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Approaches to Non-Pharmacological Modulation of Neural and Immune Communication: Therapeutic Potential of Vibration Stimulation

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ABSTRACT

Nowadays, principles of neuromuscular system activation using vibration-mediated, intensive reflex stimulation are employed in addition to conventional physical activity for clinical rehabilitation or sports performance. Studies show that vibration training is an effective, non-pharmacological way to improve various body functions, which can effectively rehabilitate movement disorders and muscle weakness, as well as treat hormonal and metabolic disorders, osteoporosis, cardiorespiratory disorders, and age-related disorders. Immune dysfunction and age-related changes are closely associated with neuroinflammation and neurodegeneration. Recent data demonstrate the positive effects of vibration training on immune responses and higher integrative brain functions, suggesting a promising therapeutic approach for treating nervous system diseases. This article evaluates the effects of vibration training for neuromuscular stimulation on cellular and molecular pathways involved in neuroimmune communications and systematizes the available data on the potential use of this non-pharmacological option for treatment of neurological and immune disorders. Various vibration training programs demonstrate their effectiveness and multifunctional performance in treating deficits and could be a promising addition to conventional exercise and physical rehabilitation options. However, the effects of proprioceptive stimulation by vibration training on the nervous system and the associated immune response remain to be elucidated. Therefore, research in various animal models and in human, as well as a comprehensive evaluation of the results and therapeutic effectiveness, will contribute to a deeper, more systematic understanding of this technology's effects on human health.

Keywords: neuromuscular system; vibration stimulation; proprioception; neuroimmune interactions.

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Подходы к нефармакологической модуляции нервной и иммунной коммуникации: терапевтический потенциал вибрационной стимуляции

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АННОТАЦИЯ

В настоящее время наряду с традиционной физической нагрузкой в целях клинической реабилитации или для достижения спортивных показателей применяются принципы активации нейромышечной системы с использованием рефлекторной интенсивной стимуляции, опосредованной вибрационным воздействием. В ряде исследований вибрационная физическая нагрузка как немедикаментозный метод воздействия на различные функциональные системы организма продемонстрировала свою эффективность в реабилитации двигательных расстройств и мышечной слабости, в коррекции гормональных и метаболических нарушений, остеопороза, кардиореспираторной и возраст-ассоциированной патологии. Иммунная дисфункция и возрастные изменения тесно коррелируют с процессами нейровоспаления и нейродегенерации. Последние данные указывают на положительное влияние вибрационного тренинга на иммунный ответ и высшие интегративные функции мозга, а также демонстрируют терапевтические возможности при заболеваниях нервной системы. В настоящей статье анализируется влияние вибрационной стимуляции нейромышечной системы на клеточные и молекулярные пути, вовлечённые в нейроиммунные коммуникации, и систематизированы имеющиеся данные о потенциале такого воздействия для немедикаментозной коррекции неврологических и иммунных нарушений. Анализ исходов различных программ вибрационной физической нагрузки подтверждает эффективность и многофункциональность данного вмешательства для коррекции соответствующего дефицита и позволяет рассматривать его как многообещающее дополнение к традиционным упражнениям и методам физической реабилитации. Однако вопросы о конкретных механизмах, посредством которых интенсивная проприоцептивная стимуляция в условиях вибрационного тренинга может влиять на различные аспекты функционирования нервной системы и иммунный ответ, остаются открытыми. Поэтому изучение данной технологии с помощью разнообразных модельных организмов и у человека, а также комплексное исследование результатов воздействия и всесторонняя оценка терапевтической эффективности будут способствовать более глубокому и системному пониманию особенностей её влияния на здоровье человека в целом.

Ключевые слова: нейромышечная система; вибрационная стимуляция; проприоцепция; нейроиммунные взаимодействия.

