Effectiveness of cognitive behavioral therapy in the treatment of fibromyalgia syndrome: a meta-analytic literature review

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SUMMARY

Fibromyalgia (FM) is a chronic disorder caused by a dysfunction of central nervous system sensitization. This syndrome is characterized by widespread pain and diffuse tenderness, but often also presents fatigue, sleep disturbances, and a whole range of symptoms such as morning stiffness, decreased physical function and dyscognition. FM is usually treated with pharmacological and non-pharmacological treatments. The non-pharmacological interventions include cognitive behavioral therapy (CBT), physiotherapy, acupuncture and patient education programs.

In order to evaluate the efficacy of CBT and compare it with other non-pharmacological treatments, we performed a review of the meta-analytic literature. We evaluated the methodological quality of publications found by following the recommendations of the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) statement. Data showed that CBT does not provide better results than other non-pharmacological treatments on outcomes of pain, fatigue, sleep disturbance and quality of life, at either a short or long-term evaluation. On the contrary, CBT seems to be more effective on symptoms of depression for a short period, whereas it considerably improves the pain self-management and reduces the number of visits to the doctor.

The data currently available indicate that cost-effectiveness studies could help us to understand whether the reduction in the number of visits to the doctor could balance the cost of CBT to the health public system.

Key words: *Cognitive behavioral therapy, fibromyalgia syndrome, meta-analysis, systematic review.*

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INTRODUCTION

Fibromyalgia (FM) is a syndrome of centralized sensitization characterized by dysfunction of the neurocircuits responsible for perception, transmission and processing of afferent nociceptors. Pain is principally in the muscular-skeletal apparatus. Besides the pain, various other accompanying symptoms can be presented that are common to other syndromes: asthenia, sleep disturbance, abdominal pain, etc. (1). This definition is the result of a growing understanding of the pathogenetic mechanisms of these centralized pain syndromes. However, in spite of the scientific knowledge from clinical research currently available, many are still skeptical about the validity of regarding FM as a separate disease entity, and are reluctant to diagnose and treat the disturbance in an appropriate manner.

Besides defining the disease, scientific results have modified and expanded the methods used to diagnose FM. In fact, criteria from the American College of Rheumatology (ACR) are not sufficient. In 1990, the ACR defined FM as a chronic illness characterized by widespread pain associated with digital-pressure sensitivity of at least 11 of 18 points, known as *tender points* (TPs), throughout the whole muscular-skeletal system. Criticism of the TP system is not only confined to the rather arbitrary choice of 11 points as a diagnostic threshold, but is also due to the fact that many individuals may not experience pain in the whole body. In fact, they may present symptoms that suggest the diagnosis of a central sensitization syndrome.

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Furthermore, ACR criteria do not take into consideration other symptoms presented by nearly all fibromyalgia patients, i.e. fatigue, sleep disturbance and, above all, allodynia, i.e. marked pain from even a light physical palpation that allows a differential diagnosis to be made between FM and other pathologies (2). Other often reported symptoms are morning stiffness, swelling of soft tissue, paresthesias, migraine, cognitive disturbances, disturbances of the temporomandibular articulation (TMA), irritable bowel (1). Given this, Wolfe and co-workers have proposed a new diagnostic system that integrates all these symptoms (3).

The basic cause of FM is still unknown. However, recent research has shown that the key factor in the physiopathology of this disturbance is represented by alterations in the sensorial processes that lead to pain developing (4). Stress is our organisms's response to all physiological and psychosocial stress-creating agents and it plays an important role in determining the onset of the syndrome and in intensifying its symptoms. Dysfunction of the hypothalamic-pituitary-adrenal (HPA) system confirms this (5). Many patients with FM show comorbidity of psychiatric disturbances. Data available in literature vary considerably. However, a recent epidemiological study (6) has shown that those disturbances most associated with FM are major depressive disorder (MDD) (12.8%), anxiety disorders with specific phobia (7.7%), alcohol abuse (4.1%) and dysthymia (4.1%).

