A Clinical Application of Biochemical Markers of Coping Intelligence: A 6-Month Integrated Rehabilitation Program for Rheumatological Patients

Andrey V. Varlamov[*]

Ryazan State Medical University named after academician I.P. Pavlov, Ryazan, Russia

Abstract. *Background and Problem*. Chronic psychosocial stress is a major modifiable factor contributing to treatment non-adherence in rheumatology patients, yet traditional approaches inadequately address this issue. Recent empirical studies (2023–2025) have identified specific biopsychological mechanisms through which stress coping regulates cortisol, inflammatory cytokines (IL-6, TNF-α, IL-4, IL-10), and neuroplasticity markers (BDNF). *Objective*. To translate these research findings into a structured, evidence-based rehabilitation program designed to enhance treatment adherence and disease outcomes in rheumatological patients by cultivating coping intelligence—the capacity to respond adaptively to complex, uncertain, and potentially threatening situations. *Method*. The program comprises 24 structured sessions organized into four modules: diagnostic-adaptation, cognitive-behavioral, physiological regulation, and consolidation-prevention. Integration of cognitive-behavioral therapy, physiological regulation techniques, and standard medical treatment addresses the psychological, neurobiological, and inflammatory dimensions of chronic rheumatological disease. Program development was based on empirical research (2023–2025) examining load tolerance profiles, biochemical and neurochemical markers of coping capacity, clinical-psychological heterogeneity in fibromyalgia, and genetic determinants of stress-coping ability. Participants: age 20–55 years, verified rheumatological diagnosis (rheumatoid arthritis, gout, or fibromyalgia), active disease, minimum 80% session attendance. *Results*. The program targets increasing medication adherence from 50–60% to 85–90%, achieving disease remission or low activity in 70% of participants, reducing pro-inflammatory cytokines (IL-6, TNF-α) by 50–65%, and improving quality of life by 40–50%. *Conclusions*. This evidence-based approach offers an alternative to traditional disease-focused care, addressing both inflammatory and psychosocial dimensions of chronic disease management. *Key Findings*. Biopsychosocial integration; genetic personalization; objectively measurable biomarker improvements; sustainable behavioral change through coping intelligence development.

Keywords: Coping Intelligence, Rheumatological Disease, Cognitive-Behavioral Therapy, Treatment Adherence, Psychosocial Stress, Fibromyalgia, Rheumatoid Arthritis, Gout

1. Introduction

1.1. The Adherence Problem in Rheumatology

Chronic rheumatological diseases such as rheumatoid arthritis (RA), gout, and fibromyalgia (FM) represent serious public health challenges in Russia and globally. Despite the pharmaceutical revolution associated with biologic agents and kinase inhibitors, a fundamental problem persists: only 40–60% of patients consistently adhere to prescribed therapy (Horne et al., 2005). This poor treatment adherence constitutes one of the primary causes of treatment failure, disease progression, complications, and costly hospitalizations.

Non-adherence factors fall into two broad

[*] Corresponding author: e-mail address: andrey.varlamov.62@gmail.com
DOI: 10.38098/nsom_2025_05_04_04

categories: medical and psychosocial. Medical factors include adverse medication effects, complex dosing regimens, and the requirement for frequent injections or monitoring (Horne et al., 2005). However, a growing body of evidence indicates that psychosocial factors—occupational stress, family conflicts, chronic pain, depression, and inadequate stress-coping skills—often play the determining role (Evers et al., 2002; Volkova, Kuvaeva, Varlamov, Volkova, & Dokuchaev, 2025). Psychosocial stress operates not merely as subjective experience; rather, it produces objective biological consequences mediated through sympathetic nervous system activation, hypothalamic-pituitary-adrenal (HPA) axis engagement, and alterations in immune function (Kiecolt-Glaser et al., 2002; McEwen, 2017).

1.2. Stress and Rheumatological Disease: Biological Mechanisms

Selye's classic stress model (1956) describes a three-phase organismal response: alarm reaction, resistance, and exhaustion. In chronic disease contexts, patients frequently become trapped in a phase of chronic sympathetic nervous system activation, producing prolonged release of epinephrine, norepinephrine, and cortisol (Black & Garbutt, 2002; Elenkov et al., 2005; Selye, 1956). This activation engages beta-2 adrenergic receptors on immune cells, suppresses Th1-mediated cellular immunity, and shifts immune balance toward the Th2 pathway, promoting synthesis of pro-inflammatory cytokines including interleukin-6 (IL-6), tumor necrosis factor-alpha (TNF-α), and interleukin-1beta (IL-1β) (Elenkov et al., 2005; Kiecolt-Glaser et al., 2002; McEwen, 2017).

However, patients exhibit differential responses to stress (Elenkov et al., 2005; Volkova et al., 2025). The critical factor involves the capacity to effectively manage stressful situations—a construct designated as coping intelligence (CI). Coping intelligence represents a biopsychological property reflecting an individual's capacity to respond adaptively to complex, uncertain, and potentially threatening situations (Kuvaeva & Volkova, 2024). Individuals with elevated CI demonstrate appropriate hormonal stress responses (cortisol normalization), activation of anti-inflammatory cytokines including interleukin-4 (IL-4) and interleukin-10 (IL-10), and preservation of cellular immunity (Volkova et al., 2025).

1.3. Coping Intelligence as an Intervention Target

Traditional rheumatological disease treatment focuses exclusively on inflammation suppression through pharmacological agents. However, this approach frequently proves insufficient because it does not address the primary modifiable factor—psychosocial stress. Furthermore, patients maintaining elevated stress levels despite anti-inflammatory therapy often demonstrate poorer clinical outcomes and heightened exacerbation risk (Black & Garbutt, 2002; Evers et al., 2002).

An alternative approach emphasizes coping intelligence development as an integral component of medical treatment. This approach recognizes that psychotherapeutic interventions produce objective biological effects. Cognitive-behavioral therapy (CBT), for example, not only modifies thoughts and emotions but also normalizes HPA axis activity, reduces pro-inflammatory cytokines, and increases cerebral neuroplasticity (Hofmann et al., 2012; Williams, Eccleston, & Morley, 2012).

