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Mindfulness-based therapy as an adjuvant treatment option for fibromyalgia: a review

Terapia basada en mindfulness
como opción terapéutica en la
fibromialgia: una revisión

Grado en Medicina

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Abstract

Fibromyalgia is a prevalent disease characterized by chronic widespread pain, fatigue, sleep disturbances, psychological disorders and autonomic symptoms. Its etiopathogenesis is unclear and seems to be multifactorial. Treatment should be individualized, and current options show poor results. Mindfulness refers to one's awareness to present thoughts, emotions, and sensations in a non-judgmental way. Therapies developed from these principles have shown results on chronic pain and mood disorders.

This narrative review aims to understand the pathogenic mechanisms behind fibromyalgia, how mindfulness may act on them, describe evidence supporting its efficacy and how mindfulness-based interventions could be used as an adjuvant treatment. Two searches were performed using PubMed, Scopus and Web of Science using the words "fibromyalgia", "pathogenesis" and "mindfulness". Sixty-four articles published in the last 5 years were considered.

Fibromyalgia seems to be a central sensitization problem shown by neuroimaging. Other factors seem to play a role such as peripheral sensitization, neuroinflammation, endocrine alterations, sleep disturbances and cognitive-emotional sensitization. Mindfulness as a trait seems to act on these factors, especially on psychological ones and is considered a protective factor. Current evidence shows efficacy of mindfulness-based interventions in fibromyalgia symptoms, mainly psychological ones and overall disease impact. More specific trials evaluating the efficacy are required as current studies are heterogenous. Cost and practicality could hinder its application but due to its reported effectiveness and safety, mindfulness-based interventions could be included in a multimodal treatment regimen and mindfulness practices outside structured programs could be recommended.

Keywords: Fibromyalgia; mindfulness; mindfulness-based therapy; meditation;, pain catastrophizing; chronic pain

Resumen

La fibromialgia es una enfermedad prevalente caracterizada por dolor crónico, fatiga, trastornos del sueño, trastornos psicológicos y síntomas autonómicos. La etiopatogenia no está clara y parece multifactorial. El tratamiento debe ser individualizado y las opciones actuales muestran malos resultados. Mindfulness es la conciencia de pensamientos, emociones y

sensaciones sin juicio. Terapias basadas en estos principios mostraron eficacia en el dolor crónico y trastornos psicológicos.

Esta revisión narrativa pretende comprender los mecanismos patogénicos detrás de la fibromialgia, cómo el mindfulness puede actuar sobre ellos, describir la evidencia de la eficacia de las terapias basadas en el mindfulness y cómo podrían usarse como tratamiento adyuvante. Se realizaron dos búsquedas en PubMed, Scopus y Web of Science utilizando las palabras “fibromyalgia”, “pathogenesis” y “mindfulness”. Se consideraron 64 artículos publicados en los últimos 5 años.

La fibromialgia parece ser un problema de sensibilización central demostrado por neuroimagen. Otros factores son la sensibilización periférica, neuroinflamación, alteraciones endocrinas, trastornos del sueño y sensibilización cognitivo-emocional. El mindfulness parece actuar sobre estos factores, especialmente los psicológicos y es un factor protector. Se demostró eficacia de las intervenciones basadas en el mindfulness en los síntomas (principalmente psicológicos) e impacto general de la fibromialgia. Se requieren más ensayos específicos que evalúen la eficacia ya que los estudios actuales son heterogéneos. El coste y la practicidad podrían dificultar su aplicación, pero debido a su efectividad y seguridad, las intervenciones basadas en el mindfulness podrían incluirse en un régimen de tratamiento multimodal y prácticas de mindfulness fuera de programas estructurados podrían recomendarse.

Palabras clave: Fibromialgia; mindfulness; terapias basadas en mindfulness; meditación; dolor crónico

Abbreviations

ACC: Anterior Cingulate Cortex

ACR: American College of Rheumatology

ACT: Acceptance and Commitment Therapy

ADS: Alfa-Delta Sleep

ANA: Antinuclear Antibodies

CBT: Cognitive Behaviour Therapy

CMT: Cognitive Meditative Therapy

CRH: Corticotropin Releasing Hormone

CSF: Cerebrospinal Fluid

CWP: Chronic widespread pain

EULAR: European Alliance of Associations for Rheumatology

FM: Fibromyalgia

GPER: G protein-coupled estrogenic receptor

HPA: hypothalamus-pituitary-adrenal

MBCT: Mindfulness-Based Cognitive Therapy

MBI/MBT: Mindfulness-Based Intervention/Mindfulness-Based Therapy

MBSR: Mindfulness-Based Stress Reduction

NSAID: Non-Steroid Anti-inflammatory Drug

OCT: Optical Coherence Tomography

OR: Odds Ratio

PDS: Polysymptomatic Distress Scale

PET: Positron Emission Tomography

PTSD: Post-Traumatic Stress Disorder

RA: Rheumatoid Arthritis

RCT: Randomized Clinical Trial

SFN: Small Fibre Neuropathy

SSD: Somatic Symptom Disorder

SSS: Symptom Severity Scale

WPI: Widespread Pain Index

1. Introduction

1.1 Definitions

1.2.1. Fibromyalgia

Fibromyalgia (FM) is a syndrome characterized by a wide array of symptoms of which the most characteristic is widespread chronic pain (CWP) with specific muscle and joint tender sites. Although pain is the most recognisable symptom of this disease, it is not its only characteristic and, included in the syndrome, are other accompanying symptoms such as sleep disturbances, fatigue, depression, anxiety, cognitive disturbances, gastrointestinal alterations, and other visceral and functional manifestations¹⁻¹⁶. The clinical manifestations of this disease can be seen on figure 1⁵.

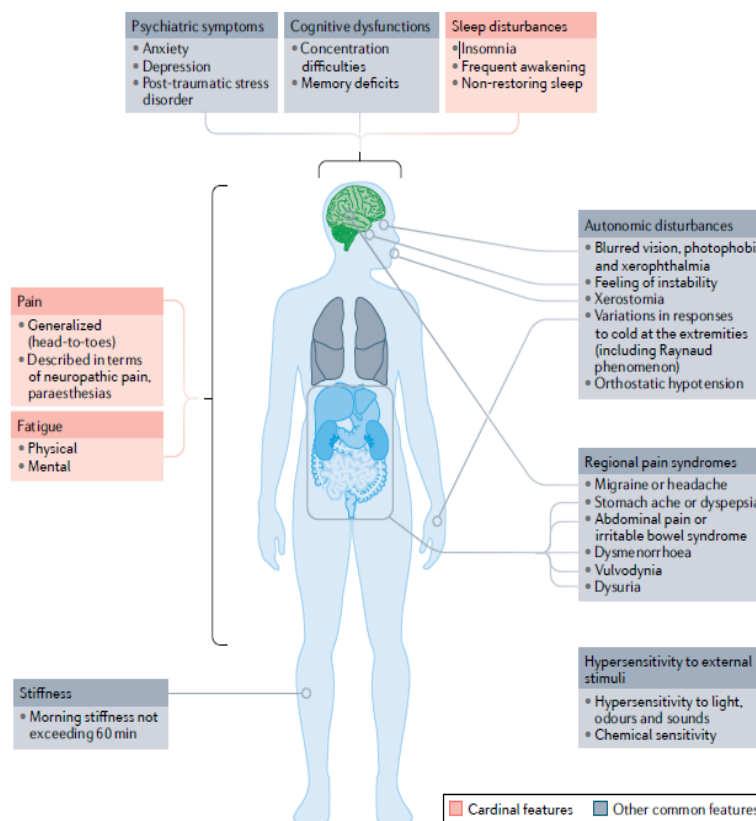


Figure 1 – Symptoms of fibromyalgia⁵

The etiology and physiopathology of this disease is still not clear and is a constant topic of debate, especially in the fields of neurology, psychiatry, and rheumatology. For some time, it was considered a purely psychogenic condition, but it is now considered a pain sensitization syndrome with organic alterations. However, there are still professionals that attribute it simply

to psychological factors and its legitimacy is still heavily discussed. It is important to note that FM is not accompanied by tissue inflammation¹⁴, which differentiates it from other rheumatological diseases and causes of CWP. The possible mechanisms behind the development of FM are discussed ahead.

The first concept of FM appeared over 60 years ago although it was first described in the 19th century under the term “fibrositis”^{5,9,14,16-18}. At the time FM was simply considered a widespread pain condition. Nowadays it is known that it is a complex syndrome comprising of more than just pain. Nonetheless the criteria used for fibromyalgia is not agreed upon as shown by two sets of criteria in which there was a 73% discrepancy between them when identifying cases⁹. The diagnosis criteria have changed along the years to establish a correct diagnosis to a widely misunderstood. Although there are many diagnostic criteria (in part due to the difficulty in defining the condition and how to classify it), the more widely used criteria is the 2010 ACR (American College of Rheumatology) criteria, later modified in 2011 and 2016⁹. These criteria take into account the Widespread Pain Index (WPI) and the Symptom Severity Scale (SSS) for both cardinal symptoms, specifically fatigue, how refreshed the patient feels when waking up and cognitive symptoms as well as for other symptoms such as muscle weakness, depression, nervousness, headaches, irritable bowel syndrome, etc⁹. With the 2011

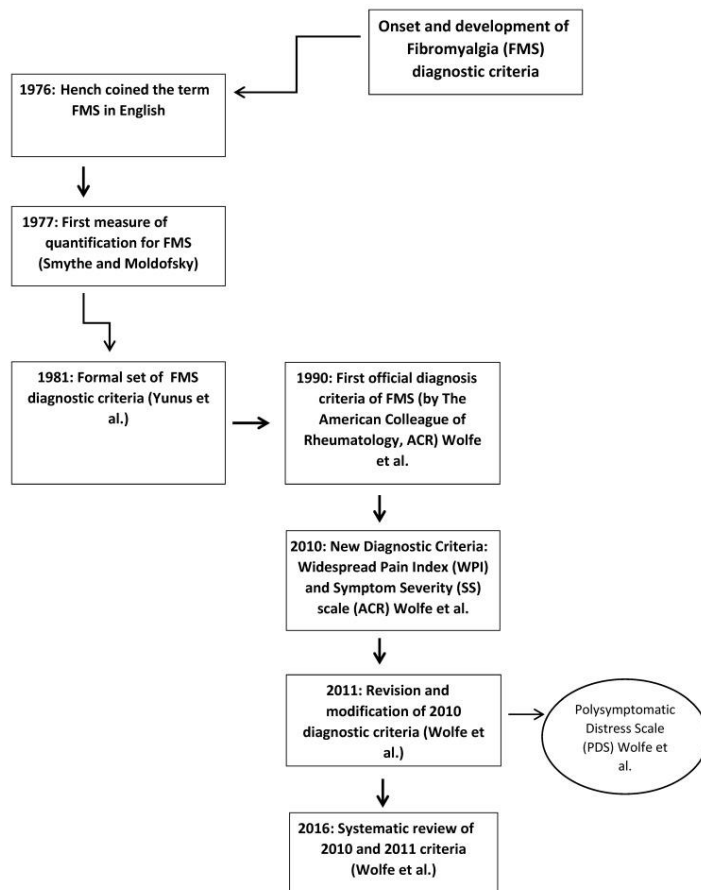


Figure 2 – Evolution of FM concept and criteria⁹

and 2016 criteria the Polysymptomatic Distress Scale (PDS) was included which measures the whole syndrome severity by combining both WPI and SSS ⁹.

So, the diagnosis of this condition is clinical and should be performed by the primary care physician after evaluating the patient according to diagnostic criteria and discarding other pathologies which could explain the patient's symptoms³. Although there are neuroimaging alterations in FM, these are not sufficiently specific and are used in trials to obtain an organic explanation for the symptoms and diagnosis method for the syndrome. The possibility for use of biomarkers such as serum haptoglobin and fibrinogen^{1,12} to establish a diagnosis has been investigated but to this day there are not reliable biomarkers that are useful to establish a diagnosis^{1,2,5,12,15,16}.

