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Invited Speaker Presentations

IS-01

Fibromyalgia Year in Review 2025

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Fibromyalgia (FM) is a chronic syndrome characterized by widespread pain, high prevalence, and a significant negative impact on quality of life. Despite extensive research, its pathogenesis and optimal treatment strategies remain insufficiently understood. Thus, it is not surprising that research has been undoubtedly active throughout 2024. Recent studies have highlighted mitochondrial dysfunction as a key area of interest, showing reduced mitochondrial biogenesis and activity in both animal models (1, 2) and human patients (3). These issues may be linked to peripheral and central sensitization, as well as compromised physical capabilities. The possibility of using mitochondrial alterations as diagnostic biomarkers is also being explored (4). Other areas of interest include the controversial roles of metabolism-regulating hormones (5), such as leptin and growth hormone, and the contribution of the immune system and low-grade chronic inflammation (6) to FM pathogenesis. Advances in neuroimaging, particularly magnetic resonance imaging (MRI), have revealed changes in brain connectivity and structure associated with symptoms such as pain threshold (7) and cognitive dysfunction (8). Integrated imaging analyses are proposed as potential biomarkers to differentiate FM patients from healthy individuals (9). Epidemiologic findings confirmed the impact of pollution and other environmental factors on FM (10), and the increasing burden on couple and family-life of patients. From a clinical perspective, some studies have focused their attention on underexplored arguments like sexual (11) and cognitive (12) dysfunction and the expanding new topic of sex and gender difference in FM. FM differential diagnosis regarding a new entity like long COVID syndrome has ignited an interesting discussion, questioning the pros and cons of considering it under the same etymology (13). On the other hand, residual pain in inflammatory conditions, another difficult differential diagnosis, remains largely underexplored. Research on different therapeutic approaches for FM treatment has confirmed the fundamental role of non-pharmacological interventions, especially for exercise and psychosocial-based interventions. New pharmacological treatments or new routes of administration, such as sublingual cyclobenzaprine (14), are being studied, while in clinical practice it is still common to use unapproved drugs like opioids. In 2024, there are also new insights into the promising field of non-invasive neuromodulation, including techniques such as TMS and TENS and the emerging field of vagal nerve stimulation, capable of modulating the parasympathetic system already found altered in FM (15). Finally, the development and use of virtual reality, artificial intelligence, and many information and communication technologies (16-18) aimed at treatment, patient management, and research herald a new era for rheumatologists and patients.

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IS-02

The molecular patterns in blood, saliva and muscle and their correlation with objective CNS alterations and clinical characteristics

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There is a need to better understand the interrelationships between peripheral inflammatory markers and pain related regions in the brain. This study aims to investigate the relationship between brain functional connectivity and levels of inflammatory markers and pain intensity, and pain characteristics in patients with fibromyalgia and healthy age- and sex-matched control subjects. The concentrations of several inflammatory substances in the different body fluids could clearly differentiate patients with FM and healthy controls. Significant associations between metabolic and inflammatory variables and pain intensity and sensitivity were found in FM. Altered insular and intraparietal sulcus (IPS) connectivity were found in FM. Functional connectivity in the insular and IPS were associated with altered levels of inflammatory markers in blood.

This study supports the fact that FM is characterized by complex interactions between peripheral tissues, peripheral and central nervous systems including nociceptive and immune processes.

IS-03

Pathogenic mechanisms of fibromyalgia: 1, 100, or 1000 mechanisms

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Fibromyalgia (FM) is a complex chronic pain disorder characterized by widespread musculoskeletal pain, fatigue, sleep disturbances, and cognitive difficulties. Despite extensive research, its pathogenesis remains elusive, reflecting a multifactorial interplay of neurological, endocrine, immunological, genetic, and psychosocial factors. Central to FM is the concept of nociplastic pain, a distinct pain mechanism characterized by altered sensory processing in the absence of clear nociceptive or neuropathic triggers (1, 2). This abstract reviews the diverse pathogenic mechanisms proposed for FM, emphasizing their intricate interactions.

Nociplastic pain and central sensitization. At the core of FM pathogenesis is nociplastic pain, where central sensitization drives heightened pain perception (3,4). This phenomenon is characterized by amplified neuronal responsiveness to normal or subthreshold stimuli, leading to hypersensitivity to mechanical, thermal, and chemical stimuli. The thalamocortical pain processing loop, involving the ventroposterolateral nucleus, primary somatosensory cortex, and thalamic reticular nucleus, plays a pivotal role in this maladaptive pain amplification.

Neuroendocrine dysregulation. Significant dysregulation of the hypothalamic-pituitary-adrenal (HPA) and hypothalamic-pituitary-gonadal (HPG) axes contributes to FM pathogenesis. Altered stress responses, dysregulated glucocorticoids, and deficiencies in neurosteroids such as allopregnanolone impair pain modulation by affecting GABAergic and glutamatergic neurotransmission. These neuroendocrine disruptions link FM to stress-related disorders and highlight the intersection of hormonal and nociplastic pain mechanisms (5).

Neurotransmitter imbalances. FM is marked by imbalances in serotonin, substance P, glutamate, and GABA – all integral to pain processing, sleep regulation, and mood. Deficiencies in serotonin and elevated cerebrospinal fluid levels of substance P disrupt normal pain signaling, while glutamate and GABA dysregulation amplify central sensitization, underpinning nociplastic pain (3, 4).

Inflammatory, immune, and CNS cellular contributions. Although FM is not traditionally inflammatory, evidence implicates inflammatory and immune processes in its pathogenesis. Elevated levels of pro-inflammatory cytokines, such as IL-6 and IL-8, and neurogenic inflammation may enhance pain sensitivity and exacerbate symptoms. Additionally, the activation of microglia and astrocytes – CNS cells with immune functions – has been

identified as a potential contributor to central sensitization and nociplastic pain. These cells release cytokines, chemokines, and neuroactive substances, further amplifying pain pathways. Autoimmune triggers and neuroimmune dysregulation may also play a role in FM's symptomatology (6).

Microbiome and gut-brain axis. Emerging research suggests the gut microbiome may play a role in FM pathogenesis via the gut-brain axis. Altered gut microbial composition and dysbiosis can influence systemic inflammation, immune responses, and central nervous system function, potentially contributing to nociplastic pain and other symptoms (7).

Genetic and epigenetic susceptibility. Genetic predisposition significantly influences FM risk, with familial clustering and polygenic contributions affecting neurotransmitter systems, stress responses, and pain pathways (8, 9). Studies have identified polymorphisms in genes such as COMT (catechol-O-methyltransferase), which impacts pain modulation via dopamine metabolism, and SCN9A, encoding the sodium channel NaV1.7, which plays a critical role in nociception. Newer studies also highlight other sodium channel variants and genes related to immune function and neuroinflammation. Beyond genetics, epigenetic modifications – such as DNA methylation and histone acetylation – mediate gene-environment interactions, linking stress, trauma, and other environmental factors to FM onset and persistence.

A groundbreaking 2024 study identified three distinct genomic signatures in FM patients, revealing new insights into the disease's heterogeneity (9). These signatures include:

1. Extracellular matrix alterations and RhoGDI signaling downregulation
2. Reduced expression of inflammatory mediators and increased CLEAR signaling pathway activity
3. Overexpression of acute inflammation pathways and global transcriptional process dysfunction

This research suggests that defective tissue homeostasis, impaired macromolecule clearance, and dysregulated inflammatory responses may play crucial roles in FM pathogenesis.

Autonomic nervous system dysfunction. Dysfunction of the autonomic nervous system (ANS) contributes to hallmark FM symptoms such as fatigue, sleep disturbances, and cognitive difficulties. Abnormalities in heart rate variability and other measures of autonomic function may interact with central sensitization and nociplastic pain mechanisms, amplifying symptom severity (10).

Psychosocial and environmental factors. Stress, trauma, and adverse life events frequently precede FM onset, influencing neuroendocrine and pain processing systems. These psychosocial factors perpetuate symptoms through cognitive-emotional sensitization and contribute to nociplastic pain. The biopsychosocial model underscores the importance of addressing these elements in comprehensive management strategies (11, 12).

Conclusion. The pathogenesis of FM involves a complex interplay of nociplastic pain mechanisms, central sensitization, neuroendocrine dysregulation, immune contributions – including microglial activation – genetic and epigenetic predisposition, microbiome influences, and psychosocial factors (13, 14). This multifaceted understanding explains the challenges in developing effective treatments and underscores the need for personalized therapeutic approaches. Future research should prioritize elucidating the relative contributions of these mechanisms, leveraging advances in microbiome science, epigenetics, and genetic studies to identify novel therapeutic targets within this intricate pathogenic network.

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IS-04

Nociplastic pain: the real epidemiology

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This talk will cover the epidemiology of conditions under the IASP classification of nociplastic pain with a specific focus on fibromyalgia and its individual features. It will cover the descriptive epidemiology (prevalence) as well as occurrence by population sub-groups (including sex, age-group and social factors). It will discuss the challenge of identifying modifiable risk factors (as opposed to factors with common causes and/or consequences of these conditions) and discuss the success in translating knowledge of modifiable risk factors into improving outcomes. The talk will review evidence linking such conditions with increased mortality and the factors which may mediate any such relationship. The talk will conclude with suggestions for priority areas for future research.

IS-05

Neuroinflammation in chronic pain: implications for fibromyalgia

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Numerous studies established the role of neuron-glia-immune interactions for pain chronification in animals and in humans (1). Central sensitization and neuroinflammation play major roles in the pathophysiology of fibromyalgia (FM), which is the most common presentation of widespread chronic pain, accompanied by sleep disturbances, fatigue and cognitive dysfunction. As the prototypical nociplastic pain condition, fibromyalgia is often part of chronic overlapping pain conditions, which suggests a common pathway sustained by central nervous system (CNS) neuroplasticity. Indeed, the main pathophysiological mechanism for developing nociplastic pain is central sensitization, which leads to pain amplification and hypersensitivity. Neuroinflammation contributes to the pathogenesis of various diseases, including most pain syndromes and neurodegenerative disorders. Neuroinflammation is characterized by activation of glial cells and production of inflammatory mediators that potentiate neurotransmission. Preclinical studies have demonstrated that the inhibition of microglial activation alleviates FM symptoms (2).

Increasing evidence from human neuroimaging supports the hypothesis that FM involves microglia-mediated neuroinflammation in the brain (3). Several proton magnetic resonance spectroscopy metabolites, such as choline and myo-inositol, have been linked with glial activity in the CNS and were shown to be altered in chronic pain patients. Cortical choline levels, a putative neuroinflammatory marker, was found to be elevated in FM patients, associated with pain interference, and correlated with astrogliosis (4). Other central metabolites, such as creatine and glutamate, have been associated with neuroinflammation in patients with FM (5). Similarly, some specific interleukins, such as IL-6 and IL-8 have been identified as peripheral biomarkers for pain severity and disability in FM patients. Mood disorders observed in FM patients may be also sustained by activated neuro-immune pathways. Thalamic mast cells may contribute to inflammation and pain in FM. Mast cells release neuro-sensitizing molecules such as histamine, IL-1 β , IL-6, tumor necrosis factor (TNF), calcitonin-gene related peptide (CGRP), and substance P, which stimulate thalamic nociceptive neurons directly, or through microglia activation in the diencephalon (6).

These findings suggest a possible role for molecules that restore physiological mast cell role and modulate microglia activation as a putative novel approach for reducing pain and symptoms of FM. Palmitoylethanolamide (PEA) is a well-known endogenous endocannabinoid-like lipid mediator, with neuroprotective, anti-inflammatory, and analgesic properties. The endocannabinoid system is an essential endogenous pathway involved in the pathophysiology of chronic widespread pain and FM (7). A retrospective observational study showed the efficacy and safety of PEA, as add-on therapy, in the treatment of FM patients treated with duloxetine (DLX) and pregabalin (PGB). After 3 months of treatment, PEA introduction provided a significant improvement in pain symptoms and a reduction in the number of tender points, compared to combined DLX + PGB only (8). A recent randomized controlled trial confirmed the effectiveness of adding PEA and acetyl-L-carnitine to a stable treatment with DLX+PGB in FM (9). Being PEA a lipid and therefore, insoluble in water, the size of the molecule is essential for appropriate absorption. Ultramicrosized palmitoylethanolamide (um-PEA) has a diameter of $0.8 \pm 2 \mu\text{m}$, which makes it optimally absorbable along the intestine and able to cross the blood-brain barrier. A retrospective analysis of 359 FM patients, prescribed with orally um-PEA, showed a statistically significant improvement in pain score, in Fibromyalgia Impact Questionnaire score, with an optimal tolerability profile (9). Further clinical investigations are warranted to confirm the therapeutic role of PEA in FM management. Advances in the understanding of the multifactorial pathophysiology of FM are essential to identify potential novel targets and treatments.

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IS-06

Neuroimmune interactions: a new frontier in fibromyalgia research

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Chronic pain conditions including fibromyalgia and complex regional pain syndrome (CRPS), fatigue syndromes, and functional gastrointestinal disorders, often present with overlapping somatic and psychiatric features are therefore also called symptom-based disorders (1). These disorders bridge the divide between physical and mental health, highlighting their complex, multifaceted nature. Recent evidence argues that many of these disorders share an autoimmune etiology based on serum or Ig transfer experiments in preclinical models. This has been specifically demonstrated in CRPS and fibromyalgia. Both diseases share the nociplastic feature of a primary chronic pain disease. In fibromyalgia, serum transfer into mice elicits mechanical hyperalgesia. Likewise, IgG transfer from chronic CRPS patients into normal mice elicits hyperalgesia but only, if a "second hit" like a plantar incision is present - emphasizing its regional character. Also in both diseases, autoantibodies have been found reacting with rodent and/or human dorsal root ganglion tissue. A systematic search documented serum autoreactivity against

satellite glia cells in fibromyalgia (2). In a large cohort of CRPS patients in the ResolvePAIN study we detected seropositivity in half of CRPS patients and a third reacted against small and/or large neurons from naïve rats. In skin biopsies, CRPS patients had increased Langerhans cells as antigen-presenting cells and mast cells (2). A transcriptomic analysis of the skin in early CRPS supported the role of autoreactivity as we observed complement activation especially in patients with poorer outcome. Complement activation has also been observed in a preclinical model of IgM serum transfer and tibia cast before (4). In summary, two primary chronic pain disorders share signs of autoreactivity – however their contribution to the pathophysiology of the disease and the specificity of the antigens need to be determined.

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IS-07

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IS-08

Mechanisms of neutrophil-mediated pain in fibromyalgia

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We have previously observed that adoptive transfer of neutrophils from patients with painful fibromyalgia confers mechanical hypersensitivity in naïve recipient mice. Our findings suggested a neuroimmune basis of pain in fibromyalgia mediated by *de novo* trafficking of neutrophils into dorsal root ganglia, and consequent chronic widespread pain. New mass spectrometry and flow cytometry data reveals a unique proteomic signature of circulating neutrophils in patients with fibromyalgia. Enhanced extracellular trap formation from fibromyalgia neutrophils demonstrates that these cells are in a hyperactivated state in circulation. Further calcium imaging studies reveal that neutrophils can sensitise dorsal root ganglia neurons *in vitro*. In order to determine whether cell-cell interaction is needed for neutrophils to sensitise neurons, we further characterised neutrophil localisation to the meningeal space of dorsal root ganglia. We then further characterised extracellular vesicles from fibromyalgia neutrophils and observed significantly different characteristics of those vesicles derived from pathophysiological fibromyalgia neutrophils. Furthermore, blocking vesicle production from patient derived neutrophils limits the capacity of these polymorphonuclear granulocytes to sensitise primary afferent neurons. Our data confirms that neutrophils are trafficked to dorsal root ganglia and release extracellular vesicle cargo that sensitises primary afferent neurones to mediate chronic widespread pain in fibromyalgia.

IS-09

Emotion regulation and the salience network: a hypothetical integrative model of fibromyalgia

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The pathophysiology of Fibromyalgia (FM) remains incompletely understood and largely controversial, even in the most objective mechanistic observations (1). This can have decisive consequences in the development of more effective therapies. The currently prevailing paradigm posits that the changes observed in the structure and function of the central nervous system represent the primary cause of this condition by fostering central amplification of pain. Small fibre neuropathy has been argued as an abnormal source of nociceptive input, but it is only observed in about half of FM patients. The recent demonstration that IgG and neutrophils can be involved in this process, underlines the complexity of the puzzle and the fuzzy nature of the underlying picture. None of these mechanisms can, however, fully encompass the important psycho-social connections of FM, supported by a wealth of accumulated evidence.

The FITSS Model (2) presents an attempt to integrate the biological and psycho-social realms of FM. The acronym stands for Fibromyalgia Imbalance of Threat and Soothing System, which directly addresses its core hypothesis: FM is characterised by an excessive perception of threat in daily life, combined with a scarce perception of safety and affiliation. This will keep the Salience Network (SN) in continuous override due to the continuous flow of menacing signals. This will be responsible for all the typical symptoms of FM, through excessive sympathetic output and the variety of effector systems under the command of the SN. Cross-amplification of potential threat signals is to be expected in this continuous alarm mode and would justify pain amplification and hypersensitivity to noise and smell. The patient is caught in a persistent and all-consuming “fight or flight” state. This hypothetical hyperactive SN can explain most, if not all, neurobiological fMRI observations in FM, as the pain and the emotion regulation circuitries of the CNS are so intricately intertwined. Experimental evidence suggests that small-fibre neuropathy might also ensue as a top-down consequence. Pathogenic neutrophils and IgG may also be originated in this context.

The Imbalance of Threat and Soothing may be the cause of the whole process, but it may also emerge as a consequence of a generalised disturbance started elsewhere in the complex interplay of factors involved in FM. A threat-dominated emotional style (classically named neuroticism) is common in FM patients. It has been attributed to genetic influences but may also be a consequence of early life adversity, precluding the learning of safety cues. In some patients, the imbalance could be derived from a primary neurobiological change leading to continuous pain, fatigue and sleep disturbance, instead of being the primary factor. Chronic auto-immune diseases might lead to similar end-result, through the generation of pathogenic neutrophils and IgG.

The FITSS model welcomes the possibility that FM may, in different patients, be a similar final consequence of different primers among the myriad of factors at play, as in a hanging toy where changes in one factor will interfere with all others, making the *chicken vs. egg* question irrelevant. Recognising the imbalance of threat and soothing, whatever its origin, may provide the unifying mechanism that must be addressed to achieve relief or resolution.

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IS-10

Psychotherapy in fibromyalgia: state of the art and new directions

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The absence of a defined pathology and the association of fibromyalgia (FM) with psychosocial stress have prompted some specialists in psychosomatic medicine to consider it a psychosomatic or functional disorder and use the diagnostic label “persistent somatoform pain disorder” (ICD-10 F45.4) for them. Indeed, 60% to 80% of FM patients meet the diagnostic criterion of either the onset or aggravation of FM symptoms by psychosocial stress and emotional conflicts. Also, the American Psychiatric Association gave a strong move to classify FM as a mental disorder, under the chapter of somatic symptom disorder (SSD). The diagnosis of SSD may, indeed, be made when there are persistent (*i.e.* typically longer than 6 months) somatic symptoms that are distressing and/or significantly disruptive of daily life and are accompanied by excessive and disproportionate symptom-related thoughts, feelings, and behaviors. There have been publications which classified FM as a SSD even though for instance in one study only 26% of FM patients met the criteria for an SSD.

If fibromyalgia is conceptualized as a mental disorder, in particular as a somatic symptom disorder, it is clear why scientific literature suggests that it can benefit from psychotherapy interventions and, in a wider sense, from psychological treatments. This issue has important clinical implications since fibromyalgia treatment is challenging because patients have a very limited benefit from pharmacological therapy. As what concerns non-pharmacological interventions are concerned, the strongest evidence has been observed for cognitive-behavioral therapy even though only about 22% of cases have a real benefit from it. In addition, typically, the contents proposed in the framework of cognitive-behavioral therapy are rather unspecific since they refer to self-monitoring, time-based pacing to increase behavioral function, progressive muscle relaxation and guided imagery to reduce pain, behavioral strategies to improve sleep, pleasant activity scheduling and cognitive reframing for mood problems, memory and thinking skills for cognitive impairment, effective communication with providers to reduce stress, and goal setting for long-term functioning. In brief, they do not really refer to the core problem of FM that is the fact that it is a psychosomatic syndrome in which physical manifestations are an expression of a psychological and mental suffering and in which physical symptoms are also due to an excessive attention on the body with catastrophic misinterpretation of its signs. This means that there is wide room for future developments of psychological interventions addressed to FM. They can include structured therapies, such as new psychotherapies or variants of existing psychotherapeutic approaches, but also less structured interventions, which pertain for instance to psychoeducation and lifestyle modifications.

IS-11

Loneliness: between chronic pain and depression in fibromyalgia

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Increasing evidence shows that social connection is a public health problem of significant relevance: social isolation and loneliness can promote the appearance of physical and mental problems (1). Loneliness is defined as a subjective feeling that occurs when one's relationships with the environment and with other people do not match one's expectations of how relationships should be (2). According to the bio-psycho-social model, the concept of loneliness concerns several areas, such as philosophical (Seneca argued that loneliness is to the spirit what food is to the body), sociological and psychological (as confirmed by growing loneliness epidemic during the era of Covid). More recently, this problem has come to the attention of the medical area, representing a significant social risk factor for health (2). If left untreated, loneliness has profound consequences on cognition, emotions, behavior, and health, thus becoming a major contributor to morbidity and mortality in humans (3). Loneliness impacts health through multiple mechanisms, such as less healthy diet, smoking and alcohol, dysregulation of the autonomic nervous system (hypothalamic-pituitary-adrenocortical axis activity) with increased systolic blood pressure and a greater release of

pro-inflammatory cytokine and other inflammatory parameters. Loneliness favors also depressive mood, insomnia with sleep fragmentation, and cognitive decline through an accelerated brain ageing, and even mortality (4). Furthermore, a growing body of scientific research has shown that loneliness can intensify the perception of physical pain, especially in chronic pain conditions, as found in pathologies such as arthritis or fibromyalgia (5). In addition to physical pain, loneliness can induce a deep sense of psychological suffering that is associated with states of anxiety, depression and higher levels of distress (6).

