DOI: 10.56871/RBR.2024.77.24.006
UDC 616.839-036.1+616.72-002.77+616.832-004.2+796.012.62

THE ROLE OF PHYSICAL ACTIVITY IN RHEUMATOLOGIC PATIENTS WITH DISTURBANCES OF VEGETATIVE REGULATION

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For citation: Akhmetova A, Basina AA, Salah Sh., Leineman YaA, Gavrilova NYu, Utekhin VI. The role of physical activity in rheumatologic patients with disturbances of vegetative regulation. Russian Biomedical Research. 2024;9(3):42–52. DOI: https://doi.org/10.56871/RBR.2024.77.24.006

Received: 30.05.2024 **Revised: 26.07.2024** **Accepted: 16.09.2024**

Abstract. The autonomic nervous system regulates all internal processes of the body, thus ensuring homeostasis. A disturbance in the balance of the autonomic nervous system can lead to clinical manifestations of autonomic dysfunction, often described in rheumatologic patients. Clinical manifestations of autonomic dysfunction vary widely in patients with rheumatoid arthritis (33–86% of cases) and systemic lupus erythematosus (9–90% of cases). The phenomena of dysautonomia in rheumatologic patients may manifest before the manifestation of specific symptoms of the disease. Signs of autonomic dysfunction reduce the quality of life of patients and pose a diagnostic challenge because of the variability of the clinical picture. An important aspect in the treatment of dysautonomia is early detection and a multidisciplinary approach. This review presents evidence that there is a positive effect of regular exercise in rheumatologic patients. It is important to remember that not all patients can be physically active due to chronic pain syndrome, joint swelling and deformity, limited spinal mobility, impaired thermoregulation and other clinical manifestations. Regular exercise can help restore the balance between the sympathetic and peripheral nervous systems. An exercise program as part of rehabilitation is developed individually based on the patient's complaints and physical parameters (strength, endurance, balance and coordination).

Keywords: autonomic dysfunction, dysautonomia, rheumatologic diseases, multiple sclerosis, physical exercises

К ВОПРОСУ О РОЛИ ФИЗИЧЕСКИХ НАГРУЗОК У ПАЦИЕНТОВ РЕВМАТОЛОГИЧЕСКОГО ПРОФИЛЯ С НАРУШЕНИЯМИ ВЕГЕТАТИВНОЙ РЕГУЛЯЦИИ

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Для цитирования: Ахметова А., Басина А.А., Салах Ш., Лейнеман Я.А., Гаврилова Н.Ю., Утехин В.И. К вопросу о роли физических нагрузок у пациентов ревматологического профиля с нарушениями вегетативной регуляции// Российские биомедицинские исследования. 2024. Т. 9. № 3. С. 42–52. DOI: https://doi.org/10.56871/RBR.2024.77.24.006

Поступила: 30.05.2024 **Одобрена: 26.07.2024** **Принята к печати: 16.09.2024**

Резюме. Вегетативная нервная система регулирует все внутренние процессы организма, обеспечивая тем самым гомеостаз. Нарушение баланса в работе вегетативной нервной системы способно привести к клиническим проявлениям вегетативной дисфункции, нередко описываемой у больных ревматологического профиля. Клинические проявления вегетативной дисфункции варьируют в широких пределах у пациентов с ревматоидным артритом (33–86% случаев) и системной красной волчанкой (9–90% случаев). Явления дизавтономии у пациентов ревматологического профиля могут проявиться до манифестации специфических симптомов заболевания. Признаки вегетативной дисфункции снижают качество жизни пациентов и представляют собой проблему для диагностики из-за вариабельности клинической картины. Важным аспектом в лечении дизавтономии является раннее обнаружение и применение междисциплинарного подхода. В обзоре представлены данные, свидетельствующие о наличии положительного влияния регулярных тренировок на пациентов ревматологического профиля. Важно помнить, что не все пациенты могут быть физически активными из-за хронического болевого синдрома, отека и деформации суставов, ограниченной подвижности позвоночника, нарушений терморегуляции и других клинических проявлений. Регулярные физические упражнения могут способствовать восстановлению баланса между симпатической и периферической нервными системами. Программа тренировок как часть реабилитации разрабатывается индивидуально на основе жалоб пациента и его физических показателей (силы, выносливости, равновесия и координации).

Ключевые слова: вегетативная дисфункция, дизавтономия, ревматологические заболевания, рассеянный склероз, физические упражнения

INTRODUCTION

The group of pathologies of the rheumatological profile includes rheumatoid arthritis, systemic lupus erythematosus, ankylosing spondylitis, gouty arthritis, multiple sclerosis and others. Pathologies of the rheumatological profile are characterized by a multitude of systemic manifestations and a high degree of disability of patients.

In recent years, the role of the autonomic nervous system in the pathogenesis of these diseases has been increasingly discussed [5, 45]. The possibility of its training to improve the quality of life of patients has been discussed too [19]. Therefore, special attention is paid to the possibility of regulating autonomic tone through physical rehabilitation.

AIM

The aim of the review is to provide an up-to-date view of the relationship between the autonomic nervous system and physical activity in rheumatologic patients.

THE AUTONOMIC NERVOUS SYSTEM AND EXERCISES

The autonomic nervous system (ANS) plays an important role in the regulation of various body functions, including the cardiovascular system (CVS). Such parameters as the heart rate (HR), conduction, myocardial contraction and relaxation force are influenced by the balance of the parasympathetic and sympathetic nervous system. When a person transitions from rest to exercise, both ANS structures must function throughout the duration of exercise, and therefore the ANS response during the transition from rest to exercise is considered to be quite complex [62].

Successful functioning of the autonomic nervous system is based on rapid analysis by brain structures of incoming information from various receptors (in blood vessels, skeletal muscles, heart, lungs) and development of an adequate response. The response is realized by the peripheral part of the nervous system, releasing the neurotransmitters acetylcholine and noradrenaline from nerve fiber endings [54]. Such signals are received by the heart, adrenal glands, and vascular smooth muscle. Changes in sympathic and vagus balance depend on the type of exercise (isometric, isotonic or isokinetic), its intensity and duration [18]. At the beginning of exercise, there is an immediate decrease in cardiac vagus nerve tone, which leads to an increase in the HR, ventricular contractility, stroke volume and, as a consequence, cardiac output [38].

The contribution of the peripheral nervous system to HR is thought to be highest during low-intensity exercise and

decreases proportionally as exercise intensity increases, especially when HR reaches 100 beats per minute or more [28]. In contrast, the contribution of the sympathetic nervous system increases linearly with increasing exercise intensity. Activation of the sympathetic nervous system and subsequent release of adrenaline from the adrenal medulla contribute to an increase in HR and ventricular contractility and cause vasoconstriction in untrained muscles and internal organs, thus redistributing cardiac output toward actively working muscles.

Physical exercise activates the release of muscle metabolites stimulating α-adrenoreceptors, which leads to a decrease in the effectiveness of sympathetic vasoconstrictor influences (functional sympatholysis) [61]. Upon cessation of exercise, there is a rapid recovery of HR, followed by a gradual decrease in HR that takes several minutes [39, 43]. Athletes with good physical training have higher activity of the peripheral nervous system. Athletes show a rapid recovery of HR after cessation of training [43] and a significant decrease in resting HR [4, 12]. Thus, the balance of the autonomic nervous system is important for proper cardiovascular response during exercise and for human well-being [28].

