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Abstracts

Invited Speaker Presentations 1-14
Oral Presentations 14-16
Poster Presentations 16-21
Author index 22
IS-01

Fibromyalgia syndrome: year in review

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The aim of this review is to describe the most recent findings concerning the diagnosis, aetiopathogenesis and treatment of fibromyalgia syndrome (FM) that were published between January 2021 and January 2022 and appearing on PubMed database.

Year 2021 saw the publication of many papers which tried to estimate the big COVID-19 impact on FM patient’s lives, both from a physical and a mental point of view (1–3). Moreover, more and more attention has been put on juvenile fibromyalgia, which is surging as a distinct clinical entity which needs prompt diagnosis (4), and, as the adult counterpart, if it is comorbid et et. Clinical and Experimental Rheumatology 2022

Invited Speaker Presentations The 4th International Virtual Congress on Controversies in Fibromyalgia

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IS-02

Chronic pain: year in review

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Chronic pain, defined as persistent or recurrent pain lasting more than three months, remains a significant health challenge, affecting more than 20% of the population in the USA, and carrying a huge social and economic burden. In last year, significant contributions have been published regarding the understanding of chronic pain syndromes, with regards to pathogenesis, clinical, psychological, and therapeutic aspects. In this review we aim to summarize some relevant – but not exhaustive- data that emerged during 2021. We will focus on new insights into the pathophysiology, related to genetics, microbiome and metabolic strategies, neuro-imaging studies, psychological factors, and the role of non-pharmacological modalities (use of virtual reality techniques) and the role of some nutrients in the management of chronic pain such as ginseng and ginsenosides.

Last but not least, we will focus on an emerging population of chronic pain syndrome due to the long-term effects of COVID-19.

IS-03

A closer look at the concept of “Nocieplastic pain”. What is it good for?

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Several years ago the membership of the International Association for the Study of Pain (IASP) formally voted to acknowledge that there was a third new mechanism/descriptor of pain, and coined the term nociceplastic pain to describe this mechanism. This term now essentially replaces terms such as central sensitization or centralized pain that had been previously used. The phenotypic features of this type of pain are very well described and include widespread or multifocal pain, often accompanied by fatigue as well as sleep, memory, and mood disturbances, and these individuals are also often sensitive to non-painful sensory stimuli such as lights, noises, and odors. The underlying mechanisms and risk factors that drive this type of pain are pleomorphic and include both intrinsic features (e.g. female sex, genetic and familial predisposition) as well as environmental factors (early life trauma, poor sleep, inactivity, low SES). The nervous system (especially the central nervous system [CNS]) is clearly playing a prominent role in nociceplastic pain conditions as changes have now been identified going back to childhood that can identify this diathesis/process that causes diffuse sensory hyper-responsiveness as well as a number of other features.

IS-04

Genetics, genomics and epigenetics in fibromyalgia and chronic pain

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Similar to other chronic conditions, the concept of “pain that runs in the family” has been long—recognized in cultural and historical aspects. Indeed, humans have inherently tended to attribute medical as well as other personal characteristics to inherited factors, even before the evolution of the science of genetics (1). Nonetheless, the scientific endeavor to decipher the genetic underpinnings of fibromyalgia and chronic pain constitute a much more recent development. In view of the controversial nature of the fibromyalgia syndrome, and particularly the paucity of objective biomarkers, the field of genetics offers not only a tool for understanding pathogenesis and treat-
ment, but also an important instrument through which fibromyalgia patients may gain legitimation and recognition. So far however despite extensive research, the precise genetic basis of fibromyalgia remains elusive (2). Early research into the genetics of fibromyalgia focused on clinical aspects such as twin studies and identification of clear familial affiliation. Subsequently, multiple candidate genes as well as SNPs were identified, followed by the application of Genome – wide association studies which have greatly enhanced our understanding.

Epi-genetics is another, complimentary strategy for tackling the fibromyalgia enigma. Focusing on the interactions between environmental factors, including trauma, and the pattern of gene expression, epigenetics may serve as a mediator explain the connection between pain and its triggers. Epigenetic studies into the pathogenesis of other trauma – related conditions such as PTSD as well as the fascinating area of intergenerational trauma, have led to better understanding of the ways in which trauma can affect our genetic composition (3).

Specific epigenetic mechanisms such as DNA hypomethylation, histone modifications, micro-RNA expression etc. have been studied and patterns of differentially methylated gens have been identified (4).

BDNF is a neurotrophin which has been specifically studied in this context. BDNF expression is partially mediated by the Val66Met polymorphism (rs6265) as well as by the methylation of specific promoters. A study on fibromyalgia patients (5) detected higher levels of serum BDNF, lower levels of DNA methylation in a promoter gene which was mediated by the Val-66Met polymorphism; serum levels of BDNF predicted patient symptoms. Thus, epigenetic mechanisms may serve as a central axis through which various factors such as genetic predistortion, environmental and lifestyle factors eventually contribute the development of complex pain conditions such as fibromyalgia. Understanding these mechanisms may greatly enhance our insight into the pathogenesis of fibromyalgia, into possible preventive efforts, as well as leading towards the development of more rational and tailored interventions.

**IS-05**

**Classification and epidemiology of chronic pain: where are we going?**

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Chronic pain is a common, complex and distressing problem that has a profound impact on the individual and society. It often occurs as a result of an illness or injury and persists beyond the normal terms of recovery. However, chronic pain is not simply an accompanying symptom, but rather a separate condition in its own right, with its own medical definition and taxonomy that has undergone a major review in recent years. The International Association for the Study of Pain (IASP) has redefined pain as follows: “an unpleasant sensory and emotional experience associating with actual or potential tissue damage.” This new definition highlights the difference between pain and nociception and implies that pain does not always result from nociceptor stimulation. Whereas nociception is a phenomenon characterized by the encoding and processing of impulses by the nervous system that can be measured instrumentally, pain cannot be measured by instrumental means and may exist independently of nociception.

Currently, there are three mechanistic descriptors of chronic pain: nociceptive, neuropathic, and nocplastic pain. According to the IASP definition, nociceptive pain arises from actual or threatened damage to non-neural tissue, is due to activation of a specific type of peripheral nervous fiber (called nociceptors), and occurs with a normally functioning somatosensory nervous system. Neuropathic pain derives from a lesion of the somatosensory nervous system, while nocplastic refers to pain not attributable either to an activation of nociceptors or to a damage of the somatosensory system, but resulting from a dysfunction of the latter leading to an increased sensory processing and an altered control of modulation systems.

Fibromyalgia (FM) belongs to the definition of nocplastic pain. The worldwide prevalence of FM is around 2.7%. Worldwide, the mean prevalence of FM is 4.2% in females and 1.4% in men, with a female-to-male ratio of 3:1. The prevalence of the disease is influenced by the diagnostic criteria adopted. In recent decades, numerous efforts have been made to establish valid diagnostic/classification criteria for FM. The 1990 American College of Rheumatology (ACR) criteria were extremely focused on chronic widespread pain (CWP) and tenderness, with little relevance of symptoms for diagnostic purposes. The 2010/2011 criteria were developed with the intention of valorizing non-painful symptoms by translating them into a symptom severity (SS) scale. In addition, the formal tender point count was replaced by the diffuse pain index (WPI), avoiding the objective examination. Recently, one of the criticisms leveled against the 2010/2011 ACR criteria is that they supposedly moved away from chronic pain. The latest development of diagnostic criteria for FM was provided by the AAPT (Analgistic, Anesthetic, and Addiction Clinical Trial Translations Innovations Opportunities and Networks [ACTTION] - American Pain Society [APS] - Pain Taxonomy) FM Working Group. In these criteria, FM was again classified as a disease characterized predominantly by chronic pain (a multi-site pain self-assessment [MSP], defined by the presence of at least six of nine pain sites throughout the body), along with fatigue and sleep problems as two key associated symptoms.

**IS-06**

**Autoimmunity of the autonomic nervous system decipherers many enigmas; fibromyalgia and CFS**

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Covid-19 virus is an autoimmune virus and more notorious than EBV. It induces autoimmune diseases by hyper-stimulation combined with induction of autoimmune disease by molecular mimicry. Post COVID-19 Syndrome (PCS) is a complex of various symptoms developing a month or more after the acute phase of the disease. The cases of PCS development among patients with asymptomatic/mild forms are frequently reported; however, the pathogenesis of PCS in this group of patients is still not completely clear.

The PCS develops on average in 30–60% of patients, mainly among women. Fatigue, shortness of breath, cough, and anosmia were reported as the most common symptoms. The possible association between the described PCS symptoms and brain damage is noted. We assume the possibility of an alternative course of COVID-19, which develops in genetically predisposed individuals with a stronger immune response, in which it predominantly affects the cells of the nervous system, possibly with the presence of an autoimmune component, which might have similarity with chronic fatigue syndrome or autoimmune dysautonomia. We will discuss all the autoimmune ramifications of the virus, the CFS / fibromyalgia / post Covid syndrome (1-7).

**References**

Urine, saliva and serum samples have been analysed with various techniques of metabolomic and proteomic analysis. The differentially expressed proteins and metabolites identified in the recent literature metabolites and proteins or metabolites in fibromyalgia. Multivariate statistical analysis showed the dysmetabolism of several biochemical pathways and the presence of abnormalities in the metabolome plays multiple roles in cellular signalling, bioenergetics and stress defence, pain mechanisms, and muscle metabolism. Have been identified. The etiology of fibromyalgia remains elusive making its diagnosis and treatment difficult. Systems biology has been widely used to explore the mechanism, aetiology and/or biomarkers of complex disease. The metabolome plays multiple roles in cellular signalling, bioenergetics and membrane structure and function. Proteomics is used for detecting diagnostic markers, understanding pathogenic mechanisms and interpreting functional protein pathways in various diseases by identifying and quantifying the ‘proteome’ of the cell, tissue or body fluids. Integrating multi-omics has been used to characterize and decipher the underlying patho-mechanisms, explore potential pathogenic factors, and provide more effective diagnosis and treatment for the disease.

**Objectives.** Identify in the recent literature metabolites and proteins or metabolites in fibromyalgia. The essence of the criteria for diagnosing chronic primary MSK pain is based on a history of the pain complaint with attention to specific characteristics of the pain and conduct of a simple clinical examination. A possible diagnosis of chronic primary MSK pain requires the following: 1) pain is regional (not discrete), has been present for at least 3 months and is not entirely explained by associated neuropathic or nociceptive pain; and 2) clinical examination findings of evoked pain hypersensitivity (by demonstration of static or dynamic mechanical allodynia, or heat or cold allodynia, or pain after sensations). A probable diagnosis requires the presence of 1) and 2) as well as the following: 3) history of pain sensitivity to touch, pressure, movement or temperature; and 4) presence of comorbidities of hypersensitivity to sound/light/odours, or sleep disturbance, or fatigue, or cognitive problems.