In this study on 110 patients with fibromyalgia, 87.13% female (mean age 52.05 years sd 10.65, BMI 25.28 sd 6.20, 39.02% is married, average duration of the disease 10.74 years) we investigated the correlations between loneliness (evaluated with 20-item UCLA Loneliness Scale), anxiety, depression and stress (DASS-21 Depression Anxiety Stress Scales), quality of life (SF-36 Short form health survey – 36 and FIQR Italian Fibromyalgia impact questionnaire).

UCLA scores were high or moderately high in 76.24% of patients, moderate in 8.91% and low in 14.85%. Our data show a positive correlation of 0.63 between the UCLA score and the FIQR score, suggesting that, as the perceived loneliness increases, so does the overall impact of fibromyalgia on patients' lives, with an aggravation of the symptoms, mainly pain, fatigue and social isolation.

Also the three dimensions of DASS were significantly linked with perceived loneliness scores: the correlation of anxiety was 0.46, stress 0.44 and depression 0.38. Therefore participants, reporting higher levels of loneliness, also tend to suffer more from depression, anxiety and stress.

To complete the survey, qualitative assessments were made about the patients' experiences and feelings concerning loneliness: the main themes that emerged were aspects of suffering, compassion, acceptance, lack and/or difficulties in interpersonal relationships.

The clinical awareness and detection of loneliness and its consequences is essential to be able to implement interventions (social, psychological, pharmacological) that demonstrate a beneficial action also on pain, fatigue and depression (7).

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IS-12

Which drugs can be effective in nociplastic pain?

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Nociplastic pain is a relatively new concept in pain science, introduced to describe pain arising from altered nociception despite no clear evidence of actual or threatened tissue damage or disease that would explain the pain. Conditions such as fibromyalgia, irritable bowel syndrome, and some cases of chronic low back pain fall under this category. Pharmacological interventions play a key role, often requiring a tailored approach that addresses the central sensitization and dysfunctions in pain processing associated with nociplastic pain.

1. Antidepressants. Antidepressants, particularly serotonin-norepinephrine reuptake inhibitors (SNRIs) and tricyclic antidepressants (TCAs), are the cornerstone of nociplastic pain management. These drugs are thought to exert their effects by modulating descending pain pathways and improving central pain inhibition.

- **SNRIs:** Duloxetine and milnacipran have shown efficacy in conditions like fibromyalgia. They increase serotonin and norepinephrine availability, enhancing the descending inhibitory pain pathways. Duloxetine is particularly effective for reducing pain intensity and improving quality of life.

- **TCAs:** Amitriptyline, though used less frequently due to side effects, remains an effective option. It works by inhibiting the reuptake of serotonin and norepinephrine and may also enhance sleep quality, which is often disrupted in nociplastic pain conditions.

2. Anticonvulsants. Anticonvulsants, particularly gabapentinoids such as gabapentin and pregabalin, are frequently employed in the treatment of nociplastic pain. These drugs modulate calcium channel activity, reducing neuronal excitability and attenuating central sensitization.

3. Muscle relaxants. Muscle relaxants, particularly cyclobenzaprine, are sometimes used in nociplastic pain management. Cyclobenzaprine has a mechanism similar to TCAs and is believed to help by improving sleep and reducing muscle tension, contributing to overall pain relief.

4. NMDA receptor antagonists. Dysregulation of the N-methyl-D-aspartate (NMDA) receptor contributes to central sensitization in nociplastic pain. NMDA receptor antagonists such as ketamine and dextromethorphan have shown potential in reducing pain by modulating excitatory neurotransmission.

- **Ketamine:** Administered in low doses, ketamine can effectively reduce pain by dampening central sensitization. However, its use is limited by potential side effects and the need for close monitoring.

5. Cannabinoids. Cannabinoids have emerged as a potential treatment option for nociplastic pain due to their effects on the endocannabinoid system, which modulates pain and inflammation. While evidence is still emerging, some studies suggest that cannabis-based medicines may provide relief for patients with fibromyalgia and similar conditions.

6. Acetaminophen. Most of the analgesic effects of acetaminophen relies on its metabolite, AM404, which is formed in the CNS. AM404 is an inhibitor of anandamide reuptake, and a weak agonist of CB1 and CB2 receptors, thus working as an enhancer of the endocannabinoid system. For these reasons, acetaminophen could be useful in some of the nociplastic conditions, in particular fibromyalgia.

6. Other pharmacological options:

- **NSAIDs and corticosteroids:** These are generally not effective for nociplastic pain, as the pain does not stem from inflammation or tissue injury.
- **Opioids:** Opioids are not recommended for nociplastic pain due to their limited efficacy and impact on cognition. In some cases, tramadol and tapentadol, which have respectively SNRI and NRI properties, may be considered.
- **Selective serotonin reuptake inhibitors (SSRIs):** While not as effective as SNRIs or TCAs, SSRIs may benefit patients with significant comorbid depression or anxiety. However, there is the hypothesis that serotonin, in chronic pain conditions, could be pronociceptive.

Future directions. Emerging therapies targeting neuroinflammation, glial cell activation, and other novel pathways are under investigation. These include monoclonal antibodies, neuropeptide modulators, and non-opioid pain relief agents.

IS-13

Mechanisms of non-pharmacological treatments in fibromyalgia

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Fibromyalgia (FM) is a complex, chronic condition characterized by widespread musculoskeletal pain, fatigue, sleep disturbances, and cognitive dysfunction. Non-pharmacological treatments have emerged as central strategies in managing FM due to their safety profiles and potential for addressing the multifactorial nature of the disorder. These treatments target diverse physiological and psychological mechanisms that contribute to FM symptoms. Below is an exploration of the primary mechanisms by which non-pharmacological interventions exert their effects in FM management.

1. Exercise therapy. Regular physical activity, particularly aerobic and resistance exercises, improves FM symptoms through multiple pathways:

- Neuromodulation: increasing levels of brain-derived neurotrophic factor (BDNF) and serotonin
- Anti-inflammatory Effects: lowering levels of pro-inflammatory cytokines such as interleukin-6 (IL-6) and tumor necrosis factor- α (TNF- α).
- Central Sensitization Reduction
- Improved Sleep and Mood

2. Cognitive-behavioral therapy (CBT). CBT improves several dimensions of FM through:

- Cognitive Restructuring: Identifying and reframing negative thought patterns
- Behavioral Activation: enhancing quality of life and reducing avoidance behaviors.
- Stress Regulation: Reducing cortisol levels and normalizing hypothalamic-pituitary-adrenal (HPA) axis activity.
- Neuroplasticity: Modifying maladaptive neural circuits

3. Mindfulness-based stress reduction (MBSR). MBSR employs meditation and yoga to cultivate present-moment awareness and reduce stress:

- Parasympathetic Activation: Enhancing vagal tone
- Neuroendocrine Modulation: Reducing cortisol and improving resilience to stress.
- Pain Perception Alteration: reducing activity in the anterior cingulate cortex and insula

4. Acupuncture. Acupuncture's analgesic effects are mediated by:

- Endorphin Release
- Neurotransmitter Modulation: Increasing serotonin and norepinephrine
- Peripheral Desensitization
- Central Sensitization Modulation.

5. Dietary interventions. Nutritional strategies aim to reduce FM symptoms by:

- Gut-brain axis modulation: Improving gut microbiota composition, which influences systemic inflammation.
- Anti-inflammatory diets: Incorporating foods rich in omega-3 fatty acids, antioxidants, and polyphenols to lower inflammation.
- Nutrient optimization: Addressing deficiencies in magnesium, vitamin D, and coenzyme Q10.

6. Transcranial magnetic stimulation (TMS). TMS is a neuromodulation technique that delivers magnetic pulses to specific brain regions:

- Cortical Excitability Reduction: Inhibiting hyperactive areas.
- Neurochemical Effects: Enhancing dopaminergic and serotonergic activity
- Network Reorganization: Promoting functional connectivity changes that reduce chronic pain.

7. Sleep interventions. Addressing sleep disturbances through cognitive-behavioral therapy for insomnia (CBT-I), relaxation techniques, or light therapy improves FM symptoms by:

- Restoring Deep Sleep
- Reducing Hypervigilance
- Normalizing Circadian Rhythms and the regulation of melatonin and cortisol cycles.

8. Biofeedback and Neurofeedback. These techniques train individuals to control physiological processes:

- Autonomic Regulation: Balancing sympathetic and parasympathetic activity to reduce stress and pain.
- Brainwave Optimization: decrease hyperexcitability in pain-processing regions.
- Enhanced Self-Efficacy.

Conclusion. Non-pharmacological treatments for fibromyalgia leverage a diverse array of mechanisms to address the multifaceted nature of the disorder. By targeting neurophysiological, psychological, and behavioral pathways, these interventions offer complementary and holistic approaches to FM management. Further research is essential to elucidate the precise mechanisms underlying these treatments and to optimize their integration into comprehensive care plans.

IS-14

Transmucosal sublingual cyclobenzaprine (TNX-102 SL¹) treatment of fibromyalgia at bedtime to target non-restorative sleep showed durable pain reduction in two double-blind randomized phase 3 studies

(Sponsored by Tonix Pharmaceuticals)

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TNX-102 SL (cyclobenzaprine [CBP] HCl sublingual tablets) provides transmucosal delivery of a tricyclic and is being developed to treat fibromyalgia with daily dosing at bedtime. Fifty years ago, Harvey Moldofsky proposed that fibromyalgia was primarily a non-restorative sleep disorder. CBP is a potent antagonist at four post-synaptic receptors, each of which have known roles in sleep quality: serotonergic-5-HT_{2A}, adrenergic- α_1 , histaminergic-H₁, and muscarinic-M₁-cholinergic. However, a clinical trial of oral CBP showed only transient pain reduction in fibromyalgia, which is inadequate for treatment of a chronic condition (Carette *et al. Arthritis Rheum* 1994; 37: 32-40). We reasoned that potential dynamic effects of CBP are swamped by the accumulation of the persistent major active metabolite norcyclobenzaprine (norCBP) after oral administration. To target the non-restorative sleep that Moldofsky described, the TNX-102 SL tablet was designed to provide faster absorption and bypass first-pass hepatic metabolism. Efficient transmucosal absorption of CBP was found to require a basic excipient to increase the local concentration of CBP free base. The TNX-102 SL tablet is based on a eutectic of CBP HCl and mannitol that protects CBP HCl from the basifying agent. Clinical pharmacokinetic (PK) studies indicated that relative to oral CBP, TNX-102 SL results in higher CBP levels of exposure during the first 2 hours and in decreased levels of norCBP in both single dose and multiple dose studies. At steady-state after 20 days of dosing TNX-102 SL, the dynamic peak level of CBP is higher than the background level of norCBP. In contrast, a PK analysis showed that after 20 days of oral CBP dosing, the simulated peak concentration of CBP was lower than the background concentration of norCBP, in which the simulated concentration-time curves were based on a Phase 1 study of single-dose oral immediate-release 5 mg CBP, along with nonparametric superposition methodology and the assumption of linear PK for both CBP and norCBP. These results are consistent with TNX-102 SL providing transmucosal absorption of CBP and bypassing first pass hepatic metabolism.

Following the pharmacokinetic studies, two 14-week double-blind, randomized, placebo-controlled Phase 3 clinical trials evaluated the safety and efficacy of TNX-102 SL as a bedtime treatment for fibromyalgia. Both Phase 3 trials (RELIEF and RESILIENT) of TNX-102 SL 5.6 mg in fibromyalgia met their pre-specified primary endpoints of significantly reducing daily pain compared to placebo ($p=0.010$ and $p=0.00005$, respectively). In both trials, TNX-102 SL was generally well tolerated with an adverse event profile comparable to prior studies and with no new safety signals observed. In both pivotal studies, the most common treatment-emergent adverse event was tongue or mouth numbness at the administration site, which was temporally related to dosing, self-limited, never rated as severe, and rarely led to study discontinuation (one participant in each study). Excluding COVID-19, rates of systemic adverse events in each of the two studies were all below 4.0%. In conclusion, TNX-102 SL was designed for transmucosal absorption of CBP in a long-term treatment regimen of daily dosing at bedtime. By improving absorption, bypassing first pass metabolism and targeting the characteristic disturbed sleep of fibromyalgia, TNX-102 SL provides dynamic effects of CBP that appear to be less impaired by the accumulation of background norCBP than oral CBP. TNX-102 SL showed durable activity in decreasing pain over 14 weeks in two Phase 3 studies with a favorable tolerability profile. Together these findings support the potential of TNX-102 SL as a non-opioid, analgesic for fibromyalgia patients. If approved, TNX-102 SL will be the first new medication for the treatment of fibromyalgia in the U.S. in more than 15 years.

¹TNX-102 SL is an investigational new drug and has not been approved for any indication.

IS-15

Interaction of fibromyalgia with inflammatory joint diseases

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Rheumatoid arthritis (RA) and psoriatic arthritis (PsA) are the most common inflammatory joint diseases. Recently, the importance of comorbidity in patients with inflammatory arthritis has gained attention of the medical community as a growing global health challenge, mainly in diagnosis and treatment. In particular, concomitant fibromyalgia has been recognized as a common comorbidity in both diseases, leading to a high disease burden and a poor prognosis despite an optimal control of inflammatory disease.

In this presentation, will discuss the different patterns of pain in arthritis, focusing on inflammatory pain versus mechanical pain and pain related to the central sensitization. Several practical tools can be used in daily practice to differentiate the origin of pain, including physical examination and imaging, such as ultrasound of joints and related structures. We will further present data on the prevalence of fibromyalgia in patients with RA and PsA, underlying the contributing factors for the development of fibromyalgia, such as depression, anxiety, and sleep disturbance. As pain is considered one of the important factors of patient-reported outcomes in the evaluation of disease activity, fibromyalgia is associated with skewed disease activity scores indicating moderate to high disease activity. Therefore, patients with fibromyalgia are commonly defined as “complicate-to-treat patients”, failing to reach treatment targets as implicated by the *treat-to-target* treatment strategy recommended in both RA and PsA.

Novel anti-cytokine biologic therapies and recently introduced small molecule treatments effectively reduce the level of pain in inflammatory arthritis. This effect may be independent of the anti-inflammatory properties. Further research is warranted to investigate the precise mechanisms of anti-rheumatic treatments on pain relief.

The key message of this presentation is the importance of recognizing and diagnosing patients with concomitant fibromyalgia among the population of patients with RA and PsA, consequently addressing the related symptoms using an integrative approach in patients' management.

IS-16

Residual pain in inflammatory rheumatic and autoimmune diseases

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Autoimmune rheumatic diseases, such as systemic lupus erythematosus (SLE), rheumatoid arthritis (RA), Sjögren syndrome (SS) and systemic sclerosis (SSc), confer multiple challenges on those living with these conditions. Apart from intermittent disease flares and irreversible organ-specific damage, patients often suffer from pain, which may take myriad forms, including arthritis, abdominal pain, Raynaud phenomenon, and comorbid fibromyalgia (FM). Pain must be dually addressed in concert with treating the underlying inflammation that characterizes rheumatic diseases (4). However, despite optimal control of inflammatory and autoimmune diseases, residual chronic pain remains a major unmet medical need (5). Pain is, in many cases, a significant issue and can have a negative impact on patients' quality of life.

Pain in rheumatoid arthritis. (RA) can be not solely attributed to immune-mediated inflammatory mechanism and joint damage secondary to inflammation but can also generate neuroendocrine responses that initiate neurogenic inflammation and enhance cytokine release, leading to persistent hyperalgesia. In addition to well-known cytokines such as TNF- α and IL-6, other cytokines and the JAK-STAT pathway play a role in pain modulation and inflammation, but involves derangement mechanisms of central pain (6-8). Therefore, understanding the dominant mechanism underlying pain in these patients should be a priority (7), also because different subgroups of patients might respond differently to treatment approaches (9-11). Therefore, it could be important to determine whether the pain is driven predominantly by disease activity or by changes in the central pain regulatory mechanisms.

Residual pain is often observed in patients even after achieving remission or low disease activity, suggesting the involvement of non-inflammatory and central sensitization mechanisms (12, 13). Moreover, FM is prevalent in RA patients and may contribute to persistent pain. Factors such as depression, sleep disturbance, and pro-inflammatory cytokines may contribute to the development of FM in RA. It is essential to identify and diagnose concomitant FM in RA patients to better manage their symptoms. In an observational longitudinal cohort consisted of long-standing RA patients at the end of the 6-month observation period, 24 of the 117 patients (20.4%) met the SDAI remission criteria. Logistic regression analysis showed that the modified Rheumatic Disease Comorbidity Index (mRDCI) ($p=0.0001$), the FM presence ($p=0.0001$), and the 36-item short-form health survey Mental Component Summary (SF-36 MCS) Score ($p=0.0088$) were the strongest predictors of not being in SDAI remission. None of the patients with concomitant FM (17.1%) achieved SDAI remission (14). Further research is needed to unravel the complexities of pain in RA. Finally, recent studies have shown that JAK inhibitors effectively reduce residual pain in RA patients, suggesting pain-reducing effects independent of their anti-inflammatory properties (1).

Pain in SLE patients. In a recent survey in SLE patients, residual pain supported substantial impairment for the majority of participants, even those who indicated that they were completely satisfied with treatments. The treatment goals most commonly reported as “very important” were reducing fatigue, pain, and the frequency or severity of flares (15).

In a prospective observational study (16) the sample comprised 107 SLE patients, with an average age of 54.1 years (SD:12.1), of whom 95.4% (102) were women. The prevalence of Fibromyalgia among SLE patients was 19.1% (21), all of whom were women with a mean age of 45.6 years (SD 9.6). The SF-36 scores of SLE patients with FM were consistently lower across all eight domains compared to those without FM, indicating a significant negative impact of this comorbidity. In a paper by Ceccarelli *et al.* (17) the analysis included 237 SLE patients [92.4% female, median age 46 years (IQR 19.5), median disease duration 156.8 months (IQR 180.6)]. At the time of enrollment, they found a mean SLEDAI-2k of 1.7 (DS 2.4); 104 patients (43.9%) had chronic damage, with a mean SDI value of 0.8 (DS 1.3). Patients diagnosed with FM were 69 (29.1%); moreover, HADS questionnaire identified a condition of anxiety and depression in 112 (47.3%) and 94 (39.7%) patients, respectively. The most compromised domain in the LupusQoL resulted “fatigue”.

Pain in Sjögren syndrome patients. FM in SS was evaluated in 134 patients; FM was present in 19%, 18%, 20%, and 29% of cases according to ACR 2016, ACR 1990 criteria, physician's opinion and the FIRST questionnaire, respectively. FM criteria-positive patients had higher EULAR SS Patient-Reported Index (ESSPRI) score, but not higher EULAR SS Disease Activity Index (ESSDAI) score (18).

Of the 13,849 patients identified with Sjögren's disease, 11,969 (86%) were women and 1,880 (14%) men, primarily white (88%) with a sex ratio of 6.4:1 women to men. The top comorbidities in patients with Sjögren's disease were fibromyalgia (25%), depression (21.2%) and pain (16.4%). Comorbidities that occurred more often in women were hypermobile syndromes (31:1), CREST (29:1), migraine (23:1), Ehlers-Danlos syndrome (EDS) (22:1), Raynaud's syndrome (15:1), SLE (13:1), systemic sclerosis (SSc) (13:1), and fibromyalgia (12:1) (19).

Pain in systemic sclerosis. In systemic sclerosis It was found that 92.9% of SSc patients suffer from different types of pain, and 45.2% of patients have pain every day. Joint pain was the most common type of pain, present in 78.6% of patients, followed by pain associated with Raynaud's phenomenon (69%), back pain (47.6%), headache (31%), chest pain (23.8%), odynophagia (21.4%) and painful digital ulcers (19%). Symptoms of neuropathic pain were noticed in 26.2% of patients. Severe joint pain, everyday pain and symptoms of neuropathic pain in SSc were associated with more severe disease and poorer quality of life. Pain related to Raynaud's phenomenon, digital ulcers, odynophagia and joint pain were associated with significant symptoms of depression (20).

FIRST detected FM in 27.8% of the 122 SSc patients, with confirmation in 30.3% (ACR1990) and 23.7% (ACR2010). ACR1990FM+ SSc patients had greater disability and pain intensity, and more diffuse pain. Secondary SS was associated with comorbid FM (21).

In conclusion, the prevalence of residual pain and particularly FM is relevant; therefore, managing pain in inflammatory arthritis like RA and other autoimmune diseases is complex and challenging. Despite advances in inflammation and joint damage control, a significant percentage of patients continue to experience persistent pain that extends beyond inflammation, involving complex mechanism of central sensitization and aberrant pain processing (22-24)

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IS-17

Metabolic syndrome and fibromyalgia

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Introduction. Fibromyalgia (FM) is a syndrome characterized by widespread musculoskeletal pain, fatigue, insomnia, depression, and cognitive impairment complaints. Fatigue, insomnia, and depression can favor physical inactivity that, associated with the overweight predisposition may promote the development of metabolic syndrome (MetS). Several studies showed higher prevalence of MetS in FM.

Methods. This abstract discusses the link between MetS of FM described in scientific papers published from 2020 and indexed in the PubMed database.

Results. A study found that FM patients had a nearly four times higher risk for MetS and the coexisting MetS can increase the FM severity (1). Loevinger *et al.* (2) found that FM patients were more prone to developing MetS with a 5.6 times higher risk than healthy females without chronic pain. In a study involving 62 female patients with FM and 4093 female controls from 35 to 75 years of age, we showed that the prevalence of hypertension, diabetes, atrial fibrillation, TIA, and CV total burden, was significantly higher in FM females than in the Italian population (3). No difference was found in blood fasting glucose, triglycerides, total and fractionated cholesterol levels, BMI, and metabolic syndrome (MetS). However, the MetS rate is underestimated for methodological aspects (3).

Conclusions. Patients with FM had a four times higher risk for MetS and the coexisting MetS can increase the severity of FM. These data suggest that in clinical practice, when evaluating a patient with FM, metabolic characteristics should also be evaluated.