Treatment of FM is directed mainly at increasing function, quality of life and symptom reduction³. It was seen that pharmacological treatment alone is not sufficient¹⁶. In fact, and according to the European Alliance of Associations for Rheumatology (EULAR), non-pharmacological treatments should be considered before pharmacotherapy because of its effectiveness, safety, and reduced costs¹⁻³. Physical exercise seems to have the most benefit and is strongly recommended for all patients^{19,20}. Because of the multifactorial origin of this disease, it is difficult to establish a universal treatment and patient management should be assessed on an individual level and multidisciplinary^{3,5,10,12,21}. Apart from pharmacological treatment for pain, such as using antidepressants, opioids, gabapentinoids among others, a more holistic approach should be considered, tackling emotional-cognitive factors, mind-body connection, etc^{5,10,12}. Non-pharmacological therapies, such as exercise, cognitive-behaviour therapy (CBT) have been shown particularly useful in reducing pain and other symptoms in patients suffering from FM^{1-3,5,8,12,15}. However, treatment of this condition still is lacking, showing poor results. Studies found that accompanying symptoms like sleep disturbances, anxiety and fatigue remained largely unchanged throughout the years whereas pain showed a moderate improvement³. One of the reasons for lacking results may be the unknown mechanisms underlying the condition²². However, one has to consider the possibility that it could also be related to the difficulty in establishing diagnosis criteria and clearly identifying patients leading to a heterogeneous group with the possible existence of FM subgroups^{5,10}.

1.2.2. Mindfulness and mindfulness-based therapy

Mindfulness is a broad concept. It consists of one being aware of thoughts, bodily sensations, facing them with an accepting attitude, without judgment^{23,24}. It is a concept that often goes

hand in hand with meditation practices²⁵. However, the two are not interchangeable although meditation practices can be included in a mindfulness context and are a means to achieve a mindful life. With its origins in Asian Buddhism, mindfulness has recently gained popularity as a way to improve mental health and reduce stress in the occident²⁵⁻²⁷. Parallel to this increase in mindfulness practices, there has been an increase in interest in its possible application in a clinical environment with the development of mindfulness-based therapies/interventions, especially in treating symptoms of depression and anxiety where it has shown promising results²⁷⁻²⁹. There has also been an increase in interest in the last 30 years in the efficacy of MBI in chronic physical conditions such as chronic pain^{25,30}.

Mindfulness-based interventions are a heterogeneous group of procedures based on the core principles of mindfulness (focusing on the present moment with a non-judgmental way, taking psychological and physical experiences as subjective and transient)²⁷. Developed as a lifestyle approach to deal with chronic pain conditions and curb their psychological impact^{23,24}, MBIs have been adapted as a short-term treatment. There are many types of MBIs, the most used in a clinical setting being mindfulness-based stress reduction (MBSR), mindfulness-based cognitive therapy (MBCT) and acceptance and commitment therapy (ACT)³⁰. The description of these interventions is detailed in figure 3²⁵. Notice how CBT is included as a MBI although most authors differentiate between the two and so does the EULAR²⁰.

Mindfulness based intervention	Similarities	Differences
Cognitive behavior therapy (CBT)	<ul style="list-style-type: none"> The umbrella term that refers to a conceptual model of treatment that target emotional awareness and regulation, cognitive flexibility, and goal-based behaviors. Mindfulness principles integrated in the therapy 	<ul style="list-style-type: none"> Mindfulness is merely a component of this intervention.
Acceptance and commitment therapy (ACT)	<ul style="list-style-type: none"> Therapeutic strategies are similar to mindfulness where its core principle is to observe self by cultivating the ability to simply observe internal phenomena, without attaching to, evaluating, or attempting to change them. 	<ul style="list-style-type: none"> An outpatient psychotherapy based in behavior-analytical principles.
Mindfulness based stress reduction (MBSR)	<ul style="list-style-type: none"> Standardized incorporation of Eastern mindfulness practices into Western cognitive-behavioral practice. 8-week program for 2-2.5-hour group-based meditation classes. Focused on learning on how to mindfully attend to body sensation using various mind-body meditative practices such as sitting meditation, body scan, gentle stretching, and yoga. 	<ul style="list-style-type: none"> Mindfulness practice is a core skill taught in treatment. Originally designed as relapse prevention for depression.
Mindfulness based cognitive therapy (MBCT)	<ul style="list-style-type: none"> Standardized incorporation of Eastern mindfulness practices into Western cognitive-behavioral practice. Follows the structure of MBSR. 	<ul style="list-style-type: none"> Mindfulness practices is core skill taught in mindfulness-based treatment. Originally designed to treat patients with chronic pain. The ultimate effect of being able to handle stressors in a more adaptive way.
Mindful socioemotional regulation (MSER)	<ul style="list-style-type: none"> Mindful practices applied in group setting. Regulation of emotions via enhancing awareness and acceptance of full range of emotions via mindfulness meditation. 12 modules, 15 minutes 	<ul style="list-style-type: none"> For emotional regulation for chronic pain patients. Focused to address social engagement deficits evident in fibromyalgia and pain patients.

Hofmann and Gómez (2017) and Davis and Zautra (2013).

Figure 3 – Common types of mindfulness-based interventions²⁵. Although CBT is included as a MBI most authors differentiate between the two

1.2 Relevance of the topic and objectives

Fibromyalgia is highly prevalent disease. It is estimated that the prevalence is somewhere between 2-8%⁵. However, as previously stated, there is not an agreement in diagnosis criteria for this disease and it still a largely misunderstood condition. So, as one can see in figure 4, prevalence is highly variable between countries and according to what criteria is used⁵. Moreover, the difficulty in establishing in diagnosis could potentially lead to a considerable number of patients underdiagnosed, meaning an even higher burden than what was previously thought.

FM has a lot of comorbidities and patients have a poor quality of life deriving from their condition affecting more than one of their life spheres (personal, professional, etc.)^{5,22}. FM is a debilitating disease with a higher impact on quality of life than rheumatoid arthritis or chronic obstructive pulmonary disease¹⁷. Additionally, patients with FM have a lot of healthcare costs, requiring frequent medical attention with high cost for the health care system ^{17,22,31}.

As previously stated, current FM treatment regimens show poor results overall and the unclear pathogenesis may be an important factor justifying the lack of defined treatment regimens²¹. First line treatments include non-pharmacological options, especially CBT which shows good results in pain and accompanying FM symptoms^{27,30}. MBCT interventions could be particularly useful in FM as cognitive behaviour therapy (CBT) is widely included in the current treatment of fibromyalgia (30), showing efficacy in symptom management and MBCT uses the principles of CBT with mindfulness ones^{25,27}. An increasing amount of attention has recently been given to MBI as a possible addition to other forms of psychotherapy in chronic pain conditions.

Therefore, the aim of this paper is to understand the possible mechanisms underlying FM, thus theorizing where mindfulness may play a role as an adjuvant treatment option in reducing symptoms as well as comorbidities and improve life quality of patients. Recent studies regarding efficacy of MBT in fibromyalgia symptoms is considered as well as the practicality and costs of implementing such therapy. The objectives are:

- a) Understand the possible etiopathogenic mechanisms underlying fibromyalgia
- b) Understand the pathophysiologic mechanisms by which mindfulness and mindfulness-based interventions could explain its use in fibromyalgia
- c) Describe current evidence supporting the efficacy of mindfulness and mindfulness-based therapies in fibromyalgia

d) Describe how mindfulness-based therapies could be used as an adjuvant treatment option in fibromyalgia

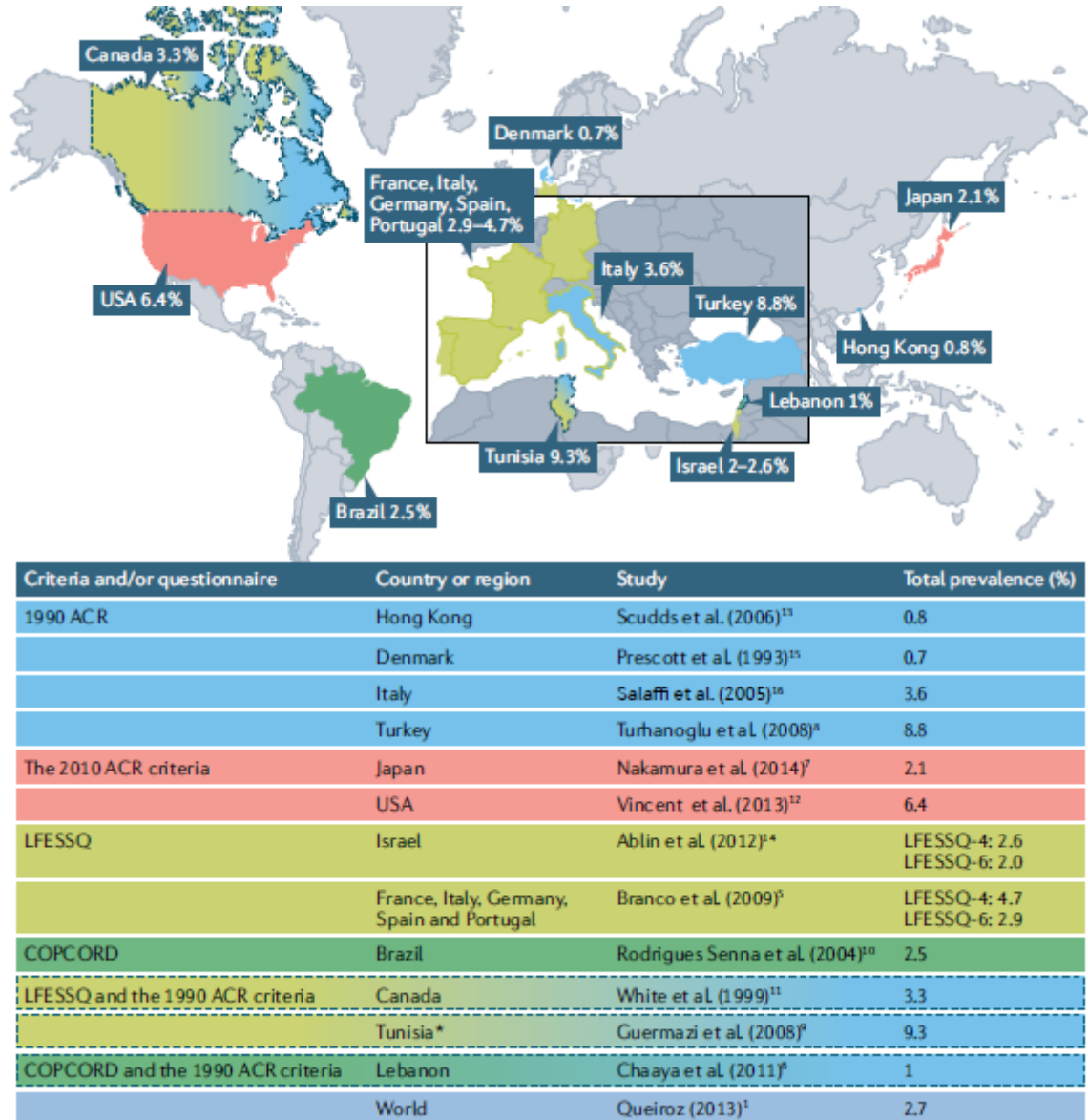


Figure 4 - Prevalence of fibromyalgia in different countries depending on the criteria used⁵

2. Methods

The sources for this narrative review were obtained by two separate searches in PubMed, Scopus and Web of Science.

The first search was made with the intent of understanding fibromyalgia, specifically its etiopathogenesis and mechanisms underlying its development. To do so, the terms “Fibromyalgia” and “Pathogenesis” were used as well as the Boolean operator “AND”. The articles used were reviews on the etiopathogenesis of FM. Included were: (a) Theoretical reviews (systematic and narrative); (b) articles that included pathogenic mechanisms behind FM; (c) Articles in English or Spanish; (d) Articles published in the last 5 years. The exclusion criteria were as follows: (a) articles about juvenile fibromyalgia; (b) experimental studies; (c) meta-analyses; (d) articles not in English nor Spanish. After applying this criteria, 28 articles were obtained.