There will be challenges to the acceptance of this new concept. To date, regional MSK complaints have been more commonly recognized as myofascial pain syndromes (MPS) with physical examination techniques used to confirm the diagnosis. With considerable similarities between these two conditions, some may question the clinical relevance of differentiating between the two. While the history of the pain complaint with specific probing questions may be familiar to those practicing in pain medicine, they do not represent the depth of interview expected in usual primary care, where we believe most patients will be seen. Similarly, the simple examination techniques may not be part of a usual examination in a patient with a pain complaint but are nevertheless simple and can be easily learned and applied. It is believed that chronic primary MSK pain does indeed exist, and this is the first step in defining criteria for the diagnosis. Patients will be reassured; unnecessary investigations will be reduced and there can be focus towards centrally rather than peripherally directed treatments.

**References.**

The discussion on animal models of pain should consider that the use of the word ‘model’ refers to three entirely separate entities: the subject (species, strain, sex, age), the assay (etiology, body part) and the measure (reflex, spontaneous, operant, pain-affected complex behaviors) (1). The choice of animal model is crucial in the discovery of candidate therapeutic targets. In fact, the translational success from animals to humans critically depends on the benefits and limitations of each model. Some animal experiments are designed to address questions about basic molecular or cellular mechanisms, whereas others are more accurately described as “clinical trials in rodents”. Rodent models of chronic pain may elucidate pathophysiological mechanisms, whereas others are more accurately described as “clinical trials in patients”. Animal models of pain are designed to recapitulate numerous visceral pain syndromes.

These represent some of the most used preclinical animal models for studying chronic pain conditions.

Transgenic animals have also been used to model diseases such as HIV and rheumatoid arthritis, chemotherapy-induced pain, and multiple sclerosis pain. Transgenic mice have been developed to model conditions such as chronic migraine pain. In these models, transgene expression is targeted to a specific tissue or cell type. The transgenic animals lack a gene or a gene product that is present in the wild type, or they have an extra copy of a gene. Transgenic animals are used to study the effects of genetic changes on disease susceptibility and the role of specific genes in disease development.

Behavioral models of chronic pain are commonly used to study the effects of different treatments on pain behavior. These models include models of chronic pain induced by peripheral nerve injury, sciatic nerve cuff or spared nerve injury (SNI), inflammatory pain induced by intraplantar injection of complete Freund’s adjuvant (CFA), and inflammatory pain induced by intraplantar injection of carrageenan. These models are used to study the effects of different treatments on pain behavior and to evaluate the efficacy of new analgesic drugs.

Suicidal behavior in fibromyalgia patients: rates and determinants of suicide ideation, risk, suicide, and suicidal attempts - a systematic review of the literature and meta-analysis of over 390,000 fibromyalgia patients

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Background. Suicide is a leading cause of death worldwide, affecting ~800,000 people every year. Fibromyalgia is an extremely prevalent rheumatic disease with a predisposition for comorbid anxiety and depression, which are known risk factors for suicidal behavior. Suicidality and relevant risk factors for suicidal behavior have not been thoroughly studied in patients with fibromyalgia.

Objectives. To investigate the risk of suicidal ideation and attempts in patients with fibromyalgia.

Methods. A systematic review and meta-analysis was conducted and reported according to the “Preferred Reporting Items for Systematic reviews and Meta-analyses” (PRISMA) standards. In addition, the gray literature was extensively searched.

Results. Thirteen studies were included in the present systematic review and meta-analysis, including 394,087 fibromyalgia patients. Sample size ranged from 44 to 199,739 subjects, mean age ranged from 45.8 to 54.5 years while the female percentage with fibromyalgia ranged from 17.1 to 100.0%. The overall suicide ideation prevalence was 29.57% [95% CI 1.84–72.07], with an OR 9.12 of (95%CI 1.42–58.77), ranging from 2.34 (95%CI 3.66) to 26.89 (95%CI 5.72–126.42). Pooled suicide attempt prevalence was 5.69% (95%CI 1.26–31.34), with an OR of 3.12 (95%CI 1.37–7.12). Suicide risk was higher with respect to the general population with an OR of 3.12 (95%CI 1.37–7.12), as well as suicide events with an HR of 1.38 (95%CI 1.17–1.71). Determinants of suicidality were found to be employment status, disease severity, obesity and drug dependence, chronic pain and co-morbidities, in particular depression, anxiety, poor sleep, and global mental health. However, in some cases, after adjusting for psychiatric conditions, the threshold of statistical significance was not achieved.

Conclusions. Fibromyalgia patients are particularly prone to suicide, in terms of ideation, attempt, risk and events, warranting a pre-emptive screening of their mental health status. Given the few studies available, the high amount of heterogeneity, the evidence of publications bias and the lack of statistical significance when adjusting for underlying psychiatric co-morbidities, further high-quality studies should be conducted.
Studies have shown that overweight and obesity are central features of fibromyalgia syndrome (FM), but the real impact of a high body mass index (BMI) on clinical severity in patients with FM is still controversial. Studies showed that obesity significantly correlated with greater pain sensitivity, tender point palpation, reduced physical strength and lower-body flexibility, shorter sleep duration, and greater restlessness during sleep; overweight and obese FM patients have higher levels of pain, fatigue, morning tiredness and stiffness in comparison with their normal weight counterparts, severely obese patients had significantly greater fibromyalgia-related symptoms and a poorer quality of life than non-obese or overweight patients. We have demonstrated that overweight/obese patients with FM are significantly more impaired in all of the symptomatological and functional domains as measured using the revised Fibromyalgia Impact Questionnaire (FIQ); the modified Fibromyalgia Assessment Status (ModFAS) questionnaire, and the Polysymptomatic Distress Scale (PDS) than Underweight/Normal patients, thus suggesting that being obese/overweight has an additional effect on symptoms and function. The mechanisms underlying the relationship between a high BMI and FM are still unclear, but it has been suggested that the reduction in physical activity induced by musculoskeletal pain may lead to a higher BMI, or that a higher BMI causes pain as a result of increased strain on weight-bearing joints.

IS-14

Long time story: data from registries?

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In the field of chronic disease, next to data from clinical trials, there is an increasing need to obtain data from real life. With the computer technology available today, it is possible to computerize the data collection process, applicable on a large scale, and organize it into a registry. A patient registry is defined as “an organized system that uses observational study methods to collect uniform data (clinical and other) to evaluate specific outcomes for a population defined by a particular disease, condition, or exposure, and that serves a predetermined scientific, clinical, or policy purpose.” For fibromyalgia, there were no European registries until the creation of the Italian Fibromyalgia Registry (IFR), the implementation of which was supported by both the Italian Society of Rheumatology (“SIR”) and the Italian Ministry of Health. The IFR, to date, has essentially allowed the achievement of multiple objectives, the main ones of which can be summarized as (1) to assess and monitor the condition of patients over time through demographic data, clinical descriptors and uniform outcome measures estimated with standardized and validated tools at each participating site; (2) establish disease severity cut-off points to support health care decision making; (3) provide researchers with reliable real-world data to answer important research questions, test hypotheses regarding various aspects of chronic widespread pain and its management, assess study feasibility, and facilitate patient recruitment into clinical research; and (4) support collaborative research projects by promoting cooperation among centers and assisting in the implementation of research projects.

IS-15

Fibromyalgia prevention – putting it all together

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Fibromyalgia (FM) is a common, chronic, widespread pain syndrome accompanied by a broad variety of functional symptoms. No single etiological cause can currently be ascribed to the development of FM, although many triggers have been associated with its appearance. Thus, triggers such as physical trauma (mainly whiplash injury), various forms of acute or chronic stress, as well as infectious and endocrine disorders have all been linked to FM onset (1). The prevalence of FM has increased over past years (2), now ranging from 2%-5% depending on the population sampled and the criteria implemented (3), and thus posed a significant social and economic burden (4). Additionally, the syndrome is difficult to manage and treat and therefore primary prevention and early diagnosis are of great importance.

That being said, prevention is difficult to obtain in potential FM patients due to the following factors:

First, when discussing pain syndromes, it is important to distinguish acute pain from chronic pain and to talk about the shift from the first to the second. Acute pain is defined as pain lasting for up to 3 months or that is related to an injury/trauma. Chronic pain is pain lasting more than 3-6 months or pain lasting beyond the usual course of injury healing. Chronic widespread pain is characterized by sensitization of central pain pathways and is currently designated as nociceptive pain, thus differentiating it from nociceptive and neuropathic pain. There is evidence that a stress response system dysfunction may play a role in central sensitization (5). Moreover, we can see that there are numerous risk factors associated with the transition from acute to chronic pain including demographic characteristics, stress, physical abilities, fear from pain and emotional state. Thus, the biopsychosocial model of chronic pain combines a genetic predisposition (e.g., genes such as COMT), a biological vulnerability (e.g., endocrine, cardiovascular, immune dysregulation etc.), psychological vulnerability (e.g., anxiety) and social vulnerability.

Although the dysfunctional descending pain-inhibitory mechanism seen in FM is primarily biological, it is greatly influenced by these risk factors (4). The problem is that while these factors can increase the risk of shifting to chronic pain, it is still hard to anticipate which patients will eventually progress into a chronic pain syndrome and what is the role of each risk factor. Secondly, there is no specific biomarker that can anticipate or identify the syndrome at an early stage, as is available for instance in inflammatory joint diseases.

Third, it is known that familial aggregation plays an important role in FM and by using genome sequencing methods an increasing number of genes have been identified as associated with centralized pain conditions in general and FM particularly (4). Yet we still haven’t found sufficiently specific genetic markers that is directly predictive of these conditions.

Based on the biopsychosocial model, tailored multidisciplinary interventions have been attempted towards the prevention of specific types of chronic pain such as low back pain and temporomandibular joint disorder. These interventions included teams consisting of a physician, a specialized nurse, physical therapist, occupational therapist and clinical psychologist. Such functional restoration programs objectively assess all aspects of patient function. Ideally such interventions should be introduced early in the course of pain, e.g., shortly after a back injury, and should try to incorporate data regarding all aspects of individual vulnerability. Similar interventions may well prove to be effective in patients considered to be at risk of developing FM, e.g., post-whiplash patients with vulnerabilities, but further research and resource allocation are called for.

In conclusion, in order to accomplish successful primary prevention it is necessary to understand if and how we can intervene and influence the different risk factors, and continue using advanced genome sequencing methods in order to locate specific genetic markers of FM and to incorporate them into a comprehensive biopsychosocial prevention strategy.

