Review

Environmental factors and fibromyalgia syndrome: a narrative review

L. Bazzichi[1], V. Giorgi[2], M. Di Franco[3], C. Iannuccelli[3], S. Bongiovanni[1], A. Batticciotto[4], G. Pellegrino[1], P. Sarzi-Puttini[1,5]

[1]*Rheumatology Unit, IRCCS Ospedale Galeazzi Sant'Ambrogio, Milan, Italy;*
[2]*Unità di Ricerca Clinica, Gruppo Ospedaliero Moncucco, Lugano, Switzerland;*
[3]*Rheumatology Unit, Department of Clinical Internal, Anaesthesiologic and Cardiovascular Sciences, Sapienza University of Rome, Italy;*
[4]*Rheumatology Unit, Internal Medicine Department, ASST Sette Laghi, Ospedale Di Circolo, Fondazione Macchi, Varese, Italy;*
[5]*Department of Biomedical and Clinical Sciences, University of Milan, Italy.*

Laura Bazzichi, MD
Valeria Giorgi, MD
Manuela Di Franco, MD
Cristina Iannuccelli, MD, PhD
Sara Bongiovanni, PhD
Alberto Batticciotto, MD, PhD
Greta Pellegrino, MD
Piercarlo Sarzi-Puttini, MD

Please address correspondence to:
Laura Bazzichi,
Reumatologia,
IRCCS Ospedale Galeazzi Sant'Ambrogio,
Via Cristina Belgioioso 173,
20157 Milano, Italy.
E-mail: l.bazzichi@gmail.com

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ABSTRACT

This in-depth review of fibromyalgia (FM), which is a complex condition characterised by chronic pain, fatigue, sleep disturbances, and a spectrum of diagnostically and therapeutically challenging symptoms, underlines the need for a comprehensive and integrated approach that also takes into account the psychological factors affecting patient responses. We focus on the substantial impact that environmental factors (climatic variations, air pollution, electromagnetic field exposure, physical and emotional traumas, dietary patterns, and infections) have on the manifestation and intensity of symptoms, and advocate personalised, holistic treatment of patients' psychological and environmental sensitivities by suggesting the benefits of tailored dietary and stress management. We also call for further research into the complex interplay of environmental, biological and psychological factors influencing FM in order to develop more effective individualised treatments that are capable of enhancing patient care and outcomes.

Introduction

Fibromyalgia (FM) is an enigmatic medical challenge that manifests itself in the form of a syndrome that is characterised by a complex array of symptoms that include widespread chronic pain, fatigue, mood alterations, and cognitive disturbances commonly known as "fibrofog" (1). The evolution of its diagnostic criteria has led to greater emphasis being placed on fatigue and cognitive symptoms (1-6), but its treatment is complicated by uncertainties concerning the exact nature of its aetiology and pathogenesis (3). These have been the subject of numerous studies and debates prompted by the significance of its estimated global prevalence of 2.7% (7), and it is currently understood to be a central sensitisation disorder that abnormally amplifies the perception of pain and involves the multifactorial dysregulation of the endocrine, sympathetic, and immune systems (1-3, 8).

The identified risk factors include female gender and a genetic predisposition that suggests a complex mechanism of response to environmental triggers such as chronic infections, vaccinations, physical and psychological traumas (1-8), and even climate as patients report worsening symptoms related to variations in temperature and weather conditions (9), thus underlining the importance of considering the external environment in treatment and patient support protocols. Recent studies have also indicated the presence of peripheral anomalies (including small fibre polyneuropathy and nociceptor dysfunctions), which suggests that the pathogenesis of FM may be even more complex than previously believed (10-11). FM often occurs together with other functional syndromes, such as chronic fatigue syndrome, affective disorders, and irritable bowel syndrome, thus highlighting the need for a holistic diagnostic and therapeutic approach (12-14). Furthermore, nutrients such as magnesium, selenium and other anti-oxidant agents may play a role in modulating musculoskeletal pain and protecting against oxidative damage (18-26); over-exposure to toxic metals has been associated with worsening symptoms (23-31); and the condition may have social and economic implications as it often limits the patients' working capacity (14-36).