Psychopathological comorbidity has increased the confusion in the diagnosis and fibromyalgia patients are often stigmatized and mistakenly considered to be psychiatric patients. In fact, it is still not clear today whether psychological factors such as anxiety, stress or psychological malaise are responsible for generating the cerebral alterations or whether these neurotransmission dysfunctions exert a secondary effect on the patient's psychological ill-being. The psychological factors are important in determining any type of pain, particularly if this is chronic, independently of the cause, and FM is no exception. In fact, the extent of psychiatric disorders presented by FM patients is in line with that of other chronic disorders that cause pain, such as rheumatoid arthritis (6). Increasingly, specific programs of physical training, relaxation techniques, self-assertion, anxiety management and emotional awareness courses are being associated with pharmacological treatment for FM. Education programs are also offered to help patients understand their illness and learn to live with it.

Cognitive behavioral therapy (CBT) is often used as a non-pharmacological treatment. Cognitive behavioral therapy was developed in the 1960s and early 1970s. It is based on the application of a procedure of *reinforcement* and *punishment* in an attempt to modify pathological behavior, thought and sentiment (7). Its basic principle is that daily behavior is supported by the consequences it produces; an action that is followed by reinforcement will be repeated in the future, while those activities that do not lead to reinforcement or that are even punished will not be repeated. Over successive years, some authors (8) have proposed a theoretical therapeutic model that went beyond the mere analysis of behavior and how it was, to a greater or lesser extent reinforced. These included fundamental cognitive aspects that play a key role in the onset of psychiatric pathologies, such as self-awareness, self-criticism, the negative expectations and degree of perception of one's own social abilities. In particular, Beck developed the CBT theory as we know it today and showed that our mood is characterized by three thought processes, the so-called *cognitive triad*. The interpretation of particular events or situations is influenced by previous personal experience and by a general vision that we have of ourselves (excessive self-criticism), of the world (seen as unfair and hostile) and of the future (distrust, pessimism) (8). Patients with FM often manifest a cognitive style that could be described as *catastrophizing*. This involves an exagerated expansion of emotional aspects with a pessimistic vision towards the self, others and the future, such as to consider pain to be something terrible and intolerable. Such

an approach contributes to pain becoming more chronic and disabling for which the *catastrophizing* is an independent factor that is only partially associated with depression. These dysfunctional thoughts lead to a greater vulnerability when faced with stressful stimuli, increasing the probability of failure and difficulty, so continuing the vicious circle.

In order to clarify the role of CBT in the treatment of FM, we carried out a review of meta-analytical literature and evaluated to what extent the papers we found corresponded to the recommendations of the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) statement concerning transparent methodology (9).

MATERIALS AND METHODS

A bibliographical search was made in Pubmed, with no limitations of year of publication, in order to find systematic reviews pertinent to the question under discussion: FIBROMYALGIA or FIBROMYALG* and COGNITIVE BEHAVIOUR* and THERAPY or BEHAVIOR* and THERAPY or COGNITIVE and THERAPY or BEHAVIOR THERAPY or PSYCOTHERAPY; SYSTEMATIC REVIEWS was used as a limiting section subset.

Systematic reviews were excluded if they:

1. did not contain a meta-analytical synthesis of results from randomized controlled trials;
2. studied patients in a single age group or disease type or with specific comorbidities;
3. studied treatment other than CBT given in a face-to-face session (e.g. online CBT);
4. were studies of chronic fatigue syndrome (for nosographic reasons).

Abstracts of the selected papers were evaluated separately by two reviewers who then decided which studies would be evaluated in full-text. Any disagreements were resolved by consensual discussion. Papers included in the analysis were then analyzed according to the PRISMA check list in order to evaluate the transparency of the method used and, therefore, to what extent the conclusions could be considered reliable. Here again, evaluation was made independently by two reviewers and any disagreements were resolved by consensual discussion.

