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Congress Chairs

Jacob Ablin
Tel-Aviv Sourasky Medical Center, Israel

Piercarlo Sarzi-Puttini
IRCCS Ospedale Galeazzi - S. Ambrogio, Milan, Italy

Abstracts

Invited Speaker Presentations

IS-01

Bridging mechanism to measure: human biomarkers and experimental provocations in nociplastic pain

Lars Arendt-Nielsen
Center for Neuroplasticity and Pain, School of Medicine, Aalborg University & Aalborg University Hospital, Aalborg, Denmark.

In 2019 the International Association for the Study of Pain (IASP) managed to get primary pain conditions (pain in its own right) approved by WHO to be included in the new ICD-11. IASP likewise introduced "nociplastic pain" as a third pain descriptor for pain from "altered nociception" not fully explained by tissue damage (nociceptive) or nerve damage (neuropathic). The IASP has published clinical criteria for identifying nociplastic pain, especially for the musculoskeletal system, requiring 1) pain lasting over 3 months, 2) a regional distribution, 3) pain not entirely explained by nociceptive or neuropathic mechanisms, and 4) signs of pain hypersensitivity (like allodynia or hyperalgesia). Patients, like fibromyalgia, with widespread pain and pain hypersensitivity may fall in this category. The problem with this classification is that we have no tools and golden standard to diagnose the 'pain hypersensitivity'.
It is the hope for the future that pain diagnosis and therapy should be mechanism based and hence pain assessment tools (pain biomarkers) should be sufficiently sensitive and advanced to provide such mechanistic information. Translating clinical observations to mechanisms and *vice versa* is not trivial, and tools to assess quantitatively the different phenomena are mandatory. This approach has provided new insight into how reorganisation of the pain system is manifested in fibromyalgia and other chronic pain conditions manifested with widespread pain. Common features across different pain patient populations have been identified utilising this approach. Peripheral and central sensitisation are important mechanisms for fibromyalgia (FM) and musculoskeletal pain conditions in general. Many similarities exist between different chronic musculoskeletal pain conditions. Musculoskeletal pain may transit from a localised pain problem through a regional representation to a widespread pain condition such as FM. As the pain condition transit from one to the other, more and more sensory abnormalities occur with many sensory abnormalities in FM. There is evidence that as well the intensity of ongoing pain as the duration of pain determines the degree of generalised hyperalgesia. This is important to realise as it underpins the importance of the ongoing nociception for the chronification process in conditions (*e.g.* osteoarthrosis) where the peripheral nociceptive drivers are known, whereas it is more complicated in *e.g.* FM where the drivers are less obvious.
Such techniques for assessing the pain sensitisation mechanisms in patients with FM and other patients with musculoskeletal pain have been developed and provide new opportunities to quantify pain mechanisms such as temporal summation, descending inhibition, spreading sensitisation, and additional modality-specific hyperalgesic reactions. Such tools can help to phenotype patients with FM based on the role of the various pain sensitisation mechanisms involved and have recently been used as tools to predict pain outcomes after pharmacological or surgical interventions in various groups of musculoskeletal pain conditions.
Relating clinical benefit of a given therapy with quantitative assessment of the pain sensitisation mechanisms involved provides new opportunities for better diagnostics and hence for tailored and individualised management regimes.
Although assessed differently in specific tissues for various musculoskeletal pain conditions, the underlying mechanisms share common underlying features An example of similar mechanisms across chronic pain conditions could be cutaneous allodynia in neuropathic pain assessed by brush, which corresponds to pain evoked by weak muscle pressure in musculoskeletal pain and to pain provoked by a weak colonic distension in visceral pain. Another example can be facilitated temporal summation and impaired descending modulation across many different chronic pain conditions including fibromyalgia. This mechanistic understanding is of importance for developing better diagnostics and for implementing tailored pain management programs. The understanding that FM and other musculoskeletal conditions share common fundamental features has positioned FM as the one extreme end as opposed to, *e.g.* a myofascial pain problem at the other end. This has provided some new insight into the development of the sensitisation processes from one extreme to the other. Some of the current available mechanistic human pain biomarkers translate back to animals, providing new possibilities for bridging findings between pre-clinical and clinical studies. Data on the clinical applicability are increasingly available. In the post-COVID aera we have identified specific groups with post-COVID pain patients manifested with widespread pain and having similar characteristics as FM patients. As such a new group of FM are now present in the clinic.
In 2019 the International Association for the Study of Pain (IASP) managed to get primary pain conditions (pain in its own right) approved by WHO to be included in the new ICD-11. At the same time, the IASP introduced *nociplastic pain* as a third mechanistic descriptor of pain, referring to pain arising from *altered nociception* that cannot be fully explained by tissue damage *(nociceptive pain)* or nerve damage (*neuropathic pain*).
The IASP proposed clinical criteria for identifying nociplastic pain including:

- Pain persisting for more than three months.
- A regional distribution of pain.
- Pain not entirely accounted for by nociceptive or neuropathic mechanisms.
- Clinical signs of pain hypersensitivity, such as allodynia or hyperalgesia.

Patients with conditions such as fibromyalgia (FM), characterised by widespread pain and pain hypersensitivity, are typical examples of this category. However, a major limitation of this classification lies in the absence of standardised and validated diagnostic tools and a *gold standard*, for assessing pain hypersensitivity.
Looking ahead, it is anticipated that pain diagnosis and treatment will increasingly become mechanism-based, requiring pain assessment tools (*i.e. pain biomarkers*) that are sufficiently sensitive and sophisticated to provide mechanistic insights. Translating clinical observations into mechanistic understanding, and *vice versa*, remains a significant challenge. Quantitative assessment tools are therefore essential for investigating the diverse phenomena underpinning chronic pain.
This mechanistic approach has yielded valuable insights into how reorganisation of the pain system occurs in FM and other chronic pain disorders characterised by widespread pain. Common features have been identified across various pain populations using this framework. Both peripheral and central sensitisation play critical roles in FM and in musculoskeletal pain conditions more broadly. Indeed, numerous similarities exist among different chronic musculoskeletal pain syndromes.
Musculoskeletal pain may evolve from a localised problem to a regional pain condition, and eventually to a widespread pain state such as FM. As this transition occurs, the number and degree of sensory abnormalities increase, reaching their peak in FM. Evidence suggests that both the intensity, duration of ongoing pain and number of pain comorbidities contribute to the degree of generalised hyperalgesia. This understanding emphasises the role of continuous nociceptive input in the *chronification* process, especially in conditions like osteoarthritis, where peripheral nociceptive drivers are well understood, in contrast to FM, where such drivers remain unclear.
Recent advances have led to the development of quantitative sensory testing (QST) and related methods for assessing pain sensitisation mechanisms in FM and other musculoskeletal pain conditions. These tools allow quantification of processes such as temporal summation, deficient descending inhibition, spatial spreading of sensitisation, and modality-specific hyperalgesia. Such assessments enable *phenotyping* of FM patients according to the specific sensitisation mechanisms involved and have been used to predict pain outcomes following pharmacological or surgical interventions across diverse musculoskeletal pain populations.
By linking the clinical efficacy of specific therapies with quantitative measures of pain sensitisation, researchers and clinicians can move toward mechanism-based diagnostics and personalised pain management strategies. Although the methods of assessment differ between tissues and pain conditions, the underlying pathophysiological mechanisms often share common features. For instance, *cutaneous allodynia* elicited by light brushing in neuropathic pain parallels pain evoked by mild muscle pressure in musculoskeletal pain, and by weak colonic distension in visceral pain. Similarly, enhanced temporal summation and impaired descending pain inhibition are shared across multiple chronic pain disorders, including FM.
Understanding these shared mechanisms is crucial for improving diagnostics and implementing targeted pain management programs. The recognition that FM and other musculoskeletal pain conditions lie along a continuum of sensitisation, with FM representing one extreme and myofascial pain the other, has deepened insight into how sensitisation processes develop and generalise. Moreover, some mechanistic *human pain biomarkers* have translational relevance in animal models, bridging preclinical and clinical research and advancing the field of pain science.
Emerging clinical data further support these mechanistic perspectives. In the post-COVID era, a subgroup of patients presenting with post-COVID pain syndromes characterised by widespread pain and hypersensitivity has been identified, sharing many features with FM. Consequently, a *new subgroup of FM-like patients* has emerged in clinical practice.

IS-02

Peripheral glial and neuroimmune alterations associated with antibodies in fibromyalgia

Camilla I. Svensson[1], Macarena Tejos-Bravo[1], Kirill Agashkov[1], Carlos E. Morado-Urbina[1], Matthew Hunt[1], Sven D. Arvidsson[1], Karolina af Ekenstam[2,3], Sigita Venckute-Larsson[1], Katalin Sandor[1], Emilie Linderoth[1], Emerson Krock[4], Lisbet Haglund[5], Theodor Arlestig[2,3], Monika Löfgren[2,3], Eva Kosek[2,3]
[1]*Department of Physiology and Pharmacology, Centre for Molecular Medicine, Karolinska Institutet, Stockholm, Sweden.*
[2]*Department of Rehabilitation Medicine, Danderyd University Hospital, Stockholm, Sweden.*
[3]*Department of Clinical Sciences, Danderyd University Hospital, Karolinska Institutet, Stockholm, Sweden.*
[4]*Faculty of Dental Medicine and Oral Health Sciences, Department of Anesthesia, Faculty of Medicine and Health Sciences, Alan Edwards Centre for Research on Pain, McGill University, Montreal, QC, Canada.*
[5]*Division of Orthopaedic Surgery, Department of Surgery, McGill University, Montreal, QC, Canada.*

Fibromyalgia (FM) is a complex pain condition characterised by altered central pain processing, with increasing evidence suggesting that peripheral neuroimmune mechanisms also contribute to disease pathophysiology. Using a translational approach, we investigated the role of the adaptive immune system in FM by combining antibody transfer experiments with analyses of dorsal root ganglia (DRG) and detailed characterisation of the cutaneous neuroimmune landscape in both mouse and human tissues.
Passive transfer of IgG from FM patients, but not healthy controls, induced robust pain-like behaviours in mice, including mechanical and cold hypersensitivity and reduced locomotor activity. Transferred FM IgG accumulated in the DRG, where limited binding to macrophages was observed, but binding occurred predominantly to satellite glial cells (SGCs). This accumulation was associated with morphological and transcriptional changes indicative of altered glial cell activity. Analysis of skin innervation revealed that 14 days after IgG transfer, mice exhibited a significant reduction in intraepidermal nerve fiber density (IENFD), assessed by PGP9.5, TrkA, and CGRP labeling, together with an increased density of thicker, NF200-positive fibers in the upper dermis.
In parallel, we examined IgG accumulation in human DRG tissue from organ donors with FM listed in their medical history and from age- and sex-matched controls. Despite the limited sample size, increased IgG accumulation was observed in FM DRG, predominantly localised to perineuronal regions enriched in SGCs and resident immune cells. Furthermore, skin biopsies obtained from the lateral hip of a well-characterised FM cohort with widespread multimodal hyperalgesia were analysed. FM skin exhibited reduced IENFD and an increased presence of myelinated NF200-positive fibers in the upper dermis, together with increased mast cell numbers, reduced non-nerve-associated Schwann cells, and decreased densities of $CD68^+$ cells accompanied by altered cell morphology. $CD163^+$ dermal macrophages were also reduced in number, and notably, $CD163^+$ macrophage density correlated negatively with epidermal innervation, suggesting a link between immune dysregulation and peripheral nerve pathology. In contrast, no differences were observed between FM and healthy controls in the densities of neutrophils, Langerhans cells, dendritic cells, T cells, or B cells.
Using a plate-based assay, we identified significantly elevated levels of SGC-binding IgG in FM sera. Importantly, increased anti-SGC IgG titres were associated with higher pain intensity. Transcriptomic profiling of FM skin revealed extensive molecular alterations, with downregulated genes enriched in mitochondrial and muscle-related pathways. Enrichment analyses demonstrated strong positive correlations between anti-SGC IgG levels and pathways related to neutrophil degranulation, innate and adaptive immune responses, and immune signaling.
In conclusion, these findings demonstrate that IgG from FM patients is sufficient to induce pain-like behaviour, glial alterations, and structural changes in peripheral innervation, mirroring key features observed in FM patients. Together, our data support a model in which autoantibody-mediated glial dysfunction and disrupted peripheral neuroimmune homeostasis contribute to chronic widespread pain in FM, highlighting novel opportunities for patient stratification and immune-targeted therapeutic strategies.

IS-03

The other side of the coin: resilience factors and positive activity interventions

Afton L. Hassett
University of Michigan, USA.

Experiencing chronic pain and can have a profound impact on every aspect of life, including mental health. In numerous studies, chronic pain conditions like fibromyalgia have been consistently associated with depression, anxiety, and diminished quality of life. Yet, a subset of individuals continues to lead productive and rewarding lives despite their chronic pain. It is from these resilient people that we may learn the most. Because the remarkable ability of some individuals with chronic pain to bounce back and lead remarkably productive and fulfilling lives is often underappreciated, this session will explore the science underlying pain resilience with a focus on fibromyalgia. The data supporting the importance of tapping into our patients' inherent strengths will be discussed, as will strategies to help them thrive despite living with chronic pain. Attendees will gain insight into practical strategies aimed at providing essential emotional support and fostering resilience in chronic pain. Drawing from evidence-based approaches, this session will provide an overview of practical tools and techniques necessary to navigate the complex experiences and emotional well-being of people with chronic pain. Also, recommendations for including resilience factors in clinical pain research will be addressed.
Learning objectives:

- Describe the concept of resilience and the processes that underlie it.
- Discuss the literature related to factors such as positive emotions, optimism, social integration and sense of purpose, and physical and emotional health.
- List at least 5 strategies and/or concrete actions that can be taken to improve resilience.
- Describe the measurement of resilience factors in chronic pain populations.

IS-04 (a)

Fibromyalgia: One year in review 2026 - clinical and pathogenetic aspects

Cristina Iannuccelli [1], Martina Favretti [2], Benedetta Bianchi[3], Giulio Dolcini[2], Carlo Cauli[4], Vincenzo Ferraro[4], Fausto Salaffi[3], Fabiola Atzeni[5], Laura Bazzichi[6], Piercarlo Sarzi-Puttini[6], Jacob N. Ablin[7], Manuela Di Franco[4], Marco Di Carlo[3]
[1]*Rheumatology Unit, AOU Policlinico Umberto I, Rome, Italy.*
[2]*Department of Molecular Sciences, Sapienza University of Rome, Italy.*
[3]*Rheumatology Unit, Università Politecnica delle Marche, Carlo Urbani Hospital, Jesi, Italy.*
[4]*Rheumatology Unit, Sapienza University of Rome, Italy.*
[5]*Rheumatology Unit, Department of Internal and Experimental Medicine, University of Messina, Messina, Italy.*
[6]*IRCCS Ospedale Galeazzi Sant'Ambrogio, Rheumatology Unit, Milan; and Dipartimento di Scienze Biomediche e Cliniche, Università degli Studi di Milano, Italy.*
[7]*School of Medicine, Gray Faculty of Medical and Health Sciences, Tel Aviv University, Tel Aviv, Israel.*

Fibromyalgia (FM) is a chronic pain condition characterised by an evolving pathogenesis and continuously updated clinical features. This report aims to summarise the most recent advances in FM research by reviewing PubMed-indexed articles published in 2025.
Recent contributions on FM pathogenesis have focused on several key domains. Emerging evidence suggests that patient-derived IgG can modulate nociceptive signalling without inducing inflammatory tissue damage, supporting the concept of a functional, non-classical autoimmune process (1). A large case-control study further identified IgG autoantibodies targeting dorsal root ganglion neurons and satellite glial cells, correlating with specific pain phenotypes (2). Growing data indicate that dysbiosis is associated with pain severity (4, 5), and that FM-associated microbiota can induce pain-like behaviours in germ-free rodent models (6). Clinical, neuroimaging, and physiological studies consistently demonstrate impaired endogenous pain inhibition, altered pain modulatory networks, and dysregulated autonomic stress responses (8, 9). However, significant gaps remain in neurochemical data necessary to fully elucidate the neurobiological basis of central sensitisation (CS) in FM (11). A recent case-control study identified two

dysregulated microRNAs (miR-4771 and miR-2115-3p), both significantly correlated with functional impairment in FM patients (12).
Beyond pathophysiology, recent studies have emphasised important clinical features of FM, particularly cognitive dysfunction and psychological factors. In addition to chronic pain, patients frequently report *fibro-fog*, a loss of mental clarity regarded as one of the most disabling symptoms, largely due to memory complaints. Evidence shows that individuals with FM exhibit significantly impaired verbal working memory compared with healthy controls, suggesting modality-specific cognitive deficits and highlighting the relevance of non-physical symptoms in disease management (13). Psychological factors are also implicated in both cognitive dysfunction and disease expression, with a systematic review identifying a strong association between post-traumatic stress disorder, increased FM risk, and greater symptom severity (14).
An additional, yet insufficiently explored, aspect of FM concerns muscle function and structure evaluation. Although sarcopenia screening tools often indicate elevated risk, patients more commonly present with dynapenia, characterised by reduced muscle strength in the absence of significant muscle mass loss (15). Moreover, residual pain in inflammatory arthritis represents a related and under-addressed clinical challenge, potentially driven by CS, psychiatric comorbidities, limited disease acceptance, and dissatisfaction with management strategies (16, 17).
Overall, these findings underscore the necessity of a multimodal management based on a biopsychosocial approach. This comprehensive framework is increasingly supported by proposed updates to FM diagnostic criteria, which advocate for the systematic evaluation of social factors alongside physical and psychological dimensions (18).

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IS-04 (b)

Pharmacological and complementary therapies: fibromyalgia year in review 2026

Laura Bazzichi[1], Piercarlo Sarzi-Puttini[1], Jacob N. Ablin[2], Silvia Sirotti[1], Greta Pellegrino[1], Roberto Casale[3], Federica Galli[4], Manuela Di Franco[5], **Cristina Iannuccelli**[5]

[1]*Rheumatology Unit, IRCCS Ospedale Galeazzi-Sant'Ambrogio and Department of Biomedical and Clinical Sciences, University of Milan, Milan, Italy.*
[2]*School of Medicine, Gray Faculty of Medical and Health Sciences, Tel Aviv University, Tel Aviv, Israel.*
[3]*OPUS Medica - Persons, Care and Research (PC&R), Piacenza, Italy.*
[4]*Department of Dynamic and Clinical Psychology and Health Studies, Faculty of Medicine and Psychology, Sapienza University of Rome, Rome, Italy.*
[5]*Rheumatology Unit, Sapienza University of Rome, AOU Policlinico Umberto I, Rome, Italy.*

Background. Fibromyalgia (FM) is a complex chronic pain disorder characterised by central sensitisation, neuroimmune dysregulation, autonomic dysfunction and a high multidimensional symptom burden, including fatigue, sleep disturbances, cognitive impairment and emotional distress. The limited effectiveness of conventional pharmacological treatments has prompted increasing interest in mechanism-based and integrative therapeutic strategies. During 2025, a growing body of literature expanded the therapeutic landscape, highlighting innovative pharmacological agents, neuromodulatory techniques and complementary interventions targeting central pain processing, neuroinflammation and cellular energy metabolism.
Objective. To summarise and critically synthesise the most relevant and innovative therapeutic approaches published in 2025 for the treatment of fibromyalgia.
Methods. A narrative review was conducted using PubMed and major scientific databases. Randomised controlled trials, systematic reviews and controlled clinical studies published throughout 2025 were analysed, with particular attention to mechanism-oriented and multimodal treatment strategies.
Results. Recent findings suggest that low-dose naltrexone improves both pain modulation and functional outcomes, while full-spectrum cannabis extracts – administered through personalized dosing – have demonstrated multi-symptomatic benefits. Psilocybin-assisted therapy has shown promising results in emotional regulation and pain reduction. Other pharmacological developments include intravenous lidocaine, which has been effective in refractory cases, and ozonated water enemas, which significantly improved fatigue and pain scores in a controlled clinical trial. On the complementary and neuromodulatory side, a multicentre trial combining millimetre-wave stimulation with motivational coaching has reported notable improvements in quality of life. Systematic reviews have also confirmed the efficacy of music therapy in reducing chronic musculoskeletal pain, while dance therapy emerged as a tool for enhancing body awareness and mood. Nutraceutical approaches, particularly combined coenzyme Q10 and magnesium supplementation, showed promise in reducing fatigue and enhancing mitochondrial function in FM patients. Additionally, non-invasive vagal nerve stimulation has shown encouraging clinical results and is gaining traction as a safe adjunctive option.
Conclusion. The 2025 literature supports an integrated model of care for fibromyalgia, combining evidence-based pharmacological interventions with complementary and neuromodulatory strategies. This evolving approach reflects a shift toward personalised, multimodal management capable of addressing the syndrome's diverse symptomatology. Larger trials are needed to validate these promising results across broader populations.

Key words. Fibromyalgia, low-dose naltrexone, cannabinoids, lidocaine, psilocybin, ozone therapy, vagal stimulation, neuromodulation, music therapy, dance therapy, integrative medicine

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IS-05

Cutaneous manifestations of fibromyalgia

Lidia Rudnicka
Department of Dermatology, Medical University of Warsaw, Poland.

Cutaneous manifestations of fibromyalgia encompass a diverse range of dermatological symptoms and disorders that are frequently experienced by patients, despite fibromyalgia not being classically characterised by specific skin findings. Common skin-related symptoms include increased skin sensitivity to touch (allodynia), and external factors such as exposure to UV light. This increased sensitivity may be characterised by itching, and erythema development without any other identifiable. These symptoms can be exacerbated by heightened sensitivity to temperature changes and reactions to skincare products containing fragrances, preservatives, or dyes. Patients often describe a burning sensation and pain as prominent complaints.
Several dermatologic disorders have been reported with increased frequency in fibromyalgia patients compared to controls. These include xerosis, lichen simplex chronicus, neurotic excoriations and dermographism. Often the conditions progress to chronic (nodular) prurigo. Hyperhidrosis is an additional symptom that can significantly impact quality of life.
A multidisciplinary approach recognising dermatological care needs is recommended to improve patients' quality of life by addressing both primary skin conditions and fibromyalgia-related skin sensitivity.

