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Evaluation of cytokines, antibodies to neurotransmitter receptors, and their interrelations in individuals with hand-arm vibration syndrome

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ABSTRACT

BACKGROUND: One of the primary objectives of the healthcare system in the Russian Federation is to preserve the health of the working population, as economic losses associated with the treatment and social support of individuals with occupational diseases is over 200 billion rubles. Hand-arm vibration syndrome and sensorineural hearing loss continue to prevail among the occupational pathologies. Patients with these conditions have been found to exhibit disturbances in the neuroimmune-endocrine system.

AIM: To compare, identify interrelations, and analyze the levels of cytokines and autoantibodies to neurotransmitter receptors in individuals with hand-arm vibration syndrome, depending on the presence/absence of sensorineural hearing loss and the type of vibration exposure.

MATERIALS AND METHODS: Serum levels of interleukins (IL-1β, IL-4, IL-6, IL-8), tumor necrosis factor (TNF-α), and autoantibodies to acetylcholine, glutamate, GABA, dopamine, and serotonin receptors were studied using enzyme-linked immunosorbent assay in patients with hand-arm vibration syndrome of various etiologies, either caused by localized vibration exposure or by combined localized and whole-body vibration exposure, with or without concurrent sensorineural hearing loss.

RESULTS: When accompanied by sensorineural hearing loss, individuals with vibration disease of any etiology exhibited higher IL-1β and IL-6 levels compared with those with hand-arm vibration syndrome due to localized vibration exposure without sensorineural hearing loss. For each subgroup, except for individuals with hand-arm vibration syndrome caused by combined localized and whole-body vibration exposure without sensorineural hearing loss, regression equations demonstrated the contribution of cytokines to the variation in antibody levels against neurotransmitter receptors.

CONCLUSION: The findings confirm a higher risk of neuroimmune inflammation in patients with hand-arm vibration syndrome caused by combined whole-body and localized vibration exposure compared to those with vibration disease resulting from localized vibration alone. The presence of concurrent sensorineural hearing loss exacerbates pathological processes due to imbalances in cytokine profiles and neurotransmitter metabolism. Distinctive interrelations between autoantibodies to neurotransmitter receptors and cytokines were identified in individuals with vibration disease of various etiologies and concurrent sensorineural hearing loss.

Keywords: cytokines; antibodies; neuronal receptors; hand-arm vibration syndrome; sensorineural hearing loss.

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Оценка цитокинов, антител к рецепторам нейромедиаторов и их взаимосвязей у лиц с вибрационной болезнью

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АННОТАЦИЯ

Обоснование. Одной из основных задач здравоохранения Российской Федерации является сохранение здоровья работающего населения, поскольку экономические потери на лечение и социальные выплаты лицам с профессиональными заболеваниями составляют более 200 млрд рублей. Лидирующие позиции в структуре профессиональной патологии продолжают занимать вибрационная болезнь и нейросенсорная тугоухость. У пациентов с данными заболеваниями установлены нарушения в нейроиммуноэндокринной системе.

Цель. Сопоставить и выявить взаимосвязь и проанализировать уровни цитокинов и аутоантител к рецепторам нейромедиаторов у лиц с вибрационной болезнью в зависимости от наличия или отсутствия нейросенсорной тугоухости и вида воздействующей вибрации.

Материалы и методы. У пациентов с вибрационной болезнью различного этиогенеза, обусловленной воздействием локальной вибрации или комбинированным воздействием локальной и общей вибрации, а также отягощённой нейросенсорной тугоухостью и без таковой, с помощью иммуноферментного анализа изучены сывороточные уровни интерлейкинов (IL-1β, IL-4, Il-6, IL-8), фактора некроза опухоли (TNF-α) и аутоантител к рецепторам ацетилхолина, глутамата, ГАМК, дофамина, серотонина.