Changes in the balance of both the sympathetic nervous system and the peripheral nervous system can lead to clinical manifestations of autonomic dysfunction. These can be characterized by a wide range of symptoms, including neurological (headache, sleep disturbances), cardiovascular (tachy- or bradycardia, hyper- or hypotension, orthostatic disorders), pulmonary (dyspnea), gastrointestinal (nausea, abdominal bloating, diarrhea or constipation, abdominal pain), genitourinary (neurogenic bladder, erectile dysfunction), secretomotor (sweating problems, dry mouth, dry eyes), vasomotor (extremity coldness, Raynaud's phenomenon), and visual (impaired pupil response to the light, tunnel vision, double vision, blurred vision, hypersensitivity to light) [46].

AUTONOMIC DISORDERS IN PATIENTS WITH RHEUMATOLOGIC DISEASES

The great variability of autonomic nervous system lesions in rheumatologic patients is most likely related to nonspecific symptoms of dysautonomia, small statistical samples in studies, and the lack of a unified approach to the examination of patients with suspected autonomic dysfunction [71]. For example, in patients with rheumatoid arthritis, ANS lesions ranges from 33 to 86% [8], and in systemic lupus erythematosus they ranges from 9 to 90% [40, 71].

The most studied manifestation of autoimmune dysautonomia is the development of cardiovascular dysfunction [71]. The increased cardiovascular risk in patients with rheumatologic diseases, especially rheumatoid arthritis (RA) (mortality is more than 50%) [2, 38] and systemic lupus erythematosus (SLE) (mortality is from 17% to 76%) [35, 51], is not fully explained by the presence of traditional risk factors (smoking, arterial hypertension, hypercholesterolemia, diabetes mellitus). The results of most studies indicate that decreased parasympathetic activity, increased sympathetic activity, altered heart rate variability and cardiac reflex activity are predictors of a higher incidence of cardiovascular disease and mortality in these patients [8].

DYSAUTONOMIA IN PATIENTS WITH RHEUMATOID ARTHRITIS

Signs of dysautonomia in rheumatologic patients may develop first before the onset of clinical symptoms of the main disease. Patients with rheumatoid arthritis have the following symptoms of autonomic imbalance: cyanosis, peripheral vasospasm, orthostatic hypotension, or postural tachycardia syndrome [8]. It has been suggested that decreased parasympathetic activity may be a part of the pathogenesis of rheumatoid arthritis [49]. It is necessary to search for significant correlations between dysautonomia and such characteristics as the duration of the initial disease, its activity, and the index of structural damage in patients with rheumatoid arthritis [71].

AUTONOMIC DISORDERS IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

Autonomic nervous system dysfunction is common in patients with systemic lupus erythematosus. Various cardiovascular cardiovascular Ewing reflex tests (Valsalva test, deep breathing test, orthostatic test, isometric exercise test) are used for its evaluation. Patients with SLE had significantly more positive tests for ANS dysfunction compared to healthy individuals. In addition, there is evidence that autonomic nervous system dysfunction does not correlate with clinical neuropsychiatric manifestations or immunoserologic markers such as antiphospholipid antibodies [70]. These data suggest that ANS dysfunction may be common in patients with SLE even in the absence of specific clinical manifestations, emphasizing the importance of monitoring of autonomic function in patients with SLE [70].

AUTONOMIC REGULATION DISORDERS IN PATIENTS WITH MULTIPLE SCLEROSIS

Dysautonomia has been documented in 45–84% of patients with multiple sclerosis (MS) [7, 21]. Autonomic

dysfunction in patients with multiple sclerosis is manifested by a variety of symptoms, including cardiovascular, genitourinary, and thermoregulatory dysfunction, sweating disorders, and signs of sexual dysfunction [7]. Disturbance of autonomic regulation of cardiovascular system can occur in the absence of clinical manifestations of the main disease [1, 6]. Both parasympathetic and sympathetic components of the cardiovascular system are selectively affected at different stages of multiple sclerosis [29, 50, 53, 76]. Parasympathetic dysfunction has been shown to correlate with increasing scores on the Disability rating scale and is more common in the late stages of the disease. In contrast, sympathetic dysfunction is associated with an outcome of the disease and thus may be associated with inflammatory mechanisms in multiple sclerosis. Autonomic dysfunction contributes to the increased fatigue felt by patients with multiple sclerosis [30]. As the disease progresses, symptoms of dysautonomia may increase, leading to orthostatic intolerance, sexual dysfunction, and decreased exercise tolerance, which are significantly affect patients' quality of life. Autonomic dysfunction in multiple sclerosis has been attributed to various mechanisms: lesion of autonomic pathways, influence of inflammatory mediators, imbalance of neurotransmitters (acetylcholine and noradrenaline), axonal degeneration, including demyelination of specific structures in the central nervous system that can disrupt ANS regulation [36, 65, 77]. Imbalance between over-activated immune system and autonomic receptors (β- and α-adrenergic and D1-like and D2-like dopamine receptors) on lymphocytes causes increased production of catecholamines by lymphocytes [16, 29]. Other factors that may be involved in autonomic dysfunction in multiple sclerosis are Epstein-Barr virus infection and vitamin D deficiency [10, 52].

DYSAUTONOMIA IN PATIENTS WITH OTHER RHEUMATOLOGIC DISEASES

In systemic scleroderma (SS), increased sympathetic activity impairs microcirculation, and impaired parasympathetic regulation can lead to impaired esophageal motor function even before the manifestation of systemic scleroderma [24]. Autonomic cardiovascular dysfunction associated with right ventricular dysfunction [74], myocardial blood flow dysregulation [34], and arrhythmias preceding the development of fibrosis [17] leads to an increased morbidity and mortality in patients with systemic scleroderma [24]. The early stages of Sjögren's syndrome are also characterized by ANS dysfunction, which causes a decrease in exocrine gland function due to impaired innervation and loss of glandular tissue due to apoptosis [20]. Symptoms such as gastrointestinal dysfunction, impaired sweating and urination, in combination with other signs of peripheral nervous system damage (sensory polyneuropathy) may occur before the onset of dry eye and mouth syndrome and later in the clinical stage [44, 57].

A common group of symptoms that include chronic fatigue, widespread pain, myalgia, arthralgia, cognitive dysfunction, and cardiovascular disorders, gastrointestinal tract and urinary tract disorders, can be described not only in patients with rheumatologic diseases, but also in patients with conditions such as myalgic encephalomyelitis/chronic fatigue syndrome, fibromyalgia (FM), breast implant illness (BII), and syndrome after COVID-19 [67]. It cannot be excluded that autonomic dysfunction in these types of pathology and rheumatologic diseases may share common pathophysiologic autoimmune mechanisms [31, 67].

THE ROLE OF PHYSICAL EXERCISE IN THE RECOVERY OF AUTONOMIC REGULATION IN PATIENTS WITH RHEUMATOLOGIC PROFILE

Regular exercise can be used to rebalance the sympathetic and peripheral nervous system.

It has been demonstrated in patients and animal models with chronic heart disease that exercise can increase vagus nerve modulation and decrease sympathetic tone [32]. Achieving autonomic balance leads to improved cardiovascular and endothelial function, normalization of blood pressure, heart rate variability and cardiorespiratory function with increased oxygen uptake and more efficient redistribution of blood flow. It is generally accepted that these changes are the main result of adaptation to regular exercise [19]. Another important effect of exercise is the induction of neuronal plasticity in autonomic centers of the CNS, such as the nuclei of the vagus nerve, nuclei of the rostral ventrolateral medulla. It has also been shown that exercise during physical rehabilitation causes reorganization of neurochemical connections in the brain, provokes neurogenesis and formation of new synapses, especially in the dentate gyrus of the hippocampus, which improves cognitive abilities [55].

