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Multimodal Non-Pharmacological Interventions for Fibromyalgia: Targeting Emotional and Cognitive Symptoms

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Abstract: Fibromyalgia (FM) is a chronic condition characterized by widespread pain, emotional distress, and cognitive impairments, significantly impacting quality of life. This study evaluated the effectiveness of three non-pharmacological interventions—stretching-based kinetic therapy, cognitive-behavioral therapy (CBT), and occupational therapy (OT)—on emotional and cognitive symptoms in FM patients. A prospective controlled study included 126 FM patients divided into four groups: CBT, stretching, OT, and a control group (CG) receiving only general education. Emotional outcomes were assessed using the Hospital Anxiety and Depression Scale (HADS) and Positive and Negative Affect Schedule (PANAS), while cognitive function was measured through Symbols and Digits tests. A follow-up assessment was conducted six months post-intervention to evaluate sustainability. CBT significantly reduced anxiety and sustained positive affect ($p = 0.01$). Stretching therapy provided long-term symptom relief ($p = 0.02$), while OT improved information processing speed ($p < 0.001$). The CG showed minimal changes. Despite observed benefits, adherence variability and the lack of randomization were study limitations. Conclusions: Multimodal non-pharmacological interventions demonstrated distinct yet complementary effects, supporting their integration into FM management. Stretching exercises contributed to sustained symptom relief, CBT was effective for emotional regulation, and OT improved cognitive function. Clinicians should consider patient-specific needs when designing rehabilitation strategies. Future studies should explore long-term adherence and comparative effectiveness across diverse FM populations.

Keywords: fibromyalgia; stretching-based kinetic therapy; occupational therapy; cognitive-behavioral therapy;

1. Introduction

Fibromyalgia (FM) is a chronic disorder characterized by widespread pain, fatigue, sleep disturbances, and a range of cognitive and emotional impairments. These symptoms, often referred to as "fibrofog," include difficulties with memory, attention, executive function, and emotional regulation, significantly impacting patients' daily functioning and quality of life [1,2]. While pharmacological treatments provide symptom relief, they often fail to address the full spectrum of cognitive and emotional challenges experienced by FM patients, highlighting the need for effective non-pharmacological interventions [3,4].

FM's pathophysiology is complex, involving central sensitization, altered neurotransmitter levels (e.g., serotonin, dopamine), and neuroinflammatory responses [5-7]. Genetic predisposition and dysregulation of the hypothalamic-pituitary-adrenal (HPA) axis contribute to increased stress sensitivity, which may exacerbate cognitive and emotional dysfunction in FM patients [8,9]. Given these mechanisms, interventions that target both stress regulation and neural plasticity—such as cognitive-behavioral therapy (CBT), occupational therapy (OT), and stretching exercises—may offer therapeutic benefits.

Similar to other rheumatologic diseases [10-12], the etiology and pathogenesis of FM remain controversial. It appears to be driven by a complex interplay of genetic predisposition [13,14], neuroendocrine dysregulation, and neural dysfunction [15,16]. The hippocampus, crucial for memory, spatial orientation, and pain modulation, emerges as a central player in FM pathology [17], with metabolic abnormalities and neuronal disruptions adding to the evidence for its involvement [18,19]. However, existing research has not sufficiently linked these neurobiological findings to targeted intervention strategies, an area this study seeks to explore.

Beyond pain, FM encompasses a wide array of symptoms, including hyperalgesia, allodynia, fatigue, stiffness, non-restorative sleep, anxiety, depression, cognitive impairments (e.g., short-term memory deficits, reduced vocabulary), and functional somatic disorders such as irritable bowel syndrome and dysmenorrhea [20-22].

Emotional disturbances such as anxiety and depression are among the most common associated symptoms in FM, affecting 30-75% of patients [20]. The exact mechanisms underlying these emotional symptoms remain unclear, but several contributing factors have been identified [23-26].

Cognitive dysfunction in FM, often referred to as "fibro fog," includes impairments in memory, attention, executive functioning, and information processing speed [27,28]. These issues have a profound impact on patients' daily lives and ability to function in work environments. Hippocampal dysfunction, characterized by reduced volume and altered metabolism, is linked to memory deficits and attentional impairments [29]. Chronic HPA axis activation contributes to emotional and cognitive impairments through excess cortisol, reducing working memory and slowing information processing [16]. Neurovascular impairment, particularly reduced cerebral blood flow in the prefrontal cortex and hippocampus, may also explain deficits in executive function [30]. Additionally, elevated oxidative stress and neuroinflammation disrupt neuronal communication, exacerbating cognitive dysfunction [31].

Despite growing recognition of these mechanisms, there remains a gap in treatment strategies that specifically target the interplay between neurobiological alterations and cognitive-emotional impairments. Although existing studies have explored CBT and kinesiotherapy as standalone interventions, few have compared their relative efficacy alongside OT. By addressing this gap, our study seeks to provide a more comprehensive understanding of multimodal intervention benefits in FM management.

The complexity of FM necessitates a multimodal treatment approach targeting both physical and psychological symptoms. Pharmacological options, including pregabalin, duloxetine, and milnacipran, have been approved for FM treatment in some regions, but their efficacy is limited, and long-term adherence remains a challenge [32]. Non-pharmacological interventions, particularly CBT and kinesiotherapy, have emerged as essential components of FM management.

Kinesiotherapy is a cornerstone of non-pharmacological management for FM, with strong evidence supporting its efficacy in alleviating pain, improving physical function, and enhancing quality of life. Among the various modalities, strength training, Pilates, aerobic or stretching exercise have been widely studied, but their impact on emotional and cognitive symptoms requires further exploration. Individualized exercise programs tailored to patient physical capabilities and symptom profiles are

essential for optimizing outcomes [33,34]. Stretching therapy, which involves systematic elongation of muscle groups and soft tissues, has shown considerable promise in managing FM symptoms. Mechanistically, stretching alleviates muscle tension and reduces stiffness, both of which are common complaints among FM patients due to prolonged muscle contraction and impaired relaxation [35,36]. By improving flexibility and joint mobility, stretching decreases physical strain during daily activities, thereby reducing the cognitive and physical load required for movement coordination [37]. Stretching has additional neurophysiological benefits. It stimulates parasympathetic nervous system activity, promoting relaxation and lowering stress levels, which are known exacerbators of FM symptoms [38]. This calming effect may indirectly mitigate emotional symptoms such as anxiety and depression by reducing stress-induced hyperalgesia. Moreover, stretching has been linked to increased endorphin release, which can enhance mood and provide a natural analgesic effect, potentially explaining its role in emotional regulation [39]. On a neurocognitive level, regular stretching sessions may enhance proprioceptive feedback and body awareness, reducing the cognitive burden of maintaining posture and coordinating movements. Studies suggest that this improved neuromuscular awareness can contribute to better executive function and reduced mental fatigue in FM patients [36]. While its direct effects on cognitive symptoms are less pronounced than those of strength training, stretching's role in stress reduction and physical relaxation makes it an essential complementary therapy for managing FM multifaceted symptoms.

