EMPIRICAL ARTICLE

A Randomized Pilot Trial Assessing the Coping Intelligence and Tolerance of Complex Loads in Patients with Rheumatoid Arthritis, Gout, and Fibromyalgia

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Abstract. Rheumatoid arthritis (RA), gout (GT), and fibromyalgia (FM) are diseases that reduce patients' working capacity and quality of life. Despite the well-studied pathogenesis of RA, GT, and FM, research on tolerance to physical load is scarce. Studies on tolerance to intellectual and communicative loads in these patient groups have not been found.

The aim of this pilot trial is to assess coping intelligence, stress index, and serum levels of hormonal and immunological parameters in patients with RA, gout, and FM compared to randomized control groups. *Methods.* The study involved 126 individuals aged 20 to 54, including 27 patients with rheumatoid arthritis (2 male/25 female; 28-54 years), 24 patients with gout (22 male/2 female; 35-48 years), and 12 patients with fibromyalgia (4 male/8 female; 26-45 years). Control groups were randomized by sex, age, and education. The assessment of coping intelligence and tolerance to complex loads included: (1) laboratory evaluation of serum hormonal and immunological parameters before and after load; (2) anthropometric measurements; (3) heart rate variability analysis; (4) load testing consisting of psychomotor, intellectual, and communicative tests; (5) scales of perceived stress from psychomotor, intellectual, and communicative loads; (6) behaviorally anchored rating scales of coping intelligence (BARS of CI). *Results.* Patients with rheumatoid arthritis exhibited higher serum IL-6 levels before and after complex load and reported lower subjective strain from communicative load compared to the control group. No significant differences in coping intelligence properties were found between RA patients and the control group.

Patients with gout, compared to controls, demonstrated a significantly lower willingness to cooperate (WE) under complex loads; had lower pre-load serum DA levels; and presented with greater weight, waist circumference, and body mass index. They also recovered more easily after physical load and reported lower strain from communicative load.

Patients with fibromyalgia showed a less positive emotional response (ER) to load, lower self-efficacy (SE) in managing it, and a reduced willingness to cooperate (WE). They had lower pre-load norepinephrine (NE) levels and lower post-load adrenaline levels compared to the control group. Serum IL-6 levels were significantly higher in FM patients both before and after the complex load. No significant differences in stress index were found between fibromyalgia patients and the control group. *Conclusion.* The findings of the research could be beneficial for rheumatologists in enhancing patient compliance with treatment for rheumatoid arthritis, gout, and fibromyalgia.

Keywords: *Rheumatoid Arthritis, Gout, Fibromyalgia, Coping Intelligence, Stress Index, Tolerance of Loads, Hormones, Interleukins, Coping Intelligence, Control groups*

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1. Introduction

The economic burden of rheumatological diseases is significant, affecting nearly one-third of the population. These diseases can reduce working capacity and lifespan, making daily activities such as walking, climbing stairs, hygiene, and cooking difficult. Smoking, overweight, genetic predisposition, aging, as well as professions associated with injuries and joint overload are considered as factors that increase the risk of developing rheumatological pathologies. At present, achieving clinical remission is becoming an increasingly realistic task. Preventing the occurrence and spread of diseases, improving well-being and ensuring the quality of life of patients is very problematic without taking into account the influence of stress factors of varying duration and nature on both professional and personal aspects of a person's life. To achieve sustainable remission, it is important to understand not only the features of the course of the disease, the external factors that provoke this disease, but also the personal characteristics of patients, their ability to cope with everyday problems and difficulties caused by a chronic disease. Prolonged overloads lead to a negative change in physiological and biochemical parameters, worsening human health. The ability to resolve difficult situations while maintaining health and personal growth is called coping intelligence.

Coping intelligence, unlike resilience, hardiness, and coping, is associated with the process of analyzing resources and choosing specific behavioral strategies consistent with personality traits, stressors, and collective coping experiences. The subjective price of resolving a difficult life situation is in the center of a person's attention. A multidimensional model of coping intelligence is presented in the monograph by E.V. Volkova and I.O. Kuvaeva (see Fig. 1, Volkova & Kuvaeva, 2022).

Clinically, patients with rheumatoid arthritis (RA), gout (GT), and fibromyalgia (FM) are characterized by a set of certain obligatory signs, which are observed in most cases, and comorbid disorders that make it difficult to verify the disease and make its course more difficult.

Rheumatoid arthritis is a multifactorial autoimmune disease of partially unknown etiology, characterized by persistent synovitis, which eventually causes damage to the articular cartilage and bone erosion. Many patients have joint deformities and various extra-articular manifestations such as cardiovascular disease, respiratory disease, lung disease, osteoarthritis and osteoporosis (Wang & Zhao, 2024), sleep disorders. The prevalence of RA in adults varies from 0.5% to 2.7%, according to various studies (Almutairi et al., 2021; Murata, 2024). This condition is more common in women, affecting them 2.5-3 times more frequently than men. It also appears to be more prevalent in industrialized countries and urban areas compared to rural settlements (Almutairi et al., 2021; Finckh & Gilbert, 2022).

Chronic stress can trigger the onset and worsening of RA. Excessive activation of the hypothalamic-pituitary-adrenal system (HPA-axis) can lead to its dysfunction, which is accompanied by reduced cortisol production and the development of chronic systemic inflammation (Lisitsyna & Veltischev, 2016).

