

Role of Cognitive Behavioral Therapy in Fibromyalgia: A Systematic Review

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Abstract

A literature search of articles from 2002-2019 was performed using Medline, Embase, Cochrane, LILACS, IBECs, CRD, and Epistemonikos databases, to analyze the effects of Cognitive-Behavioral Therapy (CBT) in the treatment of fibromyalgia. Twenty-seven articles were selected in which CBT was performed exclusively by specialist physicians, associated or not with conventional pharmacological treatment and/or physical exercise. In most articles, CBT worked with self-knowledge and cognitive restructuring, attempting to reduce pain perception, and it showed a general improvement in daily activities by decreasing patient's limitations, such as morning stiffness. The literature showed significant correlations of CBT in pain processing over time. When CBT was compared to conventional pharmacological therapy, a certain superiority of CBT could be observed concerning the quality of life, catastrophizing, and acceptance of pain. However, when they were simultaneously applied, this improvement in quality of life was not observed.

Keywords

Cognitive Behavioral Therapy, Fibromyalgia, Pain

1. Introduction

Fibromyalgia (FM) is a common disease, with a prevalence in the general popu-



lation that varies between 2% and 8%. Females are the most affected, and the disease can occur in all ages and ethnic groups [1].

It is a complex disorder characterized by generalized chronic pain, predominantly in muscles and soft tissues, although it can extend to any anatomical region [2]. Other symptoms such as fatigue, cognitive complaints, unsatisfactory sleep and mood changes are also present [3]. Such symptoms can directly impact patients' quality of life, potentially increasing likelihood of developing psychiatric disorders, including depression, anxiety, obsessive-compulsive disorder and post-traumatic stress disorder [4] [5].

Pathogenesis involves biological, psychological, behavioral and social factors. The main characteristics of the pathogenesis of fibromyalgia are related to: 1) changes in central pain modulatory processes in the spinal cord and brain; 2) a prominent role of negative affective factors in the maintenance of pain and disability; 3) a relative lack of efficacy of many pharmacological treatments [2].

Its treatment is based on different therapeutic modalities. The preferred approach is to integrate pharmacological and non-pharmacological resources, involving patients as active agents of this process [1]. The interest in alternative therapy in fibromyalgia is related to unsatisfactory results considering isolated pharmacological therapy [6].

The active participation of patients is essential for a successful treatment. Pharmacological therapies can be useful in relieving symptoms, but patients hardly improve without adopting self-management measures [1], and, in this context, cognitive-behavioral therapy (CBT) is a fundamental tool [7].

Interventions based on the basic premise that chronic pain is sustained by cognitive and behavioral factors are included in CBT. In addition to this, behavioral factors and psychological treatment lead to change through cognitive processes, such as restructuring and behavioral techniques, for example, relaxation and social skills training [8].

CBT presents itself as an important therapeutic resource, as it is capable of modifying patient's negative thoughts and expectations, improving mood, stress, coping with pain and problem solving, including behavioral interventions that specifically deal with improving the fibromyalgia symptoms (sleep hygiene, relaxation training, activity rhythm) [9].

The present study proposes a systematic review of the literature on the effects of cognitive behavioral therapy in the treatment of fibromyalgia.

2. Methodology

A systematic review was carried out, with retrieval, selection, and critical analysis of results from primary studies in the literature. This study followed the checklist Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) [10], which views amplify the quality of systematic reviews.

Systematic reviews seek to answer a clearly formulated research question in biological and health issues. It was chosen as the structure of the present study because it has well-defined stages and is considered the greatest scientific evi-

dence.

2.1. Eligibility Criteria

Developed based on the acronym PICO, adapting to their respective 4 points:

Population: Patients aged 18 years or over and diagnosed with fibromyalgia (according to the recognized diagnostic criteria) were included in the study.

Intervention: Use of cognitive behavioral therapy in fibromyalgia patients alone or associated with other therapies.

Comparison: Fibromyalgia patients undergoing other types of therapy, another type of treatment, of no treatment at all.

Outcome: All possible outcomes of patients after the use of cognitive behavioral therapy in studies.

2.2. Inclusion and Exclusion Criteria

Inclusion: Portuguese, Spanish and English languages; studies performed in humans; there was no restriction on the year of publication.

Exclusion: studies that did not address CBT, other pain syndromes or other rheumatologic diseases, secondary studies, theses and dissertations.

2.3. Study Resources

The research was carried out in September 2020, updated in April 2021 in the following online databases: Medline, Embase, Cochrane, LILACS, IBECs, CRD and Epistemonikos.

2.4. Search Strategy and Data Extraction

The search was performed with the association of terms “Fibromyalgia”, “Positive Psychology”, “Cognitive Behavioral Therapy”, and their respective synonyms, with Boolean operators according to the most appropriate search strategy for each database.

Each study was initially evaluated by its title and abstract by two researchers, using the Rayyan system (rayyan.qcri.org), allowing the evaluator to be blinded to the other’s analysis. In case of disagreement, the study was analyzed by a third party.

After the analysis by title and abstract, the articles were fully read, and those that were not in accordance with the inclusion criteria were excluded. From those selected, the following data was extracted: type of study, objective population (number of people, sex and age), study duration, use of pharmacological therapy duration of cognitive behavioral therapy, use of other types of therapy, guidance received by patients, adherence to treatment, analysis of disease progression or regression and outcome. All data obtained were extracted by a researcher and revised by a second researcher, using an excel spreadsheet.

2.5. Quality of Studies and Risk of Bias

According to the Cochrane Recommendations Manual for Systematic Reviews

[11], the quality of the work methodology, and the presence of biases in the included studies were analyzed by two independent reviewers using the HTA KMET (Standard Quality Assessment Criteria for Evaluating Primary Research Papers from a Variety of Fields) [12]. The selection of a representative sample of participants, the randomization of patients selected in the participating groups, the blinding of participants and researchers, a similar form of assessment for all groups, presence of incomplete data, selection of presented results, and other biases were evaluated. All studies were evaluated for each type of bias as low risk, high risk and doubtful risk and according to the probability of their bias, the studies as a whole were classified as low, medium or high risk. A study with low risk was one that was rated as having a low probability of bias in all of the biases analyzed. A moderate risk job was one that had 1 or 2 bias ratings as high or doubtful. Papers that had 3 or more assessments of high or doubtful biases were classified as high risk.

3. Results

3.1. Identification and Selection of Studies

A total of 1364 studies was analyzed. After excluding 296 duplicates and analyzing the title and abstract, a total of 110 articles were selected for full reading, of which 27 were included in the review. The distribution of articles can be seen in **Figure 1**.

Of the 2273 patients with fibromyalgia or strongly suspected of having fibromyalgia, according to primary studies, the majority were women, aged 18 years and over. In most studies, the average age was between 40 and 50 years old.