IS-06

Patient-centred care in fibromyalgia

J.A.P. da Silva
University of Coimbra, Portugal; MyFibromyalgia®

Abstract. Patient-centred care (PCC) is frequently presented as a desirable but optional component of fibromyalgia (FM) management. Current evidence indicates that it is, instead, a core requirement for effective and rational care. FM is classified as chronic primary (nociplastic) pain, reflecting altered central pain processing rather than ongoing peripheral tissue damage (1, 2). Experimental pain paradigms and functional neuroimaging demonstrate augmented central pain processing, impaired descending inhibition, and altered connectivity in salience and affect-related networks, providing a biological framework in which threat, uncertainty, and loss of control amplify symptoms (3, 4).
Within this context, PCC is best understood as a set of specific, evidence-based clinical behaviours that influence outcomes. First, diagnostic validation combined with a coherent mechanistic explanation reduces distress, health anxiety, and unnecessary healthcare utilisation, addressing the well-documented experience of delegitimation and epistemic injustice reported by patients with FM (5, 6). Second, shared decision-making is essential, as long-term management relies on sustained engagement with self-management strategies; across chronic pain conditions, shared decision-making improves adherence, reduces catastrophisation, and enhances functional outcomes (7, 8).
Third, PCC is central to the personalised use of pharmacological treatments, an area where uniform approaches consistently fail. Meta-analyses and guideline reviews show that medications commonly used in FM (*e.g.* duloxetine, milnacipran, pregabalin, amitriptyline) have modest average effect sizes and high interindividual variability in efficacy and tolerability (9-11). Patient-centred pharmacological care – characterised by shared goal-setting, careful phenotypic matching (pain, sleep, fatigue, mood), slow titration, early reassessment, and explicit management of expectations – improves persistence, reduces adverse effects, and limits inappropriate polypharmacy (9-12). This approach aligns with guideline recommendations that place pharmacological therapy as adjunctive and individualised, rather than central or mandatory (10, 11).
Overall, evidence supports PCC in FM not as a humanistic ideal, but as a clinically and biologically coherent strategy that integrates diagnostic validation, collaborative decision-making, tailored pharmacotherapy, and multimodal non-pharmacological care. Ignoring PCC in FM is therefore inconsistent with current pain science, guideline-concordant management, and rational use of therapeutics.

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IS-07

Biologics and pain management

Ernest Choy
Section of Rheumatology and CREATE Centre, Division of Infection & Immunity, Cardiff University, UK.

Biologics have transformed the outcome and prognosis of patients with rheumatic diseases especially rheumatoid arthritis over the last 25 years. Despite this, many patients with rheumatoid arthritis still suffer from pain and rank improvement in pain treatment as a priority unmet need (1). For a long time, clinicians assume pain is due to inflammation and switch biologic treatment when patients complain of pain. National registries and observational cohort studies have shown the number of patients who have tried and failed two or more biological agents have increased significantly. The European League of Associations for Rheumatology (EULAR) have used the term difficult-to-treat rheumatoid arthritis to describe these patients (2). The working group which developed this definition have also produced points-to-consider in the management of these patients (3). One key aspect is the assessment of comorbidities that may cause pain without inflammation. This is based on many studies and systematic reviews showing that the prevalence of fibromyalgia in patients with inflammatory arthritis is very high ranging from 13 to 21% (4). Such prevalence is much higher than the general population and suggests the need to reconsider the concept of secondary fibromyalgia. Comorbid fibromyalgia is also associated with higher disease activity scores and reduce rate of remission in inflammatory arthritis treated by biologics.
In routine clinical practice, fibromyalgia is under-recognised in inflammatory arthritis (1, 5). Fibromyalgia is the prototypical condition characterised by nociplastic pain in which central pain processing dysfunction causes amplified pain without tissue damage. Many studies assessing pain perception have showed that many patients with inflammatory arthritis have reduced pain threshold even though they do not fulfil the fibromyalgia diagnostic criteria suggesting nociplastic pain is a continuum in patients with inflammatory arthritis (6).
Mechanistically, there are many potential reasons why patients with inflammatory arthritis may develop nociplastic pain (6). Repeated stimulation of nociceptive sensory neurons can cause temporal summation, also known as windup, leading to pain amplification. Many patients with inflammatory arthritis have reduced sleep quality and mental well-being which impair coping with pain. Importantly, cytokines can sensitise directly nociceptive sensory neurons causing pain amplification. Post-hoc analyses of clinical trials of IL-6 and Jak inhibitors (7, 8), have suggested these agents can reduce non-inflammatory pain in patients with inflammatory arthritis. Therefore, the use of biological agents in the early stage of disease may well reduce nociplastic pain and the risk of development of secondary fibromyalgia in patients with inflammatory arthritis.
The Outcome Measure in Rheumatology Chronic Pain working group has highlighted in 2023 that an important unmet need in clinical trials and practice is the lack of a validated tool to assess nociplastic pain in patients with inflammatory arthritis (9). In 2025, the working group present a scoping review protocol to identify potential domains and instruments to assess nociplastic pain which will help to define pain phenotypes in patients with inflammatory arthritis.

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IS-08

Novel pharmacological therapeutics

Valeria Giorgi
Clinica Moncucco, Lugano, Switzerland.

Fibromyalgia syndrome (FMS) is a prevalent nociplastic pain disorder marked by widespread pain, sleep dysfunction, fatigue and cognitive symptoms, for which currently available agents provide modest average benefit, motivating mechanism-informed innovation. Emerging translational work supports a gut-immune-neuroaxis contribution to symptom generation, including reproducible alterations in microbiome signatures and bile-acid-related pathways, with downstream effects on neuroimmune activation and central sensitisation. Microbiome-directed strategies under evaluation include dietary and targeted microbial interventions as well as fecal microbiota transplantation (FMT); early feasibility signals and ongoing randomised controlled work suggest clinical promise but require rigorous replication with biomarker-linked responder stratification. Parallel immune-based hypotheses (*e.g.* maladaptive antibody-mediated signaling and neuroinflammation) open the door to immunomodulatory approaches that are conceptually distinct from classic centrally acting analgesics. In neurobiological models emphasising network rigidity and impaired top-down modulation, "psychoplastogens" (including serotonergic psychedelics) are being explored for their capacity to transiently increase neural plasticity and modulate affective-cognitive pain circuits; however, for FMS the clinical evidence base remains preliminary and should be framed as hypothesis-generating. Alongside these domains, the near-term pipeline is also expanding via repurposed and novel agents targeting autonomic tone, neuroimmune signaling, and symptom clusters. To illustrate the current breadth of development, ClinicalTrials.gov lists Phase 2 interventional drug studies in FMS including the norepinephrine reuptake inhibitor TD-9855 (NCT01693692) and the FcRn monoclonal antibody rozanolixizumab in severe FMS (NCT05643794). Several pharmacologic candidates have reached Phase 3 testing in FMS, including TNX-102 SL (sublingual cyclobenzaprine) and cannabidiol.
Overall, the therapeutic landscape is moving from single-pathway symptom control toward stratified, mechanism-based intervention portfolios spanning gut-immune modulation, neuroplasticity-oriented therapeutics, and targeted pharmacotherapy, with adequately powered trials needed to define efficacy, durability, safety, and clinically actionable predictors of response.

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IS-09

Cannabinoids and pharmacology in fibromyalgia

David (Dedi) Meiri
Technion Israel Institute of Technology, Israel.

Fibromyalgia is a chronic disorder characterised by widespread, diffuse musculoskeletal pain that is persistent, not explained by tissue damage, and commonly accompanied by fatigue and sleep disturbances. As of today, there is no cure or disease-specific treatment for fibromyalgia, and therapeutic strategies are limited to symptomatic management. The lack of effective treatments has raised interest in the involvement of pain-regulating systems that may contribute to disease pathophysiology. One such system is the endocannabinoid system, an endogenous signaling network involved in many physiological processes, including the regulation of pain perception. We recently demonstrated that patients with fibromyalgia and rheumatoid arthritis exhibit significant alterations in circulating endocannabinoid levels, the lipid-derived signaling molecules that activate cannabinoid receptors within the endocannabinoid system. These alterations correlated with disease severity, supporting investigation into modulation of cannabinoid signaling by plant-derived cannabinoids, which can mimic endocannabinoids at cannabinoid receptors. Medical cannabis is increasingly used by patients with fibromyalgia for symptom management, particularly for pain, sleep disturbances, and stress. However, patients may be exposed to different sets of bioactive compounds, potentially affecting therapeutic outcomes. Cannabis is a versatile plant with hundreds of cultivars and hybrids worldwide, each with a unique and distinct chemical profile. Most studies focus on just the two well-known cannabinoids THC and CBD, but there are over 160 phytocannabinoids found in the plant in addition to a milieu of terpenoids, flavonoids and other compounds with potential therapeutic activities. Moreover, the outcome of treatment with medical cannabis depends on the way these plant-derived compounds act together synergistically, in a mechanism coined as the 'entourage effect'. Given the wide range of symptoms associated with fibromyalgia, combinations of a few cannabinoids with defined mechanisms of action may represent a simple therapeutic strategy for a highly complex disease.

IS-10

A population approach to fibromyalgia: what epidemiology can tell us

Marcus Beasley
Aberdeen Centre for Arthritis and Musculoskeletal Health (Epidemiology Group), University of Aberdeen, UK.

The original 1990 ACR criteria for fibromyalgia (FM) have a requirement for chronic widespread pain, which has been operationalised for use in epidemiological studies (1). In 2010, the widespread criterion was replaced with a simple count of pain sites. Epidemiological studies have shown how this change affected associations with risk factors (2, 4) and impacted prevalence estimates in the general population (3). Although a requirement for generalised pain was reintroduced in revisions to the criteria in 2016, it has been suggested more recently that fibromyalgia is best understood as a continuous disorder (5).
However, the 2016 criteria (FM2016) may have problems in identifying cases. Recent work shows how measures of symptomatic distress used in the 2016 criteria could be improved, taking into account their continuous nature while still including a dichotomous measure of pain all over the body to identify those for whom a diagnosis is suitable (6).
Applying principles from the epidemiology of disease prevention (7) to data from the UK Biobank, we see that the bulk of the burden of fibromyalgia is in those with less severe symptomatic distress, and that the number of diagnosed cases is a function of the distribution of symptoms in the population. This implies that we should stop thinking of fibromyalgia as an individual condition and instead view symptomatic distress as a population-level phenomenon. This suggests that effect management requires treating causes across whole populations.

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IS-11

Comorbidity and fibromyalgia

Fabiola Atzeni[1], Francesca Cracò[1], Alessandra Burgio[1], Antonio Pezzano[1], Angelo Tropea[1], Maria Letizia Currò[1], Alessandra Alciati[2]
[1]*Rheumatology Unit, Department of Internal and Experimental Medicine, University of Messina, Messina, Italy*
[2]*IRCCS Humanitas Research Hospital, Department of Clinical Neurosciences, Villa San Benedetto Menni Hospital, Hermanas Hospitalarias, Albese con Cassano, Italy.*

Fibromyalgia (FM) is a chronic nociplastic pain condition characterised by widespread pain, fatigue, sleep disturbances, and cognitive dysfunction. It is frequently associated with multiple comorbidities that contribute to symptom burden, disease complexity, and reduced quality of life. Among these, metabolic syndrome rheumatic and psychiatric diseases represent particularly relevant and clinically impactful comorbid conditions. Patients with FM exhibit an increased prevalence of metabolic abnormalities, including obesity, insulin resistance, dyslipidaemia, and hypertension. These alterations may be driven by physical inactivity, neuroendocrine dysregulation, low-grade systemic inflammation, and shared pathophysiological pathways. In addition, fibromyalgia commonly coexists with both inflammatory and non-inflammatory rheumatic diseases – such as rheumatoid arthritis, spondyloarthritis, osteoarthritis, and connective tissue diseases – where it can amplify pain perception, fatigue, and functional impairment independently of underlying inflammatory disease activity. Furthermore, more than half of patients with FM present with lifetime or current psychiatric comorbidities, predominantly depressive and anxiety disorders. The coexistence of metabolic syndrome, rheumatic diseases, and psychiatric disorders further increases cardiovascular risk, worsens functional outcomes, and complicates disease assessment and management. These comorbidities appear to share overlapping mechanisms, including central sensitisation, immune-metabolic interactions, chronic inflammation, and dysregulation of stress-response systems. Recognising metabolic syndrome, rheumatic diseases, and psychiatric disturbances as key comorbidities in FM is essential for accurate clinical evaluation and effective management. A comprehensive, multidisciplinary approach addressing pain mechanisms, metabolic risk factors, mental health, and coexisting rheumatic conditions is crucial to optimise treatment outcomes and improve long-term prognosis.

IS-12

Controversies on the definition of nociplastic pain

J.A.P. da Silva
University of Coimbra, Portugal.

The concept of nociplastic pain was introduced by the International Association for the Study of Pain (IASP) to describe pain arising from altered nociception despite no clear evidence of tissue damage activating peripheral nociceptors or disease of the somatosensory nervous system sufficient to explain the pain (1). Since its introduction, nociplastic pain has gained rapid traction in pain medicine, rheumatology, and related disciplines. However, its definition has also generated significant debate, reflecting deeper tensions within contemporary pain science regarding classification, mechanism, and clinical utility.
A central controversy concerns the ontological status of nociplastic pain: whether it should be understood strictly as a mechanistic descriptor, as intended by IASP, or whether it is increasingly being used as a diagnostic category in clinical practice. This tension is amplified by the absence of nociplastic pain as a diagnosis within ICD-11, where related conditions such as fibromyalgia are classified under chronic primary pain (2). Conflation of classification systems with mechanistic descriptors risks category errors and inconsistent clinical reasoning.
A second major controversy relates to the definitional core of nociplastic pain "altered nociception". Critics argue that this phrase lacks sufficient specificity and falsifiability, potentially rendering the construct overly broad (3). Proponents counter that deliberate conceptual openness was necessary to accommodate heterogeneity and to avoid premature reductionism in the absence of validated biomarkers.
Further debate centres on the relationship between nociplastic pain and central sensitisation. While central sensitisation is a well-established neurophysiological mechanism, it is neither necessary nor sufficient to define nociplastic pain, which is intended as a higher-order clinical construct rather than a single mechanistic explanation (4). Failure to maintain this distinction has contributed to conceptual confusion.
Concerns have also been raised that nociplastic pain may function as a "diagnosis of exclusion" or wastebasket category. In response, clinical criteria and grading systems have been proposed to support structured phenotyping and to reduce the risk of overclassification (5). The relationship between nociplastic pain and fibromyalgia remains contested, with increasing consensus that fibromyalgia represents a heterogeneous clinical syndrome situated along a continuum of nociplasticity rather than a singular mechanistic prototype (6).
This presentation argues that nociplastic pain is best understood as a transitional, mechanism-informed construct that prioritises clinical utility while acknowledging current scientific limitations. Ongoing refinement through phenotyping, longitudinal research, and improved mechanistic understanding will be essential to resolving these controversies and advancing precision pain care.

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IS-13

Placebo, nocebo and pain modulation in fibromyalgia syndrome

Winfried Häuser
Medical Center for Pain Medicine and Mental Health Saarbrücken and Department Psychosomatic Medicine and Psychotherapy, Technical University Munich, Germany.

Although placebo response and effect are often used interchangeably, it is important to realise that their meaning is different. A placebo response in clinical trials is the clinical improvement following the administration of a placebo. It includes all the factors contributing to the improvement, for example, the natural course of the disease (*e.g.* spontaneous remissions), regression to the mean, patients' and clinicians' biases, as well as patients' and clinicians' expectations about the therapeutic outcome. The real placebo effect is the improvement in health or symptoms from an inert (inactive) treatment, triggered by a patient's belief, expectation, and the psychosocial context leading to real physiological changes like endorphin release, rather than the treatment's inherent properties. In order to investigate the real placebo effect, it is necessary to run a no-treatment group. What has been said for the placebo also applies to nocebo, but in the opposite direction. Nocebo responses refer to negative outcomes to active medical treatments in clinical trials or practice such as drop out due to adverse events that cannot be explained by the treatment's pharmacologic effects. The nocebo effect is explained by patient-related psychological factors such as negative expectations, conditioning of adverse reactions on medication, and personality traits (*e.g.* somatisation, anxiety) and contextual factors such as negative suggestions of the physician.
The placebo response in pharmacological drug trials in FMS is lower than in trials for diabetic polyneuropathy (DPN). A systematic review found that placebo accounted for 45% of the response in the drug groups in FMS and for 62% in painful DPN. The nocebo response in FMS trials is higher than in trials in DPN. A systematic review found that the pooled estimate of the event rate drop-out rate due to adverse events (AEs) in placebo groups was 9.6 [95% confidence control (CI): 8.6-10.7] in placebo and 16.3 (95% CI: 14.1-31.2) in true drug groups of FMS trials and was 5.8 (95% CI: 5.1-6.6) in placebo and 13.2 (95% CI: 10.7-16.2) in true drug groups of DPN trials. Nocebo effects accounted for 72.0% (44.9%) of the dropouts in true drug groups in FMS (DPN). Another systematic review with controlled trials with drug applying for approval for FMS treatment the pooled estimate of a 50% pain reduction by placebo was 18.6% (95% CI 17.4 to 19.9%). The pooled estimate of drop-out due to adverse events in placebo groups was 10.9% (95% CI 9.9 to 11.9%).
Placebo analgesia in FMS involves changes in central pain processing regions (*e.g.* reduced activity in insula and secondary somatosensory cortex and modulation of the neurological pain signature), and can be comparable in patients and healthy controls under experimental conditions. The magnitude of placebo response tends to be higher in FMS-patients with more severe symptoms, shorter disease duration, older age, and in men, and it increases in trials where the active treatment has larger effect sizes, suggesting strong contributions of expectations and learning. The high nocebo response rates in pharmacological FMS support the hypothesis that expec-

tations, prior negative treatment experiences, and high symptom vigilance amplify nocebo hyperalgesia and reduce adherence of FMS-patients.
In trials, high placebo responses reduce drug-placebo differences, making it harder to demonstrate efficacy, which has led to methodological strategies aimed at minimising placebo responses (*e.g.* enrichment designs, run-in phases). In practice, clinicians can ethically harness placebo mechanisms by optimising the therapeutic alliance, communication of realistic but positive expectations, and treatment rituals, while actively working to minimise nocebo effects by avoiding alarmist framing and providing clear, balanced information about potential side-effects.

IS-14

Fibromyalgia in clinical practice: differentiating pain mechanisms, managing comorbidities, and addressing vaccination concerns

Victoria Furer[1], Jacob Ablin[2]
[1]Department of Rheumatology, [2]Internal Medicine H Department
Tel Aviv Sourasky Medical Center, affiliated with Tel Aviv University Faculty of Medical and Health Sciences, Tel Aviv, Israel.

Background. Fibromyalgia (FM) is a frequent and clinically challenging comorbidity in clinical practice, particularly among patients with chronic inflammatory conditions. Current evidence conceptualises FM predominantly as a nociplastic pain condition, while recognising that mixed pain phenotypes – reflecting variable contributions of peripheral nociceptive input and central sensitisation – may occur. In patients with immune-mediated inflammatory diseases, failure to distinguish inflammatory pain from centralised, "top-down" pain amplification contributes to inflated disease activity assessments, misinterpretation of treatment response, inappropriate escalation of immunomodulatory therapies, and persistent symptom burden. Accurate, mechanism-based pain assessment is therefore essential for optimal care.
Methods. This presentation adopts a case-based, mechanism-oriented framework to examine three common clinical scenarios: (1) primary fibromyalgia, (2) fibromyalgia coexisting with chronic inflammatory diseases, and (3) fibromyalgia associated with chronic migraine. Drawing on contemporary models of nociplastic and mixed pain, we review clinical indicators of central sensitisation, including widespread pain, fatigue, sleep disturbance, and discordance between symptom severity and objective inflammatory findings. Strategies to differentiate inflammatory from non-inflammatory pain are discussed, incorporating clinical examination findings, laboratory and imaging data, and validated screening tools. Concepts of "top-down" versus "bottom-up" sensitisation are applied to explain heterogeneity in symptom trajectories and treatment response. Management approaches emphasise individualised, multimodal care consistent with international recommendations. Evidence regarding vaccination safety and fibromyalgia risk is integrated to address common patient concerns.
Results. Across clinical cases, fibromyalgia substantially influenced patient-reported outcomes and composite measures of disease activity, frequently in the absence of objective inflammatory activity. Centralised pain was characterised by widespread tenderness, prominent constitutional symptoms, and poor correlation with laboratory or imaging markers of inflammation. Recognition of mixed pain states clarified why adequate control of peripheral inflammation alone often failed to normalise symptoms in a subset of patients. A dual-track management strategy – addressing inflammatory disease processes and nociplastic pain mechanisms in parallel – emerged as critical to avoiding overtreatment. First-line interventions emphasised patient education, graded physical activity, and psychological therapies, with pharmacologic options selected on a symptom-driven basis and with realistic expectations regarding efficacy. Interdisciplinary care models were particularly beneficial for patients with high symptom burden and comorbid conditions. Vaccination data demonstrated that influenza vaccination is safe and immunogenic in fibromyalgia and that human papillomavirus vaccination is not associated with an increased risk of fibromyalgia.
Conclusion. Fibromyalgia is a common and impactful nociplastic pain condition that frequently coexists with chronic inflammatory disease and complicates symptom-based treatment strategies. Incorporating contemporary pain mechanisms into routine clinical assessment enables more accurate differentiation between inflammatory and non-inflammatory pain, reduces unnecessary treatment escalation, and improves patient-centered outcomes. A tailored, mechanism-based, multidisciplinary approach – combined with clear, evidence-based vaccination counselling – is essential for high-quality clinical care.

IS-15

The Fibromyalgia Registries: friends or foe?

Sonia Farah
Department of Rheumatology, Polytechnic University of Marche, Carlo Urbani Hospital, Jesi, Italy.

Background. Fibromyalgia remains one of the most clinically challenging chronic pain conditions, not because of the absence of therapeutic options, but due to the marked variability of symptoms, disease trajectories, and treatment responses observed in daily practice. Patients with the same diagnosis may present with profoundly different clinical pictures, levels of disability, and needs over time. In this scenario, registries have emerged as a pragmatic response to the limitations of traditional clinical trials, offering a longitudinal and real-world perspective on fibromyalgia. Yet, their growing influence on clinical reasoning raises an essential question: do registries truly support individualised care, or do they risk imposing simplified models on a fundamentally heterogeneous condition?
Objective. This lecture aims to explore how fibromyalgia registries interact with clinical decision-making, examining whether large-scale observational data can meaningfully assist clinicians in navigating disease complexity without diluting the individual patient experience. Using the Italian Fibromyalgia Registry as an example, the discussion focuses on how registry-derived evidence influences diagnostic framing, therapeutic choices, and the organisation of care pathways in routine clinical settings.
Methods. The Italian Fibromyalgia Registry collects standardised clinical, demographic, and psychosocial data from more than 10,000 patients, with longitudinal follow-up reflecting real-world clinical practice. The registry captures symptom severity, comorbidities, treatment strategies, and outcomes over time, allowing the observation of disease evolution beyond the constraints of experimental protocols. Advanced analytical approaches have been applied to identify recurrent clinical patterns and trajectories, while maintaining a strong focus on clinical interpretability and relevance for everyday practice.
Results. Data from the registry confirm what clinicians observe daily: fibromyalgia does not follow a single clinical course. Distinct patterns of symptom burden, functional impairment, and response to treatment emerge over time, often changing within the same patient. Longitudinal analyses suggest that patients managed through integrated approaches combining pharmacological treatment, rehabilitation, and psychological support tend to show more stable clinical trajectories. However, registry data also highlight the limits of standardisation, as fluctuations in symptoms, adherence, and follow-up challenge rigid classifications and fixed therapeutic algorithms. Rather than offering definitive answers, the registry provides a framework to contextualise clinical decisions and reduce uncertainty, supporting a more informed and reflective approach to care.
Conclusion. From a clinical perspective, fibromyalgia registries should not be viewed as prescriptive tools, but as decision-support systems that complement, rather than replace, clinical judgment. They offer a shared language to describe patterns, trajectories, and outcomes, while reminding clinicians that variability is a defining feature of the disease. When used critically, registries can enhance continuity of care, inform multidisciplinary strategies, and improve the alignment between clinical practice and real-world evidence.
Ultimately, fibromyalgia registries are neither unequivocal allies nor obstacles. Their value lies in their ability to support clinicians in managing complexity, provided that data are interpreted within the clinical context and not as substitutes for individualised patient care.