The second search intended to explore the effect and efficacy of mindfulness and mindfulness-based interventions on fibromyalgia. The terms “mindfulness” and “fibromyalgia” were used separated by the operator “AND”. The inclusion criteria were: (a) clinical trials, cross-sectional studies, reviews and meta-analyses; (b) articles that studied mindfulness or mindfulness-based interventions; (c) articles that studied fibromyalgia; (d) articles in English or Spanish; (e) published in the last 5 years. Exclusion criteria were: (a) not about mindfulness; (b) not about fibromyalgia; (c) not in English or Spanish. After applying these criteria, a total of 36 articles were considered.

The flow chart in figure 5 details the search process performed.

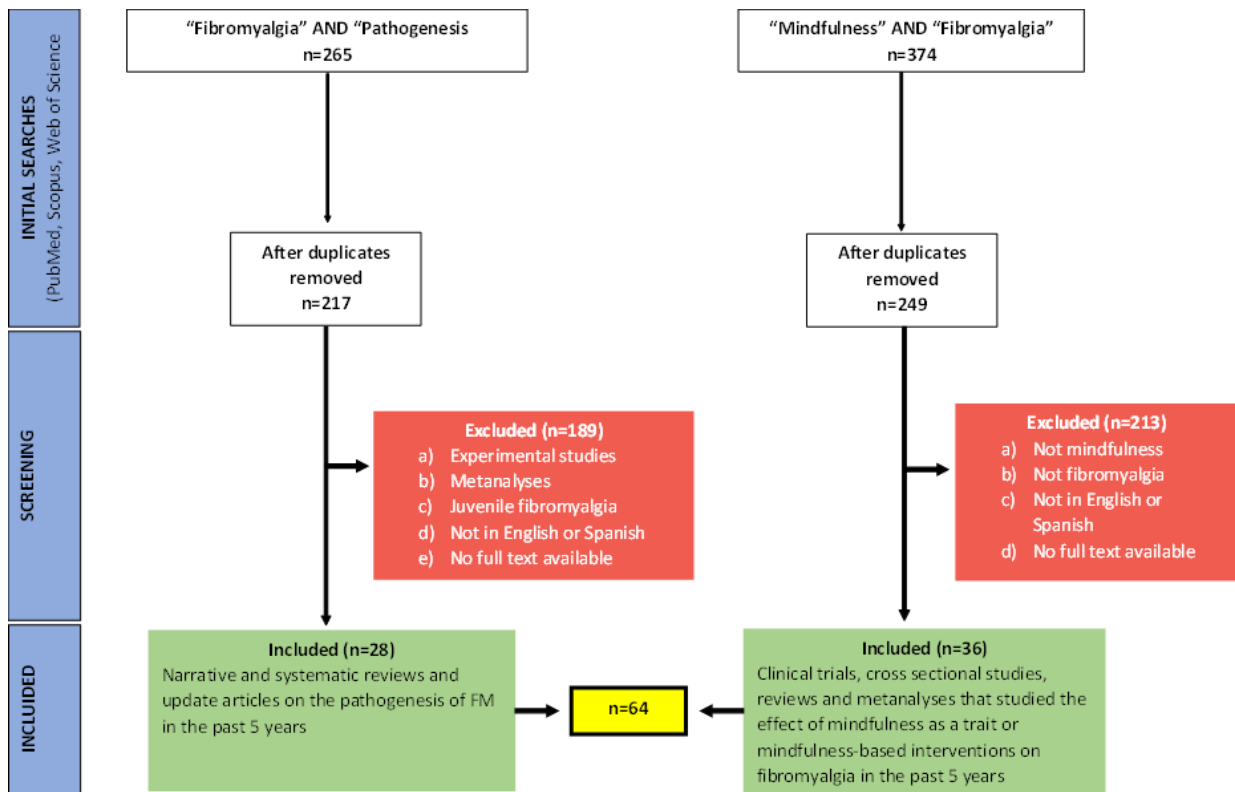


Figure 5 – Flow chart of the search method

3. Mindfulness and Fibromyalgia

3.1 Etiopathogenesis of FM

The etiology of FM is still largely unknown and assumed to be multifactorial^{14,32}. There are, nonetheless, some pathophysiologic findings which can explain in part some of the symptoms. There has also been a discussion to the field to which the disease pertains, with some arguing in a neurological/rheumatologic explanation while others attributed it to a psychological condition or a somatization since there is a high prevalence of mood disorders (anxiety, depression) among FM patients. Now it is seen as a problem pain regulation and sensitization (mainly central, peripheral, and cognitive-emotional) leading to exaggerated pain response resulting in allodynia and hyperalgesia. While there is still some controversy, FM is widely considered a multifactorial disease. Following are some of the theories and findings that try to explain the cause of this disease.

3.1.1. Central sensitization

Central sensitization is now considered the main mechanism that justifies pain, the main symptom that characterizes FM¹⁸. Cortical processing alterations, a decrease in pain modulatory mechanisms and changes in pain pathways at a molecular level all seem to contribute to this sensitization which leads to allodynia and hyperalgesia. Problems at a cortical, subcortical, and medullary levels have been identified¹⁴.

First, neuroimaging studies have shown a decrease in blood flow and grey matter in areas associated with pain processing such as the anterior cingulate cortex (ACC), periaqueductal and rostral ventromedial medulla as well as an increased activation in the posterior insula and secondary somatosensory cortex, also related with pain processing¹⁴. Moreover, a decrease in connectivity between antinociceptive areas has been observed, particularly between the ACC and the amygdala, hippocampus, and brain stem, suggesting a problem in descending inhibitory pain systems as well as an increased connectivity between the so called “default mode” areas of the brain and the insula¹⁴.

Other important findings suggesting a central sensitization are changes at a molecular level. Across FM patients, alterations in neurotransmitters, other substances and receptors have been described. There are disfunctions in monoaminergic neurotransmitters, such as an increase in excitatory substances such as glutamate and substance P (a neuromodulating neurotransmitter) in pain processing areas^{5,14,16,18,32,33}. To support the plausibility of this mechanism, the use of

NMDA, a glutamate antagonist, as well as pregabalin have shown efficacy in decreasing FM symptoms as well as low glutamate diets and exercise which reduced glutamate and increased antinociceptive neurotransmitters¹⁶. Moreover, a decrease in serotonin and norepinephrine in the spinal cord was observed, which could also explain psychiatric symptoms^{5,14,16,32,33}.

Opioid alterations have also been described in patients with FM^{5,14,18}. A decreased in μ -opioid receptor binding potential and their concentration in certain areas of the brain responsible for pain modulation such as the amygdala, dorsal cingulate cortex and accumbens nucleus was observed as well as a change in the receptor activity^{5,14}. Furthermore, an increase of opioid in the cerebrospinal fluid (CSF) of FM patients was identified⁵.

3.1.2. Peripheral sensitization

The role of peripheral sensitization in FM has also been increasingly studied and believed to play a role in the etiopathology of the symptoms. Particularly many reviews consider the possibility of small fibre neuropathy (SFN) which could explain symptoms such as pain and dysesthesia which presents in some patients^{1,5,7,8,12,14,15}. It is important to highlight that FM is not simply a small fibre neuropathy⁷. In SFN A-delta myelinated and C unmyelinated fibres are affected resulting in alterations in nociception and other sensory disfunctions as well as alterations in the autonomic nervous system¹⁴. When compared to healthy controls, FM patients have been shown to have a higher prevalence of SFN as well as a decrease in epidermal small nerve fibre density, both myelinated and unmyelinated^{7,12,14,34,35}. Moreover, FM patients scored higher in neuropathic pain questionnaires¹⁵, suggesting that there is more than the nociplastic pain related to central sensitization. Other data supporting the peripheral sensitization theory is that FM patients show alterations in thermal and nociceptive stimuli and that lidocaine injections decreased hyperalgesia¹⁶. Microneurography has also shown alteration in C fibres, demonstrating that mechanically insensitive fibres have higher spontaneous activity¹⁶.

One theory that explains some of the relationship between peripheral sensitization is that the continuous stimuli of C nerve fibres could increase release of the previously commented excitatory neurotransmitters glutamate and substance P as well as reducing opioid and serotonin levels by inducing the apoptosis of inhibitory GABAergic and opioid interneurons⁵.

As previously stated, this does not mean that FM is a small fibre neuropathy as not all patients with FM have SFN⁷. However, it could be one of the mechanisms that explain to pain, dysautonomia and other sensory symptoms as well as it could be related to the central sensitization mechanism.

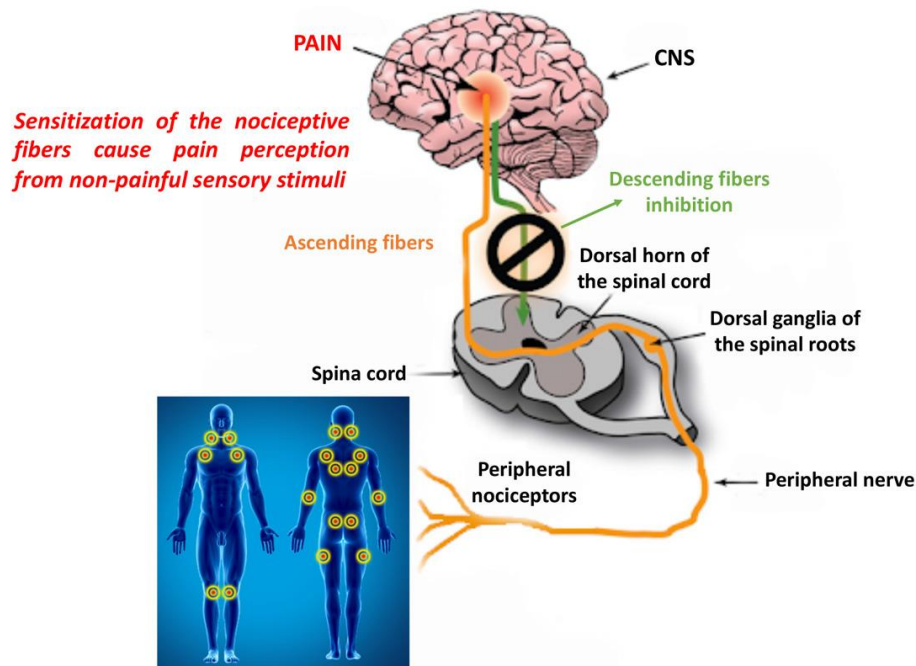


Figure 6 - Central sensitization mechanism in fibromyalgia¹⁶

3.1.3. Inflammation and immune system

Fibromyalgia is not considered an inflammatory disease and there is no evidence of tissue inflammation. It responds poorly to NSAIDs (non-steroid anti-inflammatory drugs)^{5,16} and, in fact, if tissue inflammation is observed, other diagnoses should be considered instead³. There is, however, some evidence suggesting that inflammation plays a role in its development, specifically neuroinflammation.

The hypothesis that inflammation is one of the mechanisms contributing to the etiopathogenesis of FM is supported by the fact that there is an increase in circulating pro-inflammatory cytokines such as IL-8 in the CSF and IL-6, IL-8, IL-1 β and TNF- α in the blood^{15,16,36}. Of these, the only one that showed correlation with symptom severity was IL-6¹⁶. One theory that tries to explain this is that thalamic mast cells release inflammatory and neuro-sensitising substances thus directly stimulating the thalamus or doing it indirectly through

microglial activation, particularly through TLR-4 receptors^{6,8,11} (fig.6). Moreover, CRH levels and the previously mentioned substance P have also been shown to be responsible for mast cell activation^{13,37}. When looking at skin biopsies of FM patients, a higher quantity of mast cells has also been observed^{11,37}. Glial activation has also been observed using neuroimaging techniques like PET (positron emission tomography) and OCT (optical coherence tomography)^{1,15,34}.

Additionally, the origin of some of these cytokines can be the adipose tissue, possibly explaining the higher rates of FM in obese patients¹⁶.

There is also a higher prevalence of FM among patients with other rheumatic diseases like RA which could support the involvement of inflammation in the development of FM¹⁶. There is also a subgroup of patients with positive antibodies (ANA)⁵.

The vagal nerve could also play a role through its anti-inflammatory potential via afferent and efferent fibres. A low vagal tone has been observed in fibromyalgia patients (assessed by low heart rate variability)³². One can relate this disbalance in sympathetic and parasympathetic nervous system relates to stress, a known trigger and the HPA, previously discussed. Vagal nerve stimulation could also be a potential treatment in FM and other diseases that decrease vagal tone³².