CBT has been a corner stone of chronic pain management for over two decades, targeting the interplay between emotional and cognitive dysfunction in FM by modifying dysfunction although patterns and behaviors that exacerbate symptoms [40,41]. Through cognitive restructuring and behavioral activation, CBT aims to interrupt the feedback loop between chronic pain, emotional distress, and maladaptive behaviors, leading to improved emotional well-being, coping strategies, and functional status [42]. While its effects on pain reduction are inconsistent, CBT is strongly endorsed by the European League Against Rheumatism (EULAR) as an effective intervention for enhancing function and quality of life in FM patients [32]. CBT alsodirectlyaddressespotentialmechanismscontributingtotheemotionaland cognitive symptoms in FM. Emotional disturbances, including anxiety and depression, have been linked to dysregulation of the HPA axis and heightened inflammatory responses, both of which are targeted indirectly by CBT through stress management techniques [24,25]. By teaching relaxation strategies, CBT may reduce cortisol levels and pro-inflammatory cytokines like IL-6 and TNF-α, which are known to contribute to mood disorders in FM [25,30]. Cognitive symptoms such as impaired memory and information processing may also benefit from CBT. These deficits are associated with central nervous system sensitization and hippocampal dysfunction, which exacerbate cognitive load and reduce neural plasticity [28,29,43]. CBT, by promoting adaptive coping mechanisms and enhancing emotional regulation, may mitigate some of these effects, thereby improving cognitive outcomes. Furthermore, the structured and goal-oriented approach of CBT helps patients focus their attention and maintain engagement, which could directly influence information processing and short-term memory [26].

OT plays a critical but underexplored role in managing FM. It focuses on improving daily functioning, adapting tasks, and promoting independent living, addressing the significant occupational and functional impairments experienced by FM patients [44,45]. While research on OT as a standalone intervention is limited, its techniques offer a range of benefits, particularly in managing emotional and cognitive symptoms. Techniques such as energy conservation strategies and task simplification directly reduce the physical and mental strain of daily activities. By teaching patient show to manage their work load and include rest periods, OT interventions may decrease perceived stress and anxiety, which are common in FM [46]. Stress management techniques are particularly relevant in modulating HPA axis dysregulation, a

key mechanism underlying emotional symptoms in FM [24]. Proper postural alignment can reduce pain and promote relaxation, indirectly improving mood and reducing emotional distress. Postural hygiene may also help mitigate the psychological impact of chronic pain by providing patients with practical tools to regain a sense of control over their symptoms [44]. OT interventions often focus on reintroducing meaningful activities into patients' lives, fostering a sense of purpose and social connectedness. This can alleviate feelings of isolation and depression, both of which are highly prevalent in FM [45]. The emphasis on participation in activities can reduce the burden of emotional symptoms by enhancing self-efficacy and quality of life. Some OT programs include interventions aimed at improving sleep hygiene, which is crucial for cognitive recovery and emotional regulation. Sleep disturbances exacerbate hippocampal dysfunction and emotional dysregulation in FM, making this an essential target for therapy [26].

The primary objective of this study is to assess the effectiveness of CBT, stretching-based kinetic therapy, and OT in addressing FM-related emotional and cognitive symptoms. Specifically, we aim to identify which intervention is most effective in alleviating anxiety and depression and improving information processing speed and short-term memory. A secondary objective is to evaluate the sustainability of therapeutic benefits and explore OT's potential as a standalone intervention, a topic that remains underrepresented in FM research.

By addressing two dimensions of FM, emotional and cognitive, this study offers a holistic frame work for optimizing FM care. Findings from this study could inform clinical practice, supporting the integration of non-pharmacological therapies tailored to patient-specific needs.

2. Materials and Methods

2.1. Study design

This interventional prospective study was conducted in the Department of Internal Medicine and Medical Rehabilitation Clinics at hospitals affiliated with the University of Medicine and Pharmacy of Craiova, Romania, between May 2022 and April 2024. The study included 136 patients diagnosed with FM who attended outpatient clinics. The trial involved three visits over an eight-month period. Baseline characteristics were carefully documented and are detailed in the Results section to ensure transparency in group comparisons. The absence of randomization was mitigated by ensuring balanced group allocation based on demographic and clinical profiles.

After agreeing to participate, patients provided written informed consent and were informed about the study objectives and procedures. Participants were divided into four study groups based on the type of therapy administered: Stretching Group (SG): 34 patients; Cognitive-Behavioral Therapy Group (CBTG): 34 patients; Occupational Therapy Group (OTG): 34 patients; Control Group (CG): 34 patients.

At the initial visit (T0), participants completed an interview to collect socio-demographic and clinical data, as well as an evaluation protocol.

To balance the intensity and duration of the interventions across the groups, all therapies were designed to include 24 sessions over two months. This number was chosen based on existing research, which suggests that CBT sessions typically range from 6 to 24 [47]. By standardizing at 24 sessions, the study aimed to maximize therapeutic benefits while maintaining adherence to the program.

The sessions were conducted three times per week, with the first nine sessions held at the Physical Medicine and Rehabilitation Clinic under the supervision of the same rehabilitation team. The remaining sessions were performed at the participants homes, with weekly check-ins by physiotherapists to evaluate: correct execution of stretching exercises, relaxation techniques, energy-saving strategies, activity diary updates.

The same team of professionals monitored all participants throughout the study to ensure consistency in the implementation of therapies. Participants were encouraged to report any discomfort or adverse symptoms immediately during or after the sessions.

Each session for the SG, OTG and CBTG lasted 60 minutes. At the end of the two-month intervention, participants completed the same interview and evaluation protocol (T1). A follow-up evaluation was conducted six months later (T2). At all three evaluation points (T0, T1, and T2), the interview and evaluation protocol were completed to assess progress and outcomes.

2.2. Study arms

All patients were recruited from the Rehabilitation and Physical Medicine Departments of the County Emergency Hospital and the Filantropia Municipal Hospital in Craiova, Romania. Initially, 34 patients agreed to participate in the SG, but only 32 patients completed at least 70% of the program sessions, resulting in a 94.11% adherence rate among the initially enrolled participants. Similarly, 34 patients were initially enrolled in the CBTG, OTG or CG. Of these, 32 participants in both the CBTG and OTG groups attended at least 70% of their respective program sessions and were included in the final analysis. For the CG, 30 participants completed all evaluations, resulting in an 88.23% completion rate for the group.

To ensure statistical validity, only participants meeting the following criteria were included in the final analysis (Figure 1): completed both the baseline evaluation (T1) and the follow-up evaluation (T2); attended at least 70% of the assigned sessions: stretching for the SG, CBT sessions for the CBTG, daily diary completion for the OTG, and all three evaluations for the CG; provided valid and complete data throughout the study period.