1.4. Scientific Foundation of the Program

The present program was developed based on a series of empirical studies conducted during 2023–2025 at the Institute of Psychology of the Russian Academy of Sciences (Kuvaeva & Volkova, 2024; Teplyakova, Volkova, & Kuvaeva, 2025; Varlamov et al., 2025; Volkova et al., 2024; Volkova et al., 2025; Volkova & Volkova, 2025). Key findings from these studies are briefly presented below and elaborated in corresponding program sections.

Study 1: Complex Load Tolerance (N = 56 patients: RA n = 21, gout n = 23, FM n = 12) demonstrated that rheumatological patients exhibit differentiated vulnerability profiles to various load types. Rheumatoid arthritis patients successfully manage all load categories (stress index within normal range). Gout patients demonstrate selective vulnerability to intellectual demands. Fibromyalgia patients experience systemic overload, particularly under intellectual load (stress index = 400.95 ± 200 units, indicating high distress risk). *Clinical Program Application:* These findings justify differentiated assessment in Module 1, Sessions 1, 3, and 20.

Study 2: Biochemical Markers of Coping Intelligence (N = 251 volunteers) revealed that, regardless of temperamental activity type, adequate stress coping produces the following

changes: (1) cortisol reduction ($p < .001$); (2) elevation of anti-inflammatory cytokine IL-4 ($p < .01$); (3) reduction of pro-inflammatory cytokine IL-6 from 21.6 to 2.8 pg/mL ($p = .012$) (Volkova et al., 2024). *Clinical Program Application:* Biochemical findings (IL-6 reduction 21.6→2.8 pg/mL) justify measurement schedule and expected outcomes (30–50% stress reduction, 20–30% cytokine reduction) in Modules 2–3.

Study 3: Neurochemical Markers of Coping Intelligence (systematic review of 45 publications) revealed that coping intelligence is mediated by interaction of multiple neurochemical systems: glucocorticoid (cortisol/DHEA), serotonergic, dopaminergic, noradrenergic, cytokine, and neurotrophic (BDNF) systems (Kuvaeva & Volkova, 2024). *Clinical Program Application:* The six neurochemical systems identified justify Modules 2–3's multimodal intervention structure targeting serotonergic, dopaminergic, glucocorticoid, and immune systems.

Study 4: Clinical-Psychological Characteristics of Fibromyalgia Patients (N = 3 case studies with integrative analysis) demonstrated fibromyalgia heterogeneity: different patients present distinct psychological profiles (hypochondria, reactive anxiety, trait anxiety) and different biochemical patterns (one patient exhibited fourfold IL-4 elevation; another demonstrated IL-10 reduction, indicating distinct immune dysregulation mechanisms) (Teplyakova et al., 2025). *Clinical Program Application:* Heterogeneity findings justify personalized psychological approaches in Sessions 6, 9, and 20 based on distinct phenotypes.

Study 5: Genetic Determinants of Coping Intelligence identified polymorphisms in the brain-derived neurotrophic factor (*BDNF*) gene (rs6265) and catechol-O-methyltransferase (*COMT*) gene (rs4680) that demonstrate significant association with coping cognitive style, pain sensitivity, and probability of positive response to cognitive-behavioral therapy (Volkova & Volkova, 2025). *Clinical Program Application:* Genetic findings (*BDNF* rs6265, *COMT* rs4680) justify Session 20's genetic personalization and optional testing in Session 1.

Thus, the program exemplifies translational science: moving from research on biomarkers to bedside clinical implementation. Every module, session, and outcome is grounded in specific empirical findings.

2. Objectives

2.1. Primary Objective

To enhance treatment adherence in rheumatological patients through developing coping intelligence, optimizing psychological adaptation, and normalizing immune status by reducing chronic psychosocial stress.

2.2. Specific Medical Objectives

1. Achieve clinical remission or low disease activity in 70% of program participants (Disease Activity Score 28-joint assessment [DAS28] for RA, serum uric acid level for gout, Revised Fibromyalgia Impact Questionnaire [FIQR] for FM);

2. Reduce frequency of rheumatological exacerbations by 40–50%;

3. Improve objective inflammation biomarkers (C-reactive protein [CRP], erythrocyte sedimentation rate [ESR]) by 25–35%;

4. Increase adherence to prescribed pharmacotherapy from 50–60% to 85–90%.

2.3. Specific Psychological Objectives

1. Increase coping intelligence level (reduce Baevsky stress index from 150–400 to 50–120 units);

2. Develop adaptive coping strategies (increase their utilization by 30–40% compared to maladaptive strategies per the Adolescent Coping Scale);

3. Reduce anxiety (Generalized Anxiety Disorder-7 [GAD-7]) and depression (Patient Health Questionnaire-9 [PHQ-9]) levels by 35–45%;

4. Improve quality of life (increase 36-Item Short Form Survey [SF-36] indicators by 25–40%).

2.4. Specific Biochemical Objectives

1. Normalize the ratio of anti-inflammatory to pro-inflammatory cytokines (IL-10/IL-6, IL-4/TNF-α);

2. Optimize cortisol level and circadian rhythm;

3. Normalize neuroplasticity marker (BDNF) values.

3. Program Design: Four-Module Structure

Program Duration: 6 months (24 weeks)

Format: Hybrid (weekly in-person sessions plus telemedical consultations)

Group Size: 15–20 patients

Session Frequency: 24 sessions (approximately 1 session per week, 1.5–3 hours per session)

3.1. Module 1: Diagnostic-Adaptation (Weeks 1–4, 4 Sessions)

Module Objective: Comprehensive assessment of patient baseline status and development of personalized biopsychosocial care plan.

Session 1: Individual Initial Consultation

Leaders: Rheumatologist + Clinical Psychologist

Components:

- *Medical Assessment*. Disease activity evaluation using DAS28 for RA, serum uric acid level for gout, and FIQR for FM. Analysis of current treatment adherence (percentage of doses taken during the preceding month). Pain intensity assessment using Visual Analogue Scale (VAS). Identification of adverse effects and factors limiting treatment compliance through clinical interview. Prescription of baseline laboratory studies: inflammation markers (CRP, ESR), cytokines (IL-4, IL-6, IL-10, TNF-α), hormonal parameters (cortisol, dehydroepiandrosterone [DHEA]), and neuroplasticity marker (BDNF) (Clauw, 2014; Hurley et al., 2012; Prevoo et al., 1995).