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INTRODUCTION

Vibration training (VT) involves the use of a specialized platform to expose the body to mechanical vibrations of a certain frequency and amplitude, leading to various physiological responses that contribute to positive effects and clinical benefits after short- or long-term stimulation [1]. During vibration physical exposure, skeletal muscles rapidly contract and relax reflexively at a certain frequency, activating muscle metabolism and improving stretch reflex by activation of muscle spindles [1–3]. This vibration load increases production of nitric oxide and enhances systemic blood circulation, which potentiates oxygen and nutrient delivery to organs and tissues throughout the body [4–6]. Vibration stimulation (VS) initiates endocrine responses and can increase the synthesis and secretion of hormones and growth factors, of which many contribute to skeletal muscle mass maintenance and development. Moreover, VT increases bone density, stimulates bone remodeling, and shows potential to improve neuromuscular function, which positively affects balance and sensorimotor coordination [7–13]. After a single and repeated course of vibration physical exercise (VPE), decreased pain in chronic dorsalgia, osteoarthritis, and fibromyalgia and improved bronchial patency were recorded, which may be associated with its inhibitory effect on neurons of the spinothalamic tract and vagal effects [14–16]. Overall, VT is a relatively new alternative to traditional exercises and physical rehabilitation, which has therapeutic potential, versatility, and proven effectiveness [17–19].

This study aimed to summarize and analyze current data on the mechanisms and clinical application of vibration physical effects to systematize available information on the cellular and systemic effects of intense neuromuscular activation induced by VS on the immune response and integrative functions of the brain.

A search for publications was performed in PubMed, Scopus, and RSCI using search queries and keywords. The systematic search included articles published over the past 20 years (2005–2025). The following keywords and their combinations were used: whole-body vibration, WBV, WBV training, WBV exercises, WBV therapy, vibration, nervous, immune, immunity, neurological, neuroimmune, brain, and cognitive. Based on the stated search objective, abstracts of reports, meeting minutes, books, clinical cases, and case series were excluded.

MECHANISMS OF PHYSIOLOGICAL SYSTEMS ACTIVATION

In the neuromuscular system, the mechanism of action of VT involves mechanical high-frequency stimulation of the proprioceptive system using specialized platforms and devices [20]. It is based on vibrational somatosensory perception, which is a widespread phenomenon in nature; this innate ability of animals has evolutionary significance, strengthening

the biological connection of the organism with the environment [20, 21].

The human somatosensory system is sensitive to mechanical stimulation, most commonly found in oscillatory form, with a frequency ranging from 1 Hz to approximately 100 kHz [14]. High-frequency (>100 Hz) and high-intensity (>10 mm) vibrations can lead to negative consequences, including musculoskeletal disorders or increased risks of developing vibration disease; however, low-frequency (up to 50 Hz) and low-amplitude (<10 mm) vibrations have demonstrated positive functional effects, particularly for therapeutic and rehabilitation purposes [22–24].

VS-based mechanical action promotes intensive neurogenic adaptation [3, 18]. In such cases, stimulation of muscle spindle proprioceptors is several times higher than during traditional physical activity [25]. Therefore, VPE results in muscle–hypothalamic axis activation, which causes a rapid increase in the secretion of anabolic humoral factors, including somatotropin, insulin-like growth factor-1, and testosterone, and stabilization of cortisol secretion [26]. Improvement of physical performance with this type of exposure is based on neuromuscular adaptation; VS causes a reflex reaction of skeletal muscles as a sequence of small, close to isometric, involuntary muscle contractions with a frequency equal to the stimulation frequency [2, 27]. According to electromyography data, such proprioceptive stimulation activates up to 100% of skeletal muscle fibers, with VPE causing recruitment of silent motor units and temporarily maintaining them at high activity even in fatigued muscles. In the fatigue that occurs during this process, the leading role is played by the peripheral mechanism with normal serum lactic acid levels, which do not significantly increase after VT [1, 27, 28].

VPE may be considered a conditionally passive physical exercise [13, 29]. VT requires less effort and is relatively effective, economical, and suitable for various conditions and can be adapted for clinical and home/household use. Therefore, for individuals facing physical limitations or having reduced motivation due to factors such as weakness and asthenia, psychophysiological disorders, and depression, VT is an accessible and effective technique for initiating and increasing physical activity [29–32].