Physical exercise in patients with autoimmune diseases has an immunomodulatory effect due to its effect on the expression of inflammatory marker genes, changes in the levels of hormones such as cortisol and adrenaline that inhibit the secretion of proinflammatory cytokines (tumor necrosis factor (TNF)-α), and decreased expression of toll-like receptors (TLR) on monocytes [27]. Exercise also mechanistically stimulates the promotion of immune cells and immunoglobulins through lymphatic and peripheral tissues, exerting a direct anti-inflammatory effect by

enhancing the production of anti-inflammatory cytokines. The muscle myokine IL-6 produced during exercise has a direct anti-inflammatory effect by improving glucose and lipid metabolism [58, 69].

Thus, physical exercise can serve as an additional therapy to standard immunomodulatory and immunosuppressive drugs.

Exercise is especially indicated in systemic diseases with possible impairment of self-care, as in the case of multiple sclerosis. However, patients with multiple sclerosis have motor impairment as a consequence of muscle weakness, they have impaired walking mechanics, balance problems; spasticity and fatigue complete the picture, which reduces their adherence to regular exercise [36]. Additional limitations are associated with worsening symptoms of autonomic dysfunction. Patients with multiple sclerosis may have impaired thermoregulation due to impaired sweating [42], and this makes potentially dangerous the exercise in hot conditions. Symptoms such as spasticity or paresis as the disease progresses are often irreversible, preventing patients from exercising. Moreover, these symptoms worsen with decreased physical activity. At the same time, it is well known that exercise alleviates conditions associated with hypodynamia [26]. There is evidence of a positive effect of exercise training on muscle strength in people with multiple sclerosis. Results from randomized controlled trials have shown that muscle strength increases after strength training [15, 18, 22, 23, 25, 63, 75, 78], combined aerobic exercise [48], and aquatic training [33]. Robotic mechanotherapy with the use of exoskeleton in patients with gait disturbance in multiple sclerosis allows to increase the speed and distance of walking [13]. There is evidence that progressive muscle overload training, which involves gradually increasing the weight of sports equipment or increasing the number of repetitions, improves lower limb muscle strength in people with multiple sclerosis, and these improvements are limited to the muscle groups targeted by the training [47]. Physical exercise in MS helps to restore movement coordination, stabilize balance, strengthen muscle tissue, eliminate increased spasticity, and normalize muscle tone despite the damage of the nervous system [3].

An individualized exercise program, which is recommended to be included as part of rehabilitation, should be designed taking into account the patient's chief complaints, strength, endurance, balance, coordination, and fatigue [37]. It is promising to further investigate the effects of exercise in patients with multiple sclerosis, including the effects of physical rehabilitation on cellular processes such as muscle protein synthesis, mitochondrial biogenesis, and changes in muscle fiber composition, to understand how physical activity may contribute to improving the quality of life of people with this disease [14].

A number of studies have shown the effectiveness of both endurance and weight training in improving the quality of life in people with rheumatologic diseases [60, 66]. Patients with these pathological conditions are more prone to the development of cardiovascular disease as a result of the systemic action of inflammatory mediators and are predisposed to metabolic changes due to elevated glucocorticoid levels. Unfortunately, patients with rheumatologic diseases have many reasons to be physically inactive. Chronic pain syndrome, joint swelling and deformity, limited spinal mobility, muscle weakness, fatigue, and skin rashes all contribute to patients' low adherence to an active lifestyle.

Regular physical activity is safe and well tolerated by most patients with rheumatologic diseases such as systemic lupus erythematosus, rheumatoid arthritis, systemic scleroderma, and Sjögren's syndrome [59, 66, 72]. However, there are groups of patients, predominantly with cardiac and pulmonary lesions, in whom exercise may not result in clear beneficial effects [66]. Antonioli et al. [9], who studied a group of patients with systemic scleroderma, demonstrated that exercise is useful in improving exercise tolerance by reducing the HR and dyspnea scores. Endurance and weight-bearing exercises significantly improve performance (e.g., walking time in the Cooper test) and reduce fatigue in patients with rheumatic diseases [41].

It is interesting that a recent meta-analysis of home-based exercise programs as part of the treatment plan for patients with rheumatologic diseases showed that physical activity significantly improves quality of life ($p < 0.01$), increases functional capacity ($p = 0.04$), reduces disease activity ($p = 0.03$), and decreases subjective feelings of pain ($p = 0.01$) compared to patients who do not perform any physical activity. Moreover, it has been concluded that the use of home exercise programs is as effective as exercise programs in a medical institution [68]. It is known that for patients with SLE and Sjögren's syndrome, fatigue is essentially a disabling symptom. A low-intensity exercise program is able to cause a subjective reduction in the feeling of fatigue in Sjögren's syndrome [73] and in patients with SLE [11].

Evaluation of physical activity and fatigue in patients with rheumatoid arthritis has shown that patients with a high level of daily physical activity have less fatigue. The authors noted that patients complain of increased pain and fatigue at the beginning of exercise and that symptoms decreases with continued physical activity [64].

Hypodynamia in patients with rheumatic diseases is extremely harmful both physically (decreased muscle strength, increased muscle stiffness, worsening of the condition) and psychologically (a fear of movement, depres-

sion, loss of self-confidence). It is necessary to offer patients adapted aerobic exercises with moderate intensity, which can be gradually increased as the condition improves [56].

CONCLUSION

Physical exercises during rehabilitation in rheumatologic patients with autonomic dysregulation contribute to the reorganization of neurochemical connections in the brain, neurogenesis and formation of new synapses, which improves cognitive abilities.

Exercise programs in rheumatologic patients with autonomic dysregulation have an immunomodulatory effect, reducing the level of inflammatory cytokines and stimulating the immune system, contributing to an improvement in quality of life, functional capacity and reduction of disease activity. Physical rehabilitation through exercise improves cellular processes such as muscle protein synthesis and mitochondrial biogenesis, which can lead to improved quality of life.

An individual approach to the development of exercise programs, which takes into account the patient's physical parameters and complaints, is an important aspect of successful rehabilitation. Further study of the effect of regular physical training on rheumatologic patients is necessary to fully understand the mechanisms of action of exercise and to develop optimal exercise programs for these patients. Regular physical training can be used to balance the activity of the sympathetic and parasympathetic nervous systems.

ADDITIONAL INFORMATION

Authors' contribution. Thereby, all authors made a substantial contribution to the conception of the study, acquisition, analysis, interpretation of data for the work, drafting and revising the article, final approval of the version to be published and agree to be accountable for all aspects of the study.

Competing interests. The authors declare that they have no competing interests.

Funding source. This study was not supported by any external sources of funding.

ДОПОЛНИТЕЛЬНАЯ ИНФОРМАЦИЯ

Вклад авторов. Все авторы внесли существенный вклад в разработку концепции, проведение исследования и подготовку статьи, прочли и одобрили финальную версию перед публикацией.

Конфликт интересов. Авторы декларируют отсутствие явных и потенциальных конфликтов интересов, связанных с публикацией настоящей статьи.

Источник финансирования. Авторы заявляют об отсутствии внешнего финансирования при проведении исследования.