Current treatment strategies include

various pharmacological and non-pharmacological interventions, but the lack of a clear understanding of the aetiology of FM hampers the search for effective therapeutic solutions (37-43). Nutrition is a key factor as studies have emphasised the importance of a balanced diet rich in anti-oxidants in mitigating oxidative stress and improving the quality of life (40-42). A multidisciplinary, complete approach that combines medical treatment with lifestyle and dietary changes is therefore a promising means of managing FM.

The aim of this narrative review is to describe the current evidence concerning the role of environmental factors in FM in order to provide a clearer understanding of the interactions between them.

Effects of climatic and seasonal variations on fibromyalgia

Climatic and seasonal variations in barometric pressure and temperature significantly affect the symptoms of FM. Barometric pressure fluctuations (particularly those occurring before storms) can worsen the pain of FM patients: one study of 48 patients found that low barometric pressure and high humidity levels increased pain and stress, with significant variations in individual responses (43). Temperature affects FM symptoms as the cold increases stiffness and pain, and heat exacerbates fatigue (44-45), and it has been suggested that anomalies in temperature perception among FM patients link thermoregulatory dysfunctions and pain (46-49). Seasonal changes have been associated with seasonal affective disorder (SAD) and fluctuations in FM symptoms: although one study of 471 FM patients found that there was no significant seasonal impact on symptoms (50), another involving 1.424 patients with rheumatic diseases including FM observed seasonal variations in reported symptom severity that were not corroborated by clinical measurements (51).

Effects of air and water pollution on fibromyalgia

Nascent research indicates that air pollution may increase FM symptoms as a result of systemic inflammation and oxidative stress, but there is no direct evidence of the impact of water pollution, which requires further study (52). A study carried out in south-western Sweden noted that there were health issues (including FM symptoms) related to acidic water consumption, whereas alkaline water users reported fewer health problems (53). The shared symptoms of Gulf War illness (GWI) and FM suggest that the pathogenesis of the two may have something in common, including neurotoxin exposure and altered liver function, may support the use of liver detoxification and the management of retinoid levels (54-58). The oxidative stress implicated in the development of FM emphasises the need to investigate the role of heavy metals and supports the use of comprehensive therapeutic approaches (58).

Xenobiotics

Xenobiotics are chemicals substances that are foreign to an organism and include drugs, pollutants, and cosmetics, and it has been suggested that they may exacerbate FM symptoms by increasing chemical sensitivity, oxidative stress, gut dysbiosis, and central nervous system effects (59-62). Smoking and heavy metal exposure have been related to FM and chronic fatigue syndrome, with patients often showing metal hypersensitivity (63-65). FM may also be related to the autoimmune/inflammatory syndrome induced by adjuvants (ASIA syndrome), in which environmental adjuvants trigger autoimmune reactions in susceptible individuals. This highlights the potential role of adjuvants such as those found in vaccines or silicone implants (59) in the pathogenesis of FM as the two conditions share some immune response alterations and symptoms such as fatigue, pain, and disordered sleep; it also underlines the importance of considering immune system stimulants and environmental factors in the management of both.

Infections

The complex relationship between FM, chronic widespread pain (CWP), infections, and vaccinations is multifaceted. Although no direct causality has been established, there is evidence indicating that the incidence of FM and CWP is higher in patients with infections such as Lyme disease, HIV and HCV, and possibly infections due to mycoplasma, HBV, HTLV I, and parvovirus B19 (66). Some reports suggest a potential link between vaccinations and the onset of FM or chronic pain, although this has not been definitely proven. The interactions between infections, vaccinations, and chronic pain disorders remain unclear, and need to be further investigated in order to improve their diagnosis and treatment (67). The COVID-19 pandemic introduced additional complexities by exacerbating the symptoms of FM as a result of the accompanying stress, infection-induced immune responses, disrupted care, reduced physical activity, and the FM-like symptoms of long COVID. The concept of long COVID and its implication of a continuous viral or immune response may be misleading because, prevalent in 10-80% of post-infection cases, it shares many of the symptoms of FM. The observation that long COVID was more frequent after the initial wave of the pandemic suggests it was more closely related to the stress and anxiety of the time than to the viral infection itself. This theory of a psychosomatic dimension supported the failure in the identification of any consistent biological markers and the fact that its largely unsuccessful treatment is reminiscent of the outcomes of the historical medical treatment of FM. This underlines the need to identify both the mental and physical dynamics of post-viral syndromes and suggests that the condition might be more appropriately called FM-like post-COVID syndrome in order to reflect a more nuanced understanding of post-viral conditions (68).