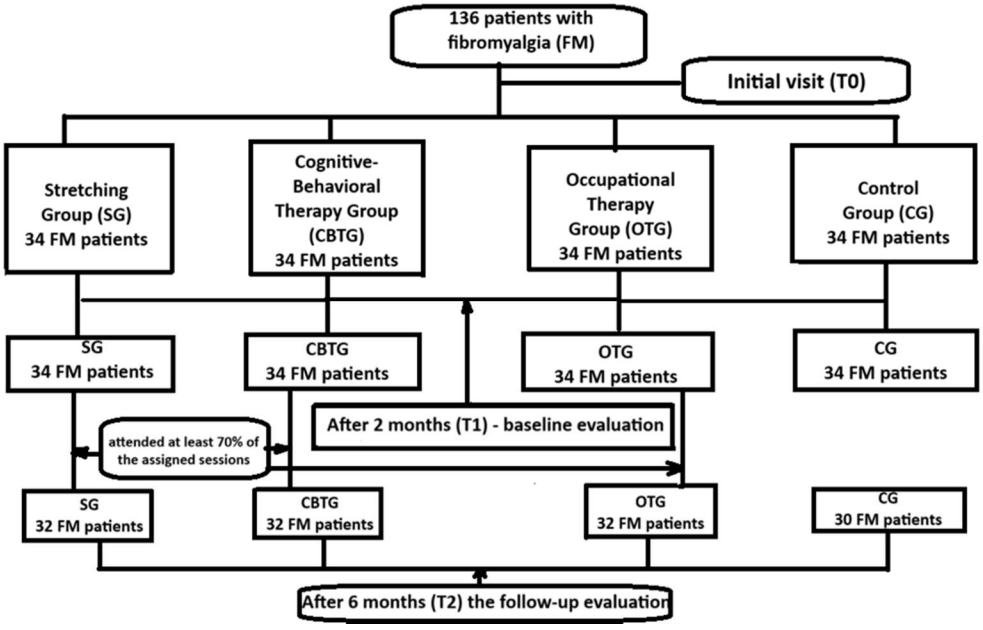

Figure 1. Study Diagram.

Sample Size Calculation: Using standard parameters for statistical validity, including a confidence level of 95% ($\alpha = 0.05$), a power of 80% ($\beta = 0.2$), and an expected effect size (ES) of 0.5 (calculated as the ratio of the score difference to the pooled standard deviation), the required sample size was determined using the formula:

$$n = Z^2 / ES^2, \text{ where } Z = z1\text{-}\alpha + z1\text{-}\beta.$$

Based on these calculations, each study group needed a minimum of 30 patients with complete data to ensure sufficient power for analysis.

Inclusion Criteria: Eligible patients met the following criteria: 1. Adults over 18 years of age. 2. Provided signed informed consent to participate in the study. 3. Had a confirmed diagnosis of FM based on the 2019 ACR criteria. 4. Proficient in the language used in the study to ensure comprehension of instructions and questionnaires. 5. No prior exposure to kinesiotherapy (stretching exercises), CBT, or OT in the past 12 months. 6. On a stable dose of analgesics or other FM-related treatments for at least three months before inclusion, with no planned changes during the study. 7. Willingness and ability to attend all required therapy sessions and complete study evaluations. None of the patients included in the study were treated with duloxetine, milnacipran, or pregabalin, as these drugs are not approved for FM treatment in Romania.

Exclusion Criteria: Participants were excluded if they met any of the following criteria: 1. Illiteracy or inability to comprehend study materials, to use self-reported scales or participate in physical assessments. 2. Active substance abuse or alcoholism. 3. Psychiatric disorders that could interfere with therapy adherence or participation. 4. Associated conditions (rheumatoid arthritis, lupus, or advanced degenerative joint diseases) that could explain the evolution of symptoms. 5. Severe musculoskeletal injuries, advanced osteoarthritis, or neurological impairments that could limit the ability to perform stretching exercises.

2.3. Study Interventions

All patients participated in group therapy sessions, led by the same team of professionals, which provided a unique combination of structured interventions and peer support. Group therapy was chosen not only for economic reasons but also for its additional therapeutic benefits. Group therapy was chosen to enhance adherence and motivation, to standardize the intervention delivery across participants as well as for its additional therapeutic benefits.

These included opportunities for patients to interact with others experiencing similar issues, share problems and solutions, learn from each other's experiences, find emotional support, and motivate one another. This approach encouraged a sense of community and mutual understanding, which amplified the therapeutic effects of the interventions.

SG: The stretching program was designed to address the unique needs of patients with musculoskeletal issues, aiming to improve functional mobility and overall well-being [48]. Its objectives included:

- Reducing muscle tension, promoting relaxation, and enhancing general well-being;
- Facilitating smoother and more coordinated movements;
- Increasing mobility and preparing the body for daily activities;
- Maintaining and improving flexibility to prevent future dysfunctions;
- Enhancing body awareness by focusing on individual muscle groups;
- Improving venous return and eliminating metabolic by products such as lactic acid.

CBTG: The CBT program incorporated innovative psychological techniques to address both physical and mental health aspects of FM [42]. Key components included:

- Pain Management: Educating participants about pain mechanisms and introducing relaxation techniques such as guided imagery and breathing exercises to alleviate discomfort;
- Energy Optimization: Teaching strategies to simplify daily tasks, conserve energy, and reduce physical and emotional strain, enabling greater participation in daily activities;

- Stress Management: Helping participants identify stressors and their effects, develop coping strategies, and understand the relationship between stress and FM symptoms;
- Cognitive Enhancement: Addressing subjective complaints about memory, attention, and concentration through practical strategies and cognitive exercises.

OTG: The OT program focused on reshaping daily activities to improve functionality and well-being.

The key components were:

- Activity Level Assessment: Helping participants evaluate their activity levels and identify high- and low-energy periods;
- Activity Diary: Introducing activity diaries as tools for self-monitoring and optimizing daily routines by balancing rest and activity;
- Restructuring Activities: Gradually increasing occupational performance while integrating rest periods and incorporating enjoyable activities.

All therapy sessions, whether CBT, OT, or ST, were supervised by trained professionals to ensure proper execution and prevent injuries or over exertion. Interventions were tailored to the participants' individual capacities and limitations. For example, exercise intensity and duration were gradually increased based on tolerance, and rest periods were incorporated to avoid fatigue or pain exacerbation.

CG: The CG was designed to receive no therapeutic intervention to allow for the observation of the natural course of FM symptoms over the study period. This approach ensures a neutral baseline for evaluating the efficacy of the active interventions without introducing potential confounding effects. However, participants were engaged through a special event featuring various recreational activities, such as reading sessions and listening to ambient music. They also attended a presentation summarizing the results of the study, fostering a sense of inclusion and participation. Each meeting was held at the association headquarters to ensure patient comfort and lasted 60 minutes.

All participants, regardless of their group, were provided with general educational sessions on symptom awareness, including recommendations for maintaining a balanced diet, avoiding sedentary behavior, adhering to a consistent sleep schedule, and limiting caffeine consumption or the use of electronic devices before bedtime. These measures were implemented to uphold ethical standards and maintain participant engagement. To maximize adherence and maintain motivation throughout the program participants were given clear, written instructions for exercises, relaxation techniques, and energy-saving strategies, helping them practice independently with confidence. A dedicated contact point was provided for participants to ask questions or seek clarification in real time, reducing errors and promoting consistency.