Stress is correlated with poor sleep quality ($r=0.27$), anxiety ($r=0.49$), and depression ($r=0.37$). In addition, depression ($r=-0.34$) and stress ($r=-0.24$) are negatively associated with mental health (Teixeira, Castelar-Pinxeiro, Rodrigues, 2025). A randomized trial of rheumatoid arthritis patients revealed that women with higher cortisol levels used in stressful situations such coping strategies as positive reappraisal, seeking emotional and instrumental support, and denial. In men, higher stress levels were associated with twice the levels of C-reactive protein compared to those with lower stress levels. As levels of C-reactive protein and the disease activity index increased (DAS28), patients used denial strategies more frequently (Wrobel et al., 2023).

Currently, rheumatologists have few parameters to make decisions about the treatment of RA (Humby et al., 2017), moreover, clinical factors and standard blood tests are not always useful prognostic markers (Isaacs et al., 2013). Patients undergo ineffective treatment, which increases the risk of irreversible damage to the joints and other consequences of the disease (Jonsson, 2024).

Gout is considered as a potentially curable disease (Cheryomushkina & Eliseev, 2022). Its prevalence varies from 0.1% to 10%, and it is more common among men than among women (Lipatov & Buksha, 2021). Typical signs of gout are severe pain, local hyperthermia, swelling of the joints, decreased joint function, or the formation of tofuses (Cheryomushkina & Eliseev, 2022). The main risk factors for the

disease include hyperuricemia, genetic predisposition, dietary factors, medication, concomitant diseases, and lead exposure (Kuo, Grainge, 2015). There is evidence that an increased risk of gout is associated with hearing loss (Fu, Zhao, 2024). Patients with GT are diagnosed with motor and cognitive impairments, and they are highly vulnerable to such diseases as dementia, Parkinson's disease, and essential tremor. The risk of developing neurodegenerative diseases in people with gout is linked to a smaller brain size and a higher concentration of iron in the brain (Topiwala & Mankia, 2023). Gout is associated with an increased risk of obesity, chronic kidney disease, hypertension, type 2 diabetes, dyslipidemia, heart disease (including coronary artery disease, heart failure, and atrial fibrillation), stroke, and peripheral artery disease (Bardin & Richette, 2017). The relationship between blood uric acid levels and the risk of cardiovascular disease remains unclear. Studies using Mendelian randomization revealed that elevated serum urate is not a direct cause of cardiovascular disease or a risk factor for it, and it is also not associated with intermediate risk factors such as kidney function, obesity, metabolic syndrome, glycemic parameters, or blood lipid concentrations (Choi, McCormick, Yokose, 2022).

Since obesity leads to increased levels of uric acid and weight gain increases the risk of developing gout, it is recommended to lose weight through daily exercise and limiting extra calorie intake. However, intense physical activity, which causes the breakdown of adenine nucleotides, and starvation, which reduces uric acid excretion, as well as dehydration, can increase uric acid levels in the blood and provoke gout attacks. Increased consumption of purine-rich foods, such as meat and seafood, can lead to higher levels of uric acid in the blood, which is associated with an increased risk of gout. In contrast, dairy products, especially those with a low-fat content, may be associated with a reduced risk of gout (Kakutani et al., 2015).

Meta-analyses suggest a positive association between mental health conditions and gout, with the overall odds ratio (OR) being 1.29 (95% confidence interval (CI) 1.07-1.56) for depression and 1.29 (95% CI 0.96-1.73) for anxiety. Four studies on the prevalence of depression in people with gout yielded an overall OR of 1.17 (95% CI 1.01-1.36). Factors that significantly influenced the risk of depression included the number of flare-ups, frequency of gout attacks, and oligoarthritis/polyarthritis. Depression and anxiety are strongly linked to gout, highlighting the need for more research into the development of mental health issues following a diagnosis of gout (Howren et al., 2020).

Fillingim and colleagues emphasize that biomarkers and psychosocial factors do not act independently, but rather synergistically, influencing the development and prognosis of pain-related diseases. Indeed, psychosocial factors are the only reliable determinants of the presence, distribution, and impact of chronic pain (Fillingim et al., 2025). One of the main markers of the body's stress response is cortisol, which is released during an acute attack of gout. The change in cortisol levels is associated with uric acid excretion in the urine (24 h UFC), as well as the levels of interleukins IL-1β and IL-6 (Zhang et al., 2023). It should be noted that the effects of specific stress hormones, such as adrenaline, norepinephrine, and cortisol, on gout are rarely the focus of large-scale research.

Despite the high prevalence of *fibromyalgia*, ranging from 2% to 7.3% (White & Tompson, 2003), it is usually diagnosed when other conditions, such as inflammation, injury, or other causes of chronic widespread pain, are ruled out. Patients seek medical attention because of generalized debilitating pain that lasts for more than three months and worsens during times of fatigue, emotional, or physical stress. Pain also worsens when the body is exposed to cold temperatures. Physical and psychological stressors contribute to a chronic pro-inflammatory state in the central nervous system and in peripheral tissues, which affects the central processing of pain. Pain syndrome is often associated with depressive disorders, asthenia, impaired sleep quality, and decreased cognitive function (Lin, Ko, Chow, 2021). Among comorbid disorders, the leading role belongs to mental, vegetative, and pain manifestations (Weier, 2006). Moreover, the higher is the BMI, the greater is the severity of the disease (Correa-Rodríguez, 2019). Characteristic features of FM patients are alpha-delta sleep (Moldofsky & Patcai, 2011), hypersensitivity, and central sensitization (Liew & Valera-Calero, 2022). Fibromyalgia is more common in women than in men (White, Speechley, 1999).