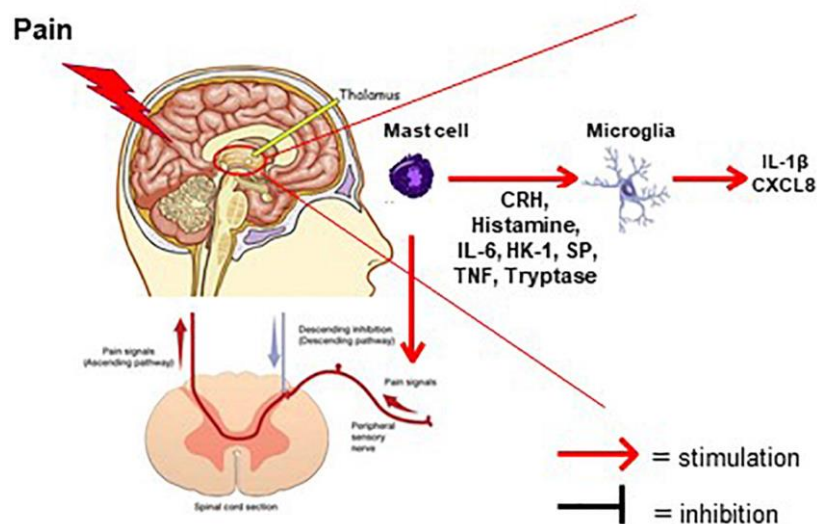


Figure 7 - Possible neuroinflammation mechanism in fibromyalgia⁶

3.1.4. Endocrine system

Endocrine factors may also be implicated in the pathophysiology of FM.

First, there is a considerably higher prevalence of FM among women with a ratio varying from 2:1 up to 9:1 comparing to males^{3,14,16}. This suggests a possible hormonal factor at play. However, when the role of oestrogens was studied, the only significant finding was a serum increase of G protein-coupled estrogenic receptor (GPER)¹⁶.

The hypothalamus-pituitary-adrenal (HPA) axis could also play a role which in turn could be related to stress and sleep disturbances. There seems to be an alteration in CRH levels among FM patients, with an increase concentration in serum when compared to healthy individuals^{6,8,13,32,33}. As previously stated, CRH can activate mast cells, therefore promoting neuroinflammation and, indirectly, central sensitization. Moreover, there seems to be an alteration of the circadian rhythm secretion among patients¹⁶. Still regarding the HPA axis, cortisol levels have been observed to be high among patients suffering from FM^{6,14,15,33}. However, this finding is not consistent in all the studies¹⁶. Additionally, it was observed that salivary cortisol showed an especially strong relation with symptoms appearing within 1 hour of being awake¹⁶. Finally, hepatic clearance of cortisol has been showed to be decreased in FM patients¹¹. Thus, the role of the HPA axis in FM is not yet fully understood and requires further investigation. However there seem to be alterations which could contribute, especially in the release of CRH. The HPA axis is closely related to stress, one of the known main triggers and aggravators of FM^{7,12}. Moreover, history of abuse and trauma could also affect the dysregulation of HPA axis and so³². It can be seen how psychological, inflammatory, and endocrine factors can interact between one another and also contribute to central sensitization. The dysfunction of the circadian rhythm could also be affected by sleep disturbances, highly prevalent in FM patients and a possible mechanism behind its physiopathology, as commented ahead.

There is also a higher incidence of obesity and glucose intolerance among patients suffering from fibromyalgia^{3,8,15}. Related to this is the lower levels of IGF-1 levels and alteration of GH secretion also because of circadian rhythm alterations¹⁴.

Contributing to inflammation (through TLR activation and cytokine production), other mechanism proposed for FM pathogenesis, although less studied, is a gut microbiome disbalance which could explain the strong relation between fibromyalgia and irritable bowel syndrome^{38,39}.

Like all other mechanisms seen, it is hard to define the causality direction of endocrine factors and fibromyalgia development.

3.1.5. Cognitive-emotional sensitization and pain catastrophizing

For some time, some professionals have viewed fibromyalgia as a psychogenic disease¹². Nowadays, it is considered more of a sensitization problem. Nevertheless, fibromyalgia is often accompanied by psychiatric illness^{3,5,9,12} and the presence of depression, abuse and trauma history and catastrophizing are prognosis factors³. Although there seems to be a psychologic/psychiatric component to fibromyalgia, it is important to make some distinctions.

Firstly, it must be noted that FM is not a somatoform disease, nor it is a somatic symptom disorder (SSD) as only 26% of patients with fibromyalgia have been shown to meet the criteria for SSD⁷.

Fibromyalgia is also not a masked depression or an affective mood disorder⁷. These types of disorders are, in fact, common in patients with FM. According to certain studies, the prevalence of anxiety in patients with fibromyalgia can be as high as 60% and depression up to 36% which is much higher than the 6.6% observed in the rest of individuals⁵. However, not every patient suffers from these conditions and this prevalence is not higher than in other chronic diseases like rheumatic diseases or cancer⁵. This points to a maladaptive response to the disease more than to it being a mechanism behind FM. On the other hand, the presence of depression indicates a worse prognosis with higher pain levels and duration and increased hyperalgesia³. Moreover, even though there was no relation between depression severity and brain activation in areas like the somatosensory cortices, there was an association with neural activation in the amygdala and contralateral insula (affective pain processing) suggesting distinct sensory and affective pain processing pathways¹⁶. So, depression and other FM symptoms could be bidirectional^{5,14}.

Stress is a known trigger and aggravator in fibromyalgia^{7,12}. It is also a predictive and prognosis factor^{3,16} and, as seen before, it can modulate pain sensitivity and release cytokines contributing to pain sensitization¹⁶. There also seems to be an association with trauma and abuse. Fibromyalgia prevalence has shown to be higher in patients with post-traumatic stress disorder (PTSD)¹⁵. One study also found that childhood mistreatment had an odds ratio (OR) of 18.92, showing a high association with FM. Childhood abuse and neglect, as well as depression and panic disorder was also more common in primary fibromyalgia when compared to FM associated to other rheumatologic diseases like RA⁸. It was also shown that domestic violence

history was significantly more associated with psychiatric conditions in FM patients than in controls¹¹ as well as increased pain intensity and associated symptoms such as depression among FM patients³².

Personality features could also be implicated in FM development and prevalence. Patients often show a hyperreactivity to stress with a presence of negative emotions and alexithymia is a very prevalent personality trait in FM patients which show a worse perspective of quality of life^{8,16}. Patients also show low levels of resilience (a protective factor) and lack effective coping strategies which could worsen symptoms^{5,11,32}. Additionally, they seem to show a state of hypervigilance¹⁶. People suffering from FM also score higher in catastrophising scales which could influence on symptom severity⁴⁰. Catastrophising can be defined as an “exaggerated amplification of emotional aspects that leads individuals to consider pain terrible and intolerable”⁵. Catastrophising is a highly prevalent trait among FM patients and has shown to be a risk factor, worsening depression, and anxiety⁴⁰ as well as pain perception⁴¹. It is a prognostic factor³ and the best predictor for patient functioning⁴². Finally, it has been proposed that there is also interpersonal sensitization, meaning that the environment and people surrounding patients can also have a role in the development of the disease through a feed-forward mechanism^{5,16}.

All these factors could lead to a cognitive-emotional sensitisation. Trauma and abuse history seem to play a role, closely related to stress and psychiatric conditions which in turn could modulate pain sensitivity. Moreover, a decrease in resilience and effective coping mechanisms, a negative outlook on events and life as well as patients being selectively attentive to body sensations and a state of hypervigilance could further contribute to the perception of pain thus leading to hyperalgesia.

Finally, in a disease that seems to have some degree of genetic predisposition, psychological factors could also contribute to its pathogenesis through epigenetic modulation⁴³.

3.1.6. Sleep disorders

As stated, sleep disorders are one of the most common symptoms among FM patients. In fact, some diagnostic criteria include sleep problems. However, there is debate over whether sleep disturbances are merely a symptom or could be one of the etiopathogenic mechanisms. Some suggest a bidirectionality between the two^{5,16}. First, it has been shown that poor sleep among FM patients seem to worsen pain and mood symptoms¹⁴. Moreover, it has been shown that sleep deprivation in healthy individuals result in the appearance of FM-like symptoms such as

hyperalgesia^{5,16}. This led some to try to label FM has a “non-restorative sleep syndrome”. Additionally, in many cases, sleep problems precede pain in FM patients and could have a predictive value¹⁶. Sleep disorders could also explain mood disorders such as depression and anxiety as well as cognitive dysfunction^{5,16}.

The mechanisms by which sleep could cause symptomatology in FM patients is not clear. Equally not clear is the direction in which one affects the other, as with other possible pathophysiologic mechanisms¹⁴. As stated, healthy individuals experience symptoms similar to FM when sleep deprived suggesting that sleep disturbances are a cause of FM. Likewise, the fact that sleep problems can precede FM symptoms also suggest this causality¹⁶. However, there are theories hypothesizing the dysfunction of the thalamus as the cause for sleep disturbances and pain in FM. These theories are based on the role of the thalamus in deep sleep and an alteration in pain signalling, specifically in this area of the brain (modulated by GABAergic and cholinergic afferents, altered in FM) is involved of alpha-delta sleep (ADS) where alpha waves are present in deep sleep phases, a phenomenon observed in FM patients¹⁶.

3.2 Possible mechanisms for the use of mindfulness in FM

Mindfulness may have its effect on more than one sphere of the multiple possible pathogenic mechanisms underlying FM. The most obvious ones are the ones pertaining to psychological factors.

Personality seems to have a strong relation to severity of symptoms in FM patients. Patients who score higher on catastrophizing, surrender and psychological inflexibility show higher scores in depression and anxiety while people who score higher in acceptance, mindfulness and positive affect seem to suffer less from these symptoms⁴⁰. Therefore, mindfulness as a trait seems to be a protective factor against psychological comorbidities in FM while catastrophizing seems to be a risk factor⁴⁰. Moreover mindfulness-based interventions lead to a greater self-care and compassion and thus more psychological flexibility, a trait lacking in patients with FM, therefore reducing one of these risk factors and possibly improving psychological functioning^{19,24,44}. Studies have shown that MBI could decrease stress (a known trigger of FM symptoms), anxiety and depression, as well as an increased ability to control anger³⁰. Mindfulness also relates to the behavioural action model of depression, specifically for FM²⁸ (figure 8). In it, it is theorized that depression is a result and/or aggravated by an interplay of distinct factors including mindfulness and pain catastrophizing. And, as described by Dorado and colleagues, mindfulness with its different facets could improve (or in some of its facets worsen) pain catastrophizing. MBI could improve mindfulness and decrease catastrophizing⁴⁵, which seems to be the stronger predictor in patient functioning⁴⁶. It also must be noted that the relation between these aspects may not be unilateral as higher levels of pain and catastrophizing could lead to less mindfulness and thus increase the likelihood to experience impaired function⁴⁶.

Figure 1. Hypothesized behavioral activation model of depression for people with fibromyalgia.

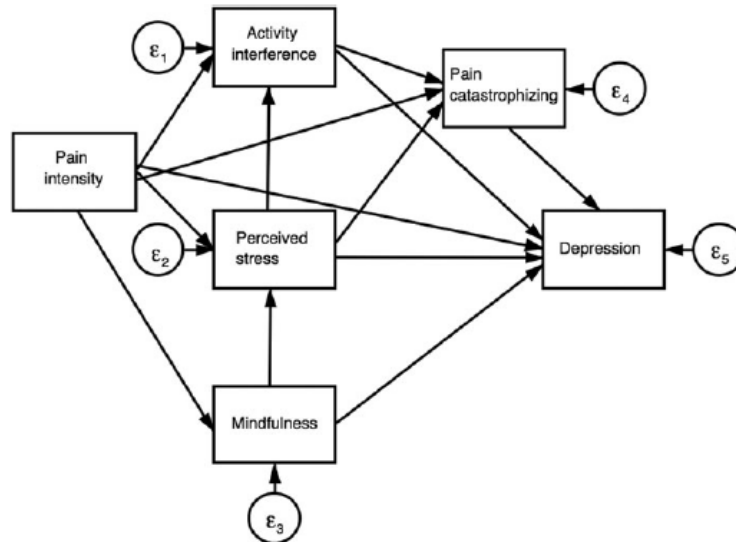


Figure 8 – Behavioural activation model of depression in fibromyalgia²⁸

In healthy individuals, cognitive and meditative therapies (CMT) was shown to reduce the affective experience of pain, improve mental health, pain self-management, control over pain, reduce anticipatory anxiety and catastrophizing and, while less consistently, it could also improve pain intensity⁴⁷. If we look at the purpose of mindfulness and MBI, we can deduce that the desired effect of pain is not the reduce it objectively but to reduce its impact and negative perception by the individual³¹, which is supported by these results.