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IS-18

Sex and gender differences in fibromyalgia: implications for treatment

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Background. Fibromyalgia (FM) demonstrates striking sex differences in prevalence, with women being diagnosed at significantly higher rates than men (1). While biological sex differences likely play a role, emerging evidence suggests that gender-related factors may be equally important in the development, manifestation, and treatment of FM. Recent research examining FM in transgender individuals has provided unique insights into the complex interplay between sex hormones, gender identity, and chronic pain conditions (2). As a prototype of nociplastic pain, FM represents altered nociceptive function without clear evidence of actual or threatened tissue damage, with distinct sex-based differences in pain processing and central sensitization (4). **Methods.** This review synthesizes current evidence from multiple sources including systematic reviews and meta-analyses of sex differences in FM prevalence and presentation, neurobiological studies examining sex-based differences in pain processing, clinical studies investigating the effects of sex hormones on pain sensitivity, original research on FM prevalence and symptoms in transgender individuals before and during hormone therapy, and psychosocial research examining gender-related stress and trauma in FM development.

Results. Current evidence suggests that both biological sex and gender-related factors contribute to FM development and expression. Sex hormone fluctuations affect pain sensitivity and symptom severity, with testosterone potentially playing a protective role against central sensitization (3). Gender-related trauma and stress contribute significantly to FM development.

Transgender individuals show unique patterns of FM prevalence and symptomatology during transition, with prevalence rates varying significantly between transgender men and women. Treatment responses vary based on both biological sex and gender identity, suggesting the need for personalized therapeutic approaches. Neuroimaging studies reveal sex-specific patterns in pain processing and neuroplasticity, with women showing enhanced pain sensitivity and distinct patterns of central sensitization in nociplastic conditions (4). **Conclusion.** Understanding sex and gender differences in FM is crucial for developing effective, personalized treatment approaches. The complex interaction between biological sex factors and gender-related psychosocial elements suggests the need for a comprehensive treatment model that addresses both hormonal and psychosocial aspects of the condition. The recognition of FM as a nociplastic pain condition with clear sex differences in central pain processing mechanisms has important implications for targeted therapies. Findings from transgender populations provide valuable insights into the relative contributions of hormonal and gender-related factors in FM development and progression. Clinical implications include the need to consider hormone levels in FM diagnosis and treatment planning, develop gender-specific psychological interventions, and account for hormonal fluctuations in treatment timing. Future research should focus on clarifying the mechanisms by which sex hormones influence nociplastic pain processing, developing gender-specific treatment protocols, and further investigating the role of gender identity in FM expression and management. **Key words:** fibromyalgia, sex differences, gender identity, hormone therapy, central sensitization, nociplastic pain, chronic pain, personalized medicine

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IS-19

What happens to small neurons in fibromyalgia?

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About 50% of patients with fibromyalgia have a reduced intraepidermal nerve fiber density as assessed with skin biopsy. This small nerve fiber loss is commonly defined as small-fiber pathology, in contrast to small fiber neuropathy (SFN), which is a different disease entity. Indeed, there are major clinical, pathological and pathophysiological differences between fibromyalgia and the classical SFN. In particular, dermal C-fibers in fibromyalgia have a smaller caliber than those of patients with SFN or healthy controls. Furthermore, the fiber reduction in most fibromyalgia patients is not distally accentuated, in contrast to length-dependent SFN. However, some clinical overlap between fibromyalgia and SFN may exist.

Small fiber pathology may underlie some of the symptoms in patients with fibromyalgia, such as ongoing burning extremity pain, or bladder and bowel disturbances. However, the relationship between small-fiber pathology and the symptoms and signs that patients with fibromyalgia experience is still an issue of controversy. Whereas several studies have reported that patients with fibromyalgia have impaired sensory profiles at the quantitative sensory testing and abnormal nociceptive evoked potentials, other studies showed that small-fiber pathology is not associated with clinically meaningful abnormalities of the somatosensory nervous system.

The reason for small-fiber pathology in fibromyalgia is as yet unknown. In healthy people, the density of skin innervation declines with age. This is not the case in fibromyalgia, at least cross sectional data do not give an indication of age-dependence. Whether the reduced caliber of dermal C-fibers in fibromyalgia is a trait or develops over time is also unknown. Thus, a pre-disposition toward pathology of the small nerve fibers, and potentially their neurons, is a possibility. In addition, any of the pathophysiological processes discussed in fibromyalgia (central sensitization, endocrine factors, immune factors etc.) may influence the peripheral nervous system. Recently, we and

others found IgG autoantibodies in patients' serum that bind to dorsal root ganglion neurons and satellite glial cells. To find out if and how these autoantibodies may alter the function of sensory neurons in fibromyalgia will greatly enhance our understanding of the pathophysiology of this disease.

IS-20

Latest diagnostic tools for small fiber neuropathy

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Small fiber neuropathy (SFN) is a disorder characterized by selective damage to small unmyelinated (C) and thinly myelinated (Aδ) nerve fibers, often presenting with symptoms of burning pain, dysesthesia, and autonomic dysfunction. In recent years, a growing body of evidence suggests that SFN may play a critical role in fibromyalgia (FM), a chronic pain condition traditionally associated with central sensitization. This potential overlap underscores the need to understand the involvement of SFN in FM pathology. Among diagnostic tools, skin biopsies remain the gold standard for diagnosing SFN. This minimally invasive technique allows for the quantification of intraepidermal nerve fiber density (IENFD) at various sites, such as the distal leg or thigh, using PGP9.5 immunostaining. A reduction in IENFD is a hallmark of SFN and provides objective evidence of small fiber involvement. Advances in spatial transcriptomics and multiplex immunohistochemistry have further enhanced the diagnostic precision by enabling the evaluation of nerve fiber morphology, axonal degeneration, and inflammatory profiles at the cellular level.

However, the assessment of IENFD does not provide any information about the function of the fibers. Quantitative Sensory Testing (QST) complements skin biopsy findings by assessing the functional integrity of small fibers through psychophysical thresholds for thermal and pain stimuli. However, QST outcomes can be influenced by patient cooperation and central sensitization, making them less specific. Corneal confocal microscopy (CCM), an emerging technique, offers a non-invasive alternative for visualizing small fiber integrity in vivo by quantifying corneal nerve fiber density, length, and tortuosity. Sudomotor function tests, including Quantitative Sudomotor Axon Reflex Testing (QSART) measures postganglionic sudomotor response to acetylcholine and provides an assessment of autonomic small fiber function. Laser-evoked potentials (LEPs) provide an objective method for evaluating the functional integrity of small nociceptive fibers by recording cortical responses to laser stimuli. This non-invasive tool is particularly valuable for detecting early small fiber dysfunction and distinguishing peripheral abnormalities from central sensitization, a key consideration in conditions like FM. Lastly, microneurography, although primarily a research tool, enables the direct recording of C-fiber activity in real time. This technique provides insights into spontaneous activity and hyperexcitability in small fibers, helping to understand mechanisms of neuropathic pain. Together, these tools enhance the diagnostic repertoire for SFN, providing functional and mechanistic data that complement morphological findings.

A subset of FM patients exhibits reduced IENFD, suggesting a possible SFN phenotype within the FM spectrum. This finding raises questions about the pathophysiological intersection between SFN and FM, with potential implications for diagnosis and treatment. Molecular and genetic profiling may identify shared biomarkers or distinct endophenotypes, guiding personalized treatment strategies. Moreover, neuroinflammation, mitochondrial dysfunction, and autoimmunity are emerging as potential mechanistic links between these conditions, warranting further exploration.

The integration of advanced diagnostic methods, such as spatial transcriptomics, artificial intelligence-assisted imaging, and multimodal biomarkers, holds promise for improving SFN diagnosis and detecting potential small fiber pathology in FM. Recognizing the overlap between SFN and FM may lead to novel diagnostic algorithms that combine morphological, functional, and molecular data. Such approaches not only enhance diagnostic accuracy but also pave the way for targeted therapies for SFN and FM with SFN component.

IS-21

Pain regulation and autonomic nervous system

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The complex interplay between the pain system and the autonomic nervous system (ANS) is fundamental to pain perception and modulation. This multifaceted relationship hinges on shared neural pathways in the brain and spinal cord that integrate nociceptive inputs with autonomic responses. The ANS, comprising sympathetic and parasympathetic divisions, exerts multifaceted influences on pain perception. The sympathetic nervous system (SNS), typically activated in acute pain, triggers the “fight or flight” response. This activation can amplify pain perception through increased muscle tension, heightened arousal, and stress hormone release. Chronic pain conditions often correlate with SNS hyperactivity, creating a feedback loop of intensified pain and persistent stress responses. In contrast, the parasympathetic nervous system (PNS), responsible for the “rest and digest” state, generally attenuates pain perception. PNS activation promotes relaxation and recovery, potentially mitigating pain through decreased heart rate and improved tissue perfusion. Moreover, the PNS may enhance endogenous pain modulatory systems, including the release of pain-alleviating neurotransmitters. These insights offer promising avenues for therapeutic interventions. Pharmacological approaches targeting the ANS can alleviate pain and enhance quality of life in chronic pain patients. Sympatholytic agents like beta-blockers can reduce excessive sympathetic activity, while parasympathetic-enhancing drugs, such as certain antidepressants, may offer dual benefits for mood disorders and pain perception. Non-pharmacological strategies, including biofeedback, relaxation techniques, and transcutaneous electrical nerve stimulation (TENS), show potential in modulating autonomic responses and influencing pain perception. Understanding the central common pathways and bidirectional influences of the SNS and PNS on pain can inform improved multidisciplinary pain management approaches. Future research should focus on elucidating specific mechanisms involved in these interactions to develop more targeted and effective pain interventions. This abstract introduces our latest findings on pain modulation and its interaction with the autonomic nervous system in both healthy individuals and those with chronic pain conditions.

IS-22

Perceived injustice in chronic pain

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Chronic pain is a multifaceted phenomenon influenced by biological, psychological, and social factors. Among these, perceived injustice has emerged as a critical psychological construct associated with the exacerbation and maintenance of chronic pain.

Perceived injustice refers to an individual's subjective appraisal of unfairness, often characterized by feelings of blame, loss, and irreparable harm. Perceived injustice in the context of chronic pain typically arises from injury or illness attributed to external factors, such as medical errors, workplace accidents, or interpersonal conflict. It is characterized by two core components: blame and retribution – the tendency to attribute fault to others, leading to feelings of anger and resentment, and irreparable loss – the belief that the consequences of the pain or injury are permanent and devastating, fostering hopelessness.

This construct has gained attention in pain research due to its strong correlation with pain severity, emotional distress, and disability. Additionally, perceived injustice can mediate the relationship between stressful life events and pain outcomes, acting as a partial mediator for centralized pain symptoms and a full mediator for pain intensity.

Mechanisms through which perceived injustice contributes to pain-related outcomes include heightened emotional responses such as anger, sadness, and anxiety; maladaptive coping strategies; activation of the HPA axis and social isolation.

Specifically, anger is a central emotional response and a critical mediator in the relationship between perceived injustice and chronic pain outcomes,

through amplification of pain perception, inhibition of adaptive coping, and negative interpersonal dynamics. This suggests that interventions targeting anger management may be beneficial in mitigating the adverse effects of perceived injustice on chronic pain. In fibromyalgia, anger is particularly prevalent due to the challenges of living with an often-dismissed and invisible illness. Patients' anger may stem from invalidation by healthcare providers or the lack of understanding from their familial and social circles, further exacerbating their emotional and physical suffering.

Furthermore, perceived injustice has been found to be a stable trait associated with poorer recovery in terms of pain intensity and depressive symptoms after traumatic injury, as it does not naturally decrease over time.

Recognizing and addressing perceived injustice in chronic pain patients, especially those with fibromyalgia, can improve pain management and rehabilitation outcomes, and enhance quality of life. Integrating psychological, physical, and social interventions can address the multifaceted nature of chronic pain and perceived injustice. Cognitive Behavioral Therapy can help patients reframe their perceptions of injustice, reducing anger and hopelessness while promoting adaptive coping mechanisms. Acceptance and Commitment Therapy (ACT) encourages patients to accept their pain and focus on value-driven actions, helping to reduce the emotional impact of perceived injustice. In fibromyalgia, ACT has shown promise in improving pain acceptance and reducing psychological distress. For patients whose perceived injustice stems from trauma, trauma-informed care can provide a safe and supportive environment for addressing these issues. This approach is particularly relevant for fibromyalgia, as many patients report histories of trauma or adverse childhood experiences.

Ultimately, addressing perceived injustice not only provides a pathway for effective pain management but also fosters emotional resilience and enhances overall well-being, offering a holistic approach to chronic pain rehabilitation.

IS-23

The effect of tetrahydrocannabinol on pain modulation paradigms in fibromyalgia: a randomized, double-blinded, placebo-controlled study

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Background. Tetrahydrocannabinol (THC) has been shown to improve pain perception in chronic pain syndromes, particularly those driven by central sensitization. Offset analgesia (OA) and conditioned pain modulation (CPM) are two commonly used biomarkers to assess central pain modulation. In this study, we aimed to compare the effects of THC on OA and CPM in patients with fibromyalgia syndrome (FMS), a well-recognized model of central sensitization.

Methods. Twenty-three FMS patients were enrolled in this randomized, double-blind, placebo-controlled crossover study. The experiment consisted of two sessions, during which patients completed the McGill Pain Questionnaire, underwent a VAS determination test, and were assessed for OA and CPM in a randomized sequence, both before and after receiving either THC-rich oil (T10/C2, 0.2mg/kg) or placebo oil sublingually.

Results. THC significantly reduced spontaneous pain ratings in the McGill Pain Questionnaire compared to baseline and placebo, respectively (95% CI [1.569, 17.34], $p=0.01$, and 95% CI [-12.66, -0.63], $p=0.02$). THC also significantly enhanced OA compared to baseline (95% CI [0.4003, 41.85], $p=0.04$) and placebo (95% CI [-26.66, -3.493], $p=0.008$), but showed no effect on CPM ($F(2.33, 32.74)=0.293$, $p=0.2738$). Furthermore, baseline OA magnitude was predictive of the extent of pain relief on the McGill scale following THC treatment ($R^2=0.404$, $F(1,21)=11.54$, $p=0.003$), whereas CPM did not show a significant correlation ($p=0.121$, 95% CI [-0.69, 0.10]).

Conclusion. This study is the first, to our knowledge, to specifically investigate the effects of THC on central pain modulation in FMS using OA and CPM. The results demonstrate that THC selectively enhances OA without affecting CPM, highlighting the possible distinct mechanisms underlying these two paradigms of central pain modulation. Additionally, this study is the first to reveal the clinical value of baseline OA measures in predicting spontaneous pain relief following THC treatment. These findings suggest the potential of OA as a biomarker for THC-related pain relief in FMS and pave the way for developing personalized cannabis-based treatments for FMS and other central sensitization disorders.

IS-24

Cannabinoids in the management of fibromyalgia syndrome: current evidence and perspectives

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Fibromyalgia syndrome (FMS) is a complex chronic condition characterized by widespread pain, fatigue, sleep disturbances and neuroinflammation and immune dysregulation. Despite existing pharmacological treatments, many patients report suboptimal symptom management, with the “30% rule” underscoring the limitations of conventional therapies. Surveys of FMS patients have highlighted a growing preference for cannabinoids as an alternative to traditional pharmacological drugs, citing better symptom management and fewer side effects (1).

Building on these surveys, clinical research has investigated the efficacy of cannabis-based therapies. The endocannabinoid system (ECS), comprising endocannabinoids, cannabinoid receptors (CB1 and CB2), and enzymes such as FAAH, represents a promising therapeutic target. Cannabinoids, including tetrahydrocannabinol (THC) and cannabidiol (CBD), exhibit antinociceptive, anti-inflammatory, and immunomodulatory effects through ECS modulation and interactions with pathways such as TRPV channels and serotonin receptors (2).

Observational studies show significant reductions in pain intensity and improved symptom management with cannabis use (3). Randomized controlled trials partially corroborate these findings, demonstrating the analgesic potential of THC-rich preparations in increasing pressure pain thresholds and improving quality of life. However, results remain inconsistent, mainly because of the low quality of the studies. Nonetheless, adverse effects such as dizziness and somnolence, particularly with THC-rich compounds, warrant cautious titration. The “entourage effect” of whole-plant cannabis extracts may enhance therapeutic outcomes.

Tailored therapeutic approaches and rigorous monitoring protocols are recommended to optimize cannabis-based interventions. Further research is needed to bridge translational gaps, clarify the ECS role in FMS, and establish long-term safety and efficacy profiles for cannabis-based medicines.

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IS-25

The role of psychedelics in the management of chronic pain

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Chronic pain is a debilitating condition affecting millions worldwide and remains a significant challenge for patients and healthcare providers due to its complex etiology and limited treatment available. Traditional pharmacological tools often provide insufficient relief and are associated with significant side effects such as dependency and tolerance (1). Psychedelics, such as lysergic acid diethylamide (LSD) and psilocybin have emerged as promising therapeutic agents in recent years due to their modulatory effects on central nervous system circuits involved in and emotional regulation and pain perception.

From a mechanistic point of view, psychedelics primarily act as agonists and partial agonists of serotonin 5-HT_{2A} receptors (2, 3), facilitating neuroplasticity and modulating the activity of brain regions implicated in pain processing, such as the anterior cingulate cortex, prefrontal cortex, and insular cortex. Limited preclinical studies suggest that psychedelics can attenuate the perception of pain (4). For instance, a study demonstrated that a single intravenous bolus administration of psilocybin can attenuate mechanical

hypersensitivity in rats displaying an inflammatory pain condition induced by formalin injection (5).

Clinical evidence supporting the analgesic properties of psychedelics is also accumulating. Recent trials have demonstrated that psilocybin therapy improves pain scores and quality of life in patients with migraine, cluster headaches and phantom limb pain (6-8). Very interesting is the application of microdose in psychedelic therapy. The term microdose refers to the administration of very low, sub-perceptual doses of a substance (9). The dose typically does not exceed the 1% of the recreational dose. Microdosing aims to elicit subtle physiological or psychological benefits without inducing the full-blown effects or hallucinations associated with higher doses (10). In this regard, a study on microdoses of LSD revealed significant reductions in pain intensity in patients with chronic neuropathic pain, underscoring the potential for sub-perceptual doses in therapeutic settings (11). Another study showed that 3 individuals who have used low-dose psilocybin to manage chronic neuropathic pain have achieved robust pain relief with decreased reliance on traditional analgesic medications. In addition, in 1 case, repeated dosing produced increased relief, suggesting a possible long-term plasticity-mediated effect (12).

Fibromyalgia is a disease characterized by widespread musculoskeletal pain, fatigue, and cognitive dysfunction, presents a unique challenge due to its multifactorial nature involving central sensitization and dysregulation of pain modulation pathways (13, 14). Psychedelics may address these underlying mechanisms by inducing changes in brain connectivity and neuroplasticity. In this regard, a single-arm study carried by Bornemann and coll. will explore the central mechanisms of psilocybin using Electroencephalogram (EEG) and functional magnetic resonance imaging (fMRI) to assess brain activity and neuroplasticity. The study also aims to evaluate pain symptomatology, mental health, and quality of life, contributing to the understanding of psilocybin's therapeutic potential for chronic pain conditions like fibromyalgia (15).

Overall, psychedelics represent a novel frontier in the management of chronic pain, offering a paradigm shift that integrates neurobiological and psychosocial dimensions. Their multimodal effects on pain perception, emotional processing, and neuroplasticity hold potential for transforming the treatment landscape of chronic pain disorders. By addressing both the sensory and affective dimensions of pain, psychedelics may provide holistic relief and improved quality of life for patients with chronic pain.

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IS-26

Non-invasive transcutaneous vagus nerve stimulation for the treatment of fibromyalgia

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The vagus nerve is the longest nerve of the autonomic nervous system and has sensory, motor, and autonomic functions. The latter aspect makes it particularly significant in the treatment of chronic pain, as it serves as the primary mediator of the parasympathetic system.

Vagus nerve stimulation (VNS) can be broadly classified into two approaches: invasive and non-invasive. The invasive method involves the implantation of devices capable of stimulating the cervical portion of the vagus nerve. The non-invasive method, on the other hand, refers to transcutaneous stimulation applied at specific anatomical sites such as the neck near the carotid region (transcervical VNS) and the cymba conchae of the auricle (transauricular VNS), where cutaneous surfaces are innervated by sensory fibers of the vagus nerve. Both transcutaneous stimulation modalities have demonstrated the ability to activate central projection areas of the vagus nerve.

VNS has long been recognized for its anti-inflammatory properties, mediated by the cholinergic pathway, with promising applications in inflammatory musculoskeletal disorders.

Although the pathophysiology is not yet fully elucidated, evidence suggests that fibromyalgia is associated with dysautonomia, characterized by a reduced vagal tone. This diminished vagal tone links fibromyalgia to other conditions, such as epilepsy and depression, for which VNS has established therapeutic indications.

Regarding the application of transcutaneous VNS in fibromyalgia, current studies, though limited in size, indicate a certain efficacy of this approach in this patient population. However, these studies are highly heterogeneous concerning stimulation parameters (*e.g.* frequency, intensity, and timing). Several open questions remain regarding the potential applications of transcutaneous VNS in fibromyalgia. The primary question concerns the method's efficacy compared to sham stimulation. Other critical issues that require resolution in the near future include identifying the most effective stimulation modality and setting, determining the optimal treatment duration, and personalizing the therapy appropriately. These questions can be addressed through large-scale, randomized controlled trials.

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IS-27

What's on the horizon? Update on novel approaches to treating nociplastic pain as of 2025

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As of 2025, several promising novel therapies have emerged for the treatment of nociplastic pain, offering new hope for patients suffering from this complex condition. These innovative approaches target various aspects of pain processing and perception, addressing the unique challenges posed by this emerging category of pain.