- *Psychological Interview*. Structured interview addressing major psychosocial stressors (occupational, familial, financial, health-related). Coping strategy assessment using the adapted Adolescent Coping Scale (Carver, Scheier, & Weintraub, 1989). Personality trait evaluation using the Structure of Temperament Questionnaire (STQ-77) (Rusalov & Trofimova, 2007). Depression screening using PHQ-9 (range 0–27, score ≥10 indicates clinically significant depression) (Kroenke, Spitzer, & Williams, 2001) and anxiety screening using GAD-7 (range 0–21, score ≥8 indicates clinically significant anxiety) (Spitzer, Kroenke, Williams, & Löwe, 2006). Social support assessment. Quality of life assessment using SF-36, comprising 36 items combined into physical and mental health components (Ware & Sherbourne, 1992). Disease management self-efficacy assessment using the Self-Efficacy for Managing Chronic Disease Scale (Lorig et al., 1999). Sleep quality evaluation using the Pittsburgh Sleep Quality Index (PSQI) (Buysse et al., 1989).

- *Biochemical Screening*. Venous blood collection for hormonal and immunological analysis. Optional genotyping of *BDNF* rs6265 and *COMT* rs4680 polymorphisms for personalized psychotherapeutic intervention planning (Varlamov et al., 2025; Volkova et al., 2024).

- *Heart Rate Variability Assessment*. Measurement of Baevsky stress index at rest and under physiological load for objective autonomic balance evaluation. The stress index is calculated from heart rate variability spectral analysis and reflects sympathetic tension level (Baevsky, Kirillov, & Kletskin, 1984).

Session 2: Group Psychoeducational Session: "Stress, Coping, and Health"

Leaders: Clinical Psychologist + General Practitioner

Components:

- Explanation of the relationship between psychosocial stress and rheumatological disease exacerbation, based on program authors' research (Kuvaeva & Volkova, 2024; Teplyakova et al., 2025; Volkova et al., 2024);

- Introduction to the coping intelligence concept as a key internal health resource (Kuvaeva & Volkova, 2024);

- Presentation of evidence regarding stress effects on the immune system and inflammation markers (Elenkov et al., 2005; Kiecolt-Glaser et al., 2002; McEwen, 2017);

- Overview of typical coping strategies with distinction between adaptive (active problem-solving, reappraisal) and maladaptive (avoidance, denial, aggression) approaches;

- Preliminary training in basic physiological regulation techniques (diaphragmatic breathing, 4-7-8 technique);

- Discussion of group rules and program expectations.

Session 3: Individual Goal Setting and Planning

Leaders: Clinical Psychologist + Rheumatologist

Components:

- Feedback on comprehensive assessment results from Sessions 1–2;

- Joint determination of SMART goals for the 6-month period:

- Medical goal: achievement of target

disease activity indicator (e.g., "DAS28 ≤3.2");

- Psychological goal: increased coping intelligence with specific load type (e.g., "reduce stress index during intellectual load from 250 to 100 units");
- Behavioral goal: increased treatment adherence (e.g., "take 100% of prescribed doses");
- Discussion of personal adherence barriers and available patient resources;
- Creation of individual session schedule (including telemedical options for busy patients);
- Recommendations for self-monitoring (pain diary, mood diary, medication calendar).

Session 4: Group Session: "I Am an Active Participant in My Health"

Leaders: Rheumatologist + Social Worker

Components:

- Presentation of success narratives from patients with elevated coping intelligence (using de-identified pilot study data);
- Dispelling common myths about rheumatological disease (e.g., "I will always be disabled");
- Practical information about prescribed medications: mechanism of action, probable adverse effects, strategies for minimization, appropriate storage and administration;
- Introduction to self-monitoring system using mobile application (pain, mood, medication tracking);
- Introduction to social support resources (patient organizations, online forums, charitable organizations).

Baseline Assessment Measures:

- Baseline stress index level (SI)
- Baseline inflammation markers (CRP, ESR) and cytokine values
- Depression (PHQ-9) and anxiety (GAD-7) levels
- Quality of life (SF-36)
- Individual-psychological characteristics (Adolescent Coping Scale, STQ-77)
- *BDNF* rs6265 and *COMT* rs4680 polymorphisms (optional)
- Self-efficacy in disease management (Self-Efficacy for Managing Chronic Disease Scale) (Lorig et al., 1999)

3.2. Module 2: Cognitive-Behavioral (Weeks 5–12, 8 Sessions)

Module Objective: Development of adaptive coping strategies for stress and pain management through structured cognitive-behavioral therapy.

Scientific rationale: Cognitive-behavioral therapy (CBT) is a well-established treatment for depression, anxiety, and chronic pain (Hofmann et al., 2012; Lumley et al., 2011; Williams et al., 2012). However, in the context of rheumatological diseases, CBT must be adapted to address specific factors associated with inflammation and disease course uncertainty (Evers et al., 2002). Our program integrates CBT components with evidence on the neurochemical basis of coping (Varlamov et al., 2025).

Session 5: "The Relationship Between Thoughts, Emotions, and Behavior"

Leaders: Clinical Psychologist

Components:

- Introduction to the cognitive triangle: how a specific situation triggers particular thoughts, which in turn generate emotions and behavioral responses;
- Identification of dysfunctional illness beliefs (automatic thoughts) such as "I will always be disabled," "My treatment is ineffective," "I am a burden to others";
- Cognitive restructuring technique: transformation of negative automatic thoughts into more realistic and functional alternatives;
- Homework: maintenance of a three-column diary (situation – automatic thought – more realistic thought) throughout the week.

Session 6: "Managing Pain Through Threat Reappraisal and Mindfulness"

Leaders: Clinical Psychologist + Physical Therapist

Scientific rationale: Study 4 demonstrated that fibromyalgia patients are particularly vulnerable to intellectual and communication stress. Threat reappraisal and mindfulness techniques are particularly effective in reducing pain catastrophizing and pain levels in this group (Häuser, Sarzi-Puttini, & Fitzcharles, 2019; Pérez-Aranda et al., 2021).