However, mindfulness seems to go further in its mechanistic influence on FM symptomatology. As previously discussed, fibromyalgia seems to mainly a sensitization problem, especially at a central level. Through neuroimaging, MBI has been shown to increase activity in areas of the brain related to the cognitive/emotional evaluation of pain and its regulation³⁰ further supporting the idea of accepting pain and how it is perceived and interpreted rather than reducing its sensation. Neuroimaging have also shown that meditators have a higher pain tolerance which seems to be a problem in patients in FM³⁰. This effect is more noticeable on expert meditators, who do not report lower pain intensity but lower pain unpleasantness³⁰.

Figure 9 illustrates the neuroimaging findings of Nascimento et al. for chronic pain, fibromyalgia and healthy patients following CMT⁴⁷.

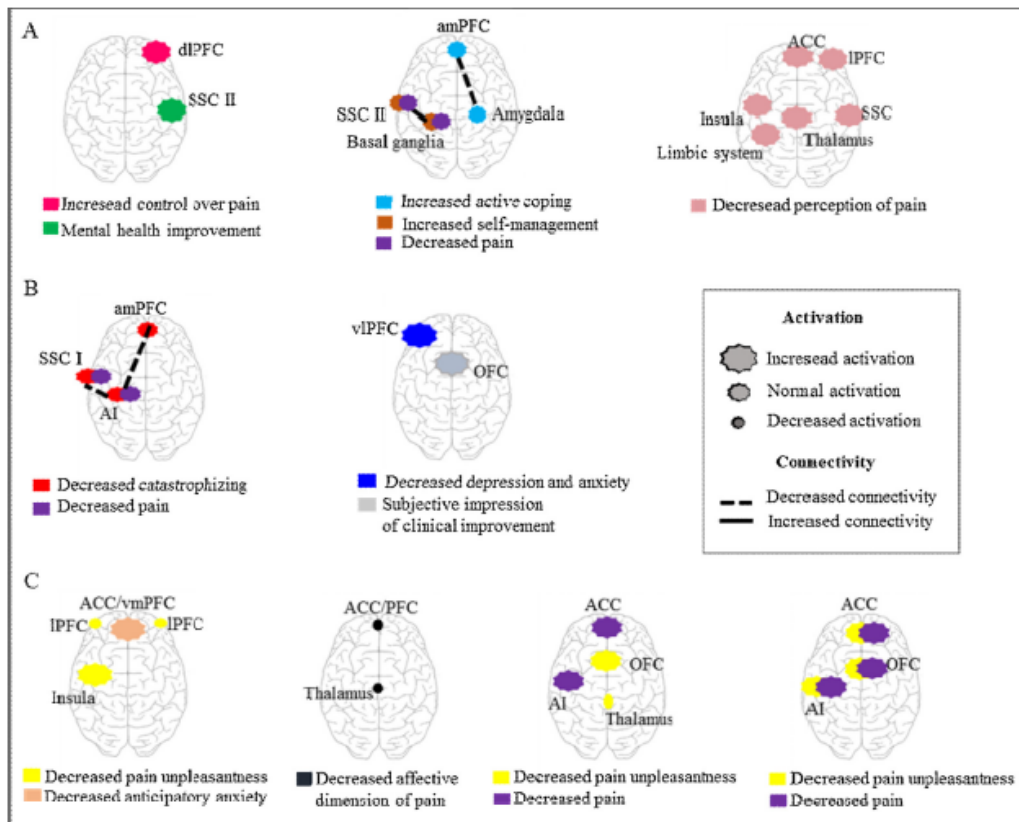


Fig. 4. Correlations between brain activity/connectivity changes and clinical pain outcomes after cognitive therapies identified in included studies with chronic pain (A), fibromyalgia (B) or healthy individuals (C). amPFC = anterior medial prefrontal cortex; ACC = anterior cingulate cortex; AI = anterior insula; dIPFC = dorsoateral prefrontal cortex; IPFC = lateral prefrontal cortex; vmPFC = ventromedial prefrontal cortex; vIPFC = ventrolateral pre-frontal cortex; OFC = orbitofrontal cortex; SSC = somatosensory cortex; SSCI = primary somatosensory cortex; SSCII = secondary somatosensory cortex.

Figure 9 – Neuroimaging findings in chronic pain patients, FM patients and healthy individuals after cognitive meditative therapies⁴⁷

Mindfulness-based therapies may also affect the inflammation mechanism described before. Andrés Rodríguez and colleagues have shown that patients treated with MBSR (one of the modalities of mindfulness-based interventions) prevents the decrease of IL-10 (an anti-inflammatory cytokine) and better the IL-6/IL-10 and CXCL8/IL-10 ratios⁴⁸. However, there was no significant improvement on these inflammatory cytokines. Nevertheless, MBI could have its role in decreasing inflammation. In another study, a decrease in IL-6 and c-reactive protein in patients treated with MBI has also been described⁴⁹. Moreover, other proposed mechanism is the decrease in sympathetic outflow and HPA activation⁵⁰. This also relates to the vagal nerve tone theory previously described. Mindfulness can increase vagal tone thus increasing its anti-inflammatory properties and decreasing HPA activation³².

Sleep disturbances, although considered a symptom of FM could be a pathogenic mechanism as previously stated. This is another way by which mindfulness could play a role directly and/or

indirectly (through relaxation, stress and pain reduction). Mindfulness as a trait has shown to improve sleep quality while decreasing sleep disturbance, possible mediated by a decrease in depression, anxiety and pain interference as seen in a cross-sectional study by Park and colleagues⁵¹.

Summarizing, mindfulness as a trait seems to be a protective factor against psychological manifestations of fibromyalgia. Since these could also be a part of its pathogenesis, MBI could improve symptoms directly and indirectly by influencing psychologic comorbidities. Moreover, the reduction of the perception of pain and the decrease in central sensitization by altering brain connectivity could be another mechanism especially in decreasing pain and/or pain perception and interference. Additionally, MBI could reduce inflammation and sleep disturbances. Figure 10 illustrates some the proposed pathogenic mechanisms behind FM, how they can interact between each other and how mindfulness, and therefore mindfulness-based interventions, could improve it.

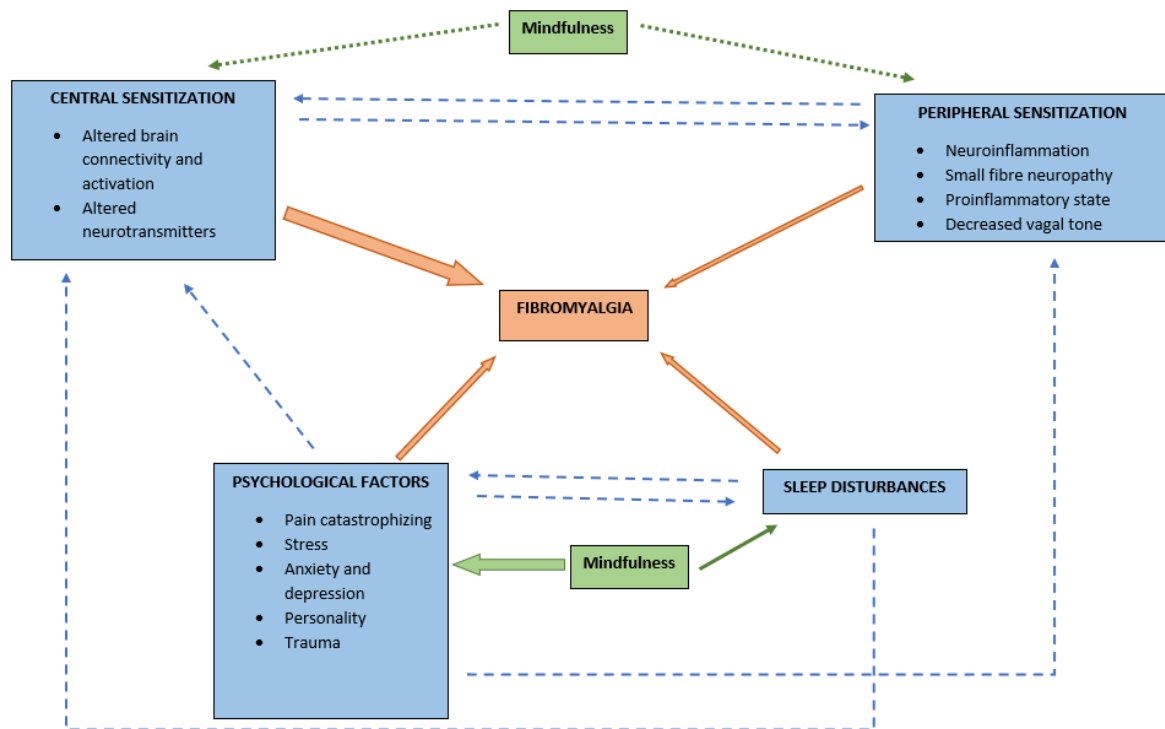


Figure 10 – Possible pathogenic mechanisms underlying fibromyalgia and how mindfulness may act therapeutically

4. Mindfulness-based interventions and fibromyalgia

4.1 Efficacy of mindfulness-based interventions in fibromyalgia

First, it must be stated that mindfulness-based interventions are an umbrella term that encompasses different types of therapy based on the principles of mindfulness. The most popular one, as previously referred, is MBSR but others like MBCT and ACT are also common, and these are the main types of therapy evaluated in current literature. Trials, cross-sectional studies, systematic reviews and meta-analyses on the use of such interventions have shown a significant increase in recent years.

Evidence seems to indicate that MBT is an effective measure in treating people with physical health conditions and chronic pain especially in pain perception, coping and mood disorders⁵²⁻⁵⁵. But how does MBT fair against FM specifically?

There are several studies that indicate an effectiveness of MBI in outcomes in FM patients

In a randomized clinical trial (RCT) comparing MBSR with treatment as usual (TAU), an improvement in functional impairment and severity was observed, as well as other positive results in anxiety and perceived stress⁴⁸. This was the same study that analysed the effect of MBSR on pro-inflammatory and anti-inflammatory cytokines.

In the RCT conducted by Pérez-Aranda and colleagues (EUDAIMON study)³¹ in which they compared MBSR, TAU and FibroQol (a multicomponent treatment without mindfulness mechanisms which has shown efficacy and served as an active control group), MBSR was significantly better than both TAU and FibroQol (and FibroQol was better than TAU) for the primary outcome, functional impairment. These results were also seen in a 12-month follow-up in comparison with TAU but not FibroQol. As for secondary outcomes (fibromyalginess[†], anxiety-depression, pain catastrophising, perceived stress, cognitive dysfunction, mindfulness facets – observing, awareness, non-judgment, psychological flexibility, and self-compassion), MBSR was largely superior to TAU and moderately superior to FibroQol. The results in follow-up were similar to the ones observed for the primary outcome.³¹ In the context of this trial, another study was made that showed that humour styles could predict response to

[†] Fibromyalginess is an outcome based on the overall symptoms of FM, based on the previously mentioned symptom scales – WPI and SSS (31)

treatment further reinforcing the psychological factor and personality trait impact on fibromyalgia⁵⁶.