Recent advancements include neurofeedback and neuromodulation techniques, which aim to retrain brain activity patterns associated with pain perception. These non-invasive approaches allow patients to actively modulate their pain experience by targeting key brain regions implicated in nociplastic pain. By restoring balance to dysfunctional neural networks, these interventions are helping redefine chronic pain management. Complementing these, hyperbaric oxygen therapy (HBOT) has shown potential in resetting central sensitization processes. This treatment, which involves exposing patients

to high-pressure oxygen environments, appears to modulate neuroinflammatory pathways, aiding in the recalibration of pain processing mechanisms.

In pharmacology, two promising classes of therapies are drawing significant attention. Sodium channel blockers, such as suzetrigine, target the Nav1.8 sodium channel, a critical component of pain signaling. Early clinical trials indicate that these agents effectively reduce both acute and chronic pain, offering a novel therapeutic option for nociplastic pain, where conventional analgesics often fall short. NMDA receptor modulators, another promising pharmacological avenue, aim to inhibit the receptors driving central sensitization. Dysregulated NMDA receptor activity is a core feature of nociplastic pain, and novel compounds targeting these pathways hold potential for providing more effective and targeted relief.

Behavioral therapies are also evolving, with pain reprocessing therapy emerging as a particularly promising approach. This therapy aims to shift the perception of chronic pain by guiding patients to reinterpret pain signals as non-threatening. By addressing the cognitive and emotional aspects of pain, pain reprocessing therapy has demonstrated success in reducing pain intensity and restoring functionality in nociplastic pain patients. Cognitive-behavioral therapy for insomnia (CBTi), a well-established method for improving sleep, continues to gain prominence in nociplastic pain management, addressing the pervasive sleep disturbances that exacerbate pain perception and reduce quality of life.

Cutting-edge technologies, such as injectrode technology, are transforming the field of neuromodulation. This minimally invasive technique employs an injectable electrode to create a pathway from the skin to deep nerves. Controlled by an external device, the injectrode delivers precise electrical stimulation to modulate dysfunctional pain pathways. This innovation provides a less invasive alternative to traditional neuromodulation devices, with the potential for widespread application in nociplastic pain syndromes. Finally, genomic advances are paving the way for personalized medicine. Multivariate genome-wide association studies have identified genetic loci associated with nociplastic pain, underscoring the potential for targeted therapies tailored to individual genetic profiles. By integrating these insights with large-scale databases, clinicians are beginning to personalize treatment strategies, enhancing both efficacy and patient satisfaction.

These therapies signify a paradigm shift toward more precise, multidimensional approaches to nociplastic pain management. By integrating novel pharmacological, behavioral, and technological advances with conventional therapies, the future holds promise for improving outcomes and quality of life for patients with nociplastic pain syndromes (1-4).

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IS-28

Full body neuromodulation: innovation in the treatment of pain (Sponsored by Ottobock)

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Full-body neuromodulation represents an innovative, rapidly developing non-invasive and non-pharmacological approach to the treatment of chronic pain, as found in fibromyalgia (1, 2), but also effectiveness in the treatment of spastic motor disorders and spasticity-induced pain as found in diseases with an upper motor neuron lesion such as Infantile Cerebral Paresis (ICP) or Multiple Sclerosis (MS) (3, 4).

The underlying mechanisms are thought to involve the substitution of missing supraspinal and afferent input, by artificial peripheral afferent input, via electrical stimulation. Inhibitory mechanisms, like reciprocal inhibition or post-activation depression, contribute to relaxation of spastic muscles (5). Recently, multiple randomized, sham-controlled clinical trials have shown the potential of full body neuromodulation in fibromyalgia patients.

Positive results were observed on the reduction of pain, improvement of bodily limitations, improvement in quality of life and improvement in fibromyalgia-related depression (2).

Other positive results have been observed on improvement of muscle oxygenation, parasympathetic modulation and pain perception (6-8). This presentation will summarize and present the latest data on the usage of full body neuromodulation in the treatment of pain.

Table I. Summary of efficacy endpoints before and after the 4-week active intervention period (open phase) (2).

Efficacy endpoints	Pre-score	Post-score	p-value	Effect size (Z/√N)
VAS _{pain}	6.73 ± 1.72	5.06 ± 2.35	<0.001	0.54
VAS _{fatigue}	6.87 ± 1.90	5.60 ± 2.34	<0.001	0.45
BPI _{total}	5.78 ± 1.98	4.79 ± 2.15	0.003	0.36
FIQ _{total}	48.83 ± 15.05	38.78 ± 18.16	<0.001	0.48
FIQ _{pain}	6.87 ± 2.17	5.15 ± 2.55	<0.001	0.46
FIQ _{fatigue}	7.19 ± 2.14	5.76 ± 2.46	<0.001	0.47
FIQ _{stiffness}	6.45 ± 2.55	5.27 ± 2.76	0.002	0.38
FIQ _{anxiety}	5.10 ± 2.78	3.75 ± 2.84	0.012	0.31
HADS _{depression}	10.09 ± 5.60	8.91 ± 5.37	0.038	0.26
HADS _{anxiety}	9.94 ± 4.44	8.54 ± 4.50	0.006	0.34
HADS _{total}	20.03 ± 9.14	17.45 ± 9.20	0.003	0.37
PCS _{total}	24.67 ± 14.98	20.36 ± 14.02	0.004	0.35
SF-36 _{role physical}	17.42 ± 26.13	45.45 ± 39.75	<0.001	0.46
SF-36 _{vitality}	24.85 ± 18.56	38.33 ± 23.14	<0.001	0.44
SF-36 _{health change}	37.12 ± 29.40	50.00 ± 34.80	0.002	0.38

Table II. t-test results comparing baseline and post-session measurement for each session and treatment. **p*<0.05.

Variables	Suit					
	1 st session		8 th session		16 th session	
	<i>p</i>	Effect size	<i>p</i>	Effect size	<i>p</i>	Effect size
NRS, 0–10	0.037*	–0.775	<.001*	–1.551	0.016*	–0.930
PPT epicondyle, kg	0.03*	0.889	0.759	0.127	0.006*	1.000
PPT knee, kg	0.049*	0.774	0.722	0.156	0.139	0.546
SmO ₂ , %	<.001*	0.229	<.001*	0.398	<.001*	0.441
THb, g/dL	<.001*	0.338	0.752	0.009	<.001*	–0.382
O ₂ Hb, g/dL	<.001*	0.263	<.001*	0.390	<.001*	0.390
HHb, g/dL	<.001*	–0.201	<.001*	–0.421	<.001*	–0.462

NRS: Numeric Rating Scale; PPT: pressure pain threshold; SmO₂: muscle oxygen saturation; THb: total hemoglobin; HHb: deoxygenated hemoglobin; O₂Hb: oxygenated hemoglobin (7).

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IS-29

The role of patient associations in fibromyalgia syndrome

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Fibromyalgia (FMS) is a disorder characterized by widespread musculo-skeletal pain accompanied by fatigue, sleep, memory and mood issues (1). It is a long-term condition, causing personal and societal impacts. The risk factors for this syndrome include being female, aged over 50, having pre-existing medical conditions, smoking, a high body mass index, and lower socioeconomic status (2). The aetiology and pathophysiology remain unknown (3), but abnormal pain processing within the central nervous system is the primary proposal. Many authors reported a significant association between prior physical or psychological trauma and the subsequent development of FMS; however, the condition can also develop in the absence of trauma. The complexity experienced by people with FMS concern not only the notion of recognition, rather different areas of everyday life (work, social, physical and legal interests) (4, 5).

Patients associations are non-profit organizations of social utility that represent and support the needs of patients (6). Their main role is to provide a correct diagnostic, therapeutic and welfare approach to patients by creating a network between health care professionals (HCPs) and patients. 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 (1). Aisf Odv (Italian Association of Fibromyalgia Syndrome), which was founded in 2005 in Milan, but operates throughout the national territory, is doing all of this. It is a clear example of collaboration between physicians, HCPs and volunteers; in fact the local sections are made up of patient volunteers and healthcare professional volunteers. It is doing an important job both for medical and social care. HCPs 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 (7, 8). HCPs 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. In some cases, the poor quality of listening and the fragmented vision of HCPs generate in many patients a feeling of loneliness and incomprehension in the face of the disease. It is therefore important to create a dialogue between the two parties, which includes respect for roles and absence of prejudices. HCPs must raise awareness of the importance of associations, must inform the patients of their existence and instruct to contact them. Conversely, volunteers must develop projects and activities for patients, whilst volunteers must acquire knowledge and skills. Associations can support training of HCPs, 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. Patient education interventions include structured educational program about understanding the disease and treatment options, self-management skills, and lifestyle modification. The management of FMS should ensure to include shared decision-making between HCPs and patients, as this helps patients to feel better informed, well supported and more satisfied with care provision (9,10). Previous research has indicated the importance of self-management strategies in the overall disease management in order to minimise the impact of the condition (9,10). Individuals living with FMS should be active in their healthcare management; FMS successful treatment is reliant upon individuals being able to be ‘active partners’; patients associations can be of great help educating patients being active partners of their disease (11-13).

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IS-30

FM Registries: do we really need them?

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Background. Fibromyalgia (FM) is a chronic condition characterized by widespread pain, fatigue, and cognitive dysfunction, often accompanied by psychiatric and somatic comorbidities. Its complex clinical presentation and variable response to treatments pose significant challenges for both diagnosis and management. Disease registries, such as the Italian Fibromyalgia Registry (IFR), have emerged as indispensable resources for collecting real-world data, enabling deeper insights into disease mechanisms, treatment effectiveness, and unmet needs. The IFR is designed not only to document patient characteristics but also to capture the dynamic evolution of the disease, providing a foundation for precision medicine.

Objectives. This lecture highlights the transformative role of the IFR, focusing on its ability to:

- Identify distinct clinical phenotypes and patterns of disease severity.
- Evaluate treatment responses and guide personalized therapeutic strategies.
- Facilitate longitudinal monitoring of disease progression and outcomes.
- Promote multidisciplinary approaches and integrated care models.
- Support the development of evidence-based guidelines and novel interventions.
- Provide a collaborative platform to foster research and clinical trials.
- Enhance patient engagement by integrating patient-reported outcomes and shared decision-making tools.

Methods. The IFR represents the largest FM-specific registry worldwide, comprising data from over 10,000 patients. It systematically records demographic, clinical, and psychosocial variables, as well as treatment histories and follow-up data. Data collection follows a standardized protocol, ensuring uniformity and comparability across centers. Advanced analytic methods, including machine learning algorithms, have been employed to identify clusters of patients with distinct clinical profiles, enabling phenotype-specific interventions and predictive modeling for treatment outcomes.

Results. Data from the IFR have revealed substantial heterogeneity in symptom burden, comorbidities, and therapeutic outcomes. The identification of patient subgroups has enabled targeted approaches, optimizing treatment efficacy and reducing trial-and-error prescribing. Longitudinal analyses have demonstrated significant improvements in symptom management when integrating pharmacological treatments with rehabilitation programs, psychological support, and lifestyle modifications. Additionally, the registry has proven valuable for monitoring the adoption of innovative therapies and assessing their real-world impact.

Preliminary analyses suggest that the IFR is also instrumental in evaluating the cost-effectiveness of treatments and identifying barriers to care. Furthermore, it has supported the validation of novel diagnostic tools, including remote monitoring systems. The ability to integrate wearable technologies and patient-reported outcome measures (PROMs) offers a future-oriented approach to data collection, providing continuous insights into disease activity.

Conclusions. The Italian Fibromyalgia Registry represents a groundbreaking platform for understanding FM and enhancing its management. It transcends the role of a data repository, functioning as a dynamic tool for precision medicine, clinical decision-making, and research innovation. The registry fosters collaboration between healthcare providers, researchers, and policymakers, fostering a unified effort to address the unmet needs of FM patients.

Future developments will focus on integrating artificial intelligence, wearable technologies, and telemedicine to enhance data acquisition, predictive modeling, and remote monitoring. These advancements are expected to support early diagnosis, refine treatment algorithms, and improve long-term outcomes. The IFR also provides an opportunity to involve patients more actively in their care, enabling a paradigm shift toward personalized and participatory medicine.

By bridging the gap between research and practice, registries like the IFR have the potential to reshape FM care and advocacy, ensuring evidence-based management, policy development, and improved quality of life for patients. The IFR sets a model for disease-specific registries worldwide, demonstrating how data-driven insights can drive innovation and meaningful change.

IS-31

ENFA: the European experience

Gunilla Göran

The European Network of Fibromyalgia Associations (ENFA)

Fibromyalgia, FM is a long-term pain disorder. The World Health Organization WHO estimates that 15 to 30 million people in Europe suffer from FM. So far, we have not had any relevant knowledge about how European countries have diagnosed, treated, and rehabilitated people with FM. The disease has been controversial for decades and by health authorities still considered difficult to treat in healthcare.

Over the past 16 years of ENFA's existence we have heard the reports of all member organization from our network, with the focus in their struggles at national level, to create a better condition for these patients. Although all reports are very similar, there is no record at European level of these difficulties or any positive achievement of each country.

The survey is conducted through the network implemented and supported by our members. Through the study we can see there is no legislation to support these patients. There is a lack of knowledge among national politicians and the profession and a consequence of this is a substandard national European health insurance system and an insufficient individual patient care. These shortcomings in society cause profound deterioration for people/patients with FM which affects families, working life, and provides a low quality of life. In addition, with enormous costs for the European countries.

IS-32

ASAF Association: the Israeli experience

Sharon Gur

Fibromyalgia patient association (ASAF), Israel

Established in 2000, the ASAF Association has represented Fibromyalgia (FM) and chronic fatigue syndrome (CFS) patients in Israel for over two decades. The association advocates for patients' rights, raises awareness within the medical community, and promotes research and clinical trials. A significant milestone was achieved in 2021 when the National Insurance Institute of Israel (NII) introduced a dedicated FM disability clause, formally recognizing patients' unique challenges.

Historically, patients faced neglect, stigma, and systemic barriers in medical care and social rights, with symptoms often dismissed as psychosomatic. The FM disability clause, implemented in March 2022, provides a structured process for disability benefits, acknowledging FM as a distinct medical impairment. Since its implementation, NII data indicates an increase in applications for FM-related disability recognition. Although the approval rate has risen slightly, concerns about an overwhelming influx of applications have proven unfounded.

Challenges persist, particularly when FM overlaps with other impairments such as physical disabilities or mental health conditions. The inclusion of mental health considerations in the clause acknowledges the psychological impact of FM but introduces complexities, such as distinguishing secondary depression from independent conditions, which can affect evaluations and benefits.

Stress is a well-documented trigger for exacerbating fibromyalgia symptoms. A study titled "A tale of two cities - the effect of low intensity conflict on prevalence and characteristics of musculoskeletal pain and somatic symptoms associated with chronic stress" (Buskila *et al.*, 2010). The research found a link between chronic stress and symptom severity.

Following Operation 'Iron Swords', heightened stress in Israel due to ongoing conflicts has likely contributed to worsening symptoms and an increase in fibromyalgia-related disability cases. Addressing this trend requires additional resources and a deeper understanding of stress's impact on the condition.

ASAF continues to support patients and their families through a hotline, seminars, a website, and publications. Recently, the association published an extensive book on fibromyalgia and chronic fatigue syndrome, providing up-to-date insights and practical resources for patients and professionals. ASAF also advocates for greater societal and institutional recognition, striving to improve patients' lives through systemic changes. These efforts help reduce patients' "invisibility" and enhance their legitimacy within the healthcare system.

While the FM disability clause is a significant achievement we continue to work towards its improvement, focusing on the following objectives:

- Developing clearer guidelines for assessing disability, especially in cases of overlapping impairments, to facilitate evaluations and reduce subjectivity in decisions.
- Collaborating with NIII and healthcare providers to monitor trends, collect data, and identify necessary policy adjustments.
- Educating policymakers, medical evaluators, and healthcare professionals about the complexities of fibromyalgia and its psychological and physical impacts, incorporating insights from leading research.
- Promoting holistic and biopsychosocial care models integrating physical and mental health treatments.

Summary

ASAF leads systemic change aimed at enhancing patients' quality of life. By promoting education, advocacy, and holistic care, and by supporting the patients and their families. The disability clause represents a significant change in the attitude towards patients. There are still challenges to address including the high stress level of patients caused by the war. Through collaboration with policymakers, healthcare providers, and researchers, we lead change. Assaf calls for international collaborations for support and research to improve the quality of patients' lives and find a cure.

Oral Presentations

P-01

Effects of immersive virtual reality-based exercise on quality of life, stress, anxiety, depression, and handgrip strength in fibromyalgia: a pilot study

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Background. Fibromyalgia (FM) is a chronic rheumatic disorder characterized by musculoskeletal pain, fatigue, and psychoemotional symptoms. Virtual reality has proven to be an innovative and motivating tool for its management. Several studies indicate that it can improve quality of life indices and reduce psychoemotional symptoms in FM, although studies with immersive virtual reality-based exercise (iVRE) are limited.

Objective. To evaluate the effectiveness of iVRE on the impact on quality of life, stress, anxiety, depression, and handgrip strength in people with FM.

Methods. A single-arm, pre-post-test pilot study was conducted. Individuals with a diagnosis of FM were recruited by convenience sampling. The iVRE protocol consisted of twelve sessions of 10 minutes of warm-up and 15 minutes of exercises applied with the Oculus Quest 2™ device. The impact on quality of life was assessed with the FIQ-R questionnaire, stress, anxiety, and depression with the DASS-21 Questionnaire, and handgrip strength with the Baseline® dynamometer. Pre-post means were compared with the T-Student test ($p=0.05$).

Results. Eleven individuals (40.6 ± 11.2 years) completed the protocol (10 women). There were significant differences in favor of iVRE in quality of life impact ($p=0.001$, Cohen's d : 1.48), handgrip strength ($p=0.05$, Cohen's d : 0.26), Depression ($p=0.05$, Cohen's d : 0.73) and anxiety ($p=0.05$, Cohen's d : 0.73).

Conclusion. A 6-week iVRE program significantly reduces the impact on quality of life, anxiety, and depression and improves handgrip strength in people with FM. Future research should investigate the physiological effects through systemic biomarkers to explain the scope of this therapeutic modality.

Table I. Effect of the iVRE program on FIQ-R, DASS21 and Handgrip.

Outcome	Pre-test		Post-test ¹		<i>p</i> -value	Cohen's <i>d</i>
	Media	SD	Media	SD		
FIQ-R	65.70	20.83	36.74	18.69	<.001	1.48
DASS21 Depression	8.54	6.54	5.27	4.45	0.03	0.73
DASS21 Anxiety	8.18	4.16	7.00	4.94	0.03	0.73
DASS21 Stress	11.36	5.18	9.54	4.61	0.11	0.51
Handgrip Dinamometry (Kg.)	16.99	6.41	20.62	6.65	0.04	0.26

iVRE: Immersive virtual reality-based exercises; DASS21: Depression anxiety and stress scales; FIQ-R: Revised Fibromyalgia Impact Questionnaire; SD: Standard Deviation; ¹measurement after 6-weeks of iVRE.

P-02

Fibromyalgia and the painful self: a meta-analysis of resting-state fMRI data

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Background and Objective. Fibromyalgia (FM) is a complex medical condition. The nested hierarchical model of self and its extension to the pain matrix could represent an integrated theoretical framework that might comprehensively captures FM clinical features.

Methods. A multi-level meta-analysis was conducted. Resting-state functional connectivity (RS-FC) studies that compared patients with FM and healthy controls (HCs) were included. The association between RS-FC among self-related brain regions and pain intensity was also explored in the FM group.

Results. Eleven studies were eligible for meta-analytic procedures. Patients with FM, compared to HCs, were characterized by an increased RS-FC between the default mode network (DMN) and areas ascribed to interoceptive (e.g. insula) and exteroceptive (e.g. premotor, visual/auditory cortices) self layers. The clinical group also showed a reduced RS-FC among regions of the pain matrix (i.e. periaqueductal gray matter, somatosensory areas) involved in pain modulation. An increased RS-FC within DMN together with a heightened RS-FC between DMN and interoceptive self areas were positively associated to pain intensity reported by patients with FM.

Conclusion. The nested hierarchical model of self and its extension to the pain matrix might represent comprehensive neurobiological backgrounds for clarifying core mind-body clinical features of FM.

P-03

Temperament, personality traits and central sensitivity: a comparative analysis in fibromyalgia, chronic migraine and comorbid patients

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Background. Fibromyalgia (FM) and chronic migraine (CM) are nociplastic pain disorders that significantly impair daily functioning and pain perception. While research highlights links between central sensitivity, temperament, and personality in FM, little is known about the combined psychological characteristics of individuals with comorbid FM and CM (Fibromig).

Objective. To compare central sensitization, temperament, and personality traits among women with FM, CM, and Fibromig. We hypothesized that the Fibromig group would exhibit higher levels of central sensitivity and more dysfunctional temperament and personality traits.

Methods. A total of 295 women from hospitals in Rome, Milan, and Pavia completed validated assessments, including the Highly Sensitive Person Scale-12, Personality Inventory for DSM-5 (PID-5), and Central Sensitivity Index (CSI).

Results. The Kruskal-Wallis test revealed significant differences across most measures: the Fibromig and FM groups reported higher scores to temperamental traits, such as ease of excitation ($p=0.001$) and aesthetic sensitivity ($p=0.003$), compared to CM. The same trend was observed for personality traits such as negative affectivity ($p=0.013$) and psychoticism (Fibromig only; $p=0.021$). No differences in detachment, antagonism, or disinhibition were shown. Central sensitivity ($p=0.001$) and low sensory threshold ($p=0.001$) were significantly greater in Fibromig than in FM and CM.

Conclusion. Fibromig and FM patients exhibit distinct traits, particularly

heightened sensitivity to stimuli, negative affectivity, psychoticism and central sensitivity symptoms. Identifying these traits is crucial for developing tailored psychological interventions to address the unique needs of this population.

P-04

Associations between fibromyalgia symptoms, psychopathology, resilience, and posttraumatic stress in psychiatric outpatients

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Background. Fibromyalgia, characterized by widespread pain and diverse somatic symptoms, is frequently associated with psychiatric comorbidities. Understanding the psychological and psychosocial factors contributing to fibromyalgia symptoms is essential for improving therapeutic interventions.