2.4. Ethical Considerations

The study was conducted in strict adherence to the principles of the Helsinki Declaration and Good Clinical Practice guidelines. It was approved by the Ethics Committee of the University of Medicine and Pharmacy of Craiova (approval no. 81/13 May 2022). Special care was taken to ensure the safety and well-being of all participants, particularly as FM patients are considered a vulnerable population.

Participants were informed that their participation was entirely voluntary and that they could withdraw from the program at any time without providing a reason or facing any negative consequences. They were also provided with detailed information regarding the protection of personal data, the potential benefits and risks of participation, and the current available treatments for FM.

The study also included periodic monitoring to ensure participant safety and to address any concerns arising during the intervention. Data confidentiality was maintained by securely storing all collected information, accessible only to authorized personnel.

Written informed consent was obtained from all participants before their inclusion in the study.

2.5. Parameters and Measurements

The assessments for this study were conducted at three key timepoints: Baseline (T0): At the start of the study; Post-Treatment (T1): At the conclusion of the two-month treatment period; Follow-Up (T2): Six months after the completion of the treatment. Different parameters were chosen to provide a comprehensive evaluation of the cognitive, emotional, and physical challenges experienced by FM patients and to assess the effectiveness of therapeutic interventions in addressing these aspects.

The following parameters were evaluated:

Cognitive Evaluation: Working memory, including information processing speed and short-term memory, was assessed using two standardized tests: Symbols and Digits. The Symbols and Digits tests were selected for cognitive assessment due to their high sensitivity in detecting cognitive dysfunctions commonly reported in FM patients, particularly in information processing speed, attention, and working memory.

- Symbols Test (Information Processing Speed) [49]: Patients were presented with nine unique symbols, each corresponding to a specific digit. They were instructed to fill in blanks with the symbols corresponding to a line of randomly ordered digits. The first ten blanks were marked as an example to ensure patients understood the task. Participants were then given 1 minute and 30 seconds to complete as many blanks as possible. The final score was the total number of blanks filled in correctly;
- Digits Test (Short-Term Memory) [50]:

  Direct Order: The evaluator presented a series of digits, which the patient was required to repeat in the exact same order. The test began with two examples to confirm the participant understood the instructions. Then, two sequences of three digits were given, progressing to sequences of four, five, six, and up to nine digits.

  Reverse Order: Participants repeated the digits in reverse order, starting with two sequences of two digits and continuing up to eight digits. The test ended when the patient failed to reproduce two consecutive sequences correctly.

  Scoring: The final score combined the largest number of digits correctly reproduced in both direct and reverse order.

Emotional Assessment: Emotional consequences were evaluated using two standardized scales:

- *HADS (Hospital Anxiety and Depression Scale)* [51,52]*:* A 14-item questionnaire assessing anxiety (7 items) and depression (7 items) over the past week. Each item was scored on a Likert scale from 0 (never) to 3 (very often). Higher scores indicated more significant anxiety or depression;
- *PANAS (Positive and Negative Affect Schedule)* [53]: A 20-item inventory measuring mood through two subscales: positive affect (e.g., excited, proud) and negative affect (e.g., guilty, upset). Patients rated their experience of each item on a 5-point Likert scale from 1 (very slightly or not at all) to 5 (extremely). Scores for each subscale were calculated by summing the ratings for the respective 10 items, with higher scores reflecting a stronger experience of positive or negative emotions;

Associated Symptoms: Symptoms experienced by participants, including nausea, dizziness, apathy, fear, and others, were recorded using a scale developed by the re-

search team. This scale assessed 27 common symptoms in fibromyalgia patients. Participants marked the presence of symptoms they experienced, and the total number of symptoms reported (score ranging from 0 to 27) was considered for statistical analysis.

2.6. Statistical Analysis

The Statistical Package for Social Sciences (SPSS) version 20 (IBM Corporation, Chicago, IL, USA) was employed for data management and analysis. Sample sizes exceeded 30 subjects per group, ensuring sufficient statistical power for detecting meaningful differences. Given that this was not a randomized study, efforts were made to ensure the validity of comparisons by detailing baseline characteristics in the Results section. Group equivalence was examined through demographic and clinical assessments before statistical comparisons were made. Multiple imputation techniques were used to address missing data, ensuring the robustness of findings.

To confirm the suitability of parametric tests, assumptions of normality and homoscedasticity were rigorously assessed using the Kolmogorov-Smirnov and Levene's tests, respectively. Variables failing the normality test were analysed with kurtosis adjustments to minimize bias.

Descriptive analyses characterized the socio demographic and clinical profiles of the samples, facilitating meaningful comparisons. Temporal evolution of variables was evaluated using paired T-tests and repeated-measures ANOVA for within-group analyses (T0, T1, T2), while independent sample T-tests and ANOVA assessed inter-group differences. Where sphericity was not assumed, the Huynh-Feldt correction was applied to ensure validity of variance analyses.

Effect sizes (e.g., Cohen's d, η^2) were calculated to quantify the magnitude of observed differences, supplementing the interpretation of p-values. For key comparisons, confidence intervals (CIs) were reported to contextualize findings. Corrections for multiple comparisons were applied to maintain statistical integrity in analyses involving numerous variables.

Visual checks, including histograms and Q-Q plots, were conducted to confirm normality and variance homogeneity assumptions. Missing data, where present, were managed using multiple imputation methods to preserve the integrity of the dataset. By addressing these critical statistical considerations, the study ensures robust and transparent analysis of emotional and cognitive symptoms in FM patients.

3. Results

3.1. Demographic Characteristics

During the study period, 136 patients with FM were initially included. The final sample consisted of 126 participants, aged between 26 and 58 years, who met the inclusion criteria by completing at least 70% of the treatment sessions in their respective groups or attending all evaluations for the CG (Table 1).

The majority of participants were female (94.44%) and actively employed (73.80%). There were no statistically significant differences between the four groups in terms of age or sex distribution ($p > 0.05$).

The results indicated no significant differences in demographic variables (age, gender distribution, professional activity status) between the four study groups ($p > 0.05$), reducing the risk of selection bias.

Patients reported an average disease duration of seven years before being included in the study. Anxiety and depression were the most common comorbidities, affecting more than 50% of participants, followed by chronic fatigue syndrome and tension headaches. These symptoms were present in more than half of the patients included in the study. No statistically significant differences in the prevalence of these conditions were observed among the groups ($p > 0.05$), further supporting the validity of inter-group comparisons.

Table 1. Baseline characteristics of patients.

Variables	SG	CBTG	OTG	CG	p values
n	32	32	32	30	
Age (Median±SD, range)	41.4±11.3 (27-55)	42.4±14.3 (28-56)	43.1±11.4 (26-56)	42.5 ±13.2 (26-58)	>0.05
Gender (n Female, %)	30(93,75)	29(90.62)	30(93.75)	30(100%)	>0.05
Professionally active (n, %)	22(68.75)	23(71,87)	26(81,25)	22(73.33)	>0.05
Professionally inactive (n, %)	10 (31.25)	9(28.13)	6(18.75)	8(26.67)	>0.01
Disease duration (years Mean±SD	6.9±3.6	8.3±3.1	8.7±2.5	8.4±4.6	>0.01
Anxiety or depression (%)	57.3	56.9	56.8	54.2	>0.05
Tension headaches (%)	28.7	25.6	31.1	27.5	>0.05
Sleep disturbances (%)	45.6	44.8	45.3	46.2	>0.05
Chronic fatigue syndrome (%)	53.1	52.6	55.1	52.7	>0.05

Variables are reported as mean and SD=standard deviation, n=number of subjects; SG=Stretching Group; CBTG=Cognitive-Behavioral Therapy Group; OTG=Occupational Therapy Group; CG=Control Group.