IS-16

Microbiome in fibromyalgia

Frances Williams
King's College London, UK.

The gut microbiome describes the genetic material contained within the microbes present in the large bowel, as assessed by stool sample. There is increasing evidence of a gut-brain axis with exchange of information (neural, cytokine, chemokine) between the two organs, and recognition that this may contribute to common complex traits such as fibromyalgia (1). TwinsUK is a cohort of same-sex adult volunteer twin pairs (n=15,500) collected over 35 years and deeply phenotyped and omityped for common complex traits at multiple timepoints. It represents an ideal way of understanding the contribution of diet, medication, lifestyle factors and genetic predisposition because of the ability to decompose the correlations between monozygotic and dizygotic twin pairs (2).
Considering chronic widespread musculoskeletal pain (CWP), a cardinal feature of fibromyalgia, we have shown using 16S rRNA sequencing of stool samples that alpha diversity is reduced (3). Genetic tools such as GWAS and Mendelian randomisation suggest that the microbiome difference observed is not causative of CWP; but this remains to be confirmed by other independent studies. Altered microbiome might reflect another known risk factor for chronic pain such as raised body mass index (BMI). Alternatively, reverse causation could be at play with diversity reduced as a consequence of CWP or medication taken for it. We have shown, for example, that opiate consumption is associated with higher abundance of Streptococcaceae (4). Other large sample studies have suggested dietary differences in those with FM, with significantly less fruit and vegetables consumed in their diet, less dairy and wholegrains compared to healthy controls (5). Interestingly, similar findings were made comparing FM patients with patients having rheumatoid arthritis as controls, suggesting the findings are indeed specific to FM.
Studies of microbiome-targeted interventions such as pre- and probiotics suggest they may be beneficial on cognition, pain and mood in FM but large, well conducted, independently funded studies are required to confirm this.

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IS-17

The FIBROKIT Project: microbiome and diagnostics in FM

Elena Durán-González[1,2], Jorge Antolín Ramírez-Tejero[2], Marta Pérez-Sánchez[2], Carmen Morales-Torres[2], Rosa Gómez-Morano[2], Claudia Díaz-López[2], Antonio Martínez-Lara[1,2], David Cotán[2]
[1]*Pablo de Olavide University (UPO), Seville, Spain.*
[2]*Pronacera Therapeutics S.L., Seville, Spain.*

Background. Fibromyalgia (FM) is a complex disease characterised by chronic widespread pain and fatigue, affecting a significant portion of the population worldwide. Its pathophysiology is multifactorial, involving oxidative stress, mitochondrial metabolism, intestinal microbiota, and inflammation. Currently, there are no validated molecular biomarkers to facilitate diagnosis, and existing studies are often limited by small cohorts. The FIBROKIT project represents a comprehensive effort to solve these limitations through a large-scale, low-interventional clinical trial (NCT05921409).
Objective. The primary objective is the development of a specific panel of FM biomarkers using a multi-omics approach (plasma proteome and intestinal microbiota) and the evaluation of their response to a six-month nutritional intervention with Extra Virgin Olive Oil (EVOO).
Methods. A final cohort of 242 women (199 FM patients and 43 age- and environmentally paired controls) was analysed. Plasma proteome analysis was performed using nLC-MS/MS, and fecal metagenome analysis was conducted via 16S rRNA gene sequencing. For the interventional phase, patients were randomised into placebo and treatment (EVOO) groups. Data was analysed using machine learning algorithms to assess diagnostic performance and longitudinal monitoring.
Results. Our baseline multi-omics analysis, recently published in *Frontiers in Microbiology*, identified a differential pattern of 30 proteins and 19 bacterial taxa between FM patients and controls. Key findings include the upregulation of *Streptococcus salivarius* and alterations in glyceraldehyde-3-phosphate dehydrogenase (GAPDH) activity, linking gut dysbiosis with mitochondrial dysfunction and oxidative stress. The integration of these markers into a diagnostic algorithm achieved a mean Area Under the Curve (AUC) of 0.85±0.07. Regarding the nutritional intervention, longitudinal analysis revealed that the EVOO-treated group showed differential modulation of these biomarkers. We identified two distinct responses: biomarkers that improved during intervention and sustained the positive trend post-treatment, and those that reversed once treatment was discontinued, highlighting the importance of adherence to diet therapy.
Conclusion. The FIBROKIT project confirms the existence of a robust signature of gut microbiota and plasma proteins in FM patients, providing a reliable tool for diagnosis as detailed in our recent publication. Furthermore, the study demonstrates that these biomarkers are responsive to non-pharmacological therapies such as EVOO, offering new avenues for personalised patient monitoring and management.

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IS-18

Non-invasive auricular vagus nerve stimulation in fibromyalgia

Marco Di Carlo
Rheumatology Unit, Università Politecnica delle Marche, Carlo Urbani Hospital, Jesi, Italy.

The vagus nerve represents the longest component of the autonomic nervous system and performs sensory, motor, and autonomic roles. Its autonomic function is of particular relevance in the management of chronic pain, as the vagus nerve is the main pathway of the parasympathetic nervous system. Vagus nerve stimulation (VNS) can be divided into invasive and non-invasive techniques. Invasive VNS involves the surgical implantation of devices that electrically stimulate the cervical branch of the vagus nerve. In contrast, non-invasive VNS consists of transcutaneous stimulation delivered to specific anatomical regions, including the cervical area near the carotid artery (transcervical VNS) and the cymba conchae of the external ear (transauricular VNS), where the skin is supplied by vagal sensory fibers. Both transcutaneous approaches have been shown to activate central vagal pathways.
VNS is widely known for its anti-inflammatory effects, which are mediated through the cholinergic anti-inflammatory pathway, and it has shown potential benefits in inflammatory musculoskeletal conditions.
Although the underlying mechanisms are not yet completely understood, research indicates that fibromyalgia is associated with autonomic dysfunction, particularly a reduction in vagal tone. This autonomic imbalance connects fibromyalgia with other disorders, such as epilepsy and depression, conditions for which VNS is already an established therapeutic option.
With respect to the use of transcutaneous VNS in fibromyalgia, available studies – despite their limited sample sizes – suggest potential effectiveness in this patient group. However, substantial variability exists among studies regarding stimulation parameters, including frequency, intensity, and treatment schedules.
Several uncertainties persist concerning the role of transcutaneous VNS in fibromyalgia treatment. The most important issue is whether its efficacy surpasses that of sham stimulation. Additional challenges include identifying the optimal stimulation technique and clinical setting, defining the most effective treatment duration, and tailoring therapy to individual patients. Addressing these questions will require well-designed, large-scale randomised controlled trials.

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IS-19

Technologies in sleep and fatigue in fibromyalgia

Francesco Porta
Interdisciplinary Pain Medicine Unit, Rheumatology Section, Santa Maria Maddalena Private Hospital, Occhiobello, Italy.

Sleep disturbances and the resulting fatigue, affecting up to 90% of patients, represent core domains of fibromyalgia and show a strong bidirectional relationship with pain. Evidence supports the presence of altered pain modulation and dysfunction of serotonergic and noradrenergic systems, which regulate both sleep and antinociceptive pathways. Neuroimaging and neurophysiological studies have demonstrated hyperactivation of pain-related brain areas and reduced conditioned pain modulation, with fragmented sleep potentially playing a role in the maintenance of central sensitisation.
In patients with fibromyalgia, sleep disturbances present with polymorphic features, including difficulty initiating sleep, early morning/night awakenings, fragmented sleep with hyperarousal, alpha-wave intrusion into deep slow-wave sleep (N3, delta sleep), restless legs syndrome, and obstructive sleep apnea.
Traditionally, sleep assessment relies on sleep diaries and validated questionnaires, which provide subjective information on sleep quality and efficiency, as well as on polysomnography, which, although considered the gold standard for objective evaluation, is not easily applicable on a large clinical scale and is conditioned by the evaluation outside the normal sleep situation.
In recent years, a wide range of devices capable of monitoring sleep have become available, including contact-based tools (such as smartwatches, rings, and other wearables) and contactless systems, often placed under the pillow or mattress. Although many of these technologies are not yet fully validated, they may represent valuable tools for screening, diagnostic support, and longitudinal follow-up.
In parallel, traditional pharmacological and non-pharmacological treatments have shown limited efficacy in addressing sleep disturbances in fibromyalgia, with encouraging results mainly reported for high-dose gabapentinoids and cognitive behavioural therapy for insomnia.
Technological advances may offer new therapeutic opportunities, including telemedicine-based cognitive behavioural therapy models, pre-sleep alpha entrainment using audio-visual stimuli delivered via smartphones combined with EEG wearables, telerehabilitation programs (via videoconferencing, apps, interactive systems, and wearables) incorporating modules on sleep hygiene, relaxation, and behavioural strategies, as well as neuromodulation techniques such as transcranial magnetic stimulation, transcranial electrical stimulation, percutaneous vagus nerve stimulation, and light therapy.

IS-20

Technology in pain management

Marta Nizzero[12], Alvise Martini[12], Patrizia Vendramin[12], Enrico Polati[12], Vittorio Schweiger[12]
[1]*Department of Pain Medicine, University of Verona, Italy.*
[2]*Department of Anesthesia and Intensive Care, University Hospital of Verona, Italy.*

Chronic pain affects over 20% of adults worldwide, causing disability, opioid dependence and reduced quality of life. Traditional pharmacological and interventional approaches often show limitations. Digital therapeutics (DTx) and emerging technologies – virtual reality (VR), mobile applications, telehealth platforms and artificial intelligence (AI) – are increasingly recognised as evidence-based tools to improve pain assessment, management and patient empowerment.
This review summarises the most recent peer-reviewed literature (PubMed, Scopus, ClinicalTrials.gov) and ongoing trials on the efficacy of these technologies in pain therapy.
VR-based DTx, such as the FDA-approved RelieVR for chronic low-back pain, produced significant pain reduction in 8 of 9 RCTs through immersive distraction and biofeedback, effective in both acute and chronic settings. Mobile apps integrating cognitive behavioural therapy (CBT), hypnosis and multidisciplinary interventions (*e.g.* ePAL for cancer pain, HelloBetter Chronic Pain) achieved 26% pain-score reductions, better functional outcomes and improved management of mental-health comorbidities. Nurse-led telehealth and web-based platforms increased accessibility, reduced healthcare utilisation and overcame barriers in older adults and underserved populations. Ongoing trials (NCT06000007, NCT07270588) confirm sustained benefits in pain intensity, anxiety and opioid consumption, with high patient acceptance. AI integration is rapidly advancing: at our centre, AI-enhanced Spinal Cord Stimulators (SCS) enable real-time, patient-specific stimulation tailored to pain type and intensity, increasing autonomy. AI-driven diagnostic algorithms improve accuracy in complex syndromes (fibromyalgia, neuropathic pain), reducing false negatives/positives and optimising personalised treatment pathways.
Challenges remain: adherence, digital divide, and the need for larger, diverse RCTs to prove long-term scalability. Nevertheless, DTx and new technologies offer transformative, equitable complements to conventional therapies and warrant broader clinical integration to address unmet needs in chronic pain care.
Key words. Chronic pain, digital therapeutics, virtual reality, telehealth, artificial intelligence, spinal cord stimulation

IS-21

Patient-centered strategies and psychosocial care in fibromyalgia

Valerie Aloush
Internal Medicine A, Tel Aviv Sourasky University Medical Center, Tel Aviv; Faculty of Health Sciences, Gray School of Medicine, Tel Aviv University, Israel.

Fibromyalgia (FM) represents a complex, multi-systemic central sensitivity syndrome characterised by widespread nociplastic pain, sleep disturbances, global sensory hypersensitivity, and a profound disruption of descending antinociceptive modulatory systems. While current pharmacological options – specifically α2δ ligands like pregabalin and SNRIs – attempt to reduce excitatory signaling or enhance descending inhibition, clinical efficacy remains constrained by substantial inter-individual variability and the persistence of non-nociceptive drivers of disability. This lecture outlines an evidence-based transition from a reductionist biomedical model toward a patient-centered framework where psychosocial care is utilised as a core biological intervention, beginning with the diagnostic encounter as a primary therapeutic event. Central to this approach is the power of clinical validation; a formal, empathetic diagnosis serves to resolve diagnostic uncertainty and mitigate the healthcare-seeking anxiety that frequently exacerbates central sensitisation. By implementing rapid psychosocial phenotyping – utilising validated instruments such as the Pain Catastrophising Scale (PCS) for cognitive distortion and the PHQ-9 for comorbid affective burden – the specialist can identify high-risk profiles and tailor interventions with precision. This shift necessitates moving beyond the 0-10 numeric pain scale toward collaborative goal setting, where therapeutic success is defined by functional metrics such as sleep architecture, vocational maintenance, and social engagement. We further examine the neurobiological impact of psychological distress and kinesiophobia, which function as robust modulators of the "pain matrix", specifically altering functional connectivity within the anterior cingulate cortex (ACC), posterior insula, and the dorsolateral prefrontal cortex (dlPFC). High-resolution neuroimaging reveals that behavioural interventions like Cognitive Behavioural Therapy (CBT) and Acceptance and Commitment Therapy (ACT) go beyond palliative support, facilitating measurable neuroplastic changes in the brain's default mode network and descending inhibitory pathways. Furthermore, we analyse the clinical deployment of personalised precision care through the integration of Prescription Digital Therapeutics (DTx). These digital platforms utilise data-driven algorithms to provide scalable, high-fidelity behavioural interventions that address the "access gap" in specialised pain psychology. By strengthening the therapeutic alliance and focusing on psychological flexibility, clinicians can better manage the autonomic and neuro-inflammatory sequelae of FM, ultimately treating the patient as a complex, integrated biological and biographical entity.

IS-22

The national perspective on fibromyalgia in Poland

Elżbieta Żuraw
Polish National Association of People with Fibromyalgia FIBRO-MY.

Fibromyalgia, despite its prevalence and serious health and social consequences, still largely remains an "invisible illness" in Poland.
One of the greatest challenges faced by patients is the diagnostic process. People with fibromyalgia encounter numerous diagnostic barriers resulting from the lack of uniform clinical guidelines and insufficient knowledge about the condition. Symptoms are often trivialised, and patients are told that their complaints are psychosomatic in nature. Chronic pain, fatigue, and cognitive disturbances are not always treated as real medical problems. Years of searching for a diagnosis, numerous consultations, and a lack of understanding lead to increasing suffering and delays in initiating appropriate treatment.
However, receiving a diagnosis does not mark the end of difficulties. Access to rheumatologists, psychological therapy and rehabilitation services is limited by long waiting times. As a result, many patients are forced to use private, costly services that are unaffordable for some, often leading to discontinuation of treatment and deterioration of health. Pain management clinics, which are too few in number, rarely have experience working with patients with fibromyalgia who require comprehensive, multidisciplinary care. There is also a lack of specialised hospital-based pain management units that could provide support during acute pain crises. Fibromyalgia also remains socially invisible. Patients experience a lack of understanding at work, within their families, and often within the healthcare system itself. This leads to isolation and stigmatisation. Results of a large study conducted in Poland show that people with fibromyalgia experience significant disability related to chronic pain, fatigue, sleep disorders, and cognitive dysfunction. Despite this, obtaining an official disability certificate is extremely difficult, and the assessment system often fails to take into account the real limitations resulting from the disease.
From the perspective of the FIBRO-MY Association, the key needs of patients include education for both physicians and patients, faster and equal access to medical specialists, access to multidisciplinary care within the public healthcare system, and full recognition of fibromyalgia in disability assessment procedures. Social awareness campaigns are also necessary, as well as systemic solutions to improve the coordination of fibromyalgia care. The FIBRO-MY Association conducts educational activities, brings patients together through a support group, and establishes contacts with medical experts. We initiated a nationwide study conducted by a team of researchers from the University of Rzeszów under the leadership of Professor Agnieszka Sozańska, concerning the assessment of disability among people with fibromyalgia in Poland. ''Disability Assessment with WHO-DAS 2.0 of People with Fibromyalgia in Poland: A Cross Sectional-Study". The Association's scientific expert is rheumatologist Tomasz Jasiński, the author of the first monograph on fibromyalgia published in Poland. Fibromyalgia will not disappear on its own. However, it can become a visible, understood, and properly treated condition. Integrating scientific knowledge, clinical experience, and the patient voice is the key to creating an effective model of care.

IS-23

The role of patient associations

Gunilla Göran
European Network for Fibromyalgia Associations (ENFA).

Patient associations are crucial for individuals affected by chronic conditions like fibromyalgia. These organisations operate at individual, national, and European levels, influencing health policy, research agendas, clinical practice, and social awareness. Through coordinated action, patient associations address medical, social, and economic challenges related to fibromyalgia.
ENFA, with its twenty-five national member organisations, focuses on advocacy, collaboration with healthcare professionals, engagement with authorities and insurance companies, and participation in European institutions. This summary is based on seventeen years of ENFA's experience, highlighting advocacy, information exchange, stakeholder engagement, and collaboration at both national and European levels. ENFA's involvement includes policy discussions, research initiatives, guideline development, and partnerships with medical and patient umbrella organisations.
While direct short-term benefits for individual patients at the European level may be limited, long-term advocacy and lobbying contribute to improved outcomes by shaping policy priorities and research directions. National associations benefit from shared knowledge, mutual support, and a deeper understanding of the daily challenges faced by people with fibromyalgia, fostering the development of European guidelines, improved research quality, and increased awareness of the disease's social and economic impact.
Well-informed patient associations become respected partners for healthcare professionals and are increasingly recognised by authorities and insurance companies as credible stakeholders, involved in policy development and discussions on access to care and social benefits. Collaboration with European umbrella organisations and medical associations strengthens advocacy and ensures the patient perspective is integrated into research and education.
ENFA thus strengthens the voice of people with fibromyalgia and contributes to better care and more equitable policies.

IS-24

Psychotherapy in fibromyalgia

Riccardo Torta, Rossana Botto
University of Turin, Italy.

An issue in the treatment of fibromyalgia (FM), a syndrome characterised by nociplastic pain, is represented by the poor effectiveness of pharmacological therapies against chronic pain. Only 40% of patients are satisfied with their pain therapy. This may depend on inadequate drug treatment or, more often, on lack of attention to the cognitive, emotional, and social aspects of pain. Moreover, it is known that a transition from acute to chronic pain reduces in the brain the activity of sensory circuits while increases that of emotional circuits. In a recent consensus on non-pharmacological therapies for FM, almost all the experts suggested psychotherapeutic interventions in the management of pain, fatigue, sleep and depression. Furthermore, the patients themselves consider the psychotherapeutic approach highly effective. In recent years, we have moved from the contrast between psycho-pharmacotherapy and psycho-therapies to an integration of the two types of interventions, also because both are characterised by similar objectives and biological bases. While the use of psychotherapies for emotional symptoms, such as anxiety, depression and distress, has been widely validated, their effectiveness in pain treatment is still partially discussed. The rationale for the use of psychotherapies in treatment of FM pain is linked to the improvement of the emotional filter on pain, the reduction of psycho-pathological interferences, and the management of cognitive, social and behavioural aspects maintaining pain, such as disadaptive behaviours, catastrophising, fear, attention, expectation, dysfunctional life styles, relational wellbeing, social support and social isolation. There are also clear demonstrations of the neurobiological effectiveness of psychotherapy, both on an immunological level *(e.g.* a normalisation of Natural Killers in depressed cancer patients and a downregulation of nuclear factor kappa B pathway reducing inflammation) and on neuroimaging studies, in which an inhibition of thalamic activity and an enhancement of pain inhibitory activity by the prefrontal and anterior cingulate cortex are demonstrated. One of the most widely used psychotherapeutic interventions in FM is Cognitive Behavioural Therapy (CBT), which has proven useful in managing emotional and cognitive symptoms, sleep disorders, dysfunctional behaviours, and painful pathology. CBT aims to identify unhelpful patterns of behaviour and beliefs and to regulate emotions, encouraging more positive attitudes toward the illness. Other interventions are the so-called "third wave" therapies including Acceptance and Commitment Therapy, Compassion-focused Therapy, and Mindfulness-Based Cognitive Therapy. They are focused on meditation, observation of internal experiences without judgment, acceptance, recognition of personal values, and experiential exercises, and contribute to patients' psychological flexibility, adaptation and wellbeing. Also problem solving techniques and mind-body practices (autogenic training, qigong, tai chi, yoga, Feldenkreis, etc.) are effective in pain management, helping patients in implementing functional solutions and self-care. Finally, experiential psychotherapies, such as EMDR, promote traumas processing by releasing tensions and defenses, and facilitating beneficial functioning. Psychoterapies work on subjective feelings and functioning around pain, managing pain-related emotions, reducing perceived pain intensity and improving pain-related disability. Non-drug therapies enhance the effectiveness of drug treatments and vice versa. As for pharmacotherapy,

the choice of non-drug therapy should be tailored to the patient, based on data of efficacy, assumed adherence, and patient resources and limitations. Non-pharmacological interventions, as the pharmacological ones, require patient's active involvement, based on adequate psychoeducation, and clinician's active involvement implementing patient care on a case-by-case basis.

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IS-25

Mind-body therapies for fibromyalgia: outcomes, contextual effects, and methodological challenges

Federica Galli, Federica Doria
Sapienza University of Rome, Italy.

Fibromyalgia is a complex chronic condition characterised by widespread musculoskeletal pain, fatigue, sleep disturbances, and cognitive symptoms. Clinical management typically involves a combination of pharmacological and non-pharmacological strategies. Although their effects vary across modalities and outcome domains, mind-body interventions have been increasingly explored as potential adjunctive components of multimodal care (Steen *et al*., 2024; Theadom *et al*., 2015; McQuillan, 2022).