Methods. This cross-sectional study included 52 psychiatric outpatients with affective, anxiety, and stress-related disorders (71.2% women, mean age 37.3±8.9 years). Associations were examined between the Score of Fibromyalgia (SIFIS questionnaire), attachment anxiety and avoidance (ECR-R), resilience (BRS), childhood resilience, psychopathology (CORE-OM), posttraumatic stress (PCL-5), and dissociation (DES). Data were analyzed using the correlational analysis and nonparametric Mann-Whitney U Test.

Results. The SIFIS score was significantly positively correlated with psychopathology, posttraumatic stress, and dissociation and negatively correlated with resilience scores. Twenty-two patients (43.5%) had a fibromyalgia score ≥4. Patients with higher fibromyalgia scores exhibited significantly elevated attachment anxiety and avoidance ($p=0.003$), greater psychopathology symptoms ($p=0.004$), higher dissociation scores ($p=0.001$), higher posttraumatic stress scores ($p=0.004$), and lower resilience and childhood resilience scores ($p=0.011$ and 0.015 , respectively).

Conclusion. Symptoms indicative of fibromyalgia are strongly associated with psychopathology, dissociation, posttraumatic stress, and attachment insecurity, while being inversely related to resilience. These findings highlight resilience and attachment security as critical therapeutic targets for managing widespread pain. Interventions focused on fostering secure attachment, alongside addressing posttraumatic stress and dissociation, may reduce fibromyalgia symptoms and improve patients' psychological well-being.

P-05

Health inequities and societal costs for patients with fibromyalgia and their spouses: a Danish cohort study

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Background. Although common, the management of fibromyalgia continues to represent a clinical challenge and studies identify ongoing issues with healthcare pathways, increased healthcare utilization and societal cost. No studies have evaluated these aspects in spouses of fibromyalgia patients.

Objective. To provide longitudinal data on the burden of illness of individuals with fibromyalgia and their spouses compared with selected match populations in Denmark.

Methods. Population-based, case-control study using Danish registry data (1994-2021). Fibromyalgia cases were identified in the National Patient Register and compared 1:4 to age, sex, spouse, and geographically matched general population comparators. Spouses/cohabitants at the time of the fibromyalgia diagnosis were identified and compared with matched controls. Healthcare and societal costs, socioeconomic status and comorbidities were evaluated for fibromyalgia patients, spouses, and matched controls.

Results. 9,712 fibromyalgia patients (94.9% females, mean age 50 years) and 5,946 spouses were included. At diagnosis, fibromyalgia patients had significantly more comorbidities, including rheumatic disorders, compared with controls. Spouses also had more comorbidities. Both groups had higher healthcare and public transfer costs and lower employment income at all timepoints. Income loss in fibromyalgia patients began years before diagnosis. Employment rate at diagnosis was 29%. Ten years post-diagnosis, 50% received disability pension versus 11% of controls. The net average increased societal cost for fibromyalgia patients was €27,193 per patient-year after diagnosis.

Conclusion. Fibromyalgia has major health and socioeconomic consequences for fibromyalgia patients, their partners, and the society and calls for improved health care strategies aiming at early diagnosis and timely interventions matching individual patient needs.

P-06

Use of cannabis liquid plant extract 10 mg/ml Δ9-tetrahydrocannabinol and 10 mg/ml cannabidiol in patients with fibromyalgia syndrome: preliminary data

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Background. An alteration of the endocannabinoid system has been hypothesized in patients with fibromyalgia (FM), but studies on the use of medical cannabis (MC) in this condition remain limited and often inconclusive. Among the available phytocannabinoid-based compounds, those containing equal doses of Δ9-tetrahydrocannabinol (THC) and cannabidiol (CBD) are known to be better tolerated, as CBD blocks the active metabolite of THC, reducing the risk of psychoactive effects without compromising efficacy.

Objective. This study aims to analyze data on the use of MC with a stable dose of THC (10 mg/ml) and CBD (10 mg/ml) in FM patients.

Methods. This prospective observational study included patients with FM diagnosed according to the 2016 ACR criteria, prescribed a liquid cannabis extract (10 mg/ml THC and 10 mg/ml CBD). Consecutive patients were enrolled from January to April 2024, with clinical and demographic data collected at baseline, after 15 days of therapy (T15), and after 30 days (T30). Patients completed self-administered questionnaires evaluating symptoms. The primary endpoint was pain reduction on the VAS scale at T30.

Results. Data from 36 female patients were analyzed. A significant reduction in VAS pain scores was observed at T30 ($p=0.0002$). Significant improvements in WPI ($p=0.002$), SSS ($p=0.001$), FIQR ($p=0.008$) and specific FIQR symptoms were noted. No significant associations were found between primary outcomes and clinical or demographic characteristics.

Conclusion. Our findings suggest that MC (CBD 10 mg/ml-THC 10 mg/ml) may represent an effective therapeutic strategy for FM. Further studies with larger cohorts and longer follow-up are planned to confirm these results.

P-07

Effect and experiences with the digital self-management program EPIO

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Background. Wide ranges of psychosocial aspects may affect patients living with various chronic pain conditions. Psychosocial treatment approaches may thus be of importance and make a difference in patients' everyday life.

Objective. The current studies aimed to examine effect and user experiences of EPIO, a digital self-management intervention for people living with chronic pain.

Methods. Participants (266), predominantly female with diverse pain conditions including Fibromyalgia or unspecific musculoskeletal pain, were assigned participants to either the EPIO intervention or a usual care control group in a 12-month randomized controlled trial (RCT). Additionally, a qualitative study explored the experiences of 25 participants after the 12 months RCT.

Results. Significant psychological benefits were noted in the RCT intervention group, including improvements in depression, vitality, mental health, reductions in anxiety and pain catastrophizing. Self-regulatory fatigue and health-related quality of life were also favorably impacted. Thematic analysis of the qualitative interviews uncovered three key areas of change after intervention access: enhanced cognition, improved coping strategies, and engagement with specific program content and functionalities. Participants specifically reported heightened insight and self-awareness, acceptance, improved emotion regulation, and acquiring practical strategies for daily pain management.

Conclusion. These studies underscore EPIO's potential in promoting psy-

chological well-being and coping mechanisms for those with chronic pain, suggesting that such digital interventions may bridge the accessibility gap in psychosocial support for these populations. The research highlights EPIO's capability to foster sustainable positive change, offering a viable option for enhancing the quality of life for individuals grappling with chronic pain.

P-08

Is the brain stem a significant part of the pain network? Long-term effects of neuromodulation by SET in FM patients

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Background. Different studies report diminished baroreflex sensitivity (BRS) in fibromyalgia (FM) patients that interferes the signal relay to the nucleus tractus solitarius (dmNTS) termed as NTS reflex arcs is associated with increased sympathetic stress responses and central sensitization in FM. The present study examined central and autonomic components of pain processing before and after systolic extinction training (SET) that combines operant-behavioral pain therapy with baroreceptor training. SET aims at new-programming of the NTS-reflex arcs in FM.

Methods. 125 FM patients were treated with SET and compared with 32 healthy controls (HC). Evoked potentials (N50, N150, P260, P390) to electrical stimuli of 3 different intensities and BRS were evaluated during either the systolic or diastolic peak of the cardiac cycle. Clinical pain, pain threshold and pain tolerance were assessed pre-, post- and at follow-up treatment.

Results. FM showed a pretreatment attenuation of early evoked potentials (N50, N150) that increased to HC levels after treatment ($p=0.01$). In addition, in FM both early and late evoked potentials were influenced by stimulus intensity (all p -values 0.01) before but not after treatment. At 6-12 months, the magnitudes of potentials evoked by all stimuli were similar to that evoked in HC. Pain threshold and tolerance significantly increased after therapy and 82% of FM reported pain remission after 6-12 months.

Conclusion. Cardiac gated peripheral afferent stimulation combined with behavioral treatment may induce changes in central pain processing that lead to pain remission. SET activates both brain stem, sensory and cognitive-affective brain regions to re-program pain inhibitory mechanisms.

P-09

Pharmacological profiling of piracetam in expression of reserpine induced fibromyalgia in mice

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Background. About 90% of patients resort to alternative therapies due to the scarcity of pharmacological options in fibromyalgia (FM). Thus piracetam was selected keeping in view its antioxidant, antiepileptic, antinociceptive, antidepressant, and neuroprotective properties.

Objective. The current study aimed to investigate the pharmacological effects of piracetam in murine model of FM. It was focused on evaluating the effects of piracetam on locomotion, hyperalgesia, allodynia, anxiety and depression in FM, followed by high performance liquid chromatography (HPLC) analysis of the neurotransmitters alterations in brain tissue samples.

Methods. FM mouse model was developed via three consecutive doses of reserpine 0.25 mg/kg dissolved in 0.9% normal saline added to acetic acid (final concentration of 0.1–0.5%). Acute study on piracetam (doses 200, 300 and 400 mg/kg) with pregabalin 30 mg/kg as standard was designed. Open field test, tail immersion test, von-Frey filaments, acetone drop test, elevated plus maze and tail suspension test were done. The level of serotonin was quantified in the brain samples via HPLC. Data was analyzed using appropriate statistical tests.

Results. Acute treatment of piracetam 400 mg/kg remarkably diminished the pain symptoms of FM with even better results than the standard on some testing days. Similarly, the non-pain symptoms, anxiety and depression were also reduced with piracetam 400 mg/kg but the effect declined on later days of study. However, depression in locomotion could not be reversed at any dose of piracetam. Lastly, neurochemical analysis revealed the decline in serotonin levels caused by reserpine could not be reversed the any dose of piracetam.

Conclusion. Reserpine causes depletion of the biogenic amines, so certain features of FM could not be reversed on once daily dosing of piracetam. Such findings warrant further studies at chronic and sub chronic levels.

Poster Presentations

P-10

Reducing fibromyalgia severity through a home-based exercise program: pilot study

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Background. It has been known for some time that strength training is one of the exercise modalities indicated to help manage fibromyalgia. Despite this growth, most studies present face-to-face proposals and use one-repetition maximum (1-RM) as a reference for prescription.

Objective. This study aimed assess fibromyalgia severity after a home-based training program and one month of detraining.

Methods. Thirteen participants (45.77±12.82 years) completed the 16-session protocol, consisting of seven main exercises performed at maximum intended velocity during the concentric phase. The sessions lasted 50 minutes (sessions 1-8) to 75 minutes (sessions 9-16) with progression from 3 sets of 8 repetitions to 5 sets of 6 repetitions. Sessions were performed via Google Meet and adaptations were made when necessary, using predefined modifications and the Borg scale for perceived exertion. Fibromyalgia severity was assessed using the Fibromyalgia Impact Questionnaire (FIQ) at baseline, post-training, and after detraining. Paired t-tests were used to compare pre- and post-training results, with significance set at $p \leq 0.05$.

Results. The protocol significantly reduced the total FIQ score ($p=0.004$) and improved domains including physical capacity ($p=0.03$), morning tiredness ($p=0.01$), stiffness ($p=0.003$), anxiety ($p=0.03$), and depression ($p=0.01$). No significant differences were observed between post-training and detraining.

Conclusion. The home-based strength training program focusing on execution velocity, was effective in reducing fibromyalgia severity, improving specific domains, such as physical capacity, morning tiredness, stiffness, anxiety, and depression. Furthermore, these effects sustained after one month of detraining.

P-11

Fibromyalgia: chronic pain due to a blood dysfunction?

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Background. Fibromyalgia (FM) is a common chronic disorder with chronic pain. The cause of FM remains undefined, but a number of factors suggest that blood features can contribute to its occurrence.

Objective. The aim of the present study was to evaluate new blood indexes and possible correlations between blood parameters and pain in FM patients.

Methods. Women diagnosed with FM for at least 6 months were asked to participate. Data were collected without a close relationship to the visit date but with the presence of FM. Blood inflammatory indices were calculated: neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR) and systemic inflammatory response index (SIRI). To evaluate a possible correlation with pain, the Visual Analogue Scale (VAS) and Fibromyalgia Impact Questionnaire (FIQ) were used.

Results. One hundred forty-four women were contacted: Pre-menopausal (n=64), menopausal (n=80). There was high variability among subjects for most of the parameters, with high percentages of values at the 'normal' low or high limit and several values outside the 'normal' ranges. All blood inflammatory indices had values outside the 'normal' range in many subjects (NLR n=23; PLR n=67; SIRI n=42), suggesting an inflammatory state and/or dysregulation of the inflammatory system. No correlations were found among blood and pain parameters.

Conclusion. The results clearly suggest the presence of blood dysfunctions. Thus the possibility of the involvement of the blood in chronic pain remains an open question, since most of the symptoms commonly present in FM patients could have their physio-pathological basis in blood components. Any findings would open up new possibilities for therapeutic intervention.

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P-12

Two weeks of home-based exercises are effective in improving the mental health of women with fibromyalgia

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During the COVID-19 pandemic, while maintaining the need for specific treatment for women with fibromyalgia, alternative home-based treatments were implemented to reduce the impacts of the disease on patients. The objective of the present study was to verify whether two weeks of home-based exercise were effective in improving the mood, anxiety, and depression of women with fibromyalgia. This study took place in 2022 at the end of the COVID-19 pandemic. The intervention consisted of 16 women, eight in the intervention group (IG) who performed two weeks of home-based resistance training, receiving through a WhatsApp group, a video with the entire exercise session to be performed, repeated three times a week, lasting up to 70 minutes each, totaling 6 sessions; and eight in the control group (CG) who maintained their usual care, remaining sedentary. Data collection was performed using Google Forms, applying the following instruments: Brunel Mood Scale, Beck Depression Inventory, and Beck Anxiety Inventory. The women in the CG had a mean age of 58.63±9.4 and the women in the IG had a mean age of 51.25±12.87 years. After two weeks of home-based physical exercise, the IG results for anxiety, depression, and mood profile remained stable, with no significant changes, while about the CG, there was a significant worsening in the mood profile, with reduced vigor and worsening of anxiety, indicating a negative mood. In this sense, home-based resistance training had a protective effect on mental health, against the impact of isolation caused by the pandemic.

P-13

Immediate effect of auricular acupuncture on pain modulation in patients with fibromyalgia: findings from a real-life experience

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Background. Acupuncture has a millennia-long history in the treatment of musculoskeletal pain. The use of microsystem-based techniques, such as auricular acupuncture, remains an underexplored area in fibromyalgia (FM).

Objective. To evaluate the 24-hour efficacy of semi-permanent needles ear application in reducing musculoskeletal pain in FM patients and to identify predictors of response.

Methods. Patients with FM were included and proposed a cycle of auricular acupuncture treatment. A baseline clinimetric evaluation was performed. Pain symptoms were reassessed 24 hours after the application of semi-permanent needles using the Numerical Rating Scale for current pain (NRS now) and the Widespread Pain Index (WPI). A reduction of 2 points on the NRS was considered a significant improvement.

Results. A total of 47 patients were included (45 women and 2 men), with a median age of 57 years (IQR 46-64) and a median baseline FIQR of 63.3 (IQR 51.0-82.3). At 24 hours after needles application, a significant reduction in pain symptoms was observed, both in terms of current pain and widespread pain (NRS now decreased from 7 [IQR 5-8] to 6 [IQR 3-7], $p=0.001$; WPI decreased from 10 [IQR 7-14] to 7 [IQR 3-11], $p=0.001$). A significant improvement was recorded in 21 (44.7%) of the 47 patients studied. Logistic regression analysis identified baseline NRS now as the only significant predictor of response, with higher baseline scores associated with greater improvements (Table I).

Conclusion. Auricular acupuncture may represent a rapidly effective treatment for pain in patients with FM.

Table 1. Logistic regression analysis of predictors for significant improvement in NRS now (variables significantly associated with significant improvement at the previous univariate analyses).

Variables	Odds ratio	Std. err.	z	p	95% CI
GAD7	0.834	0.091	-1.66	0.098	0.673-1.033
CSI9	0.910	0.093	-0.91	0.361	0.745-1.113
PHQ9	0.999	0.142	-0.00	0.998	0.755-1.322
NRS now	1.652	0.389	2.13	0.033	1.041-2.623
-cons	8.749	23.869	0.80	0.427	0.041-1837.483

P-14

Kinesiophobia: manifestation of disease or obstacle to treatment?

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Background. Fibromyalgia is a chronic condition characterized by widespread musculoskeletal pain, fatigue, sleep disturbances and neurocognitive changes. Diagnosis is clinical and treatment multidisciplinary: regular physical activity, weight control, psychological counselling and pharmacological therapies.

Objective. This study aims to assess the presence of kinesiophobia in fibromyalgia patients and its correlation with pain catastrophization and disease severity.

Methods. Forty-five consecutive patients were enrolled according to the 2016 American College of Rheumatology criteria from January to April 2023. Data on demographics, clinical status and current therapeutic strategies were collected. Kinesiophobia was assessed using the Tampa Scale of Kinesiophobia (TSK), pain catastrophizing with Pain Catastrophizing Scale (PCS), and disease severity with the Revised Fibromyalgia Impact Questionnaire (FIQR), Polysymptomatic Distress Scale (PDS) and modified Fibromyalgia Assessment Status (FASmod).

Descriptive analysis was conducted using Fisher's, Chi-square and Mann-Whitney test to compare patients with TSK scores ≥ 37 and < 37 . Statistical significance was set at p -values 0.05. Pearson correlation analysis was performed between FIQR, TSK and PCS scores.

Results. Patients with kinesiophobia (TSK ≥ 37) were older, had higher antidepressants/antispasmodic use and engaged in less physical activity. Kinesiophobia correlated with a higher disease severity (FIQR - total and subset, PDS, FASmod) and pain catastrophizing.

FIQR total score increased with TSK ($r=0.68$) and PCS ($r=0.64$) scores.

Variable	TSK ≥ 37	TSK < 37	P-value
Total patient	17	28	
Female	17 (100)	26 (92.8)	0.26
Education (degree)	2 (11.7)	11 (39.2)	0.09
Married/partnered	11 (68.7)	15 (71.4)	0.55
Pregnancy	13 (76.5)	8 (33.3)	0.006
Miscarriages	4 (23.5)	6 (25)	0.91
Antidepressants	10 (58.8)	8 (28.6)	0.045
Anticonvulsants	6 (35.3)	7 (25)	0.46
Antispasmodic	10 (58.8)	8 (28.6)	0.045
Cannabis	1 (5.9)	1 (3.6)	0.71
Opioids	3 (17.7)	2 (7.1)	0.28
Estroprogestin	0 (0)	4 (14.3)	0.10
Analgesics	7 (41.2)	9 (32.1)	0.54
Vitamin d supplementation	11 (64.7)	14 (50.0)	0.34
Aerobic physical activity	0	6 (21.4)	0.040
Age	51.0 \pm 13.1	45.7 \pm 11.8	0.030
BMI	28.0 \pm 9.0	24.5 \pm 4.0	0.23
FIQR total score	85.2 \pm 11.5	56.8 \pm 22.6	<0.0001
FIQR physical function	25.3 \pm 4.1	15.7 \pm 8.7	0.0001
FIQR overall impact	16.8 \pm 3.0	9.8 \pm 5.9	<0.0001
FIQR symptoms	43.2 \pm 6.0	31.3 \pm 10.4	<0.0001
PDS	25.4 \pm 4.1	19.7 \pm 5.8	0.001
FAS MOD	32.5 \pm 5.4	26.0 \pm 8.2	0.007
PCS rumination	17.6 \pm 1.8	10.2 \pm 4.5	<0.0001
PCS magnification	6.3 \pm 1.3	2.3 \pm 2.1	<0.0001
PCS Helplessness	19.7 \pm 3.4	10.6 \pm 5.6	<0.0001
PCS total score	43.6 \pm 5.7	23.1 \pm 10.8	<0.0001

Conclusion. Kinesiophobia is prevalent in fibromyalgia, especially in severe cases with pain catastrophizing. It poses a significant barrier to treatment, exacerbating disease severity. Catastrophizing beliefs about pain contribute to increased disability, underscoring the need for multidisciplinary approaches to address these challenges.

P-15

Nutrition and eating disorders in fibromyalgia: a topical combination in need of integrated therapies

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Background. Fibromyalgia (FM) is often associated with psychiatric changes. The spectrum of manifestations varies from moderate symptoms to severe forms.

Objective. To investigate the prevalence of nutrition and eating disorders, alterations in body image, and psychiatric symptoms in a sample of patients with FM.

Methods. A cross-sectional study was conducted on 45 consecutive patients with FM according to ACR criteria, referred to a dedicated outpatient clinic. For each patient, clinical manifestations, demographic characteristics, duration of symptoms, education level, lifestyle, clinical parameters, and PROs such as: FIQR, WPI, SSS were collected. All patients underwent to a psychometric assessment, including eating habits, using the following instruments: Eating Attitude test at 26 Items (EAT 26), Body Uneasiness Test (BUT), Self-Report Symptom Inventory-Revised (SCL- 90).

Results. In our FM population eating disorder (EAT 2620) were more frequently detected in patients with higher BMI, higher FM symptom severity, and higher BUT and SCL-90 scores. FM severity, measured by FIQR, WPI, SSS, had a low correlation with EAT 60 and BUT ($r=0.22$ and $r=0.30$), but rather high with SCL-90 ($r=0.71$).

Table. Baseline population characteristics of patients with fibromyalgia with and without nutrition and eating disorders.