Результаты. Установлено, что у лиц с вибрационной болезнью любого генеза, сопровождающейся нейросенсорной тугоухостью, уровень IL-1β и IL-6 выше при сопоставлении с вибрационной болезнью, обусловленной воздействием локальной вибрации, без нейросенсорной тугоухости. Для каждой из подгрупп, за исключением лиц с вибрационной болезнью, обусловленной комбинированным воздействием локальной и общей вибрации, не имеющих нейросенсорной тугоухости, показаны регрессионные уравнения, свидетельствующие о вкладе цитокинов в изменение уровней антител к рецепторам нейромедиаторов.

Заключение. Полученные данные подтверждают более высокие риски развития нейроиммунного воспаления у пациентов с вибрационной болезнью при комбинированном воздействии общей и локальной вибрации относительно пациентов с вибрационной болезнью, обусловленной воздействием локальной вибрации. Наличие сопутствующей нейросенсорной тугоухости усугубляет течение патологических процессов за счёт дисбаланса в цитокиновом профиле и нейромедиаторном обмене. Выявлены отличительные особенности взаимосвязей аутоантител к нейромедиаторным рецепторам и цитокинов у лиц с вибрационной болезнью различного этиогенеза и сопутствующей нейросенсорной тугоухостью.

Ключевые слова: цитокины; антитела; нейрональные рецепторы; вибрационная болезнь; нейросенсорная тугоухость.

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评估振动病患者的细胞因子、神经递质受体抗体及其相互关系

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摘要

背景。维护劳动人口的健康是俄罗斯联邦医疗卫生体系的优先任务之一，因为职业病患者的治疗和社会补助导致的经济损失超过 2000 亿卢布。在职业病谱系中，振动病及其并发的神经性听力损失仍占据主要地位。研究表明，这些患者的神经-免疫-内分泌系统功能受到显著损害。

研究目的。评估振动病患者的细胞因子水平及其针对神经递质受体的自身抗体水平，分析其相互关系，并探讨这些指标在不同振动暴露类型及伴或不伴神经性听力损失情况下的特点。

材料与方法。 研究纳入因局部振动或局部与全身振动联合暴露所致的振动病患者，分为伴或不伴神经性听力损失的亚组。采用酶联免疫吸附分析（ELISA）测定血清中细胞因子水平，包括白细胞介素（IL-1β、IL-4、IL-6、IL-8）、肿瘤坏死因子 α（TNF-α），以及针对乙酰胆碱、谷氨酸、γ-氨基丁酸（GABA）、多巴胺和血清素受体的自身抗体水平。

结果。研究发现，伴有神经性听力损失的振动病患者 IL-1β 和 IL-6 水平显著高于仅由局部振动引起但未发生听力损害的患者。此外，除局部与全身振动联合暴露但未合并听力损失的亚组外，其余各组均建立了回归方程，表明细胞因子水平与神经递质受体抗体之间的显著相关性。

结论。 研究结果证实，与单纯局部振动所致的振动病相比，局部与全身振动联合暴露可显著增加神经免疫炎症的发生风险。此外，伴发神经性听力损失的患者病理进程更为严重，这可能与细胞因子失衡及神经递质系统功能障碍相关。本研究揭示了不同病因所致振动病及其伴发神经性听力损失患者的自身抗体-神经递质受体与细胞因子的相互作用特征。

关键词：细胞因子；抗体；神经递质受体；振动病；神经性听力损失。

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BACKGROUND

In recent decades, one of the primary objectives of the healthcare system in the Russian Federation has been the preservation of the health of the working population. Despite the modernization and automation of industrial facilities, improvements in technological processes, and the implementation of robotics and artificial intelligence, a high incidence of diseases caused by harmful occupational exposures persists in several industrial sectors. Vibration disease (VD) and sensorineural hearing loss (SHL) continue to rank among the leading occupational disorders resulting from physical hazards.[1] These diseases tend to develop over a short period (5 to 7 years of work under hazardous conditions) and lead to reduced work capacity and disability, which determines the high medical and social significance of these professional disorders. The economic costs associated with treatment and social benefits for individuals with occupational diseases exceed 200 billion rubles [1].