Components:

- Explanation of pain catastrophizing

mechanisms: how negative expectations and threat exaggeration intensify pain perception;

- Threat reappraisal technique: differentiation between real physical danger ("Am I in actual danger?") and perceived threat ("Is my perception accurate?");
- Practical application: applying the technique to the patient's current pain syndrome;
- Introduction to mindfulness practice: observing sensations without judgment as a "defocusing" method from pain;
- Progressive muscle relaxation practice—a simple but effective method for reducing muscle tension (Jacobson, 1974; Pawlow & Jones, 2002);
- Homework: daily progressive muscle relaxation (10 minutes) and mindfulness meditation (5 minutes).

Session 7: "Active Problem-Solving"

Leaders: Clinical Psychologist

Scientific rationale**:** Studies 1 and 2 showed that RA patients demonstrate successful coping across all types of stressors. This suggests that active, problem-focused coping is a natural strength of this group that can be strengthened and generalized (Carver et al., 1989; Evers et al., 2002).

Components:

- Introduction to the active problem-solving algorithm (IDEAL method):
  - **I** (Identify): Define the problem;
  - **D** (Define): Clearly describe the problem;
  - **E** (Explore): List possible solutions;
  - **A** (Assess): Evaluate pros and cons of each solution;
  - **L** (Learn): Implement the best solution and evaluate results (Carver et al., 1989);
- Practical example: developing a strategy to cope with work overload or family conflict;
- Cost-benefit analysis technique for difficult decisions;
- Setting micro-goals (achievable objectives) rather than global goals;
- Homework: solve one real problem using the IDEAL method and document the result.

Session 8: "Time Management and Priority Setting"

Leaders: Clinical Psychologist + Social Worker

Scientific rationale: Study 5 found that work overload and inability to make decisions were among the most stressful factors for rheumatology patients.

Components:

- Eisenhower matrix technique: four-cell system for categorizing tasks by importance and urgency (urgent-important, urgent-unimportant, non-urgent-important, non-urgent-unimportant);
- Prioritizing activities according to patient values;
- Practicing declining requests without guilt;
- "Energy blocks" technique: alternating activity and rest according to individual energy levels;
- Day planning considering pain circadian rhythm and energy availability;
- Homework: create a weekly plan with clear task prioritization.

Session 9: "Emotional Release and Healthy Self-Expression"

Leaders: Clinical Psychologist + Art Therapist (optional)

Scientific rationale: Study 2 found that the adaptive coping strategy of emotional release (used in balance with the problem-solving strategy) helps reduce the stress index and normalize hormonal levels (Pennebaker & Beall, 1986).

Components:

- Distinction between healthy and unhealthy emotional release mechanisms;
- Safe release techniques: physical activity, creative expression, communication with trusted persons;
- Emotion expression practices: speaking, writing (forgiveness letters, anger letters), drawing;
- Setting and protecting personal boundaries in communication (assertiveness): methods for declining requests and asking for assistance;
- Constructive communication techniques (using "I-messages");

- Homework: choose one expression form and practice it 3 times per week.

Session 10: "Social Support and Life Meaning"

Leaders: Clinical Psychologist + optional spiritual counselor or chaplain

Scientific rationale: Loneliness and social isolation are independent risk factors for exacerbation of rheumatological diseases and are associated with increased pro-inflammatory cytokines (Holt-Lunstad, Smith, & Layton, 2010; Pressman & Cohen, 2005).

Components:

- Loneliness and social isolation as independent risk factors for rheumatological disease exacerbation;
- Assessment of current patient social network (family members, friends, healthcare professionals);
- Relationship strengthening techniques: regular contact, meaningful conversations, gratitude expression;
- Participation in support groups, volunteering, or other community activities;
- Finding meaning in illness context: How has disease altered my values? What positive changes have occurred? (post-traumatic growth concept) (Tedeschi & Calhoun, 1996);
- Spirituality as a coping factor (for religious patients);
- Homework: engage in one meaningful social activity per week.

Session 11: "Integration: My Personal Coping Plan"

Leaders: Clinical Psychologist

Components:

- Summary of all coping techniques learned in Sessions 5–10;
- Individualization: which techniques proved most beneficial for this patient?
- Creating a personal "quick response card"—a brief algorithm of actions for critical situations (e.g., "if severe pain occurs: (1) diaphragmatic breathing 2 minutes, (2) threat reappraisal, (3) call physician if pain intensity exceeds 7/10");
- Identification of approaching crisis warning signs and action planning;
- Homework: daily utilization of personal coping plan.

Session 12: Interim Progress Assessment

Leaders: Rheumatologist + Clinical Psychologist

Components:

- Repeat measurement of major psychological indicators (PHQ-9, GAD-7, SF-36, Adolescent Coping Scale, STQ-77);
- Analysis of pain and disease activity dynamics during the 12-week period;
- Adherence verification through direct dose counting;
- Group discussion: what difficulties occurred? Which techniques proved most beneficial?
- Motivational message emphasizing the importance of continued work in subsequent modules.

Expected Module 2 Results:

- ↓ Stress index by 30–40%
- ↓ PHQ-9 and GAD-7 by 35–45%
- ↑ Use of adaptive coping strategies by 40–50%
- ↑ Adherence to drug therapy by 20–30 percentage points
- ↓ Pro-inflammatory cytokines (IL-6, TNF-α) by 20–30%

3.3. Module 3: Physiological Regulation (Weeks 13–18, 6 Sessions)

Module Objective: Restoration of physiological balance through optimization of physical activity, sleep quality, and nutrition. Strengthening brain-derived neurotrophic factor as the foundation of neuroplasticity and recovery.

Scientific rationale: Study 2 demonstrated that adequate stress management automatically normalizes cortisol and increases anti-inflammatory cytokines. Physical activity enhances these processes by increasing BDNF, a central regulator of neuroplasticity with anti-inflammatory effects (González-Castro et al., 2019; Huang et al., 2014).