Variables	EAT26 ≥ 20	EAT26 < 20	P value
Patients	35	10	
Females	33 (94.3)	10 (100)	0.44
Education (degree)	11 (31.4)	2 (20)	0.27
Married/partners	19 (63.3)	7 (100)	0.30
Pregnancy	18 (58.1)	3 (30)	0.12
Abortions	7 (22.6)	3 (30)	0.63
Antidepressants	16 (45.7)	2 (20)	0.14
Anticonvulsants	10 (28.5)	3 (30)	0.93
Musculoskeletal relaxants	16 (45.7)	2 (20)	0.14
Cannabis	1 (2.9)	1 (10)	0.33
Opioids	3 (8.6)	2 (20)	0.31
Estroprogestinics	3 (8.6)	1 (10)	0.89
Analgesics	11 (31.4)	5 (50)	0.28
Vit D	17 (48.6)	8 (80)	0.08
Physical aerobic activity	5 (14.3)	1 (10)	0.72
Age	49.1 \pm 10.9	42.8 \pm 16.3	0.23
BMI	26.8 \pm 6.9	22.6 \pm 3.7	0.040
FIQR total	71.3 \pm 22.0	54.7 \pm 25.4	0.052
FIQR physical function	20.2 \pm 8.6	16.2 \pm 8.6	0.15
FIQR over all impact	13.2 \pm 5.9	9.8 \pm 6.1	0.12
FIQR sintoms	37.9 \pm 9.5	28.6 \pm 11.7	0.015
WPI tot	12.9 \pm 4.5	10.6 \pm 4.5	0.14
SSS tot	10.0 \pm 2.2	7.8 \pm 1.7	0.005
WPI SSS	22.9 \pm 5.5	18.4 \pm 6.0	0.017
FAS MoD	29.4 \pm 7.1	25.6 \pm 9.7	0.22
BUT global severity	1.7 \pm 1.2	0.7 \pm 1.1	0.002
BUT WP	2.2 \pm 1.3	0.8 \pm 1.0	0.003
BUT BIC	2.2 \pm 1.4	0.9 \pm 1.2	0.008
BUT A	1.4 \pm 1.3	0.5 \pm 1.3	0.020
BUT CSM	1.1 \pm 0.9	0.5 \pm 0.8	0.022
BUT D	1.3 \pm 1.2	0.4 \pm 1.1	0.003
SCL 90 total score	159.1 \pm 6.2	95.5 \pm 91.3	0.008
SCL 90 somatization	2.6 \pm 0.8	2.0 \pm 0.10	0.14
SCL 90 obsessive-compulsive	2.2 \pm 1.0	1.2 \pm 1.2	0.009
SCL 90 interpersonal sensibility	1.4 \pm 0.9	0.7 \pm 1	0.010
SCL 90 depression	2.2 \pm 0.9	1.3 \pm 1.2	0.012
SCL 90 anxiety	1.9 \pm 1.0	1.0 \pm 1.2	0.012
SCL 90 anger-hostility	1.1 \pm 0.6	0.7 \pm 0.98	0.028
SCL 90 phobic-anxiety	1.2 \pm 1.1	0.5 \pm 1.1	0.031
SCL 90 paranoid ideation	1.5 \pm 0.9	0.6 \pm 1.0	0.005
SCL 90 psychoticism	0.7 \pm 0.6	0.5 \pm 1.0	0.06

Conclusion. Our results show the high prevalence of nutrition and eating disorders in FM patients, particularly those with more severe FM symptoms. In addition, these patients have a high prevalence of body image disturbances and other psychiatric symptoms. These data support the importance of an early diagnosis of these disorders in FM patients, and the need for a multidisciplinary approach, with the involvement of the psychiatrist and psychologist, to manage such complex patients.

P-16

Severe fibromyalgia: do central sensitivity mechanisms work together?

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Objective. We aimed to evaluate in a hospital-based setting which symptoms of Fibromyalgia (FM) were more commonly associated with disease severity.

Methods. cross-sectional evaluation of consecutive patients with a diagnosis of FM who attended the dedicated outpatient clinic between 2020 and 2022. Clinical symptoms including disease duration, demographic characteristics, education level, lifestyle, clinical and laboratory parameters and therapeutic regiment were collected for each patient as well as Pros Questionnaires Categorical and continuous variables were compared between patients with FIQR ≤ 64 and those with FIQR ≥ 64 , using descriptive statistics (Chi squared test/ Fisher test and Mann-Whitney test). Thereafter, a logistic regression having as dependent variable FIQR ≥ 64 was carried out.

Results. 187 patients were included. Patients with FIQR ≥ 64 (severe disease), had a higher frequency of bowel symptoms/irritable bowel syndrome, menstrual cycle alteration or endometriosis, headache and depression, compared to those with FIQR ≤ 64 , (Table). At univariate analysis, the variables statistically associated with FIQR ≥ 64 were: male gender, active smoking, depression, bowel symptoms, sicca syndrome, and more than 4 episodes of headache each month.

In the multivariate model, the variables independently associated to FIQR ≥ 64 were depression and more than 4 episodes of headache /month.

Conclusion. Patients with severe FM more frequently present with headache, depression, irritable bowel syndrome and dysmenorrhea. All those symptoms belong to the family of central sensitivity syndromes, suggesting that some central sensitivity mechanisms play a key role in disease activity and severity.

Table. Baseline characteristics of THE fibromyalgia patient population.

	FIQR ≤ 64	FIQR ≥ 64	P
	81	106	
middle age	48.9 (13.2)	47.78 (10.6)	0.23
males	11 (13)	6 (6)	0.06
disease time, media (SD)	7.6 (8.5)	8.0 (7.3)	0.20
BMI, media (SD)	26.2 (4.2)	25.7 (4.7)	0.46
WPI, media (SD)	10.3 (4.8)	13.7 (4.1)	<0.001
SSS, media (SD)	7.4 (2.3)	10.1 (1.6)	<0.001
WPI-SSS, media (SD)	17.8 (5.9)	23.5 (5.0)	<0.001
alterations of bowel movements	34 (42)	61 (59)	0.024
Irritable bowel syndrome	27 (33)	51 (49)	0.032
Asthenia	72 (89)	54 (89)	0.89
Xerostomia o xerophthalmia	24 (30)	42 (42)	0.08
Dysmenorrhoea e/o endometriosis*	7 (10)	18 (20)	0.006
headache >4 episodes per month	37 (48)	70 (67)	0.009
Depression	30 (42)	76 (77)	<0.001
Antidepressants	24 (31)	49 (45)	0.022
Analgesic drugs	16 (20)	39 (38)	0.012
Pilates	1 (1)	8 (8)	0.046
Cognitive-behavioural therapy	1 (1)	11 (11)	0.011

Data expressed as frequency (percentage) unless otherwise specified.

*Variables calculated only for female subjects.

P-17

Pain processing and its alterations in fibromyalgia: an ALE meta-analysis of fMRI studies of multisensory task-evoked painful experiences

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Background. Fibromyalgia (FM) is a chronic syndrome characterized by widespread musculoskeletal pain. Subjective experiences of pain and related psychological processes (e.g. pain catastrophizing) are also considered core clinical features of FM. Nevertheless, the neurobiological underpinnings of these key FM clinical characteristics have not been clarified yet.

Objective. This study aims at quantitatively summarizing empirical findings of task-dependent fMRI studies evaluating neural responses toward the presentation of multisensory pain-eliciting stimuli among patients with FM compared to healthy controls (HCs).

Methods. A voxel-based ALE meta-analysis using a clustering level family-wise error correction ($p=0.05$) was conducted to evaluate: i) pain-eliciting stimuli processing (painful stimuli vs. no-pain stimuli) among FM patients and HCs (i.e. single analysis); ii) common and distinct patterns of neural responsiveness toward painful stimuli presentation (i.e. contrast and conjunction analyses); iii) areas characterized by an heightened responsiveness toward painful stimuli administration among FM patients compared to HCs.

Results. The insula was the key region of painful stimuli processing among FM patients ($n=12$ studies). The thalamus and prefrontal regions characterized pain processing among HCs ($n=12$ studies). The dorsal portion of anterior cingulate cortex and pre-supplementary motor areas showed a heightened reactivity toward pain stimuli presentation among FM patients compared to HCs ($n=13$ studies).

Conclusion. Qualitative and quantitative alterations of neural "pain matrix" responses might underpin core pain-related symptoms of FM. Psychotherapeutic implications will be discussed.

P-18

Mental disorders, psychological distress, and well-being in fibromyalgia: results from an observational study

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Background. Fibromyalgia (FM) is a central sensitization syndrome characterized by neuro-circuit dysfunction and chronic musculoskeletal pain, fatigue, alterations in sleep and cognitive disturbances. FM is also characterized by psychiatric and psychological issues.

Objective. The present project aimed to verify whether mental disorders may influence psychological distress and well-being in FM.

Methods. FM patients ($n=124$) were recruited at the Rheumatology Unit of the Academic Hospital Careggi (Florence, Italy). Patients were assessed via the Mini-International Neuropsychiatric Interview (M.I.N.I.) (Sheehan et al., 1998) to formulate mental disorder diagnoses and self-report instruments assessing psychological symptoms, distress, and well-being.

Results. The sample included 117 women and 7 men; average age was 55.04 years ($SD=12.324$). Higher levels of anxiety ($p<0.05$; $q=0.000$), somatisation ($p<0.05$; $q=0.000$), depression ($p<0.05$; $q=0.000$), anger-hostility ($p<0.05$; $q=0.000$), psychological distress ($p<0.05$; $q=0.030$), abnormal illness behavior ($p<0.05$; $q=0.00$), mental pain ($p<0.05$; $q=0.000$), sense of loneliness ($p<0.05$; $q=0.004$) and lower well-being ($p<0.05$; $q=0.000$) were found in FM patient with at least one mental disorder if compared to patients without such diagnoses.

Conclusion. Patients presenting FM and at least one mental disorder have more severe psychological symptoms and distress and poorer well-being and quality of life than FM patients without mental disorders. Investigating these aspects is seminal to reach a comprehensive understanding of FM, being a complex functional disorder.

P-19

Impact of spa therapy on physical activity, sleep and heart rate variability among individuals with fibromyalgia: results of an ancillary studyClaire Cracowski¹, Claire Colas², Enkejda Hodaj¹, Vincent Pichot²¹INSERM CIC1406, Clinical Research Center, Grenoble Alpes University Hospital, France; ²INSERM, U1059, SAINBIOSE, DVH, Department of Clinical and Exercise Physiology, Jean Monnet University, Saint-Etienne, University Hospital Center, France

Background. Spa therapy is recommended to manage symptoms of fibromyalgia, but the physiological mechanisms underlying this improvement have been poorly studied. In an original study, we explored the effect of a 3-week rheumatology spa treatment for fibromyalgia patients on quality of life and with a symptom severity questionnaire.

Objective. We present here the results of an ancillary study which explored three secondary criteria using objective measurement: diurnal actimetry for physical activity analysis, nocturnal actimetry for sleep analysis and heart rate variability.

Methods. Eighty-three fibromyalgia patients were randomized to participate in an immediate 3-week rheumatological spa therapy, either a start within 6 weeks after inclusion (interventional group, n=39) or a delayed, start 6 months after inclusion (control group, n=44). Patients were asked to wear an actimeter (n=56) to assess diurnal physical activity and sleep quality and a 24-h Holter ECG (n=60) to assess nocturnal heart rate variability at baseline, 3 months and 6 months after inclusion.

Results. Time spent in sedentary and light physical activity was reduced to ~30 min at 6 months in the interventional group ($p=0.027$). Sleep quality and heart rate variability were not improved.

Conclusion. Spa therapy made it possible to reduce sedentary activities in patients' daily life for up to 6 months afterwards, concomitant with the improvement in quality of life, pain and fatigue as highlighted in the original Thermalgi study.

P-20

Assessing the clinical validity of patient-reported outcomes measurement information system (PROMIS) surveys to trend fibromyalgia symptoms longitudinallyDevika Das, Shawn Fokken, Ivana Croghan, Ryan Hurt, Michael Mueller
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Objective. To assess and compare the longitudinal change in patient-reported survey scales for patients empaneled by the fibromyalgia treatment program.

Methods. This is a prospective observational study. Clinical and research surveys, including the Widespread Pain Index (WPI), Symptom Severity Score (SSS), Revised Fibromyalgia Impact Questionnaire (FIQR), PROMIS Cognitive Function, PROMIS Pain Intensity, PROMIS Pain Interference, PROMIS Fatigue, and the Linear Analog Scale Assessment (LASA-1) will be administered electronically to adult patients diagnosed with fibromyalgia at their baseline evaluation, 3 months, and 6 months. Percent change will be calculated at each time point for each survey. Internal consistency and convergent validity of the PROMIS surveys, WPI, and SSS will be validated against the respective FIQR domains.

Results. A total of 31 patients have been included in the study thus far. Baseline scores included a WPI of 12.6/19, SSS of 8.9/12, and FIQR of 64.8/100. Baseline PROMIS Cognitive Function score was 7.1/20, Pain Intensity was 6.5/10, Pain Interference was 16.3/20, Fatigue was 17.5/20, and LASA-1 was 4.5/10.

Conclusion. Studying and comparing important patient-reported outcomes surveys over time will allow the department to refine our clinic model and treatment algorithms. In addition, because the PROMIS surveys have been validated in several chronic conditions, results could be compared among different patient populations.

P-21

Management of psychiatric comorbidities in fibromyalgia patients treated with pregabalin versus milnacipranEduardo Espiridion¹, Angelica Arshoun², Andrew Murdock²¹Psychiatry, Tower Health-Reading Hospital, USA; ²Drexel University College of Medicine, USA

Fibromyalgia is a debilitating chronic disease with symptoms of pain and fatigue that profoundly impact a patient's quality of life. This can lead to the development of psychiatric comorbidities causing compounding decline in overall well-being. While the treatment options available for fibromyalgia are limited, pregabalin (a γ -aminobutyric acid analog) and milnacipran (a serotonin-norepinephrine reuptake inhibitor) are options for patients seeking relief. Based on these mechanisms of action, it is likely that milnacipran might be more effective at treating and preventing comorbid psychiatric conditions than pregabalin. We used TrinetX, deidentified health care organization (HCO) network, to collect and analyze our data. Patients with fibromyalgia who were not receiving opioid analgesics were included in the study, and separated into treatment groups if they were prescribed pregabalin or milnacipran. Risk ratios, hazard ratios, Kaplan Meier analysis, and log rank test were performed to analyze the differences in psychiatric comorbidities, somnolence, opioid use disorder, depressive episodes, and anxiety disorder. Our results suggest that milnacipran has a statistically significant decrease in risk of somnolence (1.3%, CI 95%= 0.9-1.8%, $p=0.00010$, opioid use disorder (0.9%, CI 95%=0.6-1.2%, $p0.0001$) and depressive episodes (2.7%, CI 95% = 1.5-4.0%, $p=0.0001$) compared to the pregabalin group, but no significant difference when comparing anxiety disorder (1%, CI 95%=0.3-2.3% $p=0.119$). log rank tests also show that all patients treated with milnacipran had a statistically significant increase in time to diagnosis for all psychiatric conditions assessed compared to pregabalin (somnolence 10.12%, $p0.001$; opioid use disorder 1.6%, $p0.001$; depressive episode 7.77%, $p=0.001$; anxiety disorder 4.48%, $p=0.008$). Overall, the data suggest that milnacipran might be more effective at reducing psychiatric comorbidities and overall increase the time to psychiatric diagnoses of these patients. However, further research is needed to determine the clinical significance of these findings.

P-22

Composite Autonomic Symptom Score 31 (COMPASS 31) for the assessment of symptoms of autonomic dysfunction in people with fibromyalgiaSonia Farah, Fausto Salaffi, Maria Giovanna Lommano, Benedetta Bianchi, Mariachiara Mangiafico, Marco Di Carlo
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Background. Fibromyalgia (FM) is associated with autonomic dysfunction, affecting heart rate, blood pressure, gastrointestinal motility, and vascular tone. The Composite Autonomic Symptom Scale (COMPASS-31) is a validated tool for assessing dysautonomia.

Objective. To evaluate autonomic dysfunction symptoms in FM patients using COMPASS-31 and explore correlations with the Revised Fibromyalgia Impact Questionnaire (FIQR), Polysymptomatic Distress Scale (PDS), 2019 Modified Fibromyalgia Assessment Status (2019 Mod FAS), and Pain Detect Questionnaire (PDQ).

Methods. This cross-sectional study included 77 women with FM (mean age 57.6) and 86 healthy controls (mean age 58.1), matched for BMI, sex, and age. Participants completed the Italian COMPASS-31, assessing six autonomic domains. Spearman's correlation, Kruskal-Wallis tests, and ROC analysis were performed.

Results. Autonomic dysfunction was observed in 64.9% of FM patients versus 3.5% of controls. The optimal COMPASS-31 threshold for confirmed autonomic dysfunction was 38.28 (sensitivity 71.4%, specificity 91.9%, LR+ 8.78). FM patients showed significantly higher COMPASS-31 total scores (47.03 ± 17.27 vs. 21.55 ± 11.48 ; $p=0.00001$) and across all autonomic domains. Positive correlations emerged between COMPASS-31 and FIQR ($rs=0.47$, $p=0.0001$), PDS ($rs=0.36$, $p=0.0001$), and 2019 Mod FAS ($rs=0.32$, $p=0.004$). Strong correlation was noted between COMPASS-31 and PDS ($rs=0.56$, $p=0.0001$). Disease severity correlated with autonomic symptoms (Kruskal-Wallis, $p=0.001$).

Conclusion. FM patients experience significant autonomic dysfunction measurable by COMPASS-31, with strong associations with FM severity and neuropathic pain indices.

P-23

Psychological profiling in nociplastic pain: insights from cluster analysis of fibromyalgia, vulvodynia, and chronic headachesMartina Mesce¹, Luigi Palla^{1,2}, Sara Bottiroli^{3,4}, Lorys Castelli⁵, Piercarlo Sarzi-Puttini^{6,7}, **Federica Galli¹**¹Department of Dynamic, Clinical and Health Psychology, Sapienza University of Rome, Italy; ²Department of Public Health and Infectious Diseases, Sapienza University of Rome, Italy; ³Department of Brain and Behavioral Sciences, University of Pavia, Italy; ⁴Headache Science and Neurorehabilitation Centre, IRCCS Mondino Foundation, Italy; ⁵Department of Psychology, University of Turin, Italy; ⁶Rheumatology Department, IRCCS Galeazzi-Sant'Ambrogio Hospital, Italy; ⁷Department of Biomedical and Clinical Sciences, Università degli Studi di Milano, Italy**Background.** Nociplastic pain (NP) arises from altered nociceptive processing and persists without identifiable tissue damage. It is commonly observed in conditions such as fibromyalgia (FM), vulvodynia (VU), and chronic headaches (CH). Despite its prevalence, the relationship between NP conditions and psychological profiles remains underexplored, particularly in the presence of comorbidities.**Objective.** This study aimed to identify NP patient subgroups through cluster analysis based on psychological variables, including central sensitivity syndrome, environmental sensitivity, traumatic experiences, personality traits, defense mechanisms, and alexithymia. A secondary goal was to evaluate whether psychological profiles align with diagnostic categories (FM, CH, VU, or comorbidity).**Methods.** A total of 895 Italian women were recruited via snowball sampling through patient associations. Participants completed a web-based survey comprising validated psychological assessments to measure central sensitivity, environmental sensitivity, traumatic experiences, personality traits, defense mechanisms, and alexithymia.**Results.** Cluster analysis revealed three subgroups representing "severe," "moderate," and "mild" psychological impairment. A one-way MANOVA showed significant differences across clusters, with central sensitivity, alexithymia, and personality traits explaining the largest variance. Chi-square tests demonstrated that NP diagnoses were distributed across clusters, suggesting overlapping psychological profiles. The FM group predominantly exhibited severe impairment, while comorbid conditions clustered similarly within moderate-to-severe profiles.**Conclusion.** The findings highlight distinct psychological profiles within NP conditions, advocating for a multidimensional approach to diagnosis and treatment. Psychological features should be integral to intervention strategies, tailoring care to individual profiles to enhance outcomes in chronic pain management.

P-24

Psychopathological and quality of life burdens in fibromyalgia, chronic migraine, and their comorbidity (Fibromig)Filippo Maria Nimbi¹, Sara Bottiroli^{2,3}, Lorys Castelli⁴, Marco Cavicchioli¹, Agata Benfante⁴, Martina Cangelosi², Martina Mesce¹, Alessandro Torelli¹, Cristina Iannuccelli⁵, Manuela Di Franco⁵, Piercarlo Sarzi-Puttini^{6,7}, **Federica Galli¹**¹Department of Dynamic, Clinical and Health Psychology, Sapienza University of Rome, Italy; ²Department of Brain and Behavioral Sciences, University of Pavia, Italy; ³Headache Science and Neurorehabilitation Centre, IRCCS Mondino Foundation, Italy; ⁴Department of Psychology, University of Turin, Italy; ⁵Rheumatology Unit, Department of Clinical Internal, Anaesthesiologic and Cardiovascular Sciences, Sapienza University of Rome, Italy; ⁶Rheumatology Department, IRCCS Galeazzi-Sant'Ambrogio Hospital, Italy; ⁷Department of Biomedical and Clinical Sciences, Università degli Studi di Milano, Italy**Background.** Fibromyalgia (FM) and chronic migraine (CM), both classified as nociplastic pain disorders, significantly impair daily functioning and psychological well-being. These conditions frequently co-occur, forming a comorbid entity termed "Fibromig". Despite their high comorbidity (45–80%), little research has focused on the combined psychological manifestations of Fibromig.**Objective.** This study aimed to compare psychopathological symptoms (somatization, depression, anxiety, obsessive-compulsive tendencies, interpersonal sensitivity, hostility, phobic anxiety, paranoid ideation, and psychoticism) and quality of life (QoL) in women diagnosed with FM, CM, and Fibromig. We hypothesized that the Fibromig group would exhibit higher

scores on psychopathological measures and report poorer mental health outcomes compared to FM or CM alone.

Methods. Data were collected from 295 women across three hospitals in Italy. Psychopathological symptoms were assessed using validated tools, including the Symptom Checklist-90-Revised, the General Anxiety Disorder Scale, the Hamilton Depression Rating Scale, and the Short Form-12 for QoL evaluation. **Results.** The Kruskal-Wallis test revealed significant differences across all measures ($p=0.001-0.004$). Fibromig and FM groups reported more severe psychopathological symptoms than the CM group, particularly in depression, anxiety, obsessive-compulsive tendencies, interpersonal sensitivity, hostility, phobic anxiety, paranoid ideation, and psychoticism. Somatization was significantly higher in Fibromig than in FM or CM. Both FM and Fibromig groups showed more compromised physical and mental QoL.**Conclusion.** Psychopathological symptoms are prevalent in CM, FM and particularly Fibromig, highlighting the need for mental health interventions alongside clinical management. Early psychological care may mitigate the impact of these symptoms on disease progression and patient outcomes.