Electromagnetic fields and fibromyalgia

Although further research is required to establish whether there is a clear causal relationship, it has been observed that electromagnetic field (EMF) exposure triggers or worsens FM symptoms in some patient. One study used gas chro-

Table I. Summary table of traumas, FM and their interrelations.

Category	Summary
Psychological traumas and FM	FM is related to emotional distress and trauma, and has parallels with PTSD in terms of stress and the quality of life. Abnormal cortisol levels and the prevalence of PTSD among FM patients reflect the association of psychological trauma and chronic pain.
Physical traumas and FM	Physical events such as road accidents and injuries are associated with FM, and suggest a direct link between physical trauma and disease onset.
Neurophysiological and genetic mechanisms	FM involves central sensitisation and altered pain processing. Genetic predisposition such as the presence of the Apo E4 allele may increase susceptibility to post-trauma FM.
Complexity of contributing factors	The development of post-trauma FM is complex and involves psychological and physical stressors, genetic predisposition, and immune responses, thus highlighting the multifactorial nature of the disease.

matography-mass spectrometry and multivariate analysis and found significant differences in the metabolomic profiles of 54 FM patients sensitive to electromagnetic radiation and 23 healthy controls, including alterations in 19 metabolites related to energy metabolism, muscle function, oxidative stress, and chronic pain (69). These findings suggest that the metabolic dysfunctions observed in the patients may be related to their symptoms and electromagnetic sensitivity although, as they were specific to patients with reported sensitivity, the results require careful interpretation and cannot be generalised to FM patients as a whole.

Fibromyalgia and traumatic stress

FM is frequently considered to be a manifestation of emotional distress related to previous emotional traumas or stressful events that may have led to changes in brain function and given rise to central sensitisation and heightened nerve activity. A relationship between psychological stress and the development of FM is supported by the frequency of post-traumatic stress disorder (PTSD) and abnormal cortisol levels related to past traumas among FM patients, which suggest a significant relationship with chronic pain (70-72). It has been shown that physical factors such as car accidents and cervical spine injuries are potential triggers of FM, and there may be a direct connection between physical traumas and the onset of FM as some studies have found a greater likelihood of FM following such events (71-76).

Description of neurophysiological mechanisms such as central sensitisation leading to increased sensitivity to pain have greatly improved our understanding of FM. Functional magnetic resonance imaging studies have shown that FM patients are affected by alterations in pain processing, including changes in neurotransmitter levels that indicate disrupted pain modulation. Genetic research has led to suggestions that factors predisposing subjects the development of FM include the presence of the Apo E4 allele and altered serum microRNA levels related to pain severity (76-80).

The relationship between FM and psychological trauma is well-documented, with many patients reporting past traumas that are often associated with depression. Studies have highlighted a significant link between FM and childhood emotional and sexual abuse, which suggests that psychological traumas can increase the likelihood of developing FM, with the possible mediation of endocrine factors such as altered cortisol secretion patterns (81-84). PTSD and FM share many symptoms, including increased stress levels and a diminished quality of life. The prevalence of PTSD among FM patients and the fact that abnormal cortisol secretion levels due to traumatic events are observed in patients with either disorder support the idea that PTSD and FM are co-morbidities with overlapping aetiologies that may emerge in subjects vulnerable to trauma (85). Determining whether a subject is likely to develop a pathological response to trauma is complex and requires further research in areas such as genetic factors, autonomic sympathetic functioning, and neurotransmitter transmission. The literature concerning the relationship between emotional trauma and FM is extensive and. although many studies are based on retrospective self-reporting and may therefore be affected by recall bias, some (including some with rheumatological control groups) have found a definite association (84).

However, there is still debate concerning the type and timing of the traumatic events related to the development of FM, which has been variably associated with childhood abuse, neglect, and adult physical and sexual abuse. The abnormal cortisol secretion observed in FM patients who have previously experienced abuse supports the theory that the development of symptoms may reflect a chronic stress reaction, although the specificity of this reaction needs further clarification as it may be affected by the confounding effects of comorbid psychological disorders such as major depressive disorder (MDD), PTSD, and anxiety.

The generally poor quality of the existing evidence provided by published studies of the association between FM and psychological trauma further highlights the need for more detailed and wide-ranging research that considers psychological as well as physical factors in order to improve the prevention, diagnosis and treatment of FM (Table I).