Session 13: "Physical Activity in Rheumatological Disease"

Leaders: Physical Therapist + Rheumatologist

Components:

- Discussion of physical activity benefits for mental and physical health: elevated BDNF, reduced cortisol, improved joint function (Clauw, 2014; Metsios et al., 2008);
- Safe activity types for RA, gout, and FM patients based on load tolerance data:
- For RA: aerobic activity (walking, swimming), resistance exercises, flexibility and balance training;
- For gout: avoiding extreme physical demands, preferring low-intensity aerobic activity;
- For FM: gentle programs beginning at very low intensity (e.g., yoga, pilates, tai chi), with gradual progression;
- Individual physical activity program planning considering baseline load tolerance profile;
- Program commencement (target result: 150 minutes of moderate-intensity activity weekly per World Health Organization recommendations) (Bull et al., 2020);
- Homework: begin assigned program.

Session 14: "Sleep Optimization as Foundation for Recovery"

Leaders: Clinical Psychologist + Neurologist (optional)

Scientific rationale: Quality sleep is essential for consolidating emotional memory, normalizing immune response (IL-4↑, IL-6↓), and recovering from stress (Besedovsky, Lange, & Born, 2012; Born, Rasch, & Gais, 2006; van Kessel et al., 2008).

Components:

- Sleep connection to immune function and inflammation regulation (IL-4↑, IL-6↓);
- Sleep hygiene techniques: consistent sleep schedule, cool dark bedroom, screen avoidance for 1 hour before bedtime;
- Sleep disturbance management: insomnia, disrupted circadian rhythm (particularly important for patients with nocturnal pain);
- Yoga nidra practice (conscious relaxation) for sleep quality improvement;
- Relaxation techniques prior to sleep;
- Homework: maintain 7–8-hour sleep duration using one relaxation technique.

Session 15: "Nutrition and Anti-inflammatory Diet"

Leaders: Registered Dietitian + Rheumatologist

Scientific rationale: Plant-based, Mediterranean, or DASH diets are associated with lower levels of pro-inflammatory cytokines and better clinical activity in rheumatology patients (Gioxari et al., 2018; Maeda & Takeda, 2017; Pedersen et al., 2006; Zhou, Xu, & Wan, 2019). Avoiding high-glycemic foods is important to minimize systemic inflammation.

Components:

- Diet and systemic inflammation connection: pro-oxidants (refined carbohydrates, trans fats) versus antioxidants (fruits, vegetables, fish);
- Anti-inflammatory diet approaches: Mediterranean, DASH, and plant-based;
- Omega-3 fatty acids (fish, flaxseed oil) as anti-inflammatory agents;
- Gut microbiome role in immune tolerance;
- Food trigger avoidance (for gout: purine avoidance; for FM: glutamate minimization);
- Individual diet planning considering cultural and economic preferences;
- Homework: implement 2–3 anti-inflammatory dietary habits.

Session 16: "Energy Management and Circadian Rhythm Synchronization"

Leaders: Clinical Psychologist + General Practitioner

Components:

- Introduction to "energy profile" concept: when during the day does the patient experience maximum energy?
- Synchronizing important activities (work, social interactions, medical procedures) with energy peaks;
- Understanding circadian rhythm effects on cortisol, pain intensity, and inflammation;
- Energy recovery techniques: microsleep (7–20 minutes), "energy transitions" (activity switching);
- Using pedometers or activity trackers for objective activity monitoring;
- Homework: plan the week according to individual energy profile.

Session 17: "Recovery After Illness and Exacerbations"

Leaders: Rheumatologist + Clinical Psychologist

Scientific rationale: Disease flare-ups are often accompanied by psychological reactions (despair, shame, social isolation), which can lead to treatment interruption and further exacerbation (Evers et al., 2002).

Components:

- Understanding psychological effects of exacerbations;
- Developing concrete action plan for exacerbations: when to contact physician? which coping techniques to employ? how to modify routine?
- Self-compassion and self-forgiveness techniques (particularly if patient attributes exacerbation to personal failings);
- Post-traumatic growth: how can exacerbation lead to positive psychological changes? (increased body awareness, priority reassessment, deeper relationships);
- Writing a letter to oneself describing how the patient has overcome difficulties previously;
- Homework: write a detailed letter to yourself titled "How I Cope with This Disease."

Session 18: Interim Physiological Assessment

Leaders: Rheumatologist + Physical Therapist

Components:

- Disease activity assessment (DAS28 for RA, serum uric acid for gout, FIQR for FM);
- Depression screening (PHQ-9);
- Anxiety screening (GAD-7);
- Neuroplasticity marker assessment (BDNF);
- Pain intensity assessment (VAS);
- Sleep quality assessment (PSQI).

Expected Module 3 Results:

- ↑ BDNF by 30–50% (neuroplasticity and recovery marker)
- ↑ Sleep quality by 40–50% (per PSQI)
- ↑ Adherence to regimen and nutrition recommendations
- Further reduction of pro-inflammatory cytokines and disease activity

3.4. Module 4: Consolidation and Prevention (Weeks 19–24, 6 Sessions)

Module Objective: Consolidation of achieved results and development of long-term strategy for preventing relapse and exacerbation.

Session 19: "My Journey: From Diagnosis to Coping with Illness"

Leaders: Clinical Psychologist

Components:

- Deep reflection on personal patient journey through the program: what changes occurred during the preceding 4.5 months?
- Creating a "success narrative" (may be voluntarily shared in the group and utilized as inspiration for new patients);
- Recognizing patient's personal contribution to results (beyond attribution to physician);
- Identifying and naming developed competencies: resilience, self-compassion, problem-solving ability, capacity to request assistance.

Session 20: "Genetics and Personalization: Understanding My Coping Type"

Leaders: Geneticist or Rheumatologist (if genotyping was performed)

Components for all patients:

- Personality activity profile typing: psychomotor, intellectual, or communicative activity? (based on Study 1 data);
- Personalized load recommendations and avoidance/modification methods;
- Understanding which life situations are most stressful for this specific patient and developing personal adaptation strategies.

Additional Components (if *BDNF*/*COMT* genotyping was performed):

- Explanation of genotyping results in accessible language (avoiding technical terminology);
- How do *BDNF* genotype (Val/Val, Val/Met, Met/Met) effects affect cognitive style and coping ability? Which learning and social interaction styles suit my genotype best? (González-Castro et al., 2019);
- How does *COMT* genotype (Val/Val versus Met/Met) affect pain sensitivity and stress response? Do I require special support in

uncertain situations?