REFERENCES

1. Basina A.A., Ahmetova A., Gavrilova N.Yu., Soprun L.A., Volovnikova V.A., Utekhin V.I., Churilov L.P. Neuropathy of small fibers in the pathogenesis of postcovid syndrome. Russian Biomedical Research. 2024;9(1):78–87. DOI: 10.56871/RBR.2024.47.88.009. (In Russian).
2. Gonchar N.V., Slizovskij N.V. Pathogenetic significance of comorbidity of juvenile rheumatoid arthritis and components of metabolic syndrome (literature review). Children's Medicine of the North-West. 2021;9(4):23–32. (In Russian).
3. Ereshko N.E., Beteva M.M. Lechebnaya fizicheskaya kul'tura pri rasseyannom skleroze. Therapeutic physical culture in multiple sclerosis. Scientific and educational basics in physical culture and sports. 2022;(4):46–51. DOI: 10.57006/2782-3245-2022-8-4-46-51. (In Russian).
4. Zemcovskij E.V., Tihonenko V.M., Reeva S.V., Demidova M.M. Functional diagnostics of the state of the autonomic nervous system. Saint Petersburg: Institut kardiologicheskoj tekhniki, 2004. EDN: WTQHQJ. (In Russian).
5. Reeva S.V. Assessment of autonomic regulation in young people. Pediatr. 2016;7(3):70–75. DOI: 10.17816/PED7370-75. (In Russian).
6. Acevedo A.R., Nava C., Arriada N. et al. Cardiovascular dysfunction in multiple sclerosis. Acta Neurol Scand. 2000;101(2):85–88. DOI: 10.1034/j.1600-0404.2000.101002085.x.
7. Adamec I., Krbot Skorić M., Habek M. Understanding and managing autonomic dysfunction in persons with multiple sclerosis. Expert Rev Neurother. 2021;21(12):1409–1417. DOI: 10.1080/14737175.2021.1994856.
8. Adlan A.M., Lip G.Y., Paton J.F. et al. Autonomic function and rheumatoid arthritis: a systematic review. Semin Arthritis Rheum. 2014;44(3):283–304. DOI: 10.1016/j.semarthrit.2014.06.003.
9. Antonioli C.M., Bua G., Frigè A. et al. An individualized rehabilitation program in patients with systemic sclerosis may improve quality of life and hand mobility. Clin Rheumatol. 2009;28(2):159–165. DOI: 10.1007/s10067-008-1006-x.
10. Ascherio A. Epstein–Barr virus in the development of multiple sclerosis. Expert Rev Neurother. 2008;8(3):331–333. DOI: 10.1586/14737175.8.3.331.
11. Ayán C., de Pedro-Múñez A., Martínez-Lemos I. Efectos del ejercicio físico en personas con lupus eritematoso sistémico: revisión sistemática [Effects of physical exercise in a population with systemic lupus erythematosus: A systematic review. Semergen. 2018;44(3):192–206. DOI: 10.1016/j.semerg.2017.12.002.
12. Barney J.A., Ebert T.J., Groban L. et al. Carotid baroreflex responsiveness in high-fit and sedentary young men. J Appl Physiol (1985). 1988;65(5):2190–2194. DOI: 10.1152/jappl.1988.65.5.2190.

13. Beer S., Aschbacher B., Manoglou D. et al. Robot-assisted gait training in multiple sclerosis: a pilot randomized trial. Mult Scler. 2008;14(2):231–236. DOI: 10.1177/1352458507082358.
14. Benito-León J. Physical activity in multiple sclerosis: the missing prescription. Neuroepidemiology. 2011;36(3):192–193. DOI: 10.1159/000328276.
15. Broekmans T., Roelants M., Alders G. et al. Exploring the effects of a 20-week whole-body vibration training programme on leg muscle performance and function in persons with multiple sclerosis. J Rehabil Med. 2010;42(9):866–872. DOI: 10.2340/16501977-0609.
16. Cosentino M., Marino F. Adrenergic and dopaminergic modulation of immunity in multiple sclerosis: teaching old drugs new tricks? J Neuroimmune Pharmacol. 2013;8(1):163–179. DOI: 10.1007/s11481-012-9410-z.
17. Cozzolino D., Naclerio C., Iengo R. et al. Cardiac autonomic dysfunction precedes the development of fibrosis in patients with systemic sclerosis. Rheumatology (Oxford). 2002;41(5):586–588. DOI: 10.1093/rheumatology/41.5.586.
18. Dalgas U., Stenager E., Jakobsen J. et al. Resistance training improves muscle strength and functional capacity in multiple sclerosis. Neurology. 2009;73(18):1478–1484. DOI: 10.1212/WNL.0b013e3181bf98b4.
19. Daniela M., Catalina L., Ilie O. et al. Effects of exercise training on the autonomic nervous system with a focus on anti-inflammatory and antioxidants effects. Antioxidants (Basel). 2022;11(2):350. DOI: 10.3390/antiox11020350.
20. Dawson L.J., Fox P.C., Smith P.M.. Sjogrens syndrome — the non-apoptotic model of glandular hypofunction. Rheumatology (Oxford). 2006;45(7):792–798. DOI: 10.1093/rheumatology/kel067.
21. de Seze J., Stojkovic T., Gauvrit J.Y. et al. Autonomic dysfunction in multiple sclerosis: cervical spinal cord atrophy correlates. 2001;248(4):297–303. DOI: 10.1007/s004150170204. Erratum in J Neurol 2001;248(12):1111.
22. de Souza-Teixeira F., Costilla S., Ayán C. et al. Effects of resistance training in multiple sclerosis. Int J Sports Med. 2009;30(4):245–250. DOI: 10.1055/s-0028-1105944.
23. DeBolt L.S., McCubbin J.A. The effects of home-based resistance exercise on balance, power, and mobility in adults with multiple sclerosis. Arch Phys Med Rehabil. 2004;85(2):290-–297. DOI: 10.1016/j.apmr.2003.06.003.
24. Di Franco M., Paradiso M., Riccieri V. et al. Autonomic dysfunction and microvascular damage in systemic sclerosis. Clin Rheumatol. 2007;26(8):1278–1283. DOI: 10.1007/s10067-006-0492-y.
25. Dodd K.J., Taylor N.F., Shields N. et al. Progressive resistance training did not improve walking but can improve muscle performance, quality of life and fatigue in adults with multiple sclerosis: a randomized controlled trial. Mult Scler. 2011;17(11):1362–1374. DOI: 10.1177/1352458511409084.
26. Döring A., Pfueller C.F., Paul F. et al. Exercise in multiple sclerosis — an integral component of disease management. EPMA J. 2011;3(1):2. DOI: 10.1007/s13167-011-0136-4.
27. Einstein O., Katz A., Ben-Hur T. Physical exercise therapy for autoimmune neuroinflammation: Application of knowledge from animal models to patient care. Autoimmun Rev. 2022;21(4):103033. DOI: 10.1016/j.autrev.2022.103033.
28. Fisher J.P., Young C.N., Fadel P.J. Autonomic adjustments to exercise in humans. Compr Physiol. 2015;5(2):475–512. DOI: 10.1002/cphy.c140022.
29. Flachenecker P., Reiners K., Krauser M. et al. Autonomic dysfunction in multiple sclerosis is related to disease activity and progression of disability. Mult Scler. 2001;7(5):327–334. DOI: 10.1177/135245850100700509.
30. Flachenecker P., Rufer A., Bihler I. et al. Fatigue in MS is related to sympathetic vasomotor dysfunction. Neurology. 2003;61(6):851–853. DOI: 10.1212/01.wnl.0000080365.95436.b8.
31. Freitag H., Szklarski M., Lorenz S. et al. Autoantibodies to vasoregulative G-protein-coupled receptors correlate with symptom severity, autonomic dysfunction and disability in myalgic encephalomyelitis/chronic fatigue syndrome. J Clin Med. 2021;10(16):3675. DOI: 10.3390/jcm10163675.
32. Fu Q., Levine B.D. Exercise and the autonomic nervous system. Handb Clin Neurol. 2013;117:147–160. DOI: 10.1016/B978-0-444-53491-0.00013-4.
33. Gehlsen G.M., Grigsby S.A., Winant D.M. Effects of an aquatic fitness program on the muscular strength and endurance of patients with multiple sclerosis. Phys Ther. 1984;64(5):653–657. DOI: 10.1093/ptj/64.5.653.
34. Gigante A., Galea N., Borrazzo C. et al. Role of autonomic dysfunction in the regulation of myocardial blood flow in systemic sclerosis evaluated by cardiac magnetic resonance. Int J Rheum Dis. 2019;22(6):1029–1035. DOI: 10.1111/1756-185X.13569.
35. Gustafsson J.T., Simard J.F., Gunnarsson I. et al. Risk factors for cardiovascular mortality in patients with systemic lupus erythematosus, a prospective cohort study. Arthritis Res Ther. 2012;14(2):R46. DOI: 10.1186/ar3759.
36. Haensch C.A., Jörg J. Autonomic dysfunction in multiple sclerosis. J Neurol. 2006;253(Suppl 1):I3–I9. DOI: 10.1007/s00415-006-1102-2.
37. Halabchi F., Alizadeh Z., Sahraian M.A.et al. Exercise prescription for patients with multiple sclerosis; potential benefits and practical recommendations. BMC Neurol. 2017;17(1):185. DOI: 10.1186/s12883-017-0960-9.
38. Harms C.A., Wetter T.J., McClaran S.R. et al. Effects of respiratory muscle work on cardiac output and its distribution during maximal exercise. J Appl Physiol (1985). 1998;85(2):609–618. DOI: 10.1152/jappl.1998.85.2.609.
39. Hautala A., Tulppo M.P., Mäkikallio T.H. et al. Changes in cardiac autonomic regulation after prolonged maximal exercise. Clin Physiol. 2001;21(2):238–245. DOI: 10.1046/j.1365-2281.2001.00309.x.
40. Hogarth M.B., Judd L., Mathias C.J. et al. Cardiovascular autonomic function in systemic lupus erythematosus. Lupus. 2002;11(5):308–312. DOI: 10.1191/0961203302lu194oa.