3.2. Emotional consequences

3.2.1. Anxiety and depression

The results of the scores computed from the Anxiety Scale of the HADS are presented in Figure 2.

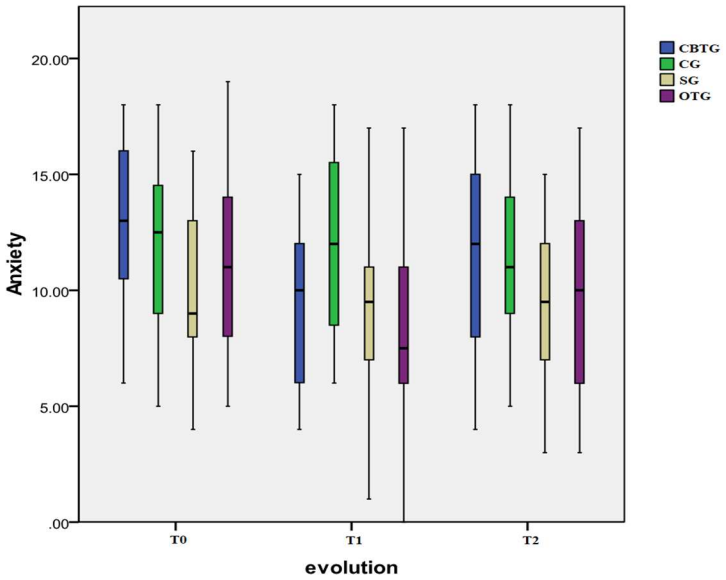

Figure 2. Boxplot representation of the distribution of Anxiety scale across four groups (CBTG, SG, OTG, CG) at three time points (T0, T1, T2)

Time Evolution: All interventional groups showed significant improvements between the baseline (T0) and post-treatment (T1) evaluations. Specifically:

- CBTG: The score decreased significantly from 12.9 (SD = 3.5) to 9.2 (SD = 3.1) (p = 0.003);
- SG: The score dropped significantly from 9.7 (SD = 3.1) to 9.0 (SD = 3.3) (p = 0.02);
- OTG: The most substantial improvement was observed, with the score decreasing from 11.2 (SD = 3.5) to 8.1 (SD = 3.8) (p = 0.000);
- In contrast, no significant changes were observed in CG.

Inter-Group Differences:

At T0 Evaluation: Significant differences were observed only between the SG and CG (p = 0.02).

At T1 Evaluation: Significant differences emerged between the CG and each of the interventional groups: CG vs. CBTG (p = 0.005), CG vs. SG (p = 0.001), CG vs. OTG (p = 0.000).

At T2 Evaluation: The only significant difference observed was between the SG and the CG (p = 0.03).

These findings indicate that all interventional groups achieved meaningful improvements by T1, with the effects of the interventions persisting more notably in the SG group at the T2 follow-up.

The results of the scores computed from the Depression Scale of the HADS are presented in Figure 3.

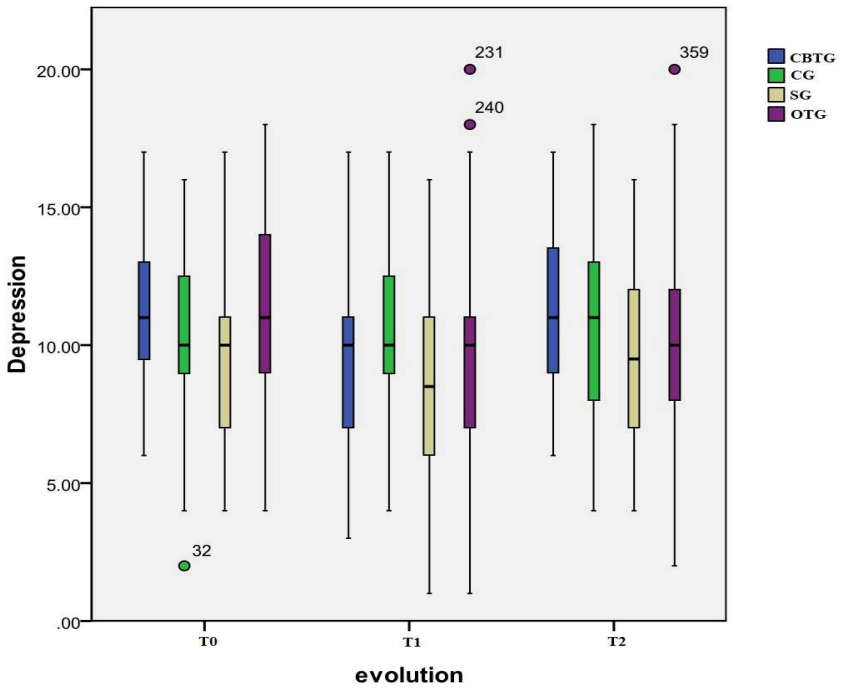

Figure 3. Boxplot representation of the distribution of Depression Scale across four groups (CBTG, SG, OTG, CG) at three time points (T0, T1, T2).

Time Evolution: All interventional groups showed significant improvements between the baseline (T0) and post-treatment (T1) evaluations. Specifically:

- CBTG: The score decreased significantly from 12.9 (SD = 3.5) to 9.2 (SD = 3.1) (p = 0.003);
- SG: The score dropped significantly from 9.7 (SD = 3.1) to 9.0 (SD = 3.3) (p = 0.02);
- OTG: The most substantial improvement was observed, with the score decreasing from 11.2 (SD = 3.5) to 8.1 (SD = 3.8) (p = 0.000);
- CG: In contrast, no significant changes were observed in CG.

Inter-Group Differences:

At T0 Evaluation: Significant differences were observed only between the SG and CG (p = 0.02).

At T1 Evaluation: Significant differences emerged between the CG and each of the interventional groups: CG vs. CBTG (p = 0.005), CG vs. SG (p = 0.001), CG vs. OTG (p = 0.000).

At T2 Evaluation: The only significant difference observed was between the SG and the CG (p = 0.03).

These findings indicate that all interventional groups achieved meaningful improvements by T1, with the effects of the interventions persisting more notably in the SG group at the T2 follow-up.

Correlations Between Scales: Significant correlations were identified between the Anxiety and Depression Scales of HADS: r = 0.598, p = 0.000 (overall correlation). Time-specific correlations: T0: r = 0.524; T1: r = 0.506; T2: r = 0.738.

These results, visualized in Figure 4, emphasize the interconnected nature of emotional responses across these scales and the impact of the interventions on participants affective states.