A 2024 systematic review (27 RCTs, 1969 participants) found Qi Gong and Tai Chi offer the most consistent short-term improvements in pain and fatigue versus controls, with heterogeneous benefits on function and mood; guided imagery, progressive muscle relaxation, neurofeedback, and meditation awareness training show select trial-level effects, often in small samples (Steen *et al*., 2024). The 2015 Cochrane review (61 trials, 4234 participants) reports movement therapies reduce pain (MD -2.3) and improve mood (MD -9.8, very low-quality evidence), relaxation therapies improve physical function (MD -8.3) and pain (SMD -1.0, low-quality evidence), while biofeedback and mindfulness yield small or inconsistent gains (very low-quality evidence) versus usual care (Theadom *et al*., 2015). Yoga-based multicomponent programs (postures, breathing, mindfulness) demonstrate moderate pain/function improvements and sustained effects in small RCTs (moderate-to-low quality) (Durusoy & Ünal, 2025; Islam *et al*., 2015).

Numerous trials document parallel improvements between mind-body interventions and controls, indicating that non-specific factors (patient expectations, therapeutic attention, engagement) substantially amplify placebo-related effects in fibromyalgia (Theadom *et al*., 2015), pending higher-quality, long-term trials clarifying efficacy, durability and intervention-specific effects (Steen *et al*., 2024; Theadom *et al*., 2015).

IS-26

From graded activity to pacing: matching exercise to complexity

Mira Meeus
MOVANT Research Group, Department of Rehabilitation Sciences and Physiotherapy, Faculty of Medicine and Health Sciences, University of Antwerp, Belgium.

Exercise therapy or physical activity management is a core component of fibromyalgia (FM) management, yet clinical outcomes remain highly variable and at best modest, with frequent symptom flares and limited long-term adherence. Although FM has long been framed as a prototype of nociplastic pain, growing evidence highlights substantial heterogeneity, with patients distributed along a continuum of pain mechanisms with varying contributions of peripheral nociceptive input and centrally driven pain amplification. Importantly, this heterogeneity extends beyond pain processing to broader biopsychosocial dimensions, including emotion, cognitions, behavioural patterns, etc.

Historically, graded activity and time-contingent exercise approaches were promoted to counter fear, avoidance, and deconditioning, gaining particular prominence following trials in, for example, chronic fatigue syndrome. Subsequent debate and re-analyses raised concerns regarding the applicability of uniform progression models in conditions marked by altered central processing, fatigue, and delayed recovery. In parallel, within the broader field of chronic musculoskeletal pain, ongoing debate concerns whether pain during exercise should be avoided, tolerated, or deliberately provoked. While limited pain exposure may reduce threat and fear in some patients, evidence indicates that exercising into pain does not consistently improve outcomes and may be inappropriate for others.

Conversely, purely symptom-contingent activity management also warrants caution. In chronic pain conditions where pain is an unreliable indicator of tissue state, strict symptom-guided pacing may be overly conservative and may inadvertently reinforce biomedical interpretations or danger-related beliefs. Contemporary pacing strategies therefore move beyond a simple symptom-versus-time dichotomy. In particular, operant learning-based pacing emphasises predefined activity blocks, strategic rest, and reinforcement of functional consistency, in contrast to energy conservation approaches that prioritise symptom avoidance.

From a pain-mechanistic perspective, altered endogenous pain modulation may further influence exercise tolerance and response. In a substantial subset of patients with FM, exercise-induced hyperalgesia has been demonstrated, reflecting impaired descending pain inhibition. The potential downside of repeated pain provocation, with impaired pain inhibition, might encompass that the insufficiently regulated pain exposure may, besides acting as negative reinforcement, function as a plasticity enhancer and reinforce central amplification in susceptible individuals. However, this phenomenon is again not universally present, underscoring once more the heterogeneity within the nociplastic pain continuum. And while such mechanistic differences may plausibly inform exercise prescription, robust evidence to guide treatment selection based on pain mechanisms remains limited.

As such, available evidence does not support clear differential effectiveness of pacing versus graded activity across FM subgroups defined by pain mechanisms or disease severity. The strongest signals for treatment matching currently emerge from behavioural phenotypes: interventions tailored to activity avoidance versus persistence patterns yield meaningful improvements, supporting a multidimensional, continuum-based framework. In consequence, rather than positioning graded activity and pacing as competing strategies, this lecture emphasises clinical reasoning and dynamic balancing, informed by pain mechanisms, behavioural profiles, and broader biopsychosocial context, to support adaptive movement without reinforcing threat, avoidance, or sensitisation.

IS-27

Oxygen-ozone autohemotherapy for fibromyalgia: NRF2 pathway activation and functional outcomes

Roberto Casale[1], Giustino Varrassi[2,3]
[1]*Opusmedica. Persons, Care & Research, NPO, Piacenza, Italy.*
[2]*Fondazione Paolo Procacci, Roma, Italy.*
[3]*College of Medicine, University of Baghdad, Iraq.*

Fibromyalgia (FM) is a chronic pain syndrome affecting approximately 2–4% of the general population and is characterised by widespread musculoskeletal pain, fatigue, sleep disturbance, and cognitive dysfunction, resulting in substantial functional impairment. Its pathophysiology is multifactorial and incompletely understood, but converging evidence supports a central role for central sensitisation, sustained oxidative stress, and mitochondrial dysfunction, which together contribute to altered pain processing and symptom persistence (1).

Oxygen-ozone autohemotherapy (O_2-O_3 AHT) consists of the withdrawal of 100–200 mL of venous blood, its controlled exposure to a calibrated oxygen-ozone gas mixture (typically 20–40 μg/mL), and immediate reinfusion into the patient (2). This procedure induces a transient, well-regulated oxidative stimulus that elicits adaptive hormetic responses (3). In contrast to local ozone infiltrations, autohemotherapy exerts systemic effects, making it conceptually suited to FM, a condition involving widespread biological dysregulation and central pain mechanisms. Standard treatment protocols generally include 10–15 sessions administered over 5–8 weeks (4).

A key mechanistic link between FM pathophysiology and the biological effects of O_2-O_3 AHT is the activation of nuclear factor erythroid 2-related factor 2 (Nrf2), a transcription factor that governs cellular antioxidant and cytoprotective responses (5). Nrf2 regulates the expression of more than 250 genes involved in redox homeostasis, mitochondrial function, and inflammatory control. In FM, persistent oxidative stress appears to impair Nrf2 signaling, leading to depletion of endogenous antioxidant defenses, mitochondrial dysfunction, and amplification of pain signaling (5, 6).

Ozone-mediated activation of Nrf2 occurs through the formation of lipid ozonation products, such as 4-hydroxynonenal and malondialdehyde, during blood exposure to the gas mixture (7). These reactive molecules interact with cysteine residues on Kelch-like ECH-associated protein 1 (Keap1), the cytoplasmic inhibitor of Nrf2, promoting Nrf2 release, nuclear translocation, and transcriptional activation of antioxidant response elements. This results in upregulation of glutathione synthesis enzymes, superoxide dismutase, catalase, and other cytoprotective proteins, thereby restoring redox balance and improving cellular resilience.

Clinical studies, although limited in size, report meaningful functional benefits following O_2-O_3 AHT in FM. Pooled analyses describe reductions in Fibromyalgia Impact Questionnaire scores of approximately 28 points, exceeding established thresholds for clinical relevance, along with 30–45% decreases in pain intensity ()]. Biomarker assessments demonstrate normalisation of oxidative stress parameters, including reductions in lipid peroxidation markers and enhancement of total antioxidant capacity. Additional reports indicate improvements in inflammatory profiles, sleep quality, and patient-reported quality of life domains [9]. Treatment is generally well tolerated, with adverse events being mild and transient, most commonly short-lived fatigue. Symptomatic improvement often emerges after 4–6 sessions and may persist for 6-12 months after treatment completion.

Overall, O_2-O_3 AHT represents a biologically plausible adjunctive intervention for FM, targeting core mechanisms related to oxidative stress and redox dysregulation through Nrf2 pathway activation. While preliminary evidence suggests clinically relevant benefits, current data are derived mainly from small observational studies and limited randomised trials. Well-designed, adequately powered randomised controlled studies are required to confirm efficacy, define optimal treatment protocols, and identify patient subgroups most likely to benefit, as well as to clarify its role within comprehensive multimodal rehabilitation strategies for fibromyalgia.

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IS-28

Immersive virtual reality in fibromyalgia

Simone Longhino[1], Luca Chittaro[2], Luca Quartuccio[1]

[1]*Rheumatology Division, Department of Medicine, University of Udine, Udine, Italy.* [2]*Human-Computer Interaction Lab, Department of Mathematics, Computer Science and Physics, University of Udine, Udine, Italy.*

Fibromyalgia (FM) is a chronic musculoskeletal syndrome marked by widespread pain, fatigue, sleep disturbance, cognitive complaints, and mood symptoms, resulting in major quality-of-life impairment and substantial healthcare and societal burden. Although guidelines recommend a multimodal strategy combining pharmacological and non-pharmacological measures, symptom control is often only partial; therefore, real-world care should prioritise effective and scalable non-pharmacological options while limiting long-term reliance on analgesics.

Virtual reality (VR) has moved from experimental use to a practical therapeutic tool in pain medicine. In acute pain settings, VR can reduce perceived pain through strong attentional engagement and modulation of affective and threat-related processing. In chronic pain, VR can also deliver structured interventions – relaxation, paced breathing, mindfulness, graded activity, and cognitive-behavioural elements – within immersive, engaging environments, which is particularly relevant to conditions involving altered central pain processing (1).

In FM, VR interventions can be broadly divided into non-immersive and immersive approaches. Non-immersive VR (screen/desktop platforms and exergames) has been mainly used as a rehabilitation adjunct, supporting exercise programs and targeting physical function, balance, activity tolerance, and global symptom impact. Immersive VR (IVR), delivered via head-mounted displays, offers higher presence and sensory isolation and has been applied both as a symptom-oriented intervention and combined with exercise. Conceptually, the higher engagement of IVR may foster adherence and strengthen therapeutic learning compared with non-immersive formats, although this remains a plausible hypothesis requiring direct comparative testing (2).

A particularly relevant development is IVR integrated with physiological biofeedback, where real-time signals (*e.g.* respiration and autonomic indices) are embedded into the virtual environment. This design shifts IVR in FM from a "distraction-only" paradigm toward skills-based self-regulation, enabling patients to practice controllable strategies with embodied feedback and immediate reinforcement. In this framework, regulation training is not merely experienced but actively learned, with the goal of supporting transfer of self-regulation skills outside the virtual session. In a pilot randomised controlled trial, *Chittaro et al*. evaluated an immersive VR plus multisensor biofeedback (IVR-BF) intervention in FM, embedding guided regulation within a virtual scenario. The study provides pragmatic evidence of feasibility and acceptability and reports improvements consistent with reduced pain and better quality-of-life/impact outcomes, supporting the clinical plausibility of IVR-BF as a non-pharmacological component addressing mechanisms relevant to FM symptom amplification (3).

In conclusion, IVR may offer a concrete, patient-centered way to deliver non-pharmacological care in FM. In real-world settings, IVR can be implemented as a structured adjunct to education, exercise, and psychological interventions, with predefined session duration, frequency, and objectives. Immersive biofeedback-enhanced approaches may be especially useful to promote engagement and train transferable self-regulation strategies.

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IS-29

A short history of fibromyalgia and nociplastic pain in OMERACT: the opportunities and challenges of definition and assessment in rheumatic disease

Philip Mease

Director of Rheumatology Research, Providence Swedish Medical Center and Clinical Professor, University of Washington School of Medicine, Seattle, USA.

Since 2004, fibromyalgia (FM) and nociplastic pain (NP) have been a focus of the OMERACT (Outcome Measures in Rheumatology) chronic pain working group. The first task of the group was to define the core set of items constituting FM/NP which should be measured in clinical trials and observational registries. The ongoing task is to raise awareness of the importance of assessing FM/NP in rheumatologic conditions and establish reliable and feasible assessment methods. The arc of the OMERACT FM/NP work and two examples of the impact and assessment of FM/NP in recent rheumatic disease studies will be discussed: the CorEvitas psoriatic arthritis registry and the UPSTAND axial spondyloarthritis clinical trial.

Oral Presentations

P-01

TNX-102 SL (cyclobenzaprine HCl sublingual tablets) provides rapid pain relief in adults with fibromyalgia

Errol Gould[1], Gregory Sullivan[2], Jean Heilman[2]
[1]*Tonix Medicines, Inc., USA.*
[2]*Tonix Pharmaceuticals, Inc., USA.*

Background. Fibromyalgia (FM) is a common, chronic nociplastic pain syndrome characterised by widespread pain, non-restorative sleep, and fatigue. Currently approved FM treatments vary in time to clinical improvement.
Objective. Examine pain improvement time course with TNX-102 SL, a sublingual cyclobenzaprine formulation, the first new FM treatment in 15 years.
Methods. RESILIENT (NCT05273749), a 14-week, randomised, double-blind, placebo-controlled Phase 3 study, evaluated TNX-102 SL efficacy and safety in adults with FM. TNX-102 SL demonstrated significant improvement *vs*. placebo for the primary endpoint: change from baseline to Week 14 in the weekly average of daily pain numeric rating scale (NRS, 0-10) scores, which was significant at Weeks 1–14. Each weekly score was the average of ~7 days of daily pain scores using 24-hour recall. A mixed-model, repeated-measures *post hoc* analysis evaluated TNX-102 SL *vs*. placebo on pain over the first 2-7 treatment days.
Results. Mean baseline (SD) NRS pain scores were 5.9 (1.08) for TNX-102 SL (n=225) and 5.9 (1.05) for placebo (n=231). During treatment Week 1, least-squares mean (LSM) differences [95% CI] in NRS pain scores favoured TNX-102 SL *vs*. placebo for each day: Day 2 (-0.2 [-0.4, 0.0]; p=0.045), Day 3 (-0.5 [-0.7, -0.3]; p=0.001), Day 4 (-0.3 [-0.5, -0.1]; p=0.014), Day 5 (-0.2 [-0.4, 0.0]; p=0.071), Day 6 (-0.4 [-0.6, -0.2]; p=0.001), and Day 7 (-0.2 [-0.5, 0.0]; p=0.046).
Conclusion. In FM patients, TNX-102 SL provided early pain reduction at Day 2 that was sustained over 14 weeks. Early pain relief may facilitate treatment adherence.

Supported by: Tonix

P-02

TNX-102 SL (cyclobenzaprine HCl sublingual tablets) for the treatment of fibromyalgia (FM): number needed to treat (NNT) and number needed to harm (NNH)

Errol Gould[1], Gregory Sullivan[2], Jean Heilman[2]
[1]*Tonix Medicines, Inc., USA.*
[2]*Tonix Pharmaceuticals, Inc., USA.*

Objective. To evaluate number needed to treat (NNT), number needed to harm (NNH), and likelihood to be helped or harmed (LHH) for TNX-102 SL in FM.
Methods. Phase 3 (NCT04172831; NCT05273749) pivotal trial data from adults with FM treated with TNX-102 SL 5.6 mg or placebo were pooled. NNT and NNH were calculated as the inverse of the absolute risk reduction (ARR). 30% pain reduction from baseline to end of treatment (Week-14) was selected for NNT, as 30% is recognised as clinically meaningful. Similar to other studies, NNH was calculated for discontinuation due to adverse events (AEs). Confidence intervals were calculated for these 2 significant outcomes. LHH (≥30% pain/discontinuation due to AE) assessed the balance between clinical benefit and harm. NNH was also calculated for other AEs.
Results. NNT and NNH were calculated using ITT (TNX-102 SL, n=479; placebo, n=480) and safety populations (TNX-102 SL, n=479; placebo, n=481), respectively (Table I). NNT (95% CI) for a ≥30% pain reduction was 7 (5-12). NNH for discontinuation due to AE was 26 (14-110). The LHH was 3.7, suggesting a nearly four-fold greater likelihood of clinical benefit than treatment discontinuation. NNH for severe AEs, severe oral AEs, dry mouth, and somnolence were 233, 159, 118, and 43, respectively.
Conclusion. TNX-102 SL was associated with favourable NNT, NNH, and LHH values, suggesting treatment benefit is more likely than AE-related discontinuation.

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Table I. NNT and NNH values for TNX-102 SL 5.6 mg (RESILIENT and RELIEF)

Outcome	TNX-102 SL			Placebo			ARR	NNT or NNH
	n	N	%	n	N	%		
Efficacy outcomes (NNT)								
≥30% pain reduction	222	479	46.3	150	480	31.3	0.151	7
Tolerability outcomes (NNT)								
Discontinuation due to AE	35	479	7.3	17	481	3.5	0.038	26
Severe AE	14	479	2.9	12	481	2.5	0.004	233
Severe oral AE	3	479	0.6	0	481	0	0.006	159
Somnolence[a]	22	479	4.6	11	481	2.3	0.023	43
Dry mouth[b]	14	479	2.9	10	481	2.1	0.008	118

[a]Somnolence includes hypersomnia, lethargy, and sedation.
[b]Dry mouth includes dry throat.
ARR = TNX-102 SL rate minus Placebo rate.
NNT and NNH = 1/ARR; calculated prior to rounding ARR.
Participants with missing efficacy data were analyzed as non-responders.

P-03

One-day multidisciplinary assessment for fibromyalgia: preliminary results from a digital registry experience

Federica Doria[1], Laura Bazzichi[2], Luigi Bonini[2], Yvelise Corradini[2], Alessandro Lucia[2], Manuela Mauri[2], Mara Vaghi[2], Federica Galli[1], Piercarlo Sarzi-Puttini[2,3]
[1]*Department of Dynamic and Clinical Psychology, and Health Studies, Faculty of Medicine and Psychology, Sapienza University of Rome, Rome, Italy.*
[2]*Rheumatology Department, IRCCS Galeazzi-Sant'Ambrogio Hospital, Milan, Italy.*
[3]*Department of Biomedical and Clinical Sciences, University of Milan, Milan, Italy.*

Background. Fibromyalgia (FM) is a complex and disabling syndrome requiring integrated and multidisciplinary management. Within the regional rheumatologic care strategy promoted by Regione Lombardia, IRCCS Galeazzi-Sant'Ambrogio implemented a one-day multidisciplinary assessment pathway to address FM's multifaceted burden. This initiative was conducted within the FibronetCare framework, the official digital platform for coordinated rheumatology care.
Objective. To describe preliminary data and feasibility outcomes of a multidisciplinary FM clinic powered by digital health support through FibronetCare.
Methods. We enrolled 93 patients who selected our center via the FibronetCare digital interface. All underwent same-day evaluations by a physiatrist, rheumatologist, nutritionist, and psychologist, followed by a final integrated report. Clinical, functional, pharmacological, nutritional, and psychological profiles were assessed using standardised tools.
Results. Patients were mostly female (94.3%), with a mean age of 51.5 years and disease duration of 6.2 years. Disease impact was high (mean FIQR 69.8, PDS 21.1, FASm 28.1), with 34.5% meeting FIQR's thresholds for severe disease. Comorbidities (mean 6.9 per patient) included musculoskeletal, psychiatric, metabolic, and gastrointestinal. Psychopathological burden included anxiety (30.6%), depression (29.7%), and trauma or major stressful events (64.5%). Patients were taking an average of 7.8 medications and followed a mean of 6.5 non-pharmacological interventions. Notably, 79.7% were receiving psychotropic drugs.
Conclusion. This one-day multidisciplinary FM model, integrated within the FibronetCare digital registry supported by Regione Lombardia, offers a feasible and replicable approach to structured patient management and may support future implementations in a patient-centered framework.

P-04

Diagnostic evaluation of ultrasound images in patients with fibromyalgia using machine learning methods

Marta Grelowska[1], Rafał Małecki[1,2], Bogna Jaszczak-Dyka[4], Łukasz Płociniczak[3]
[1]*Regional Specialist Hospital in Wrocław, Research and Development Center, Poland.*
[2]*Faculty of Medicine, Wrocław University of Science and Technology, Poland.*
[3]*Faculty of Pure and Applied Mathematics, Department of Applied Mathematics, Wrocław University of Science and Technology, Poland.*
[4]*Wrocław University of Science and Technology, Poland.*

Background. Epidemiological data indicate that fibromyalgia affects 2–5% of the adult population; however, its true prevalence may be underestimated due to the lack of reliable diagnostic methods. Ultrasonography is a readily available and relatively inexpensive imaging modality that allows correlation of tender point locations with imaging findings.
Objective. The aim of the study was to analyse differences between ultrasonographic muscle images obtained from patients with fibromyalgia and healthy volunteers using machine learning methods.
Methods. The study included patients fulfilling the 2016 American College of Rheumatology (ACR) diagnostic criteria for fibromyalgia and healthy volunteers without muscle pain. A total of 225 ultrasound images were analysed, including 163 from the fibromyalgia group and 62 from the control group. Supervised machine learning methods were applied to analyse the ultrasound images. Image features were extracted using a pre-trained VGG-19 convolutional neural network and reduced using principal component analysis (PCA). Classification performance was evaluated using cross-validation and receiver operating characteristic (ROC) curve analysis.
Results. The logistic regression classifier achieved an AUC of 0.77 and a sensitivity of approximately 0.75, indicating performance significantly better than chance. Although false-positive classification occurred, the results demonstrated that ultrasound images from patients with fibromyalgia differed from those of healthy individuals.
Conclusion. Ultrasonographic images contain diagnostically relevant information that enables differentiation between diseased and healthy individuals with certain probability, though not unequivocally. Ultrasonography may serve as a supportive tool in the diagnostic process but should not be considered a standalone method for diagnosing fibromyalgia.

P-05

The low glutamate diet effectively reduces widespread chronic pain and associated symptoms in Gulf War Illness

Fahimeh Martami[1], **Kathleen Holton**[1,2]
[1]*Health Studies, American University, USA.*
[2]*Neuroscience, American University, USA.*

Background. In previous research, the low glutamate diet (LGD), which reduces dietary exposure to excitotoxins, was shown to significantly improve the symptoms of fibromyalgia (FM) and Gulf War Illness (GWI). GWI is a multisymptom disorder associated with central sensitisation, similar to FM. A phase III clinical trial was conducted to confirm these findings in GWI.
Methods. Veterans with GWI were recruited from across the US (N=101, 55% male, age 59(5) yrs). Participants completed a baseline visit, were randomised into immediate dietary intervention or waitlisted control groups (following their own diet for one month before receiving intervention), received a 2-hour dietary training with materials, followed LGD diet for 1-month, then completed post-diet visit. At each visit, blood/urine were collected, tenderpoint exam/dolorimetry were conducted, and questionnaires were completed. Independent sample t-tests were used to compare change scores between intervention/control groups, effect size was calculated using Cohen's d; and non-parametric Wilcoxon Signed Rank tests were used for change-score analyses.
Results. After one month on the diet, significant improvements were observed for all measures (all p=0.001). Total symptom number reduced from 19(7) to 12(9), with a very large effect size (d=0.94). Myalgic score reduced from 16(17) to 7(12); tenderpoint number dropped from 3(7) to 0(3); pain threshold increased from 3(2) to 4(2); and headache days dropped from 12(20) to 7(7). Chalder Fatigue Scale reduced from 23(12) to 12(8); and metabolites related to mitochondrial function (alanine/lactate/alpha-ketoglutarate) improved, (all p0.05).
Conclusion. The LGD successfully reduces pain, fatigue, and other symptoms associated with Gulf War Illness.