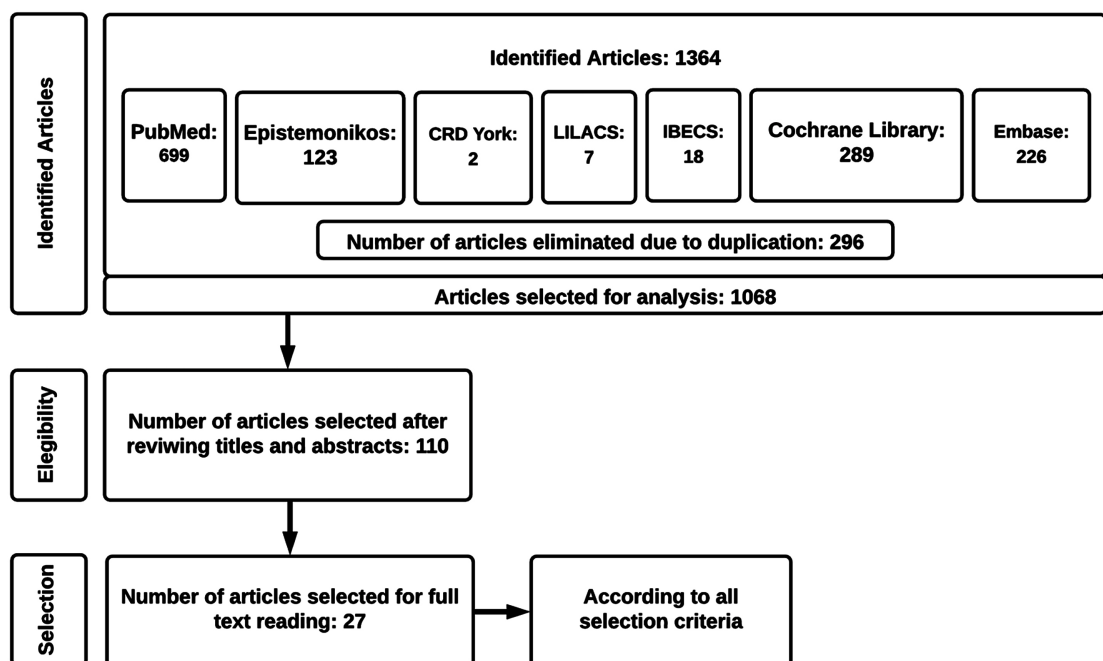


Figure 1. Article selection flowchart.

3.2. Characteristics of Included Studies

The earliest articles were published in 2002 [13] [14], and the most recent in 2019 were McCrae C. S. *et al.* 2019 [15] e Karlsson B *et al.* 2019 [16]. The majority of the studies were conducted in Spain (40.7%, n = 11) [13] [17]-[26], followed by the United States (29.6%, n = 8) [14] [15] [27]-[32], Holland (7.4%, n = 2) [33] [34], Sweden (7.4%, n = 2) [16] [35], Germany (3.7%, n = 1) [36], Brazil (3.7%, n = 1) [37], Canada (3.7%, n = 1) [38] and one shared study between Germany and the United States (3.7%, n = 1) [39], being “n” the number of articles.

Considering the 27 articles selected, all are randomized trials, due to the high level of evidence in the study design. The shortest studies lasted 3 months [27] [30] [31] [37] [38], on the other hand, the longest had duration of 3 years [21] [29]. Regarding the time of CBT, there was a variation of 4 weeks [14] [32] and 12 months [16].

3.3. Parameters and Medications Used by the Articles

In the articles analyzed, approximately 89 different parameters were utilized, such as methods of questionnaires, scales, clinical and laboratory tests, with the Fibromyalgia Impact Questionnaire (FIQ) being the most used (55.5%, n = 15) [13] [17] [18] [20]-[26] [30] [31] [37] [38] [39], followed by the Beck Depression Scale (BDI) (18.5%, n = 5) [13] [20] [23] [24] [27], the Short Form Health Survey Standardized Questionnaire 36 (SF-36) (14.8%, n = 4) [14] [23] [28] [32], the McGill Pain Questionnaire (14.8%, n = 4) [14] [15] [17] [26], the Hospital Anxiety and Depression Scale (HADS) (7.4%, n = 2) [18] [22] and the Anxiety Inventory (STAI) (7.4%, n = 2) [13] [37].

Different drug therapies were used in the analyzed articles, analgesics (n = 11) [13] [14] [17] [18] [19] [21] [23] [24] [29] [36] [37] and antidepressants (n = 9) [14] [15] [17] [18] [20] [25] [28] [30] [31], the most utilized. Followed by tricyclic antidepressants (n = 7) [13] [14] [21] [23] [24] [37] [39], anticonvulsants (n = 5) [18] [19] [25] [30] [31] and muscle relaxants (n = 3) [17] [18] [22].

3.4. CBT and Other Therapies

Of the 27 studies analyzed, only in 10 articles the patients had exclusive treatment with CBT [16] [19] [22] [23] [26] [27] [29] [32] [36] [39]. The most common association with CBT was the use of pharmacological treatment, evidenced in 8 of the studies [14] [15] [17] [21] [25] [28] [31] [35], followed by other therapies, in 6 studies [18] [20] [28] [30] [37] [38] the other association with physical exercise [13] [24] [33] [34].

Among the articles that exclusively used CBT as therapy, 7 showed improvement in pain [19] [22] [23] [26] [27] [32] [36], while 3 found no significant influence [16] [29] [39]; 6 recognized a positive emotional impact, with improvement in conditions such as depression and anxiety [16] [22] [27] [32] [36] [39], and only one did not show any change [23]. Three studies found an improve-

ment in fatigue [16] [22] [23], one did not acknowledge any difference [36], and the other 6 did not specify it [19] [26] [27] [29] [32] [39]. In regards to sleep, two articles pointed to betterment [23] [29], while the other eight studies did not specify any changes in sleep [16] [19] [22] [26] [27] [32] [36] [39].

3.5. CBT and Fibromyalgia

Cognitive Behavioral Therapy was carried out exclusively through sessions with therapist psychologists, accompanied or not by specialist physicians, over specific periods. Some articles have supported therapy with other modalities of therapeutic techniques, such as standard pharmacological treatment and hypnosis [18].

In most articles, CBT sought to work on self-monitoring, self-knowledge, and cognitive restructuring exercises to reduce the intensity and regress the main FM symptoms [16].

Overall, 78.57% of the studies observed regression of at least one FM symptom, whether physical (such as pain, stiffness, sleep, and fatigue); or psychological (such as anxiety, stress, and depression). Questionnaires [19], pain scores [21], analysis of variance [36], and subjective clinical impressions [27] were implemented to analyze the improvement in fibromyalgia as the treatment with CBT evolved. The complications of these patients were not scrutinized by the articles analyzed. The articles details can be seen in **Table 1**.

3.6. Evaluation of the Quality of Articles

Of the 27 studies, 3 papers were at low risk [21] [28] [38]. 14 at moderate risk [13] [14] [15] [18] [19] [20] [24] [25] [26] [27] [30] [33] [34] [35], and 9 at high risk [16] [17] [22] [23] [31] [32] [36] [37] [39] as shown in **Figure 2**.