- Critical point: genetics predispose but do not determine outcome. Plasticity and learning are possible regardless of genotype.

Session 21: "Relapse Prevention Plan"

Leaders: Rheumatologist + Clinical Psychologist

Components:

- Identification of early warning signs of approaching exacerbation (intensified pain, psychological distress, social isolation, sleep disruption);
- Development of individual "crisis action plan":
  - When to contact the physician? (specific symptoms or indicators)
  - Which coping techniques to immediately employ?
  - How to modify physical activity?
  - Is hospitalization indicated?
- Identification of preventive measures requiring permanent implementation:
  - Regular physical activity (minimum 3 times per week);
  - Continuous adherence to pharmacotherapy, particularly basic agents;
  - Continuous coping technique practice (relaxation, cognitive reappraisal);
  - Quarterly rheumatologist consultations (without waiting for exacerbation);
  - Social activity and maintenance of social connections;
  - Quality sleep and anti-inflammatory nutrition.
- Identification of "windows of opportunity" for preventive interventions: when is exacerbation risk highest? (e.g., following major stressful events, in particular seasons);
- Homework: write a detailed personal relapse prevention plan for 6–12 months.

Session 22: "Building My Support System"

Leaders: Social Worker + Clinical Psychologist

Components:

- Mapping patient social network: family members, friends, medical professionals, professional consultants, support groups;
- Identifying "roles" in the network: who provides emotional support? practical assistance? information support? evaluative support?
- Strengthening weak network links (e.g., if the sole contact is a general practitioner, adding a psychologist, support group);
- Discussion of methods to request assistance without shame or feeling burdensome;
- Information about available local and national resources (charitable organizations, hotlines, online patient communities);
- Discussion of patient role as "expert": can the patient support other patients? become a volunteer?

Session 23: "My Personal Health Manual"

Leaders: Clinical Psychologist (as coach)

Components:

Creating a collaborative personal "Health Manual" document (5–10 pages) including:

- Brief summary: My diagnosis, current medications, key medical indicators, my primary goals for the next year;
- My vulnerability profile: Based on Modules 1–3 data—my typical stress response profile, my pain type, my coping style;
- My most effective coping techniques: Specific (not general) techniques that work personally for me, with step-by-step instructions;
- My weekly schedule: Physical activity schedule, sleep, nutrition, relaxation, social activity;
- My pain management plan: Pharmacological (medications, doses, timing) + non-pharmacological (techniques, specialist contacts);
- How I will explain my condition to a new physician: Brief, clear description of my disease and what I require;
- Signs requiring urgent care: Specific symptoms, telephone numbers;
- My resources and strengths: What helps me cope? Who supports me? What qualities do I value in myself?

This manual becomes a "personal reference guide" for years and can be updated annually.

Session 24: Final Assessment and Graduation

Leaders: Entire interdisciplinary team (Rheumatologist, Clinical Psychologist, Physical Therapist, Social Worker, General Practitioner)

Components:

1. **Comprehensive repeat testing (baseline-to-endpoint):**

- Current treatment adherence analysis (percentage of doses taken during past month);
- Disease activity assessment (DAS28 for RA, serum uric acid for gout, FIQR for FM);
- Heart rate variability registration, Baevsky stress index at rest and under load;
- Depression screening (PHQ-9);
- Anxiety screening (GAD-7);
- Quality of life assessment (SF-36);
- Coping strategies assessment (Adolescent Coping Scale);
- Pain intensity assessment (VAS);
- Inflammation markers analysis (CRP, ESR);
- Pro- and anti-inflammatory cytokine analysis (IL-4, IL-6, IL-10, TNF-α);
- Hormonal parameters (cortisol, DHEA);
- Neuroplasticity marker analysis (BDNF);
- Sleep quality assessment (PSQI).

2. **Individual results analysis:**

- Before-after comparison for each patient;
- Discussion of achieved goals (from Session 3, Module 1);
- Identifying areas requiring continued work;
- Recommendations for next steps (continuation in maintenance mode? additional specialist consultations?).

3. **Group activity:**

- Each patient shares one key positive change attributable to the program;
- Expression of recognition and mutual gratitude (group support as a valuable resource);
- Discussion of maintenance-mode meeting plan (recommended monthly for additional 6–12 months).

4. **Document delivery:**

- Program completion certificate;
- Personal next-steps plan;
- Methodological materials for independent use;
- Information about maintaining team and group contact.

4. Assessment Methods and Expected Outcomes

4.1. Primary Outcomes

1. Treatment Adherence (primary outcome)

Measure: Percentage of correctly taken prescribed medication doses per month (based on prescription analysis, patient diaries, and telephone interviews);

Target result: Increase from baseline 50–60% to ≥85% by program completion;

Measurement timepoints: Baseline, weeks 12, 24.

2. Disease Activity

2.1. Disease Activity (Rheumatoid Arthritis)

Measure: DAS28 index including assessment of number of tender and swollen joints, overall disease activity per VAS;

Target result: Reduction ≥50% from baseline or achievement of low activity (DAS28 ≤3.2);

Measurement timepoints: Baseline, weeks 8, 16, 24.

2.2. Disease Activity (Gout)

Measure: Serum uric acid level;

Target result: Achievement of target uric acid level <360 μmol/L (or <300 μmol/L for severe tophaceous gout); reduction of acute gout attack frequency to zero during observation period;

Measurement timepoints: Baseline, weeks 8, 16, 24.

2.3. Disease Activity (Fibromyalgia)

Measure: FIQR including pain intensity assessment per VAS, functional impairment, and somatic symptom assessment; additionally, Widespread Pain Index and Somatic Symptom Severity scale per 2016 American College of Rheumatology criteria;

Target result: FIQR total score reduction ≥50% from baseline or achievement of clinically significant improvement (pain intensity reduction per VAS ≥30% and reduction of functional impairment indicators);

Measurement timepoints: Baseline, weeks 8, 16, 24.

3. Coping Intelligence

Measure: Baevsky stress index, calculated

based on heart rate variability analysis during physical, intellectual, and communicative loads;

Target result: Reduction by 60–70% (e.g., from baseline stress index = 250 ± 80 to final stress index = 80 ± 30 units);

Measurement timepoints: Baseline, weeks 12, 24.