41. Hu H., Xu A., Gao C. et al. The effect of physical exercise on rheumatoid arthritis: An overview of systematic reviews and meta-analysis. J Adv Nurs. 2021;77(2):506–522. DOI: 10.1111/jan.14574.
42. Huang M., Jay O., Davis S.L. Autonomic dysfunction in multiple sclerosis: implications for exercise. Auton Neurosci. 2015;188:82–85. DOI: 10.1016/j.autneu.2014.10.017.
43. Imai K., Sato H., Hori M. et al. Vagally mediated heart rate recovery after exercise is accelerated in athletes but blunted in patients with chronic heart failure. J Am Coll Cardiol. 1994;24(6):1529–1535. DOI: 10.1016/0735-1097(94)90150-3.
44. Imrich R., Alevizos I., Bebris L. et al. Predominant glandular cholinergic dysautonomia in patients with primary Sjögren's syndrome. Arthritis Rheumatol. 2015;67(5):1345–1352. DOI: 10.1002/art.39044.
45. Ingegnoli F., Buoli M., Antonucci F. et al. The link between autonomic nervous system and rheumatoid arthritis: from bench to bedside. Front Med (Lausanne). 2020;7:589079. DOI: 10.3389/fmed.2020.589079.
46. Kaur D., Tiwana H., Stino A. et al. Autonomic neuropathies. Muscle Nerve. 2021;63(1):10–21. DOI: 10.1002/mus.27048.
47. Kjølhede T., Vissing K., Dalgas U. Multiple sclerosis and progressive resistance training: a systematic review. Mult Scler. 2012;18(9):1215–1228. DOI: 10.1177/1352458512437418.
48. Konecný L., Pospíšil P., Vank P. et al. Combination of aerobic and resistance training in multiple sclerosis. Scripta Medica Facultatis Medicae Universitatis Brunensis Masarykianae. 2010;83:98–106.
49. Koopman F.A., Tang M.W., Vermeij J. et al. Autonomic dysfunction precedes development of rheumatoid arthritis: a prospective cohort study. EBioMedicine. 2016;6:231–237. DOI: 10.1016/j.ebiom.2016.02.029.
50. Mahovic D., Lakusic N. Progressive impairment of autonomic control of heart rate in patients with multiple sclerosis. Arch Med Res. 2007;38(3):322–325. DOI: 10.1016/j.arcmed.2006.11.009.
51. Malpas S.C. Sympathetic nervous system overactivity and its role in the development of cardiovascular disease. Physiol Rev. 2010;90(2):513–557. DOI: 10.1152/physrev.00007.2009.
52. Mann M.C., Exner D.V., Hemmelgarn B.R. et al. Vitamin D supplementation is associated with improved modulation of cardiac autonomic tone in healthy humans. Int J Cardiol. 2014;172(2):506–508. DOI: 10.1016/j.ijcard.2014.01.058.
53. McDougall A.J., McLeod J.G. Autonomic nervous system function in multiple sclerosis. J Neurol Sci. 2003;215(1-2):79–85. DOI: 10.1016/s0022-510x(03)00205-3.
54. Michael S., Graham K.S., Davis G.M. Oam. Cardiac autonomic responses during exercise and post-exercise recovery using heart rate variability and systolic time intervals — a review. Front Physiol. 2017;8:301. DOI: 10.3389/fphys.2017.00301.
55. Monje M.L., Toda H., Palmer T.D. Inflammatory blockade restores adult hippocampal neurogenesis. Science. 2003;302(5651):1760–1765. DOI: 10.1126/science.1088417.
56. Musumeci G. Effects of exercise on physical limitations and fatigue in rheumatic diseases. World J Orthop. 2015;6(10):762–769. DOI: 10.5312/wjo.v6.i10.762.
57. Newton J.L., Frith J., Powell D. et al. Autonomic symptoms are common and are associated with overall symptom burden and disease activity in primary Sjogren's syndrome. Ann Rheum Dis. 2012;71(12):1973–1979. DOI: 10.1136/annrheumdis-2011-201009.
58. Nieman D.C., Wentz L.M. The compelling link between physical activity and the body's defense system. J Sport Health Sci. 2019;8(3):201–217. DOI: 10.1016/j.jshs.2018.09.009.
59. Oliveira N.C., dos Santos Sabbag L.M., de Sá Pinto A.L. et al. Aerobic exercise is safe and effective in systemic sclerosis. Int J Sports Med. 2009;30(10):728–732. DOI: 10.1055/s-0029-1224180.
60. Rausch Osthoff A.K., Niedermann K., Braun J. et al. 2018 EULAR recommendations for physical activity in people with inflammatory arthritis and osteoarthritis. Ann Rheum Dis. 2018;77(9):1251–1260. DOI: 10.1136/annrheumdis-2018-213585.
61. Remensnyder J.P., Mitchell J.H., Sarnoff S.J. Functional sympatholysis during muscular activity. Observations on influence of carotid sinus on oxygen uptake. Circ Res. 1962;11:370–380. DOI: 10.1161/01.res.11.3.370.
62. Robinson B.F., Epstein S.E., Beiser G.D. et al. Control of heart rate by the autonomic nervous system. Studies in man on the interrelation between baroreceptor mechanisms and exercise. Circ Res. 1966;19(2):400–411. DOI: 10.1161/01.res.19.2.400.
63. Romberg A., Virtanen A., Ruutiainen J. et al. Effects of a 6-month exercise program on patients with multiple sclerosis: a randomized study. Neurology. 2004;63(11):2034–2038. DOI: 10.1212/01.wnl.0000145761.38400.65.
64. Rongen-van Dartel S.A., Repping-Wuts H., van Hoogmoed D. et al. Relationship between objectively assessed physical activity and fatigue in patients with rheumatoid arthritis: inverse correlation of activity and fatigue. Arthritis Care Res (Hoboken). 2014;66(6):852–860. DOI: 10.1002/acr.22251.
65. Saari A., Tolonen U., Pääkkö E. et al. Cardiovascular autonomic dysfunction correlates with brain MRI lesion load in MS. Clin Neurophysiol. 2004;115(6):1473–1478. DOI: 10.1016/j.clinph.2004.01.012.
66. Sharif K., Watad A., Bragazzi N.L. et al. Physical activity and autoimmune diseases: Get moving and manage the disease. Autoimmun Rev. 2018;17(1):53–72. DOI: 10.1016/j.autrev.2017.11.010.
67. Shoenfeld Y., Ryabkova V.A., Scheibenbogen C. et al. Complex syndromes of chronic pain, fatigue and cognitive impairment linked to autoimmune dysautonomia and small fiber neuropathy. Clin Immunol. 2020;214:108384. DOI: 10.1016/j.clim.2020.108384.
68. Sieczkowska S.M., Smaira F.I., Mazzolani B.C. et al. Efficacy of home-based physical activity interventions in patients with autoimmune rheumatic diseases: A systematic review and meta-analysis. Semin Arthritis Rheum. 2021;51(3):576–587. DOI: 10.1016/j.semarthrit.2021.04.004.
69. Simpson R.J., Campbell J.P., Gleeson M. et al. Can exercise affect immune function to increase susceptibility to infection? Exerc Immunol Rev. 2020;26:8–22.
70. Stojanovich L., Milovanovich B., de Luka S.R. et al. Cardiovascular autonomic dysfunction in systemic lupus, rheumatoid arthritis,