Simister and colleagues performed a RCT comparing an online ACT added to TAU versus TAU and reported less FM impact with this effect being mediated by pain acceptance in ACT + TAU group⁵⁷. The study also showed a decrease in depression, pain in kinesophobia in the ACT + TAU group as secondary outcomes.⁵⁷

In a RCT comparing Attachment-Based Compassion Therapy (ABCT), a type of mindfulness-based therapy, with an active control group treated with Relaxation condition, it was found that the group treated with ABCT showed a greater increase in mindfulness and self-compassion as well as an improvement in FM functional status although this improvement was not mediated by neither of the previous outcomes.⁵⁸

Serrat and colleagues developed a multicomponent treatment (Fibrowalk) and compared it with TAU (consistent in pharmacotherapy) in a randomized clinical trial where FM impact (primary outcome), pain, fatigue, anxiety, depression, physical function and kinesophobia. The Fibrowalk treatment included physical exercise, CBT, neuroscience education and mindfulness practices. The treatment regimen was shown to be largely effective for FM impact, pain, kinesophobia and physical function while a moderate effect was found for other outcomes when compared to TAU. The number needed to treat was 2 (95% CI=1.7-2.3) which means that 2 patients needed to be treated with Fibrowalk+TAU for one additional patient to benefit (i.e. respond). It should be noted that the benefits were reduced in the 6 month and 9 month follow-up. (59) In another trial the same comparison was made moving the Fibrowalk regiment to an online setting due to the SARS-Cov-2 pandemic lockdown where it also seemed to be effective albeit with a NNT of 5.⁶⁰

In the systematic review and metaanalysis performed by Haughmark et al. the effectiveness of mindfulness-based therapies in pain, depression, anxiety, sleep quality, quality of life and mindfulness in FM patients both at the end of treatment and in follow-ups. A moderate positive effect can be seen in all of these outcomes. Nevertheless, these results were not statistically significant for pain and anxiety in the follow-up as well as in health-related quality of life both in post treatment and in the follow-up.¹⁹

When compared with CBT in a systematic review, MBT was reported to be better than TAU (contradicting the systematic review by Lauche et al. in 2013) but not better than CBT in physical function and pain.⁶¹.

In a randomized controlled clinical trial, Amutio and colleagues found that patients undergoing Flowing Meditation (a type of MBI) improved sleep quality and reduced insomnia when compared to controls with a maintained benefit of at least 3 months⁶². Despite these promising results, the authors refer that despite this being the only study that investigated the effect of a MBI specifically on sleep, the results seem to be consistent to previous studies conclusions⁶².

Although these results seem promising there is contradicting evidence.

Referring to the systematic review performed by Lauche et al. in 2013, Hauser and colleagues report that despite the clinical improvements with MBSR when compared to wait-list controls, no statistically significant results were obtained. And referring to the review by Cache et al. it reports that no statistically significant reductions in pain, disability and fatigue were observed in MBSR compared to wait list controls.⁶³

Adler-Neal and Zeidan confirm the existence of inconsistent data when looking at trials before 2018, especially when concerning pain improvement. They affirm that there is low quality evidence for pain and quality of life improvements³⁰.

In a metanalysis performed by Pei and colleagues where MBT effectiveness in chronic pain conditions (which included fibromyalgia), no statistically significant improvement was found for pain intensity, pain interference and pain acceptance⁶⁴. It should be noted that few of the studies included in the metanalyses evaluated FM patients.

As for the subjective opinion of patients, in a patient report of various non-pharmacological interventions, it was seen that mindfulness-based interventions had a mean effectiveness of 5.67 (out of 11) and were the second lowest scored in side effects after heat pads. The consensus was that MBT worked best for anxiety and the worst side effect reported was feeling tired²¹. In a survey conducted at the end of a clinical trial, patients reported the intervention to be satisfactory, useful, recommendable, and non-aversive⁵⁶.

4.2 Other considerations

In the research conducted for this paper, very few studies referenced the cost and practicality of mindfulness-based interventions in fibromyalgia. In a review which evaluated the cost-effectiveness of MBI against other therapies for a variety of diseases, it was found that, at least in the short run, mindfulness-based interventions seemed to be cost-effective for most of the diseases evaluated including for fibromyalgia, even though only one article referred to fibromyalgia²⁹. Further studies comparing cost-effectiveness between MBI and other forms of

therapy and between different forms of MBI (MBSR, MBCT, ACT, etc.) are needed to reach a definite conclusion.

As for treatment adherence, almost no studies evaluated session adherence. Nevertheless, the two that did report a relatively high percentage of adherence to sessions (65% and 74%)^{31,56}. However, this is not enough to extrapolate adherence in a clinical setting and homework required by most MBI must be considered.

Based on the search performed, it is difficult to estimate the exact number of patients being treated with some kind of mindfulness-based therapy. Moreover, the treatment is individualized. The revised recommendations from EULAR published in 2017 (figure 11) do not differentiate MBI from other meditative movement therapies and show that it has a level of evidence of Ia with an A grade. Nevertheless, it has a percentage of agreement significantly lower than other therapies such as CBT²⁰.

Recommendation	Level of evidence	Grade	Strength of recommendation	Agreement (%)*
<i>Overarching principles</i>				
Optimal management requires prompt diagnosis. Full understanding of fibromyalgia requires comprehensive assessment of pain, function and psychosocial context. It should be recognised as a complex and heterogeneous condition where there is abnormal pain processing and other secondary features. In general, the management of FM should take the form of a graduated approach.	IV	D		100
Management of fibromyalgia should aim at improving health-related quality of life balancing benefit and risk of treatment that often requires a multidisciplinary approach with a combination of non-pharmacological and pharmacological treatment modalities tailored according to pain intensity, function, associated features (such as depression), fatigue, sleep disturbance and patient preferences and comorbidities; by shared decision-making with the patient. Initial management should focus on non-pharmacological therapies.	IV	D		100
<i>Specific recommendations</i>				
<i>Non-pharmacological management</i>				
Aerobic and strengthening exercise	Ia	A	Strong for	100
Cognitive behavioural therapies	Ia	A	Weak for	100
Multicomponent therapies	Ia	A	Weak for	93
Defined physical therapies: acupuncture or hydrotherapy	Ia	A	Weak for	93
Meditative movement therapies (qigong, yoga, tai chi) and mindfulness-based stress reduction	Ia	A	Weak for	71–73
<i>Pharmacological management</i>				
Amitriptyline (at low dose)	Ia	A	Weak for	100
Duloxetine or milnacipran	Ia	A	Weak for	100
Tramadol	Ib	A	Weak for	100
Pregabalin	Ia	A	Weak for	94
Cyclobenzaprine	Ia	A	Weak for	75

*Percentage of working group scoring at least 7 on 0–10 numerical rating scale assessing agreement.

Figure 11 – EULAR revised recommendations for fibromyalgia treatment²⁰

5. Discussion

As previously seen, mindfulness (as a trait) can influence more than one of the possible pathogenic mechanisms underlying fibromyalgia. It is obvious to deduce its possible role on psychological factors. Nevertheless, as discussed, it can directly and/or indirectly influence other factors, probably to a lesser extent, such as the main theorized mechanism of central sensitization. It also shown to improve sleep disturbances, a largely common factor among FM patients as well as possibly reducing the inflammatory state mediated by cytokines. All this creates the basis of exploring the efficacy and possibility of use of therapies based on mindfulness principles in fibromyalgia.

Literature largely supports the effectiveness of such interventions in fibromyalgia. Most trials reported at least moderate efficacy compared to controls (wait-list, TAU, and other forms of therapies) in a lot of parameters – functionality, depression, anxiety, quality of life, pain, pain interference, sleep, overall FM impact, etc. In systematic reviews and meta-analyses performed in the last 5 years there is an overall agreement of the efficacy or possible benefits of MBI in FM. Nevertheless, there is conflicting evidence, especially concerning the efficacy of these interventions in pain improvement. In fact, probably since the principles of mindfulness and MBIs do not specifically aim in reducing pain but more so in reducing its impact and increasing acceptance³⁰, there are few studies, at least in the past five years, that assess pain as an outcome. MBI seems to be more effective in psychological impact and functionality of FM than physical impact and functionality. More than conflicting evidence, the evidence for the effectiveness of MBI in FM does not seem to be of high quality. First, most of the studies apply different types of MBI (MBSR, MBCT, ACT, ABCT, etc.). Some of them include them as part of a multicomponent treatment which makes it impossible to affirm the effect of the MBI by itself. The controls used in the studies also show a high degree of heterogeneity. Some studies compare some type of MBI to wait-list controls, TAU (which varies due to the lack of an agreed protocol for FM), and other forms of therapy such as CBT (which is common among FM treatment plans due to its demonstrated effectiveness). Overall, there are few trials that evaluate the effectiveness of MBI in FM symptoms and further investigation is required.

There may be some limitations to applying mindfulness-based interventions. Although it seems cost-effective when compared to other therapies²⁹ one must consider the cost and practicality of implementing it on a large scale. This would imply training many professionals. Moreover, as previously mentioned, each type of MBI protocol aims and is constructed for different

aspects²⁷. So, identifying the one most suitable to each patient and implementing many different types of MBI could also be a logistic concern. Additionally, certain degree of learning curve and adaptation by the patients is to be expected. Although adherence was relatively high in both trials that took it into account^{31,56}, it is hard to predict how adherence would behave in clinical practice. Most regimens are time consuming and require homework (not rigorously controlled). With the most adverse effect reported by patients being feeling tired²¹ and the fatigue associated with FM it is easy to see how this could affect adherence and, therefore, efficacy.

Despite its shortcomings, as stated, most patients reported improvement and overall satisfaction with MBI²¹. Moreover, it appears to be an extremely safe intervention with few side effects to no side effects. It also must be considered that even if MBI are not implemented, mindfulness seems to be a protective trait against some of the symptoms in FM and overall impact⁴⁰ and so, mindfulness practices outside of a defined therapy regimen could be recommended by professionals (for example, recommending books or other forms of media on the topic). This could potentially increase mindfulness without the time consumption and other logistic downsides of MBI.

Cognitive-behavioural therapy is widely regarded by its effectiveness in chronic pain conditions and fibromyalgia, and it is currently recommended⁶¹. The studies comparing MBT and CBT are conflicting with some demonstrating superiority of MBT while others fail to do so^{21,61}. So, it seems that the evidence does not support a substitution of CBT for MBT but perhaps applying both could have its benefits. In this case MBCT (which combines CBT with mindfulness principles) could be the most advantageous option. It was shown that multimodal treatments with CBT and MBT are effective even when applied in an online format^{57,60}. Individualization (in overall treatment and in types of MBT applied) according to symptom prevalence and severity seems to be the best way to tackle fibromyalgia. In a review by Fonia and colleagues, they conclude that different types of MBI may be more effective than others for different symptoms and comorbidities in FM²⁷. This is what is shown in figure 12, taken from their article.

Fig. 1 Summary of MBI effectiveness for fibromyalgia symptoms

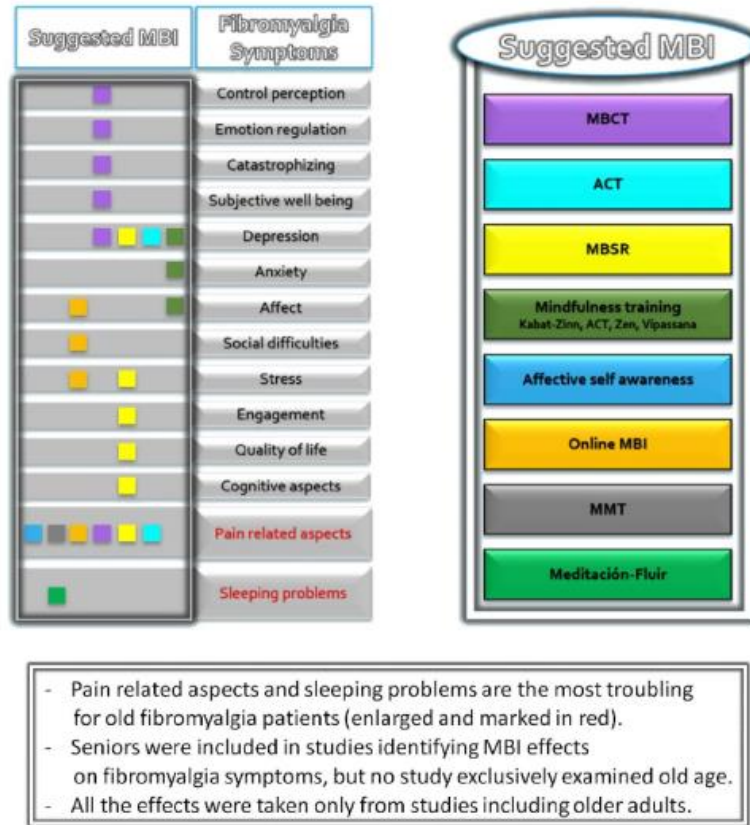


Figure 13 – Suggested types of MBI for different fibromyalgia symptoms²⁷

Based on an evidence summary, a group of experts gave their recommendations on different non-pharmacological therapies for different symptoms of fibromyalgia and whether they should be core or adjunctive. The results are exposed in figure 13. We can see that mindfulness was only recommended (by 58% of experts) for core therapy for depression while for the rest of symptoms (pain, fatigue, and sleep) as adjunctive therapy²².