4.2. Secondary Outcomes

Domain	Instrument	Baseline Example	Target Result	Measurement Timepoints
Depression	PHQ-9 (0–27)	15–18	↓60–70% (to 4–8)	Baseline, weeks 4, 8, 12, 18, 20, 24
Anxiety	GAD-7 (0–21)	12–16	↓65–75% (to 3–7)	Baseline, weeks 4, 8, 12, 18, 20, 24
Quality of Life	SF-36 (0–100)	35–50	↑40–50% (to 60–75)	Baseline, weeks 12, 24
Coping Strategies	Adolescent Coping Scale (% adaptive)	40–50%	↑35–45 pp (to 75–85%)	Baseline, weeks 12, 24
Pain Intensity	VAS (0–100 mm)	60–80	↓30–40%	Baseline, weeks 8, 18, 24
Inflammation Marker	CRP (mg/L)	10–25	↓50–60% (to 3–8)	Baseline, weeks 12, 24
Inflammation Marker	ESR (mm/h)	25–45	↓40–50%	Baseline, weeks 12, 24
Pro-inflammatory Cytokines	IL-6, TNF-α (pg/mL)	15–35	↓55–65% (to 5–12)	Baseline, weeks 12, 24
Anti-inflammatory Cytokines	IL-4, IL-10 (pg/mL)	3–5	↑50–70% (to 7–10)	Baseline, weeks 12, 24
Stress Hormone	Cortisol (nmol/L)	450–600	Circadian rhythm normalization	Baseline, weeks 12, 24
Neurotrophic Factor	BDNF (ng/mL)	15–25	↑80–100% (to 30–45)	Baseline, weeks 12, 18, 24
Sleep Quality	PSQI (0–21)	12–16	↓40–50% (to 6–8)	Baseline, weeks 12, 18, 24

4.3. Program Safety

Potential Adverse Outcome	Monitoring	Assessment Frequency	Action Plan
Mental health deterioration (suicidality risk)	Weekly observation, PHQ-9/GAD-7 every 4 weeks, direct interview	Continuous	Psychiatric referral if PHQ-9 >25 or suicidal ideation present
Rheumatological disease exacerbation	Weekly phone contact, DAS28/activity markers every 4 weeks	Continuous	Rheumatologist pharmacotherapy adjustment, optional early hospitalization
Physical injury during physical activity	Pre-program screening, post-exercise check-in	Weekly	Physical therapist program adjustment
Program dropout (>20% absences)	Contact upon absence, analysis of reasons	Per each absence	Problem-solving (schedule modification, online participation options)

5. Program Team

Minimal composition:

- Program Director (Rheumatologist): Specialization in rheumatology (≥5 years' experience), expertise in psychosocial aspects of disease
- Clinical Psychologist: Specialization in cognitive-behavioral therapy (≥5 years' experience)
- General Practitioner/Internist
- Physical Therapist: Specialization in rheumatological physiotherapy
- Nurse Coordinator
- Social Worker
- Program Coordinator (administrative support)

Optional partners: Registered Dietitian, Neurologist, Spiritual Counselor/Chaplain

Work effort: Approximately 52 hours of team work per week per group of 15–20 patients (for one rheumatologist and one clinical psychologist)

6. Inclusion and Exclusion Criteria

6.1. Inclusion Criteria

- Age 20–55 years
- Verified diagnosis of rheumatological disease (RA, gout, FM)
- Active disease (DAS28 ≥3.2 for RA, serum uric acid level ≥420 μmol/L for gout, FIQR ≥20 for FM)
- Insufficient current therapy adherence (<80% doses taken) or desire to improve quality of life
- Ability to provide informed consent
- Ability to attend program sessions (minimum 80% of 24 sessions or active telemedical participation)

6.2. Exclusion Criteria

- Acute psychiatric disorders (acute psychosis, manic episode)
- Active suicidal risk
- Severe somatic pathology (terminal renal failure, active oncology)
- Cognitive impairment preventing CBT participation
- Absence of Russian language proficiency or significant language barrier
- Simultaneous participation in another clinical program

7. Conclusion

The presented 6-month program represents a systematic translational research application, converting findings from five empirical studies

(N > 300, 2023–2025) into a structured, evidence-based rehabilitation protocol. The program exemplifies the research-to-practice pipeline: from basic findings on neurochemical mechanisms through clinical observation of disease-specific vulnerability, to genetic determination, to integrated clinical delivery (Kuvaeva & Volkova, 2024; Teplyakova et al., 2025; Varlamov et al., 2025; Volkova et al., 2024; Volkova et al., 2025; Volkova & Volkova, 2025).

Program Component	**Empirical Foundation**	**Effect Size**
Differentiated assessment	Study 1 (N=56)	RA: normal stress index; Gout: selective vulnerability; FM: systemic overload
Cytokine targets	Study 2 (N=251)	IL-6: 21.6→2.8 pg/mL (68% reduction); IL-4↑
Multimodal structure	Study 3 (n=45 publications)	Six neurochemical systems identified
Personalized approaches	Study 4 (n=3 cases)	Distinct psychological + biochemical phenotypes
Genetic personalization	Study 5	*BDNF* & *COMT* predict CBT response

Key program innovations include:

1. Differentiated approach considering specific vulnerability profiles of different disease groups (RA versus gout versus FM);
2. Biopsychosocial model integrating medical treatment, psychological interventions, and educational components;
3. Personalization based on genetic markers (*BDNF*, *COMT*) and psychological profiles;
4. Objectification of psychological results through hormonal (cortisol, DHEA) and immunological marker measurement (cytokines, BDNF);
5. Modularity and flexibility allowing program adaptation to different healthcare settings.

The program predicts improvement in treatment adherence from 50–60% to 85–90%, disease activity reduction of 50–60%, quality of life improvement of 40–50%, and normalization of inflammation markers.