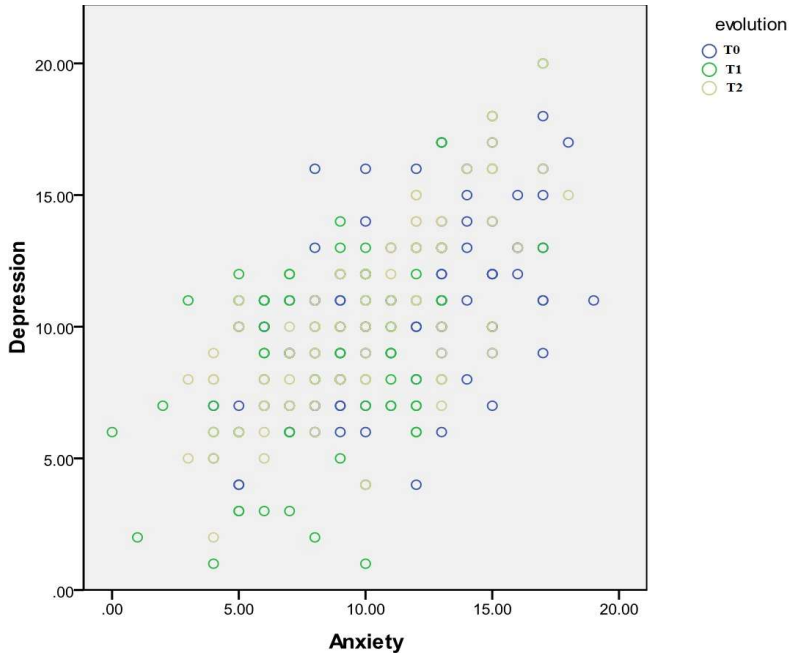

Figure 4. Scatter plot showing the relationship between anxiety (x-axis) and depression (y-axis) scores at three evaluation points: T0 (blue), T1 (green), andT2 (yellow).

3.2.2. PANAS

Positive Affect Scale: The most notable improvement over time was observed in the CBTG. The score increased significantly from 21.2 at T0 to 25.9 at T1 (p = 0.02) and remained significantly elevated at T2 (26.1, p = 0.01).

Inter-Group Differences: While the SG showed the most significant difference compared to the CG at T1 (p = 0.000), no statistically significant differences were observed at T0 (p = 0.4) or T2 (p = 0.1) between these two groups.

Negative Affect Scale: Although there was a reduction in Negative Affect Scale scores over time—dropping from 31 (T0) to 26.3 (T1) in the CBTG group and from 27.6 (T0) to 23.66 (T1) in the SG group—these changes were not significant from a statistical perspective. This suggests that while structured interventions contribute to improving mood regulation, the effects may be more pronounced in positive emotional states than in reducing negative affect.

Correlations Between Scales: Significant correlations were found between the Positive and Negative Affect Scales of PANAS, indicating an inverse relationship: r = -0.610, p = 0.000 (overall correlation). Time-specific correlations: T0: r = -0.439; T1: r = -0.664; T2: r = -0.719.

3.3. Cognitive evaluation

The mean scores and standard deviations of the two cognitive tests: Symbols and Digits are presented in Table 2.

Table 2. Cognitive functions

Cognitive functions	Symbols Mean (SD)			Digits Mean (SD)		
	T0	T1	T2	T0	T1	T2
CBTG	27.8(14)	41(22.8)	33(14.5)	8.2(1.7)	9.7(5.3)	7.9(1.5)
SG	34.7(12.4)	40.7(12.8)	39.2(10.2)	9.5(2.1)	9.4(2.2)	9.5(2.1)
OTG	18.2(5.1)	22.4(6.8)	21.6(7.1)	8.6(2.1)	9.1(1.8)	8.9(2)
CG	32.1(12.5)	43.3(41.1)	36(14)	8.5(1.2)	7.2(2.8)	8.4(1.5)

SD=standard deviation; Symbols=information processing speed; Digits=short-term memory; CBTG= Cognitive-Behavioral Therapy Group; SG= Stretching Group; OTG= Occupational Therapy Group; CG=Control Group.

3.3.1. Information Processing Speed

Time Evolution:

- CBTG: Significant improvements were observed in the average score between T0 and T1 ($p = 0.02$) and between T0 and T2 ($p = 0.03$);
- SG: The score showed a significant increase from T0 to T1 ($p = 0.000$) and from T0 to T2 ($p = 0.018$);
- OTG: The most notable improvement was observed, with significant increases between T0 and T1 ($p = 0.000$) and T0 and T2 ($p = 0.001$).

These results highlight the positive impact of all three interventions on information processing speed over time. The detailed progression of the Symbols Test scores is visualized in Figure 5, showing the improvements across all interventional groups.

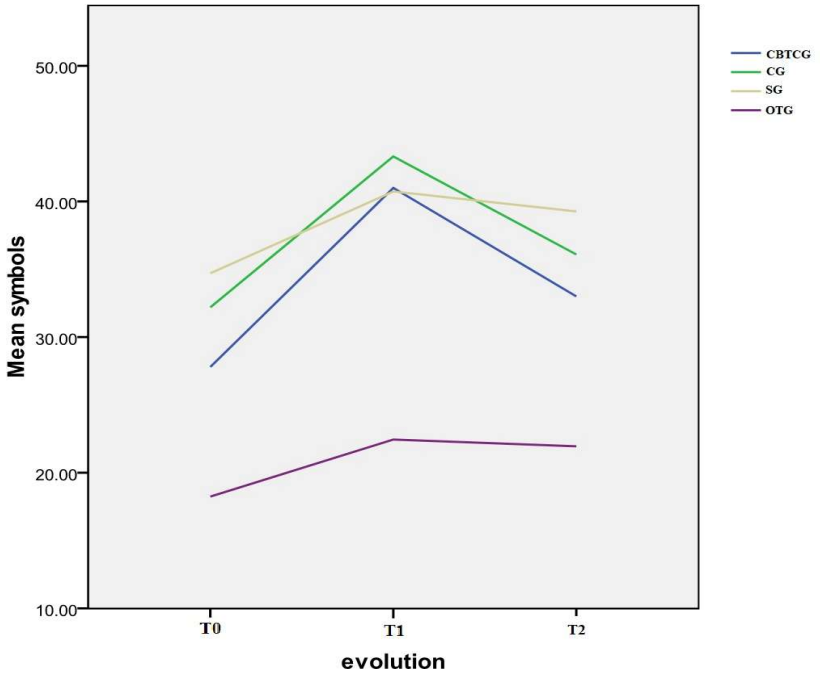

Figure 5. Line graph showing the evolution of mean Information processing speed over three evaluation moments (T0, T1, and T2) for four groups.

At all evaluation points, significant differences were found between the OTG and the other three groups:

- At T0: OTG vs. CBTG (p = 0.003), OTG vs. SG (p = 0.000), OTG vs. CG (p = 0.000);
- At T1: OTG vs. CBTG (p = 0.004), OTG vs. SG (p = 0.000), OTG vs. CG (p = 0.01);
- At T2: OTG vs. CBTG (p = 0.006), OTG vs. SG (p = 0.000), OTG vs. CG (p = 0.000).