P-25

Work disability in tertiary care chronic pain patients**Helena Jamnik**

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Background. Sustained employment maintains social roles and integration and thus counteracts the negative consequences of chronic pain. Understanding barriers to better integration into the labor market is important for the treatment of chronic pain.**Objective.** To examine characteristics associated with disability claims in patients with chronic pain who are still working and compare them with patients who are already retired due to disability.**Methods.** Clinically collected data from 389 consecutive patients presenting to the interdisciplinary pain team were analyzed.**Results.** Patients claiming full compensation had higher symptom burden compared to those who did not apply for disability (widespread pain index - WPI mean 13 vs. 9.2; painDETECT 24 vs. 17.9; NPRS pain after 6min walk test 8.7 vs. 5.6), poorer physical performance tests (timed up and go mean 20.9s vs. 7.2s; 6-minute walk test 175m vs. 310m), higher sick leave in the previous year (12 months vs. 4.3), higher unemployment (67% vs. 21%) and lower education (elementary school only 50% vs. 13%). Patients who applied for disability were younger (53.4 vs. 59.7), had higher painDETECT (23.5 vs. 18.9) and poorer hand grip strength (left - 40% vs. 69% of normal) compared to those who already had disability.**Conclusion.** Chronic pain patients with higher work disability have higher symptom burden, poorer physical performance and more difficult social background. Patients already retired on disability show fewer symptoms and better function (hand grip) than patients who are still working, despite their older age.

P-26

Prevalence of fibromyalgia symptoms among Polish rheumatologists**Tomasz Jasiński**

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Background. Fibromyalgia (FM) is a chronic generalized pain syndrome, often accompanied by symptoms such as sleep disorders, fatigue and cognitive disorders. The prevalence of this disorder is estimated at 2-8% in the general population.**Objective.** The aim of the study was to assess the incidence of fibromyalgia among doctors - participants of a conference in 2024 in Krakow.**Methods.** The study was conducted as a targeted survey - the FSQ (Fibromyalgia Survey Questionnaire). Participants were asked to complete a questionnaire assessing FM symptoms based on current diagnostic criteria - Widespread Pain Index (WPI) and the Symptom Severity Scale (SSS). Additionally, participants were asked about gender and age.**Results.** 107 people (81.3% women and 18.7% men) completed the questionnaire. The average age of the respondents was 47.4 years (26-85 years).

Seven respondents (6.5%) met the criteria for the diagnosis of FM, including five women and two men. Although the majority of respondents (93.5%) did not meet the criteria for the diagnosis of FM, the prevalence of FM symptoms was significant. Chronic pain was reported by almost half of the respondents (48.6%), the frequency of other symptoms was: fatigue - 89.7, cognitive disorders - 65.4%, sleep - 75.1%, depression - 31.8%.

Conclusion. The prevalence of FM in this study is similar to the results of another study assessing the prevalence of FM among resident physicians. Our results also indicate a high incidence of chronic pain and other symptoms such as fatigue, sleep disorders, and depressive disorders among rheumatologists.

P-27

Altered breathing pattern in women with fibromyalgia: a case-control study

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Background. Several findings have been found such as reduced muscle strength and pulmonary function in people with chronic pain compared to asymptomatic individuals. Decreased levels of carbon dioxide have also been seen in chronic pain conditions including fibromyalgia, indicating hypoventilation. Respiratory rate and tidal volume are two key components of ventilation that influence CO₂ elimination and hypoxemia may result from any condition that increases respiratory rate or tidal volume.

Objective. This study aimed to investigate breathing pattern, including tidal volume and respiratory rate, and the role of thoracic mobility in women with FM compared to healthy controls.

Methods. Thirty-eight women with fibromyalgia and 44 age-matched healthy women participated in this study. Respiratory rate was measured using a portable monitor, and tidal volume was assessed through spirometry. Thoracic mobility was evaluated by measuring chest expansion in the level of xiphoid process. Perceived stress was assessed with the Perceived Stress Scale-10 questionnaire.

Results. Women with fibromyalgia exhibited significantly higher respiratory rate and lower tidal volume compared to healthy controls. Thoracic mobility was reduced in participants with fibromyalgia. There was a significant positive correlation between tidal volume and chest expansion ($r=0.46, p=0.004$), but no correlation between chest expansion and respiratory rate for women with fibromyalgia. Group differences in respiratory rate, tidal volume, and chest expansion remained significant after adjusting for BMI, age and perceived stress.

Conclusion. Fibromyalgia is associated with altered breathing function, including higher respiratory rate and lower tidal volume. Thoracic mobility may contribute to these changes.

P-28

Exploring the impact of validation and avoiding the term 'Pain' on patient well-being and symptom perception in chronic pain management

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Background. Effective communication is pivotal in the management of chronic pain. Validating a patient's experiences fosters trust, while linguistic choices may influence symptom perception. This study evaluates the impact of combining validation techniques with the avoidance of the term "pain" on patient well-being and symptom perception.

Objective. To determine whether validating patient experiences and replacing the term 'pain' with neutral alternatives improve mood, overall well-being, and perceived symptom intensity in patients undergoing chronic pain therapy.

Methods. A two-week observational study was conducted with 12 patients. During Week 1, physicians utilized validation techniques to acknowledge and empathize with patients' experiences. In Week 2, validation was maintained, and 'pain' was systematically replaced with terms such as

'discomfort' or 'sensations'. Patients completed standardized questionnaires weekly, assessing changes in mood, well-being, and symptom perception. Data were analyzed for proportions of positive, neutral, and negative responses across both weeks.

Results. During Week 1, 83.3% of patients reported improved mood and symptom relief, with no reports of negative changes. In Week 2, 58.3% noted improvements in symptom perception, while 33.3% experienced mood enhancement. Neutral responses increased in Week 2 compared to Week 1, particularly regarding mood (66.7%). No negative effects were observed.

Conclusion. Validation significantly improved mood and symptom perception, while the avoidance of 'pain' showed moderate additional benefits, particularly for symptom relief. These findings highlight the critical role of empathic communication and linguistic precision in chronic pain management. Further studies are warranted to refine and expand these techniques.

P-29

Mental disorders and physical disease in spouses of fibromyalgia patients through the lens of different types of psychosocial adaptation

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Objective. Positive and negative reinforcement of chronic pain by the partner modify the patient's pain perception and their psychosocial adaptation. According to life event research we assume chronic pain has an impact on partners' mental and physical health. We hypothesize partners display mental and physical disorders dependent on patient's psychosocial adaptation.

Methods. Seventy-six male partners in fibromyalgia patients participated in the Structured Clinical Interview for DSM-V to assess current mental disorders. Spousal medical records were evaluated to identify disease diagnoses over the last five years. The prevalence of mental disorder and physical diseases were tested to the patient's psychosocial adaptation subgroups (Turk, 1996).

Results. Regarding mental disorders, 77.8% of the partners in dysfunctional subgroup (DYS-partners) showed anxiety disorders, 81.8% of the partners in interpersonal-distressed subgroup (ID-partners) showed depression, and 72.2% of the adaptive copers (AC-partners) did not display any mental disorders ($p=0.001$). Regarding physical diseases, partners of chronic pain patients showed cardiovascular diseases (34.2%) with the majority in DYS-partners (50%, $p=0.001$), oncological diseases (13.2%) with the majority in DYS-partners (50%, $p=0.001$), low back pain (32.9%) with the majority in ID partners (68%, $p=0.001$). Healthy partners were found in 90.9% of the AC-partners ($p=0.001$).

Conclusion. These results underscore the necessity of considering the impact of chronic pain on the partners as well as the patients. It is important to acknowledge the role of psychosocial adaptations on the partner. The presence of chronic pain not only affects the patient but his or her significant other. The influences of chronic pain are bidirectional.

P-30

The interactive effects of systolic extinction training (SET) on fibromyalgia patients and their spouses

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Background and Objective. This study investigated the effectiveness of Systolic Extinction Training (SET), combining operant pain treatment (OPT) with baroreflex training (BRT), compared to alternative treatments not only on fibromyalgia (FM) patients but importantly on their spouses.

Methods. 124 female FM patients and their male spouses were randomized into 5 groups: SET ($n=40$), OPT+TENS ($n=20$), AE+BRT ($n=21$), CBT+BRT ($n=22$), and Waiting List ($n=21$). Assessments using MPI and PRSS were conducted pre-treatment, post-treatment (5 weeks), and at 6-12-month follow-up.

Results. SET patients showed significant pain and interference reduction and increased baroreflex sensitivity compared to control groups ($p=0.01$). SET-Spouses reported greater reductions in perceptions of patients' pain and interference, maintaining improvements for over 12 months. Both SET and OPT+TENS Spouses demonstrated significant reductions in catastrophizing, while SET-Spouses additionally showed decreased in the solicitous behaviors ($p=0.005$) that maintain chronic pain.

Conclusion. While treatments incorporating OPT effectively reduced both catastrophizing, only SET produced improved pain and interference perceptions in both patients and spouses. Results highlight the necessity of spouse integration in FM treatment and the effectiveness of SET as a comprehensive approach. Further research is needed to explore patient-spouse treatment dynamics; however, these results indicate that spousal behaviors and attitudes also must change to resolve chronic pain.

P-31

Effects in sleep of NESA neuromodulation technique application in patients with fibromyalgia: a case study of three patients

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Background. In patients with fibromyalgia the prevalence of sleep problems is high. Sleep disturbances in this population exacerbate pain and poor sleep. In recent years, the NESA (Spanish name Neurestimulación superficial aplicada) has been gaining attention in sleep disorders treatment.

Objective. The aim of this study was to evaluate the changes in sleep problems of patients with fibromyalgia undergoing NESA.

Methods. The NESA neuromodulation was carried out over the ten-day cycle of 30 minutes with evaluation on the first and tenth day of therapy. Pittsburgh sleep quality index (PSQI) and the NESA protocol were completed before and after the intervention.

Results. All three patients reported the following prior to inclusion in the study: shorter and shallower sleep, problem falling asleep, nocturnal awakenings. After therapy using NESA all patients reported improvement in the NESA protocol. They assessed improvements in sleep quality and latency, faster falling asleep, long sleep duration and absence of night interruption. The sum of PSQI global score reduced after NESA in the individual patients, respectively: in the first patient by 14, in the second by 15, in the third by 10 points.

Conclusion. The observed progress in NESA is promising and exciting and may be able to push the boundaries in the treatment of fibromyalgia patients in the future.

P-32

Knowledge, attitude and practice toward fibromyalgia among fibromyalgia patients: a web-based cross-sectional study in China

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Background. This study aimed to explore the knowledge, attitude and practice (KAP) of fibromyalgia patients toward fibromyalgia.

Methods. This web-based cross-sectional study was conducted in China between February and March 2023 among fibromyalgia patients using a self-administered questionnaire.

Results. A total of 401 valid questionnaires were enrolled, including 326 (81.30%) females and with a mean age of 42.42 ± 11.78 years. The mean scores for KAP were 7.14 ± 2.72 (possible range: 0-10), 27.31 ± 4.24 (possible range: 8-40) and 28.08 ± 5.55 (possible range: 10-50), respectively. Multivariate logistic regression analysis showed knowledge (OR=1.09, 95%CI: 1.04-1.15, $p=0.001$) and patient global impression (PGI) on average pain severity in the last week (OR=0.89, 95%CI: 0.81-0.97, $p=0.011$) were independently associated with positive attitude. Attitude (OR=1.08, 95%CI: 1.02-1.14, $p=0.006$), initial consultation in orthopedics (OR=2.15, 95%CI: 1.24-3.73, $p=0.006$) and age (OR=0.98, 95%CI: 0.96-1.00, $p=0.037$) were

independently associated with proactive practice. The structural equation model demonstrated that knowledge had a positive effect on attitude ($\beta=0.21$, $p=0.006$), and Widespread Pain Index (WPI) exhibited an impact on both knowledge ($\beta=-0.04$, $p=0.001$) and attitude ($\beta=-0.52$, $p=0.001$).

Conclusion. Fibromyalgia patients showed suboptimal knowledge, moderate attitude and inactive practice toward fibromyalgia. To enhance fibromyalgia patient outcomes, recommendations include targeted education, addressing rural-urban disparities in knowledge, emphasizing early diagnosis, and adopting patient-centered approaches to promote positive attitude and better disease management.

P-33

Effect of non-invasive transcutaneous auricular vagal nerve stimulation in patients with fibromyalgia: a pilot study

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Objective. Transcutaneous vagus nerve stimulation (tVNS) represents a safe and accessible therapeutic option in patients with fibromyalgia. This pilot study evaluated the efficacy of tVNS in improving autonomic function and symptom severity.

Methods. The study enrolled 25 female patients (mean age 48.6 ± 7.3 years) with a confirmed diagnosis of fibromyalgia (ACR 2016). Inclusion criteria: minimum disease duration of 6 months and stable pharmacological treatment for at least 4 weeks. Exclusion criteria: cardiovascular or neurological disorders, uncontrolled psychiatric conditions, or implanted electronic devices. Participants underwent a 28-day tVNS treatment protocol using the Nurosom® device, which delivers non-invasive electrical stimulation via electrodes applied to the tragus of the left ear. Stimulation intensity was individually adjusted based on each patient's sensory threshold. Clinical assessments were performed at baseline (t0) and after treatment (t1) using the COMPASS31 questionnaire to evaluate autonomic dysfunction across six specific domains (Fig. 1) and the FIQR to assess perceived symptom severity. Statistical analyses were conducted using IBM SPSS Statistics 28. Data normality was assessed with the Shapiro-Wilk test. Pre- and post-treatment differences were analyzed using paired t-tests, or Wilcoxon signed-rank tests in cases of non-normal distributions. Effect sizes were calculated using Cohen's d to assess the magnitude of observed differences. Pearson's correlation coefficient (r) was employed to explore associations between changes in COMPASS31 and FIQR scores, with significance set at $p=0.30$.

Results. The total COMPASS31 score showed a significant reduction from 49.47 ± 9.2 to 43.11 ± 8.8 ($p=0.019$; Cohen's d=0.68), indicating a moderate improvement in autonomic function. Notably, the orthostatic domain exhibited a statistically significant change ($p=0.016$). Additionally, the tor domain demonstrated a positive trend ($p=0.05$), suggesting a potential enhancement in vascular regulation and circulatory response.

Conclusion. This pilot study suggests that transcutaneous vagus nerve stimulation is a safe and potentially effective therapy for improving autonomic function in patients with fibromyalgia.

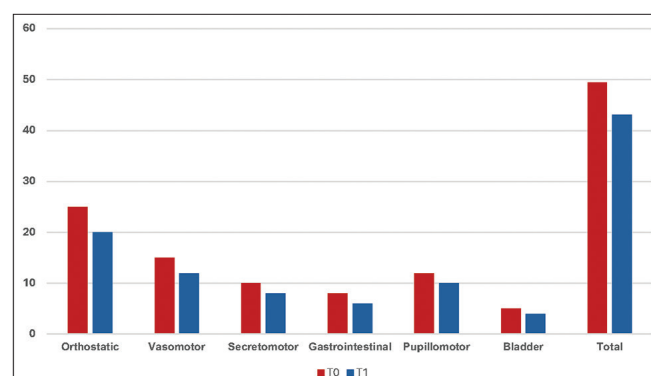


Fig. 1. Changes in mean COMPASS31 domain scores between T0 and T1, highlighting improvements in autonomic function, with significant differences in the Orthostatic ($p=0.016$) and Vasomotor ($p=0.05$) domains.

P-34

Antidepressant use in fibromyalgia, effect of duloxetine and analysis of C-reactive protein (CRP) levels: a retrospective study

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Background. Patients with Fibromyalgia (FM) exhibit higher rates of depression and anxiety and are prescribed antidepressants including duloxetine. Psychological factors can exacerbate pain, fatigue, sleep disturbances, and reduce functional capacity. C-reactive protein (CRP) is a biomarker frequently used to assess systemic inflammation.

Objective. To explore the relationship between FM, psychiatric comorbidities, and psychotropics and assess the impact of duloxetine treatment on CRP levels.

Methods. FM was identified using the ICD-9 codes (729.1). Body mass index (BMI), psychiatric conditions and history of antidepressant prescriptions were documented. Available CRP values were gathered and compared between patients prescribed duloxetine.

Results. FM=331, (289 female, 42 male), mean BMI 36.5 kg/m² (SD 9.0), depression n=242. Antidepressants ever prescribed: Duloxetine: 177 patients (53%), bupropion 115 patients (35%), selective serotonin reuptake inhibitors (SSRIs) 182 patients (55%). Currently prescribed: duloxetine (n=75, 22%, 58% decrease), bupropion (n=38, 11%, 67% decrease), and SSRIs (n=53, 16%, 71% decrease). Among with depression, 167 had previously been on an SSRI (69%), while 52 remained on an SSRI (21%, a 69% decrease). Patients were significantly more likely to be on an SSRI if they had co-morbid depression ($p=0.001$).

CRP level, total n=52 patients, first draw 2.4796 mg/L, second draw n=35, CRP rose to 4.2888 mg/L, third draw n=23, it reached 5.8926 mg/L. CRP levels and Duloxetine: n=24, 3.59 mg/L. CRP test after initiating duloxetine n=18, the average CRP level dropped to 1.91 mg/L.

Conclusion. Antidepressant maintenance decreased in FM patients; possible factors include non-compliance due to tolerability. Duloxetine may reduce CRP levels in FM.

P-35

Chronic pain co-morbidity and pain medication use in fibromyalgia: a retrospective analysis

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Background. Fibromyalgia (FM) often exhibits higher rates of comorbid health conditions. Chronic pain comorbidities in FM result in fragmented and uncoordinated care. Patients are prescribed various medications, including opioids. To optimize the care of these patients, it is crucial to enhance our understanding of the chronic pain comorbidities and pain medication use in FM.

Objective. To explore the relationship between FM, chronic pain comorbidities, and pain medication prescription patterns.

Methods. FM was identified using ICD codes. Body mass index (BMI), pain medication prescription history, and co-morbid pain condition data were gathered. The co-morbid pain conditions were compared between patients prescribed Opioids, Duloxetine and Pregabalin. Data was analyzed using Chi-square test.

Results. FM n=331, (289 female, 42 male), Mean age: 63.49, Mean BMI: 36.7±8.9. Chronic pain comorbidities: e.g. Irritable Bowel Syndrome n=150 (47%), Arthritis n=143 (44%). Pain medications ever prescribed were pregabalin (n=131, 40%), tramadol (n=190, 57%), and opioids (n=280, 84%). Duloxetine ever prescribed (n=177, 53%). Current medications are pregabalin (n=34, 10%, 74% decrease), tramadol (n=36, 11%, 81% decrease), and opioids (n=70, 21%, 75% decrease). Duloxetine currently prescribed (n=75, 22%, 58% decrease). Opioid prescriptions were associated with arthritis ($p=0.001$). 20% were maintained on an opioid compared to 29% maintained on duloxetine or pregabalin.

Conclusion. FM patients are maintained on duloxetine or pregabalin. Patients with co-morbid arthritis or severe pain condition were more likely to be prescribed opioids. Obesity is a common co-morbidity in our patient population and a common risk factor for arthritis and pain.

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Emotional patterns along the fibromyalgia continuum: a cross-cultural study

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Background. Several studies have reported disturbed emotional functioning in fibromyalgia (FM) (1, 2). Recently, FM has been conceptualized as resulting from a primary or secondary threat-soothing imbalance (3). However, whether and how threat and soothing-related emotional patterns vary along the fibromyalgic continuum remains underexplored.

Objective. The aims are two-fold: 1. identify the most predominant emotions in each fibromyalgic category; 2. characterize and compare the emotional patterns along the fibromyalgic continuum.

Methods. 2871 international participants (n=2603 women) composed of people with self-reported FM (n=2255; 94.5% women) and controls (n=616; 76.6% women) were enrolled. Sociodemographic, clinical, and trait-like affective variables were collected. Descriptive and comparative analyses were conducted.

Results. Participants were categorized into the fibromyalgic categories proposed by Wolfe (4) – absent (n=269), mild (n=170), moderate (n=177), severe (n=796), and very severe (n=1459). The five most highly rated emotions in each category were: 1) joy, love, pleasure, contentment, and enthusiasm (absent and mild); 2) joy, love, anxiety, pleasure, and contentment (moderate); 3) love, anxiety, joy, sadness, enthusiasm (severe); and 4) anxiety, sadness, upset, irritation, fear (very severe). These results show a greater imbalance between threat and soothing activation scores as FM-like symptoms become more severe, with a progressive reduction in active and safety-related positive emotions and increased threat-related emotions.

Conclusion. Results support the FITSS model by showing a link between greater threat-soothing imbalance and more severe FM-like symptoms. These findings point to the value of assessing the emotional functioning of individuals along the fibromyalgia spectrum and, when needed, targeting such imbalance through interventions aimed at improving soothing-related outputs.

Key words: fibromyalgic, emotional patterns, threat-soothing imbalance

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Emotional recognition in fibromyalgia: a pilot study using emotional faces

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Background. Emotional processing disturbances have been reported in fibromyalgia (FM) (1, 2). However, most studies have used basic emotions, failing to include more complex emotional states using the FITSS framework, which poses that FM is rooted in a threat-soothing imbalance (3).

Objective. To explore differences in emotion processing between people with FM and controls.

Methods. Eight women with fibromyalgia ($M_{age}=40.1\pm10.2$) and nine controls ($M_{age}=33.4\pm13.9$) were enrolled. Sociodemographic, clinical, and psychosocial data (e.g. FM-like and depressive symptoms, alexithymia) was collected. Participants were asked to: a) identify as fast as possible the underlying emotion from a set of faces morphing from neutral into one of seven emotional states: anger, sadness, happiness, criticism, compassion, curiosity/enthusiasm, and pain; and 2) identify the underlying emotions and their respective intensity from a set of static emotional faces displaying 25%, 50%, and 75% intensity levels.