Highlights:

- *Biopsychosocial Integration Addresses Root Cause of Non-Adherence*. The program targets psychosocial stress—a primary modifiable factor in treatment failure—rather than solely focusing on pharmaceutical suppression, offering an evidence-based alternative to traditional disease-centered rheumatological care.
- *Coping Intelligence as Measurable Biomarker*. Elevated coping capacity produces objective biological improvements: cortisol normalization, pro-inflammatory cytokine reduction (IL-6, TNF-α by 50–65%), and anti-inflammatory cytokine elevation (IL-4, IL-10), demonstrating that psychological interventions have quantifiable neurobiological consequences.
- *Differentiated Approach Based on Disease-Specific Load Tolerance*. Empirical research identified distinct vulnerability profiles: RA patients tolerate all load types; gout patients show selective intellectual load vulnerability; FM patients experience systemic overload—enabling personalized intervention strategies.
- *Four-Module Structured Intervention Combining CBT, Physiology, and Medical Care*. The 24-session hybrid program (diagnostic-adaptation, cognitive-behavioral, physiological regulation, consolidation-prevention) integrates cognitive restructuring, mindfulness, physical activity optimization, and sleep/nutrition interventions within a coordinated medical framework.
- *Sustainable Adherence Improvement Through Behavioral Change*. The program targets increasing medication adherence from 50–60% to 85–90% and quality of life by 40–50% while achieving disease remission or low activity in 70% of participants through development of adaptive coping strategies rather than external compliance monitoring.
- *Genetically Informed Personalization Enhances Treatment Precision*. *BDNF* (rs6265) and *COMT* (rs4680) polymorphisms identify

individual differences in pain sensitivity, cognitive coping styles, and CBT responsiveness, allowing tailored psychological interventions based on genetic predisposition while emphasizing neuroplasticity regardless of genotype.

Competing Interests: The author declares that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Ethics Statement: The study was reviewed and approved by the local ethics committee of the Federal State Budgetary Educational Institution of Higher Education Ryazan State Medical University of the Ministry of Health of the Russian Federation (report No. 12 dated 25/05/2021).

AI-Use Statement: Approximately 30% of the text was edited using Perplexity.ai to improve clarity and academic accuracy. Sentences generated by artificial intelligence were unusual and were reworked by the author.

Acknowledgments: The author thanks the study participants for their unpaid participation in the study to promote scientific advancement.

Funding: The development of the concept of coping intelligence and the study of its biopsychological mechanisms was supported by the Russian Science Foundation Grant No. 23-18-00293 (2023–2025, supervised by E.V. Volkova).

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Клиническое применение биохимических маркеров совладающего интеллекта: 6-месячная комплексная реабилитационная программа для пациентов с ревматологическими заболеваниями

А.В. Варламов

Рязанский государственный медицинский университет имени академика И.П. Павлова, Рязань, Россия

Резюме. *Актуальность и проблема.* Хронический психосоциальный стресс является одним из основных модифицируемых факторов отказа от лечения у ревматологических пациентов, однако традиционные подходы сопровождения данной группы пациентов учитывают его крайне недостаточно. Эмпирические исследования 2023–2025 годов показали конкретные биопсихологические механизмы, через которые способность совладания со стрессом может регулировать кортизол, воспалительные цитокины (IL-6, TNF-α, IL-4, IL-10) и маркеры нейропластичности (BDNF). *Цель.* Преобразовать результаты этих исследований в структурированную, основанную на доказательствах программу реабилитации, предназначенную для повышения приверженности к лечению и улучшения исходов заболевания у ревматологических пациентов путем развития совладающего интеллекта —способности адаптивно реагировать на сложные, неопределённые и потенциально угрожающие ситуации. *Метод.* Программа включает 24 структурированные сессии, организованные в четыре модуля: диагностико-адаптационный, когнитивно-поведенческий, физиологической регуляции и консолидации-профилактики. Интеграция когнитивно-поведенческой терапии, техник физиологической регуляции и стандартного медицинского лечения обеспечивает комплексный подход к психологическим, нейробиологическим и воспалительным аспектам хронического ревматологического заболевания. Разработка программы базировалась на эмпирических исследованиях (2023–2025), изучавших профили переносимости нагрузок, биохимические и нейрохимические маркеры совладающего интеллекта, клинико-психологическую гетерогенность фибромиалгии и генетические детерминанты способности совладания со стрессом. Участники: возраст 20–55 лет, верифицированный ревматологический диагноз (ревматоидный артрит, подагра, фибромиалгия), активное заболевание, посещение минимум 80% сессий. *Прогнозируемые результаты.* Программа ориентирована на повышение приверженности к медикаментозной терапии с 50–60% до 85–90%, достижение ремиссии или низкой активности заболевания у 70% участников, снижение провоспалительных цитокинов (IL-6, TNF-α) на 50–65% и улучшение качества жизни на 40–50%. *Выводы.* Данный подход предлагает альтернативу традиционному ориентированному на болезнь подходу, комплексно адресуя как воспалительные, так и психосоциальные аспекты ведения хронического заболевания. Особенности программы: биопсихосоциальная интеграция, генетическая персонализация, объективно измеримые улучшения биомаркеров, устойчивые поведенческие изменения благодаря развитию совладающего интеллекта.

Ключевые слова: совладающий интеллект, ревматологические заболевания, когнитивно-поведенческая терапия, приверженность лечению, психосоциальный стресс, фибромиалгия, ревматоидный артрит, подагра

Information about the author

Andrey Vitalievich Varlamov – PhD (Psychology), Lecturer, Department of General and Special Psychology with a Course in Pedagogy, Ryazan State Medical University named after Academician I.P. Pavlov; 9 Vysokovoltnaya St., Ryazan, 390026, Russia; ORCID: 0000-0002-6144-6036; e-mail: andrey.varlamov.62@gmail.com

Информация об авторе

Андрей Витальевич Варламов – кандидат психологический наук, преподаватель кафедры общей и специальной психологии с курсом педагогики, Рязанский государственный медицинский университет им. академика И.П. Павлова; 390026, Рязань, ул. Высоковольтная, д. 9; ORCID: 0000-0002-6144-6036; e-mail: andrey.varlamov.62@gmail.com

Citation: Varlamov, A.V. (2025). A Clinical Application of Biochemical Markers of Coping Intelligence: A 6-Month Integrated Rehabilitation Program for Rheumatological Patients. *Natural System of Mind, 5*(4), 49 – 66 https://doi.org/10.38098/nsom_2025_05_04_04