RESULTS

By 5 February 2012, a total of 412 abstracts had been selected (Fig. 1). Of these, 34 were confirmed to be systematic reviews. A first reading confirmed that of the 34 abstracts, 4 papers (10-13) were considered to be pertinant to the questions raised and were examined in full-text. Of these, 3 were excluded from subsequent analysis: 2 (12, 13) were excluded because they combined results from studies of different types of non-pharmacological treatment for FM and the CBT was represented by a very limited number of studies with respect to the total number of studies included (2 of 25 in the first and 6 of 49 in the second). Also, in these 2 reviews, the results from the studies on CBT had not undergone separate meta-analysis. Also, the third review (11) was excluded from the analysis since it did not specifically study the efficacy of only CBT but rather the general efficacy of 7 different types of psychological therapy of which CBT was but one, representing only a small number of studies (8 studies of 23). Since, however, the results of the study on CBT were also meta-analyzed separately, even though this only concerned the single outcome *pain intensity*, we felt that it would be useful to include themas an object of discussion.

One systematic review (10) satisfied all inclusion criteria and was considered the paper of reference for our analyses. The review included 14 randomized controlled trials traced from 30 June 2009 and published between 1994 and 2007, including a total of 910 patients on which the efficacy of CBT was evaluated and compared with a large series of other non-pharmacological treatments (attention control, physical activity, sleep hygiene, relaxation techniques,

stretching, discussion groups, keeping a diary, guided reading). When PRISMA criteria were used this was explicity stated by the authors. PRISMA criteria recommended that the presence or absence of any conflicts of interest and information regarding any financial support received should be explicitly stated in the paper. This was not always the case. However, all other PRISMA criteria were fully satisfied. Conformity to the PRISMA criteria allowed us to evaluate the *risk of bias* in each individual study (Tab. I). Cochrane evaluation critieria were used: adequate randomization, adequate access to the randomization list, degree of blindness, use of *intention to treat* (ITT) analysis.

The review distinguishes between outcome

Table I - Summary of risk of bias for each individual paper.

Study	Adequacy randomization	Adequacy allocation concealment	Blindness	Intention to treat (ITT) analysis
Astin, et al. (2003)	No	Yes	Yes	No
Burckhardt, et al. (1994)	No	No	No	No
Edinger, et al. (2005)	No	No	No	Yes
Garcia, et al. (2006)	No	No	No	Yes
Grossman, et al. (2007)	No	No	No	Yes
Kashikar-Zuck, et al. (2005)	Yes	Yes	Yes	Yes
Nicassio, et al. (1997)	Yes	No	No	No
Redondo, et al. (2004)	Yes	No	No	Yes
Sephton, et al. (2007)	Yes	No	No	Yes
Soares, et al. (2007)	No	No	No	Yes
Thieme, et al. (2003)	No	No	No	Yes
Thieme, et al. (2006)	No	No	No	Yes
Vlaeyen, et al. (1996)	No	No	No	Yes
Wigers, et al. (1996)	Yes	No	Yes	No

Table II - Efficacy of CBT compared to other non-pharmacological treatments on completion of treatment.

Outcome	Results	N. studies/n. pts
Degree of pain	NS	13 studies/664 pts
Fatigue	NS	5 studies/258 pts
Sleep	NS	4 studies/141 pts
Quality of life	NS	10 studies/517 pts
Depression	SMD (-0.24; CI 95% -0.40, -0.08)	11 studies/631 pts
Self-control	SMD (0.85; CI 95% 0.25, 1.46)	9 studies/476 pts
Visits to the doctor	NA	NA

NA, not evaluable; NS, not significant; SMD, standardized mean difference (0.2, small; 0.5, moderate; 0.8, large); pts, patients.

Table III - Efficacy of CBT compared to other non-pharmacological treatments at follow up.

Outcome	Results	N. studies/n. pts
Degree of pain	NS	10 studies/527 pts
Fatigue	NS	4 studies/200 pts
Sleep	NS	4 studies/141 pts
Quality of life	NS	7 studies/393 pts
Depression	NS	8 studies/494 pts
Self-control	SMD (0.90; IC 95% 0.14, 1.66)	7 studies/396 pts
Visits to the doctor	SMD (-1.57; IC 95% -2.00, -1.14)	2 studies/121 pts

NA, not evaluable; NS, not significant; SMD, standardized mean difference (0.2, small; 0.5, moderate; 0.8, large); pts, patients.