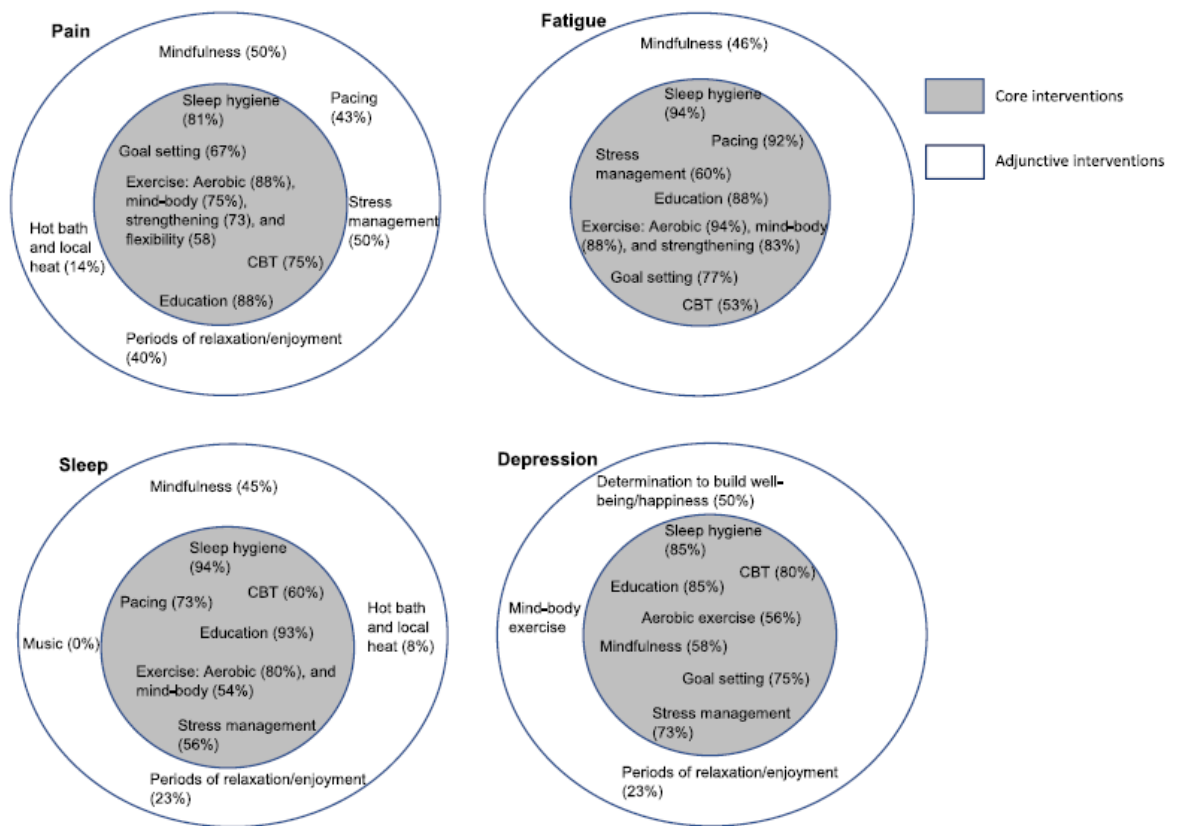


Fig. 1. The classification of accepted non-pharmacological interventions as core or adjunctive for pain, fatigue, sleep and depression. The proportion of experts recommending each intervention as core is shown in parentheses.

Figure 13 – Experts recommendation for different types of non-pharmacological treatments according to different symptoms in fibromyalgia²²

6. Conclusions

There is a theoretical basis regarding the pathogenesis of fibromyalgia that justify the use of mindfulness-based interventions. Mindfulness as a trait could act on many of the mechanisms and MBI, by increasing mindfulness, could help patients

So, should mindfulness be used as an adjuvant treatment in fibromyalgia?

It is difficult to have a definite answer to this question with the current evidence available. On one hand, studies suggest efficacy for a wide array of symptoms, especially in psychological symptoms such as anxiety and depression and it seems that MBI improves overall FM impact, improving functionality, decreasing stress, and improving quality of life. This efficacy is more prominent immediately post-treatment, and its effect seems to be less noticeable in follow-ups. This indicates that MBI would possibly need constant boosters to obtain long-term benefits. Nevertheless, due to study heterogeneity, lack of specific trials (especially comparing it to CBT, which is considered effective), among other factors, this evidence is of low quality and not enough to affirm effectiveness even if it does suggest it. This justifies the current EULAR and expert recommendations.

Moreover, the practicality of MBI must be considered and its application on a large scale could have its difficulty and the time and effort required from patients could lead to lack of adherence.

Nevertheless, due to its safety, reported effectiveness, especially on psychological impact and patient satisfaction, mindfulness could be of use as an adjuvant in fibromyalgia in a multimodal treatment setting. And, even if not in a formal regimen, mindfulness practices could be promoted to reduce FM impact and improve symptoms.

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Annexes

Introduction

- **Fibromyalgia**
 - ❖ Syndrome characterized by widespread chronic pain with specific muscle and joint tender sites as well as other symptoms such as sleep disturbances, fatigue, mood disorders, cognitive disturbances, gastrointestinal alterations, and other visceral and functional manifestations
 - ❖ Highly prevalent disease (2%-8%) with varying diagnostic criteria
 - ❖ Unknown etiopathogenesis
 - ❖ Treatment shows poor results and individualized treatment is required, preferably starting with non-pharmacological options
- **Mindfulness**: awareness to present thoughts, emotions, and sensations in a non-judgmental way
- **Mindfulness-based therapies** were developed from mindfulness principles which have shown results on chronic pain conditions and mood disorders

Results

- Fibromyalgia etiopathogenesis is unclear. Proposed mechanisms involve:
 - ❖ Central sensitization
 - ❖ Peripheral sensitization
 - ❖ Psychological factors
 - ❖ Sleep disturbances
- The directionality of these factors is not well established but together they lead to allodynia and hyperalgesia
- Mindfulness as a trait has shown to have a positive impact on all of these factors, especially on psychological ones
- Mindfulness-based interventions could improve fibromyalgia symptoms by increasing mindfulness