P-06

Ultrasonic neuromodulation for treatment of fibromyalgia

Jan Kubanek, Thomas Riis, Daniel Feldman, Akiko Okifuji
Washington University in St. Louis, USA.

Focused ultrasound is emerging as novel tool to modulate deep brain regions in humans selectively and non-invasively. The approach has the potential to provide a new way to causally interrogate the function of the human brain and to provide circuit-directed treatments of mental and neurological disorders.
We have developed an approach and a device that address the key barrier for transcranial ultrasound – the human head and hair. The approach uses ultrasound itself to measure and compensate for these aberrations in real time.
We have validated the approach and device by assessing deep brain target engagement using fMRI BOLD imaging. Moreover, we have applied the approach to subjects with fibromyalgia, targeting the anterior cingulate cortex (ACC).
The ultrasound complied with the FDA 510k levels on safe ultrasound exposure. Focused ultrasound modulation provided reliable engagement of the targeted deep brain regions. The effect was observed in single subjects.
Modulation of the ACC in subjects with fibromyalgia showed rapid and considerable (33%) improvements in the numerical rating scale scores of pain. Significant effects were observed for at least 1 week following the stimulation. These sustained effects were accompanied by target-specific changes in functional network connectivity.
These results demonstrate that low-intensity transcranial focused ultrasound has the potential to engage and reset deep brain regions that are hyperactive in fibromyalgia.

P-07

Cannabidiol versus placebo in patients with fibromyalgia: a randomised, double-blind, placebo-controlled, parallel-group, single-centre trial

Marianne Uggen Rasmussen[1], Robin Christensen[1,2], Eva Ejlersen Wæhrens[1,3], Marius Henriksen[1], Pernille Hurup Duhn[1], Henning Bliddal[1], Kirstine Amris[1]
[1]*Bispebjerg and Frederiksberg Hospital, Parker Institute, Frederiksberg, Denmark.*
[2]*Department of Clinical Research, University of Southern Denmark, Research Unit of Rheumatology, Odense, Denmark.*
[3]*Department of Public Health, University of Southern Denmark, User Perspectives and Community-based Interventions, Odense, Denmark.*

Objective. Cannabidiol (CBD) is used to alleviate fibromyalgia pain despite limited evidence for efficacy. This study assessed the efficacy and safety of CBD *vs*. placebo in patients with fibromyalgia, hypothesising that CBD would be superior to placebo in reducing pain.
Methods. In this single-centre, double-blind, randomised, placebo-controlled trial, patients diagnosed with fibromyalgia were recruited from a specialised outpatient clinic in Denmark. Eligible participants were randomised 1:1 and stratified by sex, age (45 *vs*. ≥45), and pain level (7 *vs*. ≥7) on a 0-10 numeric rating scale (NRS), to receive 50 mg plant-derived CBD or placebo tablets. The primary outcome was change in pain intensity at week 24, assessed on the NRS pain sub-item in the revised Fibromyalgia Impact Questionnaire (FIQ-R), in the intention-to-treat population. Adverse events were monitored throughout the study in the safety population.
Results. Out of 273 participants screened for eligibility, 200 were included and randomised to receive CBD (n=100) or placebo (n=100). At week 24, mean change in pain intensity was -0.4 points (95% CI: -0.82 to 0.08), in the CBD group and -1.1 points (95% CI: -1.53 to -0.63), in the placebo group, corresponding to a between-group difference of -0.7 points (95% CI -1.2 to -0.25; p=0.0028) favouring placebo. Adverse events were in general mild and evenly distributed between groups.
Conclusion. The findings do not support CBD 50 mg daily as an analgesic supplement for patients with fibromyalgia. ClinicalTrials.gov number; NCT04729179.
Key words. Cannabidiol, fibromyalgia, pain, efficacy, safety, randomised-controlled trial.

P-08

Dissociative symptoms in fibromyalgia: a systematic review and meta-analysis

Matteo Scalzeri[1], Martina Mesce[1]
Sapienza University of Rome, Italy.

Background. Fibromyalgia (FM) is a chronic pain condition characterised by heightened sensitivity to somatosensory stimuli and widespread musculoskeletal pain. Psychological comorbidities are common, and among these, dissociative symptoms (DS) – both psychological and somatoform – have been repeatedly described as potential amplifiers of symptom severity and barriers to treatment. This review systematically examines, for the first time, the role, severity, and specific features of DS in FM.
Methods. Following PRISMA guidelines, a systematic search was conducted in PubMed, Scopus, and Web of Science. The protocol was preregistered in PROSPERO. Thirteen studies met the inclusion criteria and were evaluated in terms of design, sample characteristics, assessment methods, and main findings. Factors such as childhood trauma, alexithymia, and emotional distress frequently co-occurred with DS. Somatoform dissociation, in particular, was consistently associated with greater pain intensity, functional impairment, and psychological distress. A meta-analysis of nine controlled studies was performed using a multilevel mixed-effects model to estimate the pooled effect size of DS in FM *versus* control groups.
Results. FM patients exhibited significantly higher dissociative symptoms compared to controls. The meta-analysis yielded a medium-to-high pooled effect size (d=0.73, 95% CI [0.62–0.85], p=0.001) with low heterogeneity.
Conclusion. Dissociative symptoms – especially somatoform manifestations – emerge as clinically relevant yet frequently overlooked dimensions in a subset of individuals with FM. Their assessment may help identify more complex clinical profiles, informing tailored therapeutic approaches.

P-09

Localised epidermal growth factor pathway dysregulation in the skin of fibromyalgia patients

Macarena Tejos-Bravo[1]
Karolinska Institutet, Sweden.

Background. Fibromyalgia (FM) is associated with peripheral tissue alterations that may contribute to persistent pain, yet skin-specific mechanisms remain poorly defined. We recently identified immune dysregulation in FM skin, characterised by increased mast cells and reduced dermal immunomodulatory macrophages ($CD163^+$), indicating a shift toward a pro-inflammatory environment. Immune imbalance likely disrupts local growth factor signaling involved in inflammation, tissue remodeling, and nociceptor sensitisation. In this context, epiregulin (EREG), an epidermal growth factor family member expressed by macrophages and implicated in inflammatory and nociceptive processes, emerges as a candidate linking immune dysregulation to peripheral pain in FM.
Objective. To assess epiregulin and macrophage-related gene expression in FM skin.
Methods. Skin biopsies from 62 women with FM and 70 female healthy controls (HC) were analysed using RT-qPCR and bulk RNA sequencing. Circulating epiregulin levels were measured by ELISA.
Results. RT-qPCR revealed no group differences in markers of anti-inflammatory/resolving or inflammatory macrophages. In contrast, EREG expression was significantly increased in FM skin (p=0.008), while serum epiregulin levels were unchanged. Bulk RNA sequencing identified 1,084 differentially expressed genes in FM skin. Although EREG itself was not differentially expressed, its receptors EGFR and ERBB3 were upregulated, whereas ERBB4 was downregulated. Gene ontology analysis showed reduced extracellular matrix pathways and increased skin development, ERBB, and EGFR signaling.
Conclusion. FM skin exhibits localised dysregulation of epiregulin-associated signaling independent of systemic changes. Altered EGFR/ERBB pathway activity may contribute to inflammation and impaired tissue remodeling in FM, supporting these pathways as potential peripheral targets for pain modulation.

P-10

Treatment response of long COVID and fibromyalgia to systolic extinction training

Kati Thieme[1], Dennis C. Turk[2]
[1]*Department of Medical Psychology, Clinic for Psychological Pain Therapy, Philipps-University Marburg, Germany.*
[2]*Center for Pain Research on Impact, Measurement, & Effectiveness (C-PRIME), Department of Anesthesiology and Pain Medicine, University of Washington, University of Washington, Seattle, USA.*

Both long COVID (LCOV) and fibromyalgia (FM) share common symptoms (*e.g.* pain, fatigue, cognitive impairment) although the mechanisms involved my vary. Systolic Extinction Therapy (SET) treatment combines operant-behavioural pain therapy and baroreceptor-training. SET has been shown to be effective in treating patients with FM. Thus, we hypothesised that SET could be extended to treat symptoms of LCOV.
Methods. Twenty patients reporting CNS manifestation (*e.g.* fatigue, musculoskeletal pain, cardiovascular dysregulation) were compared to 20 sex- and age- matched FM patients with comparable symptoms to receive SET in a randomised controlled trial. Standardised questionnaires were used to measure pain, interference, fatigue, and sleep. as ECG, systolic (SBP) and diastolic (DBP) BP, heart rate, BRS and HRV. The SET treatment consisted twice weekly sessions of 1 hour of operant behavioural pain therapy and 1 hour of non-invasive neuromodulation.
Results. Nineteen of 20 Long-COVID patients and 16 of 20 FM patients reported being free pain-free (P0.001), significantly statistic improved sleep (p=0.002), and reduced fatigue (p=0.003) after SET. They also reported statistically significant neuropsychological improvements (p=0.013). These results were maintained at 12-month follow-up. Neuropsychological impairments in LCOV were mild in contrast to FM patients (p=0.001). In contrast to FM patients, the physiological responses in LCOV displayed a significantly increased BRS by 117%, reduction of SBP and DBP by 56 and 38 mmHg respectively, and HR by 49 bpm (all p-values 0.01).
Conclusion. The results suggest that although different mechanisms may account for LCOV and FM. SET may be a useful treatment for both disorders

Poster Presentations

P-11

Misdiagnosis of fibromyalgia: a review of cases re-diagnosed with other diseases

Mohammad Adawi
Laniado MC, Clalit HA, Ariel University, Israel.

The presence of alternative diseases with the disappearance of fibromyalgia-like symptoms is well documented for cases of diverse ages. It suggests that revised diagnoses may depend on patient recall bias, selection bias, or physicians' beliefs. Although discrepancies in the results were seen according to the type of case series, we preliminarily identified the most frequent diseases, such as hypothyroidism-like syndrome in adult patients and familial Mediterranean fever in child cases. The prevalence of fibromyalgia in patients with legitimate diseases should be reconsidered. Synopsis Fibromyalgia is a chronic pain syndrome associated with mood disorders, poor sleep, and cognitive dysfunction, and there is no established pathological basis and no currently available cure. The presence of diverse comorbid conditions and diverse symptomatology within and between the comorbid conditions suggests that fibromyalgia may encompass more than one illness under one name. Our meta-analysis carefully demonstrates features of the diagnosis of fibromyalgia as follows: i. the number of patients allocated to other diagnoses as a result of the revised diagnosis varied depending on the type of series of fibromyalgia cases; ii. cases with congenital or chronic conditions, such as juvenile fibromyalgia, have legitimate diseases, and the rareness of the report suggests the referral and continuation bias of previous paediatric-based fibromyalgia research; and iii. a chart-based study also demonstrated the entity bias for the diagnosis of fibromyalgia, similar to previous treatment-based and database studies, thereby suggesting that fibromyalgia may not be distinct from other disorders.

P-12

Fibromyalgia and viral humoral immunity: dissecting antigen-specific responses to human cytomegalovirus as a potential trigger

Dimitrios Bogdanos[1], Eleni Patrikiou[1], Stamatis Michas[1], Sofia Zachari[1], Arriana Gkouvi[1]
Department of Rheumatology, Faculty of Medicine, Larissa, University of Thessaly, Greece.

Background and Objective. Human cytomegalovirus (HCMV) has been proposed as an infectious agent that may initiate or aggravate fibromyalgia (FM), although direct experimental evidence remains limited. In this study, we sought to investigate whether the humoral immune response directed against major immunodominant HCMV antigens is associated with the presence of FM.
Methods. We tested 30 patients with FM and demographically matched healthy controls (HC) using immunoblotting (Euroimmun) for antibodies to HCMV antigens.
Results. Overall, anti-HCMV antibody reactivity did not differ between FM (87%) and HC (93%). Including borderlines, FM patients exhibited significantly higher frequencies of antibodies against p38 (73.1% *vs*. 28.6%, p=0.003) and UL44 (57.7% *vs*. 28.6%, tendency p=0.059), along with elevated titres of UL99 (56.5±23.1 AU *vs*. 41.2±22.4, p=0.018) and UL55 (37.4±14.2 *vs*. 28.5±13.2, p=0.05). Excluding borderlines, anti-p38 remained more prevalent in FM compared to HC (62.5 *vs*. 22.7, p=0.015). In contrast, UL57 antibodies were detected less frequently in FM patients (50% *vs*. 90.9%, p=0.004). Antibody reactivity to at least 4 HCMV antigens was more frequent in FM compared to HC (46.7% *vs*. 30%), and to all 6 HCMV antigens was also more prevalent in FM (36.7%) than in HC (16.7%).
Conclusion. To our knowledge, this study represents the first systematic attempt to investigate the antigen-specific response against immunodominant HCMV antigens in patients with FM, indicating a potential association with specific HCMV antigens and elucidating the need for further assessments.

P-13

A network-based gene prioritisation framework to address molecular heterogeneity in fibromyalgia

Sveva Bonomi[1,2], Elisa Oltra[3], Tiziana Alberio[4]
[1]*Department of Medicine and Technological Innovation (DiMIT), University of Insubria, Italy.*
[2]*Escuela de Doctorado, Universidad Católica de Valencia San Vincente Mártir, Spain.*
[3]*Department of Pathology, School of Medicine and Health Sciences, Universidad Católica de Valencia San Vicente Mártir, Spain.*
[4]*Department of Science and High Technology, University of Insubria, Italy.*

Background. Fibromyalgia is a complex and heterogeneous condition whose biological underpinnings remain controversial. Multiple partially overlapping mechanisms have been proposed, including altered neurotransmission, immune dysregulation, and central sensitisation. This heterogeneity has limited the identification of consistent disease-associated genes and hampers translational progress.
Objective. To develop a systems-level, network-based framework for gene prioritisation in fibromyalgia that accounts for molecular heterogeneity without assuming a single dominant pathogenic mechanism.
Methods. A fibromyalgia-specific protein-protein interaction network was constructed starting from a multi-source disease-associated gene set. Multiple complementary topological features describing distinct network roles were computed for each gene. Redundant features were filtered, and an adaptive optimisation strategy was applied to integrate topological information into a unified gene ranking. Performance was systematically compared against multiple baseline approaches, including single-metric and established network-based methods. Functional modules among top-ranked genes were subsequently identified to support biological interpretation.
Results. The optimised network-based ranking outperformed baseline strategies in prioritising high-confidence fibromyalgia-associated genes. Module detection revealed coherent subnetworks corresponding to distinct biological processes, supporting the coexistence of multiple molecular axes rather than a single unifying pathway.
Conclusion. This framework provides a reproducible and disease-agnostic approach to gene prioritisation in fibromyalgia, explicitly addressing biological heterogeneity. By integrating network topology and modular organisation, it offers a unifying perspective to navigate ongoing biological controversies and generate testable hypotheses for future translational research.

P-14

Healthcare utilisation and its variation in people with fibromyalgia: a systematic review

Ailish Byrne[1], Helen Twohig[1], Sara Muller[1], Ian Scott[1,2]
[1]*Primary Care Centre Versus Arthritis, School of Medicine, Keele University, UK.*
[2]*Haywood Academic Rheumatology Centre, Haywood Hospital, Midlands Partnership University NHS Foundation Trust, UK.*

Background. People with fibromyalgia and their clinicians often express dissatisfaction with care provision. They commonly receive ineffective opioid prescriptions, unnecessary tests, and specialist referrals. Understanding how people with fibromyalgia use healthcare services is crucial to informing optimal service planning.
Objective. To synthesise electronic health record/insurance database studies examining healthcare use in people with fibromyalgia, including variations across geography/time and high-use subgroups.
Methods. This PROSPERO-registered review identified studies using electronic health record/insurance/registry data to assess healthcare use by adults with fibromyalgia. Outcomes comprised health service and prescription use, measured through counts, odds ratios, or percentages. Weighted means and pooled mean differences (MDs) or odds ratios (ORs) were calculated. GRADE methodology assessed evidence certainty.
Results. Twenty-six retrospective cohort studies (2007-2023) from five countries were included from 2,091 screened records. Healthcare use in people with fibromyalgia: Mean GP consultations were 5.3 (6-months) and 16.9 (12-months) per person. Mean specialist referrals and emergency visits over 12-months were 3.0 and 1.1, respectively. Compared to people without fibromyalgia (12-months): Significantly higher GP consultations (MD 8.3 [3.2, 13.4]), emergency visits (MD 0.3 [0.2, 0.4]), but not hospitalisations (MD 0.0 [-0.0, 0.1]) were observed. People with fibromyalgia had higher

odds of receiving opioids (OR 4.4 [3.6, 5.4]), gabapentinoids (OR 4.1 [1.8, 9.4]), SSRIs (OR 2.5 [1.8, 3.4]), and tricyclics (OR 7.4 [5.6, 9.8]). Evidence certainty was low across all outcomes.
Conclusion. People with fibromyalgia demonstrate substantially elevated healthcare use, particularly GP consultations and opioid/gabapentinoid use. Findings underscore the need for skilled primary care management and accessible non-pharmacological interventions.

P-15

Exploratory pilot clinical trial of Native Himalayan Shilajit as an analgesic in myofascial pain syndrome

Darshan Basavaraja[1], **Prasan Kumar Panda**[1], Rahul Katkar[2], Shailly Tomar[3], Debabrata Sircar[3], Gaurav Chikara[4]
[1]*Department of Medicine, AIIMS Rishikesh, Uttarakhand, India.*
[2]*Department of AYUSH, AIIMS Rishikesh, Uttarakhand, India.*
[3]*Department of Biosciences and Bioengineering, Indian Institute of Technology Roorkee, Uttarakhand, India.*
[4]*Department of Pharmacology, AIIMS Rishikesh, Uttarakhand, India.*

Background. Myofascial pain syndrome (MPS) is a chronic pain source frequently overlapping with fibromyalgia. Standard treatments often have inconsistent efficacy and adverse effects, necessitating safer alternatives. Native Himalayan Shilajit has traditional Ayurvedic use for analgesic properties, but clinical evidence in MPS is limited.
Objective. To evaluate the efficacy and safety of oral Native Himalayan Shilajit in reducing pain intensity and active trigger points in MPS patients.
Methods. This prospective, open-label, single-arm exploratory pilot trial involved 50 adults receiving oral Shilajit twice daily for 49 days. Outcomes included changes in Visual Analogue Scale (VAS; 0–10) scores and active trigger point counts. Clinically meaningful response was predefined as ≥30% VAS reduction. Concomitant analgesic use was quantified using WHO Defined Daily Dose and potency equivalents to control for confounding.
Results. Among 46 completers, mean VAS scores decreased significantly from 6.70±1.09 to 3.41±1.88 by Day 49 (p=0.05), a 49.1% reduction. A meaningful response (≥30% reduction) occurred in 61% of patients, yielding an Absolute Risk Reduction (ARR) of 31% and Number Needed to Treat (NNT) of 3.2. Trigger points decreased from 65 to 51 (21.5% resolution). Notably, 10% achieved relief without analgesics, and 64% maintained a low-to-very-low analgesic burden. No serious adverse events occurred.
Conclusion. Native Himalayan Shilajit is safe and associated with clinically meaningful reductions in pain intensity, trigger points, and conventional analgesic reliance, supporting further investigation through randomised controlled trials.

P-16

Impact of comorbid headache on fibromyalgia: a study of 639 patients

Annunziata Capacci[1], Giulia Calabrese[1], Marina Romozzi[2], Flora Niedda[3], Marco Moroli[3], Catello Vollono[4], Maria Antonietta D'Agostino[1,3]
[1]*Rheumatology, A. Gemelli General Hospital Foundation Rome, Italy.*
[2]*Neurology, Foundation Rome, Italy, Italy.*
[3]*Rheumatology, Catholic University of Sacred Heart, Rome, Italy.*
[4]*Neurology, A. Gemelli General Hospital Foundation Rome, Italy.*

Objective. Migraine and fibromyalgia are chronic, disabling conditions that frequently coexist and share overlapping pathophysiological mechanisms, including central sensitisation. The presence of a primary headache disorder may further aggravate fibromyalgia-related symptoms. This study aimed to compare clinical characteristics and disease severity in patients with fibromyalgia alone and those with fibromyalgia and comorbid headache and/or migraine.
Methods. This retrospective cross-sectional study included adult patients diagnosed with fibromyalgia attending the fibromyalgia clinic at Agostino Gemelli University Hospital. Demographic data, clinical characteristics, and fibromyalgia history were collected during outpatient visits, including information on anxiety, depression, and sleep disorders. Disease severity was assessed using the Revised Fibromyalgia Impact Questionnaire (FIQR), Modified Fibromyalgia Assessment Status (FASmod), Widespread Pain Index (WPI), and Symptom Severity Scale (SSS). Migraine and tension-type headache were evaluated through a structured interview based on the International Classification of Headache Disorders, 3rd edition (ICHD-3). Patients were classified as migraine-positive (EMI+) or migraine-negative (EMI-), and as headache-positive (HEADACHE+) or headache-negative (HEADACHE-).
Results. The study included 639 patients with fibromyalgia (94.7% women; mean age 52.0±18.6 years). Migraine was diagnosed in 18.6% of patients, while 73.4% reported at least one type of headache. HEADACHE+ patients showed significantly higher WPI, SSS, FIQR (total and subscales), and FASmod scores compared with HEADACHE- patients (all p=0.01). EMI+ patients also had higher combined WPI+SSS scores than EMI– patients (p=0.048). Anxiety, depression, and sleep disorders were significantly more prevalent in HEADACHE+ patients, and sleep disorders were more frequent in EMI+ patients.
Conclusion. Comorbid headache in fibromyalgia is associated with greater clinical severity and increased psychiatric and sleep comorbidity. Early recognition and a multidisciplinary approach may improve patient management and outcomes.

P-17

A mixed-methods evaluation study of an online education intervention for people with a new diagnosis of fibromyalgia at a Hospital Trust, UK

Hannah Chambers[1,2]
Therapies Department, East Kent Hospitals University NHS Foundation Trust, UK.
Canterbury Christ Church University, UK.

Background. Patient education is recommended to manage fibromyalgia. It is unclear how effective online education is in providing patients with the skills and knowledge to self-manage.
Objective. To explore the experiences of newly diagnosed patients receiving an online education intervention delivered in the UK.
Methods. A mixed methods design explored patients' views of their journey to diagnosis and experiences with the online education intervention. One hundred patients received the intervention and completed a Patient Activation Measure (PAM) February–December 2023. Online focus groups were conducted and analysed with thematic analysis. PAMs were completed at baseline and 2 months post-education.
Results. Thematic analysis identified four main themes and three subthemes aligned with the patient journey: 1. Searching for a reason for symptoms, 2. Need for compassion and understanding, 3. Contradictory and suspicious thoughts about diagnosis, and 4. Conceptions of treatment. The education intervention was viewed positively.
PAM scores indicated most participants (75%) at diagnosis showed low skills and confidence to self-manage. Post-intervention, 50% scored low, suggesting a trend toward increased skills and confidence, though not statistically significant (p=0.226).
Conclusion. Insights into patients' diagnostic journeys and views on online education indicate it was a valued intervention. Self-management skills and confidence were low at diagnosis, with positive trends of improvement post-education. Identified themes warrant further exploration.