Nutrition in the treatment of fibromyalgia

Nutrition plays a vital role in in the management of FM as its symptoms can be influenced by dietary choices and nutritional status. It has been found that obesity, food allergies, nutritional deficiencies, and certain food additives can exacerbate FM symptoms, thus indicating the therapeutic potential of dietary modification (86-88). One

Table II. The complex array of factors influencing FM.

Factor	Effect on FM symptoms	Study details and findings
Climatic and seasonal variations		
Barometric pressure	Can worsen pain, especially before storms.	A study of 48 FM patients found that low barometric pressure and high humidity levels -increased pain and stress, but individual responses varied significantly (45).
Temperature	Cold increases stiffness and pain; heat exacerbates fatigue	Temperature perception anomalies in FM patients link thermoregulatory dysfunction and pain (47-52).
Seasonal changes	Align with symptom fluctuations in FM.	Some studies have found no significant relationship, and others that seasonal changes affect symptom severity (50).
Pollution		
Air pollution	May worsen symptoms as a result of inflammation and oxidative stress	Nascent research suggests a relationship between symptoms and systemic inflammation and oxidative stress (52).
Water pollution	No direct evidence	One study has found health issues, including FM symptoms, related to acidic water consumption (53).
Xenobiotics		
Chemical exposure	May exacerbate symptoms as a result of increased sensitivity and oxidative stress	Smoking and heavy metal exposure are related to FM, thus suggesting that xenobiotics may a play a role in symptom exacerbation (61-65).
Infections		
Chronic infections	Associated with an increased incidence of FM, but causality unclear.	Evidence of an increased incidence of FM and chronic widespread pain in patients with infections such as Lyme disease, HIV, etc. (66-68).
Electromagnetic fields (EMF)		
EMF exposure	Can trigger or worsen FM symptoms.	One study found metabolic dysfunctions in FM patients who were sensitive to electromagnetic radiation, thus indicating a potential relationship with symptoms (69).
Traumatic stress		
Emotional and physical traumas	Linked to changes in brain function and chronic pain.	Studies have shown a significant relationship between traumas and FM, the incidence of which increases following a traumatic event (70-75, 82-85).
Nutrition		
Dietary factors	Obesity, food allergies, and certain additives can exacerbate symptoms.	Studies highlight the importance of anti-oxidants and dietary changes in mitigating FM symptoms, but the effects are non-specific (88-90).
Microbiome		
Gut microbiota	Altered microbiome can influence FM symptoms.	The risk of FM has been shown to be associated with specific bacteria, which suggests potential of microbiome modulation in treating FM (91-93).

comprehensive review of 36 studies involving a total of 5142 participants identified obesity and food additives as risk factors, and emphasised the significance of anti-oxidants as a means of countering FM-related oxidative stress (89). Some studies have found a correlation between vitamin D deficiency and increased pain levels (90) and others that co-enzyme Q10 (CoQ10) supplementation can considerably improve symptoms (91). It has also been shown that gluten-free and low $FODMAP_s$ (fermentable oligosaccharides, disaccharides, monosaccharides, and polyols) diets can alleviate symptoms and weight loss, and that symptoms can be improved by eliminating food additives such as monosodium glutamate and aspartame. Studies of the role of the gut microbiome in FM have shown that intestinal dysbiosis (which can be affected by genetics, age and diet) is related to the pathology of FM (90, 91), thus importance the intricate relationship between nutrition, genetics, and gut inflammation. However, the inconsistent results and methodological differences of the studies indicate that more rigorous and controlled research is required to clarify the effect of diet on FM and develop specific dietary recommendations for patients.