at two different time points: on completion of treatment and at follow up, understood to be the latest date of available follow up. The meta-analytical synthesis of the data collected on completion of treatment (Tab. II) showed no significant differences between CBT and other non-pharmacological treatments for the following outcomes: degree of pain, quality of sleep, quality of life. However, there was a significant difference between CBT and other non-pharmacological treatments for the outcome *depression* (SMD -0.24; IC95% -0.40, -0.08) and ability to self-manage pain (SMD 0.85; IC95% 0.25, 1.46).
Results at follow up (Tab. III) did not show any difference in the following outcomes: degree of pain, fatigue, quality of sleep, quality of life and depression. However, the meta-analytical synthesis of results at follow up showed a significant differences between CBT and other non-pharmacological treatments regarding ability to self-manage pain (SMD 0.90; IC95% 0.14, 1.66) and the number of visits to the doctor requested (SMD -1.57; IC95% -2.00, -1.14).

DISCUSSION

Only one systematic review (10) was found that corresponded to the statement of the authors that they had carried out the first systematic meta-analytical review on this subject. The excellent quality of the methodology of this review almost completely satisfies the requirements set out in PRISMA. However, method quality remains modest in such that the evaluation criteria of *risk of bias* shows that most of the trials had a significant *risk of bias*. The *sensitivity analysis* carried out by the authors shows that the modest effect of the CBT on mood on completion of treatment, an effect that seemed to have disappeared completely at follow up, could be due to the presence of elements that distorted the study methodology. In fact, the outcome is statistically significant when the worst quality papers are examined while this significance is lost when the studies with the best quality papers are examined. The *sensitivity analysis* was not carried out for other significant outcomes since the impact of the method quality on their significance was not reported.
In terms of efficacy, CBT was not found to be substantially superior to the other non-pharmacological treatments regarding all outcomes except for pain self-management on completion of treatment and at follow up. This agrees with the finding of a significant reduction in the number of visits to the doctor requested at follow up. On the *pain* outcome, the result of the review contrasts with data from a sub-group analysis carried out by the authors of another review (11) that showed a consistent reduction in the degree of pain observed in those who underwent CBT compared to controls (SMD 0.60; IC95% 0.43, 0.76). This disgreement was seen in spite of the fact that 5 of the 8 studies included in this last meta-analysis were also included among the 13 studies of the reference systematic review. (10) Also in this case, there was a scarse conformity to the methodological standards that could have had an important impact considering that these studies were judged to be of a low quality.
None of the studies showed *anxiety* to be an outcome even though this is an important element in all chronic disorders. In fact, *catastrophizing* is a cognitive distorsion often manifested by both FM patients (14) and by those with other chronic pathologies that cause pain. (15) This leads to very intense states of anxiety. However, none of the meta-analytical studies examined attempted to show to what extent CBT can improve this thought process and so have a positive impact on the symptoms it produces. Just how big this effect is is particularly important because the statistical significance of the results does not translate automatically into clinical significance. The clinical importance of the SMD can be evaluated according to Cohen's recommendations: 0.2 small, 0.5 moderate, 0.8 large. (16) On this basis, it is possible to show that the dimension of the effect of CBT on the outcomes in which it is shown to be significantly superior to other non-pharmacological treatments is such as to also be important from

a clinical point of view. CBT as part of FM therapeutic programs is mainly focused on the awareness and acceptance of the illness, on management of anxiety and of the cognitive distorsions associated with the illness (e.g. *catastrophic* or *absolute* thoughts associated with the symptoms or with the illness itself). Furthermore, changes in behavior and an increased ability to solve problems help patients acquire greater self-control of pain management and of the practical problems associated with their illness. (17) Gaining a greater awareness of their own problems and the potential reasons for apprehension and tension, along with a greater ability to face them and deal with them, allows the patient to achieve a greater psychic well-being that will reduce the muscular tension and pain.

The results emerging from the review of the meta-analytical literature need to be confirmed in controlled randomized trials that adopt a methodological approach the quality of which can permit reliable conclusions to be drawn. However, these results do support the efficacy of this type of targeted treatment. If the efficacy data are confirmed, cost-effectiveness must be evaluated to establish whether the economic burden of CBT can be counterbalanced by a reduction in the number of visits to the doctor requested by FM patients. Once efficacy data have been confirmed and the cost-effectiveness has been weighed up, it will be possible to formulate recommendations for clinical practice that should be included in management guidelines for this pathology.