Dysregulation of the hypothalamus-pituitary-adrenal (HPA) axis and the sympathetic nervous system is linked to chronic stress reactions and neuroinflammation. Neuroimaging and

preclinical studies confirm changes in pain and stress perception that are associated with these dysregulations. Mild inflammation and metabolic disorders, including cytokine imbalances and increased infiltration of adipose tissue, further exacerbate the symptoms. Changes in the gut microbiota contribute to impaired immune and emotional regulation. MRI studies continue to reveal changes in the brain that distinguish fibromyalgia from other chronic pain disorders. Mitochondrial dysfunction is also a key factor, as impaired energy metabolism appears to correlate with symptom severity. Physical activity and psychosocial interventions play a key role (Iannuccelli, et al., 2025).

A study of patients with FM's ability to cope with physical, intellectual, and communicative stress showed a decrease in cortisol and adrenaline levels in the blood, regardless of their phenotype. The changes in dopamine were diverse. The level of serotonin in the blood did not change significantly in any patient, but there was a four-fold increase in interleukin-4 levels in patients with over-reactive regulatory systems (Volkova, Teplyakova, & Kuvaeva, 2025).

Despite the well-studied pathogenesis of rheumatoid arthritis, gout, and fibromylagia, there are only a few studies on exercise tolerance. No studies have been found on the tolerance of intellectual and communicative loads in these groups of patients (Nature, PubMed). As noted above, patients with PA and FM have cognitive and motor impairments, which indicates a reduced tolerance to these loads in these patients and lower coping intelligence compared to the control group. Thus, the aim of the pilot trial was to compare coping intelligence (CI) and tolerance to physical, intellectual, and communicative loads (Bayevsky stress index, hormonal and immunological levels in blood serum) in patients with RA, PA, and FM compared with randomized control groups.

2. Method

2.1. Sample

The sample consists of 126 participants aged 20 to 54 years. The study participants signed a voluntary informed consent to participate in the study. The patient groups and control groups were randomized by gender, age, and education. Participants in the control groups were not diagnosed with RA, GT, FM and other chronic or autoimmune diseases, as well as mental disorders. Among the patients with RA, there were two men and twenty-five women aged between 28 and 54 years old; among those with GT, there were twenty-two men and two women, aged 35 to 48; and among those with FM, there were four men and eight women, aged between 26 and 45. None of the patients had any joint pain or swelling on the day of the study.

2.2. Procedure

The study design was approved by the local ethics committee of the Ural State Medical University of the Ministry of Health of the Russian Federation (Protocol No 5 dated 06.16.2023). The study was carried out from October 2023 to July 2024 in Moscow and Yekaterinburg. The rheumatologist informed the patient about the goals and objectives of the experimental study, the benefits and possible risks.

The experiment begins at 7:30 a.m. The patient fills out the following documents: (1) a questionnaire confirming the possibility of participating in the experiment; (2) informed voluntary consent to unpaid participation in research for the development of science; (3) consent to the collection of venous blood; (4) consent to the processing of personal data. Venous blood is taken twice on an empty stomach: at 7.40 (before the tests) and at 11.30 (after the tests). The total examination time is about 4 hours per patient. The patient's nutrition is after the end of the experiment.

2.3. The CI assessment technology includes: (1) laboratory methods for assessing hormonal and immunological parameters in the blood serum before and after complex loading; (2) assessment of anthropometric data; (3) assessment of heart rate variability; (4) stress testing, consisting of motor, intellectual and communicative tests; (5) scales of perceived strain of psychomotor, intellectual and communicative load; and (6) Behaviorally Anchored Rating Scales of Copping Intelligence (BARS of CI).

2.3.1. Laboratory methods

Hormonal studies of the level of cortisol, adrenaline, noradrenaline (NE), serotonin (5-HT), dopamine (DA) in serum are performed on the equipment of Abbott Architect i2000 SR, Abbott Diagnostics, USA. Immunological studies of the level of interleukin-4 (IL-4), interleukin-6 (IL-6), interleukin-10 (IL-10), tumor necrosis factor (TNFα) are performed on the equipment of SUNRISE, Tecan (Austria) by enzyme-linked immunosorbent assay and UniCel DXI800, Beckman Coulter (USA). The place of research is the scientific center for molecular genetic

research “DNKOM Laboratory” (Moscow).

2.3.2. Assessment of anthropometric data of study participants

Height, weight, and waist circumference are measured in each study participant; the body mass index (BMI) is calculated.

BMI less than 16	Severe underweight
16-18.5	Underweight
18.5-25	Normal
25-30	Overweight (pre-obesity)
30-35	Obesity of the first degree
35-40	Obesity of the second degree
40 or more	Obesity of the third degree (morbid)

2.3.3. Method for assessing heart rate variability

Heart rate variability reflects “the degree of tension of regulatory systems due to the activation of the pituitary-adrenal system and the reaction of the sympathoadrenal system arising in response to any stressor influence” (Baevsky & Ivanov, 2001, p. 110). Analysis of heart rate variability at rest and during stress tests is carried out using the VNS-Microcomputer electrocardiograph of Neurosoft LLC (Ivanovo). The electrodes are applied as follows: red (left subclavian region) – yellow (right subclavian region) – green (right subcostal region) – black (left subcostal region). The wires from the electrodes are fixed with a tg soft tubular bandage (size E).