As even acute and short-term effects of such exposure are accompanied by a twofold increase in blood flow in the vessels of muscles and skin, an increase in lymphatic drainage and venous return in the trained area of the body, and no pronounced systemic immunosuppressive effects are detected [33–36], VS has proven to be promising regarding effectiveness in high-performance sports and restorative medicine for patients of various age groups, including the elderly and senile [37–39].

NEUROIMMUNE COMMUNICATION

Nervous and immune regulation of functions have several communication pathways and intersystem relationships

involved in maintaining the overall homeostasis of the body [40]. In a tonic mode, the brain sends its signals to the periphery to activate immune function; conversely, the immune system transmits information in the opposite direction to modulate the activity of the central nervous system [40–42]. Such intersystem interactions affect thermoregulatory processes, sleep and wakefulness, eating behavior, brain lymphatic activity, and hormonal status [43–46]. In neurodegenerative disorders such as Alzheimer and Parkinson diseases, the immune system also plays a significant role, being directly involved in pathogenetic mechanisms and indirectly affecting disease course and progression [42, 47]. In such neuroimmune interactions, various cytokines, such as interleukins IL-1 β and IL-6, tumor necrosis factor TNF- α , transforming growth factor TGF- β 1 and TGF- α , and other immune response-related factors (e.g., Toll-like receptors and prostaglandins), play a critical role [40, 48]. Immune-mediated proinflammatory and anti-inflammatory responses, along with oxidative stress, influence the delicate balance in neurodegenerative contexts. A study and analysis of the effects of VS on immune reactivity revealed the therapeutic potential of this intervention in conditions associated with immune dysfunction and its broader implications for neurodegenerative disorders and neuroinflammatory processes [47, 48].

This review aimed to increase scientific awareness and study and analyze the complex pathways and mechanisms modulated by pulsed VS, emphasizing on the molecular and cellular aspects related to the immune response and higher integrative functions of the brain.

MODULATION OF IMMUNE SYSTEM ACTIVITY

In preclinical studies in animal models, study of macrophages from abdominal adipose tissue showed that VS in the described regimens causes a significant increase in the number of M2 macrophages with anti-inflammatory function and restores the cytokine IL-10 level in diabetic mice to resting values in control mice [49]. Immunological data indicate that vibration loading alters regulatory T-cell differentiation in mice and remodels alpha and beta diversity of the gut microbiome [49]. VS potentially alters microbiota associated with innate and mucosal immunity, which promotes anti-inflammatory effects and eliminates adverse effects by downregulating the hyperinflammatory state [43, 49–51].

Chronic inflammation as a characteristic feature of aging contributes to various age-associated diseases [52]. Serum inflammation markers are correlated with chronic processes in old and senile age, which underlies the pathogenesis of several metabolic, cardiorespiratory, and neurodegenerative disorders [52–55]. In clinical studies, VT has demonstrated potential to modulate cytokine levels in the elderly, indicating a systemic anti-inflammatory effect and lack of immunosuppression [39, 53]. Following its exposure, the expressions of TLR2 and TLR4 receptors decrease, indicating

possible biological mechanisms involved in the modulation of immune responses [56]. The identified immunological changes correlated with improved physical performance, revealing the holistic systemic effect on the participants' bodies [51, 56]. Evidence shows that traditional moderate physical activity may have anti-inflammatory effects [39, 42]. Physically active people have comparatively lower plasma concentrations of biological markers of systemic inflammation and heat shock proteins and lower proinflammatory cytokine production in mitogen-stimulated cultures, and peripheral blood monocytes express lesser Toll receptors in their membranes [42]. The effects of long-term VT on the immune response of elderly women have been studied [57, 58]. Significant changes in the cell-mediated and humoral immunity factors were noted after 12 weeks of training [57]. After 24 weeks of VPE, the main subpopulations of peripheral blood lymphocytes, expression of their activation markers, and serum concentrations of immunoglobulins and cytokines in elderly women maintained at the initial level [58]. According to the authors, obtained data indicate the stability of lymphocyte activation under such influence, which characterizes such physical activity as a weak stress factor for immune function in elderly people and allows for its wide use in medical rehabilitation [53, 58].