P-18

Real-world outcomes of auricular acupuncture in fibromyalgia

Marco Di Carlo[1], Benedetta Bianchi[1], Livio Milazzo[1], Sonia Farah[1], Fausto Salaffi[1]
[1]*Rheumatology Unit, Università Politecnica delle Marche, Carlo Urbani Hospital, Jesi, Italy.*

Background. Evidence on auricular acupuncture (AA) – a microsystem technique increasingly adopted in clinical practice – remains scarce in fibromyalgia (FM), particularly in real-world settings.
Objective. To assess the effectiveness of AA on pain, disease impact, and autonomic symptoms in FM patients, and to evaluate the durability of clinical benefits after treatment discontinuation.
Methods. This real-life observational study included consecutive FM patients fulfilling the 2016 ACR/EULAR criteria and had persistent moderate-to-se-

vere disease severity despite optimised pharmacological treatment. AA was administered once weekly for 8 weeks using semi-permanent needles applied to predefined auricular points. Clinical assessments were performed at baseline (T0), at treatment completion (T1), and 2 months post-treatment (T2). Outcome measures included FIQR, pain NRS, WPI, SSS, and COMPASS-31. Clinically meaningful improvement was defined as a ≥30% reduction in FIQR. Changes over time were analysed using repeated-measures ANOVA.
Results. Sixty patients were enrolled (88% women; median age 58 years). At T1, significant improvements were observed in disease severity (FIQR –22.3%), pain intensity, widespread pain, symptom severity, and autonomic symptoms (all $p<0.001$) (Table I). At T2, although a partial loss of efficacy was noted, all outcomes remained significantly improved compared with baseline. A clinically meaningful FIQR reduction was achieved by 43.3% of patients at T1 and persisted in 22.2% at T2.
Conclusion. In routine clinical practice, AA is associated with significant short-term improvements in the main clinical outcomes. Despite partial attenuation after discontinuation, sustained benefits were observed in a relevant percentage, supporting its role as an adjunctive non-pharmacological intervention in FM management.

Table I. Changes in disease impact, pain, symptom severity, and autonomic symptoms from baseline (T0) to the end of treatment (T1) and at 2-month follow-up (T2) in patients with fibromyalgia undergoing auricular acupuncture.

Outcome	T0	T1	T2	Δ T1–T0 (%)	Δ T2–T0 (%)	*p*
FIQR	62.7 ± 20.3	47.1 ± 22.3	55.4 ± 24.2	–22.3	–11.2	<0.001
NRS	6.95 ± 2.00	4.92 ± 2.23	5.89 ± 2.33	–13.3	–14.1	<0.001
WPI	10.4 ± 3.85	6.93 ± 4.70	8.95 ± 4.52	–16.7	–14.7	<0.001
SSS	8.32 ± 2.54	6.60 ± 2.33	7.32 ± 2.78	–13.6	–13.6	<0.001
COMPASS-31	42.7 ± 16.7	35.5 ± 17.6	35.6 ± 17.7	-29.3	–28.2	<0.001

Values are expressed as mean ± standard deviation. Δ indicates percentage change from baseline. *p*-values refer to overall comparisons across time points (repeated-measures ANOVA). A clinically significant improvement (≥30% reduction in FIQR score) was observed in 26 patients (43.3%) at T1 and persisted in 13 patients (22.2%) at T2.

P-19

Association between adherence to Mediterranean diet and disease activity in fibromyalgia and other rheumatic diseases

Giulio Dolcini[1], Martina Favretti[1], Carlo Cauli[2]
[1]*Molecular Medicine, Sapienza University of Rome, Italy.*
[2]*Rheumatology Unit, Department of Medical and Cardiovascular Sciences, Sapienza University of Rome, Italy.*

Fibromyalgia (FM) and inflammatory arthritis, including rheumatoid arthritis (RA) and psoriatic arthritis (PsA), are major causes of chronic pain. Although inflammatory arthritis is associated with increased cardiovascular risk, the role of lifestyle factors such as diet remains poorly explored. The Mediterranean diet (MedDiet) has cardiovascular and anti-inflammatory benefits, but comparative data among these conditions are limited. This study compared MedDiet adherence among patients with RA, PsA, and FM and examined associations with cardiovascular risk factors, bowel habits, and disease activity or symptom severity. A total of 442 patients were enrolled and sociodemographic, clinical, gastrointestinal, and lifestyle data were collected. MedDiet adherence was assessed using the 14-item PREDIMED questionnaire. Disease activity was evaluated using DAS28-CRP for RA, DAPSA for PsA, and FIQR for FM. FM patients were younger, predominantly female, and showed significantly lower MedDiet adherence than RA and PsA patients ($p=0.001$), with nearly half classified as low adherence and only 7% as high adherence. RA patients showed the highest adherence. FM patients reported more bowel habit alterations and food intolerances, while PsA patients had higher BMI and more frequent overweight or obesity. Overall, higher MedDiet adherence was associated with lower smoking prevalence and fewer bowel habit alterations. Moderate adherence was associated with lower DAS28-CRP in RA, and high adherence with lower FIQR scores in FM. MedDiet adherence differs across rheumatic conditions and is lowest in FM. Better adherence is associated with healthier behaviours and lower disease burden, supporting the integration of nutritional counseling into rheumatic disease management.

P-20

Efficacy of a low-FODMAP diet on clinical symptoms and intestinal permeability in patients with fibromyalgia or intestinal bowel syndrome: a pilot study

Martina Favretti[1], Giulia Scalese[2], Daniele Franculli[3], **Giulio Dolcini**[1], Lucia Pallotta[2], Emanuela Ribichini[2], Fabrizio Conti[4], Cristina Iannuccelli[5], Carola Severi[2], Manuela Di Franco[4]
[1]*Department of Molecular Medicine, Sapienza University of Rome, Italy.*
[2]*Department of Translational and Precision Medicine, Sapienza University of Rome, Italy.*
[3]*Depratment of Medicine, Acquapendente Civil Hospital, Italy.*
[4]*Rheumatology Unit, Department of Medical and Cardiovascular Sciences, Sapienza University of Rome, Italy.*
[5]*Rheumatology Unit, AOU Policlinico Umberto I, Italy.*

Background. Fibromyalgia (FM) and irritable bowel syndrome (IBS) are frequently coexisting central sensitivity disorders, in which gut–brain axis dysfunction may represent a shared mechanism. While a low-FODMAP diet (LFD) is effective for IBS, its role in FM remains unclear.
Objective. To evaluate the effects of an LFD on symptoms and quality of life (QoL) in patients with FM and/or IBS, and to explore changes in intestinal permeability markers and their relationship with clinical outcomes.
Methods. Patients with FM (2016ACR criteria), IBS (RomeIV criteria), or both were enrolled in a structured LFD. Disease severity (IBS-SSS, PDS, WPI, SSS, FIQR), central sensitisation (CSI), QoL (SF-36), and intestinal permeability markers (zonulin, LPS) were assessed at multiple time points. Longitudinal changes were analysed using mixed-effects models for repeated measures.
Results. Thirty-nine patients were included (11IBS, 9FM, 19FM+IBS; 92%female). IBS-SSS improved significantly over time in both IBS and FM+IBS groups (Fig. 1). Improvements in PDS, SSS, FIQR physical function, FIQR overall impact, and CSI were observed exclusively in the FM+IBS group (Fig. 2). Zonulin decreased at T1 in FM and FM+IBS, while a significant increase was observed at T3 in IBS; no significant changes in LPS were detected. In FM+IBS, reductions in IBS severity were associated with improvements in FM-related outcomes.
Conclusion. In patients with FM+IBS, a LDF was associated with improvements in gastrointestinal symptoms, central sensitisation, disease severity, physical function, and QoL. Screening for IBS in FM patients may help identify those who could benefit from dietary strategies within a multidisciplinary management approach.

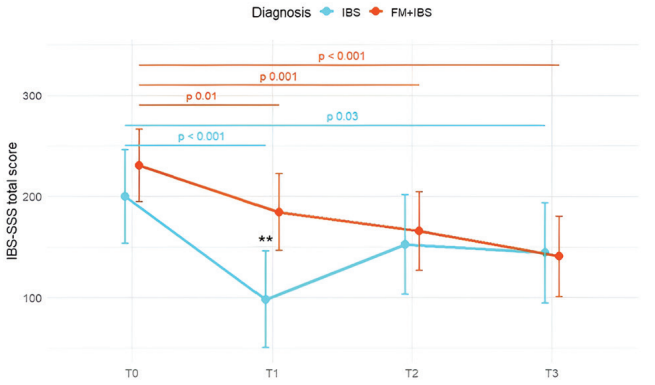

Fig. 1. Longitudinal changes in the IBS-SSS total score across four time points in the IBS and FM+IBS groups.

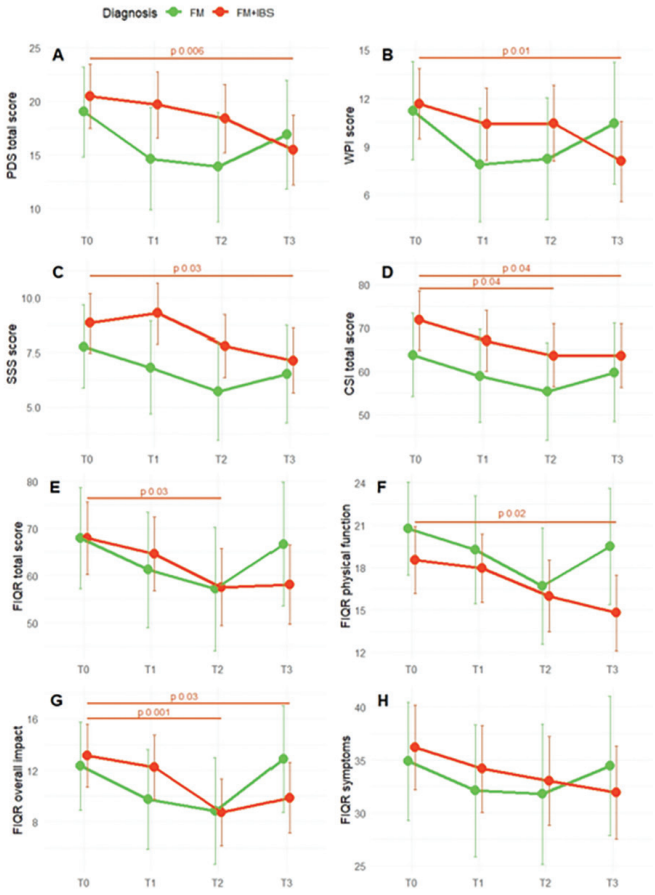

Fig. 2. Longitudinal changes in PDS total score (**A**), main domains (**B**-**C**), CSI (**D**), FIQR total score (**E**), and FIQR domain scores (**F**-**H**) across four time points in FM and FM+IBS patients.

P-21

Fibromyalgia phenotypes with and without chronic migraine: functional impact, quality of life, and reflective functioning

Martina Mesce[1], Agata Benfante[2], Alessandro Torelli[1], Martina Cangelosi[3], Marco Cavicchioli[1], Lorys Castelli[2], Sara Bottiroli[3,4], Piercarlo Sarzi-Puttini[5,6], Federica Galli[1]

[1]*Department of Dynamic and Clinical Psychology, and Health Studies, Faculty of Medicine and Psychology, Sapienza University of Rome, Rome, Italy.*
[2]*Department of Psychology, University of Turin, Turin, Italy.*
[3]*Department of Brain and Behavioural Science, University of Pavia, Pavia, Italy.*
[4]*Headache Science and Neurorehabilitation Centre, IRCCS Mondino Foundation, Pavia, Italy.*
[5]*Rheumatology Department, IRCCS Galeazzi-Sant'Ambrogio Hospital, Milan, Italy.*
[6]*Department of Biomedical and Clinical Sciences, University of Milan, Milan, Italy.*

Background. Fibromyalgia (FM) is a complex chronic pain condition characterised by significant functional impairment and reduced quality of life. In clinical practice, it often co-occurs with other pain conditions, such as chronic migraine (CM). However, the relationship between CM and FM is not fully delineated, and potential areas of overlap require further investigation. Clarifying this relationship may provide useful information for diagnosis, management, and the conceptualisation of FM.
Objective. To compare FM patients with and without CM (FibroMig) in functional impact, health-related quality of life (HRQoL), and reflective functioning, and to examine whether CM contributes to a distinct clinical profile within FM.
Methods. A total of 205 patients (116 FM; 89 FibroMig) and 106 healthy controls (HC) completed the Fibromyalgia Impact Questionnaire-Revised (FIQR), the Short Form Health Survey (SF-12), and the Reflective Functioning Questionnaire (RFQ). Group differences were analysed using ANOVA and post-hoc tests.
Results. FIQ-R scores did not differ between FM and FibroMig, indicating similar FM-related impairment. HRQoL differences emerged: FibroMig patients had lower SF-12 physical scores than FM (p=.04), and both groups scored lower than HC on physical and mental components (p=0.001). For reflective functioning, only RFQ–Uncertainty differed, with FibroMig showing greater hypomentalisation than HC (p=0.009); FM and FibroMig did not differ.
Conclusion. FM patients with and without CM display similar functional and reflective functioning profiles, although FibroMig patients report greater physical impairment. These findings support considering CM as a clinical expression within the FM phenotype rather than a separate condition.

P-22

A transdiagnostic approach to psychological risk in fibromyalgia and comorbid chronic migraine

Martina Cangelosi[1], Marco Cavicchioli[2], Martina Mesce[2], Agata Benfante[3], Alessandro Torelli[2], Lorys Castelli[3], Piercarlo Sarzi-Puttini[4,5], Federica Galli[2], Sara Bottiroli[1,6]

[1]*Department of Brain and Behavioural Science, University of Pavia, Pavia, Italy.*
[2]*Department of Dynamic and Clinical Psychology, and Health Studies, Faculty of Medicine and Psychology, Sapienza University of Rome, Rome, Italy.*
[3]*Department of Psychology, University of Turin, Turin, Italy.*
[4]*Rheumatology Department, IRCCS Galeazzi-Sant'Ambrogio Hospital, Milan, Italy.*
[5]*Department of Biomedical and Clinical Sciences, University of Milan, Milan, Italy.*
[6]*Headache Science and Neurorehabilitation Centre, IRCCS Mondino Foundation, Pavia, Italy.*

Background. Fibromyalgia (FM) is a nociplastic pain condition accompanied by substantial psychological burden. Chronic migraine (CM) frequently co-occurs with FM, but its contribution to psychological functioning remains unclear. Understanding whether FM patients with and without CM display distinct psychological profiles may support more personalised interventions.
Objective. To compare psychological functioning across women with FM, CM, and comorbid FM+CM, and to identify transdiagnostic psychological profiles through cluster analysis.
Methods. A total of 318 women participated: 130 with FM, 97 with CM, and 91 with FM+CM. Participants completed self-report measures assessing mental functioning, depressive and anxiety symptoms, global distress, and defensive functioning. Diagnostic group differences were tested using Kruskal–Wallis analyses. A k-means cluster analysis identified psychological profiles independent of diagnostic category.
Results. FM and FM+CM showed comparable levels of depressive symptoms, anxiety, distress, and defensive functioning, whereas CM displayed significantly lower symptom severity across all measures (p=0.001). Cluster analysis yielded three transdiagnostic profiles: a vulnerable cluster (n=73), with high distress and low mental functioning; an intermediate cluster (n=122); and a resilient cluster (n=76), characterised by adaptive functioning. FM and FM+CM were predominantly represented in the vulnerable and intermediate clusters, while CM participants were overrepresented in the resilient cluster ($\chi^2(4) = 21.41$, p=0.001).
Conclusion. FM patients, particularly those with comorbid CM, exhibit heightened psychological vulnerability compared to individuals with CM alone. These findings underscore the heterogeneity of psychological functioning within FM and support a dimensional, transdiagnostic framework to guide individualised clinical care.

P-23

Brief psychodynamic therapy for depressive symptoms in fibromyalgia: preliminary findings from a multicentre randomised trial

Martina Mesce[1], Agata Benfante[2], Alessandro Torelli[1], Martina Cangelosi[3], Marco Cavicchioli[1], Lorys Castelli[2], Sara Bottiroli[3,4], Piercarlo Sarzi-Puttini[5,6], Federica Galli[1]
[1]*Department of Dynamic and Clinical Psychology, and Health Studies, Faculty of Medicine and Psychology, Sapienza University of Rome, Rome, Italy.*
[2]*Department of Psychology, University of Turin, Turin, Italy.*
[3]*Department of Brain and Behavioural Science, University of Pavia, Pavia, Italy.*
[4]*Headache Science and Neurorehabilitation Centre, Centre, IRCCS Mondino Foundation, Pavia, Italy.*
[5]*Rheumatology Department, IRCCS Galeazzi-Sant'Ambrogio Hospital, Milan, Italy.*
[6]*Department of Biomedical and Clinical Sciences, University of Milan, Milan, Italy.*

Background. Fibromyalgia (FM) and related chronic pain conditions frequently involve elevated psychological distress, especially depression. While brief psychological interventions are increasingly adopted in pain care, comparative evidence remains limited. Brief Psychodynamic Therapy (BPT), focused on interpersonal patterns and emotional regulation, may offer specific benefits for these patients.
Objective. This study examined the preliminary short-term efficacy of Brief Psychodynamic Therapy (BPT), compared with Expressive Writing Technique (EWT) and Treatment as Usual (TAU), across FM, CM, and FibroMig, with a particular focus on depressive symptoms.
Methods. A multicentre randomised controlled trial including women aged 18–65 allocated participants to BPT, EWT, or TAU. Outcomes were assessed at baseline (T0) and post-treatment (T1). Measures included VAS-Pain, CSI, SF-12, MPQ, GAD-7, and PHQ-9. Three-way repeated-measures ANOVAs tested effects of time, diagnosis, and treatment.
Results. The sample included 101 participants (42 FM, 35 CM, 24 FibroMig). Diagnostic groups differed at baseline in CSI and physical functioning. No treatment × time interaction emerged for pain, central sensitisation, anxiety, mental pain, or HRQoL. However, a significant treatment effect and time × treatment interaction were found for PHQ-9, indicating that only BPT produced a clinically meaningful reduction in depressive symptoms from T0 to T1, regardless of diagnosis. EWT and TAU showed no improvement.
Conclusion. Preliminary findings suggest that BPT may serve as an effective transdiagnostic intervention for depressive symptoms in chronic pain, including FM, CM, and FibroMig. Its feasibility and selective impact support its integration within multidisciplinary pain management pathways.

P-24

Resolution of long-standing refractory fibromyalgia pain following a vitamin and nucleotide-base supplement: a case report

Sandra Gestosa[1], Luis Cantante[1], André Maciel[1], Ana Lares[1]
Pain Clinic, Anaesthesiology Department, Unidade Local de Saude do Algarve - Unidade de Faro, Portugal.

Background. Fibromyalgia is a chronic pain disorder whose pathophysiology is multifactorial and incompletely understood. Many patients remain refractory to standard pharmacological and non-pharmacological treatments. Thiamine, cobalamin and nucleotide precursors such as uridine and cytidine support neuronal metabolism and repair and may modulate pathways relevant to fibromyalgia.
Objective and Methods. A 58-year-old woman with fibromyalgia experienced persistent severe pain despite several different treatments including analgesiscs, NSAIDs, opioids, gabapentinoides and antidepressants. After 20 years of unsuccessful therapeutic attemps she iniciated a supplement containing vitamin B1, vitamine B12, uridine-5-monophosphate and cytidine-5-monophosphate. Following the introduction of this formulation she reported complete resolution of fibromyalgia-related pain with only brief exacerbations during anxiety along with improved cognition and quality of life.
Results and Conclusion. This case describes marked improvement of refractory fibromyalgia after initiaton of a vitamin-and-nucleotid-based supplement. The observed benefit may be related to the role of B vitamins and nucleotides in neuronal repair, neurotrnasmission and neuroplasticity.
While robust evidence for the supplement efficacy in fibromyalgia is lacking the complete resolution of the patient's pain cannot be neglected. This case demonstrated a potencial benefit of a vitamin and nucleotid-base supplement in a patient with long-standing treatment-resistant fibromyalgia. Further study is needed to clarify therapeutic mechanisms and efficacy.

P-25

Fibromyalgia as a microcirculatory disorder: maladaptive capillary shunting causing mild tissue hypoxia - a proposed hypothesis

Uri Gabbay
Tel Aviv University, Israel.

Fibromyalgia is a chronic pain syndrome characterised by widespread musculoskeletal pain, fatigue, and cognitive impairment. In the absence of specific clinical, laboratory, or imaging markers, diagnosis is made clinically, based on anamnesis and exclusion of alternative conditions. Despite decades of investigation, the underlying mechanisms of fibromyalgia remain poorly understood. Many mechanisms have traditionally been suggested, broadly divided into central and peripheral mechanisms. While central sensitisation has been a dominant explanatory model, emerging evidence suggests a potential role for diverse peripheral mechanisms in general, and microcirculatory impairment in particular.
Several reported findings presented alterations in oxygen dynamics. The observed oxygen-related findings include high arterial oxygen saturation, low tissue oxygen saturation, relatively high collecting venous oxygen saturation, and elevated tissue lactate levels. Other findings suggest microcirculatory abnormalities, and mitochondrial dysfunction. This oxygenation pattern indicates appropriate arterial oxygenation. Mitochondrial dysfunction is unlikely attributable as mitochondria utilise intracellular oxygen for energy production but does not directly affect the exchange of oxygen between capillaries and cells.
We propose that fibromyalgia may be driven by maladaptive microvascular regulation causing maladaptive capillary shunting via metarteriolar thoroughfare channels. It may reduce exchange capillaries blood flow and oxygen availability and extraction at the tissue level, resulting in localised mild or intermittent hypoxia. This hypoxic stress may directly contribute to muscle fatigue, pain, and tenderness. Other fibromyalgia manifestations, including sleep disturbance and psychosocial effects, may be secondary consequences that amplify the clinical presentation. This hypothesised maladaptive capillary shunting may be either primary or secondary to impaired autonomic vasomotion regulation.
The proposed model is consistent with the observed oxygenation abnormalities and may generate testable predictions to guide future research. At present, however, direct clinical evidence remains limited and circumstantial, and the hypothesis should be regarded as provisional.

P-26

Depression relief, not pain reduction, predicts fibromyalgia improvement in patients with emotional disturbances: an observational study

Chih-Hsien Hung[1]
Neurology, Kaohsiung Medical University, Taiwan.