The Baevsky Stress Index (SI) reflects the tension of the body's regulatory systems and is calculated based on the analysis of the graph of the distribution of cardiac intervals (Mikhailov, 2017, p. 28). To minimize the error in calculating the stress index, the load should last at least 5 minutes. Gradations of the Baevsky stress index:

SI<30 c.u. – a state of pronounced distress with a predominance of activity of stress-limiting systems;

31<SI<60 – a state of compensated distress with a tendency to predominate the activity of stress-limiting systems;

61<SI<120 – state of eustress (optimal physiological regulation);

121<SI<200 – state of tension of adaptation mechanisms and increased activity of stress-realizing systems;

SI >201 – a state of pronounced distress, excessive activity of stress-realizing systems, damaging the impact on systems and organs.

2.3.4. Load testing

The duration of physical activity is determined by the physical capabilities of the study participant. First, the patient lies for 5 minutes (background load). The patient then pedals on the CardioPower B37 at 120 watts until failure for at least 5 minutes. After that, the patient pedals in recovery mode for 5 minutes, i.e. at minimum power.

The intellectual load lasts for more than one hour. The study participant solves logic tests (Rusalov & Volkova, 2021) and the intelligence test “Standard Progressive Matrices” by Raven (Raven, et al., 2012). They also complete tests of conceptual thinking and collect figures from cubes according to pictures.

The communicative load lasts 45 minutes. The participant performs the Rosenzweig test (Yasyukova, 2021), answers the questions of a structured interview, reads and retells a complex text.

2.3.5. Scales of perceived stress from psychomotor, intellectual, and communicative loads

The Borg scale is used to subjectively assess the severity of symptoms (palpitations, shortness of breath, sweating) caused by physical activity. The scale ranges from 6, which is considered extremely easy, to 20, which represents maximum effort.

The scales of perceived tension of intellectual (Volkova N., 2025) and communicative (Varlamov, 2024) load are developed based on the Borg scale to assess the severity of symptoms caused by these types of loads. The grades of these loads are the same as for physical load, ranging from 1 to 20 points.

2.3.6. Behaviorally Anchored Rating Scales of Coping Intelligence (BARS of CI)

The BARS of CI is designed to identify patterns of behavior that are relevant to the successful or unsuccessful overcoming of psychomotor, intellectual, and communicative stress.

The structure of coping intelligence measurements and the technology for their assessment are presented in (Kuvaeva & Volkova, 2025). The levels of the integral indicator of coping intelligence are: 25-52 is low, 53-64 is medium, and 65-71 is high. The characteristics of CI include: (1) Analyzing the Problem (AP), (2) Transformation of the Situation (TS), (3) Emotional Response (ER), (4) Self-Efficacy, and (5) Willingness to Cooperate (WE).

The modal-specific manifestations of CI are also evaluated, namely, CI when overcoming psychomotor, intellectual, and communicative loads. The study protocol was verified in our previous studies (Teplyakova, Volkova, Kuvaeva, 2025; Volkova et al., 2025).

2.4. *Statistical data processing*

Statistical data analysis was performed using the IBM Statistics 28 software package. The Mann-Whitney U-test was used to compare the patient group with the control group. The significance of changes in hormonal and immunological parameters in blood serum before and after a complex load was assessed using the Wilcoxon test.

3. Results

3.1. Anthropometric data of the groups

Patients with RA as well as patients with FM not differ from their respective control groups in weight, height, waist circumference, or body mass index. In contrast, patients with GT exhibited greater weight, waist circumference, and body mass index compared to the control group (Table 1).

Table 1. Age, weight, height, waist circumference, and body mass index in patient and control groups

Sample	Age, years	Weight, kg	Growth (M)	Waist Circumference, sm	BMI, kg/m²
Patients with rheumatoid arthritis (N=27)	37.52±8.46	65.29±13.76	164.83±6.81	77.70± 11.95	23.95±4.27
Control Group (N=27)	38.67±7.74	63.37±13.31	166.37±5.34	75.29±11.26	22.78±4.05
p	0.659	0.749	0.179	0.476	0.401
Patients with gout (N=24)	41.92±6.61	97.92±18.55	178.71±8.33	106.42±22.99	30.54±4.56
Control Group (N=24)	38.67±7.79	87.19±22.08	180.08±10.15	89.91±16.68	26.71±5.46
p	0.107	**0.026**	0.657	**0.001**	**0.005**
Patients with fibromyalgia (N=12)	35.83±9.81	63.33±13.69	165.75±7.56	76.92±10.99	22.94±4.14
Control Group (N=12)	35.75±9.79	68.75±20.52	169.58±9.17	79.09±15.48	23.53±4.93
p	0.977	0.630	0.319	1.000	0.932

3.2. Patients with rheumatoid arthritis

No significant differences were found between the experimental and control groups in either the overall or partial measures of coping intelligence. Participants in both groups demonstrated an average level of coping intelligence, showing a tendency to analyze and transform stressful situations rather than to collaborate (Table 2).

Patients with RA showed higher serum levels of the proinflammatory cytokine IL-6 both before and after complex loads compared to the control group (Table 3). No significant within-group changes in hormonal or immunological parameters were detected following the loads (Wilcoxon test, $p > 0.05$).

The stress index in patients with RA indicated optimal physiological regulation under various loads (Table 4). They perceived physical load as heavier and communicative load as less strenuous (Wilcoxon test, $p < 0.05$). In contrast, the control group experienced distress during communication and rated the physical load as heavier than the RA patients did. It should be noted that the duration of physical load did not differ significantly between the two groups.