4. Discussion

4.1. Compliance

Patient compliance was analyzed based on attendance at sessions, completion of CBT treatment, and post-therapy follow-ups, with a mean percentage of complete adherence by the end of the research of 81.31% in 22 of the analyzed studies [13] [14] [15] [16] [17] [19]-[24] [26] [27] [28] [29] [30] [32] [33] [35] [36] [38] [39]. Lazaridou *et al.* (2017) [32] was the research with the highest compliance carried out with 16 participants, with 100% adherence. On the other hand, the research by Lami, M. J. (2018) [26] had 126 participants, of which only 57.14% completed the study. Despite the high overall compliance, even with more than half of the patients fully adhering to treatment, it conferred no connection with the success rates [14].

4.2. Pain

FM is a chronic disorder characterized by hyperalgesia, and CBT has a crucial mechanism in its reduction through the development of cognitive skills and

Table 1. Data of the articles included.

Author/year	Type of study	Objective	Population	Duration of Study	Form of analysis of the evolution of the disease	Outcome
Castel <i>et al.</i> , 2009 [17]	Randomized pilot trial	Examine effects of hypnosis in standard cognitive-behavioral therapy for pain management in patients with fibromyalgia.	N = 39	12 sessions de 90 minutes.	Numerical Pain Rating Scale, Fibromyalgia Impact Questionnaire (FIQ), McGill Pain Questionnaire (MPQ) and Harvard Group Hypnotic Susceptibility Scale-Form A (HGSHS-A).	Patients who received Cognitive Behavioral Therapy (CBT) or CBT associated with hypnosis showed a more significant improvement than those who received only conventional pharmacological treatment. CBT and hypnosis showed even greater improvement than just CBT.
McCrae <i>et al.</i> , 2019 [15]	Randomized controlled trial	Examine the effects of cognitive-behavioral treatments for insomnia and pain in patients with fibromyalgia and insomnia.	N = 113	8 months (8 sessions of treatment of 50 minutes + followup after 6 months).	Self-reported sleep diary, dysfunctional beliefs and attitudes about sleep (DBAS), actigraphy, outpatient polysomnography. Clinical pain intensity diary, MPQ, pain disability inventory (PDI); Beck Depression Inventory—Second Edition (BDI-II), State-Trait Anxiety Inventory-Form Y1 (STAI-YI).	CBT improved self-reported insomnia symptoms. CBT promoted improvements of greater magnitude that was maintained. Both caused immediate pain reductions in one-third of patients, and are effective for insomnia in patients with fibromyalgia (FM). May reduce pain in some patients.
Karlsson <i>et al.</i> , 2019 [16]	Randomized controlled trial	Evaluate the effect of cognitive-behavioral therapy on plasma substance (SP) levels in women with Fibromyalgic Syndrome.	N = 48	18 months. (20 sessions of 3 hours every week + 3 reinforcement session of the same duration for the subsequent 6 months).	Venous blood was analyzed for substance P at baseline and at each follow-up exam + the application of psychometric questionnaires: pain (The West Haven-Yale Multidimensional Pain Inventory), fatigue (Maastricht Questionnaire), stress (The Everyday Life Stress instrument) and depression (The Montgomery-Asberg Depression Rating Scale—Self Reported).	In both groups analyzed, a 33% reduction in substance P levels was observed after 6 months of treatment with CBT. However, at the 1-year follow-up after starting CBT treatment, the reduction in plasma SP levels was no longer significant in either group.
Karlsson <i>et al.</i> , 2015 [35]	Randomized clinical trial	To examine whether a stress management cognitive behavioral therapy program could influence stress, well-being, life management, and pain in women with fibromyalgia syndrome.	N = 48	18 months. (20 sessions of 3 hours every week + 3 reinforcement session of the same duration for the subsequent 6 months).	Follow-up examination and psychometric questionnaires: pain (The West Haven-Yale Multidimensional Pain Inventory), fatigue (Maastricht Questionnaire); stress (The Everyday Life Stress instrument); depression (The Montgomery-Asberg Depression Rating Scale—Self Reported).	“Life control” improved (20%), as well as “affective suffering” (15%), “Vital exhaustion” (12%), “stress behavior” (15%), “depression” (20%). Pain severity, sleep, interference, support from spouses or significant others’ showed no trend to change.

Continued

Luciano <i>et al.</i> , 2014 [19]	Randomized controlled trial	To compare the CBT versus the combination pharmacological treatment of pregabalin + duloxetine and usual care groups in the treatment of FM. Also, the 6-month cost-effectiveness.	N = 168	6 months. (9 sessions of CBT).	Utility score + application forms: EQ-5D, EQ VAS and Quality-Adjusted Life-Year.	A group-based form of CBT is more cost-effective in treating FM than the usual care and drugs recommended by the FDA.
Thieme <i>et al.</i> , 2016 [36]	Randomized clinical trial	Determine the psychosocial effects of cognitive operant and cognitive behavioral therapy in patients with fibromyalgia.	N = 115	1 year and 15 weeks. Once a week with the duration of 2 hours each + follow-ups 6 and 12 months after the end of the sessions.	After each phase, participants were asked to rate pain intensity and perceived stress on visual analogue scales (VAS) with outcomes ranging from “No pain” for “very intense pain” and “not at all” for “very stressed”, respectively.	There was reduced skin conductance and muscle tension compared to the control, which led to regulation of pain parameters. Diastolic pressure in FM patients tends to be reduced, and was regularized with therapy.
Lazaridou <i>et al.</i> , 2017 [32]	Randomized clinical trial	Evaluate the effect of CBT on the cerebral mechanism of hyperalgesia from the reduction of the catastrophizing mechanism in the patient with fibromyalgia.	N = 16	7 months. (4 sessions, once a month, with the duration of 60 - 70 min).	Generalized Pain Index and Symptom Severity, Short Health Survey Form (SF-36), Visual Analog Scale to Assess the Severity of Fatigue Experienced by Patients in the Past 2 Weeks (VAS-F 39), Outcome Measures by BPI Questionnaires, BI and PCS. Functional Magnetic Resonance Imaging.	A greater reduction in hyperalgesia and catastrophization was observed in patients undergoing CBT compared to the control group. Significant associations can be seen between brain connectivity and long-term changes in clinical outcomes of patients with fibromyalgia.
Parra-Delgado and Latorre-postigo, 2013 [20]	Randomized clinical trial	Demonstrate the effectiveness of mindfulness-based CBT, depressive symptoms, and pain intensity in women with fibromyalgia.	N = 31	3 months. (8 sessions of 2h30 of duration each).	Interview with patients + application of questionnaires MINI, ANOVA, FIQ, BDI, VAS.	CBT has been shown to be effective to reduce depressive symptoms and the impact of diseases, but there were no very relevant changes in the level of pain.
Martín <i>et al.</i> , 2014 [21]	Randomized controlled clinical trial	Evaluate the effects of an interdisciplinary pharmacological treatment, cognitive-behavioral therapy education, exercise for fibromyalgia compared to standard pharmacological treatment.	N = 110	3 years (12 sessions, six sessions lasting 1 h with a psychologist and 45 min of education activities or physical therapy.	Application of: FIQ, HADS, CAD-R, DUKE-UNC, satisfaction scale created by the researchers.	Interdisciplinary intervention promoted pain improvement, perception of social support and quality of life more than standard pharmacological therapy. Furthermore, patients were more satisfied with the interdisciplinary approach. Even though the overall quality of life has improved, no improvement in anxiety and depression symptoms have been observed.