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The 4th International Virtual Congress on Controversies in Fibromyalgia

Invited Speaker Presentations


IS-16

Long-COVID, chronic fatigue and everything in between – what have we learned and where may it impact on fibromyalgia

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As the COVID-19 pandemic made its gruesome initial appearance in the first months of 2020, it initially appeared as though nothing could be more distant from this acute, dramatic, life – threatening condition, treated in intensive care units and heroically combated behind personal protective equipment, than fibromyalgia, a chronic pain syndrome treated in clinics by primary care physicians and rheumatologists. Only gradually, as the medical community became more accustomed to the manifestations and complications of COVID-19, did the more chronic aspects of the pandemic come to light with the evolving entity of LONG-COVID syndrome (1). This syndrome was initially treated by a broad spectrum of specialties including infectious disease specialists, pulmonologists, neurologists, with rheumatologists not taking a central role. As more clinical experience was accumulated however, a surprising overlap begins to emerge between LONG-COVID and conditions such as fibromyalgia and chronic fatigue syndrome, an overlap most obvious on a clinical level to rheumatologists well acquainted with the spectrum of fibromyalgia (2).

On a clinical level, LONG COVID patients most frequently suffer from fatigue, exercise intolerance, as well as cognitive impairment, all symptoms which overlap with the chronic fatigue syndrome. Sleep disturbances, abdominal complaints, anxiety/depression and myalgia are also not unusual (3). In addition, autonomic dysregulation appears to play a role in LONG COVID (4), as in fibromyalgia.

Notably, symptoms typical of fibromyalgia among LONG-COVID patients appear to be particularly common among patients with a previous history of chronic pain, and patients who were actually diagnosed with fibromyalgia before contracting COVID-19 appear to be prone to get worse (5). Notably, an association between fibromyalgia / chronic fatigue and other chronic viral diseases such as EBV/CMV, HIV and viral hepatitis has been well known before the COVID-19 era, so that viral infection has traditionally been considered as among the triggers responsible for instigation the syndrome (6).

Another aspect of clinical importance regarding the relationship between fibromyalgia and COVID-19 relates to the effect of vaccinations. While vaccinations have previously been speculated to have a causative role in fibromyalgia, mainly based on data relating to the gulf war syndrome, the robustness of this association is not clear. In an era of significant vaccine hesitancy which often hampers effective attempts at controlling the pandemic, clear data regarding the safety and effectiveness of COVID-19 vaccinations regarding fibromyalgia is necessary.

Fascinating data has emerged indicating that patients suffering from LONG – COVID may actually have low grade persistent infection, with identification of viral antigens and RNA in tissue as long as one year after initial infection (7). While the general applicability of these findings is not yet clear, they raise the provocative possibility that similar viral vectors might be identifiable in tissues of patients suffering from chronic fatigue or fibromyalgia. Last but not least, the COVID-19 pandemic, including the social distancing measures associated with it, have taken a toll on patients suffering from fibromyalgia even when not personally infected (8). Reduced access to healthcare, lockdown and lack of exercise, anxiety and isolation may all play a role and should be considered by physicians caring for fibromyalgia patients in this era.

References


IS-17

Why patients affected by rheumatoid arthritis or other inflammatory articular syndromes may develop a concomitant fibromyalgia?

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Prevalence of comorbid fibromyalgia (FM) among patients affected by inflammatory Rheumatic diseases is considerably higher than in the general population. Although estimated prevalence should be interpreted with care because FM criteria have not been validated for patients with inflammatory arthritides, it can be considered ranging between 15 and 20% (1-3).

Centralised pain can occur because of a disease that has identifiable ongoing nociceptive input, such as inflammatory arthritides. Chronic inflammation may mediate transition from peripheral to central pain resulting in symptoms of FM. In animal models, proinflammatory cytokines such as tumour necrosis factor and interleukin-6 have been implicated in aberrant central pain processing and widespread pain sensitivity (4). However, despite early and aggressive treatment, a significant number of arthritis patients develop FM. In fact, chronic pain can be intensified by a combination of biopsychosocial factors, so that, despite the undoubted contribution of inflammation, persistent pain may develop with the contribution of multiple mechanisms (5).

Patients with RA identify pain as their most troublesome problem and advent of new disease-modifying treatments. Alternatively, as interventions to reduce peripheral nociceptive stimuli may not alter the long-term course of FM, comorbid FM may blunt the patient-reported response, leading to treatment discontinuation.

Therefore, a person-centered approach to the clinical management of pain is clearly needed, with the goal of helping patients with rheumatic diseases to reduce their pain and improve their quality of life.

References


Clinical and Experimental Rheumatology 2022
IS-18
Small fibbre neuropathy: is still relevant?
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Fibromyalgia is a chronic primary pain condition associated with autonomic symptoms, fatigue and cognitive disturbances. It affects between 2% and 4% of the general populations, with a men:women ratio of 1:3 (Häuser and Fitzcharles, 2018).

Despite the large body of studies on the topic, the mechanisms underlying this common chronic pain condition are still a matter of debate. For years, the research highlighted central nervous system abnormalities (Truini et al., 2016). However, recent preclinical investigations have indicated that dorsal root ganglia damage, due to circulating autoantibodies, may play a role in fibromyalgia (Goebel et al., 2021). Accordingly, approximately 50% of patients with fibromyalgia have a reduced intraepidermal nerve fibre density as assessed with skin biopsy. This finding, which closely resembles small-fibre neuropathy, is commonly defined as small-fibre pathology (Grayston et al., 2019).

Although patients with fibromyalgia share similar skin biopsy abnormalities with patients with small-fibre neuropathy, several studies showed that patients with fibromyalgia have different sensory phenotypes than patients with small-fibre neuropathy. In patients with fibromyalgia, sensory loss is absent and the healthy sensory phenotype is common (Fasolino et al., 2020). These findings indicate that comparable small-fibre damage shapes different sensory phenotypes and provide further support to the evidence that small-fibre pathology likely has a complex association with pain.

References

IS-19
Acetyl-L-carnitine role in fibromyalgia syndrome
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Acetyl-L-carnitine (ALC) is an endogenous molecule that plays a primary role in energy metabolism, but also has neurotrophic and neuroprotective properties. The discovery of multiple new mechanisms of action has aroused increasing interest in its potential therapeutic use. ALC is one of the metabolites into which carnitine can be transformed upon acetylation intra-mitochondrially in many brain, liver, kidney and muscle tissues by means of the action of carnitine acyltransfersases that use acetylCoA and carnitine as substrates (1, 2). It is also involved in the trans-mitochondrial membrane trafficking of acetyl units for catalobic and anabolic metabolism and in buffering the pool of acetylCoAs. ALC has an important antioxidant effect in humans (3), because it regulates the genes involved in protecting against oxidative stress, such as the heme oxidase-1 gene (HO-1) and some heat shock proteins (HSPs), and protects mitochondrial functioning (4).

The central nervous system activities of ALC include the modulation of many brain neurotransmitters; primarily, ALC can potentiate cholinergic responses (5).

ALC prevented an increase in NGF levels and normalised peripheral and central alterations in Glial-cell derived neurotrophic factor (GDNF) and Ar- temin levels, thus demonstrating an anti-hyperalgesic effect (6). ALC can increase the expression of mGlu2 receptors, thus potentiating their analgesic role during inflammatory, neuropathic, or nociceptive pain, so mGlur2Rs in the spinal cord limit the transmission of nociceptive stimuli and counter-act the establishment of central sensitisation. In the hippocampus and pre- frontal cortex, mGlur2R up-regulation may increase the synthesis and re-lease of brain-derived neurotrophic factor (BDNF) (7). It has been reported that ALC may induces antiinociception by a central cholinergic mechanism which involve M1 muscarinic receptors (8, 9).

Taking all of this into account, the administration of ALC may benefit FMS patients in various domains:
1. Neural sensitisation may improve due to the epigenetic mechanisms of ALC leading to increased mGlu2R density at nerve terminals, which provides a long-lasting effect.
2. ALC may protect FMS patients from oxidative stress and the production of inflammatory markers;
3. FMS patients, especially those with prominent depressive symptoms and mood alterations, may benefit from the neuroprotective and anti- depressive effects of ALC.
4. Cognitive dysfunctions in FMS patients may be improved by ALC sup- plements;
5. ALC may improve symptoms and nerve fibre density in FMS patients with small fibre neuropathy.

References

IS-20
Do biologics work in chronic pain?
Ernest Choy
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Chronic pain is a heterogeneous condition with a mixture of peripheral and central components in its pathophysiology. This is particularly evident in patients with musculoskeletal diseases such as osteoarthritis, inflammatory arthritides and fibromyalgia. Fibromyalgia is classified as a nociceptive condition (1) as it has many features of central pain but limited evidence of peripheral pain although the latter is controversial as some researchers found evidence of small fibre loss in the skin. In patients with inflammatory arthritides, a systematic review found that 1 in 5 patients had concomitant fibromyalgia (2). These individu- als have higher pain score. Indeed, pain score in these patients do not corre- late with inflammation measured by blood tests or imaging. Some have used the term, ‘non-inflammatory pain’ to describe this phenomenon.

Biologic agents have been used for the treatment of chronic inflammatory arthritides for more than 20 years. Biologic agents can be classified into 2 main categories: anti-cytokines and anti-lymphocytes. Cytokine receptors which involve M1 muscarinic receptors (8, 9).

Do biologics work in chronic pain?
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Biologic agents have been used for the treatment of chronic inflammatory arthritides for more than 20 years. Biologic agents can be classified into 2 main categories: anti-cytokines and anti-lymphocytes. Cytokine receptors are expressed by nociceptive neurons, spinal cord and the brain. They can sensitize nociceptive sensory neurones (3). A few studies have suggested that anti-cytokine therapy may reduce non-inflammatory pain in inflamma-

Clinical and Experimental Rheumatology 2022
tory arthritides, especially rheumatoid arthritis (4). Recently, Goebel A et al. (4) found that immunoglobulin from patients with fibromyalgia but not healthy controls can sensitize sensory neurone and raised the possibility that biologic treatment that reduce immunoglobulin level may be effective in fibromyalgia. However, this will need to be assessed in randomised control trials.

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IS-21
Could Jak inhibitors agents modulate pain and fatigue?

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Janus kinase inhibitors (JAKis) belong to a new class of oral targeted disease-modifying drugs (DMARDs) whose novel mechanism of action is able to modulate the JAK-STAT intracellular pathway. Currently, JAKis are approved and used for the treatment of Rheumatoid arthritis (RA) patients failure to conventional DMARDs, helping to achieve low disease activity or remission in a relevant percentage of cases. Several studies reported how some RA patients who have achieved inflammatory remission, as assessed through validated tools, often report residual symptoms such as pain and fatigue (1). Pain in RA is due to complex interaction of central and peripheral nervous system not always strictly related with the inflammatory pathways of the disease. Dysregulation of nervous pain pathways, in particular central and peripheral sensitization, play a fundamental role in the maintenance and expression of the RA chronic pain (2-3). While peripheral sensitization is more connected to the action of inflammatory mediators that can directly alter the responses of local nociceptive neurons, the central amplification of pain is a more complex phenomenon not only linked to the enhanced pain sensitivity of the dorsal horn of the spinal cord or different pathway activation of descending facilitatory/inhibitory central ways but also with the psycho-social aspects of pain perception of the single patient. It means that physicians should identify the pathways involved in central and peripheral pain processing in order to individualize pain treatment, improve pain efficacy and reduce the overtreatment risk of painkillers or of potentially immunosuppressive drugs (4).