The clinical presentation of VD is characterized primarily by angiodystonic syndrome, sensory polyneuropathy of the extremities, and functional disorders of the central nervous system, the severity of which increases with the duration and intensity of vibration exposure. Vibration is known to cause dysfunctions not only in the peripheral but also in the central nervous system, affecting the cerebellum, brainstem structures, hypothalamus, and reticular formation. In SHL, pathological changes occur in the auditory nerve, nerve fibers of the inner ear, as well as the brainstem and cerebral cortex [2]. In addition to nervous system involvement, patients with VD and SHL also present with immune, endocrine, and cardiovascular disorders [3, 4]. According to published data, specific autoantibodies targeting neuronal cell components and structures are detected in the serum of individuals with neurodegenerative diseases [5, 6]. Our earlier findings have revealed altered levels of cytokines and neuronal autoantibodies in patients with VD and SHL. Moreover, differences in cytokine profiles have been noted in individuals with SHL compared to those with VD, as well as depending on the etiology of VD [3, 7]. Despite numerous articles on cytokine profiles, lymphocyte subpopulations, specific antibodies, and other immunologic markers in individuals with occupational diseases, the interrelationship of these markers under combined exposure to different physical occupational hazards remains understudied.

The work aimed to compare and determine the interrelationships, as well as analyze the levels of cytokines and autoantibodies to neurotransmitter receptors, in individuals with VD, depending on the presence or absence of SHL and the type of vibration exposure.

METHODS

As part of a work project conducted by the East Siberian Institute of Medical and Ecological Research (Angarsk), a total of 153 men aged 41–58 years (mean age, 49.6 ± 0.88 years) with occupational diseases resulting from exposure to physical factors were examined.

Inclusion criteria: male sex, VD of occupational origin, no history of autoimmune disorders, and absence of acute respiratory infections at the time of examination. Exclusion criteria: unconfirmed diagnosis of VD or lack of informed consent.

Clinical and laboratory-immunological examinations were approved by the Local Ethics Committee of the East Siberian Institute of Medical and Ecological Research (Protocol No. 5, dated March 21, 2023) and conducted in accordance with the ethical principles of the Declaration of Helsinki. Written informed consent was obtained from all participants.

In all individuals, the diagnosis of VD was confirmed based on the classification criteria for diseases and conditions outlined in the International Classification of Diseases, 10th Revision (ICD-10). Among the participants, 67 men had an occupational disease resulting from exposure to local vibration (Group 1), and 86 men had combined exposure to local and whole-body vibration (Group 2). Group 1 included workers employed as riveters-assemblers, assembly fitters, tunnelers, loggers, installation workers, chippers, and sawmill operators. Group 2 comprised excavator, bulldozer, grader, drilling rig, and crane operators, as well as KrAZ log truck drivers, forklift drivers, and tractor operators. SHL as a second occupational disease was diagnosed in 47 individuals in Group 1 (local vibration) and in 64 individuals in Group 2 (combined local and whole-body vibration). Within each group, individuals with SHL were classified into separate subgroups.

Serum samples obtained from the participants were analyzed using enzyme-linked immunosorbent assay (ELISA) to determine the concentrations of cytokines, including interleukin-1β (IL-1β), tumor necrosis factor alpha (TNF-α), and interleukins 4, 6, and 8 (IL-4, IL-6, IL-8), using Vector-Best reagent kits. Additionally, levels of specific IgG autoantibodies were assessed using ELI-Neuro-Test kits (Immunkulus Research and Production Association). The autoantibodies studied included those targeting the following receptors: acetylcholine (nACh-R), glutamate (NMDA-R), gamma-aminobutyric acid (GABA-R), dopamine (DA-R), and serotonin (SER-R).

Statistical analysis was performed using STATISTICA 6.0 software. Normality of data distribution was assessed using the Shapiro–Wilk test. Comparisons of quantitative variables were conducted using the nonparametric Kruskal–Wallis test and the Mann–Whitney test. Associations between variables were evaluated using Spearman rank correlation and nonlinear regression analysis. The results are presented as median (Me) and interquartile range (25th and 75th percentiles, LQ–UQ). Differences were considered

[1] On the State of Sanitary and Epidemiological Well-Being of the Population in the Russian Federation in 2019: State Report. Moscow: Federal Service for Surveillance on Consumer Rights Protection and Human Wellbeing; 2020:299.

statistically significant at $p < 0.05$ for the Kruskal–Wallis test and Spearman correlation, and at $p < 0.0083$ for pairwise comparisons.