Continued

Williams <i>et al.</i> , 2002 [14]	Randomized Clinical Trial	Determine if there is improvement in functional physical status on CBT, and identify improvements in pain. Explore adherence to treatment in achieving improvements in physical functional status.	N = 145	6 sessions of 1 hour in the period of 4 weeks + 12 months of follow up.	Questionnaire application: PCS, SF-36 and McGill Pain Questionnaire SF.	Both therapies (pharmacological and unconventional) proved to be beneficial, but the intervention period is considered to be short.
Castel <i>et al.</i> , 2012 [18]	Randomized Clinical Trial	Evaluate the result of Cognitive-Behavioral Therapy associated and not associated with hypnosis compared to conventional pharmacological treatment of fibromyalgia.	N = 93	14 weekly sessions of 120 minutes + revaluation in 3 to 6 months.	Questionnaire application: Numerical Pain Rating Scale (NRS), CSQ (Catastrophizing Subscale of the Coping Strategies Questionnaire), HADS (Hospital Anxiety and Depression Scale), Fibromyalgia Impact Questionnaire (FIQ) and Sleep Scale Medical Outcomes Study (MOS).	Patients who received only CBT or CBT plus hypnosis showed improvements compared to patients who received only standard care. Adding hypnosis increased the effectiveness of CBT. CBT without hypnosis demonstrated changes in pain intensity, catastrophizing, psychological stress, functionalities, sleep disturbances in FM patients.
Gelman <i>et al.</i> , 2002 [13]	Randomized clinical trial	Determine the effectiveness of multidisciplinary treatment compared to standard treatment in patients with fibromyalgia.	N = 30	39 weeks (15 weekly sessions of 90 minutes + evaluation after period of 6 months).	Application of questionnaires: FIQ; the State-Trait Anxiety Inventory (STAI); the Beck Depression Inventory; visual-analog scale (EVA); number of tender points; associated symptomatology (AS); use of medications for FM.	Patients achieved a better coexistence with pain and a better adaptation and acceptance of the disorder and, therefore, a better quality of life from the lessons of cognitive-behavioral coping strategies and physical conditioning. Multidisciplinary treatment provides improved quality of life and psychological adaptation in FM patients.
Ang <i>et al.</i> , 2010 [30]	Randomized controlled trial	Explore the possibility of cognitive behavioral therapy to influence fibromyalgia symptoms through the inhibition of the descending nociceptive pathway.	N = 32	12 weeks (6 weekly sessions of 30 to 50 minutes).	Nociceptive Flexion Reflex (NFR) threshold, participants reported pain sensation for each electrical stimulus using a scale of 0 to 100. The FIQ (Fibromyalgia Impact Questionnaire) was also applied to PHQ-8 (Patient Health Questionnaire 8—item depression scale).	Both groups showed improvement, however, the intervention group was resisting higher levels of pain.

Continued

García <i>et al.</i> , 2006 [22]	Randomized controlled trial	Compare the difference in the effectiveness of Cognitive- Behavioral Therapy and pharmacological therapy in fibromyalgia.	N = 28	21 weeks (treatment phase: 9 weeks, 1 weekly session; follow-up: 3 months).	FIQ to assess the severity of the disease and its interference in the patient's work and life activities. Number of tender points (NTP). Hospital Anxiety and Depression Scale (HADS).	The results showed the superiority of CBT in reducing severity by FIQ. Combined therapy (pharmacological and CBT) does not increase efficacy, and CBT alone is more effective. In this study, time-limited CBT seems to be more effective than continuous pharmacological use, considering the side effects and the cost in the medium-long term.
Menga <i>et al.</i> , 2014 [31]	Randomized controlled trial	Evaluate the effect of CBT on FM, analyzing pain, anxiety, and depression.	N = 56	12 weeks (6 sessions of CBT).	Analysis of tender points and through the FIQ (Fibromyalgia Impact Questionnaires).	Despite the significant difference in results between the two groups at week 12, both forms of treatment were considered to have the potential to alleviate some FM symptoms (CBT treatment being well regarded for dealing with FM-related anxiety and depression).
Redondo <i>et al.</i> , 2004 [23]	Randomized Clinical Trial	To analyze the long-term effectiveness of Cognitive-Behavioral Therapy and an exercise-based strategy in patients with fibromyalgia.	N = 56	1 year and 8 weeks (treatment: once a week for 8 weeks, with 2 h 30 minutes). Evaluations: beginning, post- treatment, after 6 months and after 1 year.	Tender points score, Fibromyalgia Impact Questionnaire (FIQ), Short Form 36 (SF-36), Beck Anxiety Inventory, Beck Depression Inventory, Chronic Pain Self-Efficacy Scale (CPSS), Chronic Pain Coping Inventory (CPCI), Physical activity of vertebral column and upper and lower limbs e Measure of aerobic exercise capacity.	Both treatments, TCC and EF, showed clinical improvement in patients with FM in the short term, but there was no improvement one year after treatment. The strategies used by the patient to cope with pain were maintained, using physical activity in the PE group and relaxation in the CBT group.
Lera <i>et al.</i> , 2009 [24]	Randomized Clinical Trial	To analyze the response of patients with fibromyalgia to two multidisciplinary treatments, with or without Cognitive-Behavioral Therapy, observing symptoms and quality of life.	N = 83	4 months (14 sessions, once a week, for 90 mi- nutes) + 6-month follow-up.	The following were used: The Fibromyalgia Impact Questionnaire (FIQ), Short form 36 (SF-36), The Symptom Checklist-90—Revised (SCL-90-R). These data were collected at baseline, post-treatment and at the 6-month follow-up, and variable analysis was performed using MANOVA and ANOVA.	Both groups had an improvement in the clinical picture, but there was no significant difference to affirm that CBT is more effective. There was, however, an improvement in the Fibromyalgia Impact Questionnaire in patients with fatigue who received CBT.