Results. All participants well-tolerated the experiment, which they found interesting yet challenging due to the ambiguity and distortion of some

faces. Controls showed a reduction in anxiety levels between pre- and post-task, whereas people with FM showed an increase. People with FM rated their performance worse than controls. No between-group differences were found in reaction times, although people with FM tend to present higher reaction times than controls. No between-group differences were found for accuracy, except for sad faces (more misclassifications in FM).

Conclusion. The experimental protocol was feasible and acceptable. The results are congruent with previous studies (1, 2). Greater samples are needed to draw robust conclusions, as aberrant emotional processing is critical in interpersonal relationships and associated distress.

Key words: fibromyalgia, emotional processing, feasibility, reaction times, accuracy

P-38

Post-Covid in fibromyalgia: treatment with naturopathic complex therapy (NCT). A case study

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Background. Individuals affected with fibromyalgia (FM) have widespread pain, suffer from tiredness, exhaustion, sleep disorders, physical and psychological complaints. Post-COVID in FM, can influence the progression of the chronification process (pain progression, medication-taking behavior, need for medical help, psychosocial stress factors). Quality of life and physical functionality is reduced, disabilities associated with pain are growing. The evaluation of treatment options is still in its early stages.

Objective. A 50-year-old female FM patient with the highest degree of chronification (Gerbershagen stage 3) and post-COVID is admitted to a specialized hospital for inpatient naturopathic complex therapy (NCT) after failed outpatient therapy.

Methods. Outcome parameters are pain intensity, well-being and physical well-being (visual analogue scale), physical functionality (FFbH), and the patient's perceived disabilities (PDI) associated pain.

Results. The NCT treatment path consists of various therapeutic areas, the procedures of which are applied at high frequency in a close temporal context. The intensity of pain was reduced from VAS 7.3 to 1.8, the impairment of well-being from VAS 7.1 to 1 and the physical well-being from VAS 7.1 to 0.6. The values in the FFbH were increased from 52% to 80% and the PDI score reduced from 34.8 to 13.4 points.

Conclusion. The FM patient with post-COVID was able to benefit significantly from NCT. The integration of naturopathic procedures into conventional medicine should be considered as a therapeutic option and should be the subject of studies with large numbers of subjects.

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Prevalence of fibromyalgia in functional motor disorder: a pilot single center study

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Background. Fibromyalgia is a chronic pain condition characterized by generalized pain, fatigue, sleep disturbances and mood disorder – features that are also common in functional motor disorder (FMD). Despite evidence of syndromic overlap between FMD and fibromyalgia, little is known about its prevalence in FMD patients and its impact on health-related quality of life (HRQoL).

Objective. This study aimed to assess the prevalence of fibromyalgia in individuals with FMD using the 2016 American College of Rheumatology diagnostic criteria. Additionally, differences in clinical characteristics and HRQoL between FMD patients with and without fibromyalgia were examined.

Methods. A total of 118 FMD patients (mean age 44.0 years; mean disease duration 6.3 years) completed a validated Fibromyalgia Questionnaire assessing the Widespread Pain Index (WPI) and Symptom Severity Score (SSS). Depression, HRQoL, centrally-acting medication use, motor phenotypes, and motor symptom severity (Simplified FMD Rating Scale; S-FMDRS) were also assessed.

Results. Forty-four percent of FMD patients met FM criteria (95% CI:

5-53%). Fibromyalgia was associated with higher depression scores ($p=0.01$), greater use of centrally-acting medications ($p=0.01$), and lower HRQoL ($p=0.001$), independent of depression. No differences were found in age, FMD duration, motor phenotypes, and SFMDRS. WPI and SSS did not correlate with motor S-FMDRS scores.

Conclusion. Fibromyalgia is highly prevalent in FMD patients and linked to reduced HRQoL. These findings highlight the importance of assessing and addressing comorbid fibromyalgia in FMD management.

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Prepulse inhibition of the blink reflex in patients with functional movement disorder and fibromyalgia

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Background. Prepulse inhibition (PPI) measures subcortical pre-attentive sensory gating, protecting sensory stimulus processing from disruption. Impaired PPI of the blink reflex has been observed in functional motor disorder (FMD) and fibromyalgia. We hypothesized that abnormal PPI might be associated with pain widespreadness and somatic symptom severity in functional disorders.

Objective. To evaluate PPI of the blink reflex in patients with FMD (with and without fibromyalgia), fibromyalgia alone, and healthy controls, and to explore its relationship with pain widespreadness and somatic symptom severity.

Methods. Age- and sex-matched groups of 35 FMD patients without fibromyalgia, 35 with fibromyalgia, 35 fibromyalgia patients, and 35 healthy controls were studied. A weak electrical stimulus to the index finger (prepulse) was used to assess its effect on the R2 response of the blink reflex, induced by supraorbital nerve stimulation 100 ms following prepulse. PPI was defined as the percent decrease in R2 response. Participants completed the Fibromyalgia Survey Questionnaire, including the Widespread Pain Index (WPI) and somatic symptom score (SSS).

Results. All patient groups showed reduced PPI compared to controls, with no differences between fibromyalgia and FMD+fibromyalgia. A significant negative association was found between PPI size and WPI and SSS across all patient groups that remain significant after adjusting for age, depression and anxiety.

Conclusion. These findings suggest shared neural mechanisms in FMD and fibromyalgia, involving impaired early sensory processing at the subcortical level. Abnormal PPI could represent an objective marker of widespread pain and non-motor symptoms in fibromyalgia and other functional disorders.

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Complete dissolution of fibromyalgia symptoms with novel interoceptive therapy

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Background. Pharmacological/non-pharmacological treatments of Fibromyalgia (FM) have low effectiveness.

Objective. A 42-year-old female patient with FMS, PTSD, MDD, anxiety, and painful menstruation had been treated at an academic pain clinic and physical therapy and psychotherapy clinics for 3-5 years with no improvement. She became suicidal and in constant pain. The patient achieved significant symptom dissolution within 15 days of a novel interoceptive therapy to restructure brain areas involved in pain perception.

Methods. The patient was assessed for symptoms including chronic pain, depression, anxiety, insomnia, non-restorative sleep, fatigue, and difficulty concentrating. A novel therapy combined neural stimulation implemented via activation of peripheral mechanoreceptors and attention regulation to shift the organism into an altered state of consciousness to restructure and retrain brain areas involved in pain perception. The therapy was delivered for 4 hours a day, every day, throughout 15 days. Symptom severity was evaluated using standardized questionnaires before, during, and after the intervention over five months.

Results. By the end of the 15th day of therapy the patient experienced consistently restorative sleep, better mood, reduced fatigue, and chronic pain remission. Moderate pain appears after serious stress, but the patient is capable of resolving the pain by herself using interoceptive therapy. Menstruation became non-painful.

Conclusion. This case report suggests that novel interoceptive therapy may provide an effective treatment for reducing fibromyalgia symptoms. Further research is warranted to explore the role of interoceptive therapy in fibromyalgia management.

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The impact of fibromyalgia on the development of a ‘difficult-to-treat’ phenotype in psoriatic arthritis

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Background. Fibromyalgia (FM) is a prevalent cause of chronic widespread musculoskeletal pain and frequently coexists with chronic rheumatic diseases. In psoriatic arthritis (PsA), 16–22% of patients present with concomitant FM. FM has a critical impact on disease complexity, including increased symptom burden, altered patient-reported outcomes, and could contribute to develop a difficult-to-treat (D2T) phenotype.

Objective. This study investigates the role of FM in the development of a D2T phenotype in PsA patients.

Table I. Main demographic, anthropometric and clinical characteristics of the study population.

	PsA tot.	PsA non D2T	PsA D2T	p-value
	182	135 (74.18%)	47 (25.82%)	
Age	58.5 (53-65)	58 (52-65)	59 (53-65)	0.6
Female	119 (65.38%)	81 (60%)	38 (80.85%)	0.007
Disease Duration, months	72 (25-132)	60 (23-120)	96 (47-150)	0.01
BMI	27 (24.5-30.2)	26.6 (24.2-30.2)	27.9 (25.6-30.4)	0.2
Triglycerides	100 (80-149)	97 (80-130)	107.5 (86-160)	0.2
HDL	56 (50-65)	57 (50-65)	53.5 (44-64)	0.3
Hypertension or antihypertensive therapy	90 (53.57%)	56 (45.16%)	34 (77.27%)	<0.0001
Fasting Blood Glucose	90 (85 – 103)	90 (85-100)	98 (84-122)	0.08
MetS	73 (42.94%)	37 (29.37%)	36 (81.82%)	<0.0001
Fibromyalgia	66 (37.08%)	40 (30.08%)	26 (57.78%)	<0.0001
Smoking	67 (36.81%)	47 (34.81%)	20 (42.55%)	0.2
Axial involvement	87 (50.88%)	61 (48.8%)	26 (56.52%)	0.2
Enthesitis	72 (39.56%)	55 (40.74%)	17 (36.17%)	0.3
Dactylitis	23 (13.14%)	13 (10.08%)	10 (21.74%)	0.04
Psoriasis	113 (63.13%)	90 (68.18%)	23 (48.94)	0.01
Onychopsoiasis	34 (19.1%)	22 (16.79%)	12 (25.53%)	0.1
Uveitis	4 (2.2%)	4 (3.01%)	0	0.3
IBD	10 (5.6 %)	7 (5.3%)	3 (6.38%)	0.5
cDMARDs	78 (42.86%)	60 (44.44%)	18 (38.3%)	0.2
b/tsDMARDs	130 (71.43%)	88 (65.19%)	42 (89.36%)	0.001
TJ	1 (0-5)	0 (0- 4)	5 (2 – 9)	<0.0001
SJ	0 (0-1)	0 (0-0)	1 (0-2)	0.0001
PP	5 (3-8)	4 (1-7)	7 (6-8)	<0.0001
PtGA	5 (2-7)	4(1-7)	7(6-8)	<0.0001
EGA	0 (0-2)	0 (0-1)	1 (0-2)	0.03
LEI	0 (0-0)	0 (0-0)	0(0-0)	0.9
Dactylitis	0 (0-0)	0 (0-0)	0 (0-0)	0.2
HAQ	1 (0.13-1.63)	0.63 (0-1.38)	1.63(1.25-2)	<0.0001
PASI	0 (0-0.4)	0 (0-0.6)	0 (0-0)	0.3
DAPSA	12.3 (4.23-22)	9.2 (3.35-16.1)	22 (19.25-23.12)	<0.0001
BASDAI	5.15 (2.6-7.15)	4.15 (1.9-7)	6.625 (5.8-7.9)	<0.0001
MDA	64 (36.16%)	63 (48.09%)	1 (2.17%)	<0.0001
VLDA	30 (16.76%)	30 (22.73%)	0	<0.0001

BMI: Body Mass Index; HDL: high density lipoprotein; MetS: Metabolic Syndrome; IBD: Inflammatory Bowel Disease; cDMARDs: conventional synthetic disease-modifying anti-rheumatic drugs; b/tsDMARDs: biological or targeted synthetic disease-modifying antirheumatic drugs; TJ: Tender Joints; SJ: Swollen Joints; PP: Patient Pain; PtGA: Patient Global Assessment; EGA: Examiner Global Assessment; LEI: Leeds Enthesitis Index; HAQ: Health Assessment Questionnaire; PASI: Psoriasis Area Severity Index; DAPSA: Disease Activity for Psoriatic Arthritis; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; MDA: Minimal Disease Activity; VLDA: Very Low Disease Activity.

Table II. Univariable regression (D2T as dependent variable).

	Ods ratio	95% IC	p
Sex	2.81	1.26 to 6.29	0.01
Hypertriglyceridemia or hypocholesterolemic therapy	5.5	2.27 to 13.32	<0.0001
Hypertension or antihypertensive therapy	4.13	1.87 to 9.07	<0.0001
Fasting Blood Glucose	1.03	1 to 1.05	0.005
MetS	10.82	4.6 to 25.5	<0.0001
Fibromyalgia	3.18	1.6 to 6.4	0.001
Dactylitis	2.47	1 to 6.13	0.04
Psoriasis	0.45	0.23 to 0.88	0.02
TJ	1.2	1.1 to 1.3	<0.0001
SJ	1.5	1.15 to 1.94	0.003
PP	1.46	1.24 to 1.72	<0.0001
PtGA	1.4	1.2 to 1.62	<0.0001
HAQ	3.55	2.1 to 6	<0.0001
DAPSA	1.12	1 to 1.2	<0.0001
BASDAI	1.46	1.22 to 1.75	<0.0001

MetS: Metabolic Syndrome; TJ: Tender Joints; SJ: Swollen Joints; PP: Patient Pain; PtGA: Patient Global Assessment; HAQ: Health Assessment Questionnaire; DAPSA: Disease Activity for Psoriatic Arthritis; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index.

Methods. A cross-sectional, observational study was conducted on PsA patients consecutively enrolled at our Arthritis Center from November 2023 to June 2024. D2T. PsA was defined based on EULAR criteria readapted for PsA. Demographic, disease-related, and psychometric characteristics were assessed. Data analysis included χ^2 tests for categorical variables and Mann-Whitney/Kruskal-Wallis tests for continuous variables, using Stata v.14.

Results. A total of 182 Caucasian PsA patients were included, with 74.18% classified as non-D2T and 25.82% as D2T. The D2T group had a significantly higher prevalence of FM (57.78% vs. 30.08%, $p=0.0001$) and included a greater proportion of females, as showed in Table I. Univariable regression analysis identified FM as a significant predictor of the D2T phenotype (OR: 3.18, 95% CI: 1.6–6.4, $p=0.001$), along with metabolic syndrome, as showed in Table II.

Conclusion. FM is strongly associated with the D2T phenotype in PsA, complicating disease management and outcomes. Future research should focus on tailored management approaches that consider the dual burden of PsA and FM to enhance patient care and quality of life.

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Hope levels in fibromyalgia correlates with depression and alexithymia: a cross-sectional, monocentric study

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Background. Hope is a goal-oriented cognitive construct comprising pathways (strategies to achieve goals) and agency (motivational thoughts to pursue goals). In rheumatic diseases, hope is linked to better compliance and inversely associated with depression and symptom exacerbation. Fibromyalgia (FM), a chronic pain condition, is often accompanied by anxiety, depression, and alexithymia (difficulty identifying and expressing emotions) which exacerbate disease severity and treatment resistance.

Objective. This study evaluated the correlation between hope levels and psychometric variables, including depression and alexithymia, in FM patients.

Methods. A cross-sectional study was conducted on 61 Caucasian female FM patients (median age: 49.9 years) from the Campus Bio-Medico outpatient clinic in Rome. Participants completed psychometric and clinical assessments, including the AHS (Adult Hope Scale), HADS (anxiety and de-

pression), TAS-20 (alexithymia), and FM disease severity measures (WPI, SSS, FSS, FAS-mod, FIQ-R). Statistical analyses included univariable and multivariable regression models.

Results. Significant negative associations were observed between AHS and SSS (Coef. -0.639, $p=0.025$), HADS-Anxiety (Coef. = -0.393, $p=0.002$), HADS-Depression (Coef. = -0.687, $p=0.0001$) and TAS-20 (Coef. = -0.118, $p=0.0006$) in univariable analyses. HADS-Depression emerged as the strongest predictor of diminished hope, both in agency and pathways components, in univariable and multivariable models (adjusted for age, HADS-anxiety, HADS-depression, TAS20). All the results are showed in the tables below.

Conclusion. This study highlights the role of depressive symptoms in undermining patients' motivational drive and strategic thinking related to goal attainment. Multidisciplinary approaches targeting depressive symptoms and emotional regulation may enhance hope, coping strategies, and foster better outcomes in FM patients.

Table I. Univariable regression (AHS as dependent variable).

	Coef.	IC	p
WPI	0.232	-0.074 - 0.538	0.135
SSS	-0.639	-1.195 - (-0.082)	0.025
FSS	0.066	-0.191 - 0.323	0.610
FAS	0.008	-0.185 - 0.202	0.929
FIQ-R	-0.05	-0.111 - 0.010	0.103
HADS	-0.307	-0.437 - (-0.177)	<0.0001
HADS- Anxiety	-0.393	-0.637 - (-0.148)	0.002
HADS-Depression	-0.687	-0.928 - (-0.447)	<0.0001
TAS20	-0.118	-0.201 - (-0.357)	0.0006

Table II. Univariable regression (AHS Agency as dependent variable).

	Coef.	IC	p
WPI	0.0765	-0.108 - 0.260	0.410
SSS	-0.329	-0.663 - 0.005	0.053
FSS	0.007	-0.146 - 0.160	0.925
FAS	-0.021	-0.137 - 0.093	0.760
FIQ-R	-0.027	-0.064 - 0.008	0.129
HADS Anxiety	0.193	-0.342 - (-0.444)	0.012
HADS Depression	0.393	-0.538 - (-0.247)	<0.001
TAS20	0.0623	-0.112 - (-0.012)	0.015

Table III. Univariable regression (AHS Pathways as dependent variable).

	Coef.	IC	p
WPI	0.155	0.007 - 0.303	0.040
SSS	-0.309	-0.583 - (-0.035)	0.027
FSS	0.058	-0.067 - 0.184	0.355
FAS	0.030	-0.064 - 0.125	0.523
FIQ-R	-0.022	-0.052 - 0.007	0.140
HADS Anxiety	-0.199	-0.318 - (-0.079)	0.001
HADS Depression	-0.294	-0.420 - (-0.168)	<0.001
TAS20	-0.056	-0.097 - (-0.015)	0.008

Table IV. Multivariable regression (AHS as dependent variable; model adjusted for age, HADS-anxiety, HADS-depression, TAS20, SSS).

	Coef.	IC	p
AGE	-0.077	-0.177 - 0.023	0.130
HADS- A	0.4	-0.637 - (-0.148)	0.771
HADS-D	-0.682	-1.027 - (-0.338)	<0.001
TAS20	-0.054	-0.132 - 0.023	0.167

Table V. Multivariable regression (AHS Agency as dependent variable; model adjusted for age, HADS-anxiety, HADS-depression, TAS20, SSS).

	Coef.	IC	p
AGE	-0.036	-0.094 - 0.021	0.217
HADS- A	0.118	-0.055 - 0.293	0.179
HADS-D	-0.488	-0.686 - (-0.289)	<0.001
TAS20	-0.011	-0.055 - 0.032	0.601

Table VI. Multivariable regression (AHS Pathways as dependent variable; model adjusted for age, HADS-anxiety, HADS-depression, TAS20, SSS).

	Coef.	IC	p
AGE	-0.018	-0.071 - 0.032	0.460
HADS- A	-0.052	-0.204 - 0.100	0.497
HADS-D	-0.216	-0.390 - (-0.041)	0.016
TAS20	-0.021	-0.060 - 0.018	0.06

P-44

The impact of trauma and emotional regulation in fibromyalgia, chronic migraine, and their comorbidity: a comparative study among 3 hospitals in Italy

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Background. Research highlights a high prevalence of early traumatic experiences (psychological, physical and sexual) connected to defense mechanism and alexithymia (difficulty in identifying and expressing emotions) in nociplastic pain. However, little is known about their specificities in different diagnosis such as fibromyalgia (FM), chronic migraine (CM), and their comorbid appearance (Fibromig).

Objective. This study aimed to compare traumatic experiences, defense mechanisms, and alexithymia traits among women diagnosed with FM, CM, and Fibromig. We hypothesized that the Fibromig group would report higher levels of trauma, maladaptive defenses, and alexithymia compared to FM and CM groups.

Methods. Data were collected from 295 women across three hospitals in Rome, Milan and Pavia, Italy. Validated tools were used to assess trauma and emotional regulation, including the Traumatic Experience Checklist, the Defense Mechanism Rating Scale, and the Toronto Alexithymia Scale-20.

Results. The Kruskal-Wallis test revealed significant differences across several measures: compared to CM, the Fibromig and FM groups reported more traumatic experiences, particularly emotional neglect ($p=0.003$), with the Fibromig group also showing a higher impact of sexual harassment ($p=0.026$). No group differences were observed for emotional, physical, or sexual abuse, nor for the use of immature, neurotic, or mature defenses to cope with stress. Alexithymia was significantly higher in Fibromig and FM groups compared to CM ($p=0.001$).

Conclusion. This study highlights emotional neglect and sexual harassment as key areas of trauma in FM and Fibromig patients. Additionally, the findings underscore the importance of addressing alexithymia in these groups to improve emotional well-being and overall patient care.

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Probing deep: muscle proprioceptors play a role in somatic allodynia in fibromyalgia syndrome

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Background: Fibromyalgia is characterized by chronic widespread musculoskeletal pain. While abnormal skin innervation and sensitization of cutaneous nociceptors have been described, it is unclear how these changes relate to Fibromyalgia pain which is typically described as deep. Conversely, the contribution of muscle afferents to Fibromyalgia pain is relatively unexplored.

Objective. Since Fibromyalgia patients typically report deep muscle pain, we aimed to examine whether muscle spindle afferents (MSAs) mediate this pain.

Methods: Participants with Fibromyalgia and healthy controls (HC) underwent microneurography of the proximal radial nerve using a high-impedance electrode. We established stable recordings from individual MSAs. Intraneural microstimulation (INMS) was delivered through the electrode to selectively activate the recorded MSA. Current pulses were delivered at 1-Hz, with the strength increased in 1- μ A increments until either percept or motor threshold was reached. During test stimulations, current strength was set to percept threshold (or 80% of motor threshold, if no percept). Both cued and uncued stimulus trains (20-Hz for 5 or 30 sec) were delivered. Pain intensity was continuously recorded using an electronic visual analogue scale, and standardized questionnaires assessed the quality of evoked sensations.

Results. The current strength used for test stimulations was comparable between groups. INMS was never painful in HC, although some participants noted non-painful sensations. Conversely, INMS in Fibromyalgia patients elicited deep pain with rapid onset, typically in the muscle innervated by the stimulated MSA. Pain was described as aching, cramping, burning, and tiring/exhausting.

Conclusion. These findings implicate MSAs as mediators of deep somatic allodynia in Fibromyalgia.

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