RESULTS

The findings revealed that in the subgroups of individuals with both VD and SHL, serum IL-1β levels were significantly higher than in individuals with VD caused by local vibration exposure without SHL ($p = 0.001$ and $p < 0.001$ for the subgroups with SHL and VD due to local and combined vibration exposure, respectively; Table 1). IL-6 levels were elevated in the subgroups with VD due to combined local and whole-body vibration exposure, both with and without SHL, as well as in individuals with SHL and VD resulting from local vibration exposure. However, these intergroup differences did not reach statistical significance and demonstrated a trend compared with the subgroup with VD from local vibration exposure without SHL ($p = 0.027$, $p = 0.033$, and $p = 0.013$, respectively).

Analysis of cytokine profiles across all four subgroups revealed a similar structural pattern; however, individuals with SHL as an occupational comorbidity exhibited the highest IL-1β levels. The greatest concentration of this interleukin was observed in the subgroup with SHL and VD caused by combined local and whole-body vibration exposure. Conversely, the lowest levels of both IL-1β and IL-6 were detected in the cohort with VD resulting from local vibration exposure without SHL. These findings suggest that combined exposure to noise, local, and whole-body vibration may exert a unidirectional effect on IL-1β levels and demonstrate a synergistic proinflammatory influence.

Autoantibodies play a central role in the clearance of apoptotic cells and their components during physiological cell turnover. In this context, they may exhibit protective properties and can be detected at low concentrations in the serum of healthy individuals. However, elevated autoantibody levels may either indicate or contribute to pathological processes involving increased cell death [8].

Serum test of autoantibodies targeting neurotransmitter receptors revealed no statistically significant intergroup differences (Table 2).

Antibody production is known to be regulated by cytokines through B-lymphocyte activation [9, 10]. Consequently, elevated levels of proinflammatory cytokines and the accompanying activation of inflammatory pathways may contribute to increased serum concentrations of autoantibodies. Accordingly, a regression test was conducted to assess associations between cytokine levels and the presence of neural tissue autoantibodies. The resulting equations describe the contribution of cytokine profiles to the development of antibody responses against neurotransmitter receptors. In the subgroup of patients with VD caused by local vibration exposure without SHL, the following models were identified: $GABA\text{-}R = 1.84 - 1.44 \times (IL\text{-}1\beta) - 6.94 \times (TNF\text{-}\alpha) + 2.54 \times (IL\text{-}1\beta)^2 + 2.57 \times (IL\text{-}6)^2 + 6.87 \times (TNF\text{-}\alpha)^2$ ($R^2 = 0.89$, $p = 0.013$); $DA\text{-}R = 1.37 - 3.30 \times (IL\text{-}6) - 7.62 \times (TNF\text{-}\alpha) + 2.23 \times (IL\text{-}1\beta)^2 + 3.48 \times (IL\text{-}6)^2 + 7.40 \times (TNF\text{-}\alpha)^2$ ($R^2 = 0.86$, $p = 0.020$). In individuals with SHL, the following model was established: $NMDA\text{-}R = 1.00 - 2.49 \times (IL\text{-}6) - 2.50 \times (TNF\text{-}\alpha) + 2.41 \times (TNF\text{-}\alpha)^2$ ($R^2 = 0.85$, $p = 0.029$). In the subgroup with VD due to combined local and whole-body vibration exposure and comorbid SHL, the regression equation was as follows: $SER\text{-}R = 0.87 + 1.28 \times (IL\text{-}1\beta) - 1.72 \times (IL\text{-}1\beta)^2$ ($R^2 = 0.66$, $p = 0.021$), where GABA-R, DA-R, NMDA-R, SER-R, IL-1β, IL-4, IL-6 and TNF-α represent levels of relevant autoantibodies and cytokines. No statistically significant regression models were identified