Continued

Thieme <i>et al.</i> , 2006 [39]	Randomized Clinical Trial	To examine the effectiveness of Operant Behavioral Therapy (OBT) and CBT for patients with Fibromyalgia Syndrome, compared to the control group.	N = 100	12 months (15 weeks of 2 hour-sessions) + 2 reassessments: 1 after 6 months and another after 1 year of treatment.	Blood chemistry analysis, neurological examination, and evaluation of "tender points (TP)" by the Manual Tender Point Survey; FIQ; West Haven-Yale Multidimensional Pain Inventory (MPI); Pain-Related Self-Statements Scale (PRSS). Tübingen Pain Behavior Scale (TBS). Multivariate variance (MANOVA) for pain, function, and mood. Main effects and significant interactions were followed by post hoc analysis of variance (ANOVA) and t-tests.	Psychological treatments are clinically beneficial to patients. OBT was better for patient functionality, while CBT was better in cognitive terms. Patients treated with CBT demonstrated a clinically significant reduction in sustained pain over 12 months. OBT respondents showed reduced physical impairment, fewer visits to the doctor, and reduced pain behaviors.
Van Koulil, <i>et al.</i> 2010 [34]	Randomized controlled trial	Analyze the benefits of physical exercise, supported by CBT in high-risk patients with fibromyalgia.	N = 158	16 sessions twice a week (2 hours of CBT followed by 2 hours of physical training) + 1 booster session 3 months after completion of treatment.	Scale of the Impact of Rheumatic Diseases on General Health and Lifestyle (IRGL) instrument e o Pain Coping Inventory.	Treatment effects were significant for all primary outcomes, showing meaningful differences in physical (pain, fatigue, and functional disability) and psychological (negative mood and anxiety).
Langford <i>et al.</i> , 2008 [38]	Randomized controlled trial	Develop a manualized treatment for fibromyalgia and examine the effectiveness of treatment with Cognitive-Behavioral Therapy.	N = 105	3 months (one weekly session, for 8 weeks, of 2 hours each).	Quality of Life Scale (QOLS), FIQ, Numerical pain rating scale (NPRS), Chronic Disease Questionnaire (CDQ), Health Assessment Questionnaire (HAQ), Arthritis Self-Efficacy (ASES), Symptom Checklist 90-R (SCL90-R), Chronic Pain Coping Inventory (CPCI).	The study showed that the most significant result of CBT was the improvement in self-efficacy, which contributes to more favorable health behaviors such as exercise, relaxation training, and the continuous practice of adaptive coping strategies.
Ang <i>et al.</i> , 2013 [28]	Randomized controlled trial	Compare the effects of Cognitive Therapy Combined and Milnacipran for the Treatment of Fibromyalgia.	N = 48	21 weeks (8 sessions of 35 minutes).	Nonparametric Kruskal-Wallis. Pain sensitivity was assessed based on self-report evoked pain scores corresponding to 15 random pressure stimuli resulting from 5 pressure levels, each repeated three times. Repeated measure ANOVA was used to model this result at week 21.	Compared with milnacipran alone, combination therapy demonstrated a moderate effect in improving physical function and reducing mean weekly pain intensity.

Continued

McCrae <i>et al.</i> , 2018 [29]	Randomized controlled trial	To examine the effect of Cognitive-Behavioral Therapy for insomnia and pain on cortical thickness.	N = 37	3 years (weekly sessions of 50 minutes for 8 weeks).	Analysis of neuroimaging of cortical regions bilaterally through Magnetic Resonance.	Cognitive-Behavioral Therapy for Insomnia could delay or reverse gray matter cortical atrophy in patients with fibromyalgia and insomnia.
Jensen <i>et al.</i> , 2012 [27]	Randomized Clinical Trial	To investigate the role of the prefrontal cortex of patients with fibromyalgia in response to treatment with CBT.	N = 43	Weekly meetings for 12 weeks (6 patients in each group—each session took 90 minutes).	PGIC questionnaire and the 1) Beck Depression Inventory 2) Spielberg Anxiety Inventory 3) weekly pain intensity 4) thresholds from pain to pressure before and after treatment. Functional Magnetic Resonance was also used as a parameter.	CBT in FM patients was associated with increased activity of the ventrolateral prefrontal cortex and orbitofrontal cortex during evoked pain, which are involved in executive cognitive control. CBT has also been associated with reductions in depression and anxiety.
Falcão <i>et al.</i> , 2008 [37]	Randomized Clinical Trial	Evaluate the effects of Cognitive Behavioral Therapy in Fibromyalgia Syndrome.	N = 60	3 months (10 weeks with a weekly meeting, with 3 hours duration, of CBT combined with muscle relaxation training, cognitive restructuring, and stress management).	Progression was analyzed by a Generic Questionnaire, FIQ Visual Analog Scale (VAS) Psychological Inventory (State—Subcomponent State of the State-Trait Anxiety Inventory) Psychological assessment, including the BDI (Beck Depression Inventory) Verbal Improvement Scale (Likert Scale) The amount of acetaminophen used was another parameter used.	Both groups showed improvement with treatment. However, patients on Cognitive Behavioral Therapy had better responses regarding depression and mental health.
Van Koulil <i>et al.</i> , 2001 [33]	Randomized Clinical Trial	Evaluate the effects of CBT on pain avoidance behaviors, the pace of activities, and treatment with persistent pain.	N = 242	16 weeks of bi-weekly meetings, with 2 hours of CBT, followed by 2 hours of physical exercise + 6 months of follow-up.	A mixed linear model was used to assess physical functions, psychological functions, and the impact of fibromyalgia, taking into account the specific design features of this trial.	Patients showed improvement in all items evaluated.
Alda <i>et al.</i> , 2011 [25]	Randomized Clinical Trial	To evaluate the efficacy of CBT and the recommended pharmacological treatment compared to usual treatment at the primary care level for pain catastrophizing in patients with fibromyalgia.	N = 141	10 to 12 weeks of CBT	Pain Catastrophizing Scale. Hamilton Rating Scale for Depression (HAM-D); Hamilton Anxiety Rating Scale (HARS); Visual Analog Pain Scale (EVAP); FIQ; European Quality of Life Scale 5-D (EuroQol-5D).	CBT shows greater efficacy than recommended pharmacological treatment and usual care, not only in the main FM outcomes, such as function and quality of life, but also in relevant mediators of treatment effects, such as pain catastrophizing and pain acceptance.

Continued

Lami <i>et al.</i> , 2018 [26]	Randomized Clinical Trial	To analyze the effectiveness of CBT for insomnia and pain (CBT-IP) compared to CBT for pain (CBT-P) and usual medical care (UMC) as a means of improving sleep, pain, fatigue, and stress.	N = 126	21 weeks (9 weeks of CBT).	Pittsburgh Sleep Quality Index (PSQI), McGill Pain Questionnaire-Short Form (MPQ-SF), Multidimensional Fatigue Inventory (MFI), Fibromyalgia Impact Questionnaire (FIQ), Chronic Pain Self-Efficacy Scale (CPSS), Symptoms Check List 90-Revised (SCL-90-R), Pain Catastrophizing Scale (PCS) e Chronic Pain Acceptance Questionnaire (CPAQ).	CBT-IP didn't result in full sleep recovery in all patients. However, it has shown relevant clinical criteria, improving sleep quality and pain control. Therefore, it could be incorporated into multidisciplinary treatments.
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Alda 2011	+	+	-	?	+	+	+
Ang 2010	+	+	-	?	+	+	+
Ang 2013	+	+	+	+	+	+	+
Castel 2008	+	?	-	-	+	+	+
Castel 2012	+	+	+	+	?	-	+
Falcao 2008	-	?	?	?	+	+	+
García 2006	+	-	-	-	+	+	+
Gelman 2002	+	+	-	-	+	+	+
Jensen 2012	+	+	-	-	+	+	+
Karlsson 2015	+	+	-	-	+	+	+
Karlsson 2019	-	+	-	-	+	+	+
Lami 2018	?	+	+	+	+	+	+
Langfort 2008	+	+	+	+	+	+	+
Lazaridou 2017	-	-	-	-	?	+	+
Lera 2009	-	+	+	+	+	+	+
Luciano 2014	+	+	-	-	+	+	+
Martín 2014	+	+	+	+	+	+	+
McCrae 2018	+	+	-	-	+	+	+
Menga 2014	+	-	-	-	+	+	+
Parra-Delgado 2013	+	+	+	+	?	+	+
Redondo 2004	-	+	-	?	?	+	+
Thieme 2006	-	+	?	?	?	+	+
Thieme 2016	-	-	-	-	?	+	+
Van Kouilil 2010	+	+	-	+	+	+	+
Van Kouilil 2011	+	+	-	-	+	+	+
Williams 2002	-	+	+	+	+	-	+