Very recent works suggested that some DMARDs, in particular JAKis, may also have direct effects on pain mechanisms. For example, specific post-hoc analyses, suggested that baricitinib, a selective JAK1/2 inhibitor, is able to give greater pain relief compared to methotrexate (MTX) alone (5), or toclizumab and adalimumab monotherapy (6). Interestingly, pain reduction doesn’t seem to change if patients are opioid users (7). Therefore, JAKis could help not only to reduce disease activity, but also to modulate pain pathways through direct (IL-6, IL-17, GM-CSF) or indirect (TNF-alpha, IL-1-beta) action on cytokines involved in pain sensitivity (8).

Furthermore, both randomized controlled trials and post-hoc analysis of JAKis in patients with active RA have shown sustained improvements also in fatigue symptoms (9-10). Fatigue is another very common RA symptom having a significant impact on quality of life, even if not directly related with pain and disease activity. The complexity of the fatigue experience in patients with RA, encompassing physical, cognitive, daily living and emotional impacts, can be difficult to be managed (11, 12). Therefore, making a diagnosis remains challenging and it generally takes more than 2 years, thus leading to an important delay of treatment initiation. In addition, defining the most appropriate treatment, individualized for each patient, is complex as well. A single drug able to control every fibromyalgia symptoms is not currently available. Therefore, according to the current guidelines, fibromyalgia treatment must be based on a multimodal approach characterized by pharmacological and non-pharmacological interventions adequately combined in order to improve patients’ symptoms. In particular, treatment should pursue the following goals: minimize pain, improve

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IS-22
Should we treat fibromyalgia with a combined pharmacological approach?

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Introduction. Fibromyalgia is a complex and heterogeneous syndrome characterized by chronic widespread pain as well as a broad spectrum of neuropsychiatric, somatic and dysautonomic disorders. This syndrome is associated with a substantial patient burden, considering that fibromyalgia symptoms are able to negatively influence patients’ daily lives and up to one third of patients are physically disabled and experience a dramatically impaired quality of life. Fibromyalgia patients generally experience poorer health status and report more pain as compared not only to the general population but also to subjects affected by chronic widespread pain syndrome others than fibromyalgia. Consequently, fibromyalgia is also associated with significant health resource use and loss of productivity costs, thus leading to a considerable economic burden either for patients and society. The impact of fibromyalgia on health status, daily function, health resource use and costs also increases with greater syndrome severity. However, there is evidence that early diagnosis and prompt and appropriate treatment can significantly affect the course of this syndrome. If adequately managed and educated, patients with fibromyalgia can improve and are able to live with their disease satisfactorily.

Areas covered. To date, diagnosis of fibromyalgia is still clinical due to the lack of reliable biomarkers or specific laboratory alterations available. Therefore, making a diagnosis remains challenging and it generally takes more than 2 years, thus leading to an important delay of treatment initiation. In addition, defining the most appropriate treatment, individualized for each patient, is complex as well. A single drug able to control every fibromyalgia symptoms is not currently available. Therefore, according to the current guidelines, fibromyalgia treatment must be based on a multimodal approach characterized by pharmacological and non-pharmacological interventions adequately combined in order to improve patients’ symptoms. In particular, treatment should pursue the following goals: minimize pain, improve

Clinical and Experimental Rheumatology 2022 9
sleep, treat mood disorders and mitigate fatigue. Pharmacotherapy should be considered for those with more severe pain or sleep disturbances. Drugs that have proved most effective are centrally acting medications, such as antidepressants and anticonvulsants, but other possible treatment options are under investigation. Regarding pharmacological treatment, the potential superior effect of combined pharmacotherapy upon monotherapy remains a matter of debate mainly due to the absence of clear evidence supporting or refuting this approach. However, none of the currently available drugs are fully effective against the whole spectrum of fibromyalgia symptoms, in clinical practice, it often becomes inevitable to provide a combined pharmacological treatment, especially in presence of more severe pain or sleep disturbances. Regarding pain and sleep modulation, it is known that several concurrent neural mechanisms play a role, providing a strong rationale for combination pharmacotherapy. This approach is based on the hypothesis that combining two or more, in drugs with different molecular mechanisms of action could provide additive or synergistic effects, thus ameliorating treatment outcomes. In addition, an improved side effect profile might be noted. The addition of a second drug could directly antagonize the adverse effects of the first drug or the combination of drugs could provide the achievement of more beneficial effects with absolute lower doses, so that overall side-effects are reduced. Nonetheless, overall success rates of pharmacological treatments remain modest and only a minority of patients continue taking medication, often discontinuing them due to either lack of efficacy or development of side effects. Therefore, effective therapeutic options, able to provide a satisfactory management of this syndrome, remain an evident unmet need.

**Expert opinion.** Establishing an individualized, tailored-to-patient treatment is fundamental for fibromyalgia syndrome and it is important that patients’ management follows a multimodal and multidisciplinary approach. Pharmacological strategy should be considered, in addition to non-pharmacological treatment, only in presence of severe and difficult to treat symptoms. A step-by-step approach could be applied. First step should be mono-therapy and single medication choice should be based on patients’ clinical features and side effect profile. According to patients’ response, the medication dose could be gradually increased but it concurrently increases the risk of developing side effects. Therefore, in case of lack of efficacy or dose limiting side effects, a combined pharmacotherapy approach could be taken into account. However, maximizing clinical effectiveness of combination pharmacotherapy could be useful in order to adequately balance beneficial and adverse interactions between the co-administered treatments.

In conclusion, combination pharmacotherapy for treatment of more severe form of fibromyalgia remains an important but limited studied strategy. Further research on the best specific drug combinations is needed, due to the paucity of evidence currently available on this topic.

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Oxygen-ozone therapy is widely used as complementary therapy for inflammatory rheumatic diseases. The main actions of ozone inherent in inflammatory rheumatic diseases are analgesic, anti-inflammatory and antioxidative effects, activation of cellular metabolism, induction of the synthesis of antioxidant enzymes and improving tissue vasodilation and stimulation of angiogenesis. In fibromyalgia, this therapy is safe and free of significant adverse effects. In addition to the regulation of oxidative stress of peculiar in fibromyalgia is the induction and release of hormones and neurotransmitters, these effects induce a state of well-being, decrease widespread pain fatigue and cognitive fog.

**Conclusion.** Oxygen-ozone therapy is widely used as complementary therapy for inflammatory rheumatic diseases. The main actions of ozone inherent in inflammatory rheumatic diseases are analgesic, anti-inflammatory and antioxidative effects, activation of cellular metabolism, induction of the synthesis of antioxidant enzymes and improving tissue vasodilation and stimulation of angiogenesis. In fibromyalgia, this therapy is safe and free of significant adverse effects. In addition to the regulation of oxidative stress of peculiar in fibromyalgia is the induction and release of hormones and neurotransmitters, these effects induce a state of well-being, decrease widespread pain fatigue and cognitive fog.
es to treat resistant epilepsy in children (6). Metabolized via the cytochrome P450 enzyme system, CBD has theoretical potential for drug-drug interactions with antidepresants, anticoagulants and anti-epileptic agents. CBD is unfortunately not regulated and is manufactured by the cottage industry worldwide without regulatory oversight of quality of product, absence of contaminants or additives (especially THC) and accuracy of labelling. It is therefore recommended that patients access CBD from a provider with the certificate of Good Manufacturing Practice, avoid use by inhalation, and begin with a low daily dose in the order of 2-3 mg/day with gradual up titration. When CBD is used as a therapeutic agent, clinical care should be provided by the healthcare team and not cannabis dispensary staff. To counterbalance the vigorous marketing of CBD as a “wellness” product, patients should be fully informed of the current scientific evidence for both positive and negative effects.

References

IS-28
The role of glucocorticoids on chronic inflammatory pain
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PAIN represents mainly a circadian symptom in chronic inflammatory/immune mediated rheumatic conditions, as expression of the night neuroendocrine biochemistry of the inflammatory process (production of cytokines and other inflammatory mediators)
The use of the chronotherapy with glucocorticoids (GCs), for long-term treatment, optimize the replacement therapy of the exogenous GCs in chronic immuno-mediated diseases and induce a clear morning relief of the circadian PAIN and related symptoms
In addition, the circadian approach with treatment of chronic inflammation by acting on its pathophysiological causes, should be synergized by such modality (treatment efficacy) also with NSAIDs.

Chronic pain in fibromyalgia do not seem to get any advantage by long term treatment with GCs, even by considering the ratio efficacy/safety that might further limit such therapeutic approach in a non inflammatory condition

References

IS-29
The Brazilian experience
Caren Cunha
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Fibromyalgia has a worldwide presence affecting nearly 1 in 20 people globally. And for most fibromyalgic patients, it’s still a stigmatized and invisible disorder, hardly recognized by physicians, especially in public health systems.

Brazil is the only country in the world with more than 100 million inhabitants to have a universal health care system (SUS). 71% of the 210 million Brazilians depend on this government-maintained health system. Even so, 57.9% of all health expenditures come from private sources (2014 data).

For those who can choose an expert able to properly propose a treatment for fibromyalgia, it’s a little bit easier to face this disease. But for most citizens, the opportunity to seek a better quality of life is still lacking.

In that case, patient associations such as ANFIRO (Brazil) and LIBELLLA LIBERA (Italy) play an important role in the search for better public policies.

IS-30
Why are Patients Associations so important both for doctors and patients?
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Patient associations are non-profit organizations of social utility that represent and support the needs of patients (1). Their main role is to provide a correct diagnostic, therapeutic and assistential approach to patients by creating a network between doctors but also between doctors and patients. Physicians who take care of a chronically ill patient must also take into account his/her wellbeing. In this he/she can find considerable help from associations that carry out an action of solidarity with patients, supporting and guiding them in the difficult path of managing the disease.

It is therefore important to create a dialogue between the two parties, which includes respect for roles and absence of prejudices. Physicians must raise awareness of the importance of associations, must inform them of their existence and instruct patients to contact them. Conversely, volunteers must develop projects and activities for patients, whilst volunteers must acquire knowledge and skills. Associations can support training of healthcare professionals, support research by raising funds for scientific studies but also collaborate in study projects. They may deal for example with the recruitment of patients, the collection of feedbacks and the organization of the intervention. Associations work for prevention and listen to patients, which physicians cannot guarantee, and above all they offer health education, they help the patient to be aware both of the disease and of his/her potential to deal with it, helping he/she to become less dependent on the physician. Associations participate in health policies by soliciting interventions and participating in institutional discussions. They defend the rights of patients, support their families and through constant dialogue with the media, inform patients and fight against fake news that have a negative impact on social media (2).