Table 2. Coping intelligence in patients with rheumatoid arthritis and control group

Indicators	Descriptive statistics (mean, standard deviation)		Significance of differences between RA-patients and the control group	
	Patients with rheumatoid arthritis	Control group	U	p
Integral Index of Coping Intelligence, IICI	57.26±7.72	58.56±6.09	275.00	0.795
Scales of Coping Intelligence				
Analyzing the problem, AP	12.83±2.77	12.56±2.61	274.00	0.776
Transformation of the situation, TS	12.43±1.99	12.48±2.55	259.00	0.550
Emotional response, ER	11.70±1.52	11.60±1.58	260.00	0.560
Self-efficacy, SE	11.39±2.45	11.64±1.72	275.00	0.793
Willingness to cooperate, WE	8.65±2.28	9.48±2.48	234.00	0.265
Modality-Specific Scales of Coping Intelligence				
Coping Intelligence in overcoming motor load, CIM	15.70±2.38	15.27±4.17	286.00	0.793
Coping Intelligence in overcoming intellectual load, CII	15.96±3.05	16.00±4.09	256.00	0.510
Coping Intelligence in overcoming communicative load, CIC	16.96±3.48	16.54±4.21	284.00	0.768

Table 3. Serum cytokine and hormone levels in patients with rheumatoid arthritis and control groups before and after complex loads

Indicators	RA-patients (Before complex load/ after complex load)	Control group (Before complex load/ after complex load)	The significance of the differences (Mann-Whitney test) in indicators between RA-patients and control groups (p)	
			Before complex load	After complex load
Cortisol, nmol/l	308.64±131.49/ 184.91±78.48	335.22±116.02/ 220.60±126.30	0.983	0.364
Adrenaline, pg/ml	44.36±13.41/ 42.27±21.61	42.10±13.56/ 40.48±9.30	0.447	0.920
NE, pg/ml	395.95±198.76/ 452.41±201.74	390.70±144.03/ 504.99±214.29	0.426	0.210
DA, pg/ml	18.99±15.18/ 16.73±14.87	14.57±11.00/ 16.46±18.83	0.268	0.674
5-HT, pg/ml	187.11±73.58/ 186.19±69.59	192.30±84.44/ 192.73±87.55	0.707	0.763
IL-4, pg/ml	15.11±15.39/ 22.06±20.07	14.77±12.31/ 23.58±19.89	0.545	0.533
IL-6, pg/ml	30.04±96.75/ 9.19±14.10	16.82±57.04 / 4.02±7.55	**0.001**	**0.004**
IL-10, pg/ml	6.82±2.18/ 6.37±2.00	6.18±2.63/ 5.77±2.56	0.182	0.226
TNFα, pg/ml	2.04±4.07/ 2.92±6.72	4.15±9.36/ 5.63±12.12	0.582	0.541

Table 4. The stress index and the subjective assessment of the tolerance to psychomotor, intellectual, and communicative loads in patients with rheumatoid arthritis and control group

Indicators	Means, SD		Significance of differences between RA-patients and the control group	
	Patients with rheumatoid arthritis	Control group	U	p
Stress index (SI, c.u.)				
Background test (lying at rest)	102.22±101.33	108.51±95.08	292.00	0.920
Physical load (bicycle ergometer)	102.19±78.41	199.96±204.81	213.50	0.093
Recovery after a maximum physical load	120.28±104.99	202.61±220.96	210.50	0.273
Intellectual load	89.48±63.73	233.03±297.28	198.00	0.169
Communicative load	108.78± 83.24	212.9±147.45	123.00	**0.002**
Subjective assessment (score)				
Physical load (bicycle ergometer)	16.19±2.47	17.70±1.64	234.00	**0.022**
Intellectual load	14.09±3.80	11.96±3.14	225.50	0.146
Communicative load	9.20±3.12	9.20±2.00	69.50	0.757

3.3 Patients with gout

The overall level of coping intelligence was average in both patients with gout and the control group. However, the willingness to cooperate in difficult situations was significantly higher in the control group (Table 5).

Patients with gout presented lower morning serum dopamine levels compared to the control group (Mann-Whitney test, p=0.023; Table 6). The response to complex loads was notably different: dopamine levels decreased in the control group but showed a statistically significant increase in patients with gout (Wilcoxon test, p=0.016).

Table 5. Coping intelligence in patients with gout and control group

Indicators	Means, SD		Significance of differences between GT-patients and the control group	
	Patients with gout	Control group	U	p
Integral Index of Coping Intelligence, IICI	58.42±5.65	59.50±6.44	233.00	0.495
Scales of Coping Intelligence				
Analyzing the problem, AP	13.21±1.88	12.27±2.27	203.00	0.169
Transformation of the situation, TS	13.29±1.82	12.50±1.84	191.00	0.102
Emotional response, ER	11.88±1.62	11.68±2.12	260.50	0.938
Self-efficacy, SE	12.21±1.41	11.55±2.06	204.00	0.177
Willingness to cooperate, WE	7.79±1.88	10.73±2.05	95.50	**0.000**
Modality-Specific Scales of Coping Intelligence				
Coping Intelligence in overcoming motor load, SIM	17.46±1.56	17.18±2.57	265.50	0.867
Coping Intelligence in overcoming intellectual load, SII	16.50±1.44	15.91±2.84	236.50	0.540
Coping Intelligence in overcoming conversational load, SIC	16.67±4.23	15.68±3.37	201.50	0.164