Background. Depression and anxiety symptoms are common in fibromyalgia (FM) and negatively impact the disease. However, how emotional disturbances affect phenotypes and treatment responses remains unclear. This study aimed to investigate the impact of psychological symptoms on FM and its interactions with pain symptoms and therapeutic outcomes.
Methods. Newly diagnosed FM patients were prospectively recruited and assessed with questionnaires pertaining to emotional symptoms and disease impacts. Effects of anxiety and depression symptoms on FM were investigated through classification, correlation, regression, and mediation analyses.
Results. One hundred and twelve patients and 110 healthy controls were included. In addition to pain, emotional disturbances crucially modulated disease severity. Patients with prominent anxiety and depression symptoms (FM-AD) had more intense pain, worse disease severity, and poorer therapeutic responses than those without (FM-nAD; all p=0.001). Pain relief predicted reduced disease severity for FM-nAD cases (p=0.049), whereas re-

mission of depression but not pain severity determined the clinical improvement in FM-AD cases (p=0.039 and 0.062, respectively). Notably, depression remission exerted a direct impact (p=0.003) on disease improvement in FM-AD cases, independent of pain reduction (indirect effect: p=0.101). Despite the initially poorer treatment responses and disease severity in FM-AD cases, their long-term outcomes did not differ from those of FM-nAD cases after continuous treatment for 6 months (p=0.076).
Conclusion. Targeting pain reduction alone may not be sufficient for overall improvement in FM. Assessing and addressing depression symptoms, in addition to pain management, can offer immense help in identifying phenotypes and predicting treatment responses, thereby leading to improved long-term outcomes.

P-27

The influence of breathing pattern and thoracic mobility on physical performance in women with fibromyalgia

Kent Jonsson[1], Andreas Pikwer[2], Erik MG Olsson[3], Magnus Peterson[1]
[1]*Department of Public Health and Caring Sciences, Section of Family Medicine, Uppsala University, Sweden.*
[2]*Centre for Clinical Research Sörmland, Uppsala University, Sweden.*
[3]*Department of Women's and Children's Health, Healthcare Science and e-health, Uppsala University, Sweden.*

Background. Individuals with fibromyalgia have been shown to exhibit reduced cardiorespiratory function, including lower peak oxygen uptake, which may contribute to the impaired physical performance observed in this population. Evidence indicates that chest wall restriction at varying loads can influence exercise capacity and maximal oxygen consumption, as well as alter breathing patterns in healthy individuals. Furthermore, respiratory difficulties have been documented in fibromyalgia, including diminished thoracoabdominal mobility and compromised respiratory muscle mechanics.
Objective. To investigate the influence of respiratory parameters, including tidal volume and respiratory rate, and thoracic mobility on physical performance in women with fibromyalgia.
Methods. This case-control study included 38 women with fibromyalgia and 44 age-matched healthy women. Respiratory rate was measured using a portable monitor, and tidal volume was assessed through spirometry. Thoracic mobility was evaluated by measuring chest expansion at the level of the Xiphoid process. To evaluate cardiorespiratory fitness and lower body strength, the participants performed the six-minute walk test and the chair stand test.
Results. Respiratory rate and thoracic mobility partially mediated the relationship between fibromyalgia and the six-minute walking test. Thoracic mobility partially mediated the relationship between fibromyalgia and chair stand test. Tidal volume had no mediating effect on any of the physical tests performed.
Conclusion. Women with fibromyalgia exhibit reduced aerobic capacity and lower body strength compared to healthy controls. Respiratory rate and thoracic mobility appear to influence physical performance among these women.

P-28

Early trauma and mentalisation as factors associated with dissociation in fibromyalgia: a matched-control study

Natalia Kascakova[1,2], Jana Furstova[2], Jozef Hasto[1,2], Peter Tavel[2]
[1]*Psychiatric Outpatient Clinic, Pro Mente Sana, Bratislava, Slovakia.*
[2]*Palacky University Olomouc, Olomouc University Social Health Institute, Czech Republic.*

Background. Fibromyalgia involves widespread pain and various symptoms like dissociation, yet its etiopathogenesis remains unclear. The study explored dissociation in the context of adverse childhood experiences (ACE) and difficulties in mentalisation.
Methods. A clinical sample of women from Slovakia diagnosed with fibromyalgia (n=53, mean age 47.4 ±10.3 years) was compared to a representative pair-matched sample (n=106, mean age 46.6 ±10,6 years) in a 1:2 ratio. Participants completed electronic questionnaires on dissociation, ACE and mentalisation. Analyses included Spearman's correlations, Mann-Whitney U-test, and multiple linear regression.
Results. Women with fibromyalgia reported significantly higher dissociation, lower mentalisation, and more ACEs compared to the control group (p=0.001). Dissociation was significantly positively correlated with ACE and mentalisation difficulties. The regression model, which accounted for the pair-matched design, explained 70.6% of the variance in dissociation (R2=0.706, p=0.001). Group membership (fibromyalgia *vs*. control) was the most significant predictor (ß=0.605, p=0.001), followed by ACE (ß=0.289, p=0.001) and mentalisation difficulties (ß=0.183, p=0.001). No significant interaction was found between group and ACEs (p=0.557) indicating a universal trauma effect across both groups.
Conclusion. Dissociation in fibromyalgia is robustly and independently associated with early-life adversity and impaired mentalising. Fibromyalgia status carries a significant independent risk for dissociation, potentially functioning as a psychological defense against chronic pain or reflecting underlying autonomic dysregulation. Clinical management should prioritise multidisciplinary interventions that address trauma history, enhance mentalising capacity, and manage the physiological aspects of the condition.

P-29

Pilot analysis of the FIBRO-ATT (FIBROmyalgia ATTitudes among healthcare professionals) survey

Anna Julia Krupa[1], Mariusz Korkosz[2], Jarosław Nowakowski[2], Magdalena Kocot-Kępska[3], Jarosław Woroń[4,5,6], Marcin Siwek[1]
[1]*Department of Biological and Community Psychiatry, Jagiellonian University Medical College, Krakow, Poland.*
[2]*Department of Rheumatology and Immunology, Jagiellonian University Medical College, Krakow, Poland.*
[3]*Department for Pain Research and Treatment, Jagiellonian Univeristy Medical College, Krakow, Poland.*
[4]*Department of Clinical Pharmacology, Jagiellonian University Medical College, Krakow, Poland.*
[5]*Department of Anesthesiology and Intensive Care No. 1, Department of Internal Medicine and Geriatrics, University Hospital in Kracow, Poland.*
[6]*University Center for Monitoring and Research on Adverse Drug Effects in Krakow, Poland.*

Background. The limited data on physicians' perspectives on fibromyalgia show that doctors often express doubts/disbelief about the reported symptoms, present limited knowledge and experience in fibromyalgia management and don't feel competent consulting fibromyalgia patients.
Objective. To explore the attitudes of Polish physicians toward fibromyalgia.
Methods. This FIBRO-ATT study is a Polish anonymous online survey. Eligibility criteria are: resident/specialist in anesthesiology/intensive care, rheumatology, internal medicine, primary care, surgery/orthopedics, neurology, palliative medicine, psychiatry and stomatology. 219 responses were included in this pilot analysis.
Results. Physicians mean age was 41.93 (SD±11.5 years), mean professional experience 15,73 (SD±11.7 years). The sample consisted of specialists: internal medicine (15.5%), anesthesiology (13.2%), primary care (14.2%), neurology (9.1%), rheumatology (8.7%) and residents in primary care (11.4%), other specialties were less represented. 20.1% agreed/strongly agreed, 25.1% neither agreed nor disagreed, 54.8% disagreed/strongly disagreed with the statement "Despite my professional knowledge I have negative reactions toward people with fibromyalgia". 25.6% agreed/strongly agreed, 37.9% neither agreed nor disagreed, 36.5% disagreed/strongly disagreed with the statement "The main cause of fibromyalgia are mental health issues". 30.6% agreed/strongly agreed, 13.2% neither agreed nor disagreed, 48% disagreed/strongly disagreed with the statement "I don't know how to help people with fibromyalgia". Most respondents agreed that fibromyalgia might be the primary cause of disability 57.1% and disability benefit 59.3%.
Conclusion. Although most Polish physicians recognise fibromyalgia as a valid illness which can lead to disability, a significant percentage has negative attitudes toward fibromyalgia and people affected by it. Many physicians feel less than competent in managing fibromyalgia.

P-30

Fascia: a missing link in understanding and treating fibromyalgia pain? Muscle biopsies, genomic and proteomic data supports role of myofascial tissue in generating FM pain

Ginevra Liptan[1]
Fibromyalgia Research Library, USA.

Muscle nociceptive afferents, most of whom reside in the fascia, are important in the maintenance of FM central sensitisation. Distinct peripheral abnormalities are seen on FM muscle biopsies focusing on fascial components. Immuno-stained muscle biopsies demonstrate a 'slight, but significant increase in collagen surrounding the muscle cells of the fibromyalgia patients' (Spaeth *et al*. 2005).
Another FM muscle biopsy study showed increased endomysial staining of collagen types I, II, and VI, along with elevated markers of inflammation and oxidative stress including CD-68 positive macrophages, and advanced glycation end-products, CML staining 'was detected primarily in the interstitial tissue between the muscle fibers' (emphasis added) and colocalised with collagen. (Rüster *et al*. 2005).
Genomic studies suggest 'defective tissue homeostasis associated with the extracellular matrix' in FM. (Mohaptra *et al*. 2024) Elevated levels of proteins associated with muscle damage, muscle recovery, and oxidative stress were reported in a proteomic analysis of FM muscle.
These myofascial tissue abnormalities could be related to pathological levels of muscle tension in FM. Intramuscular pressure is almost three times higher in FM patients compared to controls. EMG studies reveal increased resting surface amplitudes and inability to reach full muscle relaxation (Bazzichi *et al*. 2009) (Anders *et al*. 2001) (Klaver-Krol 2019). Increased muscle sympathetic nerve activity is seen in FM, the level of which correlates with pain intensity.
Prolonged widespread muscle tension would cause ongoing myofascial microtrauma from even normal daily movements, generating oxidative stress and inflammation as the immune system attempts to repair the damage. (Liptan 2023).
Conclusion. Confirmation of myofascial abnormalities could be key to unraveling the enigma of fibromyalgia pain. Further biopsy studies analysed with newer quantification techniques would be useful to further explore this hypothesis. Current clinical data is strong enough to support adding myofascial treatment to standard fibromyalgia care.

P-31

Screening of pregnenolone-deficiency in patients with fibromyalgia - a potential biomarker of mitochondrial dysfunction and neurosteroidal therapeutic target

Walter Maier-Janson[1]
Neurological Practice, Specialist in Neurology & Pain Medicine, Germany.

Background. Fibromyalgia syndrome (FMS)is characterised by widespread chronic pain and fatigue. Mitochondrial dysfunction is increasingly recognised as a key contributor to its pathophysiology. We investigated whether pregnenolone deficiency is prevalent in patients with FMS. Pregnenolone (PR) is the first and rate-limiting step in steroidogenesis and is synthesised exclusively in mitochondria (Illustration) as a precursor of all steroid hormones. It acts as an active neurosteroid involved in cognition, attention and fatigue regulation.
Objective. We investigated whether pregnenolone deficiency is prevalent in patients with FMS.
Methods. Serum pregnenolone-sulfate (PR-S) was measured as a stable biomarker of pregnenolone status (age-dependent reference range :27-80 ug/L). We studied 80 patients with clinically diagnosed FMS, (68f/12 m); mean age 55.5 years. 35 had biopsy -confirmed small fiber pathology with (SFN). The results were compared with a control group of 50 patients with migraines or MS (mean age 52.6 years).
Results. The mean PR-S level in FMS patients was significantly lower (25.2 ug/l, median 25) than in the control group (44.6ug/L, median 44). No difference was observed between SFN-positive and SNF-negative FMS patients.
Conclusion. Pregnenolone deficiency is highly prevalent in FMS patients and may represent a novel biomarker of mitochondrial dysfunction. Long ago clinically reported effects of PR, which were later explained as the effect of an active neurosteroid making PR a potential therapeutic target. Given our ability now to measure PR-levels, pregnenolone represents a promising therapeutic target for fatigue in FMS patients. Pragmatic supplementation in deficient patients appears to be safe, inexpensive, and clinically effective within six to eight weeks.
Further controlled studies are warranted to evaluate its therapeutic potential and explore pregnenolone-like molecules. Routine pregnenolone screening may therefore be considered as part of the primary biological assessment.

P-32

Serum cortisol, psychiatric comorbidities and duloxetine use in fibromyalgia only versus fibromyalgia and obstructive sleep apnea

Edwin Meresh[1], Zainab Siddiqui[1], Rujuta Idate[1], Sara Tawfik[1], Laasya Gadamsetti[1], Sylwia Balata[1]
Psychiatry, Loyola University Medical Center, USA.

Background. Obstructive Sleep Apnea (OSA) is present in FM and OSA patients have chronic pain. The HPA axis for depression is hypercortisolaemia while chronic pain is related to low cortisol.
Objective. Investigate the range of cortisol serum levels in patients with FM and FM+OSA comorbid with psychiatric conditions and analyse correlation of cortisol levels in patients on duloxetine.
Methods. Using ICD codes, FM and OSA and FM only patients, serum cortisol testing, duloxetine treatment and psychiatric co-morbidities were grouped: Group 1: FM and FM+OSA without identified psychiatric conditions, 2: With adjustment disorders. 3: Depressive disorders, 4: Bipolar disorders 5: Mixed anxiety and depression 6: Panic disorders.
Results. FM only n=156, Female: 136, Male: 20, Mean age: 59.3, Average BMI: 28.76. Group 1, n=48, Group 2 =23, Group 3 =32, Group 4 =4, Group 5 =37, Group 6 =12. Serum cortisol for groups 1-6 respectively: 18.96, 18.06, 20.01, 20.94, 18.72, and 14.65 ug/dl. Upward cortisol serum value for depression (group 3) (11% increase).
FM+OSA, n= 64, Female: 59, Male: 5, Mean age: 63, average BMI: 38.8. Group 1, n=14, Group 2 n=7, Group 3 n=13, Group 4 n=3, Group 5 n=20, Group n =7. Serum cortisol: 9.06, 5.49, 13.00, 14.17, 12.25 and 16.03 ug/dl. Upward cortisol serum value for depression (44% increase).
FM patients taking duloxetine n=34, FM+OSA on duloxetine n=40. FM + OSA tended to have a lower cortisol average, not statistically significant.
Conclusion. In FM patients with OSA, prospective studies are needed on depression and cortisol levels.

P-33

Psychiatric comorbidities in fibromyalgia only patients, combined fibromyalgia and obstructive sleep apnea (OSA) patients and OSA patients without fibromyalgia

Edwin Meresh[1], Maria Matuska[1], Zainab Siddiqui[1], Vir Patel[1], Aaron Perlow[1], Tala Malo[1], Sarah Leung[1]
Department of Psychiatry, Loyola University Medical Center, USA.

Background. Fibromyalgia (FM) is a chronic pain disorder linked to adverse economic and health outcomes such as psychological distress and social isolation. FM is often comorbid with obstructive sleep apnea (OSA). Patients with FM and OSA exhibit higher rates of depression.
Objective. To explore psychiatric co-morbidities in FM only patients, combined FM and OSA patients and OSA patients without FM.
Methods. In this retrospective study, FM and OSA patients were identified, psychiatric comorbidities were assessed, and patients were stratified based on the presence or absence of psychiatric conditions, and comparisons were made regarding FM only *vs*. FM+OSA *vs*. OSA only. Data was analysed using Chi-square and Fisher's exact tests.
Results. FM only: N=45, female n=39, (87%), Mean age: 69 years, average BMI: 28 kg/m^2. Psychiatric co-morbidities n=35 participants (78%). Depression n=10, Anxiety n=9 both depression and anxiety, n=10.
OSA only: N=250 (108 male, 142 female), with 86 (34%) diagnosed with depression. Mean BMI was 33.6.
FM+OSA, among 331 patients (289 female, 42 male), the mean BMI was

36.5 (SD 9.0) kg/m². Depression was found in 242 patients. Depression in OSA only versus FM+OSA: The Fisher exact test statistic value is 0.00001. The result is significant at p=0.01.
Conclusion. The overlap between depression and FM may exacerbate symptom burden, reduce quality of life, and influence treatment adherence and outcomes. Expanding this research in a larger, more diverse cohort will be critical for developing targeted, multidisciplinary approaches that address both the physical and psychological dimensions of fibromyalgia.

P-34

Cardiovascular comorbidity in patients with comorbid fibromyalgia, obstructive sleep Apnea, ADHD, and depression undergoing treatment with continuous positive airway pressure: a cross-sectional study

Edwin Meresh[1], Liana Ysabel Bautista[1], Anne Hutchinson[1], Zainab Siddiqui[1], Aaron Perlow[1], Adam Hyde[1], Vir Patel[1]
Department of Psychiatry, Loyola University Medical Center, USA.

Background. Dysregulation of central sensitisation results in pain hypersensitivity in fibromyalgia (FM). There is a high frequency of ADHD symptoms in FM, and symptoms are worsened by sleep disturbance due to obstructive sleep apnea (OSA). Cardiovascular comorbidity is common in OSA.
Objective. Explore pain perception in patients with comorbid FM, OSA, and ADHD, Continuous Positive Airway Pressure (CPAP) treatment effects, and differences in psychiatric and cardiovascular comorbidity.
Methods. After IRB approval, FM patients with OSA were identified. After written informed consent, Adult ADHD Self-Report Scale (ASRS-v1.1) was administered. McGill Pain Questionnaire (MPQ) was administered. We analysed sleep studies and divided the FM patients into 3 groups: Mild, Moderate, and Severe OSA. We then identified OSA patients undergoing CPAP treatment and analysed their ASRS score and compared ASRS score to non-CPAP patients. REM rebound scores were analysed. Cardiovascular comorbidities included were hypertension, CAD, heart disease, dyslipidaemia, and type II diabetes.
Results. FM and ADHD+: BMI mean 35.76, MPQ mean 27.67, CPAP compliance 44%, AHI mean 22
FM and ADHD-: BMI mean 37.06, MPQ mean 19.23, CPAP compliance 55%, AHI mean 16
FM+ ADHD+ *vs*. FM+ ADHD- psychiatric diagnoses: total p-value 0.007
FM+ ADHD+ *vs*. FM+ ADHD- cardiovascular diagnoses: mild OSA p-value 0.024, total p-value 0.292
Conclusion. FM and ADHD-positive patients showed lower CPAP compliance, severe OSA and more comorbid psychiatric diagnoses compared to ADHD-negative patients. There is no significant difference in co-morbid cardiovascular diagnoses except in the mild OSA group. BMI was high in both groups.

P-35

Dermatologic comorbidity in obstructive sleep apnea: the impact of fibromyalgia

Edwin Meresh[1], Nicole Chin[1], Adam Hyde[1]
Department of Psychiatry, Loyola University Medical Center, USA.

Background. Obstructive sleep apnea (OSA) has established associations with multiple dermatologic conditions, including psoriasis, urticaria, and atopic dermatitis. Fibromyalgia (FM), another disorder linked to systemic inflammation and poor sleep, may further increase dermatologic risk.
Objective. Evaluate whether comorbid FM augments the prevalence of skin disease in patients with OSA.
Methods. In this retrospective study, OSA only and OSA + FM patients were identified. Data was collected on the presence of dermatologic conditions, including eczema, urticaria, angioedema, hyperpigmentation, contact dermatitis, acne, foot ulcers, and acanthosis nigricans. Chi-square tests were used to assess statistical significance for each comparison.
Results. OSA only n=50, OSA + FM n=50. OSA + FM were more likely to have at least one dermatologic condition compared with OSA only (74% *vs*. 54%, p=0.061). Urticaria (34% *vs*. 16%, p=0.065) and contact dermatitis (18% *vs*. 4%, p=0.055) were more frequent in the OSA + FM group, while hyperpigmentation showed a non-significant trend toward higher prevalence (18% *vs*. 6%, p=0.124). Rates of acne (10% *vs*. 2%), foot ulcers (6% *vs*. 2%), and acanthosis nigricans (4% *vs*. 0%) were also higher in OSA + FM but not statistically significant. Eczema (18% *vs*. 16%, p=1.0) and angioedema (16% *vs*. 16%, p=1.0) were similar between groups.
Conclusion. Comorbid FM appears to increase the dermatologic disease burden in patients with OSA. Larger studies are needed to confirm these associations and clarify mechanisms such as inflammation, sleep disturbance, or immune dysregulation.

P-36

Intestinal barrier dysfunction and gut microbiome composition in fibromyalgia: a pilot study

Anda Vilmane[1], Liba Sokolovska[1], Viktorija Kenina[2,3,4,5], Dita Gudra[6], Davids Fridmanis[6], Vadim Ratner[7], Zaiga Nora-Krukle[1]
[1]*Institute of Microbiology and Virology, Rīga Stradiņš University Research Center, Latvia.*
[2]*Department of Neurology, Pauls Stradiņš Clinical University Hospital, Latvia.*
[3]*Center for Neuroimmunology and Immune Deficiencies, Latvia.*
[4]*Department of Biology and Microbiology, Rīga Stradinš University, Latvia.*
[5]*Institute of Oncology and Molecular Genetics, Rīga Stradinš University, Latvia.*
[6]*Latvian Biomedical Research and Study Center, Latvia.*
[7]*Independent Researcher, Israel.*

Background. Fibromyalgia (FM) is a chronic pain condition characterised by widespread musculoskeletal pain, fatigue, and cognitive symptoms, yet its biological underpinnings remain poorly defined. Emerging evidence suggests that disturbances in intestinal barrier integrity and gut microbial composition may contribute to systemic inflammation and symptom burden in FM.
Objective. This study aimed to evaluate intestinal permeability in FM by comparing plasma zonulin and occludin levels between FM patients and healthy controls, and to characterise the gut microbiome profile within the FM cohort.
Methods. This pilot study included 30 FM patients (median age 47 years, IQR 43–55) and 25 age- and gender-matched healthy controls. Plasma zonulin and occludin concentrations were quantified using ELISAs. Gut microbiome profiling was performed on FM samples using the High-throughput Sequencing Set (FCL PE150) and DNBSEQ-G400 platform (MGI Tech Co., China), achieving an average sequencing depth of ~15 million paired-end reads per sample.
Results. Median zonulin levels were significantly higher in FM patients (293.4 ng/mL) compared with controls (167.9 ng/mL; p=0.0077). Median occludin levels were significantly lower in the FM group (2.060 ng/mL) than in controls (6.620 ng/mL; p=0.0001), supporting the presence of impaired intestinal barrier function. Microbiome analysis identified 2,061 bacterial species within the FM cohort, dominated by *Phocaeicola dorei* (10.9%), *Bacteroides uniformis* (9.46%), *Alistipes putredinis* (4.45%), and *Parabacteroides distasonis* (2.41%).
Conclusion. FM patients demonstrated biomarker patterns consistent with increased intestinal permeability alongside a diverse gut microbial community dominated by species typical of the human gut. These findings support a potential link between intestinal barrier dysfunction and FM pathophysiology, warranting further investigation in larger cohorts.