Finally, even though not strictly linked to a systematic review of efficacy, we consider it to be useful to underline that, in the absence of laboratory markers, objective characteristic signs and the presence of comorbidities with FM, constitutional symptoms need to be accurately evaluated in order to avoid diagnostic errors. One study shows a substantial inaccuracy in diagnosis in a cohort of patients who had been diagnosed with FM; a group of these patients were seen by a consultant rheumatologist and FM was confirmed in only 34% of them. (18) Given this, an accurate evaluation of the psychological condition of the patient can help exclude primary psychiatric disorders that could lead to an incorrect diagnosis and to FM patients being stigamatized as psychiatric cases.

REFERENCES

1. Ablin J, Neumann L, Buskila D. Pathogenesis of fibromyalgia - a review. Joint Bone Spine. 2008; 75: 273-9.
2. McCarberg BH. Clinical overview of fibromyalgia. Am J Ther 2011. [Epub ahead of print].
3. Wolfe F, Clauw DJ, Fitzcharles MA, et al. The American College of Rheumatology preliminary diagnostic criteria for fibromyalgia and measurement of symptom severity. Arthritis Care Res (Hoboken). 2010; 62: 600-10.
4. Bradley LA. Pathophysiology of fibromyalgia. Am J Med. 2009; 122: S22-30.
5. Geiss A, Rohleder N, Anton F. Evidence for an association between an enhanced reactivity of interleukin-6 levels and reduced glucocorticoid sensitivity in patients with fibromyalgia. Psychoneuroendocrinology. 2011. [Epub ahead of print].
6. Gonzalez E, Elorza J, Failde I. Fibromyalgia and psychiatric comorbidity: their effect on the quality of life patients. Actas Esp Psiquiatr. 2010; 38: 295-300.
7. Lewison PM. A behavioural approach to depression. Friedman R, Katz N, New York. 1974.
8. Beck AT. Depression: causes and treatment. University of Pennsylvania Press, Philadelphia. 1967.
9. Moher D, Liberati A, Tetzlaff J, Altman DG. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. J Clin Epidemiol. 2009; 62: 1006-12.
10. Bernardy K, Fuber N, Kollner V, Hauser W. Efficacy of cognitive-behavioral therapies in fibromyalgia syndrome - a systematic review and metaanalysis of randomized controlled trials. J Rheumatol. 2010; 37: 1991-2005.
11. Glombiewski JA, Sawyer AT, Gutermann J, et al. Psychological treatments for fibromyalgia: a meta-analysis. Pain. 2010; 151: 280-95.
12. Sim J, Adams N. Systematic review of randomized controlled trials of nonpharmacological interventions for fibromyalgia. Clin J Pain. 2002; 18: 324-36.
13. Rossy LA, Buckelew SP, Dorr N, et al. A meta-analysis of fibromyalgia treatment interventions. Ann Behav Med. 1999; 21: 180-91.
14. Morris LD, Grimmer-Somers KA, Spottiswoode B, Louw QA. Virtual reality exposure therapy as treatment for pain catastrophizing in fibromyalgia patients: proof-of-concept

study (Study Protocol). BMC Musculoskelet Disord. 2011; 12: 85.
15. Edwards RR, Cahalan C, Mensing G, et al. Pain, catastrophizing, and depression in the rheumatic diseases. Nat Rev Rheumatol. 2011; 7: 216-24.
16. Cohen J. Statistical power analysis for the behavioral sciences. Lawrance Erlbaum Associates, Hillsdale, NJ, USA. 1988.
17. Rodero B, Casanueva B, Luciano JV, et al. Relationship between behavioural coping strategies and acceptance in patients with fibromyalgia syndrome: elucidating targets of interventions. BMC Musculoskelet Disord. 2011; 12: 143.
18. Fitzcharles MA, Boulos P. Inaccuracy in the diagnosis of fibromyalgia syndrome: analysis of referrals. Rheumatology. 2003; 42: 263-7.