Table 6. Serum cytokine and hormone levels in patients with gout and control groups before and after complex loads

Indicators	GT-patients (Before complex load/ after complex load)	Control group (Before complex load/ after complex load)	The significance of the differences (Mann-Whitney test) in indicators between GT-patients and control groups (p)	
			Before complex load	After complex load
Cortisol, nmol/l	336.05±115.62/ 242.87±97.21	339.73±82.84/ 202.52±68.30	0.853	0.127
Adrenaline, pg/ml	37.44±14.71/ 41.44±14.52	48.49±22.42/ 45.87±14.51	0.076	0.149
NE, pg/ml	346.80±124.82/ 444.45±152.27	463.12±255.89/ 496.40±228.32	0.161	0.789
DA, pg/ml	13.77±18.51/ 19.85±19.06	17.09±11.17/ 15.08±12.41	**0.023**	0.409
5-HT, pg/ml	165.98±78.63/ 167.76±76.32/	141.39±58.34/ 144.05±61.87	0.322	0.353
IL-4, pg/ml	10.32±9.69/ 16.99±10.21	17.60±20.34/ 17.42±19.94	0.244	0.409
IL-6, pg/ml	9.15±29.52/ 3.45±4.72	7.00±22.48/ 5.17±11.45	0.173	0.577
IL-10, pg/ml	7.21±3.13/ 6.86±3.56	6.58±2.37/ 5.88±1.79	0.749	0.781
TNFα, pg/ml	0.63±0.92/ 1.01±2.80	2.45±8.06/ 1.84±4.92	0.723	0.712

Table 7. The stress index and the subjective assessment of the tolerance to psychomotor, intellectual, and communicative loads in patients with gout and control group

Indicators	Means, SD		Significance of differences between GT-patients and the control group	
	Patients with gout	Control group	U	p
Stress index (SI, c.u.)				
Background test (lying at rest)	150.34±202.05	124.47 ±120.03	204.00	0.937
Physical load (bicycle ergometer)	143.47±189.95	102.18±93.75	179.00	0.462
Recovery after a maximum physical load	96.03±90.18	**212.48±150.27**	90.00	**0.002**
Intellectual load	158.22±191.46	91.19±50.97	189.00	0.636
Communicative load	120.83±86.13	**222.10±129.87**	98.00	**0.004**
Subjective assessment (score)				
Physical load (bicycle ergometer)	22.29±36.87	15.21±3.24	265.50	0.640
Intellectual load	**15.13±4.03**	12.06±1.52	103.50	**0.010**
Communicative load	10.33±3.51	9.05±1.91	24.50	0.467

3.3. Patients with fibromyalgia

Patients with fibromyalgia demonstrated a lower level of coping intelligence compared to the control group (Table 8). The control group showed a more positive response to complex loads, greater confidence in their ability to cope with them, and a higher willingness to cooperate in difficult situations ($p<0.05$).

Patients with fibromyalgia showed lower morning levels of norepinephrine and a lower level of adrenaline after complex loads (Table 9). While norepinephrine increased post-load in both

groups, adrenaline levels decreased in fibromyalgia patients (Wilcoxon test, p=0.014) and increased in controls.

Serum IL-6 levels were significantly higher in fibromyalgia patients, both in the morning and after complex loads. In contrast to the decrease observed in the control group, IL-6 increased in patients following the loads. Furthermore, serotonin levels increased significantly after loads in the fibromyalgia group (Wilcoxon test, p=0.028) but decreased in the control group.

Table 8. Coping intelligence in patients with fibromyalgia and control group

Indicators	Means, SD		Significance of differences between FM-patients and the control group	
	Patients with fibromyalgia	Control group	U	p
Integral Index of Coping Intelligence, IICI	53.00±6.05	**59.45±7.48**	29.50	**0.023**
Scales of Coping Intelligence				
Analyzing the problem, AP	13.33±1.61	12.55±3.11	65.00	0.976
Transformation of the situation, TS	12.67±1.73	12.73±2.14	58.50	0.651
Emotional response, ER	10.17±1.26	**12.18±1.99**	27.00	**0.016**
Self-efficacy, SE	9.67±2.74	**12.27±1.84**	27.00	**0.016**
Willingness to cooperate, WE	7.42±1.67	**9.18±1.60**	29.00	**0.023**
Modality-Specific Scales of Coping Intelligence				
Coping Intelligence in overcoming motor load (CIM)	15.25±2.26	16.09±3.17	53.50	0.449
Coping Intelligence in overcoming intellectual load (CII)	15.50±2.54	16.82±2.48	47.50	0.260
Coping Intelligence in overcoming communicative load (CIC)	14.83±5.27	17.36±2.97	40.00	0.118

Table 9. Serum cytokine and hormone levels in patients with fibromyalgia and control groups before and after complex loads