primary Sjögren syndrome and other autoimmune diseases. Lupus. 2007;16(3):181–185. DOI: 10.1177/0961203306076223.
71. Stojanovich L. Autonomic dysfunction in autoimmune rheumatic disease. Autoimmun Rev. 2009;8(7):569–572. DOI: 10.1016/j.autrev.2009.01.018.
72. Strömbeck B., Jacobsson L.T. The role of exercise in the rehabilitation of patients with systemic lupus erythematosus and patients with primary Sjögren's syndrome Curr Opin Rheumatol. 2007;19(2):197–203. DOI: 10.1097/BOR.0b013e32801494e3. Erratum in Curr Opin Rheumatol. 2007;19(4):403.
73. Strömbeck B.E., Theander E., Jacobsson L.T. Effects of exercise on aerobic capacity and fatigue in women with primary Sjogren's syndrome. Rheumatology (Oxford). 2007;46(5):868–871. DOI: 10.1093/rheumatology/kem004.
74. Tadic M., Zlatanovic M., Cuspidi C. et al. Systemic sclerosis impacts right heart and cardiac autonomic nervous system. J Clin Ultrasound. 2018;46(3):188–194. DOI: 10.1002/jcu.22552.
75. Taylor N.F., Dodd K.J., Prasad D. et al. Progressive resistance exercise for people with multiple sclerosis. Disabil Rehabil. 2006;28(18):1119–1126. DOI: 10.1080/09638280500531834.
76. Tombul T., Anlar O., Tuncer M. et al. Impaired heart rate variability as a marker of cardiovascular autonomic dysfunction in multiple sclerosis. Acta Neurol Belg. 2011;111(2):116–120.
77. Vita G., Fazio M.C., Milone S. et al. Cardiovascular autonomic dysfunction in multiple sclerosis is likely related to brainstem lesions. J Neurol Sci. 1993;120(1):82–86. DOI: 10.1016/0022-510x(93)90029-x.
78. White L.J., McCoy S.C., Castellano V. et al. Resistance training improves strength and functional capacity in persons with multiple sclerosis. Mult Scler. 2004;10(6):668–674. DOI: 10.1191/1352458504ms1088oa.

ЛИТЕРАТУРА

1. Басина А.А., Ахметова А., Гаврилова Н.Ю., Сопрун Л.А., Воловникова В.А., Утехин В.И., Чурилов Л.П. Нейропатия малых волокон в патогенезе постковидного синдрома. Российские биомедицинские исследования. 2024;9(1):78–87. DOI: 10.56871/RBR.2024.47.88.009.
2. Гончар Н.В., Слизовский Н. В. Патогенетическое значение коморбидности ювенильного ревматоидного артрита и компонентов метаболического синдрома (обзор литературы). Детская медицина Северо-Запада) 2021;9(4):23–32.
3. Ерешко Н.Е., Бетева М.М. Лечебная физическая культура при рассеянном склерозе. Научные и образовательные основы в физической культуре и спорте. 2022;(4):46–51. DOI: 10.57006/2782-3245-2022-8-4-46-51.
4. Земцовский Э.В., Тихоненко В.М., Реева С.В., Демидова М.М. Функциональная диагностика состояния вегетативной нервной системы. Санкт-Петербург: Институт кардиологической техники; 2004. EDN: WTQHQJ.
5. Реева С.В. Оценка вегетативной регуляции у лиц молодого возраста Педиатр. 2016;7(3):70–75. DOI: 10.17816/PED7370-75.
6. Acevedo A.R., Nava C., Arriada N. et al. Cardiovascular dysfunction in multiple sclerosis. Acta Neurol Scand. 2000;101(2):85–88. DOI: 10.1034/j.1600-0404.2000.101002085.x.
7. Adamec I., Krbot Skorić M., Habek M. Understanding and managing autonomic dysfunction in persons with multiple sclerosis. Expert Rev Neurother. 2021;21(12):1409–1417. DOI: 10.1080/14737175.2021.1994856.
8. Adlan A.M., Lip G.Y., Paton J.F. et al. Autonomic function and rheumatoid arthritis: a systematic review. Semin Arthritis Rheum. 2014;44(3):283–304. DOI: 10.1016/j.semarthrit.2014.06.003.
9. Antonioli C.M., Bua G., Frigè A. et al. An individualized rehabilitation program in patients with systemic sclerosis may improve quality of life and hand mobility. Clin Rheumatol. 2009;28(2):159–165. DOI: 10.1007/s10067-008-1006-x.
10. Ascherio A. Epstein–Barr virus in the development of multiple sclerosis. Expert Rev Neurother. 2008;8(3):331–333. DOI: 10.1586/14737175.8.3.331.
11. Ayán C., de Pedro-Múñez A., Martínez-Lemos I. Efectos del ejercicio físico en personas con lupus eritematoso sistémico: revisión sistemática [Effects of physical exercise in a population with systemic lupus erythematosus: A systematic review. Semergen. 2018;44(3):192–206. DOI: 10.1016/j.semerg.2017.12.002.
12. Barney J.A., Ebert T.J., Groban L. et al. Carotid baroreflex responsiveness in high-fit and sedentary young men. J Appl Physiol (1985). 1988;65(5):2190–2194. DOI: 10.1152/jappl.1988.65.5.2190.
13. Beer S., Aschbacher B., Manoglou D. et al. Robot-assisted gait training in multiple sclerosis: a pilot randomized trial. Mult Scler. 2008;14(2):231–236. DOI: 10.1177/1352458507082358.
14. Benito-León J. Physical activity in multiple sclerosis: the missing prescription. Neuroepidemiology. 2011;36(3):192–193. DOI: 10.1159/000328276.
15. Broekmans T., Roelants M., Alders G. et al. Exploring the effects of a 20-week whole-body vibration training programme on leg muscle performance and function in persons with multiple sclerosis. J Rehabil Med. 2010;42(9):866–872. DOI: 10.2340/16501977-0609.
16. Cosentino M., Marino F. Adrenergic and dopaminergic modulation of immunity in multiple sclerosis: teaching old drugs new tricks? J Neuroimmune Pharmacol. 2013;8(1):163–179. DOI: 10.1007/s11481-012-9410-z.
17. Cozzolino D., Naclerio C., Iengo R. et al. Cardiac autonomic dysfunction precedes the development of fibrosis in patients with systemic sclerosis. Rheumatology (Oxford). 2002;41(5):586–588. DOI: 10.1093/rheumatology/41.5.586.
18. Dalgas U., Stenager E., Jakobsen J. et al. Resistance training improves muscle strength and functional capacity in multiple sclerosis. Neurology. 2009;73(18):1478–1484. DOI: 10.1212/WNL.0b013e3181bf98b4.
19. Daniela M., Catalina L., Ilie O. et al. Effects of exercise training on the autonomic nervous system with a focus on anti-inflammatory and antioxidants effects. Antioxidants (Basel). 2022;11(2):350. DOI: 10.3390/antiox11020350.