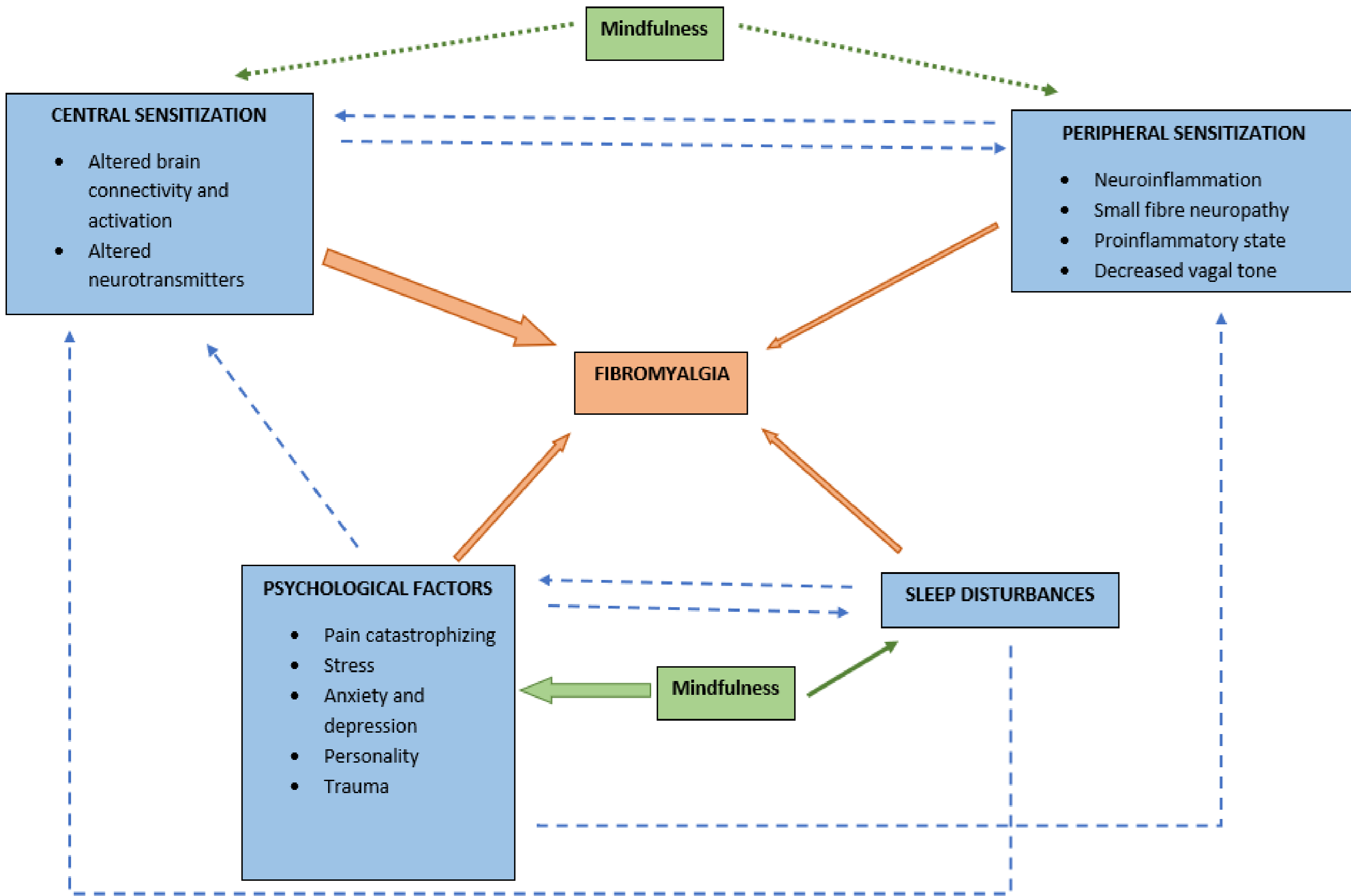


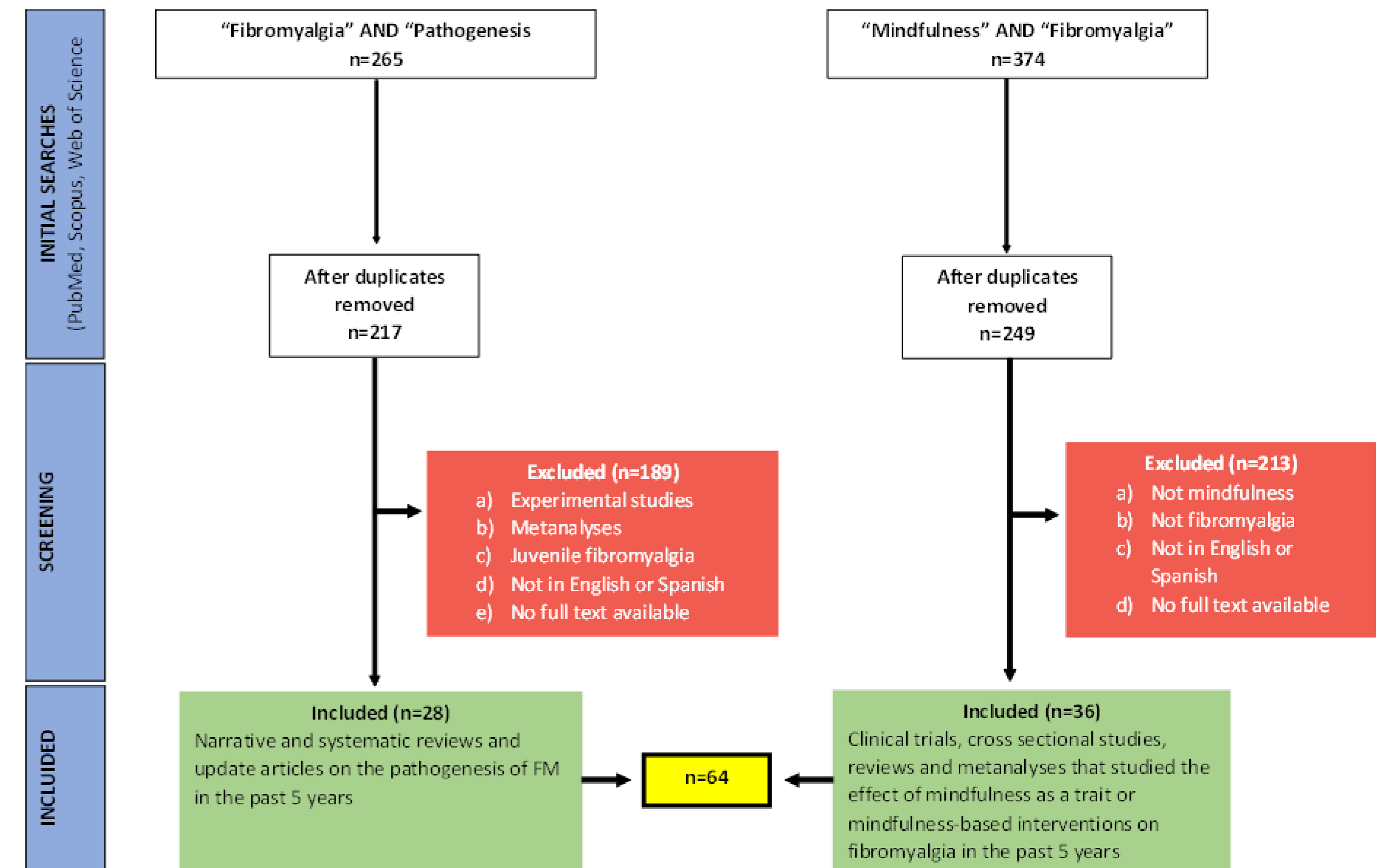
Figure 1 – Mechanisms behind fibromyalgia and how mindfulness may act on them

- Overall patients report satisfaction and the worst side effect was tiredness
- Mindfulness-based interventions seem cost-effective and have high adherence but there are few studies that evaluate these possible hindering factors
- Study heterogeneity does not allow to affirm efficacy and more specific trials are required

Objectives

- Understand possible etiopathogenic mechanisms underlying fibromyalgia
- Understand the pathophysiologic mechanisms by which mindfulness and mindfulness-based interventions could explain its use in fibromyalgia
- Describe current evidence supporting the efficacy of mindfulness and mindfulness-based therapies in fibromyalgia
- Describe how mindfulness-based therapies could be used as an adjuvant treatment option in fibromyalgia

Methods



- Current trials, systematic reviews and meta-analyses suggest that mindfulness-based therapies show efficacy in decreasing fibromyalgia symptoms, improve quality of life and decrease overall impact
- According to studies, psychological impact and symptoms are more influenced by these therapies than physical ones
- Efficacy against treatment as usual and wait-list controls has been shown while not against other non-pharmacological therapies such as cognitive behavioural therapy
- Different types of mindfulness-based interventions could be more beneficial than others for different fibromyalgia symptoms

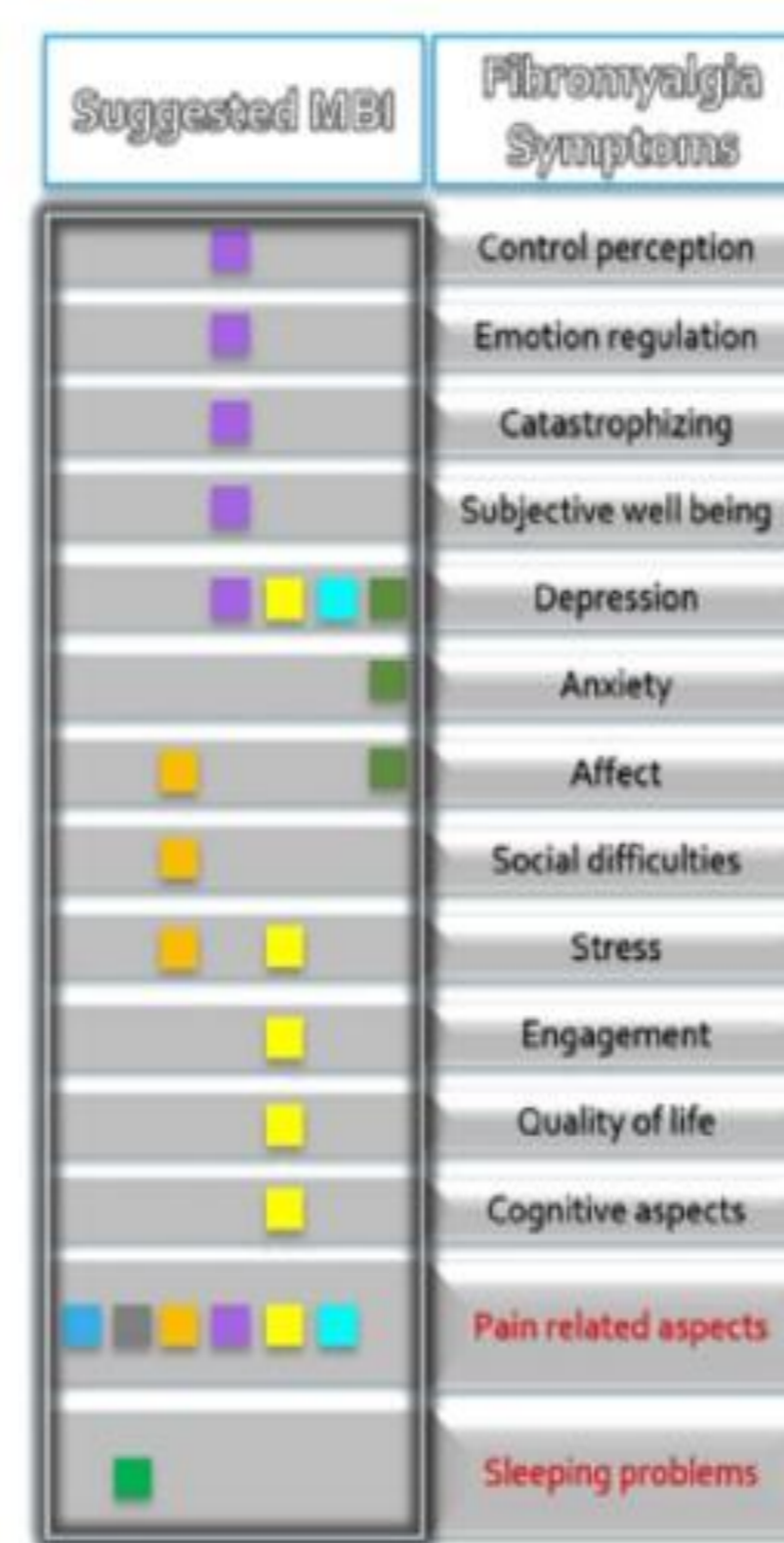


Figure 2 – Suggested types of mindfulness-based interventions for different fibromyalgia symptoms (Fonia et al., 2022)

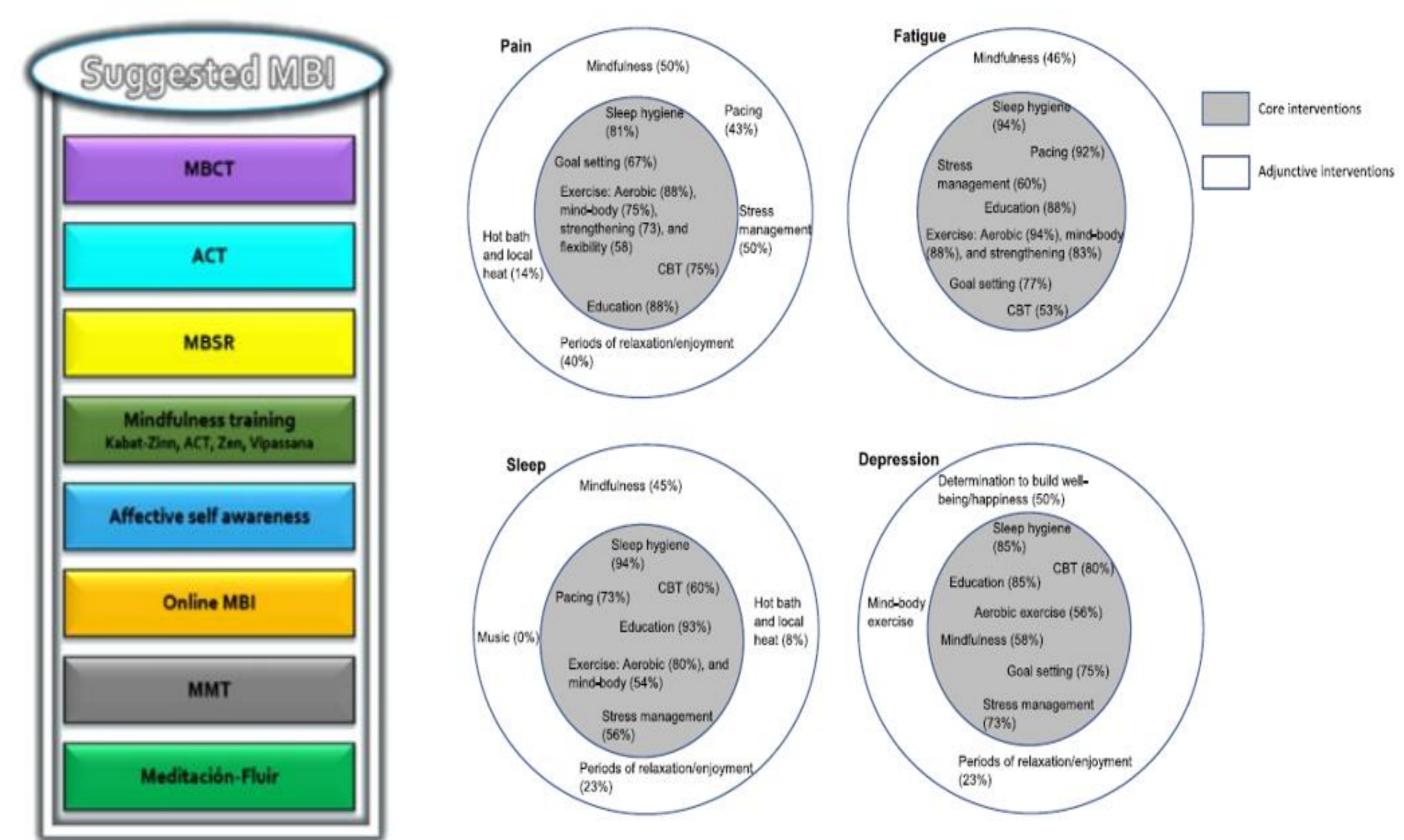


Figure 3 – Experts recommendation for different types of non-pharmacological treatments according to different symptoms in fibromyalgia (Kundakci et al., 2022)

Conclusions

- There is a theoretical basis regarding the pathogenesis of fibromyalgia that justify the use of mindfulness-based interventions
- Current evidence suggests efficacy of mindfulness-based therapies in improving fibromyalgia symptoms, especially psychological ones such as anxiety and depression as well as in decreasing overall disease impact and improving quality of life
- More specific studies are required to confirm such efficacy

- Adherence and cost could be limiting factors when implementing such programs
- Due to its safety and reported effectiveness, mindfulness-based therapies could be of use as an adjuvant option in fibromyalgia in a multimodal treatment setting
- Mindfulness practices could be promoted outside of a formal regimen to reduce disease impact and improve symptoms