- High risk

+ Low risk

? Unclear risk

Random sequence generation

Allocation concealment

Performance bias

Detection bias

Attrition bias

Reporting bias

Other Bias

Figure 2. Quality of studies and risk of bias according to the Cochrane recommendations manual for systematic reviews.

distraction techniques, showing, in neuroimaging studies, a reduction in the degree of connectivity between areas of the cerebral cortex related to pain [32].

Some clinical outcomes observed significant associations between changes in brain connectivity and long-term gains [32]. There was less pain sensation and improved resistance in those patients who underwent CBT [30], and more than half of the participants achieved declines in pain scales. Results indicate that CBT contributes to shifts in pain processing, promoting considerable improvement in clinical distress over time [27].

Few studies have not shown an improvement in the clinical status of patients. Falcão *et al.* (2008) [37] observed that patients who underwent CBT reduced the use of analgesics, but without objectively improving pain. Plasma levels of neuropeptide substance P (related to pain and stress signaling) in women with fibromyalgia who underwent CBT were reduced by 33%. However, there were no changes in the patients' state, and in some cases, the pain was considered even more significant after treatment with CBT [16]. CBT did not improve pain compared to control. However, there were immediate and clinically meaningful pain reductions in one-third of patients in both groups analyzed [15].

4.3. Fatigue and Insomnia

The study by Lera *et al.* (2009) [24] observed that the association of CBT and multidisciplinary treatment was only effective in patients with chronic fatigue. However, the multidisciplinary treatment improved the clinical picture of the other patients.

Regarding insomnia, the sleep pattern improved in patients who underwent CBT compared to the control group with the pharmacological treatment. Relaxation is a crucial component that enhances the effects of CBT on insomnia in patients with fibromyalgia. In addition, autogenic training alone showed positive effects on functional sleep disorders. Also, adding CBT content specifically targeted to treat chronic diseases resulted in significant improvements in primary insomnia in sleep disorders in patients with sleep problems and chronic pain, including fibromyalgia [18].

4.4. Cost-Effectiveness of Treatment

CBT is cost-effective when compared to pharmacological treatment (pregabalin + duloxetine), usual care groups, and FDA-recommended drugs [19].

4.5. Well-Being

CBT and pharmacological therapy have the potential to relieve FM symptoms. The first was superior in regards to anxiety and depression [20] [31] [37]. In addition, it improved the perception of clinical symptoms through an alteration of afferent pain signals, emotions, cognitions and anxiety reduction, with a significantly greater subjective impression of clinical improvement compared to controls [27].

CBT has been related to an improvement in quality of life in general, facilitating daily activities due to a decrease in functional limitation and improvement in morning stiffness [20] [22] [39].

In the study by Gelman *et al.* (2002) [13] it was achieved a better coexistence with pain and a better adaptation and acceptance of the disorder and, therefore, a better quality of life with the learning of cognitive-behavioral coping strategies in the group of patients who did CBT. Accepting the disease and managing stress are valuable tools for improving the quality of life. Additionally, patients in the CBT group had a positive effect on “life control” which was maintained 12 months after the start of treatment [35].

The study by Jensen *et al.* (2012) [27] evaluated the effect of cognitive-behavioral therapy on the cortical activation of the CNS through functional magnetic resonance in patients with FM. There was evidence of increased activation in the ventrolateral prefrontal cortex, responsible for executive cognitive control. In the clinical setting, the patients treated with CBT exhibited improvement in symptoms of depression and anxiety.

4.6. Medications, Comparison, and Association with CBT

When comparing CBT and pharmacological therapy in FM, CBT was proved to be superior, resulting in improved quality of life, reduced catastrophizing, and better pain acceptance [25]. Combined therapy improved pain, quality of life, and perception of social support compared to pharmacological therapy alone [21] [28] [31].

On the other hand, Garcia *et al.* (2006) [22] argues that CBT therapy associated with medications has not shown increased efficacy, and CBT alone would be more effective. The use of CBT for a limited time seems to be more effective and lasting than continuous pharmacological management, considering the side effects and the long-term cost [14] [22].

Patients in CBT had a lower rate of depression and higher scores in mental health compared to patients who used only pharmacological therapy, in addition to reducing the weekly use of acetaminophen for pain control. However, pharmacological therapy and CBT have shown similar results when dealing with symptoms of pain, anxiety, and quality of life [37].

4.7. Other Non-Pharmacological Therapies and CBT

Patients undergoing CBT in association with hypnosis showed significant improvement in the FIQ Total Score, a scale that assesses the impact of fibromyalgia (3.84, $p < 0.01$). There was a significant impact in patients undergoing CBT on the FIQ Total Score ($t = 2.28$; $p < 0.05$) [17].

CBT was more effective than pharmacological therapy in improving pain, stiffness, the number of tender points, catastrophizing, emotional stress, and sleep. The joining of hypnosis and CBT was even more effective [18]. Multidisciplinary therapy has led to better living with pain and better adaptation and acceptance in the short and long term [13].

The treatment effects of a combination of physical exercise and CBT in high-risk FM were significant for all primary outcomes, showing differences in physical (pain, fatigue, and functional disability) and psychological (negative mood, anxiety, and autonomy) functioning [33] [38].

On the other hand, Redondo *et al.* (2004) [23], also observed short-term clinical improvement, but without significant improvement one year after treatment. Exercise in association with motivational therapy increased physical capacity and improved clinical outcomes in patients who did not regularly use opioids. The study by Lera *et al.* (2009) [24] observed that the association of CBT with multidisciplinary treatment was only effective in patients with chronic fatigue. In other patients, only multidisciplinary treatment was effective in improving the clinical picture.

5. Conclusions

Cognitive Behavioral Therapy (CBT) has a great impact on the quality of life of patients, improving pain and fighting depression, anxiety, stress, rigidity, fatigue, and insomnia associated with the condition, facilitating daily activities and reducing functional limitations. Such improvement is maintained for a prolonged period after the end of treatment.

In addition to the monotherapeutic use, CBT can be associated with physical exercise, relaxation, psychological treatment, and hypnosis, presenting synergistic effects with each other.