Table 1. Cytokine levels in individuals with occupational diseases caused by exposure to physical factors, Me (LQ–UQ)

Indicator	Group with vibration disease due to local vibration exposure		Group with vibration disease due to combined local and whole-body vibration exposure		*p*
	Subgroup without sensorineural hearing loss	Subgroup with sensorineural hearing loss	Subgroup without sensorineural hearing loss	Subgroup with sensorineural hearing loss	
IL-1β, pg/mL	1.20 (0.10–2.19)	6.10 (2.00–29.64)*	2.83 (0.95–21.61)	8.46 (2.22–30.51)*	0.001
IL-4, pg/mL	0.98 (0.72–1.63)	0.56 (0.15–2.79)	1.28 (0.03–4.22)	1.07 (0.01–3.59)	0.676
IL-6, pg/mL	2.92 (2.04–3.87)	4.37 (3.52–5.57)#	4.68 (3.35–12.34)#	4.35 (3.16–5.49)#	0.028
IL-8, pg/mL	6.73 (5.05–7.77)	8.95 (6.93–16.02)	7.89 (6.71–15.36)	7.78 (5.40–10.81)	0.087
TNF-α, pg/mL	0.44 (0.25–0.65)	0.81 (0.30–2.71)	0.50 (0.15–1.99)	0.73 (0.31–2.30)	0.337

Note. *p*, level of statistical significance according to the Kruskal–Wallis test; differences were considered significant at $p < 0.05$; * statistically significant differences compared with the subgroup of individuals with vibration disease from local vibration exposure without sensorineural hearing loss, $p < 0.008$; # trend toward significance compared to the subgroup of individuals with vibration disease from local vibration exposure without sensorineural hearing loss, $0.008 < p < 0.017$.

for the subgroup with VD resulting from combined vibration exposure without SHL. These findings indicate that, in patients with VD due to local vibration exposure and without SHL, serum levels of autoantibodies to neurotransmitter receptors are more strongly associated with the concentrations of IL-1β, IL-4, IL-6, and TNF-α compared to individuals with combined vibration exposure or those with SHL.

DISCUSSION

It is known that IL-1β, produced by monocytes, macrophages, Kupffer cells of the liver, Langerhans cells in the epidermis, and microglial cells, exerts both local and systemic effects mediated through activation of the neuroendocrine system [9, 11]. Under normal conditions, increased IL-1β production triggers protective responses; however, it may lead to uncontrolled inflammation, tissue damage, and become part of the disease pathogenesis. Indirectly, by activating IL-6, IL-1β may promote the synthesis of antibodies of all immunoglobulin classes. In turn, IL-6 is capable of shifting the innate immune response and the development of protective mechanisms toward adaptive immunity. Elevated IL-1β and IL-6 levels in subgroups with VD and comorbid SHL may indicate the presence of chronic inflammation and autoimmune processes, as IL-6 is known to contribute to the pathogenesis of autoimmune and inflammatory conditions. The disruption of associations between cytokine levels and serum autoantibody concentrations observed in subgroups with VD caused by combined local and whole-body vibration exposure—with or without SHL—may be explained by an imbalance between pro- and anti-inflammatory cytokine production. This imbalance likely arises at a certain stage in the development of the disease under the influence of vibration and may also reflect a reduction in neuronal autoantibody levels following the clinical manifestation of the occupational disease. Previously, it was shown that patients with VD exhibit lower levels of these autoantibodies compared to experienced workers without diagnosed occupational disease [12].

In earlier studies, average serum concentrations of selected cytokines and autoantibodies were established in conditionally healthy men. For example, serum IL-1β was 3.40 (1.21–6.19), IL-4 was 0.01 (0.01–0.69), IL-8 was 5.08 (1.41–13.40), and TNF-α was 0.73 (0.01–1.47) pg/mL. Autoantibody levels were as follows (arbitrary units): nACh-R 0.34 (0.29–0.38), NMDA-R 0.27 (0.26–0.29), GABA-R 0.24 (0.22–0.28), DA-R 0.26 (0.24–0.31), and SER-R 0.46 (0.36–0.47) [3, 13]. Thus, in individuals with VD—with or without comorbid SHL—the levels of neuronal autoantibodies are approximately 1.2–2.6 times higher than those in conditionally healthy men, which is consistent with previously published data [3, 7]. Furthermore, demyelinating processes have been reported in patients with VD, along with associations between neuronal autoantibodies and impaired nerve impulse conduction in the upper and lower extremities [12].