Indicators	FM-patients (Before complex load/ after complex load)	Control group (Before complex load/ after complex load)	The significance of the differences (Mann-Whitney test) in indicators between FM-patients and control groups (p)	
			Before complex load	After complex load
Cortisol, nmol/l	392.93±94.29/ 236.46±88.44	368.40±90.99/ 205.05±76.02	0.551	0.410
Adrenaline, pg/ml	38.76±10.21/ 29.35±13.64	37.61±10.90/ 47.95±26.83	0.671	**0.033**
NE, pg/ml	341.08±121.67/ 401.65±127.12	450.14±161.09/ 517.10±179.98	**0.045**	0.114
DA, pg/ml	13.79±12.55/ 15.90±12.61	15.97±17.20/ 12.52±11.77	0.671	0.443
5-HT, pg/ml	177.32±87.85/ 182.84±79.13	154.67±72.55/ 144.95±61.99	0.713	0.266
IL-4, pg/ml	18.91±16.29/ 26.85±22.31	11.74±9.62/ 27.46±23.20	0.178	0.977
IL-6, pg/ml	2.19±1.27/ 2.25±1.05	1.83±2.93/ 1.14±0.87	**0.014**	**0.006**
IL-10, pg/ml	5.87±1.80/ 5.56±1.68	6.00±1.96/ 5.97±1.82	0.671	0.887
TNFα, pg/ml	4.67±11.98/ 2.79±6.24	0.97±2.23/ 0.39±0.79	0.551	0.378

Table 10. The stress index and the subjective assessment of the tolerance to psychomotor, intellectual, and communicative loads in patients with fibromyalgia and control group

Indicators	Means, SD		Significance of differences between FM-patients and the control group	
	Patients with fibromyalgia	Control group	U	p
Stress index (SI, c.u.)				
Background test (lying at rest)	146.67±82.72	158.60±145.11	68.00	0.843
Physical load (bicycle ergometer)	328.50±219.91	205.46±167.43	52.00	0.266
Recovery after a maximum physical load	154.58±104.00	213.50±190.83	65.00	0.713
Intellectual load	400.95±366.74	228.86±307.58	41.00	0.134
Communicative load	172.82±113.31	152.27±111.07	58.00	0.443
Subjective assessment (score)				
Physical load (bicycle ergometer)	17.67±2.10	16.50±2.81	53.00	0.264
Intellectual load	12.50±2.43	13.27±3.17	64.00	0.555
Communicative load	10.00±3.22	7.91±2.17	40.00	0.105

No significant differences were observed in the stress index or subjective tolerance to psychomotor, intellectual, and communicative loads between individuals with fibromyalgia and the control group (Table 10). However, it is important to note that during psychomotor and intellectual loads, the stress index in individuals with fibromyalgia can exceed 300, indicating a state of severe stress. This over-activation of stress-response systems may have detrimental effects on multiple organ systems.

4. Discussion

We hypothesized that all patient groups would demonstrate lower coping intelligence and lower tolerance to complex loads compared to the control group. However, this hypothesis was only partially confirmed.

Individuals with rheumatoid arthritis, gout, and fibromyalgia, as well as those in the control group, exhibited an average level of coping intelligence. They prefer to analyze (AP) and alter (TS) a challenging circumstance, rather than cooperate (WE). There are no significant differences in coping intelligence between patients with rheumatoid arthritis and the control group. Patients with gout were significantly less willing to cooperate (WE) under complex loads. Patients with fibromyalgia showed a less positive emotional response (ER) to complex loads, have less self-efficacy (SE) in managing them, and were less inclined to collaborate (WE) in challenging circumstances compared to the control group.

Patients with rheumatoid arthritis had higher serum levels of the proinflammatory cytokine IL-6 both before and after complex loads compared to the control group. Rheumatoid arthritis is characterized by a consistently high concentration of pro-inflammatory cytokines, which are considered endogenous stressors (Zeltyn et al., 2009). As emphasized by Jia and Gao (2023), the balance of pro- and anti-inflammatory macrophages is crucial for maintaining immune homeostasis and preventing excessive inflammation in RA. Their research suggests that metabolic reprogramming of pro-inflammatory macrophages via roburic acid (RBA-NP) can effectively alleviate symptoms by reducing glycolysis via the ERK/HIF-1α/GLUT1 pathway, thereby promoting a phenotypic switch from M1 to M2 macrophages.

Compared to the control group, patients with gout had lower serum dopamine (DA) levels in the morning and significant change in this hormone following complex loads.

Patients with fibromyalgia presented with lower baseline levels of norepinephrine and higher post-load levels of epinephrine compared to controls. Serum levels of IL-6 were also significantly elevated in fibromyalgia patients both before and after complex loads. Significant changes in the levels of epinephrine and serotonin

(5-HT) in response to loads were also observed in this group.

Assessment of physiological regulation revealed that patients with rheumatoid arthritis maintained optimal regulation under psychomotor, intellectual, and communicative loads. Subjectively, however, they perceived psychomotor load as heavier and communicative load as lighter. In contrast, patients with gout showed signs of regulatory system overexertion (SI >120 cu.) during psychomotor and intellectual loads. Patients with fibromyalgia also experienced significant distress during these types of loads.

While patients with rheumatoid arthritis and fibromyalgia had a standard body mass index (BMI), patients with gout had a higher BMI and larger waist circumference compared to the control group. BMI and waist circumference are established indicators of risk for obesity-related pathologies. In gout, metabolic syndrome can trigger a pronounced inflammatory cascade that exacerbates the primary pathology and promotes comorbid conditions, most notably cardiovascular disease (Zhigulina, Shilova, Aleksandrov, 2023), chronic kidney disease, and diabetes mellitus (Lipatov, Buksha, 2021). The link between gout and diabetes is associated not only with common risk factors but also with hyperuricemia and microcrystalline inflammation (Zhilyabina et al., 2022). Studies report a higher prevalence of hypertension, diabetes, hyperlipidemia, stroke, and coronary heart disease in gout patients compared to controls, as well as a significantly higher cumulative incidence of depression (Changchien et al., 2016).