20. Dawson L.J., Fox P.C., Smith P.M.. Sjogrens syndrome — the non-apoptotic model of glandular hypofunction. Rheumatology (Oxford). 2006;45(7):792–798. DOI: 10.1093/rheumatology/kel067.
21. de Seze J., Stojkovic T., Gauvrit J.Y. et al. Autonomic dysfunction in multiple sclerosis: cervical spinal cord atrophy correlates. 2001;248(4):297–303. DOI: 10.1007/s004150170204. Erratum in J Neurol 2001;248(12):1111.
22. de Souza-Teixeira F., Costilla S., Ayán C. et al. Effects of resistance training in multiple sclerosis. Int J Sports Med. 2009;30(4):245–250. DOI: 10.1055/s-0028-1105944.
23. DeBolt L.S., McCubbin J.A. The effects of home-based resistance exercise on balance, power, and mobility in adults with multiple sclerosis. Arch Phys Med Rehabil. 2004;85(2):290-–297. DOI: 10.1016/j.apmr.2003.06.003.
24. Di Franco M., Paradiso M., Riccieri V. et al. Autonomic dysfunction and microvascular damage in systemic sclerosis. Clin Rheumatol. 2007;26(8):1278–1283. DOI: 10.1007/s10067-006-0492-y.
25. Dodd K.J., Taylor N.F., Shields N. et al. Progressive resistance training did not improve walking but can improve muscle performance, quality of life and fatigue in adults with multiple sclerosis: a randomized controlled trial. Mult Scler. 2011;17(11):1362–1374. DOI: 10.1177/1352458511409084.
26. Döring A., Pfueller C.F., Paul F. et al. Exercise in multiple sclerosis — an integral component of disease management. EPMA J. 2011;3(1):2. DOI: 10.1007/s13167-011-0136-4.
27. Einstein O., Katz A., Ben-Hur T. Physical exercise therapy for autoimmune neuroinflammation: Application of knowledge from animal models to patient care. Autoimmun Rev. 2022;21(4):103033. DOI: 10.1016/j.autrev.2022.103033.
28. Fisher J.P., Young C.N., Fadel P.J. Autonomic adjustments to exercise in humans. Compr Physiol. 2015;5(2):475–512. DOI: 10.1002/cphy.c140022.
29. Flachenecker P., Reiners K., Krauser M. et al. Autonomic dysfunction in multiple sclerosis is related to disease activity and progression of disability. Mult Scler. 2001;7(5):327–334. DOI: 10.1177/135245850100700509.
30. Flachenecker P., Rufer A., Bihler I. et al. Fatigue in MS is related to sympathetic vasomotor dysfunction. Neurology. 2003;61(6):851–853. DOI: 10.1212/01.wnl.0000080365.95436.b8.
31. Freitag H., Szklarski M., Lorenz S. et al. Autoantibodies to vasoregulative G-protein-coupled receptors correlate with symptom severity, autonomic dysfunction and disability in myalgic encephalomyelitis/chronic fatigue syndrome. J Clin Med. 2021;10(16):3675. DOI: 10.3390/jcm10163675.
32. Fu Q., Levine B.D. Exercise and the autonomic nervous system. Handb Clin Neurol. 2013;117:147–160. DOI: 10.1016/B978-0-444-53491-0.00013-4.
33. Gehlsen G.M., Grigsby S.A., Winant D.M. Effects of an aquatic fitness program on the muscular strength and endurance of patients with multiple sclerosis. Phys Ther. 1984;64(5):653–657. DOI: 10.1093/ptj/64.5.653.
34. Gigante A., Galea N., Borrazzo C. et al. Role of autonomic dysfunction in the regulation of myocardial blood flow in systemic sclerosis evaluated by cardiac magnetic resonance. Int J Rheum Dis. 2019;22(6):1029–1035. DOI: 10.1111/1756-185X.13569.
35. Gustafsson J.T., Simard J.F., Gunnarsson I. et al. Risk factors for cardiovascular mortality in patients with systemic lupus erythematosus, a prospective cohort study. Arthritis Res Ther. 2012;14(2):R46. DOI: 10.1186/ar3759.
36. Haensch C.A., Jörg J. Autonomic dysfunction in multiple sclerosis. J Neurol. 2006;253(Suppl 1):I3–I9. DOI: 10.1007/s00415-006-1102-2.
37. Halabchi F., Alizadeh Z., Sahraian M.A.et al. Exercise prescription for patients with multiple sclerosis; potential benefits and practical recommendations. BMC Neurol. 2017;17(1):185. DOI: 10.1186/s12883-017-0960-9.
38. Harms C.A., Wetter T.J., McClaran S.R. et al. Effects of respiratory muscle work on cardiac output and its distribution during maximal exercise. J Appl Physiol (1985). 1998;85(2):609–618. DOI: 10.1152/jappl.1998.85.2.609.
39. Hautala A., Tulppo M.P., Mäkikallio T.H. et al. Changes in cardiac autonomic regulation after prolonged maximal exercise. Clin Physiol. 2001;21(2):238–245. DOI: 10.1046/j.1365-2281.2001.00309.x.
40. Hogarth M.B., Judd L., Mathias C.J. et al. Cardiovascular autonomic function in systemic lupus erythematosus. Lupus. 2002;11(5):308–312. DOI: 10.1191/0961203302lu194oa.
41. Hu H., Xu A., Gao C. et al. The effect of physical exercise on rheumatoid arthritis: An overview of systematic reviews and meta-analysis. J Adv Nurs. 2021;77(2):506–522. DOI: 10.1111/jan.14574.
42. Huang M., Jay O., Davis S.L. Autonomic dysfunction in multiple sclerosis: implications for exercise. Auton Neurosci. 2015;188:82–85. DOI: 10.1016/j.autneu.2014.10.017.
43. Imai K., Sato H., Hori M. et al. Vagally mediated heart rate recovery after exercise is accelerated in athletes but blunted in patients with chronic heart failure. J Am Coll Cardiol. 1994;24(6):1529–1535. DOI: 10.1016/0735-1097(94)90150-3.
44. Imrich R., Alevizos I., Bebris L. et al. Predominant glandular cholinergic dysautonomia in patients with primary Sjögren's syndrome. Arthritis Rheumatol. 2015;67(5):1345–1352. DOI: 10.1002/art.39044.
45. Ingegnoli F., Buoli M., Antonucci F. et al. The link between autonomic nervous system and rheumatoid arthritis: from bench to bedside. Front Med (Lausanne). 2020;7:589079. DOI: 10.3389/fmed.2020.589079.
46. Kaur D., Tiwana H., Stino A. et al. Autonomic neuropathies. Muscle Nerve. 2021;63(1):10–21. DOI: 10.1002/mus.27048.
47. Kjølhede T., Vissing K., Dalgas U. Multiple sclerosis and progressive resistance training: a systematic review. Mult Scler. 2012;18(9):1215–1228. DOI: 10.1177/1352458512437418.
48. Konecný L., Pospíšil P., Vank P. et al. Combination of aerobic and resistance training in multiple sclerosis. Scripta Medica Facultatis Medicae Universitatis Brunensis Masarykianae. 2010;83:98–106.
49. Koopman F.A., Tang M.W., Vermeij J. et al. Autonomic dysfunction precedes development of rheumatoid arthritis: a prospective cohort study. EBioMedicine. 2016;6:231–237. DOI: 10.1016/j.ebiom.2016.02.029.