It is well established that alterations in the levels of serotonin, glutamate, GABA, acetylcholine, and dopamine in synapses—and the resulting imbalance of these neurotransmitters within brain structures—lead to changes in the brain's bioelectrical activity in certain neurodegenerative diseases. Glutamate, one of the primary excitatory neurotransmitters, also serves as a precursor for the synthesis of GABA, the principal inhibitory neurotransmitter in the central nervous system. Glutamate is released into the synaptic cleft via exocytosis involving voltage-gated calcium

Table 2. Comparative assessment of antibody levels to neurotransmitter receptors in individuals with vibration disease and concomitant sensorineural hearing loss, Me (LQ–UQ)

Indicator	Group with vibration disease due to local vibration exposure		Group with vibration disease due to combined local and whole-body vibration exposure		*p*
	Subgroup without sensorineural hearing loss	Subgroup with sensorineural hearing loss	Subgroup without sensorineural hearing loss	Subgroup with sensorineural hearing loss	
Antibodies to nACh-R, a.u.	0.46 (0.42–0.68)	0.50 (0.17–0.65)	0.55 (0.37–0.84)	0.55 (0.20–0.77)	0.728
Antibodies to NMDA-R, a.u.	0.40 (0.36–0.60)	0.39 (0.18–0.53)	0.41 (0.29–0.66)	0.50 (0.23–0.69)	0.480
Antibodies to GABA-R, a.u.	0.55 (0.37–0.86)	0.48 (0.15–0.59)	0.47 (0.38–0.71)	0.56 (0.21–0.70)	0.349
Antibodies to DA-R, a.u.	0.49 (0.35–0.70)	0.37 (0.20–0.52)	0.45 (0.28–0.64)	0.47 (0.24–0.64)	0.153
Antibodies to SER-R, a.u.	0.49 (0.42–0.79)	0.51 (0.21–0.62)	0.51 (0.37–0.63)	0.59 (0.27–0.71)	0.682

Note. *p*, level of statistical significance according to the Kruskal–Wallis test; differences were considered significant at $p < 0.05$; * statistically significant differences compared with the subgroup of individuals with vibration disease from local vibration exposure without sensorineural hearing loss, $p < 0.008$; # trend toward significance compared with the subgroup of individuals with vibration disease from local vibration exposure without sensorineural hearing loss, $0.008 < p < 0.017$.

channels. From the synaptic cleft, it enters astrocytes, where it is aminated to glutamine. Alterations in the levels of this neurotransmitter—due to reduced astrocytic capacity to maintain optimal extracellular glutamate concentrations, impaired neuronal reuptake, and decreased receptor density—predispose to disrupted neurophysiological processes in the brain and play a significant role in neurodegenerative injury [14, 15]. Excessive glutamate production may be triggered by the proinflammatory cytokines IL-1β and TNF-α, which influence the expression of astrocytic transporter proteins. It has been established that in multiple sclerosis, TNF-α can stimulate glutamate release by microglia through autocrine mechanisms and by regulating glutaminase activity. Demyelinated axons may also contribute to increased glutamate synthesis and release due to altered localization of the pore-forming α1B subunit of voltage-gated Ca^{2+} channels on damaged axons. Additionally, glutamate itself can stimulate its synthesis via metabotropic glutamate receptors located on astrocytes [16]. Elevated levels of this neurotransmitter and hyperactivation of ionotropic glutamate receptors lead to increased Ca^{2+}release from intracellular stores into the neuronal cytoplasm, thereby enhancing lipid peroxidation, oxidative stress, and other neurotoxic processes capable of inducing neuronal apoptosis [15]. Taken together, the existing publications suggest that glutamate receptors play a critical role in modulating cellular membrane potential, ion channel activity, and free radical formation. They also participate in the regulation of cytokine secretion by T cells and contribute to neuronal death processes, particularly affecting dopaminergic neurons in the substantia nigra [15–17]. Accordingly, NMDA receptors may represent a central link in multiple pathogenetic pathways—including autoimmune responses, inflammation, and demyelination—underlying disorders associated with neurodegenerative processes, such as VD. This is supported by the present publication's findings, which demonstrate associations between GABA-R and NMDA-R levels and the concentrations of cytokines and autoantibodies to neurotransmitter receptors in subgroups of individuals with VD resulting from local vibration exposure, with and without SHL: NMDA-R = 1.42(SER-R) – 0.62 × (GABA-R)^2(R^2 = 0.82,p < 0.001); GABA-R = 0.70 × (NMDA-R) – 0.62 × (NMDA-R)^2 + 0.75 × (DA-R)^2 (R^2 = 0.99, p < 0.001) respectively, as well as in the cohort exposed to combined local and whole-body vibration without SHL: GABA-R = 0.37 + 3.95 × (nACh-R) – 4.06 × (NMDA-R) – 4.86 × (nACh-R)^2 + 5.32 × (NMDA-R)^2(R^2 = 0.93, p < 0.001).