Therefore, VS effects are crucial in modulating immune response. Direct and indirect effects on the intestinal microbiome, lymphatic clearance of metabolites, and local immune-inflammatory responses in VPE alter T-cell differentiation, cause a shift in macrophages, and modulate proinflammatory and anti-inflammatory cytokine levels [59–61]. However, stress associated with excessive physical activity can disharmonize the immune function and contribute to decreased immune reactivity to infectious agents, and decreased immunological activation and immune inflammation can be one of the mechanisms that provide positive effects of regular, moderate physical exercise; therefore, any physical activity demonstrates dose-dependent effects on the immune response system and should be limited in intensity and duration, exceeding which causes general metabolic and immune disorders [37, 62–64].

MODULATION OF NERVOUS SYSTEM ACTIVITY

Initially, the practical use of VT was aimed at improving muscle and musculoskeletal function; however, as the clinical application of VS developed, the potential impact of this nondrug method on the nervous system became more evident [18, 21, 65, 66]. The fundamental and clinical effects of VS on various aspects of brain function have been studied in healthy volunteers and animals, including models of various neuroinflammatory and neurodegenerative diseases [65–70]. Studies in animal models have found that 5 weeks of VT induce a positive effect on the cognitive performance of 18- and 30-month-old rats; the treatment demonstrated potential

in reducing anxiety, significantly improved spatial memory and rearing behavior, and increased the overall motor activity of experimental animals [71].

Complex studies of the effects of VS on neuronal function, synaptic protein expression, and neurotrophic factor levels in a rat model of chronic depression induced by restraint stress showed significant activation of neuroprotection and neuronal recovery [72]. The proposed mechanisms of such effects include inhibition of neuronal degeneration processes, reactive microgliosis and astrocyte atrophy, protective isolation of synapses, strengthening of neuronal connections, restoring impaired cellular memory, reducing dendritic and axonal damage, modulating the glymphatic pathway for removal of cerebral metabolic products, and increasing expression of neurotrophic factors [47, 73, 74]. In particular, VPE may promote neuroprotection by modulating the levels of neurotrophins and anti-inflammatory agents such as IGF-1, BDNF, and IL-10 [73]. In preclinical studies, VS has shown promising results in mitigating prefrontal cortex damage and dysfunction [75]. Moreover, activation of the SESN2/AMPK/PGC-1 α signaling pathway, which alleviates oxidative stress and local inflammation, was identified as a key mechanism mediating this effect [75, 76].

Moderate physical exercise induces a positive effect on the psychophysiological status, motor activity, and cognitive abilities of the elderly [77, 78]. Moreover, in cases where traditional physical activity is impossible owing to various limitations and concomitant pathology, VPE can be used as a form of active-passive training to achieve the required results comparable to those in physical exercise and rehabilitation, including in relation to cognitive productivity [77–80]. In some clinical studies, when exposed to VS with a frequency of 30 Hz and a session duration of <30 min per day, 4 days a week for 5 weeks, elderly people showed positive results in the Stroop test, indicating an improvement in selective attention and inhibition [80]. In a study of young participants, despite the absence of cognitive impairment, even short-term exposure showed improvement in the Stroop Color and Word Test scores and a positive effect on executive cognitive functions [81]. These reveal the potential of VPE as an adjunct to cognitive enhancement therapy programs [81, 82]. Meta-analyses and narrative reviews reported that VT demonstrates improvements in motor skills, reaction time, information processing speed, sensorimotor integration, and global executive functions [65, 78, 83, 84]. The beneficial effects extended to patients with relevant deficits, including cognitive or sensorimotor coordination impairments [85–90]. Moreover, studies have shown improvements in attention, memory, and thinking in children with attention-deficit/hyperactivity disorder and in cognitive abilities and other higher integrative brain functions in patients with multiple sclerosis, Parkinson's disease, Alzheimer dementia, and stroke [83–90].