Microbiome and fibromyalgia

There is currently considerable interest in characterising the microbiome associated with various autoimmune diseases with the aim of manipulating it for therapeutic purposes (91-93). Recent studies have begun to show that alterations in this complex ecosystem affect not only gastrointestinal disorders, but also neurological disorders, metabolic diseases, and fibromyalgia. This interest has been spurred by observations of gastrointestinal disorders such as irritable bowel syndrome (IBS) in FM patients, and the relationships between FM symptoms and immune system dysfunction, inflammation, and intestinal dysbiosis. Furthermore, the bi-directional communication system between the gastrointestinal tract and the brain offers a plausible explanation of how the intestinal microbiome may influence the central symptoms of FM such as pain modulation, and how alterations in the microbiome may contribute to its pathogenesis of FM, thus providing new impulse for potentially revolutionary treatments. Understanding how diet, probiotics, and other means of microbiome modulation can affect FM could lead to innovative therapeutic approaches to mitigating symptoms and addressing some of the underlying causes of the syndrome. One study has found that FM significantly correlates with specific gut microbiota such as *Coprococcus2*, *Eggerthella*, *Lactobacillus*, *FamilyXIIIUCG001*, and *Olsenella*. *Coprococcus, Eggerthella*, and *Lactobacillus* increase the risk of FM: *Coprococcus2* is associated with harmful effects due to the over-production of butyric acid leading to intestinal damage and inflammation; *Eggerthella* is associated with conditions frequently encountered in FM patients and may aggravate intestinal issues and inflammation; and usually beneficial *Lactobacillus* may have harmful effects on serotonin and inflammation. On the other hand, *FamilyXIIIUCG001* and *Olsenella* seem to reduce the risk of FM and it could have a potential therapeutic role. This study used Mendelian randomisation, which suggests robust findings, but limitations such as the use of broad genetic variables, the constraints of species-level analysis, and its predominantly European participants may affect the generalisability of the results. Gut microbiota is indirectly involved in the availability of neurotransmitters such as glutamate and GABA, and the metabolism of some of their precursors such as serotonin and tryptophan. It has been found that the levels of glutamate and GABA, which are key neurotransmitters in the processing of pain in the spinothalamic pathways, are altered in FM patients, who have higher levels of glutamate and lower levels of GABA than healthy controls (92). Furthermore, FM patients have lower levels of serotonin (whose multiple regulatory functions in the CNS include pain management) and its precursor, tryptophan, an essential amino acid that can only be obtained only through diet (93). Intestinal dysbiosis can increase the catabolisation of tryptophan, thus hindering its absorption and negatively affecting serotonin synthesis, whereas intestinal permeability can facilitate the absorption of glutamate and has pronociceptive effects that worsen the pain sensitivity of FM patients. The presence of intestinal dysbiosis (quantitative and qualitative imbalances in gut microbiota) has been experimentally demonstrated in patients with FM, and can negatively impact the absorption of beneficial nutrients such as GABA and tryptophan, thus compromising the synthesis of crucial neurotransmitters such as serotonin (93). The importance of gut microbiota and their interactions with the central nervous system in pain management and the pathogenesis of FM underlines the potential role of intestinal permeability and microbiota imbalances in facilitating pain transmission in FM patients. Our understanding of these mechanisms offers perspectives for new therapeutic strategies aimed at modulating gut microbiota in order to alleviate FM symptoms.

Conclusions

Given its medical complexity, the management of FM requires a holistic and highly personalised approach (94). This review underlines the fact that the disease is profoundly influenced by a variety of environmental factors, ranging from climatic and weather conditions, to pollution, psychophysical stress and trauma, dietary changes, and interactions with the intestinal microbiome. This wide array of environmental influences highlights the need to consider patients in their entirety, recognise that FM is not an isolated disorder but the epicentre of a complex interplay of external and internal factors. Possible sensitivity to changes in the climate and weather such as variations in temperature and humidity indicates the importance of understanding the specific vulnerabilities of each individual patient in order to ensure that disease management benefits from personalised strategies that take into account environmental conditions as a means of mitigating symptom intensity. Similarly, investigating the impact of air pollution and exposure to electromagnetic fields opens up new research horizons targeting preventive interventions. The critical role of diet and the microbiome in the manifestation of FM symptoms suggests the possibility of developing innovative therapeutic approaches in which personalised diet and microbiome modulation can lead to significant improvements in the quality of life. The effects of psychophysical stress and trauma on the development and course of the disease support the need to include stress management and psychological support in therapeutic strategies in such a way that addressing the psychological roots of FM and understanding and treating past traumatic experiences become crucial elements in the pathway of patient care, and offer a more comprehensive and humanised perspective of disease management (Table II).

In conclusion, there is a need for a paradigm shift in the management of FM from an approach solely based on symptom management to a more inclusive and personalised view that takes into account interactions between patients and their individual environments. Future research should therefore continue to investigate the complex network of factors influencing FM with the aim of developing more effective and personalised treatments capable of substantially improving the lives of patients afflicted by this enigmatic condition.

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