Aisudy (Italian Association of Fibromyalgia Syndrome), which was born in 2005 in Milan, but operates throughout the national territory, is doing all of this. It is a clear example of collaboration between physicians and associations, in fact the local sections are made up of patient volunteers and healthcare professional volunteers. It is doing a great job both for medical and social care. An example is Fibromyapp, an app for remote monitoring and remote support of patients. Doctors and associations together can contribute to the humanization of care and the transformation of welfare, by being among and next to people, not above them (3, 4).

References
altered muscle contraction, highlighted by the muscle fatigue. This has been done starting from the opposite: if pain precedes the cause of muscle fatigue: pain directly affects movements as well as in the point of view of muscle function (sEMG) improved with a statistically significant improvement of pain. The overall data suggesting that it could be the altered muscle contraction, highlighted by the muscle fatigue parameters in the sEMG, that precedes the development of muscle pain and not vice versa. This hypothesis must be verified on a more robust sample but could be the altered muscle contraction, highlighted by the muscle fatigue and neuromuscular efficiency before and after treatment. The results of this trial were not of immediate interpretation. In fact, the group from the data so far presented in literature, the problem should not be posed in this dualism: central vs peripheral, but rather where the decoupling between sensory afferents and motor command failed in the sensor-motor chain. sEMG is capable of discriminating whether the fatigue phenomenon is central (motor control deficit) or peripheral (muscle pathology) in relationship to a given task where the task can be cognitive or physical (Casale et al. 2019; Brustio et al. 2019).

The muscle is in fact a “station” of the sensor-motor circuit that allows us to carry out actions that are congruent with the motor task required (playing piano or running a marathon). This process requires not only a sensory evaluation (physical parameters such as weight, duration, distance, etc.) but also a more complex evaluation that we can summarize as a “cognitive understanding” of why and what our movement is for. All this information allows the CNS to develop an adequate motor strategy that will be monitored moment by moment during the entire movement in what is called sensor-motor integration. Any alteration in one of these points of the system (the muscular and extramuscular sensory afferents - the central sensor-motor integration - the “understanding of the task” - the motor command - ) can induce an aggressive derailment of the system, inducing an inadequate motor response to the task and as an extreme consequence the onset of muscle fatigue and pain. In other words, the process that leads to muscle pain and fatigue in fibromyalgia can be both top-down and bottom-up depending mainly on psychological as well on entirely physical stress (Casale & Rainoldi 2011). It was interesting to highlight how the fibromyalgia subject behaves like a oldest-old from the point of view of muscle fatigue using mainly type II fibers, even if in this study the average age of the patients was very low. This recruitment mechanism is absolutely non-physiological, not respecting Henneman’s principle of muscle recruitment (Casale et al. 2011) with a very low neuromuscular efficiency (NME). NME could be considered an estimate of the force produced per unit of EMG amplitude (Van der Hoeven et al. 1993). In practice, an individual who are capable of producing greater muscle force with lower fiber activation are considered to be more efficient. For this perspective a fibromyalgic patient is highly non-efficient. These data are of pivotal importance not only for understanding the genesis of fatigue (top-down or bottom-up) but also and above all for a correct setting of motor recovery which therefore should not be set up for a recovery of strength or endurance but rather a recovery of what a normal muscle recruitment should be with a recruitment mechanism that is absolutely non-physiological, not respecting Henneman’s principle of muscle recruitment. If, at least in the main lines, it is possible to avoid the chicken-egg problem- that is whether the genesis of fatigue and muscle pain is central or peripheral-, there remains another question that is not completely irrelevant. In fact, in some scientific literature there is a tendency to consider pain as the cause of muscle fatigue: pain directly affects movements as well as indirectly activating a pathological mechanism of compensation that leads to a spread of fatigue in other muscles.

We therefore asked ourselves if and to what extent pain preceded muscle fatigue. This has been done starting from the opposite: if pain precedes the development of muscle fatigue then a reduction in pain should precede or at least be contemporary to the normalization of muscle activity. In a proof-of-concept study a small group of patients (14 FM 12 f, 2 m; age 45.3±11.1), the development of fatigue in term of neuromuscular efficiency was studied on the biceps brachii of the dominant side at 30% and 60% of the maximal voluntary contraction (MVC). Clinically fatigue was evaluated by means of the Fibro Fatigue Scale (FFS) and pain was evaluated using the McGill Pain Questionnaire (MPQ). Patients were treated with a central analgesic (17.5 µg/h buprenorphine patches for 9 days) and assessed for pain, fatigue and neuromuscular efficiency before and after treatment. The results of this trial were not of immediate interpretation. In fact, the group from the point of view of muscle function (sEMG) improved with a statistically significant trend of muscle contraction towards normality with an improvement in neuromuscular efficiency parameters. However, as expected, this improvement in neuromuscular efficiency was not matched with a statistically significant improvement of pain. The overall data suggesting that it could be the altered muscle contraction, highlighted by the muscle fatigue parameters in the sEMG, that precedes the development of muscle pain and not vice versa. This hypothesis must be verified on a more robust sample but which, if confirmed, would open new and interesting ways of using drugs as well as controlling pain through movements.

References
This study enrolled 142 adult male patients with FM, diagnosed...
O-03
Sleep study findings in fibromyalgia and obesity
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Background. Sleep disturbance is a prominent symptom and the co-morbidity of Obstructive Sleep Apnea (OSA) in FM patients has been identified. Rapid Eye movement (REM) sleep loss is associated with hyperalgesia, suggesting sleep abnormalities and pain perception are related. REM sleep loss is associated with increased obesity. Increased REM sleep correlates to improved health, with most individuals averaging 70 min per night. By better understanding how sleep abnormalities affect pain perception and weight gain, we can effectively treat FM patients.

Objectives. Sleep study analysis will show decreased REM sleep in FM and correlate with obesity.

Methods. For this IRB-approved retrospective chart review, EPIC charts were reviewed using ICD codes to identify FM patients diagnosed with OSA between 2012-2018. Polysomnography tests results were reviewed for Stage R (REM) latency, Stage R duration and % REM total sleep time (TST), Total Apnea-Hypopnea Index (AHI), Non Rapid Eye Movement (NREM) AHI, and REM eye movement (REM) AHI. Data on weight and body mass index (BMI) were gathered from demographics.

Results, N=118. Mean age 53.8 years, female (88%), male (12%), mean weight 223.3 lb, mean BMI 37.6. Sleep studies, mean Stage R latency 140.7 minutes, mean Stage R duration 44.2 minutes, mean Stage R % TST 13.5%. Total AHI mean 21, NREM AHI mean 17.8, and REM AHI mean 27. Results show decreased REM duration, decreased REM % TST, and increased BMI.

Conclusions. Results from our pilot study identify an important relationship between decreased REM sleep and obesity in FM.

O-04
Prevalence of fibromyalgia syndrome in a cohort of patients with inflammatory bowel disease
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Background. Fibromyalgia (FM) is a common chronic disorder characterized by widespread pain, fatigue, sleep disturbances and functional symptoms, reaching a prevalence of 2-3% worldwide.

Objectives. To assess the prevalence of FM in a cohort of patients with inflammatory bowel disease (IBD).

Methods. Consecutive patients with IBD were enrolled from August to November 2021. Patients with severe disease activity according to the Crohn’s disease activity index and to the Mayo score for UC, or with other concomitant chronic diseases were excluded. Clinical and demographic data were collected. FM was diagnosed according to 2011 ACR classification criteria by an expert rheumatologist. Mann-Whitney test, chi-square test, and Student t test were used for statistical analyses.

Results. 196 IBD patients were enrolled (86 female (44%), mean age 50±15 yo), 105 with Crohn’s disease (CD) and 91 with ulcerative colitis (UC). 147 patients were in remission, 35 had low disease activity and 14 moderate disease activity. The overall prevalence of FM in the IBD cohort was 17/196 (8.7%) [95% CI 5.8% – 13.6%], 10 (11.6%) women and 7 (6.3%) men, with a prevalence of 7.6% (8/105) in CD and 9.9% (9/91) in UC. In the table are indicated the characteristics of patients with IBD + FM and IBD alone. No significant demographic and clinical differences between the two groups were detected.

Conclusions. FM is a common disorder especially in patients with other concomitant chronic diseases. This study reported a prevalence of 8.7% in IBD patients without any significant differences between CD and UC.

O-05
The effect of pain catastrophizing subdomains on disease severity levels and presenteeism-related productivity loss in female workers with fibromyalgia
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Objectives. Patients with fibromyalgia (FM) experience a decline in health-related quality of life, which is associated with increased illness severity and impairment of work abilities. Catastrophizing emerges as a highly accurate predictor and correlate of poor pain experience. The purpose of this cross-sectional study is to investigate the mediating role of pain catastrophizing subdomains in unfavorable relationships with disease severity levels and work productivity loss due to presenteeism in women with FM, with the goal of identifying potential new targets for preventive interventions.

Methods. The study used a cross-sectional design and had 232 female patients with FM. American College of Rheumatology (ACR) criteria for di-
The main objective of the present systematic review was to evaluate patients’ employment status. FM patients were grouped into categories, based on their FIQR total score. Logistic regression and receiver operating characteristics (ROC) curve analysis were used to find out which factors were most likely to be linked to presenteeism. The ROC curve analysis used presenteeism as a categorical predictor external variable.

Results. In all, the patients’ ages ranged from 1 to 20 years, with a disease duration of 5.11 (SD 6.0) years. The PCS score was ≥30 in 14/232 patients (26%). 148 of 232 FM patients (63.8%) were employed at the time of the evaluation. 88 patients (59.5%) worked full-time, while 60 (40.5%) worked part-time. The sample’s overall productivity loss was 48.8%. The majority of respondents (74.5%) reported a high degree of presenteeism with an average level of 69.8%. On the other hand, absenteeism was uncommon, with just 3.1% of respondents reporting it. The overall sample’s average level of absenteeism during the previous seven days was 11.6%. On average, among 148 workers, 14% had remission FM, 26% mild FM, 33% moderate FM, 28% severe FM, and 7% extremely severe FM. Presenteeism was associated with increased disease severity and decreased job productivity in FM (Fig 1). The pain catastrophizing scale helplessness domain score (odds ratio: 1.18, 95% CI:1.06–1.31) with an estimated value of 10 points was the factor most substantially associated with presenteeism.

Conclusions. Pain catastrophizing helplessness domain score was the factor most significantly associated with the presence of presenteeism-related productivity loss in FM patients. Overall, our findings have implications for health policy and emphasize the significance of identifying high-risk FM patients by monitoring pain catastrophism as an indicator of presenteeism and severe disease.

Methods. This review was conducted in accordance with Cochrane Collaboration guidelines and PRISMA statements. The selected articles were extracted from PubMed, Scopus and Web of Science databases. The Cochrane Risk of Bias (ROB) tool was used to assess the quality of the selected articles.