A limitation of this work is the relatively small sample size, which restricted the use of certain statistical methods and precluded a detailed analysis of associations between cytokine and autoantibody levels across different durations of occupational exposure, disease severity and stage, and time since cessation of exposure to the harmful occupational factor.

CONCLUSION

The findings of this work confirm and extend previous evidence indicating an increased risk of neuroimmune inflammation in patients with VD resulting from combined exposure to whole-body and local vibration, compared with individuals whose VD is attributable solely to local vibration [3]. The presence of concurrent SHL exacerbates the pathological process by amplifying inflammatory changes and disrupting both cytokine profiles and neurotransmitter metabolism. Distinct features of the associations between autoantibodies to neurotransmitter receptors and cytokines were identified in individuals with VD of different etiologies and coexisting SHL. In patients with VD due to local vibration exposure without SHL, levels of autoantibodies to GABA receptors were primarily associated with IL-1β, TNF-α, and IL-6; for dopamine receptors, with IL-1β, IL-6, and TNF-α. In cases with SHL, levels of autoantibodies to glutamate receptors were associated with IL-6 and TNF-α. Among individuals with VD resulting from combined local and whole-body vibration and coexisting SHL, levels of autoantibodies to serotonin receptors were linked to IL-1β concentration.

ADDITIONAL INFORMATION

Authors' contribution. L.B. Masnavieva — analysis and interpretation of results, literature review, preparation and writing of the article; G.M. Bodienkova — study conception and design, literature review, editing the article; E.V. Boklazhenko — data collection, analysis and interpretation of results. All authors confirm that their authorship meets the international ICMJE criteria (all authors have made a significant contribution to the development of the concept, research and preparation of the article, read and approved the final version before publication).

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Patients' consent. Written consent was obtained from all the study participants before the study screening in according to the study protocol approved by the local ethic committee.

ДОПОЛНИТЕЛЬНАЯ ИНФОРМАЦИЯ

Вклад авторов. Л.Б. Маснавиева — анализ и интерпретация результатов, обзор литературы, подготовка и написание текста статьи; Г.М. Бодиенкова — концепция и дизайн исследования, обзор литературы, редактирование статьи; Е.В. Боклаженко — сбор данных, анализ и интерпретация результатов. Все авторы подтверждают соответствие своего авторства международным критериям ICMJE (все авторы внесли существенный вклад в разработку концепции, проведение исследования и подготовку статьи, прочли и одобрили финальную версию перед публикацией).