CBT, despite being more cost-effective and more effective compared to drug therapy, can be used concomitantly with the latter, with analgesics and antidepressants being the most frequently used in the treatment.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

References

- [1] Clauw, D.J. (2014) Fibromyalgia: A Clinical Review. *JAMA*, **311**, 1547-1555. <https://doi.org/10.1001/jama.2014.3266>
- [2] Hawkins, R.A. (2013) Fibromyalgia: A Clinical Update. *Journal of Osteopathic Medicine*, **113**, 680-689. <https://doi.org/10.7556/jaoa.2013.034>
- [3] Vincent, A., Whipple, M.O. and Rhudy, L.M. (2016) Fibromyalgia Flares: A Qualitative Analysis. *Pain Medicine*, **17**, 463-468. <https://doi.org/10.1111/pme.12676>
- [4] Thong, I.S.K., Tan, G. and Jensen, M.P. (2017) The Buffering Role of Positive Affect on the Association between Pain Intensity and Pain Related Outcomes. *Scandinavian Journal of Pain*, **14**, 91-97. <https://doi.org/10.1016/j.sjpain.2016.09.008>
- [5] Casale, R., Sarzi-Puttini, P., Botto, R., Alciati, A., Batticciotto, A., Marotto, D., *et al.* (2019) Fibromyalgia and the Concept of Resilience. *Clinical and Experimental Rheumatology*, **37**, 105-113.
- [6] de Sousa Braz, A., de Paula, A.P., de Fátima Melo Diniz, M. and de Almeida, R.N.

- (2011) Uso da terapia não farmacológica, medicina alternativa e complementar na fibromialgia. *Revista Brasileira de Reumatologia*, **51**, 275-282. <https://doi.org/10.1590/S0482-50042011000300008>
- [7] Aman, M.M., Yong, R.J., Kaye, A.D. and Urman, R.D. (2018) Evidence-Based Non-Pharmacological Therapies for Fibromyalgia. *Current Pain and Headache Reports*, **22**, Article No. 33. <http://www.embase.com/search/results?subaction=viewrecord&from=export&id=L621530405%0Ahttp://dx.doi.org/10.1007/s11916-018-0688-2> <https://doi.org/10.1007/s11916-018-0688-2>
- [8] Bernardy, K., Füber, N., Köllner, V. and Häuser, W. (2010) Efficacy of Cognitive-Behavioral Therapies in Fibromyalgia Syndrome—A Systematic Review and Metaanalysis of Randomized Controlled Trials. *The Journal of Rheumatology*, **37**, 1991-2005. <https://doi.org/10.3899/jrheum.100104>
- [9] Hassett, A.L. and Gevirtz, R.N. (2009) Nonpharmacologic Treatment for Fibromyalgia: Patient Education, Cognitive-Behavioral Therapy, Relaxation Techniques, and Complementary and Alternative Medicine. *Rheumatic Disease Clinics of North America*, **35**, 393-407.
- [10] Page, M.J., McKenzie, J.E., Bossuyt, P.M., Boutron, I., Hoffmann, T.C., Mulrow, C.D., *et al.* (2021) The PRISMA 2020 Statement: An Updated Guideline for Reporting Systematic Reviews. *BMJ*, **372**, 9 p.
- [11] Higgins, J.P.T., Altman, D.G., Gøtzsche, P.C., Jüni, P., Moher, D., Oxman, A.D., *et al.* (2011) The Cochrane Collaboration's Tool for Assessing Risk of Bias in Randomised Trials. *BMJ*, **343**, 9 p. <https://doi.org/10.1136/bmj.d5928>
- [12] Kmet, L.M., Lee, R.C. and Cook, L.S. (2004) Standard Quality Assessment Criteria for Evaluating Primary Research Papers from a Variety of Fields. *Alberta Heritage Foundation for Medical Research*, **13**, 31 p. <https://www.ihe.ca/advanced-search/standard-quality-assessment-criteria-for-evaluating-primary-research-papers-from-a-variety-of-fields>
- [13] Gelman, S.M., Lera, S., Caballero, F. and López, M.J. (2002) Tratamiento multidisciplinario de la fibromialgia. Estudio piloto prospectivo controlado. *Revista Española de Reumatología*, **29**, 323-329.
- [14] Williams, D.A., Cary, M.A., Groner, K.H., Chaplin, W., Glazer, L.J., Rodriguez, A.M., *et al.* (2002) Improving Physical Functional Status in Patients with Fibromyalgia: A Brief Cognitive Behavioral Intervention. *The Journal of Rheumatology*, **29**, 1280-1286.
- [15] McCrae, C.S., Williams, J., Roditi, D., Anderson, R., Mundt, J.M., Miller, M.B., *et al.* (2019) Cognitive Behavioral Treatments for Insomnia and Pain in Adults with Comorbid Chronic Insomnia and Fibromyalgia: Clinical Outcomes from the SPIN Randomized Controlled Trial. *Sleep*, **42**, Article ID: zsy234. <https://doi.org/10.1093/sleep/zsy234>
- [16] Karlsson, B., Burell, G., Kristiansson, P., Björkegren, K., Nyberg, F. and Svärdsudd, K. (2019) Decline of Substance P Levels after Stress Management with Cognitive Behaviour Therapy in Women with the Fibromyalgia Syndrome. *Scandinavian Journal of Pain*, **19**, 473-482. <https://doi.org/10.1515/sjpain-2018-0324>
- [17] Castel, A., Salvat, M., Sala, J. and Rull, M. (2009) Cognitive-Behavioural Group Treatment with Hypnosis: A Randomized Pilot Trial in Fibromyalgia. *Contemporary Hypnosis*, **26**, 48-59. <https://doi.org/10.1002/ch.372>
- [18] Castel, A., Cascón, R., Padrol, A., Sala, J. and Rull, M. (2012) Multicomponent Cognitive-Behavioral Group Therapy with Hypnosis for the Treatment of Fibromyalgia:

- Long-Term Outcome. *The Journal of Pain*, **13**, 255-265.
<https://doi.org/10.1016/j.jpain.2011.11.005>
- [19] Luciano, J.V., D'Amico, F., Cerdà-Lafont, M., Peñarrubia-María, M.T., Knapp, M., Cuesta-Vargas, A.I., *et al.* (2014) Cost-Utility of Cognitive Behavioral Therapy versus U.S. Food and Drug Administration Recommended Drugs and Usual Care in the Treatment of Patients with Fibromyalgia: An Economic Evaluation alongside a 6-Month Randomized Controlled Trial. *Arthritis Research & Therapy*, **16**, Article No. 451. <https://doi.org/10.1186/s13075-014-0451-y>
- [20] Parra-Delgado, M. and Latorre-Postigo, J.M. (2013) Effectiveness of Mindfulness-Based Cognitive Therapy in the Treatment of Fibromyalgia: A Randomised Trial. *Cognitive Therapy and Research*, **37**, 1015-1026.
<https://doi.org/10.1007/s10608-013-9538-z>
- [21] Martín, J., Torre, F., Padierna, A., Aguirre, U., González, N., Matellanes, B., *et al.* (2014) Impact of Interdisciplinary Treatment on Physical and Psychosocial Parameters in Patients with Fibromyalgia: Results of a Randomised Trial. *International Journal of Clinical Practice*, **68**, 618-627. <https://doi.org/10.1111/ijcp.12365>
- [22] García, J., Simón, M.A., Durán, M., Cancellor, J., Aneiros, F.J. (2006) Differential Efficacy of a Cognitive-Behavioral Intervention versus Pharmacological Treatment in the Management of Fibromyalgic Syndrome. *Psychology, Health & Medicine*, **11**, 498-506. <https://doi.org/10.1080/13548500600745286>
- [23] Redondo, J.R., Justo, C.M., Moraleda, F.V., Velayos, Y.G., Puche, J.J.O., Zubero, J.R., *et al.* (2004) Long-Term Efficacy of Therapy in Patients with Fibromyalgia: A Physical Exercise-Based Program and a Cognitive-Behavioral Approach. *Arthritis Care & Research*, **51**, 184-192. <https://doi.org/10.1002/art.20252>
- [24] Lera, S., Gelman, S.M., López, M.J., Abenoza, M., Zorrilla, J.G., Castro-Fornieles, J., *et al.* (2009) Multidisciplinary Treatment of Fibromyalgia: Does Cognitive Behavior Therapy Increase the Response to Treatment? *Journal of Psychosomatic Research*, **67**, 433-441. <https://doi.org/10.1016/j.jpsychores.2009.01.012>
- [25] Alda, M., Luciano, J.V., Andrés, E., Serrano-Blanco, A., Rodero, B., del Hoyo, Y.L., *et al.* (2011) Effectiveness of Cognitive Behaviour Therapy for the Treatment of Catastrophisation in Patients with Fibromyalgia: A Randomised Controlled Trial. *Arthritis Research & Therapy*, **13**, Article No. R173.
<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3308108>
<https://doi.org/10.1186/ar3496>
- [26] Lami, M.J., Martínez, M.P., Miró, E., Sánchez, A.I., Prados, G., Cáliz, R., *et al.* (2018) Efficacy of Combined Cognitive-Behavioral Therapy for Insomnia and Pain in Patients with Fibromyalgia: A Randomized Controlled Trial. *Cognitive Therapy and Research*, **42**, 63-79. <https://doi.org/10.1007/s10608-017-9875-4>
- [27] Jensen, K.B., Kosek, E., Wicksell, R., Kemani, M., Olsson, G., Merle, J.V., *et al.* (2012) Cognitive Behavioral Therapy Increases Pain-Evoked Activation of the Prefrontal Cortex in Patients with Fibromyalgia. *Pain*, **153**, 1495-1503.
<https://doi.org/10.1016/j.pain.2012.04.010>
- [28] Ang, D.C., Jensen, M.P., Steiner, J.L., Hilligoss, J., Gracely, R.H. and Saha, C. (2013) Combining Cognitive-Behavioral Therapy and Milnacipran for Fibromyalgia: A Feasibility Randomized-Controlled Trial. *The Clinical Journal of Pain*, **29**, 747-754.
<https://doi.org/10.1097/AJP.0b013e31827a784e>
- [29] McCrae, C.S., Mundt, J.M., Curtis, A.F., Craggs, J.G., O'Shea, A.M., Staud, R., *et al.* (2018) Gray Matter Changes Following Cognitive Behavioral Therapy for Patients with Comorbid Fibromyalgia and Insomnia: A Pilot Study. *Journal of Clinical Sleep*

- Medicine*, **14**, 1595-1603. <https://doi.org/10.5664/jcsm.7344>
- [30] Ang, D.C., Chakr, R., Mazzuca, S., France, C.R., Steiner, J. and Stump, T. (2010) Cognitive-Behavioral Therapy Attenuates Nociceptive Responding in Patients with Fibromyalgia: A Pilot Study. *Arthritis Care & Research*, **62**, 618-623. <https://doi.org/10.1002/acr.20119>
 - [31] Menga, G., Ing, S., Khan, O., Dupre, B., Dornelles, A.C., Alarakhia, A., *et al.* (2014) Fibromyalgia: Can Online Cognitive Behavioral Therapy Help? *Ochsner Journal*, **14**, 343-349. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4171792/>
 - [32] Lazaridou, A., Kim, J., Cahalan, C.M., Loggia, M.L., Franceschelli, O., Berna, C., *et al.* (2017) Effects of Cognitive-Behavioral Therapy (CBT) on Brain Connectivity Supporting Catastrophizing in Fibromyalgia. *The Clinical Journal of Pain*, **33**, 215-221. <https://doi.org/10.1097/AJP.0000000000000422>
 - [33] Van Koulil, S., Kraaimaat, F.W., Van Lankveld, W., Van Helmond, T., Vedder, A., Van Hoorn, H., *et al.* (2011) Cognitive-Behavioral Mechanisms in a Pain-Avoidance and a Pain-Persistence Treatment for High-Risk Fibromyalgia Patients. *Arthritis Care & Research*, **63**, 800-807. <https://doi.org/10.1002/acr.20445>
 - [34] Van Koulil, S., Van Lankveld, W., Kraaimaat, F.W., Van Helmond, T., Vedder, A., Van Hoorn, H., *et al.* (2010) Tailored Cognitive-Behavioral Therapy and Exercise Training for High-Risk Patients with Fibromyalgia. *Arthritis Care & Research*, **62**, 1377-1385. <https://doi.org/10.1002/acr.20268>
 - [35] Karlsson, B., Burell, G., Anderberg, U.M. and Svärdsudd, K. (2015) Cognitive Behaviour Therapy in Women with Fibromyalgia: A Randomized Clinical Trial. *Scandinavian Journal of Pain*, **9**, 11-21. <https://doi.org/10.1016/j.sjpain.2015.04.027>
 - [36] Thieme, K., Turk, D.C., Gracely, R.H. and Flor, H. (2016) Differential Psychophysiological Effects of Operant and Cognitive Behavioural Treatments in Women with Fibromyalgia. *European Journal of Pain*, **20**, 1478-1489. <https://doi.org/10.1002/ejp.872>
 - [37] Falcão, D.M., Sales, L., Leite, J.R., Feldman, D., Valim, V. and Natour, J. (2008) Cognitive Behavioral Therapy for the Treatment of Fibromyalgia Syndrome: A Randomized Controlled Trial. *Journal of Musculoskeletal Pain*, **16**, 133-140. <https://doi.org/10.1080/10582450802161796>
 - [38] Langford, M.M. (2008) The Efficacy of a Combined Cognitive-Behavioural and Interpersonal Therapy Approach to the Treatment of Fibromyalgia Syndrome: A Randomized Controlled Trial. Doctor's Thesis, University of Saskatchewan, Saskatoon.
 - [39] Thieme, K., Flor, H. and Turk, D.C. (2006) Psychological Pain Treatment in Fibromyalgia Syndrome: Efficacy of Operant Behavioural and Cognitive Behavioural Treatments. *Arthritis Research & Therapy*, **8**, Article No. R121.