Results. Reviewed studies demonstrated using EST alterations in brain regions related to pain and emotional regulation, as well as an attentional bias and higher response time latencies (related to the words’ emotional load) in patients with CP. Further, the attentional bias towards negative information was associated with a greater presence of pain.

Key words. chronic pain, emotional stroop task, brain regions, emotional regulation, attentional bias.

P-01
Exploring emotional stroop task performance in chronic pain patients: a systematic review
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Background. Chronic Pain (CP) is an unpleasant painful sensory and emotional experience that persists more than three months and is often accompanied by symptoms such as depression, fatigue, sleep disturbances, and cognitive impairment. Emotions are known to modulate the experience of pain by influencing cognition and behavior. A useful task to explore emotional processing and emotional dysregulation, and the consequent effect on pain experience, in CP patients is the Emotional Stroop Task (EST).

Objectives. The main objective of the present systematic review was to analyze the recent body of research using EST and evaluating the behavioral performance-associated alterations of specific pain and emotion processing brain regions in CP patients.

Methods. This review was conducted in accordance with Cochrane Collaboration guidelines and PRISMA statements. The selected articles were extracted from PubMed, Scopus and Web of Science databases. The Cochrane Risk of Bias (ROB) tool was used to assess the quality of the selected articles.

Results. Reviewed studies demonstrated using EST alterations in brain regions related to pain and emotional regulation, as well as an attentional bias and higher response time latencies (related to the words’ emotional load) in patients with CP. Further, the attentional bias towards negative information was associated with a greater presence of pain.

Key words. chronic pain, emotional stroop task, brain regions, emotional regulation, attentional bias.

P-02
Changes in postural control after physiotherapy and pain relief in patients with fibromyalgia
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Fibromyalgia (FM) is an idiopathic chronic pathology characterized by wide-spread pain with a prevalence of 2.1% worldwide, and a female/male ratio over 3. A study conducted by our group has shown a beneficial effect of a pressure-controlled mesotherapy protocol for the relief of pain. This work was performed in the context of a longitudinal, non-randomized, experimental analytical study and consisted in a biomechanical evaluation of patients who completed 8 physiotherapy sessions. The biomechanical observational analysis included print amplitude measures, pressure point, balance and center of gravity registrations (before and after the 8 physiotherapy sessions) with the pressure platform and software Podoprint®. The objective was to determine the correlation between postural balance and the degree of disease severity, as well as with the improvements resulting from the treatment. The proposal was to use postural balance as a subordinated triage marker for diagnostic purposes and to monitor patient response to physiotherapy treatment. Interestingly, the biomechanical and postural analysis evidenced quantitative changes, the significance of which is currently under investigation.

P-03
The measurement of fibromyalgia severity: converting scores between the revised Fibromyalgia Impact Questionnaire (FIQR), the Polysymptomatic Distress scale (PSD), and the modified Fibromyalgia Assessment Scale (FASmod)
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Clinical and Experimental Rheumatology 2022
1. Determine TAC in blood samples from FM patients and healthy women.
2. Link TAC with the severity of the disease according to FIQ and SF-36.

Methods: We measure TAC in 40 FM patients and 20 healthy women using the e-BQC device, based on electrochemical oxidation. Healthy women fill SF-36, while patients fill the SF-36 and FIQ.

Results. TAC values are not significantly different between FM patients and healthy women.

Conclusions. The results show that TAC is not a good diagnostic single biomarker for FM patients. In addition, according with the revised Fibromyalgia Impact Questionnaire (FIQ) and SF-36, between others. Among the FM causes, alterations at the mitochondrial level and oxidative metabolism stand out. Therefore, the study of total antioxidant capacity (TAC) offers promising perspectives to understand the disease.

Objectives. The revised Fibromyalgia Impact Questionnaire (FIQ) is a widely used fibromyalgia severity assessment tool that was introduced in 2009 prior to the publication of the American College of Rheumatology (ACR) preliminary fibromyalgia criteria in 2010 and further modified in 2016. In 2020, the modified Fibromyalgia Assessment Scale (FASmod) was published. The Polysymptomatic Distress scale (PSD) and FASmod include assessments of pain location sensitivity and can be used for diagnosis as well as in non-fibromyalgia patients. The aim of this study is to provide equations for the conversion of the FIQ scores to PSD and FASmod as an aid to understanding and sharing fibromyalgia severity information.

Methods. 3089 patients with fibromyalgia, diagnosed according to the ACR 2010/2011 criteria and belonging to the Italian Fibromyalgia Registry completed FIQ, FASmod and PSD questionnaires. Spearman’s rho was used to test the correlations between indices. The least square regression approach was used to produce predictive equations for each scale based on the remaining scales.

Results. FIQ was correlated with PSD (r=0.714) and FASmod (r=0.801); PSD and FASmod showed the best correlation (r=0.897) (Fig. 1 a-b-c-). Predictive equations showing a linear model were effective in producing mean cohort values, but individual predictions deviated substantially, precluding prediction in the individual patient.

Conclusions. Conversion equations that allow for interconversion of multiple scales fibromyalgia severity assessment scales are produced. These can be useful in obtaining mean values for cohorts but are not accurate enough for use in individual patients.

P-04
Could total antioxidant capacity be a good marker for fibromyalgia diagnosis?

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Background. Fibromyalgia (FM) is a disease commonly linked to widespread pain, continuous fatigue and weakness. This condition is diagnosed following the American College of Rheumatology (ACR) criteria combined with Fibromyalgia Impact Questionnaire (FIQ) and SF-36, between others. Among the FM causes, alterations at the mitochondrial level and oxidative metabolism stand out. Therefore, the study of total antioxidant capacity (TAC) offers promising perspectives to understand the disease.

Objectives.
1. Determine TAC in blood samples from FM patients and healthy women.
2. Link TAC with the severity of the disease according to FIQ and SF-36.

Methods: We measure TAC in 40 FM patients and 20 healthy women using the e-BQC device, based on electrochemical oxidation. Healthy women fill SF-36, while patients fill the SF-36 and FIQ.

Results. TAC values are not significantly different between FM patients (15.79±6.53) and healthy volunteers (15.36±6.20). However, they correlate positively with the score obtained in SF-36, being stronger in the control group (68.4±21.15) than in the FM patients (31.78±19.83).

Conclusions. The results show that TAC is not a good diagnostic single marker to detect patients with Fibromyalgia. In addition, according with TAC results, the values of the health questionnaires showed a stronger correlation with the controls than with the patients. These values may be influenced by factors such as pharmacology, involved in antioxidant levels. However, the speed and reproducibility of the method allow it to be established as a routine in our laboratory. The validity of TAC as a monitoring biomarker for FM patients should be evaluated.

P-05
Link between central and autonomic nervous alterations in fibromyalgia patients

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Background. Fibromyalgia syndrome (FM) has been associated with central pain sensitization, autonomic alterations and neuropathy in small nerve fibers, supporting the alterations in central and autonomic nervous systems in this chronic pain condition.

Objectives. To examine the association between central pain sensitization and altered autonomic activity in FM.

Methods. Fifty-four FM patients and 22 healthy women were assessed by a slowly repeated evoked pain (SREP) protocol, as a measure of central sensitization to pain, and by skin conductance (SC) as a sympathetic autonomic measure secondarily indexing possible small nerve fiber peripheral neuropathy. Antidepressant medication and pain catastrophizing were considered as potential confounding variables.

Results. FM patients displayed lower SC and higher SREP and catastrophizing levels than healthy controls. SC was inversely associated with...
SREP sensitization, which persisted after statistically controlling for levels of catastrophizing and antidepressant use. Regression analyses confirmed that SC levels predicted SREP sensitization.

Conclusions. These results propose that central pain sensitization processes involved in the pathophysiology of FM could be related to alterations of sympathetic activity in the sweat glands, suggesting small nerve fiber neuropathy or reduced fiber density. Further studies should replicate these findings by using other central pain sensitization measures and more direct measures of neuropathy (e.g. distal electrochemical SC, quantitative sudomotor axon reflex testing or skin biopsies).

P-06
Effect of vitamin B12 on the symptom severity and psychological profile of fibromyalgia patients; a prospective pre-post study
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Background. Fibromyalgia (FM) as a prototypical nociceptive pain condition displays a difficult therapeutic situation in many cases. The promising data on the effect of vitamin B12 in improving pain and cognitive functions in various nociceptive pain conditions has been reported.

Objectives. We aimed to determine the efficacy of 1000 mcg daily dose of oral vitamin B12 on the symptom severity and psychological profile of FM patients.

Methods. This open-label, pre-post study was performed on FM patients whose diagnoses were confirmed by a rheumatologist based on the 2016 American College of Rheumatology (ACR). Patients were instructed to take a daily dose of 1000mcg vitamin B12 for fifty days. Outcome measures including the Revised Fibromyalgia Impact Questionnaire (FIQR), Hospital Anxiety and Depression Scale (HADS), 12-item Short-Form health survey (SF-12), and pain Visual Analog Scale (pain-VAS) were fulfilled by patients before and after the treatment.

Results. Of 30 eligible patients, 28 patients completed the study protocol. Patients were female with a mean age of 47.50 ±8.47 years. FIQR scores in all domains improved significantly after treatment (total FIQR: 49.8±21.86 vs 40.0±18.36, p-value 0.01; function:13.17±7.33 vs 10.3±5.84, p-value: 0.01; overall: 10.32±6.22 vs 8.25±6.22, p-value: 0.03; symptoms: 26.30±10.39 vs 21.44±8.58, p-value 0.01). Vitamin B12 also improved anxiety scores from 9.33±4.30 to 7.70±3.60, p-value: 0.01. Depression, pain-VAS, and SF-12 didn’t improve following the treatment. The Generalized estimating equations (GEE) analysis showed the improvement in total FIQR score was not cofounded by the improvement of anxiety and patients’ baseline characteristics.

Conclusions. This study showed a short course of sublingual vitamin B12, 1000 mcg daily, significantly improves the severity of FM and anxiety score. We postulate that vitamin B12 has a strong potential to consider, at least, as adjunctive therapy of FM.

P-07
Common-sense model of self-regulation to cluster fibromyalgia patients: results from a cross-sectional study in Italy
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Objectives. Fibromyalgia is a severe and disabling chronic pain syndrome affecting millions of people worldwide. Various patients’ subgroups were identified using different atheoretical measures, hardly effective to tailor treatments. Previous literature findings showed the relevance of fibromyalgia patients’ illness perceptions in adjusting to the disease. The present study aims to identify clusters of fibromyalgia patients based on their illness perceptions and investigate whether they can differ across pain, mood, physical functioning, catastrophizing, and pain acceptance measures.