These results highlight the consistent advantage of the OTG over the other groups in terms of improvements in information processing speed.

3.3.2. Short-term memory

The *time evolution* of the results from the Digits test is presented in Figure 6. There were no significant differences registered regarding the *evolution in time* of the average score in any of the four groups.

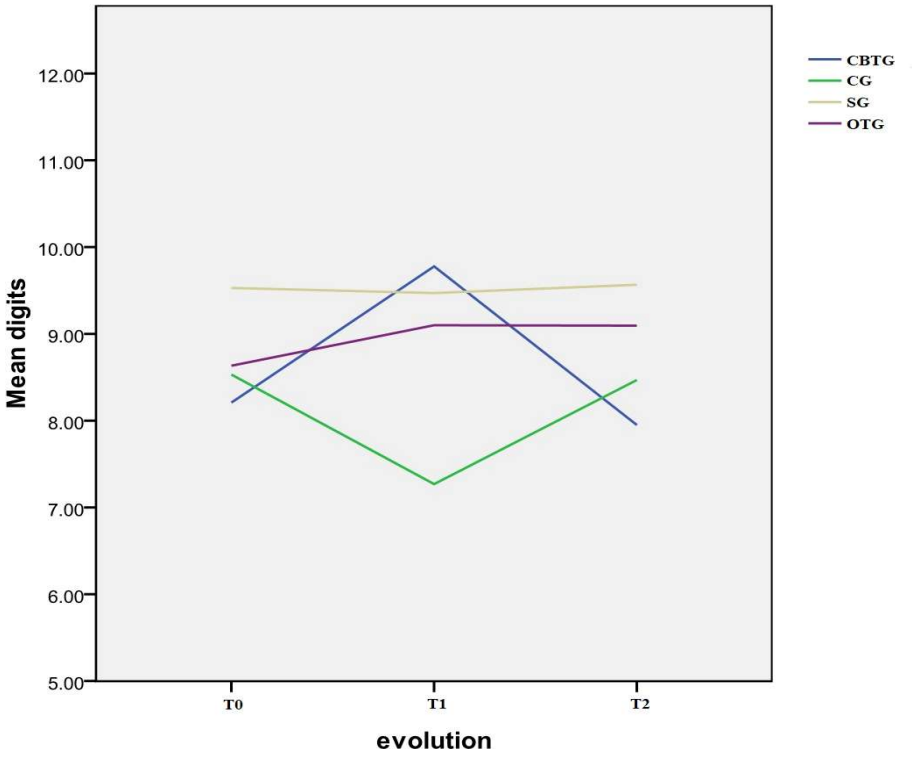

Figure 6. Line graph showing the evolution of mean Digits scores over three evaluation moments (T0, T1, and T2) for four groups.

Inter-group differences:

- At T0: The only significant difference observed was between the SG and the CG (p = 0.02);
- At T1: Significant differences emerged between the CG and all interventional groups: CG vs. CBTG (p = 0.05), CG vs. SG (p = 0.001), CG vs. OTG (p = 0.008);
- At T2: The only significant difference at this point was between the SG and CG (p = 0.02).

Correlation Between Cognitive Tests:

A weak but statistically significant correlation was identified between the two cognitive tests measuring information processing speed and short-term memory (r = 0.322, p = 0.000).

Unlike processing speed, no significant improvements were observed in short-term memory scores across any group. While minor increases were noted in the CBTG and OTG, these were not statistically significant (p > 0.05). This result aligns with prior findings that suggest working memory deficits in FM may be less responsive to behavioral interventions than processing speed.

3.4. Associated symptoms

Time Evolution: The most significant improvements in associated symptoms were observed in the SG and the CBTG (Table 3). While all interventional groups showed highly significant differences between the first (T0) and second (T1) evaluations, only the SG demonstrated significant differences between the first (T0) and third (T2) evaluations (p = 0.02).

Table 3. Associated symptoms-time evolution.

Experienced symptoms	T0 Mean	T1 Mean	T2 Mean	T0/T1 P value	T1/T2 P value
CBTG	18.1	14.5	17.7	0.01	0.01
SG	12.7	9.1	10.1	0.001	0.02
OTG	17.2	14.4	16.5	0.001	0.02
CG	16.9	14.5	16.9	0.14	1.1

CBTG= Cognitive-Behavioral Therapy Group; SG= Stretching Group; OTG= Occupational Therapy Group; CG= Control Group.

Inter-Group Differences: Compared to the Control Group (CG), the SG showed significant differences in average scores at all evaluation points: T0: p = 0.001; T1: p = 0.000; T2: p = 0.01.

The average number of associated symptoms reported by participants in these groups is presented in Table 3. These findings highlight the sustained impact of the stretching intervention on associated symptoms over time, in contrast to the other groups.

4. Discussion

Fibromyalgia (FM) is a complex condition that extends far beyond pain, encompassing a broad spectrum of symptoms such as fatigue, disrupted sleep, impaired cognition, emotional disturbances, and other somatic complaints. It is known that FM patients frequently develop digestive disorders, which may contribute to metabolic imbalances and nutritional deficiencies. Recent studies suggest that FM could be a risk factor for impaired complicating musculoskeletal symptoms [54,55]. Additionally, inflammatory processes and metabolic dysfunctions associated with FM have been linked to altered physical performance and overall functional impairment, emphasizing the need for targeted rehabilitation interventions [56,57].

These diverse manifestations highlight the importance of tailoring interventions to suit individual patients' needs, targeting not only pain but also associated symptoms. This study contributes to existing literature by evaluating the comparative effectiveness of three non-pharmacological interventions on FM-related emotional and cognitive symptoms. Unlike prior studies that typically focus on single interventions, this research highlights their distinct and complementary roles.

Emotional Outcomes: CBT emerged as the most effective intervention in reducing anxiety and depression, with significant improvements observed in the HADS and PANAS. These results are consistent with a meta-analysis conducted by Bernardy et al. (2010) [58], which reported that CBT significantly improve scoping strategies and reduces emotional distress in FM patients. CBT's structured, goal-oriented approach allows patients to address dysfunctional thought patterns and maladaptive behaviors, fostering better emotional regulation. Previous studies, such as those by Thieme et al. (2007), have highlighted CBT's ability to address comorbid emotional symptoms, particularly anxiety and depression, in FM patients [59]. Our findings expand on this evidence by showing that the positive effects of CBT on emotional symptoms were not only significant at the end of the intervention but also sustained during the follow-up evaluation, indicating a long-term benefit.

Stretching exercises also contributed to reductions in anxiety and depression, though its effects were less pronounced than those of CBT. These findings align with Busch et al. (2011) [48], who reported that exercise-based interventions enhance mood and psychological well-being in FM. The benefits observed in SG may be attributed to its impact on parasympathetic nervous system activation and endorphin release, both of which promote relaxation and stress relief [35,36]. However, these effects were less sustained at follow-up, suggesting that while stretching therapy supports emotional well-being, ongoing engagement is necessary for long-term effects.