P-37

Association of lower morningness with greater pain and stiffness but not other symptoms in patients with fibromyalgia

Jarosław Nowakowski[1], Anna Julia Krupa[2], Adrian Andrzej Chrobak[2], Marcin Siwek[2], Mariusz Korkosz[1]
[1]*Department of Rheumatology and Immunology, Jagiellonian University Medical College, Krakow, Poland, Poland.*
[2]*Department of Biological and Community Psychiatry, Jagiellonian University Medical College, Krakow, Poland, Poland.*

Background. Chronotype and its impact on pain and other symptoms remain underexplored in patients with fibromyalgia.
Objective. To measure chronotype in patients with fibromyalgia and assess its relationship with fibromyalgia symptoms.

Methods. Composite Scale of Morningness (CSM) was used to assess the chronotype. Score of 22 or below indicated an evening type, and a score above 44 a morning type. Fibromyalgia symptoms were evaluated using the number of painful body sites (AAPT 2019), Symptom Severity Scale (SSS), the Fibromyalgia Impact Questionnaire (FIQ) and duration of stiffness. Patients with lower and higher morningness were compared.
Results. We investigated 92 patients with fibromyalgia and 33 controls. CSM score was lower in patients with fibromyalgia than in healthy controls: 34 (29-38) *vs*. 39 (33-44), p=0.009. Fibromyalgia patients with lower morningness (CSM ≤ 34) reported higher pain severity on the FIQ compared with patients with higher morningness (7 [6-8] *vs*. 6 [5-7], p=0.031) but not a greater number of painful body sites. These patients also had increased stiffness severity (6 [5–7] *vs*. 5 [4-6], p=0.039) and longer duration of stiffness in hours (1.5 [1.0–2.0] *vs*. 1.0 [0.5–1.5], p=0.028) than patients with a more morning-leaning chronotype. No statistically significant differences were observed in fatigue, non-restorative sleep, cognitive symptoms, and additional somatic symptoms between fibromyalgia patients with lower and higher morningness.
Conclusion. There is an association between evening-leaning chronotype and greater pain and perception of stiffness in fibromyalgia. Importantly, this occurs despite no differences in SSS components, suggesting a pain-specific relationship.

P-38

Invisible pain-visible doubt: fibromyalgia and unintentional medical gaslighting: study

Andrea Petuchovska[1], Natalia Kascakova[2,3]
[1]*Slovak Alliance for Fibromyalgia, SAF, Slovakia.*
[2]*Olomouc University Social Health Institute, Palacky University Olomouc, Olomouc, Czech Republic.*
[3]*Psychiatric-Psychotherapeutic Outpatient Clinic, Bratislava, Slovakia.*

Background. Fibromyalgia is a real, clinically recognised condition lacking consistent objective biomarkers. This clinical invisibility challenges recognition within the biomedical model and influences how patients' symptoms are interpreted and addressed by healthcare professionals. The minimisation or dismissal of patient-reported symptoms has been described as medical gaslighting.
Objective. The aim of this study was to explore how society and healthcare system respond to invisible fibromyalgia, how this affects patients' lives and to assess diagnostic delay.
Methods. A questionnaire-based survey was conducted among Slovak patients with fibromyalgia from clinics and patient organisations (n=53, mean age 47.4±10.3 years). The survey assessed diagnostics latency and experiences of unintentional medical gaslighting.
Results. 50 (94.6%) reported symptom dismissal by healthcare professionals, with 41 (77.4%) frequent and 7 (13.2%) occasional, 2 (3.8%) once. The mean diagnostic delay was 83 months (approximately 6.9 years). 1 out of 53 respondents has been approved for a disability pension. Over 17 years, only 17 patients were assessed for disability pension eligibility (1 per year) according to the Social Insurance Agency reports.
Conclusion. The results highlight significant systematic challenges in the recognition of fibromyalgia, with patients frequently reporting symptom dismissal and extended diagnostic delays. Access to disability status based on fibromyalgia mirrors that of ultra-rare conditions. The invisibility of fibromyalgia facilitates unintentional medical gaslighting within healthcare systems, which negatively affects patient trust and care trajectories. When pain is invisible, disbelief becomes institutionalised. Increasing awareness and validating patient-reported experiences are essential steps toward improving recognition of chronic pain within healthcare systems.

P-39

Trans-anethole mitigates fibromyalgia-associated pain behaviours in a reserpine murine model

Uzair Ahmad[1], Neelam Zaman[1], Tahira Mamtaz[1], Syeda Sharmeen Shah[1], Khalid Rauf[1]
Department of Pharmacy, COMSATS University Islamabad Abbottabad Campus, Pakistan.

Background. Fibromyalgia (FM) is a complex, multifactorial, chronic disorder characterised by widespread body pain, fatigue, stiffness, sleep dysregulation, cognitive disturbances, and psychiatric signs. Pain in FM is classified as nociplastic pain because of altered nociception without known pathological causes, *i.e.* tissue injury in the affected body part, *i.e.* inflammation, trauma or infection etc. FM prevalence varies globally due to differences in sex, culture, and healthcare facilities however FM is 3rd most frequent musculoskeletal condition that affects 2–3% of the world population, with a female to male ratio of 3:1.
Objective. In this study reserpine in doses (0.25 mg/kg and 0.5 mg/kg) were used to replicate murine model of FM with pronounced and consistent signs of allodynia and hyperalgesia. Trans-anethole, commonly known as anethol, is an aromatic compound found in the in the essential oils of star anise and fennel has been documented to have antioxidant, antinociceptive and anti-inflammatory effect.
Results. This study evaluated the analgesic potential of Trans-anethole in reserpine induce FM murine model at three doses (250 mg/kg, 500 mg/kg, and 750 mg/kg). Behavioural responses to mechanical (von Frey), thermal (tail flick), and cold (acetone) stimuli were assessed. The results demonstrated a non-linear effect of trans-anethole. Doses of 250 mg/kg and 500 mg/kg were effective in significantly ameliorating pain sensitivity across all tested paradigms. In contrast, the higher 750 mg/kg dose exhibited only a mild analgesic effect.
Conclusion. Our findings suggest that trans-anethole has promising antinociceptive properties within a specific dose range for FM-related symptoms, indicating an optimal therapeutic window that may get narrow at higher doses.
Key words. Fibromyalgia, reserpine, trans-anethole, thermal hyperalgesia, mechanical hyperalgesia and cold allodynia.

P-40

Phenotyping of painful symptoms and behavioural and cognitive alterations in the reserpine-induced fibromyalgia model in male and female mice

Eva Sánchez-Robles[1], Nancy Paniagua[1], David Pascual[1], Carmen Rodríguez-Rivera[1], Miguel M García[1], Miguel Molina-Álvarez[1], Marina Sanz-González[1], Rocío Girón[1], Carlos Goicoechea[1]
Facultad de Ciencias de la Salud, Universidad Rey Juan Carlos, Madrid, Spain.

Background. The preclinical model of fibromyalgia induced by reserpine is widely described in the literature. However, there are many difficulties in comparing studies due to the different methodologies used: animals and strains, reserpine doses, vehicles or comparator groups used, study variables to assess pain and behavioural and cognitive alterations, or follow-up time. In addition, most studies focus on a single sex, which limits understanding of possible differences related to sexual dimorphism.
Objective. To perform a more comprehensive and long-term characterisation of pain symptoms and behavioural alterations induced by reserpine, including both male and female animals.
Methods. Animals: C57BL/6 mice, 10 weeks old. Experimental groups: Reserpine (1 mg/kg, s.c. for 3 days), Vehicle (0.5% acetic acid) and Untreated control; n=9-12. Signs evaluated with validated tests: spontaneous pain, mechanical and cold allodynia, heat sensitivity, muscle pain, muscle strength, motor coordination, anxiety and depression. Follow-up time: day 0 (baseline) and days 1, 5, 7, 14 and 21 after reserpine administration.
Results. Reserpine induced spontaneous pain and mechanical allodynia in both sexes, with the latter being more intense and prolonged in females. Females showed a more complex nociceptive profile, with cold allodynia and heat hyperalgesia, absent in males, while males developed muscle hyperalgesia and a more pronounced anxious phenotype, which was not observed in females. Both sexes showed alterations in motor coordination. No group

showed depressive behaviou.rs or decreased muscle strength during the follow-up period. It should be noted that the vehicle (acetic acid) is not a good comparator for reserpine, as it affects certain signs and is pronociceptive.
Conclusion. Reserpine-induced fibromyalgia model reveals a differential symptomatic pattern according to sex. Our findings underscore the need to standardise protocols and consider the impact of vehicle and sex in the interpretation of the reserpine model for fibromyalgia.

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Immuno-virologic profiling of Latvian fibromyalgia patients

Lība Sokolovska[1], Anda Vilmane[1]
Institute of Microbiology and Virology, Rīga Stradiņš University Research Center, Riga, Latvia.

Background. Fibromyalgia (FM) is a chronic, debilitating condition whose pathophysiology is unclear and diagnosis challenging, leading to significant delays in diagnosis and treatment of patients. Identifying objective markers could significantly contribute to the field and patients` overall well-being.
Objective. To characterise the immunovirological landscape in FM patients in search of new disease markers and descriptors.
Methods. Whole-blood samples were collected from 30 FM patients. Blood plasma and peripheral blood mononuclear cell (PBMC) DNA of 25 healthy controls were acquired from the Latvian National Biobank. Blood plasma was used for immunoglobulin isotyping and adrenergic and muscarinic acetylcholine receptor autoantibody (anti-β2AdR, anti-M3 AChR, anti-M4 AChR) detection and quantification. PBMC DNA was used for qPCR to detect human herpesviruses (HSV-1, HSV-2, VZV, EBV, CMV, HHV-6A/B, and HHV-7) and quantify viral loads.
Results. Multiple immunoglobulin class and subclass levels were lower in FM patients (IgG3, p=0.02; IgG4, p=0.03). FM patients were more often positive for receptor autoantibodies, B2-positive 8/30 *vs*. 6/26, M3-positive 9/30 *vs*. 4/25, M4-positive 13/30 *vs*. 5/25, although antibody levels did not differ significantly. Human herpesvirus DNA was detected in 18/30 FM patient and 19/28 control group samples. None harboured HSV-1, HSV-2, VZV, or CMV. HHV-7 was the most prevalent in both groups (FM: 13/30; CG: 15/25). Viral load did not differ between groups, but HHV-6 load in one patient exceeded 5 x 106 copies per 106 cells.
Conclusion. While herpesviruses do not seem to be associated with FM, a deeper characterisation of the immunological status of FM patients warrants further investigation

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Explorative studies on virtual embodiment and the bodily self in fibromyalgia

Justyna Świdrak[1,2], Ana Arias[3], Tamara Rodriguez[3], Xavier Torres[3,4], Maria Victoria Sanchez-Vives[1,5]
[1]*Systems Neuroscience, Institut d'Investigacions Biomèdiques August Pi I Sunyer (IDIBAPS, Spain.*
[2]*Institute of Psychology Polish Academy of Sciences, Poland.*
[3]*Rheumatology Service, Hospital Clínic de Barcelona, Spain.*
[4]*Servei de Psiquiatria I Psicologia Clínica, Institut Clínic de Neurociències, Hospital Clínic de Barcelona, Spain.*
[5]*ICREA, Spain.*

Background. The sensation of body ownership is a stable experience critical for sensorimotor interactions with the environment. Chronic pain alters this experience and leads to disturbances in body perception. Fibromyalgia (FM) is characterised by an unstable body schema, hypervigilance to bodily signals, and hyperembodiment (the body felt as an unavoidable obstacle). Virtual embodiment illusion (being in and controlling a 3D avatar) can be a powerful tool for pain modulation in both the general population and people with various chronic pain conditions.
Objective. We investigated: (1) how women with FM perceive their bodies, (2) whether they are receptive to bodily illusions in virtual reality (VR), (3) what modulates it.
Methods. The talk will include a summary of an exploratory mixed-methods online study (n=) and two experimental VR studies (n=21, n=39).
Results. Study 1 found disturbed body experiences and large individual differences in symptoms intensity, body schema, body image, distinguished three clusters (Connected, Conflicted and Disconnected body). Study 2 found that people with FM could experience virtual embodiment. The strength of embodiment was positively associated with body perception disturbances and negatively associated with FM symptoms intensity. Study 3 investigated differences between women with FM and pain-free controls. Both groups reported similar embodiment, while FM reported higher reversed out-of-body illusion.
Conclusion. FM population is characterised by a large intra- and interpersonal variety, which leads to diverse affective reactions to virtual body illusions. More disturbed body perception may facilitate the experience of bodily illusions, making it a promising tool for research and future interventions.

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Different mechanism involved in long COVID and fibromyalgia

Kati Thieme[1], Dennis C. Turk[2]
[1]*Department of Medical Psychology, Philipps-University Marburg, Germany.*
[2]*Center for Pain Research on Impact, Measurement, & Effectiveness (C-PRIME), Department of Anesthesiology and Pain Medicine, University of Washington, Seattle, USA.*

Objective. Long COVID (LCOV) and fibromyalgia (FM) share common symptoms (*e.g.* pain, fatigue, cognitive impairment); however different mechanism may be involved. Baroreflex sensitivity (BRS) and the dorsal medial nucleus tractus solitarii (dmNTS) reflex arcs regulate many homeostatic variables (*e.g.* blood pressure [BP], pain, catecholamines). Reduced BRS may play a role both in LCOV and FM; however, the heart rate variability (HRV) may display different activations.
Methods. Twenty patients with LCOV were compared to 20 FM patients reporting comparable symptoms. Standardised questionnaires were used to measure pain, interference, fatigue, and sleep. Physiological indices (*i.e.* ECG, systolic [SBP] and diastolic [DBP)] BP, heart rate, BRS and HRV) were also assessed using psychophysiological stress test as a standard procedure.
Results. The physiological responses in LCOV displayed significantly differences between the LCOV and FM patients HRV in LCOV, in particular the very high frequency band as an indicator for parasympathetic response was increased before SET. In contrast, FM showed a significantly increased low frequency band.
Conclusion. Although common symptoms were present in LCOV and FM patients, LCOV patients revealed very high frequency band as an indicator for parasympathetic response. In contrast, FM showed a significantly increased low frequency band. The results implicate different mechanisms for LCOV and FM.

P-44

Mapping emotional function in fibromyalgia: integrating alexithymia, pain catastrophising and self-compassion

Francesca Trunfio[1], Rosa Bruni[2], Damiano Currado[1], Barbara Biticchi[1], Erika Corberi[1], Francesca Saracino[1], Ludovica Lamberti[1], Leonardo Frascà[1], Annalisa Marino[1], Sebastiano Lorusso[1], Onorina Berardicurti[1,3], Luca Navarini[1,3], Roberto Giacomelli[1,3]
[1]*Rheumatology and Clinical Immunology, Department of Medicine, University of Rome Campus Biomedico, Rome, Italy.*
[2]*contract Professor at University Campus Bio-Medico of Rome, Psychiatrist, Psychotherapist, certified Teacher Mindful Self-Compassion Program, Rome, Italy.*
[3]*Clinical and Research Section of Rheumatology and Clinical Immunology, Fondazione Policlinico Campus Biomedico, Rome, Italy.*

Background. Fibromyalgia (FM) is a chronic syndrome characterised by widespread musculoskeletal pain, fatigue, sleep disturbance, and cognitive dysfunction. Alexithymia – difficulty identifying and describing emotions – has been reported in up to 48% of FM patients and is associated with increased psychological distress and pain intensity, yet its specific role in FM remains unclear.
Objective. This study seeks to assess the interplay among alexithymia, self-compassion, pain catastrophising and hope, with the aim of guiding integrated, emotion-focused interventions.

Methods. In this cross-sectional study, 112 Caucasian women fulfilling the 2016-ACR-criteria for FM were recruited between October 2023 and June 2024. Disease burden was assessed using validated FM severity indices. Psychological variables were evaluated using standardised instruments assessing alexithymia (TAS-20), hope, anxiety/depression, pain-catastrophising, and self-compassion.

Participants were stratified by TAS-20 score into non-alexithymic, borderline, and alexithymic. Group differences were analysed using χ^2 or Kruskal-Wallis tests, associations were explored through univariable and multivariable linear regression models.

Results. Alexithymic traits were identified in 51.8% of patients. Compared with non-alexithymic individuals, alexithymic patients showed significantly higher anxiety, depression, pain catastrophising, alongside lower levels of hope and self-compassion. Alexithymia scores correlated positively with FM symptom severity and psychological distress, negatively with hope and self-compassion (all p=0.001). In multivariable models, SSS (p=0.001), PCS-Helplessness (p=0.005), and SCS-Overidentification (p=0.020) emerged as independent predictors of alexithymia.

Conclusion. Alexithymia represents a marker of emotional vulnerability in FM, linked to symptom burden, maladaptive pain cognitions, and reduced psychological resources. These findings support the integration of emotion-focused and multidisciplinary strategies in FM management.

Table I. Alexithymia group comparison.

Variable	TAS20 ≤51	Borderline	TAS20≥61	P-value
Age	51 (46.25–59.25)	47.5 (39–57)	51.5 (47.25–57)	0.428
BMI	23.02 (21.49–28.21)	22.5 (22.5–28.25)	25.2 (23.09–28.91)	0.201
WPI	13 (11–15)	10 (8.5–12)	13 (9–15.2)	0.122
SSS	8 (6.5–9)	9 (7–10)	9 (6–10)	0.26
PDS	19.5 (17.25–22)	20 (16–22.25)	23.5 (19–27.75)	0.308
FASmod	27 (23–29.75)	27 (21–29.5)	29 (24–34.75)	0.228
FIQ-R	52.5 (45.38–69.25)	64 (42.22–74.5)	63 (52.43–82)	0.06
TAS20	46 (41.5–49)	56 (55–58)	72 (66–79)	0.002
HADS-anxiety	9 (6–11.75)	11 (9–13.25)	13 (9.25–15.75)	0.008
HADS-depression	9 (7.25–10)	10 (9–11)	11.5 (9–14)	0.043
HADS-total	17 (14–22)	21 (18.75–24.25)	23.5 (20–28)	0.001
AHS-total	24 (23–25.75)	24 (19.75–25)	21 (17–24)	0.024
AHS-Agency	11 (9–12)	11 (9.75–12)	10.5 (9–12.5)	0.064
AHS-Pathway	12 (10–14)	12 (10.75–13)	11.5 (9–12.75)	0.07
Helplessness	9.5 (4.5–12.75)	13 (8.5–15)	16 (11–17)	0.002
Rumination	7.5 (3.25–12.75)	13 (8–15)	14 (10–16)	0.005
Magnification	3 (2–6)	5 (3–6)	6 (4–8)	0.008
PCS-total	23 (8.75–26.75)	31.5 (21.75–38)	35.5 (28.75–42.5)	0.003
SCS- Self-kindness	3 (2–3)	3 (2–4)	2 (1–3)	0.003
SCS- Self-judgment	3.5 (1.4–4.2)	3.3 (1.8–3.5)	4.1 (2.5–4.84)	0.03
SCS- Humanity	3 (2.5–4)	3.2 (2–3.8)	3.2 (1.8–4)	0.063
SCS- Isolation	3 (1.5–4.5)	3.6 (2–4)	3.9 (3–5)	0.045
SCS- Mindfulness	3 (1.5–3.8)	3.5 (2–5.6)	3.2 (1.5–4)	0.642
SCS-Overidentification	3.38 (2.81-4.38)	3 (2.3-3.56)	2.5 (1.5-3.38)	0.003
SCS-total	3.03 (2.85-3.35)	2.94 (2.58-3.42)	2.85 (2.5-3.251	0.12

Body Mass Index (BMI); Widespread Pain Index (WPI); Symptom Severity Scale (SSS); Polysymptomatic Distress Scale (PDS); modified Fibromyalgia Assessment Scale (FASmod); revised Fibromyalgia Impact Questionnaire (FIQR); Toronto Alexithymia Scale (TAS-20); Adult Hope Scale (AHS); Hospital Anxiety and Depression Scale (HADS); Pain Catastrophizing Scale (PCS); Self Compassion Scale (SCS).

Table II. Univariable linear regression analysis, TAS20 as dependent variable.

Variable	Beta	95% CI Lower	95% CI Upper	p-value
Age	0.15	-0.09	0.39	0.213
BMI	0.34	-0.16	0.83	0.177
Smoking	1.83	-4.5	8.15	0.568
Marital status	1.52	-1.43	4.47	0.31
WPI	0.43	-0.2	1.05	0.179
SSS	3.22	2.14	4.3	<0.001
PDS	0.86	0.39	1.32	<0.001
FASmod	0.54	0.15	0.93	0.007
FIQ-R	0.34	0.22	0.47	<0.001
HADS-Anxiety	1.12	0.51	1.72	<0.001
HADS-Depression	1.75	1.03	2.47	<0.001
HADS-Total	0.91	0.54	1.28	<0.001
AHS-Total	-1	-1.46	-0.54	<0.001
AHS-Agency	-2.02	-2.92	-1.11	<0.001
AHS-Pathway	-1.69	-2.5	-0.88	<0.001
PCS-Helplessness	1.08	0.69	1.46	<0.001
PCS-Rumination	1.15	0.69	1.61	<0.001
PCS-Magnification	1.62	0.85	2.39	<0.001
PCS-Total	0.53	0.35	0.71	<0.001
SCS- Self-kindness	0.97	-1.27	3.21	0.393
SCS- Self-judgment	-3.09	-5.15	-1.02	0.004
SCS- Humanity	0.88	-1.4	3.17	0.445
SCS- Isolation	-2.91	-4.88	-0.94	0.004
SCS- Mindfulness	1.5	0.79	3.79	0.198
SCS-Overidentification	-4.35	-6.44	-2.27	<0.001
SCS-total	4.07	8.01	-0.12	0.043

Body Mass Index (BMI); Widespread Pain Index (WPI); Symptom Severity Scale (SSS); Polysymptomatic Distress Scale (PDS); modified Fibromyalgia Assessment Scale (FASmod); revised Fibromyalgia Impact Questionnaire (FIQR); Toronto Alexithymia Scale (TAS-20); Adult Hope Scale (AHS); Hospital Anxiety and Depression Scale (HADS); Pain Catastrophizing Scale (PCS); Self Compassion Scale (SCS).

Table III. Multivariable linear regression analysis, TAS20 as dependent variable, model adjusted for age, BMI, SSS, PCS-Helplessness, and SCS-Overidentification.

Variable	Beta	IC 95% Lower	IC 95% Upper	P-value
Age	0.13	-0.06	0.33	0.180
BMI	0.41	0.00	0.82	0.051
SSS	2.25	1.18	3.33	<0.001
PCS-Helplessness	0.59	0.18	1.00	0.005
SCS-Overidentification	-2.40	-4.41	-0.39	0.020

Toronto Alexithymia Scale (TAS-20); Body Mass Index (BMI); Symptom Severity Scale (SSS); Pain Catastrophizing Scale (PCS); Self Compassion Scale (SCS).

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