Methods. Fifty-three newly referred fibromyalgia patients completed clinical and psychological questionnaires. Patients’ subgroups were created by applying hierarchical cluster analysis to their answers to Illness Perception Questionnaire-Revised subscales. Potential differences across subgroups in outcome variables were tested.

Results. Cluster analysis identified two patient groups. Group A (32 patients) had a higher representation of fibromyalgia as a chronic disease with severe consequences, lower beliefs in personal and treatment control, and a higher fibromyalgia-related emotional distress than group B (21 patients). Clusters did not differ on pain intensity and duration. Group A, compared to group B, showed worse physical functioning and overall impairment due to fibromyalgia, a poorer psychological condition, a higher tendency to catastrophize, and less pain acceptance.

Conclusions. Study findings reveal two fibromyalgia subgroups differing in emotional suffering and impairment despite similar pain intensity and duration. Patients’ illness perceptions and attitudes towards pain, like catastrophizing and acceptance, might be critical in adjusting to the disease. A detailed assessment of such risk and protective factors is critical to differentiate patients’ subgroups with different needs and thus offering tailored treatments.

Key words. fibromyalgia, self-regulation, illness perception, catastrophizing, acceptance, cluster analysis

P-08
Randomized controlled trial of a new neuromodulation device in fibromyalgia patients
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Background. Fibromyalgia is a complex syndrome characterized by chronic widespread pain, sleep disturbances, fatigue, and cognitive dysfunction. A non-drug therapeutic solution based on a wristband that emits millimeter waves and a therapeutic coaching program was developed. The application of millimeter waves on an innervated area leads to neuromodulating effects, due to endorphin release and parasympathetic activation. Coaching intends to improve patient adherence to the technology and increase compliance and effectiveness of the treatment.

Objectives. Following the first positive feedback from users, we wish to demonstrate the effectiveness of this solution in improving the quality of life of fibromyalgia patients. The impact on sleep disorders, anxiety and pain levels is also investigated.

Methods. Patients are randomized into two groups. The Immediate group has access to the solution just after randomisation in addition to standard care, while the Delayed group has access to standard care and waits for 3 months before receiving the solution. The solution consists in using the device for three sessions of 30 minutes per day and four coaching sessions spread over the first two months of wristband usage. The effectiveness of the solution is evaluated by the improvement of the quality of life measured through the Fibromyalgia Impact Questionnaire after 3 months.

Results. All 170 patients are included, and follow-up is underway. Results are expected for September 2022.

Conclusions. In this randomized clinical trial, we expect to confirm the effect of the integrative approach based on endorphins stimulation and therapeutic education in nociceptive pain, and specifically for patients suffering from fibromyalgia.
Correlations between fibromyalgia and dizziness: preliminary results from a questionnaire study

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Background. Fibromyalgia (FM) is a puzzling central pain processing disorder. It comprises a wide range of symptoms, including dizziness. Objectives. We aimed to establish a prevalence rate of vestibular symptoms within a confirmed FM population group compared to healthy controls. We also evaluated the nature of the vestibular symptoms and their correlation with pain, cognitive, behavioral, and emotional dysfunctions. Methods: FM patients and matched controls were enrolled in an online survey. Information regarding socio-demographics, general symptoms, diagnosis, etc. was collected and specific validated questionnaires were used to assess the type of pain (painDETECT), the perceived vestibular symptoms (Dizziness Handicap Inventory-DHI), Situational Vertigo Questionnaire-SVQ, and the cognitive and behavioral management (CBA-H) in FM patients. Statistical analysis was performed with the software R.

Results. 357 participants completed the questionnaire (277 FM patients and 80 controls). The DHI and SVQ scores revealed a higher incidence of altered vestibular perception in FM patients with respect to controls (p = 0.001), despite only 5.6% of FM patients reported a previous vestibular diagnosis. The DHI score revealed a tendency for high dizziness handicap in FM patients, which was positively correlated with the presence of neuropathic/central pain. The most significant DHI/CBA-H correlations pertained to depressive mood and reactions, interpersonal difficulties, and an inability to relax.

Conclusions. Vestibular symptoms are significantly present in FM patients. The nature of dizziness seems to be more centrally than peripherally based. Further assessment is needed to understand how the central processing dysfunctions involved in FM pain might also affect vestibular multisensory integration.

Influence of regular physical exercise on the psychological state and life quality of fibromyalgia patients

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Background. It has been demonstrated that regular physical exercise (RPE) improves the life quality of patients with fibromyalgia (FM). However, the influence of Chronic Fatigue Syndrome (CFS) co-morbidity on this aspect remains unknown.

Objectives. To assess how CFS co-diagnosis affects the performance of RPE by FM patients and how RPE influences the psychological state of these patients with or without CFS diagnosis, majority with no time limit.

Methods. In a group of FM patients, with (FM+CFS group) or without CFS (FM group), using as reference a control group of women in the same age range. For this purpose, scientifically validated questionnaires were used, including those assessing painDETECT, the perceived vestibular symptoms Dizziness Handicap Inventory-DHI, Situational Vertigo Questionnaire-SVQ, and the cognitive and behavioral management (CBA-H) in FM patients. Statistical analysis was performed with the software R.

Results. 357 participants completed the questionnaire (277 FM patients and 80 controls). The DHI and SVQ scores revealed a higher incidence of altered vestibular perception in FM patients with respect to controls (p = 0.001), despite only 5.6% of FM patients reported a previous vestibular diagnosis. The DHI score revealed a tendency for high dizziness handicap in FM patients, which was positively correlated with the presence of neuropathic/central pain. The most significant DHI/CBA-H correlations pertained to depressive mood and reactions, interpersonal difficulties, and an inability to relax.

Conclusions. Vestibular symptoms are significantly present in FM patients. The nature of dizziness seems to be more centrally than peripherally based. Further assessment is needed to understand how the central processing dysfunctions involved in FM pain might also affect vestibular multisensory integration.

Influence of co-diagnosis of chronic fatigue syndrome on the psychological state and life quality of fibromyalgia patients

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4Nursing Department, Faculty of Medicine and Health Sciences, University of Extremadura, Spain.

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Objectives. To assess how CFS co-diagnosis affects the performance of RPE by FM patients and how RPE influences the psychological state of these patients with or without CFS diagnosis, majority with no time limit.

Methods. In a group of FM patients, with (FM+CFS group) or without CFS (FM group), using as reference a control group of women in the same age range. For this purpose, scientifically validated questionnaires were used, including those assessing painDETECT, the perceived vestibular symptoms Dizziness Handicap Inventory-DHI, Situational Vertigo Questionnaire-SVQ, and the cognitive and behavioral management (CBA-H) in FM patients. Statistical analysis was performed with the software R.

Results. 357 participants completed the questionnaire (277 FM patients and 80 controls). The DHI and SVQ scores revealed a higher incidence of altered vestibular perception in FM patients with respect to controls (p = 0.001), despite only 5.6% of FM patients reported a previous vestibular diagnosis. The DHI score revealed a tendency for high dizziness handicap in FM patients, which was positively correlated with the presence of neuropathic/central pain. The most significant DHI/CBA-H correlations pertained to depressive mood and reactions, interpersonal difficulties, and an inability to relax.

Conclusions. Vestibular symptoms are significantly present in FM patients. The nature of dizziness seems to be more centrally than peripherally based. Further assessment is needed to understand how the central processing dysfunctions involved in FM pain might also affect vestibular multisensory integration.

The Lord of the entities is One entity: suggesting a mechanism for “fibromyalgia” & “functional-psychosomatic-syndromes”

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Background. “Fibromyalgia” is a prevalent and misunderstood condition with significant burden and morbidity. Patients suffer immensely. For some reason treatments are unsatisfying. Current theories over- rely on psychological, “central sensitization” and biopsychosocial theories describe this disease as the misfortunate fate of traumatized and stressed individuals that have behavioral, cognitive, social, and/or genetic predisposition for an “infinite positive-feedback of pain with no peripheral organic lesion/injury”. Diagnostic criteria seem biologically arbitrary.

Objectives. This work offers a theoretical model with an organic mechanical mechanism to help explain “fibromyalgia” and “functional-psychosomatic syndromes”, based on cross-disciplinary empirical studies.

Methods. Systematically searched multiple phrases in MEDLINE, EMBASE, COCHRANE, PEDro, and medRxiv, majority with no time limit. Inclusion/exclusion based on title/abstract, then full text inspection. Additional literature added on relevant side topics in a scoping search. Review follows PRISMA-ScR guidelines. 831 records included.

Results. Coined “facial armoring” (Pfaut, 2022) i.e., myoblast-gener-ated-tensility-tension, these functional-psychosomatic syndromes may be one non-inflammatory non-autoimmune disease of connective-tissue that involves mechanical compression. “Facial-armoring” may explain fibromyalgia’s pain, distribution of pain, decreased pressure pain threshold,
tender spots, chronic fatigue, cardiovascular and metabolic abnormalities, autonomic abnormalities, absence of clear inflammation, silent imaging investigations, somatic symptoms, overlap with other psycho/somatic/non-specific/functional disorders, and other phenomena (e.g., complete resolution after surgery). Unhealthy lifestyle is suggested to be a major contributor to "psychosomatic" diseases, especially in genetically predisposed individuals such as those with hypermobility syndrome.

**Conclusions.** Functional/"non-specific"/"psychosomatic" conditions share a common rheuma-psycho-neuro-mechanical mechanism. "Fibromyalgia" is a mild-moderate-chronic-compartment-like-syndrome of the whole body. Early detection is key. The body and the mind are One.

**P-13**

Proprioception in patients with fibromyalgia and chronic fatigue syndrome: a systematic review

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**Background.** Previous research found impairments in postural balance and proprioception in individuals with fibromyalgia (FM) and chronic fatigue syndrome (CFS). Both constructs can be associated with proprioception, making the latter an interesting topic for further research. Moreover, an understanding of the extent and nature of proprioceptive impairments in FM and CFS is needed to identify target points for rehabilitation.

**Objectives.** To investigate the evidence for impairments in proprioception in individuals with FM and CFS and analyse differences with healthy controls.

**Methods.** Observational case-control studies that compared proprioception between patients with FM or CFS and healthy controls were selected (databases: PubMed, MEDLINE, and Web of Science). Six studies (n=422 participants) met the criteria. Data were extracted for population characteristics, diagnoses, and proprioceptive outcome measures, including study results.

**Results.** All studies applied a limb or trunk repositioning task and reported the mean positioning error as the outcome of proprioceptive performance. FM patients showed impairments in trunk-related proprioception (p < 0.005), but not in knee, shoulder, or upper limb reposition sense compared to healthy controls.

**Conclusions.** Evidence suggests trunk-related impairments may be present and relevant to the frequently reported postural imbalances in this population. However, the overall body of evidence after applying the GRADE approach was very low and further research using higher quality designs and procedures would be needed to establish strong data-based conclusions.

