, vol. 6, no. 1, pp. 392. DOI: 10.1038/s42003-02

Chistova N.P., Bodienkova G.M., Boklazhenko E.V. Neuroantibodies as risk markers for the development of autoimmune processes in case of vibration disease. Health Risk Analysis, 2025, no. 1, pp. 128–136. DOI: 10.21668/health.risk/2025.1.12.eng

Received: 29.01.2025
Approved: 19.03.2025
Accepted for publication: 27.03.2025