5. Conclusion

Data from randomized trials involving patients with various rheumatological pathologies are needed to develop a comprehensive medical management strategy. It is important not only to understand the specifics of treatment for the disease, but also how different types of load affect heart rate variability, biochemical parameters, and the patient's well-being. Without such data, health management and achieving a sustainable remission become considerably more challenging.

A pilot randomized trial revealed a range of alterations in serum hormonal parameters in patients with rheumatoid arthritis, gout, and fibromyalgia compared to control groups. Specifically, patients with fibromyalgia, compared with the control group, are characterized by lower coping intelligence, lower serum levels of NE and higher levels of IL-6; however, no differences in the stress index are found when performing different types of loads. Patients with gout have lower willingness to engage (WE), lower morning serum dopamine levels, and a higher stress index during a communication load. Patients with rheumatoid arthritis, compared with the control group, have higher serum IL-6 levels, a lower stress index during a communicative load, and a lower perceived severity of physical load.

It is important to note the limitations of this study. First, the sample size was small. Second, the analysis did not account for gender differences in coping intelligence as well as tolerance to psychomotor, intellectual and communicative loads. Third, the findings cannot be generalized to other age groups outside the range considered in this study.

CRediT author statement:

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Highlights

- Patients with rheumatoid arthritis demonstrated higher serum IL-6 levels both before and after the load and reported lower subjective strain from the communicative load compared to the control group. No significant differences in coping intelligence indicators were found between

the groups.

- Patients with gout differed from the control group by a significantly lower willingness to engage (WE) under load conditions, reduced pre-load dopamine (DA) levels, and higher values for body weight, waist circumference, and body mass index. However, this patient group demonstrated faster recovery after physical load and reported lower strain from the communicative load.

- Patients with fibromyalgia, compared to the control group, showed a less positive emotional response (ER) to the load, lower self-efficacy (SE), and a reduced willingness to engage (WE). They had a lower baseline norepinephrine (NE) level and a lower adrenaline level after the load. Serum IL-6 concentration in fibromyalgia patients was significantly higher both before and after the load. No significant differences in the stress index were found between the groups.

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Рандомизированное пилотное исследование совладающего интеллекта и устойчивости к комплексным нагрузкам у пациентов с ревматоидным артритом, подагрой и фибромиалгией

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Резюме. Ревматоидный артрит, подагра и фибромиалгия являются заболеваниями, которые снижают трудоспособность и качество жизни пациентов. Несмотря на хорошо изученный патогенез РА, ГТ и ФМ, имеются единичные исследования устойчивости к физической нагрузке. Исследований толерантности к интеллектуальной и коммуникативной нагрузке у этих групп пациентов не обнаружены. Целью пилотного исследования является оценка совладающего интеллекта, стресс-индекса Баевского, уровня гормональных и иммунологических показателей в сыворотке крови у пациентов с РА, ПА и ФМ по сравнению с рандомизированными контрольными группами. *Методы.* В исследовании приняли участие 126 человек в возрасте от 20 до 54 лет, среди них 27 пациентов с ревматоидным артритом (2 м/25 ж; 28-54 лет), 24 пациента с подагрой (22 м/2 ж;35-48 лет) и 12 пациентов с фибиромиалгией (4 м/8ж; 26-45 лет). Группы контроля рандомизированы по полу, возрасту и образованию. Технология оценки совладающего интеллекта и переносимости комплексной нагрузки включает (1) лабораторные методы оценки гормональных и иммунологических показателей в сыворотке крови до и после нагрузки; (2) оценка антропометрических данных; (3) оценка вариабельности сердечного ритма; (4) нагрузочное тестирование, состоящее из двигательных, интеллектуальных и коммуникативных тестов; (5) шкалы воспринимаемого напряжения психомоторной, интеллектуальной и коммуникативной нагрузки; (6) поведенчески выверенные оценочные шкалы совладающего интеллекта (BARS of CI). *Результаты.* Пациенты с ревматоидным артритом отличаются более высоким уровнем IL-6 в сыворотке крови до и после комплексной нагрузки и легче переносят коммуникативную нагрузку по сравнению с группой контроля. Пациенты с ревматоидным артритом достоверно не отличаются по свойствам совладающего интеллекта по сравнению с контрольной группой. Пациенты с подагрой в отличие от контрольной группы значимо реже проявляют готовность к сотрудничеству (WE) в условиях комплексной нагрузки; имеют более низкий уровень DA в сыворотке крови до нагрузки и отличаются большим весом, охватом талии и индексом массы тела; легче восстанавливаются после физической нагрузки и переносят коммуникативную нагрузку. Пациенты с фибромиалгией менее позитивно реагируют (ER) на нагрузку, меньше верят в свои силы справиться с ней (SE) и реже демонстрируют готовность к сотрудничеству (WE); отличаются более низким уровнем NE до предъявления комплексной нагрузки и более низким уровнем адреналина после нагрузки по сравнению с группой контроля. Уровень IL-6 в сыворотке крови достоверно выше у пациентов с ФМ до и после комплексной нагрузки. Значимых различий в стресс-индексе между пациентами с фибромиалгией и группой контроля не обнаружено. *Заключение*. Результаты исследования могут быть полезны ревматологам для повышения приверженности лечения пациентов с РА, ГТ и ФМ.

Ключевые слова: ревматоидный артрит, подагра, фибромиалгия, совладающий интеллект, стресс-индекс Баевского, переносимость нагрузки, гормоны стресса, интерлейкины, контрольные группы

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