SUMMARY ANALYSIS OF THE POTENTIAL IMPACT OF TECHNOLOGY ON NEUROIMMUNE INTERACTIONS

According to experimental and clinical studies, VS in the appropriate modes modulates the nervous regulation processes and higher integrative functions of the brain, including improvement of balance, coordination of movements and neuromuscular function, and development of cognitive performance and global executive functions, which determines the therapeutic potential and effectiveness of the method for people with neurological disorders [65, 71, 78, 83, 91–94]. Descriptive and systematic analyses of the outcomes of such effects on cellular and molecular pathways involved in immune and neural communication demonstrated the efficacy of VPE as a nondrug intervention to correct the corresponding deficit, which remains a debatable participant. The results may be beneficial in planning the design and protocols of future studies investigating such effects [76, 95, 96].

VS directly and indirectly affects the immune function by modulating T-cell differentiation and cytokine profile and initiating positive changes in the gut microbiome [27, 33, 40, 43, 49, 97–99]. This technology impacts the levels of proinflammatory and anti-inflammatory markers, which together shows a regulatory role in the immune response and systemic reactions [27, 33, 98]. The beneficial effects of VT in various neurological disorders may be mediated by cellular pathways that play a significant regulatory role in neuroinflammation, neuroprotection, and neurotransmission [40, 69, 89, 99]. Thus, at the molecular level, VS demonstrates involvement of several inflammatory/anti-inflammatory biomarkers (IL-1, IL-6, IL-10, CRP, and TNF- α) and neurotransmitters, such as acetylcholine, norepinephrine, dopamine, and serotonin, and neurotrophic factors, particularly TNFR-1, TNFR-2, IGF-1, and BDNF, in the modulation [27, 40, 58, 97–99].

Despite evidence of numerous clinical effects of VPE, the specific mechanisms by which intense proprioceptive stimulation in VPE modulates functional responses of the nervous system and immune response require further scientific investigation and discussion [27, 47, 53, 77]. By increasing scientific awareness, which is a basic goal of descriptive and systematic reviews, the present study can serve as an additional impetus for critical analysis of the available body of data, search for new solutions and relationships, and stimulation of basic and applied research of acute and long-term effects of VS. Further study of the effect of VPE in animal models and in humans of different age groups will contribute to a deeper understanding of the mechanisms of influence not only on neuroimmune communication but also on human health in general.

CONCLUSION

Experimental and clinical data show positive effects of VT on the immune response and higher integrative functions of the brain and demonstrate broad therapeutic potential. The present study combines and systematizes the available data of the last 20 years on the cellular and systemic effects of intense neuromuscular activation induced by VS on immune function and the central nervous system and emphasizes the importance of studying the fundamental mechanisms of such effects for the development of more optimal protocols for experimental and clinical studies in this area.

ADDITIONAL INFORMATION

Author contributions: Sh.I.V.: conceptualization, writing—original draft, writing—review & editing; P.O.N.: writing—review & editing, supervision; G.O.N.: investigation, methodology; M.P.M.: investigation, writing—original draft. All authors approved the version of the manuscript to be published and agreed to be accountable for all aspects of the work, ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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ДОПОЛНИТЕЛЬНАЯ ИНФОРМАЦИЯ

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Этическая экспертиза. Неприменимо.

Источники финансирования. Отсутствуют.

Раскрытие интересов. Авторы заявляют об отсутствии отношений, деятельности и интересов за последние три года, связанных с третьими лицами (коммерческими и некоммерческими), интересы которых могут быть затронуты содержанием статьи.

Оригинальность. При создании настоящей работы были использованы фрагменты собственного текста и данные, опубликованные ранее ([Пятин В.Ф., Шиrolapov И.В., Жестков А.В., и др. Иммунологические показатели периферической крови женщин пожилого возраста при равноускоренном тренинге: результаты 12-недельного исследования // Медицинская иммунология. 2010. Т. 12, № 4–5. С. 413–416]; [Пятин В.Ф., Жестков А.В., Шиrolapov И.В., и др. Адаптационные возможности системы иммунитета женщин пожилого возраста в условиях равноускоренного тренинга: результаты 24-недельного исследования // Аллергология и иммунология. 2010. Т. 11, № 1. С. 42–47]). Ссылки представлены в списке литературы.

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