OT demonstrated modest but significant improvements in anxiety and depression scores. These emotional benefits are likely related to the elimination of stress or sand the structured use of activity diaries and energy-saving techniques, which help patients manage daily stress. Research by Smith et al. (2021) [60], suggests that interventions targeting daily functioning and stress management can significantly impact emotional symptoms in FM patients, supporting our findings. The improvements observed in OT participants may also be attributed to the circulatory activation and relaxation promoted during therapy sessions, which could positively influence mood. The structured use of activity diaries and occupational adaptations may have contributed to improved self-efficacy and mood stabilization. However, OT's emotional benefits were less pronounced than those of CBT, highlighting its role as a complementary rather than primary psychological intervention [61].

The comparative analysis revealed that CBT was more effective in addressing emotional symptoms than stretching exercises or OT, as evidenced by the magnitude and duration of its effects on anxiety and depression scores. This superiority is supported by Miller et al. (2023) [62], which identified CBT as the gold standard for psychological interventions in chronic pain conditions, including FM. The present study findings suggest that while CBT should remain a primary recommendation for managing emotional symptoms in FM, flexibility training and OT can serve as complementary interventions, especially for patients who may not have access to CBT or prefer alternative approaches.

While our findings corroborate much of the existing evidence, some studies have reported conflicting results. For instance, Häuser et al. (2010) [35] found that the effects of CBT on FM pain and emotional symptoms are variable and may depend on individual patient factors such as baseline severity and psychological comorbidities. Similarly, kinesiotherapy interventions have shown inconsistent outcomes in reducing depression, as highlighted by Bidonde et al. (2017) [63]. These discrepancies underline the need for further research to identify the patient profiles most likely to benefit from specific interventions.

Regarding *Cognitive Outcomes*, this study demonstrated significant improvements in information processing speed across all three interventional groups, as measured by the Symbols Test. The observed enhancements in cognitive performance likely stem from the distinct mechanisms associated with each intervention:

- The structured, goal-oriented nature of CBT likely contributed to enhanced cognitive flexibility and attention by reducing anxiety and emotional distress, which are known to impair cognitive functioning in FM patients. These findings align with prior evidence suggesting that CBT can improve executive function sand attentional focus by mitigating emotional dysregulation (Bernardy et al., 2010) [55];
- Cognitive stimulation techniques, such as the use of activity diaries and memory-enhancing exercises, appeared to play a crucial role in improving attention and processing speed. These results are consistent with studies emphasizing the role of OT in enhancing cognitive skills through structured task engagement and self-monitoring (Johnson et al., 2022) [61];
- The improvements observed in SG may be attributed to the neurophysiological effects of exercise, such as increased cerebral blood flow and enhanced

neuroplasticity, which support cognitive functions like attention and processing speed. These mechanisms are well-documented in studies on exercise-induced cognitive benefits, including the work of Brown et al. (2021) [64], who highlighted the positive impact of physical activity on brain function.

While the Symbols Test revealed significant gains in processing speed, no meaningful improvements were observed in short-term memory across any group. This finding is consistent with previous studies, such as Taylor et al. (2023) [65], which reported that non-pharmacological interventions, including CBT and exercise, have limited effects on memory-specific domains in FM patients. Short-term memory deficits in FM may instead bed riven by intrinsic factors such as hippocampal dysfunction and neuroinflammation, which these interventions may not adequately address.

Associated Symptoms: Among the three interventions, stretching therapy demonstrated the greatest long-term impact on FM-associated symptoms, including fatigue, stiffness, and overall well-being. These findings align with Jones et al. (2006) [66], who emphasized stretching's role in reducing muscle tension, improving circulation, and promoting relaxation. The fact that SG maintained significant symptom reduction at T2, whereas the other interventions did not, suggests that stretching therapy may be particularly beneficial for long-term symptom management, as well as it is demonstrated for other illness [67,68].

While CBT and OT showed short-term improvements, their effects diminished over time, which is consistent with Miller et al. (2023) [62], who noted that CBT requires ongoing practice or booster sessions to sustain benefits. These findings underscore the importance of combining psychological and physical interventions to maximize treatment outcomes.

Our study had some limitations. First, while the study included a reasonable number of participants, the sample size for each intervention group may limit the statistical power to detects mall but clinically significant differences between groups. Additionally, the study did not employ random assignment to groups and selection bias may have influenced the results. Participants who chose CBT, OT, or stretching exercises might already have had specific preferences or baseline characteristics affecting outcomes. The study monitored participants for six-month safter interventions: while this provides valuable insights, FM is a chronic condition, and longer follow-up is necessary to evaluate the sustainability of benefits over time. The study focused on specific cognitive and emotional outcomes but other important domains like long-term memory, executive function, or social functioning were not assessed. The study team plans to address current limitations through future research focusing on larger sample sizes, randomized controlled designs, extended follow-up periods, and the use of advanced neuropsychological tests and imaging assessments. These efforts aim to validate findings and provide a clearer understanding of cognitive and emotional changes in FM.

The study internal validity is strengthened by its rigorous methodology, which includes well-defined inclusion and exclusion criteria, standardized intervention protocols, and the use of validated assessment tools. The application of repeated-measures analysis ensured precise tracking of changes over time, while adherence monitoring minimized biases related to intervention fidelity. Even if a single-centre design and the focus on a specific geographical area may limit the generalizability to broader populations, the study external validity is supported by the use of accessible, evidence-based interventions and a diverse sample of FM patients, ensuring the findings are relevant and translatable to routine clinical practice.

This study provides new insights into the complementary roles of different non-pharmacological strategies for FM:

- Unlike many prior studies focusing on single interventions, our research demonstrated how stretching, CBT, and OT could address different domains

of FM symptoms. This holistic approach could guide personalized treatment plans based on patient primary concerns, whether emotional or cognitive;
- While OT is typically combined with other therapies, our findings suggest its potential as an independent intervention for improving cognitive function and reducing anxiety, addressing the significant employment challenges faced by FM patients;
- The sustained effects of stretching exercises, OT and CBT on specific symptom domains highlight their utility in long-term FM management, a critical aspect given the chronic nature of the disease.

The findings from this study have implications for clinical and therapeutic applications:

- Cost-Effective Group Therapy: Group-based interventions are both affordable and beneficial, as they encourage mutual support, shared learning, and emotional connection among patients. This model can be easily implemented in clinical or community settings, helping reduce healthcare costs;
- Standardized clinical protocols can incorporate stretching exercises into outpatient rehabilitation programs to promote emotional well-being. Group workshops or virtual telehealth sessions for CBT can effectively address emotional and cognitive challenges. Additionally, customized OT programs can help patients improve their occupational performance and overall quality of life, especially those experiencing employment difficulties due to FM.

5. Conclusions

This study highlights the distinct and complementary roles of CBT, stretching therapy, and OT in FM management. While CBT was the most effective in reducing emotional distress, stretching therapy showed the most sustained benefits in symptom reduction, and OT improved cognitive processing speed. By integrating these approaches into routine care, clinicians can provide personalized, holistic management strategies that improve quality of life, reduce symptom burden, and promote functional independence in this vulnerable population.

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