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REFERENCES | СПИСОК ЛИТЕРАТУРЫ

1. Khrupachev AG, Khadartsev AA, Sedova OA, et al. Quantitative assessment of the harmful effects of industrial noise and vibration on human health. *National Interests: Priorities and Security*. 2013;9(28):44–52. (In Russ.) EDN: QIYXLR
2. Babanov SA, Vorobyova EV. Features of diagnosis and course of vibration disease in the conditions of modern production. *Trudnyj Pacient (Difficult Patient)*. 2010;8(5):28–30. (In Russ.) EDN: OGBNTL
3. Bodienkova GM, Boklazhenko EV. Immunochemical markers of effect under exposure to risk factors causing vibration disease of different etiogenesis: comparative assessment. *Health Risk Analysis*. 2023;(2):149–154. doi: 10.21668/health.risk/2023.2.14 EDN: IMBTYX
4. Lapko IV, Kir'yakov VA, Pavlovskaya NA, Zheglova AV. Changes in hormones of pituitary-thyroid and pituitary-genital systems in workers with vibration disease and neurosensory deafness. *Russian Journal of Occupational Health and Industrial Ecology*. 2015;(10):26–30. EDN: UMUIQD
5. Miteva D, Vasilev GV, Velikova T. Role of specific autoantibodies in neurodegenerative diseases: pathogenic antibodies or promising biomarkers for diagnosis. *Antibodies (Basel)*. 2023;12(4):81. doi: 10.3390/antib12040081
6. Kirschstein T, Köhling R. Functional changes in neuronal circuits due to antibody-driven autoimmune response. *Neurobiol Dis*. 2023;184:106221. doi: 10.1016/j.nbd.2023.106221
7. Bodienkova GM, Boklazhenko EV. Comparative assessment of neurochemical indicators in patients with occupational pathology due to physical and chemical factors. *Neirokhimiya*. 2021;38(4):385–390. doi: 10.31857/S1027813321040026 EDN: KDXRLT
8. Poletaev AB *Molecular medical examination (new approaches to the early manifestation of pathological changes in the human body: guidelines for doctors*. Moscow: Immunculus; 2014. (In Russ.)
9. Kashtalyan OA, Ushakova LYu. Cytokines as universal regulation system. *Meditsinskie Novosti*. 2017;(9):3–7. EDN: ZHRKTB
10. Berezhnaya NM, Sepiashvili RI. Interleukins in the pathogenesis of atopic allergic diseases. *Allergology and Immunology*. 2014;15(3):169–176. (In Russ.) EDN: UCKODP
11. Ketlinskiy SA, Simbirtsev AS. *Cytokines*. St. Petersburg: Foliant; 2008. (In Russ.)
12. Rukavishnikov VS, Bodienkova GM, Kurchevenko SI, et al. Role of neuroautoimmune integration in pathogenesis of vibration disease. *Russian Journal of Occupational Health and Industrial Ecology*. 2017;(1):17–20. EDN: XYEXFZ
13. Bodienkova GM, Kurchevenko SI. Influence of industrial vibration on the level of antibodies against regulatory proteins of the nervous tissue. *Fiziologiya Cheloveka*. 2016;42(5):550–553. doi: 10.7868/S0131164616050039 EDN: WLNKEJ
14. Maragakis NJ, Rothstein JD. Glutamate transporters in neurologic disease. *Arch Neurol*. 2001;58(3):365–370 doi: 10.1001/archneur.58.3.365
15. Mironova YuS, Zhukova NG, Zhukova IA, et al. Parkinson's disease and glutamatergic system. *S.S. Korsakov Journal of Neurology and Psychiatry*. 2018;118(5):138–142. doi: 10.17116/jnevro201811851138 EDN: XROHLV
16. Kuzmina USh, Zainullina LF, Vakhitov VA, et al. The role of glutamate in the pathogenesis of multiple sclerosis. *S.S. Korsakov Journal of Neurology and Psychiatry*. 2019;119(8):160–167. doi: 10.17116/jnevro2019119081160 EDN: LMTRSO
17. Kolobov VV, Zakharova IA, Fomina VG, et al. Effect of antibodies to glutamate on caspase-3 activity in brain structures of rats with experimental Alzheimer's disease. *Bulletin of Experimental Biology and Medicine*. 2013;154(4):425–427 doi: 10.1007/s10517-013-1967-x EDN: RFJFTJ

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