**P-15**

Validity of the Central Sensitization Inventory compared with traditional measures of disease severity in fibromyalgia

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**Objectives.** The goal of the present study was to explore additional evidence of convergent and discriminant validity of the Central Sensitization Inventory (CSI) in a large sample of subjects with fibromyalgia (FM).

**Methods.** Patients were consecutively enrolled for a cross-sectional assessment comprehensive of three FM-specific measures (the revised Fibromyalgia Impact Questionnaire [FIQR], the modified Fibromyalgia Assessment Status [modFAS], and the Polysymptomatic Distress Scale [PDS]) and of CSI. To test the convergent validity, the Spearman’s rho was used to measure the degree of correlation between the variables CSI and the FM-specific measures. To assess discriminant validity, CSI scores were grouped according to FIQR disease severity states, and differences between these groups studied with the Kruskal-Wallis test. Interpretative cut-offs were established with the interquartile reconciliation approach.

**Results.** The study included 562 FM patients, 199 (35.4%) were classified as having central sensitization syndrome (CSI ≥40). CSI was largely correlated with modFAS (r = 0.580; p<0.0001), FIQR (r = 0.542; p<0.0001), and PDS (r = 0.518; p<0.0001) and CSI cut-offs proposed for FM: 21 between remission and mild severity, 30 between mild and moderate severity, 37 between moderate and severe disease, and 51 between severe and very severe disease.

**Conclusions.** The current study successfully showed additional evidence of the convergent and discriminant validity of the CSI in FM patients.

**Key words.** fibromyalgia; Central Sensitization Inventory; central sensitization syndrome; psychometric validation; chronic pain.

**P-16**

Use and efficacy of medical cannabis in fibromyalgia patients in Malta

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**Background.** Fibromyalgia is a chronic health condition that is characterized by widespread musculoskeletal pain commonly comorbid with other symptoms such as mood disturbance, insomnia, fatigue, and cognitive problems. Due to the multi-faceted nature of this condition, treatment of Fibromyalgia has had limited success, and this underlines a need for alternative therapies. The cannabis plant has been used for healing for millennia, and recently more evidence is indicating a role for cannabis in modern medicine.

**Objectives.** The objectives of this study were to characterize of medical cannabis in Maltese Fibromyalgia sufferers and to investigate the effect of the use of cannabis on the symptoms of fibromyalgia.
medical cannabis therapy on pain, sleep quality, anxiety, functionality, and quality of life in Fibromyalgia.

**Methods.** In this study, 15 Fibromyalgia patients were asked to self-report the severity of their Fibromyalgia and co-morbid symptoms before, 1 month and 3 months after starting medical cannabis therapy. Seven validated questionnaires were used to classify the patients’ condition within the following domains: pain intensity, sleep quality, anxiety levels, fatigue, pain self-efficacy, quality of life and functionality. The patients were also asked to characterize their medical cannabis use, and questioned on societal attitudes towards medical cannabis use, notably after the recent legalization of recreational cannabis in Malta.

**Results.** The results show a significant global improvement in patients’ condition throughout all domains within the timeframe studied with minimal adverse effects.

**Conclusions.** Medical cannabis shows great promise in the treatment of Fibromyalgia. Nevertheless, more work in this field is needed to shed light on the suitability of this novel therapy.

**P-17**

**Altered quality of life in patients with inflammatory bowel disease and concomitant fibromyalgia**

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**Background.** Fibromyalgia (FM) can present as a comorbidity in patients with chronic disease.

**Objectives.** To assess the impact of FM on the quality of life of patients with inflammatory bowel disease (IBD).

**Methods.** Consecutive patients with IBD were enrolled from August to November 2021. Patients with severe disease activity according to the Crohn’s disease activity index and to the Mayo score for UC were excluded. Patient Reported Outcomes (PROs) (Widespread Pain Index (WPI), Symptom Severity Score (SSS), IBD Questionnaire (IBD-Q), Depression anxiety stress scales-21 (DASS-21), Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F), Impact of event scale-revised (IES-R), Pittsburgh Sleep Quality Index (PSQI)) were collected. FM was diagnosed according to 2011 ACR classification criteria by a rheumatologist. Mann-Whitney test, chi-square test, and Student t test were used for statistical analyses. A multivariate analysis was performed to estimate the effect of independent variables on patients’ quality of life (IBD-Q).

**Results.** 196 patients were enrolled (86 female (44%), mean age 50 ± 15 yo), 105 with Crohn’s disease (CD) and 91 with ulcerative colitis (UC). 147 patients were in remission, 35 had low disease activity and 14 moderate disease activity. Difference in PROs between the 2 groups (IBD and IBD + FM) are seen in the figure.

The variables influencing the quality of life were disease activity (p 0.0256), chronic fatigue (p 0.0061) and sleep disturbances (p 0.0440), for CD; while for UC the only variable that correlate with IBD-Q was disease activity (p 0.0129).

**Conclusion.** FM in IBD can have a considerable impact on quality of life and on measures of disease severity.

**Fig. 1.** Scatterplot with linear regression lines displays the relationship between (A) modFAS vs CSI, (B) FIQR vs CSI, and (C) FDS vs CSI score.

**Figure.** IBD-Q: inflammatory Bowel Disease Questionnaire; DASS-21: Depression anxiety stress scales-21; FACIT-F: Functional Assessment of Chronic Illness Therapy-Fatigue; IES-R: Impact of event scale-revised.
# Author Index

**A**
- Ablin Jacob N. IS-04, IS-16
- Adawi Mohammad IS-12
- Aliotti Alessandra IS-13
- Allegretti Marcello IS-10
- Aloush Valerie IS-02
- Amaro Diaz Lidia P-01
- Amral Daniela IS-12
- Ardizzone Sandro O-04, P-17
- Atzeni Fabiola IS-13, IS-17, IS-21, P-03

**B**
- Balba Nadir O-01
- Batticciotto Alberto IS-17, IS-21
- Bazzichi Laura IS-08, IS-24, P-03
- Benucci Maurizio IS-17, IS-21
- Bianchi Gerolamo P-03
- Boccella Serena IS-10
- Bogaerts Katleen P-13
- Bonastre Férez Javier P-02
- Bongiovanni S. IS-17, IS-21, P-07
- Bosson Jean-Luc P-08
- Brandolini Laura IS-10
- Browne Cherylea J. P-09
- Burlando Bruno P-09
- Butler Matthew O-01

**C**
- Casale Roberto IS-31
- Chakraborty Shitadhi O-03
- Chen Wen IS-12
- Choy Ernest IS-17, IS-21
- Clauw Daniel J. IS-03, IS-25
- La Paglia Giuliana M.C. P-17
- Cotán David P-04
- Crouzier David P-08
- Cunha Caren IS-29
- Cutolo Maurizio IS-28, P-03

**D**
- Dagna Lorenzo O-05
- de la Coba Pablo P-05
- Dell’Era Alessandra O-04, P-17
- Demorii Ilaria P-09
- Di Carlo Marco IS-05, IS-14, O-02, O-05, P-03, P-15
- Di Franco Manuela P-03, P-07, IS-22
- Di Giovanni Giuseppe P-16
- Damolard Anne P-08
- Durán-González Elena P-04

**F**
- Fabio Giuseppe IS-30
- Falaguera Vera Francisco IS-02
- Farah Sonia O-02, O-04, O-05, P-03, P-15, P-17
- Favretti Martina IS-22
- Feijen Stef P-13
- Filippou Georgios O-04, P-17
- Fischetti Fabio P-03
- Fitzcharles Mary-Ann IS-07, IS-27
- Fornasari Diego IS-26
- Fracaroli E. P-07
- Franceschini Franco P-03
- Friend Ronald O-01
- Gálvez Galán Isabel P-10, P-11
- Galvez Sánchez Carmen IS-01, IS-17, IS-19, IS-21
- Gaviria Alejandra Maria P-02
- Garcia-Hernandez Allyn P-05
- Gerli Roberto P-03
- Ghareebpoor Faeez P-06
- Giacomelli Roberto P-03
- Giordani Valeria IS-01, IS-17, IS-19, IS-21
- Giovannetti Massimo P-03
- Govoni Marcello P-03
- Gresem Elisa P-03
- Gregiemi P. P-07
- Gridavilla Daniela P-17
- Guiducci Serena P-03
- Heinricher Mary O-01
- Hierchado Sanchez-Moro Maria Dolores P-10, P-11
- Hodadov Hadas IS-12
- Iannone Florenzo P-03
- Iannuccielli Cristina IS-23, P-07
- Ilari S. P-07
- Janssens Lotte P-13
- Jones Kim O-01
- Kidron Adi IS-12
- Lim Miranda O-01
- Losacco Serena P-09
- Lotam Ely IS-32
- Luria Mijal IS-11
- Maindert Caroline P-08
- Malafoglia V. P-07
- Mariani Claudia O-05, P-15
- Marinelli Lucio P-09
- Marotti Daniella O-02
- Martin Cordero Leticia P-10
- Martin-Aguilar Aleia P-04
- Martinez-Lara Antonio P-04
- McBride Alisha O-01
- McGonagle Dennis IS-12
- Merezh Edwin O-03
- Meyns Pieter P-13
- Minier Laurent P-08

**M**
- Mist Scott O-01
- Molinari Elena O-09
- Monroy Aguilarr Casandra P-01
- Isabel
- Mozanski Flavio P-03
- Mucci Vivian P-09
- Muscoli C. P-07

**N**
- Navarro Pérez Maria del Carmen IS-09
- Nitzan Uri IS-09

**O**
- Oltra Garcia Elisa P-02
- Ortega Rincón Eduardo P-10, P-11
- Otero Calderón Eduardo P-10, P-11

**P**
- Park Yooha O-03
- Paroli M. P-07
- Plant Shiloh P-12

**R**
- Raffaeli W. P-07
- Ramakers Indra P-13
- Ramírez-Tejero Jorge P-04
- Rapallo Fabio P-09
- Reyes del Paso Gustavo P-05
- Romano Mariaeva O-04, P-17
- Romeyke Tobias P-14

**S**
- Salaffi Fausto O-02, O-04, O-05, P-03, P-15, P-17
- Samiec Sophie O-01
- Sánchez Fito Teresa P-02
- Sarzì Puttini Piercarlo IS-17, IS-21, IS-31, O-02, O-04, O-05, P-03, P-15, P-17
- Scieluna Jean Claude P-16
- Sereu Paul P-13
- Shoenfeld Yehuda IS-06
- Siroti Silvia O-04, P-17

**T**
- Tenti M. P-07
- Tirri Rosella P-03
- Traeltsi Advad IS-15
- Truini Andrea IS-18

**V**
- Vaes Michelle P-13
- Van Aken Karen P-13
- Van Den Houte Maaike P-13
- Varrassi Giustino IS-10
- Ventura Donatella O-04

**W**
- Watad Abdulla IS-12
- Wolfe Frederick P-03

**Y**
- Yavne Yarden IS-12