50. Mahovic D., Lakusic N. Progressive impairment of autonomic control of heart rate in patients with multiple sclerosis. Arch Med Res. 2007;38(3):322–325. DOI: 10.1016/j.arcmed.2006.11.009.
51. Malpas S.C. Sympathetic nervous system overactivity and its role in the development of cardiovascular disease. Physiol Rev. 2010;90(2):513–557. DOI: 10.1152/physrev.00007.2009.
52. Mann M.C., Exner D.V., Hemmelgarn B.R. et al. Vitamin D supplementation is associated with improved modulation of cardiac autonomic tone in healthy humans. Int J Cardiol. 2014;172(2):506–508. DOI: 10.1016/j.ijcard.2014.01.058.
53. McDougall A.J., McLeod J.G. Autonomic nervous system function in multiple sclerosis. J Neurol Sci. 2003;215(1-2):79–85. DOI: 10.1016/s0022-510x(03)00205-3.
54. Michael S., Graham K.S., Davis G.M. Oam. Cardiac autonomic responses during exercise and post-exercise recovery using heart rate variability and systolic time intervals — a review. Front Physiol. 2017;8:301. DOI: 10.3389/fphys.2017.00301.
55. Monje M.L., Toda H., Palmer T.D. Inflammatory blockade restores adult hippocampal neurogenesis. Science. 2003;302(5651):1760–1765. DOI: 10.1126/science.1088417.
56. Musumeci G. Effects of exercise on physical limitations and fatigue in rheumatic diseases. World J Orthop. 2015;6(10):762–769. DOI: 10.5312/wjo.v6.i10.762.
57. Newton J.L., Frith J., Powell D. et al. Autonomic symptoms are common and are associated with overall symptom burden and disease activity in primary Sjogren's syndrome. Ann Rheum Dis. 2012;71(12):1973–1979. DOI: 10.1136/annrheumdis-2011-201009.
58. Nieman D.C., Wentz L.M. The compelling link between physical activity and the body's defense system. J Sport Health Sci. 2019;8(3):201–217. DOI: 10.1016/j.jshs.2018.09.009.
59. Oliveira N.C., dos Santos Sabbag L.M., de Sá Pinto A.L. et al. Aerobic exercise is safe and effective in systemic sclerosis. Int J Sports Med. 2009;30(10):728–732. DOI: 10.1055/s-0029-1224180.
60. Rausch Osthoff A.K., Niedermann K., Braun J. et al. 2018 EULAR recommendations for physical activity in people with inflammatory arthritis and osteoarthritis. Ann Rheum Dis. 2018;77(9):1251–1260. DOI: 10.1136/annrheumdis-2018-213585.
61. Remensnyder J.P., Mitchell J.H., Sarnoff S.J. Functional sympatholysis during muscular activity. Observations on influence of carotid sinus on oxygen uptake. Circ Res. 1962;11:370–380. DOI: 10.1161/01.res.11.3.370.
62. Robinson B.F., Epstein S.E., Beiser G.D. et al. Control of heart rate by the autonomic nervous system. Studies in man on the interrelation between baroreceptor mechanisms and exercise. Circ Res. 1966;19(2):400–411. DOI: 10.1161/01.res.19.2.400.
63. Romberg A., Virtanen A., Ruutiainen J. et al. Effects of a 6-month exercise program on patients with multiple sclerosis: a randomized study. Neurology. 2004;63(11):2034–2038. DOI: 10.1212/01.wnl.0000145761.38400.65.
64. Rongen-van Dartel S.A., Repping-Wuts H., van Hoogmoed D. et al. Relationship between objectively assessed physical activity and fatigue in patients with rheumatoid arthritis: inverse correlation of activity and fatigue. Arthritis Care Res (Hoboken). 2014;66(6):852–860. DOI: 10.1002/acr.22251.
65. Saari A., Tolonen U., Pääkkö E. et al. Cardiovascular autonomic dysfunction correlates with brain MRI lesion load in MS. Clin Neurophysiol. 2004;115(6):1473–1478. DOI: 10.1016/j.clinph.2004.01.012.
66. Sharif K., Watad A., Bragazzi N.L. et al. Physical activity and autoimmune diseases: Get moving and manage the disease. Autoimmun Rev. 2018;17(1):53–72. DOI: 10.1016/j.autrev.2017.11.010.
67. Shoenfeld Y., Ryabkova V.A., Scheibenbogen C. et al. Complex syndromes of chronic pain, fatigue and cognitive impairment linked to autoimmune dysautonomia and small fiber neuropathy. Clin Immunol. 2020;214:108384. DOI: 10.1016/j.clim.2020.108384.
68. Sieczkowska S.M., Smaira F.I., Mazzolani B.C. et al. Efficacy of home-based physical activity interventions in patients with autoimmune rheumatic diseases: A systematic review and meta-analysis. Semin Arthritis Rheum. 2021;51(3):576–587. DOI: 10.1016/j.semarthrit.2021.04.004.
69. Simpson R.J., Campbell J.P., Gleeson M. et al. Can exercise affect immune function to increase susceptibility to infection? Exerc Immunol Rev. 2020;26:8–22.
70. Stojanovich L., Milovanovich B., de Luka S.R. et al. Cardiovascular autonomic dysfunction in systemic lupus, rheumatoid arthritis, primary Sjögren syndrome and other autoimmune diseases. Lupus. 2007;16(3):181–185. DOI: 10.1177/0961203306076223.
71. Stojanovich L. Autonomic dysfunction in autoimmune rheumatic disease. Autoimmun Rev. 2009;8(7):569–572. DOI: 10.1016/j.autrev.2009.01.018.
72. Strömbeck B., Jacobsson L.T. The role of exercise in the rehabilitation of patients with systemic lupus erythematosus and patients with primary Sjögren's syndrome Curr Opin Rheumatol. 2007;19(2):197–203. DOI: 10.1097/BOR.0b013e32801494e3. Erratum in Curr Opin Rheumatol. 2007;19(4):403.
73. Strömbeck B.E., Theander E., Jacobsson L.T. Effects of exercise on aerobic capacity and fatigue in women with primary Sjogren's syndrome. Rheumatology (Oxford). 2007;46(5):868–871. DOI: 10.1093/rheumatology/kem004.
74. Tadic M., Zlatanovic M., Cuspidi C. et al. Systemic sclerosis impacts right heart and cardiac autonomic nervous system. J Clin Ultrasound. 2018;46(3):188–194. DOI: 10.1002/jcu.22552.
75. Taylor N.F., Dodd K.J., Prasad D. et al. Progressive resistance exercise for people with multiple sclerosis. Disabil Rehabil. 2006;28(18):1119–1126. DOI: 10.1080/09638280500531834.
76. Tombul T., Anlar O., Tuncer M. et al. Impaired heart rate variability as a marker of cardiovascular autonomic dysfunction in multiple sclerosis. Acta Neurol Belg. 2011;111(2):116–120.
77. Vita G., Fazio M.C., Milone S. et al. Cardiovascular autonomic dysfunction in multiple sclerosis is likely related to brainstem lesions. J Neurol Sci. 1993;120(1):82–86. DOI: 10.1016/0022-510x(93)90029-x.
78. White L.J., McCoy S.C., Castellano V. et al. Resistance training improves strength and functional capacity in persons with multiple sclerosis. Mult Scler. 2004;10(6):668–674. DOI: 10.1191/1352458504ms1088oa.